Programma del
XXVI Congresso Nazionale
della Società Chimica Italiana

Centro Congressi Hotel Ariston
Paestum (SA), 10-14 settembre 2017

Divisione di Chimica Organica
XXVI Congresso Nazionale della Società Chimica Italiana

SPONSOR ISTITUZIONALI
Università degli Studi di Salerno

Dipartimento di Farmacia
Dipartimento di Chimica e Biologia A. Zambelli

GOLD SPONSOR

BRONZE SPONSOR

SUPPORTERS

Patrocinio

FEDERCHIMICA
CONFINDUSTRIA

SOMMARIO – PROGRAMMA – MEDAGLIE E PREMI – KEYNOTE – ORALI POSTER AUTORI
New promising vectors for gene delivery by a step-wise functionalization of a polyester-based non toxic dendrimer with N, N-dimethylglycine, N-methylglycine, lysine and arginine.

New polymethine dyes for photodynamic therapy.


Modification of biopolymers in ionic liquids (ILs) media to access added value materials.


Chemo-enzymatic strategies for the synthesis and functionalization of renewable polymers and composite materials.

Chemical Modifications for the Valorization of Lignin.

Multicomponent reactions on biocatalytically produced substrates.

Photocatalytic Radical Alkylation of Electrophilic Olefins by Benzyllic and Alkylic Zinc-Sulfinites.

Decrypting Transition States by Light (DTS-hv) in Brensted Acid Catalysis.

Structural and Medium Effects in the Hydrogen Atom Transfer Processes Promoted by Short-Lived Aminoxyl Radicals.

An Ultrafast Molecular Photoswitch Bio-inspired by Green Fluorescent Protein Fluorphore.

Highly selective arylation protocols to prepare bioactive and fluorescent imidazole-based compounds.

A New Antibacterial Cyclic Peptide from Hot Springs.

Recent advances in the synthesis of stemarane diterpenoids.

Easy chemical modifications to explore the ‘Janus face’ of TBA: anticoagulant vs antiproliferative properties.

The greening of protection/deprotection strategies in peptide synthesis.

Design, synthesis of new heterocyclic compounds and their biological activity against MCF-7 cell line.

Synthesis and application of bifunctional chelating agents based on AAZTA scaffold.

QU-IBX and B3-IBX: safe IBX adducts for periodonate oxidation reactions.

Light-Activated Amine Detection via Innovative Diarylthene Probes.

Handling Hydrogen Peroxide On Large Scale: Synthesis of 5-bromo-2-nitropyridine.

Zwitterionic Deep Eutectic Solvents as Effective Alternatives to Organic Solvents and to Ionic Liquids.

Innovative Two-Step Synthesis of Polysubstituted 6-Nitrolindoles.

NMR study of mixed micelles: zwitterionic – cationic surfactant systems.

Assessment of drug-induced phospholipidosis risk based on distribution coefficient in brain polar lipids.

Identification of new ErbB4 inhibitors by inverse virtual screening.

Recent advances in the discovery of novel microsomal prostaglandin E2 synthase-1 (mPGES-1) inhibitors.

Cytotoxic secondary metabolites from Mediterranean Fabaceae species display antiproliferative activity against colon cancer cell lines.

Synthesis of new peptide-drug conjugates for targeted cancer diagnosis and therapy.

Synthesis and Biological Evaluation of Some Pyrimidin-2,4-diones as Novel Non-Nucleoside Reverse Transcriptase Inhibitors.

Synthesis and decoration of small molecules targeting the Hedgehog Signaling Pathway.

Amphiphilic Guanidinocalixarenes Inhibit Lipopolysaccharide- and Lectin-stimulated Toll-like Receptor 4 Signaling.

Synthesis and stereochemical properties of axially chiral benzo[1,2-b:4,3-b’]dithiophene derivatives.

Bioinspired organocatalysis of C-C bond-forming reactions.

Highly diastereoselective synthesis of γ-butenolides and phthalides by Michael addition catalyzed by crown ethers.

Design of a new chiral nanosupported catalyst for asymmetric reactions.

Asymmetric 1,3-dipolar cycloadditions catalyzed by a new imidazolidinone organocatalyst.

A new highly efficient strategy to prepare racemic Anatabine.

Molecular Events within Confined Spaces.

Synthetic application of bacterial γ-glutamyltransferases (GGTs).

Functionalyzed triazolylidenes as versatile mesionic carbenes: metal complexes for catalysis and luminescent materials.

Copper complexes with biomimetic antioxidant activity.

Mild N-Alkylation of Amines with Alcohols Catalyzed by Acetate Ruthenium Complexes.

The power of ligand combination in redox active ruthenium and iron complexes.

Synthesis of New Carbonyl Diposphane Ruthenium Complexes for Catalytic C-H Bond Activation Reactions.

Oceans of data for informed decisions in chemistry. The shortest path from the question to insight.
XXVI Congresso Nazionale della Società Chimica Italiana

- Domino Addition/Cycloisomerization Reactions of 2-Alkynyl-Arylaldehydes: Silver Catalyzed Synthesis of 1,3-Dicarbos-Substituted-Isochromenes ................................................. 107
- Silylcarbocyclisation-desilylation reactions of N-tosyl-2-ethylnlanilines: a new protocol for the synthesis of 2-hydroxyindoline derivatives ......................................................... 108
- Er(Otf)3 in ionic liquid catalyzed [3 + 2] cycloaddition of azides with electron-deficient dipolarophile: regioselective synthesis of substituted 1,2,3-triazoles .......................................................................................................................... 109
- Synthesis of bio-based heterocycles from levulinic acid using the Ugi multicomponent reaction ................................................................. 110
- Oxidation of Hydrocarbons and Alcohols with H2O2 Catalyzed by Nonheme Iron Based Complexes ............................................................ 111
- Structural characterisation of Peripolin, a new 3-hydroxy-3-methylglutaryl flavonoid glycoside from bergamot juice .............................................. 112
- The dual role of Ionic Liquids in Gold Nanoparticles Drug Delivery-Systems ........................................................................................................ 113
- Hydroxytyrosol-controlled release from poly(vinyl) alcohol (PVA) combined with nanostructured starch .................................................................. 114
- Phytochemical analysis of Daphne sericea Vahl. from Majella National Park ........................................................................................................ 115
- Phytochemical comparison among three Sideritis taxa from Central Italy ........................................................................................................ 116
- Ethno-pharmacological value and phytochemical variability of Galeopsis ladanum subsp. angustifolia (Ehrh. ex Hoffm.) Gaudin ................................................................. 117
- N-Heterocyclic Carbones functionalized polystyrene monolithic microreactors for continuous flow stereoselective umpolung catalysis .......................................................................................................................... 118
- Disperse dyes modification by Pd-catalyzed cross coupling reactions ................................................................................................................ 119
- Novel chiral N,S-acetal cyclic structures as templates for functional, stereochemical and appendage diversity ................................................................. 120
- Synthesis and characterization of benzo[1,2-b:4,3’b]dithiophene-based organosilicon compounds ............................................................... 121
- Synthesis and structural studies towards palmitoyl ethanolamide analogues .................................................................................................. 122
- Synthesis and Investigation of Croconates as Smart Organic Coating for Noble Metals Nanoparticles ............................................................. 123
- Flow chemistry as enabling technology for controlling the reactivity of fluorocarbenoids ........................................................................ 124
- TiCl4-promoted Friedel-Crafts alkylations of arenes with alcohols ................................................................................................................ 125
- Synthesis and Characterization of DBF-based organic electrochromic materials ............................................................................................. 126
- 3-(Alkoxyaryl-2-Alkyliden)-2-Oxindoles: a new, enabling progeny of multidentate, vinylogous carbon nucleophiles for the direct, enantioselective, vinylogous michael addition to nitroolefins ........................................................................................................ 127
- New “AIE” luminogens based on π-conjugated imidazolium salts ................................................................................................................ 128
- Synthesis and biological evaluation of new heteroaryl amides active toward HIV Protease ........................................................................ 129
- Pd nanoparticles obtained by pulsed laser ablation in liquid and applied to catalyzed ligand-free Suzuki reaction ........................................................................ 130
- Homo and hetero-nuclear 2D NMR techniques as useful tool for identification of cytotoxic compounds from complex extracts of Urtica dioica ........................................................................................................ 131
- Cyclic hexameric cyclopeptoids as mimics of enniatins and beauvericin mycotoxins ........................................................................................ 132
- Development of a green and efficient flow process for the preparation of NH-sulfonoximes from sulfides and sulfoxides ......................................................................................... 133
- Synthesis and Biological Evaluation of Novel Piperidinyl Iminosugar-Based Nucleosides .................................................................................. 134
- 3-azido-6-ethylcholine derivatives as potent and selective FXR agonists ........................................................................................................ 135
- Asymmetric Phase-Transfer Catalysis by Chiral Calix[4]arene Derivatives ........................................................................................................... 136
- Antimony-oxo Porphyrrins as Promising Photocatalysts for Visible Light Induced H-Atom Abstraction .......................................................... 137
- C-terminal methyl ester helical peptides can undergo a temperature-driven, reversible screwsense inversion. A spectroscopic study ........................................... 138
- Synthesis, conformation analysis, and proteolytic stability of helical peptide inhibitors of the VEGF/VEGR protein-protein interaction ........................................................................ 139
- Tosylhydrazones as Powerful Tools for the Construction of sp2-sp3 and sp3-sp2 Carbon Bonds: A Novel Approach to Conjugated and Skipped 1-Alkoxydienes ................................................................ 140
- Multi-purpose metal-free dyes for energy and hydrogen production ........................................................................................................... 142
- Silibinin phosphate-based flavonolignans: new emerging synthetic metabolites with interesting pharmacological properties ........................................................................................................... 143
- Unprecedented “On-Water” Nucleophile Additon of Organolithiums and Grignard Reagents to Imines and Nitriles ........................................................................................................... 144
- Asymmetric Synthesis and Antiviral Activity of Novel Carbocyclic Nucleosides .............................................................................................. 145
- Elucidating the role of tanshinone IIA and cryptotanshinone in neuroinflammation through molecular docking studies ...................................................... 146
- Microwave synthesis and preliminary evaluation of 2-amino-3,4-dihydopyrimidine BACE-1 inhibitors ........................................................................ 147
- Combinatorial approach for the discovery of novel microsomal prostaglandin E2 synthase-1 (mPGES-1) inhibitors ........................................................................................................... 148
- Oxidation of amines to carbonyl compounds and nitriles by ball milling ...................................................................................................... 150

SOMMARIO – PROGRAMMA – MEDAGLIE E PREMI –
KEYNOTE – ORALI- POSTER - AUTORI
- New trimidazole derivatives: intriguing cases of photoluminescence behavior .................................................. 151
- Rational Design of Ready-to-Shape New Classes of Organo-Photocatalysts ............................................................. 152
- Visible light induced C-H α-α-difluoroacetophenone functionalization of electron-rich arenes: A viable option for difluoromethyl functionalization .......................................................................................... 153
- Rational Design of Molecular Hole Transporting Materials for Perovskite Solar Cells: Direct versus Inverted Device Configurations ...................................................................................................................... 154
- Flow synthesis of cyclobutanones via [2 + 2] cycloaddition of keteneiminium salts and ethylene gas .................... 155
- Looking for a new, isoluminol-based, molecule with improved chemiluminescence properties: a SAR study .... 156
- Efficient iminium-catalyzed Morita-Baylis-Hillman reaction on cyclopent-2-enone ............................................ 157
- Design and Synthesis of GlcNac-6-P Analogues Targeting Hexosamine Biosynthetic Pathway (HBP) with promising antitumor activity ........................................................................................................... 158
- Calix[n]arene Mediated Catalysis Under “On-water Conditions”: Hydrophobic Amplification of Weak Hydrogen-Bonds ........................................................................................................................................ 159
- Aminotriphenolates as Privileged Ligands in Catalysis ............................................................................................. 160
- Polydopamine: a versatile bioinspired material for multipurpose applications ..................................................... 161
- Lipophilic core-shell FeOx@SiOx@Au nanoparticles into nano-micelles for magnetic resonance and photoacoustic dual-imaging .................................................................................................................................. 162
- Synthesis of isoxazolidinyl-gem-bisphosphonic acids and study of protein-ligands interactions ...................... 163
- Synthesis of sulfurated heterocycles with herbicidal activity .................................................................................... 164
- Tuning morphological architectures generated through living supramolecular assembly of a helical foldamer end-capped with two complementary nucleobases .................................................................................. 165
- Enantioselective Carbolithiation of α-Arylcarbamates ............................................................................................... 166
- Asymmetric synthesis of the natural products colletochlorin A and colletorin A and their halogenated synthetic analogues ....................................................................................................................................... 167
- The role of structural and medium effects on hydrogen atom transfer from alcohols and diols to alkoxyl radicals .......................................................................................................................................... 168
- Organocatalytic Domino Methodologies to Access Important Sulfur Heterocycles: from Tetrahydrothiophenes to 1,5-Benzothiazepines ........................................................................................................................................ 169
- Dicationic Ionic Liquids (DILs): synthesis, characterization and applications ........................................................... 170
- Syntesis of multifunctional ORMOSIL nanoparticles for drug delivery ..................................................................... 171
- Discovering the biological target of 5-epi-Sinulpeptidole with a combination of proteomic approaches ............ 172
- Data-driven Ionic Liquids Modelling: a Design Opportunity for Task-specific Applications ................................. 173
- Unconventional synthetic methods towards new food additives from waste derived by olive oil industry .......... 174
- Metaboliti secondari bioattivi prodotti da funghi patogeni di piante forestali ................................................................ 175
- An expeditious and greener synthesis of functionalized cyclopenitone in deep eutectic solvents ................... 176
- Synthesis of nitro-functionalized N-heteroaromatic condensed systems ................................................................. 177
- Targeting Gastrin-Releasing Peptide Receptor expressing tumors: synthesis and characterization of new potential diagnostic and therapeutic molecular tools ......................................................................................... 178
- An unconventional helical push-pull system for solar cells ...................................................................................... 179
- Metal chelators for the multi-target therapy of Alzheimer’s Disease: isolation/synthesis and preliminary biological evaluation of new natural and synthetic compounds .................................................................................. 180
- The unexpected driving role played by substituent groups in the molecular recognition of aromatic derivatives performed through Aragonation Chromatography ....................................................................................... 181
- Facile Preparation of Metal Ions Loaded Sporopollenin Grains from Pollens, and Characterization ................... 182
- Discovery of new molecular entities able to strongly interfere with Hsp90 C-terminal domain .......................... 183
- Conformational Analysis and Absolute Configuration of Axially Chiral 1-aryl and 1,3-diaryl-xanthines .................. 184
- Synthesis and Photo-Physical Properties of Dopamine-Inspired Iridium Complexes for OLED Applications .... 185
- Visible light driven, metal-free preparation of aromatic amides from arylation sulfones ........................................ 186
- From arylation mesylates to triarylethylenes: a solar light metal-free synthesis .................................................. 187
- A Hydrogen Borrowing approach to Pyrroloubenzodiazepines ........................................................................... 188
- Synthesis of a new Riboflavin-nucleotide and its insertion into G-quadruplex forming ODNs with anti-HIV activity ............................................................................................................................................. 189
- Detecting new drugs through NMR chemosensing ................................................................................................. 190
- Synthesis of C2-modified chiral PNA using Minimally Protected Submonomer Synthesis ................................. 191
- Microsomal Prostaglandin E2 Synthase-1 potential inhibitors: design, synthesis and biological evaluation. .... 192
- Computational Study on the Gas-Phase and Aqueous Solution Acidity of Nicotine ............................................... 193
- New Mannosylcalix[n]Arenes as Multivalent Ligands for the Inhibition of Hiv/Dc-Sign Interaction ...................... 194
- Calixarene-Based Multivalent Inhibitors for Carbonic Anhydrases .................................................................. 195
- How the ring size and the side chains affect the solid state assembly of cyclopeptoids ......................................... 196
Deep Eutectic Solvents as convenient media for the synthesis of gold and platinum nanoparticles .......... 198
Enantioselective phase transfer catalyzed alkylation of phthalide-3-carboxylic esters .......................... 199
Modeling of 5,6-dihydroxyindole and caffeic acid on TiO₂: direct electron injection in Dye-Sensitized Solar Cells .................................................................................................................................................. 200
Synthesis of a new dendritic amphiphilic polyester with pentaerythritol core and a multifunctional periphery for linking amino acids and for using in gene therapy ...................................................................................... 201
Discovery of Potential Small Molecule Modulators of Macromolecular Proteins ................................ 202
Photochemical trifluoromethylation of aromatics by N-aryltrifluoromethanesulfonimides ..................... 203
Expanding the synthetic utility of the electrophilic N-transfer to the sulfur atom ................................... 204
Synthesis of dendrons and dendrimers glycoconjugates for biomedical applications ........................... 205
Studies of Electronic Properties of 5-KuQuinones .................................................................................. 206
Monomolecular G-quadruplex structures with inversion of polarity sites: new topologies and potentiality .... 207
A Trifunctional Calix[4]arene as Mimic of DNA Topoisomerase I for the Promotion of Phosphoryl Transfer Processes ....................................................................................................................................... 208
The CeCl₃ Lewis Acid Promoter in the Stereoselective Construction of Carbon-Carbon Double Bonds ...... 209
Oxidative polymerization of hydroxylated naphtalenes: Modeling free radical pathways of polycyclic aromatic hydrocarbons (PAHs) of astrochemical relevance .............................................................................. 210

Elenco degli Autori ........................................................................................................................................ 211
DIVISIONE DI CHIMICA ORGANICA

Comitato Scientifico

- Gianluca M. Farinola, Università degli Studi di Bari "Aldo Moro"
- Roberto Ballini, Università degli Studi di Camerino
- Anna Bernardi, Università degli Studi di Milano
- Maria Valeria D’Auria, Università degli Studi di Napoli “Federico II”
- Marco Lucarini, Università degli Studi di Bologna
- Alessandro Mordini, CNR ICCOM Firenze
- Gabriele Razzetti, DiPharma Francis S.r.l., Milano
- Andrea Pace, Università degli Studi di Palermo
- Claudio Villani, Università degli Studi di Roma “La Sapienza”

Delegato di Divisione

- Giuseppe Bifulco, Università degli Studi di Salerno
**Programma Scientifico**

**Divisione di Chimica Organica**

**Lunedì 11 Settembre 2017**

<table>
<thead>
<tr>
<th>Auditorium Giove</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>9:00 – 9:30</td>
<td>Opening Remarks and Awards Ceremony</td>
</tr>
</tbody>
</table>

**Plenary Session I**

*Chairperson: Cesare Gennari*

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
</tr>
</thead>
</table>
| 9:30-10:00 | **ORG MD01**: Adolfo Quilico Medal Lecture - Raffaele Riccio  
**Changing paradigms in natural product chemistry: from structural elucidation to target identification** |
| 10:00-10:30| **ORG PZ01**: Organic Chemistry for Life Science Award Lecture - Franca Zanardi  
**Playing with Peptidomimetic and Small-Molecule Drug Hybrids to Hit Cancer-Related Biomarkers** |
| 10:30-11:00| Coffee Break                                |

<table>
<thead>
<tr>
<th>Auditorium Giove</th>
<th></th>
</tr>
</thead>
</table>
| 11:00 – 11:30 | **ORG PZ02**: Organic Chemistry for Process Development and Industrial Products Award Lecture - Giorgio Bertolini  
**From few grams to multi Tons of Active Pharmaceutical Ingredients - Some tips** |

**Sala Argiva**

**Parallel Session 1A: Organic and Inorganic Chemistry Divisions’ Joint Session on Organometallic Chemistry (GICO)**

*Chairperson: Antonella Dalla Cort*

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
</tr>
</thead>
</table>
| 11:30-12:00| **ORG/INO KN01**: Alessandro Caselli  
**Catalytic Applications of Pyridine-Containing Macrocyclic Complexes** |
| 12:00 – 12:30| **ORG/INO PZ01**: EurJOC Junior Organometallic Chemist Lecture - Valentina Pirovano  
**Gold(I)-catalyzed [4+2] cycloaddition reactions of vinylindoles and allenes** |
| 12:30 – 12:45| **ORG/INO OR01**: Elia Matteucci, Andrea Baschieri, Cristiana Cesari, Rita Mazzoni, Claudia Bizzarri, Letizia Sambri  
**Functionalized triazolylidenes as versatile mesoionic carbenes: metal complexes for catalysis and luminescent materials** |
| 12:45 – 13:00| **ORG/INO OR02**: Andrea Squarcina, Martina Zonzin, Mauro Carraro, Marcella Bonchio  
**Copper complexes with biomimetic antioxidant activity** |

<table>
<thead>
<tr>
<th>Auditorium Giove</th>
<th></th>
</tr>
</thead>
</table>
| 11:30 – 11:45 | **ORG OR01**: Giuseppe Sforazzini, Augustina Jozeliunaite, Edvinas Orentas, Daniele Fazzi, Walter Thiel  
**Molecular Engineering of π-Conjugated Systems Towards Light-Responsive Organic Semiconductors** |
| 11:45 – 12:00 | **ORG OR02**: Chiara Liliana Boldrini, Norberto Manfredi, Alessandro Abbott  
**Organic sensitizers for solar fuels from dye-sensitized water splitting** |
| 12:00 – 12:15 | **ORG OR03**: Gianluigi Albano, Laura Antonella Aronica, Lorenzo Di Bari  
**Solution and solid-state supramolecular aggregates of new chiral oligothiophenes: synthesis and spectroscopic characterization** |
<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Speaker(s)</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>12:15 – 12:30</td>
<td>ORG OR04</td>
<td>Francesca Parenti, Mirko Buffagni, Alfonso Zambon, Monica Caselli, Davide Vanossi, Adele Mucci</td>
<td>Novel oligothiophenes with reduced HOMO-LUMO band gap for Optoelectronics</td>
</tr>
<tr>
<td>12:30 – 12:45</td>
<td>ORG OR05</td>
<td>Alessandra Operamolla</td>
<td>Organic and biological materials for organic electronics: adding functionality</td>
</tr>
<tr>
<td>12:45 – 13:00</td>
<td>ORG OR06</td>
<td>Roberto Grisorio, Bart Roose, Silvia Colella, Andrea Listorti, Gian Paolo Suranna, Antonio Abate</td>
<td>Molecular Tailoring of Hole-Transporting Materials for High-Performing Perovskite Solar Cells</td>
</tr>
<tr>
<td>13:00 – 13:15</td>
<td>ORG OR07</td>
<td>Pierluca Galloni, Federica Sabuzi, Barbara Floris, Francesca Valentini, Laura Micheli, Andrea Sartorel, Emanuela Gatto, Giuseppe Palleschi, Valeria Conte</td>
<td>KuQuinones as photocatalysts in Light-driven water splitting</td>
</tr>
</tbody>
</table>

13:00 – 14:00 Intervalllo Pranzo – Lunch Break

Sala Paestum B

14:00 – 15:00 Poster Session 1 (ORG PO01 – ORG PO33)

Sala Argiva

Parallel Session 2A
Chairperson: Olga Bortolini

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Speaker(s)</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>15:00 – 15:30</td>
<td>ORG PZ03</td>
<td>Methodologies in Organic Chemistry Junior Award Lecture - Giovanni Maestri</td>
<td>The chemistry of stable trinuclear all-metal aromatics</td>
</tr>
<tr>
<td>15:30 – 16:00</td>
<td>ORG PZ04</td>
<td>Organic Chemistry for Environment, Energy and Nanoscience Junior Award Lecture - Giulia Fiorani</td>
<td>Towards Bio-based Organic Carbonates and Polycarbonates via Coupling of Highly Substituted Oxiranes and CO₂</td>
</tr>
<tr>
<td>16:00 – 16:15</td>
<td>ORG OR08</td>
<td>Gianluca Salerno, Marco Consumi, Agnese Magnani, Cristina Nativi, Barbara Richichi</td>
<td>A quick and facile synthesis of stable, water-soluble CdSe/ZnS quantum dots</td>
</tr>
<tr>
<td>16:15 – 16:30</td>
<td>ORG OR09</td>
<td>Francesca Biscaglia, Santina Quarta, Gianmarco Villano, Cristiano Turato, Alessandra Biasiolo, Patrizia Pontisso, Moreno Meneghetti, Marina Gobbo</td>
<td>PreS1 Functionalized Gold Nanostructures for Liver Cancer Cells Targeting and Surface-Enhanced Raman Resonance Scattering Imaging</td>
</tr>
</tbody>
</table>

Auditorium Giove

Parallel Session 2B
Chairperson: Giuseppe Musumarra

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Speaker(s)</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>15:00 – 15:30</td>
<td>ORG PZ05</td>
<td>Organic Chemistry in Life Science Junior Award Lecture - Laura Russo</td>
<td>When glycochemistry meets biomaterials: from design to application of synthetic glyco-tools</td>
</tr>
<tr>
<td>15:30 – 16:00</td>
<td>ORG PZ06</td>
<td>Organic Chemistry for Process Development and Industrial Products Junior Award Lecture - Andrea Bonetti</td>
<td>Semisynthetic ways for the preparation of Homoharringtonine: an industrial approach</td>
</tr>
<tr>
<td>16:00 – 16:15</td>
<td>ORG OR10</td>
<td>Andrea Rozzi, Saša Korom, Alex Manicardi, Massimiliano Donato Verona, Vincenzo Verdolino, Roberto Corradini</td>
<td>Design and Synthesis of polyfunctional PNAs - A Biomolecular Engineering approach</td>
</tr>
<tr>
<td>16:15 – 16:30</td>
<td>ORG OR11</td>
<td>Laura Medve, Sonia Serna, Niels Reichardt, Silvia Achilli, Corinne Vivès, Franck Fieschi, Anna Bernardi</td>
<td>A Glycomimetic CHIP for microarray Screening of C-type Lectin Receptors</td>
</tr>
</tbody>
</table>

16:30 – 17:00 Coffee Break
### Parallel Session 3A
**Chairperson:** Maurizio Benaglia

<table>
<thead>
<tr>
<th>Time</th>
<th>ORG</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>17:00 – 17:15</td>
<td><strong>ORG OR12</strong>: Cristina Prandi, Stefano Nejrott</td>
<td><em>Gold(I)-catalyzed rearrangement of heterocycles derived 1,3-enynes</em></td>
</tr>
<tr>
<td></td>
<td><strong>ORG OR13</strong>: Francesca Ghirga, Cinzia Ingallina, Federica Aiello, Federica Balzano, Ilaria D’Acquarica, Bruno Botta, Gloria Uccello-Barretta, Deborah Quaglio</td>
<td><em>Snapshot of Ruthenium–Carbene–Resorc[4]arene Complex in an Olefin Metathesis Reaction</em></td>
</tr>
<tr>
<td>17:15 – 17:30</td>
<td><strong>ORG OR14</strong>: Mauro Sassi, Sara Mattiello, Myles Rooney, Alessandro Sanzone, Paolo Brazzo, Luca Beverina</td>
<td><em>Efficient Suzuki-Miyaura micellar Cross-Coupling in water, at room temperature and under aerobic atmosphere. Organic materials going green</em></td>
</tr>
<tr>
<td>17:30 – 17:45</td>
<td><strong>ORG OR15</strong>: Antonella Leggio, Emilia Lucia Belsito, Alessandra Comandè, Lucia Lo Feudo, Angelo Liguori</td>
<td><em>TiCl₄-Assisted Protocols in Organic Synthesis: the Case of Amides and β–Enaminones</em></td>
</tr>
<tr>
<td>18:00 – 18:15</td>
<td><strong>ORG OR16</strong>: Massimo Mella, M. Vincenzo La Rocca, Egle M. Beccalli, Silvia Gazzola, Gianluigi Broginni</td>
<td><em>Which reaction step controls regio selectivity in CuCl₂-catalyzed cyclization of alkynyl-substituted ureas and carbamates?</em></td>
</tr>
<tr>
<td>18:15 – 18:30</td>
<td><strong>ORG OR17</strong>: Raffaella Mancuso, Bartolo Gabriele</td>
<td><em>Divergent Syntheses of (E)-3-Isobenzofuran-1-(3H)-one and (1H)-Isocromen-1-one Derivatives by Palladium-Catalyzed Carbylation of 2-Alkynylbenzoic Acids</em></td>
</tr>
</tbody>
</table>

### Parallel Session 3B
**Chairperson:** Angela Zampella

<table>
<thead>
<tr>
<th>Time</th>
<th>ORG</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>17:00 – 17:15</td>
<td><strong>ORG OR18</strong>: Roberto Fiammengo, Hui Cai, Federica Degliangeli, Jia Liu, Christian Pett, Jing Hu, Horst Kunz, Ulrika Westerlind, Menji Lu</td>
<td><em>Eliciting specific humoral and cellular immune response by self-adjuvanting gold nanoparticles carrying tumor-associated MUC1 glycopeptides</em></td>
</tr>
<tr>
<td>17:15 – 17:30</td>
<td><strong>ORG OR19</strong>: Alessandro Palmioli, Carlotta Ciaramelli, Michela Spinelli, Gaia De Sanctis, Renata Tisi, Elena Sacco, Cristina Airoldi</td>
<td><em>Natural compounds in cancer prevention: effect of coffee extracts and their main polyphenolic component 5-CQA on oncogenic Ras proteins</em></td>
</tr>
<tr>
<td>17:30 – 17:45</td>
<td><strong>ORG OR20</strong>: Filippo Doria, Matteo Nadai, Matteo Scalabrin, Valentina Pirota, Vincenzo Grande, Greti Bergamaschi, Valeria Amendola, Sara N. Richter, Mauro Freccero</td>
<td><em>Synthesis and Binding Properties of a new Selective Scissoring Tool for Quadruplex Nucleic Acids</em></td>
</tr>
<tr>
<td>17:45 – 18:00</td>
<td><strong>ORG OR21</strong>: Chiara Pennetta, Alessandro Volonterio</td>
<td><em>Amino- and guanidinoglycoside based vectors for cell transfection</em></td>
</tr>
<tr>
<td>18:00 – 18:15</td>
<td><strong>ORG OR22</strong>: Carmen Festa, Simona De Marino, Maria Valeria D’Auria, Angela Zampella, Stefano Fiorucci, Vittorio Limongelli</td>
<td><em>Discovery of a new class of GPBAR1 modulators</em></td>
</tr>
<tr>
<td>18:15 – 18:30</td>
<td><strong>ORG OR23</strong>: Silvana Alfei, Gaby Brice Taptue</td>
<td><em>New promising vectors for gene delivery by a step-wise functionalization of a polyester-based non toxic dendrimer with N, N-dimethylglycine, N-methylglycine, lysine and arginine</em></td>
</tr>
<tr>
<td>18:30 – 20:00</td>
<td>Assembly of the Organic Chemistry Division</td>
<td></td>
</tr>
</tbody>
</table>
Martedì 12 Settembre 2017

### Parallel Session 4A

**Sala Argiva**

**Chairperson:** Emanuela Licandro

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
</tr>
</thead>
</table>
| 9:00 – 9:15| **ORG OR24:** Nadia Barbero, Sonja Visentin, Claudia Barolo, Roberto Buscaino, Guido Viscardi  
New polymethine dyes for photodynamic therapy |
| 9:15 – 9:30| **ORG OR25:** Paola Manini, Carmela Tania Frontera, Valeria Criscuolo, Alessandro Pezzella, Orlando Crescenzi, Michele Pavone, Marco d’Ischia, Maria Grazia Maglione, Paolo Tassini, Carla Minarini  
*From Melanins to OLED Devices: Taking Inspiration from the Black Human Pigments for the Design of Innovative Electroluminescent Materials* |
| 9:30 – 9:45| **ORG OR26:** Lorenzo Guazzelli, Andrea Mezzetta, Stefano Becherini, Cinzia Chiappe  
Modification of biopolymers in ionic liquids (ILs) media to access added value materials |
| 9:45 – 10:00| **ORG OR27:** Heiko Lange, Reza Ebrahim Majdar, Claudia Crestini  
*Towards Integrated Continuous-Flow Fractionation and Functionalisation of Technical Lignins* |
| 10:00 – 10:15| **ORG OR28:** Alice Guarnieri, Marco Cespugli, Simone Loteria, Francesca Vita, Cynthia Ebert, Lucia Gardossi  
*Chemical-enzymatic strategies for the synthesis and functionalization of renewable polymers and composite materials* |
| 10:15 – 10:30| **ORG OR29:** Zoia Luca, Anika Salanti, Marco Orlandi  
*Chemical Modifications for the Valorization of Lignin* |

### Parallel Session 4B

**Sala Mercurio**

**Chairperson:** Lucio Pellacani

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
</tr>
</thead>
</table>
| 9:00 – 9:15| **ORG OR30:** Luca Banfi, Lisa Moni, Renata Riva, Andrea Basso, Andrea Bozzano, Daniele Cartagenova, Chiara Lambruschini, Elisa Martino, Marta Nola, Gabriella Vitali Forconesi  
*Multicomponent reactions on biocatalytically produced substrates* |
| 9:15 – 9:30| **ORG OR31:** Andrea Gualandi, Daniele Mazzarella, Aitor Ortega Martínez, Luca Mengozzi, Fabio Calcinelli, Elia Matteucci, Filippo Monti, Nicola Armaroli, Letizia Sambri, Pier Giorgio Cozzi  
*Photocatalytic Radical Alkylation of Electrophilic Olefins by Benzylic and Alkylic Zinc-Sulfonates* |
| 9:30 – 9:45| **ORG OR32:** Polyssena Renzi, Johnny Hioe, Ruth M. Gschwind  
*Decrypting Transition States by Light (DTS-hν) in Brønsted Acid Catalysis* |
| 9:45 – 10:00| **ORG OR33:** Osvaldo Lanzalunga  
*Structural and Medium Effects in the Hydrogen Atom Transfer Processes Promoted by Short-Lived Aminoxyl Radicals* |
| 10:00 – 10:15| **ORG OR34:** Marco Paolino, Stefania Fusi, Andrea Cappelli, Michael Filatov, Jérémie Léonard, Massimo Olivucci  
*An Ultrafast Molecular Photoswitch Bio-inspired by Green Fluorescent Protein Fluorophore* |
| 10:15 – 10:30| **ORG OR35:** Fabio Bellina, Nicola Guazzelli, Marco Lessi, Chiara Manzini, Giulia Marianetti, Luca A. Perego, Cristofer Pezzetta, Andrea Pucci, Daniele Vergara  
*Highly selective arylation protocols to prepare bioactive and fluorescent imidazole-based compounds* |
### Auditorium Giove

**Parallel Session 4C: Biotechnology**  
**Chairperson:** Francesco Nicotra

<table>
<thead>
<tr>
<th>Time</th>
<th>ORG OR36: Short Build/Couple/Pair Approaches for the Synthesis of Novel Glyco- and Peptidomimetic Scaffolds</th>
</tr>
</thead>
<tbody>
<tr>
<td>9:00 – 9:15</td>
<td>Elena Lenci, Alessio Rossi, Gloria Menchi, Andrea Trabocchi</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time</th>
<th>ORG OR37: A New Antibacterial Cyclic Peptide from Hot Springs</th>
</tr>
</thead>
<tbody>
<tr>
<td>9:15 – 9:30</td>
<td>Roberta Teta, Viggo Thor Marteinsons, René Groben, Marie-Lise Bourguet-Kondracki, Valeria Costantino, Alfonso Mangoni</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time</th>
<th>ORG OR38: Recent advances in the synthesis of stemarane diterpenoids</th>
</tr>
</thead>
<tbody>
<tr>
<td>9:30 – 9:45</td>
<td>Francesca Leonelli, Angela La Bella, Luisa Maria Migneco, Rinaldo Marini Bettolo</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time</th>
<th>ORG OR39: Easy chemical modifications to explore the ‘Janus face’ of TBA: anticoagulant vs antiproliferative properties</th>
</tr>
</thead>
<tbody>
<tr>
<td>9:45 – 10:00</td>
<td>Veronica Esposito, Antonella Virgilio, Annapina Russo, Teresa Amato, Giulia Russo, Michela Varra, Luciano Mayol, Aldo Galeone</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time</th>
<th>ORG OR40: The greening of protection/deprotection strategies in peptide synthesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>10:00 – 10:15</td>
<td>Maria Luisa Di Gioia, Monica Nardi, Manuela Oliverio, Antonio Procopio, Rosina Paonessa, Giovanni Sindona</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time</th>
<th>ORG OR41: Design, synthesis of new heterocyclic compounds and their biological activity against MCF-7 cell line</th>
</tr>
</thead>
<tbody>
<tr>
<td>10:15 – 10:30</td>
<td>Cosimo Gianluca Fortuna, Carmela Bonaccorso, Vincenza Barresi, Cristina Satriano, Irina Naletova</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time</th>
<th>Coffee Break</th>
</tr>
</thead>
<tbody>
<tr>
<td>10:30 – 11:00</td>
<td></td>
</tr>
</tbody>
</table>

**Plenary Session 2**  
**Chairpersons:** Luca Banfi, Cinzia Chiappe and Domenico Misiti

<table>
<thead>
<tr>
<th>Time</th>
<th>ORG MD02: From ADDA to Antibody Drug Conjugates. Some Examples of Target Oriented Syntheses, a Blessing and a Curse for a Chemist</th>
</tr>
</thead>
<tbody>
<tr>
<td>11:00 – 11:30</td>
<td>Angelo Mangini Medal Lecture - Maurizio Taddei</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time</th>
<th>ORG MD03: Photocatalytic Hydrogen Atom Transfer (HAT) in Organic Synthesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>11:30 – 12:00</td>
<td>Giacomo Ciamician Medal Lecture - Davide Ravelli</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time</th>
<th>ORG PZ07: Methodologies in Organic Chemistry Award Lecture - Massimo Bietti, Tuning Reactivity and Selectivity in Hydrogen Atom Transfer from Aliphatic C–H Bonds</th>
</tr>
</thead>
<tbody>
<tr>
<td>12:00 – 12:30</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time</th>
<th>ORG PZ08: Organic chemistry for Environment, Energy and Nanoscience Award Lecture - Mauro Comes Franchini Oranic coating of Metallic nanoparticles: theranostic applications in nanomedicine</th>
</tr>
</thead>
<tbody>
<tr>
<td>12:30 – 13:00</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time</th>
<th>REAXYS-MYCS: Oceans of data for informed decisions in chemistry. The shortest path from the question to insight</th>
</tr>
</thead>
<tbody>
<tr>
<td>13:00 – 13:10</td>
<td>Carlos Rodriguez Del Rio (Elsevier)</td>
</tr>
</tbody>
</table>

**Intervallo Pranzo – Lunch Break**

**Sala Paestum B**

<table>
<thead>
<tr>
<th>Time</th>
<th>Poster Session 2 (ORG PO34 – ORG PO72)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time</td>
<td>Session</td>
</tr>
<tr>
<td>--------------</td>
<td>----------------------------------------------</td>
</tr>
<tr>
<td>14:00 – 15:00</td>
<td>Poster Session 3 (ORG PO73 – ORG PO104)</td>
</tr>
<tr>
<td>15:00 – 15:30</td>
<td><strong>Plenary Session 3</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Chairperson: Alberto Brandi</strong></td>
</tr>
<tr>
<td>15:00 – 15:30</td>
<td>ORG MD04: Piero Pino Medal Lecture - Enrico Dalcanale</td>
</tr>
<tr>
<td></td>
<td>The evolution of cavitand-based supramolecular polymers: from self-assembly to self-diagnostics</td>
</tr>
<tr>
<td>15:30 – 15:45</td>
<td><strong>Parallel Session 5A: Organic Chemistry in Industry</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Chairperson: Paolo Scrimin</strong></td>
</tr>
<tr>
<td></td>
<td>Synthesis and application of bifunctional chelating agents based on AAZTA scaffold</td>
</tr>
<tr>
<td>15:45 – 16:00</td>
<td>ORG OR43: Simone Mantegazza, Gabriele Razzetti, Emanuele Attolino, Chiara Vladiskovic</td>
</tr>
<tr>
<td></td>
<td>QU-IBX and B3-IBX: safe IBX adducts for periodinane oxidation reactions</td>
</tr>
<tr>
<td>16:00 – 16:15</td>
<td>ORG OR44: Aurelio Bonasera, Sebastian Fredrich, Virginia Valderrey, Stefan Hecht</td>
</tr>
<tr>
<td></td>
<td>Light-Activated Amine Detection via Innovative Diarylethene Probes</td>
</tr>
<tr>
<td></td>
<td>Handling Hydrogen Peroxide On Large Scale: Synthesis of 5-bromo-2-nitropyridine</td>
</tr>
<tr>
<td>16:30 – 17:00</td>
<td>Coffee Break</td>
</tr>
<tr>
<td>17:00 – 17:30</td>
<td><strong>Parallel Session 6A: Inorganic and Organic Chemistry Divisions' Joint Session on Organometallic Chemistry (GICO)</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Chairperson: Fabio Ragaini</strong></td>
</tr>
<tr>
<td>17:00 – 17:30</td>
<td>ORG/INO KN02: Lorenzo Zani</td>
</tr>
<tr>
<td></td>
<td>Conjugated Organic Compounds for Solar Energy Conversion to Electricity and Fuels</td>
</tr>
<tr>
<td>17:30 – 18:00</td>
<td>ORG/INO PZ02: EurJIC Junior Organometallic Chemist Lecture - Marco Bellini</td>
</tr>
<tr>
<td></td>
<td>Hydrogen and chemicals from renewable alcohols by Organometallic Electro-Reforming (OMER)</td>
</tr>
<tr>
<td>18:00 – 18:15</td>
<td>ORG/INO OR03: Walter Baratta, Rosario Figliolia, Salvatore Baldino, Hans Günter Nedden, Antonio Zanotti-Gerosa</td>
</tr>
<tr>
<td></td>
<td>Mild N-Alkylation of Amines with Alcohols Catalyzed by Acetate Ruthenium Complexes</td>
</tr>
<tr>
<td>Time</td>
<td>Session</td>
</tr>
<tr>
<td>--------------</td>
<td>--------------------------</td>
</tr>
<tr>
<td>18:15 – 18:30</td>
<td><strong>ORG/INO OR04</strong></td>
</tr>
<tr>
<td>18:30 – 18:45</td>
<td><strong>ORG/INO OR05</strong></td>
</tr>
</tbody>
</table>

**Auditorium Giove**

### Parallel Session 6B

- **Chairperson:** Giulia Licini

<table>
<thead>
<tr>
<th>Time</th>
<th>ORG/INO OR50</th>
<th>Title</th>
<th>Speakers and Institutions</th>
</tr>
</thead>
<tbody>
<tr>
<td>17:00 – 17:15</td>
<td>Laura Goracci, Martina Ceccarelli, Björn Wagner, Rubén Alvarez-Sanchez, Gabriele Cruciani</td>
<td>Assessment of drug-induced phospholipidosis risk based on distribution coefficient in brain polar lipids</td>
<td></td>
</tr>
<tr>
<td>17:15 – 17:30</td>
<td>Assunta Giordano, Giovanni Forte, Fabrizio Dal Piaz, Federica del Gaudio, Nunziatina De Tommasi, Patrizia Gazzarotto, Raffaele Riccio, Giuseppe Bifulco, Simone Di Micco</td>
<td>Identification of new ErbB4 inhibitors by inverse virtual screening</td>
<td></td>
</tr>
<tr>
<td>17:30 – 17:45</td>
<td>Gianluigi Lauro, Stefania Terracciano, Ines Bruno, Raffaele Riccio, Vincenza Cantone, Oliver Werz, Andreas Koeberle, Michele Manfra, Paolo Tortorella, Pietro Campiglia, Giuseppe Bifulco</td>
<td>Recent advances in the discovery of novel microsomal prostaglandin E2 synthase-1 (mPGES-1) inhibitors</td>
<td></td>
</tr>
<tr>
<td>17:45 – 18:00</td>
<td>Vittoria Graziani, Valentina Belli, Monica Scognamiglio, Brigida D’Abrosca, Angela Chambery, Severina Pacifico, Simona Piccolella, Teresa Troiani, Nicoletta Potenza, Antonio Fiorentino</td>
<td>Cytotoxic secondary metabolites from Mediterranean Fabaceae species display antiproliferative activity against colon cancer cell lines</td>
<td></td>
</tr>
<tr>
<td>18:00 – 18:15</td>
<td>Sara Piantini, Stefano Menichetti, Luisa Bracci, Chiara Falciani, Jenia Brunetti</td>
<td>Synthesis of new peptide-drug conjugates for targeted cancer diagnosis and therapy</td>
<td></td>
</tr>
<tr>
<td>18:15 – 18:30</td>
<td>Salvatore Vincenzo Giofrè, Roberto Romeo, Consuelo Celesti, Maria Assunta Chiacchio</td>
<td>Synthesis and Biological Evaluation of Some Pyrimidin-2,4-diones as Novel Non-Nucleoside Reverse Transcriptase Inhibitors</td>
<td></td>
</tr>
<tr>
<td>18:30 – 18:45</td>
<td>Elena Petricci, Fabrizio Manetti, Elena Cini, Roberta Santini, Barbara Stecca, Giuseppe Giannini</td>
<td>Synthesis and decoration of small molecules targeting the Hedgehog Signaling Pathway</td>
<td></td>
</tr>
<tr>
<td>18:45 – 19:00</td>
<td>Francesco Sansong, Stefania E. Sestito, Fabio A. Facchini, Ilaria Morboli, Jean-Marc Billod, Sonsoles Martin-Santamaria, Alessandro Casnati, Francesco Peri</td>
<td>Amphiphilic Guanidinocalixarenes Inhibit Lipopolysaccharide- and Lectin-stimulated Toll-like Receptor 4 Signaling</td>
<td></td>
</tr>
</tbody>
</table>

**Sala Argiva**

### Parallel Session 6C

- **Chairperson:** Vito Capriati

<table>
<thead>
<tr>
<th>Time</th>
<th>ORG/INO OR58</th>
<th>Title</th>
<th>Speakers and Institutions</th>
</tr>
</thead>
<tbody>
<tr>
<td>17:00 – 17:15</td>
<td>Silvia Cauteruccio, Davide Dova, Clara Baldoli, Roberta Franzini, Claudio Villani, Emanuela Licandro</td>
<td>Synthesis and stereochemical properties of axially chiral benzo[1,2-b:4,3-b’]dithiophene derivatives</td>
<td></td>
</tr>
<tr>
<td>17:15 – 17:30</td>
<td>Margherita De Rosa, Pellegrino La Manna, Carmen Talotta, Carmine Gaeta, Annunziata Soriente, Antonio Rescifina, Giuseppe Floresta, Placido Neri</td>
<td>Bioinspired organocatalysis of C-C bond-forming reactions</td>
<td></td>
</tr>
<tr>
<td>Time</td>
<td>Session</td>
<td>Authors</td>
<td>Title</td>
</tr>
<tr>
<td>-------------</td>
<td>-------------</td>
<td>------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------</td>
</tr>
<tr>
<td>17:30 – 17:45</td>
<td>ORG OR60</td>
<td>Marina Sicignano, Rosaria Schettini, Antonella Dentoni Litta, Francesco De Riccardis, Irene Izzo, Giorgio Della Sala</td>
<td>Highly diastereoselective synthesis of γ-butenolides and phthalides by Michael addition catalyzed by crown ethers</td>
</tr>
<tr>
<td>17:45 – 18:00</td>
<td>ORG OR61</td>
<td>Carla Sappino, Paolo Bovicelli, Federica Di Pietro, Giuliana Righi, Marzia Oneto, Ludovica Primitivo, Lorenza Suber</td>
<td>Design of a new chiral nanosupported catalyst for asymmetric reactions</td>
</tr>
<tr>
<td>18:00 – 18:15</td>
<td>ORG OR62</td>
<td>Vincenzo Algieri, Antonio De Nino, Loredana Maiuolo, Beatrice Russo, Pedro Merino</td>
<td>Asymmetric 1,3-dipolar cycloadditions catalyzed by a new imidazolidinone organocatalyst</td>
</tr>
<tr>
<td>18:15 – 18:30</td>
<td>ORG OR63</td>
<td>Susanna Sampaolesi, Federico Vittorio Rossi, Alessandro Palmieri, Pietro Allegrini</td>
<td>A new highly efficient strategy to prepare racemic Anatabine</td>
</tr>
<tr>
<td>18:30 – 18:45</td>
<td>ORG OR64</td>
<td>Carlo Bravin, Elena Badetti, Giulia Licini, Cristiano Zonta</td>
<td>Molecular Events within Confined Spaces</td>
</tr>
<tr>
<td>18:45 – 19:00</td>
<td>ORG OR65</td>
<td>Carlo F. Morelli, Fabio Romagnuolo, Gabriele A. Franz, Cinzia Calvio, Giovanna Speranza</td>
<td>Synthetic application of bacterial γ-glutamyltransferases (GGTs)</td>
</tr>
</tbody>
</table>
Medaglie e Premi della Divisione di Chimica Organica

Medaglia d'Oro “Adolfo Quilico”
Prof. Raffaele Riccio, Università degli Studi di Salerno

Medaglia d'Oro “Piero Pino”
Prof. Enrico Dalcanale, Università degli Studi di Parma

Medaglia d'Oro “Angelo Mangini”
Prof. Maurizio Taddei, Università degli Studi di Siena

Medaglia d'Argento “Giacomo Ciamician”
Dott. Davide Ravelli, Università degli Studi di Pavia

Premi alla Ricerca

Chimica organica per l’ambiente, l’energia e le nanoscienze
Prof. Mauro Comes Franchini, Università degli Studi di Bologna
Dott.ssa Giulia Fiorani (Junior), University of Oxford

Chimica organica per le scienze della vita
Prof.ssa Franca Zanardi, Università degli Studi di Parma
Dott.ssa Laura Russo (Junior), Università degli Studi di Milano Bicocca

Chimica organica nei suoi aspetti metodologici
Prof. Massimo Bietti, Università degli Studi di Roma “Tor Vergata”
Dott. Giovanni Maestri (Junior), Università degli Studi di Parma

Chimica organica per lo sviluppo di processi e prodotti nell’industria
Dott. Giorgio Bertolini, Olon S.p.A.
Dott. Andrea Bonetti (Junior), Indena S.p.A.
Changing paradigms in natural product chemistry: from structural elucidation to target identification

Raffaele Riccio

Dipartimento di Farmacia, Università degli Studi di Salerno
Via Giovanni Paolo II 132, 84084 Fisciano (SA), Italy - E-mail: riccio@unisa.it

Natural products have largely shown to be a huge source of bioactive molecules, often with fantastic and unprecedented structures. They have been an immense source of inspiration for the process of DD&D and many of them have reached the drug market after a long, complex and expensive process of drug development. In a series of comprehensive reviews by Newman and Cragg, analyzing the sources of new drugs from 1981-2014 [1], the contribution of natural products is estimated in about 50%, taking into account also what they cite as “natural product derived drugs”, any new drug that in some way was developed on the basis of a bioactive structural framework, a putative pharmacophoric group or bioactivity information arising from a natural product. It is indeed highly common that, in addition to the direct use of a natural product in an unmodified form, the structure of a novel natural compound or its relevant structure activity relationship information are utilized as a lead to be optimized for the development of a new drug. The scientific literature is full of such kind of examples and the valuable role of natural product scaffolds in synthesis-driven pharma exploitation has been clearly evidenced in a Danishefsky review [2]. Of course, the complete structural elucidation of a new natural product is a fundamental starting point for any DD&D process. This has been for decades an intriguing and challenging task attracting the interest of organic chemists. The extraordinary development of spectroscopic techniques and informatics tools have drastically modified the approach to a structural elucidation process and have opened new perspectives for target identification and for drug-receptor interaction studies. Our group has been largely involved in the area of natural product chemistry, isolating and investigating bioactive natural products from marine and terrestrial sources. In most recent years prominent attention has been dedicated to: application of QM calculation for structural and stereochemical determination of organic compounds [3-8]; development of an Inverse Virtual Screening (IVS) protocol for target prediction [9-12]; application of chemical proteomics approaches in bioactive natural products target profiling [13-25].

A set of investigation protocols recently applied also to the development of natural products as dietary supplements (Nutraceuticals). Solving the stereochemistry of natural product structures can still be a quite challenging task, requiring time and expertise. The knowledge of the stereochemistry, especially in complex structures with several stereocenters, is essential for undertaking total synthesis, performing conformational and structure activity relationship studies, investigating the biological mechanism of action at the molecular level. On the other end, the identification of the cellular targets of bioactive small-molecules is often a crucial step in pharmaceutical research, where the identification of target proteins and investigation of ligand-receptor interactions are recognized as essential requirements in the process of drug D&D. Protocols based on IVS or chemical proteomics appear to be attractive alternatives to in vitro binding assays, since they can be profitably applied in the early stages of the process of drug D&D. Representative case studies for the described approaches, derived from recent research activity of our group, will be illustrated in this communication.

From ADDA to Antibody Drug Conjugates. Some Examples of Target Oriented Syntheses, a Blessing and a Curse for a Chemist

Maurizio Taddei

Dipartimento di Biotecnologie, Chimica e Farmacia, Università degli Studi di Siena, Via A. Moro 2, 53100 Siena. E-mail: maurizio.taddei@unisi.it

After more than seventy years since the Woodward-Doering total synthesis of quinine, the society is still seeking for new molecules as drugs, dyes, soaps, perfumes, semiconductors, polymers and molecular tools for biology, medicine, biotechnology and nanotechnology.

As the yearned molecule has often a precise structure, only a target oriented synthesis can provide it. Science and creativity are the pillars of total synthesis but frustration is just around the corner, full of (simple) transformations that do not work or substrates with capricious reactivity. However, the reward is the creation of a matter that didn’t exist before, an achievement that the synthetic chemist shares only with God.

I report here the syntheses of several molecules we prepared in the last twenty years (with a complexity appropriate to an Italian team) through the classic trial-and-error experiment procedure. Although orchestration of the skeleton construction with functional group transformation is important, I focus herein on the issues which were key to our success as: (i) availability of starting materials and scalability of intermediate production; (ii) use of the chiral pool to solve stereochemistry problems; (iii) commitment to deliver the molecules to somebody for a specific use.

The lecture will cover also the last and mostly unpublished results on the conjugation of small molecules to antibodies with the everlasting problem to assemble simple chemicals in the complex contest of an immunoglobulin going around in the hematic torrent and in diseased tissues.

Photocatalytic Hydrogen Atom Transfer (HAT) in Organic Synthesis

Luca Capaldo, Silvia Garbarino, Stefano Protti, Angelo Albini, Maurizio Fagnoni, Davide Ravelli

PhotoGreen Lab, Department of Chemistry, University of Pavia, viale Taramelli 12, 27100 Pavia, Italy
E-mail: davide.ravelli@unipv.it

Photocatalytic reactions applied to organic synthesis have recently gained increasing attention, thanks to the unconventional pathways offered and the mild conditions involved, in accordance with the core principles of Green Chemistry. These reactions are based on the use of a photocatalyst (PC, Scheme 1), a species that is responsible for light absorption and for the subsequent activation of the substrate through a chemical step. (1) Among the activation modes of PC, two main fields can be recognized, viz. Single Electron Transfer (SET) and Hydrogen Atom Transfer (HAT) processes. The former approach is undoubtedly the most investigated one: visible light absorbing Ru- and Ir-polypyridyl complexes and organic dyes are the key actors of a "hot topic" tagged as "photoredox catalysis with visible light". (1) These reactions involve the transfer of one electron between PC* and the substrate R-X, leading to the formation of the corresponding radical ion R-X" or R-X" (Scheme 1, upper part). However, the main drawback of this strategy consists in the requirement of redox active reagents, matching the redox potentials of PC. In contrast, HAT processes offer the possibility of activating directly a C-H bond in the substrate (Scheme 1, lower part). The main limitation to the development of this pathway is represented by the limited number of PCs able to promote HAT steps. (2,3)

In recent years, we developed a number of photocatalytic methods for the photogeneration of C-centered radicals and the ensuing addition onto C=C double bonds, including electron-poor olefins (4) and vinyl aromatics. (5) This strategy is based on the use of UV-light absorbing tetrabutylammonium decatungstate (TBADT, (nBu₄N)₄[W₁₀O₃₂]) as the photocatalyst. (6,7) Upon irradiation, excited PC* cleaves homolytically (often with high chemo- and regioselectivity) C-H bonds in a variety of organic derivatives. (6,7) Thus, the functionalization of C(sp², sp³)-H bonds (R-H in Scheme 1) of aldehydes, amides, ethers and acetals, as well as alkanes, was smoothly achieved. This approach was demonstrated to proceed also under solar light irradiation (6) and could be optimized under flow conditions. (8)

Recent developments in the field of photocatalytic HAT processes involve the design and optimization of visible light absorbing photocatalysts, including porphyrin complexes, the uranyl cation and aromatic ketones.


The evolution of cavitand-based supramolecular polymers: from self-assembly to self-diagnostics

Enrico Dalcanale

Dipartimento di Scienze Chimiche, della Vita e della Sostenibilità Ambientale, Università di Parma, Parco Area delle Scienze 17/A, 43124 Parma

In the last few years the merging of polymer science with supramolecular chemistry has created a new, thriving field of research (1), known under the name of supramolecular polymer chemistry (2). The driving force behind this methodological breakthrough is the ability to control noncovalent interactions with the same precision achieved by synthetic organic chemistry. Molecular recognition is the most sophisticated form of weak interaction in terms of precise responsiveness, since it requires a well-defined arrangement of complementary non-covalent interactions to operate at its best. Some of the most relevant issues associated to the development of supramolecular polymers are: (i) achieve macroscopic expression of molecular recognition, (ii) trigger stimuli specific responses in polymeric materials and (iii) move self-assembly from the nano to the meso and macroscale. In the Medaglia Pino lecture, supramolecular polymers based on phosphonate cavitands will be presented, in which the polymerization is driven by host-guest complexation (3,4) (Figure 1). In particular, the following examples will be discussed: (i) polymer blending as macroscopic expression of molecular recognition (5) (Figure 2), (ii) electrochemical responsive host-guest polymers in the solid state (6) and (iii) strain-field self-diagnostic elastomers.

Figure 1. Crystal structure of the alternate copolymer formed by self-assembly between methyl viologen and ditopic phosphonate cavitand.

Figure 2. Polymer blending of a polystyrene HOST and a poly(butylmethacrylate) GUEST seen by AFM

References
Playing with Peptidomimetic and Small-Molecule Drug Hybrids to Hit Cancer-Related Biomarkers

Franca Zanardi

Dipartimento di Scienze degli Alimenti e del Farmaco, Università di Parma, Parco Area delle Scienze 27A, 43124 Parma, Italy
franca.zanardi@unipr.it

Relevant perspectives in modern tumor pharmacotherapy are rapidly widening, addressing several crucial issues such as drug specificity, minimization of off-target toxicities and by-passing drug-resistance mechanisms which were almost neglected by traditional, still-in-use cytotoxic chemotherapeutics. Thus, targeted drugs – either monotherapeutics, combinations, or hybrid constructs – selectively perturbing diverse and intertwined molecular targets are arising as privileged therapeutic options (1). It is well known that tumor endothelial cells show increased levels of expression of several cell-surface molecules that potentiate cell proliferation, invasion and survival during tumor vascular remodeling and angiogenesis. One such molecule is the αvβ3 integrin receptor, whose overexpression in both tumor-associated vascular endothelial cells and various tumor types – including glioblastoma and melanoma, breast, prostate, cervical, pancreatic, and ovarian carcinomas – renders it an eligible biomarker of these cancer diseases (2). In recent years, our efforts in the area of specific integrin ligands led to the discovery and development of a new series of γ-aminoproline-based Arg-Gly-Asp cyclic peptidomimetics, c(Amp)RGD, which showed low-nanomolar affinity toward the αvβ3 integrin in both cell-free and in-cell assays (3). The incorporation of these ligands within hybrid constructs – be they small molecule covalent conjugates, radioimaging active constructs or nanosized assemblies – led to the identification of multifunctional systems where the tumor-homing ability of the RGD ligands is integrated with ancillary yet crucial tumor-hitting entities (4).

The role of the c(Amp)RGD peptidomimetics in impairing tumor-associated angiogenesis and melanoma tumor growth in vitro and in vivo by using selected examples of hybrid constructs from our laboratories will be discussed; in confirmation that alliance between the science of chemical synthesis and life sciences is possible and even fruitful.

From few grams to multi Tons of Active Pharmaceutical Ingredients - Some tips

Giorgio Bertolini

Olon S.p.A., Strada Rivolta km 6/7 – 20090 Rodano (MI) - Italy; gbertolini@olonspa.it

In the phase of identification and selection of a new synthetic route for the preparation of Active Pharmaceutical Ingredients (API) all the attention is focused on the chemistry of each single steps evaluating the yield, the conditions (high vs low temperature and/or pressure) the selectivity and so on.

When the synthetic method is then identified and in some cases even optimized, several other aspects must be taken in consideration to move from a synthetic method to a chemical process that can be scale-up from Lab to the plant.

In this phase some critical points could be identified slowing down or in some cases even stop the scale-up of the process forcing the researcher to go back in the Lab to slightly change, or in some cases even completely redesign the synthetic route.

In order to have a real industrial chemical process for the production of fine chemicals or APIs, not only the simple organic chemistry has to be considered but many other aspects and for this reason a Process Development Chemist should have a multidisciplinary expertise including the knowledge, even if at high level, of Process Safety, Inorganic Chemistry, Regulatory, Chemical Engineering and Economy (process/product cost structure).

Using this knowledge he must have the ability to combine all these requests and information to design and select from the beginning the most promising synthetic route.

In this lecture some examples will be presented demonstrating that a smooth scale-up of a economic, safe and environmentally friendly chemical process depends in some cases on small details that have however a critical impact on the real success the project.
The chemistry of stable trinuclear all-metal aromatics

Giovanni Maestri

Università di Parma, Dipartimento di Scienze Chimiche, della Vita e della Sostenibilità Ambientale, Parco Area delle Scienze, 43124 Parma; giovanni.maestri@unipr.it

Aromaticity is a concept invented to account for the properties of an important class of organics. For decades, chemists played with a few bricks only to construct aromatics, mostly H, C, N and O. Nonetheless, their scope of applications is nearly boundless. This bonding mode broke the boundaries of organic chemistry with reports on all-metal aromaticity, although applications remains rare as most of them are elusive species.

Observation of this bonding mode on stable Pd$_3^+$ complexes presenting a perfectly equilateral metal kernel (1) pushed the development of a simple synthetic method to access an ample library of structures. (2) This in turn paved the way for the introduction of these prototypical subnanometric metal surfaces in catalysis, showing unique features in alkyne semireductions. (3,4) Ongoing developments highlight that tuneable all-metal aromatic frameworks can trigger complex cascades for C-C bond formation and, furthermore, that they can act as ligand to bind Lewis acidic atoms.

Towards Bio-based Organic Carbonates and Polycarbonates via Coupling of Highly Substituted Oxiranes and CO$_2$

Giulia Fiorani$^a$, Arjan W. Kleij$^{b,c}$, Charlotte K. Williams$^a$

$^a$ Department of Chemistry, University of Oxford, Chemistry Research Laboratory, 12 Mansfield Road, Oxford OX1 3TA, United Kingdom; $^b$ Institute of Chemical Research of Catalonia (ICIQ), The Barcelona Institute of Science and Technology, Av. Països Catalans 16, 43007 Tarragona, Spain; $^c$ Catalan Institute of Advanced Studies (ICREA), Pg. Lluís Companys 23, 08010 Barcelona, Spain.

Non-reductive CO$_2$ coupling reactions using highly reactive substrates (such as oxiranes) can be regarded as a topical milestone within the field of CO$_2$ conversion. These processes require an appropriate catalytic system comprising both a Lewis acid catalyst (M) and a nucleophile (Nu) and can selectively lead to heterocyclic scaffolds or CO$_2$ based polymers. The majority of this research focuses on petro-derived epoxides and CO$_2$, although promising recent reports highlight the potential for bio-derived epoxides. (1) In particular, CO$_2$ coupling with challenging di- and tri-substituted oxiranes can expand both the scope and possible applications of organic carbonates and polycarbonates. Here we report the application of highly active catalytic systems to the coupling of di- and tri-substituted epoxides and CO$_2$. The catalytic systems investigated are either Al$^{III}$ amino-triphenolate complexes which form an interesting class of modular, homogeneous catalysts (2) or bimetallic macrocycles and metal salen based systems which are selective towards polycarbonate formation. (3) These catalysts are capable of selectively forming either cyclic or polycarbonate structures. An appropriate substrate scope will be presented, highlighting sustainable, naturally occurring compounds and how they compare with more traditional epoxides. (4) The structural properties of the resulting cyclic and polymeric products will also be discussed being of interest for practical applications.

When glycochemistry meets biomaterials: from design to application of synthetic glyco-tools

Laura Russo

University of Milano-Bicocca, Department of Biotechnology and Biosciences Piazza della Scienza 2, 20126 Milan Italy.

e-mail: laura.russo@unimib.it

Glycans are ubiquitous in all living cells and organisms, where they serve essential functions, ranging from acting as structural components to regulate physiological and pathological processes. Evidence clearly indicates that glycans represent a largely untapped resource for biological discovery as well as unanticipated therapeutic opportunities. Recent studies have challenged the classical view of protein glycosylation as an intracellular event by demonstrating that glycans may experience further structural remodelling by extracellular enzymes. This makes the glycome a highly dynamic molecular entity that mirrors a biological milieu and confer to cell microenvironment an important regulatory role. The design of new synthetic strategies aimed to obtain new biomaterials able to mimic the extracellular environment and its glycosignature has impact in different biomedical fields, from tissue engineering to cell biology studies [1,2]. Here in this talk functionalization strategies of different materials and their biomedical application will be presented.

Homoharringtonine 2, a natural alkaloid obtained from various Cephalotaxus species is used in the treatment of myeloid leukemia. The mechanism of action by which Homoharringtonine exerts its antitumor activity is through inhibition of protein synthesis and promotion of apoptosis. It can be extracted from various botanical species, but its preparation by a synthetic way has always represented a challenge. An efficient industrial route for the isolation of pure omacetaxine 1 and the semisynthesis of Homoharringtonine is discussed.
Tuning Reactivity and Selectivity in Hydrogen Atom Transfer from Aliphatic C–H Bonds

Massimo Bietti, Michela Salamone

Dipartimento di Scienze e Tecnologie Chimiche, Università "Tor Vergata", Via della Ricerca Scientifica, 1 I-00133 Rome, Italy. E-mail: bietti@uniroma2.it

Hydrogen atom transfer (HAT) represents one of the most fundamental chemical reactions that plays a major role in a variety of important chemical and biological processes. Relevant examples include enzymatic and biomimetic reactions, the mechanism of action of natural and synthetic radical scavenging antioxidants, radical-induced damage to biomolecules and polymers, the degradation of volatile organic compounds in the atmosphere, as well as a large number of synthetically useful C–H functionalization procedures.

The factors that govern HAT reactivity from aliphatic C–H bonds have been discussed in detail (1-3). The main contributor is generally represented by bond strengths, but other factors such as steric, stereoelectronic, strain release and polar effects have also been shown to play an important role.

Within this framework, we have been interested in the study of HAT reactions from aliphatic C–H bonds, with the main objective of obtaining quantitative kinetic information on the role of structural and medium effects on the reactivity and selectivity patterns. This goal has been mostly achieved through time-resolved kinetic studies of the reactions of an alkoxyl radical such as cumyloxyl (PhC(CH₃)₂O, CumO•) with a large variety of substrates (hydrocarbons, alcohols, ethers, aldehydes, amines, amides) carried out employing the laser flash photolysis technique, with particular attention being devoted to the role of solvent effects and of added Lewis and Brønsted acids (4). These studies have provided a consistent set of second order rate constant values (k_H), through which useful guidelines for the description of the factors that govern these reactions have been obtained. The results of these studies will be discussed.

Organic coating OF Metallic nanoparticles: theranostic applications in nanomedicine

Mauro Comes Franchini

Department of Industrial Chemistry “Toso Montanari”, University of Bologna (Italy)

Metal nanoparticles (MNPs) have various unusual chemical and physical properties compared with those of metal atoms. The role of organic ligands and their coating of MNPs, on the other hand, are increasing the importance in nanoscience. Once grafted with organic molecules the metallic nanoparticles change their solubility and can therefore be further elaborated and/or entrapped into suitable (bio)polymers.

The functionalization of MNPs with specific organic molecules is therefore a key step in nanomedicine.

Nanomedicine is the application of nanoscience to medicine and one possible approach describe the use of multi-functional nanocarriers containing organic molecules (drugs) together with smaller lipophilic metallic nanoparticles suitable for imaging/therapy.

This concept seems to be particularly important in view of the emerging concept of theranostic in which both therapeutic and diagnostic capabilities can be present in nanocarriers.

In this talk:

Several metallic nanoparticles (Gold, Silver, Iron oxide) will be presented with specific organic coating, synthesis and characterization. Different shapes will be also considered.

Polymeric entrapment and chemical conjugation with specific biomolecules (peptides, monoclonal antibodies, aptamers) giving targeted-nanocarriers, will be also shown.

Biological results \textit{in vitro} on several cancer cells will be presented as well as some pre-clinical \textit{in vivo} experiments in tumor-bearing mice will show the final application, one step before entering in clinical trials.
Gold(I)-catalyzed [4+2] cycloaddition reactions of vinylindoles and allenes

Valentina Pirovanoa, Elisabetta Rossia, Giorgio Abbiati

a DiSFarm - Sezione Chimica Generale e Organica "A. Marchesini", Università degli Studi di Milano, Via G. Venezian 21, 20133 Milano, Italy; valentina.pirovano@unimi.it

Carbazole and tetrahydrocarbazole rings are the key structural motif in a great number of biological active molecules, including natural alkaloids and synthetic products.(1) For this reason, strategic syntheses of these indole derivatives are highly required, in particular when based on asymmetric methodologies. In this research field, 2- and 3-vinylindoles have become versatile 4C building blocks for the synthesis of complex tetrahydrocarbazole derivatives by means of [4+2] cycloadditions.(2) Among dienophiles, it has been shown that gold activated allenes could participate in [4+2] processes(3) and we published the first example of gold catalyzed reaction of 2- and 3-vinylindoles with allenamides(4) and allenyl esters.(5) In this latter work we reported also some preliminary investigations on enantioselective synthesis of tetrahydrocarbazoles, by conducting the reaction in the presence of a chiral gold(I) phosphoramidites. Prompted by these results and taking into account the importance of asymmetric tetrahydrocarbazole synthesis, we next explored the reactivity of 3/2-substituted-2/3-vinylindoles with N-allenamides under chiral gold(I) catalysis for the synthesis of a new series of dearomatized indoles bearing a quaternary C4a/C9a stereocenter (Scheme 1).(6) The results obtained in this work will be presented in the context of our investigations on gold(I) catalyzed syntheses of tetrahydrocarbazoles.

Hydrogen and chemicals from renewable alcohols by Organometallic Electro-Reforming (OMER)

Marco Bellini\textsuperscript{a}, Maria V. Pagliaro\textsuperscript{a,b}, Hamish A. Miller\textsuperscript{b}, Werner Oberhauser\textsuperscript{b}, Maria G. Follieri\textsuperscript{a}, Andrea Marchionni\textsuperscript{a}, Jonathan Filippi\textsuperscript{a}, Francesco Vizza\textsuperscript{a} and Hansjörg Grützmacher\textsuperscript{c}.

\textsuperscript{a} Istituto di Chimica dei Composti Organometallici – Consiglio Nazionale delle Ricerche, Via Madonna del Piano 10, 50019, Sesto Fiorentino (Firenze); \textsuperscript{b} Dipartimento di Chimica, Università degli Studi di Siena, Via Aldo Moro 2, 53100 Siena; \textsuperscript{c} Department of Chemistry and Applied Biosciences, ETH Hönggerberg, CH-8093 Zurigo, Svizzera. marco.bellini@iccom.cnr.it

The production of hydrogen by electrolysis of water is a well-established technology but it does not have a significant commercial impact due to its high energy cost. A recent strategy for reducing the energy cost of electrolytic hydrogen production involves the replacement of water oxidation at the anode of the electrolytic cell with the oxidation of a soluble substrate, like a bioalcohol, whose oxidation potential is much lower than that of water. This leads to a significant reduction of the potential required to produce hydrogen (1). The original idea presented here, consists in coupling the partial oxidation of renewable alcohols promoted by an organometallic complex [Rh(OTf)(trop\textsubscript{2}NH){P(4-n-buty1-Ph)}\textsubscript{3}] (trop\textsubscript{2}NH=bis(5-H dibenzo[a,d]cyclohepten-5-yl)-amine; OTf\textsuperscript{-} = CF\textsubscript{3}SO\textsubscript{3}\textsuperscript{-} = triflate; (see 1@c in figure 1 for a structure plot) with the cathodic hydrogen evolution reaction (2). We report an electrolytic device that achieves the simultaneous selective production of carboxylate compounds and high-purity hydrogen gas. This electrolyzer, that we call OrganoMetallic ElectroReformer (OMER), in contrast to electrolysis technologies based on nanoparticles, offers potentially enormous advantages as in principle every single metal atom is catalytically active, thus allowing a vastly reduced metal loading. At the same time, this technology is capable of providing simultaneously high levels of pure hydrogen production and chemicals of industrial importance by the exploitation of bioalcohols. The absence of oxygen production in the anode compartment facilitates the production of hydrogen at elevated pressures. Consequently, we hypothesize the exploitation of bioalcohol electoreforming as an essential component of the biorefinery platform using this new class of electrolyzers based on organometallic complexes.

![Figure 1](image_url): proposed mechanism for the reactions occurring on the anode coated with 1@c.

Keynote e Conferenze su Invito

- **ORG/INO KN01**: Alessandro Caselli, Università degli Studi di Milano
- **ORG/INO KN02**: Lorenzo Zani, CNR, Sesto Fiorentino (Fi)
Catalytic Applications of Pyridine-Containing Macrocyclic Complexes

Alessandro Caselli

Department of Chemistry, Università degli Studi di Milano and ISTM-CNR-Milano, Via Golgi 19, 20133
Milan, Italy. E-mail: alessandro.caselli@unimi.it

Polyazamacrocycles are a common class of macrocyclic compounds, utilized across a number of fields, including, but not limited to, catalysis, selective metal recovery and recycling, therapy and diagnosis, and materials and sensors.\(^1\) Worth of note is their ability to form stable complexes with a plethora of both transition, especially late, and lanthanide metal cations.\(^2\) Deviation of the macrocycle donor atoms from planarity often leads to rather uncommon oxidation states.\(^3\) Both the thermodynamic properties and the complexation kinetics are strongly affected by the introduction of a pyridine moiety into the skeleton of polyazamacrocycles by increasing the conformational rigidity and tuning the basicity.\(^4\) Pyridine-containing ligands engender great interest due to various potential field of applications. They have been successfully employed in biology, Magnetic Resonance Imaging, molecular recognition, supramolecular chemistry and self-assembly, molecular machines and mechanically interlocked architectures.\(^5\) In this lecture, I will provide a perspective on the catalytic applications of metal complexes of pyridine-containing macrocyclic ligands (Pc-L’s) which have been studied in our group (Figure), with a focus interest on the structural features relevant to catalysis.\(^6\) The increased conformational rigidity imposed by the pyridine ring allowed for the isolation and characterization of metal complexes which showed a rich coordination chemistry.\(^7\) The very different conformations accessible upon coordination and the easy tuneable synthesis of the macrocyclic ligands have been exploited in stereoselective syntheses.\(^8\)

**Figure.** Metal complexes of Pc-L’s and X-ray structure of a Cu(I) complex with a rare η\(^2\)-naphtyl moiety coordinated to the metal center.

**Key words:** macrocyclic ligands, homogeneous catalysis, copper, silver, C-C and C-O bond forming reactions.

References:

Conjugated Organic Compounds for Solar Energy Conversion to Electricity and Fuels

Lorenzo Zani

Istituto di Chimica dei Composti Organometallici (CNR-ICCOM), Via Madonna del Piano 10, 50019 Sesto Fiorentino (FI); lorenzo.zani@iccom.cnr.it

Over the years, conjugated organic compounds have been extensively employed in devices for solar energy exploitation, both as light-harvesting materials and semiconductors with high charge carrier mobility: relevant examples include sensitizers for dye-sensitized solar cells (DSSC) (1) and hydrogen photocatalytic production (2), small-molecule donor materials in organic solar cells (3) and hole-conductive materials for perovskite solar cells (4). In this communication, we will provide an overview of our group’s recent activity in the design, synthesis and application of donor-acceptor conjugated compounds for solar energy conversion (5-9). Compounds containing different heterocyclic rings (Figure 1) were assembled by means of typical organometallic and transition metal-catalyzed transformations, such as halogen-lithium exchange and Pd- or Cu-mediated coupling reactions, and were characterized using various spectroscopic and electrochemical techniques. The influence of their optical and redox properties on the efficiency of solar energy conversion devices will be discussed, together with the role of charge transfer processes taking place between them and other device components (such as inorganic semiconductors, electrolytes, sacrificial electron donors).

Figure 1. Examples of conjugated organic compounds employed in devices for solar energy exploitation.

Comunicazioni Orali
Molecular Engineering of \( \pi \)-Conjugated Systems Towards Light-Responsive Organic Semiconductors

Giuseppe Sforazzini\textsuperscript{a}, Augustina Jozeliunaite\textsuperscript{a,b}, Edvinas Orentas\textsuperscript{b}, Daniele Fazzi\textsuperscript{c}, Walter Thiel\textsuperscript{c}

\textsuperscript{a} Laboratory of Macromolecular and Organic Materials (LMOM), Institute of Material Science and Engineering, Ecole Polytechnique Federale de Lausanne (EPFL), 1015 Lausanne, Switzerland; \textsuperscript{b} Department of Organic Chemistry, Vilnius University, LT-03225 Vilnius, Lithuania; \textsuperscript{c} Department of Theoretical Chemistry, Max-Planck-Institut für Kohlenforschung, D-45470 Mülheim an der Ruhr, Germany; giuseppe.sforazzini@epfl.ch

Conjugated oligomers and polymers are under widespread investigation as active components in various optical and electronic technologies. The chemical-physical properties of these compounds strongly depend on the geometric arrangement of their molecular \( \pi \)-orbitals. The ability to modulate the \( \pi \)-bond geometry, e.g. the planarity, is particularly desirable as it can offer the possibility to dynamically tailor their \( \pi \)-conjugation extension, thus tuning their optical and electronic proprieties. Light-responsive switches, e.g. photochromic dyes, have been successfully used to modulate the effective conjugation length of linear \( \pi \)-systems.\textsuperscript{1,2} However, such molecules experience a drop in their photo-switching efficiency by increasing the \( \pi \)-conjugation length.\textsuperscript{3} Here, we present an alternative design philosophy called photochromic torsional switch (PTS), that exceeds the current limits of conventional photochromic molecular switches. The PTS design comprises an azobenzene-switch laterally connected to a bithiophene \( \pi \)-conjugated unit by both direct and aliphatic linker-assisted bonding. The planarity of the bithiophene can be mechanically tuned via the photochromic isomerization of the azobenzene unit. Upon exposure to 350 nm wavelength, the azobenzene moiety switches to a \textit{cis} configuration, causing the planarization of the bithiophene. In the absence of light, or upon exposure to a 254 nm wavelength, the azobenzene moiety assumes its extended \textit{trans} conformation, forcing the bithiophene backbone to be twisted out of planarity. The described PTS molecular design was then extended to thiophene-based oligomers and polymers. In order to probe the structural variations of the thiophenic backbone, as well as the reversible tuning of the optical and electronic properties of these PTS derivatives, we used state-of-the-art spectroscopic and computational quantum-chemical techniques. Noticeably, the switchability of these PTS-based oligothiophenes and polythiophenes is not adversely affected by the extension of their \( \pi \)-conjugation. Thus, PTS-based oligomers were successfully used for the fabrication of working light-responsive organic field effect transistors (OFET). This novel class of photochromic compounds open, thus, new avenues towards the design of adaptive and responsive \( \pi \)-conjugated molecular materials, and allow for the development of innovative optoelectronic technologies.

Organic sensitizers for solar fuels from dye-sensitized water splitting

Chiara Liliana Boldrini, Norberto Manfredi, Alessandro Abbotto

Department of Materials Science and Solar Energy Research Center MIB-SOLAR, University of Milano-Bicocca, and INSTM Milano-Bicocca Research Unit, Via Cozzi 55, 20125 Milano, Italy; email: c.boldrini@campus.unimib.it

The need for energy is increasing all around the world, so it is very important to find clean sources to produce it. Among the new approaches to solar energy conversion, photoelectrochemical cells (PEC) represent an interesting solution to obtain hydrogen and oxygen from water splitting. Hydrogen is a clean fuel, with zero carbon footprint, and is very versatile since it can be used to produce electricity but also as an automotive fuel that ensures a far bigger range than batteries for electric cars.

The sustainable production of fuels from Sun and water via organic dye-sensitizers is an emerging field of research, where the organic design is strategic in order to get improved technological performances. In the frame of our investigation on dye-sensitized solar cells in the last years we have pioneered a multi-branched multi-anchoring D(-π-A)2 geometry, now widely used in the field (1).

In this work we present the application of specifically engineered di-branched dyes to the dye-sensitized PEC (DS-PEC) for water splitting (Fig. 1). Namely, we tested a series of D-(π-A)2 dyes where D is a substituted phenothiazine, phenoxazine or carbazole donor core, A is the acceptor-anchoring cyano-acrylic group, and π is a thiophene spacer (Fig. 2), previously used in photocatalytic hydrogen production (2, 3). To better investigate the electron transfer process from the sensitizer to the semiconductor, a comparative study in presence of different sacrificial electron donors has been performed (namely triethanolamine, TEOA, and hydroquinone, H2Q). Compared to the reference dye (phenothiazine-based dye) (4), the new sensitizers revealed improved optical properties and enhanced photocurrent in photoelectrochemical experiments (5).

Solution and solid-state supramolecular aggregates of new chiral oligothiophenes: synthesis and spectroscopic characterization

Gianluigi Albano, Laura Antonella Aronica, Lorenzo Di Bari

Dipartimento di Chimica e Chimica Industriale, Università di Pisa, via G. Moruzzi 13, 56124 Pisa, Italy
E-mail: gianluigi.albano@dcci.unipi.it

In recent years, π-conjugated oligomers have emerged as ideal organic semiconductors for various electronic and optoelectronic applications, thanks to the possibility to modulate their electronic and optical properties (charge and exciton transport, light absorption and emission, response to external stimuli), which depend not only on their chemical structure and the conformation assumed, but also on the nano/mesoscale organization in the solid state. (1) Chirality represents one of the most sophisticated expediens to control supramolecular aggregation of similar systems, in particular their interchain spacing and/or alignment. (2) Furthermore, chiral nanostructures may display various intriguing physicochemical properties, exploited for example in sensors able to discriminate enantiomers (3) and in circularly polarized (CP) light detectors (4, 5) or emitters (6). However, since most studies have concentrated only on inorganic chiral nanomaterials, the creation of chiral organic semiconductors may open new doors for optoelectronics.

We decided to work with new oligothiophenes (π-conjugated systems well known in optoelectronic devices) functionalized with some inexpensive alkyl chiral groups derived from natural sources, seeking self-assembly properties, which would ensure supramolecular chirality and the onset of extraordinary optical and electrical properties.

In particular, we will describe: a) the synthetic route developed for the preparation of these oligomers; b) their spectroscopic characterization (UV-Vis, ECD, fluorescence) to investigate the supramolecular organization both in solution and in thin films (prepared by drop casting and spin coating techniques), in connection with standard and polarized optical microscopy analysis.

Novel oligothiophenes with reduced HOMO-LUMO band gap for Optoelectronics

Francesca Parenti,* Mirko Buffagni,* Alfonso Zambon,* Monica Caselli,* Davide Vanossi,* Adele Mucci*

* Dipartimento di Scienze Chimiche e Geologiche, Università degli Studi di Modena e Reggio Emilia, Via Campi 103, 41125 Modena; E-mail alfonso.zambon@unimore.it

Thiophene-based copolymers are conjugated materials with a wide range of interesting chemical physical properties.(1) They are widely studied as active layer in organic solar cells, light emitting diodes and field effect transistors, and other optoelectronic devices.(1, 2) The electronic energy levels of these copolymers can be fine-tuned through synthesis (e.g. choosing the backbone units, alternating electron-donor and electron-acceptor units, changing the substituents on the backbone) to optimize the HOMO-LUMO band gap in order to confer better performances to the final device. When compared to polymers, oligomers offer potential advantages, such as a defined molecular structure and molecular weight, easy purification, mass-scale production, and good batch-to-batch reproducibility. Recently, several small molecules (including oligothiophenes) with performance in optoelectronic devices comparable to that of their polymeric analogues were reported.(3, 4, 5) Here we present the synthesis of A-π-D-π-A thiophene-based oligomers (Figure 1); in the design of these materials we incorporated both electron-donor and electron-acceptor groups by having a central dithienosilole, two terminal methyldicyanovinyl acceptor groups and two bithienyl units, functionalised with alkyl or alkylsulfanyl chains, as π-bridges.

The synthesis was achieved by a multi-step route, including the formation of the dithienosilole from 5-(trimethylsilyl) protected 2-bromothiophene by a one-pot halogen-dance – homocoupling sequence followed by cyclization with dichlorodioctylsilane and subsequent Suzuki coupling with the boron derivative of the β-functionalised thiophene. The final C-C bond was formed by Stille coupling.

References:
Organic and biological materials for organic electronics: adding functionality

Alessandra Operamolla

*Dipartimento di Chimica, Università degli Studi di Bari Aldo Moro, via Orabona 4, I-70126 Bari (Italy)*

Organic materials have shown very high potential in technological applications, such as their performance as active layers in OLEDs, (1) plastic solar cells, (2) organic field effect transistors and sensors (3) and so on. The field of organic electronics, continuously in progress, poses new challenges, including the fascinating opportunity to extend the functions of organic materials by integration with biological compounds. This is an extremely attractive perspective, opening access to relevant applications as multi-functional, bio-compatible and sustainable devices.

In this communication, different strategies for the combination of the functions of organic semiconductors with the additional features of biological molecules are presented.

The decoration of conjugated polymers and oligomers with small biomolecules, like L-phenylalanine and D-glucose, enables access to organic semiconductors that show interesting interaction with chiral environment and circularly polarized light. (4)

The bioconjugation of synthetic fluorophores with a photoenzyme, the Reaction Center (RC) from the bacterium *Rh. Sphaeroides*, (5) produces enzymatically active bio-hybrids with enhanced performances. (6) An analogous chemistry is used to anchor the RC photoenzyme and streptavidin (SA) onto evaporated organic pigments thin films. The full functionality of the solid state assembly is demonstrated by photosensitization of the organic films induced by the RC photoenzyme. (7)

As new perspective, the possibility to access environmentally harmless devices drawing fully from natural raw materials represents a frontier of great technological impact. Indeed, novel cellulose nanofibers freestanding thin films, known as "nanopaper", can be part of organic devices as substrates, putting aside some plastic derivatives from the equation “disposable and flexible organic devices = oil derivatives”. Functionalization chemistry on the nanofibers, both in solution and in heterogeneous conditions, can be used to modulate surface properties of nanopaper and its environmental stability. Hydrophobization dramatically improves the water resistance yielding ideal substrates for various applications, including implantable devices. (8)

Molecular Tailoring of Hole-Transporting Materials for High-Performing Perovskite Solar Cells

Roberto Grisorio\textsuperscript{a,b}, Bart Roose\textsuperscript{c}, Silvia Colella\textsuperscript{b,d}, Andrea Listorti\textsuperscript{b,d}, Gian Paolo Suranna\textsuperscript{a,b}, Antonio Abate\textsuperscript{c}

\textsuperscript{a}DICATECh – Politecnico di Bari, Via Orabona 4, 70125 Bari, Italy. \textsuperscript{b}CNR NANOTEC – Istituto di Nanotecnologia, Via Monteroni, 73100 Lecce, Italy. \textsuperscript{c}Adolphe Merkle Institute, Chemin des Verdiers 4, CH-1700 Fribourg, Switzerland. \textsuperscript{d}Dipartimento di Matematica e Fisica - Università del Salento, Via per Arnesano, 73100 Lecce, Italy. Email: roberto.grisorio@poliba.it

Organic-inorganic lead halide perovskites have emerged (1) as one of the most promising research field in photovoltaics, due to their excellent light-harvesting, ranging from the visible to the NIR region, their high extinction coefficients and long electron-hole diffusion lengths (2). In devices, the free photo-generated holes within the perovskite material need to be extracted and transported by suitable hole-transporting materials (HTMs). To date, the highest reported efficiency values (up to 20\%) have been reached by using the expensive Spiro-OMeTAD (3). Aiming at providing convenient alternatives, we have planned and carried out the synthesis of novel phenothiazine-based HTMs (PTZ1 and PTZ2) by binding the suitable donor groups (diarylamine or triarylamine) to a phenothiazine core through straightforward Buchwald-Hartwig and Suzuki-Miyaura cross-couplings, respectively. The higher oxidation potential measured for PTZ2 could be favorable for obtaining high $V_{OC}$ in perovskite solar cells, while the relatively lower oxidation potential of PTZ1 could result in a faster hole transfer between the perovskite layer and the HTM (Figure 1). When employed as HTM in perovskite solar cells, however, a dramatic effect exerted by the presence of phenylene spacers was observed in the performances of the relevant devices. The power conversion efficiencies measured under AM 1.5 sun was boosted from 2.1\% (PTZ1) to an outstanding 17.6\% (PTZ2), a value closely rivaling the one obtained with the state-of-the-art Spiro-OMeTAD (17.7\%). By combining spectroelectrochemistry and DFT investigation, this dramatic difference in photovoltaic performances exhibited by the two phenothiazine-based derivatives could be attributed to the modulation of electron density distribution, controlling the molecules stability during the charge transfer dynamics at the perovskite/HTM interface. These results can stimulate research on phenothiazine-based materials as readily available and cost-effective promising alternatives to Spiro-OMeTAD in perovskite solar cells.

![Figure 1](https://example.com/figure1.png)

**Figure 1.** Energy level diagram of the perovskite solar cell components and molecular structures of PTZ1 and PTZ2.

KuQuinones as photocatalysts in Light-driven water splitting

Pierluca Galloni\textsuperscript{a}, Federica Sabuzi\textsuperscript{a}, Barbara Floris\textsuperscript{a}, Francesca Valentini\textsuperscript{a}, Laura Micheli\textsuperscript{a}, Andrea Sartorel\textsuperscript{b}, Emanuela Gatto\textsuperscript{a}, Giuseppe Palleschi\textsuperscript{a}, Valeria Conte\textsuperscript{a}

\textsuperscript{a} Dipartimento di Scienze e Tecnologie Chimiche, Università degli Studi di Roma Tor Vergata Via della ricerca scientifica, 00133, Roma, Italy. \textsuperscript{b} Dipartimento di Scienze Chimiche Università degli Studi di Padova, via Marzolo 1, 35131, Padova, Italy
galloni@scienze.uniroma2.it

Water splitting is a strongly endoergonic process, which requires the participation of four electrons and four protons and the formation of a new O–O bond. Consequently, it is characterized by important kinetic barriers, and the use of a catalyst is crucial to activate the splitting. Photosystem II constitutes in nature a successful model for water oxidation (1) indeed, the use of sunlight to perform water splitting appears to be a valid approach.

Few years ago, we developed a one-pot procedure for the synthesis of novel pentacyclic quinoid compounds, called KuQuinones (KuQs) (2), starting from easily available and cheap precursors. These compounds are able to harvest light in the visible region of the spectrum due to their pentacyclic and conjugated structure. Thanks to these interesting properties, we studied their ability to act as sensitive material in photoelectrochemical devices, using KuQs-functionalized ITO as working electrode and triethanolamine (TEOA) as sacrificial electron donor in solution (3). These features suggested the potential application of such novel compounds both as dyes and as electrons acceptor moiety also in the water-oxidation process. In this regard, a stable and high anodic photocurrent signal was detected in basic solution, according to the mechanism proposed in Figure 1. In this contribution, the general synthetic procedure of KuQuinones and preliminary results for the photoelectrochemical water oxidation will be presented.

![Figure 1. Structure of KuQs (left) and proposed mechanism for the photoelectrochemical cell (right).](image)

A quick and facile synthesis of stable, water-soluble CdSe/ZnS quantum dots.

Salerno G.\textsuperscript{a,b}, Consumi M.\textsuperscript{c}, Magnani A.\textsuperscript{c}, Nativi C.\textsuperscript{a}, Richichi B.\textsuperscript{a}

\textsuperscript{a} University of Florence, Department of Chemistry “Ugo Schiff”, via della Lastruccia, 13, 50019, Sesto Fiorentino (Fi), Italy.\textsuperscript{b}Institute of Atmospheric Pollution Research of the National Research Council of Italy (CNR-IIA), Via Madonna del Piano, 10 (50019) Sesto Fiorentino (Fi) Italy. \textsuperscript{c}University of Siena, Department of biotechnology, chemistry and pharmacy; via Aldo Moro, 2, 53100, Siena, Italy.

Core/shell Quantum Dots (QDs) are fascinating luminescent semiconductor nanomaterials characterized by a fine-tunable diameter size (ranging from 2 to 10 nm) (1). They display a wide range of unique and excellent electro-optical properties, such as broad absorption spectrum coupled with narrow emission band and a size-tunable photoluminescence in the visible spectral range (2). The possibility to functionalize their surface with organic molecules, allows to modulate their colloidal stability and to move their solubility from organic solvents to water environment. Water-soluble QDs can be achieved by grafting a corona of hydrophilic molecules on their surface. Ligand exchange, based on thiols containing small derivatives, is one of the most investigated approach to perform the phase-transfer step. In this regard, dihydrolipoic acid (DHLA) is the most investigating ligand to obtain water-soluble core-shell QDs, indeed, since it is bidentate, it provides quite stable interactions with QDs surfaces (3). Some examples of DHLA-based ligands have been reported to obtain water-soluble QDs, however, most of them suffer of short shelf lives: after few hours or days aggregation and precipitation phenomena take place by limiting some applications. In this framework, here is reported the efficient and reliable synthesis of hydrophilic thin coating grafted core/shell CdSe/ZnS QDs 1 (Figure 1) where the carboxylic group of a DHLA moiety was conjugated to the primary ammine group of an ethylenediamine-N,N-diacetic acid residue, named EDADA or UEDDA (4).

![Figure 1. Core/shell CdSe/ZnS QDs 1](image)

In this presentation, the long term colloidal stability of water soluble QDs 1 in different pH buffer solutions, as function of the ionic strength of the media will be discussed. Then, by manipulating the later dicarboxylic groups of the EDADA-DHLA ligand, the surface of QDs 1 can be modified, making them useful tools for diverse applications. Finally, the preparation of hybrid polymer-QDs composites is discussed.

References:
PreS1 Functionalized Gold Nanostructures for Liver Cancer Cells Targeting and Surface-Enhanced Raman Resonance Scattering Imaging

F. Biscaglia, S. Quarta, G. Villano, Cristian Turato, Alessandra Biasiolo, P. Pontisso, M. Meneghetti, and M. Gobbo

University of Padova, Dept. of Chemical Sciences, Padova, Italy; University of Padova, Dept. of Medicine DIMED, Padova, Italy; University of Padova, Dept. of Oncological and Gastroenterological Surgical Sciences DISCOG, Padova, Italy; E-mail of the presenting author: francesca.biscaglia@phd.unipd.it

The targeted delivery of biocompatible nanoparticles to malignant tumors has become a powerful tool in cancer nanomedicine for diagnostics and therapy. In particular, gold nanoparticles (AuNP) are one of the most employed nanomaterials because, besides displaying useful optical properties and a facile surface chemistry, are biocompatible, which is an essential requirement for biological application. AuNP can passively target tumors by the enhanced permeability and retention effect, but can also exhibit a high active targeting affinity and specificity when conjugated with biomolecular targeting agents, such as peptides, proteins or small molecules (1).

Recently the hepatitis B virus-preS1-(21-47) sequence has been identified as a specific ligand of Serpin B3, a member of the ovalbumin- family of serine protease inhibitor, frequently overexpressed in the majority of liver cancers (2). In this context, the aim of the present study was to synthesize preS1-functionalized gold nanostructures for targeting and detection of liver tumor cells. Nanostructures were prepared from naked AuNP obtained by Laser Ablation in Solution (3) and encoded with a Raman reporter, as shown in Figure, to achieve very intense Surface-Enhanced Raman Scattering (SERRS) signals (4,5). Peptides were synthesized on solid phase and, after deprotection and cleavage from the solid support, they were conjugated to nanoparticles, exploiting the affinity of gold for the thiol group of the ligand: a cysteine residue or a thiolated PEG chain added to the original peptide sequence. By synthesizing a few peptide analogues we were able to investigate the influence of different aspects important for Serpin B3 recognition, such as the peptide exposure and orientation on the nanostructures surface. Targeting of the nanostructures to hepatocellular carcinoma was checked on cells expressing or not Serpin B3, recording the SERRS signals cell by cell. Nanoaggregates covered with PEGs or with an anti-Serpin B3 antibody were used as negative and positive control, respectively. The results of tests in vitro and of a preliminary in vivo experiment will be presented.

Design and Synthesis of polyfunctional PNAs - A Biomolecular Engineering approach

Andrea Rozzi\textsuperscript{a}, Saša Korom,\textsuperscript{b} Alex Manicardi\textsuperscript{a}, Massimiliano Donato Verona\textsuperscript{a}, Vincenzo Verdolino\textsuperscript{c}, Roberto Corradini\textsuperscript{a,b}

\textsuperscript{a} Università degli Studi di Parma, Dipartimento di Scienze Chimiche, della Vita e della Sostenibilità Ambientale, Viale delle Scienze 17A Parma; \textsuperscript{b} National Institute for Biostructures and Biosystems (INBB)-Viale delle Medaglie d’Oro, 305, 00136 Roma, Italy. \textsuperscript{c} Facoltà di Informatica, Instituto di Scienze Computazionali, Università della Svizzera Italiana, 6900 Lugano, Switzerland; roberto.corradini@unipr.it

Peptide nucleic acids (PNAs) are polyamide analogues of nucleic acids, very effective in terms of affinity and selectivity in DNA/RNA recognition, and have been used for diagnostics, as well as for drug development.\textsuperscript{1,2} Appropriate design of modified PNAs allows to improve their properties and to increase their cellular uptake.\textsuperscript{3} This communication will describe our recent work, aimed to further improve the recognition properties of these compounds, aided by Molecular Dynamics and enhanced sampling Metadynamics (Figure 1).\textsuperscript{4} A series of synthetic modular strategies enabling a rational designing of new PNA structures, and in particular poly-functional PNAs will be described.\textsuperscript{3,6} The synthesis of PNA able to undergo programmable group shift upon interaction with DNA or RNA, and rational interpretation of experimental data based on molecular models will be presented (Figure 1a); the application of this approach in understanding the effect of nucleobase modification will also be discussed (Figure 1b). This work was carried out in the frame of the H2020 ULTRAPLACAD project (grant agreement No 633937) aimed to improve the PNA performances for early diagnosis of colorectal cancer.

![Figure 1](image-url)

Figure 1. Present approaches for the interpretation and design of PNA properties for a) poly-functional PNA (modified base and backbone); b) PNA containing modified nucleobases.

A Glycomimetic CHIP for microarray Screening of C-type Lectin Receptors

Laura Medve\textsuperscript{1}, Sonia Serna\textsuperscript{2}, Niels Reichardt\textsuperscript{2}, Silvia Achilli\textsuperscript{3}, Corinne Vivès\textsuperscript{3}, Franck Fieschi\textsuperscript{3}, Anna Bernardi\textsuperscript{1}

\textsuperscript{1} Dipartimento di Chimica, Università degli Studi di Milano, Via Golgi 19, 20133 Milano, Italy. \\
\textsuperscript{2}Glycotechnology Lab., CIC biomaGUNE, Paseo Miramón 182, 20014, Donostia/San Sebastián, Spain. \\
\textsuperscript{3}Univ. Grenoble Alpes, CEA, CNRS, Institut de Biologie Structurale, F-38000 Grenoble, France \\
email: laura.medve@unimi.it

Cell surfaces are covered by a large number of glycans (glycocalyx) which are docking sites for other cells, molecules and pathogens. Beside the sugars, these adhesion processes also involve carbohydrate-specific proteins – known as lectins, and the interactions between glycans and lectins are crucial for biological recognition and signal-initiation.

C-type lectin receptors (CLRs) were named after their Ca\textsuperscript{2+} requirement for binding carbohydrates and they play important roles in the immune response. CLR targeting can be an efficient strategy to steer the immune response toward a therapeutically desired effect. The Immunoshape European Training Network aims to develop potential lead structures for highly selective glycan-based multivalent immunotherapeutics for the treatment of cancer, autoimmune diseases and allergy.

Previous studies in our group (1) showed that mannobioside mimics (1) are capable of efficiently targeting CLRs. Their inhibitory activity and selectivity depend on the nature of the two amide moieties attached to the cyclohexane ring. With the help of chemoinformatic tools, the mannose-based library was expanded, with the aim of identifying new high-affinity ligands for different CLRs. Additionally, β-fucosylated glycomimetics (2) were synthesized to exploit the mixed fucose-mannose selectivity of some CLRs.

The glycomimetics were printed on NHS-functionalized chips, with the help of a double-functionality linker and the resulting microarrays were screened at CIC biomaGUNE against human CLRs available through the Immunoshape consortium. The preparation of the microarrays was optimized and the covalently immobilized ligands were incubated with fluorescently labeled tetravalent lectins engineered at IBS. Quantification of the fluorescent signals allowed the estimation of the affinity of glycomimetic ligands towards the lectins and selected high-affinity binders were further studied by surface plasmon resonance (SPR) technique.

Gold(I)-catalyzed rearrangement of heterocycles derived 1,3-enynes

Cristina Prandi, Stefano Nejrotti

Università degli Studi di Torino, Dipartimento di Chimica, Via P. Giuria 7, Torino, Italy.

We have previously demonstrated that the gold(I)-catalyzed reaction of N-Boc-protected 6-alkynyl-3,4-dihydro-2H-pyridines affords synthetically useful vinylogous amides (β-enaminones). The reaction has been studied in detail in order to optimize the reaction conditions, enlarge the scope and have insights into the mechanism and the structural features that selectively favor the 6-endo dig oxyauration of the triple bond.\(^1,2\) When the substrates are N-tosyl-protected 6-alkynyl-3,4-dihydro-2H-pyridines the intramolecular cyclization is prevented and an intermolecular reaction with external oxidants can be featured. Among various oxidants tested the most promising are pyridine-oxides derivatives. The oxidation of the triple bond occurs with high region and stereoselectivity, thus giving access to conjugated dienones.\(^3\) When the substrate enyne is suitably functionalized, an intramolecular trapping of the gold activated triple bond can be featured, paving the way to fused heterocycle systems.

![Reaction mechanism diagram]

References
Snapshot of Ruthenium–Carbene–Resorc[4]arene Complex in an Olefin Metathesis Reaction

F. Ghirga\textsuperscript{a}, C. Ingallina\textsuperscript{b}, F. Aiello\textsuperscript{c}, F. Balzano\textsuperscript{c}, I. D’Acquarica\textsuperscript{b}, B. Botta\textsuperscript{b}, G. Uccello-Barretta\textsuperscript{c}, D. Quaglio\textsuperscript{b}

\textsuperscript{a} Center of Life Nano Science, Istituto Italiano di Tecnologia, viale Regina Elena 295, 00185 Rome (Italy). \textsuperscript{b} Dipartimento di Chimica e Tecnologie del Farmaco, Università “La Sapienza”, P.le A. Moro 5, 00185 Rome (Italy). \textsuperscript{c} Dipartimento di Chimica e Chimica Industriale, Università di Pisa, Via G. Moruzzi, 13, 56124 Pisa, (Italy)

Previously, we envisaged the synthesis of resorc[4]arenes featuring eleven carbon side chains ending with a vinylidene group, in order to incorporate via metathesis reaction the macrocycles into polymeric architectures with intriguing mechanical properties.\textsuperscript{1} Undecenyl resorc[4]arene \textit{1a}, which featured the simplest pattern of substituent, was submitted to olefin metathesis using the second generation Grubbs complex as the catalyst. Depending on the reaction conditions, different products were isolated: a bicyclic alkene \textit{2a}, a linear dimer \textit{3a}, and a cross-linked homopolymer \textit{P1a}.\textsuperscript{2} With regard to the mechanistic pathway, we were able to detect for the first time the formation of a ruthenium-carbene-resorc[4]arene complex during the metathesis reaction of resorc[4]arene olefin \textit{2a} with the first generation Grubbs catalyst in CDCl\textsubscript{3}, by using high-resolution (600 MHz) \textit{1}H, \textit{31}P NMR and DOSY spectroscopy.\textsuperscript{3} We developed an NMR analytical protocol, which proved capable of yielding both qualitative and quantitative information. In the first case, we were able to identify the complex \textit{3a[Ru]} as a key intermediate in the ROM-CM sequence of reactions, giving us a definitive proof of the previously hypothesized mechanism. As a further feedback of the pathway, we performed a quantitative analysis using benzene in the place of CDCl\textsubscript{3}, due to the poor stability of the catalyst in such a solvent. The reaction allowed the isolation of decomposition products of the \textit{2a[Ru]} complex, which, due to the presence of still reactive alkene functions, proved to behave as propagating alkylidene species leading to further decomposition products.

\begin{figure}
\centering
\includegraphics[width=0.5\textwidth]{fig.png}
\end{figure}

References:

Mauro Sassi, Sara Mattiello, Myles Rooney, Alessandro Sanzone, Paolo Brazzo and Luca Beverina

Department of Materials Science, University of Milano, Via R. Cozzi, 55, Milano, Italy. I-20125; mauro.sassi@mater.unimib.it

Micellar coupling enables carrying out popular and versatile reactions like Suzuki-Miyaura, Sonogashira, Stille, Buchwald-Hartwig, aromatic nucleophilic substitution and many more in water environment and very frequently at room temperature, unregarding to the water solubility of reagents and products.(1) Literature reports an increasing number of “designer” surfactant specifically engineered to perform such kind of reaction.(2) Alongside, authors also explored the potentials of well established industrial surfacts like Triton X-100 and the Tween/Span series with comparable results. So far micellar coupling enabled a dramatic reduction of the overall E factor in synthetic pathways relevant for the synthesis of natural products and drugs. It is only very recently that the field of organic conjugated materials began to take into account concepts like sustainability, atom economy and E-factor. Motivated by our experience with both the encapsulation of organic fluorophores in micelles (3) and by our established experience in the field of organic semiconductors, we here present very efficient protocols for Suzuki-Miyaura, Stille and Buchwald Hartwig amination reactions representing the key steps for the preparation of molecular and polymeric semiconductors. Notably, all protocols we developed are oxygen insensitive, require moderate heating or no heating at all and feature strongly reduced reaction times with respect to the standard organic solvents enforced protocols. Reactions can be easily scaled up from hundreds of milligrams to tens of grams without relevant changes in conditions. Alongside with the demonstration of the reactions scope and efficiency, we will also discuss the very peculiar aspects ruling the kinetics and in some cases the chemo selectivity of the processes we developed.

Figure 1. Schematic representation of an oxygen insensitive, water based micellar coupling. Examples of reactions performed (red for the fragment originally carrying the halogen and black for the boronic derivative)

Titanium tetrachloride (TiCl₄) is a Lewis acid largely used in organic synthesis that has a strong affinity for oxygen-containing organic compounds. In our research activity, we had the opportunity to observe how TiCl₄ is able to coordinate to the oxygen atom by increasing the reactivity of carbonyl-containing compounds towards nucleophiles or forming a good leaving group.

TiCl₄ was used to achieve the direct one-pot conversion of aldehydes and hydroxylamine into nitriles and for condensing carboxylic acids with amines to obtain the corresponding amides. TiCl₄ can also be used in combination with a tertiary amine (NR₃), thus forming the TiCl₄/NR₃ reagent system widely used for the preparation of titanium enolates for applications in aldol and related reactions in organic synthesis.

The TiCl₄/NR₃ reagent system can easily generate an iminium ion that can evolve forming an organotitanium compound useful in the formation of carbon-carbon bonds. The reaction of variously substituted aromatic acyl chlorides in methylene chloride with triethylamine and TiCl₄, by using two different experimental procedures (Method A and Method B), afforded alternatively the corresponding amides or β-enaminones as unique or major products. The reaction occurs through the formation of the TiCl₄/NR₃ reagent system that, depending on the adopted experimental procedure, evolves differently generating two alternative reaction paths that provide the amide or β-enaminone, both important building blocks in organic synthesis. The two developed protocols were also applied successfully to a series of tertiary amines. The reactions, modulated by the presence of TiCl₄, provided the corresponding amides or β-enaminones with satisfactory yields.

Which reaction step controls regio selectivity in CuCl$_2$-catalyzed cyclization of alkinyl-substituted ureas and carbamates?

**Massimo Mella**$^a$, M. Vincenzo La Rocca$^a$, Egle M. Beccalli$^b$, Silvia Gazzola$^a$, Gianluigi Broggini$^a$

$^a$ Dipartimento di Scienza e Alta Tecnologia, Università dell’Insubria, via Valleggio 11, 22100 Como, Italy; $^b$ DISFARM, Sezione di Chimica Generale e Organica “A. Marchesini” Università degli Studi di Milano, via Venezian 21, 20133 Milano, Italy; massimo.mella@uninsubria.it

One among the most powerful methods for the synthesis of biologically important heterocycles from simple unsaturated precursors is transition metal-catalyzed intramolecular cyclization (1). In this context, copper catalysts are very attractive thanks to their low cost, tolerance toward many reactive functional groups and convenient reaction conditions. Recently, three of the Authors (EMB, SG, and GB) developed a simple and efficient method of alkoxyhalogenation of alkynyl ureas involving Cu(II) salts (2) as a catalyst in the presence of N-halosuccinimides. Spurred by such results, we wished to extend the methodology toward the synthesis of haloalkylidene-substituted heterocycles with carbamates as precursors: at variance with our expectation, however, the cycles tend to close on the nitrogen, meaning that electronic effects control the reaction regiochemistry.

With the aim of elucidating the reaction mechanism and the motivations behind the stereo chemical control and change in regio chemistry, Gibbs energy cyclization profiles are explored via DFT calculations. Four possible pathways arising from possible complexes between phenyl urea and CuCl$_2$ are followed leading to non trivial results; while the formation of urea dimers inhibits catalysis if CuCl$_2$ coordinates to the carbonyl oxygen, imposes coordination to the alkyne and controls the stereo selectivity, the relative energetic behavior of the two remaining paths rationalizes the regio selectivity. A parallel investigation is also carried out for phenyl and tosyl carbamate: it emerges that the tosyl group markedly influences the total energetics and that a detailed consideration of the possible acid-base equilibria is required to rationalize the region and stereo selectivity of the products.

![Figure 1](image.png)

Figure 1: Proposed mechanism of the Cu(II)-catalyzed reaction on urea. The mechanism consists of: preequilibrium, cyclization, cloruration from NCS, deprotonation.

Divergent Syntheses of (E)-3-Isobenzofuran-1-(3H)-one and (1H)-Isochromen-1-one Derivatives by Palladium-Catalyzed Carbonylation of 2-Alkynylbenzoic Acids

Raffaella Mancuso and Bartolo Gabriele

Laboratory of Industrial and Synthetic Organic Chemistry (LISOC), Department of Chemistry and Chemical Technology, University of Calabria, Via Pietro Bucci, 12/C, 87036 Arcavacata di Rende (CS), Italy; raffaella.mancuso@unical.it

PdI₂-catalyzed oxidative carbonylation of acetylenic substrates bearing a suitably placed nucleophilic group is a powerful methodology for the direct synthesis of carbonylated heterocycles¹. We report here a novel method for the synthesis of functionalized (E)-isobenzofuranone 2 and isochromenone 3 derivatives based on PdI₂-catalyzed oxidative heterocyclization-carbonylation of 2-alkynylbenzoic acids 1 (Scheme 1).

Reactions were carried out a 100°C and under 20 atm of 4:1 mixture of CO-air, in the presence of catalytic amount of PdI₂ (1 mol %) in conjunction with KI (10 mol %). We have found that the regiochemical output of the process may be modulated by the nature of substituents on the triple bond and by the nature of alcoholic solvents. In particular, a TMS group on the triple bond tended to promote the 5-exo cyclization mode, with sole formation of desilylated (E)-3-isobenzofuran-1-(3H)-ones 2, while a tert-butyl group, with EtOH or i-PrOH as the solvent, favored the 6-endo cyclization mode, with exclusive formation of (1H)-isochromen-1-ones 3. Products were obtained in good isolated yields (60-95%), and the structure of some representative products were confirmed by XRD analysis. The heterocyclic derivatives synthesized in this work belong to particularly important classes of heterocycles, known to possess a wide range of biological activities.

Eliciting specific humoral and cellular immune response by self-adjuvanting gold nanoparticles carrying tumor-associated MUC1 glycopeptides

Roberto Fiammengo\textsuperscript{a}, Hui Cai\textsuperscript{b}, Federica Degliangeli\textsuperscript{a}, Jia Liu\textsuperscript{c}, Christian Pett\textsuperscript{b}, Jing Hu\textsuperscript{c}, Horst Kunz\textsuperscript{d}, Ulrika Westerlind\textsuperscript{b}, and Menji Lu\textsuperscript{c}

\textsuperscript{a} Center for Biomolecular Nanotechnologies@UniLe - Istituto Italiano di Tecnologia (IIT), ViaBarsanti, 73010 Arnesano (LE) Italy; \textsuperscript{b} ISAS - Leibniz Institute for Analytical Sciences, Otto-Hahn-Str. 6b, 44227 Dortmund, Germany; \textsuperscript{c} Institute for Virology, University Hospital of Essen, Robert-Koch-Haus, Virchowstr. 179, 45147 Essen, Germany; \textsuperscript{d} Institute of Organic Chemistry, University of Mainz, Duesbergweg 10-14, 55128 Mainz, Germany.

roberto.fiammengo@iit.it

The extracellular, variable number tandem repeat (VNTR) domain of the MUC-1 (MUC1) glycoprotein is an attractive target for the development of therapeutic cancer vaccines.\(^1, 2\) Tumor-associated MUC1 (TA-MUC1) is found markedly underglycosylated compared to MUC1 on healthy cells, which results in the display of new peptide and carbohydrate epitopes. Furthermore, TA-MUC1 is found overexpressed on cancer cells.\(^3, 4\) Although a number of vaccine design strategies have been pursued, successful anticancer vaccines are yet to be obtained.\(^5\)

We are developing multivalent, TA-MUC1 vaccine candidates based on PEGylated gold nanoparticles (AuNPs)\(^6\) as the antigen carrier and we have shown that they can induce specific antibodies directed against TA-MUC1.\(^7\)

In this contribution we describe the preparation and characterization of novel AuNP-based vaccine candidates. We show that they elicit not only a robust humoral immune response but also a cellular immune response in wild-type mice without the need of any additional adjuvant. We also show that the antisera of vaccinated animals strongly react with several types of human cancer cells demonstrating recognition of TA-MUC1 antigens in the context of human cells. Antisera binding profile demonstrates that antigen delivery via AuNP-based formulations does not affect antigen processing by the immune system. Altogether these results show the great potential of TA-MUC1 vaccine candidates based on PEGylated AuNPs, especially considering their good immunogenicity and self-adjuvanting properties.
Natural compounds in cancer prevention: effect of coffee extracts and their main polyphenolic component 5-CQA on oncogenic Ras proteins

Alessandro Palmioli\textsuperscript{a}, Carlotta Ciaramelli\textsuperscript{a}, Michela Spinelli\textsuperscript{a}, Gaia De Sanctis\textsuperscript{a}, Renata Tisi\textsuperscript{a}, Elena Sacco\textsuperscript{a}, Cristina Airoldi\textsuperscript{a}

\textsuperscript{a} Dipartimento di Biotecnologie e Bioscienze, Università degli studi di Milano-Bicocca, Piazza della Scienza 2, 20126 Milano, Italy. alessandro.palmioli@unimib.it

Recent epidemiological studies demonstrate that consumption of healthy foods, especially rich in polyphenols content, might reduce the incidence of cancer and degenerative diseases\cite{1}.

In particular, chlorogenic acids (CGAs), esters formed between hydroxycinnamic acids (mainly caffeic and ferulic) and quinic acid occur ubiquitously in food, being 5-caffeoylquinic acid (5-CQA) the most abundant polyphenols in the human diet\cite{2}.

A number of beneficial biological effects, including anti-inflammatory activity, anti-carcinogenic activity and protection against neurodegenerative diseases have been described for CGAs\cite{3}.

However, the molecular mechanisms at the basis of these biological activities have not yet been investigated in depth.

Here we reports ours contribute to the elucidation of the molecular mechanism through which 5-CQA carry out its potential as chemoprotective supplements against carcinogenesis. In particular, we evaluated: 1) the molecular interaction between 5-CQA and the proto-oncogenic human protein h-Ras by mean of molecular docking and STD-NMR spectroscopy; 2) the effect of 5-CQA binding on Ras ability to switch-on the proliferative signalling; 3) the biological effects of 5-CQA in \textit{ex vivo} assay using MDA-MB-231 (Breast cancer, Ras\textsuperscript{G13D}) and of SW48 (colon rectal adenocarcinoma) cell lines; 4) the biological effects of enriched CGAs natural extracts obtained from green and roasted coffee beans.

References


Filippo Doria, Matteo Nadai, Matteo Scalabrin, Valentina Pirota, Vincenzo Grande, Greta Bergamaschi, Valeria Amendola, Sara N. Richter, Mauro Freccero.

Department of Chemistry, University of Pavia, V.leTaramelli 10, 27100 Pavia, Italy. Department of Molecular Medicine, University of Padua, via Gabelli 63, 35121 Padua, Italy.
e-mail: filippo.doria@unipv.it

It has been shown that G-quadruplex structures (G4s) have regulatory functions for telomere extension and maintenance, playing an important role in cancer biology. In addition, G4s involved in the life cycle of different viruses have been reported. Consequently, G4 selective ligands represent potential anticancer and antiviral agents. To date, more than seven thousands stabilizing G4 ligands have been published, but the fairly selective cleavage of G4s has only been achieved once, on intramolecular telomeric G4s. Nowadays, no effective and selective G4s-scissoring agents have been reported. In this frame, we synthetized and characterized a tri-substituted naphthalene diimide (NDI) embedding a diethylenetriamine (DETA) substituent (named Cu-DETA-NDI), which selectively coordinates Cu(II) at physiological pH with a very high apparent binding constant (logβ = 17.3).

Tri-substituted naphthalene diimides (NDIs) are known as potent G4 binding small molecules, with high affinity and reversibility, while the copper complexes are well known as catalytic metallodrug, also targeting G4 nucleic acids. The selective oxidation is a ROS mediated process catalysed by Cu(II) under oxidative stress. In the present study, we have investigated ligand stability using ascorbate (1 equiv.) and H2O2 (4 eq.) at neutral pH, confirming that Cu-DETA-NDI binding with G4 is fundamental to maintain the ligand undamaged. Thanks to his copper complex moiety directly embedded on the NDI core, it delivers the copper coordination sphere in close proximity to G4s, opening the opportunity to achieve an effective and site-selective cleavage.

Acknowledgment: This work was supported by ERC Consolidator (grant No. 615879)

References:
Amino- and guanidinoglycoside based vectors for cell transfection

Chiara Pennetta¹, Alessandro Volonterio¹

Department of Chemistry, Materials and Chemical Engineering ‘Giulio Natta’, Politecnico di Milano, Milano, Italy.
e-mail: chiara.pennetta@polimi.it

The development of efficient alternatives to viral vectors is a hot subject for the uptake of high molecular weight biomolecules like peptides, proteins and genes that can’t spontaneously cross the cell membrane. Aminoglycosides, such as neomycin (Neo, structure A in Figure 1) are a class of naturally occurring antibiotics while guanidinoglycosides, such as guanidinoneomycin (GNeo, structure B in Figure 1) are aminoglycosides where all the amino groups are converted into guanidino groups. The group of Prof. Tor has shown that guanidinoglycosides are very efficient molecular transporters facilitating the intracellular delivery of high molecular weight cargos at nanomolar concentrations by binding selectively cell surface heparan sulfate proteoglycans¹.

Recently, our group has been involved in the synthesis of aminoglycoside and guanidinoglycoside-based vectors for an efficient gene and drug delivery²,³. Since then different carriers have been developed including cationic lipids systems (using calix[4]arenes and cyanuric chloride as scaffolds) and colloids such as PEG-PEI nanogels decorated with Gneo. The synthetic part along with biological tests on cell viability and transfection efficiency will be reported.

Fig 2 A) Neomycin (Neo) and B) guanidinoneomycin (GNeo)

References:

1) Sarrazin, S.; Wilson, B.; Sly, W.S.; Tor, Y.; Esko J.D. Molecular Therapy, 2010, 18, 1268
Discovery of a new class of GPBAR1 modulators

Carmen Festa, Simona De Marino, Maria Valeria D’Auria, Angela Zampella, Stefano Fiorucci, Vittorio Limongelli

aDepartment of Pharmacy, University of Naples “Federico II”, Via D. Montesano 49, I-80131 Naples, Italy; bDepartment of Surgery and Biomedical Sciences, Nuova Facoltà di Medicina, P.zza L. Severi, I-06132 Perugia, Italy; cFaculty of Informatics, Università della Svizzera Italiana, Institute of Computational Science, via G. Buffi 13, CH-6900 Lugano, Switzerland; carmen.festa@unina.it

Since the discovery of the G-protein-coupled bile acid receptor GPBAR1 (also known as TGR5), there has been an increased interest to pharmacologically modulate this target involved in lipids and glucose metabolism disorders such as nonalcoholic steatohepatitis, hypercholesterolaemia, hypertriglyceridaemia, and type 2 diabetes mellitus (1,2). Most of our previous research programs were focused to explore the chemical space of the bile acids, the endogenous GPBAR1 ligands (3-7). However, the specificity of bile acid derivatives is not restricted to this receptor and their clinical use can undergo some limitations exerting a variety of pathophysiological and pharmacological activities (8). Thus, recently, our investigations have been shifted towards the development of GPBAR1 non-bile acid modulators, with the final aim of identifying privileged chemical scaffolds able to exert a fine-tuning modulation of this receptor. In this context, using a rational structure-based design and a multidisciplinary approach, we have developed a library of novel active GPBAR1 ligands, that might provide new opportunities in the treatment of several metabolic disorders.

New promising vectors for gene delivery by a step-wise functionalization of a polyester-based non toxic dendrimer with $N$, $N$-dimethylglycine, $N$-methylglycine, lysine and arginine

Silvana Alfei$^a$; Gaby Brice Taptue$^a$

$^a$Dipartimento di Farmacia, Università di Genova, Viale Cembrano 4, I-16147, Genova, Italia
e-mail: alfei@difar.unige.it

Polycationic dendrimers are able to electrostatically bind genetic material forming nanosized complexes (polyplexes). They result very appealing for applications as non-viral vectors to bring DNA or RNA within genetically defective cells for treating or solving several diseases including cancer. Commonly used cationic polymers ($b$PEI) or dendrimers (PAMAM), thanks to a good buffer capacity due to the several weakly basic amines in their structure, once in the cell, induce an osmotic swelling of endosomes that contain the polyplexes leading to content release (1). For this reason $b$PEI and PAMAM are endowed with high transfection efficiencies (2) but, if not chemically modified do not find real applications in gene therapy because of their cytotoxicity. It is also known that dendrimers containing arginine improve siRNA cellular uptake (3) and are equipped with higher efficiency of transfection and reduced toxicity (4, 5). In respect of this background in this communication we report the setting up of versatile protocols to introduce on the hydrolysable polyester-based fourth generation dendrimer (1) previously prepared, a mixture of $N$, $N$-dimethyl glycine, $N$-methylglycine, lysine, and arginine. The synergic presence of nitrogen atoms with different pKa and the arginine moiety should have promoted the cellular up-take and should have contributed to an optimal buffering capacity enhancing the endosomal escape and improving transfection activity.

The obtained products in the hydrochloride forms were subjected to volumetric titration to determine experimental molecular weight and to NMR analysis to confirm the structures. Potentiometric titration to calculate the buffer capacity ($\beta$) and then the average buffer capacity and the NMR characterization of all the intermediates were also performed.

New polymethine dyes for photodynamic therapy

Nadia Barberoa, Sonja Visentinb, Claudia Baroloa, Roberto Buscainoa, Guido Viscardia

a University of Torino, Department of Chemistry and NIS Interdepartmental Centre, Via P. Giuria 7, 10125 Torino, Italy; b University of Torino, Department of Molecular Biotechnology and Health Sciences, via Quarello 15A, 10135 Torino, Italy.

Photodynamic therapy (PDT) (1) is an emerging non-invasive technique for the treatment of cancer. It involves the systemic or topical administration of a photosensitizer (PS) that, after its excitation with light at a specific wavelength, is able to produce reactive oxygen species (ROS), causing damage to targeted cancer cells. An ideal PS should fulfil specific, clinically relevant requirements: i) sharp, intense absorption in the biological tissues’ transparency window (600-900 nm), ii) good solubility in the biological environment, iii) low dark toxicity but strong photo-cytotoxicity and iv) a high ROS sensitization quantum yield. Moreover, an ideal PS should possess a high specificity for cancer tissues and be easily and rapidly removed from the body post-treatment.

Even if some important developments have been achieved and some porphyrin-based PSs are already commercially available and clinically used (2), some problems still exist. Haematoporphyrin derivative-mediated PDT has several clinical disadvantages, including prolonged skin photosensitivity (4 weeks), relatively low quantum yield of singlet oxygen, and a limited depth of associated tissue damage of 2-5 mm. Consequently, there has been extensive research into the design of improved alternative PSs aimed at overcoming these drawbacks. Polymethine dyes (3) deserve to be counted among the innovative potential PS classes for PDT for their strong absorption in the tissue transparency window (600-800 nm).

In this work we designed and synthesised a new series of near infra-red (NIR) absorbing polymethine dyes with different substitution groups in order to investigate how the structure may influence the capacity of these molecules to produce \( \text{^1} \text{O}_2 \). The oxygen-generation ability of the new dyes was accessed in vitro by the 1,3-diphenylbenzofuran (DPBF) quenching method (4), envisioning their potential use as sensitisers for PDT. On the most promising PSs, ROS generation, cytotoxicity, cell death and DNA damage analyses were performed after the photodynamic treatment. Here we present the results obtained along with a structure-activity relationship discussion of these new potential photosensitizers for PDT. In particular, two of these squaraine dyes showed very interesting PDT performances as well as co-localization in mitochondria (5).


Paola Manini, a Carmela Tania Prontera, a Valeria Criscuolo, a Alessandro Pezzella, a Orlando Crescenzi, a Michele Pavone, a Marco d’Ischia, a Maria Grazia Maglione, b Paolo Tassini, b Carla Minarini b

*Department of Chemical Sciences, University of Naples "Federico II", via Cintia 4, I-80126 Napoli, IT; Laboratory of Nanomaterials and Devices, ENEA C. R. Portici, Piazzale E. Fermi, Portici (NA), IT; paola.manini@unina.it

The growing expansion and impact of OLED devices in our everyday life have stimulated the synthesis of a wide plethora of electroluminescent materials with the aim of improving the efficiency and the life-time of the device as well as of selectively tuning the wavelength of the emitting light.

In the frame of our research activity aimed at exploring the role of melanins, the dark pigments found in mammalian skin, hair and eyes, as soft organic semiconductors in bio-electronic devices (1), we have undertaken a new challenge: to obtain innovative electroluminescent compounds from black melanin pigments.

The strategy of this research activity has been based on the use of melanin precursors, such as 5,6-dihydroxyindole and dopamine, as starting compounds for the synthesis of fluorescent or phosphorescent materials for applications as emitting layer in OLED devices (2).

\[
\begin{align*}
\text{5,6-Dihydroxyindole} & \\
\text{Dopamine} & \\
\text{Phosphorescent Transition Metal Complexes} & \\
\text{Fluorescent Heterocyclic Platforms} & \\
\end{align*}
\]

In this communication we will discuss the synthesis of a set melanin-inspired electroluminescent compounds; we will report on their photo-physical and electrical properties; the fabrication and characterization of the corresponding OLED devices will also be presented.

References
Modification of biopolymers in ionic liquids (ILs) media to access added value materials

L. Guazzelli, A. Mezzetta, S. Becherini, C. Chiappe

University of Pisa, Via Bonanno 6, 56126 Pisa, Italy, lorenzo.guazzelli@unipi.it

Ionic liquids (ILs) are low-melting organic salts, generally composed of an organic cation and a wide range of anions. ILs are characterized by unique physicochemical properties comprising of negligible vapor pressure under ambient conditions, wide liquid range, low flammability, high ionic and thermal conductivity, wide electrochemical potential window, excellent thermal, chemical and radiochemical stability. Thanks to the variability of the constituent ions, it is possible to tune these properties, and this is the reason why they are often referred to as designer solvents. In particular, some ILs are able to disrupt the hydrogen bonding pattern present in native biopolymers. Since the pioneering work from Rogers et al. (1), ionic liquids (ILs) have become a potential new medium to dissolve biopolymers (e.g., cellulose). For instance, ILs permitted the dissolution of cellulose up to 22% w/w. Several works employed ILs and biomass, and allowed for the preparation of some new materials in the form of films, microspheres, nanofibers, hydrogels, composites, or functionalized derivatives (2).

Among the biopolymers, chitosan is an aminopolysaccharide consisting of beta-(1→4)-linked D-glucosamine units and is directly obtained by de-O-acetylation of chitin. Chitosan is biodegradable and non-toxic, and displays remarkable intrinsic properties such as antifungal, mucoadhesive and haemostatic properties, and antibacterial activity, all making chitosan and chitosan-based materials of interest for developing future biomedical applications (3). Cross-linking the chitosan backbone is one way to obtain variation of the pristine biopolymer, and we investigated this kind of modification in ILs by using CO\textsubscript{2} as a safe, non-toxic, economical C1 cross-linking agent (Scheme 1). (4) Herein, the results of this cross-linking of chitosan, a reaction which can’t be performed in aqueous media, are reported, as well as the fundamental role played by the IL. Also, our latest results in the area of obtaining new materials from the bio-feedstock by modifying them in ILs, are presented.

Towards Integrated Continuous-Flow Fractionation and Functionalisation of Technical Lignins

Heiko Lange\textsuperscript{a,}*; Reza Ebrahimi Majdar\textsuperscript{a,}\textsuperscript{b}; Claudia Crestini\textsuperscript{a}

\textsuperscript{a} University of Rome ‘Tor Vergata’ - Department of Chemical Sciences and Technologies, Via della Ricerca Scientifica, 00133 Rome, Italy; \textsuperscript{b} Gorgan University of Agricultural Sciences and Natural Resources, Golestan Province, Gorgan, Shahid Beheshti, Iran.

* corresponding author: heiko.lange@uniroma2.it

Lignin is the second-most abundant renewable polymer, contributing as much as 30% of the weight, and as much as 40% of the energy content of lignocellulosic biomass.(1,2) Sustainable and efficient biorefinery processes should not only aim at the valorization of lignin in form of fuels, but also in form of a versatile resource for oligo- and polymeric starting materials for the chemical industries.(2) Isolated lignins are highly complex polyphe-nols, exhibiting plant-specific compositions and linkage motifs as well as isolation-depending linear or branched polymer chains. The lack of a uniform defined primary structure, and the rather random arrangement of phenyl-propanoid (C9) polyphenols, prevents easy adoption of lignin, or modified lignins, as substitutes for oil-based polymers.(1) The rather broad distribution of molecular weights of the oligomers and polymers that generally characterizes most lignins presents another significant drawback to applications. However, regardless of the plant specific structural variations, lignin can be seen as naturally available, ‘functionally decorated’ polystyrene-polypropylene composite.

Fractionating lignin using physico-chemical principles(3) or filtration techniques(4), and immediately chemically re-functionalizing the (fractionated) lignin in a way that derivatives are obtained which show a more homogenized functional group profile with respect to both their ‘nature’-specific and their isolation-specific differences will facilitate, or even permit for the first time, the exploitation of new fields of application of lignin.

In one of our current research line, we have conceptually designed a new segmented continuous-flow-inspired set-up for the fractionation of lignins and the subsequent chemical functionalisations of the low polydispersity lignin fractions without un-handling steps.

Up to date, two important types of industrially available lignins, \textit{i.e.}, wheat straw organosolv lignin and softwood Kraft lignin, have been fractionated under optimized segmented flow conditions, adopting insights from non-scalable batch versions.(3) Moreover, based on advanced analytical data(5,6), selected fractions have been used for the production of structurally homogenized lignin oligomers selectively targeting the various types of hydroxyl groups in the lignin backbone. Fractionated and chemically tailored lignins - also in form of tailor-made combinations of fractions - are currently optimized for exploitation in stimuli-responsive polymers,(7,8) industrial coatings and fiber production.

The presentation thus highlights the crucial features of the continuous-flow-based fractionation-functionalization set-up, as well as the flow-compatible chemistries used for targeted functionalization of oligo- and polymeric lignins.

Chemo-enzymatic strategies for the synthesis and functionalization of renewable polymers and composite materials

Alice Guarneri, Marco Cespugli, Simone Lotteria, Francesca Vita, Cynthia Ebert, Lucia Gardossi

Dipartimento di Scienze Chimiche e Farmaceutiche, Dipartimento di Scienze della Vita, Università degli Studi di Trieste, Piazzale Europa 1, 34127 Trieste. E-mail: alliguarneri@gmail.com

Enzymes are not only renewable and sustainable catalysts but they are also endowed with unique selectivity and activity under mild conditions that enable the fine tuning of chemical structure and function of target products. In the present study, hydrolases (lipases and cutinases) were applied for the synthesis of polyesters (1,2,3) under mild conditions (50-70°C) and in solvent-free systems, while oxido-reductases (laccases) were exploited for the targeted modification of the surface of natural composite materials (e.g. rice husk). (5) The two hydrolases enabled the polycondensation of itaconic acid, a monomer displaying a C=C bond that undergoes isomerization and radical cross linking under the conditions used in conventional chemical polycondensations (T > 150 °C). A number of renewable monomers (e.g. itaconic acid, azelaic acid, adipic acid, glycerol, 1,4-butandiol, CHDM) were used for the synthesis of polymers and terpolymers with controlled architecture. The resulting polyesters have MW < 2000 Da, a desired properties for functional polyesters used in dermatologic applications or for further chemical elongation. The C=C pendant was fully conserved throughout the polycondensation and prone to further chemical modification through Michael addition. Mild and solvent-free functionalization paved the way to different synthetic routes for anchoring biomolecules on the bio-based polyesters.

Laccases enzymes were used oxidize the cellulose component of rice husk, a widely available composite material made by cellulose, hemicellulose, lignin and SiO₂. The laccase enzymes allowed the introduction of chemical functionalities under mild conditions while preserving the bulk structure of the material. The functionalized matrix was used as solid support (4) for the anchoring of 6 different enzymes that maintained their activities and were successfully applied in the synthesis of esters, polyesters, as well as in the hydrolysis of proteins and oligosaccharides. The same material can be used for the removal of toxic components from effluents.

References:
Chemical Modifications for the Valorization of Lignin

Zoia Luca\textsuperscript{a}, Anika Salanti\textsuperscript{b}, Marco Orlandi\textsuperscript{a}

\textsuperscript{a} Università degli Studi di Milano-Bicocca, Dipartimento di Scienze dell’Ambiente e della Terra, Piazza della Scienza, 1 20126 Milano.

Lignin is the most abundant renewable source of poly-aromatic moieties as its annual production is second only to cellulose. This aromatic polymer is biosynthesized for structural purposes in the plant cell walls through oxidative coupling of phenoxy radicals leading to the formation of an extremely complex three-dimensional network. The peculiar chemical nature makes lignin a potential candidate for the replacement of fossil resources. In fact large quantities of lignin by-product are made available yearly from pulping processes, as well as bio-ethanol digestion and saccharification processes. Great research efforts are made worldwide to develop physical, chemical and biological methodologies to exploit lignin as a possible substitute of petroleum-based chemical intermediates. Nevertheless, lignin valorization and upgrade to co-product status is often hindered by its complex and heterogeneous chemical and morphological structure which is strongly influenced by numerous factors, such as the botanical source and the extraction process. (1)

In this presentation we would like to summarize our results concerning lignin valorization, which mainly focuses on different chemical modification. The valorization of lignin through integrated approaches is of crucial importance to match the requirements of the biorefinery concept, which is a comprehensive utilization of all those lignocellulosic materials consisting of the residual non-food parts of current crops or other non-food sources (known as second-generation feedstock) by converting these biomasses into fuels, energy, chemicals and materials. (2)

The more interesting chemical modifications studied have been:

i. Allylation: the allylation reaction and the aromatic Claisen rearrangement of the allyl group on lignin as chemical modifications were investigated. This approach is aimed at the development of new lignin-based materials and the improvement of its compatibility and ease of processing. The allylated lignin was used for partial replacement of carbon black in tires industry. (3, 4)

ii. Epoxidation: oxirane ring were inserted on the phenolic functionalities of lignin by reaction in alkaline water with epichlorohydrin. (5) Epoxidized lignin has been used as bio-based reticulating agent in epoxy resin formulation.

iii. Carbonation: epoxide groups on lignin were converted into cyclic carbonates by the addition of CO\textsubscript{2} to oxirane rings in ionic liquid. Imidazolium based ionic liquids, acting as both solvents and catalysts, were successfully employed in the carbonation reaction. Moreover, the ionic liquid was reused up to three times without significant loss in activity. (5) Cyclocarbonate lignin was used as bio-based cross-linking agent in polyhydroxyurethane formulation. (6)

Multicomponent reactions on biocatalytically produced substrates

Luca Banfi\textsuperscript{a}, Lisa Moni\textsuperscript{a}, Renata Riva\textsuperscript{a}, Andrea Basso\textsuperscript{a}, Andrea Bozzano\textsuperscript{a}, Daniele Cartagenova\textsuperscript{a}, Chiara Lambruschini\textsuperscript{a}, Elisa Martino\textsuperscript{a}, Marta Nola\textsuperscript{a}, and Gabriella Vitali Forconesi\textsuperscript{a}

\textsuperscript{a} University of Genova, Department of Chemistry and Industrial Chemistry, via Dodecaneso, 31, 16146 Genova

Isocyanide-based multicomponent reactions represent a very useful tool for the fast generation of libraries of drug-like substances. However, stereochemical control is still an important and mostly unsolved issue. Due to this problem, and also to the limited availability of chiral starting components, often MCR products are obtained in racemic form. In this lecture I will describe an original approach to enantiopure MCR-derived products, based on the biocatalytic generation of chiral inputs and on their use in diastereoselective multicomponent reactions (1), followed by cyclization reaction (2). In this way, a fast access to interesting polyfunctionalized products and/or unusual heterocycles (3,4) was accomplished.

In particular we have used some chiral, enantiopure, monoesters derived from desymmetrization of cyclic meso-diols, as inputs for diastereoselective Passerini reactions mediated or catalysed by Lewis acids. Most of these meso diols are bio-based, since they can be derived from renewable biomass. Application to the total synthesis of Telaprevir (5) and Bengamides (6) will also be discussed.

\begin{center}
\begin{tikzpicture}
\node[draw,shape=circle,minimum size=1cm] (A) at (0,0) {\text{biocatalysis}};
\node[draw,shape=circle,minimum size=1cm] (B) at (1,0) {\text{enantiopure}};
\node[draw,shape=circle,minimum size=1cm] (C) at (2,0) {\text{1) Oxidation}};
\node[draw,shape=circle,minimum size=1cm] (D) at (3,0) {\text{2) Passerini}};
\node[draw,shape=circle,minimum size=1cm] (E) at (4,0) {\text{Telaprevir}};
\node[draw,shape=circle,minimum size=1cm] (F) at (5,0) {\text{various heterocycles}};
\node[draw,shape=circle,minimum size=1cm] (G) at (6,0) {\text{Bengamides}};
\draw[->,thick] (A) -- (B);
\draw[->,thick] (B) -- (C);
\draw[->,thick] (C) -- (D);
\draw[->,thick] (C) -- (E);
\draw[->,thick] (D) -- (E);
\draw[->,thick] (D) -- (F);
\draw[->,thick] (D) -- (G);
\end{tikzpicture}
\end{center}

Photocatalytic Radical Alkylation of Electrophilic Olefins by Benzylic and Alkylic Zinc-Sulfinates

Andrea Gualandi* a, Daniele Mazzarella a, Aitor Ortega Martínéz b, Luca Mengozzi a, Fabio Calcinelli a, Elia Matteucci c, Filippo Monti d, Nicola Armaroli d, Letizia Sambri c, and Pier Giorgio Cozzi a

a Dipartimento di Chimica “G. Ciamician”, ALMA MATER STUDIORUM Università di Bologna, Via Selmi 2, 40126 Bologna, Italy; b Institute of Organic Synthesis (ISO) Universidad de Alicante Facultad de Ciencias. Carretera de San Vicente del Raspeig S/N 03690; c Dipartimento di Chimica Industriale “Toso Montanari”, ALMA MATER STUDIORUM Università di Bologna, Viale Risorgimento 4, Bologna, Italy; d Istituto per la Sintesi Organica e la Fotoreattività, Consiglio Nazionale delle Ricerche, Via P. Gobetti 101, 40129 Bologna, Italy andrea.gualandi10@unibo.it

The decarboxylative coupling of carboxylic acids has numerous applications in photoredox catalysis. (1) In these reactions, monoelectronic oxidation of carboxylate anions, followed by carbon dioxide evolution from the so formed RCOO•, gave entry to nucleophilic radicals (R•) that were found to react with electrophilic alkenes. (2) An interesting alternative for the generation of radical species can be based on sulfinic acids or sulfinates, (3) with the advantage that the oxidation potentials of sulfinates are lower compared to carboxylate anions. A radical-based functionalization strategy that involves the use of sodium and zinc bis(alkylsulfinate) reagents has already been developed by Baran. (4)

Herein we describe a new procedure to accomplish the difficult radical alkylation of electrophilic alkenes using benzylic and alkyl sulfinates in combination with commercially available photocatalysts and visible light irradiation.

Moreover, it is shown that zinc sulfinates can be used for facile not-radical sulfonilation reactions with highly electrophilic Michael acceptors.

Decrypting Transition States by Light (DTS-\(h\nu\)) in Brønsted Acid Catalysis

Polyssena Renzi\(^a\), Johnny Hioe\(^a\), Ruth M. Gschwind\(^a\)

\(^a\)Universität Regensburg, Institut für Organische Chemie, Universitätsstraße 31 93053 Regensburg; polyssena.renzi@chemie.uni-regensburg.de

In the field of Brønsted acid catalysis, chiral phosphoric acids have been recognized as one of the most prominent class of catalysts because they combine high substrate tolerance with high activity and stereoselectivity (1). Despite their wide applicability (more than 400 asymmetric transformations published), experimental insight into the transition states is very rare and most of the mechanistic knowledge is gained by theoretical calculations.

In the context of our work on the NMR mechanistic investigation on phosphoric acids catalyzed addition of nucleophiles to imines, we sought an alternative method to go deeper into the reaction mechanism. For these transformations ternary complexes are postulated as active transition states. Four different stereochemical arrangements, denominated as Type I Z, Type I E, Type II Z, Type II E are possible considering that the imine can adopt an E- or Z-configuration and the nucleophilic attack can occur from the top (Type II) or the bottom (Type I) of the imine/catalyst binary complex (2,3). With this background we questioned whether the photoisomerization of double bonds might be used as a mechanistic tool (4).

Upon illumination, in the presence of a double bond that can be isomerized without significant photodegradation, with no change in the principal reaction mechanism and when the isomerization is slow or comparable to the enantioselective step, the photoisomerization is affecting only the E/Z-imine ratio with a direct effect on the reaction rate and enantioselectivity. The changes obtained for these values with respect to a dark reaction create a characteristic fingerprint pattern, which can be read directly in terms of transition states. Two model systems were investigated. For the asymmetric transfer hydrogenation of imines the characteristic fingerprint pattern of changes obtained (increase on reaction rate, no change on enantioselectivity) upon illumination showed the competition between the two Z-transition states (Scenario 2). According to the configuration of the major product the nucleophilic attack to the Z-imine occurs from the bottom side (Type I Z). Whereas, for the nucleophilic addition of acetylacetone to N-Boc protected imines, Type I E and Type II E were identified as the active transition states. The isomerization to the corresponding Z-imine was in fact detrimental for the reaction rate whereas the enantioselectivity was not affected (Scenario 4).

Structural and Medium Effects in the Hydrogen Atom Transfer Processes Promoted by Short-Lived Aminoxyl Radicals

Osvaldo Lanzalunga

Dipartimento di Chimica, Università di Roma “La Sapienza” and Istituto CNR di Metodologie Chimiche (IMC-CNR), Sezione Meccanismi di Reazione, P.le A. Moro, 5 I-00185 Rome, Italy
osvaldo.lanzalunga@uniroma1.it

Hydrogen atom transfer (HAT) processes from organic substrates to short-lived aminoxyl radicals such as the phthalimide-N-oxyl radical (PINO) are strongly influenced by structural and medium effects. For example we have found that addition of Brønsted or Lewis acids determines a significant deactivation of C-H bonds α to the nitrogen in amides (Figure 1) (1).

![Figure 1](image1)

In the HAT from 4-alkyl-N,N-dimethylbenzylamines to PINO a change in regioselectivity has been observed by effect of protonation. This change has been successfully applied for selective functionalization of the less activated benzylic C–H bonds para to the CH2N(CH3)2 group in the aerobic oxidation of 4-alkyl-N,N-dimethylbenzylamines catalyzed by N-hydroxyphthalimide in acetic acid (Figure 2).

![Figure 2](image2)

An increase of the HAT reactivity by addition of Brønsted or Lewis acids was instead observed with the quinolinimide-N-oxyl radical (QINO) by effect of the protonation or complexation with the Lewis acid of the pyridine nitrogen that leads to a significant decrease of the electron density in the N-oxyl radical (Figure 3).

![Figure 3](image3)

Thus, by changing the structure of the aminoxyl radical or the reaction medium it is possible to carefully control the reactivity and selectivity in the aerobic oxidations catalyzed by the N-hydroxyimides widening the synthetic versatility of the HAT process.

An Ultrafast Molecular Photoswitch Bio-inspired by Green Fluorescent Protein Fluorophore

Marco Paolino, Stefania Fusi, Andrea Cappelli, Michael Filatov, Jérémy Léonard, Massimo Olivucci

Dipartimento di Biotecnologie, Chimica e Farmacia, Università degli Studi di Siena, Via A. Moro, 53100 Siena, Italy; Department of Chemistry, School of Natural Sciences, Ulsan National Institute of Science and Technology (UNIST), Ulsan 689-798, Korea; Institut de Physique et Chimie des Matériaux de Strasbourg & Labex NIE, Université de Strasbourg, CNRS UMR 7504, Strasbourg France; Chemistry Department, Bowling Green State University, Bowling Green, Ohio, United States. paomar@oneonline.it

Light-driven molecular switches and motors are based on the conversion of light energy into molecular motion. (1) Single-molecule rotary devices are capable of funneling the energy of a photon into E/Z isomerization modes putting in motion a rotor moiety with respect to a stator framework. (2)

In the past years, we have shown a practicable strategy for achieving alternative light-driven rotary devices based on mimicking strictly the photoisomerization of biological chromophores. Indeed, we have reported the design and synthesis of a series of positively charged N-alkylated indanylidene pyrroline Schiff bases (NAIPs) structures which replicate the reactivity of the retinal chromophore of visual pigments. NAIPs have been shown to undergo a regioselective subpicosecond double bond photoisomerization similar to that observed for the protein embedded chromophore of animal and microbial rhodopsins. (3,4) Recently, our biomimetic strategy has been reemployed to design and prepare a molecular photoswitch mimicking the radiationless photoisomerization of the green fluorescent protein (GFP) fluorophore: the \( p \)-hydroxybenzylidene-2,3-dimethylimidazolinone (\( p \)-HBDI) anion.

The \( p \)-HBDI fluorophore of GFP is hosted in a tight \( \beta \)-barrel cavity, which locks its central double bond and the adjacent single bond, yielding a photochemically nonreactive molecule and, consequently, an efficient emitter. (5) The chromophore, isolated from the protein, extremely loses its fluorescence in solution due to a rapid twisting of the \( p \)-HBDI central bonds lead to radiationless deactivation via decay at a conical intersection between the first singlet excited state (S1) and the ground state (S0) of the molecule. (6) In light of this we designed a \( p \)-HBDI mimic structure which could undergo the type of regioselective double bond isomerization required for building a rotary photoswitches. We report on the computational design, preparation, and spectroscopic characterization of a synthetic \( p \)-HBDI mimic bearing a single exocyclic and ultrafast photoisomerizable E/Z double bond that connect two rigid units. (7)

Highly selective arylation protocols to prepare bioactive and fluorescent imidazole-based compounds.

F. Bellina\textsuperscript{a}, N. Guazzelli\textsuperscript{a}, M. Lessi\textsuperscript{a}, C. Manzini\textsuperscript{a}, G. Marianetti\textsuperscript{a}, L. A. Perego\textsuperscript{a}, C. Pezzetta\textsuperscript{a}, A. Pucci\textsuperscript{a}, D. Vergara\textsuperscript{b}

\textsuperscript{a}Dipartimento di Chimica e Chimica industriale, Università di Pisa, Via Moruzzi 13, 56126 Pisa; \textsuperscript{b}Dipartimento di Scienze e tecnologie Biologiche e ambientali; marco.lessi@unipi.it

Arylimidazoles are frequently used in different fields of chemistry. Particularly, arylimidazole units are found in compounds having biological activity (i.e. natural products, pharmaceutics, agrochemicals), and in precursors used for the preparation of organic functional materials. Due to their widespread applications, the improvement of synthetic protocols aimed to decorate selectively and under mild conditions the imidazole core is a challenging target in organic chemistry. In this context, the transition metal-catalyzed direct arylation reactions of imidazole (or azoles in general) with aryl halides have emerged as an attractive strategy for the effective construction of aromatic C\textsubscript{sp2}–C\textsubscript{sp2} bonds. These reactions, unlike the traditional metal-catalyzed cross-coupling procedures involving the use of preformed organometallics, enable the direct elaboration of heteroaromatic cores without the pre-activation of both the coupling partners.

In the last years, our research’s group efforts have been focused on the development of new and efficient Pd-catalyzed arylation methods involving imidazoles and (hetero)aryl halides, able to tolerate a wide range of organic functional groups.\textsuperscript{(1, 2, 3, 4)} Our results underline that it is possible to carry out highly selective direct arylation on imidazole derivatives under relative mild conditions using a proper combination of Pd precatalyst/precursor/Base/solvent.

In this talk we will show the application of our synthetic protocols to the preparation of new biological active imidazole derivative (Resveratrol analogues) and of novel imidazole-based fluorescent dyes of general formula 1.\textsuperscript{(5, 6)}

![Chemical structure of Resveratrol analogues and novel imidazole-based fluorescent dyes]

We will also present and discuss the anti-cancer properties of our new resveratrol analogues, and the peculiar optical properties of the newly synthesized imidazole-based dyes.\textsuperscript{(7, 8)}

Short Build/Couple/Pair Approaches for the Synthesis of Novel Glyco- and Peptidomimetic Scaffolds

Elena Lenci, Alessio Rossi, Gloria Menchi, Andrea Trabocchi

Dipartimento di Chimica “Ugo Schiff”, Università degli Studi di Firenze, Via della Lastruccia 13, 50019, Sesto Fiorentino (FI), Italia
e-mail: elena.lenci@unifi.it

The generation of large compound libraries is strictly necessary to increase the chance of finding new lead compounds for drug discovery programmes. In this context, Diversity-Oriented Synthesis (DOS) is one of the major opportunities for organic chemists to produce high-quality chemical libraries (1). However, considering that the synthetic efforts are not directed through a validated target, DOS synthetic strategies have to be versatile, efficient and consisting of no more than four/five economic steps. In this context, Build/Couple/Pair strategy is a powerful approach in DOS, even if, by far, only few examples of the application of this strategy starting from carbohydrates and amino acids have been reported.

However, we found that the exploitation of acetals chemistry allowed to obtain novel heterocyclic structures without the need of transitional protection/deprotection stages. Assembling D-mannose with glycine-derived aminoacetaldehyde six novel skeletally different scaffolds were achieved (Scheme 1) (2). The application of a cell-based phenotypic assay on these compounds allowed for the selection of the hexahydro-2H-furo[3,2-b][1,4]oxazine as a new biologically active scaffold, capable of inducing MDA-MB-231 cell growth inhibition (3).

In addition, four different morpholine-derived heterocyclic structures were obtained through the rearrangement of the intermediate resulting from the coupling between morpholine acetals and α-amino acids (Scheme 2) (4). Finally, new processes for the synthesis of novel skeletally different morpholine-based scaffolds using Petasis multicomponent reactions in the coupling step, are currently under development in our laboratories.

A New Antibacterial Cyclic Peptide from Hot Springs

Roberta Teta, Viggo Thor Marteinsson, René Groben, Marie-Lise Bourguet-Kondracki, Valeria Costantino, Alfonso Mangoni

The increasing incidence of bacterial infections and the rise of antibiotic-resistant bacterial strains have urged the need for novel antibiotics. Marine environment is a unique source of bioactive chemical compounds that can lead to new drugs and/or inspire the development of new medicinally relevant scaffolds. Microorganisms living in specialized ecological niche, such as submarine geothermal areas are a still untapped source of novel lead compounds in drug discovery. A strain of the thermophilic bacterium Thermactinomyces vulgaris, has been isolated from Icelandic marine hot springs. The extract has been studied following a new approach that combines liquid chromatography-high resolution mass spectrometry (LC-HRMS) with automated data analysis through molecular networking (1). Molecular networking is a visual representation of molecular relationships, due to structure similarity, of any given set of molecules as determined by tandem mass spectrometry (MS/MS) data (2). In a network, a single chemical species is represented as a node, and the relatedness between compounds is represented by an edge.

The molecular network of T. vulgaris extract contained a cluster composed by nine nodes, indicating the presence of nine closely related compounds. MS-guided purification from the extract of the most abundant compound in the cluster yielded a new antibacterial cyclic hexapeptide. The structure of the new compound was fully determined by HRMS and HRMS/MS, 1D and 2D NMR, and a modified version of Marfey's method was applied to assess the configuration of each amino acid. The new cyclopeptide showed a remarkable antibacterial activity against S. aureus. Eight minor analogues were also isolated, whose structures were partly elucidated by MS/MS.

The cyclopeptide cluster from T. vulgaris extract. Nodes are labeled with parent m/z ratio. Edge thickness is related to similarity score.

Recent advances in the synthesis of stemarane diterpenoids

Francesca Leonelli\textsuperscript{a}, Angela La Bella\textsuperscript{b}, Luisa Maria Migneco\textsuperscript{b}, Rinaldo Marini Bettolo\textsuperscript{b}

\textsuperscript{a} Dipartimento di Biologia Ambientale, \textsuperscript{b} Dipartimento di Chimica Università degli Studi di Roma “La Sapienza”, P.le Aldo Moro, 5, I-00185 Roma, Italy; francesca.leonelli@uniroma1.it

Stemarane diterpenoids, characterized by the presence of a unique bicyclo[3.2.1]octane C/D ring system within a tetracyclic skeleton, were isolated in Central and South America from plants of the genus Stemodia (1) and Calceolaria (2) respectively, and in Japan from the fungus Phoma Betae (3). Besides, a stemarane diterpenoid, (+)-oryzalexin S 1, was also isolated from Oryza sativa which produces it when attacked by the fungus Pyricularia oryzae or when exposed to UV radiations (4) or when irradiated by ultraviolet light.

\begin{center}
\begin{tikzpicture}
\begin{scope}
\node at (0,0) {\textbf{(+)-oryzalexin S 1}};
\node at (2,0) {\textbf{(+) 2}};
\end{scope}
\end{tikzpicture}
\end{center}

Its structure was elucidated by means of 2-D NMR experiments but the absolute configuration assignment is still unknown. The (+)-oryzalexin S 1 is the first stemarane type phytoalexin to be reported and it has not yet been synthesized.

Continuing our efforts in the synthesis of stemarane diterpenoids (5), whose C/D ring system can now be efficiently obtained (6), we wish now to describe the enantioselective synthesis of the key building block (+)-2, in which three out of the seven stereogenic centers of (+)-oryzalexin S 1 are correctly installed.

Easy chemical modifications to explore the ‘Janus face’ of TBA: anticoagulant vs antiproliferative properties.

Veronica Esposito, Antonella Virgilio, Annapina Russo, Teresa Amato, Giulia Russo, Michela Varra, Luciano Mayol and Aldo Galeone

Dipartimento di Farmacia, Università degli Studi di Napoli Federico II, Via D. Montesano 49, 80131 Napoli, Italy.

RNA and DNA aptamers can be defined as short synthetic ribo- and deoxyribonucleic acids able to bind with high affinity and specificity a broad range of molecular targets as small molecules, proteins and other nucleic acids (1). Under certain conditions and in aqueous solution, aptamers are able to fold in stable three-dimensional structures conferring on them the ability to bind their cognate ligands. The thrombin binding aptamer (TBA) is a 15-base long oligodeoxynucleotide (5'-GGTTGGTGTGGTTGG-3') endowed with interesting anticoagulant properties. According to both X-ray and NMR spectroscopy investigations, TBA adopts a monomolecular antiparallel G-quadruplex structure, characterized by two stacked G-tetrads and three edge loops (two TT loops and one TGT loop, Figure (2,3). Several studies have shown that G-tetrads are mostly responsible for the thermal stability of the aptamer, while loops are involved in the interaction with its target protein, namely thrombin, which is a serine protease playing a key role in the blood coagulation pathway (4). After its discovery, TBA has been subjected to a plethora of chemical modifications aimed at improving thermal stability, enhancing nucleases resistance and increasing anticoagulant activity (5). Besides the anticoagulant activity, just as other G-rich oligonucleotides, TBA has also shown antiproliferative properties (6). In this frame, the simultaneous anticoagulant activity of TBA represents a drawback in exploiting this additional biological property. In an effort to improve the anticoagulant activity or to preserve the antiproliferative properties by quenching the anticoagulant ones, we have prepared some TBA derivatives exhibiting appropriate site-specific replacement of the residues in the loops with a dibenzyl linker or commercially available thymine analogues, such as 2’-deoxyuridine (U), 5-bromo-2’-deoxyuridine (B) and 5-hydroxymethyl-2’-deoxyuridine (H). All the new quadruplex-forming TBA based sequences were studied for their structural (CD, CD melting, NMR) and biological (PT and MTT assays) properties in comparison with the parent aptamer. The whole of data open up the possibility to modulate the TBA properties by using simple tiny modifications concerning specific positions.

References
The greening of protection/deprotection strategies in peptide synthesis.

Maria Luisa Di Gioia\textsuperscript{a}, Monica Nardi\textsuperscript{b,c}, Manuela Oliverio\textsuperscript{d}, Antonio Procopio\textsuperscript{d}, Rosina Paonessa,\textsuperscript{d} Giovanni Sindona\textsuperscript{a}

\textsuperscript{a} Dipartimento di Farmacia e Scienze della Salute e della Nutrizione, Edificio Polifunzionale, Università della Calabria, Arcavacata di Rende, (CS); \textsuperscript{b} Dipartimento di Agraria, Università Telematica San Raffaele, Roma. \textsuperscript{c} Dipartimento di Chimica,Università della Calabria, Cubo 12C, Arcavacata di Rende (CS); \textsuperscript{d} Dipartimento di Scienze della Salute, Università Magna Graecia, Viale Europa, Germaneto (CZ); maria_luisa.digioia@unical.it

The presence of functional groups in a wide range of biologically active compounds makes their protection and deprotection an important and frequently mandatory exercise in synthetic organic chemistry.\textsuperscript{1} In particular, protection and deprotection of the $\alpha$-amino functionality of amino acids is one of the most important issues in peptide synthesis. Therefore, introduction as well as removal must be done in mild conditions that do not affect the remaining protecting groups or even the peptide chain.\textsuperscript{2}

Although there are hundreds of protective groups that can be introduced and removed by a variety of methods, new and milder strategies continue to be developed for many of the existing protective groups; nevertheless, most of them have their own particular drawbacks. The selection of mild reaction conditions for the use of protective groups is a crucial seek of the contemporary synthetic chemistry.

The use of ionic liquids (ILs) and deep eutectic solvents (DES) in organic synthesis has received great attention due to their unusual properties as nonconventional solvents.\textsuperscript{3} Recently, we explored the applicability of these green solvents as reaction media, for the selective introduction and removal of various protecting groups\textsuperscript{4–6} and for the synthesis of potential biologically active compounds.

Design, synthesis of new heterocyclic compounds and their biological activity against MCF-7 cell line.

Cosimo G. Fortuna\textsuperscript{a}, Bonaccorso C.\textsuperscript{a}, Barresi V.\textsuperscript{b}, Satriano C.\textsuperscript{a}, Naletova I.\textsuperscript{a}

\textsuperscript{a} Dipartimento di Scienze Chimiche, Università di Catania, Viale A. Doria, 6 95125-Catania. \textsuperscript{b} Dipartimento di Scienze Biomediche e Biotecnologiche, Sezione di Biochimica Medica, Università di Catania, Via S. Sofia, 97 95123 Catania.

In the last few years, a wide range of heterogeneous styrene systems were studied for the development of new chemical scaffolds for the design of a lead compound as new drug that could show potential antitumor activity towards MCF-7 cell line (breast cancer). The compounds previously synthesized and tested are highly conjugated structures where an electron-rich molecular portion (thiophenic, furanosic or pyrrolic) is separated from the ethylene spacer by a second low electron-poor molecular moiety (N-methylpyridinium, N-methyl-quinolinium or N,N-dimethyl-imidazolium).

In 2013, a database of 59 compounds, with antiproliferative activity towards the MCF-7 tumor cell line, has been generated (1) with the aim of carrying out QSAR studies and developing new drugs using Volsurf + software.(2)

Therefore, nine new diheteroaryl-ethylene systems (Scheme 1) have been designed, characterized by the presence of 5-phenyl-2-furanyl structures, such as electron-rich units, and a 4-pyridine salt with different substituents, as electron-poor units.

The designed compounds were projected into the Volsurf + model for prediction of their antitumor activity. The results obtained for the synthesized molecules suggest that all compounds should exhibit good anti-tumour activity against MCF-7 cells. We here reports the design, the synthesis, the biological evaluation and the study on their mechanism of action.

References:
Synthesis and application of bifunctional chelating agents based on AAZTA scaffold

Luciano Lattuada\textsuperscript{a}, Lorena Beltrami\textsuperscript{a}, Enrico Cappelletti\textsuperscript{b}, Aurelia Ferrigato\textsuperscript{a}, Giovanni B. Giovenzana\textsuperscript{a}, Loredana Sini\textsuperscript{d}

\textsuperscript{a} Bracco Imaging spa, Bracco Research Center, via Ribes 5, Colleretto Giacosa (TO) Italy; \textsuperscript{b} Dipartimento di Scienze del Farmaco, Università del Piemonte Orientale, largo Donegani 2/3, Novara, Italy
E-mail: luciano.lattuada@bracco.com

AAZTA (6-amino-6-methylperhydro-1,4-diazepinetetraacetic acid) is an innovative ligand designed to strongly chelate gadolinium ion and providing in this way a stable MRI contrast agent with increased relaxivity due to the coordination of two water molecules (1). Moreover, AAZTA proved to be an efficient chelating agent for other metal and radiometal ions, such as $^{68}$Ga and $^{44}$Sc, widely employed in PET imaging (2).

Bifunctional chelating agents (BFCA) are molecules containing two different moieties: a metal chelating unit and a reactive functional group. One well known application of BFCA is their covalent conjugation to biomolecules (e.g. peptides, antibodies) in order to obtain new entities applicable in the fields of molecular imaging, diagnostic imaging (MRI, SPECT, PET), tumor therapy (3).

A reactive group can be easily introduced on the structure of AAZTA to give BFCA based on this scaffold. For example, compound 1 was conjugated to an RGD peptidomimetic and labeled with $^{68}$Ga to target $\alpha_\beta\beta_3$ integrins (4), while compound 2 was coupled to a minigastrin derivative providing a new theranostic agent (5). In another example, compound 1 was conjugated to a set of fatty secondary amines or aminophospholipids to obtain lipophilic gadolinium complexes that were incorporated into supramolecular systems such as paramagnetic solid lipid nanoparticles (SLN) (6).

In this communication the synthesis and the application of other mono-, di- and tri-functionalized BFCA 3, based on AAZTA scaffold, will be presented.

References:

QU-IBX and B3-IBX: safe IBX adducts for periodinane oxidation reactions

Simone Mantegazza, Gabriele Razzetti, Emanuele Attolino, Chiara Vladiskovic

Dipharma Francis srl, via Bissone, 20021 Baranzate (MI)
simone.mantegazza@dipharma.com

Oxidation reactions of organic compounds are useful reactions widely employed in the pharmaceutical industry. In this field, in particular, mild and selective reagents are preferred. The well-known Dess-Martin periodinane (DMP) and its precursor 2-iodoxybenzoic acid, known as IBX, offer a plethora of chemo- and regio-selective reactions (1) but their use in industry is strongly limited by their hazardous explosive properties (2). Growing interest in industrial applications of both periodinane reagents in recent years has prompted research on safer solutions allowing the use of periodinanes even in large industrial scale synthesis. In this communication, two new oxidants QU-IBX (fig.1) and B3-IBX (fig.2), adducts of IBX with quinoline and nicotinamide (vitamin B3), respectively (3) will be presented. These adducts have been characterized by XRPD, NMR and DSC and revealed a considerable reduction of decomposition enthalpy to safer levels (table 1). Moreover both adducts show the same reactivity and selectivity of IBX and a series of oxidation reactions performed using both adducts will be presented to demonstrate their potential as a valid alternative to IBX on large scale synthesis.

Table 1.

<table>
<thead>
<tr>
<th>Compound</th>
<th>P.M. mol/kg</th>
<th>T onset °C</th>
<th>ΔH_{bdc} J/g</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBX</td>
<td>280,02</td>
<td>218,5</td>
<td>1164</td>
</tr>
<tr>
<td>DMP</td>
<td>424,15</td>
<td>136,0</td>
<td>829</td>
</tr>
<tr>
<td>QU-IBX</td>
<td>409,18</td>
<td>145,9</td>
<td>584</td>
</tr>
<tr>
<td>B3-IBX</td>
<td>402,15</td>
<td>134,9</td>
<td>724</td>
</tr>
</tbody>
</table>

Amino compounds, besides the role played in fundamental biological mechanisms (i.e. as neurotransmitters), could become toxic for living beings, beyond certain concentrations. Several biogenic amines (cadaverine, putrescine, spermidine, etc.) are products of bacteria thermal or enzymatic decarboxylation operated on aminoacids. Thus, revelation of those amines could give indication concerning food quality or hygiene levels.

In the literature, a variety of chromatographic, enzymatic and colorimetric methodologies are reported for the determination of amines concentrations, however it is still missing a protocol combining inexpensive equipment and a single-component molecular probes.

Here we describe an accurate colorimetric essay based on diarylethenes (DAEs) for the rapid detection of a wide range of amines. The molecular sensors consist of carbonyl-substituted DAEs, which undergo an amine-induced decoloration reaction, selectively in the ring-closed isomer. Thus, these probes can be activated at the desired moment by light irradiation simply using a common UV lamp for laboratories, with a sensitivity that allows amine detection in concentrations up to 10^-6 M in solution. In addition, the practical DAEs immobilization on paper allows for amine sensing on solid supports.

References:

Acknowledgements:
The European Commission (via ITN “iSwitch”), the Alexander von Humboldt Foundation and the German Research Foundation (via SFB 658, project B8) are gratefully acknowledged.
Handling Hydrogen Peroxide On Large Scale: Synthesis of 5-bromo-2-nitropyridine

Alessandro Agosti‡*, Giorgio Bertolini‡, Giacomo Bruno‡, Christian Lautz#, Thomas Glarner#, Walter Deichtmann#

‡OLON SpA, Segrate (MI), Italy  § F. Hoffmann-La Roche AG, CH-4070, Basel, Switzerland
Email: aagosti@olonspa.it

Organic chemistry oxidations are often times considered to be problematic, even more so when they have to be implemented on large scale. The very nature of the transformation in which fuel, oxidant and energy are present altogether makes it an interesting subject to be studied and very rewarding from the challenges it poses to the process safety community. Herein we wish to presents our results on the safety assessment and process development of the synthesis of the 2-nitro-5-bromopyridine. The two steps synthetic procedure utilizes a NBS bromination of 2-aminopyridine leading to the 2-amino-5-bromopyridine intermediate followed by oxidation with a mixture of H₂O₂ 30% and H₂SO₄ 98% (also known as Caro’s acid or Piranha mixture).

Process development and safety proceeded hand in hand towards the obtainment of a sound reproducible process which was applied on full scale within a short time frame. The currently optimized oxidation procedure implies the addition of a sulfuric acid solution of 2-amino-5-bromopyridine onto a pre-mixed cooled solution of hydrogen peroxide in sulfuric acid (3.6:1 w/w) in a temperature range of 15-25 °C.
A rationale for the choice of reagents, temperatures and operation conditions will be described (1).

Zwitterionic Deep Eutectic Solvents as Effective Alternatives to Organic Solvents and to Ionic Liquids

Matteo Tiecco\textsuperscript{a}, Raimondo Germani\textsuperscript{a,b}

\textsuperscript{a} Department of Chemistry, Biology and Biotechnology, University of PERUGIA, IT; \textsuperscript{b} CEMIN – Centre of Excellence on Innovative Nanostructured Materials, Department of Chemistry, Biology and Biotechnology, University of Perugia, IT.

The search for novel organic liquids that could possess environmental advantages is a key factor in the green chemistry framework. The most studied and used liquids in this field are represented by Ionic Liquids (ILs). (1) These organic liquids showed many benefits such as non-volatility, high recycle capabilities and high yields and favourable reaction conditions in many organic reactions. Unfortunately, ILs show many disadvantages due to their toxicity and to their low biodegradability. Moreover, the synthesis of these liquids often requires many steps involving the use of other organic solvents. In the recent years, Deep Eutectic Solvents (DESs) are rapidly increasing their importance as relevant alternatives to organic solvents and to ILs. (2) These novel liquids possess the same advantages of ILs (non-volatility, recycling capabilities, high yields in many chemical reactions) but they showed low or absent toxicity. Moreover, the realization of a DES is performed by simply mixing at the proper molar ratio two solid compounds, preventing the use of other organic solvents and any synthetic step. A DES is formed, in fact, by mixing a hydrogen bond donor (HBD) molecule with a hydrogen bond acceptor (HBA) one. The applications of these mixtures are wide: solvents for synthetic chemistry, nanoparticle synthesis, use as dissolution and separation liquids, solvents for extraction from natural matrixes, solar cells components and so on. The most studied DESs in literature are mixtures of choline chloride as HBA molecule with different compounds as HBD (Urea, glycerol, carboxylic acids and so on). In order to avoid the presence of chloride that could provoke unwanted side reactions, we developed novel Deep Eutectic Solvents based on quaternary ammonium methanesulfonate salts (as HBA molecules) mixed with p-toluenesulfonic acid (as HBD). (3) These novel liquids have been used as dual solvent-catalyst for esterification of several carboxylic acids with different alcohols via Fischer reaction. The step forward on the realization of novel DESs was to avoid the presence of any counterion using zwitterionic molecules, both as HBA or HBD components in different classes. These novel classes of mixtures are formed by carboxybetaine, sulfobetaine and amine-N-oxide molecules. The DESs of carboxybetaine class were successfully used as solubilizing agents of aromatic amino acids (which are normally scarcely soluble in water) and for the extraction of oxyprenylated phenylpropanoids in olive, soy, peanuts, corn and sunflower oil. (4,5) The second class of zwitterionic DESs was developed by mixing differently structured sulfobetaine molecules with (1S)-(+)-10-Camphorsulfonic acid. (6) These liquids were studied as solvents/catalysts in C-C bond formation via Claisen-Schmidt reaction. (7) The advantages of the use of this DES in this probe reaction are represented by: the green properties of the media and its low toxicity; the absence of harmful acids to catalyze the aldol condensation because of the HBD molecule composing the DES mixture; the recycling and the re-use of the DES in subsequent reaction cycles; the mild conditions and the excellent conversions and yields observed. The last class of DESs presented in this work was realized with amine-N-oxide zwitterionic molecules as HBA molecules. (8) These mixtures showed an excellent low viscosity even at room temperature and an excellent capability of solubilization of differently structured polymers.

Innovative Two-Step Synthesis of Polysubstituted 6-NitroIndoles

S. Gabrielli\textsuperscript{a}, E. Marcantoni\textsuperscript{a}, R. Ballini\textsuperscript{a}, S. Sampaolesi\textsuperscript{a}, E. Chiurchiù\textsuperscript{a}, A. Palmieri\textsuperscript{a}

\textsuperscript{a} “Green Chemistry Group”, School of Science and Technology, Chemistry Division, University of Camerino, Via Sant’Agostino 1, 62032 Camerino, MC, Italy.
Email: serena.gabrielli@unicam.it

Heterocyclic compounds are those cyclic compounds in which one or more of the ring carbons are replaced by another atom. The non-carbon atoms in such rings are referred to as “heteroatoms.” (1, 2) Such bicyclic heterocyclic compounds containing pyrrole ring with benzene ring fused to \(\alpha,\beta\)-position are known as Indoles. (3) The indole nucleus is an important element of many natural and synthetic molecules with significant biological activity, it is also a popular component of fragrances and the precursor to many pharmaceuticals. (4) Thus, the development of new and more friendly synthetic pathways, for the synthesis of this core structure, are of particular interest. In this contest, we settled a flow system-microwave two-step assisted process, for the synthesis of polysubstituted 6-nitroindoles (Scheme 1).

Scheme 1. Overall process to 6-nitroindoles

The importance of this class of indole derivatives is related to the synthesis of nucleosides starting from 6-nitroindole, which are of actual biological interest. This class of compounds is very important due to the fact that, indoles bearing nitro substituents on the benzenoid ring can be reduced to the corresponding amin indoles which are precursors to other biologically active compounds. (5, 6) Our method allows to overcome all the limitations of previous methodologies, such as low yield and regioselectivity.

NMR study of mixed micelles: zwitterionic – cationic surfactant systems

Marco Chiarini\textsuperscript{a}, Giorgio Cerichelli\textsuperscript{b}

\textsuperscript{a} Facoltà di Bioscienze e Tecnologie Agro-alimentari e Ambientali, Università di Teramo, via R. Balzarini, 1 – 64100 Teramo Italy; \textsuperscript{b} Dipartimento di Scienze Fisiche e Chimiche, Università dell'Aquila Via Vetoio s.n.c. 67100 L'Aquila Italy; mchiarini@unite.it

Surfactant molecules in a solvent self-associate into various kinds of supramolecular assemblies such as micelles, vesicles, and liquid crystals and their mixture, especially those of nonionic and ionic surfactants are used in many practical applications, such as detergents, cosmetics, oil recovery, drug delivery systems, emulsified polymerization, coating technology, and mesostructured nanofilms (1). For these applications, the structural and solution properties of the mixed surfactant systems should be controlled effectively. Therefore, it is useful to understand how the molecular structures of surfactants in mixtures affect the solution properties, such as the size, shape, and surface charge density of the mixed micelles. For these reasons, structural properties of nonionic-ionic surfactant mixed micellar solutions have been investigated theoretically and experimentally (2). In the mixture of two or more different surfactants (nonionic and ionic), the complex aggregation behavior of the mixture of surfactants in solution is a result of a delicate balance of opposing forces, i.e., the steric hindrance among the polar head groups of the surfactant molecules and electrostatic repulsion energy between charges on the polar head of the ionic surfactant molecules (3). Therefore, the structural properties of the nonionic-ionic mixed micellar solutions should be studied as a function of the molar ratio to determine the effect of molecular interaction between the surfactants in a mixed micelle on its formation. Practically, this understanding can help in choosing relevant surfactant structures that will result in the desired properties. NMR spectroscopy is one of the most convenient methods for simultaneous monitoring of changes in aggregate morphologies of interaction between components. In this study, we investigated the formation in water of mixed micelle using zwitterionic and anionic surfactants employing multinuclear NMR to study the influence of intramicellar interaction and surfactant molecular shape on the properties of mixed micelles.

In our experiments, we kept the surfactant concentration well above their cmc values, so the observed chemical shifts are those of aggregated assemblies formed upon mixing of the surfactants. Interestingly enough, NMR experiments suggest that under the chosen experimental conditions upon mixing of pure surfactants two different families of mixed aggregates are formed both larger than the original single component micelles. The fact that the different mixed micelles coexist unchanged many days after solution preparation, suggest that the system is under thermodynamic control.

Diimidazolium-based supramolecular ionogels for dye removal from wastewaters

Salvatore Marullo, Francesca D’Anna, Rossella Arrigo, Nadka Tzankova Dintcheva, Renato Noto, Carla Rizzo

Dipartimento STEBICEF-Sezione di Chimica- Università degli Studi di Palermo-Viale delle Scienze Ed. 17, 90128 Palermo, Italy; Dipartimento di Ingegneria Civile, Ambientale, Aerospaziale, dei Materiali, Università degli Studi di Palermo, Viale delle Scienze, Ed. 6, 90128 Palermo, Italy. E-mail salvatore.marullo@unipa.it

Dyes are major pollutants of industrial wastewaters deriving mainly from the textile, paper and cosmetic sectors.(1) Many strategies exist to tackle this issue, among which adsorption. In this methodology, dye-polluted waters are treated with porous materials called sorbents. Recently supramolecular gels have emerged as a promising class of nanostructured materials for the remediation of wastewaters. Supramolecular gels are originated by the self assembly of small molecules (LMWGs) in solution.(2) A recent development in this field is represented by ionogels, in which LMGWs gel ionic liquids.(3) Using organic salts as gelators for ionic liquids gives rise to fully ionic gels. Studying ionogels obtained from diimidazolium salts, we found that they possess convenient properties such as unaltered or in some cases enhanced conductivity compared with the parent components.(4)

In the light of this, we have studied the ability of ionogels originated by diimidazolium salts to act as sorbents for the removal of dyes from water. We chose salts bearing isomeric dicarboxylate anions and differing for the alkyl chain length on the imidazolium cations. Ionogels were obtained in different imidazolium based ionic liquids and characterized in terms of thermal stability, rheological properties and gelation kinetics. Dye removal capability of the ionogels was studied using rhodamine B as a model cationic dye. In general, the gelation ability of the salts considered was mainly affected by the alkyl chain length while the anion exerted a minor effect. Moreover the gelation kinetics was mainly affected by the ionic liquid anion. Finally, a more articulate behavior was found for the rheological properties and the removal efficiency of Rhodamine B from water.

References:
Assessment of drug-induced phospholipidosis risk based on distribution coefficient in brain polar lipids

Laura Goracci\textsuperscript{a}, Martina Ceccarelli\textsuperscript{a}, Björn Wagner\textsuperscript{b}, Rubén Alvarez-Sanchez\textsuperscript{b}, Gabriele Cruciani\textsuperscript{a}

\textsuperscript{a} University of Perugia, via Elce di Sotto, 8, 06123-Perugia, Italy; \textsuperscript{b} F. Hoffmann-La Roche Ltd., pRED, Pharma Research and Early Development, Pharmaceutical Research, Innovation Center Basel, CH-4070 Basel, Switzerland

laura.goracci@unipg.it

In vitro safety assessment in early drug discovery represents an important step to detect potential safety-related liabilities. It reduces late stage attrition and allows candidate optimization. Aside cell-based assays, high-throughput safety assessment screenings based on the correlation of physico-chemical properties of organic compounds with their biological effect have been successfully developed.\textsuperscript{(1)} They include both \textit{in silico} and experimental methods. In this study, we report on the use of the LogD\textsubscript{BPL} assay (a recently published assay for the determination of drug distribution coefficients between an aqueous phase and porcine brain polar lipids extract) for phospholipidosis (PLD) risk evaluation.\textsuperscript{(2)} From a mechanistic perspective, drugs inducing PLD are commonly cationic amphiphilic compounds containing an amino group protonated under physiological conditions. The combination of basic and lipophilic features in the chemical structure is responsible for the accumulation of these drugs into lysosomes due to acidic environment, inducing potential toxic outcomes. Our study \textsuperscript{(3)} showed that LogD\textsubscript{BPL} is an efficient descriptor to assess PLD risk, especially when corrected using the pKa value of compounds. A rule-based approach was developed, stating that PLD inducing drugs must possess: (i) LogD\textsubscript{BPL} \geq 1; (ii) at least an amine basic center with pK\textsubscript{A\textsubscript{MBC}} > 7, and (iii) be mostly in their protonated state at pH = 5.

Comparisons with other physico-chemical parameters related to distribution, like effective permeability by PAMPA and LogD\textsubscript{oct}, proved that LogD\textsubscript{BPL} better correlates with PLD effect of drugs.

Identification of new ErbB4 inhibitors by inverse virtual screening

Assunta Giordano,\textsuperscript{a,b} Giovanni Forte,\textsuperscript{a} Fabrizio Dal Piaz,\textsuperscript{c} Federica del Gaudio,\textsuperscript{a} Nunziatina De Tommasi\textsuperscript{a}, Patrizia Gazzero\textsuperscript{a}, Raffaele Riccio\textsuperscript{a}, Giuseppe Bifulco\textsuperscript{a}, Simone Di Micco\textsuperscript{a}

\textsuperscript{a}Dipartimento di Farmacia, Università degli Studi di Salerno, via Giovanni Paolo II, 132, Fisciano (SA); \textsuperscript{b}Istituto di Chimica Biomolecolare-Consiglio Nazionale delle Ricerche, via Campi Flegrei 34, I-80078 Pozzuoli (NA); \textsuperscript{c}Dipartimento di Medicina, Chirurgia e Odontoiatria "Scuola Medica Salernitana", Università degli Studi di Salerno; via S. Allende 84081 Baronissi (SA); sdimicco@unisa.it

We have applied the inverse virtual screening protocol (1-5) to a small library of 19 synthetic compounds that showed a weak activity against the enzyme JMJD3. Our analysis suggested the enzyme ErbB4 as a new putative target of the investigated compounds. This macromolecule is a receptor tyrosine-protein kinase, member of the epidermal growth factor receptor subfamily and identified as potential target for cancer therapy. Experimental in vitro assays show that 5 compounds present inhibitory activity against ErbB4 in the low micromolar range. We have also investigated the binding of the identified lead compounds toward the highly structural related isoform ErbB2. The experimental evidences highlight a selectivity towards ErbB4. Moreover, one of the selected compounds shows antiproliferative activity against carcinoma (HCT) and breast (MCF7) cancer cells in low micromolar range.

Recent advances in the discovery of novel microsomal prostaglandin E$_2$ synthase-1 (mPGES-1) inhibitors

Gianluigi Lauro$^{a}$, Stefania Terracciano$^{a}$, Ines Bruno$^{a}$, Raffaele Riccio$^{a}$, Vincenza Cantone$^{a,b}$, Oliver Werz$^{b}$, Andreas Koeberle$^{b}$, Michele Manfra$^{c}$, Paolo Tortorella$^{a}$, Pietro Campiglia$^{a}$, Giuseppe Bifulco$^{a}$

$^{a}$Department of Pharmacy, University of Salerno, via Giovanni Paolo II 132, 84084 Fisciano, Italy; $^{b}$Department of Pharmaceutical/Medicinal Chemistry, Institute of Pharmacy, University of Jena, Philosophenweg 14, D-07743 Jena, Germany; $^{c}$Department of Science, University of Basilicata, Viale dell’Ateneo Lucano 10, 85100 Potenza, Italy; $^{d}$Department of Pharmacy, Università degli Studi di Bari “Aldo Moro” Via Orabona 4, 70126 Bari (Italy)
glauro@unisa.it

Microsomal Prostaglandin E$_2$ synthase 1 (mPGES-1) catalyzes the conversion of prostaglandin H$_2$ (PGH$_2$) to prostaglandin E$_2$ (PGE$_2$). Its expression is increased in response to pro-inflammatory stimuli, and the involvement of this enzyme in different pathologic conditions, such as atherosclerosis and arthritis, prompts for the development of new and safer anti-inflammatory drugs (1,2). Recently, several clinical studies have also shown increased levels of mPGES-1 in various human cancers (e.g. colon, colorectal, stomach, pancreas, cervix, prostate cancer), thus encouraging the discovery of new mPGES-1 inhibitors as potential anticancer agents (3).

Thanks to the support of Associazione Italiana per la Ricerca sul Cancro (AIRC) (Investigator Grants IG_12777 and IG 17440, PI: Prof. Giuseppe Bifulco), we have developed a set of new mPGES-1 inhibitors featuring unprecedented chemical cores. The new inhibitors have been identified following two different computational approaches:

1. Structure-based drug design and optimization of new compounds obtainable by one-pot synthetic methods (4,5)
2. Lead and Fragment Virtual Screening (VS) from synthesizable and commercially available compounds (6,7)

The different compounds evaluated in silico were then selected for the subsequent phases of chemical synthesis and biological evaluation in vitro, identifying a set of new mPGES-1 inhibitors, all endowed with at least micromolar activity. The enhancements of the potency and of the pharmacokinetic properties of the identified compounds represent the next steps for disclosing new optimized mPGES-1 inhibitors prone to be tested in human cell lines, in inflammation and cancer animal models in vivo, and by small animal imaging.

Cytotoxic secondary metabolites from Mediterranean Fabaceae species display antiproliferative activity against colon cancer cell lines

Vittoria Graziani\textsuperscript{a}, Valentina Belli\textsuperscript{b}, Monica Scognamiglio\textsuperscript{c}, Brigida D’Abrosca\textsuperscript{a}, Angela Chambery\textsuperscript{a}, Severina Pacifico\textsuperscript{a}, Simona Piccolella\textsuperscript{a}, Teresa Troiani\textsuperscript{b}, Nicoletta Potenza\textsuperscript{a}, Antonio Fiorentino\textsuperscript{a}

\textsuperscript{a}Department of Environmental, Biological and Pharmaceutical Sciences and Technologies, Second University of Naples, via Vivaldi 43, I-81100, Caserta, Italy; \textsuperscript{b}Department of Internal Medicine – Clinical and Experimental Surgery “F. Magrassi and A. Lanzara”, Second University of Naples, I-80131 Via Pansini, 5 - Napoli, Italy; \textsuperscript{c}Max Planck Institute for Chemical Ecology, Hans-Knöll-Straße, Germany; vittoria.graziani@unicampania.it

Several drugs currently in clinical use are of natural product origin. This success in drug discovery is due to their high chemical variability and their well-defined three-dimensional structure (1). In this work, the crude polar extracts from Astragalus boeticus, Ononis diffusa and Trigonella corniculata have been investigated for their cytotoxic activity against a panel of colon cancer cell lines, including those resistant to the conventional drugs. An NMR-based metabolomic approach was used to completely characterise the metabolic profiles of the plant extracts (3). In particular, an extensive 2D NMR analysis identified in the mixture the main secondary metabolites. In detail: A. boeticus extract contains flavonols and cycloartane triterpenes; O. diffusa has a very complex metabolome, especially for the aromatic component and, on the contrary, T. corniculata presents little variability in terms of secondary metabolites, showing a protodioscin derivative as unique main compound. Attempting to isolate in a short term the active principles from the crude extracts, a bioguided-fractionation has been performed using different chromatographic techniques. Moreover, the combinatorial use of NMR (mainly DQF-COSY, COSY, TOCSY, HSQC, H2BC, HSQCTOCSY, HMBC, CIGAR-HMBC and NOESY experiments) and TAMDEM HR-MS, elucidated the structures of the isolated molecules. As a result, five cycloastragenols were isolated from A. boeticus and, despite their common basic skeleton, only one among them exerts the antiproliferative properties. In the same way, oxylipin compounds, differently capable of inhibiting the cellular growth, have been separated from O. diffusa. These findings revealed a clear relationship between the structure and the related function of the compounds under investigation, permitting the understanding of the chemical groups essential for the biological activity. Finally, a protodioscin glycoside has been easily isolated from T. corniculata, confirming that this is the unique molecule responsible for the cytotoxicity of the extract. In conclusion, the above-mentioned results encouraged further experiments in order to figure out the molecular mechanism of cell death induced by the cytotoxic secondary metabolites.

References
Treatment with chemotherapeutics is associated with severe side effects because of the lacking selectivity of anticancers towards cancer cells. The development of a selective treatment of cancer cells could allow a significant reduction of the drug dosage with a consequent reduction of side effects in patients. Neurotensin (NT) is an almost ubiquitary peptide hormone whose type 1 receptors (NTR1) are overexpressed by certain type of tumors. Thus NT could be used as targeting peptide for the development of a peptide-base targeting therapy. To overcome the typical low in-vivo stability of natural peptide, the Multiple Antigen Peptide (MAP) form of neurotensin was synthesized. The tetrabranched form (NT4) ensure both an enhanced resistance to proteases and peptidases(1) and a polyvalent interaction with membrane cell receptors. Through in-vitro and in-vivo tests using fluorophore-MAP-NT conjugate the targeting activity of the tetrabranched peptide was demonstrated. (2). On the base of these results, the development of drug-MAP-NT conjugate could represent a suitable tool for a selective anticancer therapy. Among anticancer drugs, taxanes, highly effective chemotherapeutic drugs against proliferating cancer, showed serious side effects because of their high toxicity and hydrophobicity. So, during my PhD, we focused the attention on the development of paclitaxel-MAP-NT conjugates, bearing one or more drug unit. The proper reversible functionalization of the cytotoxic molecule, the nature of the better linker between the drug and the MAP-NT moiety and the suitable reaction for assembling the conjugate, along with the pharmacological properties of such conjugates (Figure 1) will be the topics of this communication.

Figure 1 – MAP-NT-drug conjugates

References:
Synthesis and Biological Evaluation of Some Pyrimidin-2,4-diones as Novel Non-Nucleoside Reverse Transcriptase Inhibitors

Salvatore V. Giofrè, Roberto Romeo, Consuelo Celesti, Maria A. Chiacchio

Dept of Chemical, Biological, Pharmaceutical and Environmental Sciences, Univ. of Messina, S.S. Annunziata, 98168 Messina, Italy; Dept. of Drug Science, Univ. of Catania, V.le A. Doria 6, 95125, Catania, Italy. sgiofre@unime.it

Modified pyrimidines constitute the backbone of many antiretroviral agents acting as non nucleoside reverse transcriptase inhibitors (NNRTIs) (1, 2). 1-[(Hydroxyethoxy)methyl]-6-(phenylsulfanyl)thymine (HEPT; 1) and its analogue (TNK-651; 2) 2-alkoxy-6-benzyl-3,4-dihydro-4-oxopyrimidine (DABO; 3), diaryl-pyrimidines (DAPYs; 4) and their derivatives (Fig. 1) are all families of potent NNRTIs that, through binding at the allosteric, non-nucleoside binding pocket (NNIBP) of RT, prevent the conformational transition needed for the formation of a productive polymerase–RNA complex.

In this context, the synthesis and biological activity of a new class of 3-pyrimidinyl isoxazolidines 5, as HEPT analogues, has been reported (3). Tested in vitro for their biological activity, compounds 5 showed a nearly complete inhibition of AMV RT and HIV RT in the nanomolar range, with weak cytotoxicities towards human cells.

![Figure 1](image1.png)

We report here the design, synthesis and biological evaluation of a series of compounds amenable to derivatives 5, where structural elaborations have been performed towards inhibiting different targets of HIV-1. The replacement of the substituent at C-5 with an ethereal unit gave compounds 6 which showed an improved inhibitory activity towards HIV-1. Removal of the isoxazolidine ring led to subtypes 7 and 8 which selectively inhibited the RNase H function of RT. The redesign of N-1 and C-5 moieties afforded compounds 9 which inhibit drug-resistant HIV-1 mutants (Fig. 2).

![Figure 2](image2.png)

Synthesis and decoration of small molecules targeting the Hedgehog Signaling Pathway

Elena Petricci\textsuperscript{a}, Fabrizio Manetti\textsuperscript{a}, Elena Cini\textsuperscript{a}, Roberta Santini\textsuperscript{b}, Barbara Stecca\textsuperscript{b}, Giuseppe Giannini\textsuperscript{c}

\textsuperscript{a}Dipartimento di Biotecnologie, Chimica e Farmacia, Università degli Studi di Siena, Via A. Moro, 2 – 53100 - Siena; \textsuperscript{b}Istituto Toscano Tumori, Azienda Ospedaliero-Universitaria Careggi Viale Pieraccini, 6 - 50139 - Firenze; \textsuperscript{c}Sigma-Tau Industrie Farmaceutiche Riunite, Via Fontina, km 30,400 - 00071 - Pomezia (RM)
elena.petricci@unisi.it

The Hedgehog (HH) pathway is well recognized to be critical for embryonic development and adult tissue maintenance and repair as well as for cancer onset and progression. In addition, recent studies have highlighted HH pathway as a good therapeutic target in different viral and bacterial infections. Acylguanidine and acylurea derivatives recently developed by our group emerged as interesting SMO inhibitors (1,2). A new synthetic approach has been developed to get a more efficient and scalable preparation of the compounds and to access a family of diversely decorated derivatives. Amongst these products we found some structures active in various human cancer cell lines such as chronic myeloid leukemia, medulloblastoma, and melanoma (3, 4), as well as against several virus (5); MRT derivatives modulate alkaptonuria (AKU) a rare disease involving cartilage degradation, thus demonstrating a possible role of HH pathway in this pathology (6).

Using a virtual screening approach a new family of compounds active as Gli inhibitors has also been recently developed (7) and the synthesis of a small library of derivatives with interesting anticancer activity is reported.


\textsuperscript{a} Dipartimento di Biotecnologie, Chimica e Farmacia, Università degli Studi di Siena, Via A. Moro, 2 – 53100 - Siena; \textsuperscript{b} Istituto Toscano Tumori, Azienda Ospedaliero-Universitaria Careggi Viale Pieraccini, 6 - 50139 - Firenze; \textsuperscript{c} Sigma-Tau Industrie Farmaceutiche Riunite, Via Fontina, km 30,400 - 00071 - Pomezia (RM) elena.petricci@unisi.it
Amphiphilic Guanidinocalixarenes Inhibit Lipopolysaccharide- and Lectin-stimulated Toll-like Receptor 4 Signaling

Francesco Sansone\textsuperscript{a}, Stefania E. Sestito\textsuperscript{b}, Fabio A. Facchini\textsuperscript{b}, Ilaria Morbioli\textsuperscript{b}, Jean-Marc Billod\textsuperscript{e}, Sonsoles Martin-Santamaria\textsuperscript{e}, Alessandro Casnati\textsuperscript{b}, Francesco Peri\textsuperscript{b}

\textsuperscript{a} Dipartimento di Scienze Chimiche, della Vita e della Sostenibilità Ambientale, Parco Area delle Scienze 17/a, 43124 Parma (Italy); \textsuperscript{b} Department of Biotechnology and Biosciences, University of Milano-Bicocca, Piazza della Scienza, 2, 20126 Milano (Italy); \textsuperscript{e} Department of Chemical & Physical Biology, Centro de Investigaciones Biologicas, CIB-CSIC, C/Ramiro de Maeztu, 9, 28040 Madrid (Spain); francesco.sansone@unipr.it

Toll-like Receptors (TLRs) are receptors that recognize pathogen-associated molecular patterns. Among TLRs, TLR4 in particular is the sensor of Gram-negative bacteria endotoxins lipopolysaccharide (LPS) andlipooligosaccharide (LOS) (1). TLR4 is mainly expressed on monocytes, dendritic cells and macrophages. LPS binds sequentially to lipid binding protein (LBP), cluster of differentiation 14 (CD14), and to myeloid differentiation factor 2 (MD-2) (2) that non-covalently associates with TLR4 promoting the formation of the activated receptor multimer (TLR4/MD-2.LPS)\textsubscript{2} (Figure, left) on the plasma membrane (3). While the role of TLR4 as LPS sensor is fundamental for initiating inflammatory and immune responses, excessive and deregulated TLR4 activation leads to acute sepsis and septic shock, associated to high lethality and for which no specific pharmacological treatment is available (4,5). TLR4 can also be activated by endogenous factors called damage-associated molecular patterns (DAMPs), derived from damaged, necrotic, or infected tissues. DAMPs-activated TLR4 signaling is implicated in a large array of pathologies including atherosclerosis (6), rheumatoid arthritis (7), neuroinflammations, neuropathic pain (8) and neurodegenerative diseases such as amyotrophic lateral sclerosis (ALS) (9).

To block abnormal TLR4 signaling we proposed and synthesized a series of facial amphiphilic ligands based on a calix[4]arene scaffold, all characterized by the presence of charged heads on a rim and lipophilic tails on the other (some examples in Figure). Preliminary molecular modeling studies evidenced the possibility for these compounds to bind inside the binding pocket of CD14 and MD2. Subsequent biological tests on cells showed that some of them are strong inhibitors of TLR-4 activation even in absence of LPS. This means that their activity is due to their interaction directly with TLR-4 or its dimer with MD-2 or with one of the receptors involved in the activation pathway, rather than to the simple binding to LPS (10).

Synthesis and stereochemical properties of axially chiral benzo[1,2-b:4,3-b']dithiophene derivatives

Silvia Cauteruccio, Davide Dova, Clara Baldoli, Roberta Franzini, Claudio Villani, Emanuela Licandro

Dipartimento di Chimica, Università degli Studi di Milano, Via Golgi 19, 20133 Milano, Italia; CNR-Istituto di Scienze e Tecnologie Molecolari, Via Golgi 19, 20133 Milano, Italia; Dipartimento di Chimica e Tecnologie del Farmaco, Sapienza Università di Roma, Piazzale Aldo Moro 5, 00185 Roma 3, Italia; silvia.cauteruccio@unimi.it

Thiophene-containing fused aromatic compounds represent an interesting class of π-conjugated systems in functional organic materials (1). Among them, benzo[1,2-b:4,3-b']dithiophene (BDT) and its derivatives are widely studied, especially as units in mono and polydisperse oligomers in the field of the materials science (2), and as π-spacers in push-pull organic chromophores for photovoltaic applications (3). Moreover, BDT is a key intermediate for the synthesis of inherently chiral helical systems such as tetrathia[7]helicenes (4). For all these reasons, BDT can be identified as a key starting molecule that, through a judicious functionalization of the α-positions of the thiophene rings, can allow access to more complex and interesting systems. Exploiting the experience acquired in our laboratories on the synthesis and functionalization of BDT derivatives (5,6), we have studied a novel and simple synthetic route to prepare bis(benzo[1,2-b:4,3-b']dithiophene) systems 2, through Pd-catalyzed cross coupling reactions, starting from bromides 1 (Figure 1).

![Figure 1](image-url)

This strategy provides a convenient route to an interesting class of chiral atropisomeric heterobiaryl derivatives with C₂-symmetry, which can be selectively functionalized into bromides 3. The chiroptical properties of compounds 2 and 3 have been fully elucidated by experimental and theoretical studies. Bromides 3 are expected to have potential applications in asymmetric reactions, including the enantioselective synthesis of tetrathiahelicene derivatives.

Bioinspired organocatalysis of C-C bond-forming reactions

Margherita De Rosa, a Pellegrino La Manna, a Carmen Talotta, a Carmine Gaeta, a Annunziata Soriante, a Antonio Rescifina, b Giuseppe Floresta, b and Placido Neri a.

a Dipartimento di Chimica e Biologia, Università di Salerno, Via Giovanni Paolo II 132, Fisciano (SA), Italy; b Dipartimento di Scienze del Farmaco, Università di Catania, Viale Andrea Doria 6, 95125-Catania, Italy
maderosa@unisa.it

Over the last few decades, there has been a particular attention to the development of new and efficient synthetic strategies inspired to mimic the performance, selectivity and specificity in biological processes. (1,2) In this context, the replacement of organic solvents with more environmentally benign water and the design of "artificial" enzymes with the desirable features of natural ones but without their intrinsic drawbacks such as poor substrate versatility and ease of denaturation, represent promising fields. (3,4) We report here our recent studies on these two issues based on the use of calixarene derivatives. In fact, their hydrophobic character combined with their recognition abilities make them valid organocatalysts for the vinylogous Mukaiyama aldol reaction under "on-water" conditions (5,6) and provide a confined reaction environment to efficiently conduct 1,3-dipolar cycloaddition of nitrones to α,β-unsaturated aldehydes.(7)

Calixarenes as organocatalysts under "on-water" conditions

O OSi(CH3)3
+ R OR1
O
O O O
HO ... R4
R4
R4
n
+ Catalysis inside nanocavities

end o
exo

2. L. Marchetti, M. Levine ACS Catal. 2011, 1, 1090-1118
Highly diastereoselective synthesis of \( \gamma \)-butenolides and phthalides by Michael addition catalyzed by crown ethers

Marina Sicignano, Rosaria Schettini, Antonella Dentoni Litta, Francesco De Riccardis, Irene Izzo, Giorgio Della Sala

Dipartimento di Chimica e Biologia “A. Zambelli”, Università degli Studi di Salerno, Via Giovanni Paolo II 132, 84084 Fisciano (SA); gdsala@unisa.it

\( \gamma \)-Butenolides (1) and phthalides (2) are structural motifs found in numerous natural products and pharmaceutically useful analogues displaying a wide range of biological activities. In addition, their frameworks proved to be useful chiral building blocks for the synthesis of diverse bioactive natural compounds. Much effort has thus been devoted to the stereocontrolled construction of these lactones. An attractive strategy for the stereoselective introduction of a substituent in the C-3 position of the \( \gamma \)-lactone framework is the Michael addition to appropriate electron-poor alkenes. The vinylogous Michael addition of 2(5\( H \))-furanones or 2-silyloxyfurans to \( \alpha, \beta \)-unsaturated ketones reported to date often employ expensive chiral catalysts and usually favor the anti products (3). On the other hands the stereoselective Michael addition of phthalides has been scarcely investigated and limited to activated phthalide-3-carboxylic esters (4,5).

In this communication we report crown ethers as efficient achiral and off-the-shelf catalysts for the diastereoselective Michael addition of \( \gamma \)-butenolides and 3-aryl-phthalides to \( \alpha, \beta \)-unsaturated ketones. In particular, we have developed an unprecedented switchable diastereoselective vinylogous Mukaiyama-Michael reaction of 2-trimethylsilyloxyfuran with \( \alpha, \beta \)-unsaturated ketones, that enables the synthesis of both syn or anti adduct depending on the crown ether’s cavity size and the solvent employed (Scheme 1). The first highly diastereoselective Michael addition of 3-aryl-phthalides to diverse electron-poor alkenes is also described (Scheme 2).

Design of a new chiral nanosupported catalyst for asymmetric reactions

C. Sappino\textsuperscript{a}, P. Bovicelli\textsuperscript{b}, F. Di Pietro\textsuperscript{a}, G. Righi\textsuperscript{b}, M. Oneto\textsuperscript{a}, L. Primitivo\textsuperscript{a}, L. Suber\textsuperscript{c}

\textsuperscript{a} Dept. Chemistry, Sapienza Università di Roma, P. le A. Moro 5, 00185 Roma; \textsuperscript{b} IBPM (CNR) Dept. Chemistry, Sapienza Università di Roma, P. le A. Moro 5, 00185 Roma; \textsuperscript{c} ISM (CNR), Via Salaria km 29, 300, 00015 Monterotondo Scalo (Roma); carla.sappino@uniroma1.it

Asymmetric catalysis is nowadays considered one of the strongest tools to obtain enantiopure products: starting from prochiral molecules, it enables to synthesize optical active compounds with the help of small amount of the appropriate chiral catalyst. The opportunity to recover and reuse the catalyst, most of the times valuable molecules, has led to the adoption of new techniques belonging to material chemistry. In the last years, the growing study of nanostructured materials has given birth to a variety of new applications in many fields, among which catalysis. New chiral nanosystems have been developed, combining advantages of both homogeneous and heterogeneous catalysis: nanoparticles’ dispersibility in organic solvents makes their catalytic activity close to that of their homogeneous counterparts; at the same time, they are easily separated from the reaction mixture resulting in an economical and environmental benefit (1).

Recently, we were involved in the design and synthesis of new chiral nanosystems characterized by a β-amino alcohol fragment as catalytic site, a recurrent motif in many chiral catalysts (2), (Fig 1-A). Before immobilizing the catalyst, it was necessary to optimize the structure of the chiral ligand by proving it in the enantioselective addition of diethylzinc to aldehydes, often chosen as reaction test. After an extensive fine tuning process ligand 1 was found to be an excellent chiral catalyst in the selected reaction (yield 88-98%, \textit{ee}=90-98%, Fig 1-B), and a good one in the asymmetric version of another organic reaction, the nitroaldol or Henry reaction, source of nitroalcohols, a synthetically interesting class of compounds (Fig 1-C)

\begin{center}
\includegraphics[width=\textwidth]{fig1.png}
\end{center}

\textit{Fig 1}

In parallel, we are focusing on the optimization of the immobilization conditions and on the choice of the best solid support (Fig 2). These new β-amino alcohol nanosupported chiral catalysts will finally be tested in the same reaction previously optimized in the homogeneous phase.

\begin{center}
\includegraphics[width=\textwidth]{fig2.png}
\end{center}

\textit{Fig 2}

Asymmetric 1,3-dipolar cycloadditions catalyzed by a new imidazolidinone organocatalyst

Vincenzo Algieri\textsuperscript{a}, Antonio De Nino\textsuperscript{a}, Loredana Maiuolo\textsuperscript{a}, Beatrice Russo\textsuperscript{a}, Pedro Merino\textsuperscript{b}.

\textsuperscript{a} Dipartimento di Chimica e Tecnologie Chimiche-CTC, Università della Calabria, Ponte Bucci cubo 12C, 87036, Arcavacata di Rende (CS), Italy; \textsuperscript{b} Departamento de Síntesis y Estructura de Biomoléculas, Instituto de Síntesis Química y Catálisis Homogénea, Universidad de Zaragoza-CSIC, 50009 Zaragoza, Spain. vincenzo.algieri@unical.it

Organocatalysis exploits the small organic molecules to increase the speed of the reactions (1). Catalysis is divided into non covalent and covalent. The covalent catalysis mediated by iminium ion has been used in various applications. Pollak decarboxylation (2) was the first example of asymmetric catalysis and was performed using the L-Proline (3). According to this model, it was later developed a new type of the enantioselective imidazolidinone catalysts (4). In this work, we designed and synthesized a new type of asymmetric imidazolidinone organocatalyst, (5S)-2,2,3-trimethyl-5-thiobenzyl-4-imidazolidinone \textit{[A]}. This latter, after characterization, was initially tested on Diels-Alder reaction in which it has been possible to observe excellent catalytic efficiency at low load percentages (5).

\begin{center}
\includegraphics[width=\textwidth]{scheme1.png}
\end{center}

\textbf{Scheme 1}

In this work our research group will describe the results about 1,3-Dipolar Cycloaddition Reactions using various substituted nitrones as 1,3-dipoles and \(\alpha,\beta\)-unsaturated aldehydes as dipolarophiles (Scheme 1). The reaction yields and diastereomeric excesses are very high and excellent enantiomeric ratios of the reaction products have been observed in presence of the catalyst \textit{A}.

\textbf{References:}
A new highly efficient strategy to prepare racemic Anatabine

Susanna Sampaolesi\textsuperscript{a}, Federico Vittorio Rossi\textsuperscript{a}, Alessandro Palmieri\textsuperscript{a}, Pietro Allegrini\textsuperscript{b}

\textsuperscript{a} School of Science and Technology, Chemistry Division, University of Camerino, Via Sant’Agostino 1, 62032 Camerino, MC, Italy; \textsuperscript{b} Indena Spa, Viale Ortles, 12, 20139 Milano; susanna.sampaolesi@unicam.it

Among 4000 different compounds isolated and identified in \textit{Nicotiana tabacum} plants, Anatabine represents the most abundant of minor alkaloids (1), found with an intermediate enantiomeric ratio.

![Fig.1 Nicotine and structurally related alkaloids found in fresh leaves of \textit{Nicotiana tabacum} plants.](image)

In particular Anatabine possesses several important pharmacological properties such as anti-inflammatory activity (2); it also suppresses amyloid beta production (3), and reduces autoimmune thyroiditis (4). Furthermore, it has been demonstrated that Anatabine decreases nicotine self-administration, suggesting its possible role as agonist medication for treatment of nicotine addiction (5).

As a consequence, many methodologies for its synthesis have been developed, however they present important limitations such as low over-all yields (6), use of harsh conditions (7) or toxic agents (8). In order to overcome these drawbacks, herein we present a novel synthetic strategy to prepare racemic Anatabine within few steps, in good overall yield, starting from low-cost commercially available building blocks (Scheme 1).

![Scheme 1.](image)

Molecular Events within Confined Spaces

Carlo Bravin,* Elena Badetti, Giulia Licini,* Cristiano Zonta*

*Department of Chemical Sciences, University of Padova via Marzolo 1, 35131 Padova (PD) (Italy); cristiano.zonta@unipd.it

Self-assembly of small molecules in complex architectures is becoming the leading strategy for the formation of novel functional systems and materials. Among the different bond-formation synthetic strategies, imine condensation chemistry combined with coordination chemistry has been extensively used to obtain a large variety of molecular architectures ranging from supramolecular cages to topological structures. In the recent years we have been interested in the self-assembly of tris(2-pyridylmethyl)amine derived structures. (1) In this communication we report about a novel supramolecular cage built from the self-assembly of tris(2-pyridylmethyl)amine zinc complexes through imine condensation chemistry. The cage recognition properties over a variety of structurally related guests, together with the kinetic study of the template assembly and disassembly, have been investigated in detail. This knowledge has been used to selectively modulate the rate of both assembly and disassembly processes. In particular, a novel disassembly method induced by strain release of the guest has been developed. (2)

References:
Synthetic application of bacterial $\gamma$-glutamyltransferases (GGTs)

Carlo F. Morelli, Fabio Romagnuolo, Gabriele A. Franza, Cinzia Calvio, Giovanna Speranza

University of Milan, Department of Chemistry, via Golgi, 19 – 20133 Milano. University of Pavia, Department of Biology and Biotechnology, via Ferrata, 9 – 27100 Pavia

$\gamma$-Glutamyl dipeptides are compounds characterized by an amide bond involving the amino group of one amino acid and the $\gamma$-carboxyl group of a glutamic acid residues. They show interesting properties with respect to their parent amino acids. For example, the bitterness of aromatic and branched-chain amino acids used in oral dietary supplements is alleviated or even abolished upon $\gamma$-glutamylation, as does the unpleasant smell of seleno amino acids, the source of the micronutrient selenium.

$\gamma$-Glutamyl derivatives of $S$-substituted cysteines are naturally occurring flavor enhancers found in garlic and onion. Although their possible applications render the $\gamma$-glutamyl derivatives economically interesting compounds, their supply remains a problem. Isolation from natural sources, if any, is laborious and low-yielding, as their content may vary with cultivation and storage. Chemical synthesis is not economical, due to the need of protection/deprotection steps. A viable alternative could then rely on an enzymatic approach taking advantage by the use of a $\gamma$-glutamyltransferase.

$\gamma$-Glutamyltransferases (GGTs, EC 2.3.2.2) are widespread, conserved enzymes found in bacteria, plants and animals. They catalyze the transfer of a $\gamma$-glutamyl moiety from a donor compound, usually glutathione, to an acceptor amino acid through a $\gamma$-glutamyl-enzyme intermediate involving a catalytically active threonine residue.

As a first approach, a commercially available, crude $\gamma$-glutamyltransferase of animal origin was used in our laboratories for the synthesis of some naturally occurring flavor enhancers found in garlic. Then, our research group turned attention to bacterial enzymes, especially from GRAS (Generally Referred as Safe) microorganisms. The GGT from $B. subtilis$ seemed to be well suited for our purposes and a detailed study of this enzyme was since then undertaken. Recent findings obtained about the enzymatic activity of $B. subtilis$ GGT and related to the peculiar architecture of its active site will be presented, in relation to its application as a biocatalyst for the synthesis of $\gamma$-glutamyl derivatives of economical interest.

This work is supported by Fondazione Cariplo (TailGluTran Project, 2016-0741)

Functionalized triazolylidenes as versatile mesoionic carbenes: metal complexes for catalysis and luminescent materials

Elia Matteucci\textsuperscript{a}, Andrea Baschieri\textsuperscript{b}, Cristiana Cesari\textsuperscript{a}, Rita Mazzoni\textsuperscript{a}, Claudia Bizzarri\textsuperscript{c} and Letizia Sambri\textsuperscript{a}

\textsuperscript{a} Dipartimento di Chimica Industriale “Toso Montanari”, Università di Bologna, Viale Risorgimento 4, I-40136, Bologna, Italy.\textsuperscript{b} Dipartimento di Chimica “G. Ciamiciian”, Università di Bologna, Via Selmi 2, 40126 Bologna, Italy; \textsuperscript{c} Institute of Organic Chemistry, Karlsruhe Institute of Technology (KIT), Fritz-Haber-Weg 6 76131 Karlsruhe (D); letizia.sambri@unibo.it

1,2,3-Triazol-5-ylidene derivatives have recently emerged as a new class of so-called mesoionic (MICs) carbenes,\textsuperscript{(1)} and have found a wide range of applications as ligands in metal complexes.\textsuperscript{(2)} The success of this class of ligands is based on a combination of favorable features, as a result of their strong donor character and the easy preparation of the triazole precursors through the regioselective copper(I) catalyzed ‘click’ cycloaddition of alkynes with azides (CuAAC).\textsuperscript{(3)} Subsequent N-alkylation and deprotonation of the readily obtained 1,2,3-triazoles afford the desired mesoionic carbene ligands.\textsuperscript{(4)} The presence of a heteroatom in a suitable position of a substituent of the triazolylidene can lead to a bis-chelating ligand or to a ligand carrying an activating functionality.

We exploited such triazolylidene mesoionic carbenes to obtain a wide set of both positive and neutral Ir(III)-complexes,\textsuperscript{(5,6)} with good luminescent performances, and neutral Ru(0)-complexes, used as active catalysts in hydrogenation reactions.\textsuperscript{(6,7)}

Copper complexes with biomimetic antioxidant activity

A. Squarcina, M. Zonzin, M. Carraro, M. Bonchio

"Dipartimento di Scienze Chimiche, Università degli Studi di Padova and Istituto per la Tecnologia delle Membrane, ITM-CNR, UOS di Padova, via Marzolo, 1, 35131 Padova, Italy

The anomalous production of reactive oxygen species (ROS), generated as by-products of normal cellular metabolism, is responsible for an enhanced oxidative stress, which is ultimately associated with several disorders, chronic diseases and ageing. A major defense strategy of living systems against the ROS is represented by the antioxidant enzymes (1). These primarily belong to the superoxide dismutase (SOD) family, whose task is the disproportionation of O$_2^-$ into O$_2$ and H$_2$O$_2$. This latter oxidant is then detoxified by catalase (CAT) enzymes upon conversion into O$_2$ and H$_2$O. The active sites of the antioxidant enzymes contain metal ions as Cu(II) and Mn(III), coordinated by a set of N and O donor atoms. Despite the large availability of metal complexes showing a similar coordination environment, the efficient mimicking of the enzymatic redox activity still represents a challenging goal (2,3).

In this communication, the use of tetradeinate N$_3$O tripodal ligands, for the preparation of antioxidant synthetic enzymes, will be presented. In particular, mononuclear and dinuclear copper complexes have been prepared and tested under physiological-like conditions, in order to assess their structure-dependent catalytic behavior towards SOD-like and CAT-like reactions, showing in some cases an interesting dual activity.

Moreover, since free Cu(II) ions may also be responsible for an enhanced ROS production, the ligands have been tested to scavenge these ions from an aqueous solution, in order to convert their harmful reactivity into a benign antioxidant activity, while the peroxidase-like reactivity of the resulting complexes has been evaluated in the presence of different substrates. The speciation and the stability of the complexes will be also discussed.

Mild N-Alkylation of Amines with Alcohols Catalyzed by Acetate Ruthenium Complexes

Walter Baratta, Rosario Figliolia, Salvatore Baldino, Hans Günter Nedden, Antonio Zanotti-Gerosa

\textsuperscript{a} Dipartimento DIAA, Università di Udine, Via Cotonificio 108, 33100 Udine, Italy; \textsuperscript{b} Johnson Matthey Fine Chemicals Division 28 Cambridge Science Park, Milton Road, Cambridge, CB4 0FP, United Kingdom; E-mail: walter.baratta@uniud.it

The formation of C-N bonds for the preparation of amines compounds is a reaction of high relevance for the synthesis of bulk and fine chemicals (1). The preparation of several drug molecules involves N-substitution transformations that are usually performed by reaction of amines with alkylating agents or via reductive amination. In this context, the catalytic N-alkylation of amines using environmentally friendly alcohols as alkylating reagents and affording water as only byproduct, is an attractive atom-economic way for the C-N bond formation (2,3).

We report here the straightforward synthesis of the carboxylate ruthenium complexes of formula Ru(OAc)\textsubscript{2}(diphosphane)(CO)\textsubscript{n} (n = 0, 1). These compounds are efficient catalysts for the N-alkylation of amines using primary alcohols under mild reaction conditions, with an alcohol / amine molar ratio of 10-100. Evidence has been provided that in catalysis a monohydride species is formed through an equilibrium reaction.

\[
\begin{align*}
\text{R}^1&\text{N-H} & + & \text{R}^2\text{OH} & \overset{[\text{Ru}] \ 1 \ \text{mol} \ %}{\text{30 - 78 } \degree \text{C}} & \rightarrow & \text{R}^1&\text{N-R}^2 & + & \text{H}_2\text{O} \\
\text{R} = \text{alkyl, aryl} & & & \text{R}^1 = \text{H, alkyl} & & & \text{R}^2 = \text{alkyl}
\end{align*}
\]

References:
The power of ligand combination in redox active ruthenium and iron complexes.

Rita Mazzoni\textsuperscript{a}, Cristina Cesari\textsuperscript{a}, Andrea Cingolani\textsuperscript{a}, Valerio Zanotti\textsuperscript{a}, Fabrizio Cavani\textsuperscript{a}, Francesco Puzzo\textsuperscript{a}, Carlo Lucarelli\textsuperscript{b}, Massimo Mella\textsuperscript{b}, Andrea Tagliabue\textsuperscript{b}, Tom Baker\textsuperscript{c}

\textsuperscript{a} Dipartimento di Chimica Industriale "Toso Montanari" viale Risorgimento, 4 40136, Bologna; \textsuperscript{b} Dipartimento di Scienza e Alta Tecnologia – Università dell’Insubria-Como; \textsuperscript{c} Department of Chemistry, University of Ottawa, Canada; E-mail rita.mazzoni@unibo.it

In recent years, cyclopentadienone complexes have drawn attention due to their air-water stability, availability from cheap starting materials, and unique catalytic features arising from the presence of a non-innocent ligand.\textsuperscript{(1)} In the meantime N-heterocyclic carbenes increased their ubiquity as ancillary ligands in catalysis and other fields due to their great potential for both easy synthesis and functionalization.\textsuperscript{(2)} Our recent research interest has been thus devoted to the development of novel ruthenium and iron based complexes combining carbonyls, cyclopentadienones and variously functionalized N-heterocyclic carbenes.\textsuperscript{(3)} These complexes can be rapidly protonated on cyclopentadienone by strong acid (e.g. HOTf) giving rise, in the case of ruthenium, to active precursors for bifunctional hydrogenation and dehydrogenation catalysis.\textsuperscript{(4)}

The straightforward synthetic method allowed the design of complexes containing hydroxyl, amino and pyridine functionalized NHC directed to the improvement of their catalytic activity, to the development of supported materials and to the preparation of water-soluble complexes. Herein, we report on the chemistry of the ruthenium complexes as bifunctional catalysts in hydrogenation and dehydrogenation with particular emphasis on the peculiar role that a basic nitrogen on the lateral chain of NHC can play on the mechanism investigated by \textit{in situ} IR and DFT calculations. Joy and pain of the shift to earth abundant iron congeners will be then described. Finally the potential of these ligand-metal combinations in biphasic catalysis, bio-derived substrate transformations, electrochemistry and bio-inorganic chemistry will be also outlined.

Synthesis of New Carbonyl Diphosphane Ruthenium Complexes for Catalytic C-H Bond Activation Reactions

Rosario Figliolia, Salvatore Baldino, Walter Baratta, Steven Gibolout, Hans Günter Nedden, Antonio Zanotti-Gerosa

Dipartimento DI4A, Università di Udine, Via Cotonificio 108, 33100 Udine, Italy; Johnson Matthey Fine Chemicals Division 28 Cambridge Science Park, Milton Road, Cambridge, CB4 0FP, United Kingdom; E-mail: figliolia.rosario@spes.uniud.it

Homogeneous catalysis plays a key role in development of new chemo- and enantio-selective syntheses that point to efficiency and low environmental impact. For this purpose, great concern has been devoted to processes that employ non-toxic reagents / solvents and that can be carried out under mild reaction conditions, using low quantities of catalysts. As regards the reduction of carbonyl compounds, ketones and aldehydes are generally converted to alcohols with strongly reducing agents, namely NaBH₄ and LiAlH₄. In addition, dihydrogen at high pressure (HY) has been widely used with ruthenium based catalysts. Milder reaction conditions associated with low risks can be achieved via transfer hydrogenation (TH) using 2-propanol catalyzed by efficient ruthenium catalysts.

We report here a straightforward procedure for the preparation of a class of ruthenium carbonyl compounds RuX₂(PP)(CO)ₙ (X = Cl, OCOCH₃, OCOCF₃) (n = 0 - 2) bearing aryl and alkyl diphosphane ligands. Ruthenium hydride complexes are formed by reaction with H₂ via dihydrogen splitting or with hydrogen donor molecules. These derivatives easily react with nitrogen ligands affording efficient catalytic species for the hydrogenation and transfer hydrogenation of carbonyl compounds and other hydrogen borrowing reactions.

References:
Oceans of data for informed decisions in chemistry. The shortest path from the question to insight

Carlos Rodríguez del Río

Customer Consultant, Life Sciences, R&D Solutions, Elsevier Ltd, The Boulevard, Langford Lane, Kidlington, Oxford, OX5 1GB, United Kingdom
c.rodriguezdelrio@elsevier.com

In the last few years the amount of published has dramatically increased. A way to find the information needed in a faster way is needed to keep project funding in good shape. Reaxys provides rapid and easy access to experimental facts to empower chemistry research, chemical discovery and scientific education. Finding relevant literature, retrieving precise compound properties and reaction data has never been easier. Furthermore, universities require chemistry informatics solutions that address both teaching and research challenges. Since funding is limited, having one solution that covers more tasks is very important. Reaxys is simple enough to use with undergraduate students in the classroom, but relevant and powerful enough to help researchers prepare for his laboratory work. Reaxys provides a simple and streamlined workflow that can be applied to both education and lab work, saving precious time in both areas.
Comunicazioni Poster
Domino Addition/Cycloisomerization Reactions of 2-Alkynyl-Arylaldehydes: Silver Catalyzed Synthesis of 1,3-Dicarbo-Substituted-Isochromenes

Giorgio Abbiati, Valentina Pirovano, Elisabetta Rossi

Dipartimento di Scienze Farmaceutiche, Sezione di Chimica Generale e Organica “A. Marchesini”, Università degli Studi di Milano, Via Venezian, 21 – 20133 Milano – Italy; e-mail: giorgio.abbiati@unimi.it

One of the most efficient methods for the construction of 1-substituted isochromenes (and related heteroaryl compounds) is the metal catalyzed regioselective domino cycloisomerization/nucleophilic addition reaction of a 2-alkynyl(hetero)arylaldehyde in the presence of a suitable nucleophile. The reaction with oxygen nucleophiles is probably the most studied one. Several metal catalyst have been used, and our group recently gave a contribution in the field of silver catalyzed synthesis of 1-alkoxyisochromenes. Conversely, the reaction with carbon nucleophiles, and in particular with enolizable carbonyl compounds, is relatively less investigated. We report here our recent results regarding the silver catalyzed synthesis of 1,3-dicarbo-substituted isochromene derivatives starting from 2-alkynyl(hetero)arylaldehydes and enolizable carbonyl compounds. The reaction proceeded in a cascade fashion under mild reaction conditions with absolute regioselectivity and moderate to good yields. In some cases, the reaction produced unexpected diastereoisomeric couple of homodimeric products. The divergent formation of the 1-acylisochromenes and the alternative homodimeric products has been tentatively explained by some experiments and two conceivable competitive paths have been proposed.

Silylcarbocyclisation-desilylation reactions of N-tosyl-2-ethynylaniline: a new protocol for the synthesis of 2-hydroxyindoline derivatives

Gianluigi Albano, Margherita Lissia, Laura Antonella Aronica

Dipartimento di Chimica e Chimica Industriale, Università di Pisa, via G. Moruzzi 13, 56124 Pisa, Italy
e-mail: gianluigi.albano@dcci.unipi.it

2-Hydroxyindolines are useful building blocks for the preparation of pharmaceutical and biologically active compounds. (1) However, to the best of our knowledge only few synthetic procedures have been developed; most of them are based on the reduction of corresponding lactams or on cyclisation processes of variously substituted anilines. (2)

We found that β-lactams and β-lactones can be easily obtained from propargyl amides and propargyl alcohols by means of rhodium-catalysed silylcarbocyclisation reactions with dimethylarylsilanes; subsequent treatment with TBAF promotes a desilylation step, consisting in a 1,2-migration of aryl group from the silyl moiety to the adjacent carbon atom. (3) Very recently, we extended our silylcarbocyclisation-desilylation protocol to the preparation of various 4-(arylmethyl)isochroman-3-ones starting from 2-ethynylbenzyl alcohol and arylsilanes with different steric properties. (4)

Here we report that silylcarbocyclisations of N-tosyl-2-ethynylaniline with dimethylarylsilanes, carried out with catalytic Rh\(^{\text{II}}\)[(C\(_7\)H\(_8\))(BPh\(_4\))]\(^+\) (Rh\(^{\text{sw}}\), 0.3 mol%) under CO pressure (30 atm) at 100°C, generate (Z)-1-tosyl-3-(((dimethylsilyl)methylene)indolin-2-ols with good yields (51-68%). These compounds can be submitted to a facile TBAF-promoted desilylation step with migration of the aryl group, affording the corresponding N-tosyl-3-(methylaryl)indolin-2-ols quantitatively and with very high diastereoselectivity (anti > 90%).

Er(OTf)$_3$ in ionic liquid catalyzed [3 + 2] cycloaddition of azides with electron-deficient dipolarophile: regioselective synthesis of substituted 1,2,3-triazoles.

Antonio De Nino,$^a$ Loredana Maiuolo,$^a$ Vincenzo Algieri,$^a$ Monica Nardi,$^a$ Maria Luisa Di Gioia,$^b$ Matteo Antonio Tallarida.$^a$

$^a$ Dipartimento di Chimica e Tecnologie Chimiche-CTC, Università della Calabria, Ponte Bucci cubo 12/C, 87036, Arcavacata di Rende (CS), IT. $^b$ Dipartimento di Farmacia e Scienze della Salute e della Nutrizione, Edificio Polifunzionale, Università della Calabria, 87036 Rende (CS), IT

The 1,2,3-triazole nucleus represents a significant class of biologically active nitrogen compounds that exhibit a number of important biological properties, such as antibacterial, anticancer, antivirus, and antituberculosis.$^1$ Moreover, 1,2,3-triazoles have found industrial applications as dyes, agrochemicals, corrosion inhibitors, and photostabilizers. Therefore, the building up of a 1,2,3-triazole moiety invokes ever growing synthetic efforts. Recently, the system Er(OTf)$_3$/IL/H$_2$O used to catalyze Diels Alder reactions has emerged as a versatile tool for developing syntheses due to their numerous advantages, namely, their relatively high efficiency, water compatibility, mild reaction conditions, and eco-friendly catalytic reactions.$^2$

Herein, we report that substituted 1,2,3-triazoles can be obtained by [3 + 2] cycloaddition of azides with electron-deficient dipolarophiles catalyzed by the Er(OTf)$_3$/IL/H$_2$O system (Scheme 1), thereby providing a new synthetic method for substituted 1,2,3-triazoles formation.

Scheme 1

To the best of our knowledge, this is the first time that system Er(OTf)$_3$/IL/H$_2$O has been described for [3 + 2] cycloadditions of alkyl azide with electron-deficient dipolarophiles. In addition the IL containing the catalyst can be readily separated from the reaction products and recovered in excellent purity for direct reuse.

References:
Synthesis of bio-based heterocycles from levulinic acid using the Ugi multicomponent reaction

Luca Banfi\textsuperscript{a}, Chiara Lambruschini\textsuperscript{a}, Sirio Griva\textsuperscript{a}, Lisa Moni\textsuperscript{a}, and Renata Riva\textsuperscript{a}

\textsuperscript{a} University of Genova, Department of Chemistry and Industrial Chemistry, via Dodecaneso, 31, 16146 Genova.

Levulinic acid is one of the most important biomass derived fine chemicals. It is in the US Department of Energy (DOE) list of the 12 most important building blocks that can be derived from sugars (1). Production of levulinic acid on large scale is already a well assessed methodology. Its prize is, at the moment, about 1 $ / Kg, but it is expected to go further down, starting from waste sugar sources. Thus, the main problem now is not how to get it, but how to find new applications of it, i.e. through conversion it into high added-value compounds. Several use of levulinic acid, especially in the polymer field, are thus under study (2). However, transformations into nitrogen derivatives, especially heterocycles has not been explored very much so far, with the exception of the synthesis of δ-aminolevulinic acid (DALA), used in photodynamic therapies. Isocyanide-based MCRs can be a perfect tool to access levulinic derived heterocycles. IMCRs and levulinic acid are old friends. Actually Passerini used levulinic acid in his reaction as early as in 1923 (3) and, more recently, Ugi reactions of levulinic acid, leading to pyroglutamic acid amides, have been reported by various groups (4–7).

However, we thought that there was still ample room for further development in this area. Our plan was to combine the Ugi reaction with an intramolecular substitution reaction (8), affording, in just 2 steps, very interesting bicyclic structures like 1 or 3. They incorporate classical "privileged structures", such as pyroglutamic acid (9), ketopiperazine and diazepanone. Towards this goal we started from levulinic acid and 1,2-aminoalcohols or 1,3-aminoalcohols and developed a very efficient (in terms of yields and operational simplicity) protocol. Further diversity inputs have been introduced into compounds 1 by enolate alkylation or dehydrogenation-Michael sequences. Starting from chiral enantiopure aminoalcohols, enantiopure 1-3 could be obtained, and the diastereoselectivity in the Ugi reaction will be discussed.

\begin{equation}
\begin{array}{c}
\text{HO}_3
\text{N}^2
\text{S}_{\text{N},2}
\end{array}
\end{equation}

Oxidation of Hydrocarbons and Alcohols with H₂O₂ Catalyzed by Nonheme Imine Based Iron Complexes

Alessia Barbieri,⁷ Stefano Di Stefano,⁴ Osvaldo Lanzalunga,⁴ Giorgio Olivo²

¹Dipartimento di Chimica, Università “La Sapienza” and Istituto CNR di Metodologie Chimiche (IMC-CNR), Sezione Meccanismi di Reazione, Roma. ²Departament de Química, Universitat de Girona, Campus de Montolivi, Spagna. e-mail: alessia.barbieri@uniroma1.it

Nonheme iron complexes represent a class of powerful and versatile catalysts that are able to efficiently catalyze selective oxidations of organic compounds using environmentally benign hydrogen peroxide as the terminal oxidant. In order to avoid expensive and complex noneme ligand structures, we have synthesized and fully characterized simple nonheme iron complexes with imine-based ligands (1) assembled in one pot from cheap and commercially available reagents (2-aminopicoline and 4-substituted-2-pycolyl aldehydes).(1, 2)

The oxidation of hydrocarbons indicates that these complexes exhibit high turnover numbers in aliphatic C-H hydroxylation, comparable to the most efficient nonheme iron catalysts prepared so far. Good yields of carbonyl products were obtained in the oxidation of aliphatic alcohols, while the preferential oxidation of the aromatic ring was observed in the oxidation of benzylic alcohols (3). In line with these results, the imine iron catalyst was also very efficient and selective in the oxidation of the aryl ring in alkylaromatic compounds. A series of mechanistic studies provided evidence that oxidations are metal based. Activation of the complex likely involves an initial oxidation to the ferric state followed by a ligand arm dissociation that enables the H₂O₂ binding and activation.

Structural characterisation of Peripolin, a new 3-hydroxy-3-methylglutaryl flavonoid glycoside from bergamot juice

Lucia Bartella, Fabio Mazzotti, Giuseppina De Luca, Anna Napoli, Giovanni Sindona and Leonardo Di Donna

Department of Chemistry and Chemical Technologies, University of Calabria Via P. Bucci, cubo 12/D, 87036 - Rende (CS), Italy

In 2009 two 3-hydroxy-3-methylglutaryl flavonoid glycosides (HMG-flavonoids), Melitidin and Brutieridin, were isolated and characterized from bergamot fruit (1). Experimental and theoretical research studies report that HMG-flavonoids posses an inhibitory effect on HMGR, the key-step enzyme in the biosynthesis of cholesterol (2,3,4). In the present work, a new 3-hydroxy-3-methylglutaryl flavonoid glycoside was isolated and identified as HMG conjugate of neoeriocitrin (eriocitrin 7-(2"-α-rhamnosyl-6"-(3""-hydroxy-3""-methylglutaryl)-β-glucoside) by mass spectrometry and NMR experiments (Fig. 1). Structural characterization by NMR spectra showed that two diasteromeric forms of molecules exist, as with many flavanones in citrus fruits (5).

Fig. 3 Structure of Peripolin

Several analytical experiments were performed to assess the structure of new compound. Isolated flavonoid was evaluated by accurate tandem mass spectrometry experiments using a quadrupole time of flight instrument equipped by an electrospray source (ESI-QqTof). Moreover, basic and enzymatic hydrolysis reactions were performed on the pure sample, in order to obtained information on the ester moieties and aglycone.

The negative HRESI-MS provided the elemental composition C_{33}H_{39}O_{19}. ESI-MS/MS experiments were performed in both positive and negative ion mode and provided several diagnostic fragment ions.

\(^1\)H-NMR and 2D-NMR experiments confirm the structure of the new HMG-flavonoid glycoside and showed the presence of a mixture of diastereoisomers in bergamot juice.

References:
The dual role of Ionic Liquids in Gold Nanoparticles Drug Delivery-Systems

Cinzia Chiappe, Felicia D’Andrea, Stefano Becherini, Corinna Micheli, Elena Husanu, Valentina Cappello, Mauro Gemmi

Dipartimento di Farmacia, Università di Pisa, Via Bonanno 33, Pisa, Italy. Istituto Italiano di Tecnologia, Center for Nanotechnology Innovation@NEST, Piazza San Silvestro 12, Pisa, Italy; e-mail: stefano.becherini@farm.unipi.it

Gold nanoparticles (AuNPs) are attractive scaffolds for the preparation of organic-inorganic hybrids through the stable interaction between the gold surface and different classes of functional groups. AuNPs are used to carry and release drugs, as biological sensors or for imaging. Ionic liquids (ILs) is the term for low-melting salts obtained by the combination of a large variety of organic cations and anions. Recently, ILs were used in nanotechnology for the preparation of metal nanoparticles by electrostatic interactions.

In this work, we propose a drug delivery-system consisting of AuNPs capped with an ionic liquid, which bears a bioactive portion. First, we studied simple long-chain ILs, and evaluated the stability of the AuNPs by varying the cationic portion and the length of the alkyl chains. (Figure 1)

![Figure 1](image1.png)

These AuNPs have been synthesized in water through a simple one-pot procedure. Based on the results obtained from this preliminary study, ILs decorated with a bioactive portion were synthesized and used to obtain AuNPs. In particular, we chose a monosaccharide tail considering the role played by sugars in a plethora of biological events. (Figure 2)

![Figure 2](image2.png)

Generally, AuNPs were characterized by Ultraviolet-Visible spectroscopy (UV/Vis), Transmission Electron Microscopy (TEM) and Nuclear Magnetic Resonance (NMR).

Hydroxytyrosol-controlled release from poly(vinyl) alcohol (PVA) combined with nanostructured starch

Roberta Bernini\(^a\), Luca Santì\(^a\), Elisa Panucci\(^a\), Ermelinda Boticella\(^a\), Alessandro Di Michele\(^b\), Elena Fortunatì\(^a\), Francesca Luzi\(^c\), Luigi Torre\(^c\)

\(^a\) Department of Agricultural and Forestry Sciences (DAFNE), University of Tuscia, Via S. Camillo De Lellis, 01100 Viterbo. \(^b\) Physics and Geology Department, University of Perugia, Via Pascoli, 06123 Perugia, Italy. \(^c\) Civil and Environmental Engineering Department, UdR INSTM, University of Perugia, Strada di Pentima 4, 05100 Terni.

e-mail: berninir@unitus.it

Hydroxytyrosol (HTyr) is a phenolic antioxidant present in the olive oil and olive oil by-products (1,2) available in our laboratories on a large scale and in high purity by a selective and efficient IBX-oxidation of tyrosol, a commercially low cost compound (3).

![HTyr structure](attachment:HTyr.png)

The potentiality of using this molecule for both food and non-food applications could be increased projecting and developing novel materials that permit a controlled release to prolong the antioxidant effect over the time. In this light, on the basis of our previous results (4,5), we included HTyr into poly(vinyl) alcohol (PVA) combined with nanostructured starch. Among polymers to be used as matrix, we selected PVA, a biodegradable, biocompatible and non-toxic polymer characterized by high polarity and strong solubility in water with good optical, physical and thermo-mechanical properties. At the same time, for the production of nanomaterials, our attention has been turned on starch, a natural, renewable and biodegradable polymer consisting of amyllose, a linear macromolecule composed by \(\alpha\)-1,4-D-glucopyranose chains and amylopectin, a highly branched macromolecule with \(\alpha\)-1,4-D-glucopyranose and \(\alpha\)-1,6-D-glucopyranose chains. The ratio of these two components is generally related to the botanic origin of starch, which is also responsible for the shape, size and crystalline organization of the corresponding granules (6). In particular, our starting materials were starch extracted from the bread wheat variety Cadenza (WT, amyllose content 33\%) and a derived-high amyllose line (HA, amyllose content 75\%). For each type of starch, we prepared nanocrystals (NC\(_{WT}\), NC\(_{HA}\)) and nanoparticles (NP\(_{WT}\), NP\(_{HA}\)) by acid hydrolysis and high power ultrasound irradiation. Then, we developed novel ternary films, namely PVA/NC\(_{WT}/\)HTyr, PVA/NC\(_{HA}/\)HTyr, PVA/NP\(_{WT}/\)HTyr and PVA/NP\(_{HA}/\)HTyr, that we characterized in terms of morphological, thermal and optical properties. Finally, we tested these formulations for antioxidant food packaging applications. In this light, overall and specific migration tests were performed using a hydrophilic food simulant according to the current European legislation in order to evaluate the kinetic of release of HTyr from each film. Experimental data showed that HTyr was released in a controlled manner from all ternary films and the released HTyr still retained a strong antioxidant activity. The release profiles demonstrated the key role of the different types of nanostructured starch in the novel formulations in promoting a controlled release of HTyr.

Phytochemical analysis of *Daphne sericea* Vahl. from Majella National Park

Alessandro Venditti \(^a\), Anna Maria Serrilli \(^a\), Mirella Di Cecco \(^b\), Giampiero Ciaschetti \(^b\), Armandodoriano Bianco \(^a\)

\(^a\) Dipartimento di Chimica: Università di Roma “La Sapienza”, Piazzale Aldo Moro 5 – 00185 Rome (Italy).
\(^b\) Ente Parco Nazionale della Majella, Via Badia 28, 67039 Sulmona (L’Aquila), Italy

The genus *Daphne* (Thymelaeaceae family) comprise about 95 species worldwide distributed and several of these have been largely used in traditional medicines to treat several illnesses. The Italian territory account on about 10 species of this genus and *Daphne sericea* Vahl. (1,2) is one of these. It grows mainly in the Thyrrenian coast and in several sites with a spot distribution in the Appennines (3). The studied sample was collected in the territory of Majella National Park which represent a hot spot for biodiversity in central Italy with the presence of several endemic and rare species. Because the presence of a wide variety of biological activities in species of the *Daphne* genus much attention has been paid to their phytochemistry, but for what concern the species *sericea*, in literature is present only one study which reported on the isolation of a few flavonoid related to luteolin (4).

The phytochemical analysis of the ethanolic extract obtained from the aerial parts of *D. sericea* led to the isolation of nineteen compounds belonging to different classes of natural products. Among these the coumarins resulted the main components with the presence of two monomeric coumarins, five bis-coumarins as aglycones or in glycosidic form and one trimeric coumarin glycoside, followed by four flavonoids, two glycosidic furolignans, two glucosidic phenylpropanoids, two cyclic tetrapyrole derivatives of chlorine family and an unsaturated trygliceride.

The majority of these compounds were recognized for the first time during this study from *D. sericea* and have a chemosystematic relevance since they have been isolated from other species and subspecies of this genus (5,6). Among the identified compounds, in addition to the chemosystematic markers, have been also recognized several components which resulted to be new constituents also for the genus.

For what concern the bioactivities all these constituents are responsible of interesting biological effects, which range from the antioxidant one to the key enzyme inhibition and the anticancer ones (6), making so *D. sericea* a precious source of bioactive molecules.

Phytochemical comparison among three Sideritis taxa from Central Italy

Alessandro Venditti a, Claudio Frezza b, Mauro Serafini b, Sebastiano Foddai b, Marcello Nicoletti b, Filippo Maggi c, Armandodoriano Bianco a

a Dipartimento di Chimica, b Dipartimento di Biologia Ambientale, Università di Roma “La Sapienza”, Piazzale Aldo Moro 5 – 00185 Rome (Italy), c School of Pharmacy, University of Camerino, via S. Agostino 1, 62032 Camerino, Italy

The genus Sideritis is one of the most important genera in the Lamioideae subfamily of Lamiaceae. The Italian Flora comprises five taxa belonging to this genus (1), i.e. S. hirsuta L., S. hyssopifolia L. subsp. hyssopifolia, S. italica (Mill.) Greuter & Burdet, S. montana L. subsp. montana and S. romana L. subsp. romana, among which S. italica is considered as an endemism. Locally known as “Stregonia”, plants of the Sideritis genus are often used in infusion as tonics, carminatives, diuretics and digestives and for this reason are known as “mountain teas” (2).

In this study we reported on the phytochemical comparison of the secondary metabolites patterns in three species (S. romana, S. italica and S. montana) with particular attention to the chemosystematic markers of Lamiales (iridoids, acetylated flavonoids containing allose and glycosidic phenylpropanoids) to verify their implication in the taxonomy of these species. The presence of iridoids was confirmed in all the three species with the presence of harpagide, 8-O-acetylharpagide, 6-deoxyharpagide, 5-allosyloxyaucubin, monomelittoside, ajugoside, 8-epiloganic acid and bartioside. Yet, they resulted to be not homogeneously distributed and each species showed a characteristic composition (3,4,5). The phenylpropanoid verbascoside was detected only in S. italica, while the acetylated flavonoids containing allose (six different derivatives) were identified in all the species and, also for these metabolites, each species revealed a characteristic composition, with only one compound shared with the others. Other secondary metabolites, belonging to different classes of natural products, were also recognized, namely chlorogenic acid and methylarbutin in S. montana, siderol in S. italica; phytol and a series of acetylated glycosidic flavonoids related to apigenin and luteolin in S. romana. The presence of these constituents, with specific distribution, represents an additional marker of differentiation between the three Sideritis species. Moreover, the different metabolic profiles exhibited by these three Sideritis species is consistent with the current classification, morphologically-based, of the different sections of the genus.

Ethno-pharmacological value and phytochemical variability of *Galeopsis ladanum* subsp. *angustifolia* (Ehrh. ex Hoffm.) Gaudin

Claudio Frezza\textsuperscript{a}, Alessandro Venditti\textsuperscript{b}, Alessandra Carassiti\textsuperscript{b}, Sebastiano Foddai\textsuperscript{a}, Mauro Serafini\textsuperscript{a}, Armandodoriano Bianco\textsuperscript{b}

\textsuperscript{a} Dipartimento di Biologia Ambientale, \textsuperscript{b} Dipartimento di Chimica: Università di Roma “La Sapienza”, Piazzale Aldo Moro 5 – 00185 Rome (Italy)

*Galeopsis ladanum* subsp. *angustifolia* (Ehrh. ex Hoffm.) Gaudin (Lamiaceae) is a Mediterranean small annual herbaceous plant. It is spread all along the national territory with the only exceptions of Apulia, Calabria and Sardinia whereas its presence is uncertain in Sicily (1). *Galeopsis* species are well known to possess important pharmacological properties i.e. anti-oxidant, anti-inflammatory, astrigent, anti-anemic, expectorant, remineralizing and diuretic (1,2,3).

In this work we report a re-investigation of the secondary metabolites obtained from a sample of *G. angustifolia* collected in Civita di Oricola (Abruzzo region) at 600 m a.s.l. The aims were to compare its phytochemical pattern with that observed in a different sample collected in Latium region at 1800 m a.s.l. (4) and to evaluate the obtained results from the first sample under the ethno-pharmacological point of view, too.

Both of these scopes were achieved by analyzing the ethanolic extract of the aerial parts by means of Chromatographic and Spectroscopic techniques (NMR and MS).

Eight compounds were evidenced: verbascoside [1], 7-[(2-O-(6-O-acetyl-β-D-allopyranosyl)-β-D-glucopyranosyl)oxy]-2-(4-hydroxy-phenyl)-5,8-dihydroxy-4H-1-benzopyran-4-one [2], 7-[(2-O-(6-O-acetyl-β-D-allopyranosyl)-β-D-glucopyranosyl)oxy]-2-(4-methoxy-phenyl)-5,8-dihydroxy-4H-1-benzopyran-4-one [3], 7-[(2-O-[(6-O-acetyl-β-D-allopyranosyl)-β-D-glucopyranosyl]oxy)-2-(3-hydroxy-4-methoxy-phenyl)-5,8-dihydroxy-4H-1-benzopyran-4-one [4], harpagide [5], 8-O-acetyl-harpagide [6], chlorogenic acid [7] and quinic acid [8].

The marker compounds (iridoids [5-6] and acetylated-allsyl-flavonoids [2-4]) were reconfirmed. Indeed, several qualitative differences were evidenced and compounds [7] and [8] resulted to be new constituents of this species. The presence of these compounds suggests the hypothesis to use this species for ethno-pharmacological purposes. In fact, all of them are known to exert pharmacological activities: verbascoside as antimicrobial and anti-inflammatory (5); the three flavones as anti-oxidant and neuro-protector (6); the two iridoids as anti-tumour, anti-bacterial and anti-inflammatory (5); chlorogenic acid as cicatrizing agent (7); quinic acid as anti-oxidant and anti-inflammatory (8).

Nevertheless further and deeper studies should be made in order to better understand how they all interact with each other and participate to the phytocomplex action of this plant.

N-Heterocyclic Carbenes functionalized polystyrene monolithic microreactors for continuous flow stereoselective umpolung catalysis

O. Bortolini\textsuperscript{a}, A. Massi\textsuperscript{a}, D. Ragno\textsuperscript{a}, G. Di Carmine\textsuperscript{a}, P.P. Giovannini\textsuperscript{a}, A. Brandolese\textsuperscript{a}.

\textsuperscript{a} Dipartimento di Scienze Chimiche e Farmaceutiche, Università di Ferrara, Via Borsari 46, I-44121, Ferrara, Italia.
\textit{e-mail: olga.bortolini@unife.it}

In a previous study, our research group developed a novel synthetic route for the immobilization of racemic thiazolium salts on monolithic polystyrene and silica with the aim to investigate heterogeneous umpolung catalysis in flow-mode.(1) As a logical extension of that study, we reasoned about the utilization of polystyrene monolithic columns functionalized with chiral N-Heterocyclic Carbenes (NHCs) in stereoselective umpolung continuous-flow processes. Triazolium salt pre-catalysts have been chosen for the scope due to their well-documented activity in a wide variety of stereoselective umpolung transformations.(2)

After some experimentation, a covalent immobilization strategy of the Rovis triazolium pre-catalyst was optimized on polystyrene and the catalyst activity and recyclability were first tested under batch conditions. The stereoselective intramolecular Stetter reaction leading to optically active chromanones was chosen as the benchmark, detecting excellent results in terms of yield (>95%) and stereoselectivity (\textit{e.e.}: 81-95%). Subsequently, the continuous flow process was investigated by fabricating the corresponding monolithic microreactors (pressure-resistant stainless-steel columns) and evaluating the catalyst effectiveness during the time. Importantly, it has been demonstrated by a brief substrate scope study that the polymeric matrix and the continuous-flow regime synergistically contribute to preserve the activity of the carbene catalysts over time, thus hindering its deactivation process.

To the best of our knowledge, our study represents the first example of heterogeneous NHC-catalyzed stereoselective process under continuous-flow conditions.

Disperse dyes modification by Pd-catalyzed cross coupling reactions

Lorenzo Calugi\textsuperscript{a}, Massimo Corsi\textsuperscript{a}, Marco Bonanni\textsuperscript{b}, Roberto Bianchini\textsuperscript{a}

Dipartimento di Chimica “Ugo Schiff”, Università degli Studi di Firenze, Via della Lastruccia 3, 50019, Sesto Fiorentino (FI);\textsuperscript{b} Glycolor s.r.l., Via Madonna del Piano 6, 50019 Sesto Fiorentino (FI)

Disperse dyes are the most commonly used dyes in tinctorial processes. These dyes possess a very low solubility in water, therefore the use of surfactants is necessary to ensure a good dispersion in aqueous medium. These additives determine a substantial increase in tinctorial costs and their removal from dyeing wastewaters represents a challenge. To enhance the water solubility of disperse dyes, Bianchini and al.\textsuperscript{1} developed the naturalization process, consisting in the conjugation of the chromophore to a 6’-piperazinyl-lactose unit through an amide bond. In this work, the previously synthesized 1-amino-2-bromo-4-hydroxy-anthracen-9,10-dione carboxylic acid derivative (C.I. Disperse Violet 17 carboxylic acid derivative \textsuperscript{1}) was used as substrate in Pd-catalyzed cross coupling reactions (Fig. 1).

Different aryl derivatives were used to explore the reactivity in Suzuki, Heck and Sonogashira reactions, to extend the conjugation of the antraquinone unit and to evaluate the changes in the absorption spectrum. The naturalization process was tested on one derivative for each of the three reactions and their dyeing potential was evaluated (Fig. 2). Only for Suzuki derivative the desired water soluble compound was obtained. The desired Heck derivative (compound \textsuperscript{12}) was completely insoluble, while for the Sonogashira process the deprotection step gave a mixture of water soluble compounds including the desired one (compound \textsuperscript{12}) and a product derived from HCl addition to the alkyne. Moreover, tinctorial proprieties of compound \textsuperscript{11} are under study.

References:\textsuperscript{1} Patent WO 2014177528 A1, 2014
Novel chiral N,S-acetal cyclic structures as templates for functional, stereochemical and appendage diversity

**Vito Capaccio and Laura Palombi**

Dept of Chemistry and Biology, University of Salerno, via Giovanni Paolo II, 84084-Fisciano, Italy; e-mail: vcapaccio@unisa.it

The attainment of functionally diverse small-molecule collections based on heterocyclic structures lies at the heart of the drug discovery process, thus representing an attractive challenge for the organic chemistry community (1). An efficient way to approach this target is the design of small libraries through the functional, stereochemical and appendage diversifications of suitable “molecular platforms”.

As a part of our research program based on the asymmetric construction and functionalization of isoindolinonic architectures and related compounds (2) we have recently realized the asymmetric synthesis of a new class of multi-heteroatomic cyclic compounds 1 containing the N,S-acetal functionality by one-pot reaction of thiols and 2-cyano-N-tosylbenzylidenimine using catalysts derived from cinchona alkaloid series. As showed in scheme 1, title compounds are effectively achieved *via* an highly stereoselective heterocyclization driven by a dynamic kinetic resolution (DKR).

Scheme 1. Proposed pathway for DKR

With this innovative methodology in hand, and in view of the presence of the tertiary stereogenic center, different functional groups and reactive sites, we decided to investigate the possibility to achieve molecular diversity through additional reactions on the compounds 1.

In particular, in this communication, we will focus on the second reactivity of the title compounds aimed at obtaining enantioenriched isoindolinone-derived N(acyl),S-acetals 2 and chiral sulfoxides 3 and 4 paying attention to the configurational stability of the synthetized derivatives and, where appropriate, to the diastereoselectivity of the processes. Appendage diversity (aimed to the attainment of the products 5 and 6) at the 3rd position of the isoindolinonic core will be also considered (Scheme 2).

Scheme 2. Examples of functional, stereochemical and appendage diversity of the heterocyclic core 1

Synthesis and characterization of benzo[1,2-\textit{b}:4,3-\textit{b}']dithiophene–based organosilicon compounds

Silvia Cauteruccio\textsuperscript{a}, Alberto Bossi\textsuperscript{b}, Serena Arnaboldi\textsuperscript{a}, Patrizia R. Mussini\textsuperscript{a}, Emanuela Licandro\textsuperscript{a}

\textsuperscript{a} Dipartimento di Chimica, Università degli Studi di Milano, Via Golgi 19, 20133, Milano, Italia; \textsuperscript{b} Istituto di Scienze e Tecnologie Molecolari del CNR (ISTM-CNR), Via Fantoli 16/15, 20138, Milano, Italia and SmartMatLab Centre, Via Golgi 19, 20133, Milano, Italia.

e-mail: silvia.cauteruccio.unimi.it

Silicon-containing polymers, having a regular alternating arrangement of silanylenes and π-electron systems in a polymer backbone, are of great interest as photoresists, semiconducting materials, and precursors of silicon carbide (1). On the other hand, much attention has been paid to thiophene-based heteroaromatic compounds due to their important photoelectric properties, and their use as charge transport materials in broad range of applications including OFETs, OLEDs and Solar Cells (2). Thiophene units bridged by silylene σ-linkages, including both small molecules and polymers, have been therefore studied extensively, because of their stability, in many optoelectronic applications (3). In this context only simple thiophene rings have been studied, hence living plenty of space for further structural engineering including the use of polyconjugated thiophene-based systems.

For several years our group has been working on synthesis and functionalization of benzo[1,2-\textit{b}:4,3-\textit{b}']dithiophene (BDT, Figure 1) derivatives (4,5), which are an interesting class of π-conjugated systems in functional organic materials (6), and are key intermediates for the synthesis of inherently chiral thiahelicenes (7).

![Figure 1](image)

In this communication we will report our new field of investigation where we have focused on the development of π-conjugated BDT units bridged by silylene σ-linkages of general formula 1, as key intermediate to prepare active molecular or polymeric photoelectronic systems. We will discuss the synthesis of structures 1 along with the study of the optical, chemical and electrochemical properties.

Synthesis and structural studies towards palmitoyl ethanolamide analogues

Roberto Guizzardi, Mattia Vacchini, Sofia Magli, Giuseppe Montagna, Federica Arrigoni, Giuseppe Zampella, Barbara Costa, Laura Cipolla.

University of Milano-Bicocca, Department of Biotechnology and Biosciences, Piazza della Scienza 2, 20126 Milano, Italy;
 e-mail:laura.cipolla@unimib.it

Palmitoylethanolamide (PEA) is an endogenous fatty acid ethanolamide (FAE); FAEs are widely distributed in the central nervous system (CNS), the immune system, and the peripheral tissues of mammals, and have been shown to alleviate pain and inflammation, regulate motility and appetite, and produce anticancer, anxiolytic, and neuroprotective efficacies (1). However, despite being a NAE such as anandamide (AEA) or oleamide (OA), PEA doesn’t exhibit its affinity for the cannabinoid receptors CB1 and CB2 and cannot strictly be considered an endocannabinoid: the most robust evidence instead is for an action of PEA upon the nuclear receptor peroxisome proliferator-activated receptor alpha (PPAR-α) which is an ubiquitous transcription factor activated by various endogenous fatty acid derivatives.

PPARs are regulators of gene networks, controlling pain and inflammation. PEA’s actions are modulated mainly by its hydrolysis by two enzymes, fatty acid amide hydrolase (FAAH) and N-acylethanolamine-hydrolysing acid amidase (NAAA). These enzymes are also responsible for other acylethanolamines hydrolysis and their sequestration, in case of PEA’s pharmacological treatment, leads to an increase of other NAE’s levels, strengthening their analgesic action through different molecular mechanisms including the stimulation of cannabinoid receptor CB1, with associated undesirable side effects (2,3,4).

We propose here the synthesis of potential PPAR ligands and a preliminary computational study, based on the receptor structure, towards a library of metabolically stable PEA’s analogues with potential affinity toward PPAR-α.

References
Synthesis and Investigation of Croconates as Smart Organic Coating for Nobel Metals Nanoparticles

Beatrice Cogliati, Arturo Arduini, Andrea Secchi, Anna Painelli, Luca Seravalli

a Department of Chemistry, Life Sciences an Enviromental Sustainability – COFI unit – Parco area delle scienze 17/A. I-43124 Parma, Italy; b Istituto Materiali per Elettronica e Magnetismo IMEM-CNR, MBE Group, Parco Area delle Scienze 37/A – 43124 Parma, Italy.

Croconic acid is a cyclic organic molecule, belonging to a particular family of compounds called oxo-carbon acids. This molecule properly functionalized exhibit an absorption in NIR region and this property can be exploited in the design of NIR-harvesting materials obtained with a hybridization of a nano-material, characterized by a NIR absorption, with this organic molecule.

The purpose of this research is to combine a particular type of gold nanoparticles, called nanorods (AuNRs), with a specific aspect ratio (AR) in order to have an absorption in NIR region (900-1100 nm), with a croconic acid. This latter must be properly functionalized with an alkyl spacer (for example thiol-ending) in order to allow the anchoring to the AuNRs.

The difficulty is to detect a synthetic pathway for the synthesis of the croconic acid and here two strategies are proposed (Scheme 1), as reported in literature (1, 2). Gold nanorods are synthetized with a Seed-Mediated Growth method (3).

Flow chemistry as enabling technology for controlling the reactivity of fluorocarbenoids

Marco Colella\textsuperscript{a}, Flavio Fanelli\textsuperscript{a}, Giovanna Parisi\textsuperscript{a}, Leonardo Degennaro\textsuperscript{a}, Renzo Luisi\textsuperscript{a}

\textsuperscript{a} Department of Pharmacy-Drug Sciences, University of Bari “A. Moro” Via E. Orabona 4, Bari 70125 (Italy).

e-mail: marco.colella@uniba.it

Fluorinated compounds have attracted a great deal of interest by scientists involved in many fields of science and technology.\textsuperscript{(1)} However, despite their importance, the selective introduction of monofluoromethyl groups (-CH$_2$F) into a small organic molecule is still a challenging task. Unlike the extensive use of other halocarbenoids in organic synthesis,\textsuperscript{(2)} fluorocarbenoids are still considered the "beast" in carbenoid chemistry due to their chemical instability that severely limited its use in synthetic processes.\textsuperscript{(3)} In this communication, we report how we tried to face this challenge by employing flow microreactor technology. Fluorocarbenoids could be effectively generated and trapped with electrophiles providing a new successfully application of flash chemistry in short-lived intermediate reactions. Mechanistic insights and applications will be presented.\textsuperscript{(4)}

\textbf{Figure 1.} Strategies for the generation and trapping of highly reactive fluorocarbenoids.

References:
**TiCl₄-promoted Friedel-Crafts alkylations of arenes with alcohols**

**Alessandra Comandè, Emilia Lucia Belsito, Antonella Leggio, Valentina Papaionni and Angelo Liguori.**

*Dipartimento di Farmacia e Scienze della Salute e della Nutrizione, Università della Calabria, Edificio Polifunzionale, I-87013 Arcavacata di Rende, Italy.*
e-mail: alessandracomande@outlook.it

Alkylations of arenes are usually performed using alkyl halides and Lewis or Bronsted acids as catalysts. Complex and difficult to prepare catalysts are required when alcohols are used as the source of the electrophilic reactants needed to effect the initial step of the aromatic substitution. (1) Since titanium tetrachloride (TiCl₄) shows a great affinity for the oxygen atom (2) we chose it as suitable reagent to generate the specific electrophiles required for the Friedel-Crafts alkylation of aromatic substrates.

In a typical reaction, *p*-xylene (1 mmol) was treated, at room temperature, with benzyl alcohol (1 mmol) and pyridine (1 mmol) in the presence of non-catalytic TiCl₄ (4 mmol) using dichloromethane (CH₂Cl₂) as solvent. After 6 hours reacting 2-benzyl-1,4-dimethylbenzene was recovered as unique mono-alkylated reaction product in 65% yield. (Scheme 1)

![Scheme 1](image)

The reaction was then extended to activated and slightly deactivated aromatic systems providing mostly mono-alkylated products.

The alkylation mediated by TiCl₄ was also applied to other alkyl alcohols; in these cases the reaction proceeded at higher temperature and with longer reaction times. In particular *p*-xylene (1 mmol) was treated, at 80 °C, with 1-butanol (1 mmol) and pyridine (1 mmol) in the presence of TiCl₄ used also as solvent. The reaction was allowed to proceed for 24 hours, after which 1-sec-butyl-2,5-dimethylbenzene was obtained in 94% yield. (Scheme 2)

In all cases, small amounts of polyalkylation products are present.


---

**SOMMARIO – PROGRAMMA – MEDAGLIE E PREMI – KEYNOTE – ORALI- POSTER - AUTORI**
Synthesis and Characterization of DBF-based organic electrochromic materials

Giuseppina Anna Corrente\textsuperscript{a,b,c}, Amerigo Beneduci\textsuperscript{d}, Giuseppe Ciccarella\textsuperscript{c,e}, Agostina Lina Capodilupo\textsuperscript{e}

\textsuperscript{a}Department of Innovation Engineering, University of Salento, Via Monteroni, 73100-Lecce, Italy; \textsuperscript{b}Center for Biomolecular Nanotechnologies (CBN) Fondazione Istituto Italiano di Tecnologia (IIT), Via Barsanti 1, 73010-Arnesano, Italy; \textsuperscript{c}CNR Nanotec, Institute of Nanotechnology, Polo di Nanotecnologie c/o Campus Ecotekne, Via Monteroni, 73100-Lecce, Italy; \textsuperscript{d}Department of Chemistry and Chemical Technologies, University of Calabria, Via P. Bucci, Cubo 15D, 87036, Arcavacata di Rende, (Cs), Italy; \textsuperscript{e}Department of Biological and Environmental Sciences and Technologies, University of Salento, via Monteroni, 73100-Lecce, Italy;

e-mail: giuseppinaanna.corrente@unisalento.it

Electrochromism is the reversible change in optical properties that can occur when a material is electrochemically oxidized (loss of electron(s)) or reduced (gain of electron(s)), and it is of great academic and commercial interest. Even if, traditionally, materials have been considered as being electrochromic when they displayed distinct visible colour changes, the working definition of electrochromism has now been extended to include devices for modulation of radiation in the near infrared, thermal infrared and MW regions, so “colour” can now means a response by detectors at these wavelengths, and not just by the human eye (1,2).

Among the electrochromic materials is used to find mainly oxides of transition metals (W, V, Mo, Nb, Ti, Ni, Co and Ir), and conjugated polymers, but also organic molecules start to have a particular relevance. Among the organic molecules that present electrochromism in the NIR, the most interesting are the mixed valence (MV) compounds which are generally constituted by a conjugated core covalently linked to the arylamine groups.

We have designed and synthesized new organic compounds, T1-T2 and H1-H2 with the dibenzofulvene (DBF)-thiophene π-conjugated bridging unit and, respectively, two and four diarylamine redox centres (Fig.1). These four molecules not only differ in the number of diarylamine units but also for their anchoring positions: T1 and H1 are substituted in the 2,7- positions of the DBF instead T2 and H2 in the 3,6- (3).

![Chemical structures of 2,7- and 3,6- MVs compound.](image)

In these systems we exploited their NIR absorption capability and the electronic coupling highlighting the importance of connection through the central bridge and the importance of amine substituents in the right position on the bridge.

3-(Alkoxycarbonyl-2-Alkyliden)-2-Oxindoles: a new, enabling progeny of multidentate, vinylogous carbon nucleophiles for the direct, enantioselective, vinylogous michael addition to nitroolefins

Claudio Curti, a Lucia Battistini, a Andrea Sartori, a Gloria Rassu, b Franca Zanardi a

a Dipartimento di Scienze degli Alimenti e del Farmaco, Università di Parma, Parco Area delle Scienze 27/A, 43124 Parma, Italy; b Istituto di Chimica Biomolecolare del CNR, Traversa La Crucca 3, 07100 Li Punti Sassari, Italy
e-mail: claudio.curti@unipr.it

2-Oxindole and 2-ketoester moieties play important roles in Nature: the former is the core scaffold of a wide range of relevant biological and pharmaceutical molecules, while the latter appears in most crucial steps of biochemical processes as either donor or acceptor. In particular, due to their high degree of functionalization, α-enolizable 2-ketoesters have raised a wide interest in the field of organic synthesis, and in recent years, their role as valuable $d^2$-synthons has been reconsidered and exploited. In this context, we envisioned that merging the 2-oxindole scaffold with an enolizable 2-ketoester in the form of 3-(alkoxycarbonyl-2-alkyliden)-2-oxindoles of type C, would result in a vinylogous variant of B that retains its pro-nucleophilic character but with peculiar additional features. In fact, the C-$\gamma$ enolization of C by a suitable catalyst would generate a multidentate dienolate $C'$ embedding an exocyclic, captodative acrylate moiety, whose electronic nature and reactivity ($d^4$ vs $a^3$) is intriguing. Capitalizing on our ongoing researches on the pro-nucleophilic behavior of enolizable alkylidene heterocyclic systems, we unveiled the $d^4$-reactivity pattern of $C'$ in a direct, vinylogous, and enantioselective Michael addition to nitroolefins orchestrated by a chiral, bifunctional cinchona-thiourea catalyst. This reaction provided various almost enantiopure nitroalkylidene oxindoles D in excellent yields, complete $\gamma$-site regioselectivity, and unprecedented Z-diastereocontrol.

New “AIE” luminogens based on π-conjugated imidazolium salts

Francesca D’Anna\textsuperscript{a}, Vincenza Accurso\textsuperscript{a}, Carla Rizzo\textsuperscript{a}, Marta Feroci\textsuperscript{b}, Isabella Chiarotto\textsuperscript{b}, Salvatore Marullo\textsuperscript{a}, Renato Noto\textsuperscript{a}

\textsuperscript{a} Dipartimento STEBICEF-Sezione di Chimica, Università degli Studi di Palermo, Viale delle Scienze, Ed.17, 90128 Palermo. \textsuperscript{b} Dipartimento SBAI-Università La Sapienza, via Castro Laurenziano, 7, 00161 Rome

e-mail: francesca.danna@unipa.it

In the last few years a growing interest has been detected towards the obtainment of organic materials able to behave as luminogenic materials. These should exhibit excellent solid state fluorescence and they generally find applications in the preparation of organic photoelectric devices (1). In this context, a key role is played by the so-called “Aggregation Induced Emission luminogens”, i.e. organic compounds able to give a significant increase in the emission intensity as a consequence of an aggregation process.

Bearing in mind above information, and in the framework of our interest in studying properties and applications of fluorescent organic salts (2), we synthesized two push-pull imidazolium based systems differing in the nature of central spacer (1,4-diethynylphenyl or 1,6-diethynylpyrenyl). They were analyzed for their intramolecular charge transfer and self-assembly ability.

Results obtained using a combined approach of different techniques (DSC, TGA, CV, UV-vis and fluorescence spectroscopy, SEM) show that our organic salts behave as push-pull systems. Furthermore, they give self-assembly processes with “AIE” phenomena. Properties of organic salts as well as the ones of aggregates they are able to form, both in solution and solid state, are significantly affected by the nature of the central spacer.

References
Synthesis and biological evaluation of new heteroaryl amides active toward HIV Protease

Rosarita D’Orsi, a L. Chiummiento, a M. Funicello, a P. Lupattelli, a A. Pagano, a F. Tramutola a and F. Berti. b

a Department of Science, University of Basilicata, Via dell’Ateneo Lucano 10, 85100, Potenza, Italy.
bDepartment of Chemical and Pharmaceutical Science, University of Trieste, Via Giorgieri 1, 34127 Trieste, Italy.
e-mail: rosarita.dorsi@gmail.com

Great efforts have been done to the discovery of new drugs for the treatment of human immunodeficiency virus (HIV) infection. The knowledge of the structure of HIV protease and its substrate allowed to prepare specific HIV protease inhibitors. (1)(2) The concept of targeting the protein backbone in structure-based drug design prompted us to prepare new non-peptidic templates, (3) which can maximize interactions in the HIV-protease active site. Herein, a new synthetic strategy is proposed to obtain heteroaryl structures active toward HIV protease in few steps and high yield, from commercially available optically active epoxides. Different substitution patterns are introduced onto a given isopropanol-sulfonamide core, switching the central core, with the presence of either H or benzyl group, and the type of heteroarene connected to the core through a carboxyamide functionality (figure 1). In vitro inhibition activity will be evaluated by FRET methodology. Preliminary assaults showed a general beneficial effect of carboxyamide moiety, the IC₅₀ values ranging between 1 and 15 nM. (4) Docking analysis allowed to identify the favorable situation of benzofuryl derivatives in terms of number of interactions in the active site by extensive hydrogen bonding and hydrophobic interactions.

Pd nanoparticles obtained by pulsed laser ablation in liquid and applied to catalyzed ligand-free Suzuki reaction

Rosa D’Orsi, Lucia Chiummiento, Angela De Bonis, Maria Funicello, Paolo Lupattelli, Antonio Santagata, Roberto Teghil

*Department of Science, University of Basilicata, Via dell’Ateneo Lucano 10, 85100, Potenza, Italy. CNR-ISM, UOS Tito Scalo, C.da Santa Loja, 85010 Tito Scalo (PZ), Italy

e-mail: rosarita.dorsi@gmail.com

Nowadays nanoparticle catalysis is one of the most studied catalytic system because of their large surface area to volume ratio, their easy synthesis under mild condition and the possibility of catalyst recovery in order to replace costly metallic catalytic systems. Since palladium catalyzed cross-coupling reactions seems to be the most widely used method for generation of C-C bonds (1), it was studied a method to obtain palladium nanoparticle without use of toxic and costly solvents and reagents. Pulsed laser ablation in liquid can be considered as an efficient technique to produce metallic nanoparticles and nanostructures by one-step synthesis under benign condition.(2, 3) During the interaction of an intense laser pulse with a solid submerged in liquid, the formation of a plasma confined in a cavitation bubble can be observed. Inside the bubble, the rapid quenching of the high temperature plasma gets to the formation of polycrystalline NPs.(4) In this study we dispersed and quite spherical palladium nanoparticles were produced by pulsed laser ablation in liquid and they were used as catalyst in Suzuki cross-coupling reaction. Moreover, in order to compare the efficiency of the catalytic system, palladium nanoparticles were synthesized by direct reactions between ascorbic acid and a palladium salt, previously used in the Suzuki reaction.(5) The size and morphology of the obtained nanoparticles have been obtained by TEM and XRD techniques. Such prepared nanoparticles have been applied as catalyst for the formation of new C-C bond between methyl(E)-4-bromocrotonate and several aryl and heteroarylboronic acid. The reaction was carried out according to a protocol showing ligand-free palladium-catalyzed Suzuki cross-coupling and the better conditions using palladium nanoparticles were investigated to allow good yields of products.(6) Moreover, the catalysts were reused for different cycles of reaction without lost of activity.

Homo and hetero-nuclear 2D NMR techniques as useful tool for identification of cytotoxic compounds from complex extracts of *Urtica dioica*

Brigida D’Abrosca, Floriana Morgillo, Vittoria Graziani, Odeta Celaj, Fortunato Ciardiello, Antonio Fiorentino

Dipartimento di Scienze e Tecnologie Ambientali Biologiche e Farmaceutiche – DiSTABiF, Università degli Studi della Campania “Luigi Vanvitelli”, via Vivaldi 43 I-81100, Caserta, Italy; Dipartimento Medico-Chirurgico di Internistica Clinica e Sperimentale “F. Magrassi - A. Lanzara”, Università degli Studi della Campania “Luigi Vanvitelli” I-80131 Via Hansini, 5 - Napoli, Italy; e-mail brigida.dabrosca@unicampania.it

Nature have been a source of medicinal products for millennia with many useful drugs developed from plants. The natural product continued to play a highly significant role in drug discovery alone and/or as lead compounds (1). Most of chemotherapeutic agents for cancer treatment are molecules isolated from natural sources. In the search for new anticancer agents from plants (2), *Urtica dioica* has been investigated. Since ancient times *U. dioica* has been used in alternative medicine, but, only recently, different pharmacological properties of this plant extract, including those of an antioxidant, antimicrobial, antulcer and antiproliferative, have been documented. In particular, the effects of an aqueous extract of *U. dioica* against the MCF-7 (3), prostate cancer tissues (4) and HeLa cells (5) have been reported. Pursuing the assessment of the pharmacological properties of *Urtica dioica*, in the current work the evaluation of antiproliferative activities on panel of different NSCLC (non-small cell lung cancer) cell lines has been assayed. The active extracts have been investigated in order to identify the metabolites responsible for the activities. Extensive 2D-NMR investigations (HSQC, TOCSY, CIGAR-HMBC, H2BC, HSQC-TOCSY) allowed to identify different compounds belonging tethahydrofuranc lignans, flavonol glycosides, oxilipins classes as principal constituent of active extracts. In particular, these data suggested the presence of a ω-3 hydroxyl fatty acid derivatives as well as fatty acid derivative with cumulated double bond as constituent of polar and medium-polar extracts.

References:
Cyclic hexameric cyclopeptoids as mimics of enniatins and beauvericin mycotoxins

Assunta D’Amato, Raffaele Volpe, Giorgio Della Sala, Irene Izzo, Francesco De Riccardis

Department of Chemistry and Biology “A. Zambelli”, University of Salerno, Via Giovanni Paolo II, 132, Fisciano (SA), 84084 Italy; e-mail: asdamato@unisa.it.

Cyclic peptoids, oligomers of N-alkyl glycines, (1) have recently emerged as important examples of peptidomimetics for their interesting complexing properties and innate ability to permeate biological barriers. (2)

In the present work, we demonstrated that an assembly of properly chosen achiral oligopeptoids, once cyclized, can mimic the class of bioactive fungal cyclooligomer depsipetides enniatins and beauvericin (hybrid structures composed of α-amino acids and α-hydroxyacids), showing a broad spectrum of anticancer, antihelmintic, antibiotic, antifungal, insecticidal, hypolipidaemic and antiretroviral activities. (3) In order to understand the reasons of the enniatins/beauvericin class properties and with the idea to explore those held by the cyclic peptoids scaffold, we designed 1, 2, and 3 as structural mimics of enniatin B (enB), enniatin C (enC) and beauvericin, respectively (Figure 1). Analogs 4, 5 and 6, although not isomorph with natural enniatins/beauvericin, were included in the study in order to enlarge the scope of the investigation.

Figure 1. Cyclohexapeptoids synthetized and evaluated in the present work

Experimental data evidenced the intricate conformational and stereochemical properties of the synthesized molecules. In fact, complexation studies by NMR, in the presence of sodium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (NaTFPB) indicated that the conformationally stable host/guest metal adducts display architectural ordering comparable to that of the enniatins and beauvericin mycotoxins. Similarly to the natural depsipeptides, the synthetic cyclopeptoid analogs show a correlation between ion transport abilities in artificial liposomes and cytotoxic activity on human cancer cell lines.

The present communication demonstrates that the versatile cyclic peptoid scaffold, for its remarkable conformational and complexing properties, can mimic morphologically related natural products and elicit powerful biological activities.

Development of a green and efficient flow process for the preparation of NH-sulfoximines from sulfides and sulfoxides

Sonia De Angelis\textsuperscript{a}, Arianna Tota\textsuperscript{a}, Michael Andresini\textsuperscript{a}, Claudia Carlucci\textsuperscript{a}, Leonardo Degennaro\textsuperscript{a}, Renzo Luisi\textsuperscript{a}

\textsuperscript{a}Department of Pharmacy – Drug Sciences, University of Bari “A. Moro” Via E. Orabona 4, 70125 – Italy. FLAME-Lab–Flow Chemistry and Microreactor Technology Laboratory, Via E. Orabona 4, I-70125 e-mail: sonia.deangelis@uniba.it

A green and efficient flow process involving an heteroatom transfer (N or/and O) for the synthesis of sulfoximines from sulfides\textsuperscript{(1)} and sulfoxides\textsuperscript{(2,3)} is presented. Sulfoximines are emerging as drug motifs, ligand or auxiliaries for asymmetric synthesis and directing groups in C-H functionalization as well as agrochemical agents\textsuperscript{(4)}. We explored different N sources using flow reactors: ammonium acetate, ammonium carbamate, ammonium carbonate, ammonia in methanol and aqueous solution in the presence of diacetoxyiodobenzene (DIB) as oxidant. Interestingly the use of an aqueous solution allows the development of a greener protocol for the functionalization of a large variety of sulfides and sulfoxides.

\begin{figure}
\centering
\includegraphics[width=0.5\textwidth]{Figura1.png}
\caption{Continuous flow direct N- and O- transfer to sulfides and sulfoxides to give sulfoximines.}
\end{figure}

References:
Synthesis and Biological Evaluation of Novel Piperidinyl Iminosugar-Based Nucleosides

Maria De Fenza\textsuperscript{a}, Anna Esposito\textsuperscript{a}, Graciela Andrei\textsuperscript{b}, Robert Snoeck\textsuperscript{b}, Annalisa Guaragna\textsuperscript{a}, Daniele D’Alonzo\textsuperscript{a}

\textsuperscript{a}Dipartimento di Scienze Chimiche, Università degli Studi di Napoli Federico II, via Cintia 21, 80126, Napoli; \textsuperscript{b}Department of Microbiology and Immunology, Rega Institute for Medical Research, Herestraat 49, B-3000, Leuven, Belgium; e-mail: maria.defenza@unina.it

In recent times, the fusion of two principal concepts behind the research areas of glycomimetics and biomimetics has resulted in the development of a new class of molecules, defined as iminosugar-based nucleosides.\textsuperscript{(1)} On one hand, the structural mimicking of carbohydrates achieved by iminosugars has enabled to identify highly efficient modulators of the activity of carbohydrate processing enzymes. On the other hand, the conformational mimicking of natural nucleosides, achieved with sugar modified nucleoside analogues, revealed as a winning strategy for the treatment of viral infections.\textsuperscript{(2)} Accordingly a number of pyrrolidine-based nucleosides acting as excellent inhibitors of nucleoside processing enzymes have been identified so far, including Immucillin H (PNP inhibitor, \(K_i = 56\) pM) and Immucillin A (broad antiviral agent, e.g. anti-HCV). In this context, with the aim to expand the repertoire of such compounds, we have herein explored the synthesis of a variety of piperidinyl nucleosides 1-4.

Learning from the lesson of anti-HHV hexitol nucleosides,\textsuperscript{(2)} compounds 1-4 are conceived as conformational preorganized nucleosides, exploiting the rigidity of the piperidinyl core to improve inhibition potency and selectivity. Access to nucleosides 1-4 has been devised starting from the well-known glucosidase inhibitor 1-deoxynojirimycin (DNJ), (3) efficiently prepared with a general and highly selective procedure by a \textit{de novo} synthetic approach. (4)

Preliminary biological \textit{in vitro} assays of 3 revealed antiviral activity against a variety of DNA viruses (HSV-1 and 2, VZV, HCMV, Vaccinia Virus and Adenovirus).

3-azido-6-ethylcholane derivatives as potent and selective FXR agonists

Carmen Festa\textsuperscript{a}, Simona De Marino\textsuperscript{a}, Valentina Sepe\textsuperscript{a}, Vittorio Limongelli\textsuperscript{a,b}, Stefano Fiorucci\textsuperscript{c}, Angela Zampella\textsuperscript{a}

\textsuperscript{a} Department of Pharmacy, University of Naples “Federico II”, Naples, Italy; \textsuperscript{b} Institute of Computational Science – Center for Computational Medicine in Cardiology, Faculty of Informatics, Università della Svizzera Italiana, Lugano, Switzerland; \textsuperscript{c} Department of Surgery and Biomedical Sciences, Nuova Facoltà di Medicina, Perugia, Italy; e-mail: sidemari@unina.it

Considered for many years as the final product of cholesterol metabolism, bile acids (BAs) are experiencing a new life, being recognized as key signaling molecules. They exert their effects by interacting with membrane G-protein coupled receptors, including the bile acid receptor GP-BAR1, and nuclear receptors, mainly the farnesoid X receptor (FXR). In recent years, we have reported the chemical manipulation on chenodeoxycholic acid (CDCA) scaffold, with the aim to improve potency, efficacy and metabolic stability of endogenous BAs, affording several hit compounds with promising pharmacological profiles (1,2,3).

The introduction of an \(\alpha\)-ethyl group at C-6 on CDCA profoundly improves the activity of the endogenous BAs, giving the most potent dual FXR/GPBAR1 agonist, the 6-ethylchenodeoxycholic acid (6-ECDCA), also known as obeticholic acid. Its dual activity makes this compound a promising lead in the treatment of primary biliary cirrhosis (PBC) and steatohepatitis. However, the concomitant activation of GPBAR1 associates with potential side effects, including itching that represents a significant limitation to 6-ECDCA clinical use (4,5). As consequence, several efforts have been shifted towards the development of selective modulators. In the present communication, we have modified 6-ECDCA scaffold installing an azido/amino group at the C-3 position affording a small library with compound 2 as the most potent and selective FXR agonist of this series (6).

Asymmetric Phase-Transfer Catalysis by Chiral Calix[4]arene Derivatives

Nicola Alessandro De Simone\textsuperscript{a}, Rosaria Schettini\textsuperscript{a}, Carmen Talotta\textsuperscript{a}, Carmine Gaeta\textsuperscript{a}, Irene Izzo\textsuperscript{a}, Francesco De Riccardis\textsuperscript{a}, Giorgio Della Sala\textsuperscript{a}, Placido Neri\textsuperscript{a}

\textsuperscript{a}Dipartimento di Chimica e Biologia “A. Zambelli”, Università di Salerno, Via Giovanni Paolo II 132, I-84084 Fisciano (Salerno), Italy.

e-mail: ndesimone@unisa.it

Calix[n]arenes are a well-known class of macrocyclic compounds widely exploited in the field of molecular recognition for their three-dimensional shape and ease of functionalization, which make them good supramolecular hosts. It has long been known that calix[4]arene-amide hosts show a high affinity towards alkali metal cations, in particular K\textsuperscript{+} and Na\textsuperscript{+}. These cation-recognition abilities of calixarene-amides have been particularly exploited in many supramolecular applications, whereas their employment in phase transfer catalysis has surprisingly remained unconsidered. In particular, the approach proposed by Shinkai (3) and Taniguchi (4), using the cation-recognition abilities of calixarene-ethers, has not been considered. However, in the last years, examples of calixarene-based PTC have been proposed (5), in which the macrocycle merely acts as a scaffold bearing ammonium moieties as the real phase-transfer groups. To the best of our knowledge, no examples of asymmetric phase transfer catalysis exploiting the cation-recognition abilities of chiral calixarene-amide hosts have been so far reported. In the present communication, we will describe the synthesis of chiral calix[4]arene-amides 1-7, their recognition properties toward Na\textsuperscript{+} and K\textsuperscript{+} guests as TFPB salts, and their abilities as phase-transfer catalysts in the asymmetric alkylation of N-(diphenylmethylen)-glycine esters.

Antimony-oxo Porphyrins as Promising Photocatalysts for Visible Light Induced H-Atom Abstraction

Luca Capaldo,ᵃ Martin Ertl,ᵇ Maurizio Fagnoni,ᵃ Günther Knör,ᵇ Davide Ravelliᵃ

ᵃ PhotoGreen Lab, Dept. of Chemistry, University of Pavia, viale Taramelli 12, Pavia, Italy.ᵇ Institute of Inorganic Chemistry, Johannes Kepler University (JKU), 4040 Linz, Austria
e-mail: fagnoni@unipv.it

The use of photocatalytic reactions in organic synthesis has recently gained increasing attention due to the mild conditions involved and because they allow unconventional pathways. These reactions are based on the use of a photocatalyst (PC, Scheme 1), a species that is responsible for light absorption and, once in the excited state, for the activation of the substrates of the reaction through a chemical step. (1) Single Electron Transfer (SET) and Hydrogen Atom Transfer (HAT) are the typical activation modes of a PC. The former approach is undoubtedly the most investigated one, where visible light absorbing Ru- and Ir-polypyridyl complexes (PC_{SET}) led to the development of a hot topic, tagged as "photoredox catalysis" (Scheme 1a, left part). By contrast, HAT processes offer the possibility to cleave directly a C-H bond in the substrate (e.g. THF, Scheme 1a, right part). The main limitations to the development of this type of reactions are related to the classes of PCs able to promote HAT steps (PC_{HAT}; currently limited to the families of polyoxometalates and (aromatic) ketones) and to the use of UV light in place of visible light. (2,3)

Addressing the urgent need to develop visible light photocatalysts for promoting HAT processes, we report herein some preliminary results on the use of antimony-oxo porphyrin complexes, (4,5) such as I (Scheme 1b), for the formation of C-C bonds. We studied the Giese-type addition of tetrahydrofuran 1 onto unsaturated esters 2 as a model reaction, affording succinate 3 in up to 77% yield. Gratifyingly, the reaction could be extended also to different radical traps, such as unsaturated nitriles. Different light sources can be adopted, including (simulated) solar light and monochromatic LEDs (410 or 455 nm). The process is completely inhibited in the presence of radical scavengers, such as TEMPO, and, when the reaction is performed with an equimolar mixture of 1 and 1-ds, occurs with a kinetic isotopic effect (KIE) of 5.25.


Acknowledgements: D.R. thanks MIUR for financial support (SIR Project "Organic Synthesis via Visible Light Photocatalytic Hydrogen Transfer"; Code: RBSI145Y9R). G.K. is grateful for support by COST action CA15106 "C-H activation in organic synthesis".

---

SOMMARIO – PROGRAMMA – MEDAGLIE E PREMI – KEYNOTE – ORALI- POSTER - AUTORI
C-terminal methyl ester helical peptides can undergo a temperature-driven, reversible screw sense inversion. A spectroscopic study

Marta De Zotti\textsuperscript{a}, Giuliano Siligardi\textsuperscript{b}, Rohanah Hussain\textsuperscript{b}, Lorenzo Stella\textsuperscript{c}

\textsuperscript{a} Department of Chemistry, University of Padova, Via Marzolo 1, 35131 Padova; \textsuperscript{b} Diamond Light Source Ltd., Harwell Innovation Campus, Chilton, Didcot, Oxfordshire, UK; \textsuperscript{c} Dipartimento di Scienze e Tecnologie Chimiche, Università di Roma “Tor Vergata”, via della Ricerca Scientifica, Roma, Italy.

The C-terminus of natural peptides is never a methyl ester. However, post-translational modifications inserting esters on membrane proteins have been detected and associated with the ability of the protein to switch its 3D-structure (1). Here we describe how a methyl ester inserted at the C-terminus of the well-known, helical peptaibol trichogin GA IV dramatically reduced the rigidity of its helical 3D-structure. To this aim, we acquired synchrotron radiation circular dichroism spectra of a number of trichogin analogs in organic solvents at cryogenic temperatures, an environment that closely resembles membrane. We found that by replacing the native C-terminal 1,2-aminoalcohol leucinol of trichogin with a leucine methyl ester or free carboxylic acid, at room temperature the helical handedness was inverted from right to left at cryogenic temperatures showing an isodichroic point. Back at room temperature, the native right-handed helical conformation was regained revealing the presence of a thermally-driven peptide helical handedness switch.

On the other hand, the temperature-dependence of the peptide conformation using fluorescence and EPR spectroscopies of suitably functionalized analogs revealed that the well-characterized, mixed $3_{10}$-$\alpha$-helical structure adopted by trichogin at room temperature was also retained at cryogenic temperatures.

Synthesis, conformation analysis, and proteolytic stability of helical peptide inhibitors of the VEGF/VEGFR protein-protein interaction

M. De Zotti\textsuperscript{a}, G. Bocchinfuso\textsuperscript{b}, S. Raniolo\textsuperscript{b}, A. Palleschi\textsuperscript{b}, F. Formaggio\textsuperscript{a}, D. Arosio\textsuperscript{d}, M. Pinoli\textsuperscript{d}, U. Piarulli\textsuperscript{d}, S. Zanella\textsuperscript{e}, L. Pignataro\textsuperscript{b}, L. Belvisi\textsuperscript{e}, C. Gennari\textsuperscript{e}, L. Stella\textsuperscript{b}

\textsuperscript{a} Department of Chemistry, University of Padova, 35131 Padova, Italy; \textsuperscript{b} Department of Chemical Sciences and Technologies, University of Rome ‘Tor Vergata’, 00133 Rome, Italy; \textsuperscript{c} ISTM CNR, 20133 Milan, Italy; \textsuperscript{d} Center for Research in Medical Pharmacology, University of Insubria, 21100 Varese, Italy; \textsuperscript{e} Department of Chemistry, University of Milan, 20133 Milan, Italy;
e-mail: marta.dezotti@unipd.it

Angiogenesis is a key target in cancer therapy. With the aim at regulating this process, we recently designed, synthesized and investigated an array of peptides based on the IDNEWRTKQ sequence of the vascular endothelial growth factor (VEGF)-C. The new peptides were optimized to increase both helix stability and binding affinity towards the VEGF receptors. In particular, we exploited the known helix-inducing capabilities of C\textsuperscript{a\textprime}-tetrasubstituted \( \alpha \)-amino acids to stabilize the secondary structure of our peptides. By adding such non-coded residues we gained in proteolytic stability, as well. In addition, we inserted Trp residues at appropriate positions to enhance the binding affinity.

The conformational preferences of our peptides were investigated by CD and 2D-NMR in aqueous solution. Data analysis confirmed the onset of helical structures. Interestingly, we observed that the absorption bands in the near-UV of the indole (Trp) chromophore constitute a reliable probe to assess the conformational stability of our helical peptides. In this presentation we will correlate this CD feature to the information extracted from the NMR analysis. Our new VEGFR antagonists exhibit high binding affinity for the receptor, and biological activity against VEGF-mediated angiogenesis.
Tosylhydrazones as Powerful Tools for the Construction of $sp^3$-$sp^2$ and $sp^2$-$sp^2$ Carbon Bonds: A Novel Approach to Conjugated and Skipped 1-Alkoxydienes

Annamaria Deagostino, Stefano Parisotto

Dipartimento di Chimica – Università di Torino, via Giuria, 7, 10125 Torino.
e-mail: annamaria.deagostino@unito.it

$N$–tosylhydrazones have attracted large attention in organic synthesis as safe alternative for the *in situ* generation of unstable diazo compounds. Moreover they are easily accessible, also on large scale, by condensation between $p$-toluenesulfonyl hydrazide and carbonyl compounds, or by sulfonylation of a preformed hydrazone. Their high synthetic potential arises from the easy generation of many unstable species, with differing reactivity by choosing the appropriate procedure and tuning the reaction conditions. For instance, in the early 50’s, Bamford and Stevens discovered that upon treatment with strong bases, tosylhydrazones afford alkenes in high yields.\(^1\) Fifteen years later Shapiro reported that aliphatic tosylhydrazones containing an $\alpha$ hydrogen, react with alkyllithium reagents to yield vinyllithium intermediates.\(^2\) Later on, their ability to generate reactive metal carbenes has triggered renewed interest in these reagents. In 2007, Barluenga and co-workers reported the first example of $N$-tosylhydrazones used as nucleophilic partners in palladium catalyzed cross couplings.\(^3\)

Recently, we started to investigate over the possibility to build 1–alkoxy–1,3–dienes exploiting tosylhydrazones peculiar reactivity. Inspired by Xiao and colleagues, who reported the synthesis of highly substituted butadienes through a palladium catalyzed three component reaction between allenes, aryl iodides and diazocompounds,\(^4\) we set up a similar reaction using alkoxyallenes.

Unfortunately, due to their different electronic properties, it is not possible to promote a similar multicomponent process. Surprisingly a 4,4$'$-diaryl-1–alkoxy–1,3–diene is recovered, which clearly appears to be the product of a two component process competing with the expected reaction (Scheme 1, right). Moreover, when the same reaction conditions are applied to acetophenone tosylhydrazones, a completely different regioselectivity is observed (Scheme 1, left).

![Scheme 1](image-url)

> Scheme 1 General scheme for the Pd catalyzed cross couplings of alkoxyallenes with benzo- and acetophenone tosylhydrazones

References:
Proteomics Approaches to Elucidate Bioactivity of Monacolin K

F. del Gaudio\textsuperscript{a,b}, M. Rontogianni\textsuperscript{c,d}, K. Stecker\textsuperscript{c,d}, M.C. Monti\textsuperscript{a}, R. Riccio\textsuperscript{a}, A.J.R. Heck\textsuperscript{c,d}, A.F.M. Altelaar\textsuperscript{c,d}

\textsuperscript{a}Department of Pharmacy, University of Salerno, Via Giovanni Paolo II, 132, 84084 Fisciano (SA), Italy.
\textsuperscript{b}Farmaceutici Damor S.p.A, Via E. Scaglione 27, 80145 Naples, Ital.
\textsuperscript{c}Biomolecular Mass Spectrometry and Proteomics, BijvoetCenter for Biomolecular Research and Utrecht Institute for Pharmaceutical Sciences, Utrecht University, Padualaan 8, 3584 CH Utrecht, The Netherlands.
\textsuperscript{d}Netherlands Proteomics Centre, Padualaan 8, 3584 CH Utrecht, The Netherlands.

\textsuperscript{e}e-mail: fdelgaudio@unisa.it

MS-based proteomics represents a clever tool to disclose unclear molecular bioactivities of small molecules (1,2) such as natural compounds in nutraceuticals. The latter is raising as significant building block in prevention or/and treatment of numerous diseases (3). Monacolin K (MNK) from \textit{Monascus purpureus} is known as lovastatin, an HMG-CoA reductase inhibitor used to lower hematic concentration of cholesterol. Scientific evidences link statins to antiproliferative and apoptotic effects in a wide panel of cancers. MNK is particularly active on Triple Negative Breast Cancer (TNBC) cell lines such as MDA-MB 231(4). In this study, we investigated how MNK affects protein expression and phosphorylation in MDA-MB 231 cells. Preliminarily, a kinetic proliferation assay was performed using IncuCyte ZOOM\textsuperscript{®} system to find out the IC\textsubscript{50} of MNK and to set up proteomics experiments. Then, living MDA-MB 231 cells where treated with MNK and harvested at different time points. Each of the peptides mixtures, obtained upon extraction and digestion of proteomes, was tagged with one of the isotopomeric amine-reactive Tandem Mass Tags (TMT 10-plex\textsuperscript{™}) and then pooled together (5). After HpH fractionation and phospho-enrichment, in the case of phosphoproteome analysis, UPLC-MS/MS of the obtained multiplexed pools was carried out: bioinformatic analysis of the MS data revealed changes in proteome and phosphoproteome of MDA-MB 231 due to MNK.


Paolo Della Sala\textsuperscript{a}, Amedeo Capobianco\textsuperscript{a}, Tonino Caruso\textsuperscript{a}, Carmen Talotta\textsuperscript{a}, Margherita De Rosa\textsuperscript{a}, Placido Neri\textsuperscript{a}, Andrea Peluso\textsuperscript{a} and Carmine Gaeta\textsuperscript{a}

\textsuperscript{a}Dipartimento di Chimica e Biologia, A. Zambelli, Università di Salerno, Via Giovanni Paolo II 132, 84084 Fisciano (Salerno), Italy; e-mail: pdellasala@unisa.it

CycloParaPhenylene s ([n]CPPs) are fully conjugated macrocycles constituted by \(n\) para-linked benzene units (Figure), which exhibit size-dependent optical and electronic properties (1,2). Among them, they exhibit the narrowing of the HOMO-LUMO gap as the number of aromatic units decreases (2). Consequently, the emission spectra of CPP derivatives are red-shifted and quantum efficiency decreases as the macrocycle become smaller (2). CPPs, can be considered useful template for the bottom-up synthesis of single wall carbon nanotubes (3). Recently, many efforts have been devoted to study the triplet-triplet annihilation (TTA)-based upconversion processes (4). Upconversion represents a emerging wavelength-shifting technology, useful to convert low energy photons into light adequate for photovoltaic, photocatalysis and bioimaging (5). In TTA-based upconversion systems, the photon excitation of a triplet sensitizer (e.g.: octaethylporphyrin Pd complex, PdOEP in Figure), affords a triplet energy transfer toward an acceptor which give rise to upconverted fluorescence. Cycloparaphenylenes are known as excellent chromophores exhibiting high fluorescence quantum yields, however, to the best of our knowledge, no data is currently available about their abilities to act as emitter (acceptor) into upconversion schemes. Prompted by these considerations, we wish to describe here the synthesis of the new anthracene-incorporated [8]CPP macrocycle 1 (Figure). In addition, details on the conformational features, optoelectronic and upconversion properties of this new derivative will be given.

Multi-purpose metal-free dyes for energy and hydrogen production.

Alessio Dessì\textsuperscript{a}, Massimo Calamante\textsuperscript{a,b}, Alessandro Mordini\textsuperscript{a,b}, Lorenzo Zani\textsuperscript{a}, Gianna Reginato\textsuperscript{a}.

\textsuperscript{a} Istituto di Chimica dei Composti Organometallici (CNR–ICCOM), Via Madonna del Piano 10, 50019 Sesto Fiorentino (FI), Italy; \textsuperscript{b} Dipartimento di Chimica “U. Schiff”, Università degli Studi di Firenze, Via della Lastruccia 13, 50019 Sesto Fiorentino (FI), Italy.

\textit{e-mail: adessi@iccom.cnr.it}

Sunlight is, by far, the most abundant, economic and well distributed energy source over the world. For this reason, many different photovoltaic technologies exploit solar energy in order to produce electric current or eco-friendly fuels as hydrogen (1). Organic chemistry can play a pivotal role in the field of renewable energies because totally organic molecules are often the most suitable candidates as photoactive materials, thanks to their unique optical and electrochemical properties which can be finely tuned through a balanced modification of the structure of the compounds.

Our first interest in this field was the design and the synthesis of organic dyes as photoactive materials for Dye-Sensitized Solar Cells (DSSCs) (2), a very promising photovoltaic technology which is currently finding its market niche where the traditional silicon solar cells cannot be used. Recently we decided to broaden our horizons exploring new applications of our molecules toward other research fields which involve the exploitation of sunlight, such as in the photo-catalyzed production of hydrogen (3), or the employment of solid-state hole-transport materials (ss-HTMs) for DSSCs and PSCs (Perovskite Solar Cells) (4).

Our main interest was that of studying the influence of small structural modifications, such as the substitution of some functional groups or the insertion of alkyl chains in different regions of the molecules, on the physical and electrochemical properties of the dye, and on the efficiency of the final photovoltaic devices.

References:
Silibinin phosphate-based flavonolignans: new emerging synthetic metabolites with interesting pharmacological properties

Giovanni Di Fabio, Valeria Romanucci, Raffaele Gravante and Armando Zarrelli

Department of Chemical Sciences, University of Napoli ‘Federico II’, Via Cintia, I-80126 Napoli, Italy

Many drug candidates have been reported to possess a strong therapeutic potential in vitro but they have failed in vivo because of their poor pharmacokinetic behaviour, very often due to the low water solubility. There are many formulations and drug design strategies that can be used to overcome solubility issues. The design and synthesis of soluble pro-drugs is one of the most common approach used. In this frame, the phosphate group is a useful tool for the enhancement of aqueous solubility of phenolic and other metabolites, in addition it displayed excellent chemical stability and rapid bioconversion in vivo to the parent drug by phosphatases. On the other hand, also the conjugation of specific molecules recognized by a receptor on the target cell could be a successful strategy (1).

In our studies, we have combined both aspects through the synthesis of new phosphodiester modified Silibinin with a good water solubility, as well as, attractive antioxidant properties (2,3). In the past decade, Silibinin has received more attention due to its large variety of activities ranging from anticancer and chemopreventive actions (4,5) to hypocholesterolemic, cardioprotective and neuroprotective (6,7) activities. Unfortunately, the bioavailability and the therapeutic efficiency of Silibinin are rather limited by its low water-solubility. In this work, we present the synthesis of a new library of modified Silibinins (Figure) and related studies of their redox behaviour.

Exploiting the selective protection of the hydroxyl groups of the Silibinin, we developed an efficient strategy for the synthesis of Silibinin phosphate-based flavonolignans consisting of phosphodiester glycoconjugates and dimers of Silibinin. The water solubility, the radical scavenger efficiency and the ability to scavenge different reactive oxygen species (ROS) have been evaluated for the new phosphodiester modified Silibinins in comparison to Silibinin. Moreover, the serum stability, and their cytoprotective (X/XO assay on HepG2 cells) behaviours have been studied. The remarkable antioxidant activity and the high water solubility (compared to Silibinin) make Silibinin phosphate-based flavonolignans promising molecules for future studies.

Unprecedented “On-Water” Nucleophilic Addition of Organolithiums and Grignard Reagents to Imines and Nitriles

Giuseppe Dilauro, Marzia Dell’Aera, Paola Vitale, Filippo Maria Perna, Vito Capriati

Dipartimento di Farmacia-Scienze del Farmaco, Università degli Studi di Bari “Aldo Moro”, Consorzio C.I.N.M.P.I.S., Via E. Orabona, 4, I-70125 Bari, Italy; e-mail: giuseppe.dilauro@uniba.it

Despite their enormous synthetic relevance, the use of polar organolithium and Grignard reagents is greatly limited by their requirements of low temperatures in order to control their reactivity as well as the need of dry organic solvents and inert atmosphere protocols to avoid their fast decomposition. One of most momentous challenges in organic synthesis is to perfect the use of polar organometallics under air at room temperature, also replacing harsh and volatile organic compounds by more environmentally benign solvents (1).

Building on our recent findings (2,3,4), in this Communication we describe an unprecedented nucleophilic addition of Grignard and organolithium reagents to both aliphatic and aromatic imines and nitriles under “on water” conditions (5). It will be shown that, under optimized protocols, the above additions can be conveniently and safely run at room temperature and under air en route to secondary amines and tertiary carbinamines, which were isolated in up to >98% yield (Scheme 1). This methodology opens up new opportunities to push even more polar organometallic chemistry towards “green” horizons.

Scheme 1


Acknowledgments: This work was financially supported by the University of Bari within the framework of the Project “Sviluppo di nuove metodologie di sintesi mediante l’impiego di biocatalizzatori e solventi a basso impatto ambientale (code: Perna01333214Ricat) and the InterUniversities Consortium CINMIPS.
Asymmetric Synthesis and Antiviral Activity of Novel Carbocyclic Nucleosides

Anna Esposito\textsuperscript{a}, Maria De Fenza\textsuperscript{a}, Graciela Andrei\textsuperscript{b}, Robert Snoeck\textsuperscript{b}, Giovanni Talarico\textsuperscript{a}, Annalisa Guaragna\textsuperscript{a}, Daniele D’Alonzo\textsuperscript{a}

\textsuperscript{a}Department of Chemical Sciences, University of Naples Federico II, Via Cintia, 80126 Naples, Italy; \textsuperscript{b}Department of Microbiology and Immunology, Laboratory of Virology and Chemotherapy, Rega Institute for Medical Research, Herestraat 49, B-3000, Leuven, Belgium
e-mail: anna-esposito@outlook.com

Cyclohexenyl nucleosides (Figure 1) represent well-known biomimetic agents, working as bioactive nucleoside analogues, either at monomeric and oligomeric level (1) or as substrates/templates for enzymatic replication (2). These properties are due to the capacity by the cyclohexenyl ring to act as a conformational bioisostere of natural deoxyribose. Indeed, the flexible nature of cyclohexenyl nucleosides, rapidly fluctuating between the low energy $^2$H$_3$ and $^3$H$_2$ conformations, enables a close resemblance with the bioactive sugar ring puckers ($^2T_3$ and $^3T_2$) of natural nucleosides (Figure 1). Not surprisingly, when evaluated as antiviral agents, both D- and L-cyclohexenyl nucleosides (1 and ent-1) exhibited comparable in vitro anti-HHV (Human Herpes Virus) properties than those of some of the most efficient drugs currently in use on the market (1).

\textbf{Figure 1.} Bioactive D- and L-cyclohexenyl nucleosides 1 and ent-1.

With the aim to expand the repertoire of these bioactive nucleosides, we are currently exploring the antiviral properties of novel cyclohexenyl nucleosides 2 and ent-2, lacking the OH group at C5' position and therefore being conceived as chain terminators. Herein, the asymmetric synthesis of 2 and ent-2 (B = Pu or Py) starting from achiral cyclohexanone is reported (Figure 2). Main attention has been devoted to the key Tsuji-Trost rearrangement step of 3 and ent-3, whose unprecedented stereoconvergent outcome has been studied by chemical methods, as well as, by spectroscopic and \textit{in silico} analysis.

\textbf{Figure 2.} Synthesis of novel D- and L-cyclohexenyl nucleosides 2 and ent-2.

Preliminary in vitro assays against a variety of HHV infections are also presented, revealing interesting antiviral properties, especially against TK- strains.

Elucidating the role of tanshinone IIA and cryptotanshinone in neuroinflammation through molecular docking studies

Simona De Vita\textsuperscript{a}, Maria Giovanna Chini\textsuperscript{a}, Francesco Maione\textsuperscript{b}, Nicola Mascolo\textsuperscript{b}, Giuseppe Bifulco\textsuperscript{a}

\textsuperscript{a}Department of Pharmacy, University of Salerno, Via Giovanni Paolo II 132, 84084, Fisciano, Salerno, Italy; \textsuperscript{b}Department of Pharmacy, School of Medicine, University of Naples Federico II, Via Domenico Montesano 49, 80131, Naples, Italy.

e-mail: sdevita@unisa.it

Alzheimer's disease (AD) is a common form of dementia mainly characterized by the deposition of neurofibrillary tangles and β-amyloid (Aβ) peptides in the brain and a neuro-inflammatory state (1). Beside synthetic drugs, the use of natural compounds represents a valid therapeutic alternative for the treatment of AD. Among these, the root of \textit{Salvia miltiorrhiza} Bunge (also known as Danshen) used for the treatment of cardiovascular, cerebrovascular disease and CNS functional decline in Chinese traditional medicine is one of the most representative examples (2). Thus, we have investigated the role of tanshinone IIA (TIIA) and cryptotanshinone (CRY), two of the main components of the Danshen, in neuroinflammation by a multidisciplinary approach. Biological data showed a reduced activation of COX-2 and iNOS and an inhibition of the NF-κB/IκB-α signaling pathway (3). Therefore, we examined the ability of these compounds to bind NF-κBp65 with an in silico methodology. In particular, we performed molecular docking experiments of the active secondary metabolites on NF-κBp65 and we concluded that CRY and TIIA interact in similar way with it (Figure 1). In addition, because no structure containing NF-κBp65 has been crystallized yet, we decided to use the software SiteMap (4) to highlight the possible binding sites on the target surface. Interestingly, the most probable one (Figure 1, top), was located in the DNA-binding domain and the docking results showed that both molecules interacts with Arg30, which has been previously proven to be an important site of methylation in the NF-κBp65 activation process (5). These suggest that CRY and TIIA may be used in the treatment of AD and could act as direct inhibitors of NF-κBp65.


\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure1.png}
\caption{Binding site on NF-kBp65 (top) and binding mode of CRY (A) and TIIA (B).}
\end{figure}
Microwave synthesis and preliminary evaluation of 2-amino-3,4-dihydropyrimidine BACE-1 inhibitors

**Fulvia Felluga**, Fabio Benedetti, Federico Berti, Luca Buiatti, Sara Drioli, Giuseppe Marino, Giorgia Regini

Dipartimento di Scienze Chimiche e Farmaceutiche, Università di Trieste, Via L. Giorgieri 1, 34127 Trieste. e-mail: ffelluga@units.it

The guanidine functional group is one of the most widely used motifs in the design and synthesis of new compounds with appealing pharmacological properties. This structural unit is present in a large number of natural products (1) and bioactive compounds, (2) playing important roles in medicinal chemistry.

Of particular interest is the incorporation of this moiety into a dihydropyrimidine scaffold. Functionalized 3,4-dihydropyrimidines are accessible in a single step from readily available starting materials by Biginelli reaction, a three component cyclocondensation (3) in which urea or thiourea are reacted with an aldehyde and a β-ketoester.

A large choice of optimized experimental protocols with variations in the three building blocks is available in the literature, (3) giving access to 2-oxo- and 2-thioxodihydropyrimidine derivatives that have exhibited a large spectrum of biological properties.

On the contrary, very few general Biginelli protocols based on the use of guanidine, and leading to the corresponding substituted 2-amino-3,4-dihydropyrimidines are reported in the literature.

Due to the great potential of this functional group when included in an heterocyclic scaffold and in the frame of a research aimed at finding low molecular weight compounds of medicinal interest, we found a simple and practical method for the microwave assisted Biginelli cyclocondensation of guanidine hydrochloride with aldehydes and β-dicarbonyl compounds, affording a large set of differently functionalized 2-amino-3,4-dihydropyrimidines in short reaction times and good yields.

These compounds were found to display a marked *in vitro* inhibitory activity towards BACE 1, an aspartyl protease involved into the pathogenesis of Alzheimer Disease,(4) with IC$_{50}$ values in the micromolar and sub-micromolar range.

Combinatorial approach for the discovery of novel microsomal prostaglandin E\(_2\) synthase-1 (mPGES-1) inhibitors

**Maria Giovanna Chini**\(^a\), Assunta Giordano\(^b\), Ciro Milite\(^c\), Donatella Rescigno\(^d\), Sabrina Castellano\(^e\), Raffaele Riccio\(^a\), Vincenza Cantone\(^d\), Oliver Werz\(^d\), Giuseppe Bifulco\(^a\)

\(^a\)Department of Pharmacy, University of Salerno, Italy; \(^b\)Institute of Biomolecular Chemistry (ICB) - Consiglio Nazionale delle Ricerche (CNR), Italy; \(^c\)Department of Medicine and Surgery, University of Salerno, Italy; \(^d\)Department of Pharmaceutical/Medicinal Chemistry, Institute of Pharmacy, University of Jena, Germany.

E-mail: mchini@unisa.it

Microsomal Prostaglandin E syntase 1 (mPGES-1) has been recognized as a novel, promising target for anti-inflammatory and anticancer drugs development being involved in a number of pathologic conditions including arthritis, cancer and Alzheimer’s disease (1). MPGES-1 is the terminal enzyme in the prostaglandin (PG) biosynthesis pathway and catalyzes the conversion of prostaglandin H\(_2\) (PGH\(_2\)) to prostaglandin E\(_2\) (PGE\(_2\)). It is an inducible enzyme and its expression is increased in response to pro-inflammatory stimuli. This feature makes mPGES-1 extremely interesting for drugs development because its inhibition is connected to the suppression of inducible PGE\(_2\) responsible for inflammatory and tumor pathologies that should reduce the typical side effects of the COX-2 inhibitors commercially available (2). Thanks to the resolution human mPGES-1 X-ray structure (3), and starting from our previous results (4-6), we report the structure based drug design of new inhibitors against mPGES-1 through a combinatorial approach. We have selected two different ‘privileged structures’: a) 2-aminobenzothiazoles and b) 1,2,3,4-tetrahydro-5H-benzo[e][1,4]diazepin-5-one scaffolds, which can be easily manipulated to provide a number of highly functionalized potential ligands. Starting from the analysis of the synthetic procedures (7, 8), in fact, we have combined (Enumerate phase) (9) and evaluated (Virtual Screening Workflow) (9) all the commercially available synthons in silico before the chemical synthesis, obtaining in this way a large libraries (millions of compounds) that have been prepared and screened against mPGES-1 (dedicated software: CombiGlide, Schrödinger LLC.) (9). The possible inhibitors have been selected by a qualitative computational filter, based on the accordance with specific key interactions with the receptor counterparts, predicted free energy of binding and ligand efficiency, leading to the identification of a focused set of compounds selected for the subsequent phases of chemical synthesis and biological evaluation (cell free and cell-based assays). Following this workflow, we have identified a set of new mPGES-1 inhibitors, all endowed with low micromolar activity. Moreover, the ongoing lead optimization phases will be step-by-step supported by the prediction of the pharmacokinetic properties (dedicated software: QikProp, Schrödinger LLC.) (9), essential to discard the compounds with unfavorable predicted ADME properties that fall outside the normal range of known drugs, eliminating unnecessary testing on compounds that will ultimately fail.

Oxidation of amines to carbonyl compounds and nitriles by ball milling

Silvia Gaspa\textsuperscript{a}, Lidia De Luca\textsuperscript{a}

\textsuperscript{a} Dipartimento di Chimica e Farmacia, Università degli Studi di Sassari, via Vienna 2, 07100 Sassari, Italy

The oxidation of amines is a powerful method to produce various important synthetic intermediates such as carbonyl compounds and nitriles (1,2,3). The classical methodologies suffer of many drawbacks (4,5) such as use of toxic metal-containing reagents, toxic solvents and overoxidation of carbonyl compounds. To overcome these problems we have investigated a new mild, efficient, metal-free and solvent-free oxidation of primary amines to aldehydes, ketones and nitriles under ball-milling conditions at room temperature. This approach is simple, convenient and uses inexpensive and commercially available reagents. In addition this method is compatible with various functional groups and requires easily accessible starting materials. Simple filtration of the reaction mixture through pad of silica gel affords pure aldehydes, ketones and nitriles products.

References:
New triimidazole derivatives: intriguing cases of photoluminescence behavior

Clelia Giannini\(^a\), Elena Lucenti\(^b\), Alessandra Formi\(^b\), Chiara Botta\(^c\), Lucia Carlucci\(^a\), Daniele Marinotto\(^a\), Andrea Previtali\(^b\), Stefania Righetto\(^a\), Elena Cariati\(^a\)

\(^a\) Department of Chemistry, Università degli Studi di Milano, via Golgi 19, 20133 Milano, Italy; \(^b\) ISTM-CNR, Via Golgi 19, 20133 Milano (Italy); \(^c\) ISMAC-CNR, Via Corti 12, 20133 Milano, Italy

e-mail: clelia.giannini@unimi.it

Solid-state luminogens have been the subject of great interest because high tech applications of light emitting materials very often require their use in the condensed phase. Unfortunately, frequently, weakly or even non-emissive solid materials are obtained from highly emissive molecules due to the notorious aggregation caused quenching phenomenon. However, since the pioneering work of Tang (1), many efforts have been spent on the isolation of compounds characterized by the opposite behavior, referred to as Aggregation Induced Emission (AIE). In parallel, a strong effort has been devoted to the search of organic molecules with long-lived excited states which enable exciton migration over long distances for increased production of free charges (2). Very recently, An et al. reported ultra-long phosphorescent emission features in structures of planar organic molecules coupled in H-aggregates, which provide an effective means of stabilizing and protecting the triplet excitons formed through intersystem crossing (3). The stabilized excited state, which functions as an energy trap at a lower energy level, may delocalize on several neighboring molecules, offering suppressed radiative and non-radiative deactivation decay rates in favour of long-lived excited states and ultralong phosphorescence. Here we report three simple pure organic AIE compounds, namely cyclic triimidazole (trimidazo[1,2-a:1′,2′-c:1″-e][1,3,5]triazine) and its mono- and di-brominated derivatives, showing at room temperature in powder simultaneous molecular fluorescence and phosphorescence and aggregated ultralong phosphorescence (4). The nature of the emissive behavior is verified and interpreted through complete photophysical characterization in solution, powders and matrix dispersed thin films and by theoretical calculations and structural determination. Our experimental data reveal that luminescence lifetimes up to 1 s, which are several orders of magnitude longer than those of conventional organic fluorophores, can be realized under ambient conditions thus expanding the class of organic materials for phosphorescence applications.

Rational Design of Ready-to-Shape New Classes of Organo-Photocatalysts

Andrea Gini\textsuperscript{a,b}, Mustafa Uygur\textsuperscript{b}, Olga García Mancheño\textsuperscript{a,b}

\textsuperscript{a} Universität Regensburg, Universitätsstraße 31, 93053 Regensburg; \textsuperscript{b} Wissenschaftszentrum Straubing, Schulgasse 22, 94315 Straubing.

\textit{e-mail: andrea.gini@chemie.uni-regensburg.de}

Over the past last decade, the renewed interest around photoredox catalysis resulted in a continuous flux of many valuable light-induced synthetic transformations.(1,2) Even though there are several advantages of a photoredox-mediated approach respect to standard thermal processes, most common catalysts are based on expensive noble transition metals, such as iridium and ruthenium.(1) Moreover, they might contaminate the products, which is especially undesirable in the synthesis of pharmaceuticals. Thus, the use of organo-photocatalysts represents a valuable and attractive alternative, mainly because organic dyes are cheaper, harmless and easy to handle than the corresponding metal-based photocatalysts.(2) As follows, it is evident the advantage coming within the employment of such organic photosensitizers, but the exiguous variety of structures, which are based essentially on fluorescein, rhodamine, eosin and 9-mesityl-10-methylacridinium salt platforms, limit the possible applications. For this reason, new classes of organo-photocatalysts are highly demanding to both discover new synthetic solutions and improve the performance in standard catalytic photoredox reactions.

Following this perspective, we present herein several innovative one-pot strategies to achieve new classes of easily tunable and ready-to-shape (thio)xanthene or acridine-based photocatalysts, in which a Csp\textsuperscript{3}-H oxidative functionalization is involved as key step of the synthetic approach.(3,4) Furthermore, to show the potential and the versatility of such new structures, various applications in photoredox-catalysis are reported.

Visible light induced C-H α,α-difluoroacetophenone functionalization of electron-rich arenes: A viable option for difluoromethyl functionalization

Simone Giorgi, Olugbeminiyi O. Fadeyi, Philippe Nuhant, Enrico Marcantoni, Gabriele Lupidi, Federico V. Rossi, Neal W. Sach and Jotham W. Coe

a School of Science and Technology, Chemistry Division, University of Camerino, Via S. Agostino I, 62032 Camerino Italy. b Worldwide Medicinal Chemistry, Pfizer Inc., 445 Eastern Point Road, Groton, Connecticut 06340, United States. c Department of Chemistry, La Jolla Laboratories, Pfizer Inc., 10770 Science Center Drive, San Diego, California 92121, United States.
e-mail: simone.giorgi@unicam.it

The difluoromethyl group imparts interesting features attractive in medicinal chemistry. As a lipophilic hydrogen bond donor, it offers the rare feature to simultaneously provide hydrogen bonding interfaces and increased cell membrane permeability.(1)

In recent years a number of reactions have been developed to synthesize difluoromethylated compounds. Many of these methods require activated arenes(2) limiting scope(3,4) and regioselectivity. Baran(5) reported a new reaction that generates CF₂H radical to functionalize the more electron-deficient position in arenes owing to its electronic properties.

To complement these developments, we report a methodology that, in an efficient way, can regioselectively functionalizes the more electron-rich position of arenes (and heteroarenes). An electrophilic CF₂R radical has been developed that substitutes in this desirable position.

Inspired by photoredox catalysis which avoids potentially hazardous radical initiators, we have found that the easily prepared α-bromo-α,α-difluoroacetophenone functions as a useful reagent for the introduction of the difluoroacetophenone. These products are then readily converted to the difluoromethyl group. Ir(III) photocatalysts were studied and found successful for this easily operated CH functionalization of complex molecules. Our investigations and advances will be described.

Rational Design of Molecular Hole Transporting Materials for Perovskite Solar Cells: Direct versus Inverted Device Configurations

Roberto Grisorio\textsuperscript{a,b}, Rosabianca Iacobellis\textsuperscript{c,d}, Andrea Listorti\textsuperscript{b,e}, Luisa De Marco\textsuperscript{b}, Maria Pia Cipolla\textsuperscript{c,d}, Michele Manca\textsuperscript{c}, Aurora Rizzo\textsuperscript{b}, Antonio Abate\textsuperscript{f}, Giuseppe Gigli\textsuperscript{b,e}, Gian Paolo Suranna\textsuperscript{a,b}

\textsuperscript{a}DICATECh - Dipartimento di Ingegneria Civile, Ambientale, del Territorio, Edile e di Chimica, Politecnico di Bari, Via Orabona, 4 I-70125 Bari, Italy. \textsuperscript{b}CNR-NANOTEC, Istituto di Nanotecnologia, c/o Campus Ecotekne, Università del Salento, Via Monteroni, 73100 Lecce, Italy. \textsuperscript{c}Center for Biomolecular Nanotechnologies (CBN) Fondazione Istituto Italiano di Tecnologia, Via Barsanti 14, 73010, Arnesano, Italy. \textsuperscript{d}Dipartimento di Ingegneria dell’Innovazione, Università del Salento, via per Monteroni, 73100, Lecce, Italy. \textsuperscript{e}Dipartimento di Matematica e Fisica "E. De Giorgi", Università del Salento, Campus Universitario via Monteroni, 73100 Lecce, Italy. \textsuperscript{f}Young Investigator Group Active Materials and interfaces for stable perovskite solar cells, Helmholtz-Zentrum Berlin für Materialien und Energie, Kekuléstraße 5, 12489 Berlin, Germany.

Organic-inorganic lead halide perovskites have rapidly become one of the hottest topics in photovoltaics. Their use requires the presence, in devices, of hole-transporting materials (HTMs) to extract the photo-generated holes from the perovskite, and transport them to the electrode \textsuperscript{(1)}. The molecular tailoring of HTM for perovskite solar cells, however, still lacks in solid design criteria \textsuperscript{(2)}. Aiming at providing guidelines in this field, in marked contrast with the 3-D structure of the state-of-the-art Spiro-OMeTAD, truxene-based HTMs Trux1 and Trux2 have been employed for the first time in PSCs fabricated with a direct (n-i-p) or inverted (p-i-n) architecture, exhibiting a peculiar behavior with respect to the referential HTM.

Notwithstanding the efficient hole extraction from the perovskite layer exhibited by Trux1 and Trux2 in direct configuration devices, their photovoltaic performances were detrimentally affected by their poor hole transport. Conversely, a remarkable improvement of the photovoltaic performances in dopant-free inverted configuration devices compared to Spiro-OMeTAD (13.4\% respect to 9.5\% for Trux2 and Spiro-OMeTAD, respectively) was recorded, ascribable to the use of thinner HTM layers. The results of our investigations indicate the 3-D charge distribution of Spiro-OMeTAD radical cation as the cause of the excellent behavior of this HTM reference, favoring the hole transport across adjacent molecules. On the other hand, the trend of the photovoltaic response observed for p-i-n architecture devices was completely reversed: since in this configuration the use of a very thin HTM layer was allowed and the perovskite absorber was assembled onto the organic layer, a more favorable perovskite/HTM interface was generated due to the tailored 2-D structure of the truxene-based HTMs boosting the performances of Trux2 in comparison with the Spiro-OMeTAD reference device.

Flow synthesis of cyclobutanones via \([2 + 2]\) cycloaddition of keteneiminium salts and ethylene gas

G. Iannucci\textsuperscript{a,b}, C. Battilocchio\textsuperscript{b}, S. Wang\textsuperscript{b}, E. Godineau\textsuperscript{c}, A. Kolleth\textsuperscript{c}, A. De Mesmaeker\textsuperscript{e} and S. V. Ley\textsuperscript{b}

\textsuperscript{a} Dipartimento di Chimica e Chimica Industriale, Università di Pisa, Via G. Moruzzi 13 – 56125, Pisa (Italy); \textsuperscript{b} Innovative Technology Centre, Dept. of Chemistry, University of Cambridge, Lensfield Road, CB21EW, UK. \textsuperscript{c} Syngenta Crop Protection AG, Crop Protection Research, Schaffhauserstrasse 101, CH-4332, Switzerland; e-mail: Grazia.iannucci@for.unipi.it

In recent years, the interest of pharmaceutical and agrochemical companies toward small ring compounds, as flexible building blocks susceptible to further molecular elaboration, has increased, leading to the development of new synthetical methods based on sustainable processes (1,2). Among these compounds, substituted cyclobutanones represent a very interesting target (3), as they are associated with a reactive versatility (4), mainly due to their ring strain (3) (ca. 25 kcal/mol).

Here, a flow chemistry process for the synthesis of 2-substituted cyclobutanones, via \([2 + 2]\) cycloaddition reaction of keteneiminium salts and ethylene gas, is discussed (5). To realize the process, the flow machine was equipped with the “tube-in-tube” reactor (6), an advantageous gas-feeding technology for gas-liquid chemical reactions (Figure 1). The synthesis was carried out on substituted N,N’-diallylamides, using rapid and mild reaction conditions to access a diverse array of products with good to excellent yield (47-99% of yield), alongside a good level of functional group compatibility.

![Figure 1. Flow reaction set-up used for the synthesis of 2-substituted cyclobutanones.](image)

References:
Looking for a new, isoluminol-based, molecule with improved chemiluminescence properties: a SAR study

P. Ingallinella\textsuperscript{a}, D. Cappellini\textsuperscript{a}, A. Pighini\textsuperscript{b}, A. Prandi\textsuperscript{c}, M. De Matteo\textsuperscript{c}, L. Ferrante, P. Randazzo\textsuperscript{c}, C. Scandiuzzi\textsuperscript{a}, D. Zanin\textsuperscript{b}, L. Pallavicini\textsuperscript{b}, P. Brusasca\textsuperscript{a}, S. Maiorana\textsuperscript{c}, R. Ugo\textsuperscript{d}

\textsuperscript{a}DiaSorin Research Center, via Le petit 34, 21040 Gerenzano (VA) – Italy; \textsuperscript{b}DiaSorin SpA, via Crescentino snr, 13040 Saluggia (VC) – Italy; \textsuperscript{c}CISI Scrl, via G. Fantoli 16, 20138 Milano – Italy; \textsuperscript{d}ChemTech Srl, via V. Bellini 3, 20122 Milano – Italy; e-mail: paolo.ingallinella@diasorin.it

Chemiluminescence methods have become established in both routine clinical analysis and for clinical research applications. Historically, luminol and isoluminol were the first chemiluminescent compounds to be used as labels to be conjugated to reporter molecules (peptides, proteins, antibodies) but they were surpassed in some applications by the more sensitive acridinium esters. However, isoluminol has been successfully employed in a significant number of commercially available in vitro immunoassays, such as those marketed for use with DiaSorin’s fully automated analyzers, LIAISON\textsuperscript{®} (http://diasorin.com).

Generally, chemiluminescent labels with increased light output are highly desirable since they allow enhanced immunoassay sensitivities. With the aim of developing a new, isoluminol-based, molecule with enhanced chemiluminescence properties, we report here a Structure-Activity-Relationship (SAR) study carried out around the N-(4-aminobutyl)-N-ethylisoluminol (ABEI) core. Starting from previous studies (1,2,3), we explored different substituents in position 5 of the isoluminol ring (Fig. 1). As a result, we found that several substituents are able to confer an increased chemiluminescence signal. In particular, a gain up to more than 10-fold was observed for propyl-based substituents (i.e. sulfopropyl-, phosphopropyl-, methoxypropyl-), when the corresponding ABEI derivatives are used as labels in model assays. Moreover, the hydrophilic nature of these substituents is an interesting feature, since it should help to reduce the non-specific binding of the reporter molecule and allow its higher labeling without the risk of aggregation or precipitation. We believe that the use of such new isoluminol derivatives will lead to improved immunoassay performance, in terms of sensitivity and specificity. Further investigations are currently ongoing.

Fig. 1 The N-(4-aminobutyl)-N-ethylisoluminol (ABEI) structure and substituents used in the SAR study. The glutaric acid spacer was introduced to allow the labeling on reporter molecules.

Efficient iminium-catalyzed Morita-Baylis-Hillman reaction on cyclopent-2-enone

Innocenti Riccardo, Gloria Menchi, Andrea Trabocchi.

Dipartimento di Chimica "Ugo Schiff", Università degli studi di Firenze, Via della Lastruccia 13, Sesto Fiorentino 50019, Firenze (Italia)
e-mail: riccardo.innocenti@unifi.it

The Morita-Baylis-Hillman (MBH) reaction is an atom-economic carbon-carbon bond-forming reaction between the β position of an electron poor alkene and different carbon electrophiles under the influence of a catalyst or catalytic system. The product of a MBH reaction is a very interesting compound because of its polyfunctional character which can be used in the total synthesis of complex organic molecules or as a building block in diversity oriented Synthesis (DOS) strategies. Several electron poor alkenes have been used in this reaction such as acrylic acid derivates, nitro alkenes, α-β unsatured ketones, however the cyclic enones in particular cyclic pent-2-enone prove to be challenging substrate as only few examples of efficient catalytic systems on this compound have been reported in the literature\(^2\). In our work we proposed a new mild catalytic system based on the concomitant presence of an iminium catalyst, derived from a secondary amine, and a basic water solution of NaHCO\(_3\) for the reaction of cyclic pent-2-enone with several aldehydes, obtaining 16 compounds in moderate to excellent yields (37-99%).

![Chemical structure diagram](image.png)

Yields 37-99%

Design and Synthesis of GlcVac-6-P Analogues Targeting Hexosamine Biosynthetic Pathway (HBP) with promising antitumor activity.

_Barbora La Ferla^a, Alice Paiotta^b, Ferdinando Chiaradonna^a_

^a Dipartimento di Biotecnologie e Bioscienze, Università degli studi di Milano-Bicocca, Piazza della Scienza 2, 20126 Milano; ^b Department of Surgery and Translational Medicine, University of Milano-Bicocca, via Cadore 48, Monza, Italy.

e-mail: barbara.laferla@unimib.it

The Hexosamine Biosynthetic Pathway (HBP) is an important pathway essential in human body involved in the proliferation, survival and ability to migrate of many cancer cells lines, among which are particularly interested in pancreatic cancer cells. This pathway requires nutrients such as glutamine and glucose for the synthesis of UDP-N-acetyl-D-glucosamine, the substrate for N/O-glycosylation. The comprehension of the molecular bases of the role of the HBP could help in the identification of compounds able to interfere with this pathway, thus representing a possible strategy to arrest or kill pancreatic ductal adenocarcinoma (PDAC) cancer cells, in which protein and lipid glycosylation are actively involved in cell proliferation, cell migration and metastasis.

N-acetylglucosaminephosphate mutase (AGM1) is a key enzyme of the pathway, which catalyzes the conversion of N-acetylglucosamine-6-phosphate into N-acetylglucosamine-1-phosphate (figure 1). In the present work our aim is to interfere with the synthesis of UDP-GlcNAc through the inhibition of AGM1. To this aim we designed and synthesized a library of potential AGM1 inhibitors based on substrate/product structural similarities.

Biological evaluations in cellular cultures have identified a promising lead compound, which is under evaluation in animal models.

This work was supported by AIRC (IG2014 Id15364)

References


Pellegrino La Manna\textsuperscript{a}, Margherita De Rosa\textsuperscript{a}, Annunziata Soriente\textsuperscript{a}, Carmine Gaeta\textsuperscript{a}, Carmen Talotta\textsuperscript{a}, Neal Hickey\textsuperscript{b}, Silvano Geremia\textsuperscript{b}, Placido Neri\textsuperscript{a}

\textsuperscript{a}Dipartimento di Chimica e Biologia “A. Zambelli”, Università di Salerno, Via Giovanni Paolo II 132, I-84084, Fisciano (SA) Italy; \textsuperscript{b}Centro di Eccellenza in Biocristallografia, Dipartimento di Scienze Chimiche e Farmaceutiche, Università di Trieste, via L. Giorgieri 1, I-34127 Trieste, Italy.

In the last thirty years, calixarene macrocycles (1) have gradually gained a special role in a wide range of supramolecular applications. At this regard, many efforts have been devoted to the design and synthesis of calixarene derivatives as catalysts for organic reactions (2), and among them the development of environmentally-oriented catalytic strategies has been particularly investigated. In a pioneering work, Sharpless (4) introduced the expression "on-water conditions" to denote the rate acceleration observed in organic reactions when insoluble reactants are vigorously stirred in H\textsubscript{2}O suspension. Under "on-water conditions" the supramolecular affinities between reactants and catalyst play a key role. In fact, it is known that the hydrophobic effect forces the reactants and the catalyst to aggregate and thus amplifying the secondary interactions between them and favoring the molecular collisions. In the present communication, we will show that under “on-water conditions”, even weaker H-bond donor groups, such as amino-groups in 1 are effective to activate the substrate 2 in the Vinylogous Mukaiyama Aldol Reaction between 2 and 3 (see Figure below), on the basis of the hydrophobic amplification of H-bonds (5). Details on the catalytic efficiency of 1 and on the its recognition abilities toward the substrate 2 will be given.

Aminotriphenolates as Privileged Ligands in Catalysis

Emanuele Amadio\textsuperscript{a}, Elena Badetti\textsuperscript{a}, Davide Carraro\textsuperscript{a}, William Denis\textsuperscript{a}, Claudia Miceli\textsuperscript{a}, Paolo Zardi\textsuperscript{a}, Cristiano Zonta\textsuperscript{a}, and Giulia Licini\textsuperscript{a,***}

\textsuperscript{a} Dipartimento Scienze Chimiche and CIRCC, Università di Padova, via Marzolo, 1, 35131, Padova, Italy; e-mail: giulia.licini@unipd.it

Triphenolamines (TPA) are highly symmetric, modular molecules that form stable metal complexes with a wide variety of transition and main group elements.\textsuperscript{1} These complexes are highly active catalysts in important reactions like polymerizations, olefin metathesis, CO\textsubscript{2}/epoxide cycloadditions, and oxygen transfer processes.\textsuperscript{(1)} Here we will report our latest results related to V(V)-TPA catalysed processes. The activity of V(V)-TPA as V-haloperoxidase model \textsuperscript{(2)} and as catalyst in the aerobic carbon-carbon cleavage of vicinal diols and more complex lignin substructures \textsuperscript{(3)} will be described together with the activation of epoxides towards amine nucleophiles and CO\textsubscript{2} for cyclic carbonate synthesis.\textsuperscript{(4)}


Acknowledgement: We are grateful to the University of Padova, (PRAT-CPDA153122), Fondazione Cariparo (W.D. fellowship) and COST Action CM1205 CARISMA (C.M. Fellowship) and CM1402 CRYSTALLIZE.
Polydopamine: a versatile bioinspired material for multipurpose applications

Marco Lo Presti\textsuperscript{a}, Francesco Milano\textsuperscript{b}, Massimo Trotta\textsuperscript{c}, Roberta Ragni\textsuperscript{a}, Gabriella Leone\textsuperscript{a} and Gianluca M Farinola\textsuperscript{a}.

\textsuperscript{a} Dipartimento di Chimica, Università degli Studi di Bari “Aldo Moro”, via Orabona 4, 70126 Bari (Italy). \textsuperscript{b} CNR - IPCF; \textsuperscript{c} Istituto per i Processi Chimico Fisici - Sezione di Bari.

e-mail: marco.lopresti@uniba.it

Mussels can strongly attach to diverse substrates with high binding strength, even on wet surfaces. This observation led to a better understanding of the wet adhesion property of mussels. It was found that 3,4-dihydroxy-L-phenylalanine (DOPA) and lysine-enriched proteins near the plaque substrate interface are the major origins of the extraordinarily robust adhesion. (1,2,3,4)

On the basis of these findings, polydopamine (PDA), due to the molecular structure similarity to that of DOPA, moved into the spotlight as a novel coating material in 2007. (5) PDA presents numerous advantages: first of all PDA can be easily obtained from self-polymerization of dopamine in alkaline or oxidants contained aqueous solutions and adhere onto almost any solid surfaces without surface pretreatment (6), as seen with mussels, it can be easily deposited on virtually all types of inorganic and organic substrates, including superhydrophobic surfaces, with controllable film thickness and durable stability. Moreover this film is rich in catechol groups, which endows the PDA versatile chemical reactivity for biopolymer, biomimetic mineralization and metal nanoparticles (MNPs) in situ growth (5).

Last, but not least, polydopamine is also a major pigment of naturally occurring melanin (eumelanin), consequently, polydopamine displays many striking properties of naturally occurring melanin in optics, electricity, and magnetics, and, most importantly, it processes excellent biocompatibility. Herein, we first report that, upon dopamine polymerization in the presence of the protein, RC (a) is incorporated, (b) is capable to generate the charge-separated state, and (c) even to perform its natural photocycle (figure 1). It proved, indeed, to be effective in reducing quinone molecules to quinol by withdrawing electrons from cytochrome c. As an example of biotechnological application, a photoelectrochemical cell based on polydopamine-immobilized RC onto ITO has also been designed and successfully employed to generate photocurrents arising from the reduction of the electron-donor ferrocenemethanol.

\begin{figure}
\centering
\includegraphics[width=0.5\textwidth]{figure1.png}
\caption{Figura 1}
\end{figure}

Lipophilic core-shell Fe$_3$O$_4$@SiO$_2$@Au nanoparticles into nano-micelles for magnetic resonance and photoacoustic dual-imaging.

Erica Locatelli, a Ilaria Monaco, a Francesca Arena, b Stefania Biffi, c Enzo Terreno, b Mauro Comes Franchini a.

a Department of Industrial Chemistry “Toso Montanari”. University of Bologna. Viale del Risorgimento 4, Bologna, 40136 Italy. b Molecular & Preclinical Imaging Centers, Department of Molecular Biotechnology and Healthy Sciences, University of Torino, Via Nizza 52, Torino, 10126, Italy. c Institute for Maternal and Child Health- IRCCS “Burlo Garofolo”, Via dell’Istria 65/1, 34137, Trieste, Italy. e-mail: erica.locatelli2@unibo.it

Metal nanoparticles represent promising agents for both cancer treatment and diagnosis, opening up the novel field of theranostic (therapy and diagnostic). There is anyway an urgent need for multiple imaging technology in order to overcome the intrinsic limitations of every single imaging modality. Iron oxide nanoparticles are well known for their properties as contrast agents in magnetic resonance imaging (MRI) (1), while gold nanoparticles, have been recently investigated as promising photoacoustic imaging (PAI) contrast agents (2). The formation of a single nanosystem containing both the two nanostructures may allow an easy two imaging modality.

In this study metallic nanoparticles consisting of multiple shells of iron oxide, silica and gold were synthetized (Fe$_3$O$_4$@SiO$_2$@Au) and accurately characterized. The obtained Fe$_3$O$_4$@SiO$_2$@Au NPs were coated with a specifically designed organic ligand by exchange ligand reaction to guarantee their stability and solubility in organic solvents. The organic ligand synthetized for this purpose presents a thiol as ending group, in order to maximize interaction with the gold surface. The resulted coated nanoparticles are finally suitable for entrapment into biocompatible polymeric matrix to form a targetable water soluble nanocarrier for nanomedicine applications (3).

In conclusion, the final nanosystem is decorated with folic acid moieties and successfully tested in vivo for Photoacoustic (PA) and MRI detection of ovarian cancer.

References:
Synthesis of isoxazolidinyl-gem-bisphosphonic acids and study of protein-ligands interactions.

Loredana Maiuolo, Antonio De Nino, Vincenzo Algieri, Beatrice Russo, Monica Nardi, Matteo Antonio Tallarida, Ignacio Delso and Pedro Merino.

Dipartimento di Chimica e Tecnologie Chimiche-CTC, Università della Calabria, Ponte Bucci cubo 12/C, 87036, Arcavacata di Rende (CS), IT, Departamento de Síntesis y Estructura de Biomoléculas, Institute of Biocomputation and Physics of Complex Systems (BIFI), Universidad de Zaragoza-CSIC, 50009 Zaragoza, Spain, Servicio de RMN, Centro de Química y Materiales de Aragón, U. de Zaragoza-CSIC, 50009 Zaragoza, Spain.

Isoxazolidines mimic natural nucleosides exerting antitumor activity (1). The addition of a gem-bisphosphonate group on the heterocyclic ring increases the cytotoxicity of the obtained substrates that can be applied in clinical treatment of bone metastases and osteoporosis (2,3). In particular, this class of molecules inhibits the Farnesyl Pyrophosphate Synthase (FPPS) and the Geranylgeranyl Diphosphate Synthase (GGPP), targets of bisphosphonates for treatment of bone-related disorders (4).

In this work we will present the synthesis of a new family of isoxazolidinyl-gem-bisphosphonic acids with potential pharmacological activity.

Molecular modelling calculations and STD-NMR experiments have been used to predict and determine the affinity of our ligands towards human FPPS, as well as for characterization of the ligands binding modes. Moreover, the results of activity against Farnesyl Pyrophosphate Synthase (FPPS) and the Geranylgeranyl Diphosphate Synthase (GGPP) will be illustrated.

References:
Synthesis of sulfureted heterocycles with herbicidal activity

Raffaella Mancuso\textsuperscript{a}, Salvatore Giofrè\textsuperscript{b}, Fabrizio Araniti\textsuperscript{c}, Roberto Romeo\textsuperscript{b}, Mariarosa Abenavoli\textsuperscript{c}, Francesco Sunseri\textsuperscript{c} and Bartolo Gabriele\textsuperscript{a}

\textsuperscript{a}Laboratory of Industrial and Synthetic Organic Chemistry (LISOC), Department of Chemistry and Chemical Technology, University of Calabria, Via Pietro Bucci, 12/C, 87036 Arcavacata di Rende (CS), Italy; \textsuperscript{b}Dipartimento di Scienze Chimiche, Biologiche, Farmaceutiche ed Ambientali, Università di Messina, via S.S. Annunziata, 98168 Messina, Italy; \textsuperscript{c}Dipartimento di Agraria, Università Mediterranea di Reggio Calabria, 89124, Reggio Calabria, Italy.

e-mail: raffaella.mancuso@unical.it

The widespread development of weed resistance towards the most common herbicides is pushing the research in developing of new synthetic molecules, characterized by high phytotoxic activity and multi-target action. In this contest, we have synthesized some sulfureted heterocycle derivatives with promising herbicidal activity \textit{in vitro}.

The synthetic approach towards 1\textit{H}-isothiochromene-1-ones 2, (Z)-benzo[\textit{c}]thiophene-1(3\textit{H})-ones 3, 1\textit{H}-isothiochromene-1-thiones 4 and (Z)-benzo[\textit{c}]thiophene-1(3\textit{H})-thiones 5 is based on divergent tandem thionation-heterocyclization processes starting from readily available 2-alkynylbenzoic acids 1.

Reactions were carried out under microwave (MW) irradiation at 300W, at 100 °C, using 0.5 equiv. (for the synthesis of 2 and 3) or 1 equiv. (for the synthesis of 4 and 5) of the Lawesson’s reagent as the thionation. Products were obtained in good isolated yields (60-95%).

All the newly synthesized compounds were assayed \textit{in-vitro} on seedlings growth of \textit{Arabidopsis thaliana}, a model plant species. The results have pointed out that almost all molecules exerted a phytotoxic activity on both root and shoot. In fact, plants showed a reduction on shoot development (ED\textsubscript{50} values ≤ 64 µM) accompanied by a high decrease on pigment content. Moreover, the compounds strongly altered the root growth and morphology with ED\textsubscript{50} values ≤ 266 µM and ≤ 185 µM for primary root length and lateral root number, respectively. Finally, some of molecules significantly affected root anatomy and cells organization. Taken together these results suggest that the synthesized sulfur-containing heterocyclic derivatives represent interesting classes of chemicals with high phytotoxic activity. Further \textit{in-situ} experiments are in progress to evaluate their potential in weed management.
Tuning morphological architectures generated through living supramolecular assembly of a helical foldamer end-capped with two complementary nucleobases

Marafon, Giulia, a Crisma, Marco, b Toniolo, Claudio a,b and Moretto Alessandro a,b

aDepartment of Chemical Sciences, University of Padova, 35131 Padova, Italy; bInstitute of Biomolecular Chemistry, Padova Unit, CNR, 35131 Padova, Italy.

e-mail: giulia.marafon@studenti.unipd.it

Two appropriately functionalized nucleobases, thymine and adenine, have been covalently linked at the N- and C- termini, respectively, of two α-aminoisobutyric acid-rich helical peptide foldamers, aiming at driving self-assembly through complementary recognition(1). A crystal-state analysis (by X-ray diffraction) on the shorter, achiral foldamer 1 unambiguously shows that adenine···thymine base pairing, through Watson-Crick intermolecular H-bonding, does take place between either end of each peptide molecule (Fig. 1, upper part). In the crystals, π-stacking between base pairs is also observed(2). Evidence for time-dependent foldamer···foldamer associations for the longer, chiral foldamer 2 (Fig. 1, lower part) in solution is provided by circular dichroism measurements.

Fig. 1 Chemical structure of the achiral foldamer 1 and the chiral foldamer 2 (with a schematic representation of their expected inter- and intramolecular H-bonding interactions).

The self-assembly of foldamer 2, through living supramolecular polymerization, eventually leads to the formation of twisted fibers(3). Such a supramolecular organization can be affected by addition of either pristine adenine or thymine, that acts as a “terminator” by selectively matching a pairing nucleobase at one end of the foldamer. The co-assembly of foldamer 2 with a porphyrin-derivatized thymine, under appropriate experimental conditions, leads to the formation of vesicles which, in turn, can be converted to the fiber morphology by changing the environmental polarity. Conversely, dendrimeric, star polymer-like microstructures are generated when the supramolecular assembly of foldamer 2 is seeded by adenine-capped gold nanoparticles (Fig. 2)(4).

Fig. 2 Representation of the packing mode and the related 3D microstructures obtained.

Enantioselective Carbolithiation of α-Arylcarbamates

Giulia Marsico, Patrizia Scafato, Stefano Superchi

Dipartimento di Scienze, Università degli Studi della Basilicata, Via dell’Ateneo Lucano 10, 85100, Potenza, Italy.
e-mail: giuliamar86@hotmail.it

Carbolithiation of styrene double bonds is a practical methodology with a broad synthetic potential. In fact, the subsequent tandem reaction with carbon electrophiles allows the construction of two new C-C bonds, leading to highly functionalized systems. Despite its synthetic appealing, this class of reactions has not been much investigated because of the difficulty to control the organolithium intermediate which, reacting with a second molecule of the olefin, can trigger an unwanted anionic polymerization process. For a synthetic use of carbolithiation reactions a stabilization of the benzylthium intermediate is then required. This can be made by intra or inter-molecular organolithium coordination which, leading to an anion stabilization, prevents the polymerization. (1) This coordination occurs in the presence of coordinating groups bearing Lewis-base moieties and/or in the presence of bidentate ligands such as diamines. Aim of this study was to investigate the carbolithiation of 1-aryl-1-alkenyl N,N′-diethylcarbamates (1), a reaction poorly described in literature, and its extension to the preparation of optically active products. (1) After the carbolithiation step, the organolithium intermediate was reacted with several electrophiles, obtaining trisubstituted benzyl carbamates (2), direct precursors of tertiary benzylic alcohols. The tandem carbolithiation-trapping with electrophiles was also carried out in enantioselective manner, in the presence of chiral diamines, (2) obtaining enantioenriched tertiary benzyl carbamates. When PhCHO was used as an electrophile, a diastereomeric mixture of product 3 was obtained (3:1 by 1H NMR) which, after heating at reflux, gave rise to an intramolecular cyclization eventually leading to the single cis epoxide 4. (1) Also the enatioselective version of this reaction was investigated to provide an original approach to the synthesis of enantiomerically enriched cis-2-alkyl-2,3-diarylepoxides.

Asymmetric synthesis of the natural products colletochlorin A and colletorin A and their halogenated synthetic analogues

Giulia Marsico, Barbara A. Pignataro, Stefano Superchi, Patrizia Scafato

Dipartimento di Scienze, Università degli Studi della Basilicata, Via dell’Ateneo Lucano 10, 85100, Potenza, Italy.
e-mail: giuliamar86@hotmail.it

Fungal bioactive metabolites are an excellent source of pharmaceuticals, antifungal, and herbicidal compounds. Among these, the 3-diprenyl orsellinaldeide derivatives colletochlorins and colletorins are a class of phytotoxic metabolites isolated from Colletotrichum nicotianae, a fungus causing anthracnose in tobacco plants. Such compounds share as a common structural feature a multi-substituted polyphenolic ring and a terpenoid side chain. Moreover, in some of them, the terpenoid side chain bears one or more stereo genetic centers, which may possibly affect their biological activity. For most of these metabolites the bioactive properties are still underexplored, mainly for their scarce availability from natural sources. This is the case of colletochlorin A (1) and colletorin A (2) (2), for which the absolute configuration is also still unknown. Herein we describe the first asymmetric synthesis of both enantiomers of 1 and 2 with the aim to study the effect of the absolute stereochemistry on their biological activity. Moreover, the brominated and fluorinated unnatural analogues 3 and 4 were also prepared in optically active form to investigate the effect of the halogen substituents on their biological properties. The synthetic approach is based on the disconnection of the structure of colletochlorin A, colletorin A and their analogues into an aromatic precursor (5) and an optically active side chain (6). The enantioselective key step is the Sharpless asymmetric dihydroxylation of the geranyl acetate (7) (3), which is followed by a coupling of the chiral side chain with the poly-substituted aromatic moiety. The desired products were then obtained in good overall yields and high enantioselectivity (94-98% ee).

The role of structural and medium effects on hydrogen atom transfer from alcohols and diols to alkoxyl radicals

Teo Martin, Michela Salamone, Massimo Bietti

Dipartimento di Scienze e Tecnologie Chimiche, Università degli Studi di Roma “Tor Vergata”, Via della Ricerca Scientifica, 00133 Roma.
e-mail: teo.martin@uniroma2.it

The centrality of hydrogen atom transfer (HAT) processes is out of question, being one of the most fundamental reactions taking place in many chemical and biological processes, from radical-induced oxidative stress, to a number of new synthetically useful C-H bond functionalization procedures. Among the reactive species involved in these reactions, alkoxyl radicals have gained major attention, and the cumyloxyl radical (PhC(CH₃)₂O•, CumO•) has proven to be a very good reagent for the study of these reactions (1). CumO• can be easily generated by UV photolysis of the corresponding commercially available peroxide, can tolerate a wide range of experimental conditions and is characterized by an adsorption band in the visible region and a lifetime in the microsecond time regime, that make the direct measurement of HAT rate constants by the means of the laser flash photolysis technique particularly convenient.

Recent studies (1,2) carried out in our laboratory showed how substrate structure and medium effects could be used to finely tune the reactivity and selectivity in HAT processes from aliphatic C-H bonds. Due to the ubiquitous presence of hydroxyl functional groups in natural, commercially and biologically relevant compounds, alcohols and diols were one of the substrates of choice to broaden our comprehension of HAT reactivity and selectivity. Along this line, we have carried out a detailed time-resolved kinetic study on the reactions of a series of alcohols, 1,2-diols and 1,3-diols with CumO•, taking into particular account the role of added alkali and alkaline earth metal ion salts on the HAT reactivity. The results of these studies will be discussed.

Organocatalytic Domino Methodologies to Access Important Sulfur Heterocycles: from Tetrahydrothiophenes to 1,5-Benzothiazepines

Sara Meninno, Chiara Volpe, Alessandra Lattanzi

Dipartimento di Chimica e Biologia “A. Zambelli” Università di Salerno Via Giovanni Paolo II, 84084 Fisciano (Italy).
e-mail: smeninno@unisa.it

Organocatalytic one-pot and domino methodologies represent one of the most important achievements in organic synthesis in recent years (1,2). Small chiral organic molecules, such as squaramides and thioureas derived from simple chiral amines, are able to promote two or more successive chemical transformations in one reactor. These catalysts through the “invisible strings” of hydrogen bonds are able to orchestrate highly organized transition states accelerating and driving the sequence of reactions with high stereoselectivity. Access to differently functionalized chiral cyclic molecules, bearing one or more stereocenters, is possible without purification or separation of the intermediates. The importance of these methodologies is even more evident when applied to the synthesis of relevant biological and pharmaceutical compounds. Among sulfur containing heterocyclic compounds, particularly relevant are tetrahydrothiophenes, as naturally occurring products, targets exploited in medicinal chemistry and ligands in asymmetric catalysis. In this communication we are going to illustrate the stereoselective syntheses of highly functionalized tetrahydrothiophenes bearing three contiguous stereocenters, one of them quaternary, such as 1 (3) and more challenging spirotetrahydrothiophenes 2 (4), both of them obtained via a cascade double Michael reaction promoted by a readily available amine thiourea. The first methodology to prepare enantioenriched popular drugs N-unprotected 1,5-benzothiazepines 3, will be also described (5). An one-pot sequence involving an organocatalyzed sulfa-Michael reaction of α,β-unsaturated N-acyl pyrazoles with 2-aminothiophenols followed by silica-gel-catalyzed lactamization has been successfully exploited to develop a concise preparation of the antidepressant drug (R)-(-)-thiazesim.

Dicationic Ionic Liquids (DILs): synthesis, characterization and applications

Mezzetta Andrea\textsuperscript{a}, Guazzelli Lorenzo\textsuperscript{a}, Guglielmero Luca\textsuperscript{c}, Pomelli S. Christian\textsuperscript{a}, and Chiappe Cinzia\textsuperscript{a}

\textsuperscript{a} Department of Pharmacy, University of Pisa, via Bonanno, 33, 56126 Pisa; \textsuperscript{b} Scuola Normale Superiore di Pisa, Piazza dei Cavalieri, 7, 56126 Pisa. e-mail andrea.mezzetta@for.unipi.it.

The reduction, fixation, and use of carbon dioxide (CO\textsubscript{2}) is one of the major and urgent challenges the scientific community has demanded to address. Among the several strategies to face this problem, capture and storage of CO\textsubscript{2} in geological storages (for example saline aquifers or deep ocean storage) is considered at present the best option, while CO\textsubscript{2} utilization remains an underexploited opportunity. (1) However, CO\textsubscript{2} could be seen as an attractive option in the preparation of new added-value products. In fact, from a synthetic perspective, CO\textsubscript{2} is a non-toxic, safe, and economical C1 synthon and some methodologies to employ it in the preparation of valuable chemicals have been developed. (2) One of the typical viable routes is the synthesis of cyclic carbonates via the cycloaddition of CO\textsubscript{2} with different epoxides. Cyclic carbonates have been already used as organic solvents and in the synthesis of polycarbonates, pharmaceutical medicines and fine chemical products.

Ionic liquids (ILs) have been proven as efficient homogeneous catalysts for the synthesis of cyclic carbonates. Many task-specific ILs, combined with Lewis acids (3), are used in the cyclic carbonates formation.

Herein the preparation of a series of different di-cationic ionic liquids (DILs) is presented. The synthesized DILs were fully characterized (\textsuperscript{1}H-, \textsuperscript{13}C-NMR, FT-IR) and their thermal behavior was analyzed (thermo gravimetric analysis and differential scanning calorimetry). Finally, the effect of the structure of the DILs, (eg distance between anions/cations, type of spacer, nature of cation) on the cyclic carbonates synthesis was investigated to determine their optimal structure and their role in the catalytic cycle.

Syntesis of multifunctional ORMOSIL nanoparticles for drug delivery

Lucía Morillas Becerrila, Fabrizio Mancina, Marta Trevisanb, Ingazio Castaguoloa, Luisa Barzonb

a Organic department at University of Padova, Italy; b Molecular medicine department at University of Padova, Italy.

The probability to develop a cancer disease has been growing for the last century and although there are many therapies to treat it, cancer progresses in such manner that our knowledge is not extensive enough. Nanomedicine has emerged for its use in drug delivery, diagnosis, imaging, as well as therapy and thus nanoparticles have been used (1). Silica nanoparticles have been developed in the last years due to their great features for drug delivery(2,3), therefore in this project we synthesized organic modified silica nanoparticles loaded with an anticancer drug that were targeted to tumor cells and biocompatible.

The synthesis consist in a one pot reaction (4) in which surfactant micelles in water act as template for the nanoparticles, forming a mesoporous hydrophobic core in which our anticancer drug was loaded. Increased biocompatibility was obtained by functionalizing the nanoparticles with PEG and substituted PEG that was further conjugated with hyaluronic acid. The purpose of the use of hyaluronic acid relies on the interaction with CD44 antigen which participates in the tumor metatesis. Biological test indicated a higher effect of the drug loaded nanoparticles conjugated with hyaluronic acid compared with the free drug and unconjugated nanoparticles.

Hence, we synthesized organic modified silica nanoparticles in a one pot reaction that were loaded with an anticancer drug and functionalized with PEG conjugated with hyaluric acid showing a significant cancer cell death.

Discovering the biological target of 5-epi-Sinuleptolide with a combination of proteomic approaches

E. Morretta\textsuperscript{a}, R. Esposito\textsuperscript{a}, C. Festa\textsuperscript{b}, R. Riccio\textsuperscript{a}, M. C. Monti\textsuperscript{a} and A. Casapullo\textsuperscript{a}

\textsuperscript{a} Department of Pharmacy, University of Salerno, via Giovanni Paolo II, 132 84084, Fisciano, Italy.
\textsuperscript{b} Department of Pharmacy, University of Naples “Federico II”, Naples, Italy;
e-mail: emorretta@unisa.it

The marine surroundings include around half of the world’s biodiversity and is a huge resource of structurally relevant and biologically active compounds (1). The soft coral Sinularia produces a rich collection of secondary metabolites with a range of biological activities such as antimicrobial, anti-inflammatory, and cytotoxic (2). Among them, 5-epi-sinuleptolide (5-epi-SNEP) was selected as ideal candidate for a target discovery analysis through a combination of functional proteomic approaches.

Our strategy was based on two complementary approaches: 1) 5-epi-SNEP has been covalently bound on a solid matrix and used as a bait, fishing out its specific interactors from a complex mixture as a cell lysate by affinity. Once eluted, fished cellular targets have been identified by means of high resolution MS, bioinformatic analyses and immunoblotting (3); 2) in parallel, we applied a drug affinity responsive target stability approach (DARTS) on the native unmodified metabolite (4). The DARTS principle is based on the evidence that a protein might become less susceptible to proteolysis when is drug-bound than when it is drug-free. Both approaches pointed to the identification of actin proteins as the main 5-epi-SNEP cellular targets. Finally, a biological investigation on its effect on the cytoskeleton assembly showed the ability of 5-epi-SNEP to induce the disruption of the actin cytoskeleton and the formation of F-actin amorphous aggregates, without affecting the cell viability.

References:
4. Lomenick, B. et al.\textit{PNAS} 2009, 106, 21984-21989
Data-driven Ionic Liquids Modelling: a Design Opportunity for Task-specific Applications

Giuseppe Musumarra, Alessio Paternò, Salvatore Scire

Dipartimento di Scienze Chimiche, Università di Catania, Viale A. Doria 6, I-95125 Catania, Italy.

e-mail: gmusumarra@unict.it

In the field of ionic liquids (ILs) theory-driven modelling approaches aimed at the best fit of all available data by a unique often non-linear model have been widely adopted to develop Quantitative Structure Property Relationships (QSPR) models. Data-driven procedures have recently been proposed as a complementary approach (1). Cheminformatics and chemometrics procedures were applied to develop QSPR soft models of local validity predicting ILs toxicities (2,3,4), $E_{NR}$ solvent polarity (5) and important physicochemical properties such as heat capacity (6), viscosity (1), density (1), conductivity (1) and decomposition temperature (1). This approach uses simultaneously cations and anions VolSurf+ structural descriptors which can be easily interpreted. As experiments can hardly explore the enormous chemical space covered by ILs, data-driven modelling complements theory-driven approaches for interpretation and correlation purposes and may represent an unexploited opportunity for experimentalists in ILs industrial design.

Unconventional synthetic methods towards new food additives from waste derived by olive oil industry

Monica Nardi\textsuperscript{a,b}, Maria Luisa Di Gioia\textsuperscript{c}, Manuela Oliverio\textsuperscript{d}, Antonio Procopio\textsuperscript{d}, Giovanni Sindona\textsuperscript{b}

\textsuperscript{a} Dipartimento di Agraria, Università Telematica San Raffaele, Roma; \textsuperscript{b} Dipartimento di Chimica, Università della Calabria, Cubo 12C, Arcavacata di Rende (CS); \textsuperscript{c} Dipartimento di Farmacia e Scienze della Salute e della Nutrizione, Edificio Polifunzionale, Università della Calabria, Arcavacata di Rende, (CS); \textsuperscript{d} Dipartimento di Scienze della Salute, Università Magna Graecia, Viale Europa, Germaneto (CZ).

e-mail: monica.nardi@unical.it

People who closely follow the Mediterranean diet live longer than other Europeans and Americans due to the lower incidence of chronic and degenerative diseases; Virgin Olive Oil (VOO) is the main beneficial factor responsible for nutritional benefits of Mediterranean diet.\textsuperscript{1}

The beneficial effect connected to the olive oil consumption is directly dependent on its composition. Beside a correct ratio of saturated and unsaturated fatty acids, olive oil contains an important percentage of phenols, most of them displaying antioxidant activity. In particular, olive oil is characterized by the presence of secoiridoids phenols. The most important secoiridoid in olive oil industry is oleuropein possessing a lot of biological and pharmacological properties\textsuperscript{2} and mostly present in olive leaves, a waste of one of the more extensive agricultural production in our region. Metabolic derivatives of oleuropein are aglycones derivatives and hydroxytyrosol that have demonstrated important biological activity.\textsuperscript{3-6}

In this context, our recent research was focused to exploit the oleuropein and demethyl oleuropein, derived by wastes from olive oil industry, in environmentally friendly extraction processes. The same compounds were used as precursors for the obtainment new natural food additives through innovative synthetic methods.

Metaboliti secondari bioattivi prodotti da funghi patogeni di piante forestali

P. Noceraa, M. Masiit, B. T. Linaldedduit, A. Cimmion, L. Maddaut, A. Evidentea

a Dipartimento di Scienze Chimiche, Università di Napoli “Federico II”, Complesso Universitario Monte Sant’Angelo, via Cinthia 4, 80126, Napoli, Italia; b Università degli Studi di Padova-Dipartimento di Territorio e sistemi agro-forestali (TESAF), viale dell’Università 16, 35020 Legnano (PD), Italia; c Dipartimento di Agraria, Sezione di Patologia Vegetale ed Entomologia, Università degli Studi di Sassari, viale Italia 39, 07100, Sassari, Italia; e-mail: paola.nocera@unina.it

Le formazioni boschive in Italia sono minacciate da un crescente numero di specie fungine invasive. In particolare, i risultati di recenti ricerche indirizzate allo studio delle cause della grave moria di querce che sta interessando ampie regioni del territorio nazionale hanno evidenziato il ruolo preminente svolto da Diplodia corticola, un patogeno altamente aggressivo. Le infezioni di questo fungo hanno un grande impatto ecologico, in quanto compromettono sia la vitalità sia la produttività delle piante. Allo stesso tempo, due nuove specie fungine, Diaporthella cryptica e Sardiniella urbana associate rispettivamente ad una grave sindrome che colpisce il nocciolo e il bagolaro stanno causando gravi morie in Sardegna (1, 2). Considerata la grande valenza ecologica di questi ecosistemi forestali e dei gravi danni causati da questi funghi, si è ritenuto opportuno approfondire le conoscenze sulla bio-ecologia di queste specie e, in particolare, sui fattori di virulenza coinvolti nel processo di patogenesi. Dalle ricerche finora condotte è emersa la capacità di D. corticola di produrre in vitro una plebora di metaboliti secondari bioattivi, alcuni dei quali di particolare interesse anche sotto il profilo applicativo. I metaboliti fitosessi finora isolati appartengono a diversi classi di composti naturali quali: diterpeni pimaranici, cicloeseni epossidi, furanoni e piranoni (3, 4). Degna di nota è la potenzialità applicativa come antitumore della sphaeropsidina A, metabolita appartenente alla classe dei diterpeni pimaranici, che ha mostrato in vitro una notevole attività contro tumori maligni come il melanoma (5). Oltre la sphaeropsidina A, altri metaboliti, come il diorcinolo e il dipropyrene B, possiedono un grande potenziale applicativo in virtù della loro efficacia nei confronti di importanti patogeni appartenenti al genere Phytophthora, le cui infezioni su piante forestali sono controllate attualmente solo con pochi fungicidi di sintesi.

Nella presente comunicazione saranno presentati i risultati ottenuti sull’isolamento e la caratterizzazione chimica e biologica di metaboliti bioattivi prodotti dalle due nuove specie fungine D. cryptica e S. urbana.

References:
An expeditious and greener synthesis of functionalized cyclopentenones in deep eutectic solvents.

Fabrizio Olivito, Paola Costanzo, Antonio De Nino, Maria Luisa Di Gioia, Loredana Maiuolo, Monica Nardi, Antonio Procopio, Giovanni Sindona

*Dipartimento di Scienze della Salute, Università Magna Graecia, Viale Europa, Germaneto (CZ); Dipartimento di Chimica, Università della Calabria, Cubo 12C, Arcavacata di Rende (CS); Dipartimento di Farmacia e Scienze della Salute e della Nutrizione, Edificio Polifunzionale, Università della Calabria, Arcavacata di Rende, (CS); Dipartimento di Agraria, Università Telematica San Raffaele, Roma; e-mail: fabrizioolivito@gmail.com

In recent years, cyclopentenones have been the target of various synthetic efforts because their five member-ring structure is a characteristic of many compounds with a broad range of biological properties. Conventionally, the cyclopentenone unit has been synthesized starting from furaldehyde and primary and secondary amines but most of the reported methods suffer of some disadvantages, such as use of toxic solvents or catalysts, harsh reaction conditions, environmental problems, undesirable wastes, unsatisfactory yield, and tedious work-up procedures. Therefore, the potential important biological activity of compounds related to bifunctionalized cyclopentenones derivatives has demanded alternative, environmentally friendly strategies to synthesize bifunctionalized cyclopentenones.

In recent years much attention has been devoted to deep eutectic solvents (DESs) as new sustainable alternatives to traditional solvents and ionic liquids. Compared to ionic liquids, DESs are generally cheaper to make, are less toxic and are often biodegradable. Thus, DESs can be used as low–cost, safe and efficient solvents. We report here a practical, inexpensive, rapid and green method for the preparation of cyclopentenones derivatives in deep eutectic solvents.

Synthesis of nitro-functionalized N-heteroaromatic condensed systems

Lara Bianchi*, Massimo Maccagno*, Angela Pagano*, Giovanni Petrillo* and Cinzia Tavani*

* Dipartimento di Chimica e Chimica Industriale, Università di Genova, Via Dodecaneso 31, I-16146 Genova, Italy. 
  e-mail: angela_pagano@alice.it

The long-standing synthetic efficacy of dinitrobutadienes 1 (1) has been more recently applied to the preparation of nitrocarbazoles 3, via a sequence of two Michael-type additions (inter- and intra-molecular), followed by aromatization through nitrous acid elimination and/or oxidation processes (Scheme, path a) (2). The extension of the same reactivity of dienes 1 to azaindoles 4 or 5 (path b), as well as to pyrroles 8 (path c), would provide an appealing access to new entries, otherwise not simply attainable, in the biologically and technologically exploited field of nitroheteroaromatics and derivatives therefrom. The latest achievements in such synthetic efforts will be presented.

Targeting Gastrin-Releasing Peptide Receptor expressing tumors: synthesis and characterization of new potential diagnostic and therapeutic molecular tools.

Alessandro Palmioli\textsuperscript{a}, Cecilia Ceresa\textsuperscript{b}, Barbara La Ferla\textsuperscript{a}, Cristina Airoldi\textsuperscript{a}

\textsuperscript{a} Dipartimento di Biotecnologie e Bioscienze, Università degli studi di Milano-Bicocca, Piazza della Scienza 2, 20126 Milano; \textsuperscript{b} Department of Surgery and Translational Medicine, University of Milano-Bicocca, via Cadore 48, Monza, Italy.

e-mail: alessandro.palmioli@unimib.it

Gastrin-Releasing Peptide Receptors (GRPR) are transmembrane G-proteins coupled receptors that trigger different signaling transduction pathways, resulting, among which, in the stimulation of cell proliferation. Although GRPR are poorly distributed in normal tissues, it has been shown that they are significantly involved in the pathogenesis of different human cancers (1), including lung (small and non-small cell type), breast, prostate, exocrine pancreas, head and neck squamous cell, and glioblastoma cancers. In addition, they are recently emerged as tumoral marker in early prostate and breast cancers diagnosis (2). For these reasons, the research of new GRPR ligands as antagonists or carriers for cytotoxic and imaging molecular tools might be a promising strategy for the treatment and diagnosis of human tumoral malignancies (3).

The main aim of our work is the design, synthesis and elucidation of the structure-activity relationship of new ligands able to act as GRP agonist or antagonist. Here we presents the synthesis of a non-peptidic library of novel GRPR ligands based on a preliminary rational drug-design computational study. In particular, we synthesized a library of ligands based on a rigid and spatially defined selected glycidic scaffold, differing for the nature of potential pharmacophoric moieties. Since GRP and analogous peptides promote the activation of Phospolipase C (PLC) signaling pathway, the biological activity of the synthesized compounds was preliminarily screened by evaluating their ability to increase the level of cytosolic \(\text{Ca}^{2+}\) (agonist activity) or to contrast the stimulation mediated by natural ligands (e.g. bombesin, Bn) (antagonist activity) in a human prostate carcinoma cell line (PC-3) over-expressing the receptor.

This work was supported by AIRC (MFAG-17030 Targeting of Gastrin-Releasing Peptide receptor expressing tumors: NMR characterization of Bombesin/GRP-R interaction)

References


An unconventional helical push-pull system for solar cells

Valentina Pelliccioli\textsuperscript{a}, Silvia Cauteruccio\textsuperscript{a}, Serena Arnaboldi\textsuperscript{a}, Norberto Manfredi\textsuperscript{b}, Patrizia R. Mussini\textsuperscript{a}, Alessandro Abbonto\textsuperscript{b}, Emanuela Licandro\textsuperscript{a}

\textsuperscript{a} Dipartimento di Chimica, Università degli Studi di Milano, Via Golgi 19, I-20133, Milano, Italia;
\textsuperscript{b}Department of Materials Science and Solar Energy research Center (MIB-SOLAR), Università degli Studi di Milano-Bicocca, Via Cozzi 53, I-20125, Milano, Italia.

e-mail: valentina.pelliccioli@studenti.unimi.it

Tetrathiahelicenes (7-THs), formed by thiophene and benzene rings ortho-fused in an alternating fashion, belong to an intriguing class chiral helical-shaped molecules, that have received much attention thanks to manifold applications in different areas of science (1). In fact, the configurationally fixed helical arrangement of the \( \pi \)-system confers to helicenes a peculiar topology, and provides unique electronic and optical properties suitable for applications in optoelectronics (2), biomolecular recognition (3), and catalysis (4,5,6). Moreover, the selective functionalization of the \( \alpha \)-position(s) of the terminal thiophene ring(s) of the 7-TH allows the introduction of a variety of substituents (7), which can modulate specific properties, including electronic properties. Exploiting our well-established know-how in the synthesis and functionalization of 7-TH derivatives, we have synthesized a novel push-pull system (1, Figure 1), in which the thiahelical skeleton represents the \( \pi \)-conjugated-bridge spacer.

The optical and electrochemical properties of 1 have been studied, and its performance as organic dye in dye-sensitized solar cells (DSSCs) has been preliminary investigated.

Metal chelators for the multi-target therapy of Alzheimer’s Disease: isolation/synthesis and preliminary biological evaluation of new natural and synthetic compounds

Luca Piemontese\textsuperscript{a,b}, Daniel Tomás\textsuperscript{c}, Asha Hiremath\textsuperscript{d}, Marco Catto\textsuperscript{a}, Antonio Laghezza\textsuperscript{a}, Silvia Chaves\textsuperscript{c}, Filippo Maria Perna\textsuperscript{a}, Fulvio Loiodice\textsuperscript{e}, Maria Amélia Santos\textsuperscript{c}, Michele Solfrizzo\textsuperscript{b}, Vito Capriati\textsuperscript{a}

\textsuperscript{a}Dipartimento di Farmacia–Scienze del Farmaco, Università degli Studi di Bari “Aldo Moro”, Consortium C.I.N.M.P.I.S., Via E. Orabona 4, I-70125 Bari, Italy; \textsuperscript{b}CNR–Istituto di Scienze delle Produzioni Alimentari, via Amendola, 122/O, I-70125 Bari, Italy; \textsuperscript{c}Centro de Química Estrutural, Instituto Superior Técnico, Universidade de Lisboa, Av. Rovisco Pais 1, 1049-001 Lisboa, Portugal; \textsuperscript{d}Centre for Nano and Material Sciences, Jain University, Jain Global Campus, Jakkasandra post, Kanakapura Road, Ramanagara District, Bangalore 562112, India.

Alzheimer’s Disease (AD) is widely recognized as a social problem. Nowadays, only five drugs are FDA approved for the therapy of this widespread neurodegenerative disease, however, with poor results. Three of them (Donepezil, Rivastigmine, Galantamine) are acetylcholinesterase (AChE) inhibitors, Memantine is a NMDA receptor antagonist \cite{1}, whereas the fifth medication is a combination of Donepezil with Memantine. Because of the multiple origin of this pathology, a multi-target strategy is currently strongly pursued by physicians. This approach is based on the identification of multifunctional molecules designed in order to act simultaneously on at least two disease targets with the aim of achieving synergistic actions and of improving the therapeutic efficacy \cite{1,2}. Currently, inhibition of AChE and monoaminoxidase, NMDA receptor antagonism, antioxidant activity, inhibition of Abeta amyloid plaques (Aβ) aggregation, and chelation of copper, iron and/or zinc cations are among the most heavily investigated drug targets \cite{1}. Recent evidence, in particular, have shown that the removal and/or redistribution of metal ions at the level of the nervous system can significantly reduce the formation of Aβ and thus of reactive oxygen species, which are typical of the first stages of AD and other neurodegenerative diseases \cite{3}.

Considering that many synthetic and natural compounds possess anti-oxidant, anticholinesterase and/or metal chelation activity \cite{4}, several scaffolds have been selected in order to design new derivatives. A list of secondary metabolites of fungi, in particular, have been isolated and preliminarily tested with the aim of finding new hit compounds for future Structure-Activity Relationship studies. In addition, starting from the structure of Donepezil and two selected synthetic scaffolds, new hybrid derivatives have been synthesized aimed at obtaining a better AChE inhibitory activity, an anti-oxidant activity, and the inhibition of Aβ aggregation. In this communication, the synthetic procedures for the preparation of these compounds, jointly with the results of preliminary biological studies, will be discussed.


The unexpected driving role played by substituent groups in the molecular recognition of aromatic derivatives performed through Argentation Chromatography.

Marco Pierini\textsuperscript{a}, Alessia Ciogli\textsuperscript{a}, Francesco Gasparrini\textsuperscript{a}, Sergio Menta\textsuperscript{b}, Claudio Villani\textsuperscript{a}

\textsuperscript{a} Department of Drug Chemistry and Technology, “Sapienza” University of Rome, P.le Aldo Moro 5, 00185 Roma, Italy; \textsuperscript{b} IRBM Science Park SpA, Via Pontina km 30,600 00071 Pomezia (RM), Italy.

e-mail: marco.pierini@uniroma1.it

Argentation Chromatography (AC) is widely used nowadays as a powerful tool to separate complex mixtures of analytes containing unsaturated and/or aromatic fragments. Typically, the older types of stationary phases (SPs) employed in this kind of technique were based on either the direct process of impregnating of the silica surface with silver cations, or by the use of strong cation exchange resins. More recently, a new typology of SPs has been developed, in which the silver metal is covalently bonded to mercaptopropyl silica gel (MPSG-Ag). With respect to the older ones, which are prone to undergo both silver ion leaching and easy reduction of the metal cation, (from Ag\textsuperscript{+} to Ag\textsuperscript{0}) (1, 2), the MPSG-Ag SPs display a consistent improvement of chemical stability. The general mechanism with which, in AC techniques, the silver atom interacts with the π-electrons of unsaturated species has been thoroughly clarified, allowing to rationalize the retention pattern of such type of compounds on the basis of several simple rules related to chain length, number, configuration and position of the involved double bonds (3,4,5,6). Differently, to our knowledge, they were never achieved analogous information about the chromatographic retentive behaviour of the same technique towards aromatic analytes as a function of the effect exercised by groups directly bound onto the aromatic ring. In the perspective to afford a contribution to fill this gap, here we present the results of chromatographic and computational studies in which a series of benzene derivatives, substituted with either electron withdrawing or electron donating $G_i$ groups, have been resolved through the AC technique using a MPSG-Ag SP. In this way, clear indications (emerging from a quantum-mechanical DFT analysis that has fully rationalized the observed experimental trend) have been gained about the mechanism by which the various $G_i$ substituents have proven to modulate, in an unexpected way, the ability of the MPSG-Ag SP in retaining and discriminating the aromatic species at which they are linked.

Facile Preparation of Metal Ions Loaded Sporopollenin Grains from Pollens, and Characterization

Christian Silvio Pomelli\textsuperscript{a}, Stefano Caporali\textsuperscript{b}, Cinzia Chiapp\textsuperscript{e}, María Jesús Rodríguez Douton\textsuperscript{a}, Francesco Rossella\textsuperscript{c}, Stefania Sartini\textsuperscript{a}

\textsuperscript{a} Dipartimento di Farmacia – Università di Pisa Via Bonanno 33, 56126 Pisa; \textsuperscript{b} Affiliation and address; \textsuperscript{c} NEST, Scuola Normale Superiore and Istituto Nanoscienze-CNR, Piazza san Silvestro 12, I-56127 Pisa, Italy.
\textit{e-mail:} christian.pomelli@unipi.it

Pollen grains are 3D microstructures that can act as scaffolds or templates and can be exploited for applications in different fields including drug delivery (1). To this aim, their structural component sporopollenin must be isolated. Recently, some of us reported a novel procedure for the separation of sporopollenin from the other pollen components, using room temperature ionic liquids (ILs) (2).

Here, we present the results of functionalization protocols involving ILs including anions such as [FeCl\textsubscript{4}]\textsuperscript{-}, and we show that sporopollenin can retain a considerable amount of metal ions. We explored the use of different metals including iron, copper and zinc. The chemical and morphological main features of our systems are studied with a multitechnique approach, using X-ray photoemission spectroscopy (XPS), Fourier transform IR (FTIR) spectroscopy, elemental analysis and scanning electron microscopy (SEM). Preliminary studies suggest the onset of magnetic order in selected samples. From the chemical point of view these systems can be useful as in heterogeneous catalysts. Some preliminary results will be presented.

Discovery of new molecular entities able to strongly interfere with Hsp90 C-terminal domain

S. Terracciano\textsuperscript{a}, A. Russo\textsuperscript{a}, M. G. Chini\textsuperscript{a}, M. C. Vaccaro\textsuperscript{a}, M. Potenza\textsuperscript{a}, A. Vassallo\textsuperscript{b}, R. Riccio\textsuperscript{a}, G. Bifulco\textsuperscript{a} and I. Bruno\textsuperscript{a}

\textsuperscript{a}Department of Pharmacy, University of Salerno, Fisciano, Italy. \textsuperscript{b}Department of Science, University of Basilicata, Potenza, Italy

e-mail: mpotenza@unisa.it

Heat shock proteins (Hsps) are effective anti-apoptotic proteins involved in vital mechanisms of cancerous cells (1), and among them, the Hsp90 inhibition represents a powerful strategy in cancer therapy (2). In recent years, many natural and synthetic Hsp90 N-terminal inhibitors have been developed and have entered clinical trials, while only a few C-terminal inhibitors have been identified so far. In contrast to N-terminal modulators, the C-terminal inhibitors represent promising therapeutic alternatives for targeting malignant cells, because they do not induce the deleterious pro-survival heat shock response (HSR) (3). On these bases, in order to expand the number of Hsp90 C-terminal inhibitors, a set of twenty seven commercially available small molecules, endowed with different structural features, was subjected to surface plasmon resonance (SPR) screening on recombinant Hsp90α (4). Among these, sixteen compounds showed high affinity of binding for the Hsp90 chaperone with low $K_D$ values, and after an evaluation on their anti-proliferative activity against tumor cell lines and limited proteolysis experiments, we have disclosed two new hits targeting the C-terminal domain. On these bases, in order to rationalize the biological activity reported above, all the compounds filtered out by SPR experiments were docked onto closed active crystal structure of Hsp90α homologue (PDB code: 2CG9) (5), focusing the conformational searches in the putative ligand-binding sites disclosed by the limited proteolysis experiments. In details, we have performed molecular docking experiments using the induced fit docking protocol (Schrödinger Suite) (6), to account for flexibility of ligands and receptor. Our structural results disclose the halogen bonding as fundamental key interaction suitable for the design of novel Hsp90 inhibitors. In conclusion, through a multidisciplinary approach, we have identified two new attractive hits for Hsp90 C-terminal inhibition that provide an excellent opportunity to expand the chemical space associated with this domain.

Conformational Analysis and Absolute Configuration of Axially Chiral 1-aryl and 1,3-diaryl-xanthines

L. Prati\textsuperscript{a}, M. Mancinelli\textsuperscript{a}, S. Perticarari\textsuperscript{a}, A. Mazzanti\textsuperscript{a}

\textsuperscript{a} Department of Industrial Chemistry “Toso Montanari”, University of Bologna, Viale Risorgimento 4, 40136 - Bologna, ITALY, e-mail: luca.prati2@unibo.it

One of the most important feature of life is its intrinsic chirality. For this reason, specular chiral system interacts differently with biological systems. The xanthine scaffold is known to be the forefather of a class of biological active molecules(1). Despite its biological activity, poor attention has been given in the dynamic conformations of this scaffold. The motivation of this lack of studies has to be researched in the chemistry of the scaffold itself: it is not possible to install an ordinary center of chirality without modify one of its essential functional groups. However, it is possible to install chiral axes. The xanthine backbone is a planar framework in which an aryl substituent linked in the 1 or 3 position is driven out of the xanthine plane because of the steric hindrance, caused by the two carbonyls (2). Depending on the hindrance of the ortho-substituents, the resulting conformational enantiomers are expected to be either stereo labile or configurationally stable (atropisomers). In Figure 1 are shown the series of 1-aryl and 1,3-bis aryl-xanthines studied.

![Figure 1. 1-aryl and 1,3 bis aryl-xanthines prepared.](image)

This work aims to investigate the stereodynamics of some 1-aryl and 1,3-bis-aryl xanthines and to evaluate the steric requirements needed to produce stable heteroaromatic atropisomers or diastereoisomers, with one or two C\textsubscript{sp2}-N stereogenic axes. With these parameters in hands, it will be possible to design chiral xanthines, stable at room temperature, that can eventually interact differently with biological environment.

Synthesis and Photo-Physical Properties of Dopamine-Inspired Iridium Complexes for OLED Applications

Carmela Tania Prontera\textsuperscript{a}, Valeria Criscuolo\textsuperscript{a}, Alessandro Pezzella\textsuperscript{a}, Maria Grazia Maglione\textsuperscript{b}, Paolo Tassini\textsuperscript{b}, Carla Minarini\textsuperscript{b}, Marco d’Ischia\textsuperscript{a}, Paola Manini\textsuperscript{a}

\textsuperscript{a}University Federico II Napoli, Department of Chemical Sciences; \textsuperscript{b} ENEA, C.R. Portici, SSPT-PROMA NANO, Portici (NA), Italy.

The recent advances in the field of organic light emitting diodes (OLEDs) have been focused mainly on the need to combine the main strengths of this technology, that is the versatility (i.e. wide color tuning, ultrathin, flexible and large area devices) and the eco-compatibility (low-energy consumption), with the efficiency and the lifetime of the devices, with the aim of making OLEDs very appealing and competitive with respect to the inorganic LEDs. In the last few years, another issue has been explored in connection with the growing expansion and impact of the green electronic field, that is the challenge of integrating natural or nature-inspired materials within organic electronic devices, and so in OLEDs.

In the frame of a research plan aimed at studying the role of melanins, the dark pigment found in mammalian skin, hair and eyes, in organic electronics (1,2), we have recently explored the potentiality of new heterocyclic platforms designed taking inspiration from the mammalian pigments as electroluminescent materials for OLED applications.

Herein we report on the synthesis of a new set of phosphorescent iridium(III) complexes prepared by using ligands obtained from dopamine, the catecholic neurotransmitter and monomer precursor of the melanin polydopamine pigment (Figure 1). All the compounds obtained have been subjected to structural characterization and investigation of the photo-physical and electronic properties. Moreover, a comparative study has been carried out to delineate the role of different kind of functional groups on tuning the wavelength of the emitting light. The performances of the OLED devices fabricated with the synthesized iridium(III) complexes are also discussed.

![Diagram of dopamine-inspired iridium complexes](image)

References
Visible light driven, metal-free preparation of aromatic amides from arylazo sulfones.

Stefano Protti\textsuperscript{a}, Marco Malacarne\textsuperscript{a}, Maurizio Fagnoni\textsuperscript{a}

\textsuperscript{a}PhotoGreen Lab, Department of Chemistry, University of Pavia, V.le Taramelli 10, 27100 Pavia, Italy.
e-mail: stefano.protti@unipv.it

The amide group is present in around 25\% of top-selling pharmaceuticals. In particular, aromatic amides exhibit multifaceted bioactivity, and different compounds belonging to this class have been investigated, among others, as anticancer and antiviral agent (1). Typical approaches for the synthesis of such compounds are based on the formation of a C-N bond (via activation of carboxylic acids or their derivatives in the presence of amines) (2) as well as on the construction of an Ar-C bond, e.g. via aminocarbonylation of (hetero)aryl halides (3).

We present herein the synthesis of aromatic amides via photochemical metal-free carboamidation of arylazo mesylates in the presence of isocyanides in aqueous organic solvent. The proposed method exploited the peculiar reactivity of thermally stable arylazo sulfones (which are in turn easily synthesized from the corresponding diazonium salts) to generate aryl radicals upon visible light exposure (4).

\begin{equation}
\text{G} = \text{H, NMe}_2, \text{OMe, tBu, CN, COCH}_3, \text{COOMe, NO}_2
\end{equation}

R = tBu, C\textsubscript{6}H\textsubscript{11}, 2-morpholinoethyl

\textbf{Scheme 1}

The process allowed for the achievement of a wide range of synthetic targets, including hetero- and polyaromatic derivatives, and was also applied to the smooth preparation of antidepressant moclobemide (5).

References:
From arylazo mesylates to triarylethylenes: a solar light metal-free synthesis

Carlotta Raviola, Louis Onuigbo, Stefano Protti, Maurizio Fagnoni

PhotoGreen Lab, Department of Chemistry, University of Pavia, Viale Taramelli 12, 27100 Pavia, Italy
e-mail: carlotta.raviola01@universitadipavia.it

Recently organic chemists have made many efforts in the development of synthetic routes to triarylethylenes (TAEs), which structure is diffuse in nonsteroidal estrogen agonists and antagonists for the treatment of disorders such as breast cancer, osteoporosis and cardiovascular diseases. (1) Most protocols reported in literature involves transition metal catalyzed cross-coupling reactions and the cost and toxicity of the organometallic species along with the harsh conditions required are serious drawbacks. (2) In order to overcome these limitations we proposed herein a sunlight driven, metal-free synthesis of TAEs starting from arylazo mesylates (1, Scheme 1). These are thermally stable derivatives of aryl diazonium salts (3) bearing a coloured, photolabile moiety that exhibited a wavelength-dependent photochemistry. Indeed, aryl radicals (Ar•) and triplet aryl cations (3Ar+) (4) can be selectively generated by tuning the light source (visible light for the former ones and UVA light for the latter ones). (5) Both intermediates are generated upon solar light exposition and, in the presence of aromatics or heteroaromatics, the corresponding (hetero)biaryls were obtained in satisfactory yields. (5) In the present protocol, a straightforward uncatalyzed metal-free synthesis of TAEs (2) was efficiently achieved via solar light exposition of a solution of 1 in acetonitrile/water mixture in the presence of (substituted) 1,1-diphenylethylenes. The reaction was insensitive to both the nature (electron-donating or withdrawing) and the relative position of the aromatic substituent on 1 thus allowing to obtain a wide range of TAE cores.

References

This work has been supported by Fondazione Cariplo, project 2015-0756"Visible Light Generation of Reactive Intermediates from Azosulphones".
A Hydrogen Borrowing approach to Pyrrolobenzodiazepines.

Caterina Risi, Valentina Faltoni, Maurizio Taddei,

Dipartimento di Biotecnologie, Chimica e Farmacia, Università degli Studi di Siena, Via A. Moro 2, 53100, Siena, Italy.

The pyrrolo[2,1-c][1,4]benzodiazepines (PBDs) are a family of sequence-selective DNA minor-groove binding crosslinking agents originally discovered in Streptomyces species. They are significantly more potent than systemic chemotherapy drugs with potential applications in the field of antibiotic and anticancer therapies. Recent results showed that PBDs can be effectively employed also for antibody drug conjugate target therapy.\(^1\)

As synthetic approaches to PBDs are generally multistep complex procedures, we explored the possibility to simplify some synthetic steps applying a hydrogen borrowing (HB) mechanism to the closure of the PDB ring. Different Ru catalysts were screened on the simple amino alcohol 1 giving the cyclic compounds 2 or 3 depending on the catalyst or ligand nature. (Scheme 1). This one-pot reaction takes place with a mechanism that involves a double change in the state of oxidation of the atoms, in line with the principle of redox economy.\(^2\)

Scheme 1.

Once optimized the best conditions to obtain the general structure of PDBs, we investigated the scope of the reaction on differently functionalized analogues of 1 developing also a protecting group free synthesis of a PDB containing natural product.

Synthesis of a new Riboflavin-nucleotide and its insertion into G-quadruplex forming ODNs with anti-HIV activity

Valeria Romanucci, Armando Zarrelli, Cinzia Di Marino and Giovanni Di Fabio

Department of Chemical Sciences, University of Napoli ‘Federico II’, Via Cintia, I-80126 Napoli, Italy

In the last years, G-rich oligonucleotides (GROs) able to form G-quadruplexes, have attracted considerable interest in biological and therapeutic fields (1). G-quadruplex are among the most studied DNA structures because they are thought to be involved in important biological processes such as the modulation of gene expression; in addition they present a large variety of biological properties ranging from anticancer to antiviral activities. In all cases, the G-quadruplex formation is a crucial prerequisite for the biological effects.

Recently, we reported the synthesis and full characterization of a mini-library of G quadruplex ODNs carrying aryl groups at the 5’-end through a phosphodiester bond and endowed with prominent anti-HIV activity (2,3,4). In this frame, we report here, the synthesis of new Riboflavin-Nucleoside (RF, Vitamin B) building block in which the ribitol chain is rigidified by 2’,4’ benzylidene group, the 5’-OH function is protected with DMT group and the 3’ position is functionalized with phosphoramidite (Figure).

The new Riboflavin building block is incorporated into different ODN sequences able to form G-quadruplex structures using the well known phosphoramidite chemistry.

This research project has been encouraged by recent studies on the use of RF as useful tool for both in vivo and in vitro studies: the Riboflavin is internalized through RF transporters and is one of the most efficient natural photosensitizers (5).

Several modified ODN sequences have been synthesized with a solid phase synthetic approach in good yields; their biophysical and biological characterization has been carried out in order to evaluate the effect of RF-nucleotide insertion into G-quadruplex arrangements and their anti-HIV activity.

Detecting new drugs through NMR chemosensing

Daniele Rosa-Gastaldo\textsuperscript{a}, Luca Gabrielli\textsuperscript{a}, Fabrizio Mancin\textsuperscript{a}

\textsuperscript{a} Dipartimento di Scienze Chimiche, Università di Padova, via Marzolo 1, 35131 Padova, Italy.

\textit{e-mail: daniele.rosagastaldo@studenti.unipd.it}

A designer drug is an analog of a controlled substance designed to mimic the pharmacological effects of the original drug, while avoiding its classification as illegal and/or its detection in standard drug tests. In particular, several notable recreational drugs are members of the substituted phenethylamines class.

In order to detect new substituted phenethylamines, we apply our recently reported “NMR chemosensing” method. The rationale of this method rests upon the slow diffusion rate of the 2-nm gold core nanoparticles (AuNPs) compared to small analytes, and on the intermolecular dipolar interactions as a pathway to transfer magnetization between two interacting species (1,2,3). The NMR chemosensing experiment starts with a diffusion filter which dephases the magnetization of all the small, fast diffusing species in the sample while retaining that of the NPs. This magnetization is then transferred via NOE to the small analytes interacting with the NPs monolayer, and the resulting signals are detected (3). The main advantage is the fact that the signal produced by the sensing system is the full NMR spectrum of the analyte: this allows not only the detection and quantification of the analyte, but also its unambiguous identification.

Hence, we designed and synthesised new AuNPs able to interact selectively with the target molecules. The use of this AuNPs as NMR chemosensor, allowed the detection in water of amphetamine analogues, together with the identification of their molecular structure.


Acknowledgements: This work was funded by the ERC Starting Grants Project MOSAIC (Grant 259014) and progetto strategico NAMECA
Synthesis of C2-modified chiral PNA using Minimally Protected Submonomer Synthesis

Andrea Rozzi\textsuperscript{a}, Matteo Macchiavelli\textsuperscript{a}, Alex Manicardi\textsuperscript{a}, Roberto Corradini\textsuperscript{a}

\textsuperscript{a} Università degli Studi di Parma, Dipartimento di Scienze Chimiche, della Vita e della Sostenibilità Ambiente, Viale delle Scienze 17A Parma. 
\textit{e-mail: andrea.rozzi@studenti.unipr.it}

PNAs (Peptide Nucleic Acids, figure a) are synthetic analogous of DNA where the phosphate backbone is substituted by amide bonds. They have been used in several applications, in diagnostics and therapeutics (1). PNAs can be obtained using peptide synthesis, mainly with Boc/Z or Fmoc/Bhoc strategies using commercially available monomers, but modified PNA on the backbone, the nucleobase or on both, useful for introducing new properties, can be obtained by synthesizing appropriate precursors (2). Previously, our group showed that the insertion of a stretch of C-2 backbone-modified monomers (figure b) with D-stereocchemistry can increase the sequence-selectivity of the interaction of PNA with DNA, especially when recognition of a single point mutated DNA sequence is required (3,4). This “Chiral Box” can therefore be very useful in sensor development aiming at tumor-related point mutations, such as those of the KRas or NRas genes.

In this communication we present a simplified route to C2-modified “Chiral Box” PNA by submonomeric strategy (figure c). The procedure is based on a minimal protection approach, using the PNA backbone with only terminal amino group Fmoc-protection. This submonomer can be obtained using a simplified (figure d) metal-catalyzed reductive amination procedure (5). Incorporation into the PNA chain can be obtained, without branching side reactions, by careful choice of the coupling agent and coupling conditions; subsequent coupling with the desired nucleobase provides the incorporation of the modified PNA monomer. The optical purity of the submonomer and the effect on it of the subsequent coupling have been evaluated using a model reaction with phenylalanine methyl ester, by \textsuperscript{1}H and \textsuperscript{13}C NMR. This work was carried out in the frame of the H2020 ULTRAPLACAD project aimed to early diagnosis of colorectal cancer.

References:
Microsomal Prostaglandin E2 Synthase-1 potential inhibitors: design, synthesis and biological evaluation.

Alessandra Russo\textsuperscript{a}, Stefania Terracciano\textsuperscript{a}, Gianluigi Lauro\textsuperscript{a}, Maria Carmela Vaccaro\textsuperscript{a}, Raffaele Riccio\textsuperscript{a}, Giuseppe Bifulco\textsuperscript{a}, Ines Bruno\textsuperscript{a}.

\textsuperscript{a} Department of Pharmacy, University of Salerno, Via Giovanni Paolo II, 84084, Fisciano, Salerno
e-mail: alrusso@unisa

Microsomal prostaglandin E2 synthase-1 (mPGES-1) is a member of the MAPEG (Membrane-Associated Proteins in Eicosanoid and Glutathione metabolism) proteins family and represents an important target for anti-inflammatory and anticancer drugs discovery and development.\textsuperscript{(1)} This membrane homotrimer is an inducible GSH-dependent enzyme involved in the arachidonic acid cascade; in particular, it is responsible for the conversion of COX-derived unstable peroxide PGH2 in PGE2, a key bioactive lipid mediator of a variety of biological effects associated with inflammation disorders.\textsuperscript{(2)} The active site of this enzyme is located at the interface of the three asymmetric monomers, which in turn are formed by four $\alpha$-helices and are partially occupied by the glutathione (GSH) cofactor.\textsuperscript{(3)} Since many studies proved mPGES-1 overexpression in several inflammatory disorders as well as in different human cancers, this enzyme can be considered as a promising target in cancer and antiinflammatory therapy.\textsuperscript{(4)} Moreover the possibility of overcoming the classical side effects commonly associated with use of traditional anti-inflammatory drugs (NSAIDs), that inhibit the cyclooxygenase pathway, is another important reason that drives the discovery of new and more potent mPGES-1 inhibitors.\textsuperscript{(5)} Basing on the human mPGES-1 X-ray structure we performed a virtual screening on a huge number of synthetically accessible molecules in order to select the best candidates for chemical synthesis. Here we report the identification of a small collection of 2,4 thiazolidindiones as a new potential class of m-PGES1 inhibitors.

Computational Study on the Gas-Phase and Aqueous Solution Acidity of Nicotine

Maurizio Ciofalo, Filippo Saiano

Dipartimento di Scienze Agrarie, Alimentari e Forestali, viale delle Scienze Ed. 4, 90128 Palermo.
e-mail: omega@unipa.it

Dielectric continuum solvation models (1), recently introduced in the routine of computational chemistry, have allowed organic chemists to afford solvation free energies, thus getting a closer insight on the real thermodynamics of chemical reactions in solution. Hydron transfer reactions are by far the most studied due to their importance both in physico-chemical systems and in synthetic applications.

Since, on the other hand, molecules have almost always a notable molecular flexibility, each computational assessment should certainly address an accurate conformational analysis of each species involved in the chemical equilibrium. This rather annoying and troublesome complication has been automated and made simpler to unravel by using the application called RotAnal (Rotational Analysis), still in steady development at our laboratories. RotAnal is a smart front-end program that performs a conformational sampling, pruning, refinement and analysis through an original, multistep procedure, through any of the most widely used quantum computing packages like Gaussian™ and Firefly™, and MPI parallel computing across a PC cluster in Microsoft Windows™ environments (2).

Alkaloid nicotine has been selected in the present pilot study as a convenient model due both to the simplicity of their structure and phase space and the easy availability of the experimental aqueous sequential ionization pKa’s (3).

Calculations performed up to different theoretical levels of theory (Hartree-Fock, Kohn-Sham DFT) both in vacuo and in PCM aqueous solution have provided us with the relative and absolute pKa’s. Results show that asserting about hydronation sites of real-chemistry bases grounded mainly upon the empiric rules of introductory organic chemistry should be treated with caution.

A population analysis based on the Natural Bond Orbital (NBO) paradigm (4) has also allowed us to correlate the torsional preferences with the presence of stabilizing interactions between filled and empty orbitals through hyperconjugation effects.

New Mannosylcalix[n]Arenes as Multivalent Ligands for the Inhibition of Hiv/DC-SIGN Interaction

Francesco Sansone,a Ilaria Morbioli,a Andrea Magini,a Vanessa Porkolab,b Alessandro Casnati,a Franck Fieschi b

a Dipartimento di Scienze Chimiche, della Vita e della Sostenibilità Ambientale, Università di Parma, Parco Area delle Scienze 17/a, 43124 Parma, Italy. b Institut de Biologie Structurale, Université Grenoble Alpes, Grenoble, France.

The fight against human immunodeficiency virus is a big challenge of current times and huge efforts have been made to develop new effective therapies (1). One of the main pathway of infection exploits dendritic cells (DCs) that, used by the virus as Trojan horse, efficiently transfer virions to T-cells, where replication takes place (2). Among receptors on DCs surface, DC-specific ICAM-3 grabbing non-integrin (DC-SIGN) is strongly involved in the process, by interacting with the high-mannose glycans of glycoprotein gp120 present on the virus envelope (3). Therefore, different research groups are focusing their work on the development of glycomimetic compounds that could interfere with gp120/DC-SIGN interaction. Due to the tendency of DC-SIGN to oligomerize on the cell surface (Figure) (3), a multivalent approach seems to be a valuable strategy to design efficient and selective ligands. In this context, we designed and synthesized a small series of mannosylated calixarenes (Figure). The possibility of tuning valency and geometry of the ligating units makes calixarenes very convenient scaffold for generating multivalent ligands (4,5). Preliminary experiments by Surface Plasmon Resonance evidenced the ability of our compounds to bind to DC-SIGN.

Figure: a) Schematic representation of a DC-SIGN tetramer on the cell surface; b) multivalent mannosylcalix[n]arenes synthesized in this work.

Calixarene-Based Multivalent Inhibitors for Carbonic Anhydrases

Francesco Sansone\textsuperscript{a}, Valeria Pizzolante\textsuperscript{a}, Silvia Bu\textsuperscript{b}, Davide Sbravati\textsuperscript{a}, Fabrizio Carta\textsuperscript{b}, Alessandro Casnati\textsuperscript{a}, Claudiu T. Supuran\textsuperscript{b}

\textsuperscript{a} Dipartimento di Scienze Chimiche, della Vita e della Sostenibilità Ambientale, Università di Parma, Parco Area delle Scienze 17/a, 43124, Parma, Italy. \textsuperscript{b} Neurofarba Department, Università di Firenze, Via Ugo Schiff 6, Polo Scientifico, 50019 Sesto Fiorentino (Firenze), Italy.

e-mail: francesco.sansone@unipr.it

Carbonic anhydrases (CAs) are a group of ubiquitously expressed metalloenzymes (1) involved in numerous physiological and pathological processes, including gluconeogenesis, lipogenesis, ureagenesis, tumour progression and in the growth and virulence of various pathogens. In addition to the established role of CA inhibitors (CAIs) as diuretics and antiglaucoma drugs, it has recently emerged that CAIs could have potential as novel anti-obesity, anticancer and anti-infective drugs (2,3). Recent studies suggest that CA activation may provide a novel therapy for Alzheimer’s disease. Moreover, selectivity towards the different CAs isoforms is a valuable and challenging feature that should characterize the action of CAs inhibitors.

Primary sulphonamides, sulphamates and sulphamides act as carbonic anhydrase inhibitors (CAIs) by binding to the catalytic Zn\textsuperscript{2+} ion in the active site of the enzyme and blocking its function (4). We then designed and prepared a small family of new calixarenes functionalized with sulphonamide units (e.g. 1) to be tested as inhibitor of the CAs activity. Differently to traditional drugs, calixarenes can be functionalized in several ways exposing active units, for instance pharmacophores, in multiple copies and different orientations in space. This feature allows to exploit the so called “multivalency effect” that can result in an affinity towards the biological target significantly higher with respect to analogous monomeric ligands. Usually, multivalent ligands as those based on calixarene scaffolds show the beneficial effects of multivalency in the binding to macromolecules presenting multiple copies of equivalent recognition sites (5). However, recently some attempts have been done to verify this effect in the inhibition of enzymes (6,7). The sulphonamido calixarenes have been tested towards six different CA isoforms (hCAI, hCAII, hCAIX, VchCAβ, Can2, MgCA) and compared with two monomeric analogues and acetazolamide, a potent drug in clinical use known as CAs inhibitor. Interestingly, some of our derivatives have shown Ki values in the μM-nM range. Synthesis of the ligands and inhibition studies will be described in this presentation.

How the ring size and the side chains affect the solid state assembly of cyclopeptoids.

Rosaria Schettini, Veronica Iuliano, Irene Izzo, Consiglia Tedesco and Francesco De Riccardis

Department of Chemistry and Biology “A. Zambelli”, University of Salerno, Via Giovanni Paolo II, 132, 84084 Fisciano (Salerno), Italy. - e-mail: rschettini@unisa.it

The design of novel supramolecular architectures represents an area of growing interest that involves various fields of research such as biochemistry, crystal engineering, material science. Macrocycles are potentially applicable in different areas of nanoscience. A new class of macrocyclic systems is constituted by cyclopeptoids, cyclooligomers of N-alkyl glycines. Recently we have highlighted the role of the side chains (1) and of ring size (2) in the solid state assembly and how these strongly affects specific interactions in supramolecular architectures. For example the cyclohexapeptoid containing propargylic side chains shows a layered architecture while the cyclooctapeptoid possesses a tubular structure (figure 1). The combination of propargyl and methoxyethyl side chains in a cyclohexapeptoid provided a tubular solid state assembly, that undergoes a reversible single-crystal-to-single-crystal transformation upon guest release/uptake (figure 2). The transformation is connected to the formation of an unprecedented “CH–π zipper”, which can reversibly open and close, allowing for guest sensing. (3) In this communication the synthesis and solid-state assembly of new cyclooctapeptoids decorated with methoxyethyl and propargyl side chains in different number and position along the peptoid skeleton will be discussed (figure 3).

Figure 1. Cyclohexapeptoid: columnar assembly versus Cyclooctapeptoid: tubular structure.

Figure 2. Cyclohexapeptoid: flexible conformation.

Figure 3. Novel Cyclooctapeptoids.


Valeria Zanichelli,\textsuperscript{a} Giulio Ragazzon,\textsuperscript{b} Guido Orlandini,\textsuperscript{a} Margherita Venturi,\textsuperscript{b} Alberto Credi,\textsuperscript{c,d} Serena Silvi,\textsuperscript{b} Arturo Arduini,\textsuperscript{a} and Andrea Secchi\textsuperscript{a}

\textsuperscript{a} Dipartimento di Scienze Chimiche, della Vita e della Sostenibilità Ambientale, Università di Parma, Parco Area delle Scienze 17/A, I-43124 Parma, Italy; \textsuperscript{b} Dipartimento di Chimica “G. Ciamician”, Università di Bologna, via Selmi 2, 40126 Bologna, Italy; \textsuperscript{c} Dipartimento di Scienze e Tecnologie Agro-alimentari, Università di Bologna, viale Fanin 50, 40127 Bologna, Italy; \textsuperscript{d} Istituto per la Sintesi Organica e la Fotoreattività, Consiglio Nazionale delle Ricerche, via Gobetti 101, 40129 Bologna, Italy.

E-mail: andrea.secchi@unipr.it

A substrate can modify its chemical features, up to a change of its reactivity, as a consequence of non-covalent interactions upon inclusion within a molecular host.\textsuperscript{(1,2)} Since the rise of supramolecular chemistry, this phenomenon has stimulated the ingenuity of scientists to emulate the function of enzymes by designing supramolecular systems in which the energetics and selectivity of reactions can be manipulated through programmed host-guest interactions and/or steric confinement. In this paper we investigate how the engulfment of a positively charged pyridinium-based guest inside the π-rich cavity of a tris-(N-phenylureido)calix[6]arene host \textsuperscript{(3)} affects its reactivity towards a S_N2 reaction. We found that the alkylation of the complexed substrates leads to the formation of pseudorotaxanes and rotaxanes with faster kinetics and higher yields with respect to the standard procedures exploited so far.\textsuperscript{(4)} More importantly, the strategy described here expands the range of efficient synthetic routes for making mechanically interlocked species with a strict control of the mutual orientation of their nonsymmetric molecular components.

Deep Eutectic Solvents as convenient media for the synthesis of gold and platinum nanoparticles

Gabriella Siani\textsuperscript{a}, Antonello Di Crescenzo\textsuperscript{a}, Simona Boncompagni\textsuperscript{b}, Romina Zappacosta\textsuperscript{a}, Valeria Ettorre\textsuperscript{a}, Antonella Fontana\textsuperscript{a}, Matteo Tiecco\textsuperscript{c}, Raimondo Germani\textsuperscript{c},

\textsuperscript{a} Dipartimento di Farmacia, Università “G. d’Annunzio” - Via dei Vestini, 31 Chieti. \textsuperscript{b} Dipartimento di Neuroscienze, Imaging e Scienze Cliniche, Università “G. d’Annunzio” - Via dei Vestini Chieti. \textsuperscript{c} Dipartimento di Chimica, Biologia e Biotecnologie - Università degli Studi di Perugia- Via Elce di Sotto, 8 Perugia

e-mail siani@unich.it

Deep Eutectic Solvents (DESs) are a new class of solvents which have been developed as alternative to ionic liquids (ILs) to overcome IL toxicity, poor biodegradability and their not environmentally friendly synthesis.\textsuperscript{(1)} Even if DESs share with ILs many physicochemical features such as density, viscosity, low vapor pressure and non flammability, they chemically differ from ILs as they can be obtained also by non ionic species. Indeed DES are formed by simply mixing two components, at least an hydrogen bond donor and a hydrogen bond acceptor, resulting in an eutectic mixture with a melting point lower than those of the pure substances.\textsuperscript{(2)} The advantages of DES over ILs are their ease of synthesis, low production costs and the fact that they can be obtained from biodegradable and biocompatible components, fulfilling the green chemistry principles. DESs have been successfully used as alternative media to organic solvents in many fields\textsuperscript{(3)} such as gas adsorption, biotransformations, metal processing, organic synthesis, metal nanoparticle synthesis. Metal nanoparticles (MNPs), in particular those belonging to the noble metal group, such as gold and platinum, are very attractive functional materials due to their peculiar properties that can be potentially useful in a wide range of applications. AuNPs and PtNPs are emerging as important tools in electronics, optics, catalysis, clinical diagnostic and biomedicine.\textsuperscript{(4)} It is noteworthy that their electric, optical, magnetic and catalytic properties are strongly dependent on size and shape therefore the development of an efficient, eco-sustainable and shape/size controlling synthesis constitutes a very primary challenge.

The present communication describes the synthesis of AuNPs and PtNPs in three different DESs used as the solvent. In the studied DESs, the HBA component was the betaine N,N,N-trimethylglycine and the HBD counterpart was glycolic acid or phenylacetic acid or oxalic acid.\textsuperscript{(5)} The synthesis was performed in the presence and in the absence of a reducing agent (NaBH\textsubscript{4} or ascorbic acid). The growth and the time-dependent stability of NPs were followed by UV-Vis measurements. Transmission electron microscopy (TEM) was used to determine NP size and shape. TEM micrographs revealed distinct and well separated particles of shape and average size depending on the synthetic protocol and on the particular medium.

Enantioselective phase transfer catalyzed alkylation of phthalide-3-carboxylic esters

Marina Sicignano, Maria Leda Marino, Francesco De Riccardis, Irene Izzo, Giorgio Della Sala

Dipartimento di Chimica e Biologia “A. Zambelli”, Università degli Studi di Salerno, Via Giovanni Paolo II 132, 84084 Fisciano (SA).

E-mail: msicignano@unisa.it

Isobenzofuran-1(3H)-ones, also known as phthalides, are aromatic heterocycles of considerable synthetic interest for organic chemists since they are widely present in many natural products and therapeutically useful agents. More than 180 phthalide compounds have been identified from plants, fungi and bacteria displaying a broad range of pharmacological activities (1). Furthermore, they are useful intermediates for the synthesis of biologically active compounds. Significant efforts have been focused on synthesizing functionalized phthalides. In particular, phthalides bearing a quaternary stereocenter at C-3 are important derivatives. Most of the synthetic stereoselective strategies involve the construction of the lactone ring (2), while the stereoselective introduction of a group on C-3 has been much less investigated. Organocatalyzed Mannich reaction, Michael addition and alkylation with Morita-Baylis-Hillman carbonates has been described in literature (3-5), but alkylation under phase transfer catalysis has never reported to date.

Here we describe our preliminary results in the first enantioselective alkylation of phthalide-3-carboxylic esters promoted by cinchona alkaloid-derived and binaphthyl-derived quaternary ammonium salts (Scheme 1).

Modeling of 5,6-dihydroxyindole and caffeic acid on TiO$_2$: direct electron injection in Dye-Sensitized Solar Cells

Adalgisa Sinicropi$^{a,b}$, Maria Laura Parisi$^{a,b}$, Alessio d’Ettorre$^a$, Lorenzo Zanè, Gianna Reginato$^c$, Maurizio Taddei$^a$, Riccardo Basosi$^{a,b}$

$^a$Dipartimento di Biotecnologie, Chimica e Farmacia, Università di Siena, via A. Moro, 2, 53100 Siena, Italy; $^b$CSGI, Consorzio per lo Sviluppo dei Sistemi a Grande Interfase, via della Lastruccia 3, 50019, Sesto Fiorentino, Italy; $^c$Istituto di Chimica dei Composti Organometallici (CNR-ICCOM), Via Madonna del Piano 10, 50019 Sesto Fiorentino, Italy.

email: adalgisa.sinicropi@unisi.it

Catechol-based sensitizers have been indicated as light-harvesting molecules for Dye-Sensitized Solar Cells (DSSC). Upon binding TiO$_2$ they exhibit broad photoabsorption dye-to-TiO$_2$ charge transfer (DTCT) bands, in the longer wavelength region, whose photoexcitation leads to a direct electron injection in the TiO$_2$ semiconductor (1,2). In order to identify novel sensitizers for DSSC employing such a direct mechanism, we model the electron injection mechanism of 5,6-dihydroxyindole (DHI) and caffeic acid on (TiO$_2$)$_9$ using density functional theory (DFT) methods. The calculation of excitation energies at the time-dependent DFT level show that for both sensitizer/TiO$_2$ systems it is possible to identify a broad DTCT band along with the absorption of the isolated chromophore. The inspection of the wavefunction plots of the molecular orbitals reveals that the transitions governing the DTCT excitation include the HOMO, localized on the sensitizer, and several unoccupied orbitals whose electron density is mainly localized on the TiO$_2$ cluster with a non-negligible contribution on the TiO$_2$-bonding oxygens of the sensitizers. These features indicate a strong electronic coupling for both TiO$_2$-absorbed sensitizers, which is in favor of a direct mechanism of injection. The strong coupling is also confirmed by a Density of States (DOS) and partial DOS analysis. In conclusion, our results strongly suggest that a direct electron transfer mechanism applies for both DHI and caffeic acid when adsorbed on TiO$_2$ and used as sensitizers for DSSC.

References:
Synthesis of a new dendritic amphiphilic polyester with pentaerythritol core and a multifunctional periphery for linking amino acids and for use in gene therapy

Silvana Alfii; Gaby Brice Taptueii

aDipartimento di Farmacia, Università di Genova, Viale Cembra 4, I-16147, Genova, Italia
e-mail: brice@difar.unige.it

Dendrimers are synthetic polymers characterized by tree-like branched symmetric structure, globular shape, low polydispersity and several functions at the periphery which allow further functionalization. Their cavities can accommodate small drugs molecules protecting them from premature degradation, increasing their solubility in biological fluids, decreasing their toxicity and favoring their bioavailability. Dendrimers containing protonable nitrogen atoms can electrostatically bind nucleic acids. These reasons make dendrimers appealing materials for various biomedical applications such as drug or gene delivery non viral carriers, biosensors, bioimaging agents and theranostics. Well known polymeric systems such as bPEI or PAMAM are among the most investigated synthetic vectors with efficient transfection activity but also affected by high cytotoxicity so chemical modifications are required to reduce these drawbacks and allow a real use in gene therapy. It is known that amino acids (1, 2, 3) or peptides (4) were often used for these purposes and arginine is known to improve siRNA cellular uptake (5), efficiency of transfection and to reduce toxicity (6, 7). Hydrophobic segments in the dendrimer structure are also important in the internalization process (3) and may contribute to reduce toxicity caused by high ionic character of vectors. Looking at this background in this communication we report the step-wise protocol and NMR characterization of a new hydrolysable polyester-based dendrimer of third generation built on pentaerythritol as core and with a C-18 saturated alkyl chain as hydrophobic segment.

The peripheral 24 OH groups make this amphiphilic dendritic structure fit to the esterification with selected amino acids for obtaining polycationic non viral vectors to use in gene delivery.

Discovery of Potential Small Molecule Modulators of Macrodomain Proteins

Stefania Terracciano\textsuperscript{a}, Alessandra Russo\textsuperscript{a}, Gianluigi Lauro\textsuperscript{a}, Raffaele Riccio\textsuperscript{a}, Giuseppe Bifulco\textsuperscript{a}, Ines Bruno\textsuperscript{a}

\textsuperscript{a} Department of Pharmacy, University of Salerno, Via Giovanni Paolo II, 84084, Fisciano, Salerno
e-mail: sterracciano@unisa.it

Macromodules are a family of evolutionarily conserved proteins able to recognize ADP-ribosylation, an important reversible post-translational modification involved in many biological functions, including regulation of chromatin structure, transcription, DNA repair, cell differentiation and proliferation.\textsuperscript{1} In humans, there are at least 10 members classified in four groups, however all their functions are not yet fully clarified.

Among these, the MacroD1, MacroD2, and C6orf130 have recently been shown to act as epigenetic erasers as they are able to remove ADP-ribose from mono-ADP-ribosylated substrates.\textsuperscript{2,3} Despite the exact biological roles of MacroD1 and MacroD2 are not yet known, recent findings suggest that the dysregulation or mutation of macromodules might be related to several human diseases, including cancer and neurodegeneration. Furthermore, MacroD1 and MacroD2 overexpression is observed in endometrial, gastric and breast carcinoma and is linked to cancer progression and cell invasiveness in tissue cultures.\textsuperscript{4}

In this context, macromodule proteins can be considered strategic targets for the identification of new promising anticancer agents.

Based on these premises, using different drug discovery approaches we evaluated both commercially available fragments and synthetically accessible small molecules in order to identify new chemical entities able to interact with the macromodule-containing proteins as novel and appealing chemotherapeutics.

References:
Photochemical trifluoromethylation of aromatics by \( N \)-aryltrifluoromethanesulfonimides

*Edoardo Torti*\textsuperscript{a}, Stefano Protti\textsuperscript{a}, Maurizio Fagnoni\textsuperscript{a}

\textsuperscript{a} PhotoGreen Lab, University of Pavia, Department of Chemistry, Via Taramelli 12, 27100, Pavia, Italy. e-mail: edoardo.torti01@universitadipavia.it

Fluorine is a very popular element in lead optimization for drug discovery. Indeed, its presence in the structure of drug candidates can improve their metabolic stability, membrane permeability and bioactivity, thus enhancing their pharmacological properties.\( ^{(1)} \) Among fluorinated drugs, a great number is given by aromatics bearing a trifluoromethyl group (e.g. Fluoxetine, Leflunomide, Nilutamide, etc.). For this reason, much efforts are done to find synthetic ways to incorporate the trifluoromethyl group onto aromatic rings and researchers mainly focus their research on the formation of the Ar-CF\(_3\) bond making use of transition metal catalysis.\( ^{(2)} \) A greener and more convenient strategy relies on radical trifluoromethylation by photoredox catalysis\( ^{(3)} \) albeit expensive catalysts and reagents are usually employed.

Herein we present a simple and clean photochemical trifluoromethylation of aromatic compounds using cheap \( N \)-aryltrifluoromethanesulfonimides as trifluoromethylating agents. As an example, \( N \)-(4-acetylphenyl)-1,1,1-trifluoro-\( N \)-[(trifluoromethyl)sulfonyl]methanesulfonamide 1 was irradiated (310 nm) in deaerated dichloromethane in the presence of aromatic and heteroaromatic compounds until total conversion of 1 is reached, giving trifluoromethylated derivatives 2. A reasonable mechanism for the reaction involves a photoinduced homolysis of a N-S bond in compound 1 to afford a trifluoromethanesulfonyl radical readily prone to release SO\(_2\) thus forming a trifluoromethyl radical.\( ^{(4)} \) The latter species then reacts with aromatic rings to give eventually compound 2. Noteworthy, each of the two N-S bond may be sequentially broken during irradiation, thus improving the overall performance of the trifluoromethylation. In selected cases, the reaction can be likewise repeated with similar (or better) results upon sunlight exposition as well as by using a continuous flow apparatus. These protocols may open the ways to “window-ledge” reactions on laboratory scale as well as flow trifluoromethylations of bulk chemicals.

Expanding the synthetic utility of the electrophilic N-transfer to the sulfur atom

Arianna Tota\textsuperscript{a}, Sahra St. John-Campbell\textsuperscript{b}, James A. Bull\textsuperscript{b}, Leonardo Degennaro\textsuperscript{a}, Renzo Luisi\textsuperscript{a}

\textsuperscript{a} Department of Pharmacy-Drug Sciences, University of Bari “A. Moro” Via E. Orabona 4, Bari 70125 (Italy); \textsuperscript{b} Department of Chemistry, Imperial College London South Kensington, London SW7 2AZ (UK); e-mail: arianna.tota@uniba.it

Recently we developed straightforward strategies for the preparation of NH-sulfoximines\textsuperscript{(1,2,3)}. Our strategy holds on a direct N-transfer to sulfoxides and a simultaneous NH- and O-transfer to sulfides. With the aim of expanding N-transfer to other sulfur compounds, we investigated the reactions of thiols and sulfanimides to synthesize respectively sulfonimidates and sulfonimidamides. Literature reports that these compounds need a multistep strategy or different starting materials\textsuperscript{(4,5)}. The new strategy is carried out by using bisacetoxiodobenzene as oxidant and several N-sources, such as NH\textsubscript{2}COONH\textsubscript{4}, AcONH\textsubscript{4} and NH\textsubscript{3}. This versatile protocol could give access to useful compounds in drug discovery programs\textsuperscript{(6)}.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{strategy.png}
\caption{Strategy for synthesis of sulfonimidates and sulfonimidamides by NH-transfer}
\end{figure}

References:
Synthesis of dendrons and dendrimers glycoconjugates for biomedical applications

Mattia Vacchini, Roberto Guizzardi, Andrea Marchesi, Laura Cipolla.

Department of Biotechnology and Biosciences, University of Milano-Bicocca, P.zza della Scienza 2, I-20126 Milano.
e-mail: m.vacchini@campus.unimib.it

Dendrimers are nano-sized macromolecules, featured with a hyperbranched structure displaying a high number of functional groups on its surface, which can be exploited for further derivatisation with different kind of (bio)molecules. Given their peculiar structure and properties, dendrimers have been proposed for a variety of biomedical applications (i,ii). Interactions between cells and their environments are mediated by protein-carbohydrate recognition processes on cell surface, triggering a wide variety of biological events. In this context, highly branched glycosylated structures may be interesting tools to enhance these recognition events, helping in elucidating the biological role behind carbohydrate as signaling molecules, which mediate aspects of the immune response and of cellular recognition and adhesion (e.g. through their interactions with lectins) or acting as antagonist of important recognition events (i.e. involving viruses or bacteria) (iii). In this work, we present the synthesis of a novel hyperbranched monodisperse linear glycodendrimer, based on 2,2-bis-(hydroxymethyl)-propionic acid (bis-MPA) by convergent metathesis-mediated coupling between the alkene-terminated focal point of bis-MPA dendrons, which terminal ends expose multiple aminoxy groups that has been exploited for glycoconjugation with unprotected sugars. To the best of our knowledge, this is the first example of the use of metathesis for focal point coupling and, as carbohydrates are known to be fundamental biomolecules for cellular signaling, these hyperbranched glycodendrimers may provide good benefit to biomedical and tissue engineering applications, where high density of ligand exposure and spatial topographical presentation are crucial to bring about desired biological effects (iv,v). Dendrimers synthesis started from a bivalent, tetravalent and octavalent dendron monomers with a core double bond and Boc-protected aminoxy ends and achieves symmetrical dendrimers, doubling the branching degree of each structure by a single-step metathesis reaction with Hoveyda–Grubbs2nd generation catalyst. Deprotected aminoxy ends of the obtained symmetrical dendrimers were then reacted with maltose, as sample saccharide, yielding glycodendrimers exposing multiple sugar moieties at their ends. These hyperbranched structures are potentially capable of eliciting a biological response in a biomedical context, as the exposed α-glucoside epitopes are known to be fundamental signaling moieties in a variety of biochemical interactions (vi,vii).

i L. Wu, M. Ficker, J. B. Christensen, P.N. Trohopoulos and S. M. Moghimi. Bioconj. Chem. 2015, 26, 1198–1211. DOI: 10.1021/acs.bioconjchem.5b00031
Studies of Electronic Properties of KuQuinones

Francesca Valentini\textsuperscript{a}, Federica Sabuzi\textsuperscript{a}, Valeria Conte\textsuperscript{a}, Pierluca Galloni\textsuperscript{a}

\textsuperscript{a}Università degli Studi di Roma Tor Vergata, Dipartimento di Scienze e Tecnologie Chimiche, Via della ricerca scientifica,00133, Rome, Italy.

e-mail: francesca.valentini6@gmail.com

Few years ago we developed a new one-pot synthesis for highly conjugated pentacyclic compounds, called KuQuinones (KuQs) (1). The general synthetic procedure allowed us to prepare a small library of differently substituted KuQ derivatives. These compounds are characterized by a broad absorption spectrum in the visible region and a low reduction potential with respect to simpler quinoid compounds. In particular KuQs show three characteristic reduction processes, while no oxidation processes are observed. Due to these interesting properties, we explored the ability of KuQs to act as sensitive material in photoelectrochemical devices (2,3) obtaining interesting results.

In order to fully characterize active reduced species of KuQs we are currently investigating their nature through spectroelectrochemical measurements and DFT calculations. In this contribution, the preliminary characterization of KuQuinones anions we will be presented.

\textbf{Figure 5 (left)} Structure of a KuQ derivative. \textbf{(right)} Cyclic Voltammetry of 1-(3-Ethoxycarbonylpropyl)KuQuinone.

References:

Monomolecular G-quadruplex structures with inversion of polarity sites: new topologies and potentiality

Antonella Virgilio, Annapina Russo, Teresa Amato, Giulia Russo, Luciano Mayol, Veronica Esposito and Aldo Galeone

Dipartimento di Farmacia, Università degli Studi di Napoli Federico II, Via D. Montesano 49, 80131 Napoli, Italy.

G-quadruplex structures are secondary conformations of nucleic acids whose constitutive unit is the G-tetrad or G-quartet (1). This building block consists of a square planar arrangement of four guanosines in which each base is associated to the adjacent ones through four hydrogen bonds. Stacking of two or more G-tetrad units can form larger and more stable structures. Soon after they were discovered, these structures were subject to several chemical modifications and conjugation with the aim to promote, stabilize and investigate a particular conformation, improve their properties and encourage the formation of high-order structures (2). Among the sugar-phosphate backbone modifications, the introduction of 3'-3' and/or 5'-5' inversion of polarity sites (IPS) represents an almost “natural” and less heavy chemical structural change, since it involves only naturally occurring deoxyribonucleotides (3). In order to expand the structural variability and the topological repertoire of the G-quadruplex structures by exploiting the presence of IPSs, we designed and synthesized three oligonucleotide sequences, each containing one 3'-3' and two 5'-5' inversion of polarity sites, and four G-runs with a variable number of residues, namely two, three and four \( mTG_2T, mTG_3T \) and \( mTG_4T \) with sequence 3'-TG\(_n\)T-5'-5'-TG\(_n\)T-3'-3'-TG\(_n\)T-5'-5'-TG\(_n\)T-3' in which \( n = 2, 3 \) and 4, respectively). These oligonucleotides have been investigated by circular dichroism, nuclear magnetic resonance spectroscopy and electrophoresis methods, comparing them with their canonical counterparts \( (TG_nT)_4 \) \( (n = 2, 3 \text{ and } 4) \). Oligonucleotides \( mTG_3T \) and \( mTG_4T \) have been proven to form very stable unprecedented monomolecular parallel G-quadruplex structures, characterized by three side loops containing the inversion of polarity sites. Both G-quadruplexes have shown an all-\( \text{syn} \) G-tetrad, while the other guanosines adopt \( \text{anti} \) glycosidic conformations. All oligonucleotides investigated have shown a noteworthy antiproliferative activity against lung cancer cell line Calu 6 and colorectal cancer cell line HCT-116 \(^{53-55}\). Interestingly, \( mTG_3T \) and \( mTG_4T \) have proven to be mostly resistant to nucleases in a fetal bovine serum assay. The whole of the data suggest the involvement of specific pathways and targets for the biological activity.

References:
A Trifunctional Calix[4]arene as Mimic of DNA Topoisomerase I for the Promotion of Phosphoryl Transfer Processes

Stefano Volpi\textsuperscript{a}, Riccardo Salvio\textsuperscript{b}, Roberta Cacciapaglia\textsuperscript{b}, Francesco Sansone\textsuperscript{a}, Luigi Mandolini\textsuperscript{b}, Alessandro Casnati\textsuperscript{a}

\textsuperscript{a}Dipartimento di Scienze Chimiche, della Vita e della Sostenibilità Ambientale, Università degli Studi di Parma, Viale delle Scienze 17/A, 43124, Parma, Italy; \textsuperscript{b}Dipartimento di Chimica e Sezione Meccanismi di Reazione IMC−CNR, Università La Sapienza, P. le Aldo Moro 5, 00185 Roma, Italy.

The cone-calix[4]arene scaffold has been reported as a convenient platform for the creation, after an appropriate functionalization, of artificial catalysts able to mimic the action phosphodiesterase enzymes (1). In this poster will be presented the trifunctional calix[4]arene (1H\textsubscript{3}\textsuperscript{2+}) (2), functionalized at the upper rim two guanidinium units and a phenolic hydroxyl group in order to reproduce the catalytic triad at the active site of human DNA topoisomerase I (3).

The diprotonated form of the catalyst (1H\textsubscript{2}\textsuperscript{+}) was tested in the cleavage of the DNA model compound bis(p-nitrophenyl) phosphate (BNPP) in 80\% DMSO solution, enhancing the p-nitrophenol liberation rate up to 6.5 × 10\textsuperscript{4}-folds respect to the background hydrolysis at pH 9.5. According to the experimental data, the three active units cooperate to cleave the substrate in a two-step reaction sequence (Figure 1) that involves a phosphoryl transfer process from BNPP to the nucleophilic phenolate moiety of (1H\textsubscript{2}\textsuperscript{+}), followed by the liberation of a second equivalent of p-nitrophenol from the phosphorylated intermediate, assisted by the neighboring guanidine/guanidinium catalytic dyad.

![Figure 1: Proposed mechanism for the cleavage of BNPP by (1H\textsubscript{2}\textsuperscript{+}).](image-url)

The CeCl$_3$ Lewis Acid Promoter in the Stereoselective Construction of Carbon-Carbon Double Bonds

Pamela Piermattei$^{a}$, Samuele Bordi$^{b}$, Cristina Cimarelli$^{a}$, Marco A. Ciufolini$^{b}$, Federica Navazio$^{a}$, Enrico Marcantoni$^{a}$

$^{a}$School of Science and Technology, University of Camerino, Via S. Agostino 1, 62032 Camerino (MC) Italy; $^{b}$Department of Chemistry, The University of British Columbia, 2036 Main Mall, Vancouver, Canada

E-mail: pamela.perimattei@unicam.it

The presence of a C-C double bond in polyfunctionalized organic molecules is a crucial requirement for the control of its biologically activity.(1) The importance of having a site in the molecule that is able to generate geometrical isomerization of a carbon-carbon double bond stimulated the development of new olefination methodologies. In particular, some efforts focused on the ability of Lewis acids to provide a cheap alternative for the synthesis of molecules with C-C double bond in a highly stereoselective fashion.

For several years, we have been investigating CeCl$_3$ promoted organic reactions. This Lewis acid has been found to efficiently promote carbon-carbon (2) and carbon-heteroatom bond formation reactions.(3) In addition to being green in nature (4), CeCl$_3$ has been widely used for both inter- and intramolecular reactions for the synthesis of organic molecules with significant biological importance.

Regarding the total synthesis of biologically active small molecules containing a carbon-carbon double bond, we saw the possibility to employ CeCl$_3$ in the stereoselective construction of 2,3-dihydropyridones 1,(5) and 1,2-dihydroquinolines 2.(6)

![Chemical structures](attachment:chemical Structures.png)

The additional advantage of using CeCl$_3$ in a reaction includes its selectivity and tolerance in the presence of other functional groups. For instance, it can be used during the functionalization of molecules at late stage involving complex molecules or undesirable use of protecting groups. Introduction of C-C double bonds, which are known to increase the activity in macrolides against bacterial RNA polymerase, is currently in progress in our laboratory.

Oxidative polymerization of hydroxylated naphthalenes: Modeling free radical pathways of polycyclic aromatic hydrocarbons (PAHs) of astrochemical relevance.

Simone Potenti, Paola Manini, John R. Brucato, Orlando Crescenzi, Alessandra Napolitano, Vincenzo Barone, Marco d’Ischia

Scuola Normale Superiore, Piazza dei Cavalieri 7, 56126 Pisa, Italy; Department of Chemical Sciences, University of Naples Federico II, Complesso Universitario Monte S. Angelo, Via Cintia 4, 80126 Napoli, Italy; INAF - Osservatorio Astrofisico di Arcetri, Largo Enrico Fermi 5, 50125 Firenze, Italy

simone.potenti@sns.it

Polycyclic aromatic hydrocarbons (PAHs), which are widely diffused in the interstellar medium (ISM) accounting for more than 20% of the carbon in the universe (1), attract growing interest as possible determinants of infrared emission features seen in different astrophysical environments (2). Dust grain chemistry could be pivotal for PAHs reprocessing, since icy matrices can trap several astrochemically-relevant CHON-bearing molecules, and mineral catalysis could have played a significant role in prebiotic chemistry (3). Early experiments (4) showed that exposure of naphthalene, the simplest member of PAHs, to ultraviolet radiation in ice under astrophysically-relevant conditions leads to the generation of phenolic and quinone derivatives, allowing specific prediction of the existence and relative abundances of various oxidized naphthalenes in meteorites. The latter can undergo oxidative polymerization reactions via an interplay of competing free radical and quinone coupling pathways (5) accounting for evolution toward structurally diverse organic systems at high levels of complexity. Despite a broad and solid literature on the oxidative polymerization of monocyclic phenolic systems and their derivatives, there are still significant lacunae in the case of hydroxylated derivatives from PAHs. In this paper, we report a combined experimental and theoretical approach aimed at elucidating the mechanisms underlying the oxidative polymerization of 1-naphthol, 2-naphthol, 1,8-dihydroxynaphthalene, 1,6-dihydroxynaphthalene, and 2,6-dihydroxynaphthalene. Preliminarily, the oxidative chemistry of hydroxylated naphthalenes was investigated using an enzymatic system, peroxidase/hydrogen peroxide, as well as alkaline autoxidation and ammonia-induced solid state polymerization (AISSP) on thin films. The polymers thus obtained were characterized using mass spectrometry, electron paramagnetic resonance, UV visible spectroscopy and Diffuse Reflectance Infrared Fourier Transform Spectroscopy (DRIFTS). Main oligomeric intermediates were isolated and characterized and the underlying reactivity patterns were rationalized with the aid of DFT calculations. The results revealed marked differences in the oxidation chemistry and mode of coupling of the various derivatives which reflected the number, position and relative disposition of hydroxyl groups on the naphthalene systems. In further experiments, hydroxylated naphthalenes were adsorbed on various Martian soil analogs and exposed to UV radiation or to ammonia vapors (AISSP), and the species thus produced were compared with the reference polymers using various techniques, including mainly DRIFTS. Elucidation of this chemistry provides novel important insights into the mechanisms of processing of PAH in the ISM, a phenomenon of possible relevance to the origin and properties of complex organic matter in environments of astrochemical relevance.

### Elenco degli Autori

*Indica l’autore presentatore*

<table>
<thead>
<tr>
<th>Autore</th>
<th>Organo/Instituto</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abate Antonio</td>
<td>ORG OR06</td>
</tr>
<tr>
<td>Abbiati Giorgio</td>
<td>ORG PO048</td>
</tr>
<tr>
<td>Abbiati Giorgio</td>
<td>ORG/INO PZ01</td>
</tr>
<tr>
<td>Abbotto Alessandro</td>
<td>ORG OR021</td>
</tr>
<tr>
<td>Abenavoli Mariarosa</td>
<td>ORG PO58</td>
</tr>
<tr>
<td>Accurso Vincenza</td>
<td>ORG PO22</td>
</tr>
<tr>
<td>Achilli Silvia</td>
<td>ORG OR11</td>
</tr>
<tr>
<td>Agosti Alessandro*</td>
<td>ORG OR45</td>
</tr>
<tr>
<td>Aiello Federica</td>
<td>ORG OR13</td>
</tr>
<tr>
<td>Airoldi Cristina</td>
<td>ORG OR19</td>
</tr>
<tr>
<td>Albano Gianluigi*</td>
<td>ORG OR03</td>
</tr>
<tr>
<td>Albini Angelo</td>
<td>ORG MD03</td>
</tr>
<tr>
<td>Alfei Silvana*</td>
<td>ORG PO23</td>
</tr>
<tr>
<td>Alfei Silvana</td>
<td>ORG PO95</td>
</tr>
<tr>
<td>Algieri Vincenzo*</td>
<td>ORG PO03</td>
</tr>
<tr>
<td>Algieri Vincenzo</td>
<td>ORG OR62</td>
</tr>
<tr>
<td>Allegrini Pietro</td>
<td>ORG PO57</td>
</tr>
<tr>
<td>Allelaar A.F. Maarten</td>
<td>ORG PO35</td>
</tr>
<tr>
<td>Alvarez-Sanchez Rubén</td>
<td>ORG OR50</td>
</tr>
<tr>
<td>Amadio Emanuele</td>
<td>ORG PO54</td>
</tr>
<tr>
<td>Amato Teresa</td>
<td>ORG OR39</td>
</tr>
<tr>
<td>Amendola Valeria</td>
<td>ORG OR20</td>
</tr>
<tr>
<td>Andrei Graciela</td>
<td>ORG PO28</td>
</tr>
<tr>
<td>Andresini Michael</td>
<td>ORG PO40</td>
</tr>
<tr>
<td>Araniti Fabrizio</td>
<td>ORG PO27</td>
</tr>
<tr>
<td>Ardunii Arturo</td>
<td>ORG PO17</td>
</tr>
<tr>
<td>Arena Francesca</td>
<td>ORG PO91</td>
</tr>
<tr>
<td>Armaroli Nicola</td>
<td>ORG PO56</td>
</tr>
<tr>
<td>Arnaboldi Serena</td>
<td>ORG PO31</td>
</tr>
<tr>
<td>Aronica Laura Antonella</td>
<td>ORG PO03</td>
</tr>
<tr>
<td>Arosio Daniela</td>
<td>ORG PO33</td>
</tr>
<tr>
<td>Arrigo Rossella</td>
<td>ORG OR49</td>
</tr>
<tr>
<td>Arrigoni Federica</td>
<td>ORG PO16</td>
</tr>
<tr>
<td>Attolino Emanuele</td>
<td>ORG OR43</td>
</tr>
<tr>
<td>Badetti Elena</td>
<td>ORG OR64</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Autore</th>
<th>Organo/Instituto</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baker Tom</td>
<td>ORG/INO OR04</td>
</tr>
<tr>
<td>Baldin Salvatore</td>
<td>ORG/INO OR03</td>
</tr>
<tr>
<td>Baldoli Salvatore</td>
<td>ORG/INO OR05</td>
</tr>
<tr>
<td>Ballini Clara</td>
<td>ORG OR38</td>
</tr>
<tr>
<td>Balzani Federica</td>
<td>ORG OR47</td>
</tr>
<tr>
<td>Banfi Luca*</td>
<td>ORG OR30</td>
</tr>
<tr>
<td>Baratta Walter*</td>
<td>ORG/INO OR03</td>
</tr>
<tr>
<td>Baratta Walter</td>
<td>ORG/INO OR05</td>
</tr>
<tr>
<td>Barbero Nadia*</td>
<td>ORG OR24</td>
</tr>
<tr>
<td>Barbieri Alessia*</td>
<td>ORG PO05</td>
</tr>
<tr>
<td>Barolo Claudia</td>
<td>ORG OR24</td>
</tr>
<tr>
<td>Barone Vincenzo</td>
<td>ORG PO104</td>
</tr>
<tr>
<td>Barresi Vincenzo</td>
<td>ORG OR41</td>
</tr>
<tr>
<td>Bartella Lucia*</td>
<td>ORG PO06</td>
</tr>
<tr>
<td>Barzon Luisa</td>
<td>ORG PO65</td>
</tr>
<tr>
<td>Baschieri Andrea</td>
<td>ORG/INO OR01</td>
</tr>
<tr>
<td>Basosi Riccardo</td>
<td>ORG PO94</td>
</tr>
<tr>
<td>Basso Andrea</td>
<td>ORG OR30</td>
</tr>
<tr>
<td>Battilocchio Claudio</td>
<td>ORG PO49</td>
</tr>
<tr>
<td>Battistini Lucia</td>
<td>ORG PO21</td>
</tr>
<tr>
<td>Beccalli Egle M.</td>
<td>ORG OR16</td>
</tr>
<tr>
<td>Becherini Stefano*</td>
<td>ORG PO07</td>
</tr>
<tr>
<td>Becherini Stefano</td>
<td>ORG OR26</td>
</tr>
<tr>
<td>Belli Valentina</td>
<td>ORG OR53</td>
</tr>
<tr>
<td>Bellina Fabio</td>
<td>ORG OR35</td>
</tr>
<tr>
<td>Bellini Marco*</td>
<td>ORG/INO PZ02</td>
</tr>
<tr>
<td>Belsito Emilia Lucia</td>
<td>ORG OR15</td>
</tr>
<tr>
<td>Beltrami Lorena</td>
<td>ORG OR42</td>
</tr>
<tr>
<td>Belvisi Laura</td>
<td>ORG PO33</td>
</tr>
<tr>
<td>Benedetti Fabio</td>
<td>ORG PO42</td>
</tr>
<tr>
<td>Beneduci Amerigo</td>
<td>ORG PO20</td>
</tr>
<tr>
<td>Bergamaschi Greta</td>
<td>ORG OR20</td>
</tr>
<tr>
<td>Bernardi Anna</td>
<td>ORG OR11</td>
</tr>
<tr>
<td>Bernini Roberta*</td>
<td>ORG PO08</td>
</tr>
<tr>
<td>Berti Federico</td>
<td>ORG PO23</td>
</tr>
<tr>
<td>Bertolini Giorgio*</td>
<td>ORG PZ02</td>
</tr>
<tr>
<td>Bertolini Giorgio</td>
<td>ORG OR45</td>
</tr>
<tr>
<td>Beverina Luca</td>
<td>ORG OR14</td>
</tr>
<tr>
<td>Bianchi Lara</td>
<td>ORG PO71</td>
</tr>
<tr>
<td>Bianchini Roberto</td>
<td>ORG PO13</td>
</tr>
<tr>
<td>Bianco Armandodoriano*</td>
<td>ORG PO09</td>
</tr>
<tr>
<td></td>
<td>ORG PO10</td>
</tr>
<tr>
<td></td>
<td>ORG PO11</td>
</tr>
</tbody>
</table>
Biasolo Alessandra ORG OR09
Bietti Massimo* ORG PZ07
Bietti Massimo ORG PO62
Biffi Stefania ORG PO56
Bifulco Giuseppe ORG OR51, ORG OR52, ORG PO41, ORG PO43, ORG PO77, ORG PO86, ORG PO96
Billod Jean-Marc ORG OR57
Biscaglia Francesca* ORG OR09
Bizzarri Claudia ORG/INO OR01
Bocchinfuso Gianfranco ORG PO33
Boldrini Chiara Liliana* ORG OR02
Bonaccorso Carmela ORG OR41
Bonanni Marco ORG PO13
Bonasera Aurelio* ORG OR44
Bonchio Marcella ORG/INO OR02
Boncompagni Simona ORG PO92
Bonetti Andrea* ORG PO26
Bordi Samuele ORG PO103
Bortolini Olga* ORG PO12
Bossi Alberto ORG PO15
Botta Bruno ORG OR13
Botta Chiara ORG PO45
Botticella Ermelinda ORG PO08
Bourguet-Kondracki Marie-Lise ORG OR37
Bovicelli Paolo ORG OR61
Bozzano Andrea ORG OR30
Bracci Luisa ORG OR54
Brandolese Arianna ORG PO12
Bravin Carlo ORG OR64
Brazzo Paolo ORG OR14
Broggini Gianluigi ORG OR16
Brucato John R. ORG PO104
Brunetti Jlenia ORG OR54
Bruno Giacomo ORG OR45
Bruno Ines ORG OR52, ORG PO77, ORG PO86, ORG PO96
Brusasca PierNatale ORG PO50
Bua Silvia ORG OR89
Buffagni Mirko ORG OR04
Buiatti Luca ORG PO42
Bull James A. ORG PO98
Buscaino Roberto ORG OR24
Cacciapaglia Roberta ORG PO102
Cai Hui ORG OR18
Calamante Massimo ORG PO37
Calcinelli Fabio ORG OR31
Calugi Lorenzo* ORG PO13
Calvio Cinzia ORG OR65
Campiglia Pietro ORG OR52
Cantone Vincenza ORG OR52
Capaccio Vito* ORG PO14
Capaldo Luca ORG MD03
Capobianco Amedeo ORG PO36
Capodilupo Agostina Lina ORG PO20
Cappelletti Enrico ORG OR42
Cappelli Andrea ORG OR34
Cappellini Daniele ORG PO50
Cappello Valentina ORG PO07
Capriati Vito ORG PO39
Carassiti Alessandra ORG PO11
Cariati Elena ORG PO45
Carlo Lucarelli ORG/INO OR04
Carlos Rodríguez del Río REAXYS-MYCS
Carlucci Claudia ORG PO27
Carlucci Lucia ORG PO45
Carraro Davide ORG PO54
Carraro Mauro * ORG/INO OR02
Carta Fabrizio ORG PO89
Cartagenova Daniele ORG OR30
Caruso Tonino ORG PO36
Casapullo Agostino ORG PO66
Caselli Alessandro* ORG/INO KN01
Caselli Monica ORG PO04
Casnati Alessandro ORG OR57, ORG PO88, ORG PO89, ORG PO102
Castagoulo Ignazio ORG PO65
Castellano Sabrina ORG PO43
Cattaneo Cristian ORG PO26
Catto Marco ORG PO74
Cauteruccio Silvia* ORG OR58
Cauteruccio Silvia* ORG PO15
Cauteruccio Silvia ORG PO73
Cavani Fabrizio ORG/INO OR04
Ceccarelli Martina ORG OR50
Celaj Odeta ORG PO25
Celesti Consuelo ORG OR55
Cerichelli Giorgio ORG OR48
Cerisoli Lucia ORG PO26
Cesari Cristiana ORG/INO OR01
Cespugli Marco ORG OR28
Chambery Angela ORG OR53
Chaves Silvia ORG PO74
Chiacchio Maria Assunta ORG OR55
Chiappe Cinzia ORG OR26
<table>
<thead>
<tr>
<th>Nome</th>
<th>ORG/INO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chiaradonna Ferdinando</td>
<td>ORG PO07</td>
</tr>
<tr>
<td>Chiarini Marco*</td>
<td>ORG OR48</td>
</tr>
<tr>
<td>Chiarotto Isabella</td>
<td>ORG PO22</td>
</tr>
<tr>
<td>Chini Maria Giovanna*</td>
<td>ORG PO43</td>
</tr>
<tr>
<td>Chini Maria Giovanna</td>
<td>ORG PO41</td>
</tr>
<tr>
<td>Chiummiento Lucia</td>
<td>ORG PO23</td>
</tr>
<tr>
<td>Chiurchiù Elena</td>
<td>ORG OR47</td>
</tr>
<tr>
<td>Ciaramelli Carlotta</td>
<td>ORG OR19</td>
</tr>
<tr>
<td>Ciardiello Fortunato</td>
<td>ORG PO25</td>
</tr>
<tr>
<td>Ciaschetti Gianpiro</td>
<td>ORG PO09</td>
</tr>
<tr>
<td>Ciccarella Giuseppe</td>
<td>ORG PO20</td>
</tr>
<tr>
<td>Ciceri Daniele</td>
<td>ORG PZ06</td>
</tr>
<tr>
<td>Cimarelli Cristina</td>
<td>ORG PO103</td>
</tr>
<tr>
<td>Cicchetti Gianpiero</td>
<td>ORG PO24</td>
</tr>
<tr>
<td>Cicogna Maria Pia</td>
<td>ORG PO48</td>
</tr>
<tr>
<td>Ciolfi Emanuele</td>
<td>ORG PO75</td>
</tr>
<tr>
<td>Ciolfi Maurizio</td>
<td>ORG PO87</td>
</tr>
<tr>
<td>Cioppi Laura</td>
<td>ORG PO07</td>
</tr>
<tr>
<td>Cipolla Laura</td>
<td>ORG PZ06</td>
</tr>
<tr>
<td>Cipolla Laura</td>
<td>ORG PO16</td>
</tr>
<tr>
<td>Cinogli Alessia</td>
<td>ORG OR37</td>
</tr>
<tr>
<td>Ciriolo Antonio</td>
<td>ORG OR47</td>
</tr>
<tr>
<td>Coi Jotham W.</td>
<td>ORG PO47</td>
</tr>
<tr>
<td>Coi Jotham W.</td>
<td>ORG PO47</td>
</tr>
<tr>
<td>Cogliati Beatrice*</td>
<td>ORG PO17</td>
</tr>
<tr>
<td>Colella Marco*</td>
<td>ORG PO18</td>
</tr>
<tr>
<td>Colella Silvia</td>
<td>ORG OR06</td>
</tr>
<tr>
<td>Comandà Alessandra*</td>
<td>ORG PO19</td>
</tr>
<tr>
<td>Comande Alessandra</td>
<td>ORG OR15</td>
</tr>
<tr>
<td>Comes Franchini Mauro*</td>
<td>ORG PZ08</td>
</tr>
<tr>
<td>Comes Franchini Mauro</td>
<td>ORG PO56</td>
</tr>
<tr>
<td>Consani Marco</td>
<td>ORG OR08</td>
</tr>
<tr>
<td>Conte Valeria</td>
<td>ORG PO07</td>
</tr>
<tr>
<td>Corradini Roberto*</td>
<td>ORG PO10</td>
</tr>
<tr>
<td>Corradini Roberto</td>
<td>ORG PO85</td>
</tr>
<tr>
<td>Corente Giuseppina Anna*</td>
<td>ORG PO20</td>
</tr>
<tr>
<td>Corsi Massimo</td>
<td>ORG PO13</td>
</tr>
<tr>
<td>Costa Barbara</td>
<td>ORG PO16</td>
</tr>
<tr>
<td>Costantino Valeria</td>
<td>ORG OR37</td>
</tr>
<tr>
<td>Costanzo Paola</td>
<td>ORG PO70</td>
</tr>
<tr>
<td>Cozza Pier Giorgio</td>
<td>ORG OR31</td>
</tr>
<tr>
<td>Credi Alberto</td>
<td>ORG PO91</td>
</tr>
<tr>
<td>Crescenzino Orlando</td>
<td>ORG OR25</td>
</tr>
<tr>
<td>Crestini Claudia</td>
<td>ORG OR27</td>
</tr>
<tr>
<td>Criscuolo Valeria</td>
<td>ORG OR25</td>
</tr>
<tr>
<td>Crisma Marco</td>
<td>ORG PO59</td>
</tr>
<tr>
<td>Cruciani Gabriele</td>
<td>ORG OR50</td>
</tr>
<tr>
<td>Curti Claudio*</td>
<td>ORG PO21</td>
</tr>
<tr>
<td>D'Abrosca Brigida *</td>
<td>ORG PO25</td>
</tr>
<tr>
<td>D'Abrosca Brigida</td>
<td>ORG OR53</td>
</tr>
<tr>
<td>D'Acquarica Ilaria</td>
<td>ORG OR13</td>
</tr>
<tr>
<td>Dal Piaz Fabrizio</td>
<td>ORG OR51</td>
</tr>
<tr>
<td>Dalcantar Enrico*</td>
<td>ORG MD04</td>
</tr>
<tr>
<td>D'Alonzo Daniele</td>
<td>ORG PO28</td>
</tr>
<tr>
<td>D'Amato Assunta*</td>
<td>ORG PO26</td>
</tr>
<tr>
<td>D'Andreia Felicia</td>
<td>ORG PO07</td>
</tr>
<tr>
<td>D'Anna Francesca*</td>
<td>ORG PO22</td>
</tr>
<tr>
<td>D'Anna Francesca</td>
<td>ORG OR49</td>
</tr>
<tr>
<td>D'Auria Maria Valeria</td>
<td>ORG OR22</td>
</tr>
<tr>
<td>De Angelis Sonia*</td>
<td>ORG PO27</td>
</tr>
<tr>
<td>De Bonis Angela</td>
<td>ORG PO24</td>
</tr>
<tr>
<td>De Combarieu Eric</td>
<td>ORG PZ06</td>
</tr>
<tr>
<td>De Fenza Maria*</td>
<td>ORG PO28</td>
</tr>
<tr>
<td>De Fenza Maria</td>
<td>ORG PO40</td>
</tr>
<tr>
<td>De Luca Giuseppina</td>
<td>ORG PO06</td>
</tr>
<tr>
<td>De Luca Lidia</td>
<td>ORG PO44</td>
</tr>
<tr>
<td>De Marco Luisa</td>
<td>ORG PO48</td>
</tr>
<tr>
<td>De Marino Simona*</td>
<td>ORG PO29</td>
</tr>
<tr>
<td>De Marino Simona</td>
<td>ORG OR22</td>
</tr>
<tr>
<td>De Matteo Marilena</td>
<td>ORG PO50</td>
</tr>
<tr>
<td>De Mesmaeker Alain</td>
<td>ORG PO49</td>
</tr>
<tr>
<td>De Nino Antonio*</td>
<td>ORG OR62</td>
</tr>
<tr>
<td>De Nino Antonio</td>
<td>ORG PO57</td>
</tr>
<tr>
<td>De Nino Antonio</td>
<td>ORG PO70</td>
</tr>
<tr>
<td>De Riccardi Francesco</td>
<td>ORG OR60</td>
</tr>
<tr>
<td>De Rosa Margherita*</td>
<td>ORG OR59</td>
</tr>
<tr>
<td>De Rosa Margherita</td>
<td>ORG PO36</td>
</tr>
<tr>
<td>De Sanctis Gaia</td>
<td>ORG OR19</td>
</tr>
<tr>
<td>De Simone Nicola Alessandro*</td>
<td>ORG PO30</td>
</tr>
<tr>
<td>De Tommasi Nunziatina</td>
<td>ORG OR51</td>
</tr>
<tr>
<td>De Vita Simona*</td>
<td>ORG PO41</td>
</tr>
<tr>
<td>De Zotti Marta*</td>
<td>ORG PO32</td>
</tr>
<tr>
<td>De Zotti Marta*</td>
<td>ORG PO33</td>
</tr>
<tr>
<td>Deagostino Annamaria*</td>
<td>ORG PO34</td>
</tr>
<tr>
<td>Degennaro Leonardo</td>
<td>ORG PO18</td>
</tr>
<tr>
<td>Degliangeli Federica</td>
<td>ORG OR18</td>
</tr>
<tr>
<td>Deichmann Walter</td>
<td>ORG OR45</td>
</tr>
<tr>
<td>del Gaudio Federica*</td>
<td>ORG PO35</td>
</tr>
<tr>
<td>del Gaudio Federica</td>
<td>ORG OR51</td>
</tr>
<tr>
<td>Della Sala Giorgio*</td>
<td>ORG OR60</td>
</tr>
<tr>
<td>Della Sala Giorgio</td>
<td>ORG PO26</td>
</tr>
<tr>
<td>Della Sala Giorgio</td>
<td>ORG PO30</td>
</tr>
<tr>
<td>Della Sala Giorgio</td>
<td>ORG PO93</td>
</tr>
<tr>
<td>Nome</td>
<td>Organizzazione</td>
</tr>
<tr>
<td>---------------------------------</td>
<td>----------------</td>
</tr>
<tr>
<td>Della Sala Paolo *</td>
<td>ORG PO36</td>
</tr>
<tr>
<td>Dell’Aera Marzia</td>
<td>ORG PO39</td>
</tr>
<tr>
<td>Delso Ignacio</td>
<td>ORG PO57</td>
</tr>
<tr>
<td>Denis William</td>
<td>ORG PO54</td>
</tr>
<tr>
<td>Dentoni Litta Antonella</td>
<td>ORG OR60</td>
</tr>
<tr>
<td>Dessi Alessio*</td>
<td>ORG PO37</td>
</tr>
<tr>
<td>d’Ettorre Alessio</td>
<td>ORG PO94</td>
</tr>
<tr>
<td>Di Bari Lorenzo</td>
<td>ORG OR03</td>
</tr>
<tr>
<td>Di Carmine Graziano</td>
<td>ORG PO12</td>
</tr>
<tr>
<td>Di Cecco Mirella</td>
<td>ORG PO09</td>
</tr>
<tr>
<td>Di Crescenzo Antonello</td>
<td>ORG PO92</td>
</tr>
<tr>
<td>Di Donna Leonardo</td>
<td>ORG PO06</td>
</tr>
<tr>
<td>Di Fabio Giovanni</td>
<td>ORG PO38</td>
</tr>
<tr>
<td>Di Fabio Giovanni</td>
<td>ORG PO83</td>
</tr>
<tr>
<td>Di Gioia Maria Luisa*</td>
<td>ORG OR40</td>
</tr>
<tr>
<td>Di Gioia Maria Luisa</td>
<td>ORG PO03, PO68, PO70</td>
</tr>
<tr>
<td>Di Marino Cinzia</td>
<td>ORG PO83</td>
</tr>
<tr>
<td>Di Micco Simone *</td>
<td>ORG OR51</td>
</tr>
<tr>
<td>Di Michele Alessandro</td>
<td>ORG PO08</td>
</tr>
<tr>
<td>Di Pietro Federica</td>
<td>ORG OR61</td>
</tr>
<tr>
<td>Di Stefano Stefano</td>
<td>ORG PO05</td>
</tr>
<tr>
<td>Dilauro Giuseppe*</td>
<td>ORG PO39</td>
</tr>
<tr>
<td>Dintcheva Nadia Tzankova</td>
<td>ORG OR49</td>
</tr>
<tr>
<td>d’Ischia Marco</td>
<td>ORG OR25, OR79, PO104</td>
</tr>
<tr>
<td>Doria Filippo*</td>
<td>ORG OR20</td>
</tr>
<tr>
<td>D’Orsi Rosarita*</td>
<td>ORG PO23</td>
</tr>
<tr>
<td>D’Orsi Rosarita*</td>
<td>ORG PO24</td>
</tr>
<tr>
<td>Dova Davide</td>
<td>ORG OR58</td>
</tr>
<tr>
<td>Drioli Sara</td>
<td>ORG PO42</td>
</tr>
<tr>
<td>Ebert Cynthia</td>
<td>ORG OR28</td>
</tr>
<tr>
<td>Ebrahim Majdar Reza</td>
<td>ORG OR27</td>
</tr>
<tr>
<td>Ertr Martin</td>
<td>ORG PO31</td>
</tr>
<tr>
<td>Esposito Anna</td>
<td>ORG PO28</td>
</tr>
<tr>
<td>Esposito Anna*</td>
<td>ORG PO40</td>
</tr>
<tr>
<td>Esposito Roberta</td>
<td>ORG PO66</td>
</tr>
<tr>
<td>Esposito Veronica</td>
<td>ORG PO101</td>
</tr>
<tr>
<td>Esposito Veronica*</td>
<td>ORG OR39</td>
</tr>
<tr>
<td>Ettorre Valeria</td>
<td>ORG PO92</td>
</tr>
<tr>
<td>Evidente Antonio</td>
<td>ORG PO69</td>
</tr>
<tr>
<td>Facchini Fabio A.</td>
<td>ORG OR57</td>
</tr>
<tr>
<td>Fadeyi Olugheminiyi O.</td>
<td>ORG PO47</td>
</tr>
<tr>
<td>Fagnoni Maurizio</td>
<td>ORG MD03, PO80, PO81, PO97</td>
</tr>
<tr>
<td>Fagnoni Maurizio*</td>
<td>ORG PO31</td>
</tr>
<tr>
<td>Falciati Chiara</td>
<td>ORG OR54</td>
</tr>
<tr>
<td>Faltoni Valentina</td>
<td>ORG PO82</td>
</tr>
<tr>
<td>Fanelli Flavio</td>
<td>ORG PO18</td>
</tr>
<tr>
<td>Farinola Gianluca Maria</td>
<td>ORG PO55</td>
</tr>
<tr>
<td>Fazzi Daniele</td>
<td>ORG OR01</td>
</tr>
<tr>
<td>Felluga Fulvia*</td>
<td>ORG PO42</td>
</tr>
<tr>
<td>Feroci Marta</td>
<td>ORG PO22</td>
</tr>
<tr>
<td>Ferrante Luca</td>
<td>ORG OR50</td>
</tr>
<tr>
<td>Ferrigato Aurelia</td>
<td>ORG OR42</td>
</tr>
<tr>
<td>Festa Carmen</td>
<td>ORG PO29</td>
</tr>
<tr>
<td>Festa Carmen*</td>
<td>ORG OR22</td>
</tr>
<tr>
<td>Fiammengni Roberto*</td>
<td>ORG OR18</td>
</tr>
<tr>
<td>Fieschi Franck</td>
<td>ORG OR11</td>
</tr>
<tr>
<td>Fieschi Franck</td>
<td>ORG PO88</td>
</tr>
<tr>
<td>Figliolia Rosario</td>
<td>ORG/INO OR03</td>
</tr>
<tr>
<td>Figliolia Rosario*</td>
<td>ORG/INO OR05</td>
</tr>
<tr>
<td>Filatov Michael</td>
<td>ORG OR34</td>
</tr>
<tr>
<td>Filippi Jonathan</td>
<td>ORG/INO PZ02</td>
</tr>
<tr>
<td>Fiorani Giulia*</td>
<td>ORG PZ04</td>
</tr>
<tr>
<td>Fiorentino Antonio</td>
<td>ORG OR53</td>
</tr>
<tr>
<td>Fiorucci Stefano</td>
<td>ORG OR22</td>
</tr>
<tr>
<td>Floresta Giuseppe</td>
<td>ORG OR59</td>
</tr>
<tr>
<td>Floris Barbara</td>
<td>ORG OR07</td>
</tr>
<tr>
<td>Fodda Sebastiano</td>
<td>ORG PO10</td>
</tr>
<tr>
<td>Folliero Maria G.</td>
<td>ORG/INO PZ02</td>
</tr>
<tr>
<td>Fontana Antonella</td>
<td>ORG PO92</td>
</tr>
<tr>
<td>Formaggio Fernando</td>
<td>ORG PO33</td>
</tr>
<tr>
<td>Forni Alessandra</td>
<td>ORG PO45</td>
</tr>
<tr>
<td>Forte Giovanni</td>
<td>ORG OR51</td>
</tr>
<tr>
<td>Fortuna Cosimo Gianluca*</td>
<td>ORG OR41</td>
</tr>
<tr>
<td>Fortunati Elena</td>
<td>ORG PO08</td>
</tr>
<tr>
<td>Franza Gabriele</td>
<td>ORG OR65</td>
</tr>
<tr>
<td>Franzini Roberta</td>
<td>ORG OR58</td>
</tr>
<tr>
<td>Freccero Mauro</td>
<td>ORG OR20</td>
</tr>
<tr>
<td>Fredrich Sebastian</td>
<td>ORG OR44</td>
</tr>
<tr>
<td>Frezza Claudio</td>
<td>ORG PO10</td>
</tr>
<tr>
<td>Frezza Claudio*</td>
<td>ORG PO11</td>
</tr>
<tr>
<td>Funicello Maria</td>
<td>ORG PO23</td>
</tr>
<tr>
<td>Fus Stefania</td>
<td>ORG OR34</td>
</tr>
<tr>
<td>Gabriele Bartolo</td>
<td>ORG PO58</td>
</tr>
<tr>
<td>Gabriele Bartolo*</td>
<td>ORG OR17</td>
</tr>
<tr>
<td>Gabrielli Luca</td>
<td>ORG PO84</td>
</tr>
<tr>
<td>Gabrielli Serena *</td>
<td>ORG OR47</td>
</tr>
<tr>
<td>Gaeta Carmine</td>
<td>ORG OR59</td>
</tr>
<tr>
<td>Galeone Aldo</td>
<td>ORG OR39</td>
</tr>
<tr>
<td>Galloni Pierluca</td>
<td>ORG PO101</td>
</tr>
<tr>
<td>Galloni Pierluca*</td>
<td>ORG PO100</td>
</tr>
<tr>
<td>Gambina Andrea</td>
<td>ORG PZ06</td>
</tr>
<tr>
<td>Garbarino Silvia</td>
<td>ORG MD03</td>
</tr>
<tr>
<td>García Mancheño Olga</td>
<td>ORG PO46</td>
</tr>
<tr>
<td>Gardossi Lucia</td>
<td>ORG OR28</td>
</tr>
<tr>
<td>Gaspa Silvia*</td>
<td>ORG PO44</td>
</tr>
<tr>
<td>Gasparrini Francesco</td>
<td>ORG PO75</td>
</tr>
<tr>
<td>Gatto Emuela</td>
<td>ORG OR07</td>
</tr>
<tr>
<td>Gazzero Patrizia</td>
<td>ORG OR51</td>
</tr>
<tr>
<td>Gazzola Silvia</td>
<td>ORG OR16</td>
</tr>
<tr>
<td>Gemmi Mauro</td>
<td>ORG PO07</td>
</tr>
<tr>
<td>Gennari Cesare</td>
<td>ORG PO33</td>
</tr>
<tr>
<td>Geremia Silvano</td>
<td>ORG PO53</td>
</tr>
<tr>
<td>Germani Raimondo</td>
<td>ORG OR46</td>
</tr>
<tr>
<td>Ghirga Francesca*</td>
<td>ORG OR13</td>
</tr>
<tr>
<td>Giannini Clelia*</td>
<td>ORG PO45</td>
</tr>
<tr>
<td>Giannini Giuseppe</td>
<td>ORG OR56</td>
</tr>
<tr>
<td>Giboulot Steven</td>
<td>ORG/INO OR05</td>
</tr>
<tr>
<td>Gigi Giuseppe</td>
<td>ORG PO48</td>
</tr>
<tr>
<td>Gini Andrea*</td>
<td>ORG PO46</td>
</tr>
<tr>
<td>Giofrè Salvatore Vincenzo</td>
<td>ORG PO58</td>
</tr>
<tr>
<td>Giofrè Salvatore Vincenzo*</td>
<td>ORG OR55</td>
</tr>
<tr>
<td>Giordano Assunta</td>
<td>ORG OR51</td>
</tr>
<tr>
<td>Giorgi Simone*</td>
<td>ORG PO47</td>
</tr>
<tr>
<td>Giovannini Pier Paolo</td>
<td>ORG PO12</td>
</tr>
<tr>
<td>Giovenzana Giovanni Battista</td>
<td>ORG OR42</td>
</tr>
<tr>
<td>Glarner Thomas</td>
<td>ORG OR45</td>
</tr>
<tr>
<td>Gobbo Marina</td>
<td>ORG OR09</td>
</tr>
<tr>
<td>Godineau Edouard</td>
<td>ORG PO49</td>
</tr>
<tr>
<td>Goracci Laura*</td>
<td>ORG OR50</td>
</tr>
<tr>
<td>Grande Vincenzo</td>
<td>ORG OR20</td>
</tr>
<tr>
<td>Gravante Raffaele</td>
<td>ORG PO38</td>
</tr>
<tr>
<td>Graziani Vittoria</td>
<td>ORG PO25</td>
</tr>
<tr>
<td>Graziani Vittoria*</td>
<td>ORG OR53</td>
</tr>
<tr>
<td>Grisorio Roberto*</td>
<td>ORG PO06</td>
</tr>
<tr>
<td>Grisorio Roberto*</td>
<td>ORG PO48</td>
</tr>
<tr>
<td>Griva Sirio</td>
<td>ORG PO04</td>
</tr>
<tr>
<td>Groben René</td>
<td>ORG OR37</td>
</tr>
<tr>
<td>Grützmacher Hansjörg</td>
<td>ORG/INO PZ02</td>
</tr>
<tr>
<td>Gschwind Ruth M.</td>
<td>ORG OR32</td>
</tr>
<tr>
<td>Guarani Andrea*</td>
<td>ORG OR31</td>
</tr>
<tr>
<td>Guaragna Annalisa</td>
<td>ORG PO28</td>
</tr>
<tr>
<td>Guarneri Alice*</td>
<td>ORG OR28</td>
</tr>
<tr>
<td>Guazzelli Lorenzo</td>
<td>ORG PO64</td>
</tr>
<tr>
<td>Guazzelli Lorenzo*</td>
<td>ORG OR26</td>
</tr>
<tr>
<td>Guazzelli Nicola</td>
<td>ORG OR35</td>
</tr>
<tr>
<td>Guiglianero Luca</td>
<td>ORG PO64</td>
</tr>
<tr>
<td>Guizzardi Roberto</td>
<td>ORG PO16</td>
</tr>
<tr>
<td>Hasanu Elena</td>
<td>ORG PO07</td>
</tr>
<tr>
<td>Hecht Stefan</td>
<td>ORG OR44</td>
</tr>
<tr>
<td>Heck Albert J.R.</td>
<td>ORG PO35</td>
</tr>
<tr>
<td>Hickey Neal</td>
<td>ORG PO53</td>
</tr>
<tr>
<td>Hoe Johnny</td>
<td>ORG OR32</td>
</tr>
<tr>
<td>Hiremathad Asha</td>
<td>ORG PO74</td>
</tr>
<tr>
<td>Hu Jing</td>
<td>ORG OR18</td>
</tr>
<tr>
<td>Hussain Rohanah</td>
<td>ORG PO32</td>
</tr>
<tr>
<td>Jacobellis Rosabianca</td>
<td>ORG PO48</td>
</tr>
<tr>
<td>Iannucci Grazia*</td>
<td>ORG OR49</td>
</tr>
<tr>
<td>Ingallina Cinzia</td>
<td>ORG OR13</td>
</tr>
<tr>
<td>Ingallinella Paolo*</td>
<td>ORG PO50</td>
</tr>
<tr>
<td>Innocenti Riccardo*</td>
<td>ORG PO51</td>
</tr>
<tr>
<td>Iuliano Veronica</td>
<td>ORG PO90</td>
</tr>
<tr>
<td>Izzo Irene</td>
<td>ORG OR06</td>
</tr>
<tr>
<td>Jozeliunaite Augustina</td>
<td>ORG OR01</td>
</tr>
<tr>
<td>Kleij Arjan W.</td>
<td>ORG PZ04</td>
</tr>
<tr>
<td>Knör Günther</td>
<td>ORG PO31</td>
</tr>
<tr>
<td>Koeberle Andreas</td>
<td>ORG OR52</td>
</tr>
<tr>
<td>Kolleth Amandine</td>
<td>ORG PO29</td>
</tr>
<tr>
<td>Korom Saša</td>
<td>ORG OR10</td>
</tr>
<tr>
<td>Kunz Horst</td>
<td>ORG OR18</td>
</tr>
<tr>
<td>La Bella Angela</td>
<td>ORG OR38</td>
</tr>
<tr>
<td>La Ferla Barbara</td>
<td>ORG PO72</td>
</tr>
<tr>
<td>La Ferla Barbara*</td>
<td>ORG PO52</td>
</tr>
<tr>
<td>La Manna Pellegrino</td>
<td>ORG OR59</td>
</tr>
<tr>
<td>La Manna Pellegrino*</td>
<td>ORG PO53</td>
</tr>
<tr>
<td>La Rocca M. Vincenzo</td>
<td>ORG OR16</td>
</tr>
<tr>
<td>Laghezza Antonio</td>
<td>ORG PO74</td>
</tr>
<tr>
<td>Lambruschini Chiara</td>
<td>ORG OR30</td>
</tr>
<tr>
<td>Lange Heiko*</td>
<td>ORG OR27</td>
</tr>
<tr>
<td>Lanzalunga Osvaldo</td>
<td>ORG PO05</td>
</tr>
<tr>
<td>Lanzalunga Osvaldo*</td>
<td>ORG OR33</td>
</tr>
<tr>
<td>Lattanzi Alessandra</td>
<td>ORG PO63</td>
</tr>
<tr>
<td>Lattuada Luciano*</td>
<td>ORG OR42</td>
</tr>
<tr>
<td>Laura Russo*</td>
<td>ORG PO35</td>
</tr>
<tr>
<td>Laura Russo*</td>
<td>ORG PO26</td>
</tr>
<tr>
<td>Lauro Gianluigi</td>
<td>ORG OR86</td>
</tr>
<tr>
<td>Lauro Gianluigi*</td>
<td>ORG OR52</td>
</tr>
<tr>
<td>Lautz Christian</td>
<td>ORG OR45</td>
</tr>
<tr>
<td>Leggio Antonella</td>
<td>ORG PO19</td>
</tr>
<tr>
<td>Leggio Antonella*</td>
<td>ORG OR15</td>
</tr>
<tr>
<td>Lenci Elena*</td>
<td>ORG OR36</td>
</tr>
<tr>
<td>Léonard Jérémie</td>
<td>ORG OR34</td>
</tr>
<tr>
<td>Leone Gabriella</td>
<td>ORG PO55</td>
</tr>
<tr>
<td>Leonelli Francesca*</td>
<td>ORG OR38</td>
</tr>
<tr>
<td>Lessi Marco*</td>
<td>ORG OR25</td>
</tr>
<tr>
<td>Ley Steven V.</td>
<td>ORG PO49</td>
</tr>
<tr>
<td>Licandro Emanuela</td>
<td>ORG OR58</td>
</tr>
<tr>
<td>Licini Giulia</td>
<td>ORG PO15</td>
</tr>
<tr>
<td>Licini Giulia*</td>
<td>ORG PO73</td>
</tr>
<tr>
<td>Liguori Angelo</td>
<td>ORG OR19</td>
</tr>
<tr>
<td>Limongelli Vittorio</td>
<td>ORG OR22</td>
</tr>
<tr>
<td>Linaldeddu B.T.</td>
<td>ORG OR69</td>
</tr>
<tr>
<td>Lissia Margherita</td>
<td>ORG OR02</td>
</tr>
<tr>
<td>Listorti Andrea</td>
<td>ORG OR06</td>
</tr>
<tr>
<td>Liu Jia</td>
<td>ORG OR48</td>
</tr>
<tr>
<td>Lo Feudo Lucia</td>
<td>ORG OR15</td>
</tr>
<tr>
<td>Lo Presti Marco*</td>
<td>ORG OR55</td>
</tr>
<tr>
<td>Locatelli Erica*</td>
<td>ORG OR56</td>
</tr>
<tr>
<td>Loiodice Fulvio</td>
<td>ORG OR74</td>
</tr>
<tr>
<td>Lombardo Marco</td>
<td>ORG PO26</td>
</tr>
<tr>
<td>Lotteria Simone</td>
<td>ORG OR28</td>
</tr>
<tr>
<td>Lu Menji</td>
<td>ORG OR18</td>
</tr>
<tr>
<td>Lucenti Elena</td>
<td>ORG PO45</td>
</tr>
<tr>
<td>Luisi Renzo</td>
<td>ORG PO45</td>
</tr>
<tr>
<td>Lupattelli Paolo</td>
<td>ORG PO23</td>
</tr>
<tr>
<td>Lupidi Gabriele</td>
<td>ORG PO47</td>
</tr>
<tr>
<td>Luzzi Francesca</td>
<td>ORG PO08</td>
</tr>
<tr>
<td>Maccagno Massimo</td>
<td>ORG PO71</td>
</tr>
<tr>
<td>Macchiavelli Matteo</td>
<td>ORG PO85</td>
</tr>
<tr>
<td>Maddau Laura</td>
<td>ORG PO69</td>
</tr>
<tr>
<td>Maestri Giovanni*</td>
<td>ORG PO23</td>
</tr>
<tr>
<td>Maggi Filippo</td>
<td>ORG PO10</td>
</tr>
<tr>
<td>Magini Andrea</td>
<td>ORG PO88</td>
</tr>
<tr>
<td>Magli Sofia</td>
<td>ORG PO16</td>
</tr>
<tr>
<td>Maglione Maria Grazia</td>
<td>ORG OR25</td>
</tr>
<tr>
<td>Magnani Agnese</td>
<td>ORG PO79</td>
</tr>
<tr>
<td>Maione Francesco</td>
<td>ORG PO41</td>
</tr>
<tr>
<td>Maiorana Stefano</td>
<td>ORG PO50</td>
</tr>
<tr>
<td>Maiuolo Loredana</td>
<td>ORG OR62</td>
</tr>
<tr>
<td>Maiuolo Loredana*</td>
<td>ORG PO03</td>
</tr>
<tr>
<td>Malacarne Marco</td>
<td>ORG PO70</td>
</tr>
<tr>
<td>Manca Michele</td>
<td>ORG PO57</td>
</tr>
<tr>
<td>Mancin Fabrizio</td>
<td>ORG PO80</td>
</tr>
<tr>
<td>Mancin Fabrizio</td>
<td>ORG PO48</td>
</tr>
<tr>
<td>Mancinelli Michele</td>
<td>ORG PO65</td>
</tr>
<tr>
<td>Mancuso Raffaella</td>
<td>ORG PO84</td>
</tr>
<tr>
<td>Mancuso Raffaella*</td>
<td>ORG PO78</td>
</tr>
<tr>
<td>Mandolini Luigi</td>
<td>ORG OR17</td>
</tr>
<tr>
<td>Manetti Fabrizio</td>
<td>ORG PO58</td>
</tr>
<tr>
<td>Manfra Michele</td>
<td>ORG PO102</td>
</tr>
<tr>
<td>Manfredi Norberto</td>
<td>ORG OR56</td>
</tr>
<tr>
<td>Mangoni Alfonso</td>
<td>ORG OR85</td>
</tr>
<tr>
<td>Manicardi Alex</td>
<td>ORG OR02</td>
</tr>
<tr>
<td>Manini Paola</td>
<td>ORG PO79</td>
</tr>
<tr>
<td>Manini Paola*</td>
<td>ORG OR18</td>
</tr>
<tr>
<td>Mantegazza Simone*</td>
<td>ORG OR43</td>
</tr>
<tr>
<td>Manzini Chiara</td>
<td>ORG OR35</td>
</tr>
<tr>
<td>Marafon Giulia*</td>
<td>ORG PO59</td>
</tr>
<tr>
<td>Marcantoni Enrico</td>
<td>ORG OR47</td>
</tr>
<tr>
<td>Marchesi Andrea</td>
<td>ORG PO09</td>
</tr>
<tr>
<td>Marchionni Andrea</td>
<td>ORG/INO PZ02</td>
</tr>
<tr>
<td>Mariangeli Giuseppa*</td>
<td>ORG OR35</td>
</tr>
<tr>
<td>Marino Bettolo Rinaldo</td>
<td>ORG OR38</td>
</tr>
<tr>
<td>Marinotto Danielle</td>
<td>ORG PO45</td>
</tr>
<tr>
<td>Marsico Giulia*</td>
<td>ORG PO60</td>
</tr>
<tr>
<td>Marsico Giulia*</td>
<td>ORG PO61</td>
</tr>
<tr>
<td>Marteinsson Viggo Thor</td>
<td>ORG OR37</td>
</tr>
<tr>
<td>Martin Teo*</td>
<td>ORG PO62</td>
</tr>
<tr>
<td>Martino Elisa</td>
<td>ORG OR30</td>
</tr>
<tr>
<td>Martin-Santamaria Sonsoles</td>
<td>ORG OR57</td>
</tr>
<tr>
<td>Marullo Salvatore</td>
<td>ORG PO22</td>
</tr>
<tr>
<td>Marullo Salvatore*</td>
<td>ORG OR49</td>
</tr>
<tr>
<td>Masocol Nico</td>
<td>ORG PO41</td>
</tr>
<tr>
<td>Maso Marco</td>
<td>ORG PO69</td>
</tr>
<tr>
<td>Massi Alessandro</td>
<td>ORG PO12</td>
</tr>
<tr>
<td>Matteucci Elia</td>
<td>ORG OR31</td>
</tr>
<tr>
<td>Matteucci Elia</td>
<td>ORG/INO OR01</td>
</tr>
<tr>
<td>Mattiello Sara</td>
<td>ORG OR14</td>
</tr>
<tr>
<td>Maurizio Taddei*</td>
<td>ORG MD02</td>
</tr>
<tr>
<td>Mayol Luciano</td>
<td>ORG OR39</td>
</tr>
<tr>
<td>Mazzanti Andrea</td>
<td>ORG PO78</td>
</tr>
<tr>
<td>Mazzarella Daniele</td>
<td>ORG OR31</td>
</tr>
<tr>
<td>Mazzoni Rita</td>
<td>ORG/INO OR01</td>
</tr>
<tr>
<td>Mazzoni Rita*</td>
<td>ORG/INO OR04</td>
</tr>
<tr>
<td>Mazzotti Fabio</td>
<td>ORG PO06</td>
</tr>
<tr>
<td>Medve Laura</td>
<td>ORG OR11</td>
</tr>
<tr>
<td>Mella Massimo</td>
<td>ORG/INO OR04</td>
</tr>
<tr>
<td>Mella Massimo*</td>
<td>ORG OR16</td>
</tr>
<tr>
<td>Menchi Gloria</td>
<td>ORG OR36</td>
</tr>
<tr>
<td>Meneghetti Moreno</td>
<td>ORG OR09</td>
</tr>
<tr>
<td>Mengozzi Luca</td>
<td>ORG OR31</td>
</tr>
<tr>
<td>Menichetti Stefano</td>
<td>ORG OR54</td>
</tr>
<tr>
<td>Meninno Sara*</td>
<td>ORG PO63</td>
</tr>
<tr>
<td>Menta Sergio</td>
<td>ORG PO75</td>
</tr>
<tr>
<td>Merino Pedro</td>
<td>ORG OR62</td>
</tr>
<tr>
<td>Mezzetta Andrea</td>
<td>ORG OR26</td>
</tr>
<tr>
<td>Mezzetta Andrea*</td>
<td>ORG PO64</td>
</tr>
<tr>
<td>Micelz Claudia</td>
<td>ORG PO54</td>
</tr>
<tr>
<td>Micheli Corinja</td>
<td>ORG PO07</td>
</tr>
<tr>
<td>Micheli Laura</td>
<td>ORG OR07</td>
</tr>
<tr>
<td>Migneco Luisa Maria</td>
<td>ORG OR38</td>
</tr>
<tr>
<td>Name</td>
<td>Organization</td>
</tr>
<tr>
<td>-----------------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Milano Francesco</td>
<td>ORG PO55</td>
</tr>
<tr>
<td>Milite Ciro</td>
<td>ORG PO43</td>
</tr>
<tr>
<td>Miller Hamish A.</td>
<td>ORG/INO PZ02</td>
</tr>
<tr>
<td>Minarini Carla</td>
<td>ORG OR25</td>
</tr>
<tr>
<td>Monaco Ilaria</td>
<td>ORG PO56</td>
</tr>
<tr>
<td>Moni Lisa</td>
<td>ORG OR30</td>
</tr>
<tr>
<td>Montagna Giuseppe</td>
<td>ORG PO16</td>
</tr>
<tr>
<td>Monti Filippo</td>
<td>ORG OR31</td>
</tr>
<tr>
<td>Monti Maria Chiara</td>
<td>ORG PO35</td>
</tr>
<tr>
<td>Morbioli Ilaria</td>
<td>ORG OR57</td>
</tr>
<tr>
<td>Mordini Alessandro</td>
<td>ORG PO37</td>
</tr>
<tr>
<td>Morelli Carlo*</td>
<td>ORG OR65</td>
</tr>
<tr>
<td>Moretto Alessandro</td>
<td>ORG PO59</td>
</tr>
<tr>
<td>Morgillo Floriana</td>
<td>ORG PO25</td>
</tr>
<tr>
<td>Morillas Becerril Lucia*</td>
<td>ORG PO65</td>
</tr>
<tr>
<td>Morretta Elva*</td>
<td>ORG PO66</td>
</tr>
<tr>
<td>Mucchi Adele</td>
<td>ORG OR04</td>
</tr>
<tr>
<td>Mussini Patrizia R.</td>
<td>ORG PO15</td>
</tr>
<tr>
<td>Musumarrà Giuseppe*</td>
<td>ORG PO67</td>
</tr>
<tr>
<td>Nadai Matteo</td>
<td>ORG OR20</td>
</tr>
<tr>
<td>Nalëtova Irina</td>
<td>ORG OR41</td>
</tr>
<tr>
<td>Napoli Anna</td>
<td>ORG PO06</td>
</tr>
<tr>
<td>Napolitano Alessandra</td>
<td>ORG PO104</td>
</tr>
<tr>
<td>Nardi Monica</td>
<td>ORG OR40</td>
</tr>
<tr>
<td>Nardi Monica*</td>
<td>ORG PO68</td>
</tr>
<tr>
<td>Nativi Cristina</td>
<td>ORG OR08</td>
</tr>
<tr>
<td>Navazio Federica</td>
<td>ORG PO103</td>
</tr>
<tr>
<td>Nedden Hans Günter</td>
<td>ORG/INO OR03</td>
</tr>
<tr>
<td>Nejrotti Stefano</td>
<td>ORG OR12</td>
</tr>
<tr>
<td>Neri Placido</td>
<td>ORG OR59</td>
</tr>
<tr>
<td>Nicoletti Marcello</td>
<td>ORG PO10</td>
</tr>
<tr>
<td>Nocera Paola*</td>
<td>ORG PO69</td>
</tr>
<tr>
<td>Nola Marta</td>
<td>ORG OR30</td>
</tr>
<tr>
<td>Noto Renato</td>
<td>ORG OR49</td>
</tr>
<tr>
<td>Noto Renato</td>
<td>ORG PO22</td>
</tr>
<tr>
<td>Nuhant Philippe</td>
<td>ORG PO47</td>
</tr>
<tr>
<td>Oberhauser Werner</td>
<td>ORG/INO PZ02</td>
</tr>
<tr>
<td>Oliverio Manuela</td>
<td>ORG OR40</td>
</tr>
<tr>
<td>Olivito Fabrizio*</td>
<td>ORG PO70</td>
</tr>
<tr>
<td>Olivo Giorgio</td>
<td>ORG PO05</td>
</tr>
<tr>
<td>Olivucci Massimo</td>
<td>ORG OR34</td>
</tr>
<tr>
<td>Oneto Marzia</td>
<td>ORG OR61</td>
</tr>
<tr>
<td>Operamolla Alessandra*</td>
<td>ORG OR05</td>
</tr>
<tr>
<td>Orentas Edvinas</td>
<td>ORG OR01</td>
</tr>
<tr>
<td>Orlandi Marco</td>
<td>ORG OR29</td>
</tr>
<tr>
<td>Orlandini Guido</td>
<td>ORG PO91</td>
</tr>
<tr>
<td>Ortega Martínez Aitor</td>
<td>ORG OR31</td>
</tr>
<tr>
<td>Ounigbo Louis</td>
<td>ORG PO81</td>
</tr>
<tr>
<td>Pacifico Severina</td>
<td>ORG OR53</td>
</tr>
<tr>
<td>Pagano Angela</td>
<td>ORG PO23</td>
</tr>
<tr>
<td>Pagano Angela*</td>
<td>ORG PO71</td>
</tr>
<tr>
<td>Pagliaro Miaria V.</td>
<td>ORG/INO PZ02</td>
</tr>
<tr>
<td>Painelli Anna</td>
<td>ORG PO17</td>
</tr>
<tr>
<td>Paiotta Alice</td>
<td>ORG PO52</td>
</tr>
<tr>
<td>Pallavicini Luca</td>
<td>ORG PO50</td>
</tr>
<tr>
<td>Palleschi Antonio</td>
<td>ORG PO33</td>
</tr>
<tr>
<td>Palleschi Giuseppe</td>
<td>ORG OR07</td>
</tr>
<tr>
<td>Palmieri Alessandro</td>
<td>ORG OR47</td>
</tr>
<tr>
<td>Palmioli Alessandro*</td>
<td>ORG OR19</td>
</tr>
<tr>
<td>Palmioli Alessandro*</td>
<td>ORG PO72</td>
</tr>
<tr>
<td>Palombi Laura</td>
<td>ORG PO14</td>
</tr>
<tr>
<td>Pannucci Elisa</td>
<td>ORG PO08</td>
</tr>
<tr>
<td>Paolino Marco*</td>
<td>ORG OR34</td>
</tr>
<tr>
<td>Paonessa Rosina</td>
<td>ORG OR40</td>
</tr>
<tr>
<td>Papianni Valentina</td>
<td>ORG PO19</td>
</tr>
<tr>
<td>Parenti Francesca</td>
<td>ORG OR04</td>
</tr>
<tr>
<td>Parisi Giovanna</td>
<td>ORG PO18</td>
</tr>
<tr>
<td>Parisi Maria Laura</td>
<td>ORG PO94</td>
</tr>
<tr>
<td>Parisotto Stefano</td>
<td>ORG PO34</td>
</tr>
<tr>
<td>Paternò Alessio</td>
<td>ORG PO67</td>
</tr>
<tr>
<td>Pavone Michele</td>
<td>ORG OR25</td>
</tr>
<tr>
<td>Pelliccioli Valentina*</td>
<td>ORG PO73</td>
</tr>
<tr>
<td>Peluso Andrea</td>
<td>ORG PO36</td>
</tr>
<tr>
<td>Pennetta Chiara*</td>
<td>ORG OR21</td>
</tr>
<tr>
<td>Peregò Luca A.</td>
<td>ORG OR35</td>
</tr>
<tr>
<td>Peri Francesco</td>
<td>ORG OR57</td>
</tr>
<tr>
<td>Perna Filippo Maria</td>
<td>ORG PO39</td>
</tr>
<tr>
<td>Perticarari Sofia</td>
<td>ORG PO78</td>
</tr>
<tr>
<td>Peterlongo Federico</td>
<td>ORG PZ06</td>
</tr>
<tr>
<td>Petricci Elena*</td>
<td>ORG OR56</td>
</tr>
<tr>
<td>Petrillo Giovanni</td>
<td>ORG PO71</td>
</tr>
<tr>
<td>Pett Christian</td>
<td>ORG OR18</td>
</tr>
<tr>
<td>Pezzella Alessandro</td>
<td>ORG OR25</td>
</tr>
<tr>
<td>Pezzetta Cristofer</td>
<td>ORG OR35</td>
</tr>
<tr>
<td>Piantini Sara*</td>
<td>ORG OR54</td>
</tr>
<tr>
<td>Piarulli Umberto</td>
<td>ORG PO33</td>
</tr>
<tr>
<td>Piccolella Simona</td>
<td>ORG OR53</td>
</tr>
<tr>
<td>Piemontese Luca*</td>
<td>ORG PO74</td>
</tr>
<tr>
<td>Pietini Marco*</td>
<td>ORG PO75</td>
</tr>
<tr>
<td>Piermattei Pamela*</td>
<td>ORG PO103</td>
</tr>
<tr>
<td>Pigilini Andrea</td>
<td>ORG PO50</td>
</tr>
<tr>
<td>Pignataro Barbara A.</td>
<td>ORG PO61</td>
</tr>
<tr>
<td>Name</td>
<td>ORG/INO Code</td>
</tr>
<tr>
<td>--------------------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Pignataro Luca</td>
<td>ORG PO33</td>
</tr>
<tr>
<td>Pinoli Monica</td>
<td>ORG PO33</td>
</tr>
<tr>
<td>Pirotta Valentina</td>
<td>ORG PO20</td>
</tr>
<tr>
<td>Pirovano Valentina</td>
<td>ORG PO01</td>
</tr>
<tr>
<td>Pirovano Valentina*</td>
<td>ORG/INO PZ01</td>
</tr>
<tr>
<td>Pizzolante Valeria</td>
<td>ORG PO89</td>
</tr>
<tr>
<td>Pomelli Christian Silvio</td>
<td>ORG PO64</td>
</tr>
<tr>
<td>Pomelli Christian Silvio*</td>
<td>ORG PO76</td>
</tr>
<tr>
<td>Pontisso Patrizia</td>
<td>ORG OR09</td>
</tr>
<tr>
<td>Porkolab Vanessa</td>
<td>ORG PO88</td>
</tr>
<tr>
<td>Potenti Simone</td>
<td>ORG PO104</td>
</tr>
<tr>
<td>Potenza Marianna*</td>
<td>ORG PO77</td>
</tr>
<tr>
<td>Potenza Nicoletta</td>
<td>ORG OR53</td>
</tr>
<tr>
<td>Prandi Adolfo</td>
<td>ORG PO50</td>
</tr>
<tr>
<td>Prandi Cristina*</td>
<td>ORG OR12</td>
</tr>
<tr>
<td>Prati Luca*</td>
<td>ORG PO78</td>
</tr>
<tr>
<td>Previtali Andrea</td>
<td>ORG PO45</td>
</tr>
<tr>
<td>Primitivo Ludovica</td>
<td>ORG OR61</td>
</tr>
<tr>
<td>Procopio Antonio</td>
<td>ORG PO40</td>
</tr>
<tr>
<td>Prontera Carmela Tania</td>
<td>ORG PO25</td>
</tr>
<tr>
<td>Prontera Carmela Tania*</td>
<td>ORG PO79</td>
</tr>
<tr>
<td>Pronti Stefano</td>
<td>ORG MD03</td>
</tr>
<tr>
<td>Pronti Stefano*</td>
<td>ORG PO81</td>
</tr>
<tr>
<td>Pucci Andrea</td>
<td>ORG PO97</td>
</tr>
<tr>
<td>Puzzo Francesco</td>
<td>ORG/INO OR04</td>
</tr>
<tr>
<td>Quaglio Deborah</td>
<td>ORG OR13</td>
</tr>
<tr>
<td>Quarta Santina</td>
<td>ORG OR09</td>
</tr>
<tr>
<td>Ragazzon Giulio</td>
<td>ORG PO91</td>
</tr>
<tr>
<td>Ragni Roberta</td>
<td>ORG PO55</td>
</tr>
<tr>
<td>Ragno Daniele</td>
<td>ORG PO12</td>
</tr>
<tr>
<td>Randazzo Pietro</td>
<td>ORG PO50</td>
</tr>
<tr>
<td>Raniolo Sofia</td>
<td>ORG PO33</td>
</tr>
<tr>
<td>Rassu Gloria</td>
<td>ORG PO21</td>
</tr>
<tr>
<td>Ravello Davide</td>
<td>ORG PO31</td>
</tr>
<tr>
<td>Ravello Davide*</td>
<td>ORG MD03</td>
</tr>
<tr>
<td>Raviola Carlotta*</td>
<td>ORG PO81</td>
</tr>
<tr>
<td>Razzetti Gabriele</td>
<td>ORG OR43</td>
</tr>
<tr>
<td>Reginato Gianna</td>
<td>ORG PO37</td>
</tr>
<tr>
<td>Regini Giorgia</td>
<td>ORG PO42</td>
</tr>
<tr>
<td>Reichardt Niels</td>
<td>ORG OR11</td>
</tr>
<tr>
<td>Renzi Polyszena*</td>
<td>ORG OR32</td>
</tr>
<tr>
<td>Rescifina Antonio</td>
<td>ORG OR59</td>
</tr>
<tr>
<td>Rescigno Donatella</td>
<td>ORG PO43</td>
</tr>
<tr>
<td>Riccio Raffaele*</td>
<td>ORG MD01</td>
</tr>
<tr>
<td>Riccio Raffaele</td>
<td>ORG OR51</td>
</tr>
<tr>
<td>Richichi Barbara</td>
<td>ORG OR08</td>
</tr>
<tr>
<td>Richter Sara</td>
<td>ORG OR20</td>
</tr>
<tr>
<td>Righetto Stefania</td>
<td>ORG PO45</td>
</tr>
<tr>
<td>Righi Giuliana</td>
<td>ORG OR61</td>
</tr>
<tr>
<td>Risi Caterina*</td>
<td>ORG PO82</td>
</tr>
<tr>
<td>Riva Renata</td>
<td>ORG OR30</td>
</tr>
<tr>
<td>Rizzo Aurora</td>
<td>ORG PO48</td>
</tr>
<tr>
<td>Rizzo Carla</td>
<td>ORG OR49</td>
</tr>
<tr>
<td>Rodríguez Douton María Jesús</td>
<td>ORG PO76</td>
</tr>
<tr>
<td>Romagnuolo Fabio</td>
<td>ORG OR65</td>
</tr>
<tr>
<td>Romanucci Valeria</td>
<td>ORG PO38</td>
</tr>
<tr>
<td>Romanucci Valeria*</td>
<td>ORG PO83</td>
</tr>
<tr>
<td>Romeo Roberto</td>
<td>ORG OR55</td>
</tr>
<tr>
<td>Rontogiani Matina</td>
<td>ORG PO35</td>
</tr>
<tr>
<td>Rooney Myles</td>
<td>ORG OR14</td>
</tr>
<tr>
<td>Roose Bart</td>
<td>ORG OR06</td>
</tr>
<tr>
<td>Rosa-Gastaldo Daniele*</td>
<td>ORG PO84</td>
</tr>
<tr>
<td>Rossella Francesco</td>
<td>ORG PO76</td>
</tr>
<tr>
<td>Rossi Alessio</td>
<td>ORG OR36</td>
</tr>
<tr>
<td>Rossi Elisabetta</td>
<td>ORG/INO PZ01</td>
</tr>
<tr>
<td>Rossi Federico Vittorio</td>
<td>ORG PO47</td>
</tr>
<tr>
<td>Rozzi Andrea</td>
<td>ORG OR10</td>
</tr>
<tr>
<td>Rozzi Andrea*</td>
<td>ORG PO85</td>
</tr>
<tr>
<td>Russo Alessandra</td>
<td>ORG PO96</td>
</tr>
<tr>
<td>Russo Alessandra*</td>
<td>ORG PO86</td>
</tr>
<tr>
<td>Russo Annapina</td>
<td>ORG OR39</td>
</tr>
<tr>
<td>Russo Beatrice</td>
<td>ORG OR62</td>
</tr>
<tr>
<td>Russo Giulia</td>
<td>ORG OR39</td>
</tr>
<tr>
<td>Sabuzi Federica</td>
<td>ORG PO101</td>
</tr>
<tr>
<td>Salamone Michela</td>
<td>ORG PO75</td>
</tr>
<tr>
<td>Salamone Michela</td>
<td>ORG PO06</td>
</tr>
<tr>
<td>Salani Anika</td>
<td>ORG OR29</td>
</tr>
<tr>
<td>Salerno Gianluca*</td>
<td>ORG OR08</td>
</tr>
<tr>
<td>Salerno Gianluca*</td>
<td>ORG OR08</td>
</tr>
<tr>
<td>Sambri Riccardo</td>
<td>ORG PO102</td>
</tr>
<tr>
<td>Sambri Letizia</td>
<td>ORG OR31</td>
</tr>
<tr>
<td>Sambri Letizia*</td>
<td>ORG/INO OR01</td>
</tr>
<tr>
<td>Sampaolesi Susanna</td>
<td>ORG OR47</td>
</tr>
<tr>
<td>Sampaolesi Susanna*</td>
<td>ORG OR63</td>
</tr>
<tr>
<td>Sansone Francesco</td>
<td>ORG PO102</td>
</tr>
</tbody>
</table>

SOMMARIO – PROGRAMMA – MEDAGLIE E PREMI – KEYNOTE – ORALI- POSTER - AUTORI
XXVI Congresso Nazionale della Società Chimica Italiana

SOMMARIO
– PROGRAMMA
– MEDAGLIE E PREMI
– KEYNOTE – ORALI - POSTER - AUTORI

Sansone Francesco* ORG OR57
Sansone Francesco* ORG PO88
Sansone Francesco* ORG PO89
Santagata Antonio ORG PO24
Santi Luca ORG PO08
Santini Roberta ORG OR56
Santos Maria Amélia ORG PO74
Sanzone Alessandro ORG OR14
Sappino Carla* ORG OR61
Sartini Stefania ORG PO76
Sartorel Andrea ORG OR07
Sartori Andrea ORG PO21
Sassi Mauro* ORG OR14
Satriano Cristina ORG OR41
Sbravati Davide ORG PO89
Scafato Patrizia ORG PO60
Scalabrin Matteo ORG OR20
Scanduzzi Cristina ORG PO50
Schettini Rosaria ORG PO30
Schettini Rosaria* ORG PO90
Scire Salvatore ORG PO67
Scognamiglio Monica ORG OR53
Secchi Andrea ORG PO17
Secchi Andrea* ORG PO91
Sepe Valentina ORG PO29
Serafini Mauro ORG PO10
Serafini Mauro ORG PO11
Seravalli Luca ORG PO17
Serna Sonia ORG OR11
Serrili Anna Maria ORG PO09
Sestito Stefania E ORG OR57
Sforazzini Giuseppe* ORG OR01
Siani Gabriella* ORG PO92
Sicignano Marina ORG PO60
Sicignano Marina* ORG PO93
Siligardi Giuliano ORG PO32
Silvi Serena ORG PO91
Sindona Giovanni ORG OR40
Sini Loredana ORG OR42
Sinicropi Adalgisa* ORG PO94
Snoeck Robert ORG PO28
Snoeck Robert ORG PO40
Solfrizzo Michele ORG PO74
Soriente Annunziata ORG OR59
Speranza Giovanna ORG OR65
Spinelli Michela ORG OR19
Squarcina Andrea ORG/INO OR02
St. John Campbell Sahra ORG PO98
Stecca Barbara ORG OR56

Stecker Kelly ORG PO35
Stefano Caporali ORG PO76
Stella Lorenzo ORG OR32
Suber Lorensa ORG OR61
Sunseri Francesco ORG PO58
Superchi Stefano ORG PO60
Supuran Claudiu T. ORG PO89
Suranna Gian Paolo ORG OR06
Suranna Gian Paolo ORG PO48
Taddei Maurizio ORG PO82
Tagliaabue Andrea ORG/INO OR04
Talarico Giovanni ORG PO40
Tallarida Matteo Antonio ORG PO03
Talotta Carmen ORG OR59
Tassini Paolo ORG PO25
Tavan Cinzia ORG PO79
Tedesco Consiglia ORG PO90
Teghil Roberto ORG PO24
Terricciano Stefania ORG OR52
Terricciano Stefania* ORG PO96
Terreno Enzo ORG PO56
Teta Roberta* ORG OR37
Thiel Walter ORG OR01
Tiecco Matteo ORG PO92
Tiecco Matteo* ORG OR46
Tisi Renata ORG OR19
Tomás Daniel ORG PO74
Toniolo Claudio ORG PO59
Torre Luigi ORG PO08
Torti Edoardo* ORG PO97
Tortorella Paolo ORG OR52
Tota Arianna ORG PO27
Tota Arianna* ORG PO98
Trabocchi Andrea ORG OR36
Tramutola Francesca ORG PO23
Trevisan Marta ORG PO65
Troiani Teresa ORG OR53
Trotta Massimo ORG PO55
Turato Cristian ORG OR09
Uccello-Barretta Gloria ORG OR13
Ugo Renato ORG PO50
Uygur Mustaga ORG PO46
<table>
<thead>
<tr>
<th>Vaccaro Maria Carmela</th>
<th>ORG PO77</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vacchini Mattia</td>
<td>ORG PO16</td>
</tr>
<tr>
<td>Vacchini Mattia*</td>
<td>ORG PO99</td>
</tr>
<tr>
<td>Valderrey Virginia</td>
<td>ORG OR44</td>
</tr>
<tr>
<td>Valentini Francesca</td>
<td>ORG OR07</td>
</tr>
<tr>
<td>Valentini Francesca*</td>
<td>ORG PO100</td>
</tr>
<tr>
<td>Vanossi Davide</td>
<td>ORG OR04</td>
</tr>
<tr>
<td>Varra Michela</td>
<td>ORG OR39</td>
</tr>
<tr>
<td>Vassallo Antonio</td>
<td>ORG PO77</td>
</tr>
<tr>
<td>Venditti Alessandro</td>
<td>ORG PO11</td>
</tr>
<tr>
<td>Venditti Alessandro*</td>
<td>ORG PO09</td>
</tr>
<tr>
<td>Venditti Alessandro*</td>
<td>ORG PO10</td>
</tr>
<tr>
<td>Venturi Margherita</td>
<td>ORG PO91</td>
</tr>
<tr>
<td>Verdelino Vincenzo</td>
<td>ORG OR10</td>
</tr>
<tr>
<td>Vergara Daniele</td>
<td>ORG OR35</td>
</tr>
<tr>
<td>Verona Massimiliano Donato</td>
<td>ORG OR10</td>
</tr>
<tr>
<td>Villani Claudio</td>
<td>ORG OR58</td>
</tr>
<tr>
<td>Villano Gianmarco</td>
<td>ORG OR09</td>
</tr>
<tr>
<td>Virgilio Antonella</td>
<td>ORG OR39</td>
</tr>
<tr>
<td>Virgilio Antonella*</td>
<td>ORG PO101</td>
</tr>
<tr>
<td>Viscardi Guido</td>
<td>ORG OR24</td>
</tr>
<tr>
<td>Visentin Sonja</td>
<td>ORG OR24</td>
</tr>
<tr>
<td>Vita Francesca</td>
<td>ORG OR28</td>
</tr>
<tr>
<td>Vitale Paola</td>
<td>ORG PO39</td>
</tr>
<tr>
<td>Vitali Forconesi Gabriella</td>
<td>ORG OR30</td>
</tr>
<tr>
<td>Vivès Corinne</td>
<td>ORG OR11</td>
</tr>
<tr>
<td>Vizza Francesco</td>
<td>ORG/INO PZ02</td>
</tr>
<tr>
<td>Vladiskovic Chiara</td>
<td>ORG OR43</td>
</tr>
<tr>
<td>Volonterio Alessandro</td>
<td>ORG OR21</td>
</tr>
<tr>
<td>Volpe Chiara</td>
<td>ORG PO63</td>
</tr>
<tr>
<td>Volpe Raffaele</td>
<td>ORG PO26</td>
</tr>
<tr>
<td>Volpi Stefano*</td>
<td>ORG PO102</td>
</tr>
<tr>
<td>Wagner Björn</td>
<td>ORG OR50</td>
</tr>
<tr>
<td>Wang Anna</td>
<td>ORG PO49</td>
</tr>
<tr>
<td>Werz Oliver</td>
<td>ORG OR52</td>
</tr>
<tr>
<td>Westerlind Ulrika</td>
<td>ORG OR18</td>
</tr>
<tr>
<td>Williams Charlotte K.</td>
<td>ORG PZ04</td>
</tr>
<tr>
<td>Zambon Alfonso*</td>
<td>ORG OR04</td>
</tr>
<tr>
<td>Zampella Angela</td>
<td>ORG OR22</td>
</tr>
<tr>
<td>Zampella Giuseppe</td>
<td>ORG PO16</td>
</tr>
<tr>
<td>Zanardi Franca</td>
<td>ORG PO21</td>
</tr>
<tr>
<td>Zanardi Franca*</td>
<td>ORG PZ01</td>
</tr>
<tr>
<td>Zanella Simone</td>
<td>ORG PO33</td>
</tr>
<tr>
<td>Zani Lorenzo</td>
<td>ORG PO37</td>
</tr>
<tr>
<td>Zani Lorenzo*</td>
<td>ORG/INO KN02</td>
</tr>
<tr>
<td>Zanichelli Valeria</td>
<td>ORG PO91</td>
</tr>
<tr>
<td>Zanin Davide</td>
<td>ORG PO50</td>
</tr>
<tr>
<td>Zanotti Valerio</td>
<td>ORG/INO OR04</td>
</tr>
<tr>
<td>Zanotti-Gerosa Antonio</td>
<td>ORG/INO OR03</td>
</tr>
<tr>
<td>Zappacosta Romina</td>
<td>ORG PO92</td>
</tr>
<tr>
<td>Zardi Paolo</td>
<td>ORG PO54</td>
</tr>
<tr>
<td>Zarrelli Armando</td>
<td>ORG PO38</td>
</tr>
<tr>
<td>Zarrelli Armando</td>
<td>ORG PO38</td>
</tr>
<tr>
<td>Zoia Luca*</td>
<td>ORG OR29</td>
</tr>
<tr>
<td>Zonta Cristiano</td>
<td>ORG PO54</td>
</tr>
<tr>
<td>Zonta Cristiano*</td>
<td>ORG OR64</td>
</tr>
<tr>
<td>Zonta Cristiano*</td>
<td>ORG OR64</td>
</tr>
<tr>
<td>Zontin Martina</td>
<td>ORG/INO OR02</td>
</tr>
</tbody>
</table>