Società Chimica Italiana
Divisione di Chimica Organica

Atti

del

XXXIX Convegno Nazionale

della

Divisione di Chimica Organica

della

Società Chimica Italiana

CD TORINO CO 2019

Torino 8-12 Settembre 2019

UNIVERSITÀ DEGLI STUDI DI TORINO

CAMERA DI COMMERCIO INDUSTRIA ARTIGIANATO E AGRICOLTURA DI TORINO

UPO UNIVERSITÀ DEL PIEMONTE ORIENTALE

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Benvenuto

Cari Soci,

benvenuti al **XXXIX Convegno Nazionale della Divisione di Chimica Organica, CDCO Torino 2019**, organizzato dai Colleghi dell'Università di Torino e dell'Università del Piemonte Orientale.
Ci incontreremo dall'8 al 12 settembre 2019 nella capitale piemontese dove saremo ospitati presso la nuova aula magna "Cavallerizza Reale" dell'Università di Torino per le giornate di apertura e di chiusura, mentre nelle giornate centrali le sessioni si svolgeranno nelle vicine strutture di "Torino Incontra", il centro congressi della Camera di Commercio.

Ci prepariamo a trascorrere intense giornate scientifiche, con le conferenze plenarie dei vincitori di medaglie e premi della Divisione di Chimica Organica 2019 e degli speakers invitati, e con numerose comunicazioni orali e poster per aggiornarci sui progressi della ricerca nella Chimica Organica italiana. Anche quest'anno alle attività scientifiche affiancheremo momenti di riflessione sul ruolo sociale ed economico della Chimica Organica nel nostro paese: in collaborazione con la Camera di Commercio di Torino incontreremo chimici organici che lavorano nel tessuto professionale ed industriale della Regione Piemonte ed in tutta Italia; organizzeremo, insieme al Gruppo Interdivisionale di Diffusione della Cultura Chimica, una sessione aperta al pubblico con personalità di richiamo nella divulgazione scientifica; i Soci giovani saranno attivamente coinvolti nella programmazione di eventi e conferenze.

Ci incontreremo poi nell'Assemblea dei Soci, dedicando ampio spazio a discutere delle attività divisionali, ed a pianificare le direzioni future della nostra comunità in seno alla SCI. Non ultimo, condivideremo il piacere dello stare insieme nei momenti sociali, per i quali i Colleghi Organizzatori ci riserveranno ambientazioni molto suggestive nella cornice della loro bellissima città.

Potrete seguire tutti gli aggiornamenti dell'organizzazione su questo sito, facendo pervenire a me, al Consiglio Direttivo ed al Comitato Organizzatore i vostri suggerimenti per il nostro CDCO Torino 2019.

Vi invito a non mancare all'evento più importante della nostra Divisione nel 2019, portando i vostri contributi ai lavori scientifici e le vostre voci alla discussione.

Molti cari saluti

Gianluca Farinola

Presidente della Divisione di Chimica Organica

Medaglie e Premi

Medaglie

Medaglia d'oro *Angelo Mangini:*

Alessandro Casnati – *Università di Parma*

Per i suoi contributi fondamentali alla chimica dei calixareni, che partendo dalla messa a punto di strategie di funzionalizzazione regio- e stereoselettiva e dallo studio delle proprietà conformazionali di tali piattaforme macrocicliche, hanno portato allo sviluppo razionale di derivati multivalenti con molteplici applicazioni di grande interesse quali la catalisi, il riconoscimento e la veicolazione di principi attivi.

Medaglia d'oro *Adolfo Quilico:*

Marco d'Ischia – *Università di Napoli "Federico II"*

Per l'originalità, l'ampiezza ed il valore delle sue ricerche sulla chimica ossidativa dei composti fenolici. Tali studi hanno spaziato, con rigore ed eleganza scientifica, dalla sintesi biomimetica, alla definizione dei meccanismi di reazione, fino alla caratterizzazione di polimeri melanici, consentendo una razionalizzazione delle relazioni struttura-proprietà di rilevante importanza per applicazioni biomediche e tecnologiche.

Medaglia d'argento *Giacomo Ciamician:*

Luca Dell'Amico – *Università di Padova*

Per i brillanti risultati ottenuti nell'ottimizzazione di protocolli sintetici esplorando percorsi innovativi che spaziano dall'organocatalisi polare e fotoorganocatalisi radicalica alla fotocatalisi in reattori microfluidici.

Medaglia *Piero Pino:*
delle Divisioni di Chimica Organica e di Chimica Industriale

Maurizio Benaglia – *Università di Milano*

Per aver contribuito con creatività e rigore metodologico allo sviluppo di nuovi sistemi organocatalitici, caratterizzati da elevata efficienza e basso impatto ambientale. I suoi studi hanno sviluppato protocolli di grande interesse in ambito industriale utilizzando reagenti supportati e riciclabili e progettando metodiche di sintesi basate su reazioni in flusso continuo. Le ricerche del Prof. Benaglia contribuiscono a colmare lo spazio concettuale e sperimentale tra le metodiche di laboratorio ed i processi di sintesi su larga scala.

Premi alla Ricerca

Premio alla ricerca "Chimica Organica per l'Ambiente, l'Energia e le Nanoscienze" (Senior):
Valeria Conte - *Università di Roma Tor Vergata*

Per i suoi importanti contributi all'avanzamento degli studi di sistemi di ossi-funzionalizzazione di substrati organici in ambienti prevalentemente acquosi, che mimano i processi biologici puntando allo sviluppo di percorsi sintetici sostenibili.

Premio alla Ricerca "Chimica Organica per l'Ambiente, l'Energia e le Nanoscienze" (Junior):
Giulio Ragazzon - *Università di Trieste*

Per i suoi contributi allo sviluppo di originali costrutti supramolecolari dinamici ed alla loro implementazione in sistemi catalitici cooperativi ed in nano-assemblati basati sugli acidi nucleici.

Premio alla ricerca "Chimica Organica nei suoi Aspetti Metodologici" (Senior):
Andrea Basso - *Università di Genova*

Per i suoi contributi rigorosi e creativi allo sviluppo di nuove metodologie fotochimiche e multicomponenti per la generazione di diversità chimica di rilevanza biologica.

Premio alla ricerca "Chimica Organica nei suoi Aspetti Metodologici" (Junior):
Damiano Tanini - *Università di Firenze*

Per il suo contributo allo sviluppo di originali metodi di sintesi e di caratterizzazione chimico-fisica di derivati calcogenati con interessanti e peculiari attività.

Premio alla ricerca "Chimica Organica per le Scienze della Vita" (Senior):
Cristina Nativi - *Università di Firenze*

Per avere saputo coniugare in modo originale ed innovativo la ricerca di nuovi percorsi di sintesi efficiente e stereoselettiva di molecole di natura saccaridica con lo sviluppo di glicoconiugati e mimetici in ambito biomedico.

Premio alla ricerca "Chimica Organica per le Scienze della Vita" (Junior):
Alberto Dal Corso - *Università di Milano*

Per i suoi studi sull'incremento dell'affinità di legame tra farmaco e proteina bersaglio e sulla sintesi di composti citotossici coniugati a ligandi selettivi di antigeni tumorali.

Premio alla ricerca "Chimica Organica per lo Sviluppo di Processi e Prodotti nell'Industria" (Senior):
Augusto Canavesi - *Teva Active Pharmaceutical Ingredients - TAPI*

Per i suoi studi rivolti all'ottimizzazione di processi di produzione di farmaci con particolare riguardo alle strategie sintetiche ed al fenomeno del polimorfismo.

Premio alla ricerca "Chimica Organica per lo Sviluppo di Processi e Prodotti nell'Industria" (Junior):
Maria Pia Catalani - *Evotec*

Per i suoi studi sulla sintesi stereoselettiva di derivati policiclici della piperazina con potenziali attività biologiche.

Premi di Dottorato

Premio Tesi di Dottorato "Chimica Organica per l'Ambiente, l'Energia e le Nanoscienze":

Gianluigi Albano - *Università di Pisa*

Per i suoi originali studi sulle proprietà chirottiche di film sottili di oligotiofeni chirali.

Premio Tesi di Dottorato "Chimica Organica nei suoi Aspetti Metodologici":

Luca Capaldo - Università di Pavia

Per i suoi studi sullo sviluppo di processi sintetici fotocatalizzati ad alta efficienza.

Premio Tesi di Dottorato "Chimica Organica per le Scienze della Vita":

Chiara Platella - Università di Napoli "Federico II"

Per i risultati ottenuti nella messa a punto di protocolli per l'identificazione di piccole molecole in grado di legare specifiche strutture G-quadruplex.

Programma

Programma Scientifico

Domenica 8 Settembre (Presso Aula Magna, Cavallerizza, Università di Torino, via Verdi 9, Torino)		
	14.00-14.30	Saluti, Inizio Lavori e Premiazioni
Sessione Plenaria #1	Chairperson: **P. Scrimin**	
	14.30-15.00	**M-01** Medaglia A. Mangini **Casnati A.** *Calixarenes: from Chemical Curiosity and Basic Research to Industrial Implementation*
	Chairperson: **R. Riccio**	
	15:00-15:30	**M-02** Medaglia Adolfo Quilico **d'Ischia M.** *The Melanin Code: Deciphering Nature's Paradigms for Chemical Functionality*
	Chairperson: **E. Licandro**	
	15:30-16:00	**PR-S1** Premio: "Chimica Organica nei suoi Aspetti Metodologici" **Basso A.** *Isonitrili al Pesto (Isocyanides in Pesto Sauce)*
	16:00-16:30	**PR-S2** Premio: "Chimica Organica per le Scienze della Vita" **Nativi C.** *[4+2] Cycloadditions: Vintage Reactions for New Glycan-based Epitopes*
16.30-17.00 Coffee Break		
Sessione Plenaria #2	Chairperson: **F. Sannicolò**	
	17:00-17:30	**M-03** Medaglia P. Pino **Benaglia M.** *Development of catalytic stereoselective methodologies: sense and sensibility*
	Chairperson: **F. De Angelis**	
	17:30-18:00	**EurJOC Lecture** in ricordo di Cinzia Chiappe **Welton T.** *Ionic Liquid Effects on the Rates of Reactions - A Lecture in Memory of Prof. Cinzia Chiappe*
	Chairperson: **A. Brandi**	
	18:00-18:30	**KN-01 Laus M.** *Toward deterministic doping*
	18:30-19:00	**PR-S3** Premio "Chimica Organica per l'Ambiente, l'Energia e le Nanoscienze" **Conte V.** *V-catalysis in Oxidation Reactions: from Mimesis of HalPO Enzymes to Sustainable Synthesis*
	19.30	**Buffet di benvenuto. Cortile del Rettorato**

Lunedì 9 Settembre - Mattino (Presso Sala Cavour, Centro Congressi Torino Incontra, via Nino Costa 8, Torino)		
Sessione Plenaria #3	Chairperson: **M. Menicucci**	
	9:00-9:15	Apertura Lavori
	9.15-11.00	Imprese e Ricerca: storie di connessioni.
11.00-11.30 Coffee Break		
Sessione Plenaria #4	Chairperson: **M. Menicucci**	
	11.30-11.45	Il Cluster SPRING per un sistema nazionale che integri ricerca e imprese.
	11.45-13.00	La Chimica si rinnova, Green Chemistry, Nuove Tecnologie ed Open Innovation.

Lunedì 9 Settembre - Pomeriggio (Presso Sala Cavour, Centro Congressi Torino Incontra, via Nino Costa 8, Torino)		
	13.00-15.00	**Sessione Poster #1 (Torino Incontra – Foyer)**
Sessione #1 (Sala Cavour)	Chairperson: **M. Taddei**	
	15:00-15:30	**PR-S4** Premio: "Chimica Organica per lo Sviluppo di Processi e Prodotti nell'Industria" **Canavesi A.** *Challenges and creativity in API process development: facing unexpected impurities formation.*
	15:30-15:50	**IC-01 Roletto J**. *Efinaconazole process development and scale up through unconventional use of Grignard reagent*
	15:50-16:10	**IC-02 Carcone L.** *Development and Scale-up of a Stereoselective Synthesis to Droxidopa*
	16:10-16:30	**IC-03 Lombardo A.** *Pentetrazol: development and industrialization of the manufacturing process*
Sessione #2 (Sala Giolitti)	Chairperson: **G. Oliviero**	
	15:00-15:30	**PR-J1** Premio: "Chimica Organica nei suoi Aspetti Metodologici" (Junior) **Tanini D.** *Reactivity and synthetic applications of new chalcogen-containing small molecules*
	15:30-15:50	**OC-01 Esposito A.** *Synthesis and biological evaluation of novel antimicrobial and antibiofilm agents*
	15:50-16:10	**OC-02 Clemente F.** *Stereoselective synthesis of C-2 alkylated trihydroxypiperidines: effect of the chain length and the configuration at C-2 on their activity as Pharmacological Chaperones for Gaucher Disease*
	16:10-16:30	**OC-03 Teta R.** *Deciphering the metabolome of marine microbiome through molecular networking*
Sessione #3 (Sala Einaudi)	Chairperson: **O. Bortolini**	
	15:00-15:30	**PR-J2** Premio: "Chimica Organica per l'Ambiente, l'Energia e le Nanoscienze" (Junior) **Ragazzon G.** *Supramolecular dynamic systems away from equilibrium*
	15:30-15:50	**OC-04 Da Pian M.** *A Kinetic and Morphological Study of P3HT Nanowhiskers Formation in the Presence of either PCBM or PCL.*
	15:50-16:10	**OC-05 Decavoli C.** *Design of Organic Based Photosensitizer-Catalyst Systems for Photoelectrochemical Solar Fuels*
	16:10-16:30	**OC-06 Cordaro M.** *Synthesis of self-assembled BODIPY heterodimer for energy transfer investigations*
16.30-17.00 Coffee Break		

Sessione #4 (Sala Cavour)	Chairperson: **L. Di Bari**	
	17:00-17:30	**PR-J3** Premio: "Chimica Organica per lo Sviluppo di Processi e Prodotti nell'Industria" (Junior) **Catalani M. P.** *Novel NK1 receptor antagonists*
	17:30-17:50	**IC-04 De Combarieu E.** *Investigation of optical purity of natural Cephalotaxine*
	017:50-18:10	**OC-07 Bandini M.** *Catalytic manipulations of arenes with light and graphene oxide I*
	18:10-18:30	**OC-08 Salamone M.** *Metal-Ion Induced C-H Bond Deactivation in the Hydrogen Atom Transfer Reaction from Diol Substrates to the Cumyloxyl Radical*
	18:30-18:50	**OC-09 Martin T.** *Hydrogen Atom Transfer based Aliphatic C–H Bond Functionalization of Cycloalkane Derivatives. Kinetic and Product Studies on the Role of Torsional Effects*
	18:50-19:10	**OC-10 Galeotti M.** *Selective aliphatic C−H bond hydroxylation promoted by in situ generated dioxiranes*
Sessione #5 (Sala Giolitti)	Chairperson: **F. Nicotra**	
	17:00-17:30	**PR-J4** Premio: "Chimica Organica per le Scienze della Vita" (Junior) **Dal Corso A.** *New-generation Self-Immolative Spacers Enable Fast Release of Anticancer Drugs*
	17:30-17:50	**OC-11 Valgimigli L.** *The strange case of quinones and hydroperoxyl radicals*
	017:50-18:10	**OC-12 Doria F.** *Photoresponsive molecular tools targeting DNA G-quadruplex structures*
	18:10-18:30	**OC-13 Montesarchio D.** *The intriguing world of G-quadruplex-based aptamers*
	18:30-18:50	**OC-14 Sabuzi F.** *Encapsulation and controlled release of thymol derivatives into lignin microcapsules*
	18:50-19:10	**OC-15 Roviello G. N.** *Novel insights on peptide-G4 DNA interaction: a study on the binding behaviour of polyamine peptides on different G4 DNA structures*
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	17:20-17:40	**OC-17 Zinna F.** *Chiral functionalized fluorescent macrocycles as a scaffold for remarkable chiroptical properties*
	17:40-18:00	**OC-18 Francesconi O.** *Development and binding properties of a synthetic receptor for the molecular recognition of caffeine and related xanthines*
	18:00-18:20	**OC-19 Cringoli M. C.** *Spike of Sulfur for Photo-Chemistry on Self-assembling Tripeptides*
	18:20-18:40	**OC-20 Patamia V.** *Self-Assembled nicotinic acid-based tetrahedral hosts as supramolecular catalysts: synthesis and first applications*
	18:40-19:00	**OC-21 Di Stefano S.** *How to Make Autonomous the Motions of a Chemically Fueled Molecular Machine*

Martedì 10 Settembre - Mattino (Presso Sala Cavour, Centro Congressi Torino Incontra, via Nino Costa 8, Torino)		
Sessione Plenaria #5 (Sala Cavour)	Chairperson: **M. Prato**	
	9.00-9.30	**KN-02 Marchesan S.** *Entry to peptide Wonderland through the rabbit hole*
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	09:30-09:50	**OC-22 Porcheddu A.** *Mech@nochemistry: an Appealing Marriage of Innovation and Tradition*
	09:50-10:10	**OC-23 Guazzelli L**. *Bio-based ionic liquids: synthesis and applications*
	10:10-10:30	**OC-24 Chiurchiù E.** *A new efficient flow chemical synthesis of thiophene-2-carboxylates*
Sessione #8 (Sala Giolitti)	Chairperson: **M. Melucci**	
	09:30-09:50	**OC-25 Schettini R.** *Multivalent effect of cyclopeptoid-iminosugar conjugates in glycosidase inhibition*
	09:50-10:10	**OC-26 Corradini R.** *PNA- and modified-PNA-based systems: applications to genetic diseases*
	10:10-10:30	**OC-27 Cardullo N.** *Synthesis of bisphenol neolignans as bioactive compounds*
Sessione #9 (Sala Einaudi)	Chairperson: **M. Maggini**	
	09:30-09:50	**OC-28 Russo L.** *3D Printable biomaterials for tissue models, functionalization strategies*
	09:50-10:10	**OC-29 Locatelli E.** *Photoluminescent decoration of iron oxide magnetic nanoparticles for dual-imaging applications*
	10:10-10:30	**OC-30 Sambri L.** *Phosphorescent iridium-containing nanomicelles: synthesis, characterization and preliminary applications in nanomedical imaging*
10.30-11.00 Coffee Break		
Sala Cavour	11.00-13.00	Assemblea Soci

Martedì 10 Settembre - Pomeriggio (Presso Sala Cavour, Centro Congressi Torino Incontra, via Nino Costa 8, Torino)		
	13.00-15.00	**Sessione Poster #2 (Torino Incontra – Foyer)**
Sessione #10 (Sala Cavour)	Chairperson: **E. Beccalli**	
	15:00-15:15	**PD-01** Premio Dottorato: "Chimica Organica nei suoi Aspetti Metodologici" **Capaldo L.** *The Triangle of Photocatalysis: Different Approaches for Ecosustainable Synthesis*
	15:15-15:35	**OC-31 Minassi A**. *Photochemical angular-to-linear switch of the triterpenoid A,B,C ring system: discovery, mechanistic aspects, and biological translation*
	15:35-15:55	**OC-32 Leggio A.** *A $TiCl_4$-based effective protocol for the synthesis of peptides*
	15:55-16:15	**OC-33 De Luca L.** *Metal-free Chlorination of Toluenes and Aldehydes Mediated by Visible Light*
	16.15-16.35	**OC-34 Volpe C.** *New applications of ester surrogates in organic synthesis*
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	15:00-15:15	*Tavola Rotonda*
	15:15-15:35	**PD-02** Premio Dottorato: "Chimica Organica per le Scienze della Vita" **Platella C.** *Towards DNA-targeting magic bullets: searching for potential conformation-selective G-quadruplex ligands*
	15:35-15:55	**OC-35 Mancuso A.** *Structural modifications of glycoamino OPEs: synthesis and properties*
	15:55-16:15	**OC-36 Finamore C.** *Synthesis of new oxadiazole derivatives as potent and selective FXR antagonists*
	16.15-16.35	**OC-37 Bucci R.** *Enantioselective Syntheses of Morpholino β-Amino Acids for the preparation of different nanomaterials*
Sessione #12 (Sala Einaudi)	Chairperson: **M. Bonchio**	
	15:00-15:15	**PD-03** Premio Dottorato: "Chimica Organica per l'Ambiente, l'Energia e le Nanoscienze" **Albano G.** *Outstanding chiroptical features in thin films of chiral π-conjugated oligomers: from synthesis to applications*
	15:15-15:35	**OC-38 D'Anna F.** *Ionic Liquid Gels: Tunable and Multifaceted Materials*
	15:35-15:55	**OC-39 Riela S.** *Clay minerals: a challenge for chemists*
	15:55-16:15	**OC-40 Giacalone F.** *Carbon Nanoforms-based Hybrid Catalysts*
	16.15-16.35	**OC-41 Melucci M.** *Graphene oxide composites-based filters for tap water purification*
16.35-17.00 Coffee Break		

Sessione #13 (Sala Cavour)	Chairperson: **M. Funicello**	
	17:00-17:20	**OC-42 Tiecco M.** *Novel Hydrophobic Deep Eutectic Solvents (DESs) as water-immiscible H-bond-based solvents*
	17:20-17:40	**OC-43 Benassi A**. *Light meets click chemistry: development of novel, photoactivable, 2,5-diaryl tetrazoles for labelling nucleic acids*
	17:40-18:00	**OC-44 Risi C.** *Hydrogen Borrowing reactions in water medium*
	18:00-18:20	**OC-45 Ferlin F.** *Combining Safer Solvents Heterogeneous Catalysis and Flow Technology Toward Sustainable C-H Activation Methodologies*
	18:20-18:40	**OC-46 Martina K.** *Green approach to aerobic alcohol oxidation and transfer hydrogenation of nitro benzene derivatives*
	18:40-19:00	**OC-47 Valentini F.** *Highly selective toluene oxidation to benzaldehyde: a sustainable process*
Sessione #14 (Sala Giolitti)	Chairperson: **A. Liguori**	
	17:00-17:20	**OC-48 Casertano M.** *Development and synthesis of simplified analogs of a bioactive natural polyketide*
	17:20-17:40	**OC-49 Cardano F.** *Spiropyrans for light-controlled delivery of Aspirin*
	17:40-18:00	**OC-50 Forgione R. E.** *The interplay between NMR spectroscopy and molecular modeling: a powerful tool to investigate protein-glycoconjugate interactions*
	18:00-18:20	**OC-51 Maranzana, A.** *Degradation of Ochratoxin A in a wide pH range: experimental and computational study*
	18:20-18:40	**OC-52 Hawala I.** *Innovative synthetic approach based on the Native Chemical Ligation for development of new dual PET/OI peptide imaging probes*
	18:40-19:00	**OC-53 Marafon G.** *α-Amino Aldehydes as Monomers for the Synthesis of Imine-/Amide-based Foldamer Structures*
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	17:20-17:40	**OC-55 Magli S.** *Multimodal Functionalization of Nanoparticles for b-cells Imaging: new diagnostic tools for pancreatic regenerative therapies*
	17:40-18:00	**OC-56 Fiammengo R.** *Site-selective immobilization of leptin on gold nanoparticles*
	18:00-18:20	**OC-57 Scala A.** *Engineered Polylactide-based Nanoparticles as Multifunctional Drug Delivery Systems*
	18:20-18:40	**OC-58 Sacco M.** *Azomethine ylides: a powerful tool for Nanodiamonds-based contrast agents and drug delivery systems*
	Chairperson: **G. Reginato**	
	18:40-19:00	**ChemPubSoc Europe Editor's Lecture** **Novara F.** *Current Challenges in Chemistry Publishing*

Mercoledì 11 Settembre - Mattino (Presso Sala Cavour, Centro Congressi Torino Incontra, via Nino Costa 8, Torino)		
Sessione Plenaria #6 (Sala Cavour)	Chairperson: **E. Marcantoni**	
	9.00-9.30	**KN-03 Pace V.** *Designing new synthetic concepts for imparting molecular complexity with C-1 sources*
Sessione #16 (Sala Cavour)	Chairperson: **L. Dell'Amico**	
	09:30-09:50	**OC-59 Brandolese A.** *N-Heterocyclic Carbene (NHC)-Organocatalyzed kinetic resolution of biologically active Biginelli compounds*
	09:50-10:10	**OC-60 Rizzo S**. *High Enantioselection Performances of Inherently Chiral Ionic Liquids with Axial, Helical and Central Stereogenicity*
	10:10-10:30	**OC-61 Lauro G.** *DFT/NMR approach for the configuration assignment of groups of diastereoisomers by the combination and comparison of experimental and predicted sets of data*
Sessione #17 (Sala Giolitti)	Chairperson: **V. Costantino**	
	09:30-09:50	**OC-62 Piccialli V.** *Synthesis and antitumor activity of polybrominated C15 acetogenin derivatives*
	09:50-10:10	**OC-63 Zongo L.** *Folate-Tannin Microcapsules for Oncologic Theragnosis Applications*
	10:10-10:30	**OC-64 La Ferla B.** *Sweet and Smart Nanovectors for Live-Cell Drug Delivery and in vivo Bone Targeting*
Sessione #18 (Sala Einaudi)	Chairperson: **A. Goti**	
	09:30-09:50	**OC-65 Toniolo G.** *Stable and Water-Dispersible Quantum Dots: Modular Fluorescent Tools for Bioimaging Applications*
	09:50-10:10	**OC-66 Viglianisi C.** *Macromolecular and nano-supported antioxidants for practical applications*
	10:10-10:30	**OC-67 Nitti A.** *Photopolymerization of Selected Monomers Initiated by Arylazo Sulfones*
10.30-11.00 Coffee Break		

Sessione #19 (Sala Cavour)	Chairperson: **L. Pellacani**	
	11:00-11:20	**OC-68 Lanzalunga O.** *N-hydroxyphthalimide: an Efficient Hydrogen Atom Transfer (HAT) Mediator in Hydrocarbon Oxidations Promoted by Nonheme iron(IV)-oxo complexes*
	11:20-11:40	**OC-69 Navazio F**. *Efficient Lewis Acid Multicomponent-Promoting System in the Carbon-Nitrogen Bond Formation*
	11:40-12:00	**OC-70 Cauteruccio S.** *Non photochemical route to functionalized thiophene-based [7]helicenes*
	12:00-12:20	**OC-71 Caprioglio D.** *Iodine-mediated deconstructive annulation of isoprenylchromenes to benzo[c]chromenes. Development of a one-step synthesis of cannabinol (CBN)*
	12:20-12:40	**OC-72 Menichetti A.** *Nitroso Diels-Alder chemistry on 1,2-dihydropyridines as a platform to obtain novel anti-diabetic agents*
	12:40-13:00	**OC-73 Citarella A.** *Direct and Chemoselective Transfer of the Difluoromethyl (CHF_2) Unit Into Carbon-Electrophiles under Nucleophilic Regime*
Sessione #20 (Sala Giolitti)	Chairperson: **F. Cardona**	
	11:00-11:20	**OC-74 Molinaro A.** *A new biopolymer skeleton formed by a dimer of carbohydrate and aminoacid produced by Rhizobium radiobacter and useful for plant immunity evasion*
	11:20-11:40	**OC-75 Chini M. G.** *Application of quantum chemical integrated multistep protocol in the stereochemical determination of natural products*
	11:40-12:00	**OC-76 Martinelli J.** *Mn^{II}-complexation / $Al^{18}F$-labeling of new AMP-based chelators for applications in Magnetic Resonance Imaging and Positron Emission Tomography*
	12:00-12:20	**OC-77 Gentile D.** *Ligand Based Identification of FABP4 Inhibitors: Synthesis and Biological Screening*
	12:20-12:40	**OC-78 Masi M.** *Fungal phytotoxins with potential herbicidal activity for Cenchrus ciliaris biocontrol*
	12:40-13:00	**OC-79 Petricci E.** *Synthetic approaches to the development of new Antibody-Drug Conjugates charged with unconventional payloads*
Sessione #21 (Sala Einaudi)	Chairperson: **V. Capriati**	
	11:00-11:20	**OC-80 Rossi S.** *Technology-driven catalysis: (SLA) 3D-printed devices for organic synthesis*
	11:20-11:40	**OC-81 Pinna A.** *Synthesis of new chiral catalysts through multicomponent processes*
	11:40-12:00	**OC-82 Castagnolo D.** *Chemo-Enzymatic Cascades for the Synthesis of Heteroaromatic and Sulphur Containing Pharmaceutical Ingredients*
	12:00-12:20	**OC-83 Ziccarelli I.** *Synthesis of 1,3-oxazinan-2-ones by catalytic incorporation of carbon dioxide into N-alkyl-3-yn-1-amines*
	12:20-12:40	**OC-84 Filippini G.** *Highly Performing Iodoperfluoroalkylation of Alkenes Triggered by the Photochemical Activity of Perylene Diimides*
	12:40-13:00	**OC-85 Zappimbulso N.** *C–H Bond arylations of 1,2,3-triazoles by reusable Pd/C catalyst in solvent-free condition*

Mercoledì 11 Settembre - Pomeriggio (Presso Sala Cavour, Centro Congressi Torino Incontra, via Nino Costa 8, Torino)		
	15.00-15.10	**Foto di Gruppo**
Sessione #22 (Sala Cavour)	Chairperson: **A. Evidente**	
	15:15-15:35	**OC-86 Foschi F**. *Memory of Chirality Approach to the Synthesis of α-Quaternary Amino Acid Derivatives*
	15:35-15:55	**OC-87 Massolo E.** *Tetrachlorosilane mediated direct amidation method*
	15:55-16:15	**OC-88 Colella M.** *Straightforward Tactics and Enabling Technologies as useful tools for Fluoroalkylations*
	16.15-16.35	**OC-89 Lenci E.** *Diversity-Oriented Synthesis and chemoinformatic analysis of sp^3-rich molecular scaffolds using imine-based multicomponent reactions*
Sessione #23 (Sala Giolitti)	Chairperson: **L. Cipolla**	
	15:15-15:35	**OC-90 Marzano M.** *A new symmetric G-rich Oligonucleotides incorporating a 3'-3' inversion of polarity site as an interesting model for ligand binding studies.*
	15:35-15:55	**OC-91 Falanga A. P.** *Synthesis and characterization of a PNA probe targeting the Bcl-2 gene promoter: a promising tool in anticancer treatment*
	15:55-16:15	**OC-92 Leone L.** *Combined effect of amide protons and second sphere water molecules on the relaxivity of Gd(III)-DO3A-hydroxypropionamide complexes*
	16.15-16.35	**OC-93 Fioretto L.** *From microalgae to vaccine adjuvant: immunomodulant activity of sulfavants and its correlation with colloidal self-assembly*
Sessione #24 (Sala Einaudi)	Chairperson: **M. Salamone**	
	15:15-15:35	**OC-94 Dughera S.** *Gold Catalysed Coupling Reactions of Arenediazonium o-Benzenedisulfonimides*
	15:35-15:55	**OC-95 Veltri L.** *A Palladium Iodide – Catalyzed Oxidative Carbonylation Process for the Synthesis of Functionalized Imidazopyridines*
	15:55-16:15	**OC-96 Gualandi A.** *Allylation of Aldehydes by Dual Photoredox and Nickel Catalysis*
	16.15-16.35	**OC-97 Galloni P.** *Sustainable Catalytic Bromination of porphyrins*
16.40-17.00 Coffee Break		

Sessione Plenaria #7 (Sala Cavour)	Chairperson: **F. Novara**	
	17.00-17.20	Premiazione poster e Flash 1° premio
Sessione #25 (Sala Cavour)	Chairperson: **R. Noto**	
	17.20-17.40	**OC-98 Ceccarelli J.** *Pyridyl and quinolyl methanols: applications in metal-free reductions of aromatic nitro compounds*
	17.40-18.00	**OC-99 Benzi A**. *A convenient access to imidazo[1,2-a]pyridines and fluorescent polycycles from nitrodienic building-blocks*
	18.00-18.20	**OC-100 Maiuolo L.** *Base Mediated 1,3-Dipolar Cycloaddition of Azides with Substituted Enaminones for Regioselective Synthesis of Trisubstituted 1,2,3-Triazoles*
	18.20-18.40	**OC-101 Giofrè S.** *Divergent reactivity of N-allyl-2-aminophenols in domino reactions exploiting hypervalent iodine(III) reagents*
	18.40-19.00	**OC-102 Romeo R.** *Synthesis of 1,2,3-Triazole/MWCNT Conjugates for Environmental Application*
(Sala Giolitti)	17.20-19.00	Riunione Gruppo Interdivisionale Biotecnologie
Sessione #26 (Sala Einaudi)	Chairperson: **S. Menichetti**	
	17.20-17.40	**OC-103 Cerveri A.** *Phosphine-catalyzed stereoselective dearomatization of 3-NO_2-indoles with allenoates*
	17.40-18.0	**OC-104 Pomelli C. S.** *Dicationic Ionic Liquids: Synthesis, Characterization and catalytic Properties*
	18.00-18.20	**OC-105 Dessì A.** *Photocatalytic hydrogen production by means of Pt/brookite TiO2 sensitized with dithienosilole-based organic dyes*
	18.20-18.40	**OC-106 Matassini C.** *Copper-free methodologies for the multimerization of bioactive iminosugars*
	18.40-19.00	**OC-107 Moran Plata M. J.** *Non-conventional technologies for copper heterogeneous catalysts production and its applications in organic synthesis*
20.30 - Cena Sociale: Sala dei Re – Museo Egizio		

Giovedì 12 Settembre (Presso Aula Magna, Cavallerizza, Università di Torino, via Verdi 9, Torino)		
Sessione Plenaria #8	Chairperson: **A. Abbotto**	
	9.00-9.30	**M-04** Medaglia G. Ciamician **Dell'Amico L.** *The Ciamician Up-To-Date Lesson to a Ciamician Medalist. Organo-, Stereoselective-, and Photocatalysis in Sustainable Organic Synthesis.*
	Chairperson: **L. Triggiani – M. Da Pian**	
	9:30-10.00	**Elsevier Lecture** **Rodriguez del Rio C.** *Finding novel lead compounds in pesticide discovery inspired by pharmaceutical research*
	10.00-10:15	**Premio Reaxys**
	Chairperson: **D. Misiti**	
	10:15-10:45	**KN-04 Cevasco G.** *I primi 150 anni della Tavola Periodica degli Elementi Chimici: tra Chimica, Storia e Letteratura*
10.45-11.15 Coffee Break		
Sessione Plenaria #8	Chairperson: **S. Tortorella, - E . Lenci**	
	11.15-11.20	**Apertura evento**
	11:20-11:40	**Redazione FRidA** *Tu la conosci FRidA? Una piattaforma web, un laboratorio di comunicazione, tutta la ricerca di UniTO*
	11.40-12.10	**Garlaschelli L.** *Chimica e Mysteri*
	12.10-12.40	**Malvaldi M.** *L'acqua di Babele, ovvero come non fare un esperimento*
	12.40-12.45	**Chiusura evento**
	12.45-13.00	Conclusione Lavori

Lunedì 9 Settembre 2019: Prima sessione Poster – h 13.00-15.00.

Autore Presentatore	Titolo	Codice
T. Tedeschi	Study of Milk Proteins' Digestibility: Characterization of the Peptide Fraction Released and Potential Impact on Allergenicity	**PC-01**
C. Coppola	Design of novel organic hole transport materials for perovskite solar cells	**PC-02**
S. Tallarico	Alternative Chemocatalytic Methods for Selective Conversion of Cellulose into Lactic Acid	**PC-03**
S. Nejrotti	Natural deep eutectic solvents as an efficient and versatile catalytic system for the Nazarov cyclization	**PC-04**
A. Rinaldi	Synthesis of Indenes by Tandem Gold(I)-Catalyzed Propargyl Claisen Rearrangement/Hydroarylation Reaction	**PC-05**
R. Mancuso	PdI2-Catalyzed Carbonylative Approach to Benzothiophene Derivatives from (2-Alkynyl)(methylthio)benzenes	**PC-06**
C. Rizzo	Hybrid ionogels as potential antioxidant agents	**PC-07**
F. Billeci	Gluconic acid for eco-friendly Ionic Liquids: chemical and biological investigations.	**PC-08**
S. Marullo	Conversion of carbohydrates into 5-HMF in Deep Eutectic Solvents under mild reaction conditions	**PC-09**
M. Massaro	Zinc oxide nanoparticles supported on halloysite nanotubes for environmental remediation	**PC-10**
E. Azzi	Visible-Light-Driven Synthesis of Tetrahydropyridazines from γ-δ Unsaturated N-Tosylhydrazones	**PC-11**
E. Mezzina	Synthesis and EPR investigation of a new stable diradical macrocycle	**PC-12**
T. Laurita	Regio- and diastereoselective organo-zinc promoted arylation of trans 2,3-diaryloxiranes by arylboronic acids: stereoselective access to trans 2,3-diphenyl-2,3-dihydrobenzofuran.	**PC-13**
P. La Manna	Green and Mild Friedel-Crafts Benzylation of Arenes and Heteroarenes Under On Water Conditions	**PC-14**
R. D'Orsi	From HIV protease inhibitors to anticancer agents: diversity-oriented synthesis of new compounds with double biological activity	**PC-15**
A. Campofelice	New Molecules as Translational Readthrough Promoters of Nonsense Mutations: Rescuing the CFTR Protein	**PC-16**
F. Buonsenso	A novel procedure for rapid and accurated quantification of amino functionalities bonded to solid porous matrices	**PC-17**
C. Capacchione	Synthesis of new Water Reducer Plasticizers for concrete, gypsum and clay	**PC-18**
L. Menduti	Boron-functionalized benzodithiophenes	**PC-19**
M. Novello	New Synthesis of 4-Iodothienopyranone Derivatives by Iodocyclization Reaction	**PC-20**
M. Cirillo	Development of new beta-lactam-based integrin ligands: Synthesis and Applications	**PC-21**
A. Massi	Enantioselective Desymmetrization of 1,4-Dihydropyridines by Oxidative NHC-Catalysis	**PC-22**
C. Bellomo	Functionalization of the BODIPY core with styryl carboranes: synthesis, characterization and photophysical properties.	**PC-23**
M. Blangetti	Chemoselective Addition of Highly Polar Organolithium Reagents to Carboxamides in Deep Eutectic Solvents (DESs)Under Air: Novel Opportunities for the Synthesis of Ketones in Unconventional Solvents	**PC-24**
P. Russo	A New Synthesis Of 2-(imidazo[1,2-a]pyridin-3-yl)acetamides By Palladium-Catalyzed Oxidative Aminocarbonylation Of (N-Prop-2-yn-1-yl)pyridin-2-amines	**PC-25**

S. Ghinato	An Unusually Divergent Reactivity of Basic Organolithium Compounds in Protic Unconventional Media: Novel Opportunites for the Synthetic Elaboration of Aryl Carboxyamides in Deep Eutectic Solvents	**PC-26**
S. De Vita	CI.O.E.: An automated workflow to simplify the early steps of Structure-Based Inverse Virtual Screening	**PC-27**
A. Gelain	Unravelling the interactions between an antiproliferative 1,2,5-oxadiazole derivative and STAT3	**PC-28**
F. Franco	One-pot synthesis of a-trifluoromethylthiolated carboxylic acid derivatives	**PC-29**
F. Migliorini	Synthesis and development of linker for bioconjugation of Smo inhibitors	**PC-30**
D. Gentili	Synthesis of substituted 1,2-dihydropyridines by cerium(III) catalyzed amine-aldehyde polycondensation	**PC-31**
C. Del Plato	Resorc[4]arene-based site directed immobilization of antibodies for immunosensors development	**PC-32**
L. Forti	The marine worm *Hermodice carunculata* is a promising biocatalyst for aldol reactions	**PC-33**
L. Zongo	Chemical Derivatisation of Tannins for Functional Materials	**PC-34**
L. Zongo	Stability Profiles of Lignin Microcapsules	**PC-35**
G. Pastore	Bio-based renewable polymeric materials from research to industrial point of view	**PC-36**
G. Lupidi	Novel Synthetic Analogues of Climacostol as Potent Anticancer Nature-Inspired Small Molecules	**PC-37**
G. Marsico	Synthesis of the fungal metabolites radicinin and its natural precursor deoxyradicinin: potential bioherbicides for invasive species control	**PC-38**
G. Marsico	Enantioselective Carbolithiation-Trapping Reaction of 1-Aryl-1-Alkenyl Carbamates	**PC-39**
P. Musci	Intriguing role of iodine on the stability and reactivity of dihalomethyllithium carbenoids	**PC-40**
M. Barbero	Diastereoselective synthesis of axially chiral styrenes	**PC-41**
G. Biagiotti	GLYCOG Lab 4.0, the sweet nanofiller: a tangible case of transfer of technology (TOT)	**PC-42**
L. Leone	Accelerating water exchange in GdIII-DO3A-acetophenone derivatives by favouring the dissociative mechanism through hydrogen bonding	**PC-43**
J. Martinelli	MnEDTA-based multimeric contrast agents based on G0 and G2 PAMAM dendrimers	**PC-44**
E. Colarusso	Targeting mPGES-1 by a combinatorial approach: identification of 2-aminobenzothiazoles as scaffold for new PGE2 modulator in human cancer cells	**PC-45**
S. Baldino	Unprecedented use of a deep eutectic solvent as hydrogen source for Ru(II)-catalyzed transfer hydrogenation of carbonyl compounds under mild conditions	**PC-46**
A. D'Amato	Quinoline cyclic tripeptoids as novel DNA bis-intercalating agents	**PC-47**

Martedì 10 Settembre 2019: Seconda Sessione Poster - h 13.00-15.00.

Autore Presentatore	Titolo	Codice
S. Terracciano	Modulation of biological target selectivity through an appropriate scaffold decoration	**PC-48**
M. Potenza	A multistep computational protocol towards the identification of 2-amino-1,3,4-thiadiazole-based molecules as novel mPGES-1 inhibitors	**PC-49**
F. Cardona	Synthesis of bifunctional inhibitors to address type 2 diabetes by dual enzyme targeting	**PC-50**
P. Quagliotto	Micellar Assisted Synthesis of Chalcones as Intermediates for Bipyridines	**PC-51**
M.M.H. Desoky	Synthesis and characterization of polymers as HTMs for perovskite solar cells	**PC-52**
M.M.H. Desoky	Synthesis of a donor-acceptor polymer for perovskite solar cells	**PC-53**
M. Gastaldi	Azodyes based polymers for 3D printing	**PC-54**
G. Viscardi	Squaraine dyes: interaction with bovine serum albumin to investigate supramolecular adducts with aggregation-induced emission (AIE) properties	**PC-55**
V. Patamia	Sigma-1 Receptors: Computational Model to Predict the Agonist/Antagonist Effect	**PC-56**
C. Carlucci	Flow technology for the preparation of Active Pharmaceutical Ingredients	**PC-57**
G. Siani	Zwitterionic Natural Deep Eutectic Solvents as green alternative for the CO_2 capture	**PC-58**
R. Di Lecce	Bioactive metabolites produced by the fungal pathogens Diplodia fraxini and Hymenoscyphus fraxineus isolated from infected Fraxinus spp. trees	**PC-59**
M. Masi	Natural products as stimulants and inhibitors of parasitic seed germination and radical growth	**PC-60**
A. Zarrelli	New degradation products of Irbesartan: Analysis and identification from a simulated chlorinated disinfection treatment	**PC-61**
D. Tanini	Sulfur, Selenium, and some silicon: A new access to disulfides and mixed chalcogenides with GPx-like activity	**PC-62**
G. Di Fabio	New Phosphate-Linked Tyrosol Dimers: Synthesis, antioxidant activity, metal chelating capacity and effect on Aβ aggregation1	**PC-63**
G. Di Fabio	A general synthetic strategy and preliminary investigations of pro-drug Silibinin conjugates	**PC-64**
D. Franchi	Structural modification of pyridine-containing ligands: customize optical and electrochemical properties of Cu complexes	**PC-65**
E. Licandro	Luminescent rhenium(I)-peptide nucleic acids conjugates for microRNA targeting	**PC-66**
V. Pelliccioli	Synthesis and characterization of chiral bis-benzo[1,2-b:4,3-b']dithiophenes	**PC-67**
M. Vagnoni	Lipase catalyzed oxidation in sugar-derived Natural Deep Eutectic Solvents	**PC-68**
S. Menichetti	Synthesis of heterohelicenes through the Povarov reaction	**PC-69**
G. Forti	Sustainable and Water-Soluble Non-Fullerene Acceptors for Bulk Heterojunction Solar Cells	**PC-70**
F. Formaggio	Influence of flat and helical peptide spacers on the redox properties of two covalently bound, ferrocenyl moieties	**PC-71**
O. Yildirim	Squaraine-Based Porous Organic Polymers Containing Trigonal Linkers	**PC-72**
V. Marsicano	Coinage-metal catalyzed functionalizations of propargylic amine derivatives	**PC-73**

O. Celaj	Spectroscopic elucidation and antimicrobial screening of myrtogalloyl glicosides from Myrtus communis	**PC-74**
K. Fidecka	Collagen capped halloysite nanotubes as multifunctional drug carriers	**PC-75**
A. Pagano	Visible-Light Promoted Dearomatizing Spirocyclizations of Ynone-Tethered Indoles	**PC-76**
F. Trapani	Plasticizers from Natural Resources	**PC-77**
F. Pollastro	Synthesis of Pre-cannabinoid Terpenyl esters, an Unexplored Class of Native Phytocannabinoids	**PC-78**
D. Mattoteia	Molecular Editing of Cannabichromene (CBC)	**PC-79**
V. Algieri	Synthesis of Nucleobase-Containing 1,2,3-Triazoles with Potential Biological Activity through Metal Catalyzed Azide-Alkyne 1,3-Dipolar Cycloaddition	**PC-80**
A. Fontana	Preparation and characterization of graphene oxide foils for applications in the biomedical field	**PC-81**
A. Menichetti	Developing new ways to introduce the boron atom in organic molecules by ring-opening reactions	**PC-82**
R. Stefania	Synthesis of fluorinated curcumin-based molecules for detecting amyloid plaques by ^{19}F-MRI	**PC-83**
M. S. Christodoulou	Ruthenium-catalyzed ring transformation of 4,4-disubstituted isoxazolin-5-ones to different heterocyclic systems	**PC-84**
S. V. Giofrè	N,N-bis-Triazol-Sulphenamides: A New Family of Halogen Free Flame Retardants	**PC-85**
M. C. Ligi	Decoration of carbon nanotubes for the combined therapy of cancer	**PC-86**
V. Raglione	Synthesis of new amphiphilic Zn-Salophen complexes derivatized by bile acids	**PC-87**
J. Mateos	Naphtochromenones as Cross-Border Light Photoredox Catalysts	**PC-88**
A. Vega Peñaloza	Microfluidic Dearomatisation of Indoles by a Light-Driven [2+2] Paternò-Büchi Process	**PC-89**
G. Bertuzzi	Higher order cycloadditions: from a stereoselecrive rediscovery to a computational fascination	**PC-90**
M. De Angelis	Stereocontrolled synthesis of pyrrolidine iminosugars' lipophilic derivatives	**PC-91**
L. Primitivo	Synthesis of new 1,2-diaminic ligand for the asymmetric Henry reaction	**PC-92**
A. Vasco Corti	Catalytic Asymmetric Oxidative γ-Coupling of α,β-unsaturated Aldehydes with Air as the Terminal Oxidant	**PC-93**
P. Capurro	Synthesis of α-Amido Silyl Enol Ethers via Silylative Ketene 3-Component Reactions: Synthetic Applications in Organic and Natural Products Synthesis	**PC-94**

Lectures Medaglie

M-01

Calixarenes: from Chemical Curiosity and Basic Research to Industrial Implementation

A. Casnati

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Although the story of the cyclic oligomers obtained by basic condensation of p-alkylphenols and formaldehyde traces back in the early 1940s, it was at the end of the 1970s that the potentiality of these macrocycles in supramolecular chemistry was apparent thanks to the work of C. D. Gutsche, who developed their selective syntheses, and of R. Ungaro and A. Pochini at Parma University that definitely demonstrated their cyclic structure by X-ray crystallography.[1] Since then, their synthesis and functionalization were deeply studied worldwide and calixarenes became extremely popular platforms giving rise to a burst in basic research publications for these macrocycles.[2] Starting from the early 1990s, we have proposed a series of calixarene-based receptors for spherical metal ions, especially caesium and potassium, anions and ion-pairs which, in some cases, still remain among the most selective ligands for these ions known so far. More recently,[3] we moved our interests towards the targeting of biologically relevant species thus obtaining derivatives possessing antimicrobial activity, able to inhibiting the adhesion of lectins on cell surface or to selectively bind specific amino acid residues on proteins. Multivalency, moreover, was properly exploited to implement a series of calixarene-based delivery systems able to bind and transfect nucleic acids (NAs) into cells with efficiency even better than that observed for commercially available formulations. Calixarenes also exhibited to be proper scaffolds for the design of multifunctional catalysts for the cleavage of carboxylic or phosphoric esters. Mechanistic studies disclosed a high level of cooperation between catalytic units especially in the enhancement of the rates of cleavage of NA models, di- or oligonucleotides.

Altogether, these studies highlight that calixarenes are special scaffolds for the development of highly efficient receptors, functional materials, catalysts and ligands for bio(macro)molecules, exploiting different tools typical of supramolecular chemistry such as preorganization and cooperativity of ligating/catalytic sites, multivalent effects and self-assembly. Their lipophilic backbone can be, moreover, exploited to give rise to peculiar amphiphilic structures extremely useful for applications in (bio)nanotechnology, separation science and formulation chemistry. Two special industrial implementations of studied calixarenes will be also discussed in radioactive waste treatment[3] and lubricant additive formulation.[4]

References:

[1] G. D. Andreetti, R. Ungaro, A. Pochini, *J. Chem. Soc., Chem. Commun*. **1979**, 1005-1007.
[2] A. Casnati, *Chem. Commun.* **2013**, *49*, 6827-6830.
[3] M. Giuliani, I. Morbioli, F. Sansone, A. Casnati, *Chem. Commun.* **2015**, *51*, 14140-14159.
[4] M. Notari, A. Roselli, A. Casnati, F. Sansone, A. Burlini, PCT Int. Appl. (2017), WO 2017025900 A1 20170216.

M-02

The *Melanin Code*: Deciphering Nature's Paradigms for Chemical Functionality

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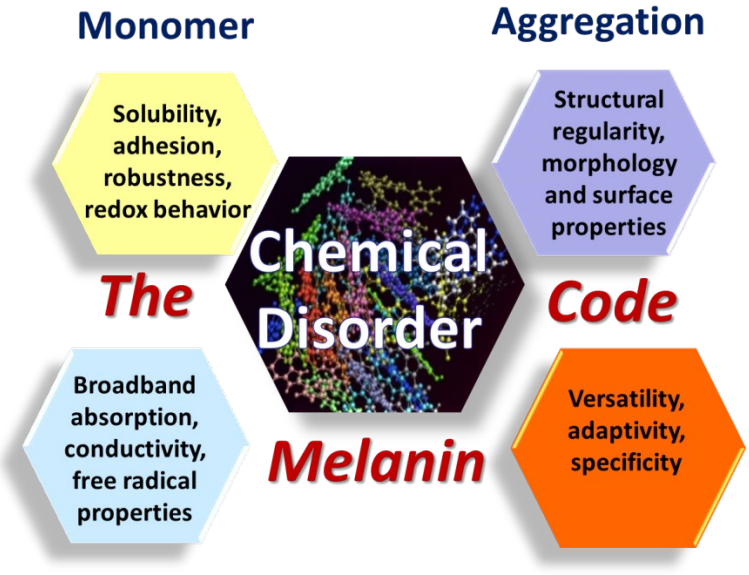
Melanins are a class of black-to-reddish brown functional pigments derived biogenetically from the oxidative polymerization of tyrosine and other phenolic precursors. Found widespread in nature, from man and mammals to birds, cephalopods, plants and microorganisms, melanins provide a paradigm system for translating biological concepts into innovative biomedical and technological solutions. This is due to the highly disordered and heterogenous nature of these polymeric pigments, which share unique physicochemical properties, including high insolubility, a semiconductor behavior, efficient light-dissipation capacity, a permanent free radical character and an amorphous supramolecular architecture. Although melanins are believed to play a broad range of biological roles, from photoprotection to antioxidant defense, metal and toxin binding and radioprotection, the evolving scenario of theories and observations still suffers from the lack of a complete frame of structure-property-function relationships that could be translated into innovative applications in biomedicine and materials science.

Aim of this presentation is to critically discuss Nature's counterintuitive logic of selecting a single class of insoluble and structurally disordered polymers (the melanins) to implement multipurpose multifunctional systems for diverse biological roles. Following a brief survey of recent advances, a possible rationale is proposed, which is referred to as "***The Melanin Code***". **Chemical disorder**, which is both **monomer-** and **aggregation**-dependent, is the key to unveil this "Code". It provides an ingenious means of generating and combining unique opto-electronic and paramagnetic properties, via intrinsically and extrinsically controlled π-electron delocalization, with versatility, adaptivity and site-specificity to ensure dynamic responses in different biological contexts.



M-03

Development of catalytic stereoselective methodologies: sense and sensibility

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Organic synthesis has traditionally been performed in batch that means in round-bottomed flasks, test tubes or closed vessels; however, continuous flow processes have gained lately much attention from synthetic organic chemists. Application of these systems for the preparation of fine chemicals, such as natural products or active pharmaceutical ingredients (APIs) is becoming very popular. Although pharma industry still relies on multipurpose batch or semi-batch reactors, it is evident that interest is arising towards continuous flow manufacturing of APIs.[1]

Aim of the presentation will be to highlight some of the stereoselective catalytic methodologies developed by our group, with a special focus on the very recent advances concerning the continuous flow multistep synthesis of chiral organic molecules.

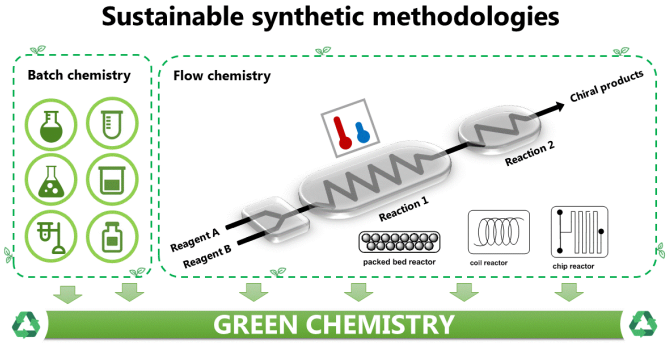

Figure 1: technology-driven organic synthesis

Organocatalytic stereoselective transformations using catalytic reactors will be presented; both packed-bed and monolithic reactors, either made by silica and/or organic polymers, have been successfully used in reactions promoted by immobilized enantiopure amines. Furthermore, the use of different chiral metal-free catalysts in micro- and mesofluidic devices, to perform technology-assisted stereoselective transformations will be also discussed, including reactions of nitroacrylates and metal-free catalytic synthesis of biologically active chiral amines.[2]

Catalytic reactions in (micro)-mesoreactors will be compared with stereoselective catalytic in-flow reactions in 3D-printed reactors.[3] The fabrication of *ad hoc* designed reactors and other devices, to perform different organic reactions, may give new impulse to the use of enabling technologies in the synthesis of complex (chiral) molecules.

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M-04

The Ciamician Up-To-Date Lesson to a Ciamician Medalist. Organo-, Stereoselective-, and Photocatalysis in Sustainable Organic Synthesis.

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Sustainability has nowadays become not only a priority but a way-of-life we all must adopt. Since the past centuries, the utilisation of renewables for the generation of new substances or for energy production has been recognised as one of the main needs of our society. This was limpidly highlighted by Giacomo Ciamician back in 1912.[1] He recognised the renewables, such as light and CO_2, as indispensable ingredients towards a modern chemical synthesis.

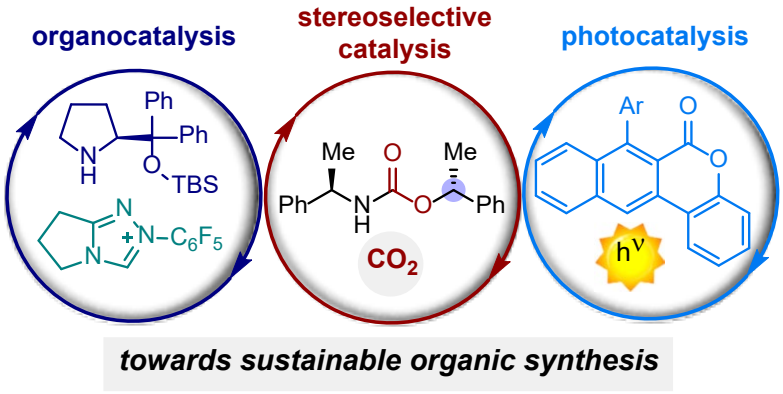

Figure 1: development and application of diverse types of catalysis towards sustainable organic synthesis.

About a hundred year later, also the research I performed has always – sometimes unconsciously – been guided by the principles of sustainable synthesis (Figure 1). Starting from the use of small organic molecules as organocatalysts,[2] to the catalytic stereoselective construction of complex molecular architectures using CO_2,[3] through the use of light as key reagent[4] to the progress of innovative reaction pathways.[5]

The lecture will focus on the key features of the different types of catalysis (organo-, stereo-, and photocatalysis), highlighting my personal contributions to the fields. Finally, perspectives towards the sustainability aspects will be discussed.

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Lectures Premi Senior

PR-S1

Isonitrili al Pesto (*Isocyanides in Pesto Sauce)*

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Searching for a common thread able to connect the research topics investigated in recent years in Genova, isocyanides[1] are indeed a constant presence (and fragrance!). We have employed them not only as building blocks in classic multicomponent reactions, such as the Passerini and Ugi ones, but also:

- as building blocks in the development of novel multicomponent reactions[2,3]
- as activators of arylacetic acids to generate ketenes, further elaborated to captodative olefins[4]
- as dipolarophiles in cycloaddition reactions to assemble complex tetrazole compounds[5]
- as nitrogen source in the synthesis of combinatorial libraries of polycyclic (spiro)compounds[6]
- as fluorescent probes during *in cellulo* activation of prodrugs

This communication will be a journey through the multiple applications of this extremely versatile class of compounds, with main focus on the most recent results and on the combination of isocyanide chemistry with photoinduced and photocatalyzed processes.

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PR-S2

[4+2] Cycloadditions: Vintage Reactions for New Glycan-based Epitopes

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Inverse electron-demand [4+2] cycloadditions involving glycals as electron rich dienophiles and alpha,alpha'-dioxothiones as electron poor dienes, are powerful reactions to afford glycosides chemo-, regio- and stereoselectively.[1] Relying on these versatile reactions, diastereomerically pure O-glycosides have been prepared and employed as starting material to obtain oligosaccharides, glycopeptides and glycoproteins. Among recent applications, the synthesis of a fucose mimetic (**1**) and of two saccharidic antigen mimetics (the mimetic of the melanoma antigen GM3 lactone, **2** and the mimetic of the mucin antigen Tn, **3**) have been developed (Figure 1).[2,3]

Thanks to their structure versatility, these three mimetics have been used to decorate multivalent constructs, including nanoparticles,[4,5] nano fibers,[6] a cyclopeptidic (RAFT) scaffold[7] as well as proteins. In particular, the synthesis, the multivalent presentation and biological assays run with a structurally constrained Tn antigen mimetic will be presented.

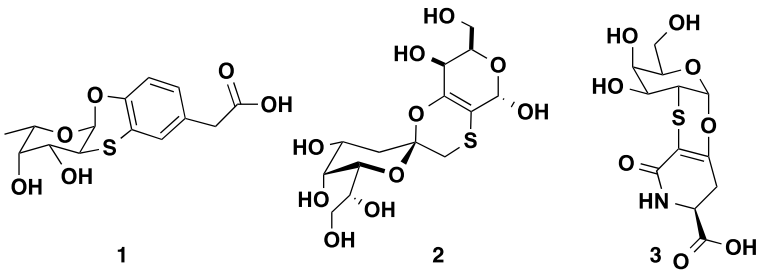

Figure 1: Structure of the fucose mimetic, **1**, of the GM3 lactone saccharide mimetic, **2** and of the MUC1 TnThr antigen mimetic **3**.

References:

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PR-S3

V-catalysis in Oxidation Reactions: from Mimesis of HalPO Enzymes to Sustainable Synthesis

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In the course of the years, elucidation of the mechanistic details of vanadium based oxidative catalytic systems has been the focus of the research in my group, performing *inter alia* kinetic, NMR, electrochemical and spectroscopic experiments, as well as theoretical calculations.[1] These studies allowed to establish correlation between the nature of the ligands bound to vanadium centre and catalytic activity in benchmark oxidations.

Meanwhile,[2] in our labs we developed a mild and efficient system for metal (V and Mo) catalyzed oxybromination of alkenes inspired by the activity of haloperoxidases enzymes. In particular we used a two-phase system where a brominating intermediate is formed in water from the metal catalyst, H_2O_2 and bromide ion. The peroxometal complex then oxidize the substrate dissolved in the organic phase. Yields and selectivities obtained, together with replacement of Br_2 with Br^-, provide a procedure of significant synthetic interest. Indeed, excellent results were obtained with different substrates: aromatics, alkenes and alkynes. To render our system even more interesting from the sustainable point of view, we have improved it by substituting molecular chlorinated solvents with ILs, testing both hydrophilic and lipophilic ones. Also with such modification, first-class results in terms of reaction rates and selectivities have been obtained with alkenes and alkynes.[1,2] More recently, we applied our procedure to the bromination of toluene and similar molecules;[3,4] the reaction proceeds under very mild conditions, and nicely the substrates can be used as solvent, thus further improving the sustainability of the process.

Possible industrial applications of such procedure in the functionalization of natural products[5] will be presented.

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PR-S4

Challenges and creativity in API process development: facing unexpected impurities formation.

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Control of impurities is one of the major aspects in API development. A deep chemical knowledge of impurities formation mechanism is always very useful for setting a good control strategy for each and every possible impurity. Case studies are discussed for unexpected impurities formation: the origin of the impurities and the theoretical formation mechanisms are explored and analyzed in order to set the appropriate control strategy during process development.

Lectures Premi Junior

PR-J1

Reactivity and synthetic applications of new chalcogen-containing small molecules

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Organochalcogen compounds are valuable intermediates in organic synthesis and have additional applications in biology, medicinal chemistry, materials science, and catalysis. Sulfur- and selenium-containing small molecules and enzymes have been demonstrated to play a key role in a wide range of biological functions and biochemical mechanisms.[1] Recently, the synthesis and the use of organotellurium compounds have also faced a strong development, due to their unique properties and reactivity. Furthermore, over the past years a high number of selenium- and tellurium-containing catalytic antioxidants have been proposed as synthetic mimics of glutathione peroxidase (GPx).[1] In this context, the development of novel methodologies to access chalcogen-containing organic small molecules is highly sought after.

Our long standing interest in the study of the reactivity of silyl chalcogenides led us to disclose silicon mediated routes for the synthesis of new variously functionalized S-, Se-, and Te-containing derivatives.[2] Such procedures have been applied to the synthesis of novel cyclic and open chain derivatives, useful in organic synthesis, biology, and medicinal chemistry. In this communication, the reactivity of novel chalcogen-containing reagents, as well as their application to the synthesis and the evaluation of the antioxidant activity of novel GPx-like catalysts will be discussed. The modulation of chalcogen-bonding interactions as an effective strategy to enhance the catalytic antioxidant properties of functionalized selenides and tellurides will also be described.[2,3]

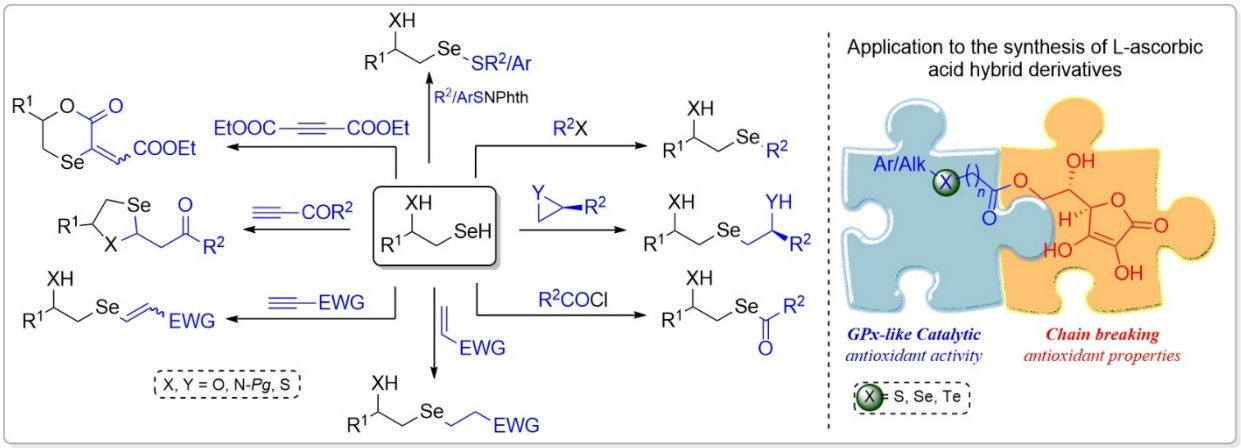

Figure 1: Examples of reactivity and synthetic applications of chalcogen-containing small molecules

References:

[1] V. K. Jain, K. I. Priyadarsini, Organoselenium Compounds in Biology and Medicine: Synthesis, Biological and Therapeutic Treatments, Royal Society of Chemistry, London, **2018**.

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PR-J2

Supramolecular dynamic systems away from equilibrium

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Weak interactions underlie recognition events at the nanoscale. In most cases, these interactions have been studied in static systems, mostly at equilibrium. However, supramolecular chemistry is transitioning to the study of dynamic systems, that exist and operate away from equilibrium while dissipating energy.[1] Such a new domain might open new opportunities for both material and biological science. Ultimately, Life is a nonequilibrium phenomenon.

We approached this innovative domain merging our previous experiences in molecular machines and self-assembly,[2] as well as exploiting the opportunities offered by DNA nanotechnology.[3] In particular, we have rationalized current experimental approaches to nonequilibrium self-assembly, disclosing general underlying principles for driven (endergonic) self-assembly.[4] It emerged that energy consumption is not a sufficient requirement for driving chemical reactions away from equilibrium. Cooperative catalysis instead is a useful prerequisite to obtain high-energy assemblies (figure 1, left). For this reason, the substrate-induced self-assembly of cooperative catalysts has been investigated, engineering the formation of catalytic vesicles in which a transesterification reaction occurs at the surface, owing to a Zn^{2+} mediated cooperative mechanism (figure 1, right).[5]

An overview of the work performed in this area will be presented.

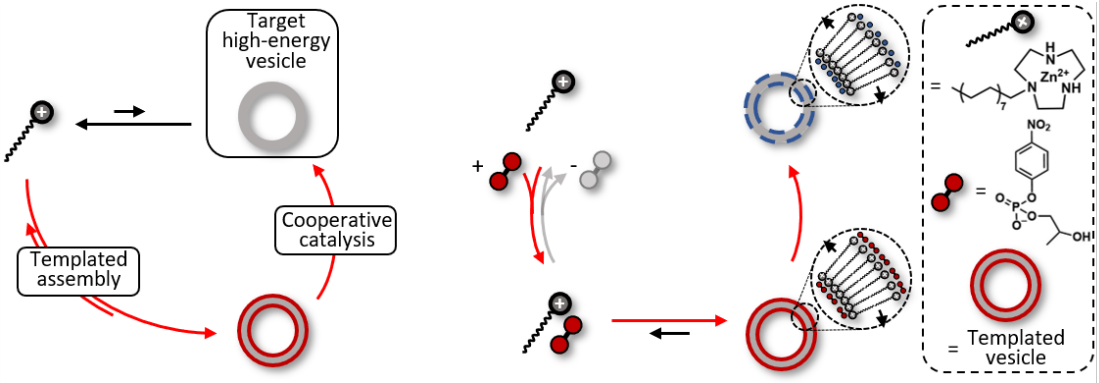

Figure 1: Reaction schemes for driven self-assembly; left: a minimal strategy to obtain a high-energy assembly; right: steps implemented in a studied artificial system.

References:

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PR-J3

Novel NK_1 receptor antagonists

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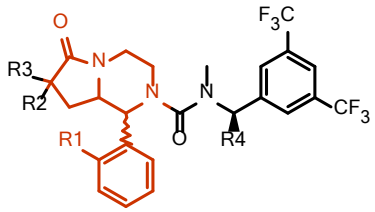
NK_1 receptor[1] (G- protein – coupled - receptor) research has been pursued aggressively over the last two decades by several pharmaceutical companies, in an effort to develop drugs that might be useful in a wide range of pathological affections: inflammatory conditions, migraine, emesis, schizophrenia, depression, anxiety, tinnitus, hearing loss, bronchoconstriction and regulation of gastrointestinal effects. Chemically diverse non-peptide NK_1 receptor antagonists have been identified since the discovery of CP-96,345 by Pfizer in 1991[2]. In 2003 a NK_1 receptor antagonist (Aprepitant)[3] was approved and launched onto the market for the prevention of chemotherapy – induced nausea and vomiting (CINV).

New NK_1 receptor antagonists, incorporating a bicyclic core, with potential activity in the treatment of inflammatory skin diseases, have been identified and synthetized.

The bicyclic core, containing the piperazine ring (Figure 1), has been obtained through a diastereoselective approach.



R_1= H, CH_3
R_2= H, chain, ring
R_3= H, chain, ring
R_4= H, CH_3, chain

Figure 1

The synthesis involved two crucial cyclization steps: a first step mediated by [bis (trifluoroacetoxy)iodo]benzene (PIFA) [5] and a second condensation step that gave as product only the ***ANTI-***derivative.

References:

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PR-J4

New-generation Self-Immolative Spacers Enable Fast Release of Anticancer Drugs

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The covalent conjugation of anticancer drugs to small ligands, capable of selective binding to tumor-overexpressed receptors, has been proposed as a suitable strategy to overcome important pharmacokinetic limitations of large monoclonal antibodies.[1] The so-called small molecule-drug conjugates are often designed to release the anticancer agent in the presence of tumor-associated enzymes, which cleave a specific chemical bond (i.e. the linker) between the drug and the ligand.[2] In particular, a spacer between the linker and the drug is fundamental to lower the steric hindrance around the substrate and to allow an efficient enzymatic action. These spacers, often referred to as "self-immolative units", are designed to undergo spontaneous degradation upon linker cleavage, thus releasing the free drug in its active form. To ensure therapeutic efficacy, the design of self-immolative spacers must take into account different aspects, such as synthetic accessibility, the anchoring point on the anticancer drug and plasma stability. Moreover, high drug release rates may be fundamental, as long half-lives of the inactive prodrug may lead to suboptimal therapeutic efficacy and toxicity to healthy tissues.

In this work, different diamine spacers where synthesized and conjugated to anticancer drugs at OH groups, through the formation of hydrolytically-stable carbamate bonds. The cyclization rates of the prodrugs' amine moieties onto the carbamate bonds were measured, resulting in the formation of a cyclic urea and the release of the free drug (Figure 1).

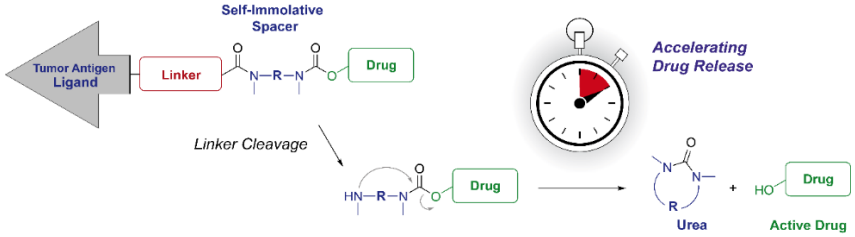

Figure 1: Mechanism of action of cyclization-based self-immolative spacers installed on a linker-drug module in a small molecule-drug conjugate. The rate-limiting step of the drug release process is highlighted, consisting in the intramolecular nucleophilic attack of the amine moiety to the carbonyl.

Structurally modified self-immolative units were found to influence significantly the drug release rates, being in some cases much more efficient than benchmark spacers. The evaluation of the impact of the accelerated drug release mechanism on the therapeutic effects is in progress. Besides holding promises on the development of new generation prodrugs, the structural basis for producing efficient self-immolative spacers may find important applications in analytical chemistry and material sciences.[3]

References:

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KEYNOTES

KN-01

Toward Deterministic Doping

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Atomic scale devices represent the cutting edge of Si technology[1]. Control over concentration and exact positioning of impurity atoms in semiconductor structures is the key to support device scaling down to atomic scale. On the other side, scaling down of microelectronic devices posed several challenges in terms of short-channel-effect control and leakage current issues determining the development of non-planar architectures as multigate FETs such as FinFETs (Fin shaped Field Effect Transistors), thus in turn requiring a conformal doping technology. Ion implantation, the standard industrial technique for doping, is highly effective in modulating the concentration of non-isoelectronic impurities in semiconductors but it is mono-directional in nature and consequently not suitable for advanced device architectures. In addition, it lacks adequate control over the dopant atom positioning, being even destructive to the crystal structure. Conversely, solid- and gas-phase source diffusion processes, still representing alternative doping technologies, do not allow precise control over the dopant dose and atom positioning.

A novel conceptual approach was recently introduced[2] by our group by developing functional polymers, featuring controlled molar mass and narrow molar mass distribution, terminated by a dopant containing moiety. This polymeric architecture allows the chemistry of grafting reaction to be kept constant whereas tuning of the number of polymeric molecules linked to the substrate is achieved simply by changing the molar mass of the polymer. Pushing the self-limited "grafting to" reaction to the corresponding pseudo-plateau thickness values of two times the gyration radius of the grafted macromolecule allows to obtain a very high degree of reproducibility in the dopant dose amount. The amount of dopant atoms deposed on the substrate was found to decrease from $8*10^{13}$ to $2*10^{12}$ atoms/cm^2 as the molar mass of the polymeric carrier increases from 2.3 kg/mol to 25 kg/mol. In addition, the nature of the end groups was found able to outperform the dopant dose control. Moreover, the proposed approach was demonstrated to significantly reduced carbon contamination with respect to conventional approaches, thus increasing the activation rate of the P atoms incorporated into the Si substrate. These results suggest the possibility to integrate this technology into the conventional process flow of semiconductor device fabrication.

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KN-02

Entry to peptide Wonderland through the rabbit hole

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Nature's preference for homochirality (*e.g.*, L-peptides, D-carbohydrates) has animated our investigations, as we question it with heterochiral D,L-peptides. We took inspiration from Alice, who steps through the mirror into Wonderland, whereby everyday life elements are combined in fantastic ways.[1] Similarly, we discovered new self-assembly scenarios by using L-amino acids in combination with their mirror-image D-enantiomers at selected positions in short, D,L-peptide sequences. The use of small peptide libraries with variations in amino acid sequence or stereoconfiguration is leading to the emergence of self-assembly rules to obtain nanostructures or nanostructured hydrogels.[2,3] We monitored the divergent path of homochiral and heterochiral tripeptides through self-assembly from the molecular, to the nano-, micro- and macroscopic scale. In this manner, we could link back the final material properties with fine structural variations of the building blocks.[3]

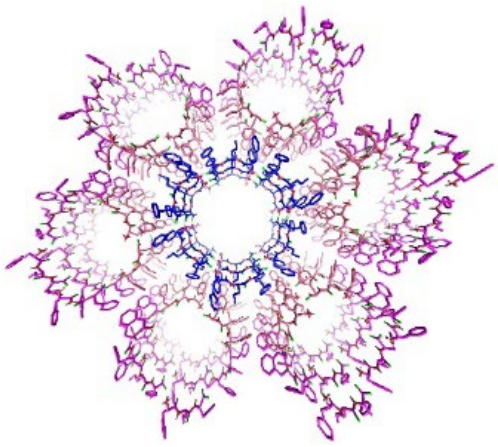

Fig. 1: XRD structure of D,L-tripeptide reveals 2 nm-wide water channels.[3]

As Alice enters Wonderland through the rabbit hole,[4] we can follow the self-assembly into supramolecular water channels of D,L-tripeptides (**Fig. 1**) that form nanostructured hydrogels, while their L-stereoisomers do not. Present studies are focussing on a more diverse library with various functional groups. Applications go from biomaterials[3,5] to supramolecular catalysis[6] and embedding of other components, such as carbon nanostructures[7] or metal-organic cages for selective chemical separation.[8] An attractive feature of these systems is the ability to have a function that can be switched on/off with assembly/disassembly, as well as biodegradability.

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KN-03

Designing New Synthetic Concepts for Imparting Molecular Complexity with C-1 Sources

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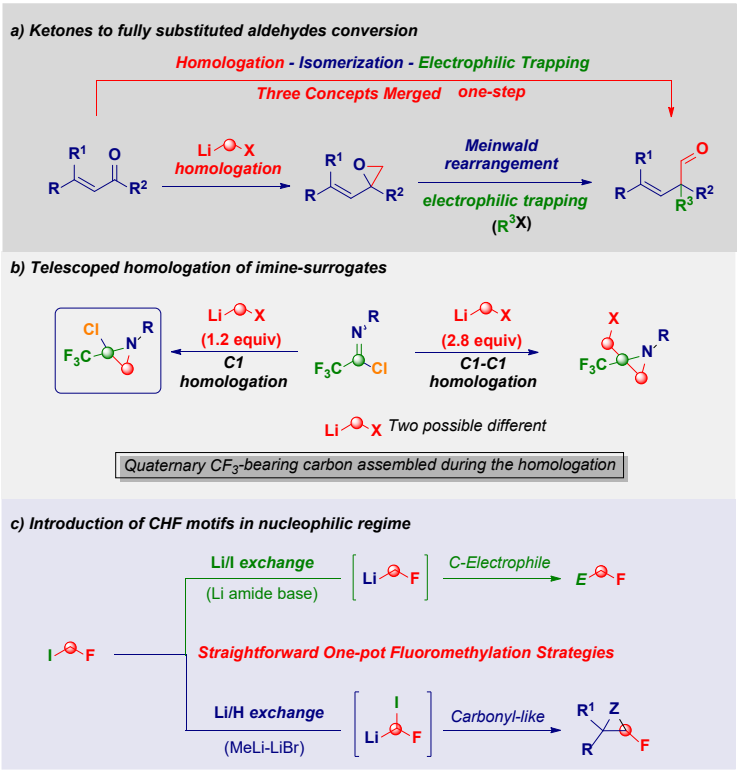
The direct transfer of a reactive nucleophilic CH_2X unit into an existing linkage enables the formal introduction of the moiety with the precisely defined degree of functionalization.[1] Upon the fine tuning of the reaction conditions governing the transformation, the initial homologation event can serve as the manifold for triggering unusual rearrangement sequences leading to complex architectures through a unique synthetic operation. The direct – full chemoselective - conversion of a ketone into the homologated all-carbon quaternary aldehyde (*via* a)[2] and, the telescoped homologation of imine-surrogates to quaternary aziridines (*via* b)[3] will illustrate these unprecedented concepts. Additionally, the one-step mono-fluoromethylation of carbon electrophiles with extremely labile fluoromethyllithium reagents will provide a novel entry to valuable fluorinated building-blocks without the needing of using protecting elements for fluoro-containing carbanions (*via* c).[4]



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KN-04

I primi 150 anni della Tavola Periodica degli Elementi Chimici: tra Chimica, Storia e Letteratura

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L'UNESCO ha proclamato l'anno 2019 Anno Internazionale della Tabella Periodica degli Elementi per celebrare i 150 anni dalla pubblicazione della tabella dello scienziato russo Dmitri Mendeleev che è alla base di quella che oggi tutti conoscono. Gli elementi, come mattoncini elementari, costituiscono il nostro mondo, noi stessi e tutto ciò che ci circonda, visibile od invisibile e da ciò deriva la straordinaria importanza, scientifica e non solo, della Tabella Periodica.

Lo stesso Mendeleev riconobbe pubblicamente che alla base della sua tavola periodica c'era in larga misura il lavoro di uno scienziato italiano, Stanislao Cannizzaro, che negli anni 1855-1861, quando era professore di chimica all'Università di Genova, mise a punto un metodo per determinare con precisione il peso atomico degli elementi. Cannizzaro in realtà non fu solo un chimico. Partecipò ai moti siciliani del 1848, fuggì in Francia, tornò poi in Italia (partecipò alla seconda spedizione di Garibaldi del 1860) e infine divenne vicepresidente del Senato realizzando importanti riforme nell'ambito dell'istruzione e della salute pubblica.

Ma nel 2019 ricorrono altri importanti anniversari ed uno di questi è il centenario della nascita di Primo Levi che fu chimico e scrittore, vittima e lucido testimone della tragedia della Shoah, i cui libri più importanti e noti a livello internazionale sono certamente "Se questo è un uomo", un resoconto scientifico della tragedia dei lager, e "Il Sistema Periodico" una serie di affascinanti racconti dedicati appunto agli elementi e dunque è evidente lo strettissimo legame che unisce questi due anniversari.

Nel racconto intitolato Ferro del Sistema Periodico Levi scrive: "…il Sistema Periodico di Mendeleev, era una poesia, più alta e più solenne di tutte le poesie digerite in liceo: a pensarci bene, aveva perfino le rime!"

E allora immaginiamo la Tabella Periodica come una tastiera perché come dice Levi: "… non è detto che il mestiere di cucire insieme lunghe molecole presumibilmente utili al prossimo, non insegni nulla sul modo di cucire insieme parole ed idee."

Ancora una volta ci rendiamo così conto che non esiste differenza tra la cultura umanistica e quella scientifica in quanto esse coesistono in una sola!

EurJOC Lecture

EurJOC Lecture

Ionic Liquid Effects on the Rates of Reactions

A Lecture in Memory of Prof. Cinzia Chiappe

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Since the introduction of air and water stable salts that are liquid at room temperature, there has been an explosion of interest in the application of these as solvents for chemicals synthesis and processing. Much of this interest has been centered on the possibility that the ionic media provided by these solvents offer a different kind of chemical environment to molecular solvents perhaps leading to novel behaviors that cannot be achieved with molecular solvents.

Using a combination of detailed kinetic investigations of both Diels-Alder and S_N2 reactions in a range of ionic liquids and measurements of the spectra of probe compounds, we have identified how ion-solute interactions in ionic liquids can be used to change the reactivity of solutes.

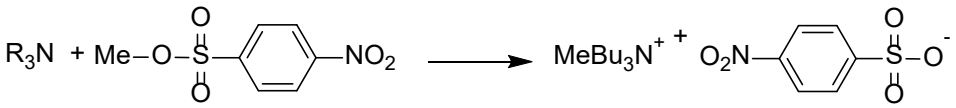

Figure 1: S_N2 reactions of neutral nucleophiles with neutral substrates are accelerated in ionic liquids.

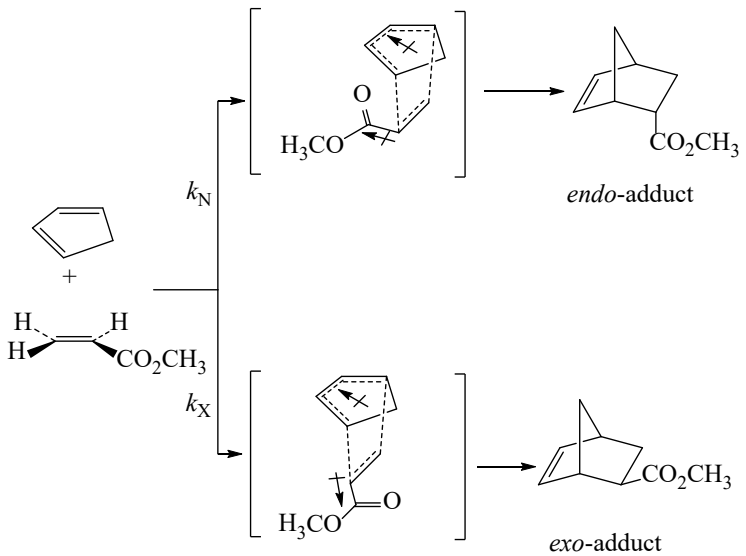

Figure 2: Selectivity of Diels-Alder reaction towards endo- and exo- adducts.

ChemPubSoc Lecture

ChemPubSoc Lecture

Current Challenges in Chemistry Publishing

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Scholarly publishing is crucial to the advancement of chemistry and has a fundamental role in connecting scientists and providing them with a platform to share their findings with the appropriate audience. In this contribution, current developments and trends within chemistry publishing will be addressed and questions and concerns will be answered. Topics to be covered include open science and open access, good publication practices, and future trends.

Figure 1: Two journals owned by ChemPubSoc Europe.

References:

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Elsevier Lecture

Elsevier Lecture

Finding novel lead compounds in pesticide discovery inspired by pharmaceutical research

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The use of high throughput (HTP) methodologies for supporting discovery and development of new agrochemical products opens up new opportunities to test many new compounds potentially acting on biological targets in various organisms. Finding new lead compounds which might act as a new pesticide can sometimes be a lengthy process; we present a method which can provide lead compounds by using the breath of information available from pharmaceutical research. This talk will give an overview of the chemical and biological informatics methods and data used to map compounds active against biological targets in parasites in humans to fungal targets. The talk will also explore how information solution workflow enabling tools such as Reaxys and AI and Machine Learning techniques recently developed for pharmaceutical research projects can augment these developments. Thereby demonstrating how findings from pharmaceutical research can be transferred to crop protection research.

Lectures Premi di Dottorato

PD-01

The Triangle of Photocatalysis: Different Approaches for Ecosustainable Synthesis

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Over the past decades, photochemical synthesis, i.e. organic synthesis that uses light as source of energy to break and forge bonds, has vehemently re-emerged as an ecosustainable methodology in organic chemistry. A natural speed up in this direction was represented by the emergence of photocatalysis: in these reactions, a purposely added molecule (photocatalyst, PC) is responsible for the conversion of light energy into chemical energy for the activation of a substrate in a highly predictable and selective way. This activation can occur via three different mechanisms: Single-Electron Transfer (SET), Hydrogen-Atom Transfer (HAT) or Energy Transfer (EnT), as shown in Figure 1. In my Ph.D. thesis I decided to explore the potentialities of each approach for the generation of highly reactive intermediates under extremely mild conditions and for the ensuing development of novel ecosustainable synthetic protocols. One case for each activation manifold will be presented.

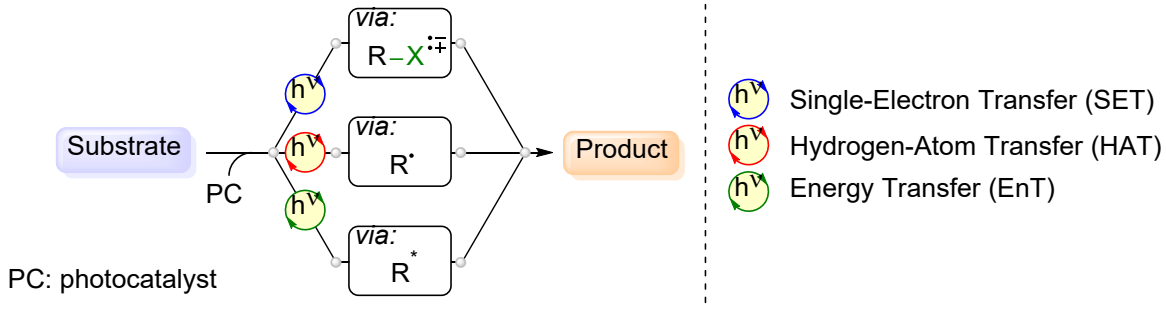

Figure 1: Different activation manifolds in organic photocatalysis.

Generally speaking, one of the most remarkable goals achieved is the generation of fleeting intermediates such as benzyl[1] and acyl radicals[2] via SET and aliphatic radicals via HAT[3]. Moreover, detailed investigations on novel classes of photocatalysts able to promote the C-H to C-C bond conversion under visible-light are reported.[4] Finally, interesting results on the use of transition metal complexes as photosensitizer via EnT for the synthesis of cyclobutanes via [2+2] photocycloadditions are included.[5]

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[5] manuscript in preparation

PD-02

Towards DNA-targeting magic bullets: searching for potential conformation-selective G-quadruplex ligands

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In the search for effective and minimally toxic anticancer therapies, G-quadruplex (G4) structures emerged as appealing targets for their crucial roles in human telomeres and oncogene promoters.[1] G4s are non-canonical nucleic acid secondary structures exhibiting marked structural polymorphism.[1,2] To achieve an optimal recognition selectivity, thus reducing drug toxicity, a major challenge is the identification of ligands which are not only structure-selective, *i.e.* able to discriminate G4 *vs.* duplex DNA, but also conformation-selective, *i.e.* able to specifically recognize different G4 conformations. Thus, considerable efforts are currently devoted to the design of molecules able to selectively target conformationally different G4s and discriminate duplex DNA. To be effective, the huge impulse to synthesize libraries of potential conformation-selective ligands has to be coupled with fast and reliable High Throughput Screening assays.

In this context, during my PhD I developed: i) a method for the on-line synthesis of glass support-bound, fully deprotected secondary structure-forming oligonucleotides,[3] and ii) an affinity chromatography-based assay, named G-quadruplex on Controlled Pore Glass (G4-CPG), for the screening of libraries of putative conformation-selective G4 ligands.[4]

After full optimization of the G4-CPG assay, two different libraries of putative G4 selective ligands, based either on a furobenzoxazine naphthoquinone[5] or a naphthalene diimide[6] scaffold, were designed, synthesized and evaluated. The strongest and most selective ligands, selected by the G4-CPG assay, were further investigated in their binding to G4 structures having different conformations by several biophysical techniques, as well as subjected to *in vitro* biological assays.

In this presentation, I will describe the novel developed G4-CPG method based on our newly designed CPG support that allowed us selecting promising candidate drugs for *in vivo* studies, endowed with strong activity against cancer cells (IC_{50} in the low nM range) and very good selectivity in killing cancer cells *vs.* normal cells.

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[6] Manuscript in preparation.

PD-03

Outstanding chiroptical features in thin films of chiral π-conjugated oligomers: from synthesis to applications

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In the last years, chirality has gained an increasing interest in the fields of metamaterials and organic optoelectronics as an important parameter for controlling supramolecular arrangement of π-conjugated systems at different hierarchy levels, opening the way to highly innovative technological applications.[1] Most of these devices are based on the different interaction of the active layer with left- and right-handed circularly polarized light, therefore a current research goal is to obtain thin films of organic π-conjugated systems displaying significant chiroptical properties in absorption (*i.e.* electronic circular dichroism, ECD) or in emission (*i.e.* circularly polarized luminescence, CPL).

In the present work we developed a family of novel chiral π-conjugated oligomers functionalized with inexpensive alkyl chiral groups from natural sources, studying their ECD and CPL features in thin films. Although in general we found a manifold of situations, revealing the central role of different local supramolecular structures (strictly related to chemical structure, deposition technique and post-deposition operations), in some cases we discovered outstanding chiroptical features.

Concerning the ECD properties, for some of them we found the very uncommon property of ECD signal inversion upon sample flipping (**Figure 1a**):[2] due to the interference between linear dichroism and linear birefringence (called LDLB effect), it could be exploited for the realization of new devices, able to discriminate the direction of sample illumination. For the CPL properties, in general quite large dissymmetry factors g_{lum} values (in the order of 10^{-2}) on a wide wavelengths range were obtained, despite their structural differences. Encouraged by promising results, we investigated their possible application in circularly polarized organic light-emitting diode (CP-OLED) devices: a *multilayer* device based on a 9*H*-carbazole-oligothiophene as active layer was developed (**Figure 1b**), representing to the best of our knowledge the first example of CP-OLEDs based on chiral oligothiophenes.

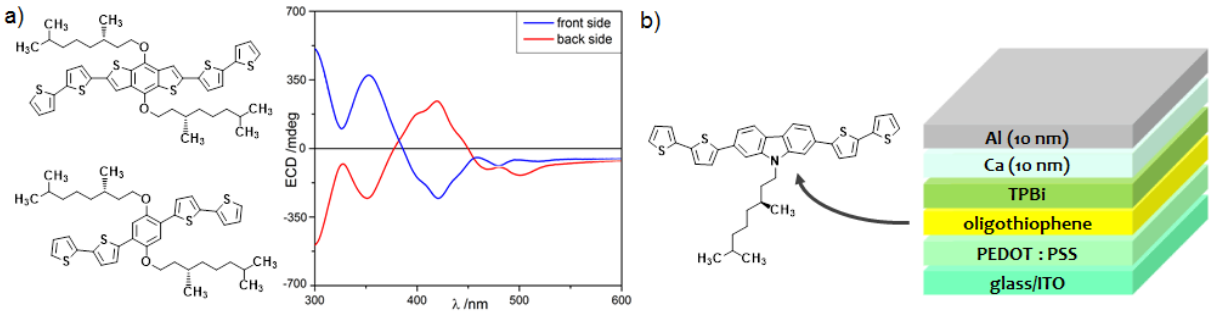

Figure 1: a) ECD spectrum inversion by sample flipping due to LDLB effect in thin films of our compounds; b) architecture of the *multilayer* CP-OLED based on 9*H*-carbazole-oligothiophene developed in this work.

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Contributi Orali

OC-01

Synthesis and biological evaluation of novel antimicrobial and antibiofilm agents

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Bacterial infections represent a serious threat in the public health due to the emergence of antibiotic-resistant pathogens resulting from the wide use and abuse of antimicrobial agents.[1] In addition, bacteria ability to form biofilms increases the difficulties to eradicate the pathogens leading to chronic and resistant infections. Therefore, development of novel candidates active against bacteria in planktonic state, as well as growing in biofilm, represents an important issue. In this context, our interest in the development of novel small molecules endowed with biological activity led us to identify two class of compounds, *N*-alkyl-L-iminosugars and corticosteroid derivatives (**Figure 1**) as novel potential antibacterial and antibiofilm agents. Despite the interesting biological properties for both of these classes of compounds,[2] to the best of our knowledge, only few data are reported on their action on bacterial infections. Regarding *N*-alkyl-L-iminosugars, a recent study aimed to explore their inflammatory potential in Cystic Fibrosis lung disease, suggested a possible role as molecules able to control microbial infection. In our lab a *de novo* synthesis has been tuned up to gain access to the iminosugar core,[2] along with a scalable procedure for the alkyl chains assembly (**Figure 1a**). On the other hand, our attention has been attracted by a series of steroid derivatives whose synthesis has been realized starting from the commercially available tetraene acetate (3TR) (**Figure 1b**).

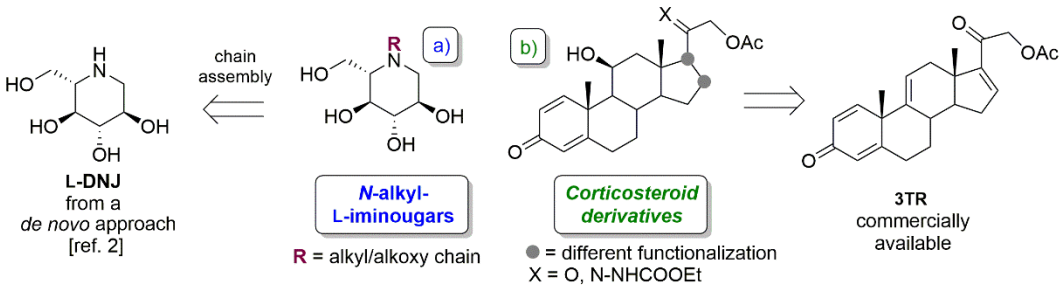

Figure 1: Synthesis of *N*-alkyl-L-iminosugars (**a**) and of corticosteroid derivatives (**b**).

Both classes of compounds were subjected to preliminary biological assays showing interesting antimicrobial activity against both Gram-positive (*S. aureus*) and Gram negative (*P. aeruginosa and S. maltophilia*), as well as a good ability to prevent biofilm formation and, in some cases, to disperse pre-established existing biofilms. These first data prompted us to explore the therapeutic potential of these compounds, also by studying their behaviour when used in combination or jointed to form a single molecular system.

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OC-02

Stereoselective synthesis of C-2 alkylated trihydroxypiperidines: effect of the chain length and the configuration at C-2 on their activity as Pharmacological Chaperones for Gaucher Disease

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A synthetic strategy based on the addition of Grignard reagents onto nitrone **1**, derived from aldehyde **2**, followed by intramolecular reductive amination, provides access to C-2 alkylated trihydroxypiperidines bearing different alkyl chains (octyl, nonyl, undecyl, dodecyl and tridecyl). Lewis acid addition during the Grignard reaction allowed access to both epimers at the newly created stererocentre, providing the target trihydroxypiperidines with both configuration at C-2. The overall synthesis was achieved in 8 steps from low cost D-mannose and provided the final compounds in 35-45% overall yield.[1,2] With this approach, a small library of new iminosugars of biological interest was accessed as potential Pharmacological Chaperones (PCs). PCs are small molecules that bind and stabilize enzymes, rescuing the enzymatic activity of misfolded or deficient enzymes when they are used at sub-inhibitory concentration.[3] In particular, it is of great interest the search for PCs able to improve the cellular folding and trafficking defects associated with Gaucher disease (GD), the most common autosomal recessive lysosomal storage disorder. GD is caused by point mutations in the gene encoding for acid-β-glucosidase (β-GCase), the enzyme responsible for glucosylceramide metabolism into glucose and ceramide. The effect of the chain length and the configuration at C-2 on GCase inhibition, in extracts from human leukocytes homogenate isolated from healthy donors and on chaperoning activity, in human fibroblasts derived from Gaucher patients bearing the N370 and L444P mutation, will be presented. Furthermore, the selectivity towards other human glycosidases was determined on these molecules together with their cytotoxicity and mechanism of action.[2]

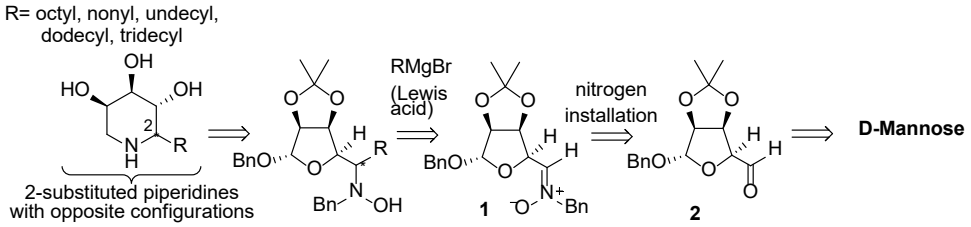

Figure 1: Retrosynthetic strategies to access 2-substituted piperidines.

Acknowledgements: Fondazione Cassa di Risparmio di Pistoia e Pescia (Bando Giovani@Ricerca scientifica 2017).

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OC-03

Deciphering the metabolome of marine microbiome through molecular networking

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Marine environment provides an unrivaled degree of biodiversity that is paralleled with biochemical and chemical diversity, making it a cornucopia for the discovery of new chemical entities of potential clinical efficacy. Our research is focused on the study of the chemistry of natural products from marine organisms (sponges) and microorganisms (sponge symbionts, cyanobacteria) that are extremely prolific in new bioactive natural products.

In this context, we have explored the use of molecular networking,[1] a recently-developed method for automated LC-MS data analysis and mining,[2,3] to discover novel lead compounds for anticancer, antibiotic and anti-inflammatory drug design.[4]

In our most recent studies, in the Caribbean sponges *Smenospongia aurea* and *Smenospongia conulosa* we have found a series of chlorinated mixed-biogenesis NRPS/PKS compounds, namely smenamides[5] and smenothiazoles[6] from *S. aurea* and conulothiazoles[7] from *S. conulosa*, showing a potent cytotoxic activity at the nanomolar level. The bloom-forming cyanobacteria *Trichodesmium* sp. have been recently shown to produce some of the chlorinated peptides/polyketides previously isolated from the marine sponge *S. aurea*.[8] A comparative analysis of the organic extracts of *S. aurea* and *Trichodesmium* sp. was performed combining high-resolution LC-MS/MS and molecular networking, showing that both *S. aurea* and *Trichodesmium* sp. contain a wide range of such chlorinated compounds, many of which are present in both organisms. Following this integrated approach, new antiproliferative chlorinated polyketides, smenolactones A-D, were isolated from *S. aurea*, and two new conulothiazole analogues, isoconulothiazole B and conulothiazole C were isolated from *Trichodesmium* sp., and their structures elucidated. These findings confirmed molecular networking as a powerful tool in the discovery and development of new drug leads.

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OC-04

A Kinetic and Morphological Study of P3HT Nanowhiskers Formation in the Presence of either PCBM or PCL.

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Poly-3-(hexyl thiophene) (P3HT) is currently the benchmark semiconducting polymer for organic photovoltaics. Its physical, electrical, photophysical properties are strongly dependent on its morphology in the solid state. However, several issues remain unclear, regarding the forces that drive the assembly/crystallization of P3HT to form fibrillar nanocrystals (NCs) in marginal solvent conditions (anisole)[1,2].

This work reports the results of a systematic study on the aggregation/crystallization behavior of P3HT to NCs under different solution conditions and in the presence of different relative contents of either PCBM[3] or poly(ε-caprolactone) PCL.[4] PCBM and PCL confined the aggregation/crystallization process of P3HT NCs allowing the formation of extended crystallites, on the other hand at high concentrations in solution it hindered the formation of NCs slowing down their assembly. The results obtained in this work offer a promising perspective for the obtainment of functional all-polymeric NCs.

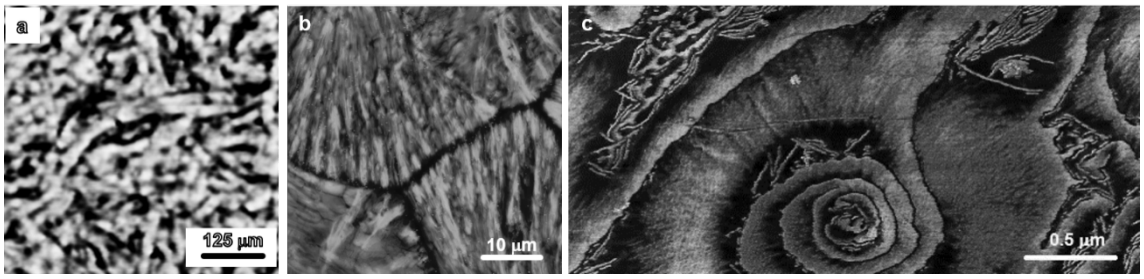

Figure 1: AFM phase micrograph of P3HT NCs mixture obtained from a) P3HT:PCBM 1:1, b) and c) P3HT:PCL 160:1 relative concentrations (w/w).

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OC-05

Design of Organic Based Photosensitizer-Catalyst Systems for Photoelectrochemical Solar Fuels

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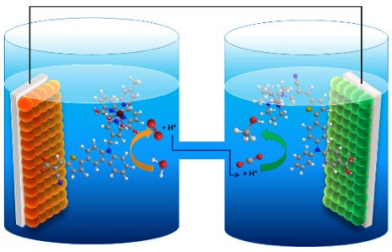

Figure 1: Scheme of a DS-PEC.

Photoelectrochemical cells (PEC) are the new frontier for the conversion of water and solar radiation into oxygen and hydrogen with zero carbon footprint. Two electrodes, soaked into two different half-cells and connected by an external circuit, compose the cell. The electrodes are p-type and n-type semiconductors (SC), both dye-sensitized (e.g by organic molecules) to enhance light harvesting. In the media either a water oxidation catalyst and a hydrogen evolution catalyst are solubilized to oxidize water and to reduce protons. The goal of a dye-sensitized PEC (DS-PEC) is to mimic the nature, achieving an artificial leaf able to produce solar fuels like hydrogen and/or hydrocarbons from the reduction of water or carbon dioxide (**Figure 1**). The organic dye is the strategic center of the device and, upon irradiation, generates the electron/hole couple. Organic dyes have been playing an emerging role in photocatalysis and in DS-PEC due to their easy synthesis, low cost, and abundance of precursors.[1] This work focuses on the design and the synthesis of new types of organic push-pull dyes that can be connected to the corresponding catalysts exploiting various types of photosensitizer-catalyst interactions (**Figure 2**). The first series of dyes will exploit the host-guest properties of calix[4]arene moiety to direct the catalytic process. In the second series, the sensitizer is covalently linked to a carbon based π-framework to exploit π-π interactions with the catalyst.[2] Finally, in order to reach the most ambitious goal achieving an integrated artificial photosystem, catalyst and sensitizer are directly covalently linked. The type of interaction between catalyst and dye is important for the efficiency of the device because can control the charge transfer and define the arrangement on the SC surface that can reduce charge recombination reactions.

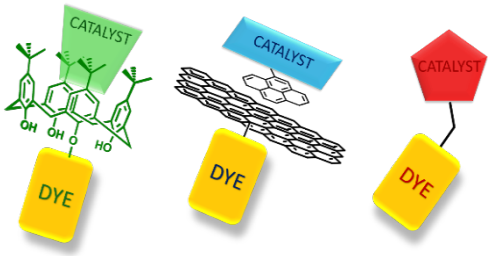

Figure 2: Investigated molecular designs.

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OC-06

Synthesis of self-assembled BODIPY heterodimer for energy transfer investigations

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The crucial step in the conversion of solar to chemical energy in photosynthesis takes place in the reaction center, where the absorbed excitation energy is converted into a stable charge-separated state by ultrafast electron transfer events. However, the fundamental mechanisms responsible for efficiency of these processes are still largely unknown. The development of 2D spectroscopic techniques has shown that coherent transfer of electronic wave-packets is an essential step.[1] These findings are raising questions also about the role of quantum coherence in artificial devices, but only few papers have been devoted to the investigation of not-biological complexes.[2] One of the key challenges for the future will be to learn how to construct artificial molecular materials enabling the harvesting of sunlight exploiting quantum effects. Here we will report the synthesis and experimental investigations on an innovative Bodipy-type multichromophoric self-assembled system (Figure 1). The synthetic strategies for Bodipy building blocks linked to peripheral complementary triple hydrogen bonding moieties, will be presented.

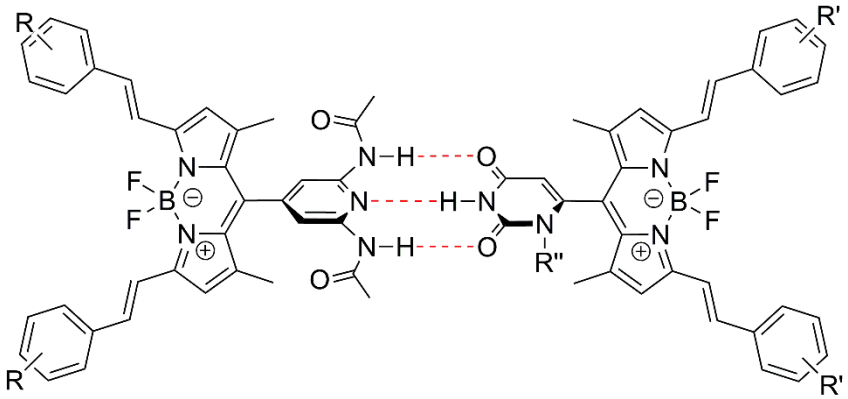

Figure 1: Heterodimer of DAPA-BODIPY and Orotic-BODIPY

The spectroscopic characterization of the heterodimer and preliminary studies of electron transfer by 2D technique, will be also shown.

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OC-07

Catalytic Manipulations of Arenes with Light and Graphene Oxide

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Aromatic motifs are contained in countless number of organic species with applications spanning from pharma to molecular machines. The current trends in synthetic methodologies dealing with aromatic systems can be organized in three major areas: synthesis of the ring, site-selective functionalization of the arene periphery and dearomatization protocols. Catalysis represent the ultimate strategy for all these fields.[1]

Over the past decade our group has been engaged in this intriguing field by means of metal (Au, Ni) and metal-free (Brønsted acid, phosphine) catalysis, generating a wide portfolio of chemical diversity within 2D- and 3D-heterocyclic realms.

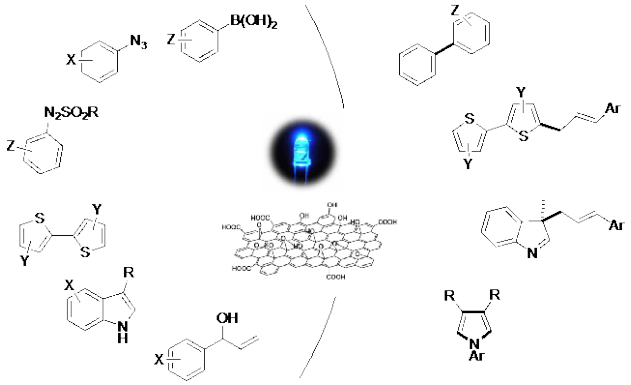

Figure 1: Visible-light photoredox and carbo-catalytic tools in arene chemistry.

In the present communication, our latest findings in the synthesis as well as functionalization of hetero-aromatic compounds via visible-light photoredox processes[2a,b] and carbo-catalytic tools will be presented (Figure 1).[2c,d]

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OC-08

Metal-Ion Induced C–H Bond Deactivation in the Hydrogen Atom Transfer Reaction from Diol Substrates to the Cumyloxyl Radical

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Aliphatic C−H bond functionalization procedures based on hydrogen atom transfer (HAT) to radical and radical-like species are attracting considerable interest in view of the possibilities they offer to introduce a variety of functional groups and to promote highly selective transformations.[1-3]

Within this framework, medium effects have recently emerged as a powerful tool that has been successfully employed to control reactivity and site-selectivity in an increasing number of synthetically useful examples.[4]

From a mechanistic point of view, recent studies in our group have provided a quantitative evaluation of the effect of Lewis acid-base interactions on HAT from aliphatic C−H bonds to the electrophilic cumyloxyl radical ($PhC(CH_3)_2O^{\bullet}$, $CumO^{\bullet}$). In acetonitrile solution, deactivating effects have been observed following alkali or alkaline earth metal ion addition for HAT from the α-C–H bonds of a series of basic substrates such as amines, amides and ethers, with the magnitude of these effects that has been shown to depend on the nature of the metal ion and on the substrate Lewis basicity.[4,5]

The study has been extended to the reactions of $CumO^{\bullet}$ with acyclic and cyclic alkanols and alkanediols. The results of a detailed time-resolved kinetic study in acetonitrile solution on the effect of alkali and alkaline earth metal ion salts on these latter reactions as a function of the nature of the metal ion and the substrate structure, and the possible implications in terms of synthetically useful C–H bond functionalization procedures will be discussed.

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OC-09

Hydrogen Atom Transfer based Aliphatic C–H Bond Functionalization of Cycloalkane Derivatives. Kinetic and Product Studies on the Role of Torsional Effects

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The direct functionalization of aliphatic C−H bonds is currently one of the main goals of modern synthetic organic chemistry, because these reactions can offer advantages both in terms of decreased waste generation and reaction step economy.[1] Methodologies based on Hydrogen Atom Transfer (HAT) to radical and radical-like species have proven to be successful in pursuing this challenging goal.[2]

The factors that govern reactivity and selectivity in HAT reactions from aliphatic C−H bonds have been discussed in detail.[1a,3,4] A major role is generally played by the C−H bond dissociation energy (BDE), but other factors can also play a relevant role. Among them, we can enlist electronic, stereoelectronic, and medium effects. Torsional effects have also been shown to play an important role in the reactions of cyclohexane derivatives with HAT reagents,[5,6] where in particular tertiary equatorial C−H bond activation and tertiary axial C−H bond deactivation has been observed.

In view of these findings, and in order to provide a quantitative evaluation of the role of torsional effects on HAT from the C−H bonds of cycloalkane derivatives, we have carried out detailed time resolved kinetic study on the reactions of an extended series of monosubstituted and disubstituted cycloalkanes with a prototypical HAT reagent such as the cumyloxyl radical ($PhC(CH_3)_2O^{\bullet}$, $CumO^{\bullet}$). These studies have been accompanied by product studies on the reactions of the same substrates with $CumO^{\bullet}$ and with *in situ* generated dioxiranes. The results thus obtained will be presented.

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OC-10

Selective aliphatic C−H bond hydroxylation promoted by *in situ* generated dioxiranes

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The selective oxidation of nonactivated aliphatic C−H bonds represents one of the most challenging reactions in modern organic synthesis.[1] Among the methodologies that have been developed for this purpose, procedures based on hydrogen atom transfer (HAT) from aliphatic C−H bonds have aroused great interest. Within this framework, dioxiranes have been shown to promote the hydroxylation of these bonds[2] and a mechanism that proceeds through initial HAT followed by fast OH-rebound has been recently proposed.[3] In this context, a recent article by Hilinski and coworkers has described the development of a new method for *in situ* dioxirane generation that has been then applied to aliphatic C−H bond oxidations.[4] Taking the results of this study as the starting point, in order to obtain information on the effect of dioxirane structure on the oxidation reaction we have carried out a detailed mechanistic investigation, taking adamantane as the reference substrate and employing a wide range of ketones as precursors of the dioxiranes. The optimized conditions have been then extended to the oxidation of a variety of hydrocarbons. The results thus obtained will be discussed.

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OC-11

The strange case of quinones and hydroperoxyl radicals

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Hydroperoxyl radiicals (HOO•), along with alkylperoxyl radicals (ROO•) are the main chain-carrying oxidizing species in organic systems and in biology. On the other hand, catechols and hydroquinones are among the most important antioxidants both in nature and among synthetic compounds. While catechols (e.g. **1**H_2) efficently trap 2 peroxyl radicals being oxidized to the corresponding quinones (**1**), hydroquinones (e.g. **2**H_2) have lower efficency due to competing pro-oxidant behavour based on the formation of HOO• by reaction of their seminiquinone radical (**2**H•) with O_2.[1] Quinones (*ortho* or *para*), instead, have no known antioxidant activity, being unable to trap peroxyl radicals. We have recently shown that, paradoxycally, HOO• could have co-operative antioxidant effect upon interaction with species like nitroxyl radicals, affording antioxidant systems of unmatched effiency based on a catalytic redox cycle.[2] It was also shown that HOO• can act as reducing agent toward phenoxyl radicals.[3] Here we will show how this chemistry can be called into action to afford extremely effective antioxidant systems based on the interplay of quinones and semiquinones with hydroperoxyl radicals, as summarized in Figure 1.

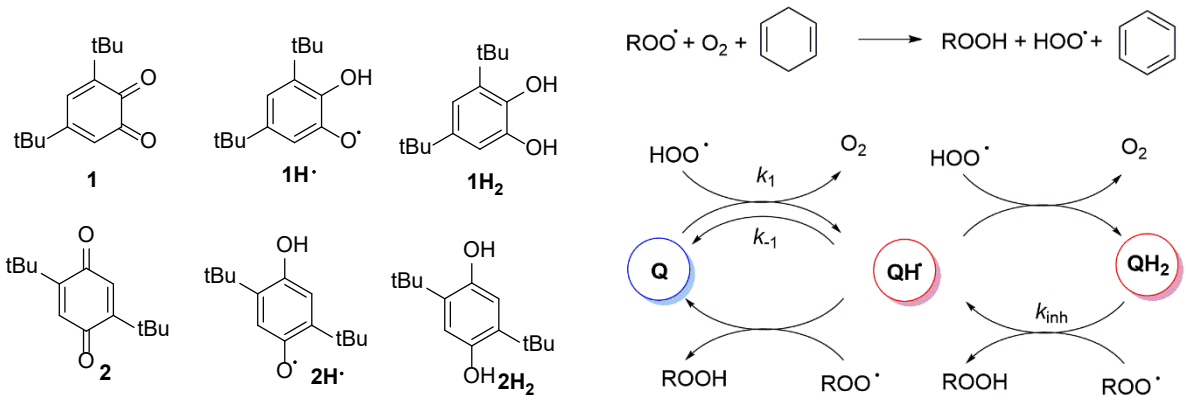

Figure 1: Key reactions explaining the antioxidant activity of quinones mediated by HOO•, **Q** = **1** or **2**.

The picture arising from this study eventually clarifies the controversial antioxidant behaviour of quinones and hydroquinones, both in nature and in man-made materials and sets the basis for the rational use of this fascinating chemistry.

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OC-12

Photoresponsive molecular tools targeting DNA G-quadruplex structures

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In the last few years a nucleic acid secondary structures known as G quadruplex (G4) have been extensively investigated for their critical role in the regulation of biological processes. G4s are non-canonical supramolecular structures formed by guanine-rich oligonucleotides. Four Gs bind via Hoogsteen-type hydrogen bonds base-pairing to yield G-quartets, which in turn stack on top of each other to form the G4. In the human genome and in prokaryotes, have been found G4- forming sequences at the telomeres and in proximity of transcription starting sites, within regulatory elements (e.g., promoters, untranslated regions, rDNA). Recently, the presence of G4s in viruses and their involvement in virus key steps has also been provided. All these experimental evidences have been validated G4s as therapeutic (e.g., anticancer, antiviral) targets suitable for chemical intervention. New methodologies for selectively sensing G4 formation, both in vitro and in vivo, are therefore urgently needed. Optical light-up probes are perfectly suited for such applications, allowing fast, simple, and ultrasensitive detection of biomolecules. For this purpose our group developed different selective G4 ligand starting from Naphthalenediimide core (NDI).

NDIs are very versatile molecules for the design of new molecular systems; their optoelectronic properties can be effectively tuned by substituents on the aromatic core, thus giving origin to absorption and emission in the red spectroscopic window, which makes them appealing for fluorescence imaging and photodynamic therapy (PDT). In addition, their well-known binding properties toward G-quadruplex (G4), make the NDIs the best candidates for a selective G4 fluorescence sensing[1-7].

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OC-13

The intriguing world of G-quadruplex-based aptamers

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Among the known aptamers, many are guanine-rich oligomers. The relatively high abundance of guanine-rich aptamers identified by SELEX, coupled with their ability to recognize very different targets, is not surprising.[1-3] In fact, guanine-rich oligonucleotides share a distinctive ability to fold into stable but also extremely different G-quadruplex (G4) structures, which are non-canonical nucleic acid conformations stabilized by guanine tetrads, i.e. cyclic planar arrangements of four guanines linked through Hoogsteen-type hydrogen bonds. Stacking of two or more guanine tetrads generates the G4 motif, further stabilized by cations complexed in the central cavity of the G4.[4] The apparently rigid G4 structure is indeed rather plastic and can fit into a variety of nucleic acid architectures. Thus, even very similar DNA sequences can exhibit an extraordinarily wide structural variability, and therefore provide precious and versatile scaffolds to evolve highly specific aptamers, accounting for very different biological effects.

In this frame, we are currently investigating several G4-forming aptamers, specifically targeting inflammation- and cancer-related proteins. Our recent results concerning aptamers selectively recognizing two peculiar systems, i.e. the proteins VEGF and IgM, widely recognized biomarkers of different cancer forms, will be here presented as case studies. For these proteins, we studied brand new G4-based aptamers (IgM),[5] or provided conspicuous new knowledge on known G4-based aptamers (VEGF).[6]

The conformational behaviour of these aptamers, analysed by multiple biophysical methods, proved to dramatically depend on their solution environments. In pseudo-physiological buffers mimicking extra- or intracellular media, the studied aptamers proved to be highly polymorphic, folding into stable, unimolecular G-quadruplex structures in K^+-rich solutions. In all cases, their functional conformations have been identified and characterized.

These findings demonstrate the key role of G-quadruplex folding in the molecular recognition and efficient binding of both anti-mIgM and anti-VEGF aptamers, providing a precious rational basis for the design of effective aptamer-based biosensors potentially useful for the detection of cancer-relevant biomarkers.

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OC-14

Encapsulation and controlled release of thymol derivatives into lignin microcapsules

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Thymol and the corresponding brominated derivatives constitute important biological active molecules as antibacterial, antioxidant, antifungal and antiparasitic agents.[1,2] However, their use as preservatives in food industry or in packaging materials is often limited because of their pronounced fragrance, their poor solubility in water and their high volatility. Among the others, active molecules encapsulation represents a successful strategy to overcome such limitations.

In this communication, preliminary results related to the encapsulation of different thymol derivatives into biocompatible lignin-microcapsules will be presented. As a matter of fact, the adoption of an encapsulating material possessing relevant antibacterial and antioxidant activity as well as high biocompatibility -such as lignin-[3,4] allows the easy development of new materials that are suitable for the application in several industrial fields. To this purpose, lignin microcapsules containing thymol, 4-bromothymol, 2,4-dibromothymol and the corresponding methoxy derivatives have been efficiently prepared through ultrasonication (Fig. 1). Studies of encapsulation efficiency, morphology and release will be presented.

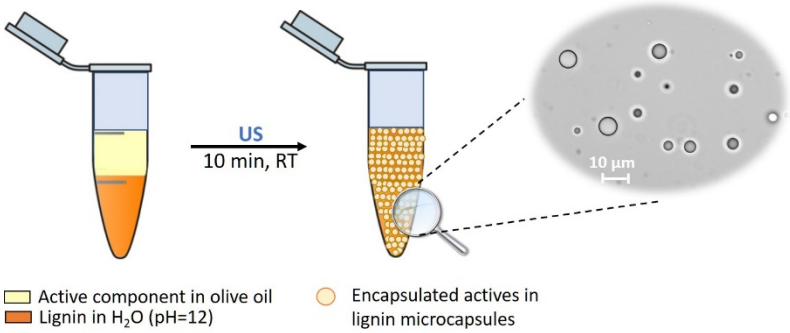

Figure 1: Encapsulation process of the active components in lignin microcapsules. In the zoom: microscope images of lignin microcapsules.

Acknowledgments:
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OC-15

Novel insights on peptide-G4 DNA interaction: a study on the binding behaviour of polyamine peptides on different G4 DNA structures

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Guanine-rich sequences are found in DNAs able to fold into intramolecular G-quadruplex structures, which may play a relevant role in a number of biological processes and disease related mechanisms[1].Thus, the discovery and the characterization of new supramolecular G4 assemblies represent a very interesting challenge[2]. Apart cations, such as potassium or sodium, also molecules such as polyaminines and triethylene tetraamine contribute to the stability of G4 structures to which they bind provoking noteworthy biological effects, including telomerase inhibition.[3,4]

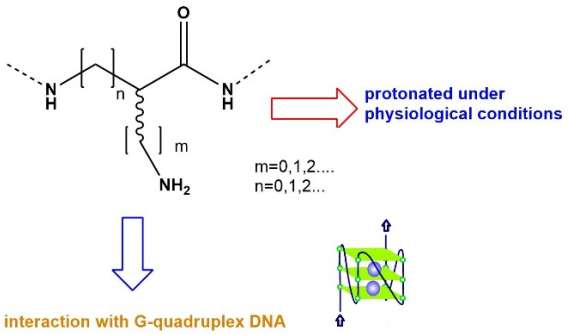

Figure 1: Schematic representation of the repeating unit of a generic diamino acid-based peptide to be studied in G4-DNA targeting

In this study we investigate the potential as G4 binders of artificial polyamine peptides, unnatural peptides based on the oligomerization of diamino acids, synthesized by solid phase synthesis and fully characterized. The effects on different models of G4-DNAs, including the parallel topology-forming c-myc and tel_{22} in a hybrid mixed paralle/antiparallel topology, are discussed on the light of CD, UV and fluorescence binding evidences that seem to indicate polyamine peptides, positively charged under physiological conditions, as G4 binders able to induce specific structural modifications in the different G4 topologies.

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OC-16

Novel [2]-Rotaxanes Incorporating a Nitroxide Radical Motif

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Dialkyl nitroxide radicals (R_2N-O•) are an important example of open-shell molecules largely employed in many fields of chemistry and related sciences.[1] If compared to related diamagnetic functional groups, the use of nitroxides in molecular-level assembly processes remains, however, basically unexplored. This is somewhat surprising given their desirable intrinsic properties: nitroxides possess one of the largest dipole moments known for any functional-group type (close to 3 D), making them potentially useful for control of molecular orientation. In particular the N-O• motif is a good hydrogen and halogen-bond acceptor,[2] and offers a simple reversible route to diamagnetic oxammonium species via one-electron electrochemical oxidation.[1] On this basis, we investigated the possibility to prepare the first examples of nitroxide-containing bistable rotaxanes in which the N-O• motif would act not only as EPR probe for the shuttling process, but can be also directly involved in the recognition process both in its radical state[3] or in its diamagnetic oxidized form. In the reported [2]rotaxanes, the wheel is a 2,5-dimethyl-2,5-diphenylpyrrolidine-N-oxyl radical bound to a crown ether fragment at the *meta* positions of both aromatic rings (**1,** Figure 1). Two different interlocked molecules were investigated: in one case the thread contained 4,4'-bipyridinium (BPY^{2+}) and dialkylammonium (NH_2^+) stations (**2**) while in the other, the BPY^{2+} unit was replaced by a triazole fragment (**3**). Shuttling of the paramagnetic ring along the threads was induced by applying both acid-base or electrochemical inputs and was monitored by using different spectroscopic techniques, including EPR. It will be shown that the ability to switch between different states in these rotaxanes, using electrochemical power-source or by pH variation, highlights the possibility of creating elaborated molecular architectures, capable of progressively complex functions.

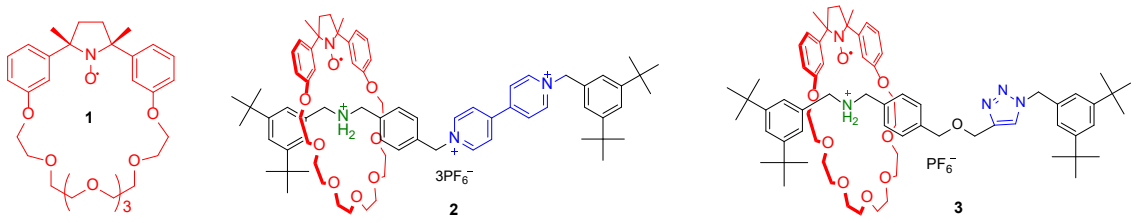

Figure 1: Structures of macrocycle **1** and rotaxanes **2**-**3**.

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OC-17

Chiral functionalized fluorescent macrocycles as a scaffold for remarkable chiroptical properties

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We investigated a series of chiral macrocycles, di-functionalized with various fluorescent moieties. These compounds display strong intramolecular excimer fluorescence and allied highly circularly polarized luminescence (CPL) with a circular polarization degree in the upper range of the ones reported for non-aggregated chiral molecules (g_{lum} up to $1.7.10^{-2}$). Upon interaction with alkaline and alkaline earth cations (Na^+, Ba^{2+}), the systems undergo deep conformational rearrangements which can result in a complete quenching of the excimer fluorescence and CPL (on/off), while the ECD profile is strongly modified, with some bands showing a sign inversion (+/−).[1]

Upon reversible decomplexation excimer fluorescence and the original ECD and CPL spectra are almost perfectly recovered. Such effect can be observed over several complexation/decomplexation cycles.[1]

In this way, rare examples of completely reversible switching of both +/− ECD and on/off CPL were attained.

Moreover, taking advantage of such molecular scaffold, we obtained the first example of circularly polarized electrochemiluminescence stemming from an organic molecule.[2]

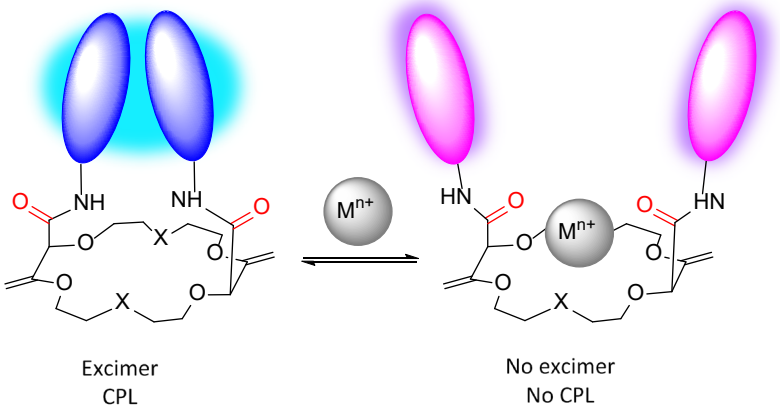

Figure 1: (Chiro)optical response upon cation binding by functionalized macrocycles.

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OC-18

Development and binding properties of a synthetic receptor for the molecular recognition of caffeine and related xanthines

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Caffeine and related xanthines, are among the most widely used psychoactive substances in the world, since they are consumed with traditional drinks, such as tea and coffee, but also with commercial energy drinks and with different kind of analgesics.[1] Xanthines have various pharmacological activities,[2] such as central nervous system stimulation, in addition to diuretic, anti-tussive and anti-bronchospastic properties. Furthermore, a protective role of caffeine seems to be involved in neurovegetative diseases, such as Parkinson's, Alzheimer's and ischemia.

Because biological functions of caffeine and of its main metabolites, theophylline and theobromine, are mediated by specific molecular recognition receptors, the study of their recognition is fundamental to understand their role in biological systems. The use of artificial receptors, possessing a very simplified structure and accessibility is essential for mimicking the function of the biological counterpart and for defining the structural and functional requirements that determine binding ability and selectivity. In this context, the realization of water-soluble synthetic receptors with high affinity and selectivity remains a goal pursued with much interest.

In recent years, in our research group, a family of synthetic receptors designed for carbohydrate recognition have been successfully developed.[3] The architecture of these receptors consists of aromatic platforms bridged by aminocarbazole units and endowed with hydrosolubilizing groups, an architecture that seems structurally and functionally appropriate to recognize xanthines as well. On the basis of receptors developed up to now, the synthesis of a new structure has been carried out and recognition ability towards xanthines of particular interest has been evaluated.

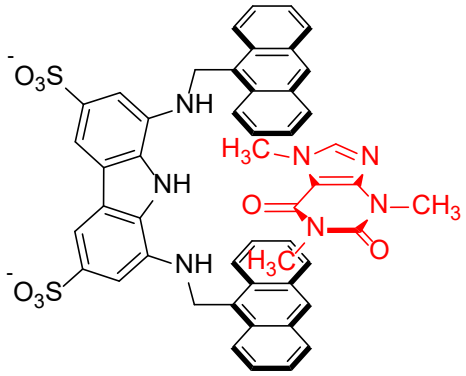

Figure 1: Schematic representation of receptor·caffeine complex.

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OC-19

Spike of Sulfur for Photo-Chemistry on Self-assembling Tripeptides

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Tripeptides are attractive minimalistic bioactive motifs and low-cost building blocks for supramolecular hydrogels.[1] Amongst the various design approaches, combination of D- and L-amino acids is proving successful for hydrophobic sequences.[2,3] The identification of new motifs containing cysteine or methionine could be interesting for added properties, such as the possibility to undergo redox cycles, metal coordination, or sulfur-based reversible chemistry to develop dynamic functional materials.

We report on a series of self-assembling D,L-tripeptides containing either methionine or cysteine to give dynamic materials that can undergo reversible cycles of assembly. The supramolecular behaviour of these materials is characterized by circular dichroism, single-crystal XRD, FT-IR, Thioflavin T fluorescence, and TEM.

The possibility to control the supramolecular behaviour by means of a photo-switch is an attractive strategy to obtain new smart materials, useful for technological and medical applications. Popular photo-switches are reversible and often based on *cis-trans* isomerization. However, for specific applications, such as cargo delivery or final disposal of the functional material, irreversible photo-switches could be desirable.

The observation that an alanine-containing tripeptide is not able to self-assemble into a hydrogel, while its cysteine containing analogue does, suggests that a cysteine-to-alanine conversion, through a photo-induced desulfurization, could be a good strategy to disassemble a supramolecular nanostructured hydrogel in an irreversible manner. In literature, several reactions of desulfurization are reported in the context of native chemical ligation, but they typically require harsher reaction conditions or bring to the formation of several side products. Photo-activated desulfurization of cysteine in water is reported and applied to D,L-tripeptides that self-assemble into hydrogels, to convert them into analogues that do not gel. In this way, irreversible disassembly can be spatially-resolved by using a photo-mask (Fig. 1).

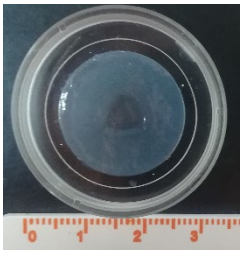

Figure 1: Photograph of a hydrogel irradiated with UV light using a triangle-shaped mask.

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OC-20

Self-Assembled nicotinic acid-based tetrahedral hosts as supramolecular catalysts: synthesis and first applications

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The field of supramolecular chemistry has its foundation in mimic the nature catalysts, in which microenvironments promote reactions with remarkable rate acceleration, substrate specificity, and product selectivity.[1,2] Drawing inspiration from early studies, self-assembled supramolecular hosts continue to capture a significant amount of interest toward their development as catalysts for increasingly complex transformations.[3]

This communication describes our recent developments in the application of new nicotinic acid-based tetrahedral hosts as catalysts for organic transformations. The monomer for the tetrahedral complex was synthesized by simple amide coupling reactions, and the tetrahedral catalyst was then self-assembled in the presence of gallium(III) (Figure 1). The formation of the tetrahedral structure was confirmed by NMR and MS analyses. The catalytic capabilities of the novel nicotinic acid-based tetrahedral host have been firstly studied by different uninvestigated examples of reaction. 1,3-dipolar cycloaddition and reductive amination are here reported. The mechanism of the reaction and the inclusion of reagents and products in the supramolecular catalyst have been studied and rationalized by NMR spectroscopy experiments and molecular modeling calculations.

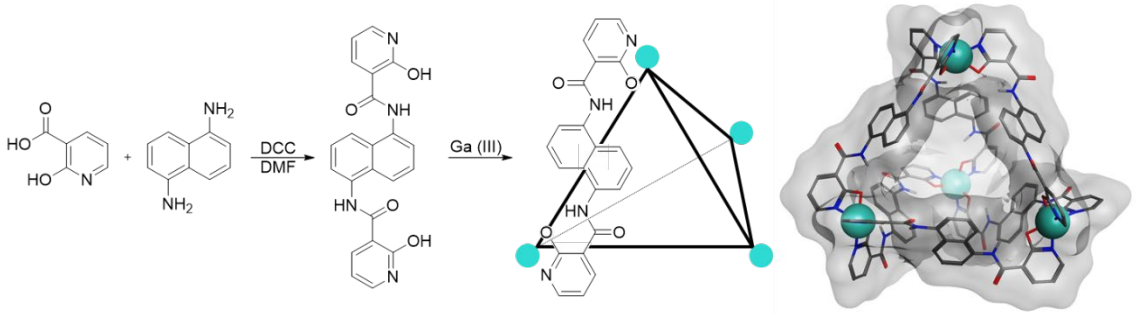

Figure 1: Synthesis and schematic representation of the nicotinic acid-based tetrahedral hosts.

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OC-21

How to Make Autonomous the Motions of a Chemically Fueled Molecular Machine

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In recent years, molecular machines (switches and motors) have been one of the hottest topic in chemical science. Applications of the principles and concepts developed in this field to future nanosciences and nanotechnologies are so promising that the related advantages for mankind are nowadays hardly imaginable.

Our main contribution to molecular machines is the use of the decarboxylation reaction of activated carboxylic acids as a source of energy for molecular motions. In particular, back and forth motions of an acid-base operated molecular machine (a switch) were demonstrated to occur on addition of such fuel acids with no need of subsequent addition of any counter-stimulus.[1,2,3] Our system was of inspiration to Leigh and co-workers who used the decarboxylation reaction of trichloroacetic acid as source of energy for the unidirectional operation of rotary and linear molecular motors.[4] However, a main drawback related to the use of our acids lied in the impossibility to use an excess fuel with respect to the molecular machine, which posed severe limitations to an "autonomous" operation of the machine itself.

In this communication we report that the use of a pre-fuel allows to overcome the above drawback. Indeed, we found that the slow and continuous transformation of the pre-fuel into the acid fuel triggers the back and forth motions of machine.[5] Importantly, the chemical reaction that transforms the pre-fuel into the fuel and the cyclic motions of the switch turned out to be matched in such a way that excess of acid (fuel) with respect to the switch (machine) is never present in solution. As a consequence, the machine does not require a reloading after each cycle, but repeatedly switches back and forth as long as fuel is present. This system represents the first example of a chemically fueled molecular machine that autonomously carries out a number of motion cycles with no need of supply of material or radiant energy during the operation.

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OC-22

Mech@nochemistry: an Appealing Marriage of Innovation and Tradition

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In the not too distant past, the design of a synthetic process was mainly focused on maximizing yields by neglecting all aspects related to safety and environmental impact. For this reason, in public opinion chemistry, pollution and disaster sound the same way. Nowadays, it is possible to improve a chemical process by using very advanced technologies switching from conventional heating to photochemistry. Unfortunately, solvents are still today the primary source of pollution and represent the most significant portion of chemical waste in an organic transformation. Toxic solvents can be replaced with greener one, but in the end, the problem remains unresolved. The most sustainable solvent is the solvent that is not used. Mechanochemical reactions, conducted by milling, grinding, or shearing, are rapidly emerging as an attractive, clean, energy- and materials-efficient alternative to conventional solution-based synthesis and are considered to be promising candidates in solvent-free synthesis. In this scenario, "*mechanical energy*" represents an alternative mean to activate chemical processes, which have not been widely explored yet. Moreover, the *mechanochemical activation* of organic synthesis allows overcoming some of the issues of classical synthesis in solution, enables the design of unexplored synthetic strategies, thus expanding the scope of chemical reactions to insoluble starting materials (Scheme 1). In this communication, the potential of "*Mechanochemistry*" applied to some significant reactions recently developed in our laboratories, and some of the related challenges will be discussed in detail.[1-3]

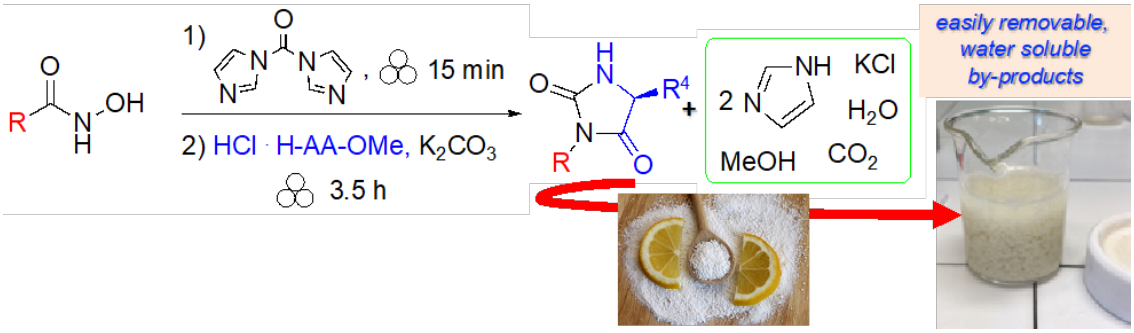

Figure 1: An eco-compatible synthesis of 3,5-disubstituted hydantoins by CDI-mediated "*mechanochemical Lossen transposition*".

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OC-23

Bio-based ionic liquids: synthesis and applications

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Ionic liquids (ILs) are salts composed by an organic cation and either an organic or an inorganic anion, which are in the liquid state at temperatures below 100 °C. ILs are characterized by unique physico-chemical properties such as high thermal stability, low combustibility, negligible vapor pressure, and favorable solvating properties for a range of polar and non-polar compounds.

Since the beginning of the century, ILs attracted growing interest and found use in a wide range of applications which span for instance from alternative reaction media for organic reactions, to materials science and biological science.

During the last ten years, questions related to the real green character and even sustainability of ILs have been posed. Therefore, a recent trend in the ILs field is to select more carefully the constituting ions looking with increasing interest to natural and bio-based options[1]. Replacement of petrol-derived ions with natural or bio-based ones, could represent a way to address both issues by reducing ILs toxicity and enhancing their biodegradability.

Figure 1: preparation of bio-based ionic liquids and potential applications.

Here we present our results in the preparation of ILs and protic ILs comprised of ions with natural origins (eg fatty acids, terpenoids, levulinic acid)[2-4].

Characterization of the obtained ILs as well as potential fields of applications explored thus far will be presented (Figure 1).

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OC-24

A new efficient flow chemical synthesis of thiophene-2-carboxylates

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Thiophenes, especially 2-carboxylate derivatives **4**, are key building blocks for synthesizing biologically active compounds used for the treatment of cancer, neurological, inflammatory and fibrotic diseases.[1,2,3] Synthetic methods for their preparation reported in literature[4,5,6] show significative drawbacks such as the use of expensive metal catalysts, harsh reaction conditions or restricted substrates generality.

Following our studies related to the reactivity of β-nitroacrylates,[7,8,9,10] we propose a new efficient, fast and general procedure to prepare the title compounds in good to excellent overall yields. The method is based on the reaction between β-nitroacrylates of type **1** and thioacetic acid using a continuous flow system. The three step synthesis involves: (i) promoter-free conjugate addition of thioacetic acid to the β-nitroacrylates (intermediate **2**); (ii) base-induced nitrous acid elimination (intermediate **3**) and (iii) acid-promoted cyclization-aromatization. The use of solid supported reagents avoids any intermediate purification and leads to the target compounds in a one-pot procedure that is applicable to a wide variety of β-nitroacrylates.

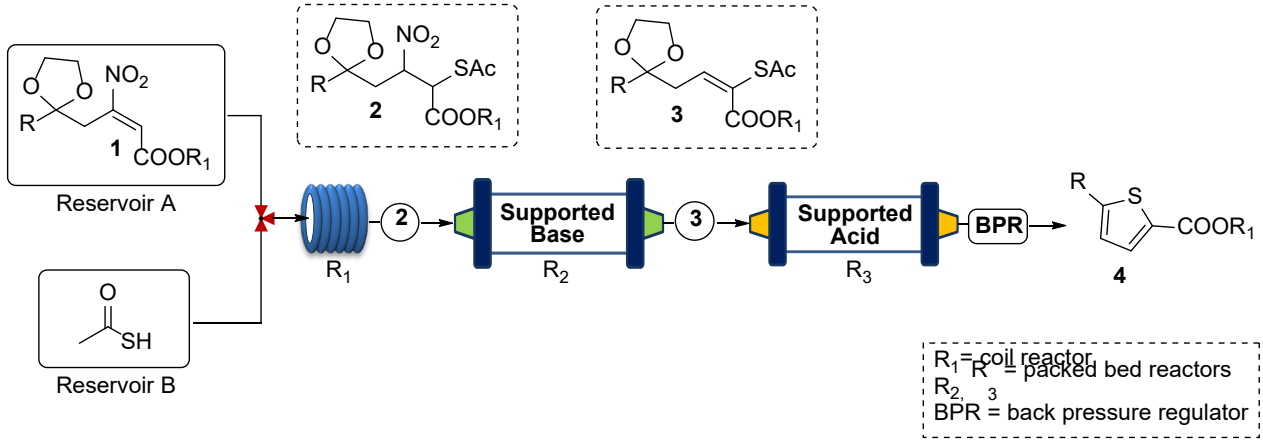

Figure 1: Continuous flow apparatus for the synthesis of 2-carboxythiophenes.

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OC-25

Multivalent effect of cyclopeptoid-iminosugar conjugates in glycosidase inhibition

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An attractive class of carbohydrate mimics, known as inhibitors of glycosidases, are the iminosugars, which are emerging drugs for an impressive variety of diseases[1] such as viral infections, diabetes, cancer, lysosomal storage disorders, cystic fibrosis.[2] Multivalent effect can be a powerful tool to improve the therapeutic potential of enzyme inhibitors, increasing binding potencies.[2] The first evidence of a significant multivalent effect in glycosidase inhibition was reported for a fullerene-based iminosugar cluster, which displayed a strong binding enhancement to α-mannosidase.[3] In 2014, the first examples of iminosugar clusters, based on cyclic peptoid core were reported.[4] In few years, a series of cyclic peptoid-based iminosugar conjugates has been evaluated and in 2016 the largest binding enhancement ever reported before was observed for 36-valent cyclic peptoid-based inhibitor, against Jack bean α-mannosidase.[5] More recently, the first high resolution crystal structure of Jack bean α-mannosidase in presence of the cyclic peptoid-based inhibitor has been reported (figure 1).[6] In order to rationally design more efficient multivalent inhibitors the synthesis of new cyclic peptoidic cores cointaining different number and position of propargylic side chains has been realized. Design, synthesis and biological activities will be discussed.

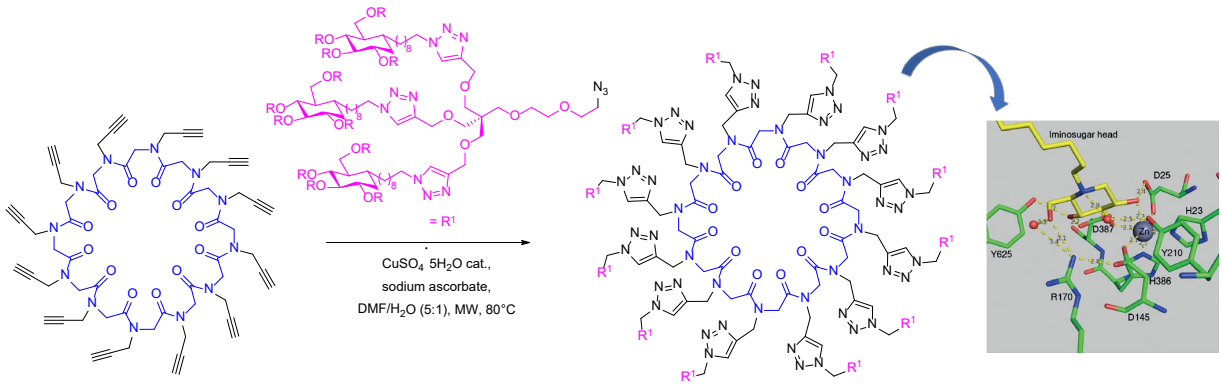

Figure 1: Cyclic peptoid-based imonosugar clusters.

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OC-26

PNA- and modified-PNA-based systems: applications to genetic diseases

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The development of Peptide Nucleic Acids (PNAs) and their analogs allows to produce very important tools for personalised therapies (Figure 1).[1] We have approached the design of new PNA structures using rational tools, such as molecular dynamics and metadynamics analysis;[2] synthetic modular strategies, have been developed enabling to rationally create PNAs with improved cellular uptake, biostability and recognition properties,[3] and the use of nanocarriers has created new possibilities for PNA cellular delivery.[4] Recently our group has designed PNAs and modified PNAs able to regulate gene expression as potential treatments for presently intractable genetic diseases.[5] In these applications, PNA can be designed in order to: a) target microRNA, short RNAs which down-regulate protein production through RNA binding and activation of the RISC silencing complex; b) target defective DNA by strand invasion, which has been show by P.Glazer and co-workers to enhance the homologous recombination process, thus allowing efficient gene editing.[6]

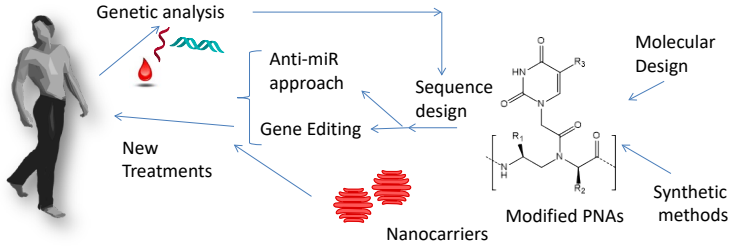

Figure 1: PNA-based personalized medicine for genetic diseases.

The design and synthesis of new PNAs for these applications will be described, and illustrated by examples of our recent work on the PNA-based treatment of cystic fibrosis (CF) by modulation of the Cystic Fibrosis conductance Transmembrane Regulator (CFTR) functionality by anti-miR PNAs. In this approach several key proteins, such as partially inactive CFTR or auxiliary proteins enabling the correct CFTR folding could be up-regulated.

Perspectives in the use of PNA-based systems and their conjugates with nanostructures for gene-editing will also be discussed. New strategies for co-delivery of different PNAs, and of PNAs and other therapeutic components (small drugs, RNA and DNA) using nanocarriers will be presented.

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OC-27

Synthesis of bisphenol neolignans as bioactive compounds

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Lignans and related compounds (neolignans, oxyneolignans,and mixed lignans) represent a large family of natural products, showing an interesting variety of structures and biological activities.

In recent years, two simple dimeric neolignans, namely the bisphenols magnolol and honokiol, have gained growing attention for their multiple biological activities. Both are natural products originally isolated from the bark of *Magnolia* spp., used in Japanese and Chinese traditional medicine for various diseases such as gastrointestinal disorders, anxiety, allergy, inflammation and others.

The biological properties of the two neolignans have been the subject of many studies, and a non-exhaustive list includes antitumor, antiangiogenic, anti-inflammatory, antimicrobial, antiviral, antioxidant and neuroprotective effects.[1] These properties prompted a number of research groups to synthesize magnolol and honokiol analogues as potential bioactive molecules.

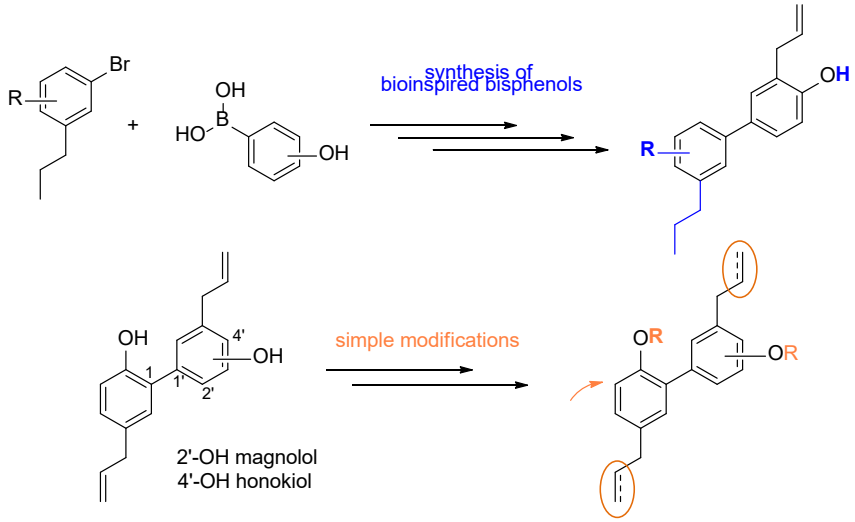

Figure 1: Schematic representation of the synthesis of bisphenol neolignans

The main objective of the present work is to obtain bisphenol neolignans inspired by honokiol and magnolol through Suzuki-Miyaura coupling or simple modifications of natural leads. The new compounds will be subjected to several biological evaluations, including the study of antiproliferative and hypoglycemic activity.

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OC-28

3D Printable biomaterials for tissue models, functionalization strategies

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In the last decades, the development of regenerative medicine was in charge of the design of biomaterials because of their capability to mimic the complex Extracellular Matrix (ECM) microenvironment. To develop new biomaterials able to mimic mechanical, morphological and biochemical role of ECM, natural and synthetic polymers can be synthetized and modified in order to control the properties of final hybrid biomaterial. The 3D bioprinting technology represents today a transformative approach to generate customizable living scaffolds. The design of new synthetic strategies aimed to obtain new nano- and 3D bioprintable materials (bioinks) biologically inspired, has high impact in different biomedical fields, from nanomedicine, to tissue engineering and cell biology studies [1,2]. Taking inspiration from ECM role in cell-cell and cell-ECM interactions, different functionalized hybrid biomaterials are needed.
We will present our results in the functionalization of biomaterial with complementary functional groups for chemoselective ligation, and the subsequent crosslinking, in order to generate bioinks for 3D-bioprinting with different architectures.

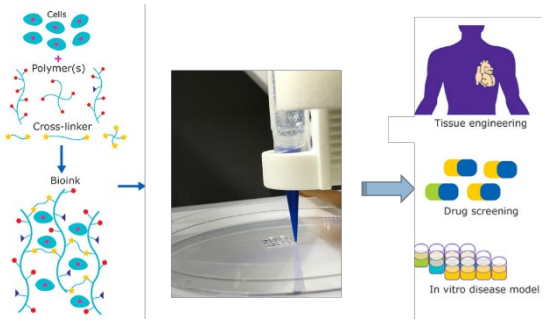

Figure 1: Bioinks and 3D bioprinting

Acknowledgments: Ministero della Salute, RICERCA FINALIZZATA 2016 RF-2016-02362946 (1/3/2018-28/2/2021) Theoryenhancing Projects. Title: Dissecting the link between pulmonary stromal changes and lung cancer progression for biomarkers discovery and therapeutic intervention

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OC-29

Photoluminescent decoration of iron oxide magnetic nanoparticles for dual-imaging applications

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The design of multifunctional nanosystems for dual- imaging applications has been largely investigated in order to improve cancer diagnosis and treatment by creating a synergism of different imaging techniques.[1] In this light a fluorescent magnetic nanoparticle has been synthesized from a nitrobenzofurazan (NBD)-labeled dopamine (DA) capping agent. The selective functionalization of dopamine with the photoluminescent moiety was achieved through a one-pot protection-functionalization-deprotection sequence leading to the DA-NBD derivative. Capping of iron oxide nanoparticles with DA-NBD and further embodiment into PLGA-b-PEG polymeric nanocarriers[2] produced an "onion-like" nanoparticle with latent photoluminescent properties. Indeed, disassembling of the polymeric layer fully restored the fluorescence of the capping agent. The controllable photoluminescence of the obtained multilayered magnetic nanoparticles encourages their use as multimaging systems for both optical imaging and magnetic resonance.

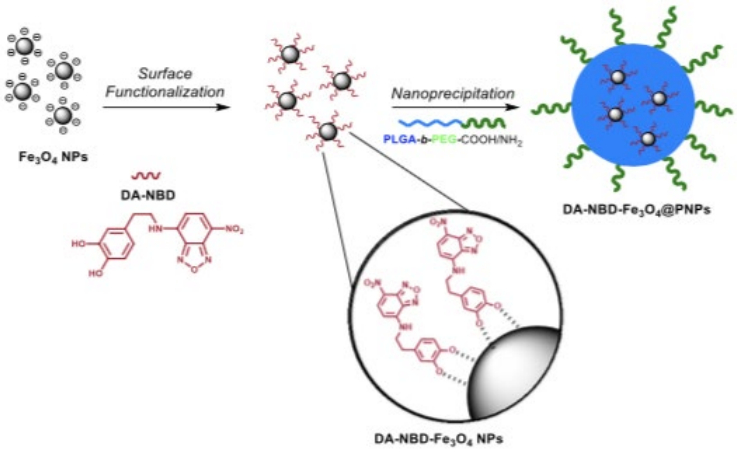

Figure 1: schematic representation of the nanosystem preparation.

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OC-30

Phosphorescent iridium-containing nanomicelles: synthesis, characterization and preliminary applications in nanomedical imaging

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Nanoparticle technology represents a great promise for drug delivery applications in nanomedicine due to its beneficial properties such as better encapsulation, bioavailability, controlled release, and a lower toxic effect. The opportunity to ingrate an imaging/diagnostic approach can produce important results due to the fast advance of imaging techniques, and the opportunity to map biochemical pathways in vivo at an unprecedented level.[1]

Among various imaging techniques, optical imaging has emerged as an easy, non-ionizing and flexible imaging modality. Recently, the use of phosphorescent transition metal complexes, such as cyclometalated Ir(III)-complexes, as intra- cellular sensors and bioimaging reagents has received great attention. This is by virtue of some of their unique properties, such as large Stokes' shifts, high quantum yields, long-lived phosphorescence, high photostability, and cell permeability, making them ideal candidates for bioimaging agents.

From a synthetic point of view, a straightforward approach is to conjugate the "diagnostic luminescent tag" onto the surface of the nano- systems used for drug delivery. We report here, our recent studies[4,5] about the potential of nanoscale phosphorescent iridium-containing micelles as a novel platform for the design of luminescent hybrid nano- particles with high contrast for optical imaging and nanomedicine applications (Figure 1).

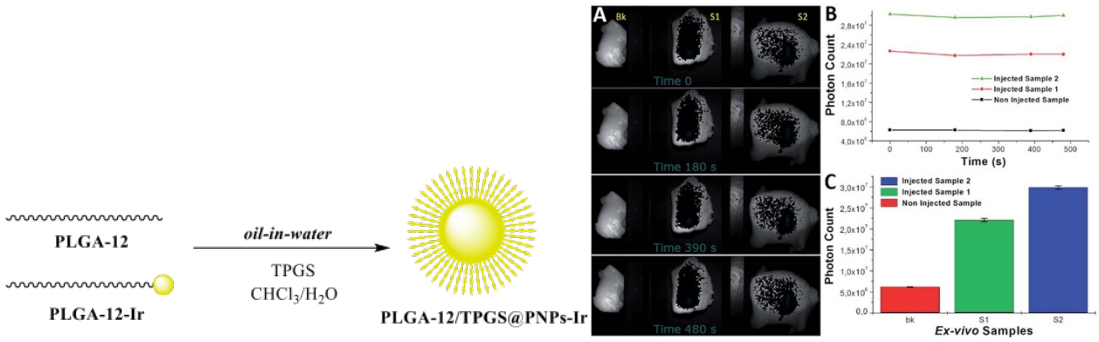

Figure 1: Schematic representation of luminescent nanoparticles

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OC-31

Photochemical angular-to-linear switch of the triterpenoid A,B,C ring system: discovery, mechanistic aspects, and biological translation

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Remodeling the carbon skeleton of natural compounds represents a powerful tool in organic chemistry to rapidly generate new natural-like libraries to study different biological processes.[1] Bond breaking and structure rearrangements are dominant features in the photoreactivity of 4,4-dialkyl-2-cyclohexenones that irradiated undergo to the lumiketone rearrangement giving bicyclo [3.1.0] hexenones as well demonstrated in Δ^4-cholesten-3-one (**1**).[2]

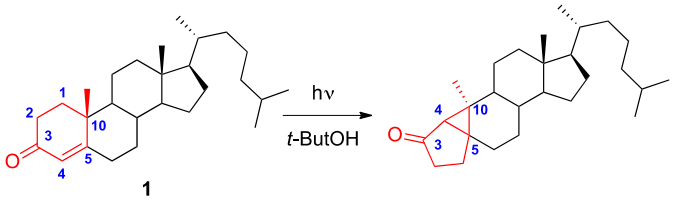

Figure 1: Lumiketone rearrangement of Δ^4-cholesten-3-one.

Pentacyclic triterpenic acids (PCTTAs) are a class of isoprenoids targeting different macromolecular endpoints, facing a "*biological renaissance*" after the discovery of two pre-clinical potent derivatives: the anti-viral bevirimat and the antioxidant inflammation modulator bardoxolone methyl. Compared to steroids, they have long been considered as "*chemical pariahs*" remaining ignored by the greats of chemistry and with their chemical space largely untouched. In search of new ideas to fertilize the field, we have focused our attention on the photoreactivity of the Δ^1-3-enones of easily available PCTTAs (**2**), that under irradiation gave a complete rearrangement of the A/B rings leading a new class of *iso*-PCTTA-3-enones (**3**).

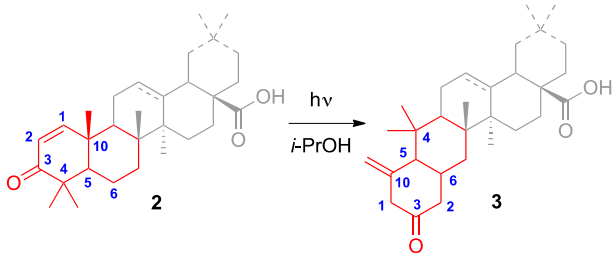

Figure 2: Lumiketone rearrangement of Δ^1-PCTTA-3-enones.

The mechanism of this remarkable rearrangement along with the scope, the limitations and the biological translation will be discussed.

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OC-32

A $TiCl_4$-based effective protocol for the synthesis of peptides

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The synthesis of peptides constitutes a major application of amide bond formation chemistry. The most commonly used methods for amidation involve the activation of carboxylic function through its conversion into acyl chloride, anhydride or activated ester or through the use of a coupling agent.[1-3]

Having recently developed a method for general amidation using $TiCl_4$,[4] we investigated the applicability of this approach in the synthesis of peptide systems. The synthesis of a selection of dipeptides by using $TiCl_4$ as coupling agent was designed.

Dipeptide systems were synthesized easily and in high yields through a $TiCl_4$-assisted condensation reaction between *N*-protected amino acids and amino acid methyl esters in pyridine that acts both as solvent and base.

The reaction was applied successfully to amino acids protected on the α-amino function with different protecting groups. The adopted experimental conditions allowed preserving not only the α-amino protecting groups but also the side chain protecting groups.

Instead, the pyridine-free treatment of dipeptides protected by acid-labile groups with $TiCl_4$ provided the corresponding dipeptides deprotected on the amino function that were also employed for obtaining tripeptide systems by using the $TiCl_4$/pyridine reagent system.

Furthermore, the preservation of the stereochemical integrity at the amino acid chiral centres has been verified.

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OC-33

Metal-free Chlorination of Toluenes and Aldehydes Mediated by Visible Light

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One of the most interesting research themes in modern organic synthesis is the development of new methodologies induced by visible light.[1] Photosynthesis can be described as the conversion of sunlight into chemical energy effectively employed to carry out chemical reactions, allowing the development of sustainable and efficient procedures. Solar energy is a promising tool as the green energy source because it is a reliable, renewable and valuable source of energy. For these reasons, a reaction that occurs by means of solar radiation is an ideal goal. Many photochemical reactions require complexes of heavy or rare metals such Ru and Ir, so a photoreaction that arises without any metal catalyst represents a great aim. In this context we have developed efficient metal-free, mediated by both sunlight and artificial visible light, procedures. By these methodologies was possible to chlorinate substituted toluenes to corresponding benzyl chloride[2] (Figure 1, path a) and aldehydes to corresponding acyl chloride, which were then converted, in one pot fashion, to esters, carboxylic anhydrides and amides[3] (Figure 1, path b).

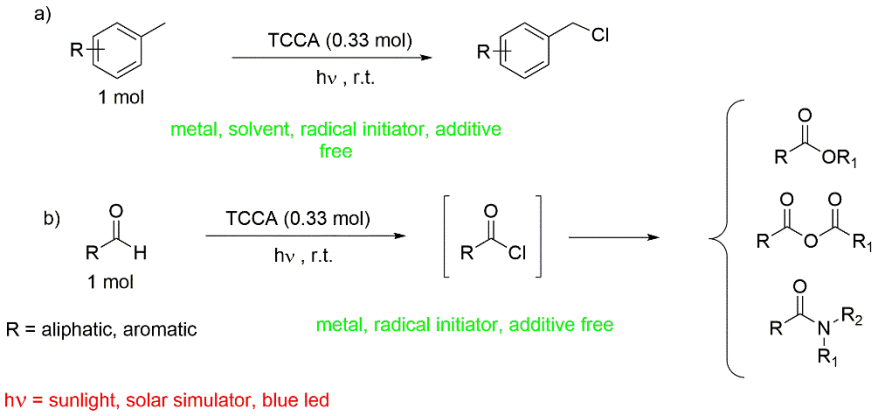

Figure 1: Chlorination of toluenes and aldehydes.

The methodologies have shown to have a big versatility and applicability on differently substituted toluenes and both aliphatic and aromatic aldehydes. The stoichiometric ratio of the reactants is optimal and the use of visible light as source of energy is very appealing from an ecological point of view. A key advantage of this process is that avoids the use of expensive and toxic transition metals-based catalysts. The reactions can be driven using different visible light sources, such as blue led, solar simulator and, more importantly, the sun. The procedures are operationally simple and the starting reagents as well as the visible light sources are inexpensive and readily accessible.

Acknowledgements: Regione Autonoma della Sardegna (CRP 72, "Capitale Umano ad Alta Qualificazione, 2015_L.R. 7/8/07, no. 7") and (RASSR81788,"INVITO A PRESENTARE PROGETTI DI RICERCA DI BASE -Annualità 2017")

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OC-34

New applications of ester surrogates in organic synthesis

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Masked esters/amides are scaffolds with great potential in organic synthesis.[1] Ester surrogates of proper acidity can be converted into enolates which react with opportune electrophiles. In the presence of cyclic azomethine ylides a [3+2] cycloaddition occurs thanks to the leaving group ability of corresponding heterocycle. We developed a convenient methodology to obtain bicyclic pyrazolidinones by using readily available reagents and working under mild reaction conditions.[2] Moreover, we worked out a facile synthesis of α-iminoesters derivatives by reacting nitrosobenzenes with masked esters. This scaffold is very useful, since subsequent reactions allow the elaboration to important intermediates frequently applied in organic synthesis.[3]

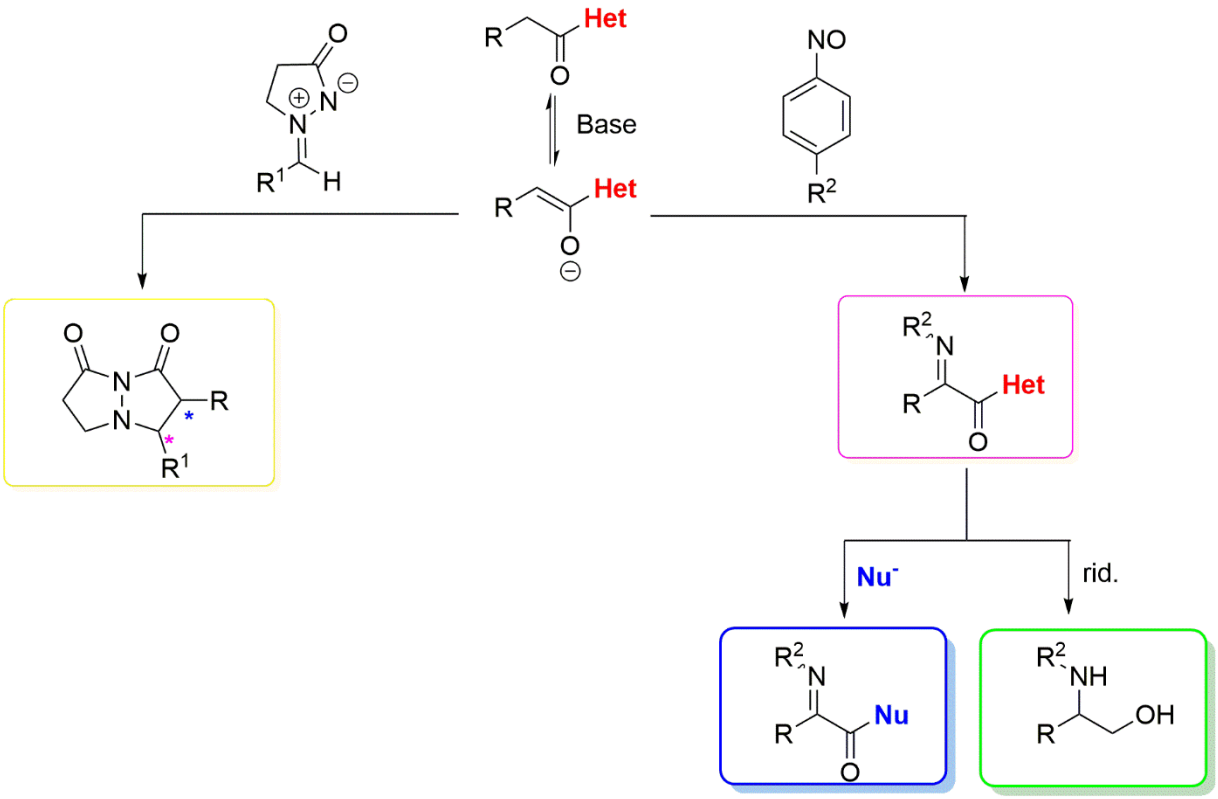

Figure 1: General scheme for the use of masked esters/amides.

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[3] Unpublished results.

OC-35

Structural modifications of glycoamino OPEs: synthesis and properties

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The synthesis of sugar-decorated molecular systems represents a significant tool in biotechnological, pharmaceutical and medical fields. In fact, conjugation with carbohydrates provides a guidance mechanism for sick cells, enabling drugs to arrive there with precision and act properly without (or with minimum) side effects.[1]

In the last years, the introduction of glucose moieties as chain terminations of Oligo(phenylene-ethynylene)s (OPEs) gave to this class of compounds one of the first applications in the bioimaging field. In fact, the joint presence of the hydrophilic sugar moieties, the hydrophobic conjugated system and the dimethylamino (**Figure 1**) group allows the permeation to the cellular membrane, showing their potential uses as cellular dyes.[2] Otherwise, their production of singlet oxygen opened the way in their use as Photosensitizers in superficial Photodynamic Therapy (PDT).[3]

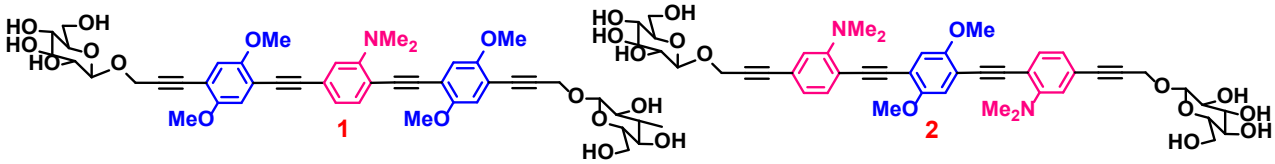

Figure 1

On the basis of these results, in order to explore the possibility to improve their use in this kind of medical procedures, the aim of our research has lately been to modify the structure of glycoamino-OPEs. First of all, the nitrogen quaternarization has been realized; as result, the presence of the new positive charges, joint with the peculiar structural features of compounds **1** and **2**, such as the biologically relevant sugar moieties and the flat aromatic cores, makes these luminescent dyes soluble in aqueous media and able to strongly interact with DNA.[4]

Moreover, the introduction of sugar terminations different from glucose (galactose, mannose, maltose) has been realized; among them, the functionalization with the disaccharide maltose has improved the water solubility of these compounds. Biological studies on the new systems are now ongoing. Finally, new strategies for the elongation and desymmetrization of the chain are underway, giving us the opportunity to extend their use in different fields: the anchoring of our biocompatible systems to upconverting lanthanide nanoparticles is one of these aims.

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OC-36

Synthesis of new oxadiazole derivatives as potent and selective FXR antagonists

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Farnesoid X Receptor (FXR) is a member of the nuclear receptor super-family and is highly expressed in liver, intestine, kidney, and adrenals. This receptor is involved in bile acid homeostasis[1] and governs lipid and glucose metabolism in the liver.[2] For all these reasons, FXR represents a promising pharmacological target in the management of metabolic disorders. In the last few years, several FXR agonists, belonging to steroidal and non-steroidal scaffolds, have been identified as potential leads for the treatment of metabolic disorders, with some of them progressed in advanced clinical trials for the treatment of patients with primary biliary cirrhosis (PBC) and non-alcoholic steatohepatitis (NASH). However, recently, has been discovered that the FXR gene ablation protects from liver injury caused by bile duct ligation (BDL), moving the attention towards the FXR antagonism in the treatment of obstructive cholestasis. As in the case of the agonists, the speculation around both steroidal and non-steroidal scaffolds led to the identification of several FXR antagonists. In order to discover novel non-steroidal FXR antagonists, we started from a recent work of Flesch *et al.*[3] where is showed that the structural fragmentation of GW4064,[4] a highly potent and selective non-steroidal FXR agonist, can lead to the shift of the receptor modulation from the agonism to the antagonism.

In particular, the replacement of the isoxazole ring in GW4064 with a 3,5-disubsituted oxadiazole led to compounds with different activity profiles, from agonism, partial agonism to antagonism. This is the case of compound **1**, a highly simplified GW4064 derivative, endowed with an antagonistic profile toward FXR. Therefore, we have decided to manipulate further the oxadiazole scaffold, modifying both substituents at C-3 and C-5, developing a small library of derivatives some of which characterized by a potent FXR antagonistic activity and promising pharmacokinetic properties.

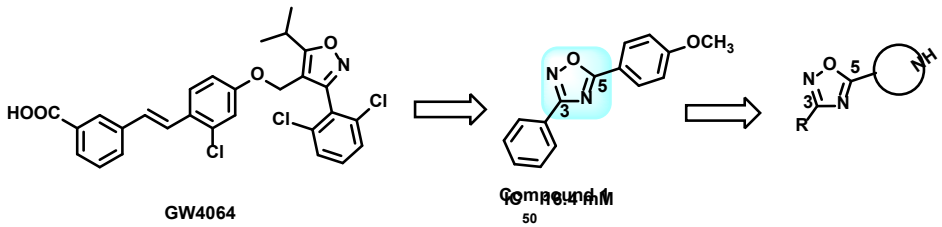

Figure 1. Fragmentation pathway on GW4064 in the identification of FXR antagonist

References:

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OC-37

Enantioselective Syntheses of Morpholino β-Amino Acids for the preparation of different nanomaterials

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Molecular self-assembly is a powerful approach for the building of novel supramolecular architectures and it is ubiquitous in natural world. In billions of years of evolution, Nature has produced a basic set of 'Molecular Lego', such as 20 amino acids, few nucleotides, lipid molecules and sugars as well as naturally modified building blocks apt to self-organize, thanks to weak and noncovalent bonds[1]. Nowadays, one of the most challenging efforts of scientist is to reproduce these organized architectures in laboratory for disparate applications, from biomedicine to electrochemistry and catalysis[2].

Here we reported the enantioselective syntheses of differently functionalized constrained morpholino β-amino acids (AAs). As β-AAs, they could confer a high stability in proteolytic environment and the presence of the oxygen on the ring, as H-bond acceptor, leads to conformational stabilization.

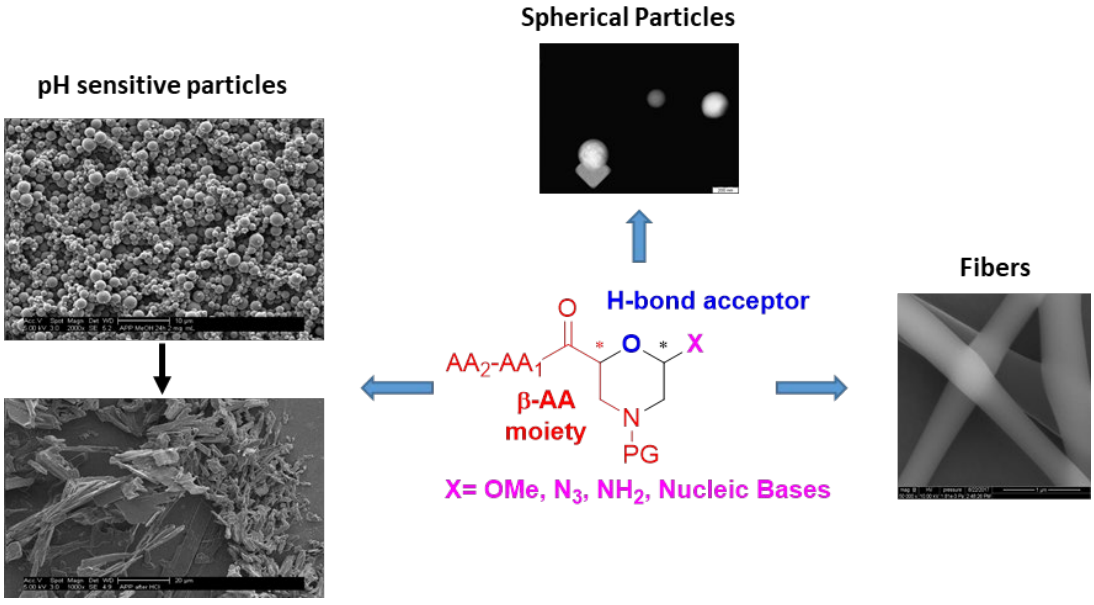

Figure 1: Nanomaterials obtained from ultra-short peptides containing β-Morpholino Amino Acids.

These new β-AAs have been inserted in ultra-short peptides. We found that, depending on the stereochemistry, the substitutions on C-2 and C-6, the protecting group on the *N*-terminus, they are able to form different type of nanomaterials. All these obtained nanostructures were characterized by DLS, TEM, SEM, FT-IR and NMR techniques.

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OC-38

Ionic Liquid Gels: Tunable and Multifaceted Materials

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Materials based on ionic liquids retain properties of solvent components, like low vapor pressure, high thermal stability and structure tunability. The latter allows changing properties of materials by making small variations in the cation or anion structure, opening the way to a plethora of different applications.

In this context, ionic liquid gels can represent a challenge especially if they are obtained from gelation of ionic liquid binary mixtures or of organic salts in ionic liquids.

In the framework of our interest in studying ionic liquids properties and applications, in the last few years, we have addressed our attention to the obtainment of ionic liquid gels.[1] We have deeply investigated their properties and analyzed the possible applications, preparing systems used for environmental preservation[2] or remediation,[3] as well as to avoid deterioration of materials.[4]

In this communication, a brief overview of results collected in the last few years will be presented.

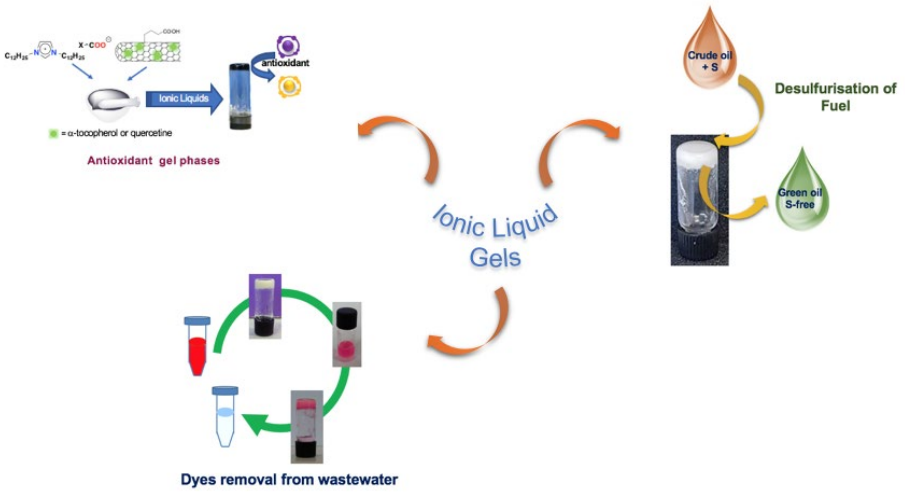

Figure 1: Applications of Ionic Liquid Gels.

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OC-39

Clay minerals: a challenge for chemists

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Halloysite nanotube, an aluminosilicate of the kaolin group, is an emerging nanomaterial which possesses peculiar chemical characteristics. By means of suitable modifications, such as supramolecular functionalization or covalent modifications, it is possible to obtain novel nanomaterials with tunable properties for several applications.[1,2] In this context the covalent grafting of suitable organic moieties on the external surface or in the halloysite lumen has been exploited to improve the loading and release of several biologically active molecules. The resulting hybrid nanomaterials have been applied as drug carrier and delivery systems, as fillers for hydrogels, in tissue regeneration and in the gene delivery field.[3] Furthermore the loading and release of specific molecules have been also investigated for environmental purposes.

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OC-40

Carbon Nanoforms-based Hybrid Catalysts

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Carbon nanoforms such as fullerene, nanotubes, graphene, nanohorns etc. are emerging as useful scaffolds in the preparation of last generation nanostructured catalysts,[1] due to a series of features comprising high chemical inertness under many conditions, thermal stability and mechanical resistance along with a lightness that other conventional materials cannot match. Moreover, in several cases, the use of these nanomaterials as support structures offers better performances than conventional supports.[2] On the other hand, CNFs are nanoobjects with well-defined structure and dimensions often displaying sharp size distribution, which allow for a homogeneous dispersion of the functionalities and active sites all over their surface, allowing obtaining reproducible hybrids with reproducible properties.

In the last recent years, our research group has investigated the use of different nanocarbons as platforms for anchoring catalytic moieties directly or for covalently linking dendrimers and polymers for the stabilization of palladium nanoparticles (Figure 1).

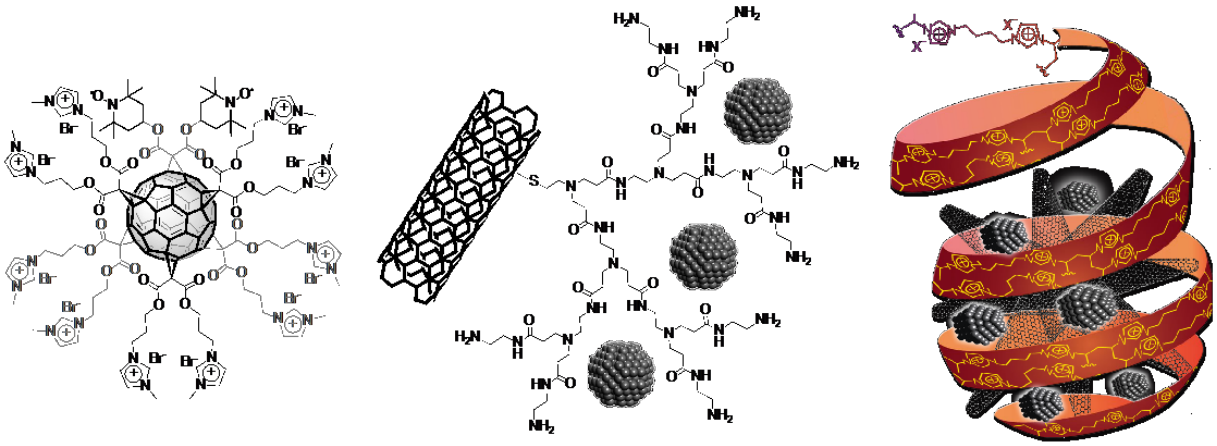

Figure 1: Examples of nanocarbon-based hybrid catalysts.

In such a way, the resulting hybrids have been successfully employed as recyclable materials in organocatalysis[3] as well as in organometallic catalysis[4] showing in some case synergistic effect or enhanced performances compared to other supported catalysts.

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OC-41

Graphene oxide composites-based filters for tap water purification

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Much of our tap water comes from rivers, streams, lakes and groundwater. These water resources are increasingly contaminated by discharges of chemicals from industries and urban areas, most of them not fully removed by basic water treatment. Traces of prescription medications, antimicrobial chemicals, pesticides, cosmetics, with suspicious or even proved toxic effects have been found in several EU water bodies, this calling for the development of new efficient, low cost and sustainable purification technologies. In the last years, due to their outstanding adsorption properties, high processability and versatile chemical modification options, graphene-based materials have emerged as the most promising nanomaterials for advanced water treatment technologies.

Here, we report the preparation of new polysulfone-graphene oxide composites (PSGO) specifically designed for the simultaneous filtration and adsorption of organic contaminants of emerging concern from tap water.[1] Stable fixation of GO and chemically modified GO on commercial PS membranes (Medisulfone®) is achieved by thermal activation under mild conditions.[2] The unique combination of numerous adsorption sites and interlayer enabled filtration provided by GO with the porosity of the PS scaffolds, significantly enhances the removal performances of several selected contaminants, including drugs, from tap water with respect to PS-only and to activated carbon (the industrial standard). Working mechanism, regeneration and GO release have been also investigated. The proposed approach is also exploited to revalue and reuse scraps of the industrial production of PS membranes (≈10% of the total year production, ≈1,5 tons).[3]

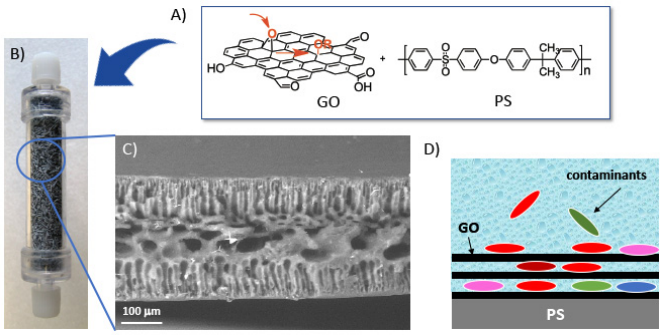

Figure 1: a) composition of the active materials, b) representative PSGO filter, c) structure of a PSGO composite membrane, d) working mechanism of a PSGO membrane.

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OC-42

Novel Hydrophobic Deep Eutectic Solvents (DESs) as water-immiscible H-bond-based solvents

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Deep Eutectic Solvents (DESs) are a class of liquids formed by H-bond interactions between two species: a hydrogen bond donor (HBD) compound and a hydrogen bond acceptor (HBA) compound. The intra- and inter-molecular H-bonds between the two species lead to a difficult regular crystal lattice formation, therefore to a liquid phase.[1]

DESs represent a novel class of green liquids for many reasons: they can be obtained from natural source molecules (NADESs: NAtural Deep Eutectic Solvents); they have low or absent vapour pressure; they are showing low toxicity; they can be easily recycled and reused; their synthesis does not involve any use of solvents because they are obtained by simply mixing and heating the two solid compounds. In addition to their ecological advantages, DESs have many practical advantages that promote their use in many topics such as: their active role in many chemical reactions (i.e. acid catalyst; reactants or reagents); their chiral organocatalytic properties in the case they are formed by chiral molecules,[2] the possibility of “out of the hood” procedures and so on.

Even if they are formed by H-bonds, their behaviour with water is peculiar and it depends on the chemical structures used as HBD or HBA and on their concentration: they can be dissolved in it, they can form clusters of HBD-HBA aggregates, they can be separated from it.[3]

In this work, we present the realization and the characterization of the properties of novel hydrophobic DESs.[4] We chose a set of water-miscible and -immiscible HBA and HBD molecules; this permitted us to define the role of the components for the proper development of H-bond-based mixtures that can result water-separable. We performed the characterization of the properties of these liquids (density, eutectic profiles), the water separation ranges and the phases contamination via Karl Fischer titration and with ^{1}H-NMR spectroscopy. Finally, we successfully performed the extraction of polluting phenol compounds and a dye from water with efficiencies >90-95%. Further experiments at pH = 2 and at pH = 9 showed these mixtures as well-separable and excellent extracting liquids even in these conditions.

The novel hydrophobic Deep Eutectic Solvents are promising tools as hydrophobic extraction agents and as hydrophobic green reaction media.

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OC-43

Light meets click chemistry: development of novel, photoactivable, 2,5-diaryl tetrazoles for labelling nucleic acids

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Click chemistry represents a useful method to create covalent bonds among two reagents, with high yields, fast reaction kinetic and under mild conditions. During the last years, this powerful strategy has been extensively employed in bioorthogonal ligation for labelling biological molecules (proteins, DNA, RNA), in order to monitor and understand the mechanism of many physiological processes [1].

Although targeting nucleic acids has become fundamental, currently just few click reactions are reported for this kind of application, such as azide-alkyne cycloaddtion (CuAAC) and inverse-electron demand Diels-Alder (IEDDA)[2].

However, these approaches present some limitations: azide-alkyne cycloaddition requires copper as a catalyst, which is not very compatible with systems and fluorescent probes must be used to observe product formation, so in order to overcome these drawbacks, we decided to employ a new strategy: recently, Lin and co-workers reported the use of a 2,5-diaryl tetrazole as photoactivable mojety for bioorthogonal ligation on proteins[3]. This compound, under irradiation, generate a 1,3-nitrile imine dipole (NI), an intermediate able to react with different types of dipolarophiles, to generate a fluorescent pyrazoline. Despite these promising properties, when this reaction is performed in physiological enviroment, many byproducts are formed and this represents a relevant impediment for previously described applications.

Here, we reported the synthesis of a library of 2,5-diaryl tetrazoles, properly functionalized in order to investigate how substituents can modulate NI generation and reactivity, in particular in aqueos solution.

In our preliminary studies, for each compound, we measured quantum yield of NI generation at 310 nm. Furthermore, photoreactivity was explored by irradiation of substrates in presence of various dipolarophiles and products distribution has been analyzed, in order to identify the best candidates for labeling of biomolecules.

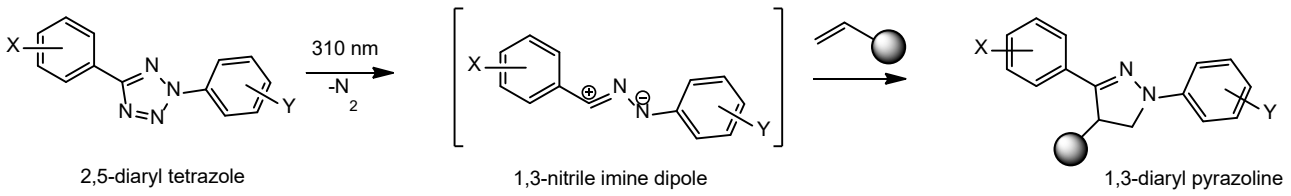

Figure 1: Photogeneration of 1,3-nitrile imine dipole.

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OC-44

Hydrogen Borrowing reactions in water medium

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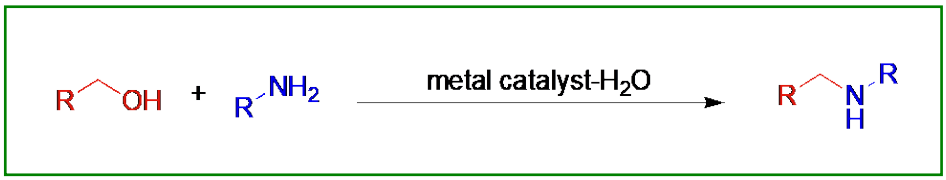
Hydrogen Borrowing (HB)[1] is very useful reaction to access amines and other molecules in a sustainable way in terms of redox and atom economy. The reaction mechanism basically involves the dehydrogenation of an alcohol to form the corresponding aldehyde, which reacts with a nucleophile such as an amine to generate an imine. In the same catalytic cycle, the hydrogen produced during the alcohol oxidation is involved in the further hydrogenation of the imine giving the alkylated amine as the reaction product. In spite of the excellent results in terms of efficacy and selectivity obtained with this methodology on different substrates, the high temperatures,[2] the use of not environmentally friendly solvents (i.e. toluene)[3] in the presence of noble metals based catalysts still represent important issues.[4] In order to find more sustainable conditions and to extend the reaction scope, we decide to investigate the possibility to carry out the HB reaction in water, in the presence of surfactants. The micellar environment worked well with standard Ru catalysts and, once the reaction conditions have been optimized, different secondary and tertiary amines have been obtained in good yields. An intramolecular HB cyclisation has been also successfully explored. The use of micelles has been extended as well to other reactions based on hydrogen transfer processes.



Scheme 1: Hydrogen borrowing using metal catalysts in H_2O.

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OC-45

Combining Safer Solvents Heterogeneous Catalysis and Flow Technology Toward Sustainable C-H Activation Methodologies

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In recent years C–H activation has proven to be a powerful synthetic tool for the direct and selective construction of C–C bonds.[1] Generally, metal-catalyzed C–H bond cleavage relies on the use of a homogeneous metal catalyst and it is often performed in petrol-based toxic organic solvents.[2b-c] Both aspects render the available methodologies for C–H activation/functionalization limited from the sustainability point of view.

In this communication, we report our results on the definition of novel protocols for C–H functionalization reactions based on the combined use of heterogeneous catalysts, safer biomass-derived reaction media and customized flow reactors. Our protocols have been specifically developed to feature advantages in terms of safety, waste minimization and minimal catalyst leaching in order to minimize purification procedures and preserve the catalyst stability and longevity.

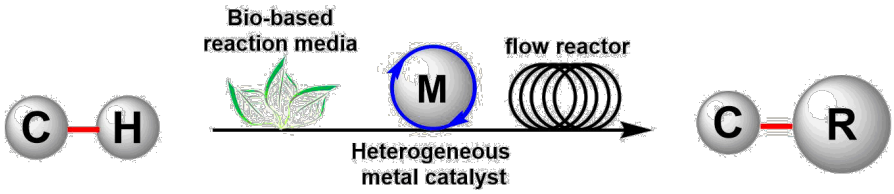

Figure 1: Our approach to sustainable C–H functionalization technology.

This contribution is part of our research program dedicated to the definition of environmentally and chemically-efficient procedures for C–H functionalization[2] in order to access highly valuable materials while minimizing waste production.[3]

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OC-46

Green approach to aerobic alcohol oxidation and transfer hydrogenation of nitro benzene derivatives

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Selective oxidation and reduction are fundamental organic transformations of critical importance to produces value-added products from simple organic molecules. The use of green reagents and the study of efficient procedures under mild conditions with cost-effective and environmentally friendly characters provide the reduction of cost and of environmentally hazardous by-products. Catalytic aerobic oxidation and transfer hydrogenation have recently become the center of research in organic synthesis and these synthetic methods enabled breakthroughs in product synthesis, materials science, and bioorganic chemistry.

The so called “enabling technologies” such as microwave, ultrasound, ball mill besides an efficient heat and mass transfer, may generate high energy micro-environments that strongly enhance reactivity and reaction rate. Herein we report the development of convenient and efficient strategies in the field of Pd catalysed aerobic oxidation of alcohol to methyl ester under MW irradiation. [1]
In the search of new procedures, mechanochemical activation was exploited to efficiently reduce nitro benzene and alkyl/aryl azide in a stainless steel jars without catalyst addition. Copper nanoparticles were also used in glycerol for efficiently reducing nitro benzene in a tunable way.

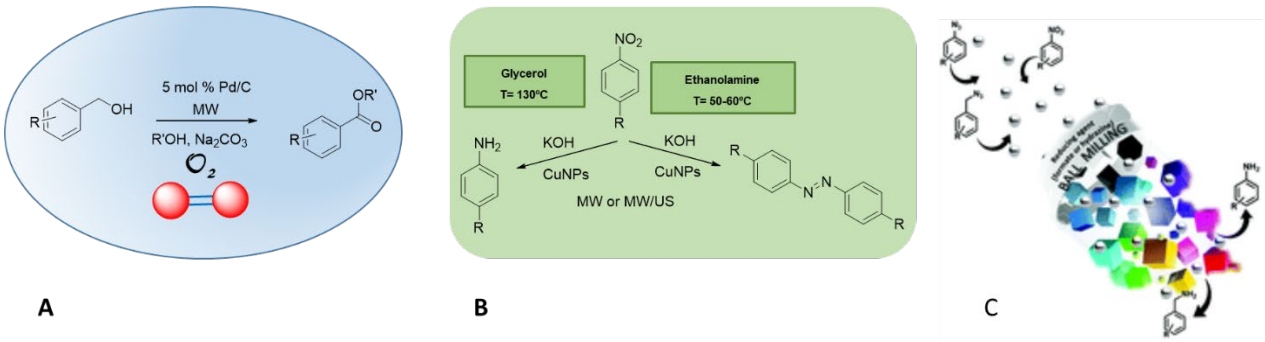

Figure 1: Schematic representation of A) MW promoted aerobic oxidation of benzylic alcohols B) tunable reduction of nitro benzenes with CuNPs, C) mechanochemically promoted nitro benzene and alkyl/aryl azide reduction.

References:

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OC-47

Highly selective toluene oxidation to benzaldehyde: a sustainable process

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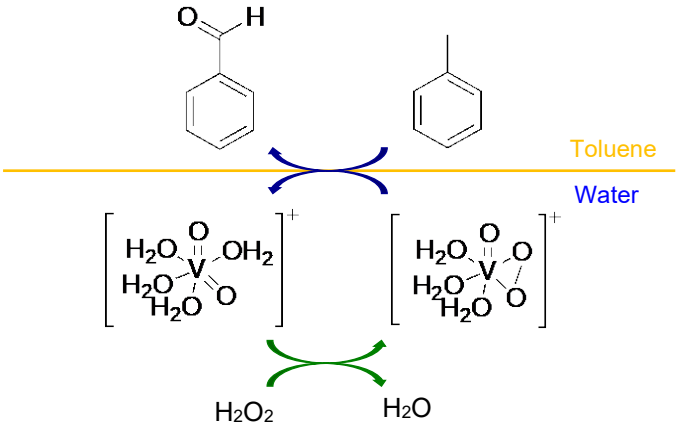
Selective toluene oxidation to benzaldehyde is one of the most challenging oxidation reactions because oxidation products such as benzyl alcohol or benzoic acid are produced in large quantity. Benzaldehyde is an important chemical intermediate in the manufacture of pesticides, pharmaceuticals, perfumes and food industry.[1] Traditionally benzaldehyde has been produced from chlorination of toluene on benzylic position followed by hydrolysis.[2] This process is not environmental friendly due to very harsh condition required and hazardous waste produced. Moreover, benzaldehyde obtained is not suitable for usage in pharmaceuticals and food application because of chlorinating contaminants. In the last years several attempts using homogenous catalysis have been done in order to obtain benzaldehyde from toluene in high selectivity and yield possibly with an environmental friendly process, but the results are still unsatisfactory mostly in terms of selectivity.[3]

In our previous work,[4] we found that monoperoxo V(V) species are able to perform oxidative bromination of toluene in the presence of hydrogen peroxide and a bromine source at acidic pH, one of the by products of the reaction being benzaldehyde.

In this contribution highly selective toluene oxidation to benzaldehyde using cheap and environmental friendly starting materials as ammonium vanadate, hydrogen peroxide and an inorganic salt with a sustainable process will be presented.



Scheme 1: Vanadium based system for toluene oxidation

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OC-48

Development and synthesis of simplified analogs of a bioactive natural polyketide

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Natural compounds are characterized by a considerable structural diversity that remain a key inspirational factor in the search for new therapeutic agents. In the marine environment, one of the largest and most interesting family of complex natural products is represented by polyketides.[1] These compounds are generally produced by specific enzymatic systems of microorganisms, bacteria and/or fungi, associated to marine invertebrates finding a wide range of pharmaceutical applications.[2] Marine polyketides are often built by polyhydroxy and polyoxy substituents in their structure with respect to sulphate and phosphate groups that are more rarely present.[3]

In this view, the recent isolation of the phosphoeleganin (**Figure 1**), a novel phosphorylated polyketide from the Mediterranean ascidian, *Sydnium elegans,*[4,5] characterized by a significant inhibitory activity against the human protein tyrosine phosphatase 1B (PTP1B), encouraged the development of several simplified analogs of the natural metabolite.

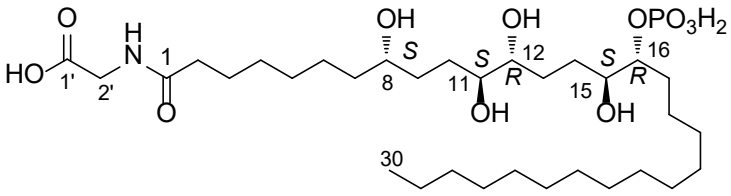

Figure 1: Structure of phosphoeleganin.

This research was aimed by the possibility to synthesize diastereoisomeric model compounds as profitable instrument to assign the absolute configuration of complex, acyclic and polysubstituted molecules. In addition, the synthesis and the pharmacological evaluation of these phosphorylated polyols represent the starting point to understand the essential structural requirements for the activity against PTP1B. In this communication, it's reported the synthetic protocol based on the combination of organic stereoselective reactions and chiral derivatization allowing to obtain a small chemical library of phosphorylated products.

References:

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OC-49

Spiropyrans for light-controlled delivery of Aspirin

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The study and development of new stimuli responsive nano-devices is an appealing research field[1,2]. In the nano-medicine realm, the possibility to create new smart platforms, for the selective delivery of active agents, using simple and bio-compatible external stimuli such as visible light is a promising field of investigation. For this purpose, we have designed and synthesised a smart platform based on a photo-switchable spiropyran (SP) taking advantage of its well-known capabilities to coordinate metal ions and form stable merocyanine (ME)-metal complexes[3,4,5]. We have selected Zinc(II) for its intrinsic properties and for its essentiality in the human being and Aspirin as the biologically active compound. We have planned the study of a ternary Visible light regulated system (figure 1) for the delivery of two active agents at the same time. The system has been investigated through spectroscopic techniques to define its features and its ON/OFF switching properties. Our results show the formation of the ternary system ME:Zn:ASA in solution and its Visible light photo-controlled properties paving the way for its use in the assembly of new devices for medicinal chemistry purposes.

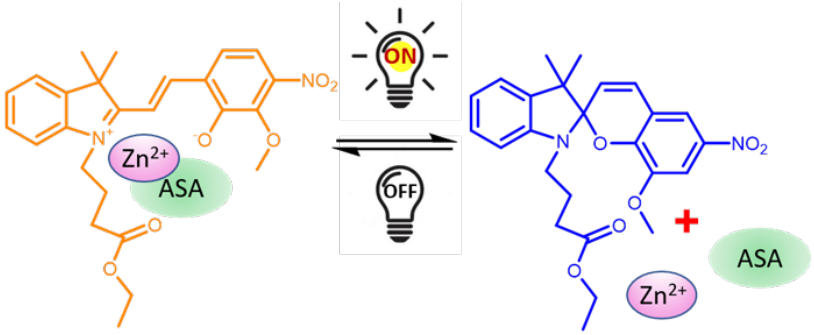

Figure 1: Schematic representation of the proposed drug-delivery system.

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OC-50

The interplay between NMR spectroscopy and molecular modeling: a powerful tool to investigate protein-glycoconjugate interactions.

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Protein–carbohydrates interactions set the basis of molecular recognition processes, indeed, they are involved in events like cell–cell interactions, signal transduction, inflammation, viral entry, and host bacteria recognition, thereby participating in disease, defense and symbiosis[1,2]. Understanding the roles that complex carbohydrate such as glycans plays in the aforementioned biological events offers opportunities for developing therapeutic strategies for the treatment of various diseases[3].

However, comprehending the dynamic of protein- glycoconjugates interactions represents a major challenge due to extreme structural complexity and variability of both mammalian and bacterial glycans, as well as the multivalent nature of their interactions with proteins[4,5]. The present work applies magnetic resonance (NMR) techniques to dissect the binding events occurring between sialylated glycans and their receptors, mainly through a ligand-based approach[6]. Furthermore, computational methods are implemented to provide a complete picture of protein- glycoconjugate binding mechanisms. With the raised awareness that the presentation of a glycan epitope can affect its recognition by proteins[3], the aim of the work is to rigorously define the bioactive conformation and binding epitope of the selected ligand for a deeper comprehension and modulation of biological processes closely related to biomedicine applications[7].

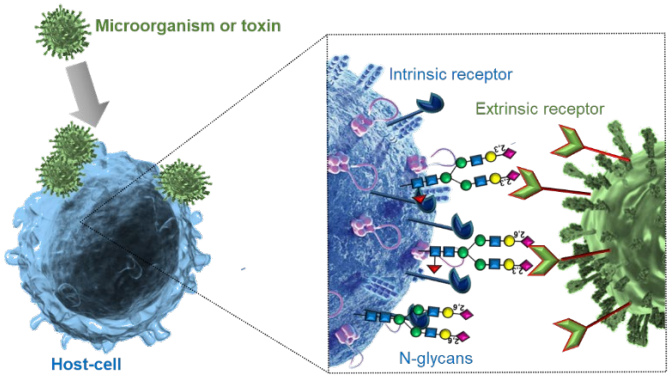

Figure 1: Molecular recognition of sialylated glycans by intrinsic and extrinsic receptors. Sia's can act as marker of self in the immune system, as such residues are absent in most microbes. On the other hand, host Sias are frequently exploited as attachment sites by pathogens including protozoa, viruses, bacteria, and toxins.

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OC-51

Degradation of Ochratoxin A in a wide pH range: experimental and computational study

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Ochratoxin A (OTA) is a potent toxin that is able to cause negative effects on animal and human health: it can affect a large variety of alimentary commodities such as cereals, wine, spices and animal feed.[1-2] OTA is considered one of the most important dietary risk factor, and a possible carcinogen to humans.[3] The behaviour of OTA in aqueous solutions in a pH range from 1.0 to 12.5 was studied by two independent spectroscopic techniques (UV-Vis absorption spectrophotometry and fluorescence spectroscopy) and Density Functional Theory (DFT) calculations. ωB97XD functional with Pople's 6-311++G(d,p) basis set were used in the DFT optimizations. Excitation energies were calculated by Time Dependent-DFT calculations. OTA shows three levels of proton dissociation in the pH range from 1.0 to 8.0 and under alkaline conditions, it displays degradation processes. Some of the reaction products were revealed at pH higher than 12, such as OTA with hydrolyzed lactone ring and ochratoxin alpha (OTα) with hydrolyzed ring. The product of lactone ring opening and OTα are less toxic than the protonated forms of OTA.

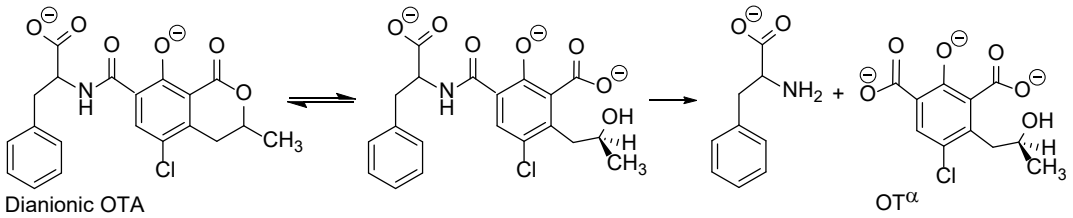

Figure 1: Ochratoxin A degradation steps.

However, the reversibility studies showed that the species obtained upon re-acidification depend on those initially present under alkaline conditions, that can differ depending on pH and storage time. Dianionic and trianionic forms of OTA at pH 12.5 in fresh solution return to the neutral form of OTA when the acidic conditions are quickly restored, representing again a hazard to humans. Conversely, OTα with the hydrolyzed ring does not return to the neutral OTA, but only to the neutral OTα. Irreversible fragmentation can be completed only after a very long time (more than one week) in strongly basic solutions. These conditions are necessary to achieve an effective OTA inactivation. The theoretical study suggests a reaction pathway that matches experimental data and facilitates their interpretation. Also, the computed absorption maxima of the intermediates along the suggested pathway resulted consistent with experiments.

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OC-52

Innovative synthetic approach based on the Native Chemical Ligation for development of new dual PET/OI peptide imaging probes

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Dual Optical/PET peptide imaging probes are considered as efficient tools for disease diagnosis and/or monitoring. Their preparation is still a challenging task due to the complicated synthetic protocols requiring fully-protected peptide segments (in solution) or the use of orthogonal protection groups (solid phase) to achieve the dual site-specific labelling. An advantageous strategy for peptide site-specific modification of unprotected peptide in solution, overcoming most of the above mentioned limitations, relies on the use of native chemical ligation (NCL)[1].

Targeting peptide AE105 (reported antagonist of uPAR) was synthetized using a solid phase peptide synthesis approach and functionalized with a cysteine to allow the condensation with AAZTA-C4-COOH, pre-activated as thioester with 2-Mercaptoethanesulfonic acid sodium salt (MESNA). After the reaction between the free thiol of the cysteine and the AAZTA thioester derivative, a rearrangement gives a stable amide bond between the N-terminus of the same cysteine and the carboxylic group of the arm of AAZTA-C4-COOH. The transposition of the chemical bond on the amine, made the thiol accessible to the subsequent reaction with a maleimide pre-activated fluorophore (i.e. cy 5.5). With this approach, it was possible to use the same thiol group of the peptide cysteine residue to achieve two chemoselective reactions in sequence, reducing significantly the formation of side products. The desired product (Figure 1) was afforded from preparative HPLC with a chemical purity over 95%. Final complexation with ^{nat}Ga was performed at pH 4, in order to evaluate the labelling efficiency with the metal and to demonstrate, by *in vitro* binding evaluations monitored by Flow Cytometry, that all the above modifications on the native peptide structure, did not affect the affinity for the uPAR receptor. Herein we developed a standard synthetic strategy to easily obtain a targeting molecule functionalized with a fluorophore to be employed in optical imaging applications and a cage, to allow the complexation with PETs radionuclides.

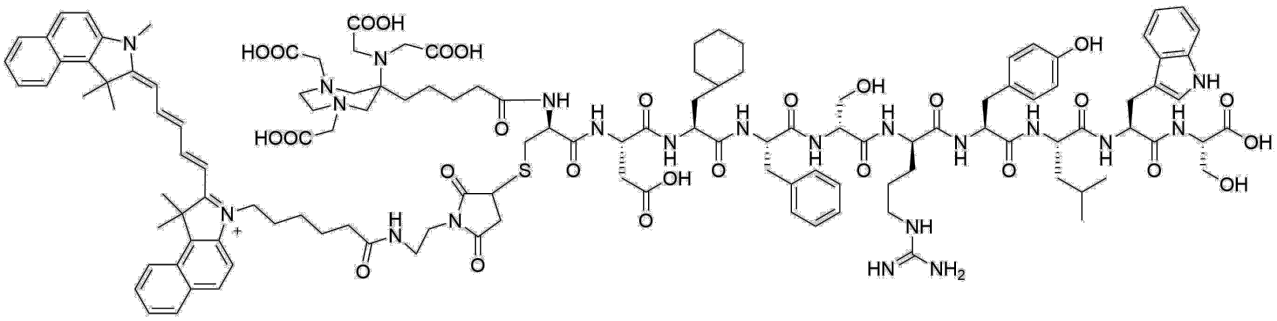

Figure 1: Chemical structure of AAZTA-C4-CO-Cys(Cy 5.5)-AE105

References:

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OC-53

α-Amino Aldehydes as Monomers for the Synthesis of Imine-/Amide-based Foldamer Structures

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Schiff bases (imines) are condensation products of primary amines with carbonyl compounds.[1] Natural and non-natural α-amino acids can be easily chemically converted into their α-amino aldehyde derivatives.[2] Surprisingly, despite of their potential interest, incorporation of these non-natural α-amino acid derivatives into peptide sequences has not been investigated so far.

We found that self-polymerization of different types of α-amino aldehydes provides formation of stable conjugated polymers, which display different colors and enhanced fluorescent properties depending on their length. In our strategy, a Boc-protected α-amino aldehyde was treated with trifluoroacetic acid (TFA) in dichloromethane to remove the Boc group. Subsequently, the resulting free amino group was able to react (in methanol solution) with the aldehyde function of another unit forming an imine bond. Repeating this reaction, leads to formation of different all-imide, linear and cyclic, polymeric structures. During polymerization, solutions of Nα-deprotected amino aldehydes rapidly change their color. This phenomenon was accompanied by the occurrence of fluorescence emission which indicated formation of extensive π–π backbone conjugation generated by the tautomeric equilibrium between the imine/enamine forms. Moreover, we found that in their polymerization short peptides based on Boc-Xxx-Aib-H (Xxx, chiral α-amino acid; Aib-H, α-aminoisobutyric aldehyde), when made to react as mentioned above, underwent repetition of the H-Xxx-Aib-H unit into a well-defined, chiral foldamer structure, where peptide bonds alternate with imine bonds (Figure 1, where Xxx is Val).

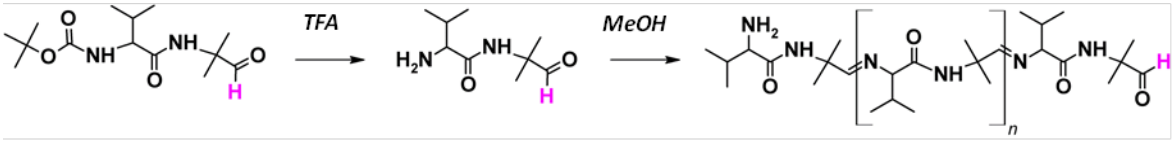

Figure 1: foldamers composed by alternation of amide/imide groups.

Finally, imine/amide polymer chains were analyzed in terms of H-Xxx-Aib-H release by virtue of the imine bond cleavage that we found to be prone to hydrolysis under mild conditions (37°C at pH 7.2). In particular, the polymer structure was, slowly and quantitatively, hydrolysed in 48 hours. These polymeric systems may represent an interesting platform in the pharmaceutical field for the time-controlled release, under nearly physiological conditions, of small-peptide drugs “masked” in large polymeric matrix.

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OC-54

Modified Carbon Nanoforms Systems for Asymmetric Catalysis

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In the last years the chemistry of carbon nanoform (CNFs) attracted attention in the field of catalysis, especially in the preparation of last generation nanostructured catalysts. Here are reported synthesis and catalytic applications of chemically modified nanocarbons such as C_{60}, carbon nanohorns and nanotubes The well-developed chemistry for CNFs functionalization allows operating multiple additions on their structures, and this can be exploited for sensibly increasing catalyst loading or for adding different functionalities.[1] In this way, it is possible to explore synergistic or detrimental effects due to the close proximity of catalytic moieties. In addition, the peculiar solubility profile of CNFs-derivatives may be used for recovering a homogeneous catalyst by simple precipitation.

Herein CNFs were functionalized with a series of chiral bisoxazoline (BOX) ligands, widely used in asymmetric catalysis.[2] In the case of C_{60}-adducts, these were functionalized in order to obtain mono- and hexakis-adducts as well as monoadducts endowed with ten 1,2-dimethylimidazolium moieties in order to get hybrid with a different solubility profile (Figure 1a). All the CNFs-BOX systems were employed, along with copper(II) salts as catalysts in asymmetric Henry and Diels-Alder reactions (Figure 1b). Furthermore, their ease separation from the reaction mixture allow for a facile reuse in multiple cycles.

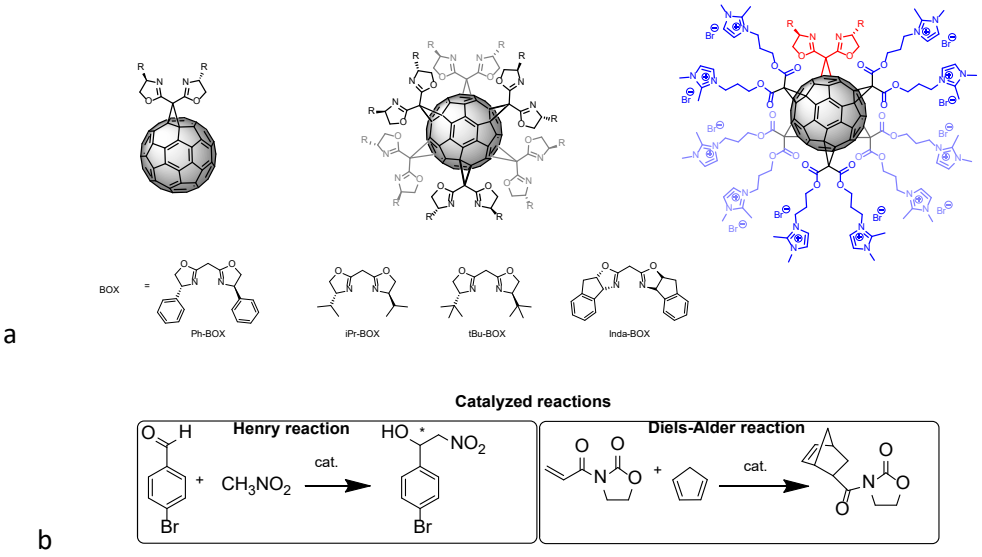

Figure 1 a) Fullerene and BOX based catalysts. b) Asymmetric Henry and Diels-Alder reactions.

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OC-55

Multimodal Functionalization of Nanoparticles for β-cells Imaging: new diagnostic tools for pancreatic regenerative therapies

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In the context of the H2020 project iNanoBIT, a new medical device able to produce insulin for diabetic patients will be experimented. The device, once implanted, undergoes vascularization. It will be filled with transgenic porcine beta-cells that produce insulin. The vascularization allows insulin to exit and nutrients to get into the device. The viability of the porcine pancreatic cell however must be monitored to program the substitution. For this purpose we generated nano-diagnostics with multiple functionalization, able to interact with a ligand of living beta cells and suitable for two different diagnostic protocols applicable on patients. Specifically, we selected peptide exendin-4 as ligand of the GLP1 receptor overexpressed at the surface of living beta-cells, 99-Tc for SPECT and/or 64-Cu for PET, and IRDye® 800CW a new optoacustic diagnostic protocol (MSOT). The multifunctional nano-diagnostics have been generated on FDA approved nanoparticles, obtained by aggregation of cationic and anionic biopolymers, chitosan and polyglutamic acid. We developed synthetic strategies to decorate chitosan and polyglutamic acid with functional groups suitable for chemoselective ligation of: i) exendin-4, ii) DOTA as chelator of 99-TC and 64-Cu, iii) IRDye® 800CW.
In order to perform the chemoselective ligation, exendine-4, DOTA and IRDye® 800CW were functionalised with the complementary chemoselective group. The obtained multifunctionalised nano-diagnostics were characterized for their capacity to interact with pancreatic beta-cell and are under evaluation for the diagnostic potential.

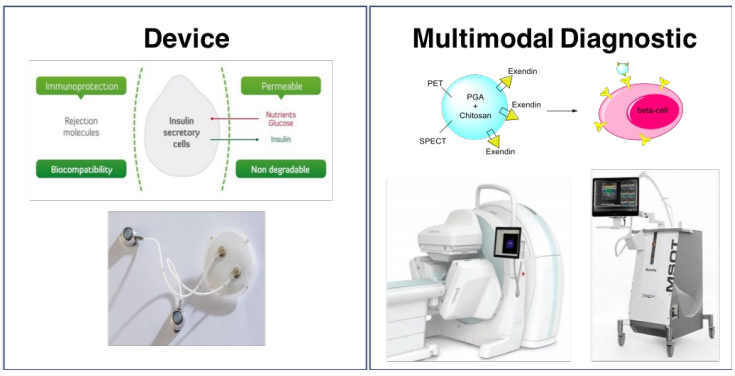

Figure 1: BioArtificial Pancreas Device and Multimodal NPs

Acknowledgments: this project is funded by H2020-NMBP-15-2017- GA-760986 — iNanoBIT (1.10.2017-30.9.2022) Integration of Nano- and Biotechnology for beta-cell and islet Transplantation. **http://inanobit.eu/**

OC-56

Site-selective immobilization of leptin on gold nanoparticles

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The immobilization of proteins on nanoparticles has a significant impact on the ultimate performances of the nanoconstructs.[1] Choosing correctly the most suitable conjugation strategy can be determinant to direct the interaction between protein-functionalized nanoparticles and biological systems, to achieve more effective diagnostic tools and eventually to improve the targeting efficiency of drug formulations based on nanoparticles.

Leptin is a non-glycosylated pleiotropic cytokine of 16 kDa that plays a key role in body energy homeostasis and is involved in cell differentiation and proliferation, immunity, and tumorigenesis.[2] Leptin is primarily produced by adipocytes, but carries out its biological action on many peripheral cell types, including on neurons after crossing the blood-brain barrier (BBB) through an active transport mechanism.[3] We propose that immobilization of leptin on nanoparticles may facilitate the understanding of some aspect of leptin biological activity, including receptor binding and transport across the BBB. This latter aspect is of special relevance in the context of targeted brain delivery.

In this contribution, we describe the site-selective immobilization of full length leptin on PEGylated AuNPs following a disulfide rebridging strategy.[4] We show that these nanoparticles target the leptin receptor in vitro significantly better than control AuNPs obtained via a more commonly employed, random immobilization strategy. Furthermore, leptin signaling via phosphorylation of the signal transducer and activator of transcription 3 (STAT3) is retained only when leptin is immobilized site-selectively on the AuNPs.

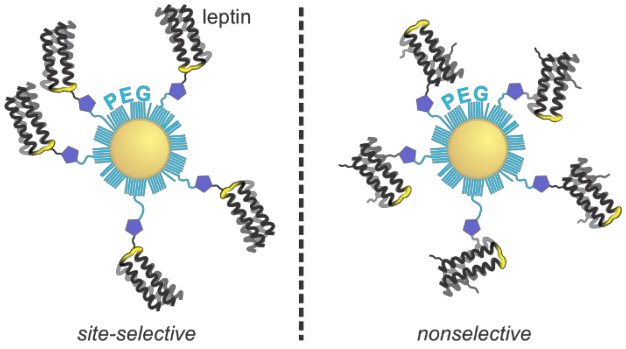

Figure 1: Site-selective *vs.* nonselective immobilization of leptin on PEGylated AuNPs.

References:

[1] C. D. Spicer, C. Jumeaux, B. Gupta, M. M. Stevens, *Chem. Soc. Rev.* **2018**, *47*, 3574-3620.

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OC-57

Engineered Polylactide-based Nanoparticles as Multifunctional Drug Delivery Systems

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In the last few years, engineered polymeric nanoparticles with tailor-made functionalizations have attracted increasing interest for drug delivery and tissue engineering applications.[1]

PolyLactic Acid (PLA) is frequently used for nanoparticles fabrication due to its biodegradability, biocompatibility and properties tunability by chemical modification.[2]

Herein, different synthetic strategies for the grafting of acetylene groups on PLA backbone will be discussed, leading to alkyne-grafted PLA derivatives, useful building blocks for click chemistry exploitations (Figure 1).[3] The reactions of "*clickable*" PLA derivatives with azide-functionalized compounds, such as polyethylene glycol (PEG), azide-fluor 545, folic acid and integrin-targeting RGD peptide, have been investigated to access a variety of functionalized polymers by Cu(I)-catalyzed cycloaddition reaction (CuAAC). Finally, different formulation strategies have been used to produce multifunctional PLA nanoparticles armed with targeting agent and fluorescent probes for biomedical applications.

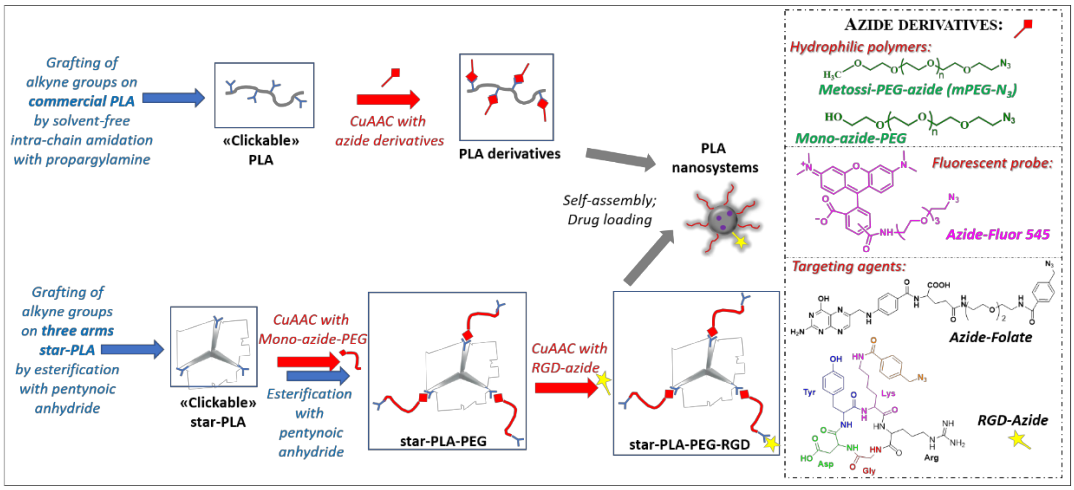

Figure 1: Overview of our recent exploitation of *click chemistry* for PLA functionalization.

References:

[1] V. Beer, K. Koynov, W. Steffen, K. Landfester, A. Musyanovych, *Macromol. Chem. Phys.* **2015**, *216*, 1774-1781.

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OC-58

Azomethine ylides: a powerful tool for Nanodiamonds-based contrast agents and drug delivery systems

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Specific and uniform surface functionalization of carbon nanomaterials is an intriguing topic. In recent years the research is focusing on Nanodiamonds (NDs), a promising nanometric scale carbon allotrope useful for technology (lubricants, abrasive materials...) and biomedicine (drug delivery, biosensors, imaging...) applications. Despite of inertness of its diamond-like core, NDs surface is reactive and it can be modified by covalent attachment of functional moieties. Whereas the linkage of oxygen, halogen or sulphur atoms is relatively simple to achieve, the covalent conjugation of nitrogen, with high yield, is a growing challange[1]. Amino groups are suitable for further functional moieties grafting, in order to link biomedical relevant molecules, such as antibodies, drugs or contrast agents. The already known procedures[2,3] provide surface functionalization by formation of pyrrolidine or tetrahydroindolizine rings.

In this work we modify NDs surface with amino groups, by means of 1,3-dipolar cycloaddition via amminoacids-generated azomethine ylides (Figure 1). The 1,3-dipoles irreversibly react with the partially graphitized surface, giving N-grafted nanomaterials, with the aim to obtain Nanodiamonds-based contrast agents (CA) and drug delivery systems (DDS).

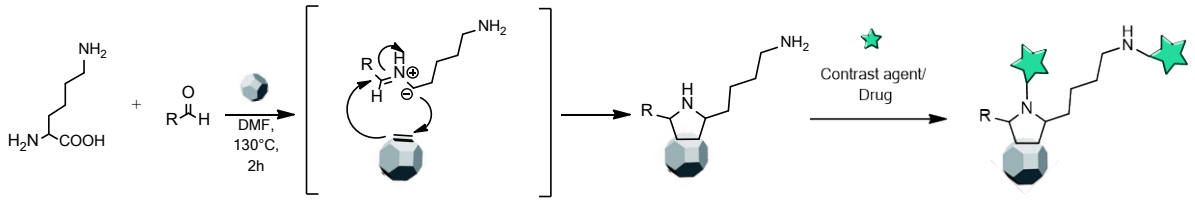

Figure 1: Synthesis of Nanodiamonds-based CA and DDS, by mean of prior surface ammination via a *in situ* aminoacid-formed azomethine ylide.

The surface functionalization was characterized by zeta potential, FTIR and thermogravimetric analyses.

The irreversibility of the process, which allows to carry out more than one functionalization step, together with the easiness of reaction preparation and the wide reagents choice, make 1,3-dipolar cycloadditions via aminoacids-generated azomethine ylides an interesting and flexible route for nanodiamonds surface N-grafting, in a non-destructive manner.

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[3] D. Lang, A. Krueger, *Diam. Relat. Mater.* **2011**, *20*, 101-104.

OC-59

N-Heterocyclic Carbene (NHC)-Organocatalyzed kinetic resolution of biologically active Biginelli compounds

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Dihydropyrimidones (DHPMs), well known as Biginelli products, can be simply synthetized through an efficient multicomponent reaction using highly accessible aldehydes, active methylene compounds and (thio)ureas in acidic medium.[1] In recent years, DHPMs have attracted considerable attention, thanks to their several biological and pharmaceutical applications. Optically active DHPMs represent challenging synthetic targets accessible through direct asymmetric synthesis or chemical resolution processes.[2] Kinetic resolution constitutes a useful method in asymmetric synthesis representing one of the most widely used industrial procedure for the preparation of chiral compounds.

In the present work, optically enriched DHPMs have been synthetized through N-heterocyclic carbene catalysed kinetic resolution of racemic Biginelli compounds.[3]

The aim of this study was to carry out a stereoselective N-3 acylation of racemic DHPMs. The reaction promoted by chiral N-heterocyclic carbene catalyst (NHC) in oxidative conditions leads to optically active N-acylated products and enantioenriched unreacted DHPMs (Figure 1). Reaction conditions were optimized to reach satisfactory level of conversion (up to 45%) and stereoselectivity (up to 80:15 er).

To the best of our knowledge, this work represents the first example of kinetic resolution of amides and in the future could be extended to other biological and pharmaceutical interesting amide compounds.

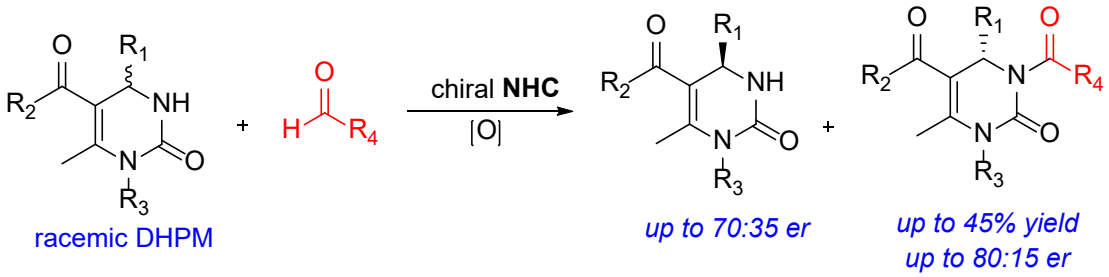

Figure 1: Kinetic resolution of DHPMs promoted by NHC in oxidative conditions.

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OC-60

High Enantioselection Performances of Inherently Chiral Ionic Liquids with Axial, Helical and Central Stereogenicity

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We define as "inherently chiral" functional materials the compounds in which the stereogenic scaffold responsible for chirality and the molecular group responsible for their specific properties coincide.[1,2] This structural combination results in outstanding enantioselection properties, much higher than those exhibited by compounds in which stereogenic unit and functional group are independent moieties. The validity of this concept was proved in the design of high symmetry (D_n) macrocyclic oligo-thiophenes in which chirality results from a tailored torsion of regio-regular thiophene sequences. They were employed as highly stereoselective electrode surfaces.[2]

Here we report the results of the application of the inherent chirality concept to Chiral Ionic Liquids (CILs). We checked first the effects produced by a stereogenic axis and then extended the research to Inherently Chiral Ionic Liquids (ICILs) based on helices and stereocenters.

In our project the ICILs based on a stereogenic axis are characterized by suitably substituted 3,3'-bipyridinium (**1**) or 1,1'-bibenzimidazolium (**2**) atropisomeric scaffolds.[1] Considering that pyridinium and imidazolium groups are classical IL functionalities, and that a pair of them are involved in the hindered rotation around the interanular bond, responsible for chirality, it is evident that the attribute of ICILs to these compounds is correct. Aza- and di-aza-hexahelicenium cations (**3**) also fulfill the requirements to be defined as ICILs, since the pyridinium unit is essential part of the helical scaffold. As for ICILs based on stereogenic centers, we have planned the alkylation of configurationally stable phosphanes (**4**) like DIPAMP. (Figure 1).

Synthesis and characterization of all new ICILs and electrochemical enantiodifferentiation performances of the antipodes of several chiral probes are discussed in comparison with the behavior of CILs designed according to classical strategies (**5**).[3]

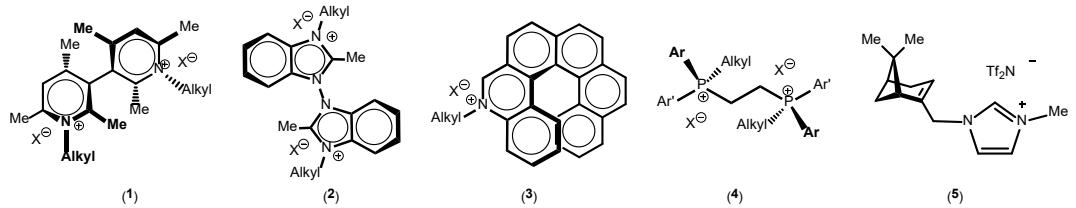

Figure 1: Prototypes of inherently chiral organic salts characterized by stereogenic axis (**1**,**2**), helix (**3**) and stereocenter (**4**), and example of a new traditionally designed CIL (**5**).

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OC-61

DFT/NMR approach for the configuration assignment of groups of diastereoisomers by the combination and comparison of experimental and predicted sets of data

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DFT/NMR approaches have been widely used for the configuration assignments of organic compounds generally comparing one cluster of experimentally determined data (e.g. $^{13}C/^{1}H$ chemical shifts) with those predicted for all the possible theoretical diastereoisomeric species.[1,2] However, more than one set of experimental data, each related to a specific diastereoisomer (e.g. pairs, triads, tetrads etc.), may occur in some specific cases. Accordingly, the accurate configurational assignment of each species can be obtained combining the experimental/computed data in different ways.[3]

We here introduce a novel straightforward methodology based on the simultaneous analysis, combination, and comparison of all the available sets of experimental/calculated $^{13}C/^{1}H$ chemical shifts for the configuration assignment of groups of diastereoisomers. This method relies on mathematical manipulations on both the experimental and predicted data, avoiding errors arising from the calibration procedures and, as a consequence, strongly reducing systematic errors. Also, we noticed a remarkable benefit in simultaneously accounting and comparing all the experimental/calculated chemical shifts: specifically, aligned values drive the results towards the correct assignment and, accordingly, disarranged data aid in excluding incorrect stereoisomers.

As a proof of concept, we have applied this methodology on a tetrad of synthesized cladosporin diasteroisomers (cladologs),[4] showing the identification of the correct correspondences between experimental/calculated sets of data.

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OC-62

Synthesis and antitumor activity of polybrominated C_{15} acetogenin derivatives.

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C15 acetogenins are typical metabolites from red algae belonging to the genus *Laurencia*. They are usually halogenated substances including one or more cyclic ethers with different ring sizes and an enyne or a bromoallene terminal group.[1]

In 1990 we isolated a new member of this class of substances from the encrusting sponge *Mycale rotalis*[2] (**1**, Figure 1). This finding was rather unusual and was explained by hypothesizing that the sponge could preferentially grow on a *Laurencia* species engulfing it entirely.

Our group is currently actively involved in the search of new antitumor lead substances either of synthetic or natural origin. In this context, the effect of compound **1** on the proliferation of human tumor cells such as melanoma (A375), adenocarcinoma (HeLa), breast cancer (MCF-7) and human normal dermal fibroblasts (HDF), was tested. It showed a good activity on Hela and A375 cell lines as well as pro-apoptotic ability. Based on this result a number of variously functionalised and degraded derivatives of **1** (Figure 1) were prepared and tested. The chemistry developed, and the preliminary biological results obtained will be presented in this communication.

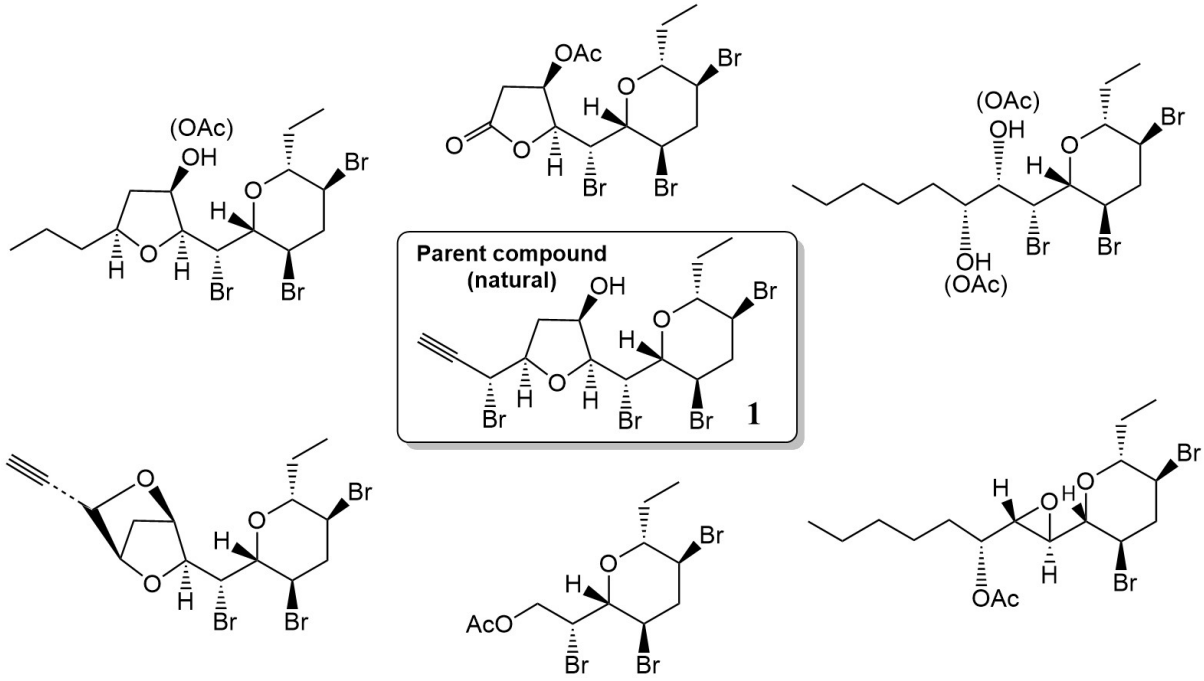

Figure 1: Polybrominated C_{15} acetogenin derivatives.

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OC-63

Folate-Tannin Microcapsules for Oncologic Theragnosis Applications

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Cell surface receptors for folic acid are generally overexpressed in human cancer. In several studies folate has been used as a targeting moiety of various anti-cancer agents to avoid their non-specific attacks on normal tissues as well as to increase their cellular uptake within target cells.[1] Tannins possess several relevant biological activities such as antioxidant and anti-inflammatory properties, anti-mutagenic and anti-carcinogenic activities, prevention and delay of cardiovascular diseases, increase in lifespan and retarded the onset of age-related markers. Such activities are due to their specific chemical and physical properties as significant chelating and stacking capacity.[2] In addition, the polyphenolic character of tannins displays further functionalisation possibilities.

Tannins thus represent a very versatile class of compounds with respect to the use of both as substrate of functionalisation[3] and as shell material in the generation of microcapsules for pharmaceutical and biomedical applications.[4,5] Consequently, the folate functionalized tannins represent one of the most plausible ideal candidates for the development of a new class of microcapsules for oncologic theragnosis.

In the present study these unique combinations of interesting properties of tannins were exploited in the synthesis of folate-tannin moieties, which have been used as shell material for the generation of gadolinium reinforced folate-tannin microcapsules containing 5-fluorouracil for cancer therapy and diagnosis purpose.[6]

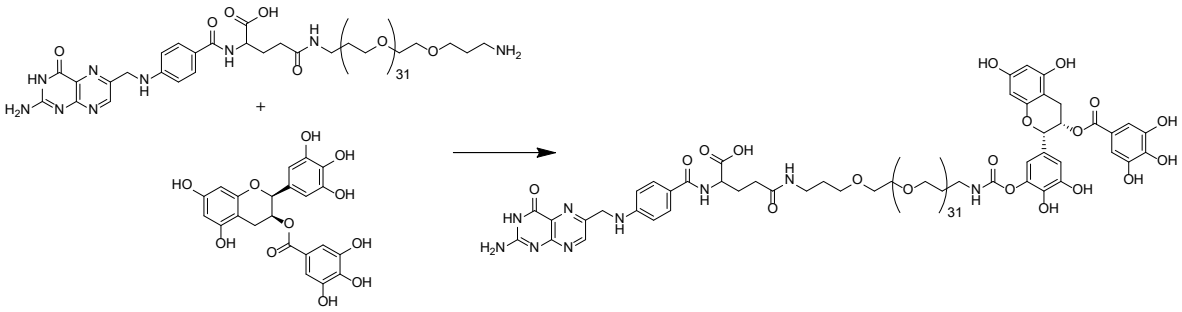

Figure 1: Folate-tannin synthesis using PEG-ylated folic acid and epigallocatechin gallate.

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OC-64

Sweet and Smart Nanovectors for Live-Cell Drug Delivery and *in vivo* Bone Targeting

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Surface functionalized nanoparticles (NPs) are gaining great importance in the biomedical field due to the emerging role of nanomedicine. Nanotechnology is orienteering towards the development of nano-medical devices as drug delivery and diagnostic systems with improved properties and reduced side effects if compared to traditional medicine. The presence of a specific molecular entity (ligand) on the NPs' surface, can target the nanodevice to specific tissue; this can be used for direct tumor targeting, exploiting its overexpression of specific receptor recognized by specific ligands, or can allow to reach biological districts, such as bones, for which drugs usually show a very low tropism. In this context, we have realised two different types nanoparticles where sugar moieties play different crucial roles.

The first type is a sugar decorated polymeric NP loaded with cytotoxic drugs, designed to engulf immune cells and use them as Live-Cell Drug Delivery systems.[1,2] As polymer we selected poly(lactic-co-glycolic acid) (PLGA), and for the surface decoration we used different sugars and sugar-dendrimers, that exploit specific receptors on cell surface. In this context we adopted a chemoselective method applied on a free sugar, that can be extended to the conjugation of any sugar/oligosaccharide moiety bearing a reducing end.[3]

The second type consist in Cellulose-Nano-Crystals (CNCs). We differently functionalised the surface of these NPs with Ca++ chelating moieties (sulfates, pyrophosphonates and carboxylates) to address bone tropism. On these NPs we carried out a careful evaluation of the biodistribution, accumulation and clearance in filter organs of CNCs in mice, using fluorescent labelled CNCs detectable by in vivo Optical Imaging2.[4]

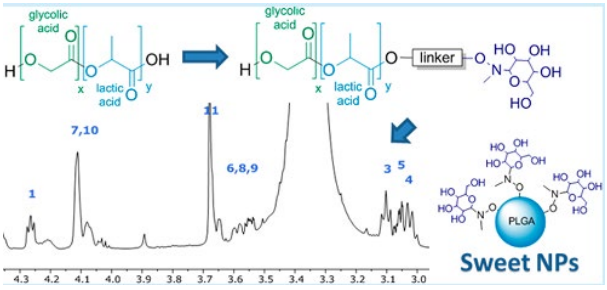

Figure 1: Derivatization and characterization of PLGA-sugar derivatives.

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OC-65

Stable and Water-Dispersible Quantum Dots: Modular Fluorescent Tools for Bioimaging Applications

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Quantum dots (QDs) are luminescent semiconductor nanomaterials displaying a wide range of unique electro-optical properties.[1,2] The decoration of QDs with synthetic organic molecules is fundamental since it gives these nanoparticles excellent stability in aqueous media, which is the basis to rely on for any biological applications.[3] Also, by taking advantage of the functional groups of the organic layer, further functionalization of the QDs opens up a virtually-unlimited range of bio-related opportunities. In other words, water-dispersible QDs are extremely versatile and can be used as stable and efficient probes for bioimaging, diagnostic and drug delivery combining the optical/electrochemical properties with the biological function of a chosen biomolecule.

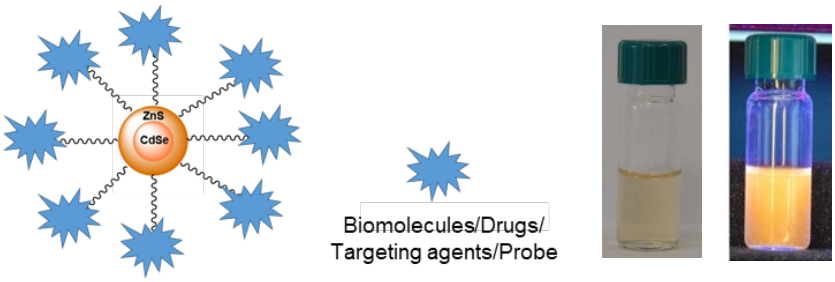

Figure 1: a) Schematic representation of conjugated QDs; b) DHLA-EDADA coated CdSe/ZnS QDs water dispersion under white and UV light.

The presentation will give an overview on the enormous potential of water-stable QDs by reviewing the most impactful papers in the field, along with the most recent results of our group. The attention will be focused on the applications and advantages of water-dispersible QDs, such as bio-imaging, where the QDs serve as imaging tag while the attached molecule may serve as a targeting agent. Also, the conjugation of QDs with biomolecules will be taken into consideration. Such conjugates can be used as probes toward specific biological mechanisms in immunoassays and live-cell imaging as well as in a variety of other fluorescence-based detection assays, which could give the opportunity to explore further certain biological functions.

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OC-66

Macromolecular and nano-supported antioxidants for practical applications

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All organic materials exposed to air will degrade over time as function of chemical structure, use and storage. In addition, the products of certain degradation processes pose a potential safety risk if present at high levels. Polyolefins and ethereal solvents, two very common classes of organic materials, require special handling and storage considerations, and the addition of stabilizers to inhibit or retard thermo- and/or photo-oxidative degradation. Several additives are low molecular weight polar compounds, such as hindered phenols and amines, which however are structurally different from the apolar polyolefinic matrices. This causes poor compatibility with stabilizer and physical loss by migration.

To overcome these drawbacks, we proposed different families of macromolecular additives[1] consisting in ethylene- and propylene-based copolymers containing tuned amounts of suitable olefinic comonomers bearing a stabilizing functionality (Figure 1). On the other hand, additives used in ether solvents must be removed before use with time, cost and safety concerns. In this communication we report also the synthesis of novel graphite-coated magnetic cobalt nanoparticles[2] decorated with hindered phenolic antioxidant for easily removable nanoantioxidants capable of preventing the autoxidation of organic solvents such as THF (Figure 1).

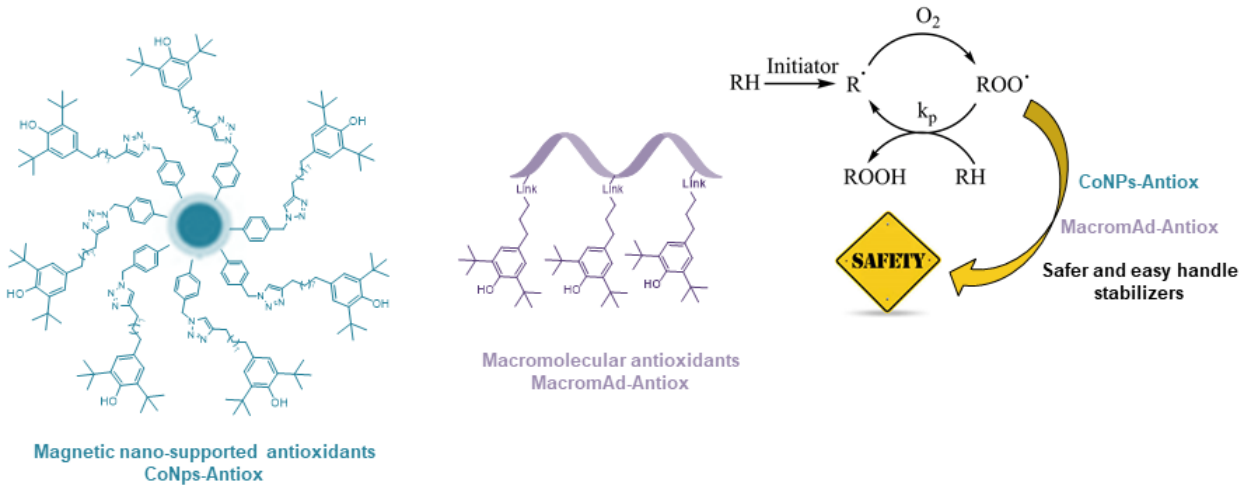

Figure 1: Nano-supported and macromolecular antioxidants.

References:

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OC-67

Photopolymerization of Selected Monomers Initiated by Arylazo Sulfones

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Photopolymerization offer several advantages over classical thermal polymerizations such as rapidity of execution, solvent-free conditions and reduced emission of volatile organic compounds as the consequence of the mild reaction conditions. Photoinitiators are essential for the photopolymerization because their light-induced dissociation lead to the formation of radical, cationic or anionic intermediates responsable for initiating the polymerization. Photopolymerizations have been traditionally developed for 2D printing technological applications such as photolithography,[1] and they are currently experiencing a resurgence of interest for applications in the fields of stereolithographic 3D and 4D printing.[2] The possibility to photogenerate different intermediates in the same material with good spatial and temporal control of the process, has been recently addressed in multimaterial, 2D and 3D printing applications.[3] There is therefore a demand for dually-activatable photoinitiators, in order to address more precisely the multimaterial printing.

Arylazo sulfones are compounds studied as radical initiators in thermal polymerizations during ’60 and ’70, and recently arylazo sulfones, as thermally stable derivatives of aryl diazonium salts, were studied as arylating agents for the photoinduced metal-free direct arylation of (hetero)aryls.[4] They can, according to the irradiation wavelength, produce radicalic or cationic species. We describe the use of arylazo sulfones as new class of photoinitiators for the radical and cationic polymerization of several vinyl monomers. Their efficiency, in terms of polymerization yields, dispersity and degree of polymerization, will be presented in relation to different class of monomers used.

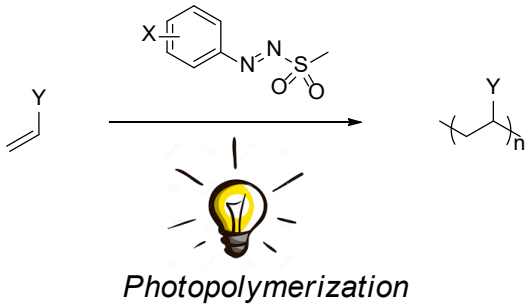

Figure 1: Photopolymerization of selected monomers using arylazo sulfones as initiators.

References:

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OC-68

N-hydroxyphthalimide: an Efficient Hydrogen Atom Transfer (HAT) Mediator in Hydrocarbon Oxidations Promoted by Nonheme iron(IV)-oxo complexes

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Oxidation processes mediated by *N*-hydroxyphthalimide (NHPI) have attracted a special attention in recent years. For example NHPI is an efficient mediator in the aerobic oxidation of organic compounds promoted by laccase, a multicopper oxidase active in wood delignification.[1] After oxidation by the Cu(II) form of the enzyme, the oxidized mediator phthalimide-*N*-oxyl radical (PINO) diffuse into the woody fibres and oxidize the lignin polymer with a hydrogen atom transfer (HAT) process regenerating the mediator. NHPI plays also an important role as redox mediator under electrochemical conditions. PINO can be easily generated at the electrode surface after electron removal from NHPI enabling a wide range of electrosynthetic organic transformations.[2]

We have recently discovered that NHPI is an efficient mediator in the oxidations of hydrocarbons promoted by nonheme-iron(IV) oxo complexes, biomimetic models of the active species formed in nonheme-iron oxygenases.[3] Kinetic studies of the reaction of hydrocarbons (triphenylmethane, cumene, ethylbenzene, toluene and cyclohexane) with the nonheme iron(IV)-oxo complex, $[(N4Py)Fe^{IV}(O)]^{2+}$ showed a faster decay of the oxidant in the presence of NHPI. The increase of reactivity is associated to the oxidation of the mediator to PINO (Figure 1, step a) which efficiently abstracts hydrogen atom from the substrates regenerating the mediator NHPI (Figure 1, step b).

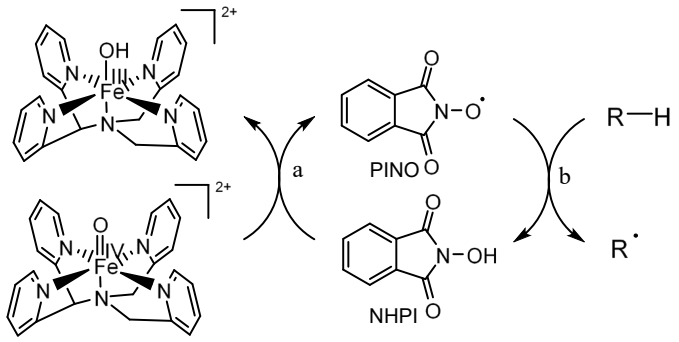

Figure 1: NHPI mediated oxidation of organic compounds promoted by $[(N4Py)Fe^{IV}(O)]^{2+}$

The mediation effect of NHPI in the oxidations promoted by $[(N4Py)Fe^{IV}(O)]^{2+}$ is confirmed by the results of product analysis of the oxidation of triphenylmethane, ethylbenzene and toluene showing that significant higher product yields are observed in the presence of the NHPI mediator.

References:

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OC-69

Efficient Lewis Acid Multicomponent-Promoting System in the Carbon-Nitrogen Bond Formation

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The Lewis acid promoters, widely used for carbon-nitrogen bond formation are an active area of research in organic chemistry. They play an important role in such reactions, and thus they find wide application in the synthesis of polysubstituted nitrogen-containing heterocycles.[1] The function of many biologically active molecules requires the presence of carbon-nitrogen bonds in strategic positions and chemical synthesis allows to synthesize natural products more efficiently than biosynthetic pathways. For this reason the efficiency in the preparation of carbon-nitrogen bonds has an environmental impact.

Recent studies by us and by others have shown that a multicomponent-promoting system based on the combination of Ce(III) salts and inorganic iodides provides a new approach for one-pot formation of nitrogen-containing heterocycles. In the course of our program aimed at studying new synergetic promoting system, we were able to develop the selective hetero-cyclocondensation to provide 2-substituted benzimidazoles.[2] The strategy has found application in our synthesis of Hoechst molecule **1**, which is useful for many different therapeutic and diagnostic purposes, as well as in the synthesis of other important building blocks in medicinal chemistry such as julolidine-type compound **2**, which has proved to have anticancer activity.[3]

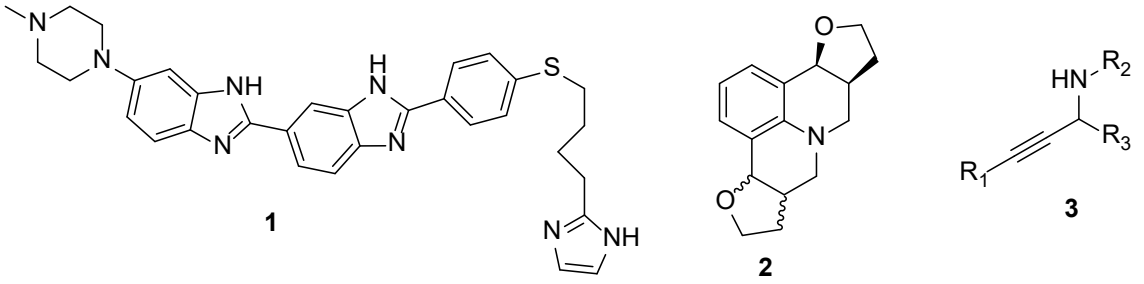

Figure 1.

Efficiency in synthesis of acyclic precursors is often the key factor in having good yield in target heterocycles: through the appropriate combination of the components of the promoting system, by A^3 coupling reaction[4] we obtained also useful secondary propargylamines **3**, a class of building blocks involved in the synthesis of several important heterocyclic scaffolds.

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OC-70

Non photochemical route to functionalized thiophene-based [7]helicenes

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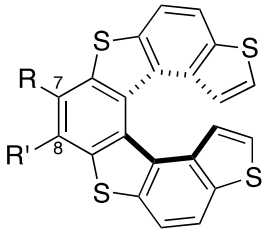
Helicenes are an intriguing class of *ortho*-annulated polycyclic aromatic or heteroaromatic compounds endowed with inherent chirality owing to the helical shape of their π-conjugated system. These curved organic molecules provide unique opportunities for applications in manifold fields, including materials sciences, chiroptical devices, and asymmetric synthesis.[1] Among helicenes, thiahelicenes are emerging as one of the most popular class of heterohelicenes thanks to their unique characteristics combining the electronic properties of oligothiophenes, with the chiroptical properties of helical shape molecules.[2] For several years, we have been interested in the study of the synthesis and functionalization of thiahelicenes, such as tetrathiahelicene (7-TH) derivatives (Figure), that are configurationally stable and potentially very interesting for applications in optoelectronics,[3] catalysis,[4] and biology.[5]



R, R: aryl, heteroaryl

Figure: general structure of 7-TH derivatives

Recently, we have developed a versatile non-photochemical procedure to prepare functionalized thiahelicenes, including a novel class of 7,8-diaryl substituted 7-TH compounds. This strategy involves the synthesis of chiral heterobiaryl derivatives as key intermediates, whose configurational stability have been elucidated in order to design an asymmetric version for the synthesis of enantioenriched thiahelicenes.

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OC-71

Iodine-mediated deconstructive annulation of isoprenylchromenes to benzo[c]chromenes. Development of a one-step synthesis of cannabinol (CBN)

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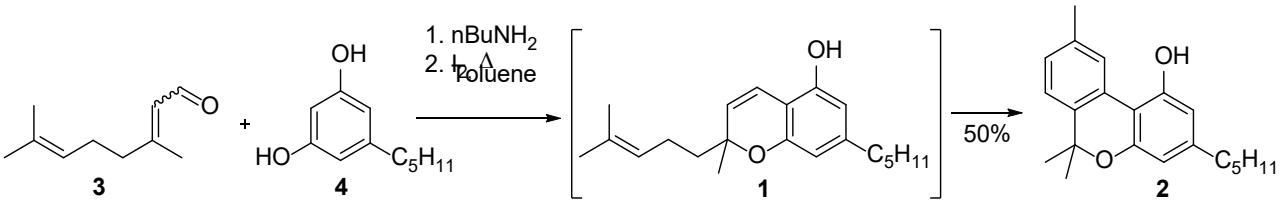
Based on model reaction and calculations, the thermal degradation of the non-narcotic phytocannabinoid cannabichromene (CBC, **1**) has been suggested to generate a mixture of psychotropic tetrahydrocannabinols (THCs).[1] We found no evidence for this mechanistic and socially relevant conversion under a variety of pyrolytic conditions, but CBC could be converted in the benzochromene cannabinol (CBN, **2**) by refluxing with iodine.

Iodine can trigger the cyclization of isoprenylated chromenes to benzochromenes via a process that includes a couple of regiochemically distinct electroreversion and electrocyclization steps eventually evolving into a formal benzoannulation: the reaction involves cycloreversion of the chromene system to quinone methide, and this is next trapped in a hetero Diels-Alder fashion by the distal terminal isoprenyl double bond; the final iodine promoted aromatization terminates the reaction.[2]

Since isoprenylated chromenes are easily available by cyclo-condensation of phenolics with terpenyl aldehydes, the reaction has broad application for the preparation of natural- and non-natural products, as exemplified by an expeditious one-step synthesis of CBN from citral (**3**) and olivetol (**4**) that outperforms in terms of simplicity, scalability, and yield all its previous syntheses.

This deconstructive annulation is added to our meagre inventory of expedite benzochromene synthesis and of complex isoprenoids rearrangements involving aromatic moieties,[3] and the remarkable atom-economy and simplicity of the reaction make it ideal to explore the chemical space of complex benzochromenes like cannabinoids and related bioactive biphenyls.



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OC-72

Nitroso Diels-Alder chemistry on 1,2-dihydropyridines as a platform to obtain novel anti-diabetic agents

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Diabetes is among the most common and prominent diseases in various countries of the world, and in particular type-2 diabetes (T2DM) is prevalent in 90% of the population suffering from this pathology.[1] Glucagon-like peptide-1 (GLP-1) is an incretin hormone that enhances insulin release from pancreatic *β*-cells in both normal and type 2 diabetic subjects. GLP-1 receptor agonists and drugs that slow the degradation of active GLP-1 are therefore under development as novel treatments for T2DM. Some GLP-1 mimetics are now commercially available, but all of these are peptides with problems of stability and administration route.[2] For this reason, there is a huge interest in novel treatments that have similar physiological effects to GLP-1, but which can be administered orally and minimize side effects.

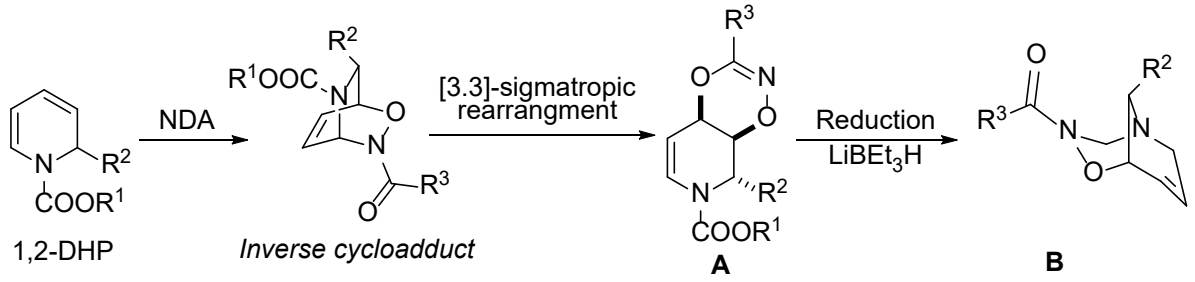

Figure 1: Synthesis of new bicyclic scaffold **B**.[5]

A previous deep study by our group about nitroso Diels-Alder reactions of 1,2-dihydropyridines and subsequent [3.3]-sigmatropic rearrangement of inverse cycloadducts afforded bicyclic dioxazines of type **A** (Figure 1).[3] Reductive elaborations of a variety of compounds of type **A** allowed the obtainment of oxadiazabicyclo[3.3.1]-nonene scaffolds of type **B**. The latter compounds have shown the ability to bind the GLP-1 receptor and they seem to be promising candidate to explore in terms of structure-properties relationship.[4,5]

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OC-73

Direct and Chemoselective Transfer of the Difluoromethyl (CHF_2) Unit Into Carbon-Electrophiles under Nucleophilic Regime

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The difluoromethyl group (CHF_2) plays a crucial role in synthetic chemistry because of the capability to act as an isoster of the carbinol group (CH_2OH), manifesting a remarkable hydrogen donor characteristic. As a consequence, difluoromethylated analogues of biologically active substances are strong, ideal candidates for pharmaceuticals.[1] In contrast to the lipophilic CF_3 group, the CHF_2 group is weakly acidic and exhibits a natural tendency to make strong H-bonding interactions. [2]

In line with Pace's group studies on nucleophilic halomethylations,[3,4] the highly challenging introduction of a CH_2F group, herein we disclose a highly effective difluoromethylation – under nucleophilic regime – for the one-pot, straightforward formal transfer of a CHF_2 motif into a carbon electrophile. Tactic's development, optimization, and study of the scope – as well as the application in synthetic relevant transformations of the accessed structures – will be presented.[5]

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OC-74

A new biopolymer skeleton formed by a dimer of carbohydrate and aminoacid produced by *Rhizobium radiobacter* and useful for plant immunity evasion

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Microbial surface antigens are key molecules for both symbiotic and pathogenic bacteria in the interaction with other organisms and in the physico-chemical interaction with the external environment. They are mostly carbohydrate based molecules such as glycolipids, glycoprotein and (capsular) polysaccharides. In Gram negative bacteria the lipopolysaccharide (LPS) represents the most important and the most abundant membrane/surface antigen. LPSs play a key role in the elicitation of innate immune response in all eukaryotes and is recognised as MAMP (Microbe Associated Molecular Pattern) by the eukaryotic immune system. LPS are amphiphilic essential outer membrane constituents of Gram negative bacteria, they comprise three chemically and genetically distinct regions: the endotoxic moiety termed Lipid A, the core region and the O-specific polysaccharide, which together form the so-called smooth(S)-form LPS; a rough(R)-form LPS (LOS) lacks, partially or totally, the O-specific polysaccharide. From a structural point of view, the O-specific polysaccharide, often referred to as the O-chain, is the predominant part of the LPS, usually it is a regular polysaccharide whose repeating unit is made up of a discrete number of residues, ranging from two to six.

In the present communication, it will be illustrated that the *Rhizobium radiobacter* strain expresses a polymer resulting to be a novel type of biopolymer in which the repeating unit is formed by a monosaccharide and an aminoacid derivative so that the whole molecule has alternating glycoside amide bonds.

OC-75

Application of quantum chemical integrated multistep protocol in the stereochemical determination of natural products

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The correct stereo-assignment of two metabolites as two atropisomeric forms (**1** (*M*, 10'*S*) and **2** (*P*, 10'*S*)) of the same glucopyranosylbianthrone (*Asphodelus tenuifolius)* was achieved applying a quantum chemical integrated multistep protocol (Fig. 1).[1] The correct assignment of the stereochemical pattern of **1** and **2** was resolved accounting two main issues, i.e., the atropisomerism around the biaryl axis and the configuration at C-10′ as the unique point of difference between them.[1]

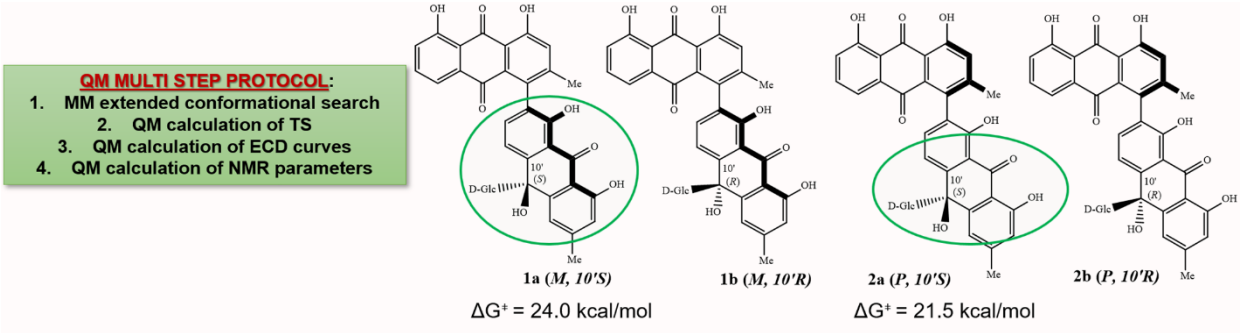

Figure 1: Schematic representation of the QM multistep protocol and molecular structures of the four possible diastereoisomers of **1** and **2** (**1a**, **1b**, **2a**, and **2b**).

With this aim, after defining the 2D structure of the two C-glucosidic metabolites and assuming the presence of a D-glucose, four different phases of the multistep protocol were applied, namely: 1) extended conformational search at empirical level; 2) computation of the rotational energy barrier related to the interconversion between the atropisomeric forms (*P* and *M*) for each possible isomer at C-10' (*R* and *S*) at DFT level, demonstrating their hindered interconversion; 3) computation and comparison of the experimental and calculated ECD curves of **1a**, **1b**, **2a**, **2b** suggesting that the Cotton effects are not influenced by the 3D arrangement at C-10'; 4) calculation and comparison between the experimental and calculated ^{13}C NMR chemical shifts (DFT/NMR), singling out the better fit with the experimental data of **1a** and **2a**, and suggesting the (10'*S*) absolute configuration for both atropisomers. The results highlighted the elevated applicability and versatility of this integrated quantum chemical approach to a real case for resolving correct structure, stereochemistry and 3D arrangement of natural products (NP),[2] that represent a fundamental aspect for complete comprehension and rationalization of the molecular recognition events responsible for the biological activities of NPs.

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OC-76

Mn^{II}-complexation / $Al^{18}F$-labeling of new AMP-based chelators for applications in Magnetic Resonance Imaging and Positron Emission Tomography

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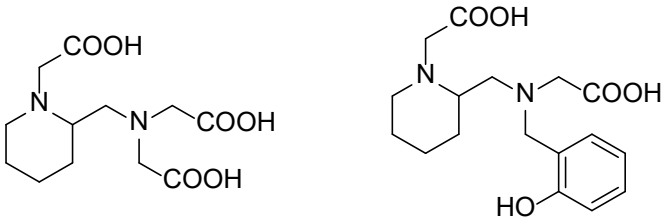
Magnetic resonance imaging (MRI) and positron emission tomography (PET) are non-invasive molecular imaging technologies constantly expanding, with a high demand for specific imaging probes. Contrast-enhanced MRI requires the use of suitable paramagnetic metals to increase the water-protons relaxation rate (R_1). Also, PET tracers based on $[Al^{18}F]^{2+}$-complexes have been recently developed to label temperature-sensitive biomolecules. Thus, we designed pentadentate chelators based on the structure of aminomethylpiperidine (AMP) with acetic and/or hydroxybenzyl pendant arms, where the presence of the rigid piperidine cycle allowed to increase the metal complexes' stability.

Several AMP-based chelators were designed and synthetized: **2-**, **3-**, **4-AMPTA**; **2-**, **3-**, **4-AMPDA-HB**. All the ligands were characterized by HPLC-MS analysis and NMR spectroscopy. The relaxometric characterization of the Mn-complexes was performed by measuring the variation of R_1 as a function of pH, temperature and magnetic field strengths. The AlF-18 labeling reactions were performed at different pH values (4 and 5) and temperatures (rt, 37 and 80 °C); all the products were analyzed by radio-TLC and radio-HPLC and the stability of the tracers was investigated at 10-240 minutes *via* incubation in human serum, EDTA 5 mM, PBS and NaCl solutions. The MRI performance of the Mn-complexes is comparable to that of other mono-aquo Mn-based contrast agents. The $Al^{18}F$ radiolabeling efficiency at 37 °C was 60% for **2-AMPDA-HB** and 75% for **2-AMPTA**. High stability in human serum was measured for the ligand **2-AMPDA-HB** with a 90% of complexed $Al^{18}F$, and 55% for **2-AMPTA** after 120 min. After 240 min in human serum the $Al^{18}F$ complexed by **2-AMPDA-HB** was 68%, and 33% for **2-AMPTA**.

In a preliminary screening of the reported chelators, promising results have been obtained in terms of radiolabeling efficiency at rt and 37 °C, and good stability in physiological conditions. The selection of the best chelator will lead to the synthesis of the bifunctional derivative followed by conjugation to temperature-sensitive biomolecules (*e.g.* Fab fragments and/or nanobodies), labeling and then *in vivo* applications.



2-AMPTA **2-AMPDA-HB**

Figure 1: two of the ligands prepared and investigated to form MRI and PET contrast agents.

OC-77

Ligand Based Identification of FABP4 Inhibitors: Synthesis and Biological Screening

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Following on the recent publication of pharmacologically relevant effects, small molecule inhibitors of adipocyte fatty-acid binding protein 4 (FABP4) have attracted high interest.[1] FABP4 is mainly expressed in macrophages and adipose tissue, where it regulates fatty acid storage and lipolysis, being also an important mediator of inflammation. In this regard, FABP4 recently demonstrated an attractive molecular target for the treatment of type 2 diabetes, other metabolic diseases, and some cancers. In the past years, hundreds of effective FABP4 inhibitors have been synthesized. This communication describes our recent developments of a ligand-based (3D-QSAR model, Figure 1) approach for the identification of novel structures as FABP4 inhibitors. One hundred twenty of the already reported FABP4is were used to build the 3D-QSAR model. The development of the model has been undertaken with the use of Forge software using the PM3 optimized structure and the experimental IC_{50} of each compound. The model was then employed to predict the activity of 3000 new isosteric derivatives of BMS309403.[2] The isosteric replacement was validated by the synthesis and the biological screening of three new compounds (AST_**1**–**3**).[2,3] Their effective binding properties toward FABP4 were tested through a displacement assay and the three molecules results as FABP4 binders with an IC_{50} between 3.70 and 5.79 μM.

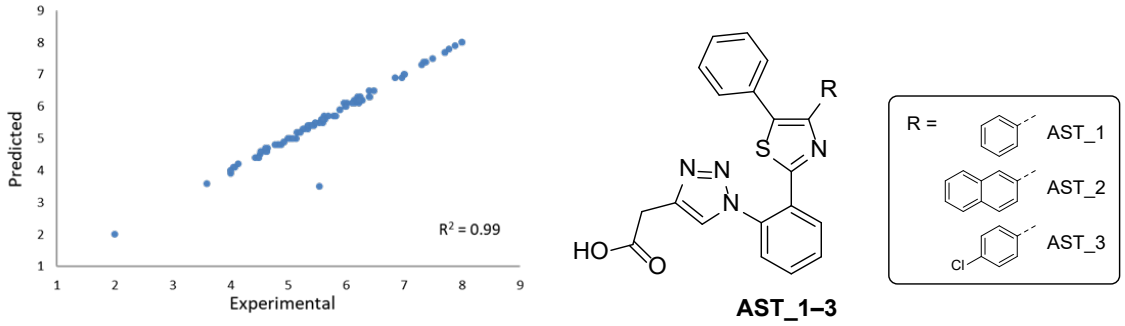

Figure 1: Left: 3D-QSAR model - Experimental *vs*. Predicted activity of the compounds in the training set. Right: Structures of AST_**1**–**3**.

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OC-78

Fungal phytotoxins with potential herbicidal activity for *Cenchrus ciliaris* biocontrol

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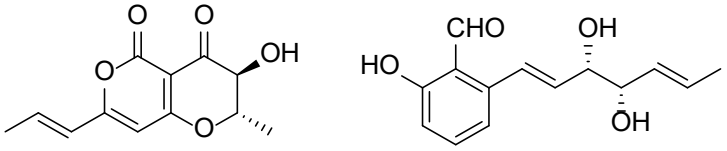
Cenchrus ciliaris, also known as buffelgrass or *Pennisetum ciliare*, is a plant native to the Old World which was intentionally introduced in many semi-arid regions of the world as a pasture grass. However, it has become highly invasive in western North America negatively affecting the native vegetation and altering the wildfire regime, especially in the Sonoran Desert of southern Arizona. Broad-spectrum herbicides have been extensively used to manage this weed with a negative environmental and ecological impact. Phytotoxins produced by weed pathogenic fungi might be an efficient alternative to these synthetic substances. Thus, some fungal pathogens, isolated from buffelgrass in North America, have been studied to evaluate their ability to produce phytotoxic metabolites that could be used to design natural and potential safe bioherbicides for *Cenchrus ciliaris* biocontrol. Fourteen secondary metabolites, belonging to different classes of natural compounds, have been isolated from *in vitro* cultures of *Cochliobolus australiensis* and *Pyricularia grisea.*[1-3] Some of these phytotoxins resulted to be new natural products and have been characterized by spectroscopic and chemical methods. Their relative and absolute configurations were also determined using a combination of spectroscopic, chiroptical and computational methods. When tested by leaf puncture assay on the host plant at different concentrations, radicinin and (10*S*, 11*S*)-*epi*-pyriculol (**1** and **2**, Fig. 1) proved to be the most promising compounds and their phytotoxic activity was also evaluated on non-host indigenous plants. Radicinin demonstrated high target-specific toxicity on buffelgrass, low toxicity to native plants, and no effects on zebrafish (*Brachydanio rerio*) embryos.[4] This communication will give an overview on the work carried out and will illustrate the results obtained. The possibility to use radicinin for the development of a target-specific bioherbicide against buffelgrass will be also discussed.



1 **2**

Figure 1: The structures of radicinin and (10*S*, 11*S*)-*epi*-pyriculol (**1** and **2**).

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OC-79

Synthetic approaches to the development of new Antibody-Drug Conjugates charged with unconventional payloads

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With more than 50 antibody−drug conjugates (ADCs) in clinical trials for cancer treatment, the ADC approach opens a new era of chemotherapy especially after Adcetris and Kadcyla approval for treatment of Hodgkin lymphoma and Her-2-positive metastatic breast cancer, respectively.[1] ADCs activity is strictly related to the chemical properties of both linker and payload, while the conjugation methodologies impact their homogeneity. Here we report our experience in the development of novel ADCs that can deliver to human tumors hystone deacetylase (HDAC) inhibitors[2-3] and other payloads (i.e. Smo inhibitors)[4] with low cytotoxicity. Different payloads were prepared using both cleavable and non-cleavable linkers and conjugated to Cetuximab and Trastuzumab resulting in ADCs exhibiting unmodified ability to recognize EGFR and efficient internalization into tumor cells.[2-3] Animal models of human solid tumors showed high anti-tumor efficacy of the conjugates without the toxicity of traditional ADCs charged with highly potent cytotoxic drugs. These new bioconjugates proved to be suitable for targeted epigenetic modulation possibly extending the ADC strategy to therapeutic applications beyond cancer.

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OC-80

Technology-driven catalysis: (SLA) 3D-printed devices for organic synthesis

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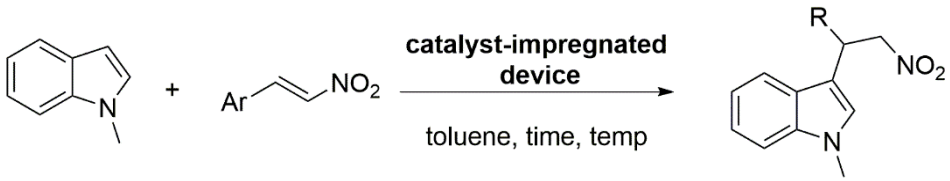
Three-dimensional (3D) printing has the capability to transform scientific ideas in bespoke and low cost devices that previously required expensive and dedicate facilities to make. By a simple additive manufacturing process, these appliances could be realized on a layer-by-layer basis through a series of cross-sectional slices.[1] Among all 3D Printing technologies developed to realize objects, FFF and SLA approaches are the most developed. Stereolithography (SLA) 3D printing technology involves the use of an ultraviolet laser that is focused onto a vat containing a photopolymer resin.

The manufacturing of a three-dimensional product from a computer-driven digital model (3D printing) has found extensive applications in several fields. In chemical sciences (FFF) 3D-printers were used to build research equipment, but had also a significantly impact in the field of fluidics devices for the realization of mesoreactors.[2] Despite all these developments, no examples of chemical-impregnated 3D printed devices realized with stereolithography technology are known. In this context, we focused our attention in the preparation of (SLA) 3D-printed catalyst-impregnated devices and their evaluation for batch and flow reactions in organic synthesis.

Using a low-cost SLA 3D printer and freeware design software, different devices were designed and printed using a photopolymerizable resin containing different organocatalysts. These devices were used to investigate different organic transformations such as the Friedel-Crafts alkylation of aromatic and heteroaromatic systems with nitroolefins leading to the formation of desired products with good results (Scheme 1).[3] Furthermore, some 3D-printed mesoreactors have been employed in preliminary investigations of visible-light promoted reactions.



Scheme 1: Friedel-Crafts alkylation of aromatic systems with nitroolefins

References:

[1] S. Rossi, A. Puglisi, M. Benaglia, *ChemCatChem* **2018**, *10*, 1512-1525.
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OC-81

Synthesis of new chiral catalysts through multicomponent processes

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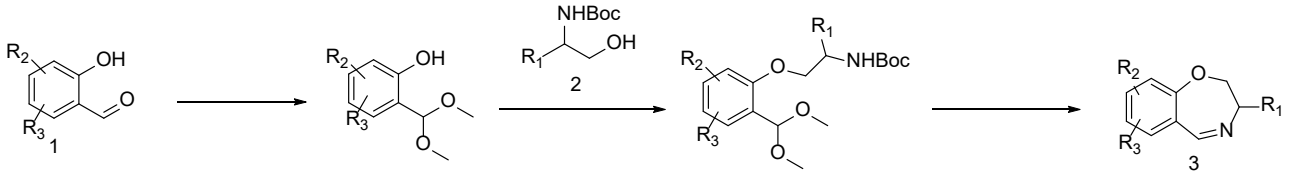
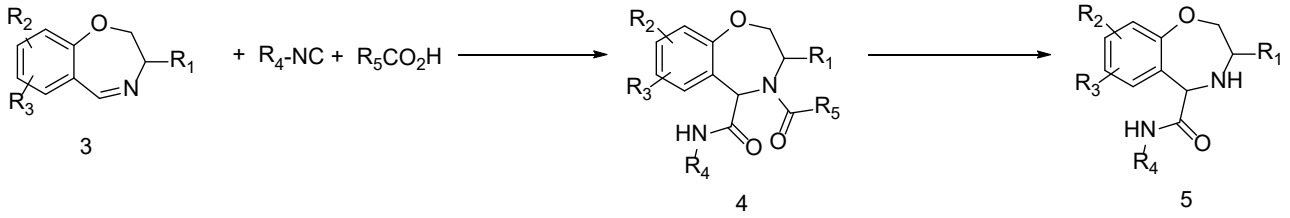
The examples of processes that are catalysed by secondary amines are many in the literature. They are involved in catalysis via enamine or iminium ion. The most famous and applied catalysts are proline derivatives, so finding an efficient method to synthesize new kind of catalysts would be desirable. The multicomponent reactions are ideal to get this goal in a combinatorial way, because they allow us the get a product in a single step, introducing various diversity inputs.[1]
Recently a new methodology for the synthesis of chiral cyclic imines starting form salycilaldehydes **1** and Boc-amino-alcohols **2** has been developed (Scheme 1).[2]



Scheme 1: Synthesis of chiral cyclic imines

Involving theses imines in a Ugi-Joullié reaction[3] allow us the get easily the product with high diasteroselectivity. Although the product **4** has an amidic group in its structure, a method to get the free amino group can be found (Scheme 2).



Scheme 2: Synthesis of new potential organo-catalyst

References:
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OC-82

Chemo-Enzymatic Cascades for the Synthesis of Heteroaromatic and Sulphur Containing Pharmaceutical Ingredients

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The use of biocatalysis in synthetic chemistry has grown exponentially in the last decade due to the tremendous progresses made in the field of gene cloning, DNA sequencing and protein expression. Biocatalysis represents nowadays a robust and sustainable method for the synthesis of many chemical tools and pharmaceutical ingredients under mild and more sustainable reaction conditions. However, one of the most intriguing challenges for chemists and biologists is still represented by the possibility to combine chemo- and biocatalysis in a concurrent fashion to outperform sequential transformations with a high degree of selectivity. Chemo-enzymatic cascade reactions are highly appealing for industrial processes as they can offer multiple benefits such as the immediate succession of individual transformations and the in-situ consumption of toxic or unstable intermediates without the requirement of intermediate isolation or functional group protection strategies, thus leading to safer processes and to the reduction of undesired side products. Our research group is interested in the development of novel chemo-enzymatic methods for the synthesis of drug-like compounds. Since most drugs contain a heteroaromatic ring, we developed a chemoenzymatic approach to access heterocycles such as pyrroles, pyridines and furans from appropriate aliphatic precursors through a ring-closing metathesis/enzymatic aromatization cascade. In parallel, we developed a photo-biocatalytic method for the synthesis of 1,3-mercaptoalkanols, a class of volatile flavouring compounds used as excipients in pharmaceutical preparations. The 1,3-mercaptoalkanols were synthesised from ketone precursors using KRED enzymes. Two different KRED biocatalysts with opposite enantioselectivity were identified in this study.

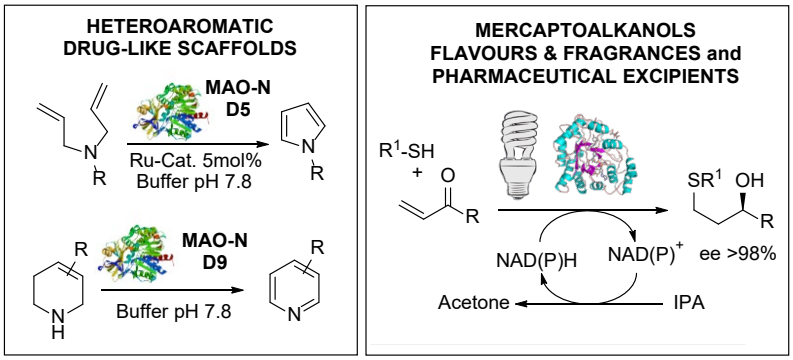

Figure 1. Chemoenzymatic approaches for the synthesis of aromatic heterocycles and mercaptoalkanols

References:

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OC-83

Synthesis of 1,3-oxazinan-2-ones by catalytic incorporation of carbon dioxide into N-alkyl-3-yn-1-amines

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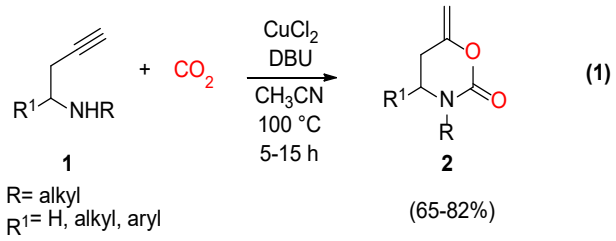
Carbon dioxide, continuously emitted in the atmosphere from the combustion of fossil fuels, is considered to be one of the major greenhouse gases responsible for increasing global temperature. For this reason, the efficient conversion of CO_2 into high value-added products currently represents one of the most innovative strategies for the valorization of this important waste.[1]

In this contribution, we report a new synthetic process to obtain 1,3-oxazinan-2-ones, which are heterocycles of pharmaceutical interest,[2] using CO_2 as a key building block. In particular, starting from the results in the field of CO_2 fixation recently achieved in our research group,[3] we have investigated the reactivity of *N*-alkyl-3-yn-1-amines **1** under carboxylation conditions for the synthesis of cyclic carbamates **2**, using $CuCl_2$ as simple and inexpensive catalyst (*Eq. 1*)



1
R= alkyl
R^1= H, alkyl, aryl

2
(65-82%)

In the presence of 2 mol % of $CuCl_2$ and DBU (40 mol%), under relatively mild reaction conditions (100°C under 40 atm of CO_2), different *N*-alkyl-3-yn-1-amines **1** were converted into the corresponding 1,3-oxazinan-2-one **2**. Formation of **2** can be interpreted as occurring through an ordered sequence of steps, involving the initial DBU-promoted formation of a carbamate, followed by 6-*exo*-*dig* intramolecular nucleophilic attack of the carbamate oxygen on the triple bond coordinated to $CuCl_2$ and protonolysis.

The reaction is regioselective and leads to the oxazinan-2-one derivatives in good to high yields (65-82%)

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OC-84

Highly Performing Iodoperfluoroalkylation of Alkenes Triggered by the Photochemical Activity of Perylene Diimides

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Visible light photocatalysis has recently emerged as a powerful strategy for the implementation of radical chemical transformations.[1] This approach relies on the ability of light-absorbing metal complexes and organic dyes (photocatalysts) to generate, upon direct visible-light excitation, reactive radicals from suitable precursors at ambient temperature. In 2014, the König group exploited the ability of perylene diimides (PDIs) to function as visible light photocatalysts for the reductive dehalogenation of aryl halides.[2] Despite the excellent optical and redox properties of PDIs, their application in organic photochemistry remains rare.

Within this research field, we envisaged the use of PDIs as effective photocatalysts for atom-transfer radical addition (ATRA) reactions. Specifically, we describe a novel efficient photochemical procedure for the direct iodoperfluoroalkylation of terminal olefins (**1**, Figure 1).[3] The process uses a simple and inexpensive perylenediimide (PDI) in an extremely low catalytic loading (0.05 mol%, corresponding to 500 parts per million) and occurs with visible light irradiation. The reported methodology is highly viable from a synthetic point of view, since it proceeds under mild reaction conditions with a significant rate of production. In addition, products (**3**) can be used as suitable building blocks to prepare new relevant chemical species by employing common organic synthetic methodologies.

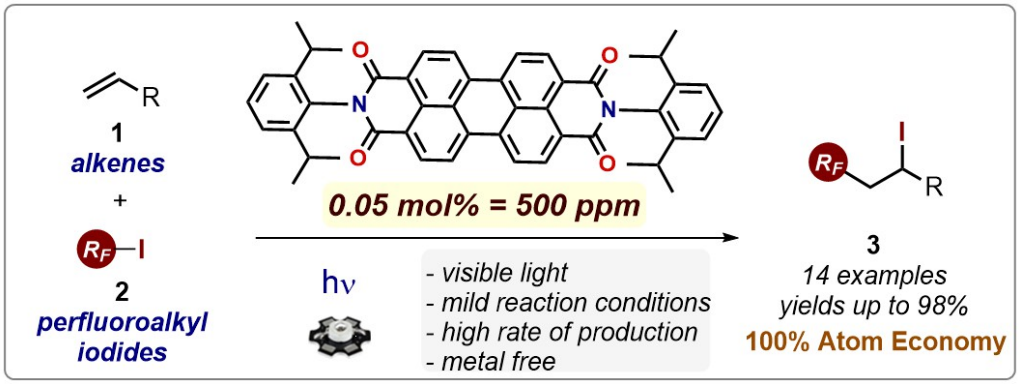

Figure 1: PDI initiated Atom Transfer Radical Addition (ATRA)

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OC-85

C–H Bond arylations of 1,2,3-triazoles by reusable Pd/C catalyst in solvent-free conditions

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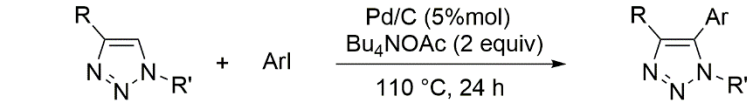
The 1,2,3-triazole ring represents a key structural motif in various applied areas, such as drug discovery,[1] bioconjugation,[2] and materials science.[3] Among the known methods for the regioselective synthesis of fully substituted 1,2,3-triazoles, the Pd-catalyzed direct arylation of the easy available 1,4-disubstituted 1,2,3-triazoles turns out to be the most general approach.[4] The major drawback of this synthetic methodology is still represented by the use of toxic solvents. Only few examples of direct arylation protocols of 1,4-disubstituted 1,2,3-triazoles based on the use of more sustainable conditions have been reported in the literature. For example, protocols for Pd-catalyzed direct arylations in environmentally-benign reaction media, such as polyethylene glycol (PEG) [5] or biomass-derived γ-valerolactone, in the presence of reusable palladium catalysts, were developed by Ackermann and coworkers.

In the frame of our studies on triazole-based materials[6] as well as on Pd-catalyzed reactions for the synthesis of heteroaromatic compounds,[7] we report here in the first Pd-catalyzed direct arylation protocol of 1,4-disubstituted 1,2,3-triazoles that is performed in (i) solvent-free, (ii) non-anhydrous conditions, (iii) without exclusion of air, and (iv) in the presence of a reusable catalyst.



R = Ph, R' = $C_{16}H_{33}$
R = C_5H_{11}, R' = CH_2CH_2Ph
R = *p*-CH_3Ph, R' = C_8H_{17}
R = Ph, R' = *p*-CH_3Ph
R = C_6H_{13}, R' = *p*-CH_3Ph

Then, with the aim of making the reaction conditions more sustainable, we evaluated the possibility of using only tetra-n-butylammonium acetate (Bu_4NOAc) as the base and the reaction medium, in the absence any other additive. Using Pd/C (5 mol %) as the catalyst, we examined the role of the halogen, reaction temperature and catalyst loading. To probe catalyst reusability, we recovered the Pd/C by a modified literature protocol and evaluated the catalytic activity of the recycled material in the subsequent run. We observed an unchanged catalytic activity of the recycled Pd/C until the third run, while a halving of its activity is detected at the fourth run. Having selected Pd/C (5 mol %) in the presence of neat Bu_4NOAc as the best reaction system, we investigate the substrate versatility reacting the 1,2,3-triazoles, having a different ring substitution pattern, with various aryl iodides.

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OC-86

Memory of Chirality Approach to the Synthesis of α-Quaternary Amino Acid Derivatives

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Quaternary amino acids have an essential role to play in the design of peptidase-resistant antibiotics and in the control of secondary structure in designed peptidomimetics.[1] In this communication we report the stereoselective conversion of a series of *N*-alkyl, *N*-aryl-sulphonyl-α-amino acid derivatives into the corresponding *N*-alkyl-α-aryl-α-amino esters (*ee* up to 98%). This methodology has been applied to the rearrangement of sulphonamides bearing different electron withdrawing functional groups *via* a 'memory of chirality' approach. The high enantioselectivities obtained indicate that the stereochemical information is transferred from the *N*-alkylated sulphonamide **1** to the final rearranged product **2** via a chiral nonracemic enolate **A**. This latter, evolves through a *Re*-face attack into a chiral spiro-Meisenheimer intermediate **B** that, in turn, undergoes the stereoselective *Ns*→*C*α migration of the aryl group and loss of sulphur dioxide (Figure 1).[2]

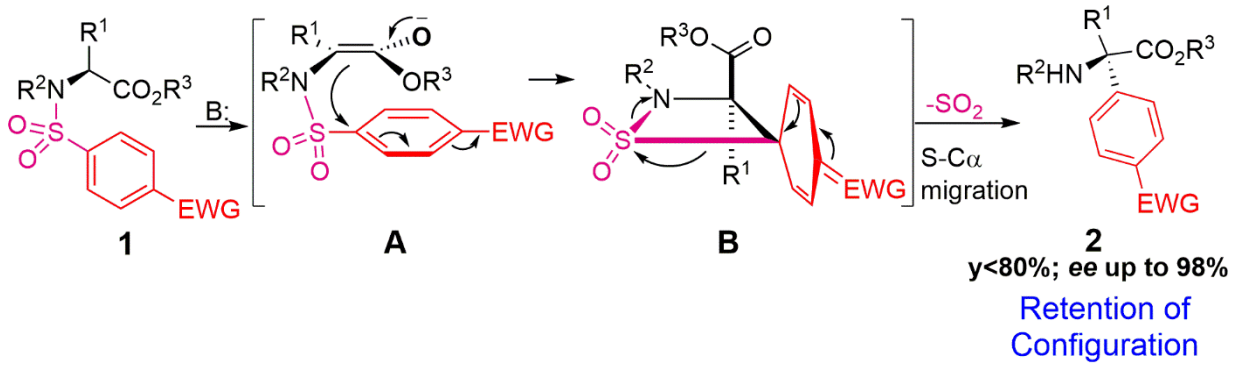

Figure 1

Interestingly, the pentafluoro sulphonamido derivatives do not promote the aryl migration reaction, but the ring closure, forming the correspondent sultam in high yield and enantiomeric excess.[3]

References:

[1] C. Cativiela, M. D. Díaz-de-Villegas, *Tetrahedron: Asymm.* **2009**, *18*, 569-623.
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OC-87

Tetrachlorosilane mediated direct amidation method

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The developments of general methods for sustainable direct amide formation is still one of the Key Green Chemistry Research Areas.[1] Several highly effective methods have already been reported, but they often suffer from drawbacks, including the need for harsh conditions, the involvement of expensive and/or toxic reagents and the formation of by-products that impede easy purifications.

Considering the relevance of the topic, our group developed a direct amidation method bond based on the use of tetrachlorosilane ($SiCl_4$)[2] as a mediator. Other silicon-based species have already been employed to promote the amide bond formation, but the most of them rely on organosilicon compounds,[2] intrinsically less effective in terms of atom economy.[3] Tetrachlorosilane appears rather convenient, being cheap and readily available and implying the formation of inorganic by-products that are easily removed from the reaction crude during the work-up phase.

Conditions optimization allowed good yields for a wide substrate scope, including both aromatic and aliphatic amines; the desired amides were obtained clean upon aqueous work-up. An in-flow version of the method can also be implemented, leading to advantages from a productivity standpoint.

Control experiments have been carried out to gain an insight into the reaction mechanism.

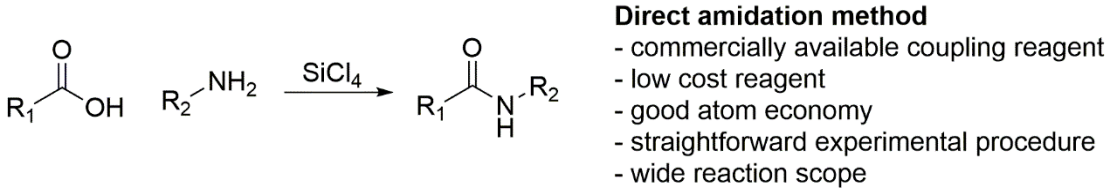

Figure 1: General reaction scheme for the developed amidation method

References:

[1] M. C. Bryan, P. J. Dunn, D. Entwistle, F. Gallou, S. G. Koenig, J. D. Hayler, M. R. Hickey, S. Hughes, M. E. Kopach, G. Moine, P. Richardson, F. Roschangar, A. Stevenh, F. J. Weiberth, *Green Chem.* **2018**, *20*, 5082-5103.

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OC-88

Straightforward Tactics and Enabling Technologies as useful tools for Fluoroalkylations

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Organofluorine compounds are interesting molecules with broad applications in medicinal chemistry, material chemistry and agrochemistry.[1,2] The development of new synthetic strategies to access new molecules with fluorinated moieties still remains a challenge for organic chemists and a "hot topic" in modern synthesis. The importance of organofluorine chemistry is showcased by the presence of fluorine in nearly 20% of all pharmaceuticals and 35% of agrochemicals on the market.[3] It is therefore noteworthy to develop effective synthetic strategies, either for the incorporation of fluorine atoms into organic scaffolds or for the preparation of fluorinated building blocks. In this communication, we report our contribute in the development of strategies for direct fluoroalkylation.[4] The potential of flow microreactor technology in fluoroalkylation chemistry will be also reported.[6]

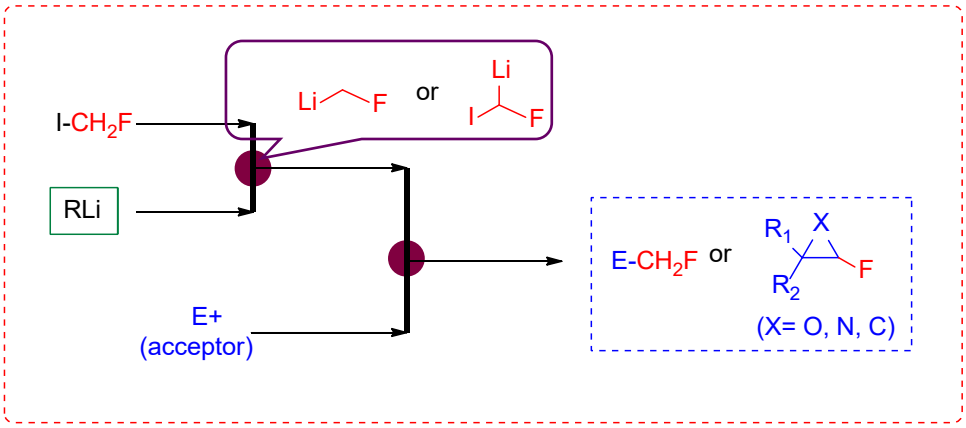

Figure 1: Flow Microreactor Technology as useful tool for Fluoroalkylations.

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OC-89

Diversity-Oriented Synthesis and chemoinformatic analysis of sp^3-rich molecular scaffolds using imine-based multicomponent reactions

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Modern chemical biology requires efficient synthetic processes to produce high-quality small-molecule collections as probes to investigate biological pathways. In this view, Diversity-Oriented Synthesis[1] (DOS) allows to explore the chemical space by generating structurally complex small molecule libraries, and multicomponent reactions (MCRs) represent a great tool to efficiently give a polyfunctional product for subsequent pairing reactions. In particular, imine-based MCRs, involving imines as a substrate or an intermediate, have gained considerable attention in recent years, due to substrate-dependent reactivity of imines, and commercial availability of several hundred amines and aldehydes to access a large number of imines.

Our contribution in this field involves the development of amino-acid derived molecular scaffolds, and to increase the complexity and the sp^3 character of the synthesized heterocyclic scaffolds, we recently applied the Petasis[2] and the copper-catalyzed A3 and KA2 reactions as imine-based MCRs to build novel structurally complex molecules. Chemoinformatic analysis demonstrated such MCRs being instrumental to access new areas of the chemical space, and to achieve molecular scaffolds possessing high Fsp^3 ratio and three-dimensional complexity.

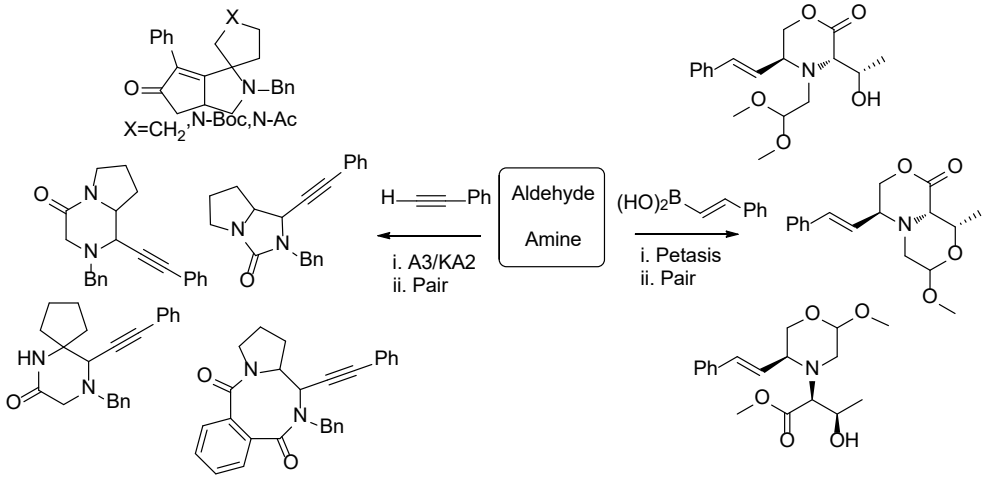

Figure 1: Petasis and A3/KA2 imine-based MCR reactions as coupling steps in couple-pair approaches.

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OC-90

A new symmetric G-rich Oligonucleotides incorporating a 3'-3' inversion of polarity site as an interesting model for ligand binding studies.

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G-quadruplexes are secondary structures of DNA, which are formed by guanine-rich oligonucleotides (GRO) annealed in the presence of monovalent cations such as Na^+ and K^+. The basic unit of a G-quadruplex is the G-quartet or G-tetrad, which is composed of a planar arrangement of four guanine bases stabilized by eight Hoogsteen hydrogen bonds. GRO and G-quadruplex structures have attracted the attention of researchers in medicinal chemistry and more recently in supramolecular chemistry and nanotechnology. In recent years, G-quadruplexes have also been used to build supramolecular structures by exploiting the multimerization between several G-quadruplex units [1]. In accordance with the topological arrangement, in a previous work we have studied the ability of the 5'-CGGT-3'-3'-GGC-5' (Figure 1) to form long G-wires [2]. In this context, we have synthesized a new GRO incorporating the 3'-3' inversion of polarity site and have studied the interaction of this type of longer stacked G-wires assembly.

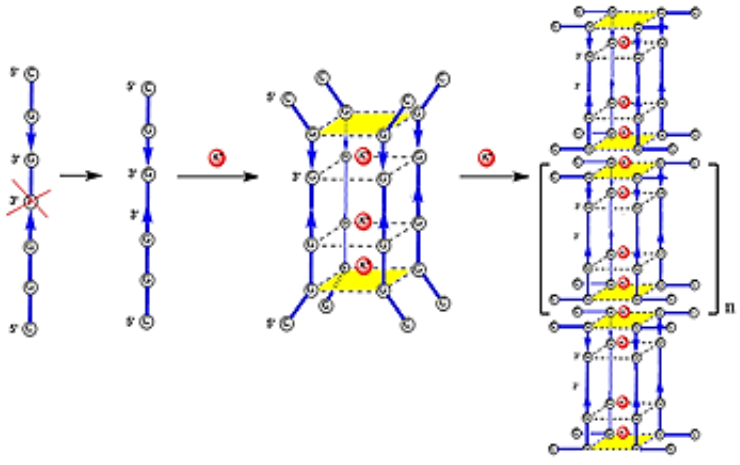

Figure 1. Formation of the G-quadruplex building block Q_1 and its multimerization into Q_n G-wire polymers.

References:

[1] A. B. Kotlyar, N. Borovok, T. Molotsky, H. Cohen, E. Shapir, D. Porath, *Adv. Mater.* **2005**, *17*, 1901.

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