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Journées Franco-Italiennes de Chimie

16 – 18 April 2018

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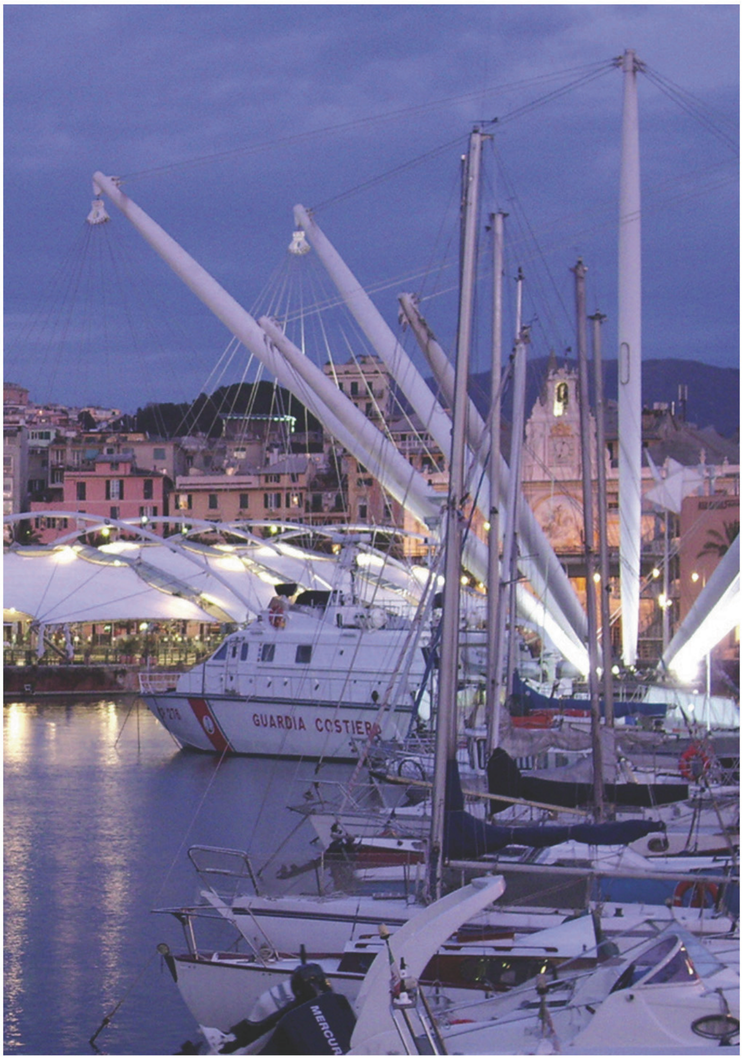
Genova



BOOK OF ABSTRACTS

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Scientific Program

Monday 16/4/18			**Registration and poster posting**		14,00-15,30
			Opening Ceremony		15,30-15,45
			Chair: Prof. Philippe Knauth, Past President SCF PACA		
	PL1	Ravera Mauro	Piemonte Orientale	*An "inorganic chemistry" overview on platinum anticancer drugs: the past, the present, the future*	15,45-16,30
	IL1	Martinez Alexandre	Aix-Marseille	*Catalysis in confined spaces: endohedral functionalization of hemicryptophane molecular cages*	16,30-17,00
	OC1	Dufond Maxime	Marseille	*Effect of photodoping on TiO2-coated n-type Si for water splitting*	17,00-17,15
	OC2	Ricchiardi Gabriele	Torino	*On the structure of superbasic (MgO)n sites solvated in a faujasite zeolite*	17,15-17,30
	OC3	Reeves Benjamin	Nice	*Bioaccumulation and speciation of uranium in sea urchins*	17,30-17,45
	OC4	Malegori Cristina	Genova	*Hyperspectral imaging for forensics sciences: revealing the hidden*	17,45-18,00
	OC5	Fenoglio Gaia	Torino/ Piemonte Orientale	*An unusual blue-turquoise pigment found on a painting at Novalesa abbey (Piemonte)*	18,00-18,15
	OC6	Chendo Christophe	Marseille	*Ion mobility/mass spectrometry: a powerful coupling for detailed characterization of synthetic polymers*	18,15-18,30
			1st poster session		18,30-20,00
			Welcome cocktail		20, 00
Tuesday 17/4/18			*Chair: Prof. Pinuccia Cerrato, SCI Piemonte e Valle d'Aosta*		
	PL2	Michelet Véronique	Nice	*Gold- and silver-catalyzed cycloisomerization and domino reactions – A journey in molecular diversity*	8,45-9,30
	IL2	Trotta Francesco	Torino	*Dextrin-based nanosponges*	9,30-10,00
	OC7	Canepa Ester	Genova	*Interaction of anionic and cationic nanoparticles with phospholipid membranes*	10,00-10,15
	OC8	Berezhnaia Veronika	Marseille	*Helicene-based chiral nanographenes*	10,15-10,30
	OC9	Uehara Ayaka	Nice	*Characterization of the odorant constituents of Helichrysum italicum essential oil*	10,30-10,45
	OC 10	Bisio Angela	Genova	*Sesterterpenes from Salvia tingitana Etl. (Lamiaceae)*	10,45-11,00

Tuesday 17/4/18, morning		**Coffee Break**			11,00-11,30
		Chair: Prof. Sylvain Antoniotti, SCF PACA			
	OC 11	Capurro Pietro	Genova	*a-Silyloxy acrylamides: synthesis and reactivity*	11,30-11,45
	OC 12	Elhadj Yacoub MS	Toulon	*Superabsorbant polymers for application in agriculture*	11,45-12,00
	OC 13	Taptue G. Brice	Genova	*N,N,N-Tris(tert-butoxycarbonyl)-L-arginine: five isoforms whose obtainment depends on procedure and a scrupulous NMR confirmation of their structures*	12,00-12,15
	OC 14	Alberti Stefano	Genova	*Porous PDMS membranes loaded with TiO2 NPs for detachable antibacterial coatings*	12,15-12,30
	OC 15	Pasquini Luca	Marseille	*Polymer electrolyte membranes for energy storage and conversion*	12,30-12,45
	OC 16	Delorme Marion	Marseille	*[2+2+2]-Cycloaddition Reaction for a new access to polycyclic cobalt complexes*	12,45-13,00
		Lunch			13,00-14,00
Tuesday 17/4/18, afternoon		**2° poster session**			14,00-15,30
		Chair: Prof. Chiara Brullo, SCI Liguria			
	PL3	Fossa Paola "ChemPub Soc Europe Lecture"	Genova	*Recent updates in CFTR structural studies: opportunities and challenges for cystic fibrosis drug development*	15,30-16,15
	IL3	Lucas Yves	Toulon	*A biogeochemical view on soil formation and functioning*	16,15-16,45
	OC 17	Pippione A Chiara	Torino	*Hydroxytriazole and hydroxybenzoisoxazole derivatives as potent and selective aldo-keto reductase 1C3 (AKR1C3) inhibitors: application of a bioisosteric scaffold hopping approach to target Prostate Cancer.*	16,45-17,00
		Coffee Break			17,00-17,30
		Chair: Prof. Valter Maurino, SCI Piemonte e Valle d'Aosta			
	OC 18	Martin Anthony	Nice	*Original nucleoside analogues to combat drug resistance in haematological malignancies*	17,30-17,45
	OC 19	Tang Yue	Nice	*Asymmetric catalysis: an entry to functionalized cyclohexene derivatives*	17,45-18,00

	OC 20	Figliola Carlotta	Marseille	*Diastereoselective functionalization of NHC-boranes through radical intermediates*	18,00-18,15
	OC 21	Marini Elisabetta	Torino	*New tools for the development of direct NLRP3 inflammasome inhibitors*	18,15-18,30
			Gala Dinner		20,30
Wednesday 18/4/18			*Chair: Prof. Elisabet Dunach, SCF PACA*		
	PL 4	Léger Christophe "Laureate Award"	Aix-Marseille	*Mechanistic studies of the enzymes that make dihydrogen*	9,00-9,45
	IL4	Di Carro Marina	Genova	*Emerging contaminants in waters: a challenge for analytical chemistry*	9,45-10,15
	OC 22	Derraji Kaouther	Toulon	*Study of Phase Change Materials (P.C.M) for thermal energy storage by latent heat*	10,15-10,30
	OC 23	Pourcin Florent	Marseille	*Hybrid materials using multi-layer architectures with near-ideal tunable large band absorption for stealth applications*	10,30-10,45
	OC 24	Alberti Diego	Torino	*A theranostic approach for Boron Neutron Capture Therapy (BNCT) treatment based on the use of Gd/B multimodal probes*	10,45-11,00
			Coffee Break		11,00-11,30
			Chair: Prof. Giovanni Petrillo, Vice President SCI Liguria		
	OC 25	Pagano Angela	Genova	*Nitrobutadienes: suitable substrates for the original synthesis of novel polyfunctional indole derivatives*	11,30-11,45
	OC 26	Caprioglio Diego	Piemonte Orientale	*Carbonyl activation in electrophilic polyene cyclizations: a toolbox for the design of isoprenoid libraries*	11,45-12,00
	OC 27	Butscher Teddy "Thesis price winner"	Marseille	*Role of radical reactivity in the formation of complex organic molecules in interstellar ices*	12,00-12,15
	OC 28	Signorile Matteo "Thesis price winner"	Torino	*Extending the applicability of Raman spectroscopy: from labile systems to in situ and operando approaches*	11,15-12,30
			Award Ceremony		12,30-12,45
			Concluding Remarks		12,45-13,00

List of Posters (according to alphabetic order of presenting Authors)

1st session, Monday 16th April

Num	**Cognome**	**Nome**	**Contatto**	**Titolo**
PO1	Aboudou	Soioulata	Soioulata@hotmail.fr	Synthesis, purification and characterization of antimicrobial peptides isolated from animal venoms
PO2	Ajmalghan	Muthali	Ajmalghan.muthali@etu.univ-amu.fr	Coverage dependent recombination mechanisms of hydrogen from tungsten surfaces via density functional theory
PO3	Alberto	Gabriele	Gabriele.alberto@unito.it	Hybrid squaraine-silica nanoparticles as nir probes for biological applications: optimization of the photoemission performances
PO4	Alkarsifi	Riva	Rivakarsifi@hotmail.com	Synthesis of doped metal oxide nanocrystals for solution-processed interfacial layers in organic solar cells
PO5	Anceschi	Anastasia	Aancesch@unito.it	Maltodextrins nanosponges as precursor for porous carbon materials
PO7	Arnodo	Davide	Davide.arnodo@edu.unito.it	First racemic total synthesis of heliolactone
PO8	Azzi	Emanuele	Emanuele.azzi@edu.unito.it	Synthesis of boronated analogue of curcumin as potential therapeutical agents for alzheimer's disease
PO9	Barzan	Giulia	Sci piem	Study of Nanobiomaterials with Bio-based Antioxidants: Interaction of Polyphenol Molecules with Hydroxyapatite and Silica
PO10	Battaglia	Luigi Sebastiano	Luigi.battaglia@unito.it	Methotrexate loaded solid lipid nanoparticles: protein functionalization to improve brain biodistribution
PO11	Begni	Federico	Federico.begni@gmail.com	On the adsorption of toluene on porous materials with different chemical composition
PO12	Ben Khalifa	Eya	Benkhalifaeya@gmail.com	Synthesischaracterization of activated carbon from modified banana peels for hexavalent chromium adsorption
PO13	Benvenuti	Martino	Mbenvenuti25@gmail.com	The maturation of the co-dehydrogenase from thermococcus sp. Am4 depends on the accessory protein cooc
PO14	Boufroua	Naouel	Naouel.boufroua@unice.fr	an efficientcatalytic one-pot coupling method for the synthesis of novel pyranfuran derivatives
PO15	Brullo	Chiara	Brullo@difar.unige.it	Development of new pde4d inhibitors for alzheimer disease
PO16	Butnarasu	Cosmin	Cosmin.butnarasu@gmail.com	An innovative screening tool to predict the mucus permeability for efficient cystic fibrosis drugs
PO17	Calà	Elisa	Elisa.cala@uniupo.it	The messale rosselli: scientific investigation on an outstanding 14th century illuminated manuscript from avignon
PO18	Calsolaro	Federica	Federica.calsolaro@edu.unito.it	Effect of simultaneous ultrasoundmicrowave irradiation in the production of superparamagnetic iron oxide nanoparticles as negative contrast agent in mri
PO19	Cavalera	Simone	Scavaler@unito.it	Inorganic quantum dotscarbon-nitride quantum dots fluorescence quenching for biosensors
PO20	Cecone	Claudio	Ccecone@unito.it	Controlled release of deet loaded on fibrous mats from electrospun pmda/cyclodextrin polymer
PO21	Chen	Jiaxuan	Cjxisbest@hotmail.com	Synthesis of bola-amphiphilic dendrimers for on-demand drug delivery
PO22	Chen	Xi	Xi.chen@unice.fr	Gold-catalyzed 6-endo cycloisomerization reactions of 1,6-enynes

PO23	Coquerel	Yoann	Yoann.coquerel@univ-amu.fr	Helicene-based chiral nanographenes
PO24	Corazzari	Ingrid	Ingrid.corazzari@unito.it	Swcnt-porphyrin nano-hybrids selectively activated by ultrasound: a new tool for sonodynamic therapy.
PO25	Cutini	Michele	Michele.cutini@unito.it	What is the driving force for collagen protein folding? Insights from hybrid dft simulations
PO26	Darrigo	Giulia	Gdarrigo@unito.it	Exploring nuclear receptors variability with innovative computational tools
PO27	Derraji	Kaouther	Kaouther.derraji@univ-tln.fr	Synthesischaracterization of nanostructured CoMoO4 : Thermochromismpiezochromism.
PO28	Di Vona	Maria Luisa	Divona@uniroma2.it	Composite anion-conducting membranes based on polysulfonelayered double hydroxides
PO29	Fabbiani	Marco	Marco.fabbiani@unito.it	Formic acid adsorption mechanism on anatase tio2 (101) surfaces
PO30	Gal	Jean-Francois	Gal@unice.fr	Quality control of an indium solid polymer for catalytic use by energy dispersive x-ray spectrometry (edx/eds)
PO31	Gastaldi	Simone	Simone.gastaldi784@edu.unito.it	Covalent nlrp3 inhibitors: design strategies, synthesispharmacological characterization
PO32	Giacchello	Ilaria	Giacchello@difar.unige.it	3-cyano-4,6-diphenyl-pyridine amino acid derivatives active as influenza a polymerase inhibitors
PO33	Giordana	Alessia	Alessia.giordana@unito.it	Aromatic compounds profile of doc piedmontese wines by gc-ms with hs-spme
PO34	Giordana	Alessia	Alessia.giordana@unito.it	Hetergeneous catalysts for biomass valorisation: the case of t-zro2
PO35	Greco	Chiara	Greco.phd@difar.unige.it	Synthesis of a small library of potential sgk1 inihibitors
PO36	Hooshyari	Maryam	Hooshyari.phd@difar.unige.it	Effect of storage in plastic bottles on the quality of extra virgin olive oil
PO37	Ivanchenko	Pavlo	Pavlo.ivanchenko@unito.it	Study of nanobiomaterials with bio-based antioxidants: interaction of polyphenol molecules with hydroxyapatitesilica
PO38	Kilinc	Volkan	Kilinc@cinam.univ-mrs.fr	Selective ionic sensor development: deposition of lipid dielectric monolayers on organicinorganic semi-conductor
PO39	Knauth	Philippe	Philippe.knauth@univ-amu.fr	Electrodeposition of ionomer membranes for energy storageconversion
PO40	Knauth	Philippe	Philippe.knauth@univ-amu.fr	Laboratory ionomer materials for energy
PO41	Lan	Wenjun	Wenjun.lan@etu.univ-amu.fr	Sirna-based personalized nanomedicine for cancer treatment
PO42	Lavaud	Lucien	Lavaud@cinam.univ-mrs.fr	N,n’-disubstituted diamino-benzoquinone-diimines : coordination propertiesquinone-zwitterion equilibrium
PO43	Leinardi	Riccardo	Riccardo.leinardi@unito.it	"revisiting the paradigm of quartz pathogenocity: interaction mechanism of surface silanols and biomembranes"
PO44	Leone	Loredana	Loredana.leone@uniupo.it	Structuralnmr relaxometric studies on gdiii complexes of hydroxy-, methoxyacetophenone functionalised do3a chelators
PO45	Mabrouk	Kamel	Kamel.mabrouk@univ-amu.fr	Alkoxyamine peptide ligation (apl): a straightforward method for non native peptide conjugation using intermolecular radical 1,2-addition

2nd Session, Tuesday 17th April

PO6	Argenziano	Monica	Monica.argenziano@unito.it	Hybrid polysaccharide/cyclodextrin nanostructures for the delivery of acyclovir
PO46	Mandrile	Luisa	L.mandrile@inrim.it	Surface enhanced raman scattering substrates for food contaminants detection
PO47	Marchesi	Stefano	Stefano.marchesi@uniupo.it	Extraction of lanthanides from aqueous solutions with saponite clays
PO48	Mateo	Lou	Lou.mateo@unice.fr	Mck-140, is a new antagonist for cxcr1-2, exerting both anti-inflammatory and anti-angiogenic effect in in-vitro and in-vivo.
PO49	Maurino	Valter	Valter.maurino@unito.it	Toward traceable measurements of photocatalytic activity
PO50	Mino	Lorenzo	Lorenzo.mino@unito.it	In situ growth of graphene-like layers on tio2 from molecular precursors
PO51	Mouzay	Julie	Julie.mouzay@univ-amu.fr	Uv-vis light induced aging of titan’s haze and ice
PO52	Musumeci	Francesca	Francesca.musumeci@unige.it	Pyrazolo[3,4-d]pyrimidines as tyrosine kinase inhibitors: synthesis and biological evaluation
PO53	Nejrotti	Stefano	Stefano.nejrotti@unito.it	Gold(i)-catalysed transformations of heterocyclic 1,3-enynes
PO54	Neytard	Cyril	Cyril.neytard@univ-tln.fr	Role of natural organic matter in silicon speciation in soils
PO55	Obah Kosso	Anne	Anneobah@gmail.com	Efficient selenocyanation of imidazoheterocycles and chromen-4-ones
PO56	Ottonelli	Massimo	Massimo.ottonelli@unige.it	Molecular design of benzodithiophenebenzothiadiazole conjugated systems for photovoltaic applications
PO57	Parisotto	Stefano	Stefano.parisotto@unito.it	Cooperative iodide pd(0) catalyzed coupling of n-tosylhydrazonesalkoxyallenes: a selective synthesis of conjugatedskipped dienes
PO58	Pellegrino	Francesco	Francesco.turci@unito.it	Shape controlled anatase nanoparticles for the optimization of functional properties: synthesis, characterization and applications
PO59	Pieraccini	Stefano	Stefano.pieraccini@unimi.it	In silico designexperimental characterization of an oligopeptide targeting the ebola virus vp24 protein
PO60	Poyer	Salomé	Salome.poyer@univ-amu.fr	Kendrick mass defect (kmd) plots for convenient reading of messages stored in sequence-controlled synthetic polymers
PO61	Priola	Emanuele	Emanuele.priola@unito.it	Engineering of gold(i)-zinc(ii) bimetallic complexes for visible light emitting materials: a structuralspectroscopic study.
PO62	Rebba	Erica	Ericarebba23@gmail.com	Applicative aspect of bionanomaterials: leather coatings for firewater resistance
PO63	Righetti	Giada	Righetti@difar.unige.it	Computational approaches for the designchemical synthesis of novel f508del correctors in the treatment of cystic fibrosis
PO64	Rossi	Daniela	simona.collina@unipv.it	Sigma 1 Receptor eligible target for counteracting neurodegeneration. The lead compound (R)-RC-33
PO65	Sainas	Stefano	Stefano.sainas@unito.it	Targeting myeloid differentiation using potent human dihydroorotate dehydrogenase (hdhodh) inhibitors
PO66	Santalucia	Rosangela	Rosangela.santalucia@edu.unito.it	Formation of glycinealanine homo-peptides on the surface of a-quartz from non-activated amino acids
PO67	Sartori	Emanuela	Emanuela-sartori@libero.it	Lead halide perovskite nanocrystals
PO68	Seijo	Lorenzo	Lorenzoseijo@hotmail.com	Hf(otf)4–catalysed hydride transfer reactions in the cyclisation of trifunctional compounds

PO69	Sordello	Fabrizio	Fabrizio.sordello@unito.it	Size-shape-controlled baso4 particles for functional applications
PO70	Spano	Giulia	Giulia.spano@unito.it	Molecularly imprinted polymers: could surfactant influence the molecular recognition properties?
PO71	Sperandio	Céline	Celine.sperandio@etu.univ-amu.fr	Multi-catalytic cascade to access fluorinated keto-diols
PO72	Tintori	Guillaume	Guillaume.tintori@etu.univ-amu.fr	Base-free generation of organic electron donors from air-stable precursors
PO73	Tonelli	Michele	Tonelli@difar.unige.it	Synthesis of benzimidazole derivativesin vitro screening for antileishmanial activity
PO74	Toso	Stefano	Tosostefanots@gmail.com	Collective properties of bright emitting perovskites nanocrystals
PO75	Turci	Francesco	Cristina.pavan@uclouvain.be	Revisiting the paradigm of quartz pathogenicity:silanols as key descriptor of the mechanism of toxicity
PO76	Turco	Francesca	Francesca.turco@unito.it	Discerning between natural and artificial pozzolanic materials by FTIR spectroscopy
PO77	Uehara	A	baldovin@unice.fr	Characterization of the odorant constituents of Helichrysum italicum essential oil
PO78	Vitali Forconesi	Gabriella	gabriella.vitali.f@gmail.com	Application of MCRs to the stereoselective synthesis of diverse heterocycles starting from chemoenzymatycally obtained chiral aldehydes
PO79	Vittoni	Chiara	chiara.vittoni@uniupo.it	Unravelling the Effects of the Adsorbent Porosity on the CO2 Adsorption Process
PO80	Vittoni	Chiara	chiara.vittoni@uniupo.it	CO2 Adsorption on Hybrid Organic-Inorganic Materials: A Multidisciplinary Study
PO81	Yildirim	Onur	onur.yildirim@unito.it	Synthesis of Covalent Organic Frameworks Containing Structural Linkers with Donor-Acceptor Characteristics and Investigation of Their Optoelectronic and Energy Storage Properties".
PO82	Zamirri	Lorenzo	lorenzo.zamirri@unito.it	Computer simulations of interstellar silicates: energeticspectroscopic characterization of forsterite nanoparticle models
PO83	Zampieri	Daniele	dzampieri@units.it	Antitubercular activity of novel 3-(2-oxo-2-arylethylidene)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-ones derivatives
PO84	Zampieri	Daniele	dzampieri@units.it	New hybrid derivatives of 3,4-dihydroquinolin-2(1H)-one5-phenyl-1,3,4-oxadiazol-2(3H)-one scaffolds as sigma-2 ligands
PO85	Zuccarello	Lidia	Lidia.ZUCCARELLO@cea.fr	Probing cysteine and water molecules in redox proteins by FTIR difference spectroscopy

PLENARY LECTURES

An "inorganic chemistry" overview on platinum anticancer drugs: the past, the present, and the future.

Mauro Ravera[*]

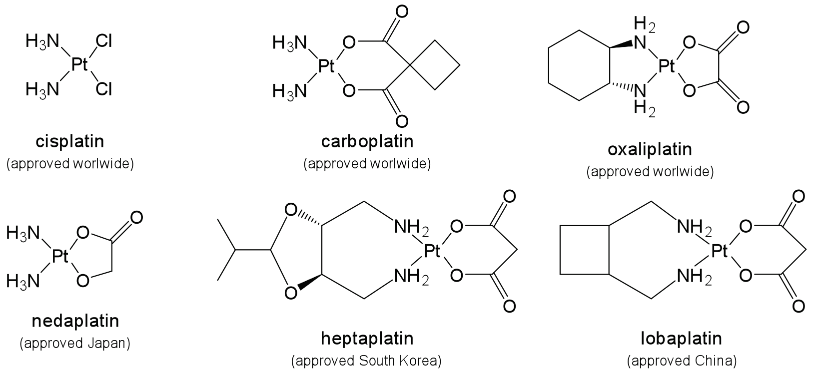
Dipartimento di Scienze e Innovazione Tecnologica, Università del Piemonte Orientale, Viale Teresa Michel 11, 15121 Alessandria (Italy)

The 40th anniversary of the approval by the US Food and Drug Administration (FDA) of the use of cisplatin (*cis*-diamminedichloridoplatinum(II), $[PtCl_2(NH_3)_2]$) as an anticancer drug, may be the occasion to take stock of the situation.

The discovery of the cytotoxic properties of cisplatin in the late '60s and its clinical use have marked the origin of an enormous interest in the chemistry of Pt compounds. Unfortunately, cisplatin and other Pt-based cytotoxic agents display limited activity against certain types of cancer, trigger drug resistance and cause adverse effects (*e.g.*, kidney toxicity, nausea, bone marrow disruption, etc.). Thus, the design of new antitumoral drugs with greater activity than cisplatin and lower adverse side effects was one of the main challenges of research in bioinorganic chemistry. However, it is clear that playing with the basic chemical structure of cisplatin, according to the empirical structure–activity relationships summarized by Cleare and Hoeschele, is unlikely to produce the "metallodrug of the third millennium".

Attempts to obtain molecules with lower systemic toxicity and better pharmacological profiles have provided important results, although these are too few and far between, considering the tremendous efforts made [1].

In this presentation, the past and the present of Pt-based drugs will be recalled and will be the starting point for new and/or different strategies to be adopted for the design of the "cisplatins" of the future (*e.g.*, non-classical platinum complexes with different DNA binding modes or targets different from DNA, Pt-complexes that accumulate selectively at the tumour site by virtue of the drug targeting and delivery (DTD) strategy [2-4], Pt-complexes that are activated only in tumour tissues or cells (prodrugs), bifunctional Pt complexes [5], etc.).



cisplatin
(approved worlwide)

carboplatin
(approved worlwide)

oxaliplatin
(approved worlwide)

nedaplatin
(approved Japan)

heptaplatin
(approved South Korea)

lobaplatin
(approved China)

Figure 1 : Platinum complexes actually used in clinic.

[1] M. Fanelli, M. Formica, V. Fusi, L. Giorgi, M. Micheloni, P. Paoli, *Coord. Chem. Rev.*, **2016**, *310*, 41-79.
[2] E. Gabano, M. Ravera, D. Osella, *Curr. Med. Chem.*, **2009**, *16*, 4544-4580.
[3] T.C. Johnstone, K. Suntharalingam, S.J. Lippard, *Chem. Rev.*, **2016**, *116*, 3436-3486.
[4] R.J. Browning, P.J.T. Reardon, M. Parhizkar, R.B. Pedley, M. Edirisinghe, J.C. Knowles, E. Stride, *ACS Nano*, **2017**, *11*, 8560-8578.
[5] E. Gabano, M. Ravera, D. Osella, *Dalton Trans.*, **2014**, *43*, 9813-9820

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Gold- and Silver-Catalyzed Cycloisomerization and Domino Reactions – A Journey in Molecular Diversity

Véronique Michelet

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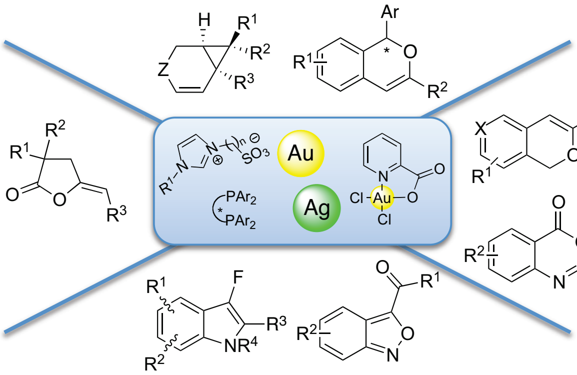
Over the past few years, significant research has been directed toward the development of new methodologies for synthetic efficiency and atom economy processes in the presence of gold and silver catalysts.[1] We have been engaged in a wide project dedicated to the development of catalytic methodologies for the synthesis of original and functionalized carbo- and heterocycles. Our interest has been focused on the cyclization and/or functionalization of alkynes including enynes,[2] carboxylic acid-[3] and aniline-[4] functionalized alkynes, alkynyl silyl enolethers[5] and o-alkynyl benzaldehydes.[6] We also got interested in cycloisomerization reactions of allenols[7] and developed sustainable catalytic systems.[8] This presentation will show an overview of the latest results implying achiral and chiral gold and silver complexes.



References

[1] *Gold Catalysis: An Homogeneous Approach* (Eds.: Toste, F.D.; Michelet, V.), Imperial College Press, London, **2014**. *Silver in Organic Chemistry*; Harmata, M. Ed.; J. Wiley & Sons, Inc. **2010**.
[2] Chao, C.-M.; Beltrami, D.; Toullec, P. Y.; Michelet, V. *Chem. Commun.* **2009**, 6988. Chao, C.-M.; Vitale, M.; Toullec, P. Y.; Genêt, J.-P.; Michelet, V. *Chem. Eur. J.* **2009**, *15*, 1319.
[3] Tomas-Mendivil, E.; Toullec, P.Y.; Borge, J.; Conejero, S.; Michelet, V.; Cadierno, V. *ACS Catal.* **2013**, *3*, 3086.
[4] Arcadi, A.; Chiarini, M.; Del Vecchio, L.; Marinelli, F.; Michelet, V. *Eur. J. Org. Chem.* **2017**, 2214 and *Chem. Commun.* **2016**, *52*, 1458. Arcadi, A.; Pietropaolo, E.; Alvino, A.; Michelet, V. *Org. Lett.* **2013**, *15*, 2766.
[5] Carrër, A.; Péan, C.; Perron-Sierra, F.; Mirguet, O.; Michelet, V. *Adv. Synth. Catal.* **2016**, *358*, 1540.
[6] Mariaule, G.; Newsome, G.; Toullec, P. Y.; Belmont, P.; Michelet, V. *Org. Lett.* **2014**, *16*, 4570. Tomas-Mendivil, E.; Starck, J.; Ortuno, J.-C.; Michelet, V. *Org. Lett.* **2015**, *17*, 6126. Tomas-Mendivil, E.; Heinrich, C.; Ortuno, J.-C.; Starck, J.; Michelet, V. *ACS Catal.* **2017**, *7*, 380.
[7] Le Boucher d'Herouville, F.; Millet, A.; Scalone, M.; Michelet, V. *Synthesis* **2016**, *48*, 3309.
[8] Moragues, A.; Neatu' F.; Pârvulescu, V.I.; Marcos, M. D.; Amorós, P.; Michelet, V. *ACS Catal.* **2015**, *5*, 5060. Leseurre, L.; Le Boucher d'Herouville, F.; Millet, A.; Genêt, J.-P.; Scalone, M.; Michelet, V. *Catal. Commun.* **2015**, *69*, 129.

Recent updates in CFTR structural studies: opportunities and challenges for cystic fibrosis drug development

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Cystic Fibrosis (CF) is the most common lethal monogenic disorder in Caucasians. It is due to different mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) which are classified in five groups, according to the mechanism of CFTR loss-of-function [1]. The most common one, occurring in 70–90% of CF patients, is the deletion of phenylalanine 508 (ΔF508) in the nucleotide binding domain 1 (NBD1). This mutation causes an inappropriate folding and structural instability of CFTR, that, for this reason, remains trapped in the endoplasmic reticulum and is rapidly degraded by the ubiquitin/proteasome system. The deficit of CFTR at the plasma membrane has a major impact on the respiratory system, determining an impairment of innate defense against bacteria [2]. Current therapies are mostly aimed at treating CF symptomatically and although they have significantly pushed forward the mean survival age of patients, the burden of CF care continues to be very high and life quality and expectancy for most CF patients are still limited.

An ambitious therapeutic alternative is to address CF systemically, by means of small molecules able to restore the trafficking (correctors) or the gating (potentiators) capacity of mutated CFTR. Some interesting compounds are emerging in academic laboratories and pharmaceutical companies, however they need a better elucidation concerning their molecular mechanism of action. To this lack of knowledge surely contributes the fact that up to now, the available experimental structures of human wild type (WT) or mutated NBD1 are largely incomplete and also the experimental structure of the human WT CFTR presents some unsolved portions [3], making thus difficult to gain useful insights into the binding mode of small ligands.

Based on these considerations, an overview on recent progress in CFTR structural studies will be presented and discussed, focusing the attention on the ability of the available experimental and homology models to support the efficient screening of large compound libraries and the rational design and synthesis of new compounds for the rescue of the mutated protein. In addition, the combination of a computational approach and Surface Plasmon Resonance will be reported as a good strategy for better clarifying the molecular mechanism of action of some known modulators.

[1] Fanen P., Wohlhuter-Haddad A., Hinzpeter A. Genetics of cystic fibrosis: CFTR mutation classifications toward genotype-based CF therapies. Int. J. Biochem. Cell Biol. 2014, 52, 94–102.
[2] Rivas Caldas R., Boisrame S. Upper aero-digestive contamination by Pseudomonas aeruginosa and implications in Cystic Fibrosis. J. Cyst. Fibros. 2015, 14, 6–15.
[3] Liu F., Zhang Z., Csanady L., Gadsby D.C., Chen J., Molecular Structure of the Human CFTR Ion Channel. Cell 2017, 169, 85-95 e8.

Mechanistic studies of the enzymes that make dihydrogen.

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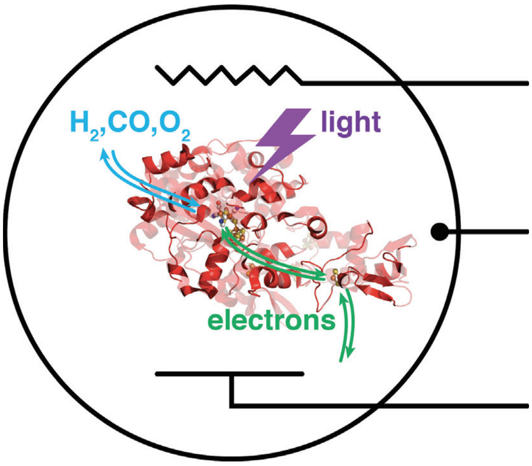
The enzymes that consume or produce « solar fuels » are large protein complexes that embed inorganic cofactors. Understanding their mechanisms requires a combination of biochemistry, molecular biology, spectroscopy, crystallography, theoretical chemistry and kinetics. As part of kinetics, electrochemistry has become very important in this field. I will illustrate how we use it in Marseille to study hydrogenases, the biological catalysts of dihydrogen production and oxidation.



[1] M. Del Barrio, Melisa and M. Sensi and C. Orain and C. Baffert and S. Dementin and V. Fourmond and C. Leger, "*Electrochemical investigations of hydrogenases and other enzymes that produce and use solar fuels*" Acc. Chem. Res. 51 769 (2018). doi:10.1021/acs.accounts.7b00622
[2] M Sensi, M del Barrio, C Baffert, V Fourmond, C Leger "*New perspectives in hydrogenase direct electrochemistry*", Current Opinion in Electrochemistry (2017) doi:10.1016/j.coelec.2017.08.005
[3] V Fourmond and C. Leger, "*Modelling the voltammetry of adsorbed enzymes and molecular catalysts*", Curr. Op. Electrochem 1:1, 110-120 (2017) doi:10.1016/j.coelec.2016.11.002
[4] C. Leger and P. Bertrand. "*Direct electrochemistry of redox enzymes as a tool for mechanistic studies*" Chem. Rev. 108, 2379 (2008) doi:10.1021/cr0680742
[5] Christophe Orain, Matteo Sensi, Carole Baffert, Vincent Fourmond, Christophe Léger, "*La réaction des hydrogénases FeFe avec le dioxygène : étude expérimentale et théorique*", L'actualité chimique 426, 33-37 (2018)
[6] Carole Baffert , Sebastien Dementin , Vincent Fourmond , Christophe Leger, "*L'électrochimie, un outil pour étudier les mécanismes enzymatiques*", L'actualité chimique, 392, 9-1 (2015)
[7] http://bip.cnrs-mrs.fr/bip06/publications.html

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INVITED LECTURES

Catalysis in Confined spaces : Endohedral Functionalization of Hemicryptophane Molecular Cages

Alexandre Martinez*(1)

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Hemicryptophanes are molecular cages that combine a CTV unit with another C_3 symmetrical unit.[1] They have recently received a growing interest and were found to act as efficient receptors, or chiral molecular switches, but their most remarkable feature is the possibility to achieve the endohedral functionalization of their molecular cavity. The resulting confined catalysts have been tested for instance in C-H oxidation or CO_2 conversion. The encapsulation of the catalytic species was found to improve the stability, rate or selectivity of the reaction making this class of supramolecular catalyst specially promising.

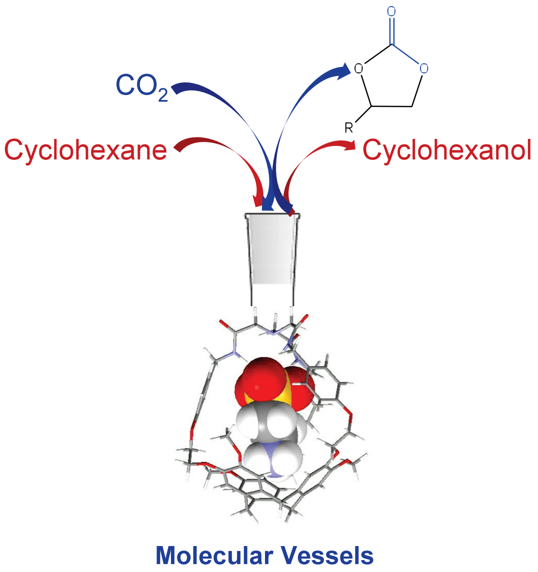

Figure 1 : Catalysis in confined spaces with hemicryptophane cages

[1] D. Zhang, A. Martinez, J.-P; Dutasta, *Chem. Rev.* **2017**, *117*, 4900–4942.

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Dextrin-based Nanosponges

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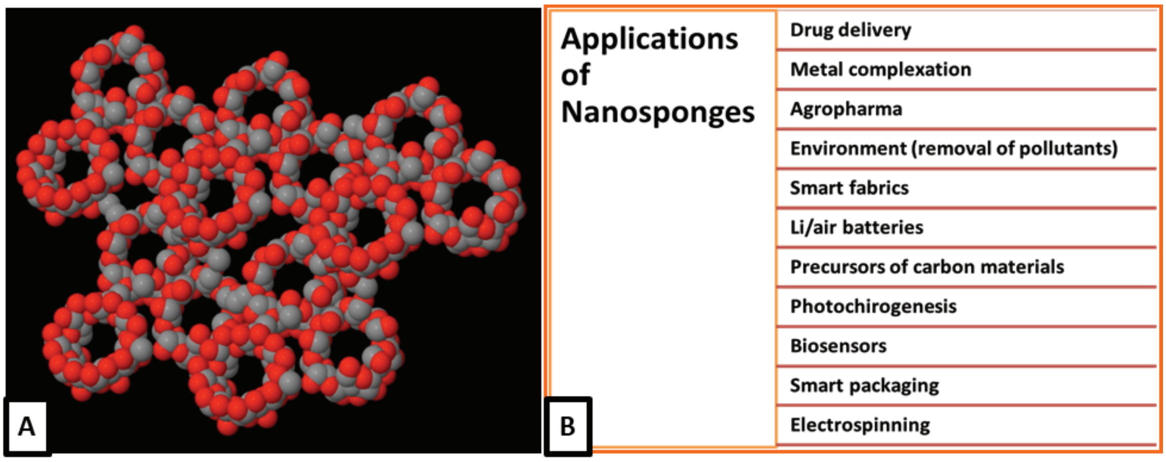
Dextrin-based nanosponges (NS) are cross-linked insoluble polymers nanostructured within a three-dimensional network. Cyclodextrins (CDs), and more recently also linear dextrins, can be cross-linked into NSs bringing significant benefits compared to the respective native dextrin used. In particular, NSs are able to form more stable inclusion complexes with a wider series of molecules thanks to the presence of interstitial spaces among the dextrins, which can host even more hydrophilic guests. (Figure 1, inset A).

Thanks to their outstanding encapsulation properties and the absence of toxicity, NSs find applications in several scientific and technological fields, including drug delivery system, targeted drug delivery nanocarriers, chemistry, agriculture, waste water remediation, catalysis, food, cosmetics, and energy production. (Figure 1, inset B),[1].

In this presentation NSs synthesis and applications were reviewed and some more recent findings will be discussed.



Applications of Nanosponges	
	Drug delivery
	Metal complexation
	Agropharma
	Environment (removal of pollutants)
	Smart fabrics
	Li/air batteries
	Precursors of carbon materials
	Photochirogenesis
	Biosensors
	Smart packaging
	Electrospinning

Figure 1: A – Possible molecular structure of a CD-NS; B - Overview on applications of NS

[1] F. Caldera, M. Tannous, R. Cavalli, M. Zanetti, and F. Trotta, "Evolution of Cyclodextrin Nanosponges," *Int. J. Pharm.*, 2017.

[2] F. Trotta, M. Zanetti, and R. Cavalli, "Cyclodextrin-based nanosponges as drug carriers," *Beilstein J. Org. Chem.*, vol. 8, pp. 2091–2099, 2012.

[3] S. Swaminathan, R. Cavalli, F. Trotta "Cyclodextrin based nanosponges: a versatile platform for cancer nanotherapeutics development "*WIREs Nanomed Nanobiotechnol* 2016. doi: 10.1002/wnan.1384

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A biogeochemical view on soil formation and functioning

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Soils are the result of the interaction between rock, atmosphere, hydrosphere and biosphere. On the surface of the emerged lands, rocks are weathered by aqueous solutions: part of their constitutive minerals are dissolved and part of the dissolved elements reprecipitates as neoformed minerals. On a global scale, the distribution of mineralogy and soil chemistry can be well explained using thermodynamics of major ions and minerals in aqueous solutions. Soils in high rainfall areas, in which aqueous solutions are diluted, are composed of less soluble elements and minerals than soils under drier climates.

A more detailed examination of the structure and composition of soils, however, shows the limits of an abiotic approach of soil genesis. Studies done in the last 30 years have shown how plants and related microorganisms can change the pH, Eh and complexing capacity of the soil solutions, and how the recycling by plants of the elements constitutive of soil minerals impacts the mineralogical composition of soils and can control the cycle of several elements on a global scale.

Here we give the example of Si and Al, the most abundant elements in the earth's crust after oxygen, and of C, whose behavior is of particular interest in the context of climate change.

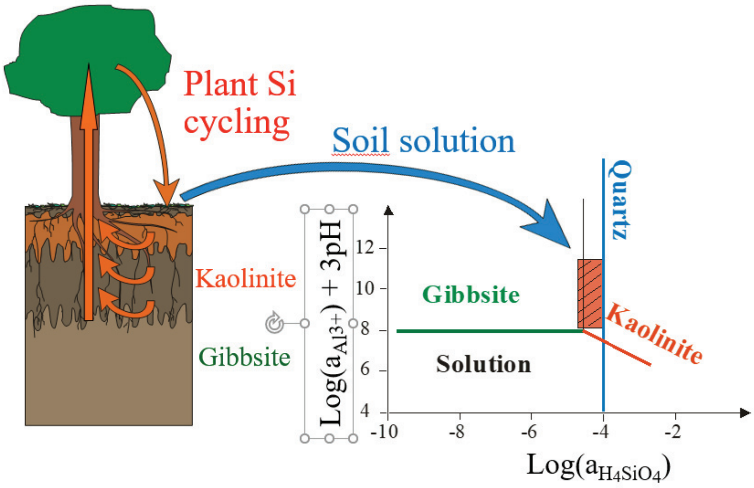

Figure 1

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IX Giornate Italo-Francesi di Chimica
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Emerging contaminants in waters: a challenge for analytical chemistry

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In the past decade, the focus of environmental research has partly shifted from the analysis of conventional priority pollutants to the analysis of emerging contaminants, especially those widely used in everyday life [1]. Many of these are not new chemicals, since they have been present in wastewaters for decades, but are only now being recognized as potentially significant water pollutants, even if no guidelines or legislative interventions are currently available to regulate their presence in the environment. Emerging pollutants include a wide array of different compounds: personal care products, pharmaceuticals, new pesticides, industrial compounds, and byproducts. Their occurrence in waters is mainly due to the incomplete removal in sewage treatment plants, which are principally designed to control suspended solids emissions and oxygen demand of the final effluent [2]. They are less persistent than priority pollutants, but continuously discharged into the environment, where they are usually present in extremely small concentrations, from $\mu g\ L^{-1}$ to $ng\ L^{-1}$ [3].

Such low concentration levels represent a real challenge for the determination of these compounds in environmental waters, together with the presence of potential interferents [4]. Therefore, a combination of effective preconcentration methods and sensitive and selective analytical techniques is required to tackle this complex problem. While liquid chromatography coupled to mass spectrometry or tandem mass spectrometry is considered as the technique of choice for the analysis of emerging pollutants, different sample preparation methods are available, and new ones are proposed in the literature every year.

In this contribution, an overview of the most innovative sample preparation techniques will be described; in particular, various methods developed by our research group for the determination of different classes of emerging pollutants in waters will be presented and discussed, together with the application to diverse types of environmental waters (seawater, wastewater and groundwater).

[1] Mirasole, C., Di Carro, M., Tanwar, S., Magi, E., J. Mass Spectrom. 2016, 51, 814–820.
[2] S. Tanwar, S., Di Carro, M., Ianni, C., Magi, E., Occurrence of PCPs in Natural Waters From Europe, Springer, Berlin Heidelberg 2014, 1–35.
[3] Lapworth D.J., Baran N., Stuart M.E., Ward R.S., Environ. Pollut. 2012, 163, 287–303.
[4] Fatta-Kassinos D., Meric S., Nikolaou A., Anal. Bioanal. Chem. 2011, 399, 251-275.

ORAL COMMUNICATIONS

Effect of photodoping on TiO_2-coated n-type Si for water splitting

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Water photosplitting under solar illumination appears to be a leading approach to produce H_2, a solar fuel, and O_2. Unfortunately, the best efficiencies are reached with non-earth abundant or expensive materials (such as Ga, As, In…) which is an obstacle to their large scale development. In the present work, silicon is used as photoanode in a photoelectrochemical cell. It absorbs light in the visible range and its electronic structure and properties are well-suited to drive the water photooxidation [1]. However, it suffers from a strong corrosion in alkaline media. A thin TiO_2 film can thus be used as protection because this material is highly stable at high pH and a synergic effect is also expected due to its electronic structure and its absorption in the UV range [2,3]. To perform this step, Atomic Layer Deposition (ALD) is carried out using TTIP or TDMAT and water. This technique allows a perfect control of both thickness and composition of the layer. A long time stability is obtained in strong alkaline media, but, the photocurrent (j_{ph}) can be further improved [2,3]. It has been demonstrated that, TiO_2 layer can be doped by cathodic polarization (electrodoping) [4,5] or by illumination (photodoping) [5,6]. This step leads to the reduction of Ti(IV) to Ti(III) in the near surface region with the incorporation of protons inside the layer [6,7,8]. Photodoping is an easy way to dope a layer and leads to the improvement of both the photocurrent and the fill factor, nevertheless, this is partially reversible [6].

In this work, a systematic study of the n-Si/TiO_2/KOH photodoping is proposed in order to drastically improve both the fill factor and the j_{ph}. An enhancement of the photoelectrochemical properties are directly correlated with the duration, the light power and the wavelength used during the doping step. This spontaneous electron accumulation is monitored by infrared spectroscopy as well as open circuit measurement (under illumination) since the Fermi level is shifted with the reduction of Ti (IV). A direct impact of the capping layer thickness and of the parameters of the ALD step are also observed. To assess the doping stability, chronoamperometry and sequential voltammograms are performed after the photodoping step. The j_{ph} of the first polarization is incredibly high and a photocurrent drop appears at the second polarization but, a long time stabilization above the reference photocurrent is highlighted. The best efficiency is reached with TTIP at 120°C.

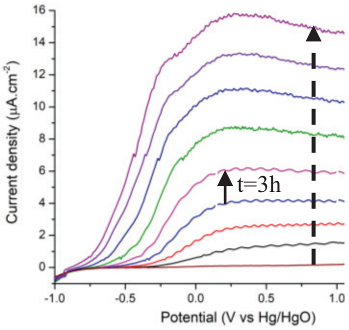

Figure 1: Sequential cyclic voltammograms of TiO_2-coated n-Si in 1M KOH under white light illumination (100 mW.cm^{-2})

[1] K. Sun et al., *Chem. Rev.*, **2014** 114, 8662
[2] Y. J. Hwang et al., *Nano Lett.*, **2009**, 9, 410
[3] L. Santinacci et al., *ACS Appl. Mater. Interfaces*, **2016**, 8, 24810
[4] L. A. Harris et al., *J. Electrochem. Soc.*, **1979**, 126, 850
[5] M. F. Weber et al., *J Electrochem Soc.*, **1982**, 129, 2022
[6] T. Berger et al., *Electrochem. Commun.*, **2006**, 8, 1713
[7] J. Idigoras et al., *J. Phys. Chem. C*, **2016**, 120, 27882
[8] B. J. Trzesniewski et al., Energy Environ. Sci., 2017, 10, 1517

On the Structure of Superbasic $(MgO)_n$ sites solvated in a Faujasite Zeolite

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Basic zeolite catalysts are experiencing a renewed interest due their application in many novel industrial processes involving oxygen-containing substrates, connected with the growing field of the integration of renewable feedstock in refinery processes. We report the synthesis and characterisation of a HY/MgO zeolite/oxide composite material with high crystallinity and highly dispersed superbasic MgO sites. Preparation was optimized in order to preserve sample crystallinity, to avoid the formation of mesoporosity and to minimize the formation of separate Mg-containing phases. These features were checked by means of electron microscopy, X-ray powder diffraction, porosimetry and IR spectroscopy. A single-phase material was obtained, comprising clusters of magnesium oxide and hydroxide hosted by the microporous zeolite framework. The material has been studied by means of Rietveld refinement high quality quantum mechanical molecular simulations. The refinement has shown the presence of magnesium and oxygen atoms in the double six-membered ring cages, consistent with the presence of mononuclear Mg moieties. However, composition and IR spectroscopy demonstrate that other Mg species must exist, likely located in the supercages. In order to propose candidate structures for these species, several hypothetic periodic models of the material were built by placing $(MgO)_n$ clusters in different locations of the zeolite structure, taking into account the material composition and other constraints imposed by the experimental observations. The models were optimized at the B3LYP-D*/DZVP level and classified according to their stability. Two families of possible sites were identified: isolated sites containing a single MgO moiety and larger clusters. The reactivity of representative models with CO_2 has been modeled. CO2 forms very stable linear end-on adducts with low coordinated Mg ions in most cases (Figure 1). Isolated sites give rise to bridge bidentate complexes (Figure 1a) in agreement with previous spectroscopic observations. The formation of hydrogen-carbonates is observed only on specific sites, through a process having a low adsorption energy because of the high deformation of the adsorption site.

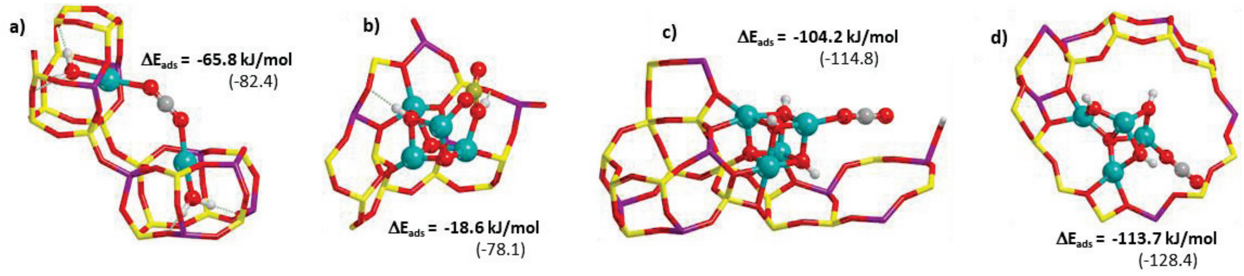

Figure 1 : Models of CO_2 adsorption on selected $(MgO)_4$ cluster

[1] D. Barthomeuf, Catal. Rev., 1996, 38, 521-612.
[2] K. Kwapien, M. Sierka, J. Dobler, J. Sauer, M. Haertelt, A. Fielicke and G. Meijer, Angewandte Chemie-International Edition, 2011, 50, 1716-1719.
[3] H. V. Thang, L. Grajciar, P. Nachtigall, O. Bludsky, C. O. Arean, E. Frydova and R. Bulanek, Catalysis Today, 2014, 227, 50-56.

Bioaccumulation and speciation of uranium in sea urchins

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Further to nuclear waste discharges, leaks or nuclear accidents, non-negligible amounts of uranium can be released in the environment and, in particular, in seawater, which often represents the final environmental repository for contaminated waters. In environmental and biological conditions, uranium mainly occurs under its hexavalent oxidation state, in the form of the di-oxo uranyl cation, UO_2^{2+}. Previous studies reveal that uranyl is mainly present in seawater as a dicalcium uranyl tricarbonate complex $Ca_2UO_2(CO_3)_3$.(1) However, the bioavailability and the mobility of uranium strongly depends on its speciation. It is therefore of great importance to further study the bioaccumulation of uranium in living organisms and to understand its speciation.

The accumulation of several heavy metals (among which radionuclides) in marine organism has been widely studied.(2) Nevertheless, the speciation of uranium in marine organisms has never been investigated, probably due to the very low concentration of uranium in natural seawater (ppb level), which makes really challenging the use of spectroscopic methods.

This work aims at assessing new insights about the speciation of uranium in a model marine species: sea urchins *Paracentrotus Lividus*. Multiple bioaccumulation experiments over ten days were performed, after which the sea urchins were sacrificed, and the three compartments (intestinal tract, gonads and test = spikes + shell) separated. Uranium content was later quantified, via ICP-OES (Inductively Coupled Plasma - Optical Emission Spectrometry). The speciation inside each compartment was studied by EXAFS (Extended X-ray Absorption Fine Structure) spectroscopy at the MARS beam line of SOLEIL synchrotron.

Bioaccumulation results, biodistribution in the sea urchins and speciation in the three different compartments of the sea urchins will be presented.

[1] M. Maloubier et *al*., XAS and TRLIF spectroscopy of uranium and neptunium in seawater, *Dalton Trans*., 2015, 44, 5417-5427

[2] R.A Jeffree et *al*. Comparison of the bioaccumulation from seawater and depuration of heavy metals and radionuclides in the spotted dogfish *Scyliorhinus canicula* (Chondrichthys) and the turbot *Psetta maxima* (Actinopterygii: Teleostei), *Science of the Total Environment* 368 (2006) 839–852

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Hyperspectral imaging for forensics sciences: revealing the hidden

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There is a large interest in developing customised analytical methods based on non-destructive chemical imaging in several fields of application, especially when it is fundamental to spatially visualise the results as an unequivocal proof of the crime and without damaging the evidences, because further investigations could be required during legal inquiries. For these reasons, the present work aims at developing a reliable method for the application of hyperspectral imaging in the near infrared region (HSI-NIR) to detect biological traces on the crime scene; in this way, a screening procedure is proposed to detect areas of interest in which collecting micro-samples for applying the conventional more targeted DNA analyses. In more detail, this work will give a fundamental contribute to forensic scientists in identifying biological traces directly on specimens, recognising the type of trace (e.g. blood, urine, semen and their mixtures as well as food traces) regardless of the material constituting the collected evidences (e.g. paper, glass and cloth).

HSI-NIR is the newest technology developed in the NIR spectroscopy field; it is based on the interaction between radiation − in the region of the electromagnetic spectrum between 1000 and 2500 nm − and the sample, to obtain chemical information about its composition, thanks to the spectroscopic absorption of characterising compounds. The advantages of this approach are exploited when samples to be evaluated are characterised by a non-uniform distribution of chemicals inside the whole matrix. In this situation, the validity of traditional chemical analyses is strictly dependent upon the design of a correct sampling plan; the extent of sampling required to account for such a variability of distribution is necessarily quite large and the method of collecting samples is also critical. All these limits become serious when data collected have to be used for drawing conclusions at the service of law. In fact, sampling limitations leave an analytical crack in which crime is still acting.

HSI-NIR instrumentations are not directly applicable because they require optimisation steps in terms of both instrumental setup and image acquisition; furthermore, acquiring the image is not enough for extracting robust results from samples. For these reasons, in this work, HSI-NIR is supported by a proper chemometric strategy particularly suited to account for the spatial information, allowing to define a customised method for the specific application.

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An unusual blue-turquoise pigment found on a painting at Novalesa abbey (Piemonte)

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In the analysis of paintings it is always interesting to compare the identified colourants with the recipes reported in ancient treatises; but there are cases, however, in which a colourant is identified on a painting for which it is not possible to find any confirmation on ancient literary source. This is definitely the case of a blue-turquoise pigment found on a 12th century mural painting at the abbey of Novalesa (Piemonte), an ancient Benedictine settlement funded in 8th century AD along the route that crosses the Moncenisio pass between Italy and France. In the cloister of the abbey, a wonderful lunette (Fig.1) contains a *mandorla* with the Pantocrator Christ. *In situ* non-invasive measurements identified the presence of natural ultramarine blue in the vast bright blue background area, but the borders of the *mandorla*, however, coloured in blue, turquoise and green, told us a completely different story. *In situ* non-invasive measurements with X-ray Fluorescence spectrometry (XRF) detected only Fe together with Si, Al, K and Ca, all common elements in a mural painting. UV-visible diffuse reflectance spectrophotometry with optic fibres (FORS) analysis highlighted an apparent absorbance maximum at ca. 900 nm which suggests the presence of Fe^{3+} ion in a chemical environment similar to *goethite*, but with an apparently different colour. In the end, the pigment used on the borders has no correspondence with any known blue or turquoise. At least, it was possible verifying that the green hue was obtained with a mixture of the blue-turquoise pigment and yellow ochre. In order to elucidate the chemical nature of this anomalous pigment, micro samples were taken to perform more in-depth analyses. Raman analysis highlighted the presence of a thin upper layer made of gypsum, possibly laid in order to tune the colour; in fact the same layer was not found on other painted areas. The spectrum of the underlying blue-turquoise area only suggested that a silicate material was present. Scanning Electron Microscopy-Energy Dispersive X (SEM-EDX) analysis confirmed the presence of gypsum only on the uppermost layer, while in the blue-turquoise layer a clear correlation between Fe, Si, Al, K, Mg and Ca was found, allowing hypothesising that the pigment could be a clay-like material. Further measurements by means of X-ray Diffraction on sample treated with acetic acid, to eliminate the $CaCO_3$ fraction are in progress in order to identify the exact structure of the clay minerals. This information will be interesting with concern to the identification of the possible source of the material and will send light on the artists working at Novalesa in that period.

Figure 1: Lunette containing the blue-turquoise pigment

Ion mobility/mass spectrometry: a powerful coupling for detailed characterization of synthetic polymers

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Mass spectrometry is increasingly used as a fast and accurate technique to characterize the structure of synthetic polymers. On the one hand, these macromolecules can be generated as intact ions in the gas phase using soft ionization techniques such as electrospray (ESI) or matrix-assisted laser desorption/ionization (MALDI). On the other hand, mass analyzers such as time-of-flight (TOF) devices offer sufficient resolution capabilities to enable safe mass spectral assignments. While analysis in the MS mode allows repeating units to be readily identified, experiments conducted in the MS/MS mode are performed to characterize the structure of end-groups. However, this technique has also some limitations, particularly when considering very complex samples such as polymer blends or mixtures sampled from reaction media during the development of new polymerization processes. Efficient separation of species prior to their mass analysis can be achieved by advanced liquid chromatography techniques, but this approach highly increases the whole analysis time (MS typically operates on a microsecond timescale while LC separations require at least some minutes). Alternatively, ion mobility spectrometry (IMS) can separate ionic species on a millisecond timescale and can hence advantageously be coupled to MS(/MS) for polymers analysis. Moreover, since IMS separates ions based on their mass, charge and shape,[1] it can also be employed to get insights in conformational properties of the analytes.

This study shows the two main uses of IMS-MS coupling in the field of synthetic polymers. The first case shows the benefits of using IMS to improve the separation of isobaric species prior their activation, allowing individual MS/MS spectra to be acquired and hence accurate assignments of chain terminations. It is illustrated by data obtained for polylactides (PLA) or polystyrenes (PS).[2] In the second example, IMS was employed to evidence conformational changes of synthetic polymers as a function of i) their repeating units, as illustrated for poly(vinylpyridine) chains composed of either 2- or 4-vinylpyridine monomers, or ii) the nature of cations adducted to their skeleton, as shown for an hybrid polymer composed of a poly(ethylene oxide) (PEO) chains capped by a poly(amidoamide) (PAMAM) dendrimer.[3]

[1] Giles K., Williams J.P., Campuzano I., Rapid Commun. Mass Spectrom., 25, 1559 (2011).
[2] Chendo C., Le D. Phan T.N.T., Gigmes D., Charles L., J. Polym. Sci. Pol. Chem., 54, 3388, (2016).
[3] Tintaru A. Chendo C., Wang Q., Viel S.,Quéléver G., Peng L., Posocco P., Pricl S., Charles L. Anal. Chim. Acta., 808, 164, (2014).

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Interaction of anionic and cationic nanoparticles with phospholipid membranes

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Ligand-protected inorganic nanoparticles (NPs), functionalized by organic and biocompatible coatings, offer several opportunities in biomedicine. In particular, monolayer-protected gold NPs (AuNPs) have emerged as a reference system in the field, as their optical properties can be exploited for *in vitro* sensing and *in vivo* imaging, drug delivery applications and photothermal therapies. However, there is concern about the possible toxicological effects of these nanosized materials, since they also involve potential risks of harmful side effects on health. Therefore, a number of studies is aimed at investigating the chemico-physical mechanisms which take place in the interaction between ligand-protected NPs and biological membranes. Current results on the molecular mechanisms involved and on the role played by positively and negatively charged NP ligands are still debated. We focused our attention on the interaction between charged monolayer-protected AuNPs and model lipid membranes. We studied the effect of the NP coating charge on the interaction of NPs with neutral zwitterionic 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC) membranes. We synthetized charged AuNPs with diameter between 4 and 6 nm, passivated with both hydrophobic and charged alkanethiols. We used $-COO^-$ ω-functionalized thiols for anionic NPs (NP−) and $-N^+(CH_3)_3$ ω-functionalized thiols for cationic NPs (NP+). The NPs diameter was measured by FESEM and DLS techniques; the monolayer surface charge and composition were characterized by Z-Potential and NMR analyses. To investigate the perturbation induced by NP− and NP+ on neutral lipid membranes we quantified experimentally the NPs-induced leakage from POPC liposomes loaded with calcein. Our leakage assays show that NP+ induce a slightly larger transient permeabilization of POPC liposomes than NP− do. We rationalised this finding based on the tendency of the NP− anionic ligands to get protonated when interacting with the membrane. This result has been validated by means of metadynamics and unbiased molecular dynamics simulations.

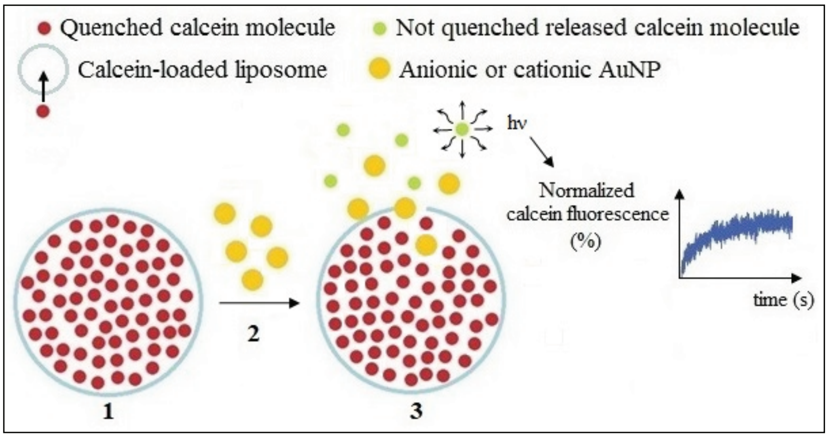

Figure 1: NPs-induced leakage assay on calcein-loaded liposome (not to scale)

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Helicene-Based Chiral Nanographenes

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Curved polyaromatic hydrocarbons (PAHs) with extended π-systems are of great interest in organic chemistry and in materials science, especially in research on nanographenes, nanoribbons, and distorted graphene sheets with peculiar topology.[1] An increasing number of large, nonplanar, and molecularly defined PAHs have lately been reported. However, the ultimate challenge in this field is probably to exploit chirality as an additional parameter to fine-tune and to fully exalt organic materials properties, such as their physical, supramolecular (solid-state packing, homochiral/heterochiral interactions), photophysical, conductive, chiroptical, molecular recognition, and switching properties.[2] Because helicenes[3] are typical units that can be used to induce chirality, several nonplanar PAHs incorporating multiple helicene units have been proposed, but only a few are stereochemically stable.[4] In this communication, the design, the synthesis and the properties of a configurationally stable *D3*-symmetric propeller-shaped PAH embedding six helicene moieties will be discussed (Figure 1).[5]

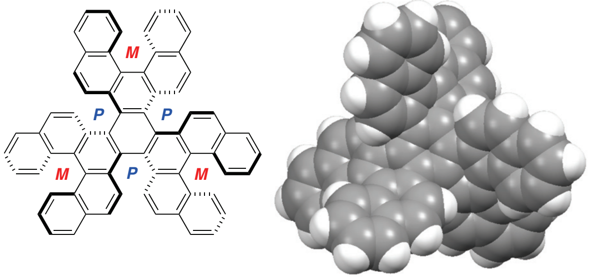

Figure 1 : D3-symmetric propeller-shaped nanographene ***1*** *embedding six enantiomerically stable [5]helicenes*

References:

[1] Reviews: a) R. Rieger, K. Müllen *J. Phys. Org. Chem.* **2010**, *23*, 315-325. b) R. A. Pascal, Jr., *Chem. Rev.* **2006**, *106*, 4809-4819. c) Y.-T. Wu, J. S. Siegel, *Chem. Rev.* **2006**, *106*, 4843-4867. d) V. M. Tsefrikas, L. T. Scott, *Chem. Rev.* **2006**, *106*, 4868-4884.

[2] A. Scarso, G. Borsato, In *Chirality at the Nanoscale, Nanoparticles, Surfaces, Materials and More* (Ed.: D. Amabilino), Wiley-VCH: Weinheim, 2009; Chapter 2, pp 29−65.

[3] a) *Helicene Chemistry From Synthesis to Applications* (Ed.: C.-F. Chen, Y. Sheb), Springer: Berlin, 2017. b) Y. Shen, C.-F. Chen, *Chem. Rev.* **2012**, *112*, 1463-1535. c) M. Gingras, *Chem. Soc. Rev.* **2013**, *42*, 968-1006. d) M. Gingras, G. Félix, R. Peresutti, *Chem. Soc. Rev.* **2013**, *42*, 1007-1050. e) M. Gingras, *Chem. Soc. Rev.* **2013**, *42*, 1051-1095. f) S. Goretta, C. Tasciotti, S. Mathieu, M. Smet, W. Maes, Y.M. Chabre, W. Dehaen, R. Giasson, J.-M. Raimundo, C. Henry, C. Barth, M. Gingras, *Org. Lett.* **2009**, *11*, 3846-3849.

[4] Review: C. Li, Y. Yang, Q. Miao, *Chem. Asian J.* DOI: 10.1002/asia.201800073.

[5] a) V. Berezhnaia, M. Roy, N. Vanthuyne, M. Villa, J.-V. Naubron, J. Rodriguez, Y. Coquerel, M. Gingras, *J. Am. Chem. Soc.* **2017**, *139*, 18508-18511.

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IX Giornate Italo-Francesi di Chimica
IX Journées Franco-Italiennes de Chimie
Genova
April 16-18, 2018

Characterization of the odorant constituents of *Helichrysum italicum* essential oil

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Helichrysum italicum ssp. *italicum* (Asteraceae) is widespread all over the Mediterranean basin. It is sometimes called "curry plant" because of the typical strong spicy smell of its leaves. In the flavour & fragrance industry, this species is extracted for the production of absolute, or hydrodistilled to furnish an essential oil which is widely used in cosmetics and in aromatherapy. The composition of the essential oil has been extensively studied, and depending on the geographical origin of the plant, the main constituent is either neryl acetate **1** or monoterpenes like α-pinene **2**. Some uncommon 2-methyl-1,3-diketones such as **3-6** appear to be specific components of *H. italicum*, and have never been observed in other species so far [1, 2].

In the course of our analytical studies devoted to the identification of the key odorants of fragrant plants, we performed a Gas Chromatography Olfactometry (GC-O) analysis of a sample of Corsican *H. italicum* essential oil (neryl acetate type), using the Aroma Extract Dilution Analysis (AEDA) methodology. The identification of the odorants was realized by a detailed fractionation of the essential oil by liquid-liquid basic extraction, distillation and column chromatography, followed by the GC-MS and GC-O analyses of some fractions, and coinjection of commercial and synthesised reference compounds.

We could demonstrate that the characteristic curry/spicy odor of the plant is mostly due to the saturated diketones **3** - **4**, together with some volatiles more common as essential oil constituents (such as 1,8-cineole **7**, nerol **8**, eugenol **9**, *p*-cresol **10**…). In contrast, the olfactory contribution of **1** and of the unsaturated diketones **5** - **6** was much less significant.

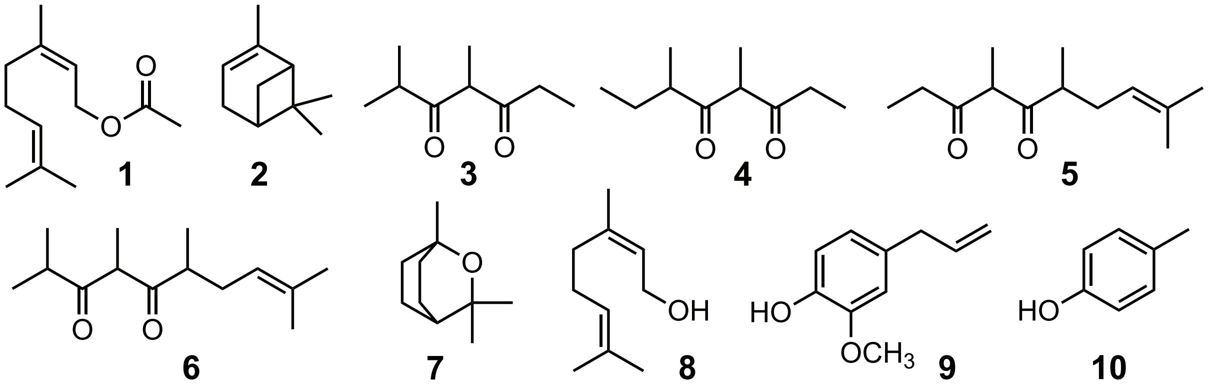

Figure 1: Main constituents and odorants of Helichrysum italicum *essential oil.*

[1] Manitto, P.; Monti, D.; Colombo, E., *Phytochemistry,* **1972,** *11* (6), 2112-2114.
[2] Tira, S.; Di Modica, G., *Tetrahedron Letters,* **1967,** *8* (2), 143-148.

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IX Giornate Italo-Francesi di Chimica
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Sesterterpenes from *Salvia tingitana* Etl. (Lamiaceae)

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Salvia tingitana Etl. is an aromatic woody-based perennial shrub original from the Arabian region [1]. The plant was historically used as rubefacient, solving, digestive, and against colds and drunkenness [2]. In the course of our research on new plant compounds from *Salvia* species able to face the constantly increasing resistance to antibiotics [3], the antimicrobial properties of the dichloromethane extract obtained from the aerial parts of *S. tingitana* was investigated following a bioassay-oriented fractionation approach. The surface extract showed moderate antimicrobial activity against Gram positive multi-resistant bacterial strains; no activity was observed on the Gram-negative strains or on *Candida albicans*.

The hexane insoluble fraction of the crude extract was separated by silica gel column chromatography into six fractions (I_a-VI_a); the hexane soluble fraction was separated into seven fractions (I_b-VII_b); all fractions were evaluated at doses corresponding to that of the crude extract. Among the tested fractions, fraction IV_a V_a V_a were active against various *Staphylococcus* spp including *S. aureus* and *S. epidermidis*. Fractions III_b and IV_b were active against various *Staphylococcus* spp. and *Enterococcus faecium*, and fraction V_b was active against *Staphylococcus* spp.

The chemical separation of the fractions afforded eight new and five known sesterterpenes, along with other known compounds including five labdane and one abietane diterpenes, one sesquiterpene and four polymethoxylated flavonoids, identified by IR, 1D and 2D NMR, HR-MS analysis. The antimicrobial activity of the pure compounds was analysed on several Gram positive multi-resistant bacterial strains, also of marine origin (*S. aureus*, *S. epidermidis*, *S. haemoliticus*, *S. hominis*, *S. capitis*, *S. lugdunensis*, *S. saprophyticus*, *S. mitis*, *E. faecium*, *E. faecalis*, *E. durans*, *E. gallinarum*, *E. casseliflavus*, *E. gallolyticus*). The compounds showed various antimicrobial activities against Gram positive bacteria, with the exception of manool and sclareol, which exhibited MIC values ranging from 4 to 64 µg/mL.

[1] Foley, MJY, Hedge, IC, Möller, M. (**2008**) The enigmatic *Salvia tingitana* (Lamiaceae): a case study in history, taxonomy and cytology. *Willdenowia*, ***38***, 41-59.
[2] Alpini, P. (**1627**) *De plantis exoticis: libri duo. De plantis exoticis*, ed. Alpini, A. Apud Io. Guerilium, Venetiis [Venice]
[3] Pontes, DS, de Araujo, RSA, Dantas, N, Scotti, L, Scotti, MT, de Moura, RO, Mendonca-Junior, FJB. (**2018**) Genetic Mechanisms of Antibiotic Resistance and the Role of Antibiotic Adjuvants. *Current topics in medicinal chemistry*.

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IX Giornate Italo-Francesi di Chimica
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α-Silyloxy Acrylamides: Synthesis and Reactivity

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The photoinduced, multicomponent reaction of α-diazoketones, silanols, and isocyanides affords α-silyloxy acrylamides (Figure 1), formally derived from α-keto amides. The presence of a secondary amido group makes classic preparative methods for silyl enol ethers unfeasible in this case, while the mild conditions required by this photochemical approach allow their synthesis in good yields; moreover, the general structure can be easily modified by varying each component of the multicomponent reaction. Fine-tuning of the reaction conditions (i.e., solvents, radiation, additives) can be exploited to obtain complete Z selectivity. The reactivity of this overlooked class of silyl enol ethers has been investigated, and features that could pave the way to new applications have been found.[1]

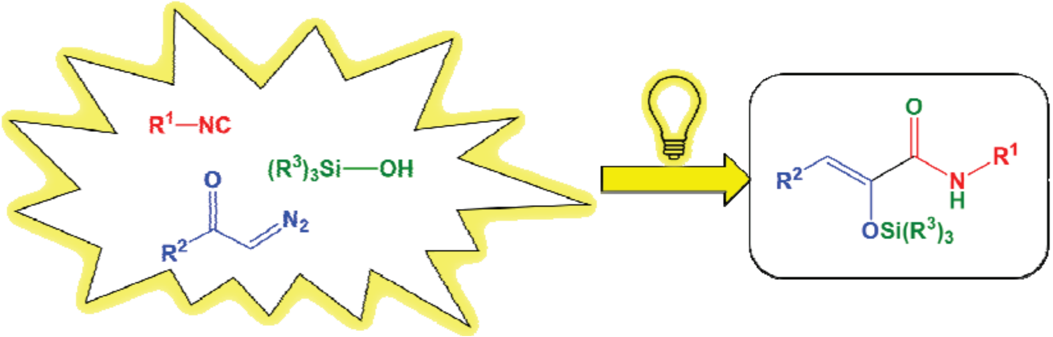

Figure 1: Photoinduced multicomponent approach to α-silyloxy acrylamides.

[1] Ibba, F.; Capurro, P.; Garbarino, S.; Anselmo, M.; Moni, L. and Basso, A., *Org. Lett.*, **2018**, *20* (4), pp 1098–1101

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Superabsorbent polymers for application in agriculture

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Hydrogels are homopolymeric or copolymer hydrophilic networks absorbing large quantities of water without dissolution or loss of three-dimensional structure. The high water retention capacity of hydrogels can reduce the vulnerability to droughts and, therefore, meet the major challenge for agriculture in arid or semi-arid region. The development of hydrogels with high water absorption and water holding capacities is one of the objectives of PROWPER project (ERA-NET WaterWorks2015). The hydrogels were prepared by simultaneous polymerization and crosslinking of acrylic acid and acrylamide with N,N'-methylene-bis-acrylamide (MBA) as crosslinking agent. The influence of the degree of neutralization of acrylic acid, the proportion of acrylamide and the level of crosslinking agent on the swelling and water retention properties of hydrogels have been investigated. Uniaxial tensile tests were conducted to evaluate the mechanical strength of the swelled acrylic hydrogels. The water retention properties were found to strongly depend on the type of stress applied, pressure or temperature, during the desorption test. As a representative example, the figure below shows that the water retention capacity after centrifugation increases when the degree of crosslinking increases while it decreases under temperature desorption conditions.

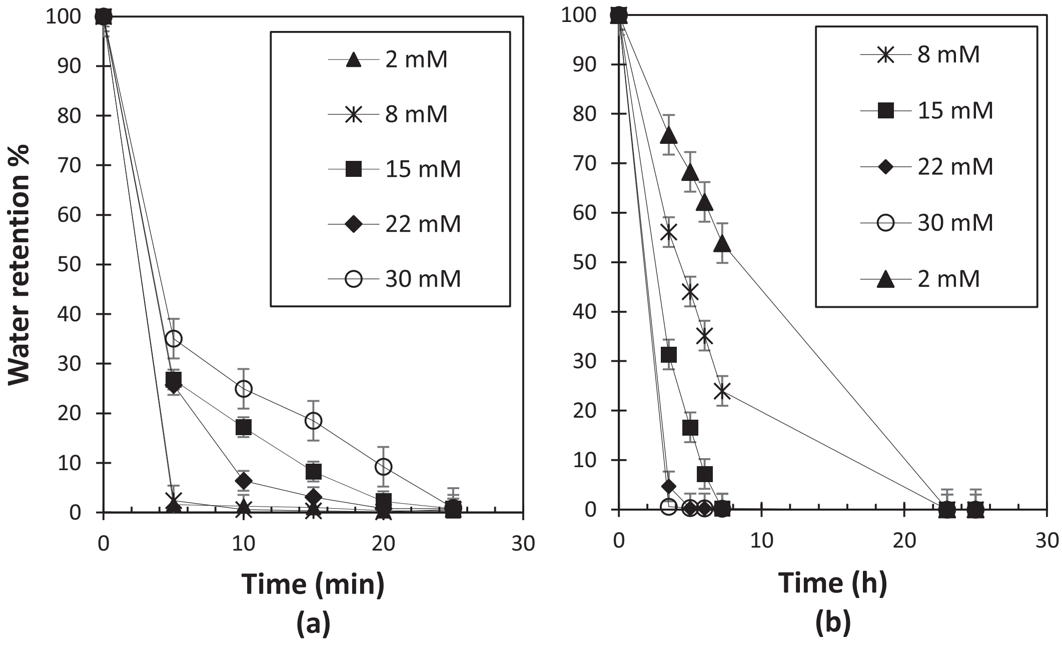

Figure: Water retention as a function of centrifugation time (a) and drying time at 60 ° C (b) for poly(acrylic acid) gels obtained at different MBA concentration

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N,N,N-Tris(*tert*-butoxycarbonyl)-*L*-arginine: five isoforms whose obtainment depends on procedure and a scrupulous NMR confirmation of their structures

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L-arginine is often covalently linked to delivery systems for increasing their transfection activity and reducing toxicity and its basic nitrogen atoms need protection for example with *tert*-butoxycarbonyl group. Following three reported protocols which assured the goal of obtaining the widely cited $^{\alpha}N,^{\omega}N,^{\omega'}N$-tris(*tert*-butyloxycarbonyl)-*L*-arginine, surprisingly we achieved also other four isoforms (Figure 1). With the first selected procedure [1] $^{\alpha}N,^{\omega}N,^{\omega'}N$-Tris(*tert*-butyloxycarbonyl)-*L*-arginine was never obtained. The second one [2] provided the desired compound but as a mixture of geometric isomers *E/Z* while the third [3] protocol led to a single very pure isoform in high yield but with an unreported symmetrical structure. Since BOC protection is transient this discovery would seem of poor interest but results obtained from following investigations about the behavior of each one of the isoforms obtained in the esterification reactions of our interest shown that their reactivity depends on their structure. With this work we reported a detailed description of this unexpected results and the NMR investigation performed with particular care for double bonds geometry and position which confirmed the structures.

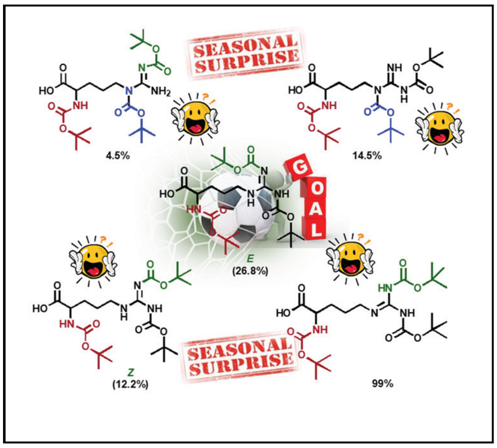

Figure 1: The unexpected five isoform obtained

[1] H. Konno, K. Kubo, H. Makabe, E. Toshiro, N. Hinoda, K. Nosakaa, K: Akaji, *Tetrahedron* **63**, 9502 (2007) doi:10.1016/j.tet.2007.06.082
[2] J. Izdebski, T. Gers, D. Kunce, P. Markovsky, *J. Pept. Sci.* **11**, 60 (2005) doi: 10.1002/psc.585
[3] M. A. Jones, A. D. Hislop, J. S. Snaith, *Org. Biomol. Chem.* **4**, 3769 (2006) doi: 10.1039/b611170j

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Porous PDMS membranes loaded with TiO_2 NPs for detachable antibacterial coatings

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Poly (dimethyl siloxane) "PDMS" is a highly hydrophobic mechanically and thermally stable polymer whose features are attributable to its Si-O bonds, which can resist to TiO_2 activity with respect to average carbon-based polymers. Therefore, PDMS is widely used in different fields, such as sealants, separating membranes and biomedical devices [1]. PDMS hydroxyl terminated prepolymers with two different molecular weights and therefore viscosities (20.000 e 50.000 cSt); TEOS (tetraethyl orthosilicate) as multifunctional cross-linking agent; THF as solvent and HNO_3 for hydrolysis reactions were used [2]. The electrospinning process can guarantee a fibrous structure with microscale dimensions (Fig. 1). In order to obtain the cross-linked PDMS membranes coupled with TiO_2, a Sn-based catalyst was used [3]. Bare TiO_2 was synthesized through a sol-gel synthesis, using titanium tetraisopropoxide, 2-propanol and water (1:35:5, V/V), in presence of a minimal amount of nucleation seeds [4]. An amorphous gel was obtained and it was then subjected to a hydrothermal synthesis, to get crystalline anatase TiO_2. This composite appears as a white soft sheet and combines the high adsorbent capacity and the macroscopic handling of the membrane with the photocatalytic antibacterial features of TiO_2. The photocatalytic activity of this system can be activated by a neon light source, whose photons have an energy at least equal to the TiO_2 energy gap. For this work, different synthetic conditions were investigated, varying the PDMS prepolymers ratio, the temperature and the time of the polymer synthesis and the electrospinning conditions (voltage, flow, distance from the electrodes). The synthesized samples were characterized by means of rheological measurements, FE-SEM and recycling photocatalytic activity by means of methylene blue degradation while the antibacterial activity was evaluated on the abatement of some controlled E. Coli cultures.

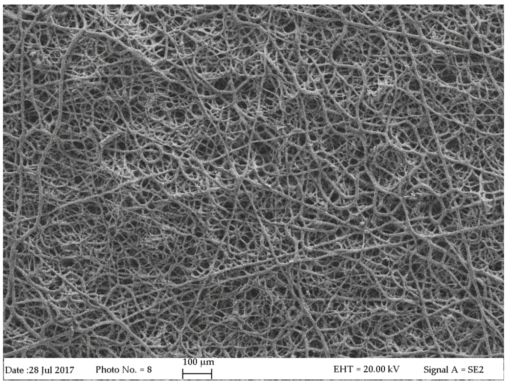

Figure 1. FE-SEM image for a PDMS membrane loaded with TiO_2

References: [1]. Lin, J.; Moller, S.; Obermeier, E. *Sens. Actuators B,* **1991**, 5, 219.
[2]. Castellano, M.; Cantù, R.; Mauri, M. et al. J. *Nanosci. Nanotechnol*., **2016**, 16-6, 6587-6594.
[3]. Caratto, V.; Setti, L.; Campodonico, S. et al. *J. Sol-Gel Sci. Technol*., **2012**, 63, 16–22.
[4] Villa, S. ; Caratto, V. ; Locardi, F. et al. *Materials*, **2016**, 9, 771.

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Polymer electrolyte membranes for energy storage and conversion

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Energy storage and conversion devices are at the forefront for the development of the smart grid, at a macro as well as at a micro and nano scale. Energy storage assures a stable filter between energy production, sometimes intermittent, and demand. Moreover, it is important to efficiently convert back the stored energy. The improvement, in terms of cost, durability and performances, of fuel cells, redox flow batteries and microbatteries seems fundamental for the future. Among the main issues affecting these devices, the performance and the durability of the solid electrolyte, if considering Polymer Electrolyte Membrane (PEM) type devices, is challenging.

In our research, we develop new polymer electrolytes to be easily transformed in membrane shape and capable to attain a good ionic conductivity, selectivity and stability. Our approach consists not only in changing the polymer skeleton (aromatic polymers like poly(etheretherketone) or polysulphone instead of perflorinated polymers), but also in changing the functional moieties (like sulfonic acid or secondary and tertiary amino groups to have protonic, anionic, or amphoteric[1] conduction) and cross-linking the polymer. Moreover, with the final objective to miniaturize device size, we explore the possibility to directly synthetize and depose the polymers in membrane shape by using the electrochemical deposition[2], a versatile bottom-up technique to obtain conformal deposition of materials allowing the designing of objects with complicated shape at nanometric scale. It was demonstrated that an enhancement of ion conductivity, cycling[2], stability in severe conditions, selectivity[3], and mechanical strength can be obtained and that the properties can be easily tuned. The results are promising for the application of these electrolytes in high technology storage and conversion devices.

[1] R. Narducci, L. Pasquini, et al;ChemPlusChem 81 (2016) 550-556
[2] M. Braglia, I.V. Ferrari, L. Pasquini, T. Djenizian, M. Sette, M.L. Di Vona, P. Knauth, Electrochimica Acta (2018) In Press
[3] P. Knauth, L. Pasquini, M. L. Di Vona, Solid State Ionics 300 (2017) 97-105

[2+2+2]-Cycloaddition Reaction for a New Access to Polycyclic Cobalt Complexes

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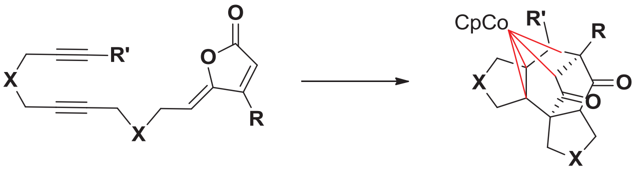
The discovery of new chemical tools and the development of new methodologies that would allow for a rapid, straightforward and controlled synthetic access to the expected target molecules is a topical issue for both academic and industrial research. More precisely, a viable and sustainable route for the future preparation of relevant and highly complex molecular scaffolds from simple and achiral substrates still constitutes a real challenge for a synthetic chemist. Among all the transformations that we have at our disposal to access functionalized polycyclic compounds, the purely atom economy couplings are rare and cycloaddition reactions address this goal efficiently.

In this context, we propose to explore the reactivity of the captodative *exo*-cyclic double of alkylidenebutenolides towards [2+2+2] cycloaddition reactions for a new access to bicyclo[3.2.2]nonane cobalt(I) complexes.



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IX Giornate Italo-Francesi di Chimica
IX Journées Franco-Italiennes de Chimie
Genova
April 16-18, 2018

Hydroxytriazole and hydroxybenzoisoxazole derivatives as potent and selective aldo-keto reductase 1C3 (AKR1C3) inhibitors: application of a bioisosteric scaffold hopping approach to target Prostate Cancer.

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Prostate cancer is the most commonly diagnosed cancer in men. The aldo-keto reductase 1C3 (AKR1C3) isoform plays a vital role in the biosynthesis of androgens and is considered an attractive target in prostate cancer. No AKR1C3-targeted agent has to date been approved for clinical use. Flufenamic acid and indomethacin are non-steroidal anti-inflammatory drugs known to inhibit AKR1C3 in a non-selective manner as COX off-target effects are also observed.[1] Since 2006, the authors have directed their efforts towards the investigation of hydroxylated pentatomic heterocyclic systems in order to create a sophisticate tool able to bioisosterically mimic the carboxylic acid function, as well as other acidic moieties.[2] This bioisosteric tool, combined with a more general scaffold hopping approach, was applied to design innovative AKR1C3 inhibitors:[3] starting from flufenamic acid and indomethacin scaffolds, both containing an acidic function, three classes of structurally different AKR1C3 inhibitors were identified. Their design, synthesis, binding mode (from co-crystallisation experiments) and biological evaluation are here discussed. Notably, the best compounds, besides being active on the target, were found to be highly selective for AKR1C3 over the C2 isoform and COX enzymes, able to reduce the cell proliferation, the prostate specific antigen (PSA) and testosterone production in cellular models of prostate cancer.

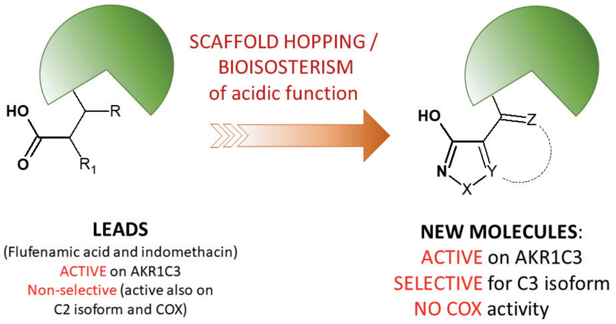

Figure 1: the approach used to design the described AKR1C3 inhibitors.

[1] Penning T.M., Expert Opin Ther Pat, 2017, 27:1329-1340.
[2] Pippione A. C. et al., MedChemComm, 2015; 6:1285-1292.
[3] Pippione A. C. et al. Eur J Med Chem., 2017;139:936-946.

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IX Giornate Italo-Francesi di Chimica
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Original nucleoside analogues to combat drug resistance in haematological malignancies.

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Chemo-resistance in anticancer therapies is unfortunately a common and highly occurring feature. Whether acquired or innate, this resistance phenomenon limits the efficiency of chemotherapies. It allows cancer cells to survive and contributes to the progression of cancers.

In this research work, we focused our efforts on the development of new nucleoside analogues to combat drug resistance in models of myelodysplastic syndromes (MDS). MDS are characterised by the production of immature blood cells within the bone marrow. Additionally, MDS may lead to acute myeloid leukaemia in a third of the cases.[1] Since 2009, the hypomethylating agent, vidaza® (5-azacytidine), has been used as first-line treatment; although response rate, toxicity effects and acquired resistances are still limiting its use. Hence, the development of new therapeutic strategies to overcome drug resistance, particularly for high-risk MDS patients after vidaza® failure, is an urgent and vital need.

To circumvent this chemo-resistance issue we worked on the development of structural analogues of acadra® (acadesine, Figure 1) as this compound was shown to overcome vidaza® resistance in MDS cell lines (*e.g.* SKM1-R) while inducing type II programmed death (autophagy).[2] While acadesine is a low potent anti-neoplastic agent (IC_{50} of 1 mM) we managed to produce analogues (Figure 1) that exhibited about 3000-fold increased potency (0.34 μM). These latters feature a 1,2,3-triazolyl aglycone moiety bearing the 5-alkynyl motif. [3]

In this communication, we will present general trends in the structure-activity relationship that led us to our original nucleoside analogues, as well as insights in their mode of action. We will also present our latest results in the elucidation of the molecular targets of our antineoplastic agents.

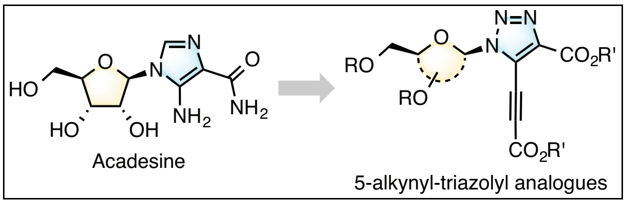

Figure 1 : From acadesine to 3000-fold more potent analogues against MDS.

[1] K. Raj, G. J. Mufti *Ther. Clin. Risk Manag*. **2006**, *2*, 377-388.
[2] T. Cluzeau, G. Robert, *et al. 55th ASH annual meeting and exposition* - poster 1568.
[3] H. Amdouni, G. Robert, M. Driowya, N. Furstoss, C. Métier, A. Dubois, M. Dufies, M. Zerhouni, F. Orange, S. Lacas-Gervais, K. Bougrin, A. R. Martin, P. Auberger, R. Benhida, *J. Med. Chem.* **2017**, *60*, 1523-1533.

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Asymmetric catalysis:
an entry to functionalized cyclohexene derivatives

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Gold catalyzed cycloisomerization reactions and domino processes have become in recent years a straightforward and atom-economical tool for access to highly functionalized carbo- and heterocycles.[1] Considering our continuous interests on asymmetric gold-catalyzed cyclizations,[2] and for diversity-oriented synthesis (DOS),[3, 4] we focus on cyclofunctionalization reactions on enyne units [5] with different chiral gold catalysts based on atropisomeric ligands and imidazo[1,5-a]pyridinylidene ligands.(*Figure 1*)

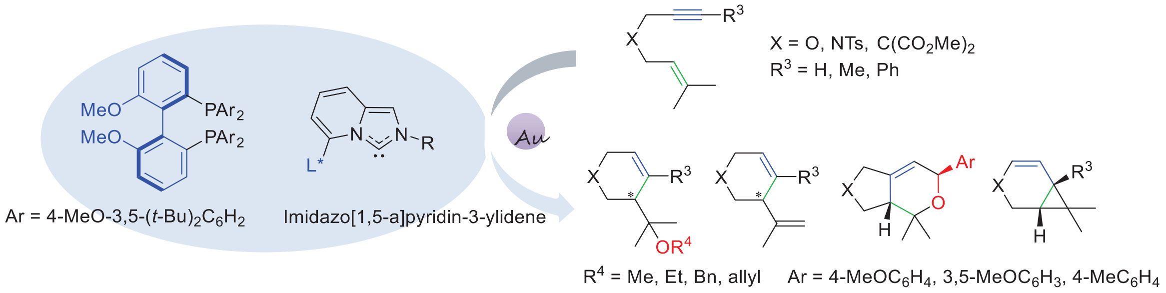

Figure 1 : Gold-catalyzed cyclofunctionalization reactions of enynes

The scope and limitations as well as recent results will be presented.

References:

[1] *Gold Catalysis: An Homogeneous Approach* (Eds.: F. D. Toste, V. Michelet), Imperial College Press, London, **2014**. *Silver in Organic Chemistry* (Ed. M. Harmata), J. Wiley & Sons, Inc. **2010**.

[2] Pradal, A.; Chao, C.-M.; Toullec, P. Y.; Michelet, V. *Beilstein J. Org. Chem.* **2011**, *7*, 1021. Chao, C.-M.; Beltrami, D.; Toullec, P. Y.; Michelet, V. *Chem. Commun.* **2009**, 6988. Le Boucher d'Herouville, F.; Millet, A.; Scalone, M.; Michelet, V. *Synthesis* **2016**, *48*, 3309. Pradal, A.; Toullec, P. Y.; Michelet, V. *Synthesis* **2011**, 1501.

[3] *Diversity-Oriented Synthesis: Basics and Applications in Organic Synthesis, Drug Discovery, and Chemical Biology*; Trabocchi, A., Ed.; John Wiley & Sons: New-York, **2013**.

[4] Tomás-Mendivil, E.; Heinrich, C.; Ortuno, J.-C.; Starck, J.; Michelet, V. *ACS Catal.* **2017**, *7*, 380. Carrër, A.; Péan, C.; Perron-Sierra, F.; Mirguet, O.; Michelet, V. *Adv. Synth. Catal.* **2016**, *358*, 1540.

[5] Michelet, V.; Toullec, P.Y.; Genêt, J.-P. *Angew. Chem. Int. Ed.* **2008**, *47*, 4268.

Diastereoselective functionalization of NHC-boranes through radical intermediates

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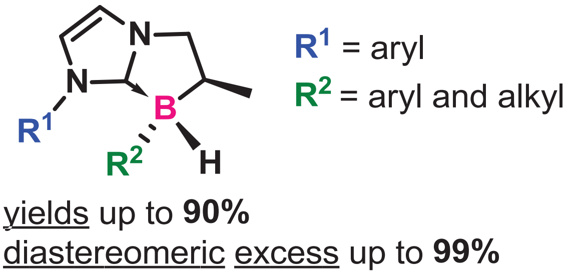
The increasing need of reproducible and scalable enantioselective processes to synthesize molecules of pharmaceutical, agrochemical or biochemical interest, is a constant source of inspiration for the organic chemist community. The optimization of milestone chemical transformations in an asymmetric, metal-free and atom economical version is the center of the modern era of synthetic chemistry.

Since the pioneering work of Brown, Soderquist, Itsuno and Corey on the synthesis of small chiral borane reagents for asymmetric hydroboration and reduction reactions,[1] a large number of boron-containing species has been developed and new catalytic processes and synthetic challenges have emerged. However, the easy access to chiral boranes still calls for improvements.

Recently our group developed an unprecedented class of enantiopure bicyclic *N*-Heterocyclic Carbene (NHC) borane scaffolds.[2] Following on this work, we discovered an easy, highly diastereoselective and versatile process to functionalize the boron center (R^2 = aryl or alkyl) using commercially available Grignard reagents (Figure 1). In order to understand the reaction mechanism, Electron Paramagnetic Resonance (EPR) studies were carried out. Strategies, synthesis of precursors, scope and limits of the reaction and mechanistic studies will be described and discussed.



R^1 = aryl
R^2 = aryl and alkyl

yields up to **90%**
diastereomeric excess up to **99%**

Figure 1: Diastereoselective functionalized NHC-boranes.

[1] a) Brown, H. C.; Zweifel, G. *J. Am. Chem. Soc.* **1961**, *83*, 486; b) Zweifel, G.; Brown, H. C. *J. Am. Chem. Soc.* **1964**, *86*, 397; c) Brown, H. C.; Chandrasekharan, J.; Ramachandran, P. V. *J. Am. Chem. Soc.* **1988**, *110*, 1539; d) Brown, H. C.; Ramachandran, P. V. *Pure Appl. Chem.* **1991**, *63*, 307; e) Gonzalez, A. Z.; Román, J. G.; Gonzalez, E.; Martinez, J.; Medina, J. R.; Matos, K.; Soderquist, J. A. *J. Am. Chem. Soc.* **2008**, *130*, 9218; f) Itsuno, S.; Nakano, M.; Miyazaki, K.; Masuda, H.; Ito, K.; Hirao, A.; Nakahama, S. *J. Chem. Soc. Perkin Trans. 1* **1985**, *2039*; g) Corey, E. J.; Bakshi, R. K.; Shibata, S. *J. Am. Chem. Soc.* **1987**, *109*, 5551.
[2] Toure, M.; Chuzel, O.; Parrain, J.-L. *J. Am. Chem. Soc.* **2008**, *130*, 9218.

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New tools for the development of direct NLRP3 inflammasome inhibitors

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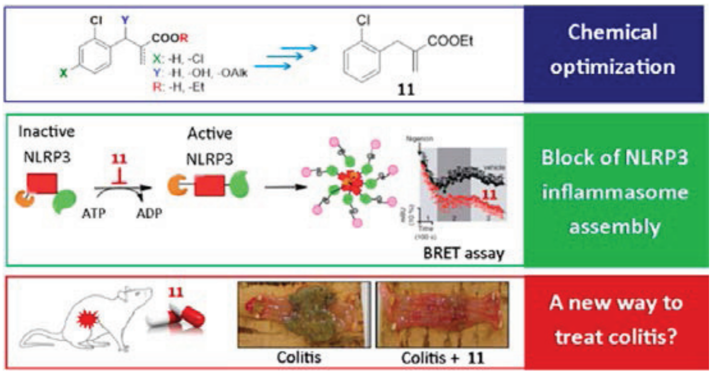
In the last decades, several studies have highlighted the pivotal role of inflammasomes in the molecular control of inflammatory processes and the pathological role of NLRP3 inflammasome has been well established in different pathological settings. The discovery of agents able to prevent inflammasome activation is a promising therapeutic strategy to decrease chronic inflammation and associated damage. To date, different approaches have been pursued, among which reversible or irreversible modification of reactive cysteine residues of relevant proteins seems to be the prevalent one. In view of the above, we designed a library of electrophilic warheads bearing α,β-unsaturated nitrile and carbonyl-substituents.[1] These compounds were able to significantly prevent NLRP3-dependent pyroptosis of THP-1 cells. We demonstrated via a thiol trapping kinetic assay and ^{1}H NMR experiments that the biological activity of this series of compounds is dependent on their reactivity as Michael acceptors. The most promising warheads identified also proved able to directly inhibit the NLRP3 ATPase activity of isolated enzyme; unfortunately, these compounds exerted a certain degree of cytotoxicity on THP-1 cells, which could be related to their high reactivity. Thus, we developed new series of safer compounds by tuning down the reactivity of the electrophilic warhead through the chemical modulation of the acrylate scaffold. Thanks to this approach, we were able to obtain INF39 (**11**), a noncytotoxic molecule able to counteract NLRP3 activation through direct irreversible interaction with NLRP3 protein.[2] We better investigated his mechanism of action, and **11** has revealed able to block the conformational change required for inflammasome activation (Bioluminescence Resonance Energy Transfer experiment on recombinant NLRP3). Our preliminary in vitro ADME studies showed that INF39 was stable in simulated gastric and intestinal fluids, and it was absorbed into the intestinal epithelium, where it can act locally and generate a nontoxic active metabolite. On the basis of the preliminary ADME profile, INF39 was selected for in vivo studies in a model of DNBS-induced colitis in rats. After oral administration, INF39 significantly reduced systemic and colonic inflammation.



[1] Cocco, M. et al. Electrophilic Warhead-Based Design of Compounds Preventing NLRP3 Inflammasome-Dependent Pyroptosis. J. Med. Chem. 57, 10366-10382 (2014).
[2] Cocco, M. et al. Development of an Acrylate Derivative Targeting the NLRP3 Inflammasome for the Treatment of Inflammatory Bowel Disease. J Med Chem 60, 3656-3671 (2017).

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Study of Phase Change Materials (P.C.M) for thermal energy storage by latent heat.

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Generally, the availability of the resource does not coincide with the energy needs. Latent heat storage in Phase Change Materials (PCM) is one of the most efficient energy solutions for industries.

A synthesis of the bibliographic studies was carried out and supplemented by characteristic data of chemicals. This approach allowed for a first selection of candidate materials for thermal energy storage by latent heat in two temperature ranges [70-85 °C] and [120-155 °C]. Currently, in industry a significant amount of thermal energy is lost each year during cooling in these temperature ranges. This energy could be recovered and stored in PCM and used later.

The selected materials were characterized by calorimetry. A semi-industrial scale calorimeter has been built and patented. It allows the observation of phase changes on samples of more than 0.6 L contained in an enclosure of the same nature and the same geometry as that provided on an industrial scale.

On criteria of industrial applicability of thermal storage which takes into account the environment, 13 materials were retained including 2 eutectic mixtures based on nitrates, 5 hydrated salts and 6 organic materials.

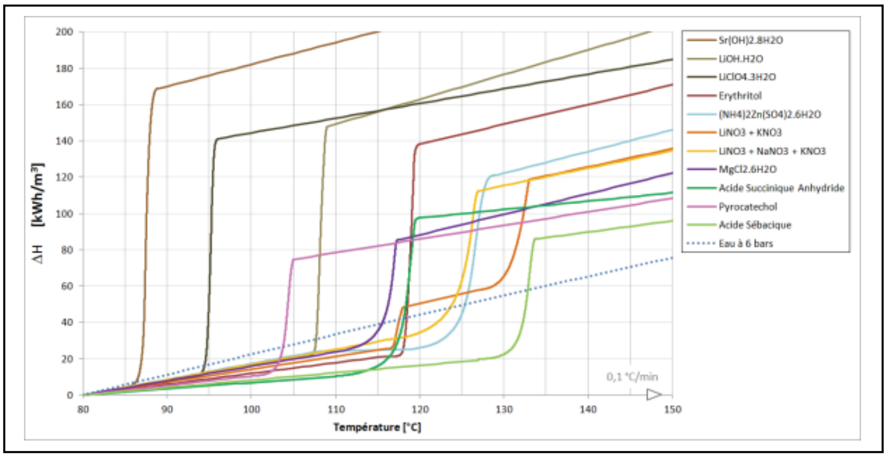

Figure 1. Materials retained for a thermal storage application.

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Hybrid materials using multi-layer architectures with near-ideal tunable large band absorption for stealth applications

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Nowadays, plasmonic nanoparticles are an interesting class of metallic nano-objects thanks to their unique optical properties which open up multiple opportunities toward practical applications. In general, the light absorption, reflection and scattering depend on different parameters such as size, shape, material and environment of the particles. Moreover, when these nanoparticles are embedded in a transparent polymer matrix, new hybrid materials can be obtained with enhanced and/or tunable optical properties which are different from those of the individual nanoparticles [1]. Collective effects arising from nanoparticle coupling in the layer are indeed of primary importance in thin films elaborated from these hybrid materials.

The aim of this work is to obtain a perfect absorber [2] in the visible and short infrared range by mainly controlling the optical properties of such hybrid materials, which have several applications related to stealth technologies. We focus our study on silver nanocubes since they possess a strong high electric field enhancement over the whole domain of the visible region and on tungsten oxide nanowires to fulfill the infrared region. In this context, we propose an interesting simple method for generating a sequence of thin layers of hybrid materials having tunable optical properties, based on controlling the dispersion and the aggregation state of the nanoparticles within the non-absorbing polymer matrix.

Depending on how nanocubes are dispersed in the polymer matrix, it is possible to obtain a localized absorption controlled by the size of the nanocubes or a large band absorber when aggregates appear in the bulk. We thus propose a novel method in order to tune the nanocubes density and their organization within the thin layer in order to strongly modify the optical properties of these materials without changing its composition. This study opens the way towards simple processable methods to modify the optical properties of hybrid materials in thin films on large scale, in order to obtain the optimal response for the specific application of interest.

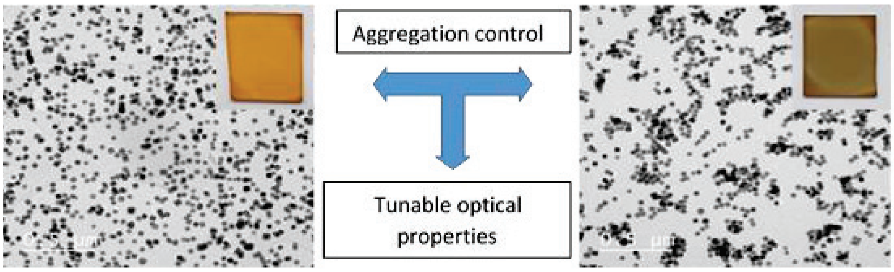

Figure 1: Aggregation effect in thin layer for the same nanocubes density

[1] Carlberg, M., Pourcin, F., Margeat, O., Le Rouzo, J., Berginc, G., Sauvage, R.M, Ackermann, J., and Escoubas, L., Opt. Mater. Express **7**, 4241-4248 (2017)

[2] Akselrod, G. M., Huang, J., Hoang, T. B., Bowen, P. T., Su, L., Smith, D. R. and Mikkelsen, M. H. Adv. Mater., 27: 8028–8034(2015),

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A theranostic approach for Boron Neutron Capture Therapy (BNCT) treatment based on the use of Gd/B multimodal probes

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This study aims at investigating a new theranostic approach for the treatment of primary tumours and metastasis based on the use of BNCT that combines low energy neutron irradiation with the presence of boron-containing compound at the targeted cells. This makes BNCT a promising option for the treatment of metastasis disseminated, for example, in the thoracic cavity that cannot be treated by methods requiring a precise localization, such as surgery or conventional radiotherapy. The innovation of this study lies on the development of novel theranostic agents, able to maximize the selective uptake of boron atoms in tumour cells and, at the same time, to quantify boron distribution in the tumour and in other tissues by Magnetic Resonance Imaging (MRI). The measurement of local boron concentration is crucial to determine the optimal neutron irradiation time, to calculate the delivered radiation dose and to evaluate the toxicity of the treatment by determining differences in boron concentration between tumour and healthy tissues. To this purpose a new dual BNCT/MRI agent has been synthesized and delivered to tumour cells using Low Density Lipoproteins as specific carriers. In particular, this study has been focused on the treatment of lung metastases generated by intravenous injection of a Her2 + breast cancer cell line (i.e. TUBO) in BALB/c mice, transgenic EML4-ALK mice used as primary lung tumor model [1] and of a subcutaneous tumour mouse model of Malignant Mesothelioma (MM). The latter is an aggressive tumour with a poor prognosis whose incidence and mortality is a function of past exposure to asbestos, after a latency period of 30-50 years. MM is a disseminated tumour against which conventional radiotherapy has limited effectiveness. Therefore, to improve both the clinical diagnostics and treatment, the discovery of new MM potential target molecules is of great interest. BNCT has been performed after MRI analysis at the TRIGA-Mark II reactor at the University of Pavia. With respect to controls, in boron treated group, tumour growth was significantly reduced.

References

[1] D. Alberti, et al. *Nanomedicine*. **11,** 741-50 (2015)

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Nitrobutadienes: suitable substrates for the original synthesis of novel polyfunctional indole derivatives

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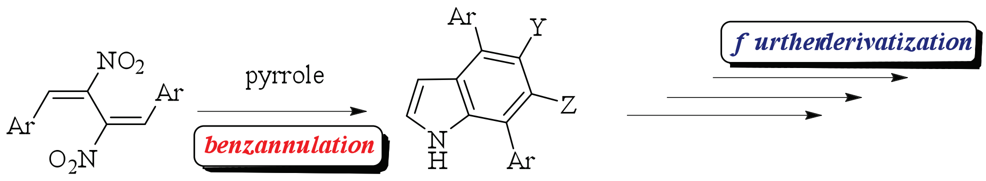
Through an original strategy based on the construction of the benzene ring onto pyrrole (Figure 1), 5-nitro- **2**, 6-nitro- **3**, and, even more interestingly, 5,6-dinitroindoles **4** (a substitution pattern never reported in literature so far) have been synthetized starting from dinitrobutadienes **1** [1].



1

2: Y = NO_2, Z = H
3: Y = H, Z = NO_2
4: Y = Z = NO_2

Figure 1

Nitroindoles **2-4** represent valuable precursors of other important indole derivatives, due to the possibility to convert the nitro group *e.g.* into an amino group and different functionalities therefrom.

Latest achievements in the preparation and derivatization of such functionalized indole scaffolds will be presented and discussed on both synthetic and mechanistic grounds, as well as preliminary results on biological/pharmacological tests currently under way.

[1] L. Bianchi, G. Giorgi, M. Maccagno, G. Petrillo and C. Tavani, *Eur. J. Org. Chem.*, in press. C. Tavani, L. Bianchi, A. De Palma, G.I. Passeri, G. Punzi, C.L. Pierri, A. Lovece, M.M. Cavalluzzi, C. Franchini, G. Lentini and G. Petrillo, *Bioorg. Med. Chem. Lett.* **2017**, *27*, 3980-3986. L Bianchi, G. Giorgi, M. Maccagno, G. Petrillo, C. Scapolla and C. Tavani, *Tetrahedron* **2016**, *72*, 7050-7058. L. Bianchi, A. Carloni-Garaventa, M. Maccagno, M. Pani, G. Petrillo, C. Scapolla and C. Tavani, *Tetrahedron* **2015**, *71*, 7550-7461. L. Bianchi, A. M. Maccagno, M. Pani, G. Petrillo, C. Scapolla and C. Tavani, *Tetrahedron* **2015**, *71*, 7421-7435. L. Bianchi, M. Maccagno, G. Petrillo, C. Scapolla, C. Tavani and A. Tirocco, *Eur. J. Org. Chem.* **2014**, 39–43. L. Bianchi, F. Ghelfi, G. Giorgi, M. Maccagno, G. Petrillo, D. Spinelli, M. Stenta and C. Tavani, *Eur. J. Org. Chem.* **2013**, 6298-6309, and references cited therein. R. Ballini, N. Araujo, M. V. Gil, E. Roman and J. A. Serrano, *Chem. Rev.* **2013**, *113*, 3493-3515.

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Carbonyl Activation in Electrophilic Polyene Cyclizations: A Toolbox for the Design of Isoprenoid Libraries

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The development of new strategies for the synthesis of complex molecules is hotly pursued in organic chemistry. In this context, the transannular cyclization of polyolefins is an important tool to generate complex polycyclic scaffolds and major natural products-like skeletal diversity.[1] In search of new ideas to fertilize the field, we have focused on the 11-membered cyclic trienone zerumbone (**1**), a humulane derivative from shampoo ginger (*Zingiber zerumbet*) endowed with a multi-faced bioactivity and chemical reactivity.[2] Using its cross-conjugated dienone system, we have explored the possibility to trigger intramolecular polyene cyclizations by generation of a Nazarov allyl cation rather than by the mechanistically simpler protonation of a double bond or a hydroxyl. While zerumbone could be recovered unscathed after treatment with Brønsted acids, it generates a different range of cyclized derivatives by treatment with Lewis acids, with the nature of the acid dramatically influencing the course of cyclization (Figure 1).

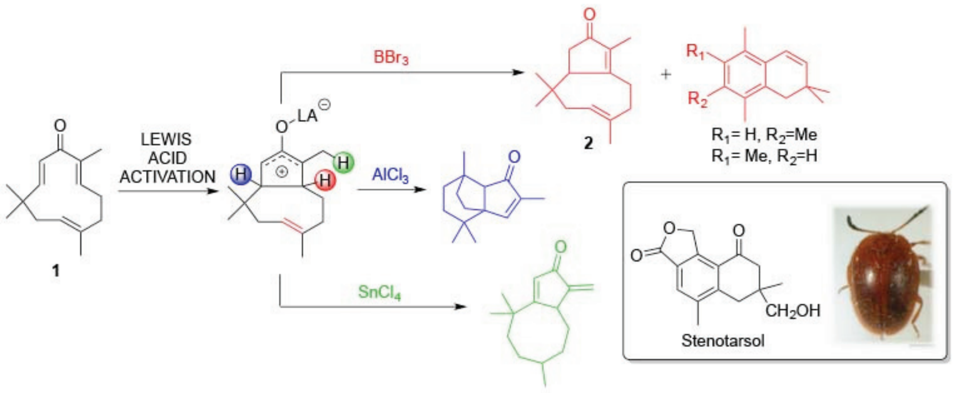

Figure 1

The structure of the compounds generated in the reaction holds remarkable mechanistic relevance, as exemplified by the cyclizative generation of a *trans*-cyclooctene derivative (**2**),[3] a reaction not yet observed in organic chemistry, and by the biogenetic deorphanization of the enigmatic stenotarsane skeleton, a putative isoprenoid whose constitution had so far eluded biogenetic derivation, and that our result can reconduct to a humulane precursor.

[1] Foo, K.; Usui, I.; Götz, D.C.G.; Werner, E.W.; Holte, D.; Baran, P.S. Angew. Chem. Int. Ed. 2012, 51, 11491-11495
[2] Appendino, G.; Minassi, A.; Collado, J. A.; Pollastro, F.; Chianese, Taglialatela-Scafati, O.; Ayyari, M.; Garcia, V.; Muñoz, E. Eur. J. Org. Chem. 2015, 3721–3726.
[3] Minassi, A.; Pollastro, F.; Chianese, G.; Caprioglio, D.; Taglialatela-Scafati, O.; Appendino, G. Angew. Chem. Int. Ed. 2017, 56, 7935-7938

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IX Giornate Italo-Francesi di Chimica
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Role of radical reactivity in the formation of Complex Organic Molecules in interstellar ices

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Astrophysical observations led to the identification of numerous organic molecules in the Interstellar Medium (ISM). Although the main part of these are simple molecules, some have an important number of atoms and are so called Complex Organic Molecules (COMs).
Although COMs characterization is confident, their formation mechanisms are still under investigation. The particular conditions – UV photons, hydrogen bombardments, thermal effects – makes formation mechanisms hard to be clearly identified, as no usual formation pathways can be applied. Several formation mechanisms were proposed, either in gas phase or in solid state, each of them dealing with different kinds of reactivity. We focus here on radical reactivity in astrophysical like conditions. Interstellar ice analogues are made in laboratory and submitted to ISM-like processes-hydrogenation, VUV irradiation, thermal effect- while their chemical composition is monitored by spectroscopic techniques – IR, MS and, if required, GC-MS.

Radical species produced during these experiments are difficult to study, due to their short lifespan and high reactivity. To overcome this problem, we use cryogenic matrix isolation technique combined with IR spectroscopy to characterize unstable species and observe their reactivity[1,2]. Also,by using EPR spectroscopy, we are able to focus only on radical species and to detect them even in low amount. Our work focused on two main processes observed in the ISM: carbon monoxide CO hydrogenation and methanol CH3OH photolysis. To do so, we performed formaldehyde H2CO and methanol CH3OH ice analogues and submitted them to VUV irradiation and heating. During these experiments, we found out that, among the two possible radicals that can be produced from H2CO hydrogenation, CH2OH and CH3O, only CH2OH is formed. We also showed that radical species can be formed and be stored inside the ice at low temperature before reacting whenever diffusion is triggered by any process. Moreover, produced radical species – CH2OH, HCO, CH3O, HOCO - are precursors of detected COMs, such as glycolaldehyde GA, ethylene glycol EG, methylformate MF or even carboxylic acids[4, 5, 6]. But radical reactivity is not limited to simple recombination reactions: radical-induced polymerization can occur in ISM-like conditions. Also, radical-radical recombination does not lead mandatorily to an increase in molecular complexity: indeed, HCO dimerization tend to produce H2CO and CO with H-abstraction mechanism instead of glyoxal HCOCHO from direct recombination.

[1] Butscher, T. ; Duvernay, F. ; Theulé, P. ; Danger, G. ; Carissan, Y. ; Haugebaum-Reignier, D. ; Chiavassa, T. ; *MNRAS* **2015**, *453*, 1587-1596.
[2] Butscher, T. ; Duvernay, F. ; Rimola, A. ; Segado-Centellas, M. ; Chiavassa T. ; *Phys. Chem. Chem. Phys.*, **2017**, *19*, 2857-2866.
[3] Woods, P. M.; Slater, B.; Raza, Z.; Viti, S.; Brown, W. A.; Burke, D. J.; *ApJ* **2013**, *777*, 90.
[4] Feedoseev, G.; Cuppen, H.; Ioppolo, S.; Lamberts, T.; Linnartz, H.; *MNRAS* **2015**, *448*, 1288.
[5] Hudson, R. L.; Moore, M. H.; Cook, A. M.; *Adv. Space Res.* **2005**, *36*, 184.
[6] Bennett, C. J.; Kaiser, R. I.; *ApJ* **2007**, *661*, 899.

Extending the applicability of Raman spectroscopy: from labile systems to in situ and operando approaches

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Raman spectroscopy is a versatile characterization technique, often considered complementary to IR spectroscopy. With respect to the latter, Raman spectroscopy can be straightforwardly applied in the characterization of complex materials, such as liquids or high optical absorption materials. Still, the application of Raman spectroscopy is limited in comparison to IR, principally because of the low cross-section of the Raman process, leading to 1-3 orders of magnitude longer measurement times. This limitation can be partially overcome by exploiting extremely bright excitation sources, *i.e.* lasers. The need of high power sources however introduces new drawbacks, mostly related to the stability of the sample upon the exposure to the intense incident light.

In order to come through this side effect and fully exploit the possibilities offered by Raman spectroscopy, we recently developed an innovative setup based on the magnetic stirring of the sample,[1,2] dramatically reducing the extent of the beam damage. Such device allows to exploit the full power of the excitation sources even in the case of labile materials: as an example, in Figure 1 the effect of rotation in the study of methanol adsorbed over a ZSM-5 zeolite is shown.

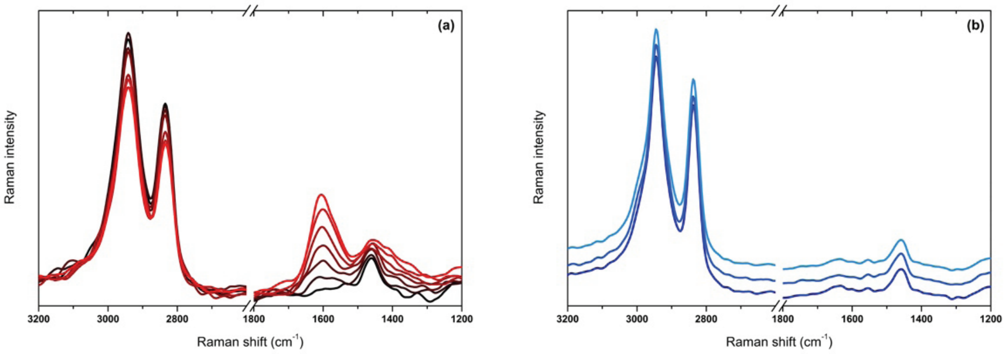

Figure 1. Raman spectra (λ = 244 nm) of bulk methanol adsorbed from gas phase on H-ZSM-5 collected with static sample (a) with a 30 s/spectrum exposure or rotating sample (b) with a 300 s/spectrum exposure.

The possibility to exploit the full excitation power while avoiding sample damaging allows the collection times to be significantly reduced, thus increasing the time resolution of Raman. Taking advantage of such improvement, deactivation processes occurring during the Methanol to Hydrocarbon process have been investigated through an *operando* approach: the effect of the topology of the zeolite catalysts will be discussed.[3]

[1] Signorile M.; Bonino, F.; Damin, A.; Bordiga, S. *Top. Catal.* **2018**, *under revision*
[2] Damin, A.; Signorile, M.; Bonino, F.; Bordiga, S.; Disa, R. *WO2017077513 (A1)*, **2017**.
[3] Rojo-Gama, D.; Signorile, M.; Bonino, F.; Bordiga, S.; Olsbye, U.; Lillerud, K. P.; Beato, P.; Svelle, S. *J. Catal.* **2017**, *351*, 33–48.

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POSTERS

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Synthesis, Purification and Characterization of Antimicrobial Peptides isolated from Animal Venoms

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The frequency of Candida infections has increased in recent years, largely due to the growing size of the population at risk, which includes transplant, cancer patients and other immunodeprimed patients. In Europe, Candida species are among the top 10 most frequently isolated nosocomial pathogens. More particularly, yeast Candida Albicans (C. albicans) is the most common opportunistic pathogen in humans and represents the fourth leading cause of nosocomial infections. Candidiasis ranges from superficial and local infections to deadly septic mycosis in compromised patients. For the medical treatment of fungal infections, amphotericin B has been considered the drug of choice and azoles are mainly used in common clinical situations. However, the toxicity and resistance to these antifungals are more and more frequent. Indeed, an increased amount of amphotericin B should be administered to patients because of its low permeability across the membrane which can lead to serious side effects such as kidney damage. To overcome these side effect problems, natural products can be considered as promising antimicrobial and antifungal agents. Animal venoms are a rich source of antifungal (AFP) and antimicrobial (AMP) peptides. We screened over 180 venoms on multidrug against multidrug resistant gram-negative, gram-positive bacteria and fungi. Several venoms showed a strong antimicrobial activity. Bioactive fractions have been identified, purified and characterized. The AMP obtained par chemical synthesis confirmed the activity.

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Coverage dependent recombination mechanisms of hydrogen from Tungsten surfaces via Density Functional Theory

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One of the main challenges of modern society is to find a reliable source of energy other than fossil fuels. Nuclear fusion energy emerges as a possible source proposed to have the advantage of being clean and extremely energy efficiency. One key aspect of feasible fusion power reactors is the choice of a suitable plasma facing material (PFM). Tungsten (W) is a prime candidate and will be used in the divertor of the ITER and WEST tokomaks due its low tritium retention, high melting point, and high thermal conductivity. The diverter must withstand high-energy flux particles of Hydrogen isotopes, which penetrate through the surface of tungsten and are expected to diffuse in depth, creating defects, embrittlement, and finally damaging the material. For these reasons, material scientists extensively study the interaction of hydrogen with tungsten at the interface of the surface and within the bulk.

One of our goals is to determine the adsorption/desorption mechanisms of hydrogen and its isotopes to/from the surface of tungsten. Activation energies for the recombination of atomic hydrogen atoms into molecular hydrogen depend upon the surface structure itself as well as its Hydrogen to Tungsten (H/W) coverage ratio. On the surface, the hydrogen to tungsten surface coverage ratio depends on the temperature and the pressure. As the temperature increases, coverage is expected to change from saturation to zero.

On the basis of Density Functional Theory (DFT) calculations, we previously determined the many configurations that exist for hydrogen on top of the W (100) and W (110) surfaces from low coverage to saturation and beyond. These findings were corroborated by experimental studies [1].

In the present DFT work, we extend our investigation by examining the paths that lead atomic hydrogen from the bulk to the W (100) and W (110) surfaces at various coverage's. Following this, from the most stable adsorption configurations we study the recombination and desorption mechanisms of molecular hydrogen. We confirm that indeed, the recombination mechanism and related activation energies are strongly dependent on the coverage ratio.

[1] Piazza, Z. A., M. Ajmalghan, Y. Ferro, and R. D. Kolasinski. "Saturation of Tungsten Surfaces with Hydrogen: A Density Functional Theory Study Complemented by Low Energy Ion Scattering and Direct Recoil Spectroscopy Data." *Acta Materialia* 145 : 388–98. https://doi.org/10.1016/j.actamat.2017.12.029.

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Hybrid squaraine-silica nanoparticles as NIR probes for biological applications: optimization of the photoemission performances

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In the last decade, Near Infra-Red (NIR) dyes have emerged as a promising tool for both biological applications and *in vivo* fluorescence imaging due to the deep photon penetration in tissue and the negligible self-fluorescence of the biological molecules in the so called "tissue window" of the electromagnetic spectrum. Among the other organic fluorophores, squaraine dyes are of particular interest because of the versatility of the molecular structure allowing the easy design of NIR dyes [1] with high extinction coefficients, narrow absorption and photoemission peaks, high photostability and low cytotoxicity. However, the general low degree of hydrophilicity, with the consequent tendency to form aggregates in solution, limited their use as fluorescent markers for biological applications. In this respect, several works proposed the incorporation of these dyes within organic [2] or inorganic [3] frameworks in order to confer different physico-chemical properties by maintaining the photophysical behaviour unaltered. As for the inorganic matrices, the use of amorphous silica is usually preferred due to the possibility to obtain nanoparticles (NPs) with different morphology, size and porosity and easily and stably suspendable in physiological media and then highly suitable for biological applications. It is known that non-porous siliceous hybrid NPs highly homogenous in shape and size can be obtained by the microemulsion technique, where the NPs formation is ruled by the partition equilibria of the silica precursor (TEOS) and dye molecules between the oil and water phases, separated by the surfactant palisade of the reverse micelles. However, the photoemission performances of the encapsulated dyes are strongly affected by the homogeneity of dispersion throughout the silica matrix that, in turn, is strictly related to the physico-chemical properties of the fluorophore: in a previous work [4] we demonstrated how it is possible to optimize the distribution of trimethine cyanine dyes within NPs by controlling the diffusion rates ratio of the dye and TEOS between the two phases of the microemulsion during the synthesis. On this basis, in this work we explored the possibility to prepare NIR emitting nanoparticles using squaraine dyes; three fluorophores with different chemical structure and degree of hydrophilicity were selected. The photophysical properties of each sample were qualitatively and quantitatively investigated by absorption and steady state/time-resolved photoemission spectroscopies in order to define structure-properties relationships useful for the optimization of the photoemission performances.

[1] Barbero N., et al *Org Lett* 2015; 17: 3306.
[2] Sreejith S. et al *ACS Nano* 2015; 9: 5695.
[3] Conterosito E., et al *ChemSusChem* 2016; 9:1279.
[4] Alberto G. et al *Chem. Mater* 2012; 24: 2792

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Synthesis of Doped Metal Oxide Nanocrystals for Solution-Processed Interfacial Layers in Organic Solar Cells

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High band gap semiconducting metal oxide films have been widely used as charge extraction layers in organic solar cells over two decades because of their superior electronic properties and stability compared to their organic counterparts. Among these, MoO_x, WO_x, GO and NiO_x are well studied for hole extraction. However, these oxides suffer from high resistivity and can therefore only be included as very thin layers in the solar cells. In order to increase layer thickness and thus processing robustness without sacrificing performance, increase in conductivity can be reached by creating metal vacancies and doping with some elements. [1] Several chemical and physical methods were reported for the preparation of these oxides but to meet the requirements for large-scale, low cost and roll-to-roll production; the solution processable methods are more desirable.

Recent works were dedicated to doping of n-type metal oxides such as ZnO demonstrating that doping leads not only to robust processing, but also to improved air processibility [2], device performance as well as color tuning of the solar cells [3].

Here, we focus on the development of doped p-type metal oxide semiconductor nanocrystals for solution-processing of hole transporting layers applied in both normal and inverted device structures. Amongst the large variety of metal oxides used, we focus on doped NiO_x and WO_x using different dopants (Li, Cu, and Sn). We applied these materials to high efficiency polymer solar cells using both fullerene and non-fullerene acceptors. The impact of the doping on the performance, air and thick layer processing will be discussed.

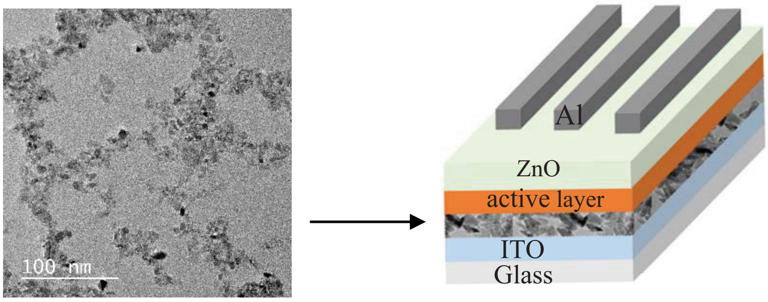

Figure 1: TEM image of Sn doped NiOx nanoparticles as a hole extraction layer in organic solar cells

[1] Matsubara, K., Huang, S., Iwamoto, M., Pan, W. Nanoscale 6, 688–692, (2014).

[2] Prosa et al., ACS Appl. Mater. Interfaces 8, 1635–1643, (2016).

[3] Gaceur et al., Adv. Funct. Mater. 26, 243–253, (2016).

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MALTODEXTRINS NANOSPONGES AS PRECURSOR FOR POROUS CARBON MATERIALS

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Porous carbon materials are promising products in the fields of catalysis and energy. They are also used in the adsorption and storage of carbon dioxide and in the removal of pollutants such as arsenic from water. Such porous materials are generally produced by pyrolysis of biomasses [1].

Recently the synthesis of porous carbon using maltodextrins in form of nanosponges was investigated [2].

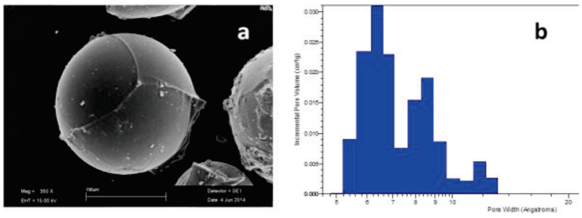

Figure 1 : a) SEM picture of the carbon particle obtained by nanosponge pyrolysis; b) DFT pore size distribution plot obtained by N2 gas-volumetric adsorption at 77K

The carbons produced show a very narrow pore size distribution, in the range of 5-17 Å and a quite high surface area. Furthermore, the porous carbon obtained from nanosponges have a spherical shape as revealed by the SEM analysis.

These carbons have successfully found out different possible industrial applications. For instance, in the field of water treatment, they can be used for removing some organic pollutants. The adsorption capacity of such materials was tested toward the removal of charged dyes from aqueous environment. Isothermal experiments carried out at circumneutral pH indicated an important charge-selectivity, which encourages their use as sustainable alternative materials in wastewater purification treatments.

Another possible application of these porous carbon materials is the selective uptake of gases for future industrial applications. Basically, these materials were tested in the adsorption of gases through several techniques. Different gases were used, such as CO_2, CO, N_2 and O_2 and surprisingly, the carbon produced from nanosponge was able to adsorb only CO_2.

Recently, these carbons are giving good results even in flux reactors.

In the end, it was find out the possibility to improve the physical properties of the carbon activating them with the KOH. This activation allows to improve the ability of the carbons in all above mentioned fields.

[1] F.C. Wu, R.T. Tseng, C.C. Hu, C.C.J. Wang, Power Sources, 2004, 351-359.
[2] A. Anceschi, G. Magnacca, F. Trotta, M. Zanetti, RSC Advance, 2017, 36117–36123.

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Hybrid polysaccharide/cyclodextrin nanostructures for the delivery of acyclovir

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Acyclovir (ACV), a nucleoside analog, is the drug of choice for the treatment of herpes simplex virus (HSV) infections. For ACV vaginal therapy of HSV-2 sexually transmitted infections, high drug concentrations in genital tissues are desirable. Unfortunately, ACV low and highly variable bioavailability, associated with low retention at the vaginal mucosa and short action duration limit the effectiveness of vaginally administered ACV. Nanoparticulate systems are recently proposed to overcome current challenges associated with antiviral therapy, since they could facilitate targeted antiviral delivery [1]. Previously, polymer nanodroplets, spherical core/shell nanostructures filled by vaporizable compounds (i.e. decafluoropentane), were developed as versatile multifunctional nanocarriers for the delivery of drugs and genes [2]. The aim of this work was the development of advanced core-shell nanostructures with an hybrid polysaccharide/cyclodextrin (CD) shell to improve the drug loading capability of the nanosystem. For this purpose, sulfobutyl ether-β-cyclodextrin decorated chitosan nanostructures called hybrid nanodroplets were designed. This nanoplatform was investigated for ACV vaginal delivery, in order to provide sustained release and improved antiviral efficacy for the local treatment of genital herpes. The hybrid chitosan/CD shell was tuned by studying the influence of several parameters including chitosan molecular weight and chitosan/CD ratio. To prepare acyclovir-loaded hybrid nanodroplets, the drug was previously complexed with sulfobutyl ether-β-cyclodextrin (Captisol®), which can then be associated to the nanodroplet chitosan surface, exploiting electrostatic interaction. Desirable application viscosity can be achieved by hybrid nanodroplet incorporation in a vehicle suitable for vaginal administration. The inclusion of ACV in sulfobutyl ether-β-cyclodextrin was confirmed by phase solubility, DSC, FTIR studies. Hybrid nanodroplet formulations were *in vitro* characterized determining sizes, surface charge, drug loading, morphology, mucoadhesion and drug release studies in simulated vaginal fluid. They showed sizes of about 400 nm, spherical shape and a positive surface charge. A prolonged release kinetics of ACV from the nanodroplets was demonstrated without initial burst effect. The antiviral activity of ACV loaded into hybrid nanodroplets was evaluated against a clinical isolate of HSV-2 in cell cultures by specific HSV infectivity assays. The ACV-loaded nanodroplets exhibited a statistically superior antiviral activity compared with that of the free drug. Of note, blank nanodroplets were able to suppress the cell to cell spread of HSV-2. Based on these results, ACV-loaded hybrid nanodroplets might represent a new strategy for developing a future nanomicrobicide for the HSV-2 infections.

Acknowledgments
The work was funded by Compagnia di San Paolo 2014 (Torino_call2014_L2_207). The authors thank Captisol for kindly purchasing sulfobutyl ether-β-cyclodextrin.

[1] D. Lembo, M. Donalisio, A. Civra, M. Argenziano, R. Cavalli. *Expert Opin Drug Deliv.,* **2017**, *1*, 22.
[2] R. Cavalli, M. Soster, M. Argenziano, *Ther Deliv.* **2016**, *7(2),* 117.

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First racemic total synthesis of Heliolactone

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Strigolactones (SLs) are a subject of increased scientific interest since 2008. Originally identified as allelochemicals involved in plant–parasite interactions, more recently SLs have been shown to play multiple key roles as signalling molecules, plant hormones and anticancer agents. For these reasons they have become a cutting-edge topic in plant biology and agronomy, and have great potential in modern agriculture for regulation of plant development and interactions.[1] Classic SLs feature a common structural framework including a tricyclic ring system (ABC-ring) linked to a butenolide ring (D-ring) via an enol ether bond. Recently, a novel subclass of strigolactones (non-canonical) lacking the canonical ABC-ring moiety has been identified: an open-chain unit links structurally diverse A-ring moieties to the D-ring, however the low natural abundance paired with the intrinsic instability of non-canonical SLs has so far hampered the investigation of these natural products. Among them, Heliolactone is the most abundant SL in sunflower and a germination stimulant for seeds of root parasitic weeds. Heliolactone has been recently isolated from sunflower root exudates through bioassay-guided purification. Detailed NMR spectroscopic studies performed on this molecule established a methylfuranone group, a common structural component of SLs connected to a methyl ester of a C_{14} carboxylic acid via an enol ether bridge.[2]

At the present, no synthetic approaches leading to Heliolactone have been developed yet. To this purpose, we envisaged the first racemic total synthesis of Heliolactone starting from natural terpene citral and other renewable chemicals. Our strategy is focused on a convergent synthetic approach where the "non-canonical" SL's skeleton is assembled by means of a cross metathesis reaction as the key synthetic step. This methodology is also suitable for a future development of an enantioselective synthesis of the Heliolactone scaffold. The preliminary results will be discussed.

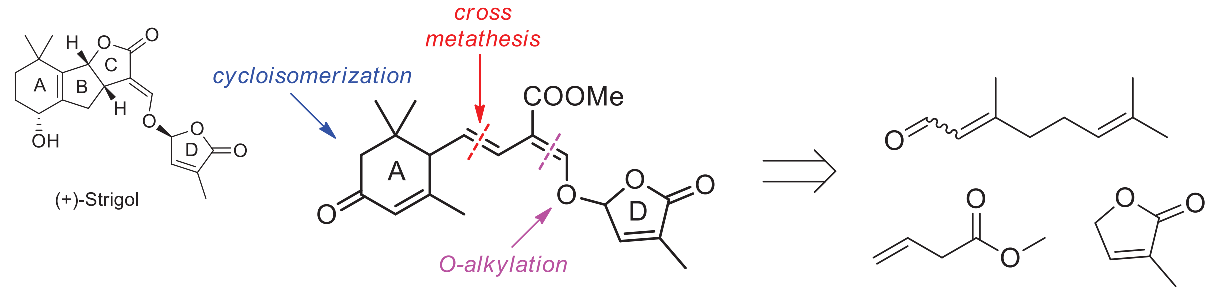

Figure 1 : Heliolactone retrosynthetic analysis

[1] Koltai, H.; Prandi, C. *Planta* **2016**, *243*, 1309.
[2] Sugimoto, Y. *et al. Phytochemistry* **2014**, *108*, 122–128.

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Synthesis of Boronated Analogue of Curcumin as Potential Therapeutical Agents for Alzheimer's Disease

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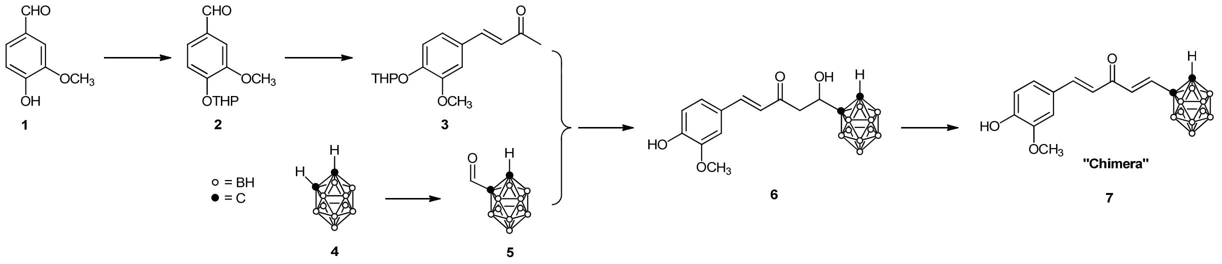
Alzheimer's Disease (AD) is a kind of neurodegenerative dementia. The accumulation of β-amyloid peptide fragments known as "plaques" is a symptom involved in the pathogenesis of this disease.[1] Nowadays, the natural molecule curcumin ((1*E*,6*E*)-1,7-bis-(4-hydroxy-3-methoxyphenyl)-epta-1,6-dien-3,5-dione) has shown a promising efficacy in the disaggregation and inhibition of association of these plaques.[2] BNCT (boron neutron capture therapy) is a binary radiation therapy for the treatment of cancer, based on the capture of thermal neutrons by ^{10}B nuclei that have been selectively delivered to tumour cells. The neutron capture event results in the formation of excited ^{11}B nuclei that undergo fission to yield highly energetic $^{4}He^{2+}$ and $^{7}Li^{3+}$ ions. Cell death is triggered by the release of these charged particles which create ionisation tracks along their trajectories, resulting in cellular damage.[3] In order to exploit for the first time the NCT effects towards brain plaques instead of tumor cells, we planned to combine curcumin natural efficacy against β-amyloid and the destructive effects provided by BNCT. Thus, we envisaged the synthesis of a hybrid compound which contains both a curcumin moiety and a boron derivative. The key step of our strategy was the aldol condensation between formyl-carborane **5** (where the *ortho*-carborane cage ideally replaces an aromatic ring) and the appropriate curcumin-like enone **3**. Preliminary biological essays on hen egg-white lysozyme (HEWL) fibrils showed that the efficacy against amyloid aggregation of our hybrid compound **Chimera 7** was totally comparable to that of curcumin itself. These results are encouraging, considering that this effect could be furtherly enhanced by neutron irradiation of boron atoms in NCT treatments.



Scheme 1. Synthetic route to Chimera 7

References:
[1] D. J. Selkoe, J. Dennis, EMBO Mol. Med. 8, (2016), 595.
[2] T. Esatbeyoglu, P. Huebbe, I. M. A. Ernst, M. D. Chin, A. E. Wagner, G. Rimbach, Angew. Chem. Int. Ed. 51 (2012), 5308.
[3] R. F. Barth; J. A. Coderre,; M. G. H. Vicente,; T. E. Blue, Clin. Canc. Res. 11, (2005) 3987. M. F. Hawthorne, M. W. Lee, J. Neuroonc. 62, (2003), 33.

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Study of Nanobiomaterials with Bio-based Antioxidants: Interaction of Polyphenol Molecules with Hydroxyapatite and Silica

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In the last decade, nanoparticles arouse the great interest in the field of biotechnology due to their small dimensions and unique properties. They can be synthetized with a surface area that allow large load capability and tissue-specific release. In order to improve their biocompatibility it is possible to functionalize their surface with tannic polyphenol molecules. These natural molecules are present in many fruits and vegetables and known for their great anti-carcinogenic and anti-oxidant properties.[1] They can be obtained from biomass that make them particularly attractive in industrial context.

In this work, we focused on the absorption/desorption of benzoic acid, phenol, pyrocatechol, gallic acid, tannic acid, and hydrated morin on/from amorphous pyrogenic silica (AOX50) and hydroxyapatite (HA) nanoparticles.

The first three smaller molecules were sent in form of vapor phase on the surface of the two materials that were both in their native state or had been thermo-activated with the aim of modify their surface centres (SiOH for silica and Ca^{2+} for HA). Then the respective FTIR spectra were analyzed. Also, citrate-functionalized HA (HA-cit) was tested in this respect, that turned out to be more efficient in delivery. The thermal treatment showed two different effects on AOX50 and on HA. Thermal treatment of AOX50 caused condensation of free silanols which lead to reduction of the analyte absorption[2] while the treatment of HA caused the removal of water remaining adsorbed on the surface leaving the room for absorption of analyte[3]. The citrate functionalization may promote the molecules with a carboxylic group to pass from a deprotonated form to a protonated one by rising the acidity of the environment.

Desorption of the molecules from the materials in H_2O over time was evaluated with UV-Vis spectroscopy analysis both in static or agitated environments. The analytes were previously absorbed on the surfaces of the two materials with the purpose to create a theoretical single or double layer with the impregnation technique. It was observed that the release of the double layer was not addictive to that of the mono-layer, this may be a consequence of a change in the interaction structure between the molecules and the surface of the material depending on the amount of absorbed compound with effects on their solubilisation. This hypothesis was confirmed by FTIR and diffuse reflectance UV-Vis analyses of one of the polyphenol molecules largest in size: hydrated morin impregnated on AOX50 and HA. These analyses demonstrated that the system is not addictive not only due to changes in the molecular organization, but also because the absorption modifies the molecule's electronic structure. Thus, the results of the current work confirm the hypothesis that a change in the solubility of the molecules is possible.

[1] Y. Zuo, et.al., *J. Agric. Food Chem.* **2002**, *50*, 3789–3794.
[2] A. Rimola, et.al., *Chem. Rev.* **2013**, *113*, 4216–4313.
[3] F. Chiatti, et.al., *J. Phys. Chem. C* **2013**, *117*, 25526–25534.

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Methotrexate loaded solid lipid nanoparticles: protein functionalization to improve brain biodistribution

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Glioblastoma Multiforme (GB) is the most common and invasive primary central nervous system (SNC) tumour, with a negative prognosis. The brain-blood barrier (BBB) is the main obstacle to GB pharmacological treatment. Nanoparticles emerged as versatile vectors that can overcome the BBB, particularly through the active targeting strategies.

In this experimental work, solid lipid nanoparticles (SLN), prepared by fatty acid coacervation [1], were loaded with an active lipophilic ester of methotrexate (MTX), didodecylmethotrexate (ddMTX) [2], and functionalized with transferrin and insulin, two proteins whose receptors are abundantly expressed on the BBB. Functionalization was achieved by grafting on the SLN surface a maleimidic mojety and exploiting its reactivity toward thiolated proteins. The derivatization was confirmed by SDS-PAGE followed by Blue Coomassie staining. SLN biodistribution was tested *in vitro* on BBB model and *in vivo* on Wistar rats. Drug metabolism and its tissue amount, in particular the enzymatic synthesis of 7-hydroxymethotrexate (7OH-MTX) - the only active metabolite of MTX - was also investigated in the animal model by mass spectroscopy.

Data obtained, although preliminary, are very interesting, ddMTX-SLN functionalization with PEGilated linkers improved BBB overcoming in cell model, as well as in rats. The drug was extensively metabolized *in vivo*, but 7OH-MTX was not the major metabolite in the model under study.

Further studies on *in vivo* glioma models will be performed in order to evaluate the potential application of this approach to GB therapy.

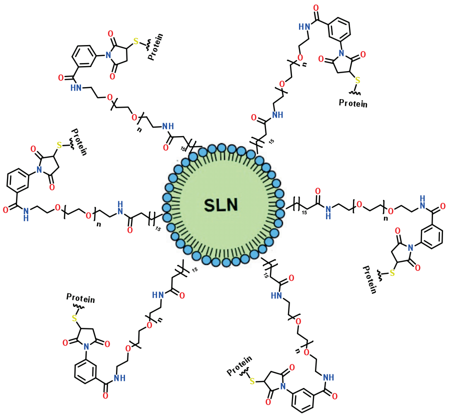

Figure 1 : Scheme of functionalized SLN

[1] Battaglia L, Gallarate M, Cavalli R, Trotta M. Solid lipid nanoparticles produced through a coacervation method J. Microencaps. 2010;27:78–85.

[2] Rosowsky A, Forsch RA, Yu CS, Lazarus H, Beardsley GP. Methotrexate analogues. 21. Divergent influence of alkyl chain on the dihydrofolate reductase affinity and cytotoxicity of methotrexate monoesters. J Med Chem. 1984;27:605–609.

On the adsorption of toluene on porous materials with different chemical composition

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Various methods for the removal of organic contaminants from groundwater have been developed in recent years such as oxidation, reverse osmosis, ion exchange etc. Nevertheless adsorption is considered a very promising alternative [1] a growing number of porous materials have been developed, ranging from microporous to mesoporous materials with different chemical composition.

In this work, the performances of hyper cross-linked polymers (HCPs) towards toluene adsorption via gas phase were evaluated and compared with those of silica-based materials with micro and mesoporosities (*i.e.* zeolites and ordered mesoporous MCM-41 and SBA-15 silicas). Synthetic route for HCPs consists of employing a Friedel–Crafts alkylation to promote the formation of a rigid and highly cross-linked framework formed by aromatic rings. HCPs-like materials (named UPOs) were prepared in our research group varying different synthetic parameters [2] in order to obtain a modulation of their micro and mesoporosity. This was done to evaluate the effect of their textural properties on toluene adsorption. Adsorption data obtained by volumetric measurements (Fig. 1) showed a higher toluene uptake for UPOs with respect to zeolites and silica based materials. This suggests that the high surface area and the nature of the aromatic framework displayed by UPOs are key properties to improve adsorption capacities of the materials towards aromatic molecules.

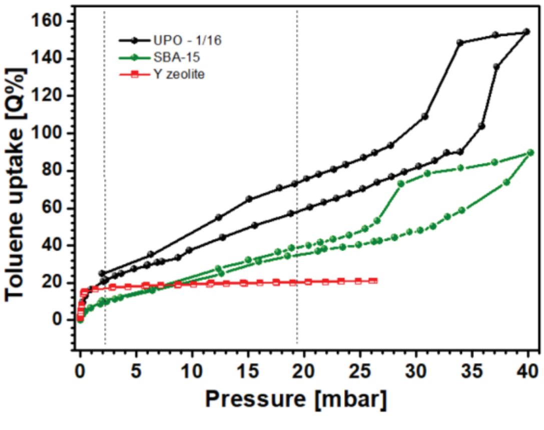

Figure 1. Adsorption isotherms of toluene adsorbed on a selected UPO material compared with SBA-15 mesoporous silica and Y Zeolite.

[1] I. Ali. *Journal of Environmental Management.* 113. **2012**. 170-183.
[2] M. Errahali. *J. Phys. Chem.* **2014**, 118, 28699−28710.

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Synthesis and characterization of activated carbon from modified banana peels for hexavalent chromium adsorption

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In this work, banana peels were used to produce activated carbon. A chemical activation step was carried out by impregnation of the biomass with zinc chloride (1 : 0.5 (w/w)) in order to increase the specific area of the adsorbent. The modified biomass was then activated at a carbonization temperature of 500°C for 1 hour. Fourier transform infrared spectroscopy (FTIR), Scanning electron microscope (SEM), Thermogravimetric analysis (TGA), BET and pH of zero charge were used to characterize the modified adsorbent. The efficiency of this material to remove hexavalent chromium was studied and the effect of the contact time, pH and adsorbent amount on chromium uptake were performed.

The results showed that the adsorption uptake of Cr (VI) reached 90%.

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The maturation of the CO-dehydrogenase from *Thermococcus* sp. AM4 depends on the accessory protein CooC

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Ni-containing CODHs are the biological catalysts that perform the reversible conversion of CO into CO_2 (with turnover frequencies up to 40000 s-1).

$$CO + H_2O \text{ « } CO_2 + 2H^+ + 2e^-$$

The active site of these enzyme, called C-cluster, is a [Ni-4Fe-4S] center. The maturation mechanism of the active site is not fully understood. In most cases, it seems to depend on the accessory protein CooC, but there are exceptions [1][2][3][4]. This protein is indeed required to increase the content of Ni of the C-cluster of the heterologously produced CODH from *Desulfovibrio vulgaris* (*Dv*) and the CODH I from *Carboxydothermus hydrogenoformans* (*Ch*)[3][5]. However, CooC is apparently not required for the insertion of Ni into the C-cluster of CODH II and CODH IV from *Ch,* which can be produced and matured in *E. coli*in the absence of any specific maturase[2]. Moreover, even if Ni-loaded, some CODH have to be activated *in vitro* to become fully active. The activation protocols vary. For example the *Dv* CODH is activated by $NiCl_2$ under reducing conditions whereas the CODH II and CODH IV from *Ch* require a reductive treatment with sodium dithionite (NaDT) and DTT [2][3].
Here we describe the first production and characterization of a CODH from the archea *Thermococcus* sp. AM4 (*Tc*) produced in *Desulfovibrio fructosovorans* either in the presence or in the absence of CooC (the CODH is called $CooS^c$ and CooS, respectively). $CooS^c$ is fully Ni-loaded (1 Ni/monomer), active (250 mmol/mg/min) and cannot be further activated by exogenous Ni under reducing condition. Produced in the absence of CooC, CooS is partially Ni-loaded (0.4 Ni/monomer), almost inactive (6 mmol/mg/min), as observed before with *Dv* CooS.
The results show that this thermococcal CODH is a CooC-dependent enzyme. CooC is involved in the insertion of Ni and is necessary to obtain an active form of the CODH which does not need additional activation treatment. The crystal structures of $CooS^c$ and CooS will help us to understand the role of CooC in CODH maturation and the implications on the activation mechanism of these enzymes.

[1] R. L. Kerby and P. W. Ludden, vol. 179, no. 7, pp. 2259–2266, 1997.
[2] L. Domnik, , *Angew. Chemie - Int. Ed.*, vol. 56, no. 48, pp. 15466–15469, 2017.
[3] J. Hadj-Saïd, *Biochim. Biophys. Acta - Bioenerg.*, vol. 1847, no. 12, pp. 1574–1583, 2015.
[4] T. INOUE, *Biosci. Biotechnol. Biochem.*, vol. 75, no. 7, pp. 1392–1394, 2011.
[5] T. Inoue, , *Biosci. Biotechnol. Biochem.*, vol. 78, no. 4, pp. 582–587, 2014.

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An efficient and catalytic one-pot coupling method for the synthesis of novel pyran and furan derivatives

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Pyran derivatives are found in various natural products. They gained considerable attention due to their wide spectrum of biological activities such as antibacterials, antitumor agents and HIV protease inhibitors [1]. Also, many furan-ring structures were evaluated for their applications in pharmacology and medicinal chemistry such as antidepressant, anxiolytic and anti-inflammatory agents [2].

The aim of this work is to develop a simple and efficient one-pot method for the synthesis of this class of compounds, starting from pyrone and allylic acetate derivatives, using metal triflates ($M(OTf)_n$) as the catalyst.

In Figure 1, we describe an example of the condensation of 4-hydroxycoumarin **1a** with prenyl acetate **2a**, under metal triflate catalysis, to give a mixture of 3,3-dimethyl-3,4-dihyropyrano- [3,2-b]chromen-10(2H)-one **3aa** and 2,2- dimethyl-3,4-dihyro-pyrano[3,2-c]chromen-5-(2H)-one **4aa**, in 86 % yield in a ratio of 77/23. The protocol was extrapolated to the synthesis of various pyranofuran, pyranopyrone and furanopyran derivatives. Moreover, we report some rearrangement studies of linear pyranchromone **3aa** to angular pyranocoumarin **4aa**.

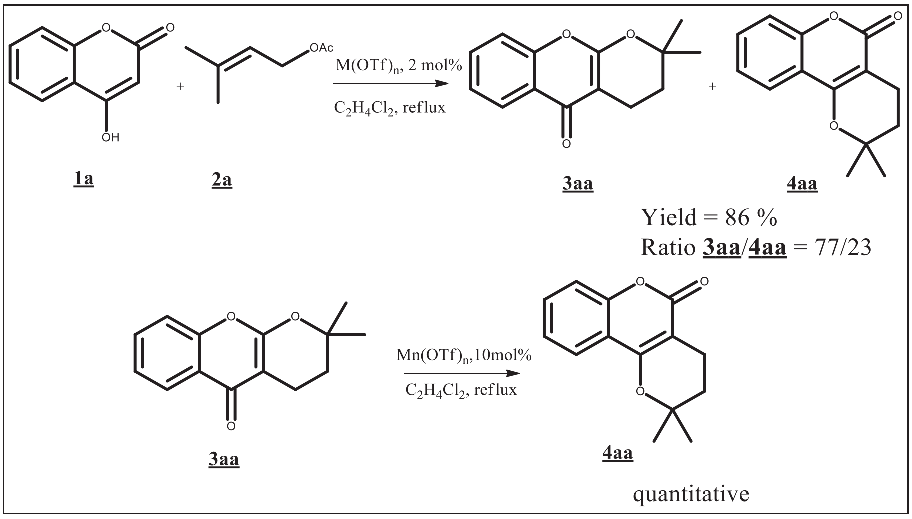

Figure 1: synthesis of linear pyranochromone ***3aa*** *and angular pyranocoumarin* ***4aa***

[1] Sari, E., Aslan, H., Dadi, S., Oktemer, A., Logoglu, E. «Biological activity studies of some synthesized novel furan and pyran derivatives». / GU J Sci, 30 (4), 49-55, (2017).

[2] Katırcıoğlu, H., Loğoğlu, E., Tilki, T., Öktemer, A. «Synthesis of 2, 4-dihalogenofluorobenzenes and their antimicrobial and antifungal activity studies». / Med. Chem. Res, 16 (5), 205-212, (2007).

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Development of new PDE4D inhibitors for Alzheimer Disease

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In the last few years, PDE4 (Phosphodiesterases type 4) is considered a new important pharmacological target due to its crucial involvement in the cAMP/PKA/CREB pathway. Isoform D3 inhibitors (PDE4D3Is) improve memory and cognitive functions both under physiological and pathological condition, with reduced side effects (mostly emesis and sedation) [1]. During the last ten years, a large library of compounds, commonly referred to as the GEBR library, with partial selectivity for the PDE4D isoform has been synthesized by us; all these molecules bear a catecholic moiety (typical of Rolipram-related PDE4Is) and an amino function, linked to the aromatic portion by an iminoether chain or an heterocycle nucleus (pyrazole, isoxazole or isoxazoline, Figure 1 [2,3]. The most active and selective componds **GEBR-7b** [3] and **GEBR-32a** [4] (Figure 1) improve spatial and objects recognition memory and increase hippocampal cAMP levels in transgenic mice [1,5].
With the aim at identifying key structural features able to bind stably the compounds into the catalytic pocket and to interact with the enzyme regulatory domains and to obtain more selectivity, we designed and synthesized a new small library in which pyrazole nucleus of **GEBR-32a** was substituted with pyrrole one (componds **1**, Figure 1). Crystallographic studies and molecular modelling simulation, in progress, will clarify if the presence of 2 nitrogen atoms in the heterocycle nucleus is essential to improve the interaction with the enzyme and therefore increase the selectivity towards the D3 isoform.
Synthesis and pharmacological results of new pyrrole analogues **1-5** will be reported in the poster session.

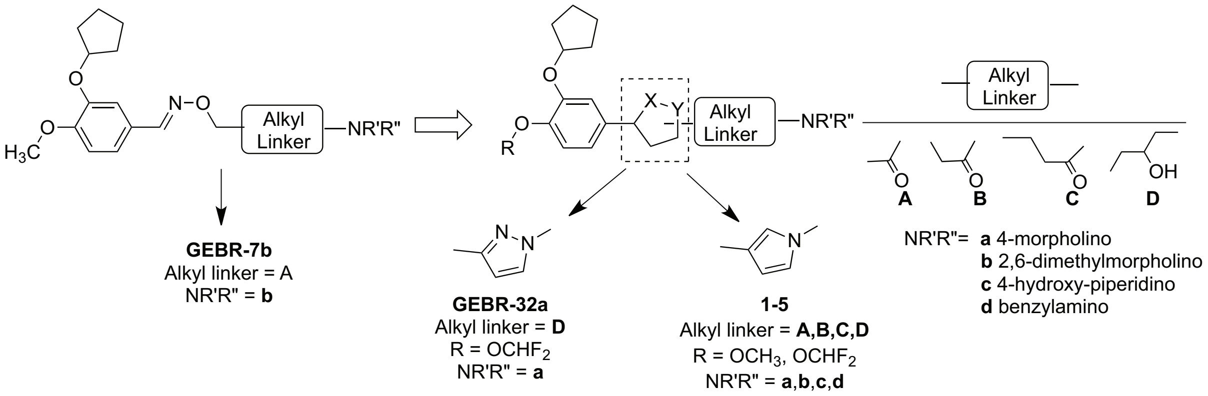

***Figure 1** : structure of previous **GEBR-7b** and **GEBR-32a** and of new derivatives **1-5**.*

[1] Sierksma, A.S. et al. *Neuropharmacology* **77**, 120-30 (2014).
[2] Brullo, C. et al. Eur. J. Med. Chem., **124**, 82-102 (2016).
[3] Bruno, O. et al. *J. Med. Chem*. **52**, 6546–6557 (2009).
[4] Ricciarelli, R. et al.. *Sci. Rep*. **7**, 46320 (2017).
[5] Bruno, O. et al. *Br J Pharmacol*. **164**, 2054-2063 (2011).

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AN INNOVATIVE SCREENING TOOL TO PREDICT THE MUCUS PERMEABILITY FOR EFFICIENT CYSTIC FIBROSIS DRUGS

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Aim: A number of chronic respiratory diseases including chronic bronchitis, asthma, cystic fibrosis and bronchiectasis are characterized by mucus hypersecretion**.** In this work, an airway mucus model composed by alginate and mucin is herein proposed aiming to model both composition and rheological properties of the pathologic CF-mucus (1-3). This mucus model could be used for HTS purposes in drug discovery.

Methods: Alginate (from brown algae)/mucin (from porcine stomach, type III) hydrogels were produced in NaCl 7 mM. Rheological measurements were carried out to access the viscoelastic and shear thinning behaviour of the developed gels and further compared to the pathological CF-mucus. Stability analysis was also conducted to acquire using both water and PBS, at 25°C, to analyse changes on weight percentage and volumetric increase. Finally, both drug diffusion and interaction through alginate and alginate/mucin gels were carried out using aspirin, cephalexin and epirubicin, as well as gold nanoparticles (GNP) as model drugs.

Results: The viscosity of the mucus model decreases with the increasing of shear stress, with no differences observed between both mucus model and CF mucus. Additionally, no differences on the dissipative modulus were detected between the CF and model mucus, although differences were detected over storage modulus. Weight and size increased in both H_2O and PBS, at 25°C. Diffusion studies of drugs and gold nanoparticles through the gels exhibited compositional and structural dependency, thus effecting the interaction with mucin. The diffusion of drugs was also related to both alginate drug interactions or steric barrier effect of the gel.

Discussion : A mucus model was proposed to study drug permeability in presence of mucus secretion. This platform will serve as the basis to implement the complexity of the model in terms of components, also including the effect of bacteria.

[1] M. Robinson et al. J. Aerosol Med Pulm Drug Deliv. (2016), 337-345.
[2] Y. Shaopeng et al. Sci Transl Med. (2015),1–19.
[3] S.K. Lai et al. J.Adv Drug Deliv Rev. (2009), 86-100

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The *Messale Rosselli*: scientific investigation on an outstanding 14th century illuminated manuscript from Avignon

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The manuscript D.I.21 kept at Biblioteca Nazionale Universitaria in Torino, better known as *Rossell Missal* or *Messale Rosselli*, is one of the richest fully illustrated Missals surviving from the mid-14th century (Fig.1). It was produced for the Aragonese cardinal Nicolas Rossell (1314-1362), as indicated both by the *colophon* at the end of the manuscript, where the scribe Alamannus states that the book was completed in 1361 [1]. The vast illustrative programme, painted in tempera by a different workshop, is based on historiated initials introducing the masses in the liturgical year, while the most important festivities are highlighted by fully illuminated borders. The Missal stayed in the Avignon curia after the patron's death, passing into the hands of cardinal Guillaume de Bragose and of archbishop Pierre II de Cros, before 1383 [1]. The *Messale Rosselli* has recently been the object of a thorough interdisciplinary study, involving full characterisation of the colourants with non-invasive techniques (FORS, fluorimetry, XRF spectrometry, optical microscopy). The full set of colourants was identified, highlighting the systematic use of precious pigments such as lapis lazuli, cinnabar and gold, a feature reinforcing the symbolic value of the manuscript; in addition, less valuable but interesting dyes such as brazilwood and folium were also identified, used either pure or in a mixture with pigments in order to obtain a wide range of hues. The overall palette has been evaluated according to the availability of raw materials in the geographic area around Avignon, finding that most of the colourants could be at easy disposal of the artists. Information has also been obtained concerning the preparation of the parchment and the volume itself. The systematic measurement of the width of folios allowed hypothesising the number of the animals slaughtered to produce parchment, and the way of using skins. XRF analysis on the folios suggested that two different preparations were used, one with clay material and one with white lead. Finally, using ZooMS (ZooArchaeology by Mass Spectrometry), a non-invasive technique able to provide information on the animal species from which parchment was produced [2], it was found that both calf and goat were used to produce the parchment in the *Messale Rosselli*.

Figure 1 : Miniature of the Messale Rosselli (337r and 1r)

[1] Manzari F., La miniatura ad Avignone al tempo dei Papi. 1310-1410 (2006) Modena.
[2] Fiddyment S. et al., Animal origin of 13th-century uterine vellum revealed using noninvasive peptide fingerprinting, P. Natl. Acad. Sci. USA, 112 (2015) 15066-15071.

Effect of simultaneous ultrasound and microwave irradiation in the production of superparamagnetic iron oxide nanoparticles as negative contrast agent in MRI

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Superparamagnetic iron oxide (SPIO) nanoparticles have been widely used as MRI negative contrast agents and they are composed of nano-sized coated iron oxide nanoparticles. The two most extensively used methods in preparation of SPIONs are co-precipitation and thermal decomposition techniques. The development of new synthetic methods that provide control over size, morphology, and nano/microstructure of nanoparticles is nowadays object of great interest and high intensity ultrasound offers a facile, versatile synthetic tool for the preparation of nanostructured materials that is often unavailable by conventional methods. The combination of ultrasound (US) and microwave (MW) irradiation can furthermore be considered as a non-conventional strategy to achieve efficient heating as well as mass transfer. The objective of present work is the preparation of coated iron oxide nanoparticles to form core-shell structured system as negative MRI contrast agent. A series of iron oxide magnetic nanoparticles (MNPs) were prepared and coated with and without US-MW irradiation. MNPs were characterized and field-cycling relaxometry NMRD profiles was acquired. In the present study the efficacy of US-MW combined irradiation in the preparation as well in the coating procedure was proved. Citric acid, dextran, carboxy-methyl dextran (CDM) and silica coated MNPs were compared and the results showed that US-MW irradiation influence the size as well the stability of their colloidal dispersion. Several attempt to graft β-cyclodextrins on the surface of coated MNPs were performed with modest grafting loading. On basis on their ability to reduce T_2 value, these systems can be defined like potential negative MRI contrast agents.

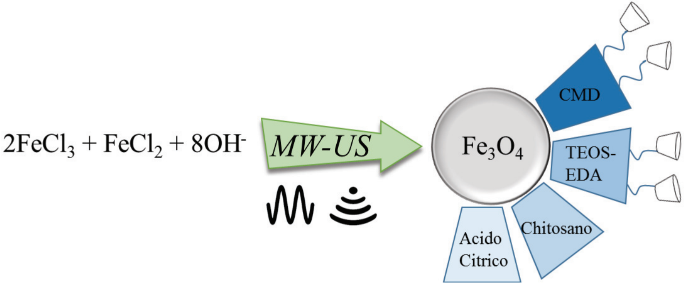

Figure 1 : Ultrasound and microwave irradiation in the production of coated superparamagnetic iron oxide nanoparticles

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Inorganic Quantum Dots and Carbon-Nitride Quantum Dots fluorescence quenching: application in biosensors

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Nowadays, Therapeutic Drug Monitoring (TDM) became a very important topic due to the crescent knowledge about bio-diversity and personalized medicine sensitization. One of the most important supporting technique to this philosophy is the self-testing realized by so-defined 'point-of-care tests'. Among them, lateral flow assays (LFAs) are becoming increasingly popular as a diagnostic tool on their simplicity, specificity, and sensitivity. The gold nanoparticles (GNPs) based LFA gives colorimetric readout and allows rapid screening but lacks of quantitative information, especially for small molecules such as many therapeutic drugs; while LFAs with fluorescence readout (F-LFA) allows quantitative and sensitive detection.

Among fluorescent probes, inorganic semiconductor Quantum Dots (QDs) and Carbon-Nitride Quantum Dots (CNQD) show unique luminescent properties: concerning QDs high quantum yields, size-tunable fluorescence, broad absorption spectra, narrow and symmetric emission spectra, and high resistance to photo-bleaching; concerning CNQDs low cost synthesis, customizable functional groups and high hydro-solubility. Some QDs based LFAs have been reported [1] whereas there are no application using CNQDs in LFAs at the moment. The two main figures of merits of the QD-based LFA are higher sensitivity and improved precision, thus consolidating them as promising labels for small molecule detection [2]. More interestingly, QDs fluorescence is quenched by resonant energy transfer to gold nano-particles when these are kept at a convenient distance, i.e.: the distance achieved by antibody-antigen complex formation [3]. Quenching of QD emission also occurs due to the high extinction coefficient of GNPs through the inner filter effect. Quenching fluorescence allows for increasing sensitivity of competitive immunoassays that applies for measuring small compounds such as therapeutic drugs. Furthermore, the sensitive detection of the target drugs is accomplished in "positive mode" by monitoring the increment of the fluorescence intensity that is proportional to the target amount. The presentation will discuss the properties and advantages of CNQDs and inorganic QDs as convenient probes for developing fluorescence quenching immunoassays to monitoring therapeutic drugs. The ultimate goal is the use in a multi-analyte LFA for detecting anti-retroviral therapeutic drugs in saliva and blood exploiting tunability and multi-responsive behavior.

[1] Huang X, Aguilar ZP, Xu H, Lai W, Xiong Y. Biosens Bioelectron., 2016, 75:166-80.
[2] Anfossi L.; Di Nardo F.; Cavalera S.; Giovannoli C.; Spano G.; Speranskaya E. S.; Goryacheva I. Y. Baggiani C. Microchimica Acta (2018), 185(2), 1-10
[3] Anfossi L, Calza P, Sordello F, Giovannoli C, Di Nardo F, Passini C, Cerruti M, Goryacheva IY, Speranskaya ES, Baggiani C. Anal Bioanal Chem., 2014, 406:4841-9.

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Controlled release of DEET loaded on fibrous mats from electrospun PMDA/cyclodextrin polymer

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Francesco Trotta(1), Pierangiola Bracco(1), Marco Zanetti(1)

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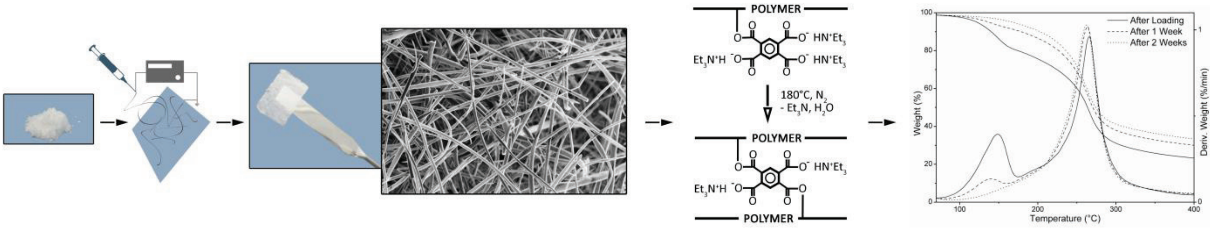

Figure 1 : Processing, curing and loading of PMDA-linked βCD-based polymer.

β-cyclodextrin (βCD) is a cyclic oligosaccharide obtained by enzymatic degradation of starch, consisting of seven α(1,4)-linked glucopyranose units characterized by a truncated cone-shaped structure, producing a slightly hydrophobic cavity, which can accommodate guest molecules through the formation of inclusion complexes [1].

Electrospinning is a powerful technique which is commonly used to obtain fibrous samples from polymeric solution characterized by an high surface-to-volume ratio. Both synthetic and natural polymers have been successful spun giving polymeric fibers widely studied over the past years. In particular, the eco-compatibility and bio-compatibility features offered by polysaccharide-based materials joined to electrospinning processing, increased the use of bio-based fibers in many scientific, medical and industrial fields.

Obtaining performing fibrous materials, which can be used to load and release specific molecules, starting from simple and cheap natural source, such as βCD, would be a challenging result.

We report the possibility to load one of the most common mosquito repellant molecule, diethyltoluamide (DEET), into an insoluble fibrous polymeric matrix. The polymeric mat sample was obtain starting from an hyper-branched water-soluble βCD-based polymer [2] which can be easily processed using an electrospinning device. A one-step simple thermal treatment [3] was used to crosslink the spun polymer and render it insoluble. Finally, it was proved how the treated mat resulted capable to offer a controlled release of the loaded DEET over the time. The DEET releasing resulted more than 2 weeks lasting, starting from a polymeric matrix loading capacity of 200 mg/g (mg DEET/g fibrous matrix).

[1] F. Caldera, M. Tannous, R. Cavalli, M. Zanetti anf F. Trotta, Int. J. Pharm. **2017**, DOI: 10.1016/j.ijpharm.2017.06.072

[2] F. Trotta, F. Caldera, R. Cavalli, A. Mele, C. Punta, L. Melone, F. Castiglione, B. Rossi, M. Ferro, V. Crupi, D. Majolino, V. Venuti and D. Scalarone, Beilstein J. Org. Chem. **2014**, 10, 2586–2593.

[3] M. Zanetti, A. Anceschi, G. Magnacca, G. Spezzati, F. Caldera, G. P. Rosi and F. Trotta, Microporous Mesoporous Mater. **2016**, 235, 178–184.

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SYNTHESIS OF BOLA-AMPHIPHILIC DENDRIMERS FOR ON-DEMAND DRUG DELIVERY

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On-demand drug delivery capable of responding to stimuli intrinsic to diseases are extremely important for the targeted delivery of therapeutics.[1] We have recently developed a fluorinated bola-amphiphilic dendrimer Bola4A, which is sensitive to the reactive oxygen species (ROS) and capable of on-demand delivery of small interfering RNA (siRNA) in ROS-rich cancer cells.[2] Here we will report the different synthesis of these bola-amphiphilic dendrimers which bear a ROS-sensitive thioacetal in the hydrophobic core and poly(amidoamine) dendrons at the two terminals. Also their ROS-sensitive structural feature has been studied using NMR and MS analysis.

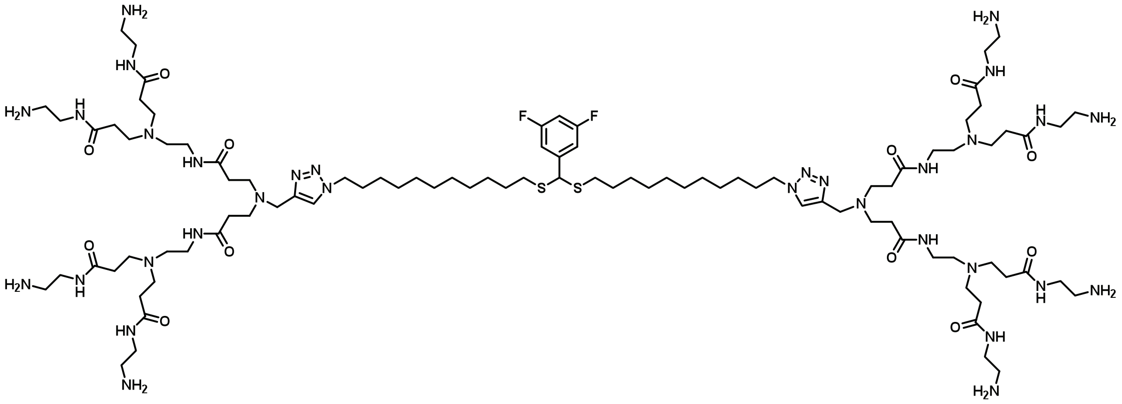

Figure 1 : Structure of Bola4A dendrimer reported in this work

[1] Vladimir Torchilin, “Multifunctional, stimuli-sensitive nanoparticulate systems for drug delivery”, *Nat. Rev. Drug Discov.* **2014**, *13*, 813

[2] Xiaoxuan Liu, Yang Wang, Chao Chen, Aura Tintaru, Yu Cao, Juan Liu, Fabio Ziarelli, Jingjie Tang, Hongbo Guo, Roseline Rosas, Suzanne Giorgio, Laurence Charles, Palma Rocchi, Ling Peng, “A fluorinated bola-amphiphilic dendrimer for on-demand delivery of siRNA via specific response to reactive oxygen species”, *Adv. Funct. Mater.* **2016**, *26*, 8594.

Gold-catalyzed 6-*endo* cycloisomerization reactions of 1,6-enynes

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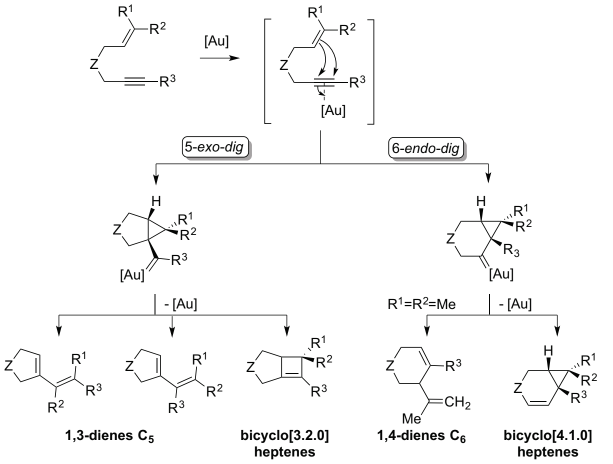
Over the past few years, significant research has been directed toward the development of new methodologies for synthetic efficiency and atom economy processes in the presence of gold catalysts.[1] We have been interested in the development of catalytic methodologies for the synthesis of original and functionalized carbo- and heterocycles starting from enyne derivatives.[2] The stereoselective addition of the alkene to the activated carbon–carbon triple bond may occur via two different pathways, a 5-*exo*-dig or 6-*endo*-dig one.[3] In the general case of 1,6-enynes, the 6-*endo* cyclization is not always observed and a 5-*exo* cycloisomerization generally occurs.



The modification of the substituents on the 1,6-enyne and the optimization of the catalyst may therefore induce the formation of endocyclic derivatives.[5]

This presentation will show our latests results on the 6-*endo* approach. Some recent domino processes as well as challenging enantioselective approaches[6] will also be presented.

References

[1] *Gold Catalysis: An Homogeneous Approach* (Eds.: Toste, F.D.; Michelet, V.), Imperial College Press, London, **2014**.
[2] Michelet, V. in *Comprehensive Organic Synthesis 2nd Edition*, **2014**, Ed. Molander, G.; Knochel, P. "Noble Metal-Catalyzed Enyne Cycloisomerizations and Related Reaction", 1483-1536
[3] Michelet, V.; Toullec, P.Y.; Genêt, J.-P. *Angew. Chem. Int. Ed.* **2008**, *47*, 4268. Lee, S. I.; Chatani, N. *Chem. Commun.* **2009**, 371. Toullec, P. Y.; Michelet, V. *Top. Curr. Chem.* **2011**, *302*, 31. Zhang, D.-H.; Zhang, Z.; Shi, M. *Chem. Commun.* **2012**, *48*, 10271.
[4] Shibuya, T.; Nakamura, N.; Tanaka, K. *Beilstein J. Org . Chem.* **2011**, *7*, 944. Lee, S. I.; Kim, S. M.; Kim, S. Y.; Chung, Y. K. *Synlett* **2006**, 2256. Lee, Y. T.; Kang, Y. K.; Chung, Y. K. *J. Org. Chem.* **2009**, *74*, 7922. Wilckens, K.; Uhlemann, M.; Czekelius, C. *Chem. Eur. J.* **2009**, *15*, 13323.
[5] Tang, Y.; Chen, X.; Michelet, V. unpublished results.
[6] Watson, I. D. G.; Toste, F. D. *Chem. Sci.* **2012**, *3*, 2899.

Helicene-based chiral nanographenes

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Curved polyaromatic hydrocarbons (PAHs) with extended π-systems are of great interest in organic chemistry and materials science, especially in research on nanographenes, nanoribbons, and distorted graphene sheets with peculiar topology.[1] Accordingly, a rapidly increasing number of large, nonplanar, and molecularly defined PAHs have been designed and synthesized in the past decade. However, the ultimate challenge in this field is probably to exploit chirality as a parameter to fine-tune and to fully exalt organic materials properties, such as their physical, supramolecular (solid-state packing, homochiral/heterochiral interactions), photophysical, conductive, chiroptical, molecular recognition, and switching properties.[2] Helicenes are typical units that can be used to induce chirality in PAHs.[3] Recently, a new series of nonplanar PAHs have received great attention: the multiple helicenes, that is PAHs containing two or more helicene moieties.[4] In this communication, the design, syntheses and properties of *D3*-symmetric propeller-shaped PAHs containing six helicene moieties, e.g. **1** in Figure 1, will be discussed.[5]

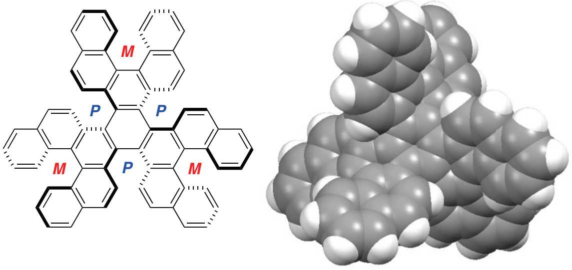

*Figure 1 : The D3-symmetric propeller-shaped nanographene **1** embedding six enantiomerically stable [5]helicenes*

[1] Reviews: a) R. Rieger, K. Müllen *J. Phys. Org. Chem.* **2010**, *23*, 315-325. b) R. A. Pascal, Jr., *Chem. Rev.* **2006**, *106*, 4809-4819. c) Y.-T. Wu, J. S. Siegel, *Chem. Rev.* **2006**, *106*, 4843-4867. d) V. M. Tsefrikas, L. T. Scott, *Chem. Rev.* **2006**, *106*, 4868-4884.
[2] A. Scarso, G. Borsato, In *Chirality at the Nanoscale, Nanoparticles, Surfaces, Materials and More* (Ed.: D. Amabilino), Wiley-VCH: Weinheim, 2009; Chapter 2, pp 29–65.
[3] a) *Helicene Chemistry From Synthesis to Applications* (Ed.: C.-F. Chen, Y. Sheb), Springer: Berlin, 2017. b) Y. Shen, C.-F. Chen, *Chem. Rev.* **2012**, *112*, 1463-1535. c) M. Gingras, *Chem. Soc. Rev.* **2013**, *42*, 968-1006. d) M. Gingras, G. Félix, R. Peresutti, *Chem. Soc. Rev.* **2013**, *42*, 1007-1050. e) M. Gingras, *Chem. Soc. Rev.* **2013**, *42*, 1051-1095.
[4] Review: C. Li, Y. Yang, Q. Miao, *Chem. Asian J.* DOI: 10.1002/asia.201800073.
[5] V. Berezhnaia, M. Roy, N. Vanthuyne, M. Villa, J.-V. Naubron, J. Rodriguez, Y. Coquerel, M. Gingras, *J. Am. Chem. Soc.* **2017**, *139*, 18508-18511.

SWCNT-porphyrin nano-hybrids selectively activated by ultrasound: a new tool for sonodynamic therapy.

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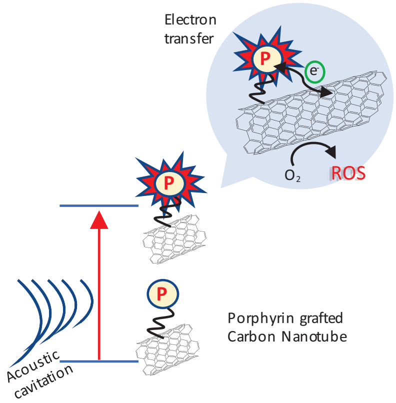

Figure 1 : Mechanism of ROS production by SWCNT-porphyrin nano-hybrid upon US excitation

Sonodynamic therapy (SDT) is an innovative anticancer approach, based on the excitation of a given molecule (usually a porphyrin) by inertial acoustic cavitation that leads to tumour-cell death via the production of reactive oxygen species (ROS). The study was aimed to produce and characterize an innovative hybrid nanosystem based on porphyrin-grafted Single Walled Carbon Nanotubes (SWCNT) for enhancing SDT in vitro citotoxicity. Three different porphyrins were covalently linked to SWCNT via Diels-Alder or 1,3-dipolar cycloadditions. ROS production and tumour-cell viability upon ultrasound (US) irradiation were evaluated. Such nanosystem showed high ROS yield and effective tumour-cell killing activity in vitro. A SWCNT-porphyrin electron transfer mechanism is proposed to explain the observed activity (fig. 1).

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What is the Driving Force for Collagen Protein Folding? Insights from Hybrid DFT Simulations

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Collagen is one of the most abundant protein in mammals. It is the building block of complex hierarchical structures such as bones and tendons.[1] Its structural peculiarity is the geometrical motif in which three parallel polypeptides strands coil about each other to form a triple helix (see Figure 1).[1] The primary structure of collagen is mainly restricted to a triplet repeated sequence, which occurs in all types of collagens.[2] In each triplet, glycine (Gly) always occupies the first position, while proline (Pro) and its derivatives, e.g. hydroxyl-proline (Hyp), are the most common amino acids in the second and the third positions, respectively. Within all collagens, Gly appears most frequently (33%), and Pro and Hyp represent the ~22% of all residues.[3] Hyp is not directly incorporated in the protein. Indeed, the process of hydroxylation of the Pro ring occur after collagen formation in cells. It has the relevant role of increasing the stability of the collagen protein preventing rapid denaturation at human body temperature. In the last decade, several experimental studies were carried out to explain energetic reasons of this stabilization effect. Despite the large amount of work done,[4] the scenario is still not clear.

Molecular simulation at the DFT level combine atomic resolution and chemical accuracy, and can be an useful tool for investigating biological systems. Its main limitation is the size of the systems investigable, which is very limited, so it is a method rarely employed in protein science. Thanks to highly symmetrical collagen protein models, we reduced the computational cost of our calculations, thus succeeding to simulate the folding process of a single polypeptide strand into a collagen triple helix. We focused on the role of the proline hydroxylation by comparing several aminoacidic compositions. From our simulation, dispersion forces seem to guide the formation of the triple helix in vacuum. Water molecules, which have a very delicate role in the folding process, must be included explicitly in the simulations for a reliable representation of this natural phenomenon.

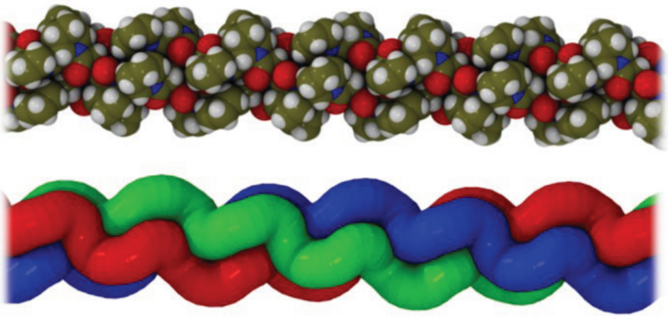

Figure 1. Collagen protein. Top: all atoms. Down: the three polypeptide strands reported in different colours.

[1] Fratzl, P. *Collagen. Structure and Mechanics*. (Springer Berlin / Heidelberg, 2008).
[2] Bella, J. Collagen structure: new tricks from a very old dog. *Biochem. J.* **473,** 1001–25 (2016).
[3] Ramshaw, J. A. M., Shah, N. K. & Brodsky, B. Gly-X-Y tripeptide frequencies in collagen: a context for host-guest triple-helical peptides. *J. Struct. Biol.* **122,** 86–91 (1998).
[4] Shoulders, M. D. & Raines, R. T. Collagen structure and stability. *Annu. Rev. Biochem.* **78,** 929–58 (2009).

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Exploring Nuclear Receptors Variability with Innovative Computational Tools

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Nuclear receptors (NRs) are a superfamily of transcription factors that regulate the expression of a lot of genes playing a role in every aspect of development, physiology and diseases in humans. NRs are formed by different domains, two of which, the DNA-binding domain (DBD) and the ligand-binding domain (LBD), are highly conserved. In particular, LBD is responsible for substrates, agonist and antagonist recognition, for co-activator and co-repressor binding and for receptor dimerization. Even if conserved in the overall folding, LBD sequence varies substantially between NRs. Thus, retrieving similarity between binding sites could have a great impact for enhancing selectivity in drug design. The comparison of protein binding sites can also be a useful technique to approach drug repurposing, polypharmacology and off-target effects. To this aim we used BioGPS, a new computational algorithm for comparing and clustering protein pockets in terms of their three-dimensional structure. BioGPS combines the GRID Molecular Interactions Fields (MIFs) with pharmacophoric fingerprints having the advantage to be a MIF-based approach and to compare protein binding sites by their ligand "image". Here we provide the application of the BioGPS procedure to the NRs superfamily. Pockets detection and comparison was computed on the six big families of NRs and on each of the subfamilies inside. This work helps to discriminate which classes are more or less variable, in terms of structural flexibility of both orthosteric and possible allosteric binding sites, and to find correlation among them. Finally, it is valuable to detect receptors with few or none crystallographic structure that would be further investigated by means of molecular dynamics simulations.

[1] Moore, J. T., Collins, J. L., & Pearce, K. H. The nuclear receptor superfamily and drug discovery. ChemMedChem, 2006, 1(5), 504-523.
[2] Siragusa L, Cross S, Baroni M, Goracci L, Cruciani G. BioGPS: navigating biological space to predict polypharmacology, off-targeting, and selectivity. Proteins. 2015, 83(3), 517–32.

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IX Giornate Italo-Francesi di Chimica
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Synthesis and characterization of nanostructured $CoMoO_4$: Thermochromism and piezochromism.

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Cobalt molybdate $CoMoO_4$ has some interesting properties such as thermochromic [1], piezochromic [2], photoluminescence and photocatalysis under UV excitation are well know [3].

In the present study, the material has been succefully synthesized by a new EDTA-Citrate method, and various heat treatments were applied. It may exist in two polymorphic phases α (green) and β (purple), they depend of two parameters pressure and temperature. Afterwards, the polycrystalline samples are characterized by thermogravimetric analysis, X-ray diffraction and scanning electron microscopy.

The results obtained by XRD, showed the possibility of obtaining a β phase (at 500 °C) and a highly textured α phase according to the family of planes (hh0). The results obtained by scanning electron microscopy confirmed the existence of two phases α and β with very different morphologies. The β phase consists of agglomerated grains of about 200 nm. However, the α phase is organized in the form of nanosheets (20 nm) and aggregate of beads nanostructured assembled into faceted crystallites of sub-micron sizes.

At last but not least, photocatalysis and photoluminescence tests are in progress and will be discussed in this paper.

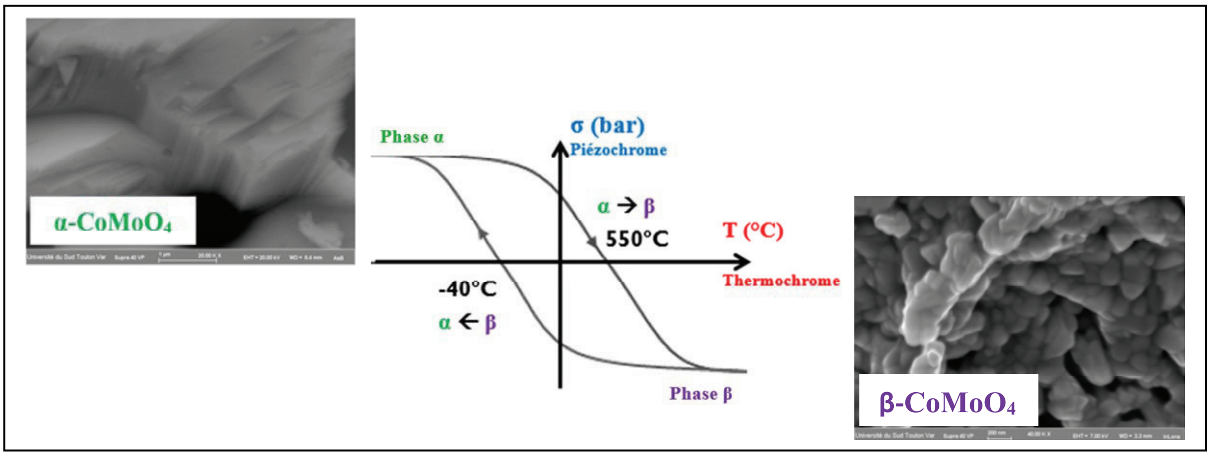

Figure 1. Phase transition of $CoMoO_4$.

[1] C. Livage, A. Hynaux, & G. Férey. Materials Chemistry **12**. 1423 – 1425 (2002).
[2] M. Gaudon, A. E. Thiry & A. Largeteau. Inorganic Chemistry **47**. 2404 – 2410 (2008).
[3] G. Kianpour & H. Emadi. Superlattices and Microstructures **58.** 120 – 129 (2013).

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Composite anion-conducting membranes based on polysulfone and layered double hydroxides

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The synthesis of anion exchange membranes (AEM) are based on inexpensive aromatic polymers, such as polysulfone (PSU) which is easy to produce and recycle with relatively little environmental pollution problems, is stable in alkaline media and presents a low gas permeability. The AEM were prepared by chloromethylation and amination of PSU; the composite anion-conducting membranes were made by dispersion of nanoparticles of layered double hydroxide (LDH) with composition $Mg_{0.62}Al_{0.38}(OH)_2(Cl)_{0.38}\cdot 0.6H_2O$ as inorganic filler. Two types of amines were used: small and flexible trimethylamine (TMA) and bulky and rigid 1,4-diazabicyclo[2.2.2]octane (DABCO). These amines were chosen because they are strong bases, and especially DABCO presents high values of steric hindrance and the positive charge is delocalized through long-range interactions or resonance; these features can help to prevent the S_n2 elimination by OH^- and the ylide formation [1].

The composite membranes have a distinctly lower water uptake and swelling and they can be hydrated at 60 °C without dissolution. Composites with DABCO have slightly lower water uptake and ionic conductivity than those with TMA. Their mechanical properties in fully humidified conditions are clearly enhanced with especially a nearly 3-fold increase of the Young modulus. In spite of their strongly reduced hydration, the conductivity of the composite membranes is comparable with that of the pristine ionomers, being in the range 2-4 mS cm^{-1} at 25 °C. Furthermore, the membranes can be treated in alkaline conditions at 60 °C without losing their properties [2].

[1] M.L. Di Vona, R. Narducci, L. Pasquini, K. Pelzer, P. Knauth, Int. J. Hydrog. Energy, 39 (2014) 14039-14049
[2] M.L. Di Vona, M. Casciola, A. Donnadio, M. Nocchetti, L. Pasquini, R. Narducci, P. Knauth, Int. J. Hydrog. Energy, 42 (2017) 3197-3205

Formic Acid Adsorption Mechanism on Anatase TiO_2 (101) surfaces

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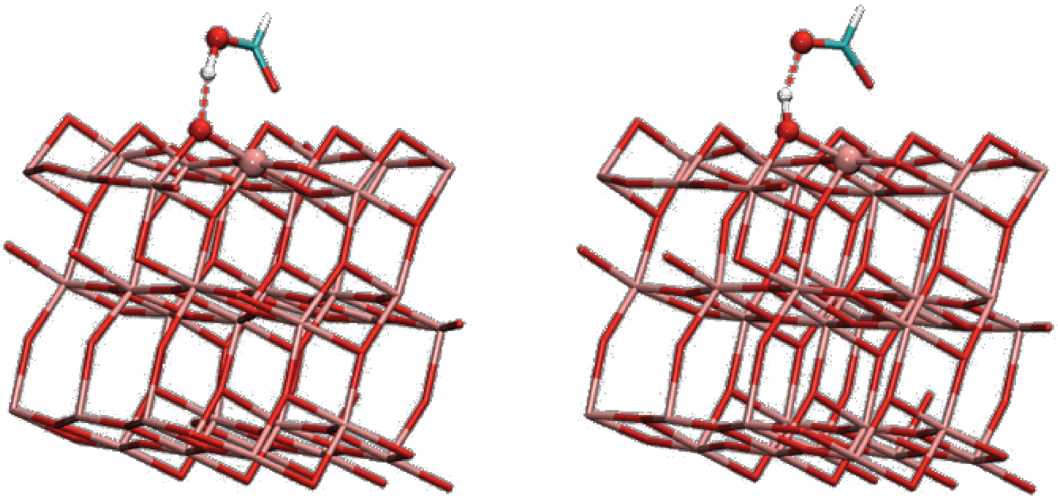
The interaction of carboxyl groups with mineral surfaces is of key relevance in chemistry. Nevertheless, how formic acid adsorbs on the most abundant TiO_2-anatase facets is still controversial: whereas ab initio structural optimizations predict molecular absorption, several experiments evidenced formic acid dissociation. [1, 2] In this work, by using IR spectroscopy and first principles molecular dynamics, evidence is provided of a fast equilibrium taking place, at the experimental room-temperature conditions, between formate and formic acid on anatase TiO_2 (101) facets. The microscopic process, a femtosecond-scale proton shuttling between the carboxyl group and the surface oxygen atoms, implies the coexistence of molecular formic acid and dissociated formate on anatase TiO_2 (101) under normal conditions. With this study, the aim is to shed some light on the interactions of organic acids with titania and once more underlines the importance of the temperature variable in modelling approaches. Furthermore, these insights are a new starting point for the subsequent reaction of FA with MA.



Optimized structures of HCOOH on anatase-TiO_2 (101).

[1] Xu M., Noei H., Buchholz M., Muhler M., Wöll C., Wang Y., *Catalysis Today* **2012** 182, 12-15.
[2] Deiana C., Sakhno Y., Fabbiani M., Pazzi M., Vincenti M., Martra G., *ChemCatChem* **2013** 5, 2832-2834.

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Quality control of an indium solid polymer for catalytic use by energy dispersive X-ray spectrometry (EDX/EDS)

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Indium (III) catalysts have found a wide arrange of applications in organic synthesis, in particular as triflate (trifluoromethanesulfonate) salts.[1] In the context of Green Chemistry, there is a need for the most efficient use of metal as catalysts, and recycling is a must for minimizing the environmental impact of they use. Solid catalysts that can be easily separated from a liquid reaction mixture were prepared by sulfonation of the chemically and thermally stable PEEK polymers (PolyEtherEtherKetone). Sulfonate functionalization followed by formation of an indium salt was selected as mean to mimic the metal triflate catalyst.[2]

The full characterization of such compounds is challenging. The indium content (In^{3+}) is a crucial data for assessment of the synthetic steps, the initial activity of the catalyst and its stability after recycling. Using Scanning Electron Microcopy (SEM), energy dispersive X-ray spectrometry (EDX) is a simple and rapid elemental analysis for metal and metalloids with atomic numbers above 6.[3] The sample preparation is minimal, only routine metallization was used in our case. A typical spectrum of the functionalized polymer is shown in Fig. 1. We focused on the S/In ratio, expected to be 3/1 for a perfect sulfonate salt $(RSO_3)_3In$. The potential value of quantitative EDX analysis for our application was assessed. Calibrations using indium sulfide and indium sulfate indicated good accuracy. In addition, the homogeneity of metal distribution, microstructure of the material and possible impurities can be examined.

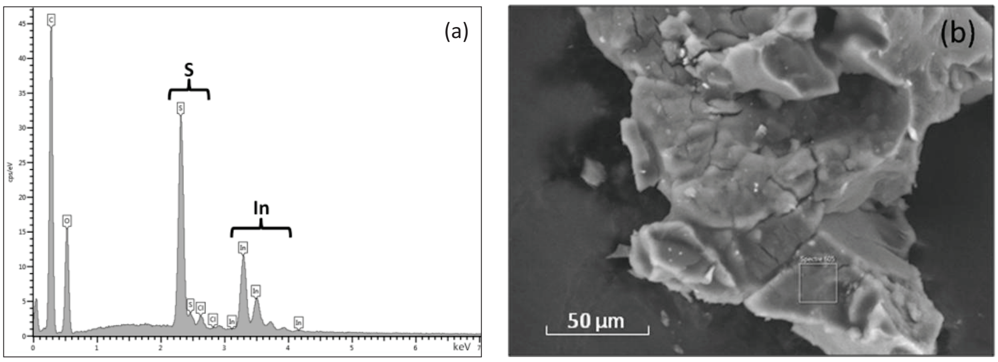

Figure 1: (a) Characteristic EDX spectrum of an indium (III) salt of a 100% sulfonated PEEK polymer. (b) SEM image of a typical catalyst particle, showing the spot where the EDX spectrum was taken.

The experimental conditions and results will be detailed in the poster.

[1] C. Frost, E. Levesque, "Indium(III) Triflate", e-EROS Encyclopedia of Reagents for Organic Synthesis, **2015**, 1-6. R. Ghosh, S. Maiti, *J. Mol. Catal. A*, **2007**, *264*, 1-8.

[2] V. Morizur, D. Hector, S. Olivero, J. R. Desmurs, E. Duñach, *Eur. J. Org. Chem*. **2016**, 3126-3129.

[3] J. I. Goldstein et al., "Scanning Electron Microscopy and X-ray Microanalysis", 3rd Ed., Springer, New York, 2003.

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Covalent NLRP3 inhibitors: design strategies, synthesis and pharmacological characterization

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NLRP3 inflammasome is a multiprotein complex that plays a key role in the intracellular activation of caspase-1, processing of pro-inflammatory interleukins (IL)-1β, IL-18 and pyroptotic cell death. The overactivation of NLRP3 is involved in a variety of diseases, including cryopyrin-associated periodic syndromes (CAPS), inflammatory bowel disease (IBD), neuroinflammatory diseases and many others. NLRP3 inflammasome activation is emerging as promising drug target. In previous proof of concept studies our team discovered that α,β-unsaturated carbonyl derivatives are able to inhibit NLRP3 signalling. The synthesis of the Michael acceptor moiety was performed using the reaction of an electron-deficient alkene and a carbonyl compound under Morita-Bayles-Hillman (MBH) conditions. Different reactivities of the adopted starting materials required a set-up of the literature reaction conditions. From the first electrophilic warhead compound series, **INF4E**, appeared to be the primary hit compound (pyroptosis decrease on PMA-differentiated LPS-primed THP-1 cells: 75.1 ± 2.6% at 10 µM, NLRP3 ATPase inhibition on isolated enzyme: 72 ± 14% at 100 µM, reactivity with cysteamine: $k_2 = 0.866\ M^{-1}s^{-1}$, caspase-1 inhibition in THP-1 cells: 30.3 ± 2.5% at 10 µM, $TC_{50} = 67.0 \pm 3.4$ µM on HK-2 cells).[1] Unfortunately, **INF4E** displayed a certain degree of cytotoxicity, which could be due to its not perfectly tuned reactivity. In order to increase its activity while reducing its cytotoxicity, we investigated the modulation of four molecular moieties, as reported in *Fig.1*. Two series of compounds (acrylate and acrylamide series) were designed and synthetized accordingly, and their cytotoxicity and anti-pyroptotic activity was determined.[2,3] This communication presents the synthesis, structure-activity relationship determination and studies of cytotoxic properties leading to the identification of a new electrophilic hit compound, **INF39**.

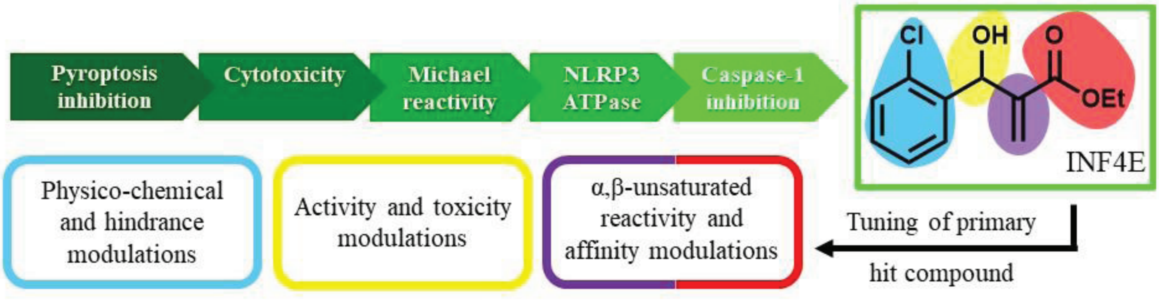

Fig. 1:Schematic representation of the conducted screening on INF4E and modulated molecular moieties.

1. Cocco, M. et al. Electrophilic Warhead-Based Design of Compounds Preventing NLRP3 Inflammasome-Dependent Pyroptosis. J. Med. Chem. 57, 10366-10382 (2014).
2. Cocco, M. et al. Development of an Acrylate Derivative Targeting the NLRP3 Inflammasome for the Treatment of Inflammatory Bowel Disease. J. Med. Chem. 60, 3656-3671 (2017).
3. Cocco, M. et al. Design, Synthesis, and Evaluation of Acrylamide Derivatives as Direct NLRP3 Inflammasome Inhibitors. Chem. Med. Chem. 2016, 11, 1790-1803.

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3-Cyano-4,6-diphenyl-pyridine amino acid derivatives active as influenza A polymerase inhibitors

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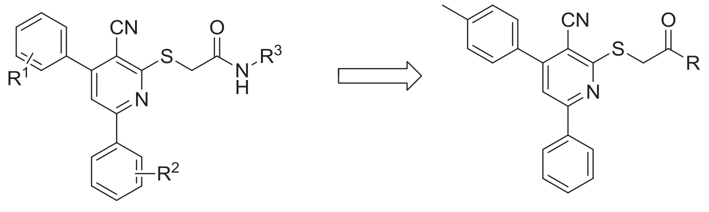
Influenza (Flu) is an infectious disease caused by negative-single-stranded and segmented RNA viruses, which belong to the *Orthomyxoviridae* family. These are classified in type A, B, C and D. Among them, influenza A virus (FluA) is responsible for the most important human pandemics of the last century and it is very difficult to prevent and to treat because of the high mutation rate and genomic reassortment. The RNA-dependent RNA polymerase (RdRp) is widely recognized as one of the more promising anti-flu target, since it has a critical role in FluA infection progression and possesses a high genomic sequence conservation. RdRp is constituted by three subunit: PA (polymerase acid protein), PB1 and PB2 (polymerase basic protein 1 and 2) [1]. Our group has already identified the 3-cyano-4,6-diphenyl-pyridine scaffold **1** (Figure) as an interesting disruptor of the PA-PB1 complex of RdRp, by mimicking the N-terminal portion of PB1 and the most important interactions with the C-terminal domain of PA [2,3]. Starting from this background, we decided to explore the chemical space around the C2 side chain of the pyridine scaffold, synthesizing derivatives **2a-p** (Figure). We introduced in C2 one, two or three amino acids as free acids or as esters, to ensure membrane permeability. The majority of the molecules are not cytotoxic (CC$_{50}$ values >250 μM) and some of them show a good antiviral activity. In particular, the most active derivative possesses an IC$_{50}$ of 36 μM and EC$_{50}$ values of 39 μM and 53 μM in plaque reduction assay (PRA) and in minireplicon assay, respectively. Detailed biological data will be reported in the poster section.



1

2a-p

R^1, R^2 = H, halogens, small alkyl groups
R^3 = aromatic groups

R = L-amino acid-COOH, -COOBn or -COOCH$_3$
L-Val-L-Asp-COOH, -COOAll or -COOCH$_3$
L-Val-L-Asp-L-Met-COOCH$_3$

*Figure: General structures of first (**1**) and second (**2**) generations of 3-cyano-4,6-diphenyl-pyridine derivatives*

[1] Zhou, Z. *et al.* Drug Discovery Today (2018) [Epub ahead of print].
[2] Tintori, C. *et al.* Bioorg. Med. Chem. Lett. 24 (2014) 280-282.
[3] Trist, I. M. L. *et al.* J. Med. Chem. 69(6) (2016) 2688-703.

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Hetergeneous catalysts for biomass valorisation: the case of t-ZrO_2

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Zirconium oxide because of its interesting physical and chemical properties has been widely used for many technological application [1]. Limiting factor for applications are its intrinsic polymorphism resulting in the difficulty to obtain a pure stable phase. Microwave-assisted processing can help to overcome disadvantages of common synthesis techniques by reducing reaction time, improving yield and leading the preparation of a metastable phase [2]. We report a quick and green procedure to obtain zirconia: microwave-assisted sol-gel synthesis, followed by microwave-assisted calcination. The product obtained is highly crystalline, as confirmed by different techniques (Powder X-Ray Diffraction, Raman and FT-IR spectroscopies). Morphology of tetragonal ZrO_2 has been investigated by means of HR-TEM, showing small spherical particles with an homogeneous shape distribution. BET specific surface area and porosity have also been determined. Thanks to its thermal stability and its bifunctional acid/basic properties, ZrO_2 can act as catalyst support or catalyst by itself. The product will be tested as catalyst in the transformation of platform molecules from biomass into value-added chemicals.

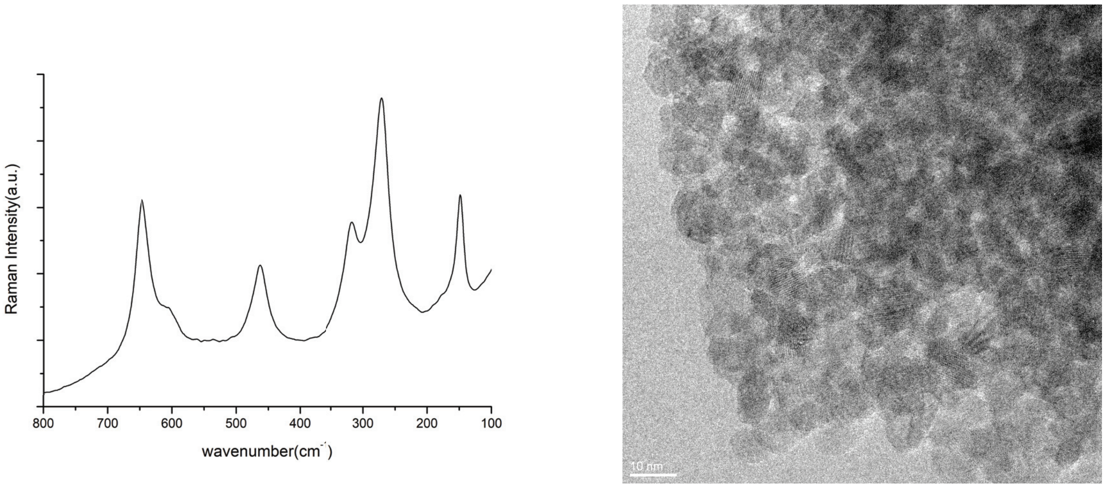

Figure 1 :On the left Raman spectrum, on the right HR TEM of zirconia nanoparticles.

[1] J. Joo, T. Yu, Y.W. Kim, H.M. Park, F. Wu, J.Z. Zhang and T. Hyeon, *J. Am. Chem. Soc.*(2003) **125,** 6553–6557

[2] H.J. Kitchen, S.R. Vallance, J.L. Kennedy, N. Tapia-Ruiz, L. Carassiti, A. Harrison, A.G. Whittaker, T.D. Drysdale, S.W. Kingman and D.H. Gregory, *Chem. Rev.*(2014) **114**, 1170–1206

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Aromatic compounds profile of DOC Piedmontese wines by GC-MS with HS-SPME

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Gas chromatography-mass spectrometry is widely employed to obtain important information on the aromatic profiles of red wine, as it is recognized that it is associated with human diet: the worldwide consumption of red wines reached over 240 mhl in 2017 [1]. On the basis of the general approach to consume local and sustainable products, we decided to focus our attention on some not yet studied Piedmont hillock wines. The aromatic molecules we wanted to evidence, extracted by means of headspace microextraction (HS-SPME) with a triphasic fiber (CAR/PDMS/DVB 30/50µm), have been quantified by means of a Focus GC DSQ Thermo corporation-single quadrupole spectrometer. This hyphenated extraction technique has gained universal approval and is employed in many application as aromas and fragrances recognition in food area, in toxicology, in environmental and biological matrixes [2]. Multivariate chemometric approach will allow the identification of the representative profile of the selected typical Piedmontese wines, which will be useful for traceability and safeguard from food frauds.

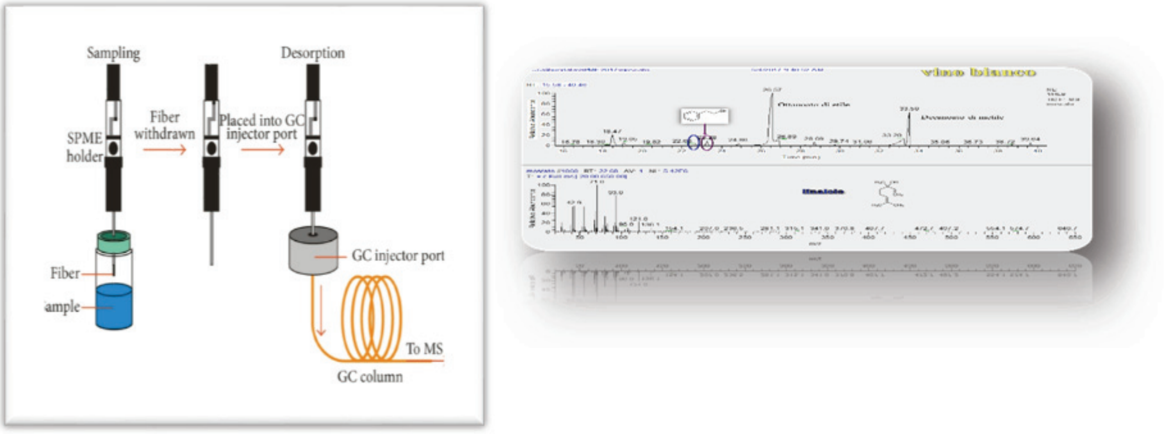

Figure 1 : FIG. 1: Solid phase microextraction and GCMS analysis

[1] OIV – Organisation Internationale de la Vigne et du Vin, april 2017 report
www.oiv.int/public/medias/5287/oiv-noteconjmars2017-en.pdf
[2] S. Camara, M.Arminda Alves, J.C. Marques, Anal. Chim. Acta, 555 (2006), 191-200.

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Synthesis of a small library of potential SGK1 inihibitors

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The serum- and glucocorticoid-regulated kinase 1 (SGK1) is a serine-threonine kinase which is emerging as an essential and non-redundant target in medicinal chemistry. SGK1 has demonstrated to be involved in cancer development and resistance, and in the metabolic syndrome, a pathological state mainly characterized by hypertension and obesity [1, 2]. Only few SGK1 inhibitors have been reported in the literature to date.
Our research group synthesized a wide library of 4-amino-substituted pyrazolo[3,4-*d*]pyrimidines active as dual Src/Abl inhibitors, two tyrosine kinases which are involved in many malignancies. Recently, we decided to virtually screen our in house library against SGK1 to evaluate the activity towards this emerging target. The most promising *in silico* compounds have been tested *in vitro* and, among these, SI113 (*Figure*) showed an IC_{50} value of 600 nM on SGK1 and resulted selective for this kinase compared with AKT-1, Src and Abl. Furthermore, SI113 resulted active *in vitro* as antiproliferative agent on different cancer cell lines and also in glioblastoma and hepatocarcinoma xenograft mouse models [3,4]. For this reason we synthesized a new generation of SI113 derivatives, with the aim to find molecules with a higher activity and a better pharmacokinetic profile. We explored the effects of substitutions on N1 phenyl ring, and on C4 and C6 positions. In particular, we inserted polar groups such as the ethanolamino and diethanolamino moieties in C6 to improve the solubility of such molecules.
Synthesis and biological results will be reported in the poster section.

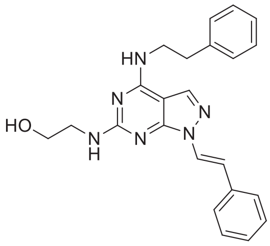

Figure: the SGK1 inhibitor SI113

[1] Bruhn, MA et al. *Growth Factors*, **2010**, 28, 394-408.
[2] Lang, F. et al. *Hormons*, **2013**, 12, 160-71.
[3] Talarico, C. et al. *Oncotarget*, **2015**, 6, 37511-25.
[4] Abbruzzese, C. et al. *Oncotarge*t, **2017**, 8, 11043-55.

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IX Giornate Italo-Francesi di Chimica
IX Journées Franco-Italiennes de Chimie
Genova
April 16-18, 2018

Effect of storage in plastic bottles on the quality of extra virgin olive oil

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According to Reg. (CE) 1019/02, concerning the olive oil marketing standards, oils must reach the consumer packaged in containers with a capacity not exceeding five litres with an airtight seal. In the case of extra virgin olive oil, the packaging plays the fundamental role of protective barrier against light and oxygen and it is therefore a mean of preserving the quality of the oil.

In this study, the effect of storage in plastic or glass bottles on extra virgin olive oil (EVOO) was investigated by Near-Infrared Spectroscopy (NIRS). In order to reach this goal, 32 extra virgin olive oils, from different cultivars and geographical origins, were collected. For each sample, 100 mL were poured from the amber glass bottle into dark plastic (PET) little bottles purchased from a company that guarantees them as suitable for storing essential and food oils. The samples were stored for 2 weeks under constant temperature and humidity conditions, protected from light.

The NIR spectra of the oils were recorded, immediately after opening the bottle and after 2 weeks of storage, with an NIR-Buchi spectrophotometer (NIRFlex N-500), in the 4000-10000 cm^{-1} range and 4 cm^{-1} resolution.

After a suitable pre-processing to reduce unwanted variability (SNV transform), NIR profiles revealed that the band around 5200 cm^{-1} was affected by the difference between storage conditions, in glass or PET. Principal Component Analysis highlighted a clear distinction between the oils stored in the two different conditions along PC1, direction of maximum variance.

Further tests were carried out to investigate the cause of this difference; in particular, 2 samples were exposed to the air under stable and controlled conditions of temperature and humidity; the results obtained supported the hypothesis that the oils stored in the plastic bottles undergo an oxidation due to the permeability of PET to atmospheric oxygen.

The results of this study led to a careful choice of the storage conditions for the extra virgin olive oil samples subject of the Project.

Acknowledgment:
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Study of Nanobiomaterials with Bio-based Antioxidants: Interaction of Polyphenol Molecules with Hydroxyapatite and Silica

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In the last decade, nanoparticles arouse the great interest in the field of biotechnology due to their small dimensions and unique properties. They can be synthetized with a surface area that allow large load capability and tissue-specific release. In order to improve their biocompatibility it is possible to functionalize their surface with tannic polyphenol molecules. These natural molecules are present in many fruits and vegetables and known for their great anti-carcinogenic and anti-oxidant properties.[1] They can be obtained from biomass that make them particularly attractive in industrial context.

In this work, we focused on the absorption/desorption of benzoic acid, phenol, pyrocatechol, gallic acid, tannic acid, and hydrated morin on/from amorphous pyrogenic silica (AOX50) and hydroxyapatite (HA) nanoparticles.

The first three smaller molecules were sent in form of vapor phase on the surface of the two materials that were both in their native state or had been thermo-activated with the aim of modify their surface centres (SiOH for silica and Ca^{2+} for HA). Then the respective FTIR spectra were analyzed. Also, citrate-functionalized HA (HA-cit) was tested in this respect, that turned out to be more efficient in delivery. The thermal treatment showed two different effects on AOX50 and on HA. Thermal treatment of AOX50 caused condensation of free silanols which lead to reduction of the analyte absorption[2] while the treatment of HA caused the removal of water remaining adsorbed on the surface leaving the room for absorption of analyte[3]. The citrate functionalization may promote the molecules with a carboxylic group to pass from a deprotonated form to a protonated one by rising the acidity of the environment.

Desorption of the molecules from the materials in H_2O over time was evaluated with UV-Vis spectroscopy analysis both in static or agitated environments. The analytes were previously absorbed on the surfaces of the two materials with the purpose to create a theoretical single or double layer with the impregnation technique. It was observed that the release of the double layer was not addictive to that of the mono-layer, this may be a consequence of a change in the interaction structure between the molecules and the surface of the material depending on the amount of absorbed compound with effects on their solubilisation. This hypothesis was confirmed by FTIR and diffuse reflectance UV-Vis analyses of one of the polyphenol molecules largest in size: hydrated morin impregnated on AOX50 and HA. These analyses demonstrated that the system is not addictive not only due to changes in the molecular organization, but also because the absorption modifies the molecule's electronic structure. Thus, the results of the current work confirm the hypothesis that a change in the solubility of the molecules is possible.

[1] Y. Zuo, et.al., *J. Agric. Food Chem.* **2002**, *50*, 3789–3794.
[2] A. Rimola, et.al., *Chem. Rev.* **2013**, *113*, 4216–4313.
[3] F. Chiatti, et.al., *J. Phys. Chem. C* **2013**, *117*, 25526–25534.

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Selective ionic sensor development: deposition of lipid dielectric monolayers on organic and inorganic semi-conductor

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Human activities gradually lead to the degradation of the environment and cause adverse effects on human health by the release in food, water, air or soil of various pollutants or harmful molecules. Quantifying their presence and their impact on both the environment and the human health is crucial. The development of innovative analytical techniques that encompass selectivity, sensitivity, easiness-to-handle, high-throughput, integration and wearable associated to real-time monitoring capabilities has therefore unlimited applicative potential.

In that way, we focused out our researches on the development of an OFET sensor where the selectivity and the sensitivity are brought by an original way on using a chemically engineered ultra-thin versatile lipid monolayer as gate dielectric.

As part of this project I have been working on the formation of lipid monolayers on P3HT and SiH. I have shown using indentation measurements by AFM that such layers can be stabilized by a two-dimensional reticulation process which gives them high mechanical and dielectric stability.

The lipids are chemically modified such that their head-group offers a hydroxyl function that can be further used to graft a probe using a siloxane function for example. Both reticulation and grafting of probes have been studied by XPS and FTIR-ATR.

The probes that I am synthesizing are derivatives of calix-4-arene. I have shown that by using a 1,3 alternated conformation with aromatic ring in the chelating area, we can have probes with high affinity to Cs^+ with a 1:1 stoichiometry. Affinity constant measurements for other ions confirmed the high specificity towards Cs^+.

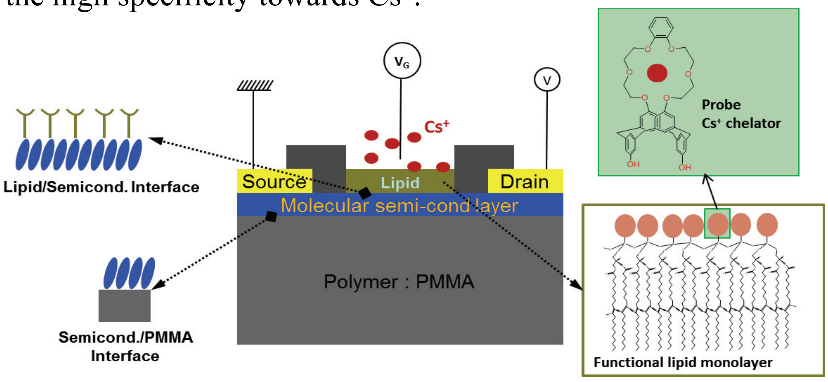

Figure 1 Illustration of the FET-sensor for Cs^+ detection

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LABORATORY IONOMER MATERIALS FOR ENERGY

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The objective of the International Associated Laboratory “LIME” is to prepare and characterize ionomer materials for electrochemical energy technologies. Aromatic polymers are very attractive given their easy functionalization, low cost and easy recycling. Among the many aromatic polymers, we focus mainly on Poly(ether-ether-ketone) (PEEK), Poly(phenyl-sulfone) (PPSU) and Polysulfone (PSU).

1. Proton conducting ionomers

Proton conducting ionomers are materials of choice for fuel cells and water electrolysis. The properties can be improved by innovative thermal treatments for annealing and cross-linking (XL-SPEEK) the macromolecules.

2. Cation conducting ionomers

Various cations can be introduced by ion exchange or chemical reaction (e.g. with butyl-Li). The ionomers can be used as separators for rechargeable batteries (in anhydrous state) or for aqueous metal batteries.

3. Hydroxide conducting ionomers

The most common ionomers contain quaternary ammonium groups. The basic operating conditions allow using non-noble electrocatalysts for the oxygen reduction reaction and thus an important cost reduction for alkaline fuel cells and water electrolysers.

4. Anion conducting ionomers

They can be prepared by ion exchange from hydroxide conducting ionomers or by innovative synthesis by reaction of acids with basic groups (e.g. sulfonamides). Such ionomers are especially useful for redox flow batteries, where the cation permeability must be minimized.

5. Amphoteric ionomers

Acidic and basic groups coexist in a single macromolecule: the type and value of the ionic conductivity depends on the pH of its environment. This versatility and the low ionic permeability are very useful for technologies requiring low ion permeability.

Ionomer separators for electrochemical energy technologies are produced from the microscale (microbatteries based on TiO_2 nanotubes) to the macroscale (redox flow batteries). The characterization techniques include spectroscopies (FTIR, UV and NMR), thermogravimetry, mechanical tests, permeability measurements, impedance spectroscopy and electrochemical measurements, such as cyclovoltammetry and galvanostatic polarization.

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Electrodeposition of ionomer membranes for energy storage and conversion

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Electrochemical synthesis is a powerful tool for the preparation of conformal, thin solid electrolytes directly on the electrodes, particularly with complex shapes, such as nanotubes or nanowires.

Such separators should present the highest possible single ion conductivity, negligible electronic conductivity combined with high chemical and mechanical stability.

These requirements drive our development work: we use aromatic polymers as base, given their excellent mechanical properties, which are decisive for a high durability of the separators; furthermore they can impede lithium dendrite growth when cycling rechargeable lithium batteries. Single-ion conductivity is assured by grafting the counter-ions on the polymer chain.

For cation-conducting membranes, we synthesized ionomers with grafted sulfonate groups. These ionomers (including poly(styrene sulfonate), PSS) can be used for proton exchange membrane fuel cells and Li batteries [1-3].

Anion-conducting membranes contained quaternary ammonium as fixed cationic groups. These ionomers can be applied for example in hydroxide exchange membrane fuel cells [4].

We present the electrochemical synthesis procedures and the structural, microstructural and electrical properties of the ionomers, including relevant data for applications, such as Li battery cycling.

[1] M. Braglia, I. V. Ferrari, F. Vacandio, P. Knauth, M. L. Di Vona, Chemistryselect 2016, 1, 3114-3119.
[2] I. V. Ferrari, M. Braglia, T. Djenizian, P. Knauth, M. L. Di Vona, Journal of Power Sources 2017, 353, 95-103.
[3] M. Braglia, I. V. Ferrari, T. Djenizian, S. Kaciulis, P. Soltani, M. L. Di Vona, P. Knauth, ACS Applied Materials & Interfaces 2017, 9, 22902-22910.
[4] M. Braglia, I. V. Ferrari, L. Pasquini, T. Djenizian, M. Sette, M. L. Di Vona, P. Knauth, Electrochim. Acta 2018, in press.

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siRNA-based personalized nanomedicine for cancer treatment

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The promise that siRNA can efficiently and specifically down-regulate any gene with known sequence offers great potential for personalized medicine in treating various diseases, provided there is safe and easy-to-handle siRNA delivery system.[1] We have recently established self-assembling supramolecular dendrimers as excellent nanocarriers for siRNA delivery. [2-5] Here, we present that using our dendrimer nanovector to validate siRNA target and siRNA therapeutics to elaborate effective personalized cancer treatment using patient derived pancreatic cancer models in our proof-of-concept study. This study will open new perspectives in establishing siRNA therapeutics for personalized precision medicine in cancer therapy.

[1] Dowdy, *Nat. Biotechnol*. 2017, *35*, 222

[2] Cao et al, *Front Chem. Sci. Eng.* 2017, 11(4), 663-675.

[3] Yu et al, *Angew. Chem. Int. Ed.* 2012, *51*, 8478; Chen et al, *Small* 2016, *12*, 3667; Liu et al, *Nanoscale* 2015, 7, 3867-3875.

[4] Liu et al, *Angew. Chem. Int. Ed.* 2014, *53*, 11822; Wei et al, *Proc. Natl. Acad. Sci. U.S.A.* 2015, *112*, 2978.

[5] Liu et al, *Adv. Funct. Mater.* 2016, *26*, 8594.

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N,N'-disubstituted diamino-benzoquinone-diimines : coordination properties and quinone-zwitterion equilibrium

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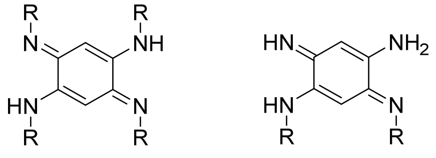
Benzoquinonediimines (BQDI) of type **1** have been extensively investigated because of their remarkable fundamental and applied aspects especially in coordination chemistry as ligands for the preparation of mono or polynuclear complexes.[1] BQDI are particularly interesting because of the unusual distribution of their overall 12-π electrons system which can be described as two nearly-independent 6-π electrons subunits chemically connected through two C-C single bonds.[2]

Until recently, *N*,*N*'-disubstituted analogues of type **2** were unknown whereas the absence of *N*-substituents in the "upper part" of **2** would indeed induce drastically different properties compared to **1**.



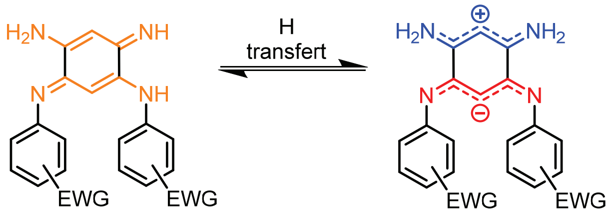
R= H, Alkyl or Aryl

R= Alkyl or Aryl

1 **2**

Figure 1: 2,5-diamino-[1,4]benzoquinone-diimine

Herein, we present the synthesis of these derivatives and some of their properties including their ability to produce extended metal-ligand complexes with absorptions that reach the near infrared domain.[3] The equilibrium between canonical (**3**) and zwitterionic form (**4**) of BQDI substituted by two electron-withdrawing aryls groups will also be presented together with their solvato- and vapochromic properties.[4]



3 **4**

Figure 1: canonical/zwitterionic equilibrium of N,N'-disubstituted BQDI

[1] a) J. Rall et al., *Angew. Chem. Int. Ed.* 37, 2681 (**1998**) b) S. Frantz et al., *Chem. Eur. J.* 10, 149 (**2004**) c) I.-R. Jeon et al., *J. Am. Chem. Soc.* 135, 16845 (**2013**) d) N. Deibel et al., *Organometallics* 33, 4756 (**2014**) e) K. Ohno et al., *Dalton Trans.* 44, 368 (**2015**) f) H. Audi et al., *Chem. Commun.* 50, 15140 (**2014**).
[2] a) S. Dähne et al., *Angew. Chem. Int. Ed.,* 5, 984 (**1966**) b) O. Siri et al., *J. Am. Chem. Soc.* 125, 13793 (**2003**).
[3] L. Lavaud et al., *Dalton Trans*., 38, 12794 (**2017**).
[4] S. Pascal, L. Lavaud, et al. *Submitted for publication.*

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The pathogenicity of silica: crystallinity and surface disorder. Revisiting the paradigm with synthetic quartz crystals.

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An impressive body of scientific reviews and experimental works,[1-2] has evidenced two key aspects in the interaction between crystalline silica and cells: i) the crucial role played by the particle surface in triggering the adverse biological response, and ii) the extreme variability in the pathogenic potential among different sources of particulate silica.[3] Such a variability is the consequence of differences in silica bulk and surface chemistry, including the nature, abundance, and spatial disposition of silanol (–Si-OH) families. Silanols, acidic moieties with a potential for H-bonding, have a key role in defining silica interaction with cells: silica surface is characterized by different families of –Si-OH groups, including isolated (the most common), geminal, and vicinal silanols. The long-range order and distribution of silanol patches on silica surface impart specific characteristics to different silica specimen. Quartz dusts used so far in particle toxicology assays have been obtained by grinding rock containing natural quartz, a process that affects crystallinity and yields samples with extreme variable and complex surface states. To overcome such a variability, we have developed an innovative method to grow highly-pure quartz crystals in respirable size (< 4 μm) with controlled surfaces, in order to investigate, at the molecular level, the mechanisms related to quartz toxicity. Surprisingly, the as-grown synthetic quartz crystals with regular faces, characterized by silanol patches with a long-range order, did not show any perturbative activity towards membrane models at increasing complexity (liposome and red blood cells), developed to investigate the molecular determinants in the interaction. On the contrary, after inducing the loss of the long-range order of silanol patches by ball milling, synthetic quartz elicited strong reactivity toward same models. Crystal milling also led to the formation of surface radical species,[4] which are held to be involved in the alteration of the ROS metabolism of cells. Overall, data are consistent with the hypothesis that most of the biological reactivity of quartz dusts is not due to crystallinity *per se,* but it is originated via fragmentation *(fig. 1)*, which entails the formation of conchoidal fractures and new faces, characterized by the strong disorganization of surface functionalities.

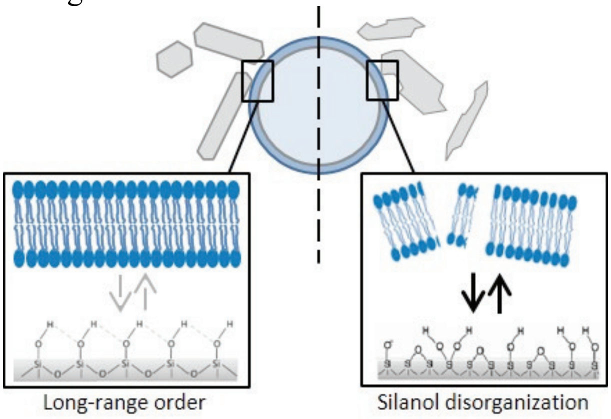

Fig. 1: Mechanical milling imparts strong membrano-perturbative potential to synthetic quartz crystals, due to disorganization of surface functionalities.

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References

1. K. Donaldson, A. Seaton, *Part Fibre Toxicol.*, 2012, 9:13
2. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Silica, some silicates, coal dust and para-aramid fibrils. Lyon, 15-22 October 1996. *Monogr. Eval. Carcinog. Risks Hum.* 68:1 – 475; 1997.
3. B. Fubini, W. E. Wallace, In: Papirer. E, ed. Adsorption on silica surfaces. New York: Marcel Dekker, 1999:645-664
4. A. Rimola, D. Costa, M. Sodupe, J. Lambert, P. Ugliengo, *Chem. Rev.*, 2013, 113(6): 4216-313

IX Giornate Italo-Francesi di Chimica
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Structural and NMR relaxometric studies on Gd^{III} complexes of hydroxy-, methoxyacetophenone functionalised DO3A chelators

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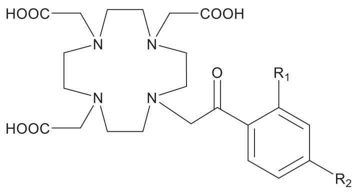
Magnetic Resonance Imaging (MRI) contrast agents (CAs) are paramagnetic metal complexes able to reduce the relaxation times (T_1 or T_2) of protons in their vicinity. Their efficiency depends on several structural features of the complex, typically Gd^{III} or Mn^{II}, affecting the mode of interaction and magnetic coupling between the paramagnetic ion and the surrounding water molecules. For example, the exchange rate (k_{ex}) of the water molecule coordinated to the metal center is a parameter of paramount importance. It can be modulated by modifying the structural and electronic features of the complex and it can be determined by variable-temperature ^{17}O-NMR studies.[1] In this work, we were interested in exploring the coordination mode of a novel family of chelators consisting of DO3A (1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid), bearing one acetophenone-based pendant arm. Thus, we have synthesized (Figure) and characterized five DO3A-like ligands with a fourth pendant arm consisting of a phenacyl group (**DO3A-AP**), 2'-hydroxyphenacyl and 4'-hydroxyphenacyl groups (**DO3A-*o*-HyAP** and **DO3A-*p*-HyAP**) and their methoxyphenacyl analogues (**DO3A-*o*-MeOAP** and **DO3A-*p*-MeOAP**). The presence of the phenol group in GdDO3A-HyAP complexes leads to deprotonation already at neutral pH due to the presence of the enolate anion coordinating the metal center. The synthesis of ligands and complexes, a detailed ^1H and ^{17}O NMR relaxometric characterization of the Gd^{III} complexes and an UV-Vis spectrophotometric analysis at variable pH have been carried out. The relaxivity values obtained for such complexes are unexpectedly high with respect to Gd-complexes with similar molecular weight. Finally, the X-ray crystal structure of the protonated form of GdDO3A-*o*-HyAP, coupled to molecular modeling allowed to shed light on the structural changes occurring as response to pH changes.



R_1= H, R_2= H;	**DO3A-AP**
R_1= OH, R_2= H;	**DO3A-*o*-HyAP**
R_1= H , R_2= OH;	**DO3A-*p*-HyAP**
R_1= OMe, R_2= H;	**DO3A-*o*-MeOAP**
R_1= H, R_2= OMe;	**DO3A-*p*-MeOAP**

Figure: Structures of the ligands involved in this work

Reference:

[1] The Chemistry of Contrast Agents in Medical Magnetic Resonance Imaging, Eds. A. Merbach, L. Helm and E. Toth, Wiley, Chichester, 2nd ed., 2013.

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ALKOXYAMINE PEPTIDE LIGATION (APL): A STRAIGHTFORWARD METHOD FOR NON NATIVE PEPTIDE CONJUGATION USING INTERMOLECULAR RADICAL 1,2-ADDITION

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Many chemoselective ligation methods have emerged over the two past decades for coupling of peptide fragments or for peptide modification with biomolecules of interest. These methods include native chemical ligation, imine or oxime ligation, Staudinger ligation, triazole formation through alkyne-azide addition, decarboxylative condensations of N-alkylhydroxylamines and α-ketoacids or, more recently, bis(2-sulfanylethyl)amino native peptide ligation. However, to our knowledge, free radical chemistry based reactions have not been exploited yet as a peptide conjugation/ligation strategy. In this study we describe a novel conjugation method, namely Alkoxyamine Peptide Ligation (APL), based on intermolecular radical 1,2-addition (IRA) of SG1 nitroxide based alkoxyamines onto double bonds [1]. This strategy implies simple peptide pre-derivatization to obtain (i) a SG1 nitroxide functionalized resin peptide at its N–terminus (SG1-peptide alkoxyamine), (ii) a vinyl functionalized peptide (either at its C-terminus or N-terminus), and does not require any coupling agents. This is the first example of chemoselective peptide conjugation based on a radical reaction.

(Alkoxyamine, Peptide, Ligation, Radical, addition)

[1] Trimaille, T., Autissier L., Rakotonirina MD, Guillaneuf Y., Villard C., Bertin D., Gigmes D., Mabrouk K. Chem. Commun, 50, 2744 (2014)

Surface Enhanced Raman Scattering substrates for food contaminants detection

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The present study concerns in the food safety field of study. It concerns the development of new strategies to improve the sensitivity of Raman spectroscopy, exploiting the surface enhancement effect provoked by metal nanostructured materials, thanks to their plasmonic activity [1]. The surface enhanced Raman scattering (SERS) has been demonstrated to be a promising technique because of its high sensitivity. However, many efforts to optimize SERS systems and to provide a good compromise between signal intensity and repeatability, reproducibility and stability are still needed [2]. The idea is to set up stable and easy-to-use strategies for the analysis of chemicals deposited on contaminated surfaces, and to fix the critical points, such as low repeatability and high uncertainty budget, that usually affect innovative analytical methods. Although the Raman intensity to concentration dependence is well known, the same thing is not obvious when enhancement factors are concerned. A metrological calibration strategy for surface contamination analysis using SERS is proposed. An application of SERS for pyrimethanil fungicide detection on apples is discussed, with the objective to confirm the potential for broad application, by standardized quantitative SERS methods [3]. Moreover, the development of a flexible and versatile SERS substrate for the detection of surface contaminants is presented [4].

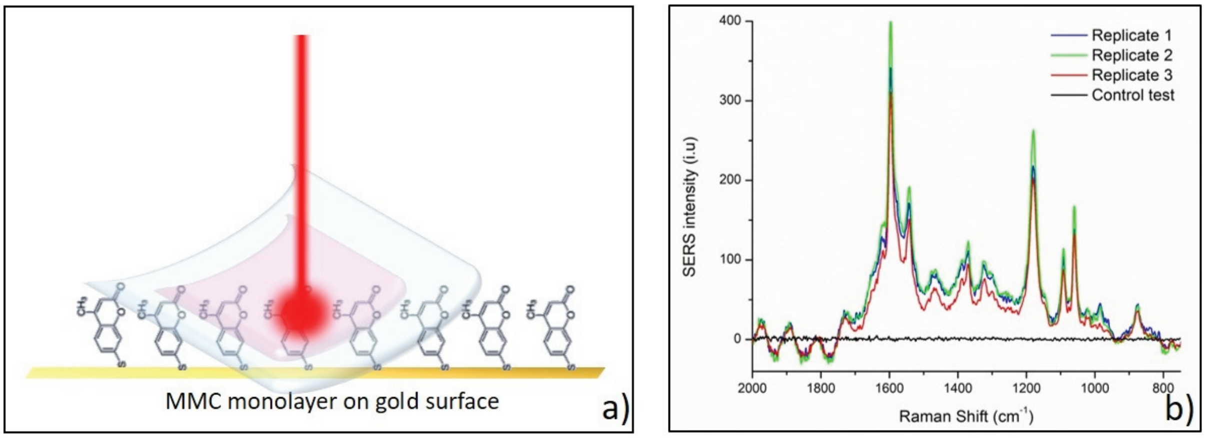

Figure 1: a) graphical representation of PDMS SERS support for surface contamination analysis in its use configuration, b) mean spectra of three analogue measurements and control test spectrum (black) collected on the contaminated model surface before SERS tape application.

[1] Willets, K. A., Van Duyne, R. P. (2007), Localized surface plasmon resonance spectroscopy and sensing, Annual Review of Physical Chemistry, 58, 267-297.
[2] Zheng, J., He, L. (2014). Surface□Enhanced Raman Spectroscopy for the Chemical Analysis of Food. Comprehensive reviews in food science and food safety, 13(3), 317-328.
[3] Mandrile, L., Giovannozzi, A. M., Durbiano, F., Martra, G., Rossi, A. M. (2018). Rapid and sensitive detection of Pyrimethanil residues on pome fruits by surface enhanced Raman scattering. Food Chemistry, 244, 16-24. Reference (Times New Roman 10).
[4] Singh, J. P., Chu, H., Abell, J., Tripp, R. A., Zhao, Y. (2012). Flexible and mechanical strain resistant large area SERS active substrates. Nanoscale, 4(11), 3410-3414.

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IX Giornate Italo-Francesi di Chimica
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Extraction of Lanthanides from Aqueous Solutions with Saponite Clays

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Due to their unique electronic, magnetic, optical and catalytic properties, the rare-earth elements (REEs) have been extensively used in the last decades in renewable energy and for state-of-the-art energy-efficient technologies (*i.e.* batteries, solar panels and high-performance magnets).[1] Thus, the recycling of REEs is of great importance to advance the efficient use of these precious technological resources. In addition, there is also an environmental problem related to the release of lanthanide ions associated to nuclear accidents, resulting from the fission of uranium and plutonium isotopes, and from other sources.

Actually, the traditional processes employed for the REEs recovery are based on solvent extraction, which need repetitive steps and involve great amounts of harmful and expensive extractants. The development of new *green* environmental remediation/recovery methods with higher efficiency and lower cost is an important challenge for the scientific community. In this respect, several solid sorbents based on carbon, porous silica and layered materials have been selected for their high chemical affinity for *f*-block species.

In light of these considerations, in this work we explored two synthetic saponite clays (SAP) as solids sorbents for the extraction of lanthanides with different ionic radius (La^{3+}, Gd^{3+} and Lu^{3+}) from aqueous solutions. The synthetic saponites prepared were characterized by different particle size and cation exchange capacity (CEC). The uptake of Gd^{3+} was performed in pure water and simulated seawater solutions, in wide concentration ranges of [Gd^{3+}] (10-0.1 mM). Both the solids showed good sorption capacity, with an effective extraction of Gd^{3+} around 70% after 5 hours. A relationship between the uptake capability of Gd^{3+} and the CEC of the clays was observed. The uptake of Gd^{3+} is comparable to that of other layered and microporous materials reported in literature (*Figure 1*). The same behaviour was found for the extraction of La^{3+} and Lu^{3+} ions. The solids were also tested in the presence of an equimolar mixture of La^{3+}, Gd^{3+} and Lu^{3+} ions: in this case, a strong selectivity for Lu^{3+} was observed respect to the other lanthanides.

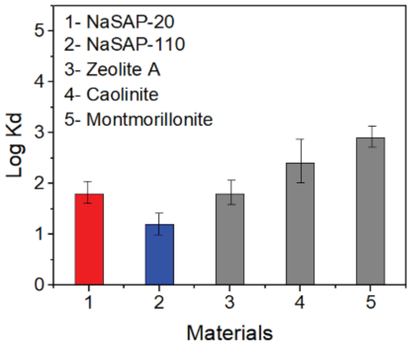

Figure 1 : Gd^{3+}-uptake sorption performance of the two synthetic saponites in comparison to other layered and porous materials.

[1] C R. Ronda *et al.*, *J. Alloys Compd.*, 1998, **275-277**, 669-676.

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MCK-140, is a new antagonist for CXCR1-2, exerting both anti-inflammatory and anti-angiogenic effect in in-vitro and in-vivo.

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2. *Institute for Research on Cancer and Aging of Nice, IRCAN UMR CNRS 728 INSERM U1081, Université Côte d'Azur, Nice, France*
3. *Département de Chimie, Faculté de Pharmacie & UFR Biomédicale des Saint-Pères, Université Paris-Descartes*

The current anti-angiogenic therapies fail to fully eradicate cancer cells, since the tumors always relapse after an initial period of clinical benefit. Therefore, new therapeutic approaches are urgently needed to overcome drug resistances. In this context, our project aims at developing a new strategy to concomitantly tackle inflammation and angiogenesis by interfering with the ERL+CXCL cytokines signaling pathway. Therefore, we hypothesized that small-sized organic CXCR1/CXCR2 antagonists might exert a dual activity on both angiogenesis and inflammation. [1,2]

We report herein the rational design and the synthesis of a series of new CXCR antagonists, structurally-related to SB-225002, a CXCR antagonist developed by GSK.[3,4] Among these new compounds, two potential hits emerged, MCK133 and MCK140.

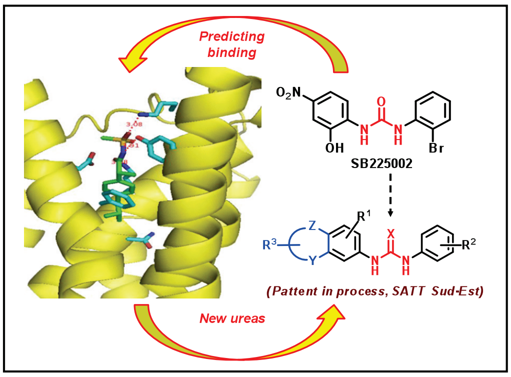

Figure 1 : New envisaged drug design according to a predicting binding.

[1] F. Chang, L.S. Steelman, J. T. Lee, J. G. Shelton, P. M. Navolanic, *Leukemia* **2003**, *17*, 1263-1293.
[2] A. Sparmann, D. Bar-Sagi, *Cancer Cell* **2004**, *6*, 447-458.
[3] L. M. Campbell, P. J. Maxwell, D. J. J. Waugh, *Pharmaceuticals*, **2013**, *6*, 926-959.
[4] M. Alleretti, M. C. Cesta, A. Garin, A. E. I. Proudfoot, *Immunol. Lett.* **2012**, 145, 68-78.

Toward traceable measurements of photocatalytic activity

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The possible market for photocatalytic materials, in the form of powders, built-in powders, thin films and nano-structured materials, as well as devices directed to specific applications, is estimated in exponential growth. However, the central problem is the standardization of the procedures for photocatalytic efficiency evaluation of an illuminated catalyst. For gas/solid experiments different reactors, like batch or flow-through either continuous stirred-tank reactor (CSTR) or plug flow reactor (PFR), were proposed [1,2], in order to measure the rate of conversion of a standard substrate under controlled conditions. Experiments show that a CSTR configuration presents a lot of advantages for practical use, as any volume, any shape of catalyst and any flow of gas into the reactor can possibly be used [3]. In the framework of the SETNanoMetro EU project we developed and patented a portable CSTR photoreactor with controlled illumination and purposely designed fluidodynamics in order to obtain a photocatalytic rate evaluation independent on the measurement conditions, characteristic only of the catalyst [4]. The reactor allows fast (minutes) and on site measurements with a choice of different substrates. This is a step in the direction to obtain a traceable measurement of photocatalytic activity and properly compare different catalysts.

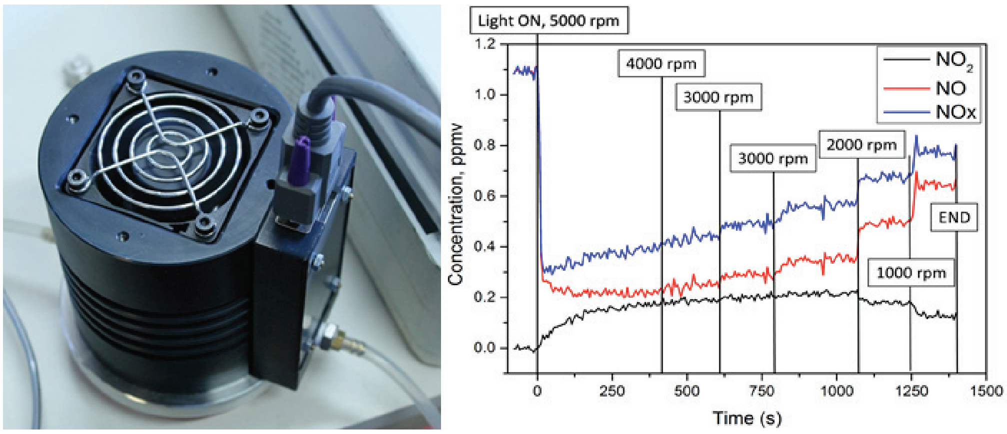

Figure 1 : Portable photoreactor developed for photocatalytic activity evaluation and example of a test using NO as substrate

[1] UNI NORM 11484/2013
[2] ISO NORM 22197/2017
[3] C. Minero, A. Bedini, and M. Minella, International Journal of Chemical Reactor Engineering 2013; 11(2): 717–732
[4] Maurino V., Minero C., Pellegrino F., Zangirolami M. – European Patent: “System for Lighting and measuring the Photo-Catalytic Activity of the Reactive Surface of a Material” - Application Number: 17000861.9-1554” - 19/05/2017

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In situ growth of graphene-like layers on TiO_2 from molecular precursors

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The efficient conversion of solar energy into electrical power by photovoltaic devices or into fuels by artificial photosynthesis is among the most challenging goals of modern science. The strategies aimed at these purposes include the use of photoactive systems based on oxide semiconductors, which are particularly attractive owing to their photo-stability, affordable cost and low toxicity. However, a further improvement of their efficiency in solar energy conversion is needed to promote large-scale applications: this has been attempted by doping with metal and non-metal impurities or by coupling different oxide semiconductors. In this context, metal oxide/graphene composites have recently attracted increasing attention due to their high electron conductivity, large specific surface area and good adsorption properties [1]. Various methods have been developed for the synthesis of graphene, including micro-mechanical exfoliation, epitaxial growth and reduction of graphite oxide. In this contribution we explore the possibility to directly grow graphene-like structures on TiO_2 surfaces using a bottom-up strategy. We consider two different molecular precursors: acetylene and furfuryl alcohol. Acetylene can oligomerize already at room temperature to produce polycyclic condensed hydrocarbons in close contact with the TiO_2 surface (see Figure 1), while furfuryl alcohol shows a limited reactivity in the same conditions. However, both molecules, upon mild heating, are able to produce extended carbonaceous structures tightly anchored to the TiO_2 surface. These products can represent intermediate steps toward the *in situ* synthesis of graphene layers on TiO_2 in very mild conditions, allowing to avoid the anatase to rutile transformation. The reactions have been monitored by IR and UV-vis spectroscopies and via continuous wave Electron Paramagnetic Resonance (CW-EPR) [2, 3].

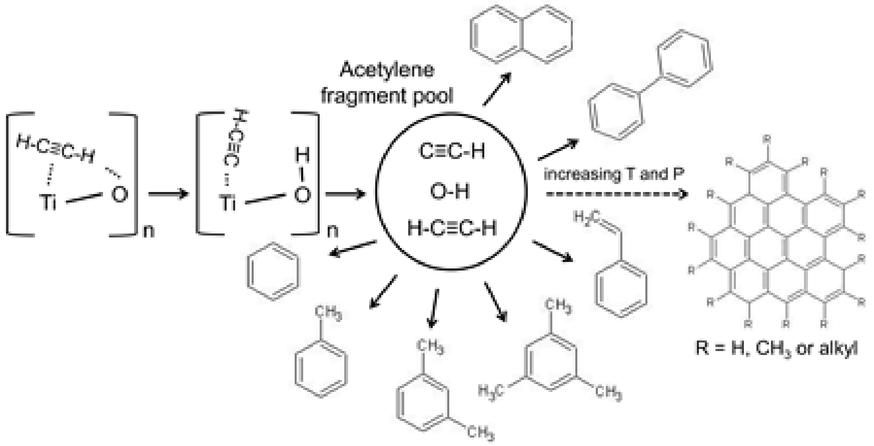

Figure 1: Schematic representation of the reaction of acetylene on TiO_2 showing the first steps of the reaction (adsorption and dissociation of C_2H_2 on the oxide surface) and the main reaction products.

[1] Q.J. Xiang, J.G. Yu, M. Jaroniec, *Chem. Soc. Rev.* 41 (2012) 782.
[2] S.M. Jain, J.J. Biedrzycki, V. Maurino, A. Zecchina, L. Mino, G. Spoto, *J. Mater. Chem. A* 2 (2014) 12247.
[3] J.J. Biedrzycki, S. Livraghi, I. Corazzari, L. Mino, G. Spoto, E. Giamello, *Langmuir* 31 (2015) 569.

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UV-Vis Light Induced Aging of Titan's Haze and Ice

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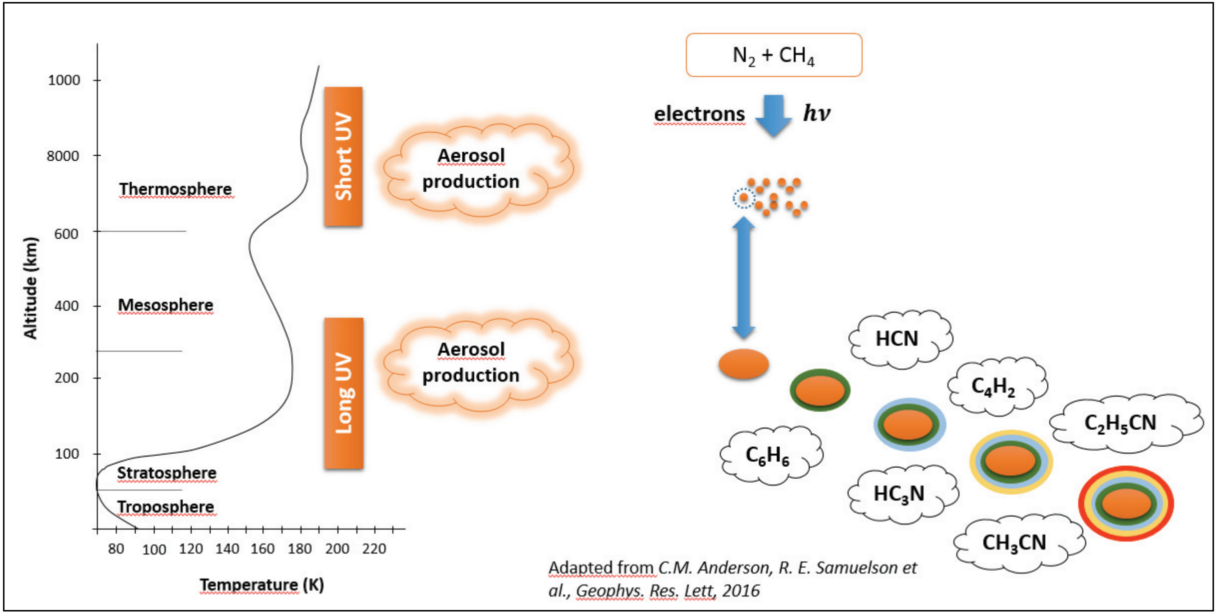
Titan's aerosols are the final product of complex carbon-nitrile photochemistry occurring from the upper atmosphere (>1000 km) (Horst, 2017). UV photons, photoelectrons, energetic ions and magnetospheric electrons induce the dissociation and the ionization of N_2 and methane leading to the formation of complex organic molecules including nitriles and hydrocarbons.

Atmospheric gaseous species produced in the upper atmosphere sediment until the surface. Depending to the stratosphere temperature, complex organic molecules like C_6H_6 and HCN can condense, forming microscopic ice particles or aerosols (Horst, 2017). Once they are formed, these particles are submitted to long UV radiation (λ>230 nm) during the sedimentation process. We present here, the results obtained during the photochemistry of HCN and C_6H_6 ices isolated or co-condensed in the conditions of the Titan low atmosphere.



Adapted from C.M. Anderson, R. E. Samuelson et al., Geophys. Res. Lett, 2016

Figure 1 : Sedimentation aerosol's process occurring in the Titan atmosphere

[1] Horst, S. M. 2017, J. Geophys. Res. Planets, 122, 432

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Pyrazolo[3,4-*d*]pyrimidines as tyrosine kinase inhibitors: synthesis and biological evaluation

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Tyrosine kinases (TKs) are a large class of enzymes which play a key role in many phases of cell life, such as differentiation, adhesion and survival. These proteins are overexpressed and/or hyperactivated in a variety of tumor cells and their inhibition has been widely recognized as a successfully strategy in cancer therapy. So far, more then twenty TK inhibitors have been approved for clinical use. Most of them are small molecule ATP competitive inhibitors endowed with a heterocyclic scaffold [1]. In particular, the pyrazolo[3,4-*d*]pyrimidine nucleus, an isostere of adenine, has gained importance in the search for TK inhibitors, as confirmed by the recent approval of Btk TK inhibitor ibrutinib for the treatment of mantle cell lymphoma [2].

In this context, our research group synthesized a wide library of 4-amino-substituted pyrazolo[3,4-*d*]pyrimidines active as ATP-competitive inhibitors of Bcr-Abl and/or Src, two cytoplasmic TKs involved in solid and haematological cancers. These kinases show high structural homology, but the introduction of a different substitution pattern on the scaffold allowed us to obtain either selective inhibitors or dual inhibitors. Both selective and dual (or multitargeted) inhibitors are important in drug discovery, since the former can reduce the risk of side effects, and the latter can be more effective in multifactorial pathologies such as cancer. Interestingly, several in-house compounds resulted active in *in vivo* tumor models [3,4].

Starting from this solid background, we decided to synthesize a new generation of derivatives in order to discover potent selective or multikinase inhibitors. To achieve this goal, we differently decorated the N1 and C6 positions of the pyrazolo[3,4-*d*]pyrimidine scaffold, and introduced an anilino derivative in C4, since the presence of this substituent was often related to a good activity profile in previous generation compounds. The molecules are currently being tested on a panel of kinases, i.e. Bcr-Abl, Src and Fyn (another cytoplasmic TK belonging to the same family of Src). Interestingly, we have already identified a selective Fyn inhibitor, which possesses an ID_{50} value of 384 nM in an enzymatic assay. Synthesis and available biological data will be reported in the poster section.

[1] Wu P. et al. *Drug Discov. Today* **2016**, *21*, 5-10.
[2] Schenone S. et al. *Chem. Rev.* **2014**, *114*, 7189-7238.
[3] Radi M. et al. *J. Med. Chem.* **2013**, *56*, 5382-5394.
[4] Vignaroli G. et al. *J. Med. Chem.* **2017**, *60*, 6305-6320.

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Gold(I)-catalysed transformations of heterocyclic 1,3-enynes

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Gold complexes are well-known efficient and selective catalysts for the activation of C-C triple bonds towards the attack of nucleophilic species. The good tolerance of various functional groups and the generally mild conditions required make gold catalysis a useful tool for the synthesis of complex molecules.[1] In recent years, we investigated the gold-catalysed functionalisation of lactam-derived heterocyclic 1,3-enynes, by using the oxygen atom of the *N*-protecting group as an internal nucleophile.[2] In addition, we extended the potential of the methodology by using a pyridine *N*-oxide as source of external oxidant. In this case, the gold activation goes through an α-oxo gold carbene intermediate (Figure 1, a) which leads to a variety of lactam derived vinyl ketones.[3] We then stepped further and envisaged the possibility of reacting the gold-activated triple bond of the lactam derived substrate with an internal nucleophilic C. To this purpose, we synthesized a lactam-derived enyne in which an aryl group is tethered to the position of the heterocycle adjacent to the alkyne moiety (Figure 1, b). With aryl groups as internal nucleophiles, a *6-exo-dig* hydroarylation of the triple bond, followed by aromatization, leads to polycyclic products, such as tetrahydrobenzo[g]quinolines.

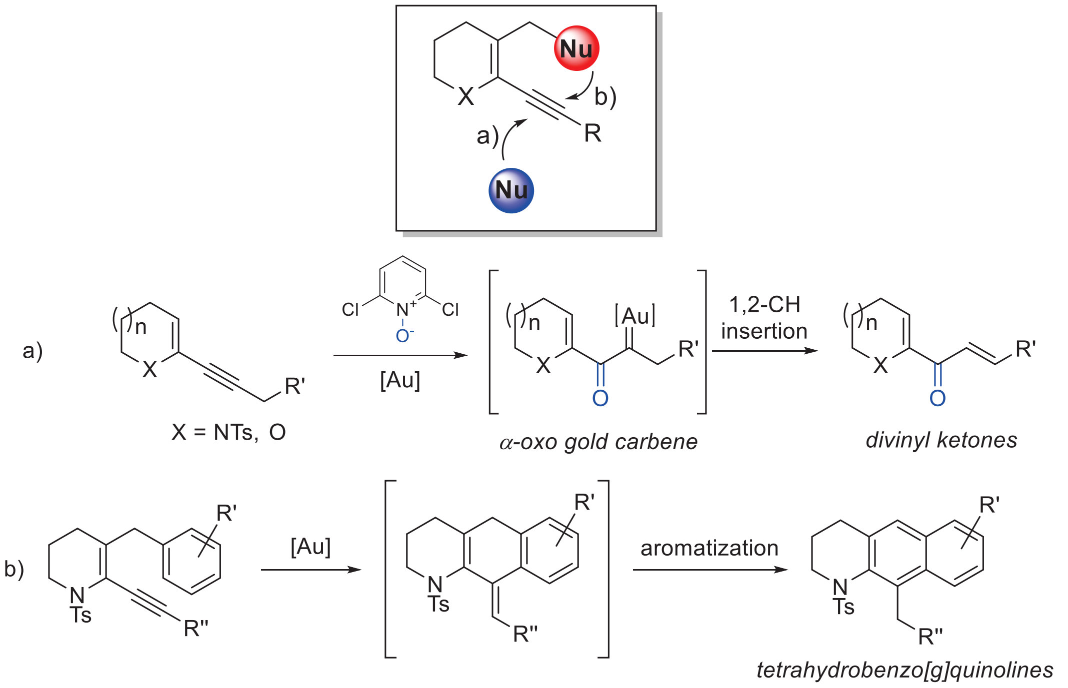

Figure 1 : Gold-catalysed transformations of heterocyclic 1,3-enynes with external and internal nucleophiles.

[1] a) D. Pflästerer, A. S. K. Hashmi, *Chem. Soc. Rev.* **2016**, *45*, 1331-1367; b) R. Dorel, A. M. Echavarren, *Chem. Rev.* **2015**, *115*, 9028-9072; c) Q. Wang, M. Shi, *Synlett* **2017**, *28*, 2230-2240

[2] a) A. Oppedisano, C. Prandi, P. Venturello, A. Deagostino, G. Goti, D. Scarpi, E. G. Occhiato, *J. Org. Chem.* **2013**, *78*, 11007-11016; b) D. Scarpi, S. Begliomini, C. Prandi, A. Oppedisano, A. Deagostino, E. Gómez-Bengoa, B. Fiser, E. G. Occhiato, *Eur. J. Org. Chem.* **2015**, 3251-3265

[3] S. Nejrotti, G. Prina Cerai, A. Oppedisano, A. Maranzana, E. G. Occhiato, D. Scarpi, A. Deagostino, C. Prandi, *Eur. J. Org. Chem.* **2017**, 6228-6238

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IX Giornate Italo-Francesi di Chimica
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Genova
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Role of Natural Organic Matter in Silicon speciation in soils

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In the ANR project BIOSISOL, we are interested in the status of silicon (Si) in soils and in particular in the bioavailability of Si in soils for plants. The land use and particularly agriculture can modify the Si cycle through a depletion of soil available Si. Silicon fertilization by natural silicates has the potential to mitigate environmental stresses and soil nutrient depletion and as a consequence is an alternative to the extensive use of phytosanitary and NPK fertilizers for maintaining sustainable agriculture (Guntzer et al, 2012). Indeed, recent studies have shown the benefits of Si in the field of agriculture, resulting for example on better plant growth, or better resistance to biotic or abiotic stresses (Epstein, 1994). However, the beneficial effect of Si in agriculture has never been shown in Europe whereas in countries like China, Japan, India and other countries in South America, Si is already integrated in their agriculture to overcome the depletion of bioavailable Si (Ma, 2004). As long as Si interactions with soil components will not be fully understood, it will not be authorized as fertilizer in Europe.

In this broad context of study, we attempt to identify the potential interactions between natural organic matter of soil (NOM) and Si. In fact, although Si is commonly accepted as not interacting with the NOM, some interferences in isotopy analysis seem to show the opposite (Pokrovski and Schott, 1998). We have attempted to use molecular fluorescence spectroscopy to identify potential complex NOM-Si in aqueous solution. The first results have shown that there would be no direct coordinated bonds between NOM and Si, but perhaps a bridging connection through Al ions. The complexing capacities (C_L) and 1:1 stability constants (K) of fluorescing ligands with Al and Si were determined with the method of Ryan and Weber (Ryan and Weber, 1982). Moreover, potentiometry was developed to determine the acid-base properties of the NOM and those of the NOM-Si complexes, in the same chemical conditions as previously. Modelling will be able to provide the speciation of Si in the binary NOM-Si and ternary NOM-Si-Al systems. We also carried out the monitoring of the size distribution of the complexes coupled with fluorescent Si-specific probe in different systems by NTA spectroscopy (Nano Tracking Analysis) to distinguish free Si from complexed Si. Moreover, in order to study the solid phase, we used Raman and FTIR spectroscopy for identifying the potential NOM-Si-Al complexes in the solid samples.

[1] Guntzer, F., Keller, C., & Meunier, J. D. (2012). Benefits of plant silicon for crops: a review. Agronomy for Sustainable Development, 32(1), 201-213.
[2] Epstein, E. (1994). The anomaly of silicon in plant biology. Proceedings of the National Academy of Sciences, 91(1), 11-17.
[3] Ma, J. F. (2004). Role of silicon in enhancing the resistance of plants to biotic and abiotic stresses. Soil Science and Plant Nutrition, 50(1), 11-18
[4] Pokrovski, G. S., & Schott, J. (1998). Experimental study of the complexation of silicon and germanium with aqueous organic species: implications for germanium and silicon transport and Ge/Si ratio in natural waters. Geochimica et Cosmochimica Acta, 62(21-22), 3413-3428.
[5] Ryan, D. K., & Weber, J. H. (1982). Fluorescence quenching titration for determination of complexing capacities and stability constants of fulvic acid. Analytical Chemistry, 54(6), 986-990.

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IX Giornate Italo-Francesi di Chimica
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Efficient selenocyanation of imidazoheterocycles and chromen-4-ones

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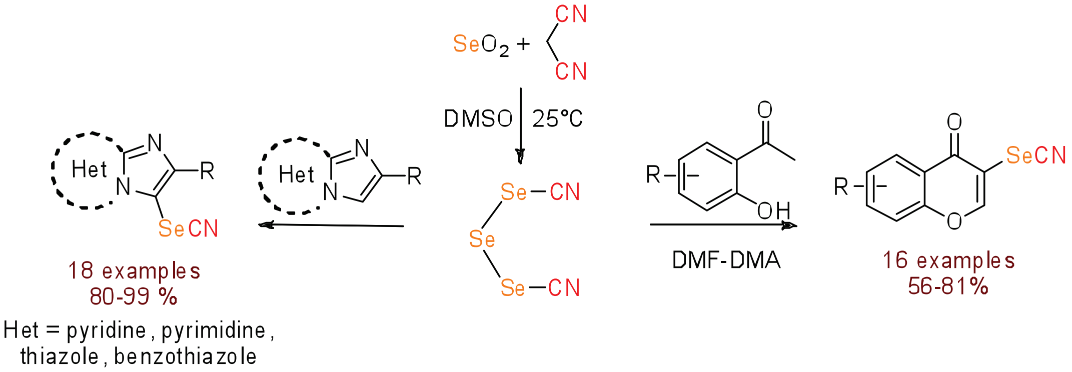
Selenocyanate substituted heterocycles have shown interesting activities as antileishmanial agents.[1] In continuation of our research program centered on the medicinal chemistry of electron-rich heterocycles, we investigated the reactivity of triselenodicyanide for the selenocyanation of various imidazoheterocycles and chromones. Selenocyanate function can be introduced using KSeCN, as electrophilic source with *N*-iodosuccinimide,[2a] or as radical source with an oxydant.[2b] These methodologies present several disadvantages: using very smelly and air sensitive KSeCN, blue LED and tedious column chromatography. In order to develop a more attractive industrial process, it is of high importance to offer a straightforward, odorless, inexpensive and scalable method. To do so, the triselenodicyanide represents the ideal electrophilic source, especially since its novel generation from malononitrile and odorless selenium dioxide.[3] We present here an efficient methodology for the regioselective C-3 selenocyanation of imidazoheterocycles[4a] and a one pot C-3 selenocyanation of chromen-4-ones derivatives.[4b]



These selenocyanations are characterized by the use of odorless and inexpensive starting materials and an ease of purification by filtration. In this study, we also explored interesting reactivities of the SeCN function toward decyanations.

Preliminary *in vitro* activities against *Leishmania donovani* promastigotes and their cytotoxicities will be presented.

[1] Baquedano, Y.; Alcolea, V.; Toro, M. A.; Gutierrez, K., J.; Nguewa, P.; Font, M.; Moreno, E.; Espuelas, S.; Jimenez-Ruiz, A.; Palop, J. A.; Plano, D.; Sanmartín, C. *Antimicrob. Agents Chemother*. **2016**, *60*, 3802.
[2] a) Muniraj, N.; Dhineshkumar, J.; Prabhu K. R. *ChemistrySelect* **2016**, *5*, 1033. b) Mitra, S.; Ghosh, M., Mishra, S.; Hajra, A. *J. Org. Chem*. **2015**, *80*, 8275.
[3] Kachanov, A. V.; Slabko, O. Y.; Baranova, O. V.; Shilova, E. V.; Kaminskii. V. A. *Tetrahedron Lett*. **2004**, *45*, 4461.
[4] a) Redon, S.; Obah Kosso, A.R; Broggi, J.; Vanelle P. *Tetrahedron Lett*. **2017**, *58*, 2771. b) Obah Kosso, A. R.; Broggi, J.; Redon, S.; Vanelle P. *Synlett* **2018** accepted.

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Molecular design of benzodithiophene and benzothiadiazole conjugated systems for photovoltaic applications

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In the last few decades up to now, organic semiconductors (OS) achieved great relevance as active materials in a broad typology of devices such as: field effects transistors, light-emitting diodes, photodetectors and new generation solar cells [1]. Indeed, the great interest towards organic photovoltaic (OPVs) devices lies in the peculiar electronic properties of the conjugated systems for the basic research and, from the technologic point of view, in the easily tuning of their manufacturing characteristics such as flexibility, cost-effective, capability to be produced in large area systems from low-temperature solution processing techniques [2,3].

In order to increase the power conversion efficiency (PCE) of OPVs it was demonstrated that one of the most suitable architecture of the device implies a nanoscale interfacing between the donor and acceptor active layers [4]; giving the so-called bulk heterojunction (BHJ) solar cells. To achieve efficient PCE values, the donor and acceptor molecules should have: (*i*) a suitable molecular energy level alignment, (*ii*) a high charge mobility to facilitate charge transport, (*iii*) a broad absorption spectrum with a high extinction coefficient at least one of the two active components, in order to maximize the harvesting of the solar energy. Among these requirements. it is was also found that the most efficient chemical structure for OS is constituted by the presence of both donor and acceptor moieties in the same molecule and a large number of works in literature are focused on this kind of compounds. Nevertheless, the wide examples of available donor and acceptor groups indicate that new systems can be potentially designed and synthesized to further improve the performance of OPV devices.

In this framework, the *in-silico* molecular design by the selection, connections and functionalization of the donor/acceptor moieties can easily build molecular library for the selection of potential structures with the above characteristics . Here, the theoretical results obtained from the study of a novel class of molecules in a typical donor-bridge-acceptor architecture are presented. The donor moieties are triphenylamine functionalities, whereas the bridge is constituted by dithiophene or benzodithiophene groups and the acceptor moieties are represented by benzodithiophene substituents. This type of active system was investigated in order to provide a general guideline for the molecular design of potential photovoltaic materials with enhanced performance.

[1] M. C. Beard, J. M. Luther, O. E. Semonin and A. J. Nozik, Acc. Chem. Res., 2013, 46, 1252-1260.
[2] G. Dennler, M.C. Scharber, C.J. Brabec Adv. Mater. 2009, 21, 1323–1338.
[3] J.Y. Kim, K. Lee, N.E. Coates, D. Moses, T.Q. Nguyen, M. Dante, A.J. Heeger Science 2007, 317, 222□225.
[4] N.S. Sariciftci, L. Smilowitz, A.J. Heeger, F. Wudl Science 1992, 258, 1474–1476.

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Cooperative Iodide - Pd(0) Catalyzed Coupling of *N*-Tosylhydrazones and Alkoxyallenes: a Selective Synthesis of Conjugated and Skipped Dienes

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Palladium catalyzed cross couplings involving tosylhydrazones are today a well-established protocol for the synthesis of polysubstituted olefins and dienes with almost universal generality with respect to the coupling partners.[1] Recently, their ability to react with *in situ* formed allyl Pd(II) complexes has been exploited for the construction of 1,3-dienes starting from allyl halides or allenes.[2]

In this context, we envisioned that alkoxyallenes could in turn give access to alkoxydienes,[3] whose synthetic potential has been largely investigated by our group.[4] Surprisingly, we found out that no aryl halide is required for this coupling and that the reactive allyl palladium species can come from an initial allene hydropalladation. Tosylhydrazones deriving from benzophenones and acetophenones smoothly react affording the corresponding dienes in good yields. Moreover, with enolizable tosylhydrazones a different regioselctivity arises in the final β-hydride elimination, which produces skipped 1,4-dienes.

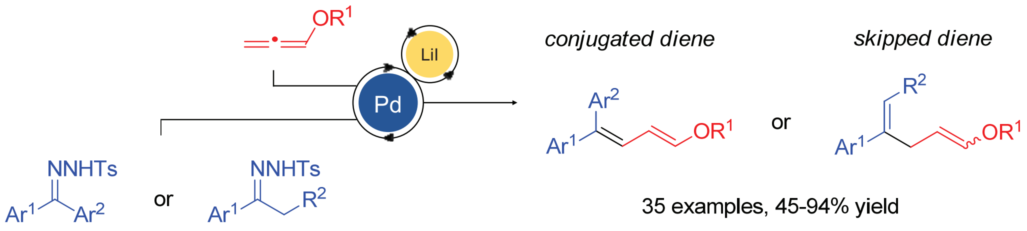

Figure 1 : Pd(0) catalyzed coupling of alkoxyallenes and tosylhydrazones

[1] J. Barluenga, C. Valdés. *Angew. Chem. Int. Ed.* **2011**, *50*, 7486.

[2] a) K. Wang, S. Chen, H. Zhang, S. Xu, F. Ye, Y. Zhang, J. Wang. *Org. Biomol. Chem.* **2016**, *14*, 3809. b) Q. Xiao, B. Wang, L. Tian, Y. Yang, J. Ma, Y. Zhang, S. Chen, J. Wang. *Angew. Chem. Int. Ed.* **2013**, *52*, 9305.

[3] a) T. Boi, A. Deagostino, C. Prandi, S. Tabasso, A. Toppino, P. Venturello. *Org. Biomol. Chem.* **2010**, *8*, 2020. b) A. Deagostino, C. Prandi, A. Toppino, P. Venturello. *Tetrahedron* **2008**, *64*, 10344.

[4] A. Deagostino, C. Prandi, C. Zavattaro, P. Venturello. *Eur. J. Org. Chem.* **2006**, 2463.

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IX Giornate Italo-Francesi di Chimica
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Shape Controlled Anatase Nanoparticles for the optimization of functional properties: synthesis, characterization and applications

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The synthesis of TiO_2 nanoparticles (NPs) with well-defined morphology and size is fundamental for the development of advanced nanomaterials in various application fields. Synthetic routes were developed for bipyramidal TiO_2 facet-controlled anatase NPs with low truncation along the c-axis and acicular morphology, through hydrothermal treatments of aqueous solutions of Ti^{IV}(triethanolamine)$_2$ [1,2] complex. The shape control agents used were pH, temperature and triethanolamine. Bipyramidal TiO_2 anatase NPs (that largely expone (101) surfaces) with low truncation along the c-axis were produced. Through a careful experimental design the influence of many process parameters on the synthesis outcome (size, shape and polydispersity), a predictive soft model was developed that is able to predict reasonably well the synthesis outcome. The synthesis of TiO_2 anatase nanosheets which presents high percentage of (001) facets are carried out with a solvothermal synthesis using hydrofluoric acid as capping agents [3].
Bipyramids and nanosheets were then tested against three different organic substrates (phenol, melamine and formic acid) that undergo three different photo-oxidation mechanism on TiO_2 NPs. Moreover, they were tested in the production of H_2 by formic acid photoreforming using Pt as co-catalyst. The results allow to rationalize the effect of the shape (and shape controllers) on the photocatalytic activity of TiO_2 anatase nanoparticles.

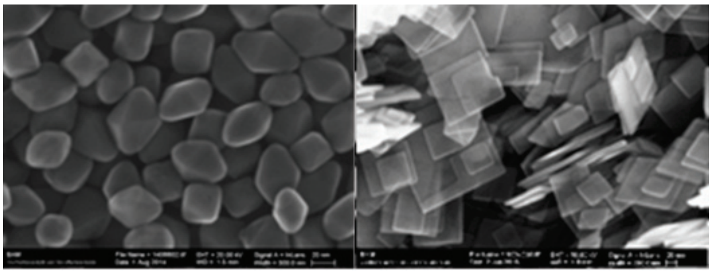

Figure 1 : Shape controlled TiO2 Nanoparticles: bipyramids (left) and nanosheets (right)

[1] Deiana, C.; Minella, M.; Tabacchi, G.; Maurino, V.; Fois, E.; Martra, G. Phys. Chem. Chem. Phys. 2013, 15, 307-315.
[2] Sugimoto, T.; Zhou, X. P.; Muramatsu, A.J. Colloid Interface Sci. 2003, 259, 53-61.
[3] X Han, Q Kuang, M Jin, Z Xie and L Zheng; JACS Vol 131, NO. 9 (2009), 3152-3153.

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IX Giornate Italo-Francesi di Chimica
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In silico design and experimental characterization of an oligopeptide targeting the Ebola virus VP24 protein

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(2) *DISFARM-Dipartimento di Scienze Farmaceutiche, Sezione Chimica Generale e Organica "A. Marchesini", Università degli Studi di Milano, Via Venezian 21, 20133, Milano, Italy*
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Ebola virus virulence and high lethality are due to different factors, in particular to its ability to inhibit both the innate immune response in the early stages of infection and the subsequent adaptive specific immune responses of the host organism[1]. The Ebola viral Protein 24 (VP24) inhibits interferon signaling through its interaction with the human protein Karyopherin, thus impairing the immune response of the host against the infection and increasing its rate of diffusion into the organism and its lethality[2]. This makes VP24 a potential pharmacological target, as the inhibition of its interaction with Karyopherin could reduce Ebola virulence. We carried out an atomic level study of the network of interactions between VP24 and Karyopherin using molecular dynamics and computational alanine scanning[3]. Modeling the VP24–Karyopherin complex (Fig. 1) allowed us to identify the amino acid residues responsible for protein–protein binding and led to the identification of a nonapeptide with VP24 binding potential. Subsequently, the ability of this peptide to actually bind VP24 in solution has been assayed using Saturation Transfer Difference NMR and Circular Dichroism. Experimental and molecular modeling data concerning the VP24–peptide complex have been compared and putative peptide binding sites and modes will be discussed.

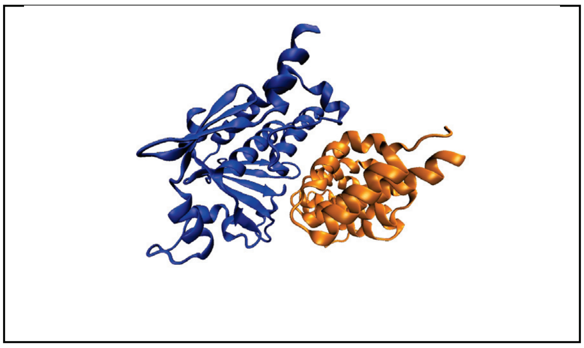

Figure 1: Structure of the complex between VP24 (blue) and Karyopherin (orange)

[1] M. Bray and T. W. Geisbert, Int. J. Biochem. Cell Biol., 2005, 37, 1560.
[2] S. P. Reid, C. Valmas, O. Martinez, F. M. Sanchez and C. F. Basler, J. Virol., 2007, 81, 13469.
[3] F. Dapiaggi *et al.* New J.Chem., 2017, 41,4308.

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Kendrick mass defect (KMD) plots for convenient reading of messages stored in sequence-controlled synthetic polymers

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The Kendrick mass defect plot is used to allow fast and extremely useful visualization of many structural features in complex mass spectra. The concept of simplification was extended to polymer chemistry by using the repeat unit of a polymer as the base unit for the calculation of the Kendrick mass [1]. Accordingly, the plot of a blend of homopolymers of the same monomer will display as many horizontal lines as distributions in the sample. On the opposite, a homopolymer distribution containing another repeating unit, different from the base unit, will line up in an oblique direction.
The assets of these horizontal/oblique lines can be extended to decrypt by MS/MS messages encoded in sequence-controlled synthetic polymers recently developed as new data storage media [2]. These macromolecules are composed of uniform chains with a precise location of co-monomers building units, intentionally defined as 0-bit and 1-bit to store information at the molecular level. As co-monomers have different masses, so-encoded messages can be readily deciphered by MS/MS sequencing [3]. Therefore, the KMD plot of such MS/MS data exhibits fast visualization deciphering as 0-bit-monomers will have a different direction than 1-bit-monomers.

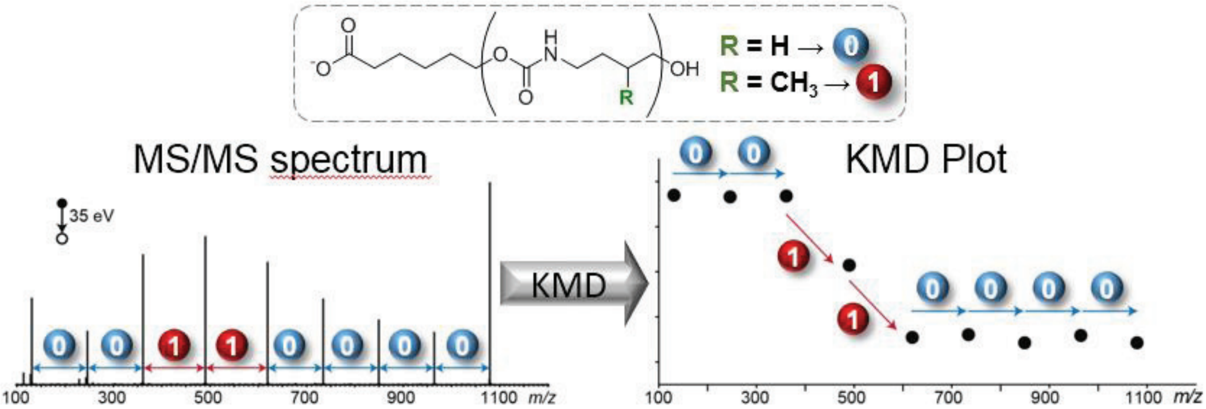

Figure 1: Convenient graphical visualization of messages encoded in sequence-defined synthetic polymers using Kendrick mass defect analysis of their MS/MS data

In this study, performance of KMD analysis were hence evaluated to improve the decoding step of messages encrypted in two families of sequence-controlled synthetic polymers, namely, polyurethanes and poly(alkoxyamine phosphodiester)s.

[1] H. Sato, et al., J. Am. Soc. Mass Spectrom. 25 (2014), 1346–1355.
[2] J.-F. Lutz et al., Nat. Rev. Mater. 1 (2016), 16024.
[3] L. Charles et al., Macromolecules 48 (2015), 4319-4328.

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Engineering of Gold(I)-zinc(II) bimetallic complexes for visible light emitting materials: a structural and spectroscopic study.

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Materials for lighting technology are of great interest in modern coordination chemistry research. Parallelism between photoluminescence and electroluminescence is the base of most of research, and a great effort to obtain high yield and low cost materials has been spent. Metals centers with d^{10} electronic configuration have been specifically considered for the lower price by respect to usual d^6 and d^8 metal complexes.[1] However, their complex chemistry, dominated by low energy effects, make difficult to optimize new materials, but results are often very good. We considered the possibility to construct new zinc(II)-gold(I) systems based on common and substituted chelating organic molecules. These compounds could be of general interest thanks to the low-price chemistry of zinc and the specific intermolecular interactions of gold that could enhance the luminescence properties of resulting solids. [2] This goal has been obtained by a tuned use of multiple equilibria that make possible the bridging attack by terminal cyanide of the linear building block dicyanoaurate. In this study, we analyse with a multi-technique approach (ESI-MS, solution absorption and emission spectroscopy, XANES) the solution behaviour of the molecular fragments and we correlate it to the solid state structure of 4 different products obtained. The judicious choice of the system made possible to obtain pure, single-phase, highly crystalline products. The crystal structure has been studied through SCXRD, demonstrating the presence of both the metals. The structural behaviour of the different fragments has been correlated with the luminescence in the solid state: the presence of gold(I) clearly shifts the emission of the $[Zn(L)_2]^{2+}$ fragment, and this phenomenon has been demonstrated by a spectroscopic analysis of similar systems with non-relativistic elements.

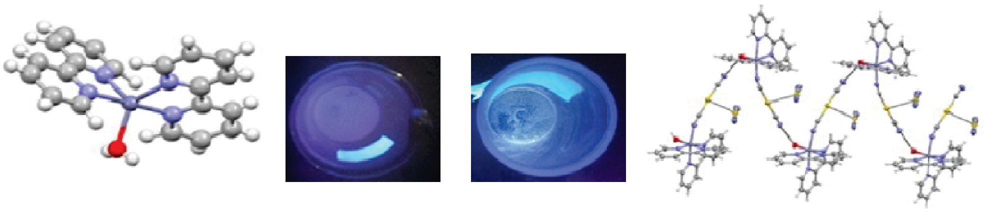

Figure 1 : Effect on solid state luminescence in the $[Zn(L)_2][Au(CN)]_2$ tecton built from the monometallic fragment.

[1] V.W.W Yam, K.M.C. Wong – Chem. Commun., 2011, 47, 11579-11592.
[2] P. Pyykko, Angew. Chem. Int. Ed., 2004, 43(34), 4412–4456.

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Applicative Aspect of Bionanomaterials: Leather Coatings for Fire and Water Resistance

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Leather, widely used in everyday life are mainly composed of proteins containing amino-, hydroxyl, carboxyl groups, naturally causing its hydrophilicity. Consequently, leather products are exposed to a damage by water and bacteria. Currently, this problem is addressed by coating leather with perfluoralkyl substances that are toxic and persistent in the environment.[1] Besides that, leather treatment includes measures for the increase of resistance to the flame, as finishing with triphenyl phosphate or resorcinol bis-(diphenyl phosphate), but these substances are known for poor compatibility and low reactivity with leather fibers[2].

Hereby, we propose to exploit the potential of nanomaterials for improvement leather production process and decrease environmental impact of tanning/retanning and leather finishing.

Alumina nanoparticles were an object of studies of environmentally safe and effective formulation of hydrophobic surface with application of relatively short hydrocarbon chains[3]. On such a basis, we have performed surface modification of Aeroxide Alu C with branched isostearic acid (FINEOXOCOL ®, by Nissan Chemical America Corporation) in order to apply it as leather coating. The functionalization resulted in a significant decrease of hydrophilicity of surface of Alumina nanoparticles measured by sessile drop method. The next step of this study is the application of the modified nanoparticles in sprays for leather coating.

The choice of hydroxyapatite (HA) as flame retardant (FR) additive is motivated by its high phosphorus content that is the measure of the efficiency of FRs. Furthermore, HA has high affinity for proteins, which is, for example, is exploited by nature in the nanocomposite structure of bone tissue.

In this context, the preliminary study of interaction of HA with bovine serum albumin (BSA) as a simple model protein has been carried out. From a structural point of view, the HA crystal can be described as an A-B-A-A-B-A- sequence of $Ca_3(PO_4)_2$ (A) and $Ca_4(PO_4)_2(OH)_2$ (B) layers parallel to $\{01\bar{1}0\}$ crystal planes. Hence, for such facets the surface-exposed layers results as ...-A-B-A, ...-A-A-B, or ...-B-A-A giving rise to the stoichiometric $\{01\bar{1}0\}$ and the nonstoichiometric $\{01\bar{1}0\}$_Ca-rich and $\{01\bar{1}0\}$_P-rich surfaces, respectively. These surfaces can be detected by combination of in-situ IR-controlled probing with CO and modelling[4]. This approach allowed to establish that two types of HA nanoparticles prepared by different methods exposed Ca-rich and P-rich surfaces (representing the overwhelming majority of particles facets in a 2:1 and 1:2 ratios.

Once BSA has been adsorbed at HA agglomerates by incubation in a BSA solution buffered with HEPES, average changes in the secondary structure of proteins in the multilayers were found to depend on the ratio of the two types of terminations of the same type of crystallographic facets: Ca-rich terminations seemed to induce limited conformational changes in adsorbed BSA, whereas the prevailing P-rich terminations resulted in an opposite effect. In summary, it was found that the relative amount of Ca-rich and P-rich HA surface terminations has a significant effect on the secondary structure of adsorbed proteins.

Acknowledgements. Project 'NanoSusLeather' funded by Compagnia di San Paolo

[1] J. Ma, et.al, Colloids Surfaces A Physicochem. Eng. Asp. 2015, 472, 21–25.
[2] Y. Jiang, et.al., Polym. Degrad. Stab. 2015, 115, 110–116.
[3] S. Alexander, et.al., ACS Appl. Mater. Interfaces 2016, 8, 660–666.
[4] F. Chiatti, et.al., J. Phys. Chem. C 2013, 117, 25526–25534.

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Computational approaches for the design and chemical synthesis of novel F508del correctors in the treatment of cystic fibrosis

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In cystic fibrosis patients, the function of CFTR is lost. Defective function of this channel can be caused by a variety of mutations with F508del being the most common. The primary defects can be treated with drug-like small molecules, known as “CFTR modulators”.

During the last years, several efforts have been performed to identify new active modulators [1]. The most promising data came from high-throughput screening (HTS) strategies, towards the discovery of thiazole-containing correctors [2]. In previous studies, we identified a class of compounds called aminoarylthiazoles (AATs) that potentially correct the CF basic defect and also showed a strong additive effect when combined with VX809 [3].

Herein we discuss the effectiveness of performing QSAR analyses to guide the search of thiazole-containing derivatives as F508del modulators. Indeed, in an attempt to construct more active molecules, it was thought to generate chemically hybrid compounds, merging a portion of VX809 with the thiazole scaffold. The derived QSAR model allowed us to guide and prioritize the most promising hybrids to be synthesised in the following synthetic routes [4, 5]. The newly derived compounds have been tested in functional and biochemical assays on CFBE41o- cells expressing F508del-, showing a promising corrector activity. Notably, the QSAR model efficiently predicted the biological trend of these new derivatives, being therefore worthy of a further development and optimization process towards the design of novel derivatives. Indeed, such molecules may represent lead compounds for the search of drugs that correct the basic defect in CF patients.

References
[1] M. Lopes-Pacheco, Front. Pharmacol. 7 (2016) 275. doi: 10.3389/fphar.2016.00275
[2] N. Pedemonte, G.L. Lukacs, K. Du, E. Caci, O. Zegarra-Moran, L.J. Galietta, A.S. Verkman, J. Clin. Invest. 115 (2005) 2564-2571. doi: 10.1172/JCI24898
[3] E. Pesce, M. Bellotti, N.Liessi, S. Guariento, G. Damonte, E. Cichero, A. Galatini, A. Salis, A. Gianotti, N. Pedemonte, O. Zegarra-Moran, P. Fossa, L. J. Galietta, E. Millo, Eur. J. Med. Chem. 99 (2015) 14-35. doi: 10.1016/j.ejmech.2015.05.030.
[4] Liessi N, Cichero E, Pesce E, Arkel M, Salis A, Tomati V, Paccagnella M, Damonte G, Tasso B, Galietta LJV, Pedemonte N, Fossa P, Millo E. 144 (2017) Eur J Med Chem. 2017 Dec 8;144:179-200. doi: 10.1016/j.ejmech.2017.12.030.
[5] FFC#6/2017 "Pharmacophore and pharmacokinetic filtering tools guiding for the design and synthesis of novel thiazole-containing and VX-809 hybrid derivatives as F508del correctors" (P.I Dott. E. Millo).

Sigma 1 Receptor eligible target for counteracting neurodegeneration. The lead compound (*R*)-RC-33

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The progressive loss of structure and/or function of neurons, within the Central Nervous System (CNS), is the prototypical event leading to neurodegeneration. Over the years, neurodegenerative disorders have gained the attention of the scientific community, since they represent one of the main causes of death worldwide [1]. Among the plethora of eligible targets useful for counteracting neurodegeneration, Sigma 1 Receptor (S1R) is note of worthy. Indeed, it is widely accepted that S1R agonists could be attractive modulators for the treatment of neurodegenerative diseases. In support of this evidence, the S1R macroscopic distribution at the CNS, as well as the overt involvement of S1R molecules in different neuropathies (Parkinson's, Amyotrophic Lateral Sclerosis, Alzheimer's and Multiple Sclerosis), allow to define S1R modulators as beneficial neuroprotective agents [2]. Our research is part of this scenario and in our previous investigations, (*R*)-RC-33 emerged as a potent and selective S1R agonist. Herein, we report the optimized gram-scale synthesis, pharmacokinetic profile and CNS distribution of (*R*)-RC-33 in mice to determine the most suitable dosage schedule for *in vivo* administration. For comparative purposes, the same experiments were also performed with PRE-084, the gold standard of S1R agonists. From these results arose that (*R*)-RC-33 possesses a similar pharmacokinetic profile and a better CNS distribution when compared with PRE-084. Therefore, (*R*)-RC-33 may be a promising candidate for *in vivo* studies in animal models of neurodegenerative diseases [3].

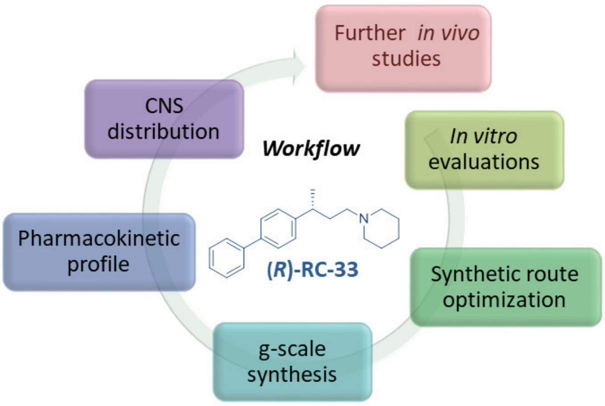

Figure 1: Workflow

[1] Przedborski, S. *et al. J Clin Invest.* **2003**; *111*(1): 3–10.
[2] Collina, S. *et al. Expert Opin Ther Pat.* **2013**; *23*(5):597-613.
[3] Marra, A. *et al. Future Med Chem.* **2016**; *8*(3):287-95.

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IX Giornate Italo-Francesi di Chimica
IX Journées Franco-Italiennes de Chimie
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Targeting myeloid differentiation using potent *human* dihydroorotate dehydrogenase (*h*DHODH) inhibitors

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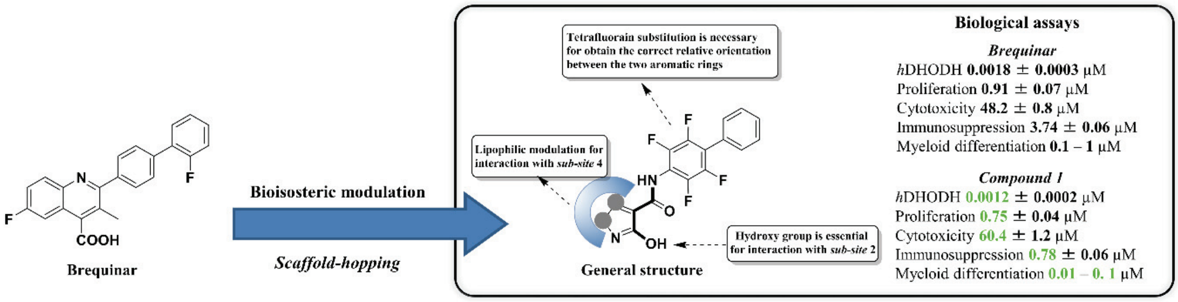
Human dihydroorotate dehydrogenase (*h*DHODH) catalyses the fourth step in the *de novo* pyrimidine biosynthesis where dihydroorotate (DHO) is converted to orotate (ORO).[1] Being already validated as therapeutic target for the treatment of autoimmune diseases, as rheumatoid arthritis or multiple sclerosis [2], quite recently *h*DHODH was associated to acute myeloid leukaemia (AML) [3], a disease where the standard of intensive care has not changed in the last four decades.[4] The success of brequinar (Figure 1), one of the most potent known *h*DHODH inhibitors, to induce *in vitro* and *in vivo* differentiation in mouse AML models[3], highly encourages researches to design *h*DHODH inhibitors with better drug-like profiles. Starting from brequinar, by applying innovative *scaffold-hopping* replacement, we recently designed a first generation of potent *h*DHODH inhibitors presenting nM activity on the isolated *h*DHODH.[5] Following that early affords, in this occasion we are presenting a second generation of inhibitors (Figure 1) able to reach the brequinar *h*DHODH potency levels. Compound **1**, the best of two series, was found able to restore the myeloid differentiation in leukaemia cell lines (U937 and THP-1) at concentrations one digit lower than those achieved in experiments with brequinar. Theoretical design, modeling, synthesis, SAR, X-ray crystallographic data, biological assays (enzymatic assays, proliferation, cytotoxicity, immunosuppression and myeloid differentiation), preliminary ADME and *in vivo* toxicity are here presented and discussed.



Biological assays

Brequinar
*h*DHODH **0.0018 ± 0.0003** μM
Proliferation **0.91 ± 0.07** μM
Cytotoxicity **48.2 ± 0.8** μM
Immunosuppression **3.74 ± 0.06** μM
Myeloid differentiation **0.1 – 1** μM

Compound 1
*h*DHODH **0.0012 ± 0.0002** μM
Proliferation **0.75 ± 0.04** μM
Cytotoxicity **60.4 ± 1.2** μM
Immunosuppression **0.78 ± 0.06** μM
Myeloid differentiation **0.01 – 0. 1** μM

*Figure **1**: Brequinar structure and general strategy for the design of new hDHODH inhibitors.*

[1] Marco, L. L.; *et al*., Recent Patents on Anti-Cancer Drug Discovery 2018, 13, 86-105.
[2] Leban, J.; Vitt, D. Arzneim. Forsch. 2011, 61, 66-72.
[3] Sykes, D. B.; *et al*., Cell 2016, 167, 171-186.e15.
[4] Tzelepis, K *et al*., Cell Reports 2016, 17, 1193-1205.
[5] Sainas, S.; *et al*., Eur. J. Med. Chem. 2017, 129, 287-302.

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Formation of Glycine and Alanine homo-peptides on the surface of α-quartz from non-activated amino acids

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The chemistry of silica and the role of its surface features in the adsorption of biomolecules has been widely studied and reviewed over the last decades. [1] For their ubiquity on Earth's crust, silicate minerals have also been addressed as possible candidates for amino acids polymerization in prebiotic conditions. Among all studies, the effectiveness in the formation of long homo-peptides of Gly from non-activated amino acids using a Chemical Vapour Deposition approach was lately reported. [2]

In this study, we extend the CVD approach to the surface of α-quartz. Gly and Ala are sublimated on samples of both amorphous silica and α-quartz.

The final products are extracted with water from the surface of quartz and analyzed by High Resolution Mass Spectrometry. The results show the formation of homo-peptides of Gly and Ala long up to 11-mer and 10-mer, respectively.

Furthermore, in the case of Ala, it was possible to analyze the extracted species by UV-Circular Dichroism. Could the surface of silica influence the chirality of the formed poly-Ala species?

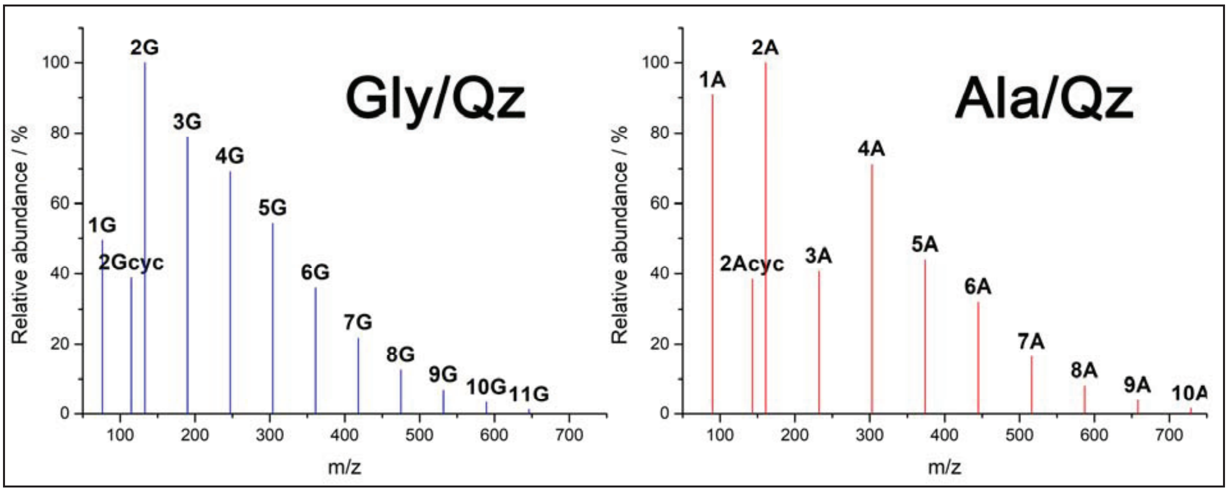

Figure 1 : ESI-MS spectra of solution resulting from washing (with pure water) of αQz contacted with Gly and Ala vapours for 30 minutes. The number on the bars indicates the n-mer of Gly and Ala, respectively.

[1] A. Rimola, D. Costa, M. Sodupe, J-F. Lambert, P. Ugliengo, *Chem. Rev.* **2013**, 113, 4216-4313.
[2] G. Martra, C. Deiana, Y. Sakhno, I. Barberis, M. Fabbiani, M. Pazzi, M. Vincenti, *Angew. Chem. Int. Ed.* **2014**, 53, 4671-4674.

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Lead Halide Perovskite Nanocrystals

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Lead halide perovskites (LHPs) in the form of colloidal nanocrystals (NCs) have been given increasing importance in the yield of materials science due to their unique optical versatility, high photoluminescence quantum yields (PL QYs) and facile synthesis [1].
They are expected to be promising candidates for the next-generation cost-effective lighting and display sources and for the solar cells, since solution-deposited absorbing layers of perovskites are able to increase the power conversion efficiencies reaching 20% [2].
In the $APbX_3$ LHPs crystal structure, A can be either organic (like methylammonium (MA, $CH_3NH_3^+$) or formamidinium (FA, $CH(NH_2)_2^+$) or inorganic, like Cesium (Cs^+), and X is one or more halides (Cl^-, Br^- or I^-). Due to the nature of the constituent elements, LHP NCs have a "soft" and rather ionic lattice, and their optical and electronic properties are highly tolerant to structural defects and surface states [1].
In this study, we have synthesized monodisperse colloidal nanocubes (7–12 nm edge lengths) of fully inorganic Cesium lead halide perovskites ($CsPbX_3$, X = Cl, Br, and I or mixed halide systems Cl/Br and Br/I), in order to investigate the change of luminescence due to the nature of the halide and the structural defects in mixed halide perovskites.

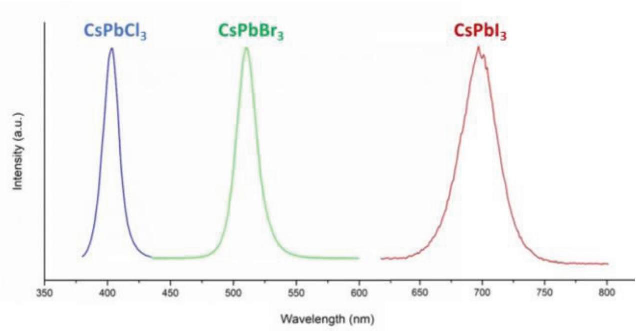

Figure 1: Emission spectrum and photo of $CsPbX_3$ [$X = Cl^-$, Br^- and I^-]

[1] Quinten A. Akkerman, Gabriele Rainò, Maksym V. Kovalenko and Liberato Manna, Genesis, challenges and opportunities for colloidal lead halide perovskite nanocrystals, *Nature Materials* (2018).
[2] Chung, I.; Lee, B.; He, J.; Chang, R. P. H.; Kanatzidis, M. G., Perovskite solar cells with a planar heterojunction structure prepared using room-temperature solution processing techniques, *Nature* (2012), 485, 486-489.

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$Hf(OTf)_4$–catalysed hydride transfer reactions in the cyclisation of trifunctional compounds

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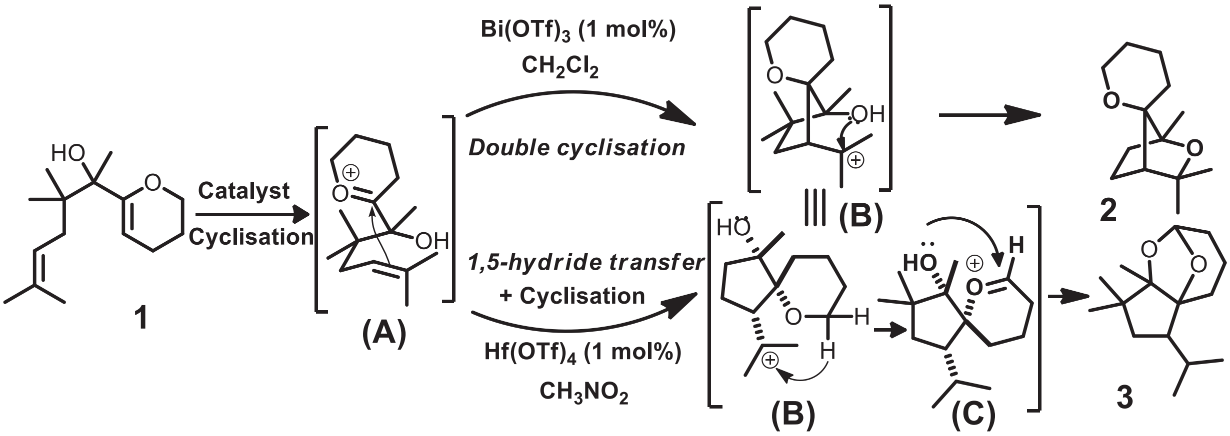
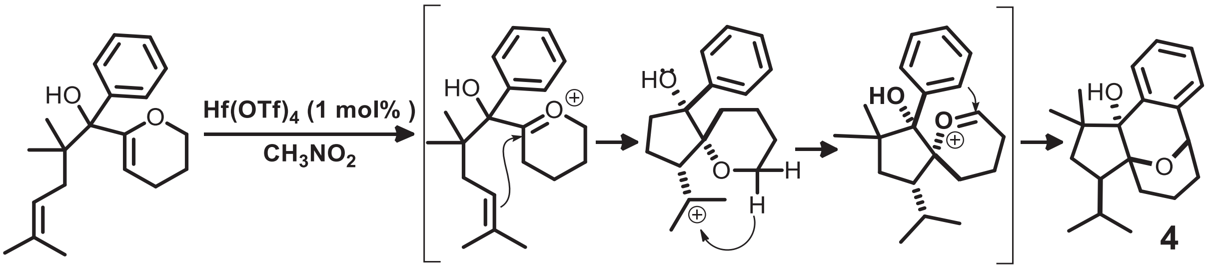
The quest for green and efficient catalysts in organic chemistry is never ending. In this context, metal triflates are often-sought resources not just because their selectivity and mild reactions conditions but also because the metal's nature keep the door open to new unexpected reactivities.[1,2] In the search of new odorant molecules, a novel synthetic methodology of interest for the cyclisation of polyfunctionalized dienols such as **1** is being examined in our group. [3] In dichloromethane, with $Bi(OTf)_3$ as the catalyst, compound **1** allows to obtain a tricyclic diether **2,** *via* a double cyclisation mechanism by the proposed intermediates **A** and **B**. On the other hand, in nitromethane, the catalyst $Hf(OTf)_4$, drove us to the structure **3** *via* a 1,5-hydride transfer, process which is proposed to undergo via intermediate **C**.



This last conditions were applied to others enol ether substrates. One of them, including an aromatic ring, allowed to confirm the hydrogen's conveyance and to observe a different reactivity to the tetracyclic structure **4**.



Some of these new compounds, presenting woody and green notes, are of potential interest in the field of odorant compounds.

[1] P. Ondet, G. Lemière, E. Duñach, *Org. Lett.* **2015**, *17*, 1002-1005.
[2] P. Ondet, L. Lempenauer, G. Lemière, E. Duñach, *Org. Chem. Front.* **2016**, *3*, 999-1003.
[3] P. Ondet, L. Lempenauer, G. Lemière, E. Duñach, *Eur. J. Org.Chem.* **2017**, 20*17*, 761-780.

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IX Giornate Italo-Francesi di Chimica
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Size- and shape-controlled $BaSO_4$ particles for functional applications

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Chemists approach barium sulfate early during their formation, because $BaSO_4$ is paradigmatic for its low solubility, and therefore taken as an example to introduce solvation, ionic bond and precipitation equilibria. During the second half of the 20th century, the precipitation of Ba as $BaSO_4$ has progressively lost importance, owing to the substitution of gravimetric methods with the most sensitive and less work-intensive instrumental techniques. Conversely, the industrial relevance of $BaSO_4$ has experienced the opposite trend, with world production passing from $4.2 \cdot 10^6$ tons in 1994 to $9.2 \cdot 10^6$ tons in 2012. Thanks to its chemical inertness, thermal stability, white color, abundance and low price, $BaSO_4$ finds indeed applications as pigment, contrast agent, weighting agent in rubber, paints and plastics, in high-density concrete for radiation shielding, and automobile brake and clutch pads.

The properties of $BaSO_4$ play a crucial role in many of its applications, and, as it is observed for many materials, particle size has a striking effect on scattering properties, solubility, specific surface area and tribology. Nevertheless, $BaSO_4$ is mainly available, and employed, as powders obtained from the crushed mineral. Therefore, the commercial powders lack of size and shape control, being composed of fractured particles with irregular shape and size varying from nanoparticles to several hundreds of micrometer. The potential of $BaSO_4$ are indeed underexploited, limiting the performance in the commercial applications.

For these reasons we considered two synthetic procedures already known from geochemistry and gravimetric analysis, but not yet exploited for the preparation of barite with controlled morphology. The first procedure is inspired by the observation that $BaCO_3$ deposits are converted to $BaSO_4$ if they come in contact with sulfate-containing water. We then decided to employ $BaCO_3$ as a precursor for $BaSO_4$ synthesis. The second synthetic procedure stems from Ba gravimetric determination. The simplest way to precipitate Ba consists in adding sulfate to the solution, to form insoluble barite. Nevertheless the particles obtained in this way are small and difficult to sediment. To overcome this issue, the precipitation of $BaSO_4$ with sulfamic acid, NH_3SO_3, was proposed. While $Ba(NH_2SO_3)_2$ is soluble, NH_3SO_3 can be hydrolyzed generating sulfate in situ, and resulting in coarser, flocculating precipitate, particularly suitable for gravimetric determination.

In the present work we studied the synthesis of $BaSO_4$ employing $BaCO_3$ or NH_3SO_3 as precursors, which are inexpensive and already employed in industrial processes. We devoted particular attention to unravel the effects of the different experimental variable involved in determining the synthesis output, aiming to obtain particles with controlled size and shape.

Molecularly imprinted polymers: could surfactant influence the molecular recognition properties?

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The artificial receptors known as Molecularly Imprinted Polymers (MIPs) represent one of the most successful type of man-made materials developed to mimic the binding properties of natural receptors like antibodies and enzymes[1]. One of the most significant application concerns the use of MIPs as substitutes of natural antibodies in immunoaffinity extraction, in the so-called Molecularly Imprinted Solid Phase Extraction (MISPE). In this technique, the target analyte contained in the sample is loaded onto an imprinted solid phase, and after a washing step, it is recovered to be quantified. Of consequence, to enhance the MIP's selectivity and to assure high recoveries of the analyte it is of paramount relevance to minimize non-specific interactions between MIP and the sample matrix. Such non-specific interactions are generally based on weak hydrophobic forces between the surface of the MIP and the less hydrophylic components of the sample matrix. Consequently, additives able to interfere with such interactions should be able to significantly reduce any non-specific binding effect[2]. Among the possible additives, surface active agents represent an interesting class of substances as they are cheap, easily available and compatible with the organic solvents commonly used in MISPE technique. Here we report a study about the effect of several surfactants on the binding properties and the selectivity of a trichlorophenoxyacetic acid-imprinted polymer[3]. HPLC columns packed with imprinted and non-imprinted polymers were eluted with mixtures of water/acetonitrile (containing acetic acid 2% v/v) added with variable amounts of three different surfactants: the anionic sodium dodecylsulphate (SDS, 0-0.2% w/v), the cationic cetyltrimethylammonium bromide (CTAB, 0-0.2% w/v) and the non-ionic polyoxyethylene-(20)-sorbitan monolaurate (Tween 20, 0-2.5% w/v). The binding ability of the polymers towards the template 2,4,5-T and two related ligands 2,4-D and 4-M was evaluated by measuring the capacity factors of these ligands and calculating the normalized imprinting factor:

NIF= (k MIP – k NIP) / k MIP)

The relative selectivity was measured in the same experimental conditions as:

a = (k template – k ligand) / k ligand

From the experimental results, it is possible to observe that surfactants are able to increase the imprinting effect by decreasing the non-specific binding. This effect is less marked with the non-ionic surfactant respect to the two ionic ones. This indicates that surfactants act mainly by inhibiting the ionic pair interaction between the acidic ligands and the basic functional monomer 4-vinylpyridine. About selectivity, all the surfactants show no influence, as any increase of selectivity observed can be directly related only to the amount of water present in the mobile phase.

[1] K. Haupt, "Molecular Imprinting", *Springer*, **2013**.
[2] J.W Goodwin. *Colloids and Interfaces with Surfactants and Polymers-An Introduction* (1st ed.), *John Wiley & Sons, New York*, **2004**.
[3] C. Baggiani, L. Anfossi, C. Giovannoli, C. Tozzi, "Binding properties of 2,4,5-trichlorophenoxyacetic acid-imprinted polymers prepared with different molar ratios between template and functional monomer", *Talanta,* **2004,** (5), 1029-1034

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Multi-catalytic cascade to access fluorinated keto-diols

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Combining multiple catalytic activation modes notably based on widely available cheap catalytic systems such as iron-, copper- or organo-catalysts is a powerful approach for eco-compatible synthesis. Our laboratory has taken advantage of this strategy to discover innovative synthetic routes for the synthesis of crucial building blocks.[1] In this context, we recently focused on discovering an alternative strategy to access in one single cascade to keto-diols, key precursors of extended 1,3-polyols, a motif widely present in numerous biologically active molecules. Using iron or copper complexes in cascade, a bi-directional aldolization occurred directly forming the synthetically valuable keto-diols albeit the development of an enantioselective version remained hampered by the good coordinating ability of the starting keto-diacid (a).[2] To overcome this issue, we recently designed a multi-catalytic cascade allowing the generation of enantioenriched aldehydes and their direct trapping forming complex acyclic keto-diols possessing 4 stereocenters with excellent stereocontrol (b).[3]

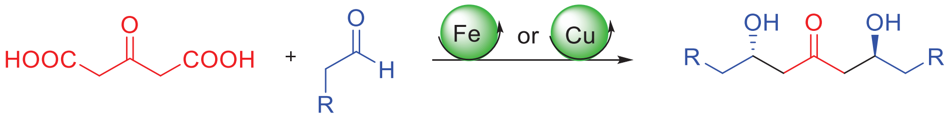
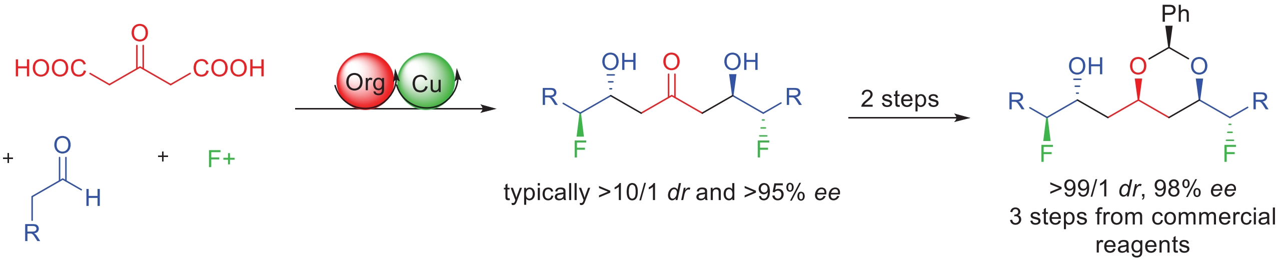


Figure 1 : Racemic approach



typically >10/1 *dr* and >95% *ee*

>99/1 *dr*, 98% *ee*
3 steps from commercial reagents

Figure 2 : Enantioselective multi-catalytic approach

[1] a) A. Quintard, T. Constantieux, J. Rodriguez, *Angew. Chem. Int. Ed.* **2013**, *52*, 12883; b) M. Roudier, T. Constantieux, A. Quintard, J. Rodriguez, *Org. Lett.* **2014**, *16*, 2802 ; c) A. Quintard, J. Rodriguez, *Chem. Commun.* **2015**, *51*, 9523 ; d) M. Roudier, T. Constantieux, A. Quintard, J. Rodriguez, *ACS Catal.* **2016**, *6*, 5236.
[2] A. Quintard, J. Rodriguez, *Chem. Eur. J.* **2015**, *21*, 14717.
[3] A. Quintard, J. Rodriguez *ACS Catal.* **2017**, *7*, 5513-5517.

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Base-free generation of organic electron donors from air-stable precursors

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Reducing agents, based on totally neutral organic structures and with exceptionally negative redox potentials, emerge as an attractive novel source of reducing electrons. Organic electron donors (OEDs) showed their potency and chemoselectivity in the reduction of challenging substrates. [1] They promote the formation of radical or anionic intermediates by single- or double-electron transfers. These strong reducing agents are now attracting more and more the interest for original applications in diverse domains (coupling partners, polymerization initiators, redox switches). [2] Nonetheless, their stability issues in atmospheric oxygen or over time complicate their manipulation and storage.

To overcome these constraints and enhance OED's practicality, new air- and moisture-stable aminopyridinium carboxylate and carbonate precursors were synthesized and thermally activated to in-situ generate the potent electron donor. [3] Carboxylate adducts proved to be excellent OED-latent systems allowing easy and efficient reduction of challenging substrates. Their reducing properties are correlated to their structural characteristics by thermogravimetric and spectrometric analysis.

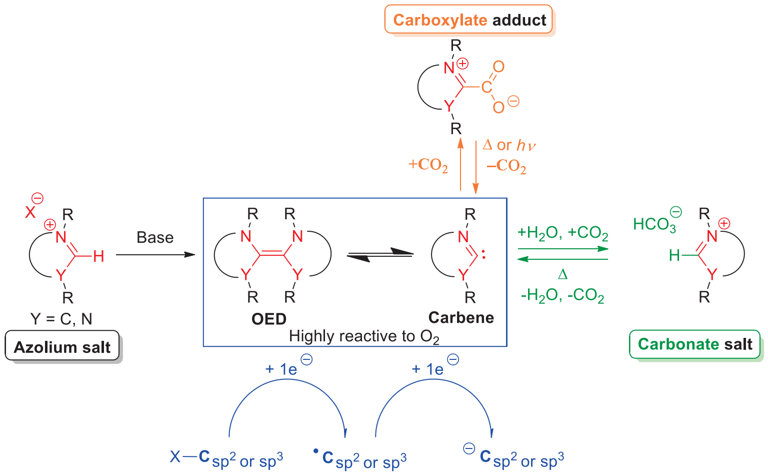

Figure 1: In-situ generation of OEDs from air-stable precursors.

[1] a) J. Broggi, T. Terme, P. Vanelle, Angew. Chem. 2014, 126, 392-423, Angew. Chem. Int. Ed. 2014, 53, 384-413; b) J.A. Murphy, J. Org. Chem. 2014, 79, 3731-3746.
[2] a) J. Broggi, M. Rollet, J.L. Clément, G. Canard, T. Terme, D. Gigmes, P. Vanelle, Angew. Chem. 2016, 128, 6098-6103, Angew. Chem. Int. Ed. 2016, 55, 5994- 5999; b) F. Cumine, S. Zhou, T. Tuttle, J.A.Murphy, Org. Biomol. Chem. 2017, 15, 3324-3336.
[3] G.Tintori, P. Nabokoff, R. Buhaibeh, D. Bergé-Lefranc, S. Redon, J. Broggi, P. Vanelle, Angew. Chem. Int. Ed. 2018, *Early View*, doi: 10.1002/anie.201713079.

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Synthesis of benzimidazole derivatives and in vitro screening for antileishmanial activity

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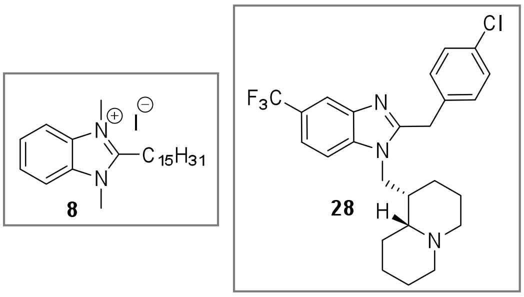
Leishmaniasis is caused by a protozoa parasite from over 20 *Leishmania* species, and is transmitted by the byte of infected female phlebotomine sandflies. There are three main forms of leishmaniases – visceral (the most serious form of the disease), cutaneous (the most common), and mucocutaneous. In the absence of effective and sustainable vaccines, the current therapies are based on pentavalent antimonials and require long-term treatments, burdened by toxicity, severe side-effects, pain and cost. Moreover the onset of drug resistance, associated with treatment failures, point out the crucial need for new anti-leishmanial agents. In this context we designed and synthesized two sets of benzimidazole derivatives that were screened for their antiparasitic activity against promastigotes of *L. tropica* and *L. infantum*. A first set was formed by 2-(long chain)-alkyl/benzyl benzimidazoles (**1**-**22**), whose heterocyclic head was mainly quaternized to mimic the ammonium head of miltefosine. The second set was composed of 2-benzyl and 2-phenyl benzimidazoles (**23-39**) decorated in position 1 with a basic side chain. Most of the tested compounds of both sets proved to be active against *L. tropica* and *L. infantum* with IC_{50} values in the low micromolar/sub-micromolar range. The best-performing representative derivatives of the two sets were, respectively, compounds **8** and **28** (Figure 1), which resulted about 200-fold (IC_{50}= 0.19 µM, *L. Tropica*; 0.34 µM, *L. infantum*) and 10-fold (IC_{50}= 3.70 µM *L. Tropica*, 4.76 µM *L. infantum*) more potent than miltefosine, used as positive control. Therefore, compounds **8** and **28**, whose activity was also confirmed on intramacrophagic amastigote stage of *L. infantum*, represent interesting hit compounds, worthy of structural optimization to improve their safety profiles.



8 **28**

Figure 1: Chemical structure of the best-performing benzimidazole derivatives studied.

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Collective properties of bright emitting perovskites nanocrystals

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Thanks to international efforts inorganic lead halogen perovskites, $CsPbX_3$, are now quite well known both as bulk and as nanocrystals. In this second shape remarkable sharp and bright direct band – gap emission, finely tunable through stoichiometry, makes them excellent candidates for a wide range of optoelectronic applications, from solar cells to LED devices.[1,2] Until now exploitation attempts have focused on dispersing nanocrystals into a polymeric matrix, or simply drop casting them onto various substrates.

The aim of this work is studying how collectives properties are related to those of individual nanocrystals and bulk; we expect changes in optoelectronic properties along with effects related to electronic interactions between nanocrystals (being them quantum confined structures).[3]
These results will lead to a deeper comprehension of self-assembled nanocrystals behaviour, and will possibly represent the first step towards new multiphasic self-assembled structures.

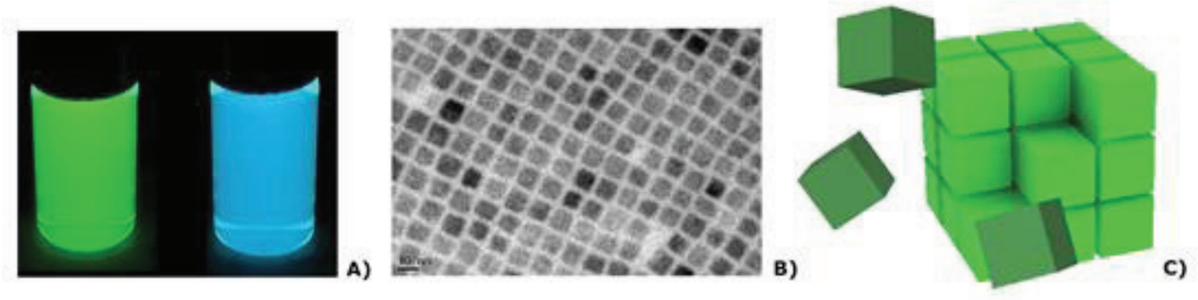

Figure 1: A) Bright emitting 11 nm (green) and 6 nm (blue) $CsPbBr_3$ nanocrystals dispersed in hexane; B) TEM image of $CsPbBr_3$ nanocrystals; C) Rendering of a possible self-assembled structure;

[1] Quinten A. Akkerman *et al.*, Genesis, challenges and opportunities for colloidal lead halide perovskite nanocrystals, Nat. Mat. (2018), doi:10.1038/s4156-018-0018-4
[2] Guilherme Almehida *et al.*, Role of Acid-Base Equilibria in Size, Shape, and Phase Control of Cesium Lead Bromide Nanocrystals, J. Am. Chem. Soc. 138 (2016), 7240 – 7243
[3] Michael C. Brennan *et al.*, Origin of the Size – Dependent Stokes Shift in $CsPbBr_3$ Perovskite Nanocrystals, J. Am. Chem. Soc. 139 (2017), 12201 – 12208

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Revisiting the paradigm of quartz pathogenocity: investigation of the interaction between surface silanols and biomembranes

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An impressive body of scientific reviews and experimental works,[1-2] has evidenced two key aspects in the interaction between crystalline silica and cells: i) the crucial role played by the particle surface in triggering the adverse biological response, and ii) the extreme variability in the pathogenic potential among different sources of particulate silica.[3] Such a variability is the consequence of differences in silica bulk and surface chemistry, including the nature, abundance, and spatial disposition of silanol (–Si-OH) families. Silanols, acidic moieties with a potential for H-bonding, have a key role in defining silica interaction with cells: silica surface is characterized by different families of –Si-OH groups, including isolated (the most common), geminal, and vicinal silanols. The long-range order and distribution of silanol patches on silica surface impart specific characteristics to different silica specimen. Quartz dusts used so far in particle toxicology assays have been obtained by grinding rock containing natural quartz, a process that affects crystallinity and yields samples with extreme variable and complex surface states. To overcome such a variability, we have developed an innovative method to grow highly-pure quartz crystals in respirable size (< 4 µm) with controlled surfaces, in order to investigate, at the molecular level, the mechanisms related to quartz toxicity. Surprisingly, the as-grown synthetic quartz crystals with regular faces, characterized by silanol patches with a long-range order, did not show any perturbative activity towards membrane models at increasing complexity (liposome and red blood cells), developed to investigate the molecular determinants in the interaction. On the contrary, after inducing the loss of the long-range order of silanol patches by ball milling, synthetic quartz elicited strong reactivity toward same models. Crystal milling also led to the formation of surface radical species,[4] which are held to be involved in the alteration of the ROS metabolism of cells. Overall, data are consistent with the hypothesis that most of the biological reactivity of quartz dusts is not due to crystallinity *per se,* but it is originated via fragmentation *(fig. 1)*, which entails the formation of conchoidal fractures and new faces, characterized by the strong disorganization of surface functionalities.

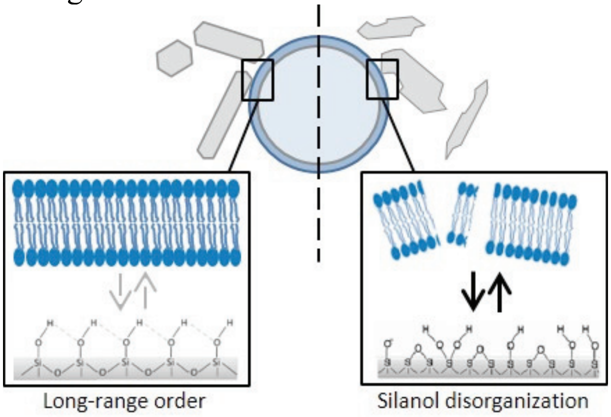

Fig. 1: Mechanical milling imparts strong membrano-perturbative potential to synthetic quartz crystals, due to disorganization of surface functionalities.

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References

1. K. Donaldson, A. Seaton, *Part Fibre Toxicol*., 2012, 9:13
2. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Silica, some silicates, coal dust and para-aramid fibrils. Lyon, 15-22 October 1996. *Monogr. Eval. Carcinog. Risks Hum.* 68:1 – 475; 1997.
3. B. Fubini, W. E. Wallace, In: Papirer. E, ed. Adsorption on silica surfaces. New York: Marcel Dekker, 1999:645-664
4. A. Rimola, D. Costa, M. Sodupe, J. Lambert, P. Ugliengo, *Chem. Rev*., 2013, 113(6): 4216-313

Discerning between natural and artificial pozzolanic materials by FTIR spectroscopy)

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Discerning between natural (i.e. *pozzolana*) o artificial (i.e, crushed bricks or ceramics) pozzolanic materials in hydraulic plaster and mortars is usually performed by means of Optical Microscopy (OM) thin section observation, by thermal techniques (TGA-DTA) and XRD analysis. (Chiari et al., 1992; Moropoulou et al., 2005, 1995). In the present work a new option based on FTIR spectroscopy is proposed. FTIR spectra collected on geological material (Pozzolana di Torre del Greco, Museo Regionale di Scienze naturali) and a certified reference material (SARM69 powdered ceramic, MINTEK**,** Johannesburg, SA) indicate the possibility of discriminating between *pozzolana* and ceramic materials in typical 1170-470 cm^{-1} frequency range. Analysis of archaeological mortar fragments, containing *pozzolana* and crushed ceramic respectively, confirms the suitability of the proposed FTIR technique in discerning between natural and artificial pozzolanic materials on real samples. Nature of the pozzolanic aggregate in these samples was previously ascertained by mean of OM, XRD, TGA and SEM-EDX.

FTIR is a fast and economic technique, both in sample preparation and analysis and could be usefully applied when a great number of samples has to be examined, as an alternative to the XRD technique in the case of disaggregated samples or when pozzolanic materials are present in the form of fine particle, i.e. below the resolving power of the OM. Finally, a scale-up to portable equipment could allow *in situ* determinations leading to the mapping of the different technological horizons in an archaeological site or complex.

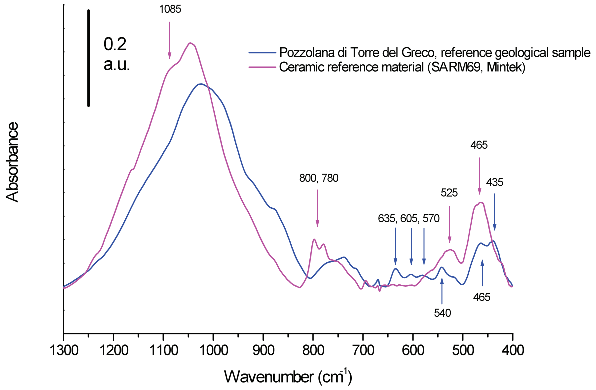

Figure 1 : FTIR spectra of reference materials

[1] Chiari, G., Santarelli, M.L., Torraca, G., 1992. Caratterizzazione delle malte antiche mediante l'analisi di campioni non frazionati. Mater. e Strutt. Probl. di Conserv. II, 111–137.
[2] Moropoulou, A., Bakolas, A., Anagnostopoulou, S., 2005. Composite materials in ancient structures. Cem. Concr. Compos. 27, 295–300.
[3] Moropoulou, A., Bakolas, A., Bisbikou, K., 1995. Characterization of ancient, byzantine and later historic mortars by thermal and X-ray diffraction techniques. Thermochim. Acta 269–270, 779–795.

Characterization of the odorant constituents of *Helichrysum italicum* essential oil

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Helichrysum italicum ssp. *italicum* (Asteraceae) is widespread all over the Mediterranean basin. It is sometimes called “curry plant” because of the typical strong spicy smell of its leaves. In the flavour & fragrance industry, this species is extracted for the production of absolute, or hydrodistilled to furnish an essential oil which is widely used in cosmetics and in aromatherapy. The composition of the essential oil has been extensively studied, and depending on the geographical origin of the plant, the main constituent is either neryl acetate **1** or monoterpenes like α-pinene **2**. Some uncommon 2-methyl-1,3-diketones such as **3**-**6** appear to be specific components of *H. italicum*, and have never been observed in other species so far [1, 2].

In the course of our analytical studies devoted to the identification of the key odorants of fragrant plants, we performed a Gas Chromatography Olfactometry (GC-O) analysis of a sample of Corsican *H. italicum* essential oil (neryl acetate type), using the Aroma Extract Dilution Analysis (AEDA) methodology. The identification of the odorants was realized by a detailed fractionation of the essential oil by liquid-liquid basic extraction, distillation and column chromatography, followed by the GC-MS and GC-O analyses of some fractions, and coinjection of commercial and synthesised reference compounds.

We could demonstrate that the characteristic curry/spicy odor of the plant is mostly due to the saturated diketones **3** - **4**, together with some volatiles more common as essential oil constituents (such as 1,8-cineole **7**, nerol **8**, eugenol **9**, *p*-cresol **10**…). In contrast, the olfactory contribution of **1** and of the unsaturated diketones **5** - **6** was much less significant.

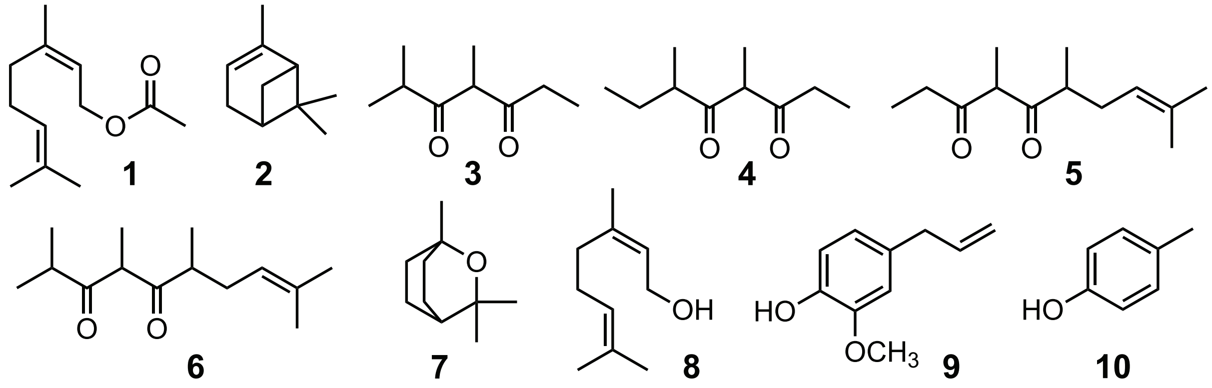

Figure 1: Main constituents and odorants of Helichrysum italicum *essential oil.*

[1] Manitto, P.; Monti, D.; Colombo, E., *Phytochemistry,* **1972,** *11* (6), 2112-2114.
[2] Tira, S.; Di Modica, G., *Tetrahedron Letters,* **1967,** *8* (2), 143-148.

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Application of MCRs to the stereoselective synthesis of diverse heterocycles starting from chemoenzymatycally obtained chiral aldehydes

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Exploitation of biomass as starting material for fine chemicals production is of particular interest. The bio-based building blocks obtained can be further transformed into high added-value compounds.
Within this context our group is implementing an overall strategy for obtaining polyfunctionalized products starting from biomass in an efficient and sustainable manner.
In particular, we choose as starting materials a cyclic meso-diol derived from erythritol, a meso natural polyalcohol, that is considered a promising intermediate building block for the synthesis of sugar derived structures.
The strategy involves three steps: first the enantioselective generation of enantiomerically pure chiral inputs, bearing a variety of alternative appendages, via biocatalysis; then the use of these inputs in diastereoselective Passerini reactions; finally the cyclization to afford heterocyclic scaffolds.
The result is the diversity-oriented synthesis of chiral, biobased, densely functionalized heterocycles, with control of relative and absolute stereochemistry of the stereogenic centres. These compounds could find useful applications in drug discovery

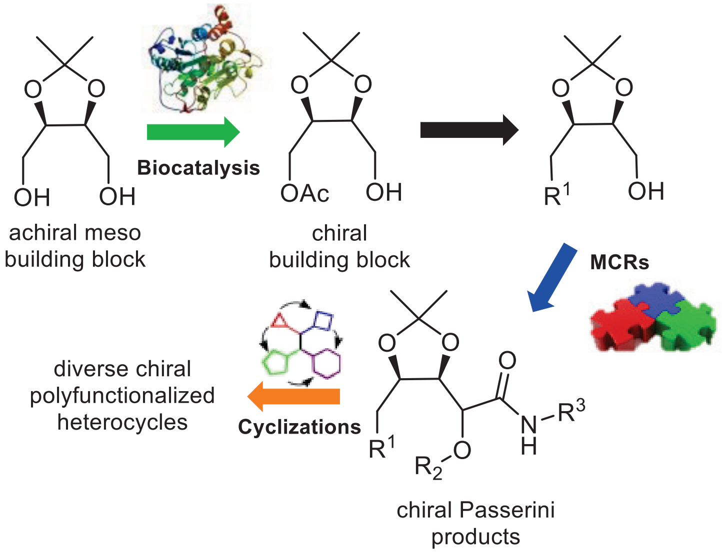

Figure 1 : Coupling of three different techniques

[1] V. Cerulli, L. Banfi, A. Basso, V. Rocca, R. Riva, Org. Biomol. Chem. 2012, 10, 1255.
[2] L. Moni, L. Banfi, A. Basso, E. Martino, R. Riva, Org. Lett. 2016, 18, 1638.

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CO_2 Adsorption on Hybrid Organic-Inorganic Materials: A Multidisciplinary Study

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In order to decrease the amount of CO_2 emitted to the atmosphere, several CO_2 capture methods have been studied in literature. Among the various technologies, gas phase adsorption on solid adsorbents has been the focus of many investigations, due to their economical and eco-friendly advantages. In this work, different organic-inorganic hybrid materials have been synthesized, characterized and tested as sorbents for CO_2 in post combustion conditions (35 °C, partial pressure CO_2 = 0.1 bar). On one side, hybrid organic-inorganic SBA-15 silicas functionalized with increasing amounts of amino groups were studied. Three different amino-silane species were used: 3-aminopropyltriethoxysilane (APTS), 3-(2-aminoethyl)aminopropyltrimethoxysilane (EAPTS) and 3-[2-(2-aminoethyl)aminoethyl] aminopropyltrimethoxysilane (PAPTS). A detailed study on the interactions of organosilane species with the silica surface was performed by using a combination of IR and SS-NMR spectroscopy, with particular emphasis to the determination of the silane chain length effect on the mobility of organic species on the silica surface.[1] On the other side, we considered MCM-41 silica samples with different particle diameter, passing from micrometric to nanometric scale, in order to study the size effect of the support on the adsorption properties. The adsorption process was studied both qualitatively and quantitatively by using different techniques (*i.e.* FT-IR and SS-NMR spectroscopies, volumetric measurements, TGA and Zero Lenght Column analysis) with a special focus on the reversibility of the reactions. Since the coal-fired power station flue gas is typically vented to the atmosphere at higher temperature respect room temperature, we finally studied the CO_2 adsorption process on the materials at increasing temperatures: 35-50-70-90 °C.[2]

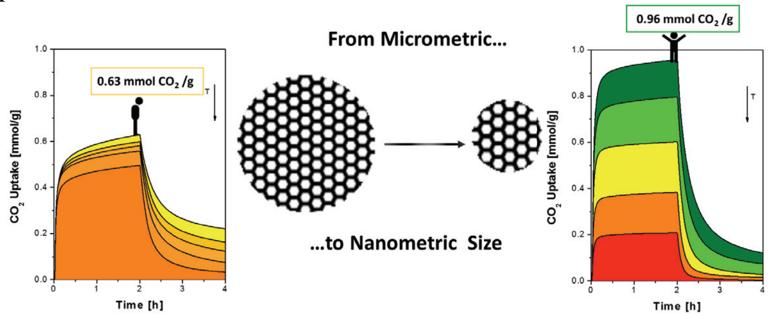

Figure 1: TGA analysis of CO_2 adsorbed on micrometric and nanometric MCM-41 samples grafted with PAPTS.

[1] G. Gatti, et al. PCCP, 19 (2017), 14114-14128.
[2] G.Gatti et al. PCCP, 19 (2017), 29449-29460.

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Unravelling the Effects of the Adsorbent Porosity on the CO_2 Adsorption Process

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In the present study, the CO_2 adsorption properties of an organo-modified Stöber silica were evaluated for the first time in comparison with a mesoporous material based on MCM-41 silica. The use of Stöber silica as support is interesting for real technological applications mainly due to economic factors. In fact, during the synthesis of the Stöber silica, no expensive templating agents are used, as occurs for the preparation of ordered mesoporous silicas. Furthermore, a direct comparison between the organo-modified Stöber sample with an ordered porous material (based on MCM-41 silica) allowed to evaluate the effect of the porosity on the CO_2 adsorption properties. In order to make both materials reactive toward CO_2, they were functionalized by introducing amino groups via grafting of 3-[2-(2-aminoethyl)aminoethyl]aminopropyltrimethoxysilane (PAPTS). From the comparison, obtained by coupling FTIR and SS-NMR spectroscopies, it was highlighted that a greater amount of physisorbed CO_2 is observable for the Stöber-based material with respect to the MCM-41-based one, due to the higher pore accessibility (inter-particle porosity). Viceversa, the chemisorbed component is present in greater amount in the ordered mesoporous sample, due to the higher amount of PAPTS chains grafted in this material. Finally a quantitative determination of CO_2 adsorption capacity, performed by TGA and Zero Length Column techniques, revealed that the mesoporous materials are more efficient if compared to the Stöber-based one (adsorption capacity values of 0.49 and 0.58 mol/kg for Stöber-based and mesoporous samples respectively). However, since the difference in the adsorption capacity is not large (about 15%) and the Stöber-based sample is considerably cheaper, the non-porous sample should be considered a very interesting adsorbent material for carbon dioxide capture applications.

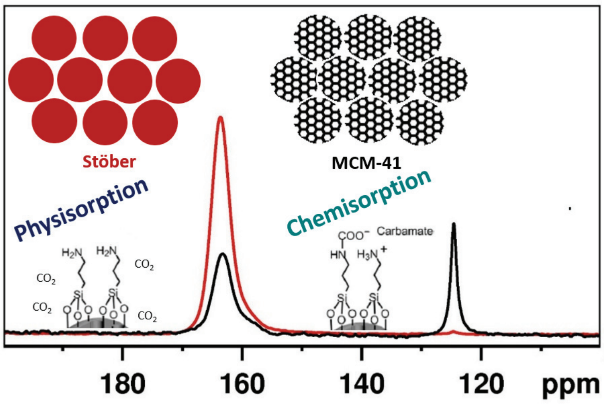

Figure 1: SS-NMR spectra of 60 mbar of $^{13}CO_2$ adsorbed on Stöber and MCM-41 samples grafted with PAPTS.

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Synthesis of Covalent Organic Frameworks Containing Structural Linkers with Donor-Acceptor Characteristics and Investigation of Their Optoelectronic and Energy Storage Properties

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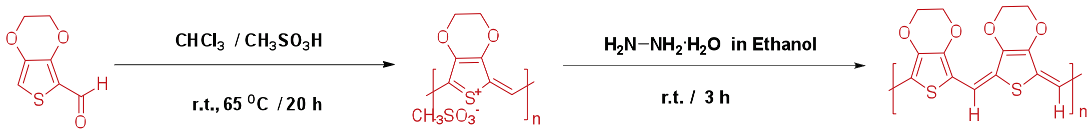
Covalent organic frameworks (COFs) are a class of crystalline organic porous materials.[1,2] While COFs are generally studied for gas storage and catalysis, their optoelectronic and energy storage properties have been explored only recently.[3,4] For example, thiophene-based COFs, synthesized starting from highly conjugated linkers, have shown semiconducting and luminescent properties.[5]

This research aims at synthesizing new conductive COFs based on thiophene moieties. Our target structure is composed by a tritopic linker (i.e. : tris(4-thiophene-2-yl)phenyl)amine) and a series of ditopic linker (i.e. :thiophene-2,5-dicarboxaldehyde and derivatives) linked through a condensation reaction that will define a methine bridge. These materials, containing modulated donor-acceptor moieties, can offer different optoelectronic properties respect to the previous COFs based on boronate anhydride, boronate ester, borosilicate, nitrile, imine, hydrazone and anionic silicate bridges. Poly(EDOT-methine) have been also synthesised (Scheme 1) as reference conducting material based on a thienylmethine bridge.



Scheme 1: Reaction of Poly(EDOT-methine)

[1] San-Yuan Ding and Wei Wang, Chem. Soc. Rev., 2013, 42, 548-568.
[2] Peter J. Waller, Felipe Ga□ndara, and Omar M. Yaghi, Acc. Chem. Res. 2015, 48, 3053□3063.
[3] Mirjam Dogru and Thomas Bein, Chem. Commun., 2014, 50, 5531-5546.
[4] Long Hao, Jing Ning, Bin Luo, Bin Wang, Yunbo Zhang, Zhihong Tang, Junhe Yang, Arne Thomas, and Linjie Zhi, J. Am. Chem. Soc. 2015, 137, 219□225
[5] Mirjam Dogru, Matthias Handloser, Florian Auras, Thomas Kunz, Dana Medina, Achim Hartschuh, Paul Knochel, and Thomas Bein, Angew. Chem. 2013, 125, 2992 –2996.

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IX Giornate Italo-Francesi di Chimica
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Computer simulations of interstellar silicates: energetic and spectroscopic characterization of forsterite nanoparticle models

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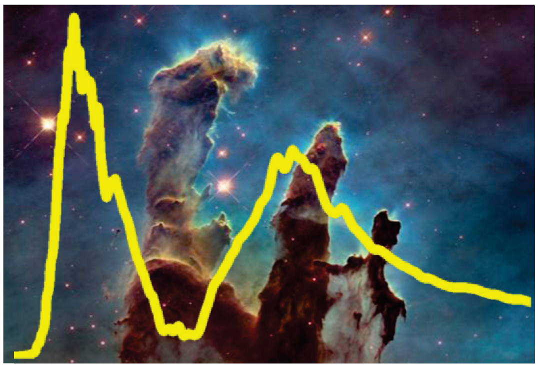
The observation of the interstellar medium (ISM) by means of rotational spectroscopic techniques has revealed, according to the Cologne database [1], the presence of more than 200 molecular species. Further observations in the IR region of the electromagnetic spectrum have also revealed the presence of solid nano-particles (NPs) in form of dust grains. These particles belong to two different classes, namely C-based (carbonaceous) and Si-based (silicates). Among silicates, NPs with an olivine-like stoichiometry ($Mg_{2x}Fe_{2-2x}SiO_4$, $0 \leq x \leq 1$) represent one of the main components. In colder regions, pure Mg_2SiO_4 (forsterite, Fo) NPs are expected to be predominant over Fe-bearing ones [2]. The presence of these NPs is fundamental since they are expected to have a surface catalytic activity that would allow the formation of the large variety of molecules that have been observed: for example, it has been suggested that H_2, the most abundant molecule in the ISM, could form on selected Fo surfaces [3]. While the chemical composition of these silicates can be easily inferred from their IR spectra, their actual physical properties cannot be properly derived from direct observations. For example, interstellar silicates are usually assumed to be highly amorphous because of the broadness of both the Si–O stretching (~ 10 μm) and O–Si–O bending (~ 18 μm) features [2]. However, it has been reported that in some environments, the percentage of crystalline NPs could become predominant over the amorphous one [4]. In order to shed some light on the important issue of the actual composition of interstellar silicates, we built, thanks to computer simulation techniques, two different sets of forsterite NPs that could represent reliable models for amorphous- and crystalline-like dust grains. We fully characterized these models both from an energetic and spectroscopic point of view. The full IR spectra that we were able to collect suggest that, at least for nanometer-sized particles, crystalline and amorphous forsterite NPs cannot be properly distinguished only from their vibrational features. We hope that our models could represent the basis of further works dealing with the computer simulation of surface-catalyzed formation routes for molecular species of astrochemical interest.



Simulated full IR spectrum for a selected forsterite nano-particle.

[1] Endres, C. P.; Schlemmer, S.; Schilke, P.; Stutzki, J.; Müller, H. S. P.; *J. Mol. Spectrosc*. **2016**, *327*, 95−104.
[2] Henning T.; *Annu. Rev. Astro. Astrophys*., **2010**, *48*, 21–46.
[3] Navarro-Ruiz, J.; Sodupe, M.; Ugliengo, P.; Rimola, A.; *Phys. Chem. Chem. Phys*., **2014**, *16*, 17447–17457
[4] Li, A.; Draine, B. T.; *Astrophys. J.,* **2001**, *550*, L213–L217.

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Antitubercular activity of novel 3-(2-oxo-2-arylethylidene)-3,4-dihydro-2*H*-benzo[b][1,4]oxazin-2-ones derivatives

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Few years ago, Li et al.[1] have identified several 1,4-benzoxazine derivatives, targeting MenB (1,4-dihydroxy-2-naphtoyl-CoA synthase), endowed with high antibacterial activity against *Mycobacterium tuberculosis* $H_{37}Rv$ with the best MIC value of 0.6 µg/ml. Menaquinone is one of the essential components of the electron transport chain in many pathogens and consequently, enzymes in its biosynthesis pathway are potential drug targets for the development of novel antibacterial agents. The authors also investigated the 2-chlorophenyl substitution in the side chain of the benzoxazine core and they found a promising antitubercular activity of their derivatives (3.1 µg/ml), but the lack of MenB inhibition. In order to deepen the SAR and the enzymatic inhibition, we synthesized and biological evaluated different aryl substitution in the side chain of the benzoxazin-2-one scaffold.

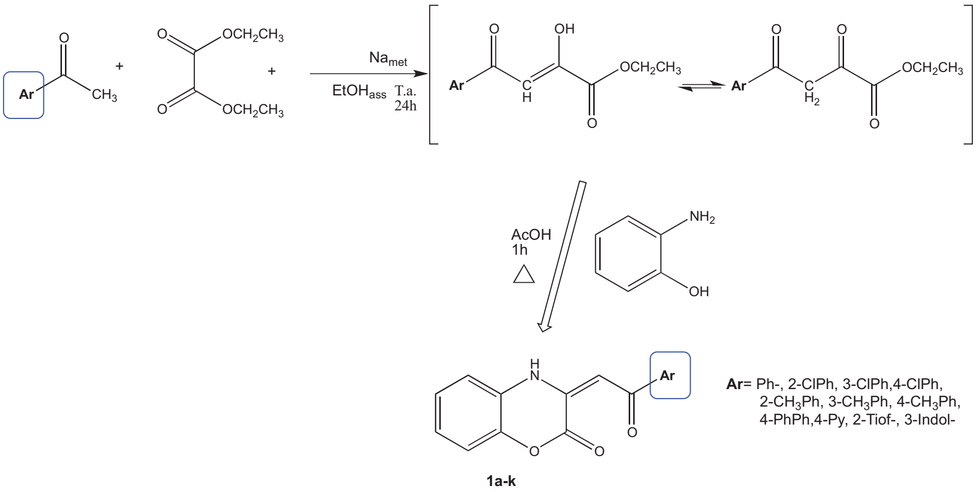

Figure 1: Synthetic route for the 3-(2-aryl-2-oxoethylidene)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-ones

The results obtained showed MIC values ranging from 2 to 4 µg/ml with the best data for the heterocyclic 2-thiophen-2-yl and 2-indol-3-yl derivatives. Cytotoxicity studies towards mammalian cells (Vero) revealed a safe cytotoxic profile with CC_{50} values ranging from 125 up to 500 µg/ml and a selectivity index (S.I.) of 250.

[1] 1. Li, X.; Liu, N.; Zang, H.; Knudson, S.E.; Slayden, R.A.; Tonge, P.J. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 6306-6309.

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New hybrid derivatives of 3,4-dihydroquinolin-2(1*H*)-one and 5-phenyl-1,3,4-oxadiazol-2(3*H*)-one scaffolds as sigma-2 ligands

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Continuing our efforts in the sigma receptor field, and encouraged from the recent results obtained in the discovery of σ2 protein identified as TMEM97 [1], we planned to synthesized, and biological evaluate, some novel hybrids as a combination of two distinct scaffolds, that appear in some ligands gifted with both σ1 and σ2 receptor affinity [2,3], with others (like 3,4-dimethoxytetraisoquinoline, 3H-spiro[isobenzofuran-1,4-piperidine], etc.) present in many known σ2 selective receptor ligands. The moieties are linked through a butyl spacer and the synthesis is depicted in the figure 1.

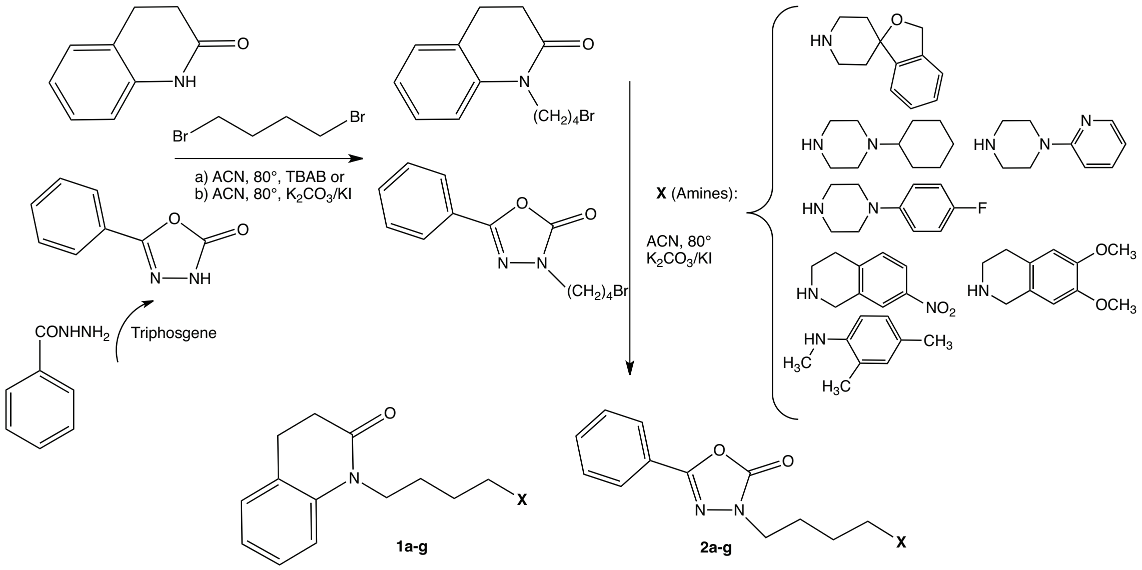

Figure 1: Synthesis of new σ2 hybrids

The aim of this research is to develop new compounds gifted with a selective σ2 profile and, in this regard, our molecules are currently under biological investigation also for their potential cytotoxic effect towards different tumor cell lines.

[1] Alon, A.; Schmidt, H.R.; Wood, M.D.; Sahn, J.J.; Martin, S.F.; Kruse, A.C. Identification of the gene that codes for the σ2 receptor. *Proc. Nat. Ac. Sc.*, **2017**, *27*, 7160-7165.
[2] Zampieri, D.; Fermeglia, M.; Vio, L.; Pricl, S.; Wu□nsch, B.; Schepmann, D.; Romano, M.; Mamolo, M.G.; Laurini, E. Computer-assisted design, synthesis, binding and cytotoxicity assessments of new 1-(4-(aryl(methyl)amino)butyl)-heterocyclic sigma 1 ligands. *Eur. J. Med. Chem.* **2016**, *121*, 712-726.

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Probing cysteine and water molecules in redox proteins by FTIR difference spectroscopy

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Cytochromes and ferredoxins are excellent models of redox proteins involved in the bioenergetics of the cell. Two c-type cytochromes, Tll0287 [1] and PsbV2 [2] with peculiar Cys/His axial coordination, and two ferredoxins, Fd1 and Fd2 characterized by the [Fe_2S_2] cofactor coordinated by 4 cysteines, have been studied. Although their structures are known, their function does not. We wonder which factors determine the regulation of their midpoint potential and what task they have in the energetic exchanges of the cell and particularly the role of cysteine as ligand to the iron in the control of the midpoint potential and the role of the overall proteic environment in its fine-tuning.
With this aim, electrochemistry coupled with UV-visible and infrared spectroscopies [3] make feasible the correlation between structural and electrochemical properties of the metalloproteins. Notably, FTIR difference spectroscopy is a rare technique to investigate the amino acids sensitive to the oxidation state of the cofactor and how their protonation state is related to it. When extended to the far infrared region (670-100 cm^{-1}), FTIR difference spectroscopy coupled with electrochemistry allows direct investigation of metal-ligand interactions [4].
For cytochromes with Cys/His axial coordination we have identified characteristic IR signatures between 400 and 280 cm^{-1} and, in the case of PsbV2, the presence of a redox and pH sensitive water molecule involved in the activity of the cofactor.
On the other hand, in ferredoxins we have identified the presence of a protonated cysteine depending on the type of Fd so that a correlation between the midpoint potential and proteic environment of the cluster is pointed out.

[1] Motomura, T. et al., *J. Biol. Chem.* 292, 9599 – 9612 (2017)
[2] Kerfeld, C. A. et al., *Plant Cell Physiol* 44, 697 – 706 (2003)
[3] Dalla Bernardina, S. et al., *Vibrational Spectroscopy* 75, 154 – 161 (2014)
[4] Berthomieu, C., et al., *Biopolymers* 82, 363 – 367 (2006)

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