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Supramolecular Chemistry 2022

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ORGANIZATORI

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Pod pokroviteljstvom Hrvatskog kemijskog društva

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Zagreb, 2022.

PROGRAM

8:00 – 9:00	Registracija sudionika
9:00 – 9:30	Otvaranje konferencije Goran Pichler , tajnik Razreda za matematičke, fizičke i kemijske znanosti HAZU David Matthew Smith , ravnatelj Instituta Ruđer Bošković Mirko Planinić , dekan Prirodoslovno-matematičkog fakulteta Mladen Žinić , predsjednik Odbora za kemiju HAZU Leo Frkanec , Institut Ruđer Bošković Predsjedavajući sekcije: Dražen Vikić-Topić
9:30 – 10:00	Ilija Čorić (University of Zurich): <i>Site-selective C–H arylation of arenes ortho to small alkyl groups</i>
10:00 – 10:30	Nives Galić (PMF): <i>Praziquantel/Cyclodextrin Inclusion Complexes</i>
10:30 – 11:00	Stanka za kavu Predsjedavajući sekcije: Vladislav Tomišić
11:00 – 11:30	Vitomir Šunjić (HAZU): <i>Supramolekulski katalitički kompleks [Mo7O24-6 x aldoza] u „kombi procesu“ na putu prema alditolima</i>
11:30 – 12:00	Ana Budimir (FBF): <i>Host-Guest Interaction Between Nabumetone and Cucurbit[7]uril in Aqueous Solutions</i>
12:00 – 12:30	Branimir Bertoša (PMF): <i>3D-QSAR study of activity of a group of quinolone compounds</i>
12:30 – 13:30	Stanka za ručak Predsjedavajući sekcije: Leo Frkanec
13:30 – 14:00	Tomica Hrenar (PMF): <i>Machine Learning Determination of Hidden Correlations in Big Data Sets</i>
14:00 – 14:30	Nadica Ivošević DeNardis (IRB): <i>Marine-Bioinspired Self-assembled Vesicles as Potential Drug Carriers</i>
14:30 – 14:45	Antonija Ožegović (IRB): <i>Molekulski oblik i mikrosegregacija – pokretači mezogenih svojstava</i>
14:45 – 15:00	Milenko Korica (Sveučilište J. J. Strossmayera): <i>Anion influence on crystal structure in coordinated silver(I) complexes with N₂O₂ Schiff base macrocycle</i>
15:00 – 15:30	Stanka za kavu Predsjedavajući sekcije: Dominik Cinčić
15:30 – 16:00	Krešimir Molčanov (IRB): <i>Strong π-Hole Interactions Involving Charge Transfer</i>
16:00 – 16:15	Barbara Panić (PMF): <i>Self-Assembly, Dimerization and Polymerization of Aromatic C-Nitroso Derivatives on Gold Surface</i>
16:15 – 16:30	Lea Čolakić (PMF): <i>Electrical Properties of Flexible Coordination Compounds of Copper(II) Halides with 3-nitropyridine</i>
15:00 – 16:45	Posterska sekcija (predsjedavajući sekcije: Vladislav Tomišić, Leo Frkanec)
16:45 – 17:00	Zatvaranje konferencije Leo Frkanec, Mladen Žinić

POZVANA PREDAVANJA

Ilija Čorić (University of Zurich): *Site-selective C–H arylation of arenes ortho to small alkyl groups*

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Vitomir Šunjić (HAZU): *Supramolekulski katalitički kompleks [Mo7O24-6 x aldoza]*

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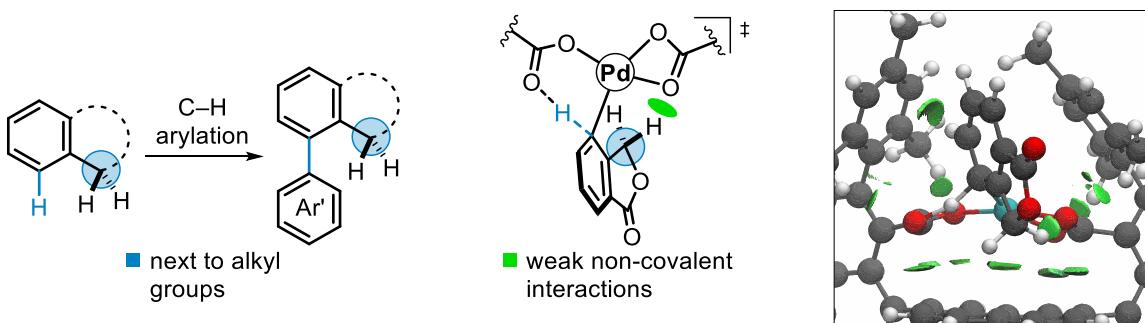
Site-selective C–H arylation of arenes ortho to small alkyl groups

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Direct transformation of C–H bonds to C–C bonds using transition metals such as palladium shows great promise for the synthesis of complex molecules and materials. However, the development of catalytic systems that offer high reactivity and control over site-selectivity is an outstanding challenge.^{[1],[2]} We have recently developed spatial anion control as a concept for the design of catalytic sites for C–H bond activation, thereby enabling nondirected C–H arylation^[3] of arenes at ambient temperature.^[4] In this presentation, our recent progress on the development of site-selective C–H arylation reactions will be described. In particular, the role of non-covalent interactions in the site-selective functionalization at uncommon positions next to alkyl substituents will be discussed.^[5]



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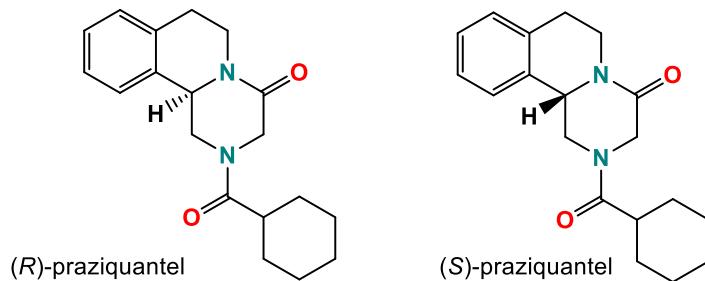
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- [3] L.-Y. Liu, J. X. Qiao, K.-S. Yeung, W. R. Ewing, J.-Q. Yu, *Angew. Chem. Int. Ed.* **2020**, *59*, 13831-13835.
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Praziquantel/Cyclodextrin Inclusion Complexes

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Praziquantel (PZQ) is an anthelmintic drug used for therapy and prevention of schistosomiasis.¹ The drug is administrated as a racemate, where *R*-enantiomer is eutomer, while *S*-enantiomer is responsible for extremely bitter taste of the drug. PZQ has aqueous solubility of 0.04 mg/mL, and is classified as type II drug according to the Biopharmaceutical Classification System (BCS). Bitter taste and limited solubility of the drug can be efficiently solved by inclusion complexation with both natural and chemically modified cyclodextrins (CDs).^{1,2}



A comprehensive investigation of PZQ complexes with β -cyclodextrin (β -CD) and its hydroxypropyl (HP β CD), sulfobutylether (SBE β CD), and randomly methylated (RM β CD) derivatives was conducted by means of UV-Vis spectroscopy, spectrofluorimetry, NMR spectroscopy, LC-HRMS/MS and molecular modelling.² Among four CDs tested, the RM β CD and the SBE β CD resulted in the highest increase in PZQ solubility (approximately 16-fold). The formation of 1:1 inclusion complexes was confirmed by HRMS, NMR and molecular modelling. The influence of CDs on PZQ stability was investigated in solution (HCl, NaOH, H₂O₂) and in the solid state (accelerated degradation, photostability) by UPLC-DAD/MS. CD complexation promoted new degradation pathways of the drug. In addition to three already known PZQ degradants, seven new degradation products were identified (*m/z* 148, 215, 217, 301, 327, 343, 378) and their structures were proposed based on HRMS/MS data.² Complexes in the solid state were prepared by grinding and analyzed by standard methods (differential scanning calorimetry (DSC), X-ray power diffraction (XRPD), infrared spectroscopy (FT-IR)).¹

¹ M. Cugovčan, J. Jablan, J. Lovrić, D. Cinčić, N. Galić, M. Jug, Biopharmaceutical characterization of praziquantel cocrystals and cyclodextrin complexes prepared by grinding, *J. Pharm. Biomed. Anal.* **2017**, 137 42–53.

² T. Kezele Špehar, M. Pocnić, D. Klarić, B. Bertoša, A. Čikoš, M. Jug, J. Padovan, S. Dragojević, N. Galić, Investigation of praziquantel/cyclodextrin inclusion complexation by NMR and LC-HRMS/MS: mechanism, solubility, chemical stability and degradation products, *Mol. Pharm.* **2021**, 18 4210–4223.

Supramolekulska katalitička kompleks $[\text{Mo}_7\text{O}_{24}^{4-} \times \text{aldoza}]$

u „kombi procesu“ na putu prema alditolima

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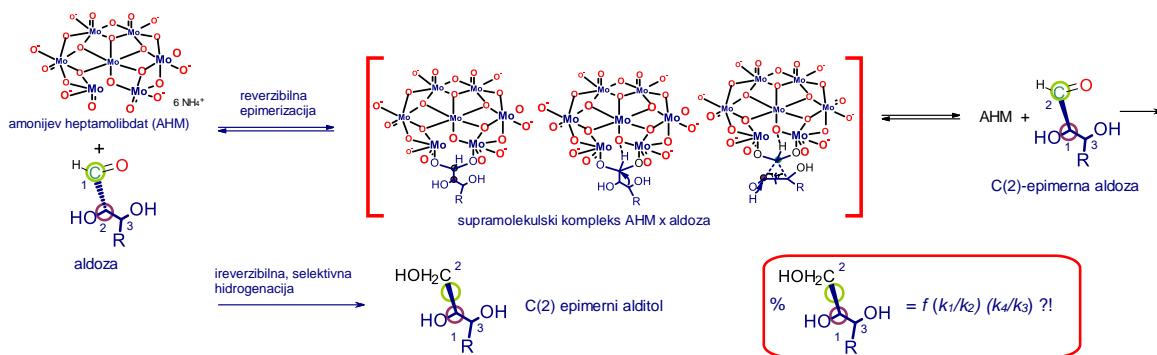
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Epimerizacija aldoza inverzijom konfiguracije na C(2) atomu katalizirana je amonijevim heptamolibdatom (AHM).¹ Katalitički proces uključuje migraciju C(1)-C(2) atoma, odn. specifično pregradnju ugljikohidratnog skeleta unutar katalitičkog, supramolekulskog kompleksa [polioksomolibdat anion x aldoza], Slika 1.

Ova reakcija pruža mogućnost dvokoračnog „kombi procesa“, transformaciju lako dostupnih aldoza, na pr. D-glukoze, D-ksiloze ili D-arabinoze, zatim selektivnu redukciju C(2) epimerne aldoze, D-manoze, D-liksoze ili D-riboze u alditole visoke dodane vrijednosti, D-manitol, D-liksitol ili D-ribitol.

Katalitička epimerizacija ravnotežni je proces, i rezultira smjesom C(2) epimernih aldoza, na pr. za D-Glc/D-Man ravnotežni omjer je ca. 65-70/35-30, za D-Ksl/D-Liks ca. 50:50, za D-Arab/Rib ca. 40/60. Selektivna hidrogenacija C(2) epimernih aldoza u alditole visoke dodane vrijednosti moguća je na osnovu Le Chatelierovog principa; „kada se sustav u ravnoteži podvrgne promjeni koncentracije (temperature ili tlaka) sustav se prilagođava tako da se suprotstavlja tom efektu uspostavom nove ravnoteže“.

Da bi se postigla visoko selektivna hidrogenacija jedne aldoze u poželjni, C(2)-epimerni alditol predviđeno je modeliranje kinetike za oba reakcijska koraka, prvog ravnotežnog i drugog nepovratnog procesa, Slika 1.



Slika 1. Ravnotežna epimerizacija i ireverzibilna, selektivna hidrogenacija, sastavnice „kombi procesa“.

1. V. Šunjić, K. Kovačević, Stereochemistry of Skeletal Rearrangement of Aldoses, u, „Organic Stereochemistry in Croatia and Prelog School“, izd. Hrvatska akademija znanosti i umjetnosti, Hrvatsko hemijsko društvo, Sveučilište u Zagrebu, Fakultet kemijskog inženjerstva i tehnologije, 2000, str. 50-55.

Host-Guest Interaction Between Nabumetone and Cucurbit[7]uril in Aqueous Solutions

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Despite the rapid developments in modern medicine, the pharmaceutical field still faces many challenges. The biggest of these is that the majority of existing drugs belong to the class II drugs (low solubility, high permeability) according to the Biopharmaceutics Classification System (BCS). The encapsulation of drug molecules within macrocyclic molecular containers, using supramolecular noncovalent interactions in aqueous solution, is a method of improving their bioavailability and bioactivity.

Cucurbit[n]urils ($\text{CB}[n] = 5\text{-}8, 10, 13\text{-}15$) are a family of macrocyclic molecules with remarkable host-guest chemistry in water.¹ They consist of n glycoluril units bridged by $2n$ methylene units forming a macrocycle with a hydrophobic cavity accessible through two identical portals (Figure 1). CBs have been shown to form host-guest complexes with a variety of organic and inorganic small molecules. Encapsulation is favored by hydrophobic effects within the cucurbituril cavity and further stabilized by hydrogen bonding or ion-dipole interactions with the cucurbituril portal. Specific advantages of using CBs for encapsulation of drug molecules include improved stability and solubility of the drug, controlled or triggered release, induction of pKa shifts of the drug, and use as an antidote. The $\text{CB}[7]$ (Figure 1) has received the most attention of the $\text{CB}[n]$ family due to its superior solubility in water.

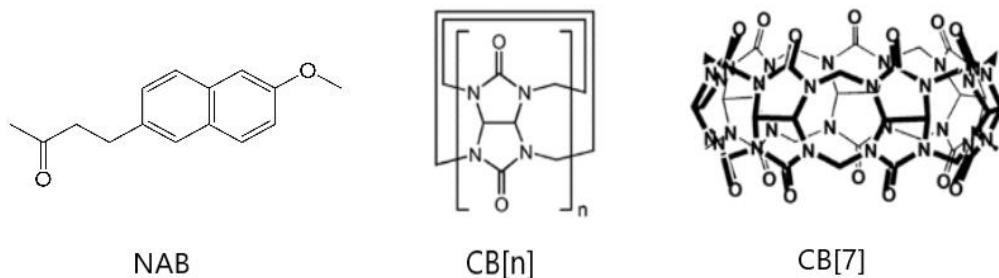


Figure 1. Structures of nabumetone, cucurbit[n]urils and cucurbit[7]uril.

Nabumetone, (NAB, Figure 1) is a nonsteroidal anti-inflammatory prodrug with extremely low water solubility, which is the reason for its limited bioavailability. It is used to treat pain and inflammation associated with rheumatoid arthritis and osteoarthritis.² In this presentation, our experimental results of complexation of NAB with $\text{CB}[7]$ in aqueous solution will be presented.

Reference

¹ S. J. Barrow, S. Kasera, M. J. Rowland, J. del Barrio, O. A. Scherman, *Chem. Rev.* **2015**, *115*, 12320–12406.

² T. Hedner, O. Samulessen, P. Währborg, H. Wadenwik, K.-A. Ung, A. Ekbom, *Drugs* **2004**, *64* 2315–2343.

3D-QSAR study of activity of a group of quinolone compounds

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Biological activity of small organic compounds is usually achieved through their interactions with a target in a cell. A target is usually biological macromolecule, most often protein or DNA or RNA. The interaction between small organic molecule and target triggers a cascade of reactions that lead to biological response. However, the activity of a small molecule depends not only to its adequate interaction with target, but also to its ADME properties that enable a molecule to reach the target in a cell. Computational studies of such systems are limited by identification of the target in the cell as well as by availability the 3D structure of the target. In addition, most computational chemistry methods do not take into account ADME properties that can have significant influence on activity of studied small molecules. One of computational methods that is not limited by the identification of the target nor by the availability of its 3D structure is QSAR modelling. QSAR stands for Quantitative Structure – Activity Relationship. It is an approach that aims to develop mathematical model that provides quantitative description of the relationship between biological activity and structural features of studied group of compounds. Depending on the approach, QSAR models might take into account, at least partially, also ADME properties of studied compounds. In the lecture, one of the 3D-QSAR approaches will be presented and its application to study antiproliferative activity of a group naturally occurring quinolones will be shown.

Machine Learning Determination of Hidden Correlations in Big Data Sets

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In today's research, it is easy to collect massive data sets. Among these data, there is often a linear dependence, which is reflected as an association between the variables. However, exploring these datasets and uncovering hidden correlations is far from trivial, starting from proper variable selection, missing or misrepresented data, data space coverage, using the correct setting in the machine learning method, the right type of software, adequate hardware, etc.

Comprehensive and highly efficient machine learning (ML) technique¹ for the investigation of hidden correlations present in the big data set (Fig. 1) will be presented and applied to various types of chemical problems. Dimension reduction is the first step followed by multivariate linear regression using singular value decomposition to calculate the coefficient matrix \mathbf{B} . Each possible regression model will be built and thoroughly validated by *leave-one-out cross-validation* (LOO-CV). Models will be inspected, and the most optimal representations will be selected based on the adjusted and predicted R^2 values, LOO-CV mean squared error, as well as the number of variables in the models. The final results represent all possible correlations among the big data set that can be used for conceptual inference or numerical prediction (extra- or interpolation).

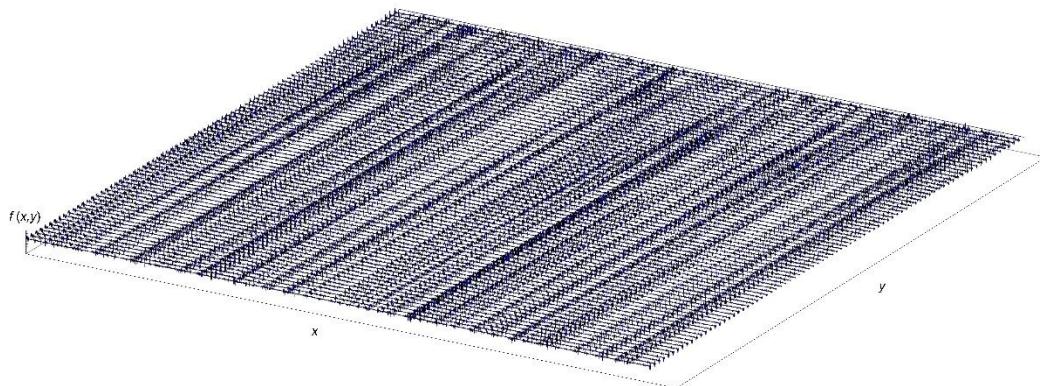


Figure 1. Investigated big data set and the existing variations.

¹T. Hrenar, **moonee**, Code for Manipulation and Analysis of Multi- and Univariate Big Data, rev. 0.68268, 2022.

Marine-Bioinspired Self-assembled Vesicles as Potential Drug Carriers

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The development of drug carriers that mimic natural biological membranes is of great biotechnological interest. Since lipid-based, inorganic, and polymeric drug carriers do not approach the complexity of the natural membrane, numerous studies in the last decade have focused on the development of cell-based drug carriers.^{1,2} Our research focuses on marine microalgae as important primary producers that form the basis of the aquatic food web. In addition to their ecological importance, algae are widely used as food, pharmacological agents, and energy sources, and yet their potential has not been adequately explored. Since it is a sustainable and environmentally friendly material, our interest lies in the development of drug carriers from microalgae. When soft microalgae are subjected to hypoosmotic shock, the cells burst, intracellular material is released, and the remaining membrane fragments self-assemble due to various non-covalent interactions to form spontaneously reconstructed membrane vesicles.³ This presentation will provide insight into the morphology, properties, composition, and ability of the vesicles to encapsulate a model drug. This unique membrane system could open a new avenue for the use of marine-bioinspired materials to develop a new generation of supramolecular self-assembled drug delivery systems, thus connecting the ocean to human health.

Acknowledgments

This work is supported by the Croatian Science Foundation Project “From algal cell surface properties to stress markers for aquatic ecosystems” (IP-2018-01-5840) and International Visegrad Grant “Research network VF-Croatia for the development of novel drug carriers from algae”(No. 22220115).

References

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- ² I. K. Herrmann, M.J.A. Wood, G. Fuhrmann, *Nat. Nanotechnol.* **2021**, 16, 748-759.
- ³ N. Ivošević DeNardis, G. Pletikapić, R. Frkanec, L. Horvat, P.T. Vernier, *Bioelectrochemistry*, **2020**, 134, 107524.

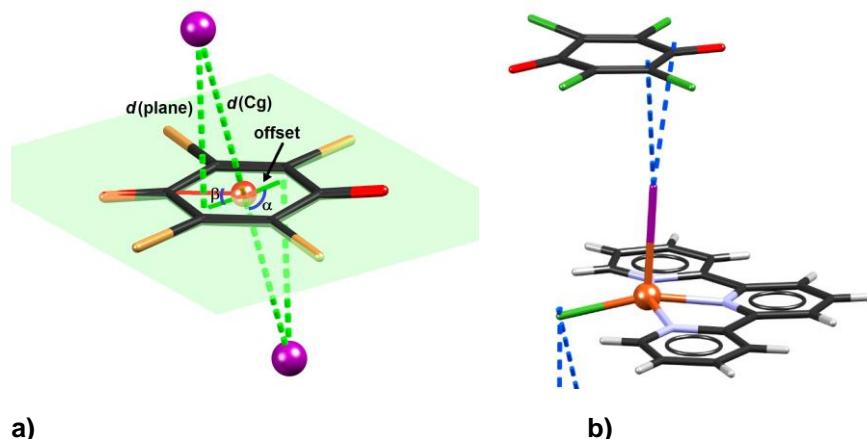
Strong π -Hole Interactions Involving Charge Transfer

Krešimir Molčanov,^{*a} Valentina Milašinović,^a Lidija Molčanov,^a Vedran Vuković,^b Anna Krawczuk,^c and Christoph Hennig^d

^a Ruđer Bošković Institute, Bijenička 54, Zagreb, Croatia. ^b Universität Regensburg, Universitätsstrasse 31, Regensburg, Germany. ^c Universität Göttingen, Tammanstrasse 4 Institution, Göttingen, Germany. ^d European Synchrotron Radiation Facility, 71 Avenue des Martyrs, Grenoble, France
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Unusually strong π -hole interactions with short distances between an iodide anion and a quinoid ring were discovered by us recently.^{1,2} These compounds typically comprise sandwich-like groups $\text{I}^- \cdots \text{quinone} \cdots \text{I}^-$ (Fig. 1a). Black colour of the crystals indicates charge transfer from the iodide to the electron-depleted quinone (which therefore has a partial radical character). A co crystal of 3-chloro-*N*-methylpyridinium iodide with tetrabromoquinone (3-Cl-*N*-MePy-I·Br₄Q) which involves a sandwich-like $\text{I}^- \cdots \text{quinone} \cdots \text{I}^-$ moiety was chosen as a model system for a detailed quantum crystallographic study (combining X-ray charge density with quantum chemical modelling). The π -hole interaction involves an $n \rightarrow \pi^*$ charge transfer, so the quinoid ring has a partial negative charge (estimated to 0.08 – 0.11 e) and a partial radical character. X-ray charge density study revealed two symmetry-independent bonding critical points between the iodide and carbon atoms of the ring with maximum electron density of 0.065 e Å⁻³, which were reproduced by quantum chemical modelling. Energy of the interaction is estimated to -13 kcal mol⁻¹, which is comparable to hydrogen bonding; it is dominantly of electrostatic nature, with a considerable dispersion component.

This π -hole interaction was also found in co-crystals of [Cu(phen)XCl] (phen = 1,10-phenanthroline; X = Br, I) with tetrachloro- and tetrabromoquinone (Fig. 1b). Due to the close contact of X and the quinoid ring, the Cu-X bond is elongated by as much as 0.18 Å.



¹ K. Molčanov, G. Mali, J. Grdadolnik, J. Stare, V. Stilinović, B. Kojić-Prodić, *Cryst. Growth Des.*, **2018**, 18, 5182-5193.

² V. Milašinović, K. Molčanov, *CrystEngComm*, **2021**, 23, 8209-8214.

KRATKA USMENA PRIOPĆENJA

Antonija Ožegović (IRB): *Molekulski oblik i mikrosegregacija – pokretači mezogenih svojstava*

Milenko Korica (Sveučilište J. J. Strossmayera): *Anion influence on crystal structure in coordinated silver(I) complexes with N₂O₂ Schiff base macrocycle*

Barbara Panić (PMF): *Self-Assembly, Dimerization and Polymerization of Aromatic C-Nitroso Derivatives on Gold Surface*

Lea Čolakić (PMF): *Electrical Properties of Flexible Coordination Compounds of Copper(II) Halides with 3-nitropiridine*

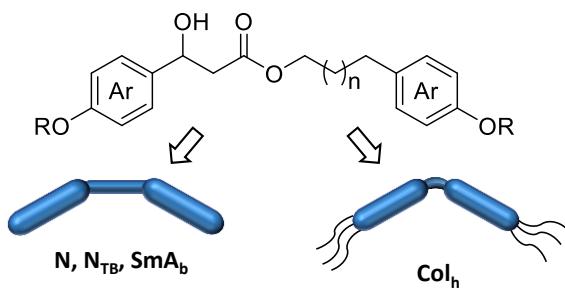
Molekulska oblik i mikrosegregacija – pokretači mezogenih svojstava

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Tekući kristali (LC), koji su najpoznatiji po svojoj primjeni u zaslonima, predstavljaju jedinstveno stanje materije karakterizirano mobilnošću i redom na molekulskoj i supramolekulskoj razini, a pojavljuje se kao međufaza između trodimenzionalno uređene krutine i potpuno neuređene tekućine. Molekule u LC fazi posjeduju orientacijsko uređenje, a u nekim slučajevima i pozicijsko uređenje pa tako razlikujemo nematičke (N) i smektičke (Sm) faze.¹ Ključnu ulogu u formiranju LC faza imaju oblik i međumolekulske interakcije, a nedavno je potvrđena i spontano kiralna faza (N_{TB}) za koju je zaslužan svijeni oblik molekula.²

Naše istraživanje je fokusirano na određivanje utjecaja strukture na mezogena svojstva dimera svijene geometrije (slika 1). LC dimeri sastoje se od dvije mezogene jedinice povezane fleksibilnom razmaknicom, a svijena geometrija je posljedica neparnog broja atoma u razmaknici. Dosadašnji rezultati pokazuju kako male promjene u strukturi rezultiraju promjenom u topologiji molekule i jačini međumolekulske interakcije. Time se posljedično utječe na samoorganizaciju molekula unutar mezofaze. Zbog prisutnosti terciarne hidroksilne skupine u razmaknici omogućeno je proučavanje racemičnih i enantiomerno čistih formi što daje perspektivu dalnjim istraživanjima, a posebno utjecaju intrinzične kiralnosti na samoorganizaciju pojedinih mezofaza. To može doprinijeti razvoju novih organskih materijala i pojašnjenu spontanu kiralnost prisutnu u mnogim živim sustavima.



Slika 1. Generalna struktura sintetiziranih dimera te faze dobivene promatranjem dimera svinute geometrije i polikatenarnih dimera.

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Zavale

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Anion influence on crystal structure in coordinated silver(I) complexes with N₂O₂ Schiff base macrocycle

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Metal ion can be bound inside (*endo*) or outside (*exo*) macrocyclic cavity depending upon the flexibility of a molecule, cavity size (interdonor distance), and design of macrocyclic ligand [1]. As we have found in our previous investigations some level of ligand preorganization for the preparation of *exo*-coordinated species can be achieved by the presence of a rigid C=N bond in close proximity to an aromatic system [2]. *Exo*-coordinated macrocyclic species are quite uncommon, but these compounds could become very attractive due to remarkable structural diversity and potential formation of 3D porous structures. *Exo*-coordinated complex compounds with macrocycles are usually prepared by the substitution of stronger ligand in existing *endo*-macrocyclic complex or by an employment of a specifically designed macrocyclic ligand. Anions can also be a major factor in the formation and overall topology of *exo*-coordinated macrocyclic species. It was found for silver(I) oxa-thia macrocyclic coordination compounds that choice of an anion can induce formation of *exo*-coordinated (presence of ClO₄⁻) and *endo*-coordinated complex (presence of PF₆⁻) [3].

Silver(I) complexes with aza-oxa macrocyclic Schiff bases L (L = 1,5-daza-2,4:7,8:16,17-tribenzo-9,15-dioxa-cyclooctadeca-1,5-dien) were prepared by the reaction of the corresponding macrocycle with four different silver salts (AgX; X=ClO₄, PF₆, SbF₆ and BF₄).

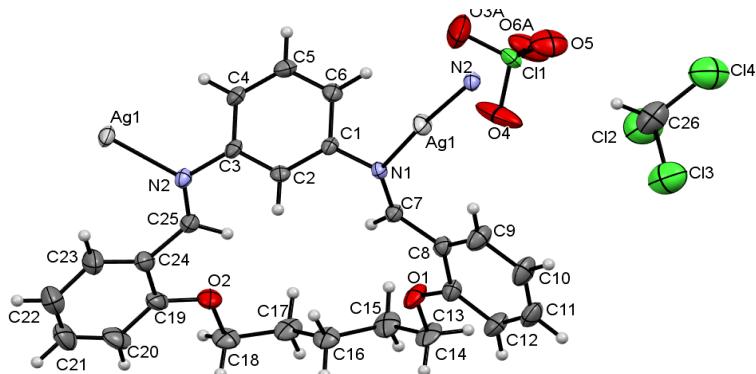


Figure 1. ORTEP plot of (AgLCIO₄)₂·CH₂Cl₂ with displacement ellipsoids of non-hydrogen atoms drawn at the 50 % probability level.

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Self-Assembly, Dimerization and Polymerization of Aromatic C-Nitroso Derivatives on Gold Surface

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Aromatic C-nitroso compounds are promising candidates for studying the adsorption of organic molecules on metal surfaces, their self-assembly into monolayers and multilayers, and for the design of new functional materials with potential application in areas such as molecular switches and organic semiconductors. Our recent studies have shown that aromatic C-nitroso compounds functionalized with a sulfur-containing group have a great tendency to bind to the gold (111) surface through a strong covalent S–Au bond and form self-assembled monolayers.^{1–3} Owing to the property of aromatic C-nitroso compounds to dimerize and polymerize to the corresponding azodioxides, it is also possible to design self-assembled bilayers (SABs) and multilayers by interactions of nitroso groups exposed at the monolayer interface and free nitroso groups in solution through azodioxy bonds.

In the present study, we first examined the experimental conditions for the design of monolayers and bilayers of nitrosobenzene derivatives with thiocyanate headgroup for adsorption on the gold (111) surface. The growth of monolayers and bilayers was studied at different solution concentrations and adsorption times by using ellipsometry, atomic force microscopy (AFM) and scanning tunneling microscopy (STM). It was found that a higher solution concentration and longer adsorption times result in the formation of more ordered adlayers and an increased tendency towards bilayers. The obtained results were then used for the targeted preparation of monolayers with exposed nitroso groups which were employed as initiation sites for the formation of azodioxy multilayers by interactions with aromatic dinitroso derivatives. Various aromatic dinitroso derivatives and different adsorption times were used to examine the influence of structural and experimental parameters on the possible formation of azodioxy multilayers on the gold (111) surface. Morphological characteristics and thicknesses of the adlayers were investigated by atomic force microscopy (AFM) and ellipsometry, respectively, which indicated formation of azodioxy adlayers. This was strongly supported by nano-FTIR spectroscopy which enabled chemical identification of the adlayers at the nanoscale.

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Electrical Properties of Flexible Coordination Compounds of Copper(II) Halides with 3-nitropiridine

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The physical properties of crystalline substances depend not only on their molecular structure, but also on the arrangement of molecules in the solid state. Consequently, supramolecular interactions are recognized as one of the important parameters for tuning the physical properties of crystalline solids. Precisely for this reason, crystal engineering is experiencing its upswing because it provides insights into the understanding and control of intermolecular interactions with the aim for preparing crystalline substances with the desired supramolecular outcome and desired physical properties.¹ However, the brittleness and stiffness of the crystals have so far proved to be a limiting factor in their practical implementation. On other hand, the recent discovery of molecular crystals adaptable to external mechanical stimuli results in a significant shift towards considering these materials as potential candidates for application in advanced technologies.^{2,3} So far, mechanical flexibility has been reported for a significant number of organic molecular crystals, but mechanical properties of metal–organic crystalline solids have been much less explored and understood. Coordination polymers have proven as ideal models of metal–organic systems that result in flexible crystals.⁴

In order to improve our understanding on structure–function correlation in mechanically flexible crystalline coordination polymers, we have prepared needle-like crystals of coordination polymers of copper(II) halides with 3-nitropyridine. An external mechanical force was applied to the obtained needle-like crystals, whereby the type of mechanical response was determined and, at a later step, also quantified. The mechanical response of the crystal is correlated with the strength and directionality of the intermolecular interactions present in the crystal packings. In addition, electrical properties were studied using impedance spectroscopy, as the first step in a potential application of these flexible crystalline materials.

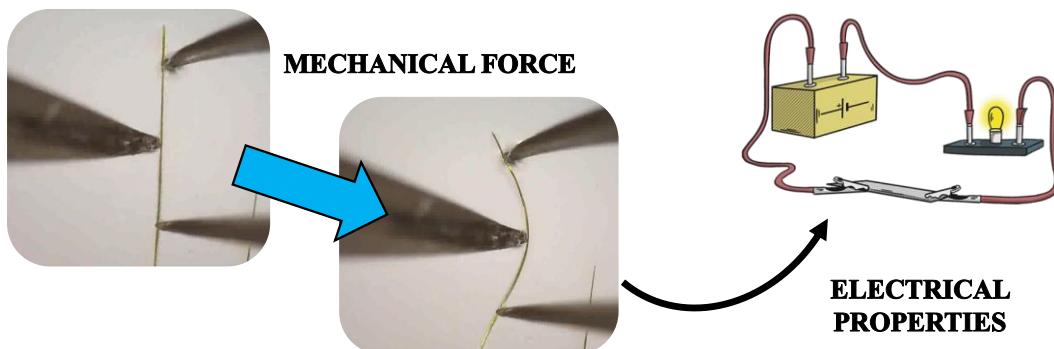


Figure 1. Electrical properties of flexible crystals of copper(II) coordination polymers

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The Role of Hydrogen Bonds in Proton-Conductive Homo- and Heterometallic Compounds with Ammonium Cations

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The oxalate group, $C_2O_4^{2-}$, used in the preparation of metal-organic coordination compounds, has the ability to bind to metal ions in various modes, which allows the synthesis of various structures, of different dimensionality and nuclearity. Its ability to mediate magnetic interaction between the paramagnetic metal centers, depending on the nature of the bridged metal ions, makes it a good ligand that can form compounds with ferro-, antiferro- or ferrimagnetic ordering. These compounds can combine several properties of the interest; intrinsic properties of the host with additional functionalities originating from the selected guest molecules can result in materials with multifunctional properties. Oxalate polymers are mostly negatively charged and therefore can associate with different molecular cations, and combine cooperative magnetism with another property of interest.¹ The proton conductivity of metal-organic networks has been intensively researched because of their crystallinity, high porosity, designability and tunability in structure and properties. As a new functionality of metal-organic compounds it can be achieved by incorporating a counterion such as hydronium (H_3O^+), ammonium [NH_4^+ , $(CH_3)_2NH_2^+$, ...] or an anion (SO_4^{2-}) into the anionic network during synthesis. The counterions form the hydrogen bonds with the guest water or other components of compound and create proton-conducting pathways consisting of hydrogen bonding networks. The oxygen atoms of the oxalate group can construct complex hydrogen-bonded networks with water, which are more than suitable for proton conduction.²

We investigated the proton conductivity behaviour of the novel oxalate-based coordination compounds: $(NH_4)_2[Fe(H_2O)Cl_3(C_2O_4)] \cdot H_2O$ (**1**), $\{[NH(CH_3)_2(C_2H_5)][FeCl_2(C_2O_4)]\} \cdot H_2O \cdot n$ (**2**), $\{[NH(CH_3)(C_2H_5)_2]_8[Mn_4Cl_4Cr_4(C_2O_4)_{12}]\}_n$ (**3**) and $\{[NH(CH_3)_2(C_2H_5)]_8[Mn_4Cl_4Cr_4(C_2O_4)_{12}]\}_n$ (**4**). The discrete mononuclear compound **1** exhibits remarkable humidity-sensing properties and a very high proton conductivity of $2.17 \times 10^{-3} (\Omega \text{ cm})^{-1}$ at 298 K under 74% relative humidity (RH). The one-dimensional (1D) compound **2** containing infinite anionic zig-zag chains $[FeCl_2(C_2O_4)]_n^{n-}$ and cations $(CH_3)_2(C_2H_5)NH^+$ located between them, shows an increase in conductivity of six orders of magnitude with increasing RH, reaching values of $2.00 \times 10^{-4} (\Omega \text{ cm})^{-1}$ at 298 K and 93% RH. Compounds **3** and **4** consisting of two-dimensional (2D) oxalate-bridged anionic layers $[Mn_4Cl_4Cr_4(C_2O_4)_{12}]_n^{8n-}$ interleaved by the hydrogen-bonded templating cations $(CH_3)(C_2H_5)_2NH^+$ (**3**) or $(CH_3)_2(C_2H_5)NH^+$ (**4**), exhibit extraordinary humidity-sensing properties and very high proton conductivity of $9.6 \times 10^{-4} (\Omega \cdot \text{cm})^{-1}$ at 298 K under 94% RH and $1.60 \times 10^{-3} (\Omega \cdot \text{cm})^{-1}$ at 298 K under 90% RH, respectively.

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Kompeticijsko određivanje konstanti vezanja dipiridamola i varfarina za humani serumski albumin polarizacijskom fluorescencijom

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Pri određivanju terapijskih doza lijekova potrebno je voditi računa o njihovom vezanju za proteine krvne plazme. Imajući na umu da je samo nevezani udio lijeka farmakološki aktivan¹, kod lijekova poput varfarina² i dipiridamola³ koji su u terapijskim dozama preko 95% vezani na albumin, a imaju vrlo malu terapijsku širinu, ta je interakcija od kritične važnosti. Varfarin je u trenutno najšire upotrebljavani oralni antikoagulans i koristi se za prevenciju tromboembolije⁴. Važnost točnosti njegovog doziranja pokazuje činjenica da se osobama na terapiji varfarinom svakih nekoliko tjedana mjeri protrombinsko vrijeme kako bi se ispitao učinak lijeka. Dipiridamol se ne propisuje često kao varfarin i ima veću terapijsku širinu, ali s varfarinom je indiciran kod pacijenata s umjetnim srčanim zališćima kojima prijeti opasnost od embolije unatoč adekvatnoj dozi varfarina⁵. Za takve slučajeve rezultati ovog rada mogli bi biti relevantni.

Interakcija albumina i njegovo vezanje s lijekovima temelji se na stvaranju kompleksa uglavnom putem nekovalentnih interakcija. U ovom radu naglasak je stavljen na mjerjenje interakcije između albumina i navedenih lijekova koji se reverzibilno vežu na vezna mesta na albuminu. Dipiridamol je fluorescentna molekula koja nakon ekskcitacije polariziranim svjetlošću određene valne duljine emitira svjetlost čiji je stupanj polarizacije obrnuto proporcionalan brzini njezine rotacije. Kako se radi o maloj molekuli, ona u se slobodnom obliku rotira velikom brzinom i stoga znatno zakreće polarizacijsku ravninu te time smanjuje stupanj polarizacije. Vezanje na druge molekule dovodi do smanjenja takvog učinka, a kada se radi o velikim molekulama (npr. albuminu) taj učinak gotovo da izostaje. Zahvaljujući tim svojstvima moguće je mjerjenjem polarizacije fluorescencije odrediti stupanj vezanja⁶ dipiridamola na albumin. U ovom radu prvo je ispitivano izravno vezanje, a zatim u kompeticiji s varfarinom te su temeljem rezultata izračunane konstante vezanja oba lijeka.

U izračunima su obrađena dva teorijska modela. U prvom modelu predviđeno je vezanje dipiridamola na samo jedno vezno mjesto na albuminu, a u drugom na dva. Mjerjenja i izračuni su pokazali da varfarin čak ni u suvišku ne istiskuje sav dipiridamol s albumina što ukazuje na mogućnost postojanja veznog mesta za dipiridamol na albuminu na koje se varfarin veže slabo ili nikako.

Naglasak ovog rada ujedno je i na praktičnoj primjeni polarizacijskih mjerjenja u svrhu opisa procesa uzrokovanih supramolekulskim, odnosno nekovalentnim interakcijama, budući da su te interakcije osnova velikog broja biokemijskih procesa u kojima je bitan proces molekulskog prepoznavanja.

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Application of thermal analysis and Raman microscopy in the study of cadmium(II) coordination polymers' flexibility

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Mechanical properties of crystalline materials are closely related with their structure and their potential applications in various areas of industry. Crystals are generally considered to be stiff and inflexible, and can crack or break due to the action of mechanical force.¹ By studying the crystals of organic compounds, it was established that the application of external mechanical force can lead to plastic or elastic deformation of a crystal.² Elastic materials undergo reversible bending (returning to their initial position when mechanical force is removed) upon applied mechanical stimuli, while plastic materials exhibit a permanent change in their shape (irreversible deformation). In the last few years, research on the mechanical flexibility of metal-organic crystalline solids has been carried out, but it is still, compared to crystals of organic compounds, much less explored and understood. As a significant contribution to the hitherto poorly researched mechanical flexibility of metal-organic crystals, the most recent research on cadmium(II) coordination polymers' flexibility should be mentioned.³⁻⁶ By systematic study of those crystals, different flexible responses upon application of mechanical force (from elastic, elastic→plastic up to plastic) was established. The crystal structure of coordination polymers is based on coordination bonds and much weaker non-covalent interactions and our goal was to elucidate the relative role and importance of these two features on mechanical properties of the crystals. Detailed structural studies revealed that small differences in the strength and directionality of non-covalent interactions can significantly impact on type and degree of mechanical response of such crystals.

In order to examine possibilities of the thermal analysis methods and Raman microscopy in the study of the crystals with plastic response, we prepared coordination polymers of the cadmium(II) halides with 3-chloropyridine (3-Clpy) and 3-bromopyridine (3-Brpy). The crystals of required morphology (needle-like) of the coordination polymers were prepared by a liquid diffusion method. The effect of the bending on the strength of the intermolecular interactions was examined by Raman spectroscopy are correlated with results obtained by means of thermal analysis methods (TGA, DSC and Hot stage microscopy).

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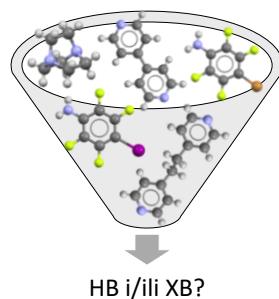
ACKNOWLEDGEMENTS: This work has been fully supported by Croatian Science Foundation under the project "From form to function: Mechanically flexible crystalline materials with controllable responses" (IP-2019-04-1242).

Perhalogenirani amini kao bifunkcionalni donori halogenske i vodikove veze u kokristalima s akceptorima koji sadrže dušik

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Usmjerene i predviđljive međumolekulske interakcije glavni su predmet istraživanja u kristalnom inženjerstvu višekomponentnih kristala.¹ Većina istraživanja usmjerena je na sustave u kojima su dominantne samo vodikove veze ili samo na halogenske veze, dok je vrlo malen broj radova u kojima je proučavana kompeticija ili kooperativnost tih dviju interakcija u istom kristalu.² U ovom radu istraživani su kokristali 4-brom-2,3,5,6-tetrafluoranilina (**btfa**) i 4-jod-2,3,5,6-tetrafluoranilina (**itfa**) s tri odabrana akceptora koji sadrže dušik: 4,4'-bipiridin, 1,2-bis(4-piridil)etan i 1,4-diazabiciklo[2.2.2]oktan. Perhalogenirani amini odabrani su kao bifunkcionalni donori halogenske veze (atom broma ili joda) i vodikove veze (amino skupina) kako bi se proučila mogućnost kompeticije ili kooperativnosti vodikovih i halogenskih veza koje usmjeravaju povezivanje molekula u kristalima. Mehanokemijskom sintezom i kokristalizacijom iz otopine pripremljeno je devet kokristala u kojima su donor i akceptor u stehiometrijskom omjeru 1:1 ili 2:1. Pripravljeni spojevi karakterizirani su difrakcijskim metodama (difracija rentgenskog zračenja na jediničnom kristalu i praškastom uzorku), te je njihova termička stabilnost određena razlikovnom pretražnom kalorimetrijom. Strukturnom analizom utvrđeno je da su u četiri kokristala molekule povezane vodikovim vezama N–H···N i halogenskim vezama N···I ili N···Br, u četiri kokristala s **btfa** dominantna veza je vodikova veza N–H···N, dok je u jednom kokristalu s **itfa** dominantna samo halogenska veza N···I. Dobiveni rezultati u skladu su s očekivanima jer je jakost donora halogenske veze i vodikove veze u molekuli **itfa** približno jednaka te se stoga u većini kokristala stvaraju supramolekulski lanci u kojima se naizmjence ostvaruju obje interakcije. S druge strane, ukoliko se usporede atom broma i amino skupina kao donori u molekuli **btfa**, donor halogenske veze slabiji je od donora vodikove veze. Iz toga razloga u kokristalima s **btfa** dominantna je samo vodikova veza, a atom broma sudjeluje u slabijim međuhalogenim kontaktima Br···Br tipa I.



Slika 1. Molekule donora i akceptora korištenih za pripravu kokristala

¹ G. R. Desiraju, *J. Am. Chem. Soc.* **2013**, 135, 9952.

² C. B. Aakeröy, S. Panikkattu, P. D. Chopade and J. Desper, *CrystEngComm* **2013**, 15, 3125.

Mechanosynthesis and Magnetic Properties of Cocrystals Containing Mono- or Dinuclear Copper(II) Complexes and Perhalogenated Halogen Bond Donors

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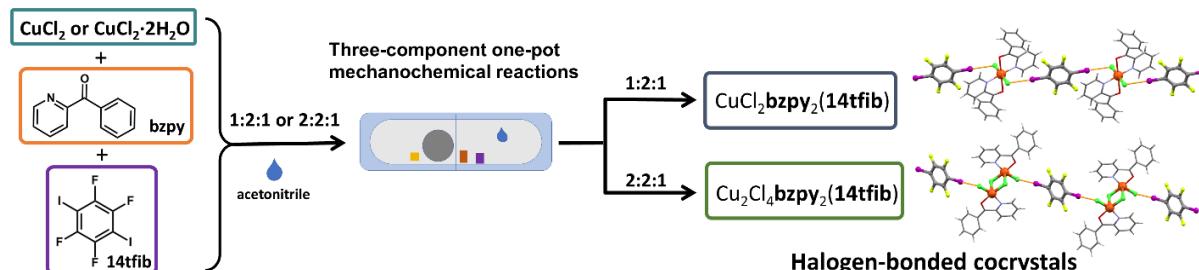
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In the last decade design and synthesis of halogen-bonded metal-organic cocrystals has thrived greatly.¹ Mechanochemical synthesis has proven to be convenient technique enabling fast and simple preparation of halogen-bonded metal-organic cocrystals by grinding metal complex and halogen bond donor, but one-pot mechanochemical approach where coordination bonds and supramolecular bonds form in the same step of synthesis have not been sufficiently studied yet.² Here we present a systematic investigation of three-component one-pot mechanochemical reactions to obtain cocrystals containing copper(II) complexes and perhalogenated halogen bond donors. Grinding CuCl₂ · 2H₂O or CuCl₂, 2-benzoylpyridine (**bzpy**) and perfluorinated iodobenzenes (1,4-diiodotetrafluorobenzene, 1,3-diiodotetrafluorobenzene, 1,2-diiodotetrafluorobenzene and 1,3,5-triiodotrifluorobenzene) in different stoichiometric ratios has shown as useful approach in the preparation of halogen-bonded cocrystals containing mononuclear or dinuclear copper(II) complexes as halogen bond acceptors. It is shown that the presence of hydrate water of CuCl₂ · 2H₂O directs the reaction towards the formation of a cocrystal containing the mononuclear copper(II) complex, while in the absence of hydrate water, using CuCl₂, a reaction occurs towards the formation of cocrystal containing the dinuclear copper(II) complex. This study has yielded a series of seven new cocrystals: five cocrystals containing the mononuclear complex [CuCl₂(**bzpy**)₂] and two cocrystals containing the dinuclear complex [Cu₂Cl₄(**bzpy**)₂]. All obtained cocrystals were also prepared from the solution and single-crystal X-ray diffraction revealed that the cocrystals display different crystal packing governed by Cu–Cl···I halogen bonds. Also, we conducted the first magnetization measurements on halogen-bonded cocrystals containing neutral metal-organic units made to determine how halogen bonding influences the magnetic properties of these systems. Magnetization measurements revealed that all cocrystals are paramagnetic in the entire measured temperature range.



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² D. Cinčić and T. Friščić, *CrystEngComm*, **2014**, 16, 10169.

NMR methods for determining crude oil stability

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Crude oil samples are organic mixtures composed of many different macromolecules.¹⁻⁴ The stability of such complex compounds is a matter of many approaches based on different analytical methods, such as spectroscopic (NMR, MS, IR, Raman), chromatographic (LC-MS, GC-MS), microscopic and electrochemical.³ Spectroscopic methods are usually coupled with statistical tools to disentangle complicated spectral patterns.

NMR spectroscopy can provide valuable data on the structure and chemistry of crude oils and has been frequently used to study their stability. In this work, we will show examples of using one- and two-dimensional NMR techniques to study crude oil residues, asphaltenes, resins and vacuum gas oils. Depending on the polarity of the crude oil, the components are often divided into four main groups: asphaltenes, saturates, aromatics and resins. Asphaltenes and resins are of special importance because they can cause serious problems in refining process and production, such as reduction in oil flow, clogging of production pipes, coke formation, corrosion, catalyst deactivation and poisoning.

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<https://doi.org/10.1021/acs.energyfuels.7b01358>

Solvent-free mechanochemical synthesis of HostGuest Complexes with Cucurbit[n]uril

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Cucurbit[n]urils ($n = 5-10$) are rigid host molecules with hydrophobic cavities that can bind guests in 1:1, 2:1, or 1:2 complexes and have been used previously to bind hydrophobic guests in water often with extreme binding affinities up to $7.2 \times 10^{17} \text{ M}^{-1}$.[1-3]

Solvent-free mechanochemical synthesis (ball milling) has been shown to be a useful method for the preparation of inclusion complexes with cucurbit[7]uril and adamantane and phenyl derivates as model molecules of guests.[4] Therefore, we researched various phenylenediamine derivatives and ferrocene inclusion complexes with Cucurbit[n]uril. Studies included mechanochemical formation of inclusion complex in vibrational mill. *In situ* monitoring of grinding reactions by Raman spectroscopy enabled direct insight into the successful formation of the Host-Guest complex and the mechanochemistry of grinding.[5]. Host-guest complexation in the solid-state was studied and characterized by X-ray powder diffraction, FTIR, NMR spectroscopy, and differential scanning calorimetry.

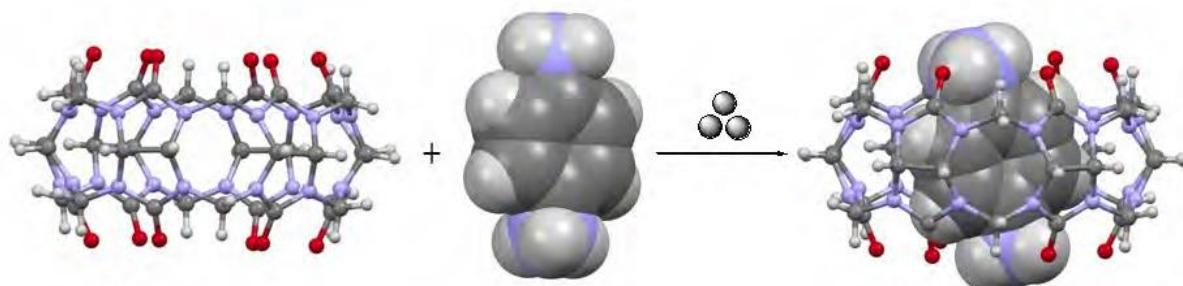


Figure 1. Schematic representation of inclusion complex formation by milling consisting of a *p*-phenylenediamine (space-filling model) bound within a Cucurbit[6]uril (ball and stick).

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Electron Spin Relaxation Times of Copper(II) Ions in MOF-525 and PCN-223 Measured by Pulsed EPR Spectroscopy

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The spin-lattice (T_1) and phase-memory electron spin (T_m) relaxation times of metal-organic frameworks (MOFs) MOF-525 and PCN-223 doped with 10% copper (II) ions were examined by pulse electron paramagnetic resonance (EPR) spectroscopy. Investigation of these MOFs was performed in order to determine their potential as molecular spin qubits. Both MOFs exhibit electron spin coherence detectable up to 80 K. MOF-525 shows longer relaxation times than PCN-223. Incorporation of fullerene into PCN-223 increases both spin-lattice and phase-memory electron spin relaxation times. It was observed that PCN-223 with a maximum filling of fullerene shows better performance in both relaxation times compared with the previously surpassing MOF-525.

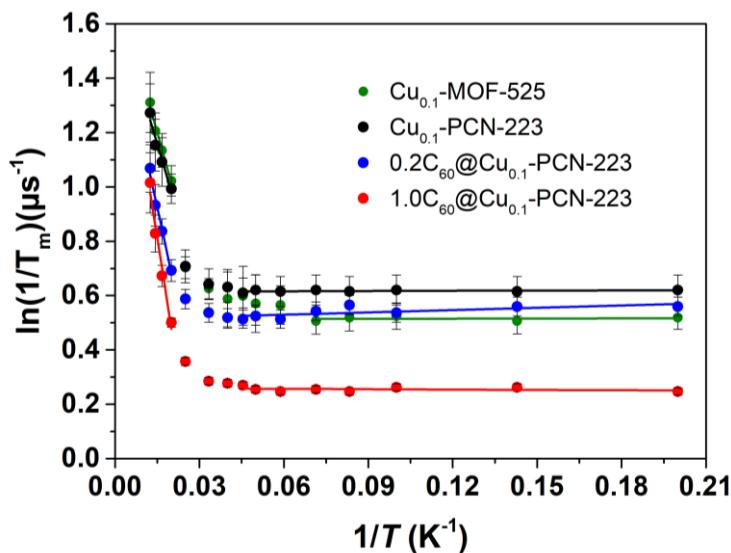


Figure 1. Temperature dependence of the electron spin phase-memory relaxation time, T_m , in various MOFs at $g_{||}$ spectral position. The best fits according to the Arrhenius equation (full line) are indicated.

ACKNOWLEDGEMENTS:

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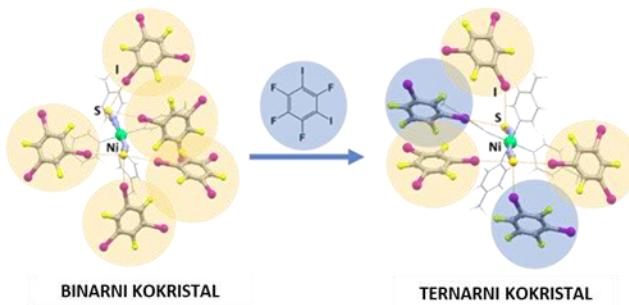
Strategija za dizajn ternarnih metaloorganskih kokristala temeljenih na halogenskim vezama

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Dizajn binarnih kristala je područje koje je posljednjih nekoliko desetljeća u fokusu kristalnog inženjerstva, a temelji se na razumijevanju međumolekulske interakcije i supramolekulske sintone. Usklađivanje i ugradnja više vrsta molekula u kristal i kontrola specifičnih međumolekulske interakcije je vrlo zahtjevno, zbog čega je sinteza ternarnih ili kvaternih kokristala izazovno područje.¹⁻³ U literaturi se može pronaći oko 200 istraživanih ternarnih kokristala, od kojih ih je samo četvero kokristala u kojima su halogenske veze dominante međumolekulske interakcije.⁴

U ovom istraživanju osmišljena je strategija za sintezu ternarnih kokristala koja se temelji na metalnom kompleksu specifičnih svojstava kao osnovnoj građevnoj jedinici. Sintetiziran je Wernerov koordinacijski spoj $\text{Ni}(\text{CH}_3\text{C}_5\text{H}_5\text{N})_4(\text{NCS})_2$ - **K1**, koji sadrži dvije izotiocijantne skupine u *trans* položaju, koje su sterički izbočene u odnosu na ostale ligande i fleksibilne. Na taj način je dizajniran ditopični metaloorganski akceptor koji je zbog svojih geometrijskih svojstava idealan kandidat za stvaranje halogenskih veza s perhalogeniranim benzenima. Ovaj koordinacijski spoj sklon je raditi klatrate, a poznata su tri njegova polimorfa, od kojih je jedan mikroporozan, te se njegova jedinična ćelija može proširiti za više od 10% prilikom umetanja molekula gosta ili povišenjem temperature. Za sintezu ternarnih kokristala korištene su kombinacije sljedećih donorskih molekula: 1,2-dijodtetrafluorbenzen (**12tfib**), 1,3-dijodtetrafluorbenzen (**13tfib**), 1,4-dijodtetrafluorbenzen (**14tfib**) i trifluor-1,3,5-trijodbenzen (**135tfib**). Sintetizirana je serija od 5 ternarnih kokristala koji su okarakterizirani difrakcijom rentgenskog zračenja na jediničnom kristalu: $(\text{K1})(\text{135tfib})(\text{13tfib})$, $(\text{K1})(\text{135tfib})(\text{12tfib})$, $(\text{K1})(\text{13tfib})_3(\text{14tfib})$ te dva polimorfa $(\text{K1})(\text{135tfib})(\text{14tfib})$. Kokristali su pripremljeni kristalizacijom iz otopine te mehanokemijskom sintezom. Strukturnom analizom utvrđeno je da sumpor izotiocijanatnog liganda može biti povezan s čak tri donora halogenske veze dok cijeli koordinacijski spoj može biti povezan s pet donora, što je značajno više od dosad proučavanih kokristala koordinacijskih spojeva. Višestruke halogenske veze koje se mogu ostvariti s **K1** omogućuju strukturu mimikriju molekula donora i stvaranje ternarnih kokristala. Sintetizirani kokristali predstavljaju prve poznate ternarne metaloorganske kokristale temeljene na halogenskim vezama.



Slika 1. Strukture binarnog kokristala $(\text{K1})(\text{135tfib})_2$ i ternarnog kokristala $(\text{K1})(\text{135tfib})(\text{13tfib})$

¹ C. B. Akeröy, P.D. Chopade, J. Desper, *Cryst. Growth Des.* **2011**, *11*, 5333–5336.

² S. Tothadi, G. R. Desiraju, *Chem. Commun.* **2013**, *49*, 7791–7793.

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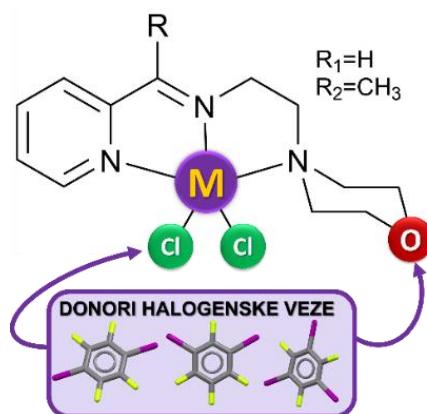
Kompeticija vs. kooperativnost halogenskih veza I...O_{morf} i I...Cl-M u kokristalima koordinacijskih spojeva cinka i bakra(II)

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Posljednjih desetak godina istraživanja halogenskih veza u metaloorganskim kokristalima usmjerena su na kristale koji sadrže neutralne organske doneore halogenske veze (u pravilu perhalogenirane spojeve) i neutralne metaloorganske jedinice, koordinacijske spojeve metala koji sadrže akceptorske skupine. Istraživanja takvih sustava mogu se podijeliti¹ u tri smjera: prvi smjer obuhvaća kelatne koordinacijske spojeve s npr. karbonilnom skupinom na periferiji iminskog liganda, s kisikovim atomima acetilacetonačnih liganada, ili s piridinskim dušikovim atomima na periferiji acetilacetonačnog liganda, u drugom smjeru ulogu akceptora imaju neutralne molekule koordinirane na metal, kao što su morfolin i tiomorfolin, dok treći pristup uključuje halogenide koordinirane na metalni centar organometalnog ili koordinacijskog spoja gdje halogenid ima ulogu akceptora halogenske veze.

U ovom istraživanju pripravljeni su koordinacijski spojevi cinka i bakra(II) koji kao moguće akceptore halogenske veze posjeduju morfolinski fragment lociran periferno na ligandu i kloridne ione vezane izravno na metalni centar. Koordinacijski spojevi pripravljeni su iz metalnih klorida i imina dobivenih kondenzacijskom reakcijom 2-piridinkarbalodehyda ili 2-acetylpiridina s aminoetilmorfolinom. Literaturno poznati spojevi^{2,3} okarakterizirani su difracijom rentgenskog zračenja u polikristalnom uzorku, a novopripravljeni difracijom rentgenskog zračenja u monokristalnom uzorku. Pripravljeni koordinacijski spojevi kokristalizirani su s komercijalno dostupnim donorima halogenske veze (supstitucijskim izomerima dijodtetrafluorbenzena i 1,3,5-trijod-2,4,6-trifluorbenzenom) u polarnim protičnim otapalima. Dobiveno je i strukturno okarakterizirano 11 kokristala. U svim kokristalima molekule se povezuju halogenskim vezama, pri čemu su u najvećem broju slučajeva (7 kokristala, 64 %) istovremeno akceptorji halogenske veze i morfolinski kisikov atom i kloridni ligand. U tri kokristala dominantna je samo halogenska veza I...Cl-M, dok je u jednom kokristalu dominantna samo halogenska veza I...O_{morf}. Prema navedenome može se zaključiti da se morfolinski kisikov atom pokazao kao koristan i kompetitivan akceptor kloridnom ligandu vezanom na metalni centar pri čemu je omogućeno povezivanje molekula u složene supramolekulske arhitekture.



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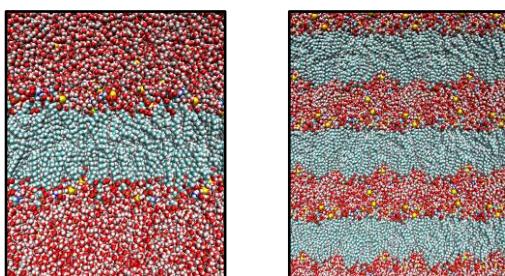
³ N.A.I.Hisham, N.S.Gwaram, H.Khaledi, H.M.Ali, *Acta Cryst.*, **2011**, E67, m55

Discerning the Structure and Hydration of Unilamellar and Multilamellar Phosphatidylserine Bilayers Using Molecular Dynamics

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Dipalmitoylphosphatidylserine (DPPS) is an anionic lipid that serves as a major constituent of the eukaryotic membrane¹. The experimental research of PS membrane models often prefers multilamellar (ML) systems due to higher stability, while computational studies model unilamellar (UL) bilayers^{2,3}. Here, classical molecular dynamics was employed to simulate both ML and UL DPPS systems in gel and fluid phase. Lipid bilayer containing 122 DPPS and 6 dipalmitoylphosphatidylglycerol (DPPG) molecules was simulated using GROMACS software. DPPG was added to be consistent with previous experimental work. Both systems employed periodic boundary conditions. UL systems contained a thick layer of water on both sides of the bilayer, thus preventing the interaction of the membrane with its periodic images. ML systems contained only a 2 nm layer of water between the images, mimicking the thickness of interbilayer water observed experimentally. The simulations were run for 150 ns. Structural parameters of the bilayer, hydration and the effects of water on both interfaces were evaluated. Membrane thickness, lipid ordering and lateral lipid diffusion indicated slightly higher packing and rigidity of ML systems. In both cases the bilayer was fully hydrated and water formed extensive hydrogen bonding network with lipid headgroups and the glycerol backbone. Lipids influenced water organization in the same way within the first hydration shell, however in ML systems the structuration of water persisted throughout the interlamellar space. Coupled with the 2-fold reduction in water diffusion coefficients between UL and ML, this leads to the conclusion that water in UL simulations behaves predominantly as bulk water, while in ML simulations the majority of waters behave as interfacial water. These findings will be combined with our experimental research in order to provide insight into differing thermotropic and molecular properties of UL and ML liposomes.



¹ A. Gupta, T. Korte, A. Herrmann, T. Wohland. *J. Lipid Res.* **2020**, 61, 252–266.

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Thermotropic Properties of Unilamellar and Multilamellar DPPS Bilayers

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Biological membranes have a complex composition and consist of hundreds of different lipids, asymmetrically distributed between the inner and outer bilayer leaflets. A lipid of special interest in eukaryotic membranes is the negatively charged phosphatidylserine (PS), located on cytosolic leaflet.¹ One of its primary functions seems to be to impart a negative charge to the inner surface of the membrane lipid bilayer which is required for the binding and activation of various peripheral membrane proteins.² Liposomes (lipid vesicles) are suspensions of membrane lipids in which a lipid bilayer surrounds an aqueous lumen and they serve as model system for cell membrane.³ Commonly used phosphatidylserine-constituted lipid membranes are multilamellar liposomes (MLV) while unilamellar liposomes (LUV) are more realistic model membrane system, not researched enough because of instability. The liposomes prepared in this experiment form as MLV and LUV. In order to examine their thermotropic properties we performed calorimetric and spectroscopic study of both, MLV and LUV, constituted from 2-dipalmitoyl-sn-glycero-3-phosphatidylserine (DPPS).

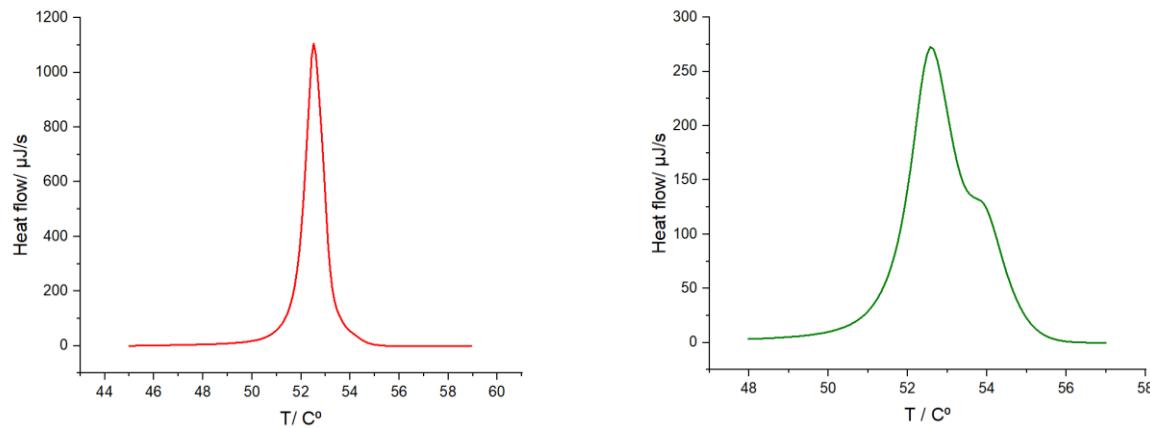


Figure 1. DSC curves of MLV DPPS (left) and LUV DPPS (right)

¹ H.L. Scott, F.A. Heberle, J. Katsaras, F.N. Barrera, *Biophysical Journal*, **2019**, 116, 1495.

² R. N. A. H. Lewis, R. N. McElhaney, *Biophysical Journal*, **2000**, 79, 2043.

³ B. Li, E. London, *Langmuir*, **2020**, 36, 12521.

Kompeticijsko određivanje konstanti vezanja dipiridamola i varfarina za humani serumski albumin polarizacijskom fluorescencijom

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Pri određivanju terapijskih doza lijekova potrebno je voditi računa o njihovom vezanju za proteine krvne plazme. Imajući na umu da je samo nevezani udio lijeka farmakološki aktivan¹, kod lijekova poput varfarina² i dipiridamola³ koji su u terapijskim dozama preko 95% vezani na albumin, a imaju vrlo malu terapijsku širinu, ta je interakcija od kritične važnosti. Varfarin je u trenutno najšire upotrebljavani oralni antikoagulans i koristi se za prevenciju tromboembolije⁴. Važnost točnosti njegovog doziranja pokazuje činjenica da se osobama na terapiji varfarinom svakih nekoliko tjedana mjeri protrombinsko vrijeme kako bi se ispitao učinak lijeka. Dipiridamol se ne propisuje često kao varfarin i ima veću terapijsku širinu, ali s varfarinom je indiciran kod pacijenata s umjetnim srčanim zaliscima kojima prijeti opasnost od embolije unatoč adekvatnoj dozi varfarina⁵. Za takve slučajeve rezultati ovog rada mogli bi biti relevantni.

Interakcija albumina i njegovo vezanje s lijekovima temelji se na stvaranju kompleksa uglavnom putem nekovalentnih interakcija. U ovom radu naglasak je stavljen na mjerjenje interakcije između albumina i navedenih lijekova koji se reverzibilno vežu na vezna mjesta na albuminu. Dipiridamol je fluorescentna molekula koja nakon ekscitacije polariziranim svjetlošću određene valne duljine emitira svjetlost čiji je stupanj polarizacije obrnuto proporcionalan brzini njezine rotacije. Kako se radi o maloj molekuli, ona u se slobodnom obliku rotira velikom brzinom i stoga znatno zakreće polarizacijsku ravninu te time smanjuje stupanj polarizacije. Vezanje na druge molekule dovodi do smanjenja takvog učinka, a kada se radi o velikim molekulama (npr. albuminu) taj učinak gotovo da izostaje. Zahvaljujući tim svojstvima moguće je mjerjenjem polarizacije fluorescencije odrediti stupanj vezanja⁶ dipiridamola na albumin. U ovom radu prvo je ispitivano izravno vezanje, a zatim u kompeticiji s varfarinom te su temeljem rezultata izračunane konstante vezanja oba lijeka.

U izračunima su obrađena dva teorijska modela. U prvom modelu predviđeno je vezanje dipiridamola na samo jedno vezno mjesto na albuminu, a u drugom na dva. Mjerena i izračuni su pokazali da varfarin čak ni u suvišku ne istiskuje sav dipiridamol s albumina što ukazuje na mogućnost postojanja veznog mesta za dipiridamol na albuminu na koje se varfarin veže slabo ili nikako.

Naglasak ovog rada ujedno je i na praktičnoj primjeni polarizacijskih mjerjenja u svrhu opisa procesa uzrokovanih supramolekulskim, odnosno nekovalentnim interakcijama, budući da su te interakcije osnova velikog broja biokemijskih procesa u kojima je bitan proces molekulskog prepoznavanja.

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Effect of cyclodextrins on solubility enhancement of loratadine

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Loratadine (LOR) is antihistaminic drug, classified as BCS class II drug due to its low solubility and high permeability.¹

Cyclodextrins (CD) are cyclic oligosaccharides containing 6 (α -CD), 7 (β -CD) or 8 (γ -CD) glucose subunits linked with (α -1,4)-glycosidic bond. Their cone like shape with hydrophobic cavity and hydrophilic surface enables formation of inclusion complexes with drugs, which affects physicochemical properties of drugs, such as solubility and stability.²

The influence of natural cyclodextrins (α -CD, β -CD, γ -CD) and its hydroxypropyl derivative (HP β CD) on LOR solubility in water and buffered solutions at different pH has already been studied.^{1,3} However solubility in biorelevant media has not been studied yet.

The aim of this study was to investigate the influence of β -CD and its hydroxypropyl (HP β CD), randomly methylated (RM β CD) and sulfobutylether (SBE β CD) derivatives on the solubility of LOR in water and simulated intestinal media (pH 6.8). Based on the enhancement of solubility, β -CD and HP β CD were selected for phase solubility studies, performed according to the method presented by Higuchi and Connors.⁴ Phase solubility diagrams were constructed, and stability constants, complexation efficacies and solubility enhancement were determined.

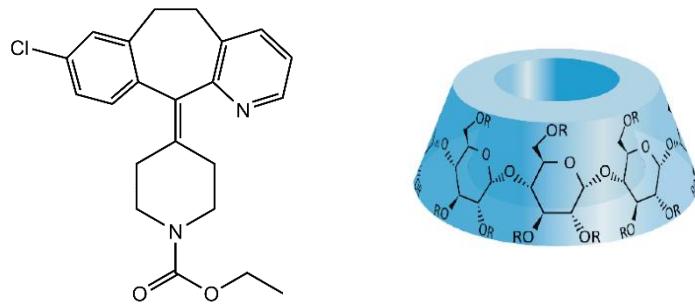


Figure 1. Structures of loratadine and β -cyclodextrin.

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Phenanthridine – Nucleobase Conjugates: Supramolecular pH-dependent Fluorescent Hydrogelators

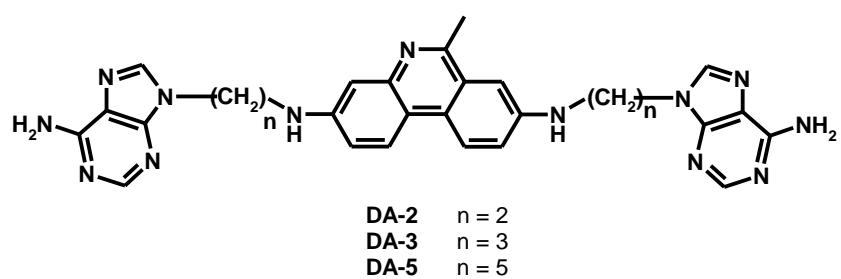
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Numerous small organic molecules self-organize to form gels by spontaneous and reversible self-assembly. Gel-to-sol transitions can be controlled and induced by temperature, pH, light, ultrasound, or a specific solute. Steric and electronic properties of gelator molecules determine both type and direction of inter- and intramolecular non-covalent interaction, and thereby structure of gel, its properties and functions.^[1]

Small molecules containing nucleobase moiety showed gel formation that was caused by H-bond formation between nucleobases.^[2] Introduction of fluorophoremoiety introduces additional functionalisation of gelator: aggregation - induced emission enhancement properties – AIEE. This gel property can be used for design and development of new functional fluorescent materials, e.g. for biosensors and chemosensors.^[3]



a)

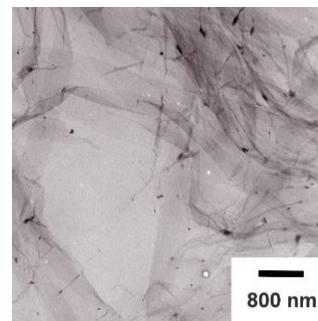


Figure 1. a) Phenanthridinium – adenine conjugates b) TEM image of DA-3 hydrogel PWK-stained

New phenanthridine – adenine conjugates were prepared in order to study the influence of the linker length to the intramolecular conformation, self-association in water and gel properties. Phenanthridine – adenine conjugates **DA-3**^[4] and **DA-5** showed self-aggregation and gel-formation in acidic water solution. Self-aggregation was probably caused by inter-and intramolecular π - π aromatic stacking interactions of aromatic subunits and H-bonding between protonated adenines^[5].

ACKNOWLEDGMENT

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Direct Measurement of Heat Effects for Solid-State Reactions by Isothermal Calorimetry

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Chemical reactions in solid-state gained significant popularity in recent years¹ due to their ability to expand the chemical space of organic synthesis,² which provides novel routes towards advanced materials for various applications.³ An important beneficial aspect of mechanochemistry is the fact that it requires environmentally acceptable conditions which includes the use of little or no organic solvent. Among the techniques for monitoring and characterization of solid-state reactions used so far (XRD methods, temperature and/or pressure monitoring, Raman, NMR and IR spectroscopy),⁴ isothermal calorimetry (ITC) studies were scarcely applied, especially at ambient temperatures.^{5,6} A lack of reaction enthalpy data for reactions in solid-state makes full thermodynamic characterization of these processes impossible without using thermodynamic cycles (requiring many different, long-lasting calorimetry experiments). Therefore, a crying need for direct detection of heat effect upon mixing of two or more solid reactants emerges in this research area, the response to which, to the best of our knowledge, was not yet reported.

In this work, a robust Calvet-type calorimeter (Setaram®), equipped with a cell originally designed for studies of dissolution processes, was used to directly measure the enthalpy of reactions between solid compounds at room temperature. Investigated reactions were complexation of KHSO_4 with 18-crown-6 ether⁷ and proton transfer from salicylic acid to *N,N*-dimethylpyridin-4-amine combined with cocrystal formation. The reliability of the data was tested by comparing the directly obtained values of solid-state reaction enthalpies with the ones calculated using the appropriate thermodynamic cycles.

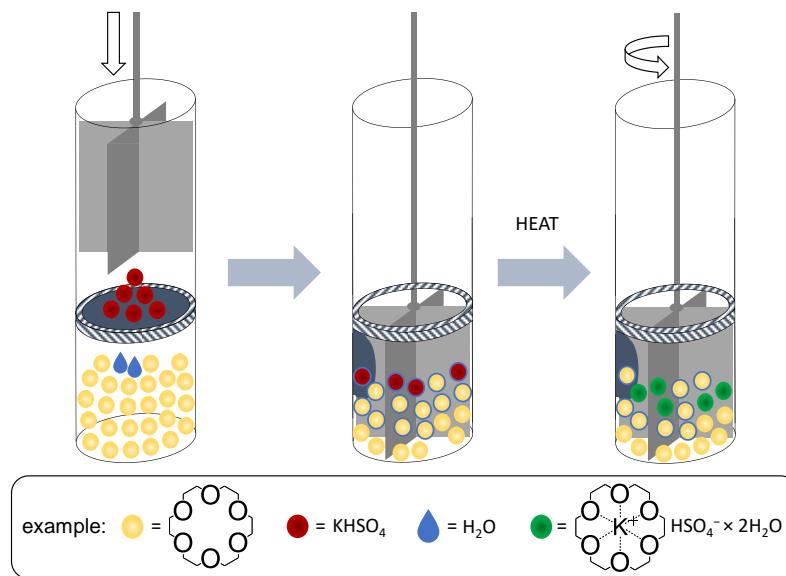


Figure 1. Direct measurement of heat effect for solid-state reaction (such as complexation of KHSO_4 with 18-crown-6 ether) by isothermal calorimetry.

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Thermodynamic and structural studies on the complexation of methyl ester of pentaisoleucine with anions in acetonitrile

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Over the past few decades anion receptors have attracted increasingly more interest in the field of supramolecular chemistry. Particularly interesting receptors are cyclic peptides. They have good complexation properties due to the extraordinary donor properties of the amide groups¹, the flexibility of the macrocyclic ring and the variability of the subunits.² Cyclic peptides are formed by cyclization from linear analogs in which a conformationally more rigid macrocyclic ligand is formed from a flexible chain. The main factor that affects successful ring closure is the conformational preorganization, which is the ability of a linear precursor to bring its reactive termini in close spatial proximity. This can be achieved by using favorable template ions. Determination of the stability constants for the anion-receptor complexes of linear peptides can be useful for the determination of the best template agent in macrocyclization reaction.³ In this work, binding affinities of pentaisoleucine methyl ester with several anions in acetonitrile were studied using ¹H NMR and ITC titrations as well as classical molecular dynamics simulations.

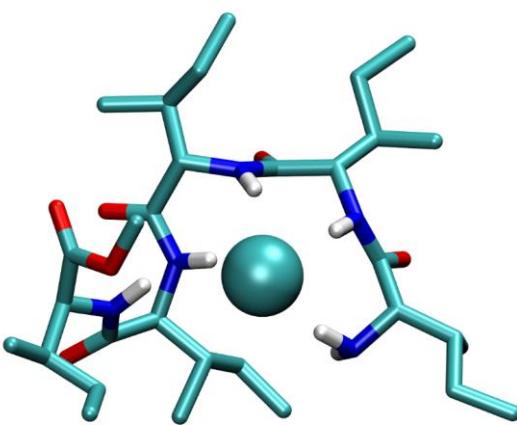


Figure 1. Structure of pentaisoleucine methyl ester complex with chloride anion.

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Characterization of Host-Guest Interaction Between Nabumetone and Selected β -cyclodextrins in Aqueous Solutions

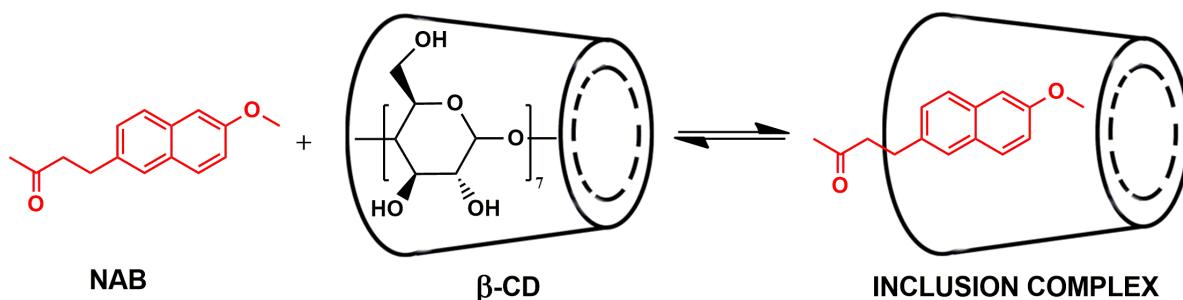
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Nabumetone (NAB) is a nonsteroidal anti-inflammatory prodrug that is clinically used for reducing pain and inflammation in the treatment of patients with osteoarthritis or rheumatoid arthritis.¹ Since NAB possesses low aqueous solubility, it can be classified as a Class 2 drug substance according to The Biopharmaceutics Classification System.²

Cyclodextrins (CDs) are a group of cyclic oligosaccharides containing six (α -CD), seven (β -CD), or eight (γ -CD) D-glucopyranose units which are α -(1,4)-linked in a ring formation. Their structure is visualized as a truncated cone with a hydrophilic outer surface and a hydrophobic central cavity. Their ability to form water-soluble inclusion complexes with lipophilic drug molecules has been intensively studied.³



This study aims to evaluate the influence of β -CD and its hydroxypropyl (HP β CD), sulfobutylether (SBE β CD), and randomly methylated (RM β CD) derivatives on intrinsic solubility of NAB in water through phase-solubility analysis according to the existing Higuchi-Connors method.³ To estimate total drug solubility changes in the presence of increasing CD concentration phase-solubility diagrams were constructed. Quantitative determination of NAB was performed by developed and validated UV/Vis spectrophotometric and spectrofluorimetric methods. The complexation of NAB with selected β -CDs in water was studied by fluorescence spectroscopy as well since CD-induced variation of native NAB fluorescence was noticed. Additionally, complexation in water was studied by isothermal titration calorimetry to determine the thermodynamic profile of the inclusion complexes (enthalpy of complex formation (ΔH), the Gibbs energy of complex formation (ΔG) and the entropy of complex formation (ΔS)). Experimental results, i.e. values of binding constants obtained by the above-mentioned techniques were compared.

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Synthesis of Glycine and Phenylalanine Containing Cyclopeptides and their Anion Binding Properties in Acetonitrile

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In the last few decades cyclic peptides have become compounds of interest due to their potential biological activity as well as their ability to act as molecular receptors.¹⁻² Cyclic peptides are especially attractive as biologically active compounds due to their increased bioavailability and metabolic stability. To gain further insight into the reactivity and anion binding properties of cyclopeptides we synthesized three peptides, tetrapeptide Phe-Phe-Gly-Gly **1**, pentapeptide Phe-Phe-Gly-Gly-Phe **2** and hexapeptide Phe-Phe-Gly-Gly-Phe-Phe **3** using solution-based synthesis. The cyclization of this linear oligopeptides was then explored using a chloride-assisted macrocyclization reaction recently developed in our group³ enabling the synthesis of **C2** and **C3** while the tetrapeptide **1** failed to cyclize. The complexation affinity of **C2** and **C3** towards both cations and anions in acetonitrile was studied using fluorescence spectroscopy.

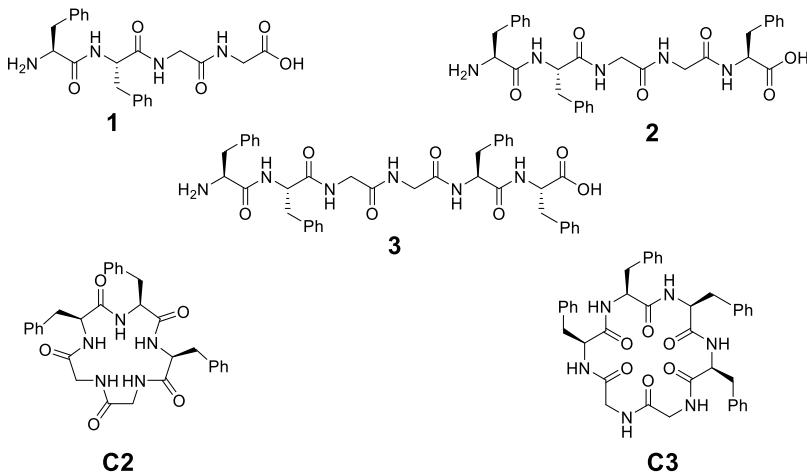


Figure 1. The chemical structure of the synthesized peptides.

¹ P. A. Gale, *Chem. Commun.* **2011**, 47, 82.

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Supramolecular Self-assembled Peptide Hydrogels Ac-L-Phe-L-Phe-L-Ala-NH₂ for Vaccine Delivery with Adjuvant Activity

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Adjuvants are used in order to enhance vaccine potency by improvement of the humoral and cell-mediated immune response to vaccine antigens. Adjuvants of new generation often include different biocompatible nanomaterials for sustained release of antigen and at the same time have adjuvant properties themselves. Supramolecular self-assembled peptide hydrogels have a great potential for applications in bionanotechnology and it has been shown that certain peptides possess immunostimulatory activity (1).

We report here the adjuvant system based on supramolecular hydrogel of a self-assembling tripeptide Ac-L-Phe-L-Phe-L-Ala-NH₂ (2) and evaluated for their *in vivo* adjuvant activity. The results of our experiment have shown that the examined hydrogels based on Ac-Phe-Phe-Ala-NH₂ and tripeptides Ac-Phe-Phe-β-Ala-OMe and Ac-Phe-Phe-Ala-OH induce a strong specific immune response in mice compared to the antigen itself. Also, these three adjuvant formulations modulated the type of specific immunoreaction,

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² Pospišil T et al. (2016) Biomater Sci 4, 1412–1416.

We acknowledge the financial support of Croatian Science Foundation (HrZZ, Project No: IP-2018-01-6910).

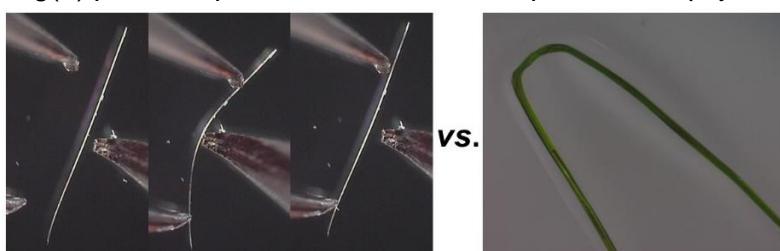
Utjecaj kationa metala na mehaničkim putem izazavanu savitljivost kristala na primjeru koordinacijskih polimera kadmijevih(II) i bakrovih(II) halogenida s 3,5-lutidinom

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Donedavno je u kristalografskoj zajednici bilo uvriježeno pojmanje kristala kao statičnih, krtih i neelastičnih tvari koje se lako lome pod djelovanjem vanjske mehaničke sile. Takav pogled promijenjen je otkrićem dinamičnih kristala koji pod utjecajem vanjskog podražaja daju drugačiji odziv. Tako kristali pod utjecajem vanjskog toplinskog ili svjetlosnog podražaja mogu skakati, puzati, savijati se ili čak eksplodirati, dok se pod utjecajem mehaničkog podražaja kristali najčešće plastično ili elastično savijaju. Uzrok ovakvog ponašanja kristala leži u samoj kristalnoj strukturi te reakcijama i transformacijama koje se u njemu događaju kao odgovor na vanjski podražaj.¹ Kristali s ovakvim svojstvima otvorili su cijeli novi svijet mogućnosti primjene koji je do tada za kristale bio nepojmljiv. Tako su se kristali pokazali kao dobri kandidati za primjenu u aktuatorima² i optoelektroničkim uređajima³, a mogli bi poslužiti i kao materijali koji se mogu samostalno opraviti od vanjskih oštećenja⁴. Ono što kristale zasigurno izdvaja od ostalih materijala koji se trenutno koriste u industriji i čini ih toliko poželjnima njihova je vrlo uređena struktura. Međutim, prije ikakve stvarne primjene ovakvih kristala, potrebno je detaljno ispitati njihova svojstva i razumjeti kako različiti strukturni čimbenici utječu na mehanički odziv, to jest na njegovu vrstu i izraženost.

Jednodimenzijski koordinacijski polimeri pokazali su se idealnim sustavima za istraživanje utjecaja strukture na mehanički odziv te za njegovo kontroliranje. Pokazano je da međumolekulske interakcije ortogonalne na smjer pružanja jednodimenzijskih lanaca imaju značajan utjecaj na vrstu i izraženost mehaničkog odziva kristalnih jednodimenzijskih polimera.⁵ Kako bismo upotpunili razumijevanje poveznice između strukturnih značajki i mehaničkog odziva, u ovome smo radu istražili utjecaj kationa metala na mehanički odziv koordinacijskih polimera. U tu svrhu odabrali smo polimere kadmijeva(II) i bakrova(II) bromida s 3,5-lutidinom: $[CdBr_2(lut)_2]_n$ i $[CuBr_2(lut)_2]_n$, lut = 3,5-lutidin. Kristali bakrovog(II) polimera pokazali su se izrazito plastičnim, dok su kristali kadmijevog(II) polimera pokazali elastičan odziv pri nižim stupnjevima zakrivljenosti.



Slika 1. Elastično savitljivi kristali kadmijevog(II) (lijevo) i plastično savitljivi kristali bakrovog(II) polimera.

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Catalyzed carboxylative C-C cross coupling reactions of propargyl alcohols

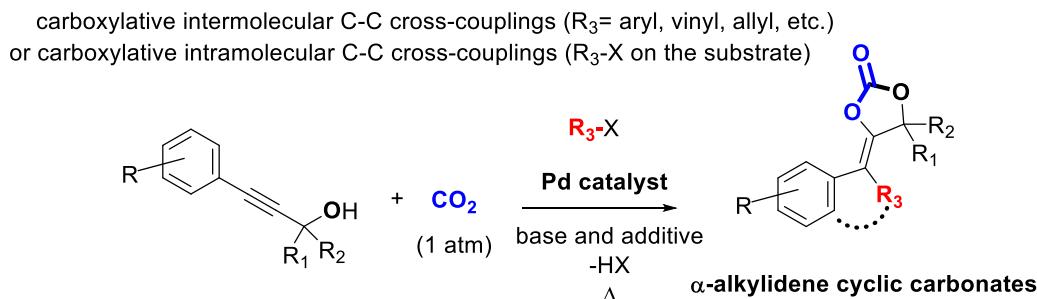
Maria Kolypadi Markovic,^a Filip Vranješević,^b Dario Matulja,^b Marija Jozanović,^c Nikola Sakač,^d Gabriela Ambrožić,^a Davor Šakić,^e Valerije Vrček,^e and Dean Marković^{*b}

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Valorization of carbon dioxide (CO_2) gas as C1 building block for producing highly valued and biologically active chemicals following the principles of green chemistry represents a current challenge in modern organic synthesis.¹ Metal catalyzed CO_2 capture by propargylic substrates - alcohols or amines- affords α -alkylidene cyclic carbonates or carbamates, respectively.² Domino reactions that combine CO_2 capture followed by a C-C cross-coupling reaction may give direct access to complex products that otherwise require multistep syntheses.³ We have accordingly envisaged energetically favored Pd-catalyzed intermolecular or intramolecular C-C cross-coupling reactions on suitable propargylic alcohol substrates, which can overcome the thermodynamic and kinetic stability of CO_2 . Notably, our calculations based on density functional theory (DFT) method predict that these reactions are exergonic owned to product stabilization through the formation of additional C-C bonds. We are currently examining the role of additives, such as Cu salts, which are mediating the Pd catalysis, probably due to their reducing and complexing properties, and increase the reaction yields under atmospheric pressure of CO_2 .

Our combined studies -experimental and computational- enable the rational design of new CO_2 trapping substrates and the preparation of useful fine chemicals such as cyclic carbonates.



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Scale-Up of Agrochemical Urea-Gypsum Cocrystal Synthesis Using Thermally-Controlled Mechanochemistry

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Nitrogen fertilizers have been an important part of supporting the growing human population by enabling increased food production. However, there are ongoing challenges in their sustainability, both during their production, and during their use. For instance, urea, one of the most common nitrogen fertilizers, decomposes under ambient conditions, releasing ammonia and causing losses in the nitrogen cycle, as well as lower fertilizer efficiency.¹ Increasing urea retention time can be achieved by incorporating it into adducts that stabilize it, and preferably also provide additional nutrients.²

We here explore the atom- and energy-efficient synthesis of crystalline calcium urea sulfate ($[\text{Ca}(\text{urea})_4]\text{SO}_4$, CSD code: URCASU³), a combined calcium, nitrogen, and sulfur fertilizer. We study its mechanochemical formation from urea and three different calcium sulfate sources ($\text{CaSO}_4 \cdot x\text{H}_2\text{O}$, $x=0, 0.5, 2$), one of which – gypsum – is a common waste product of the construction industry. We monitor the kinetics of URCASU formation on a small scale (0.5 g) in a mixer mill (MM) by *in situ* Powder X-ray Diffraction (PXRD) and Raman spectroscopy, to establish the catalytic effects of water contained in the starting materials, at both room temperature and elevated temperatures. We then use the obtained results to inform scale-up procedures, using planetary milling (PM – 50 g and 100 g scale) and twin-screw extrusion (TSE – 300 g/h scale). We compare the time-space yield and energy consumption of both methods, as well as the conversion efficiency, to ascertain the most efficient and sustainable scale-up procedure. Dissolution and stability studies of the prepared URCASU adducts show significantly higher urea retention in both laboratory and real-world conditions, compared to pure urea.



Figure 1. Reaction scheme for the small and large scale synthesis of calcium urea sulfate (URCASU, the crystal

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Parametrization of the Mn²⁺ Binding Site of Protein SloR (*S. mutans*) Starting from the Zn²⁺ bound Crystal Structure

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The primary causative agent of human dental caries is *Streptococcus mutans*, an oral pathogen that grows as a plaque biofilm on the tooth surface. Metal ion homeostasis is essential for the growth and survival of most microorganisms, including the bacteria *S. mutans*.¹ Divalent metal ions, such as Fe²⁺ and Mn²⁺, are important enzyme cofactors and stabilizing components of proteins in various key metabolic pathways. The metaloregulatory protein SloR has an important role in maintaining homeostasis of Mn²⁺ ions in *S. mutans*. As a transcriptional factor, SloR regulates metal ion transport upon binding to DNA in response to manganese availability.² In order to investigate the structural and dynamical properties of the protein and their changes upon Mn²⁺ binding to SloR. Adequate parametrization of interaction between Mn²⁺ ions and protein is necessary fro such study. The parametrisas using a bonded model scheme that was presented by Pengfei and Merz³ was used.

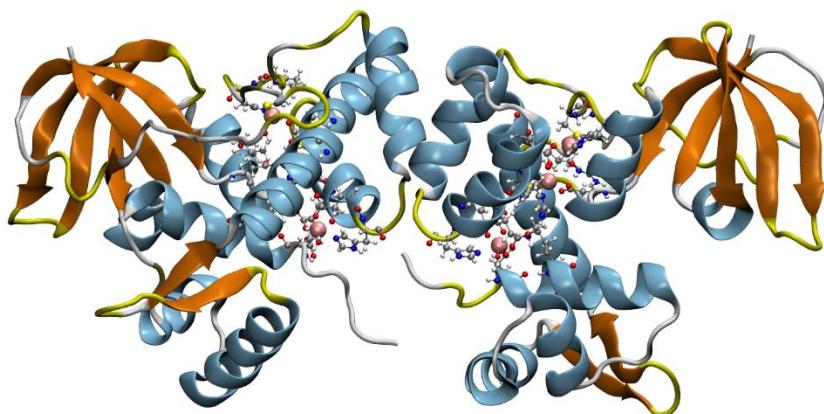


Figure 1. Structure of the SloR protein with bound Mn²⁺.

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The complexity of brain sphingomyelin

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Multiple lipids and proteins make up the myelin sheath, a multilamellar membrane surrounding the axons of neurons in both the central (CNS) and peripheral (PNS) nervous system.¹ Due to the extremely complex structure, the characterization of myelin is often performed on simpler models, such as membranes made only of lipids, such as sphingomyelin (SM). One of the main characteristics of SM is formation of lateral heterogeneity and immutability in the membrane plane.² Brain SM, found in high concentrations in myelin, is a mixture of SM molecules with different lengths of hydrocarbon chains, which makes its characterization challenging. In addition, the effect of changing acyl chain length on the physical behavior of SM remains poorly understood.¹ By using the fluorescent probe Laurdan (L) for fluorescence measurements, its response and influence on thermal changes in the SM lipid bilayer will be observed.³ Besides using fluorescence spectroscopy, the analysis of thermotropic behavior of brain SM multilamellar liposomes, also includes differential scanning calorimetry (DSC) and temperature-dependent UV/Vis spectroscopy with the addition of using appropriate chemometric tools.⁴

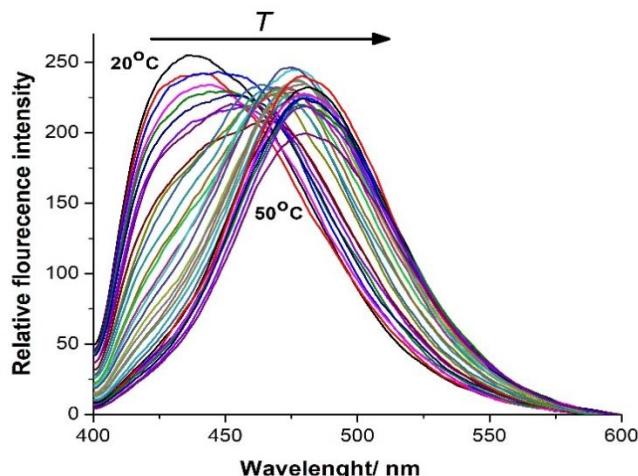


Figure 1. Temperature-dependent fluorescence spectra of SM liposomes with Laurdan.

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Macrocyclic Receptors and Benzene Derivatives: Complexation Thermodynamics and Substituent Impact

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Macrocyclic receptors such as cucurbit[7]uril (**CB7**) and β -cyclodextrin (**β -CD**) are excellent hosts for hydrophobic guests in aqueous solutions.^{1,2} The host-guest interactions are weak van der Waals interactions yet high stability complexes are often formed due to the thermodynamically favourable dehydration of the host cavity³ and the guest.⁴ Unlike in the case of **β -CD**, the hosting of aromatic compounds by **CB7** is far less thoroughly explored. We have therefore decided to study the complexation of simple mono- and 1,4-disubstituted benzene derivatives with different electron-donor (-acceptor) properties. The corresponding complexation reactions were explored calorimetrically and by means of ¹H ROESY NMR spectroscopy in a wide temperature range. **CB7** always formed complexes of higher stability than **β -CD** due to more exothermic binding. The guests with electron-donating groups formed more stable complexes compared to those acting as electron-acceptors. An almost complete compensation of $\Delta_r H^\circ(T)$ with $-T\Delta_r S^\circ(T)$ for complexation of explored aromatic compounds was observed.⁴

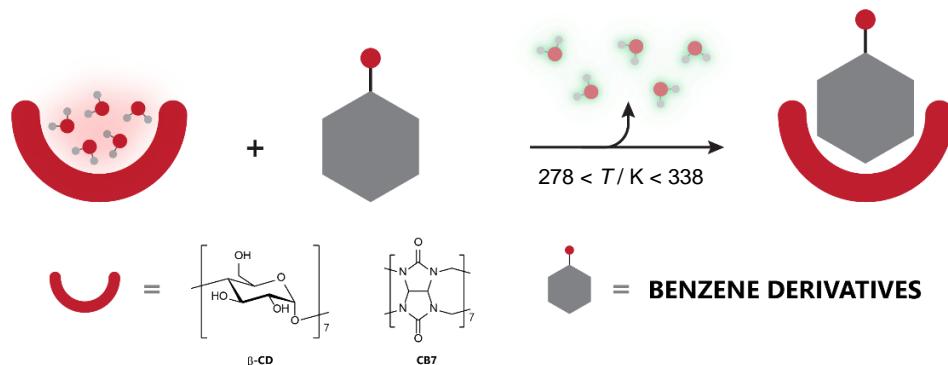


Figure 1. Schematic representation of the complexation process

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