SARS-COV-2 METHYLTRANSFERASE INHIBITORS CONTAINING (ADENOSYLTHIO)METHYL BENZOIC ACID ANALOGUES

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Considering the recent global COVID-19 pandemic, it is important to develop new SARS-CoV-2 antiviral drugs and it is vital to study them to prevent future possible spreading of coronavirus Coronaviral methyltransferases NSP14 and NSP16 are considered valid antiviral targets.

Recently we have discovered 3-phenyl benzoic acid containing adenosine derivative **1** as a bisubstrate inhibitor of SARS-CoV-2 methyltransferase NSP14. Here we report the development of new coronavirus methyltransferase inhibitors based on structure **1**. We explored 3-phenyl benzoic acid scaffold of the structure to complement the structure-activity relationship of adenosylthiobenzoic acid derivatives. Another approach is the fragmentation of the structure **1**. We prepared several analogs of compound **1** without the adenine moiety resulting in a new class of coronavirus methyltransferase inhibitors [1].

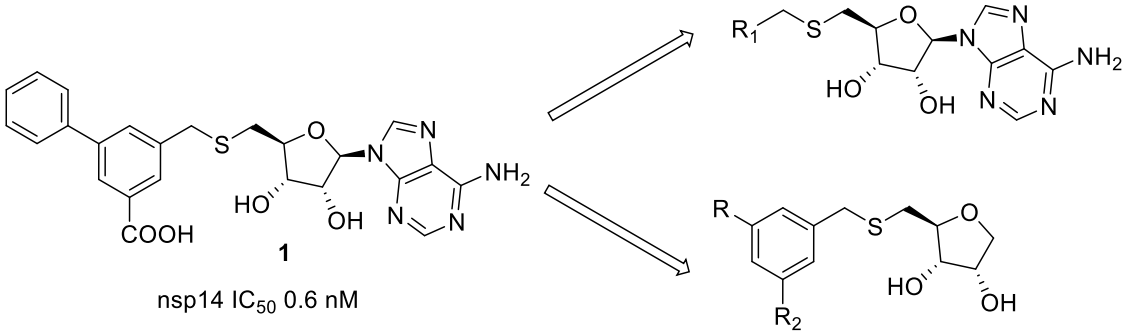

Fig. 1. Design of SARS-CoV-2 methyltransferase inhibitors

References:

[1] Olga Bobileva, Raitis Bobrovs, Evelina Elva Sirma, Iveta Kanepe, Anna L. Bula, Liene Patetko, Anna Ramata-Stunda, Solveiga Grinberga, Aigars Jirgensons, Kristaps Jaudzems *Molecules* **2023** 28, 768

ELABORATING THE NEW ROUTE TOWARD METHANOINDENE CAGE KEY INTERMEDIATE

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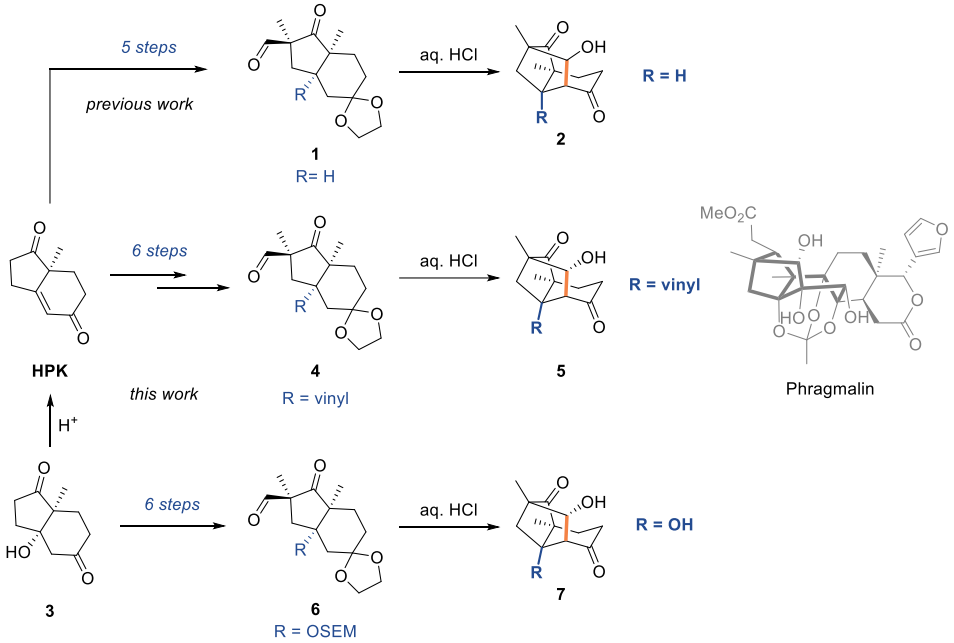
Phragmalin-type limonoids stand out as intricate natural compounds, showcasing a diverse array of biological activities including anti-cancer, anti-bacterial, and anti-inflammatory properties [1]. These compounds feature an unconventional octahydro-*1H*-2,4-methanoindene cage structure (Scheme 1, bolded), whose synthetic approaches prior to this work were limited to racemic versions [2]. To construct this scaffold, the Hajos–Parrish ketone (HPK) has been chosen as the readily available starting material for the synthesis of key intermediate **1**. Subsequently, through the strategic aldol reaction (Scheme 1), aldehyde **1** can be transformed into the product **2** with distinctive cage framework [3].

Herein, we focused on the installation of the hydroxy group or its precursor (vinyl moiety) at the bridgehead position in order to construct the target methanoindene frameworks (Scheme 1). Therefore, the HPK and Hajos–Parrish ketol (**3**) were used as affordable optically pure starting materials in proposed synthetic approaches, yielding the desired products **5** and **7** in 7 steps. Further work will be devoted to the synthesis of phragmalin-type limonoids employing compounds **5** and **7** as key building blocks.



Scheme 1. The new routes toward the methanoindene derivatives.

Acknowledgements:

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References:

[1] Liu, S.-B. et al. *RSC Adv.* **2017**, *7*, 28994.
[2] a) *J. Am. Chem. Soc.* **1969**, *91*, 2806; b) *Org. Lett.* **2011**, *13*, 2130; c) *Org. Lett.* **2017**, *19*, 6172.
[3] Becica, J.; Rāciņš, O.; Ivanova, M.; Jirgensons, A. *J. Org. Chem.* **2023**, *88*, 10306–10309.

ELECTROCHEMICAL SYNTHESIS OF PYROLLIDINE AND PIPERIDINE FRAGMENT-CONTAINING COMPOUNDS BY UTILIZING THE INTRAMOLECULAR HOFER-MOEST REACTION

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Pyrrolidine and piperidine fragment-containing molecules play a vital role in drug research due to their versatile pharmacological properties and structural diversity, making these heterocycles valuable scaffolds for drug discovery and development. Pyrrolidines and piperidines have been integrated into various pharmaceuticals, including anticancer, antibacterial, and anti-inflammatory drugs, which renders these compounds attractive targets for medicinal chemistry studies [1].

Recently, the synthesis of tetrahydropyran and tetrahydrofuran fragment-containing unnatural amino acids was achieved via the electrochemical decarboxylation/oxidation of readily available *N*-acetylamino malonic acid monoesters followed by the intramolecular cyclization with a tethered *O*-nucleophile [2]. In the current research, the scope of tethered nucleophiles has been expanded by introducing *N*-tethered nucleophiles to afford pyrrolidine and piperidine fragment-containing compounds.

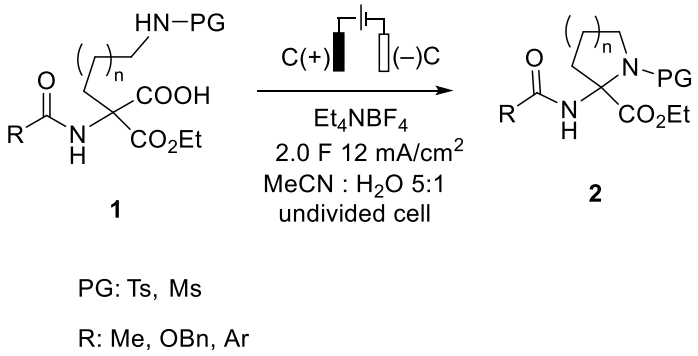

Fig. 1. Electrochemical synthesis of *N*-heterocyles **2**.

The developed electrochemical method provides access to pyrrolidine and piperidine fragment-containing amino acid derivatives. These novel compounds hold significant promise for drug discovery efforts, particularly in the development of bioactive molecules.

References:

[1] Li Petri, G., Raimondi, M.V., Spanò, V. et al. Pyrrolidine in Drug Discovery: A Versatile Scaffold for Novel Biologically Active Compounds. Top. Curr. Chem. **2021,** 379, 34.
[2] Koleda, O.; Prane, K.; Suna, E. Electrochemical Synthesis of Unnatural Amino Acids via Anodic Decarboxylation of N-Acetylamino Malonic Acid Derivatives. *Org. Lett.* **2023**, *25*, 7958–7962.

ORGANO-PHOTOREDOX CATALYZED RADICAL FLUOROMETHYLATION-CASCADE CYCLIZATION OF ARYL *N*-ACRYLAMIDES

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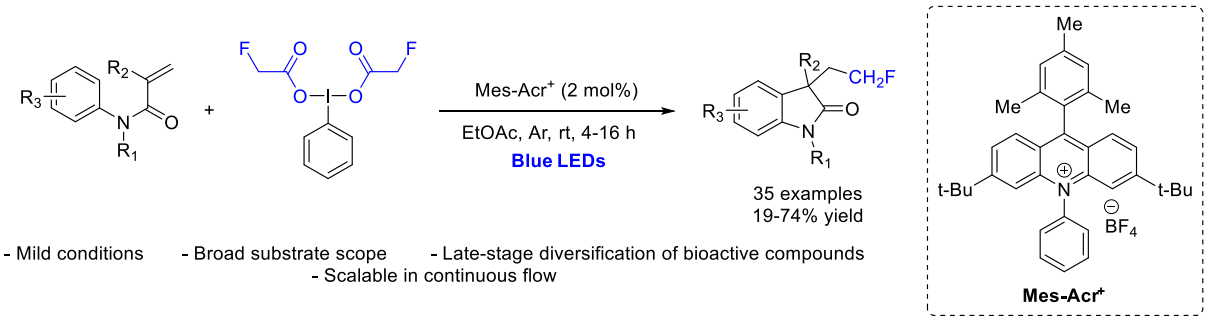
2-Indolones are common motifs in many natural products and some commercially available drugs. Currently researchers are focusing on developing methods for accessing bioactive 3,3-disubstituted 2-indolones with diverse substitution patterns. Incorporation of fluorine atoms or fluoroalkyl groups into organic compounds has been shown to improve physiochemical and biological properties such as conformation, lipophilicity, potency etc. [1]. Introduction of trifluoromethyl group is well developed, however methods for incorporating monofluoromethyl group are less explored.

Herein, we report a method for accessing monofluoromethylated 2-indolones using an iodine (III) reagent as a fluoromethyl radical source under visible-light photoredox catalysis [2]. Contrary to the previous reports employing metal-photocatalysts for this process [3,4], our method uses an organophotocatalyst – 9-mesityl 10-phenylacridinium (a metal-free approach). This protocol is also applicable to synthesis of other polycyclic nitrogen heterocycles containing fluoromethyl group.



References:

[1] Gillis E.P., Eastman K.J., Hill M.D., Donnelly D.J., Meanwell N.A. *J. Med. Chem.* **2015**, *58*, 8315-8359
[2] Ramkumar N., Baumane L., Zacs D., Veliks J. *Angew. Chem. Int. Ed.* **2023**, *62*, e202219027
[3] Tang X., Thomoson C.S., Dolbier Jr. W.R. *Org. Lett.* **2014**, *16*, 4594-4597
[4] Duhail T., Messaoudi S., Dagousset G., Marrot J., Andre-Barres C., Magnier E., Anselmi E. *Adv. Synth. Catal.* **2023**, *365*, 2392-2399

INVESTIGATION OF RETRO-BROOK REACTION ON PROTECTED 2-PROPARGYL PHENOL

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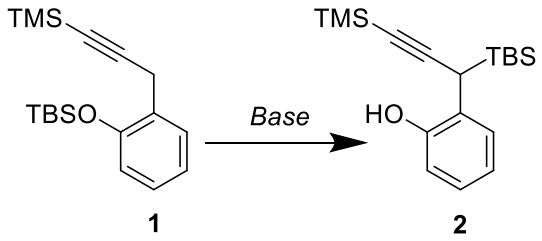
We report a new use of retro-Brook rearrangement in protected 2-propargyl phenols to yield propargyl silanes **2**. In 2014, benzylic retro-Brook [1,4]-rearrangements were investigated in substituted *o*-cresols with LDA in refluxing THF [1]. Five years later, retro-Brook rearrangement was reported for TBS-protected terminal alkynols using 2 equivalents of butyllithium [2]. In this work, we aim to examine the utility of base-promoted retro-Brook [1,4]-rearrangement in 2-propargyl phenols.

We also propose a convenient synthetic pathway to protected propargyl phenol **1** from commercially available *o*-cresol, which can be carried out in 3 steps involving silylation, bromination and alkylation.



Scheme. 1. Retro-Brook rearrangement in 2-propargyl phenol.

References:

[1] Wang, X., Gao, Q., Buevich, A.V., Yasuda, N., Zhang, Y., Yang, R.-S., Zhang, L.-K., Martin, G.E., Williamson, R.T. *J. Org. Chem.* **2019**, *84*, 10024–10031.
[2] Wang, Z., Wang, Y., Zhang, L. *J. Am. Chem. Soc.* **2014**, *136*, 8887–8890.

TRIMETHYLENEMETHANE CYCLOADDITION TO SULFUR DIOXIDE AS A NEW METHOD FOR SULTINE SYNTHESIS

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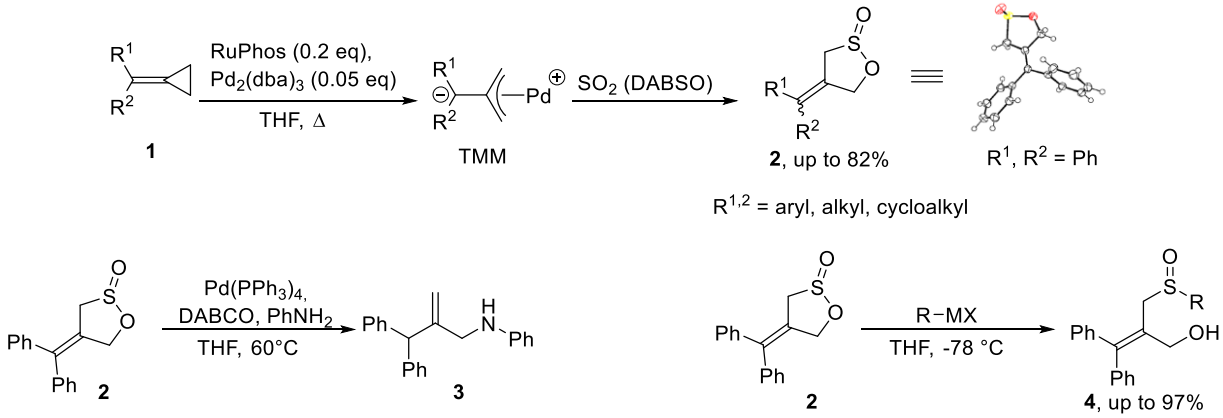
Sultines (cyclic sulfinate esters) are largely unexplored class of compounds, even though they have been known since late 19th century, which is mostly attributed to difficult and wasteful synthesis. For the past 20 years, research into novel synthetic methods has not ceased, since sultines are potentially versatile building blocks for preparation of biologically active molecules as they undergo ring opening, alkylation, reduction and oxidation reactions yielding variety of useful products. [1,2]

Experimental research yielded new synthetic method for γ-sultine synthesis through trimethylenemethane intermediates reaction with sulfur dioxide. Optimization of reaction conditions and catalytical system allowed yields up to 82% of various γ-sultines.

Further investigation into synthetic utility of the obtained products uncovered possibility to practically "regenerate" trimethylenemethane from these γ-sultines and sequentially form adduct to aniline. Additionally, ring opening reactions with carbon nucleophiles were performed achieving various sulfoxides with allyl alcohol moiety.



Scheme 1. New method for γ-sultine synthesis and explored derivatization pathways

References:

[1] Zhu Z., Deng Z., Ouyang X., Shu C. *Synlett* **2023**, *34* (17), 1943–1947.
[2] Zhang Y., Li H., Yang X., Zhou P., Shu C. *Chem. Commun.* **2023**, *59* (42), 6272–6285.

SYNTHETIC APPLICATION OF 2-FLUOROCYCLOPROPYL-1-SULFINATE

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Fluoroalkyl containing compounds (e.g. $–CF_3$, $–CF_2H$, $–CFH_2$) are of high significance in research of pharmaceuticals [1], agrochemicals [2] and advanced materials [3] as fluoroalkyl groups can alter physiochemical properties of a molecule, for example, metabolic stability and bioavailability [4]. Monofluorocyclopropyl group is an intriguing moiety with potential application in medicinal chemistry, therefore, monofluorocyclopropylsulfinate **1**, being similar to *Langlois* reagent [5], could be an attractive, yet little explored, source of this moiety in fluorine chemistry.

Herein, we demonstrate application of little explored monofluorocyclopropylsufinate **1** to access monofluorocyclopropanes via reaction with primary or secondary alkyl halides **2**. This strategy significantly complements our group's developed approach to monofluorocyclopropylsulfones **3** using the Johnson-Corey-Chaykovsky reaction [6], since now not only aromatic, but also aliphatic monofluorocyclopropylsulfones **3** can be obtained.

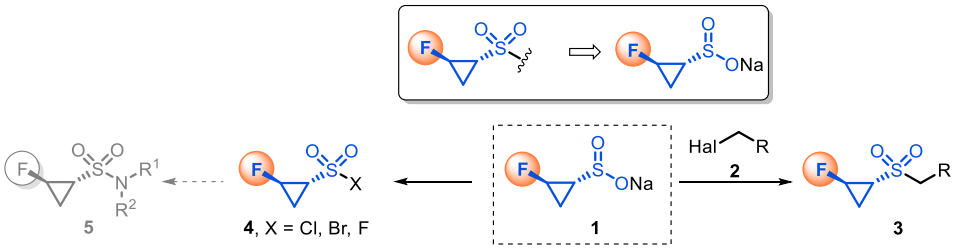

Fig. 1. Synthetic application of 2-fluorocyclopropyl-1-sulfinate **1**.

Acknowledgements:

This work has been supported by the Latvian Council of Science project lzp-2022/1-0335.

References:

[1] Wang, J., Sánchez-Roselló, M., Aceña, J., L., del Pozo, C., Sorochinsky, A., E., Fustero, S., Soloshonok, V., A., Liu, H. *Chem. Rev.* **2014**, *114* (4), 2432-2506.
[2] Fujiwara, T., O'Hagan, D. *J. Fluorine Chem.* **2014**, *167*, 16-29.
[3] Begrer, R., Resnati, G., Metrangolo, P., Weber, E., Hulliger, J. *Chem. Soc. Rev.* **2011**, *40* (7), 3496.
[4] Meanwell, N.A. *J. Med. Chem.* **2018**, *61* (14), 5822-5880.
[5] Zhang, C. *Adv. Synth. Catal.* **2014**, *356* (14-15), 2895-2906.
[6] Melngaile, R., Sperga, A., Baldridge, K., K., Veliks, J. *Org. Lett.* **2019**, *21* (17), 7174-7178.

SYNTHESIS OF SUBSTITUTED CHROMANES VIA TANDEM 1,2-SILYL SHIFT – FRIEDEL–CRAFTS CYCLIZATION

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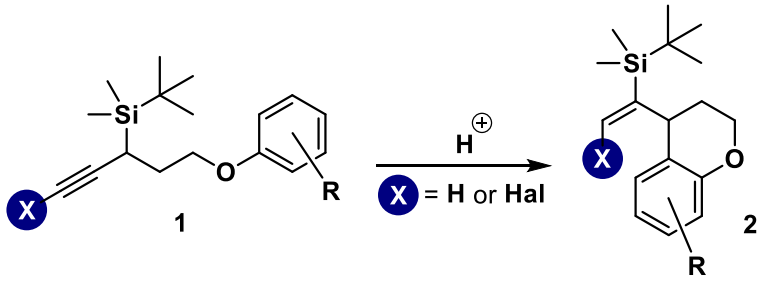
Previously our scientific group has found 1,2-silyl shift approach to be a powerful tool to the formation of 5-membered cycles, both carbocycles [1] (indenes) and heterocycles [2] (tetrahydrofuranes, pyrrolidines, tetrahydrothiophenes and isoxazolidines).

In this work, we apply acid-induced 1,2-silyl shift for the formation of 6-membered rings. We have developed a convenient synthetic pathway to substituted chromanes. Key synthetic step (Scheme 1) to substituted chromane **2** involves protonation of alkynes **1** and 1,2-silyl shift with consequent Friedel–Crafts cyclization with yields up to 99 %.



Scheme 1. Chromane synthesis via tandem 1,2-silyl shift – Friedel–Crafts cyclization.

The starting material **1** can be obtained in 70-80 % yield from commercially available pent-4-yn-1-ol in 3 or 4 steps: O-silylation, retro-Brook rearrangement [3] under Schlosser conditions and modified Mitsunobu reaction [4] with corresponding phenols. In the additional step, haloalkyne (Hal = Cl, Br, I) synthesis was conducted, and the resulting aryl ether **1** undergoes acid-catalysed cyclization in the same fashion yielding chromane with *E*-selective alkene side chain.

References:

[1] Puriņš M., Mishnev, A., Turks, M. *J. Org. Chem.* **2019**, *84*, 3595-3611.
[2] Kroņkalne R., Beļaunieks, R., Ubaidullajevs, A., Mishnev, A., Turks, M. *J. Org. Chem.* **2023**, *88*, 13857-13870.
[3] Wang, X., Gao, Q., Buevich, A. V., Yasuda, N., Zhang, Y., Yang, R.-S., Zhang, L.-K., Martin, G. E., Williamson, T. R. *J. Org. Chem.* **2019**, *84*, 10024-10031.
[4] Hirose, D., Gazvoda, M., Košmrlj, J., Taniguchi, T. *J. Org. Chem.* **2018**, *83*, 4712-4729.

C2 MODIFICATION OF QUINAZOLINE DERIVATIVES VIA AZIDE-TETRAZOLE TAUTOMERISM

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Quinazoline derivatives exhibit a broad range of biological activities, finding use as anticancer, antimicrobial, antimalarial, and antiviral agents. Numerous 2-amino-6,7-dimethoxyquinazoline analogs are extensively employed as α_1-adrenoreceptor blockers and in recent years quinazoline-based OLED materials have also gained attention[1–3].

Several methods of selective C4 position modification are known, but the modification of the C2 position is still challenging[4].

In this research, we employ the sulfonyl group dance[5] to achieve 4-azido-2-sulfonylquinazolines, which inverse the regioselectivity and further undergo C2 substitution, yielding 2-amino-4-azidoquinazolines. The regioselectivity of the transformation was proven by chemical synthesis, NMR, and X-ray crystallography.

Furthermore, we show the applications for these products in the synthesis of phosphoronylidenes, fluorescent 4-triazolylquinazolines, and the development of a novel synthesis pathway toward α_1-adrenoreceptor blockers terazosin and prazosin.

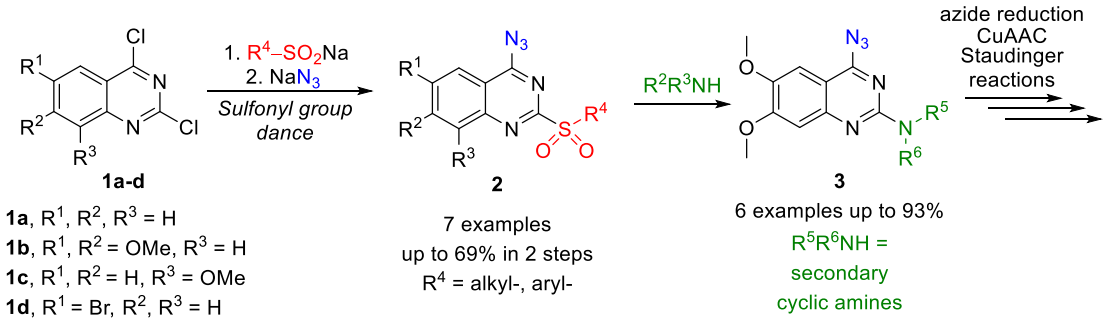

Fig. 1. Inversion of the regioselectivity of the quinazoline core via sulfonyl group dance.

Acknowledgments:

Dr. phys. A. Mishnev for X-ray analysis. Una Ušacka for assistance in acquiring the experimental data. This work was supported by the Latvian Council of Science grant No. LZP-2020/1-0348.

References:

[1] Karan, R.; Agarwal, P.; Sinha, M.; Mahato, N. *ChemEngineering* **2021**, *5* (4), 73.
[2] Minarini, A.; Bolognesi, M. L.; Tumiatti, V.; Melchiorre, C. *Expert. Opin. Drug. Discov.* **2006**, *1* (5), 395–407.
[3] Li, B.; Wang, Z.; Su, S.; Guo, F.; Cao, Y.; Zhang, Y. *Adv Opt Mater* **2019**, *7* (9), 1801496.
[4] Connolly, D. J.; Cusack, D.; O'Sullivan, T. P.; Guiry, P. J. *Tetrahedron* **2005**, *61* (43), 10153–10202.
[5] Zaķis, J. M.; Ozols, K.; Novosjolova, I.; Vilšķērsts, R.; Mishnev, A.; Turks, M. *J. Org. Chem.* **2020**, *85* (7), 4753–4771.

SYNTHESIS AND ENERGETIC PROPERATIES OF NOVEL ANNULATED POLYAZIDOPYRIMIDINES AND THEIR SOLVATES

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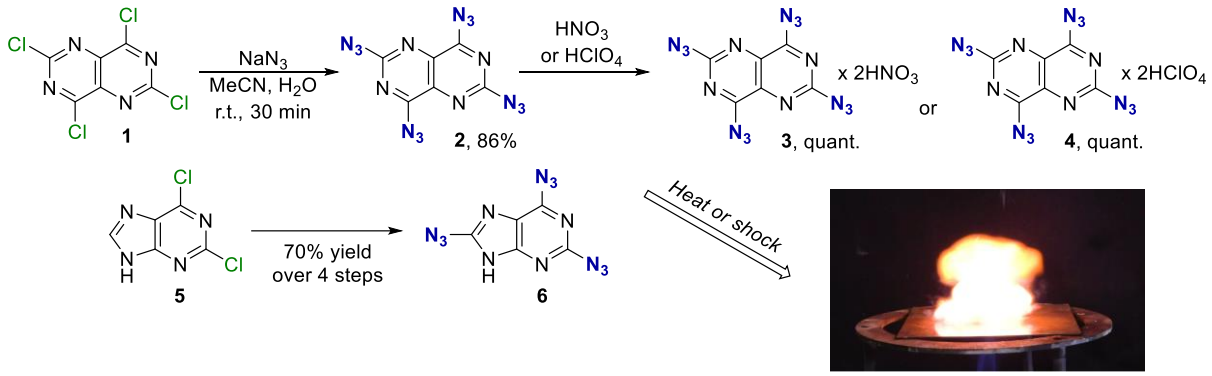
Binary C_xN_y organic compounds are impact-sensitive and possess explosive properties due to the high nitrogen content. The performance of nitrogen-rich compounds is attributed to the high heat of formation. Moreover, the main combustion product of such nitrogen-rich compounds is non-toxic nitrogen gas rather than the CO_2 from oxidation of a carbon backbone as in traditionally used explosives (TNT, RDX). Hence, nitrogen-rich compounds are currently the most promising candidates for the next-generation "green" explosives [1].

To the best of our knowledge, purine and its homologue - pyrimido[5,4-*d*]pyrimidine have not been used in the synthesis of energetic materials before. However, the nitrogen-rich backbone presents excellent features for application such as high energy density materials. Recently, we have designed an approach towards binary C_6N_{16} compound **2**, triazidopurine (**6**), and their solvates. Also, energetic properties of these compounds have been tested (**Scheme 1**) [2].



Scheme 1. Synthesis of polyazidopyrimidines and their solvates

References:

[1] Herweyer D., Brusso J. L., Murugesu M. *New J. Chem.* **2021**, *45*, 10150–10159.
[2] Leškovskis K., Mishnev A., Novosjolova I., Krumm B., Klapötke T. M., Turks M. *Cryst. Eng. Comm.* **2023**, *25*, 3866–3869.

MELDRUM'S ACID BASED ANTIOXIDANT SYNTHESIS AND ANTIRADICAL ACTIVITY EVALUATION

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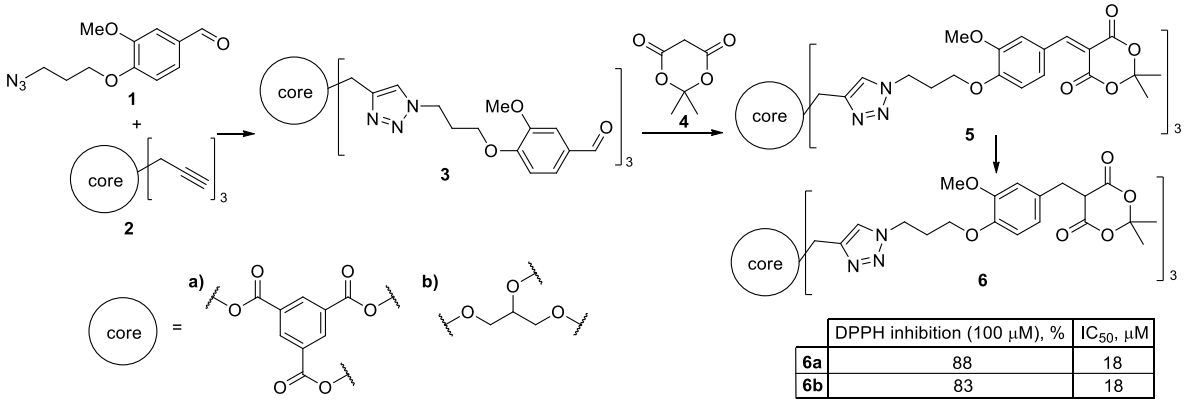
Antioxidants are molecules which inhibit oxidation processes, consequently improving the longevity of various products and, in the case of living organisms, preventing illnesses associated with oxidative stress [1].

Our work is focused on carbon-centered 1,3-dicarbonyl type antioxidants [2], more specifically arylmethyl Meldrum's acids – compounds which have shown promising radical scavenging ability [3]. Previously we have found that dendrimeric structures containing multiple Meldrum's acid moieties show consistently high antiradical activity [4]. In this work we have synthesized dendrimers which contain 1,2,3-triazole linkers between the core and surface groups.

The key steps of the synthesis are cycloaddition of azide **1** with alkynes **2a** and **2b**, Knoevenagel condensation of the resulting aldehydes **3** with Meldrum's acid (**4**), and the reduction of the arylidenes **5** to the final products **6**.



	DPPH inhibition (100 μM), %	IC_{50}, μM
6a	88	18
6b	83	18

Fig. 1. Synthesis and antiradical activity of dendrimers **6**

The obtained products have higher radical scavenging ability (inhibition at a 100 μM concentration AA = 88% and 83%, respectively) in the DPPH assay than commercial antioxidants ascorbic acid (AA = 14%) and BHT (AA = 16%) under the same experimental conditions.

References:

[1] Halliwell B., *Adv. Pharmacol.* **1996**, *38*, 3–20.
[2] Bērziņa L., Mieriņa I., *Molecules* **2023**, *28*, 6203.
[3] Mierina I., Jure M., Zeberga S., Makareviciene V., Zicane D., Tetere Z., Ravina I., *Eur. J. Lipid Sci. Technol.* **2017**, *119*, 1700172.
[4] Mieriņa I., Peipiņa E., Aišpure K., Jure M., *New J. Chem.* **2022**, *46*, 607–620.

ETHER-FUNCTIONALIZED IMIDAZOLIUM IONIC LIQUIDS

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Ionic liquids (ILs) are ambient-temperature liquid salts composed entirely of ions. The combination of organic cations and inorganic anions allows for the creation of ILs with desirable physical properties such as low melting points, tunable viscosities, increased electrochemical stability, and relatively high ionic conductivity. The first known IL was reported by the Latvian chemist Paul Walden in 1914 [1].

Fluorinated anions produce ILs of low melting points and viscosities, and high electrochemical stability. Ether functionalization has demonstrated to significantly reduce pure IL viscosities and densities [2].

In this work, we have developed multigram synthetic routes to novel PEG-monomeric and PEG-dimeric imidazolium ILs based on bis-(trifluoromethanesulfonyl)imide $[NTf_2]^-$ anion (**Figure 1**) for energy storage applications. Density and viscosity analysis has been carried out using rolling ball viscometry and vibrating tube densimetry.

To understand the role of connectivity between the PEG chain and the ionic core, the linker length in cations has been varied from one (**1, 2, 3**) to two (**4**) carbon atoms. To facilitate cooperative interactions of the two chains with plausible solute ions, the chains have been placed in a parallel (1,2-substituted) fashion (**3**). Controls (1,3-substituted) have also been prepared (**1, 2, 3**).

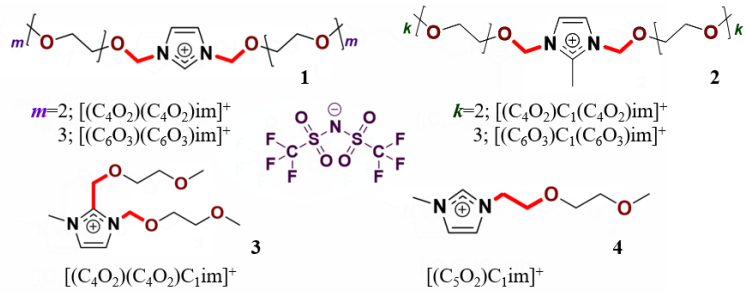

Figure 1. Structures of the cations of intermediates and $[NTf_2]^-$ ILs prepared

Acknowledgments

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References

[1] Welton, T. Ionic Liquids: A Brief History. *Biophysical Reviews*. Springer Verlag June 1, 2018, lpp 691–706. https://doi.org/10.1007/s12551-018-0419-2.

[2] Philippi, F.; Rauber, D.; Zapp, J.; Prãsang, C.; Scheschkewitz, D.; Hempelmann, R. Multiple Ether-Functionalized Phosphonium Ionic Liquids as Highly Fluid Electrolytes. *ChemPhysChem* **2019**, *20* (3), 443–455. https://doi.org/10.1002/CPHC.201800939.

SYNTHESIS OF ORGANIC LIGANDS FOR DEVELOPMENT OF METAL ION SENSORS

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In recent years, significant attention has been directed towards environmental pollution and its monitoring. With the development of industrialization, heavy metals have emerged as one of the primary pollutants capable of accumulating in various living organisms [1]. However, the most widely used methods for the determination of heavy metal concentration, such as ICP-MS, entail significant costs and are only available in specialized laboratories. Consequently, in collaboration with the Institute of Atomic Physics and Spectroscopy, we are developing an organic ligand sensor, that could enable on-field analysis of metal ion concentration.

The Salen-type ligand **1** is employed in coordination chemistry due to its ability to form stable metal complexes [2]. Additionally, the inherent properties of the ligand structure often impart selectivity towards particular metal ions. In this report, we delve into the structural patterns of ligand **1** and explore its potential applications in metal ion detection (Fig. 1).

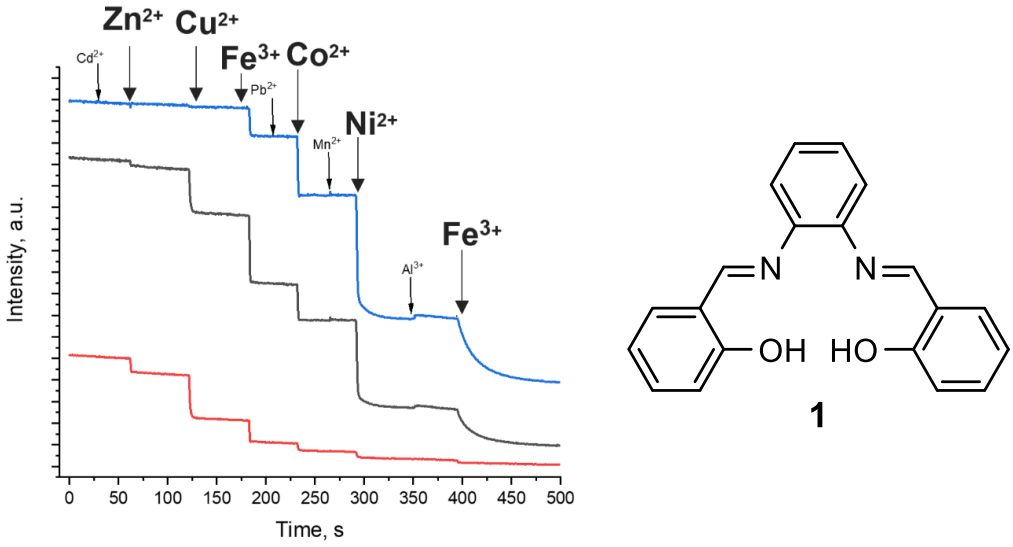

Fig. 1. Preliminary transmittance test with metal ions for ligand **1**.

References:

[1] Zamora-Ledezma, C.; Negrete-Bolagay, D.; Figueroa, F.; Zamora-Ledezma, E.; Ni, M.; Alexis, F.; Guerrero, V. H. Heavy Metal Water Pollution: A Fresh Look about Hazards, Novel and Conventional Remediation Methods. *Environ. Technol. Innov.* **2021**, *22*, 101504.
[2] Cozzi, P. G. Metal–Salen Schiff Base Complexes in Catalysis: Practical Aspects. *Chem Soc Rev* **2004**, *33* (7), 410–421.

SYNTHESIS AND USE OF BIFUNCTIONAL NON-COVALENT MOLECULARLY IMPRINTED POLYMERS (MIPS) FOR SELECTIVE EXTRACTION OF CATECHOLAMINES AND THEIR METABOLITES

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Catecholamines (CAs) are an important group of hormones and neurotransmitters. Abnormal CA levels in bodily fluids can be linked to neurodegenerative diseases as well as adrenogenic tumors (e.g. neuroblastoma). Simultaneous determination of both CAs and their metabolites in biological fluids is an efficient way of reliably diagnosing the aforementioned diseases. Molecularly imprinted polymers (MIPs) are slowly replacing conventional sorbents for use in solid-phase extraction (SPE) to achieve superior selectivity for target analyte isolation from biological matrices. Simultaneous isolation of CAs and their acidic metabolites using MIPs is a novel and potentially viable approach that is being studied by our group [1].

To provide better recovery and molecular recognition for both CAs and their metabolites, the MIP is synthesized using a non-covalent approach. Methylenebisacrylamide (MBAA, cross-linker **4**) is polymerized in the presence of a salt of (4-vinylbenzyl)trimethylammonium (VBTMA, **1**) and homovanillyl alkoxide (**2**) and a salt formed by homoveratric acid (**3**) and **2**, which act as dual-purpose templates/monomers for CAs and their metabolites, respectively.

Non-covalent MIP sorbents and non-imprinted polymers (NIPs) with variable cross-linker/monomer ratios were synthesized and packed into cartridges. Standard analyte mixture was passed through. The imprinting factor (IF) and recovery for each compound were calculated and compared to the NIPs. Preliminary results show that two MIPs show better retention and IF of CAs compared to the NIPs. These polymers will be used for further studies.

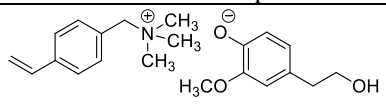
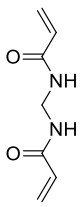
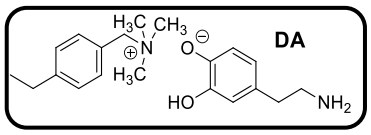
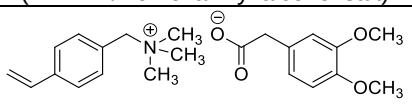
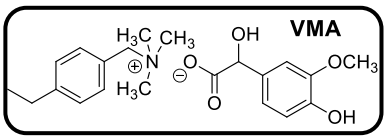
Analyte	Combined Functional Monomer/Template	Cross-linker	Analyte Binding Site
CAs, MN and NM	 **1** **2** (VBTMA/Homovanillyl alcohol salt)	 **4**	 DA
HVA and VMA	 **1** **3** (VBTMA/DMPAA salt)		 VMA

Table 1. Structural formulas of the compounds chosen for synthesis of the MIPs.

Acknowledgements

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References:

[1] Podjava, A.; Šilaks, A. Synthesis and sorptive properties of molecularly imprinted polymer for simultaneous isolation of catecholamines and their metabolites from biological fluids. *J. Liq. Chromatogr. Relat. Technol.* **2021**, *44*, 181–188.