**Hírlevél**

**MTA Szénhidrát, Nukleinsav és Antibiotikumkémiai Munkabizottság**

**2019. április**

1.) A 2019. évi munkabizottsági ülés időpontja:

**2019. 05. 22. (szerda) - 2019. 05. 24. (péntek), Mátrafüred**

**A jelentkezéseket, szállásfoglalást lezártam. Módosítási kérelmet csak nagyon indokolt esetben email címemre kérném. (csavas.magdolna@science.unideb.hu)**

http://mta-szenhidrat-nukleinsav-es-antibiotikumkemiai-mu.mozello.hu/

2.) Ülésünket idén

**International Workshop on Chemistry and Chemical Biology of Carbohydrates, Nucleic Acids and Antibiotics**

néven és formában rendezzük meg. A program összeállításához kérem az alábbi határidő **SZIGORÚ** betartását .

**Előadás bejelentés: 05.14.**

**(email címemre kérném az előadás címét, preferált időpontját, csavas.magdolna@science.unideb.hu)**

3.) M E G H Í V Ó

Az MTA Szerves és Biomolekuláris Kémiai Bizottság

**„Bruckner-termi előadás” sorozatának következő előadói ülésére**

Időpont: 2019. május 24. (péntek), délután 2 óra.

Helyszín: ELTE TTK Kémiai Épület (1117 Budapest, Pázmány Péter sétány 1/A.) 0.63-as előadóterem („Bruckner-terem”)

Program:

1. Kégl Tamás, PhD, tudományos főmunkatárs, Pécsi Tudományegyetem, TTK Kémiai Intézet, Szervetlen Kémia Tanszék

Katalitikus karbonilezési reakciók számításos vizsgálata

2. Kiss Nóra Zsuzsa, PhD, egyetemi adjunktus, BME Szerves Kémia és Technológia Tanszék

Foszfinátok, foszfonátok és foszfátok előállításának újabb megközelítései

Várjuk szíves megjelenésüket ezen a fontos előadói ülésen.

Huszthy Péter Hazai László

MTA levelező tagja a kémia tudomány doktora

az MTA Szerves és Biomolekuláris az MTA Szerves és Biomolekuláris

Kémiai Bizottságának elnöke Kémiai Bizottságának titkára

3.) A munkabizottság nevében gratulálunk Kövér Katalin Professzor Aszzonynak és Huszthy Péter Professzor Úrnak az MTA rendes tagjává való választáshoz.

<https://mta.hu/mta_hirei/bemutatjuk-a-magyar-tudomanyos-akademia-ujonnan-megvalasztott-tagjait-109669>

4.) Szeretnénk a Munkabizottság tagjainak legújabb eredményeit, megjelent közlemények kivonatait hírlevelünkben is közzétenni. Kérem, aki élni szeretne a lehetőséggel, továbbítsa közleménye absztraktját.

**New syntheses towards C-glycosyl type glycomimetics**

**László Somsák, Éva Bokor, László Juhász, Sándor Kun, László Lázár, Éva Juhász-Tóth,Marietta Tóth**

**Pure and Applied Chemistry, 2019**

DOI: <https://doi.org/10.1515/pac-2019-0208>

**Abstract**

Glycomimetics are compounds that resemble carbohydrate molecules in their chemical structure and/or biological effect. A large variety of compounds can be designed and synthesized to get glycomimetics, however, C-glycosyl derivatives represent one of the most frequently studied subgroup. In the present survey syntheses of a range of five- and six membered C-glycopyranosyl heterocycles, anhydro-aldimine type compounds, exo-glycals, C-glycosyl styrenes, carbon-sulfur bonded oligosaccharide mimics are described. Some of the C-glycopyranosyl azoles, namely 1,2,4-triazoles and imidazoles belong to the most efficient glucose analog inhibitors of glycogen phosphorylase known to date. Biological studies revealed the therapeutical potential of such inhibitors. Other synthetic derivatives offer versatile possibilities to get further glycomimetics.

**Kilogram scale chemical synthesis of 2′-fucosyllactose**

**Károly Ágoston, Markus Jondelius Hederos, István Bajza, Gyula Dékány**

**Carbohydrate Research 476, 2019, 71-77**

Abstract

A scalable synthetic procedure to high quality 2′-fucosyllactose, the most abundant oligosaccharide in human breast milk, has been designed and validated in kilogram scale. The synthetic route has been developed to suit industrial environment and contains only a single chromatographic purification step.

**Studies on the reversible enzyme reaction of rabbit muscle glycogen phosphorylase b using isothermal titration calorimetry**

**Kármen Szabó, Lili Kandra, Gyöngyi Gyémánt**

**Carbohydrate Research 477, 2019, Pages 58-65**

**Abstract**

Glycogen phosphorylase enzymes (GP) catalyse reversible reactions; the glucose transfer from glycogen to inorganic phosphate (Pi, phosphorolysis) or the reverse glucose transfer from glucose-1-phosphate (G-1-P) to glycogen (synthesis). Rabbit muscle GPb (rmGPb) was used as a model enzyme to study the reversible enzyme reaction. To follow both directions of this reversible reaction, we have developed a novel isothermal titration calorimetry (ITC) method for the determination of the direct reaction rate. The preference of forward or reverse reaction was ensured by the 0.1 or 10 concentration ratios of G-1-P/Pi, respectively. Substrate specificity was studied using different maltooligosaccharides and glycogen. Based on the KM values, glycogen and 2-chloro-4-nitrophenyl maltoheptaoside (CNP-G7) were found to be analogous substrates, which allowed to optimize the method by taking advantage of the CNP chromophore being detectable in HPLC. In case of CNP-G7, substrate inhibition was observed and characterised by Ki of 23 ± 7 mM. Inhibition of human GP is a promising strategy for the treatment of diabetes. Our ITC measurements have confirmed that caffeine and glucopyranosylidene-spiro-thiohydantoin (GTH), as known GPb inhibitors, inhibit the rmGPb-catalysed reversible reaction in both directions. Ki values obtained in the direction of synthesis (1.92 ± 0.14 mM for caffeine and 11.5 ± 2.0 μM for GTH) have been shown to be in good agreement with the Ki values obtained in the direction of phosphorolysis (4.05 ± 0.26 mM for caffeine and 13.8 ± 1.6 μM for GTH). The higher difference between the inhibition constants of caffeine was explained by the non-competitive mechanism.The described ITC method using the developed experimental design and reaction conditions is suitable for activity measurements of different phosphorylase enzymes on various substrates and is applicable for inhibition studies as well.

**Synthesis of the chiral selector heptakis(6‐O‐methyl)‐β‐cyclodextrin by phase‐transfer catalysis and hydrazine‐mediated transfer‐hydrogenation**

**Mihály Bálint, András Darcsi Gábor Benkovics Erzsébet Varga Milo Malanga Szabolcs Béni**

**Electrophoresis 2019, DOI 10.1002/elps.201900065**

**Abstract:** The exhaustive primary-side alkylation of cyclodextrins has never been achieved directly.The undesired and simultaneous derivatization of the secondary hydroxyl moieties gener-ates intricate isomeric mixtures that are challenging to purify, analyse and characterize. Theaim of this study was to develop a chromatography-free and up-scalable strategy towardsthe preparation of per-6-O-methylated cyclodextrin and to test the compound as potentialchiral selector. The target molecule was prepared according to a five-step synthesis by us-ing methyltriphenylphosphonium bromide as catalyst under heterogeneous conditions.The removal of benzyl moieties, used as temporary secondary-side protecting groups, wasattained by applying hydrazine-carbonate in the presence of Pd/C. All the intermediateswere obtained in high yields, thoroughly characterized and their purity was assessed byad-hocdeveloped HPLC methods. The per-6-O-methylated-cyclodextrin showed promis-ing chiral recognition ability as background electrolyte additive in cyclodextrin-modifiedcapillary electrophoresis using the recreational drug methylene-dioxypyrovalerone asmodel compound. Additionally, a model for the inclusion geometry between the singleisomer host and the selected drug was developed based on the extensive 2D NMR analysis.The versatility of the proposed synthetic strategy opens the way to the industrial productionof homogeneously primary-alkylated cyclodextrins and to their wide application in chiralseparation of various drugs.

**A Three‐Color Fluorescent Supramolecular Nanoassembly of Phototherapeutics Activable by Two‐Photon Excitation with Near‐Infrared Light**

**Dr. Aurore Fraix Dr. Vladimir Kirejev Dr. Milo Malanga Dr. Éva Fenyvesi Prof. Szabolcs Béni Prof. Marica B. Ericson Prof. Salvatore Sortino**

**Chem. Eur. J. 10.1002/chem.201900917**

**Abstract**

A supramolecular nanoassembly, of about 30 nm in diameter, that consists of a green‐fluorescent, β‐cyclodextrin‐based, branched polymer co‐encapsulating a red‐emitting singlet oxygen (1O2) photosensitizer and a nitric oxide (NO) photoreleaser, which comprises a blue fluorescent reporter, is here reported. The system exhibits “five‐in‐one” photofunctionalities. All components can be simultaneously excited in the phototherapeutic window with two‐photons by using near‐infrared light at 740 nm and despite their close proximity, behave as independent units. This allows for their in vitro visualization in carcinoma cancer cells, due to their distinct green, red, and blue fluorescence, and for the production of both cytotoxic 1O2 and biofunctional NO.

**α/β-Chimera peptide synthesis with cyclic β-sugar amino acids: the efficient coupling protocol**

**Adrienn Nagy, Viktória Goldschmidt Gőz, István Pintér, Viktor Farkas, András Perczel**

**Amino Acids (2019) 51: 669.**

**Abstract**

The synthesis of α/β-chimeras comprises peptide bond formation from α- to β-, from β- to β-, and from β- to α-amino acid residues. The fine-tuned solid phase synthesis of –GXXG– chimera peptides containing the simplest achiral α-amino acid glycine and two cyclic SAAs of different ring size [X denoting cyclic β-Sugar Amino Acids (β-SAA)] is reported, variants containing Fmoc–RibAFU(ip)–OH a furanoid-, and Fmoc–GlcAPU(Me)–OH a pyranoid-type structural “Lego-element”. Systematic search for the best coupling strategy with both H–β-SAA–OHs is described, including the comparison of the different coupling reagents and conditions. Selecting the optimal reagent (from commonly used PyBOP, HATU and HOBt) was assisted by time-resolved 1H-NMR: formation and stability of the Fmoc protected active esters were compared. We found that PyBOP is the best choice for successfully coupling both H–β-SAA–OH prototypes. The present comparative results open a reasonable route for building efficiently various –β-SAA– containing homo- and heterooligomers.

**Zanichelli, A.; Tamburello, D.; Jicsinszky, L.; Rosetti, L.; Cravotto, G.; Martina, K. & Caporaso, M. N.**

**A Process to Remove Bad Smell and Odours from Plastic Materials WO2018047205**

**Abstract:** A process to remove bad odours from plastic materials is disclosed, wherein said materials contain at least a polymer and at least a plasticiser. According to the process, natural or synthetic mono-, linear, branched or cyclic oligomeric carbohydrates are added during the compounding of the plastic formulation in order to fulfill the above indicated aim. The process is particularly suitable when said polymer is a polyvinyl chloride resin (PVC), chosen so as to exhibit a K value in the range K50-K85, and preferably in the range K64-K80. The invention also relates to a plastic material, containing at least a polymer and at least a plasticiser, on which natural or synthetic, mono-, linear, branched or cyclic oligomeric carbohydrates are grafted, once the formulation compounding already happened.

**Jicsinszky, L.**

**Some Comments on the Cyclodextrin Solubilities *MOJ Bioorganic & Organic Chemistry,* 2019*, 3*, 11-13. *DOI: 10.15406/mojboc.2019.03.00091***

**Abstract:** The cyclodextrin (CD) solubilities in various solvent systems are discussed. The erroneous aqueous solubility-temperature equations have been substituted with simpler ones. The new equations calculate the CD solubilities in water more accurately. Re-calculation of the literature data of organic solvent-water mixtures from molar fractions to volume percentage of organic solvents resulted in a more user friendly data

**Argenziano, M.; Haimhoffer, A.; Bastiancich, C.; Jicsinszky, L.; Caldera, F.; Trotta, F.; Scutera, S.; Alotto, D.; Fumagalli, M.; Musso, T.; Castagnoli, C. & Cavalli, R. In Vitro Enhanced Skin Permeation and Retention of Imiquimod Loaded in Βcyclodextrin Nanosponge Hydrogel**

***Pharmaceutics,* 2019*, 11*, 138. *DOI: 10.3390/pharmaceutics11030138***

**Abstract:** Imiquimod (IMQ) is an immune response modifier clinically used for the treatment of various topical diseases. However, its poor aqueous solubility and skin penetration capability make the topical delivery of IMQ a challenging task. This work aims at developing a nanomedicine-based topical formulation, carrying IMQ to control the scarring process for the treatment of aberrant wounds. For this purpose, IMQ was loaded in β-cyclodextrin-based nanosponges and dispersed in a hydrogel suitable for dermal application. The formulation was characterized in vitro and compared with IMQ inclusion complexes, with (2-hydroxy)propyl βcyclodextrin(HPβCD) and carboxymethyl β-cyclodextrin (CMβCD) showing enhanced penetration properties. The hydrogel containing IMQ-loaded nanosponges could act as a drug reservoir and guarantee the sustained release of IMQ through the skin. A greater inhibitory effect on fibroblast proliferation was observed for IMQ loaded in nanosponges compared to the other formulations.

**Ge, X.; Wu, Z.; Manzoli, M.; Jicsinszky, L.; Wu, Z.; Nosyrev, A. E. & Cravotto, G.**

**Adsorptive Recovery of Iopamidol from Aqueous Solution and Parallel Reuse of**

**Activated Carbon: Batch and Flow Study**

***Ind. Eng. Chem. Res.,* 2019 *DOI: 10.1021/acs.iecr.9b00516***

**Abstract:** The present study demonstrates the adsorptive recovery of Iopamidol (IOP), which is a highly valuable X-ray iodinated contrast media (ICM) from aqueous solution and the reuse of the adsorbent activated carbon (AC) via elution with alcohol. Of the adsorbents selected, coconut powder AC (CPAC) displayed the best adsorption performance for IOP. The results of batch investigation into adsorption kinetics, isotherms, activation energy and thermodynamic calculations support the occurrence of a physisorption process. The adsorption mechanism has been determined using the intra-particle diffusion model. A Boyd plot has revealed that IOP adsorption onto CPAC was mainly governed by particle diffusion. CPAC also exhibited excellent adsorptive performance towards IOP, which was efficiently eluted and recovered using methanol in a semi-continuous flow system. Moreover, the spent CPAC was efficiently regenerated and reused in five adsorption/desorption cycles. The characterization of CPAC samples by SEM, DRIFT and TGA show that IOP is absorbed onto CPAC, leading to significant decreases in the BET surface area, pore volume and shift of pore diameter. p-p interactions, donor-acceptor complex, Van der Waals and hydrogen bonds interactions are governed the IOP adsorption. Hydrogen bonds interactions between IOP and alcohols play a crucial role in desorption process. IOP was completely eluted and the surface properties of CPAC were recovered after elution in the flow system. This study demonstrates that many benefits can be achieved from adsorption/desorption processes, such as those in wastewater treatment and the recovery of valuable compounds, as adsorbent recycling simplifies the operations and reduces treatment costs.

*A havi rendszerességű hírlevélben megjelentetni kívánt anyagot kérjük minden hónap utolsó napjáig elküldeni a* [*csavas.magdolna@science.unideb.hu*](mailto:csavas.magdolna@science.unideb.hu) *email címre.*

Üdvözlettel: Csávás Magdolna

a munkabizottság titkára

2019. április