**Hírlevél**

**MTA Szénhidrát, Nukleinsav és Antibiotikumkémiai Munkabizottság**

**2017. január**

1.) A 2017. évi munkabizottsági ülés időpontja: **2017. 05. 31. (szerda) - 2017. 06. 02. (péntek), Mátraháza**

Nagy örömünkre szolgál bejelenteni, hogy elfogadta felkérésünket az MB ülésen való részvételre és plenáris előadásra **Alberto Marra** (Franciaország) és **Michaela Wimmerová** (Csehország).

Kutatási területük az alábbi linken megtekinthetőek:

<https://ibmm.umontpellier.fr/spip.php?page=pageperso&nom=marra&prenom=alberto&lang=fr>

<https://www.muni.cz/en/people/854-michaela-wimmerova>

**Az idei árajánlat:**

Szállás reggelivel kétágyas elhelyezéssel 7.200.-Ft/fő/éj

Szállás reggelivel egyágyas elhelyezéssel 8.700.-Ft/fő/éj

Ebéd, vacsora (3 fogásos menüválasztással): 2.500.-Ft/fő/alkalom

Ebéd, vacsora (2 fogásos menüválasztással): 2.000.-Ft/fő/alkalom

(italfogyasztás nélkül)

Terem használat 1.500.-Ft/ fő/nap

2.) Szeretnénk a Munkabizottság tagjainak legújabb eredményeit, megjelent közlemények kivonatait hírlevelünkben is közzétenni. Ízelítőül néhány közlemény:

**C-Glycopyranosyl Arenes and Hetarenes: Synthetic Methods and Bioactivity Focused on Antidiabetic Potential**

Éva Bokor, Sándor Kun, David Goyard, Marietta Tóth, Jean-Pierre Praly, Sébastien Vidal, and László Somsák

*Chem. Rev*., Article ASAP, DOI: 10.1021/acs.chemrev.6b00475, Publication Date (Web): January 25, 2017

Abstract: This Review summarizes close to 500 primary publications and surveys published since 2000 about the syntheses and diverse bioactivities of C-glycopyranosyl (het)arenes. A classification of the preparative routes to these synthetic targets according to methodologies and compound categories is provided. Several of these compounds, regardless of their natural or synthetic origin, display antidiabetic properties due to enzyme inhibition (glycogen phosphorylase, protein tyrosine phosphatase 1B) or by inhibiting renal sodium-dependent glucose cotransporter 2 (SGLT2). The latter class of synthetic inhibitors, very recently approved as antihyperglycemic drugs, opens new perspectives in the pharmacological treatment of type 2 diabetes. Various compounds with the C-glycopyranosyl (het)arene motif were subjected to biological studies displaying among others antioxidant, antiviral, antibiotic, antiadhesive, cytotoxic, and glycoenzyme inhibitory effects.

**Tri- and tetravalent mannoclusters cross-link and aggregate BC2L-A lectin from Burkholderia cenocepacia**

Magdolna Csávás, Lenka Malinovská, Florent Perret, Milán Gyurkó, Zita Tünde Illyés, Michaela Wimmerová, Anikó Borbás

*Carbohydr. Res.,* 437 (2017) 1-8.

Abstract: The opportunistic Gram-negative bacterium *Burkholderia cenocepacia* causes lethal infections in cystic fibrosis patients. Multivalent mannoside derivatives were prepared as potential inhibitors of lectin BC2L-A, one of the virulence factors deployed by *B. cenocepacia* in the infection process. An (α1→2)-thio-linked mannobioside mimic bearing an azide functionalized aglycon was conjugated to different multivalent scaffolds such as propargylated calix[4]arenes, methyl gallate and pentaerythritol by azide-alkyne 1,3-dipolar cycloaddition. The interaction between the glycoclusters and the mannose binding BC2L-A lectin from *B. cenocepacia* was examined by isothermal microcalorimetry, surface plasmon resonance, inhibition of yeast agglutination and analytical ultracentrifugation.

**Synthesis of carotenoid-monosaccharide conjugates via azide–alkyne click-reaction**

Attila Agócs, Éva Bokor, Anikó Takátsy, Tamás Lóránd, József Deli, László Somsák and Veronika Nagy

*Tetrahedron* 73 (2017) 519-526.

Abstract: Carotenoid pentynoates were coupled to protected and unprotected sugar azides via an azide-alkyne click-reaction using bis-triphenylphosphano-copper(I)-butyrate (C3H7COOCu(PPh3)2) complex. Protected sugars delivered the conjugates with excellent yields, whereas with unprotected ones amphipathic carotenoid-sugar derivatives were obtained in good or moderate yields in a simple way.

**Xanthines studied by femtosecond fluorescence spectroscopy.**

Changenet-Barret, P.; Kovács, L.; Markovitsi, D.; Gustavsson, T.,

*Molecules* **2016,** 21, (12), 1668:1-11. DOI: 10.3390/molecules21121668; <http://www.mdpi.com/1420-3049/21/12/1668/html>

Abstract: Xanthines represent a wide class of compounds closely related to the DNA bases adenine and guanine. Ubiquitous in the human body, they are capable of replacing natural bases in double helices and give rise to four-stranded structures. Although the use of their fluorescence for analytical purposes was proposed, their fluorescence properties have not been properly characterized so far. The present paper reports the first fluorescence study of xanthine solutions relying on femtosecond spectroscopy. Initially, we focus on 3-methylxanthine, showing that this compound exhibits non-exponential fluorescence decays with no significant dependence on the emission wavelength. The fluorescence quantum yield (3 × 10−4) and average decay time (0.9 ps) are slightly larger than those found for the DNA bases. Subsequently, we compare the dynamical fluorescence properties of seven mono-, di- and tri-methylated derivatives. Both the fluorescence decays and fluorescence anisotropies vary only weakly with the site and the degree of methylation. These findings are in line with theoretical predictions suggesting the involvement of several conical intersections in the relaxation of the lowest singlet excited state.

**Synthesis and biological evaluation of triazolyl 13α-estrone–nucleoside bioconjugates.**

Bodnár, B.; Mernyák, E.; Wölfling, J.; Schneider, G.; Herman, E. B.; Szécsi, M.; Sinka, I.; Zupkó, I.; Kupihár, Z.; Kovács, L.,

*Molecules* **2016,** 21, (9), 1212. DOI: 10.3390/molecules21091212; <http://www.mdpi.com/1420-3049/21/9/1212>

Abstract: 2'-Deoxynucleoside conjugates of 13α-estrone were synthesized by applying the copper-catalyzed alkyne–azide click reaction (CuAAC). For the introduction of the azido group the 5′-position of the nucleosides and a propargyl ether functional group on the 3-hydroxy group of 13α-estrone were chosen. The best yields were realized in our hands when the 3′-hydroxy groups of the nucleosides were protected by acetyl groups and the 5′-hydroxy groups were modified by the tosyl–azide exchange method. The commonly used conditions for click reaction between the protected-5′-azidonucleosides and the steroid alkyne was slightly modified by using 1.5 equivalent of Cu(I) catalyst. All the prepared conjugates were evaluated in vitro by means of MTT assays for antiproliferative activity against a panel of human adherent cell lines (HeLa, MCF-7 and A2780) and the potential inhibitory activity of the new conjugates on human 17β-hydroxysteroid dehydrogenase 1 (17β-HSD1) was investigated via in vitro radiosubstrate incubation. Some protected conjugates displayed moderate antiproliferative properties against a panel of human adherent cancer cell lines (the protected cytidine conjugate proved to be the most potent with IC50 value of 9 μM). The thymidine conjugate displayed considerable 17β-HSD1 inhibitory activity (IC50 = 19 μM).

**A three-component reagent system for rapid and mild removal of *O*-, *N*- and *S*-trityl protecting groups.**

Kicsák, M.; Bege, M.; Bereczki, I.; Csávás, M.; Herczeg, M.; Kupihár, Z.; Kovács, L.; Borbás, A.; Herczegh, P.,

*Organic and Biomolecular Chemistry* **2016,** 14, (12), 3190-3192. DOI: 10.1039/C6OB00067C; <http://dx.doi.org/10.1039/C6OB00067C>.

Abstract: A new reagent system consisting of a Lewis acid such as BF3·Et2O or Cu(OTf)2, the mild protic acid hexafluoroisopropanol and the reducing quenching agent triethylsilane was elaborated for *O*-, *N*- and *S*-detritylation of nucleoside, carbohydrate and amino acid derivatives. The method is compatible with acetyl, silyl, acetal and Fmoc groups.

**Synthesis and biological evaluation of lipophilic teicoplanin pseudoaglycon derivatives containing a substituted triazole function.**

Szűcs, Zs., Csávás, M., Rőth, E., Borbás, A., Batta, G., Perret, F., Ostorházi, E., Szatmári, R., Vanderlinden, E., Naesens, L., Herczegh, P.

*J. Antibiot.* 2017 70 (2): 152-157. doi: 10.1038/ja.2016.80

Abstract: A series of lipophilic teicoplanin pseudoaglycon derivatives, including alkyl-, aryl-, calixarene- and protected sugar-containing conjugates, were prepared using azide-alkyne click chemistry. Out of the conditions applied, the CuSO4-ascorbate reagent system proved to be more efficient than the Cu(I)I-Et3N-mediated reaction. Some of the new compounds have high in vitro activity against glycopeptide-resistant Gram-positive bacteria, including vanA-positive *Enterococcus faecalis*. A few of them also display promising in vitro anti-influenza activity.

**A Modular Synthetic Approach to Isosteric Sulfonic Acid Analogues of the Anticoagulant Pentasaccharide Idraparinux**

E. Mező, D. Eszenyi, E. Varga, M. Herczeg and A. Borbás

*Molecules* 2016, 21(11), 1497; doi:10.3390/molecules21111497

Abstract: Heparin-based anticoagulants are drugs of choice in the therapy and prophylaxis of thromboembolic diseases. Idraparinux is a synthetic anticoagulant pentasaccharide based on the heparin antithrombin-binding domain. In the frame of our ongoing research aimed at the synthesis of sulfonic acid-containing heparinoid anticoagulants, we elaborated a modular pathway to obtain a series of idraparinux-analogue pentasaccharides bearing one or two primary sulfonic acid moieties. Five protected pentasaccharides with different C-sulfonation patterns were prepared by two subsequent glycosylation reactions, respectively, using two monosaccharide and four disaccharide building blocks. Transformation of the protected derivatives into the fully O-sulfated, O-methylated sulfonic acid end-products was also studied.

**Inhibitory Effect of Multivalent Rhamnobiosides on Recombinant Horseshoe Crab Plasma Lectin Interactions with Pseudomonas aeruginosa PAO1**

M. Herczeg, E. Mező, N. Molnár, S-K. Ng, Y.-C. Lee, M. Dah-Tsyr Chang A. Borbás

*Chemistry An Asian Journal*, 11, 23, 2016, 3398–3413

DOI: 10.1002/asia.201601162

Abstract: Less is sometimes more: Two sets of glycoclusters with up to four α(1–3)-rhamnobiosides were prepared to study their inhibitory effect on recombinant horseshoe crab plasma lectin (rHPL)–bacteria interactions. Trivalent rhamnobiosides on a pentaerythritol or a Tris central core showed a stronger inhibitory effect on P. aeruginosa PAO1 binding than either the corresponding tetravalent derivatives or the less flexible methyl gallate-based trivalent clusters (see figure).

*Továbbra is bátorítok és kérek mindenkit, aki élni szeretne ezzel a lehetőséggel, továbbítsa felém a megjelent közleményeinek kivonatát.*

*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:

Somsák László Csávás Magdolna

a munkabizottság elnöke a munkabizottság titkára

2017. február 14.