German-Polish-Baltic Conference on Organic Chemistry

Hamburg, 15th-19th May 2018, Book of Abstracts

Programme

Tuesday 15 May 2018	
15:00-18:00	Arrival, Registration and Check in
18:30	Dinner
Wednesday 16 May 2018	
8:00	Breakfast
	Synthetic Methodology I Chair: Christian B. W. Stark, Hamburg
9:00-9:10	Welcome
9:10-9:40	**Jacek Mlynarski**, Cracow, Keynote Lecture: *Zinc Instead of Noble Metals: Enantioselective Reduction and Carbon-Carbon Bond Forming Reactions Promoted by Zinc Complexes*
9:40-10:00	**Krista Suta** et al., Riga: *Application of Liquid SO_2 as a Solvent for Organic Synthesis*
10:00-10:10	**Krzysztof Gutkowski** et al., Warsaw: *Synthesis and Photophysical Properties of N-Arylated Diketopyrralopyrroles*
10:10-10:30	**Lukasz Albrecht**, Łódź, Invited Lecture: *Vinylogous synthetic strategies in asymmetric organocatalysis*
10:30-10:50	Coffee break
	Glycoscience I Chair: Ernst Schaumann, Clausthal
10:50-11:20	**Slawomir Jarosz**, Warsaw, Keynote Lecture: *Stereoselective Synthesis of Sugar Mimetics from Simple Monosaccharides*
11:20-11:30	**Sven O. Jaeschke** et al., Kiel: *Maltose as a Scaffold Molecule for the Synthesis of Heteromultivalent Glycoclusters*
11:30-11:40	**Sophia Boden** et al., Düsseldorf: *Varying Hydrophobicity of Precision Glycomacromolecules and the Effect on Lectin Binding*
11:40-11:50	**Matylda Stefaniak** et al., Cracow: *Synthesis of Ulosonic Acids via Zinc- and Iron-promoted Asymmetric Hetero Diels-Alder Reaction*
11:50-12:10	**Ulrika Westerlind**, Dortmund, Invited Lecture: *Exploring Bacterial Lectin Recognition Events of Synthetic Mucin Glycopeptide Ligands*
12:10-14:00	Lunch break

	Natural Product Chemistry I Chair: Daniel T. Gryko, Warsaw
14:00-14:30	**Jeroen Dickschat**, Bonn, Keynote Lecture: *Tracing Terpenes with Isotopes*
14:30-14:45	**Christian B. W. Stark**, Hamburg: *Biomimetic Natural Product Synthesis*
14:45-15:00	**Nina Schützenmeister** et al., Hamburg: *Total Syntheses of Marine Natural Products*
15:00-15:20	**Malte Brasholz**, Rostock, Invited Lecture: *New Catalytic Photooxygenations of Indole Alkaloids*
15:20-15:30	**Gunnar Ehrlich** et al., Hamburg: *Synthesis of Cytospolides D, M, O, and Q and Late-Stage Diversification of Derivatives Thereof*
15:30-15:40	**Christian Bartens** et al., Hannover: *New seco-Progeldanamycin Derivatives: Tools to Study the Substrate Flexibility of the Amide Synthase GdmF*
15:40-15:50	**Fabian Schneider** et al., Konstanz: *Studies towards the Total Synthesis of Canataxpropellane*
15:50-16:30	Coffee break
16:30-16:45	**Johannes Panten**, Holzminden: *Aroma Molecules from Renewable Resources*
16:45-16:55	**Dominik Rekow** et al., Stuttgart: *A Chemoenzymatic Approach to Cembranoid Analogue*
16:55-17:05	**Caroline Poock** et al., Hannover: *Total Synthesis of Nannocystin Ax*
17:05-17:15	**Jevgenija Luginina** et al., Riga: *Synthesis of Novel Betulin Conjugates*
	Supramolecular Chemistry Chair: Paul Margaretha, Hamburg
17:20-17:40	**Riina Aav**, Tallinn, Invited Lecture: *Hemicucurbiturils and their Dynamic Chemistry*
17:40-18:00	**Marcin Stępień**, Wroclaw, Invited Lecture: *From Coronoid Macrocyles to Stable Biradicaloid Systems*
18:00-18:10	**Monika Chwastek** et al., Warsaw: *Towards New Macrocylic Scaffolds*
18:10-18:20	**Agnieszka Czapik** et al., Poznań: *Trityl Group as a Tool for Construction of Multicomponent Supramolecular Materials*
18:20-18:30	**Sandra Kaabel** et al., Tallinn: *Template-driven Assembly of Hemicucurbit[n]uril Macrocycles in the Solid State*
18:30-18:50	**Agnieska Szumna** et al., Warsaw, Invited Lecture: *Dynamic Peptidic Containers - a Road towards Bio-inspired Self-assembly*
19:30	Dinner

Synthesis of Novel Betulin Conjugates

Jevgeņija Luginina[1], Rūdolfs Beļaunieks[1], Andis Melderis[1], Uldis Peipiņš[1], Reinis Vilšķērsts[2] and Māris Turks1

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Keywords: betulin, triazole, isoxazole

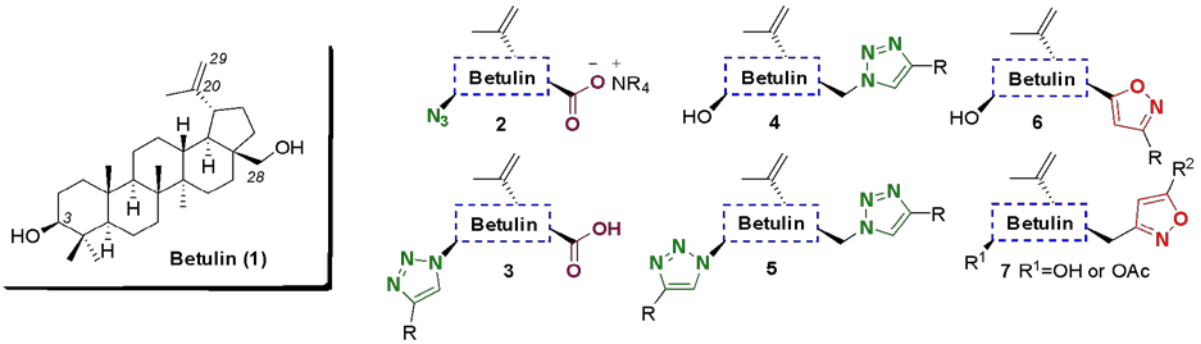
Betulin is an abundant naturally occurring triterpene, most commonly found in birch bark. Research shows that betulin and its derivatives possess wide spectrum of biological activities such as anti-HIV, anti-inflammatory, and anticancer properties.[1,2] Use of betulin is limited by its low solubility in water. Therefore, structural modifications of betulin with new functional groups to improve both the bioactivity and solubility in water are being made.[3]

In this work, various conjugates were obtained starting from betulin (**1**). 3-Azido betulinic acid was prepared by standard Jones oxidation, reductive amination at C(3) position and diazotransfer reaction sequence. Subsequently, it was converted into corresponding salts **2** with ammonia, choline, and some amino acids. Compound **2** was also employed in Cu(I) catalyzed azide-alkyne 1,3-dipolar cycloaddition reactions to obtain C(3)-triazolyl conjugate **3**.

To obtain C(28) betulin-triazole monoconjugates **4**, primary alcohol was chemoselectively oxidized. The obtained aldehyde was treated with hydroxylamine hydrochloride to obtain corresponding oxyme. Following catalytic hydrogenation gave amines with or without reduced C(20)-C(29) double bond. From the obtained amines corresponding azides and triazoles **4** were created *via* described two-step procedure. Betulin derivatives containing two triazole substituents **5** were synthesized in 5 steps, starting with Swern oxidation that gives ketoaldehyde. The treatment with hydroxylamine hydrochloride provided dioxyme that was used in reductive amination with $NaCNBH_3$ to obtain corresponding diamine, which again through azide intermediate provided target compounds **5**.

Finally, betulin-isoxazole derivatives **6** were prepared using alkynyl-betulin as a dipolarophile component in 1,3-dipolar cycloaddition reaction with different oxymes, while compound **7** was generated using nitroethyl-betulin as a dipole precursor.

Novel triterpene conjugates were tested on a rare cancer cell lines and observed cytotoxicity will be reported.



References

[1] Alakurtti, S., Makela, T., Koskimies, S., Yli-Kauhaluoma, J. *Eur. J. Pharm. Sci.* **2006**, *29*, 1.
[2] Murniece, R., Namniece, J., Nakurte, I., Jekabsons, K., Rieksina, U., Jansone, B. *Pharmacol. Res.* **2016**, *113*, 760.
[3] Khlebnicova, T. S., Piven, Y. A., Baranovsky, A. V., Lakhvich, F. A., Shishkina, S. V., Zicāne, D., Tetere, Z., Rāviņa, I., Kumpiņš, V., Rijkure, I., Mieriņa, I., Peipiņš, U., Turks, M. *Steroids.* **2017**, *117*, 77.