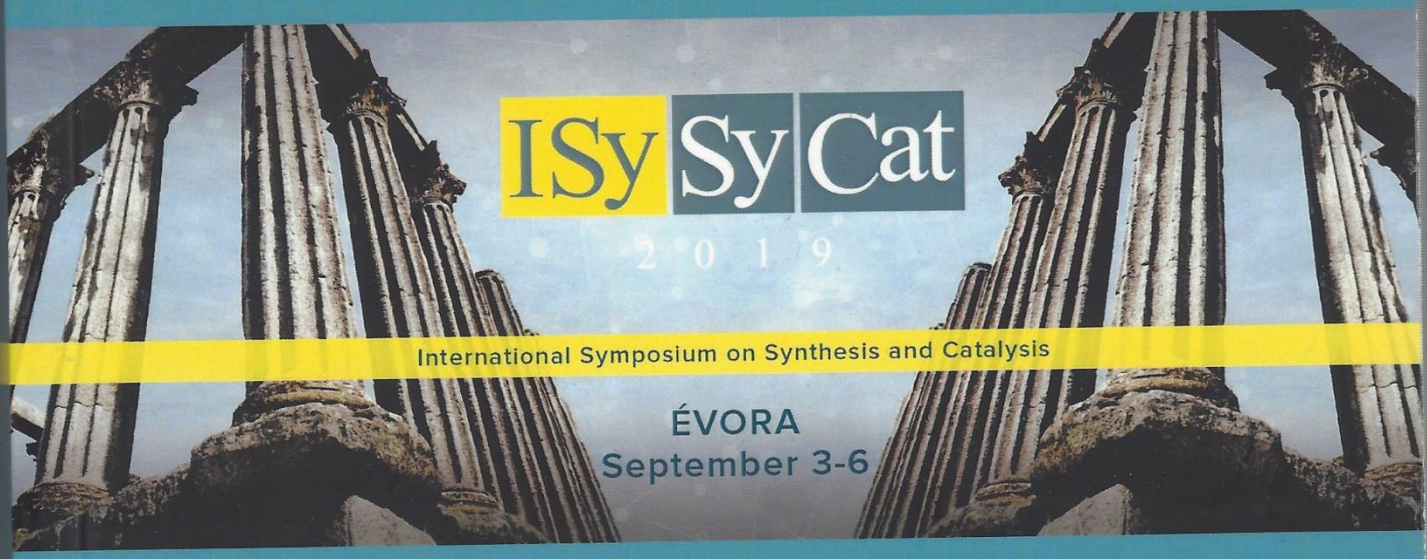


Book of Abstracts

UNIVERSIDADE DE ÉVORA

SOCIEDADE PORTUGUESA DE QUÍMICA

Synthesis of Novel Betulin-Triazole Conjugates and Exploration of Their Biological Activity

Rūdolfs Beļaunieks,[a] Andis Melderis,[a] Daina Zicāne,[a] Jevgeņija Lugiņina,[a] Reinis Vilšķērsts,[b] Uldis Peipiņš,[a] Māris Turks[a]*

[a]*Institute of Technology of Organic Chemistry, Faculty of Materials Science and Applied Chemistry, Riga Technical University, P. Valdena str. 3, Riga, LV-1048,* [b]*Faculty of Pharmacy, Riga Stradins University, Dzirciema str. 16, Riga, LV-1007*

Email: rudolfs.belaunieks@rtu.lv

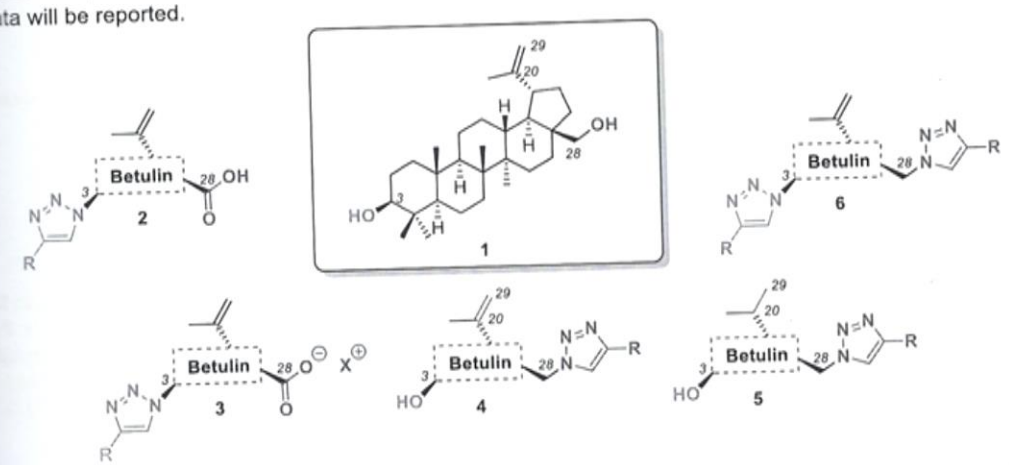
Betulin (**1**) is an abundant naturally occurring triterpene that is most commonly found in birch bark. Research shows, that betulin and its derivatives possess wide spectrum of biological activity – antiinflammatory, anti-HIV and anticancer properties.[1] To improve the latter, structural modifications with new biological activity are being made.[2]

The synthesis of triterpenoid-triazole monoconjugates at C(3) position (**2**) was initiated by Jones oxidation. Obtained ketocarboxylic acid was used in reductive amination followed by diazotransfer reaction. In CuAAC reaction from azido derivative 1,2,3-triazoles were synthesised and converted to corresponding salts (**3**) with ammonia, choline and some amino acids.

The synthesis of triterpenoid-triazole monoconjugates at C(28) position (**4** and **5**) was initiated by selective primary alcohol oxidation. The latter were threated with hydroxylamine hydrochloride followed by catalytic hydrogenation. By differentiating reaction conditions we were able to obtain products with or without reduced double bond at C(20)-C(29) position. Obtained amines were used in diazotransfer reaction to obtain correspoding azides. The latter were used in CuAAC reaction to obtain sets of 1,2,3-triazole conjugates.

The synthesis of triterpenoid-triazole diconjugates at positions C(3) and C(28) was initiated by employing betulin in Swern oxidation conditions. Obtained ketoaldehyde was threated with hydroxylamine hydrochloride followed by reductive amination. From the obtained diamine respective diazide and following bistriazoles were easily synthesised similarly to monoconjugate synthesis.

Novel triterpene-1,2,3-triazole conjugates were tested on rare cancer cell lines and obtained cytotoxicity data will be reported.



Scheme or Figure 1: Novel betulin-1,2,3-triazole conjugates.

Acknowledgements: This work was supported by ERA.NET RUS Plus project No. RUS_ST2017-139 // W3478 "Development of pentacyclic triterpenoid – azole conjugates: from cancer chemopreventive agents and adjuvants in cancer chemotherapy to novel anti-cancer drug candidates".

References:

1. Xiao, S.; Tian, Z.; Wang, Y.; Si. L.; Zhou, D. Med. Res. Rev. **2018**, *38*, 951.
2. 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.