SELECTIVE PROTECTION OF GLYCEROL

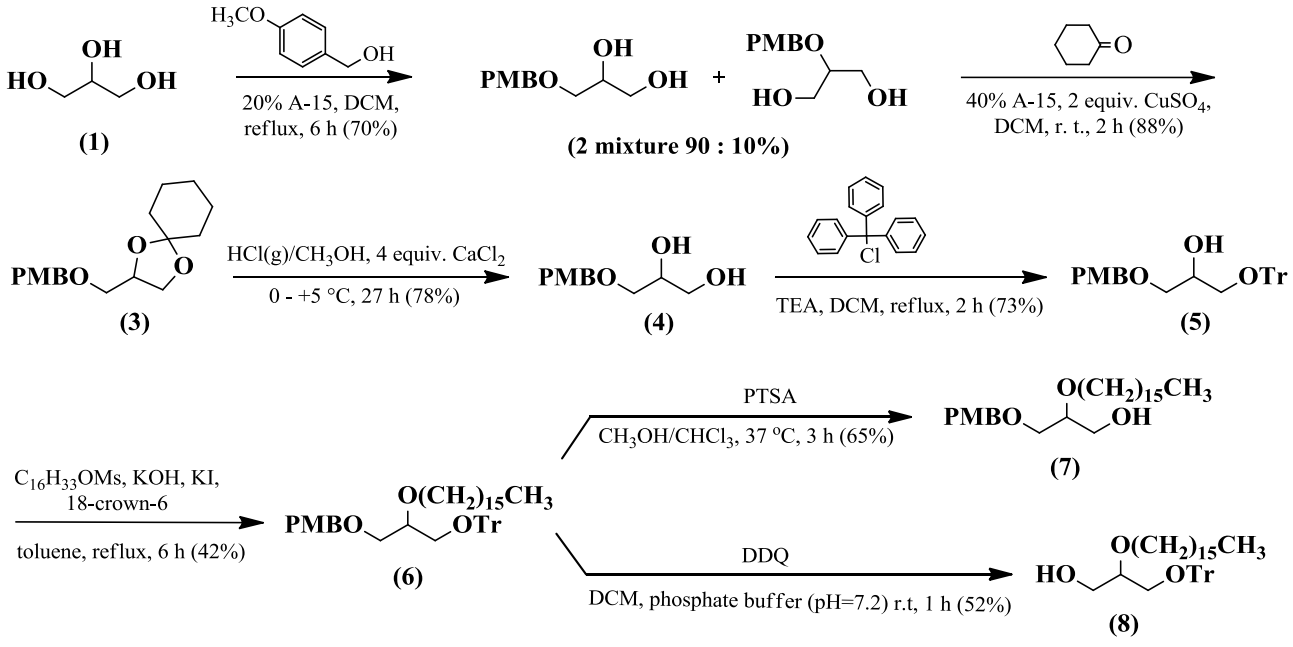
Greta Olimpija Remeikytė[1], Rytis Deržinauskas[1], Tatjana Charkova[2]

[1] Faculty of Chemistry and Geosciences, Vilnius University, Lithuania
[2] Department of Organic Chemistry, Center for Physical Sciences and Technology, Lithuania
greta.remeikyte@gmail.com

A simple, economic glycerol is an abundant source for a great variety of glycerol ethers with useful biological and physical properties such as immunostimulatory, anti-inflammatory, antimicrobial, antibacterial, antifungal, antitumor activity etc. The similarity of hydroxyl groups remains a main problem in glycerol etherification reactions – isomeric mono-, di- and triproducts are synthesized under similar conditions [1]. Many hydroxyl protecting groups have been reported to resolve this problem, but only not many of them are in common use [2, 3].

In our ongoing project of developing glycerol-based molecular systems, we have chosen to protect hydroxyl group by using p-methoxybenzyl (PMB) alcohol. PMB group can be selectively removed under acidic or mildly oxidizing conditions that do not affect alkenes, benzyl ethers, ketones, tosylates and some others derivatives [2, 3]. This open alternative way to use PMB glycerols in the synthesis of functionally complex compounds, where extensive selective protection-deprotection protocols are required.

We successfully found a new synthesis route of primary PMB monoprotected glycerol (Scheme 1, compound 4). Firstly, we protect commercial glycerol by using PMB alcohol. The primary product is isolated from produced mixture of isomers (90% and 10% respectively) by two simple steps: selective coupling with cyclohexanone and acidic hydrolysis of new synthesized cyclohexylidene-1-(4-methoxybenzyl)glycerol (compound 3). Hereby, we suggest inexpensive reagents and safely low temperature regimes for all protection-deprotection steps. All used resins and inorganic reagents are simply removed by filtration, neutralization and extraction procedures; this also makes isolation of products easier and more convenient. Then, monoprotected PMB glycerol is tritylated (synthesis of compound 5) and used for synthesis of monoalkyl glycerol ether (compound 6). Two selective deprotection methods have been shown: with p-toluenesulfonic acid (PTSA) and with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) reagent. Undoubtedly, it will be used for the synthesis of more complex structures in the near future.



Scheme 1. Selective protection-deprotection of glycerol.

[1] M. Sutter, E. Da Silva, N. Duguet, Y. Raoul, E. Métay, M. Lemaire, Glycerol ether synthesis: a bench test for green chemistry concepts and technologies, Chemical Reviews **115**, 8609-8651 (2015).
[2] P. J. Kocieński, *Protecting groups*, (3rd edition, Thieme, New York, 2003).
[3] T. W. Greene and P. G. Wuts, *Protective groups in organic synthesis*, (3rd edition, Wiley, New York 1999).