

Review of the PhD thesis titled “Enantioselective Vinylogous Mukaiyama-Michael Reaction with Acyclic Silyl Dienolates” by Smita Basu

The Doctoral Thesis of Mr. Smita Basu titled “Enantioselective Vinylogous Mukaiyama-Michael Reaction with Acyclic Silyl Dienolates”, completed under the supervision of Prof. Dr. Christopher Schneider (University of Leipzig) and Prof. Dr. Jacek Młynarski (Jagiellonian University), describes a remarkable class of carbon-carbon bond forming reactions, which can provide highly functionalized intermediates in one synthetic operation in an asymmetric fashion.

The term vinylogy, which describes a unique property of π systems where electron density and reactivity are amplified along conjugated bonds, was proposed 75 years ago by Fuson. To date, several enantioselective vinylogous processes have been described, among which vinylogous aldol and Mannich reactions have been extensively studied. Very recently, Schneider and co-workers reported the first catalytic, enantioselective vinylogous Mukaiyama-Michael reaction of acyclic dienol silyl ethers, which furnished valuable chiral 1,7-dioxo compounds with good yields and excellent regio- and enantioselectivity. However, this spectacular process is impeded by a number of limitations. The most important of them is the high catalyst loading employed (20 mol% of Hayashi-Jorgensen diphenylproline catalyst) and the problematic functionalization of the obtained products. The need to solve these two problems prompted the thesis research of Mr. Smita Basu.

In the first part of his dissertation, the author discusses the basic ideas and principles of organocatalysis. In the next chapter the author briefly describes the principles governing vinylogous-type reactions. This short introduction facilitates further reading of the text. Unfortunately, the references given in Section 3.4 are different from those listed in Section 8 (references). This is the only serious flaw I found in the theoretical part of the dissertation under review.

The next section presents a synthesis of vinylketene silyl-*N,O*-acetals and vinylketene silyl-*Si,O*-acetal respectively. Three new nucleophiles were synthesized by replacing the mesityl group (difficult to further modify) within the dienolate component with either a sterically and electronically similar 2,5-dimethyl pyrrole unit

or a trimethyl silyl group. Vinylketene silyl-*N,O*-acetals were prepared through enolization and silylation of the corresponding α,β -unsaturated *N*-acyl-2,5-dimethyl pyrroles, whereas the vinylketene silyl-*Si,O*-acetal was obtained by α -regioselective reaction of (1-silylallyl)lithiums with carbon monoxide (correct reference: *Organometallics*, **1996**, *15* 5459–5461).

After the successful synthesis of the vinylketene silyl-*N,O*-acetal, it was subjected to vinylogous Michael reaction. The candidate showed that vinylogous Mukaiyama-Michael reaction of DPMS-substituted dienolate with a broad range of enals is efficiently promoted by a combination of Hayashi-Jorgensen catalyst with PNBA as co-catalyst (10 mol % each) in toluene-ethanol (1:1) at room temperature. Finally, one of the 1,7-dioxo compounds was derivatized into a number of useful synthetic building blocks. In the next step the silyl-*Si,O*-acetal was also subjected to optimization studies with cinnamadehyde. The author stated that under the optimal reaction conditions the reaction gave only the desired γ -regioisomer in 78% yield and with excellent enantioselectivity (99%). In this chapter, the author clearly showed that the previous limitations concerning nucleophile reactivity, catalyst loading and subsequent product manipulation have been overcome by employing new dienolates.

I've found a few typographical errors in the submitted copy. This is a common problem, of no great importance and does not influence my excellent opinion on the reviewed thesis.

I would like to stress that the thesis provides very interesting material. The described transformations are simple and effective, asserting the candidate's knowledge, creativity and understanding of asymmetric organic synthesis. All reported reactions were carefully performed, the products were obtained in good yields and well characterized by NMR spectroscopy and mass spectrometry. These facts affirm the candidate's excellent acquaintance with modern organic chemistry.

I am strongly convinced that the thesis of Mr. Smita Basu fulfills all international standards of the PhD degree in organic chemistry. Therefore I recommend to the Jagiellonian University, Department of Organic Chemistry the granting of the PhD degree to Mr. Smita Basu.

Bartłomiej Furman

