

An Efficient Synthesis of Methallyl sulfoxides: Application of Sulfur Dioxide in C-S Bond Formation

Agnese Stikute¹, Vilnis Peipiņš², Māris Turks³
¹⁻³Riga Technical University

Keywords — Silyl sulfinates, Grignard reagents, sila-ene reaction, sulfoxides.

INTRODUCTION

Structural motif of sulfoxides is present in many naturally occurring [1] and biologically active compounds [2], that are used as medication [3]. Sulfoxides are also well-recognized synthetic intermediates. They form complexes with transition-metals and are used in catalysis [4]. The most common approaches for synthesis of sulfoxides are oxidation of sulfides and C-S bond formation in nucleophilic substitution reactions [5].

Herein we report an application of silyl sulfinates **1** in the synthesis of variously substituted methallyl sulfoxides **2** (see Scheme 1) [6]. Silyl sulfinates **1** are obtained in sila-ene reaction of allylsilanes **3** with sulfur dioxide.

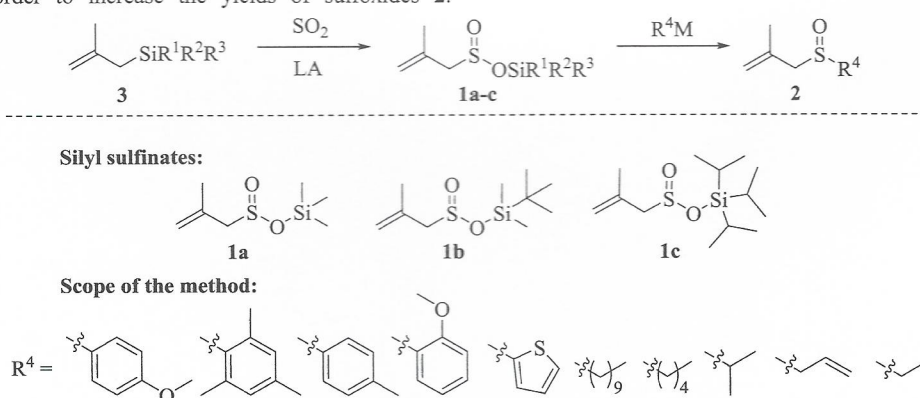
RESULTS AND DISCUSSIONS

In order to optimize the reaction conditions for sulfoxide **2** synthesis we investigated influence of solvent, temperature, organometallic reagent (including Grignard reagents, copper and cerium salts) and Lewis acid (e.g. LiCl, ZnCl₂, TMSOTf, TBSOTf, BF₃·OEt₂) additive on sulfoxide **2** yield. We have also diversified silyl moiety in sulfinates **1** structure, examining trimethylsilyl- (**1a**), *tert*-butyldimethylsilyl- (**1b**) and triisopropylsilyl sulfinates (**1c**) in order to increase the yields of sulfoxides **2**.

Experiments with Grignard reagents as nucleophiles and silyl sulfinates **1a,b** as sulfinyl transfer reagents showed the most promising results. The nucleophilic attack of Grignard reagents was accelerated in toluene and in the presence of LiCl or ZnCl₂ as Lewis acidic additives. The scope of the method has been demonstrated with the successful incorporation of aryl-, alkyl-, allyl-, and heterocyclic Grignard reagents. Under the given experimental conditions trialkylsilyloxy groups act as good leaving groups. The method described above gives opportunity to synthesize methallyl sulfoxides **2** in up to 83 % yield.

REFERENCES

- Jacob, C. A scent of therapy: pharmacological implications of natural products containing redox-active sulfur atoms. *Nat. Prod. Rep.* 2006, vol. 23, p. 851.
- Bentley, R. Role of sulfur chirality in the chemical processes of biology. *Chem. Soc. Rev.* 2005, vol. 34, p. 609.
- Zeng, Q., Gao, S., Chelashaw, A. K. Advances in Titanium-Catalyzed Synthesis of Chiral Sulfoxide Drugs. *Mini-Rev. Org. Chem.* 2013, vol. 10, p. 198.
- Mellah, M., Voituriez, A., Schulz, E. Chiral sulfur ligands for asymmetric catalysis. *Chem. Rev.* 2007, vol. 107, 5133.
- Wojaczynska, E., Wojaczynski, J. Enantioselective Synthesis of Sulfoxides: 2000–2009. *Chem. Rev.* 2010, vol. 110, 4303.
- Stikute, A., Peipiņš, V., Turks, M. Synthesis of allyl sulfoxides from allylsilanes via silyl sulfinates. *Tetrahedron Lett.* 2015, DOI: 10.1016/j.tetlet.2015.06.018.



Scheme 1. Strategy of sulfoxide **2** synthesis.

Search for Nitrogen

Krista Suta¹, Diāna
¹⁻³Riga Technical University

Keywords — Aziridine triazole conjugates, aziridine inhibitors.

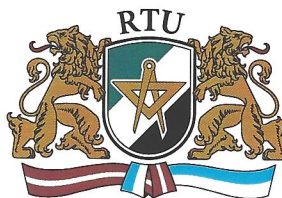
Matrix metalloproteinases (MMPs) are endopeptidases that are involved in the degradation of extracellular matrix proteins such as collagen, elastin and casein. Because of their role in physiological and pathological processes, they have become interesting targets for drug development. In addition, it is known that MMPs play a role in tumour growth and metastasis.

Previously our research group has reported on aziridine derivatives with 1,4-disubstituted triazole side chain as a new class of MMP inhibitors. Herein we report further studies on these derivatives as well as on the synthesis of compounds containing 1,5-disubstituted triazole side chain containing 1,4-disubstituted triazole side chain.

Synthesis of target compounds was carried out catalyzed Huisgen 1,3-dipolar cycloaddition between azide (**±**)-**1** or **2** and alkyne (**±**)-**3** (Scheme 1). Derivatives of azetidine containing 1,4-disubstituted triazole side chain were obtained using well established Huisgen 1,3-dipolar cycloaddition reaction yields 61–88 %. Whereas for synthesis of compounds containing 1,5-disubstituted triazole side chain complex Cp*RuCl(CO)₂ catalyzed cycloaddition was employed and 89 %.

For aziridines *N*-protected aziridines were used in small excess of TFA in toluene and the reaction proceeded in 64–85 % yield. Derivatives of triazoles (**±**)-**3a-j** and 1,5-disubstituted triazoles (**±**)-**4a-j** were obtained. The deprotection of azetidines the deprotected azetidines and isolated yields were 74 % and 74 %.

RIGA TECHNICAL UNIVERSITY
Faculty of Materials Science and Applied Chemistry



ABSTRACTS

**of the Riga Technical University
56th International Scientific Conference**

Section
Materials Science and Applied Chemistry
October 14–16, 2015, Riga, Latvia



Riga 2015