M6

From Methallylsilanes to Methallyl Sulfoxides

Agnese Stikute, Vilnis Peipiņš,
Faculty of Material Science and Applied Chemistry, Riga Technical University, P. Valdena 3, LV-1007, Riga, Latvia
E-mail: agnese.stikute@rtu.lv

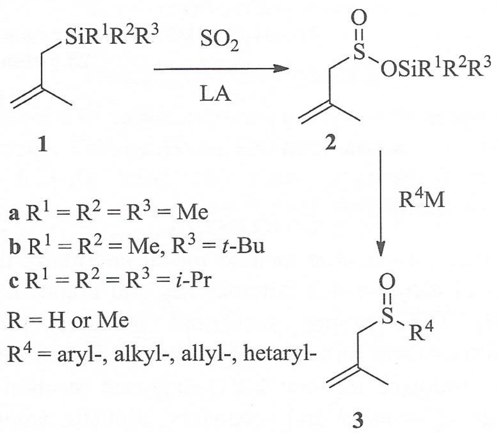
Introduction

Sulfur dioxide is widely used in synthetic organic chemistry as a solvent and reagent [1]. *Ene*-reaction of allyltrialkyltin, allylgermanes, allylsilanes and enoxysilanes with sulfur dioxide are well known [1]. An example worth mentioning is application of Vogel's silyl sulfinate (obtained by sila-*ene* reaction between methallylsilane and SO_2) as silylation reagent for GC-MS quantitative analysis [2]. Our research is focused on application of silyl methallylsulfinates in the synthesis of methallyl sulfoxides.

Sulfoxides exhibit a wide range of biological properties and are used as medication [3]. Chiral sulfoxides are used as chiral auxiliaries in transition metal catalysed reactions [3] and as intermediates in the synthesis of polypropionate antibiotics [4]. The most common approaches for synthesis of sulfoxides are oxidation of sulfides and C-S bond formation in nucleophilic substitution reactions [3].

Results and Discussions

We report here a novel method for synthesis of sulfoxides with general formula **3** (Scheme 1). It is based on addition of organometallic reagent to silyl methallylsulfinate **2**. The latter is obtained in sila-*ene* reaction of allylsilanes **1** with sulfur dioxide.



Scheme 1. Strategy of methallylsulfoxide **3** synthesis.

In order to optimize the reaction conditions for sulfoxide **3** synthesis, we investigated the influence of solvent, temperature, organometallic reagent and Lewis acid additive on the yield of sulfoxide **3a** (R=Ph) using trimethylsilyl sulfinate **2a**. Experiments with different organometallic reagents including copper and cerium salts showed low reactivity (isolated yields of sulfoxide **3a** were 30 – 40 %). The best results were obtained using Grignard reagent as a nucleophile. Addition of Lewis acids (e.g. LiCl, TMSOTf, TBSOTf, $BF_3{\cdot}OEt_2$) and the use of toluene as solvent instead of THF increased the isolated yield of sulfoxide **3a** to ~ 60 % – 80 %. The best of all conditions turned out to be addition of 1.0 equivalent of PhMgBr/LiCl in toluene at -100 °C (the isolated yield of **3a** was 79 %). When a premixed mixture of PhMgBr/$ZnCl_2$ was added to sulfinate **2a** competitive yield (69 %) of compound **3a** was obtained. The use of optimized reaction conditions with other Grignard reagents (R=aryl-, heterocyclic- and *n*-alkyl- (C_{10} and C_5)) gave good yields of sulfoxides **3** (66 % – 83 %). The present reaction conditions turned out to be ineffective when isopropyl-, allyl- and ethylmagnesium halides were used, but in these cases the premixed mixture of RMgX/$ZnCl_2$ gave good yields of corresponding sulfoxides **3** (~ 60 % – 75 %).

We also tested the ability of *t*-butyldimethylsilyl methallylsulfinate **2b** and triisopropylsilyl sulfinate **2c** to form sulfoxides **3** in the reactions with the corresponding Grignard reagents. When used without additives, the sterically more bulky starting material **2b** gave slightly higher yields of sulfoxides **3** than its trimethylsilyl counterpart **2a**. Also in this case addition of LiCl improved the yields of target sulfoxides **3**. Addition of Lewis acids such as TMSOTf, TBSOTf and $BF_3{\cdot}OEt_2$ gave similar results to the reactions in the presence of LiCl. We have found that premixing of Grignard reagent (R=isopropyl- or allyl-) with $ZnCl_2$ followed by addition of **2b** gave even better results of corresponding sulfoxides **3** (~ 80 %). Unfortunately, the use of triisopropylsilyl sulfinate **2c** gave lower results in comparison with sulfinates **2a,b** – the highest isolated yield of sulfoxide **3a** was 51 % when mixture of PhMgBr/$ZnCl_2$ was used.

In conclusion, we have developed a novel approach to sulfoxide synthesis which is based on sila-*ene* reaction between allylsilanes and SO_2 followed by LiCl- or $ZnCl_2$-assisted Grignard reagent addition to the *S*-center of silyl sulfinate. The scope of the method has been demonstrated with the successful use of aryl-, alkyl, allyl- and heterocyclic Grignard reagents.

Supervisor: Dr. chem. M. Turks.

Acknowledgement

A.S. thanks the Latvian Academy of Sciences for scholarship. This work was financed by the Latvian Council of Science Grant No 12.0291.

References

[1] (a) Lugiņina, J. *Synlett* 2014, *25*, 2962-2963; (b) Deeming, A. S.; Emmett, E. J.; Richards-Taylor, C. S.; Willis, M. C. *Synthesis* 2014, *46*, 2701-2710; (c) Vogel, P.; Markovic, D.; Turks, M. *Sulfur Dioxide: A Powerful Tool for the Stereoselective Construction C-C Bonds.* In *Stereoselective Synthesis of Drugs and Natural Products*, Chap. 22; Andrushko, V.; Andrushko, N., Eds.; John Wiley & Sons: Hoboken, New Jersey, 2013, 623-666.

[2] Novosjolova, I.; Turks, M. *Phosph. Sulf. Silicon Rel. Elem.* 2015, *in press* [doi: 10.1080/10426507.2014.996644].

[3] Wojaczynska, E.; Wojaczynski, J. *Chem. Rev.* 2010, *110*, 4303-4356.

[4] Turks, M.; Laclef, S.; Vogel, P. Construction of polypropionate fragments in natural product synthesis. *Stereoselective Synthesis of Drugs and Natural Products*, 1st ed.; John Wiley & Sons, Inc.: Hoboken, 2013; Vol. 2, pp 271-318.