Pergamon

Tetrahedron Letters 39 (1998) 7827–7830

TETRAHEDRON LETTERS

New Tandem Reactions with Sultones

Bernd Plietker, Peter Metz*

Institut für Organische Chemie, Technische Universität Dresden, Mommsenstraße 13, D-01062 Dresden, Germany

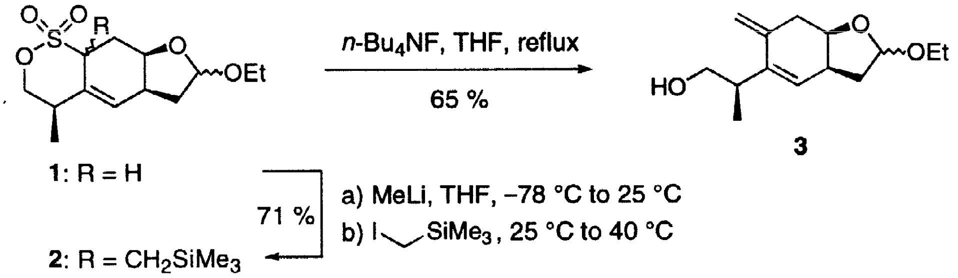
Received 16 June 1998; revised 17 August 1998; accepted 18 August 1998

Abstract

New one-pot procedures for the synthetic elaboration of sultones with concomitant desulfurization have been developed. Alkylation of α-metalated allylic sultones prepared either by deprotonation, radical cyclization/transmetalation or conjugate 1,6-addition with iodomethylmagnesium chloride is immediately followed by β-elimination to give highly substituted sulfur-free methylidene cyclohexenes. An advanced intermediate for the synthesis of several 1,10-*seco*-eudesmanolides is efficiently available by this new method.

Keywords: Alkenylation; Carbenes and carbenoids; Desulfurisation; Terpenes and terpenoids

A two-step desulfurization of sultones [1-3] with simultaneous methylenation to give bishomoallylic alcohols (cf. **1** → **3**) has recently been achieved by alkylation with (iodomethyl)trimethylsilane followed by fluoride-induced β-elimination (Scheme 1) [4].



Scheme 1. Desulfurization of sultone **1** with simultaneous methylenation

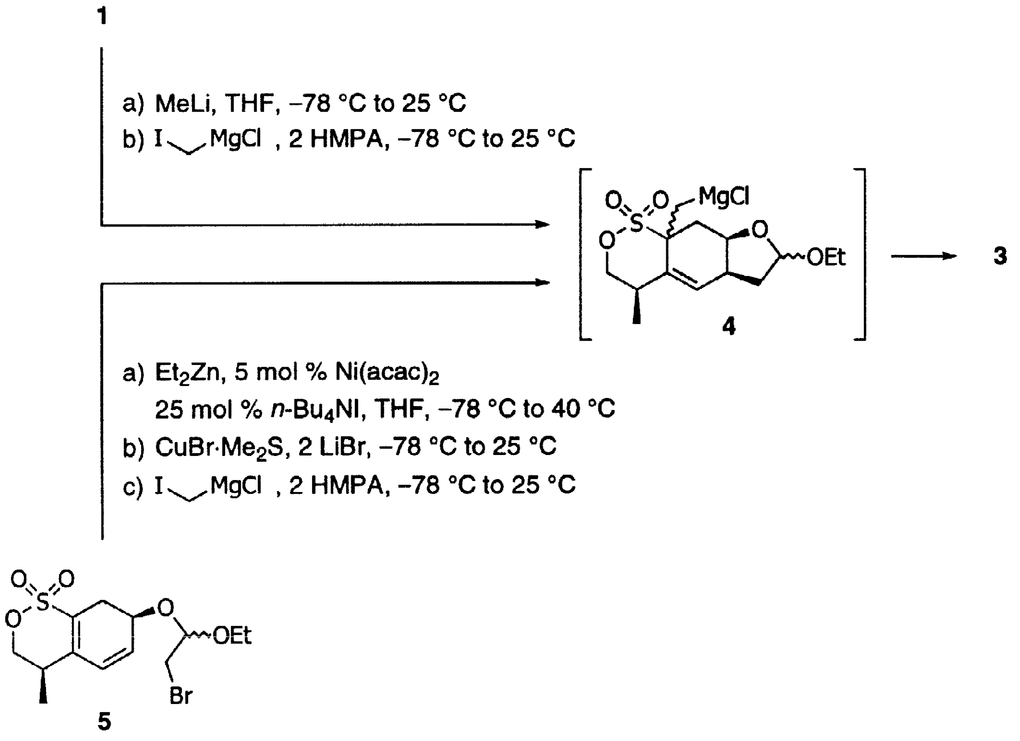
---

*E-mail: metz@coch01.chm.tu-dresden.de

0040-4039/98/$ - see front matter © 1998 Elsevier Science Ltd. All rights reserved.
PII: S0040-4039(98)01743-2

Since the 1,3-diene **3** currently serves us as a central intermediate for the synthesis of several highly oxygenated 1,10-*seco*-eudesmanolides, e. g. eriolanin and eriolangin [5], we were interested in finding a more rapid access to **3** through the application of sequential transformations [6-9]. Here we report that a considerable shortening of our previous route to **3** is possible by using the carbenoid reagent iodomethylmagnesium chloride [10] as an alkylating agent for a suitable metalated derivative of **1**. In addition, we disclose an efficient one-pot transformation of furan-derived sultones to highly substituted sulfur-free methylidene cyclohexenes that stems from these observations.

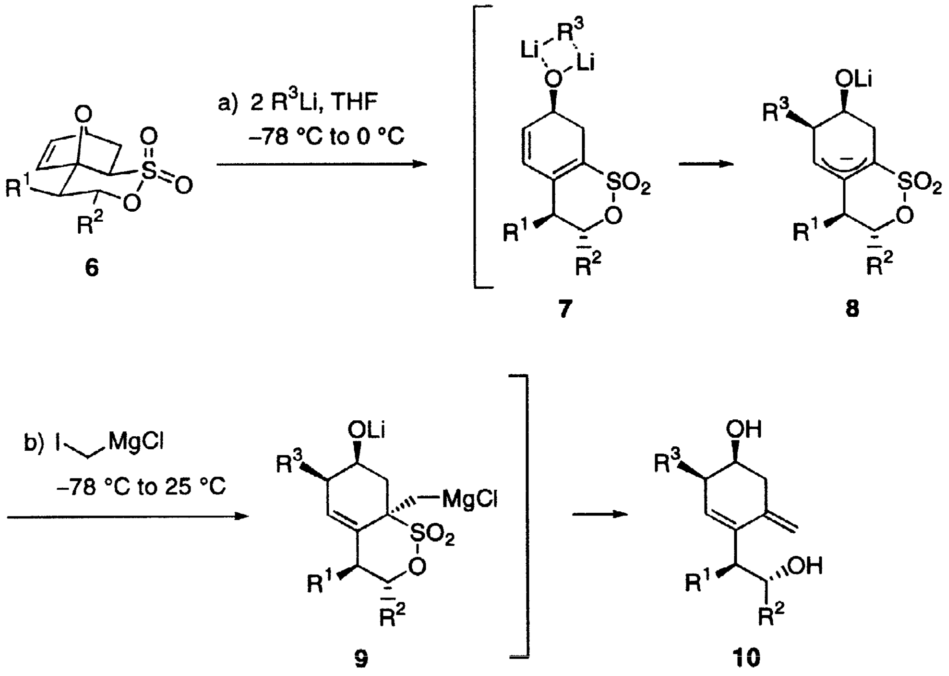
Whereas first attempts to alkylate lithiated sultone **1** with chloromethylmagnesium chloride [11] met with failure, the iodo carbenoid reacted smoothly in the presence of HMPA (Scheme 2). As anticipated, the intermediate Grignard species **4** spontaneously undergoes a β-elimination with rupture of the δ-sultone to deliver the desired dienol **3** in 69 % yield. Using the same conditions for the alkylation event, it even proved possible to directly convert bromoacetal **5**, the precursor of sultone **1** [12], to **3** in 68 % yield when the original chromium(II)-mediated cyclization of **5** to **1** was replaced by a nickel-catalyzed ring closure with diethylzinc followed by transmetalation of the resultant allylmetal compound to copper(I) [13,14]. Presumably, the latter process again leads to intermediate **4** or a related metal species that suffers a β-elimination with sultone cleavage.



Scheme 2. Tandem processes to dienol 3

The clean production of **3** from **1** and **5** implies a regioselective alkylation of the allylmetal species involved with the carbenoid reagent α to sulfur, which has precedent in corresponding sultone alkylations with methyl iodide [12,15] or (iodomethyl)trimethylsilane [4]. Moreover, since no protonation of **4** to give the methylated derivative of **1** was observed after aqueous workup, the endocyclic carbon sulfur bond in **4** is easily cleaved at or below room temperature.

Encouraged by these results, we investigated if the tandem alkylation/desulfurization described above could be coupled to the generation of lithiated sultones *via* tandem elimination/alkoxide-directed 1,6-addition [15] with furan-derived substrates **6a** [12] and **6b** [1]. Indeed, upon treatment of sultones **6** with 2 equivalents of an organolithium reagent and subsequent alkylation of the resultant allyllithium intermediates **8** with iodomethylmagnesium chloride, the 1,3-dienes **10** were obtained in good yield as single diastereomers (Scheme 3, Table 1). Interestingly, HMPA was not required for the C–C bond formation event **8** → **9**.



Scheme 3. One-pot conversion of sultones **6** to dienols **10**

Table 1
One-pot conversion of sultones **6** to dienols **10**

Substrate	R^1	R^2	R^3	Product	Yield **10** (%)[a]
6a	Me	H	Me	**10a**	62
6a	Me	H	*n*-Bu	**10b**	66
6b	H	*n*-Pr	Me	**10c**	61
6b	H	*n*-Pr	*n*-Bu	**10d**	70

[a] Isolated yield after purification by flash chromatography.

Conjugate addition of R^3Li *syn* to the lithium alkoxide moiety has been rigorously established before, and axial attack of the electrophilic carbenoid on **8** seems reasonable in view of the stereochemical course of the corresponding methylation [15].

General procedure for the transformation of sultones **6** to dienols **10**: 6.2 ml (12.3 mmol) of a 2M solution of isopropylmagnesium chloride in ether (Aldrich) are diluted with 20 ml of THF under argon. The solution is cooled to –78 °C, 3.3 g (12.3 mmol) of diiodomethane are added dropwise with vigorous stirring and the resultant yellowish suspension is vigorously stirred for 1 h at –78 °C to give the carbenoid reagent. In a separate flask, a solution of 2.05 mmol of sultone **6** in 20 ml of THF cooled to –78 °C is treated dropwise with 2.6 ml (4.1 mmol) of a 1.6M solution of methyllithium (Acros) in ether (**10a**,**c**) or *n*-butyllithium in hexane (**10b**,**d**) under argon. After stirring for 15 min at –78 °C and 1 h at 0 °C (**10a**,**c**) or 1 h at –78 °C (**10b**,**d**), the solution cooled to –78 °C is transferred by syringe to the carbenoid reagent. The resultant mixture is stirred for 15 min at –78 °C and allowed to warm to room temperature over a period of 8 h. The mixture is treated with 10 ml of sat. aqueous NH_4Cl and the aqueous layer is extracted 3× with ether. After acidifying the aqueous layer to pH 5-6, it is again extracted with ether, and the combined organic layers are successively washed with sat. aqueous $NaHCO_3$, water, brine, and dried over $MgSO_4$. After filtration and concentration *in vacuo*, flash chromatography (pentane/ether 1:1) yields the dienol **10** [selected data of **10a**: ^1H NMR ($CDCl_3$) δ ppm: 4.94 (s, 1 H), 5.18 (s, 1 H)), 5.37 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ ppm: 111.74 (CH_2), 129.03 (CH), 137.29 (C), 139.02 (C)] as a colorless oil.

Acknowledgment. Financial support of this work by the *Deutsche Forschungsgemeinschaft* and the *Fonds der Chemischen Industrie* is gratefully acknowledged.

References

[1] Metz P. J. Prakt. Chem. 1998;340:1–10.
[2] Buglass AJ, Tillett JG. In Patai S, Rappoport Z, editors. The Chemistry of Sulphonic Acids, Esters and their Derivatives. New York: John Wiley, 1991:789–878.
[3] Roberts DW, Williams DL. Tetrahedron 1987;43:1027–1062.
[4] Metz P, Seng D, Plietker B. Tetrahedron Lett. 1996;37:3841-3844.
[5] Kupchan SM, Baxter RL, Chiang C-K, Gilmore CJ, Bryan RF. J. Chem. Soc., Chem. Commun. 1973:842–843.
[6] Tietze LF. Chem. Rev. 1996;96:115–136.
[7] Tietze LF. Chem. Ind. 1995:453–457.
[8] Tietze LF, Beifuss U. Angew. Chem. 1993;105:137–170; Angew. Chem. Int. Ed. Engl. 1993;32:131–163.
[9] Ho T-L. Tandem Organic Reactions, New York: John Wiley, 1992.
[10] De Lima C, Julia M, Verpeaux J-N. Synlett 1992:133–134.
[11] Hahn RC, Tompkins J. Tetrahedron Lett. 1990;31:937–940.
[12] Metz P, Stölting J, Läge M, Krebs B. Angew. Chem. 1994;106:2275–2276; Angew. Chem. Int. Ed. Engl. 1994;33:2195–2197.
[13] Vaupel A, Knochel P. J. Org. Chem. 1996;61:5743–5753.
[14] Knochel P, Singer RD. Chem. Rev. 1993;93:2117–2188.
[15] Metz P, Meiners U, Fröhlich R, Grehl M. J. Org. Chem. 1994;59:3687–3689.