Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

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Published online: 04 Dec 2007.

To cite this article: Doo Ok Jang , Yung Hyup Joo & Dae Hyan Cho (2000) Efficient Synthesis of Epoxides from Vicinal Diols Via Cyclic Sulfates, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 30:24, 4489-4494

To link to this article: http://dx.doi.org/10.1080/00397910008087077

SYNTHETIC COMMUNICATIONS, 30(24), 4489–4494 (2000)

EFFICIENT SYNTHESIS OF EPOXIDES FROM VICINAL DIOLS *VIA* CYCLIC SULFATES

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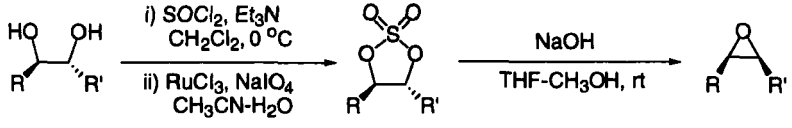
ABSTRACT: Reaction of cyclic sulfates of *vic*-diols with sodium hydroxide in THF-MeOH produced the corresponding epoxides in excellent isolated yields at room temperature. Cyclic sulfates of *trans*-diols gave *cis*-epoxides, and cyclic sulfates of *cis*-diols afforded *trans*-epoxides exclusively. Various cyclic sulfates of *vic*-diols can be converted into the epoxides under the conditions.

Epoxides are versatile intermediates in organic synthesis.[1] There are many biologically important natural products containing epoxide functionality.[2] A number of methods for the preparation of epoxides have been reported.[3] Oxidation of alkenes with peroxides or peroxy acids is the most widely used method for the epoxide preparation.[3-4] Another important procedure for the synthesis of epoxides is intramolecular nucleophilic displacement of an appropriate leaving group by an α-oxyanion. Thus, epoxides can be prepared from β-functionalized alcohols[5] and vicinal diols. To obtain epoxides from *vic*-diols, one hydroxyl group of two should be activated regioselectively. Sulfonates are most frequently used for the

purpose.[6] However, sulfonation of *vic*-diols showed low regioselectivity giving undesired bis-sulfonated by-products.

It has been reported that cyclic sulfates can be used as an activator of *vic*-diols in nucleophilic substitution reactions.[7] We anticipated that the cyclic sulfates might used as the activating group for the preparation of epoxides from *vic*-diols. In this communication, we report that epoxides can be obtained from the cyclic sulfates of *vic*-diols by treatment with sodium hydroxide in methanol at room temperature in high isolated yields (Scheme 1).

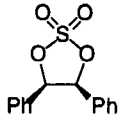
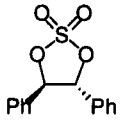
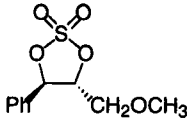
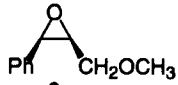
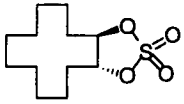
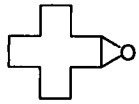
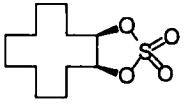
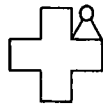
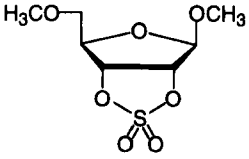
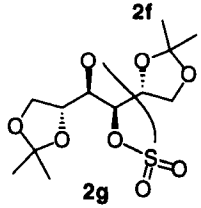
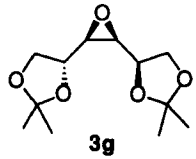


1 2 3

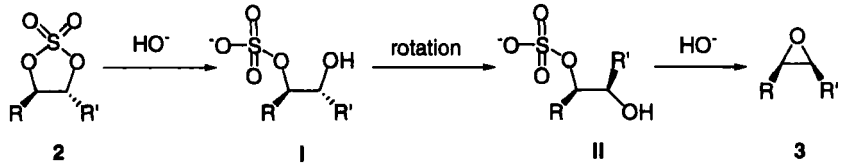
Scheme 1

Diols were first converted into the corresponding cyclic sulfates by treatment with $SOCl_2/Et_3N$ and RuO_4 ($NaIO_4$/cat. $RuCl_3$) in MeCN-H_2O sequentially in one pot.[7b] When the cyclic sulfate of *meso*-hydrobenzoin (**2a**) was treated with 1 M NaOH (2 equiv.) in THF/MeOH (3:1) at room temperature for 1 h, *trans*-stilbene epoxide (**3a**) was obtained in 86% yield. The reaction using NaOMe as a base instead of NaOH was not effective giving the epoxide in 43% yield. NaOH is the choice of the base for the synthesis of epoxide from cyclic sulfates. From the previous report, the cleavage of S-O bond of cyclic sulfate **2** is occurred by a hydroxyl anion to generate an intermediate **I** (Scheme 2).[8] The ring-opened intermediate **I** changes the conformation to give intermediate **II** that has suitable stereochemistry for intramolecular nucleophilic displacement. Then, the intermediate **II**, undergoes intramolecular S_N2 reaction to yield epoxide **3**.

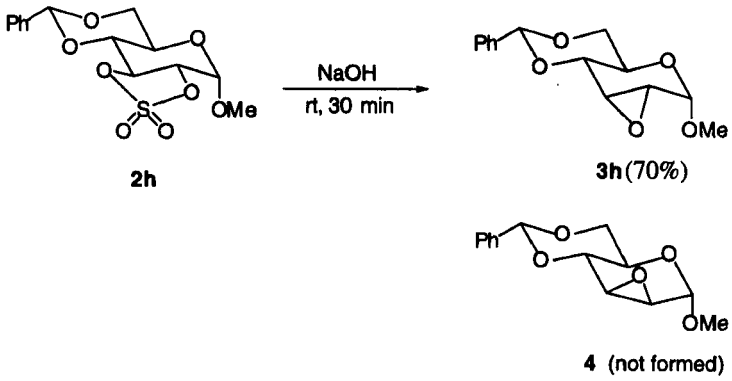
Table 1. Synthesis of Epoxides from *vic*-Diols

Cyclic Sulfate	Epoxide	Time (h)	Yield (%)[a]
 **2a**	 **3a**	1	86
 (±)-**2b**	 **3b**	0.8	80
 (±)-**2c**	 **3c**	1.5	74
 (±)-**2d**	 **3d**	26	85
 **2e**	 **3e**	27	83
 **2f**		26	-[b]
 **2g**	 **3g**	0.5	86

[a]Isolated yield. [b]Salt of ring-opened sulfate was obtained.



Scheme 2



Scheme 3

As expected, *trans*-cyclic sulfates **2b** and **2c** gave *cis*-epoxides **3b** and **3c** in high yields under these conditions. In cyclic systems, both *cis*- and *trans*-cyclic sulfates **2d** and **2e** that are conformationally flexible gave the corresponding epoxides **3d** and **3e**, while *cis*-diols in conformationally rigid rings such as D-ribose derivative (**2f**) did not proceed to the epoxide. Sugar epoxides can be prepared under the conditions. Cyclic sulfate of diacetone mannitol (**2g**) was transformed into the epoxide **3g** in 86% yield that is higher than the previous report.[6g] In the epoxide formation of methyl 4,6-O-benzylidene-α-D-glucopyranoside using tosylation /base sequence, the epoxide that came from the sulfonylation of the carbon-2 hydroxyl group, methyl 2,3-anhydro-4,6-O-

benzylidene-α-D-mannopyranoside (**4**) was obtained exclusively.[6f] Interestingly, the reaction of cyclic sulfate of methyl 4,6-O-benzylidene-α-D-glucopyranoside (**2h**) with NaOH gave only methyl 2,3-anhydro-4,6-benzylidene-α-D-allopyranoside (**3h**) (Scheme 3). The result indicated that the oxy anion was formed at C-2 position exclusively.

In conclusion, an efficient process for the epoxide formation from cyclic sulfates of *vic*-diols has been developed. This method shows several advantages including stereospecificity and its easiness, simplicity, rapidity, and mildness of conditions.

Typical experimental procedure: To a solution of a cyclic sulfate (0.4 mmol) in THF (3 mL) and MeOH (1 mL) was added 1 M NaOH (0.8 mL) at room temperature. The reaction mixture was stirred for an appropriate time. The progress of the reaction was monitored by TLC. The reaction mixture was diluted with ether, and washed with 0.1 M HCl, water and brine successively. Drying over anhydrous $MgSO_4$ and evaporation of the solvent afforded the crude product that was purified by column chromatography on silica gel.

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(Received in Japan 14 January 2000)