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GENERAL SYNTHESIS OF 2-HYDROXY, 3-HYDROXY-, AND 4-HYDROXY-ALKYLDIMETHYLSULFONIUM SALTS FROM CYCLIC ETHERS

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Abstract-Epoxides, oxetane, and tetrahydrofuran were successfully transformed to 2-hydroxy-, 3-hydroxy-, and 4-hydroxyalkyldimethylsulfonium triflates by the reaction with dimethyl sulfide in the presence of trifluoromethanesulfonic acid. Several reactions of these salts are described.

Recently, the reaction of chlorinated epoxides with dimethyl sulfide was reported by two groups.[1] They utilized these reactions for the synthesis of chlorinated ketones which are important synthons. Methods for the preparation of 2-hydroxysulfonium salts (1) include the alkylation of 2-hydroxysulfide,[2] nucleophilic ring opening reaction of cyclic sulfonium salts,[3] and degradation of S-adenosylmethionine.[4] However, there is no report on the synthesis of the title compounds from epoxides (2), oxetane (3) or tetrahydrofuran (4).[5] In this communication, we would like to report a highly effective and convenient synthesis of 1, 3-hydroxypropyldimethylsulfonium salt (5), 4-hydroxybutyldimethylsulfonium salt (6) by the reaction of cyclic ethers with dimethyl sulfide (7) in the presence of trifluoromethanesulfonic acid (8).

A typical reaction was run as follows: To a solution of cyclohexene oxide (2a) (10 mmol) in 7 (15 ml) was added dropwise a solution of 8 (10 mmol) in 7 (8 ml) at 20 °C. After stirring for 2 h, colorless crystals were precipitated. These crystals were collected by filtration to give 2-hydroxycyclohexyldimethylsulfonium triflate (1a) (9.6 mmol, 96%). Other sulfonium salts were obtained as viscous oils which were converted into tetraphenylborate salts (1b,d~f'). As shown in Table 1, salts 1, 5, and 6 were obtained in excellent yields.

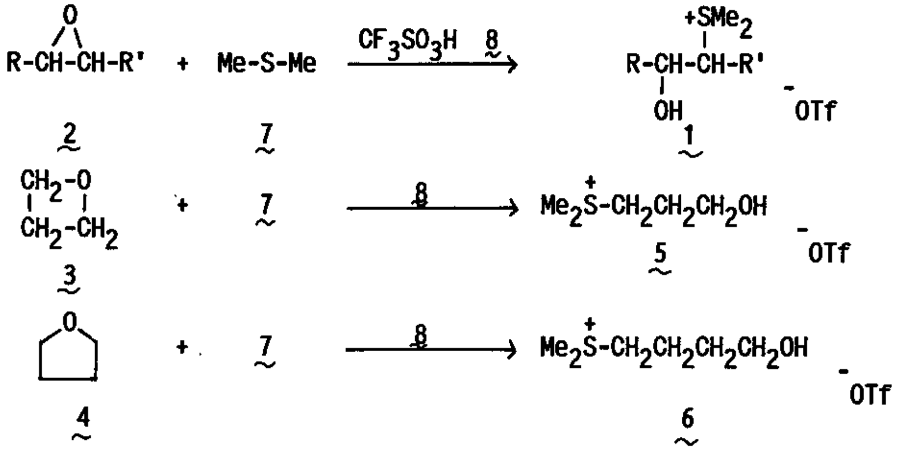
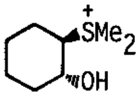


Table 1. Preparation of Hydroxyalkyldimethylsulfonium Salts 1, 5, and 6.

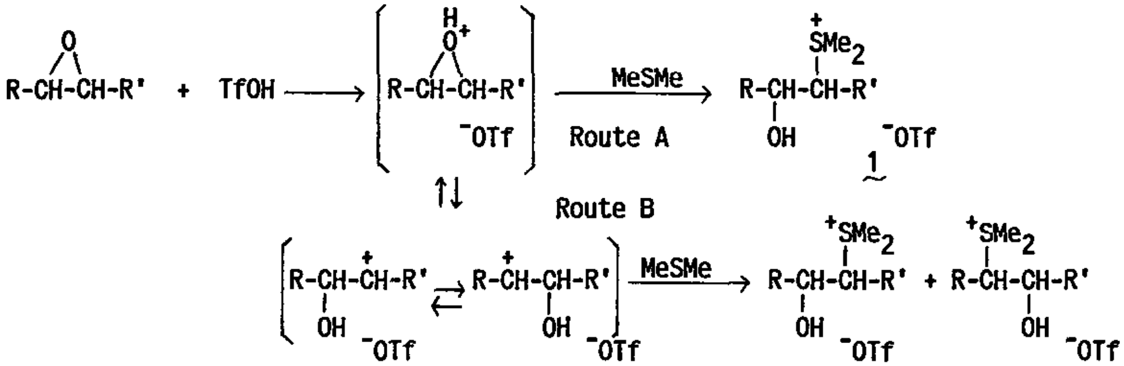
Cyclic Ether	Product[a)]			Yield (%)	Mp (°C)
Epoxides (2)					
cyclohexene oxide		^{-}OTf	1a	96	72-73
ethylene carbonate[b)]	$Me_2\overset{+}{S}-CH_2CH_2OH$	$^{-}BPh_4$	1b	88	191-192
trans stilbene oxide	$Me_2\overset{+}{S}-CH(Ph)CH(Ph)OH$	^{-}OTf	1c	90	145-146
propene oxide	$Me_2\overset{+}{S}-CH_2CH(Me)OH$	$^{-}BPh_4$	1d	92	164-165
butene oxide	$Me_2\overset{+}{S}-CH_2CH(Et)OH$	$^{-}BPh_4$	1e	90	148-149
styrene oxide	$Me_2\overset{+}{S}-CH(Ph)CH_2OH$	$^{-}BPh_4$	1f	77	134-135
	$Me_2\overset{+}{S}-CH_2CH(Ph)OH$	$^{-}BPh_4$	1f'		oil
trimethylene oxide (3)	$Me_2\overset{+}{S}-CH_2CH_2CH_2OH$	$^{-}BPh_4$	5	90	163-164
tetrahydrofuran (4)	$Me_2\overset{+}{S}-CH_2CH_2CH_2CH_2OH$	$^{-}BPh_4$	6	90	123-124

a) Satisfactory elemental analyses were obtained for all compounds except 1f'.
b) Instead of ethylene oxide, ethylene carbonate was used.

Previously, sulfocholine 1b was obtained by the reaction of 2-chloroethanol with sodium methylthiolate followed by the addition of methyl iodide.[6] Johnson and Schroeck prepared optically active 2-hydroxy(2-phenyl)ethylsulfonium salt by three step reactions starting from corresponding sulfide.[7] The present method requires only one step and the yields are higher than any other methods. The reaction is not always regioselective but stereospecific. The acidic ring opening reactions of epoxides were previously reported: preparation of episulfide[8], formation and decomposition of episelenide[9], and preparation of 2-

hydroxycarbonyl compounds[10]. It is also well known that reactions of epoxides with trimethylsilyltrifluoromethanesulfonate followed by addition of many nucleophiles give ring-opened products.[11] However, there is no report on the acid activated reaction of cyclic ethers with sulfides.

As to the formation of 1, following two mechanisms are possible: treatment of epoxide with acid formed the corresponding oxonium ion, which was directly attacked by dimethyl sulfide to give 1 (route A); the oxonium ion was transformed to carbocation which resulted in the formation of 1 (route B).



The stereospecificity observed in the reactions of cyclohexene oxide and trans stilbene oxide and the regiospecificity observed in the reactions of propene oxide and butene oxide in which dimethyl sulfide attached the less hindered methylene carbon, suggested that the reaction might proceed in S_N2 mechanism via the oxonium intermediate (route A). However, the nonstereospecificity in the reaction of styrene oxide suggested that the reaction preceeded via not only the oxonium intermediate (route A) but also the carbocation intermediate (route B). In this case, the carboncation is stabilized by the phenyl group.

Since products can be seen as intermediates of Corey-Chaykovsky reaction,[12] we then tried the reaction of 1a with a base. Treatment of 1a with diazabicyclo[5.4.0]undecene (DBU) afforded cyclohexene oxide in 86% yield. Other reactions summarized in Scheme 1 were also carried out.

Scheme 1

We are now continuing the synthetic application of this reaction.

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