A CONVENIENT METHOD FOR A PREPARATION OF OXIRANES

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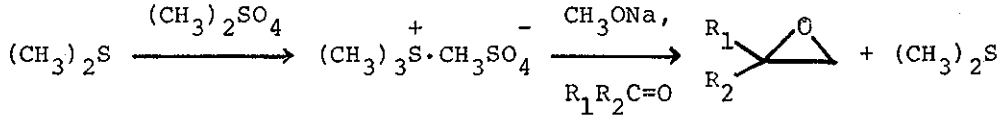
Oxiranes have been prepared in moderate to excellent yields *via* an one-pot process under a very mild condition. To an acetonitrile solution of dimethylsulfonium methylide prepared *in situ* by treating dimethyl sulfide with dimethyl sulfate, followed by sodium methoxide, was added carbonyl compounds at an ambient temperature to give oxiranes.

Carbonyl compounds have been converted into oxirane derivatives by treating with dimethyloxosulfonium methylide[1] or dimethylsulfonium methylide[1,2]. Although in a small scale reaction,the both conversions are general and effective, those reactions require specific conditions such as use of a large excess of dried dimethyl sulfoxide(DMSO) and/or dried tetrahydrofuran(THF) as the solvent and oil free sodium hydride or potassium *t*-butoxide as the base under a limited reaction temperature[1,2,3]. For a large scale production, those condition might be unsuitable. We now wish to report a modification of the second method[1,2] which allows a convenient one-pot three stage preparation of oxiranes in either a small scale or a large scale without

using DMSO and/or THF as the solvents and sodium hydride as the base.

Thus, a solution of dimethyl sulfide(1.6 equiv.) was mixed with dimethyl sulfate(1.5 equiv.) at room temperature and the mixture was treated with carbonyl compounds(1.0 equiv.) (1), followed by with sodium methoxide(1.5 equiv.) at the same temperature to give corresponding oxiranes (2) in yields as shown in the table. In the reaction, an accompanied by-product, dimethyl sulfide, which has disagreeable odor was trapped and recycled by distilling with the reaction solvent into a receiver containing dimethyl sulfate to form trimethylsulfonium methylsulfate[4] in acetonitrile. Trimethylsulfonium methylsulfate was prepared for polarographic study[5], which has not been applied for oxirane synthesis.



(1) (2)

In comparison with the conventional methods[1,2], this process would be more favorable for preparing oxiranes in a large scale under a mild condition without using any of expensive alkylating agents and intractable solvents. In a large scale preparation, it is preferable to treat the sulfonium salt with the base, and finally with carbonyl compounds. A typical example was shown to be a synthesis of 2-(4-isobutylphenyl) -2-methyloxirane which has been used as an excellent precursor for the synthesis of an anti-inframmatory agent, 2-(4-isobutylphenyl)-propionic acid(Ibuprofen)[6].

2-(4-isobutylphenyl)-2-methyloxirane: To a solution of dimethyl sulfate 189.2 g(1.50 mole) in acetonitrile(700 ml) was

Table

Entry	Oxirane		mp or bp (mmHg) °C		yield %
	R_1	R_2	observed	reported	
1	H	C_6H_5	67-68 (8)	80 (5)[1];80 (18)[2]	82.6
2	H	(4-MeO)C_6H_4	98-99 (3)	51 (0.001)[1]	87.0
3	H	(4-Cl)C_6H_4	74-75 (3)[7]		82.2
4	Me	C_6H_5	70 (8)	30 (0.001)[1];84-85 (16)[8]	84.9
5	Me	(4-C_6H_5)C_6H_4	76-81[9]		86.4
6	Me	4-pyridyl	86-88 (10)[9]		60.0
7	Me	2-naphthyl	77-78[9]		85.2
8	Me	2-benzofuranyl	60-61[9]		87.4
9	Me	6-MeO-2-naphthyl	107-109[10]		84.5
10	C_6H_5	C_6H_5	55.5-56.5	58[1];55-56[2]	91.2
11	-$(CH_2)_5$-		60-63 (40)	148 (760)[1];61-62(39)[11]	57.6
12	-$(CH_2)_6$-		51 (8)	61 (14)[1];63 (14)[2]	68.0

added a solution of dimethylsulfide 102.5 g(1.65 mole) in acetonitrile(300 ml) with stirring at room temperature(25 —30°) and the mixture was allowed to stand overnight at ambient temperature. To the stirred mixture, sodium methoxide 89.1 g(1.65 mole) was added at room temperature(25 —30°) and then 4-isobutylacetophenone 176.3 g(1.0 mole) was added at the same temperature in such a rate over a period of 30 min. The reaction mixture was heated to distil dimethyl sulfide and most of the solvent into the receiver containing dimethyl sulfate 189.2 g(1.50 mole) in acetonitrile(100 ml) in order to form a solution of trimethylsulfonium methylsulfate which was recycled for next synthesis. The residue was added with water(200 ml) and the organic layer was separated, washed with water(150 ml), dried over sodium sulfate, and distilled under a reduced pressure to give 2-(4-isobutylphenyl)-2-methyloxirane 174.5 g(91.7 %), bp 110-112°(7 mm Hg), δ^{CDCl_3}(p.p.m.) 0.89(6H, d, J=7.5 Hz), 1.67(3H, s), 1.4-2.1(1H, m), 2.43(2H, d, J=7.5 Hz), 2.80(1H, d, J=6 Hz), 2.90(1H, d, J=6 Hz), 6.95(2H, d, J=8 Hz), 7.15(2H, d, J=8 Hz).

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4 More than 75 % of dimethyl sulfide could be recoverd as trimethylsulfonium methylsulfate[5].

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