Regioselective Reaction of Oxiranes with *S*-Phenyl Thioesters Catalyzed by Quaternary Onium Salts or Crown Ether-Metal Salt Complexes

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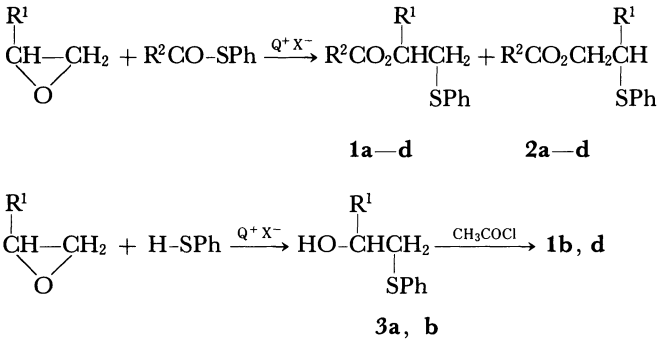
Synopsis. Regioselective addition reactions of 2-substituted oxiranes with *S*-phenyl thioesters gave 2-aceyloxy-1-phenylthio derivatives in high yield using some 18-crown-6-metal complexes as well as tetrabutylammonium salts as a catalyst under relatively mild conditions.

The addition reaction of oxiranes with esters has attracted much attention in the field of polymer chemistry since two distinct functional groups are introduced into their molecules at the same time.[1] Since these substrates do not show a high reactivity, it is very important to select suitable catalysts for the reaction. Funahashi[2] previously undertook the reaction of oxiranes with esters using such bases as tertiary amines or potassium *t*-butoxide as a catalyst at high reaction temperatures. Recently, we found[3] that the reaction of a pendant epoxy group in a polymer with an active ester and thioester proceeded smoothly upon the addition of onium salts, which had much higher catalytic activities than the bases as a catalyst, under relatively mild conditions; crown ether-metal complexes were also available catalysts for this reaction.

We wish to report herein the identification of the addition products of 2-substituted oxiranes with *S*-phenyl thioesters, and to discuss the catalytic effect of crown ether-metal salt complexes on this reaction in comparison with that of tetrabutylammonium salt.

The addition reaction of 2-(phenoxymethyl)oxirane and 2-(methoxymethyl)oxirane with *S*-phenyl thiobenzoate and *S*-phenyl thioacetate was carried out in DMF using Bu_4NBr as a catalyst. The reactions did not occur without a catalyst; however, the addition of Bu_4NBr caused the reaction to proceed with high conversion, as shown in Table 1. The reaction could be expected to give two products, the corresponding 2-acyloxy-1-phenylthic derivatives (**1**) and 1-acyloxy-2-phenylthio derivatives (**2**), as shown in Scheme 1. However, the reaction of oxirane with *S*-phenyl thioester yielded only one product other than a very small amount of 2-hydroxy-3-(phenylthio) propyl ether (**3**). The reaction product agreed with **1** obtained from an acylation of **3**. **3** was also prepared from an addition reaction of the oxirane with thiophenol. Furthermore, it is easy to distinguish between **1** and **2**, which show very different ^1H NMR spectra.[4] The addition products of oxirane with *S*-phenyl thioester showed similar chemical shifts of methine and methylene protons to those of the known compounds **1**.[4a] These results strongly substantiated that the reaction of oxirane with *S*-phenyl ester proceeded regioselectively to give **1**.



Q^-X^-: quaternary onium salt, crown ether-metal complex

1, 2a: R^1=$PhOCH_2$ R^2=Ph
b: R^1=$PhOCH_2$ R^2=Me
c: R^1=$MeOCH_2$ R^2=Ph
d: R^1=$MeOCH_2$ R^2=Me

3a: R^1=$PhOCH_2$
b: R^1=$MeOCH_2$

Scheme 1

The catalytic effect of crown ether-metal salt complexes on the addition reaction of 2-(phenoxymethyl) oxirane with *S*-phenyl thiobenzoate was investigated at 90 °C in diglyme, as shown in Table 2. Tertiary amines have been used as catalysts in the reaction of oxirane with ester;[2] however, tertiary amines, such as tributylamine and triethylamine, hardly showed any catalytic activity under these conditions. The reaction took place upon the addition of a mixture of 18-crown-

Table 1. Reaction of Oxiranes with *S*-Phenyl Thioester

Entry	Reagents		Reaction		Product	Yield[a] of **1**
	R^1	R^2	Temp / °C	Time / h		%
1	$PhOCH_2$	Ph	110	25	**1a**	71.0
2	$PhOCH_2$	Me	110	10	**1b**	75.9
3	$MeOCH_2$	Ph	110	50	**1c**	69.7
4	$MeOCH_2$	Me	110	10	**1d**	60.4

a) Isolated yield.

Table 2. Reaction of 2-(Phenoxymethyl)oxirane with *S*-Phenyl Thiobenzoate in Diglyme at 90 °C for 5 h

Entry	Catalyst	Yield %	Entry	Catalyst	Yield %
5	Et_3N	2.6	13	18-C-6/KI	69.1
6	Bu_3N	4.3	14	18-C-6/$KHSO_4$	0
7	AcOK	0	15	18-C-6/$KClO_4$	0
8	18-C-6[a)]	0	16	Bu_4NCl	91.0
9	18-C-6/AcOK	89.5	17	Bu_4NBr	70.7
10	18-C-6/KF	73.7	18	Bu_4NI	2.6
11	18-C-6/KCl	0.9	19	Bu_4NHSO_4	0
12	18-C-6/KBr	75.6	20	Bu_4NClO_4	0

a) 18-C-6: 18-crown-6.

6 and potassium salts as well as quaternary ammonium salt. Since neither 18-crown-6 nor potassium salt individually showed any catalytic activity, the 18-crown-6-metal salt complexes produced from the mixture worked as catalysts. The catalytic activity was markedly affected by the counter ions in the catalysts. The effect of a counter ion in tetrabutylammonium salt and 18-crown-6-potassium salt complex changed in the order; $HSO_4^- = ClO_4^- < I^- < Br^- < Cl^-$ and $AcO^- > Br^- > F^- > I^- > Cl^- > HSO_4^- = ClO_4^-$, respectively. The counter-ion effect was much different between the tetrabutylammonium salt and 18-crown-6-potassium salt complex. On the other hand, 18-crown-6-potassium acetate showed almost the highest catalytic activity of tetrabutylammonium salts and the crown ether-potassium salt complexes. These results suggest that 18-crown-6-potassium salt complexes are also suitable catalysts for an addition reaction of oxiranes with thioesters.

Experimental

General Procedure for Synthesis of 2-Acyloxy-3-(phenylthio)propyl Ethers (Table 1). 2-Benzoyloxy-3-(phenylthio)propyl Phenyl Ether (1a): The mixture of 2-(phenoxymethyl)oxirane (7.51 g, 50 mmol), *S*-phenyl thiobenzoate (10.70 g, 50 mmol), Bu_4NBr (1.61 g, 5 mmol), and dry DMF (50 ml) was stirred at 110 °C for 25 h. The conversion was 82.4%, measured by GLC. Ether (150 ml) was added to the reaction mixture, and the etheral solution was washed with water (50 ml×3), dried with $MgSO_4$, and evaporated in vacuo. The residue was recrystallized from hexane to afford **1a** (12.90 g, 71.0%); mp 39—40 °C; IR (KBr) 1720 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ=3.35 (d, 2H, S-CH_2), 4.32 (d, 2h, O-CH_2), 5.36—5.70 (m, 1H), 6.80—8.10 (m, 15H). Found: C, 72.55; H, 5.80%. Calcd for $C_{22}H_{20}O_3S$: C, 72.50; H, 5.53%.

2-Acetoxy-3-(phenylthio)propyl Phenyl Ether (1b): Bp 190—195 °C/0.05 mmHg (1 mmHg≈133.322 Pa); IR (neat) 1740 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ=1.98 (s, 3H), 3.28 (d, 2H, S-CH_2), 4.14 (d, 2H, O-CH_2), 5.10—5.40 (m, 1H), 6.76—7.56 (m, 10H). Found: C, 67.56; H, 6.27%. Calcd for $C_{17}H_{18}O_3S$: C, 67.52; H, 6.00%.

2-Benzoyloxy-3-(phenylthio)propyl Methyl Ether (1c): Viscous oil; IR (neat) 1720 cm^{-1} (C=O). ^1H NMR ($CDCl_3$) δ=3.34 (d, 2H, S-CH_2), 3.38 (s, 3H), 3.76 (d, 2H, O-CH_2), 5.24—5.56 (m, 1H), 7.10—8.20 (m, 10 H). Found: C, 67.82; H, 6.25%. Calcd for $C_{17}H_{18}O_3S$: C, 67.52; H, 6.00%.

2-Acetoxy-3-(phenylthio)propyl Methyl Ether (1d): Bp 96—100 °C/0.03 mmHg; IR (neat) 1740 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ= 2.00 (s, 3H), 3.18 (d, 2H, S-CH_2), 3.34 (s, 3H), 3.60 (d, 2H, O-CH_2), 5.00—5.24 (m, 1H), 7.10—7.52 (m, 5H). Found: C, 60.02; H, 6.81%. Calcd for $C_{12}H_{16}O_3S$: C, 59.97; H, 6.71%.

3-Hydroxy-3-(phenylthio)propyl Phenyl Ether (3a): The mixture of 2-(phenoxymethyl)oxirane (15.02 g, 0.10 mol), thiophenol (11.02 g, 0.10 mol), Bu_4NBr (1.61 g, 5 mmol), and dry diglyme (50 ml) was stirred at 90 °C for 5 h. After the usual work-up, the residue was distilled under reduced pressure to give **3a** (20.32 g, 78.1%); bp 179—180 °C/0.03 mmHg; IR (neat) 3450 cm^{-1} (OH); ^1H NMR ($CDCl_3$) δ=2.76 (d, 1H, O-H), 3.16 (d, 2H, S-CH_2), 3.90—4.30 (m, 1H, CH), 4.02 (d, 2H, O-CH_2), 6.20—7.60 (m, 10H). Found: C, 69.20; H, 6.19%. Calcd for $C_{15}H_{16}OS$: C, 69.61; 6.20%.

3-Hydroxy-3-(phenylthio)propyl Methyl Ether (3b): Yield 67.2%; bp 110—112 °C/0.02 mmHg (lit,[5] 103—104 °C/0.03 mmHg); IR (neat) 3450 cm^{-1} (OH); ^1H NMR ($CDCl_3$) δ=2.80 (d, 1H, O-H), 3.00 (d, 2H, S-CH_2), 3.08 (s, 3H, CH_3), 3.40 (d, 2H, O-CH_2), 3.70—4.10 (m, 1H, CH), 7.00—7.50 (m, 5H).

Synthesis of 1b from 3a: To a solution of **3a** (0.200 g, 73 mmol) in pyridine (5 ml) was added acetyl chloride (0.576 g, 73 mmol) at 5 °C. After allowing the mixture to stand at room temperature for 1 h, the mixture was poured into water, and extracted with ether. The etheral extract was washed with a dilute hydrochloric solution, dried, and evaporated in vacuo. The residue was chromatographed on silica gel, using benzene-ethyl acetate (10 : 1), to give **1b** (0.245 g, 95%) as a colorless viscous oil.

Synthesis of 1d from 3b: Yield 85.0%, after purification from chromatography on silica gel using hexane-ethyl acetate (7 : 3).

Reaction of 2-(Phenoxymethyl)oxirane with *S*-Phenyl Thiobenzoate (Table 2): A mixture of 2-(phenoxymethyl)-oxirane (10 mmol), *S*-phenyl thiobenzoate (10 mmol), catalyst (quaternary onium salt or potassium salt and 18-crown-6, 0.5 mmol), and dried diglyme (5 ml) was stirred at 90 °C under nitrogen flow. The amount of **1a** was monitored by GLC.

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