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Polyethylene Glycol (PEG) 4000 Catalysed Regioselective Nucleophilic Ring Opening of Oxiranes - A New And Convenient Synthesis of ß-Hydroxy Sulfone and ß-Hydroxy Sulfide

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Abstract : Oxiranes and sodium p-toluene sulfinate salt react smoothly in a regioselective manner in the presence of PEG4000 to furnish ß-hydroxy sulfone and ß-hydroxysulfide. The reaction was extended for the preparation of alkylsulfones and ß-oxosulfones from alkylhalide and ß-oxohalide respectively.

INTRODUCTION

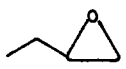
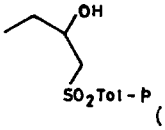
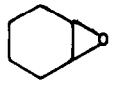
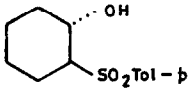
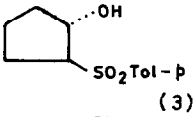
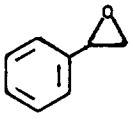
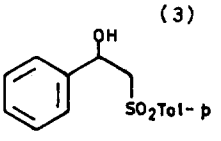
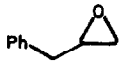
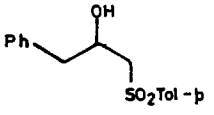
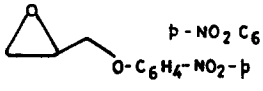
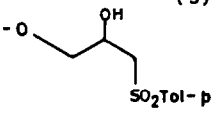
The ring opening of oxiranes[1] with various nucleophiles is an important synthetic transformation in organic systhesis because this leads to a 1,2-difunctionalised system which is a valuable intermediate for the synthesis of natural products. These transformations are generally promoted by different types of Lewis acid. We now report the successful application of Polyethylene glycol 4000, a phase transfer agent and solvent for promoting a variety of reactions[2], for the preparation of ß-hydroxy sulfone and ß-hydroxy sulfide from different oxirane under neutral condition in fairly good yield. In addition to above it has also been found that PEG 4000 successfully transformed alkyl halide and ß-oxo halide to corresponding alkyl sulfone and ß-oxo sulfone in good yield.

The high efficiency of PEG 4000 is probably due to the fact that it allows the transport of the sulfinate ion into the organic layer very effectively leading to the successful displacement reaction (in the preparation of alkyl sulfone and ß-oxo sulfone). It is also likely that the nucleophilicity of thiophenol is increased due to the presence of PEG 4000 which facilitates nucleophilic attack on the oxirane leading to the formation of ß-hydroxy sulfide. Moreover, the low cost, ready availability, non-toxicity of PEG 4000 and easy work up procedure makes this process very easy and practical.

RESULTS AND DISCUSSION

Various methods for the preparation of ß-hydroxy sulfones reported earlier[3] took longer time for completion of the reaction whereas in case of PEG 4000 shorter times are required for the reaction with satisfactory yield. The results are shown in Table 1.

Table 1 : PEG 4000 Catalysed Synthesis of ß-Hydroxy Sulfone

Substrate	Product	Time(h)	Yield(%)[a]
	 (1)	2	85
	 (2)	3	80
	 (3)	3.5	70
	 (4)	2.5	85
	 (5)	3	75
	 (6)	2	90

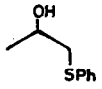
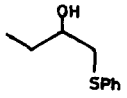
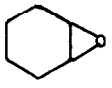
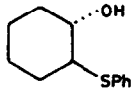
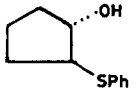
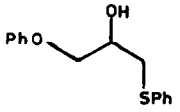
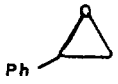
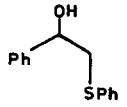
[a]Isolated yield after column chromatography based on starting material.

The opening always takes place with high regioselectively and definitely with antisteroselectively and generally the nucleophile attacks at the less hindered side.

The opening of oxiranes using benzenethiol is of more obvious value.

Although a number of methods using neutral alumina[4], a lanthanide complex[5] and Cobaltous Chloride[6] have been reported, none of these methods are free from either extended reaction times or by-products. Although in the case of neutral alumina a good yield is obtained in short time but several equivalents of nucleophile are required, whereas in case of PEG 4000 high yield is obtained using a molar equivalent of nucleophile. The reaction also proceeds with high regioselectively. The results are shown in Table 2.

Table 2 : PEG 4000 Catalysed Synthesis of β-Hydroxy Sulfide

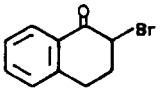
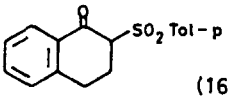
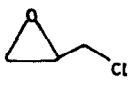
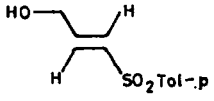
Substrate	Product	Time(h)	Yield(%)[a]
	 (7)	1.5	80
	 (8)	1.5	75
	 (9)	3	70
	 (10)	3.5	65
	 (11)	2.5	60
	 (12)	2	72

[a]Isolated yield after column chromatography based on starting material.

Considering the importance of alkyl sulfone[7] and β-oxo sulfone[8] in organic synthesis, the reaction was extended to reactions with alkyl

halides and ß-oxo halides respectively. Although there were a number of methods[9-12] available, our method was found to be better with respect to reaction time and yield. Different sulfones prepared by this method are shown in Table 3. In case of 1-chloro-2,3-epoxy propane some what different result was obtained. This may be due to the fact that the intermediate ß-epoxy sulfone suffers ß-elimination under reaction condition[10].

Table 3 : PEG 4000 Catalysed Synthesis of Alkyl Sulfone And ß-Oxosulfone

Substrate	Product	Time(h)	Yield(%)[a]
$(H_3C)_2CHBr$	$(H_3C)_2CHSO_2Tol\text{-}p$ (13)	1.5	85
$H_3C(CH_2)_3Br$	$H_3C(CH_2)_3SO_2Tol\text{-}p$ (14)	1.5	80
$PhCH_2Br$	$PhCH_2SO_2Tol\text{-}p$ (15)	1.0	85
	 (16)	1.0	90
$PhCOCH_2Br$	$PhCOCH_2SO_2Tol\text{-}p$ (17)	1.0	90
$p\text{-}BrC_6H_4COCH_2Br$	$p\text{-}BrC_6H_4COCH_2SO_2Tol\text{-}p$ (18)	0.5	90
	 (19)	2.0	85

[a]Isolated yield after column chromatography based on starting material.

EXPERIMENTAL

Melting points were uncorrected. ^1H NMR spectra were measured in $CDCl_3$ with a JEOL-FX-100 spectrometer (100 MHz). Chemical shifts were reported in ppm relative to tetramethyl silane (δ units). Infrared (IR) spectra were recorded on a Shimadzu IR-408 spectrometer using thin liquid films or KBr pellets. Mass spectra were recorded on a Shimadzu

QP-1000 instrument. PEG 4000 was purchased from Fluka, Switzerland.

Preparation of ß-hydroxy sulfone, ß-oxo sulfone and alkyl sulfone. General procedure . To the solvent system water : benzene (1:1), the sodium salt of p-toluene sulfinic acid (3 gm; 0.03 mole) PEG 4000 (0.5 gm) oxirane/alkyl halide/ß-oxo halide (0.02 mole) was added and refluxed for the stipulated period of time (as mentioned in Table 1 and 3). The course of the reaction was monitored by TLC. After the indicated period of time, benzene layer was concentrated under reduced pressure and chromatrographed over silica gel. On elution with chloroform the desired sulfones were obtained in pure form.

Preparation of ß-hydroxy sulfides. General procedure . To a solution of PEG 4000 (0.5 gm) in CH_2Cl_2 (40 ml) benzenethiol (0.03 mole) and the oxirane (0.03 mole) were added and the mixture was stirred for the indicated period of time (as mentioned in Table 2) under a nitrogen atmosphere. The resulting mixture was then concentrated under reduced pressure and chromatographed over silica gel. On elution with chloroform ß-hydroxy sulfides were obtained in pure form.

1-Tosyl-butane-2-ol (1) [14]. Semisolid. ν_{max}(film) 3475, 1310, 1150 cm^{-1}. ^1H NMR : δ 0.94 (t, 3H), 1.36(m,2H), 2.44(s,3H), 3.0(d, 2H, J=6.5 Hz) 4.0 (m, 1H), 7.40 and 7.80 (d, 2H, J=8.2 Hz). M^+ 228. Anal. Calcd for $C_{11}H_{16}O_3S$, C, 57.89; H, 7.02. Found, C, 57.91; H, 7.08.

1-Tosyl-Cyclohexane-2-ol (2) [10]. m.p. 121°C; ν_{max} (KBr) 3500, 1275, 1150 cm^{-1}. ^1H NMR : δ 1.20-2.0(m, 8H), 2.44(s,3H), 3.0 (m, 1H), 3.9 (m, 1H), 7.40 and 7.80 (d, 2H, J=8.2Hz). M^+ 254. Anal Calcd for $C_{13}H_{18}O_3S$, C, 61.42; H, 7.08. Found C, 61.43; H, 7.1.

1-Tosyl-Cyclopentane-2-ol (3) . Semisolid; ν_{max} (film) 3515, 1300, 1170 cm^{-1}. ^1H NMR : δ 1.0-1.8 (m, 6H), 2.44 (s, 3H), 2.8 (m, 1H) 3.8 (m, 1H) 7.40 and 7.80 (d, 2H, J=8.2 Hz). M^+ 240. Anal Calcd for $C_{12}H_{16}O_3S$, C, 60.00; H, 6.66. Found, C, 60.20; H, 6.71.

2-Phenyl-1-tosyl-ethane-2-ol (4) [3g]. m.p. 131°C; ν_{max} (KBr) 3500, 1600, 1300, 1150 cm^{-1}. ^1H NMR : δ 2.40(s,3H), 4.0-4.72 (m,3H), 7.08-7.48 (m, 9H). M^+ 276. Anal Calcd for $C_{15}H_{16}O_3S$, C, 65.21; H, 5.79; Found C, 65.32; H, 5.82.

1-Phenyl-3-tosyl-2-propanol (5) [3f]. m.p. 85°C. ν_{max} (KBr) 3470, 1300, 1150 cm^{-1}. ^1H NMR : δ 2.44 (s, 3H) 2.8 (2d, 2H, J=6Hz) 3.2(d, 2H, J=6Hz) 4.30 (m, 1H), 7.30-7.90 (m,9H). M^+ 272. Anal Calcd for $C_{16}H_{18}O_3S$, C, 66.18; H, 6.25, Found, C, 6.36.

3-(p-nitrophenoxy)-1-tosyl-propane-2-ol (6) [3g]. m.p. 107°C. ν_{max} (film) 3490, 1600, 1300, 1145 cm^{-1}. ^1H NMR : δ 2.44(s,3H) 3.44(d,2H) 4.15(d,2H) 4.60(m,1H) 7.4 and 7.9 (d, 2H, J=8.2 Hz) 7.0 and 8.20(d,2H,J=7.8HZ). M^+ 351. Anal Calcd for $C_{16}H_{17}NO_6S$,C, 54.70; H, 4.84. Found C, 54.82; H, 4.96.

2-Phenylthio-propan-2-ol (7) [6]. Oil, ν_{max} (film) 3700 cm^{-1}. ^1H NMR : δ 1.18(d, 3H, J=6.8 Hz) 2.88(d, 2H, J=7Hz) 3.76 (m,1H) 7.0-7.6 (m, 5H). M^+ 168. Anal Calcd for $C_9H_{12}OS$, C, 64.28; H, 7.14 Found C, 64.30; H, 7.21.

2-Phenylthio-butan-2-ol (8) [15]. Oil, ν_{max} (film) 3760 cm^{-1}. ^1H NMR : δ 0.95(t, 3H), 1.50 (m, 2H) 2.8 (dd, 1H, J_1=18Hz, J_2=8Hz), 3.12(dd, 1H, J_1=16Hz, J_2=6Hz), 3.56(m, 1H) 7.18-7.56(m. 5H); M^+ 182. Anal Calcd for $C_{10}H_{14}OS$, C, 65.93; H, 7.69. Found, C, 66.02; H, 7.78.

2-Phenylthio-Cyclohexan-1-ol (9) [6]. Oil, ν_{max} (film) 3340 cm^{-1}. ^1H NMR : δ 1.3-2.15 (m, 8H) 2.9 (m, 1H) 3.4(m, 1H) 7.3-7.6 (m, 5H). M^+ 208. Anal Calcd for $C_{12}H_{16}OS$, C, 69.23; H, 7.69. Found C, 69.30; H, 7.72.

2-Phenylthio-Cyclopentan-1-ol (10) . Oil, ν_{max} (film) 3340 cm^{-1}. ^1H NMR : δ 1.24-2.2 (m, 6H), 2.94 (m, 1H) 3.44(m, 1H), 7.28-7.6 (m, 5H). M^+ 194. Anal Calcd for $C_{11}H_{14}OS$, C, 68.04; H, 7.22. Found C, 68.08; H, 7.25.

3-Phenoxy-1-phenylthio-propan-2-ol (11) [6]. Oil, ν_{max} (film) 3420 cm^{-1}. ^1H NMR : δ 3.10(d, 2H, J=6.8 Hz) 3.8 (d, 2H, J=7Hz) 4.2(m, 1H) 6.76-7.82 (m, 10 H). M^+ 260. Anal Calcd for $C_{15}H_{16}O_2S$, C, 69.23; H, 6.15. Found, C, 69.30; H, 6.21.

2-Phenylthio-1-phenyl-ethane-1-ol (12) [15]. Oil, ν_{max} (film) 3345 cm^{-1}. ^1H NMR : δ 3.18(d, 2H, J=6.8 Hz) 4.4 (t, 1H, J=6.8 Hz) 7.2-7.5 (m,10H). M^+ 230. Anal Calcd for $C_{14}H_{14}OS$, C, 73.04; H, 6.08. Found, C, 73.05; H, 6.10.

1,1-Dimethyl-tosylmethane (13) [9]. m.p. 78°C. ν_{max} (KBr) 1300, 1150 cm^{-1}, ^1H NMR :δ1.32 (d, 6H, J=6.8Hz), 2.44 (s, 3H), 3.10(m, 1H) 7.44 (d, 2H, J=8Hz), 7.88(d, 2H, J=8 Hz) M^+ 198. Anal Calcd for $C_{10}H_{14}O_2S$, C, 60.60; H, 7.07. Found, C, 60.68; H, 7.12,

1-Tosyl-butane (14). m.p. 49°C, ν_{max} (KBr). 1310, 1150 cm^{-1}. ^1H NMR : δ1.08(t, 3H), 1.40(m, 4H) 3.0 (m, 2H), 7.45(d, 2H, J=8Hz), 7.80(d, 2H, J=8Hz). M^+ 212. Anal Calcd for $C_{11}H_{16}O_2S$, C, 62.26; H, 7.55. Found, C, 62.30; H, 7.73.

Phenyl-tosyl-methane (15) [9]. m.p. 142°C. ν_{max} (KBr) 1300, 1150 cm^{-1}. ^1H NMR : δ2.44(s,3H) 4.25 (s,2H) 7.32(m, 9H). M^+ 246. Anal Calcd for $C_{14}H_{14}O_2S$, C, 68.29; H, 5.69. Found, C, 68.32; H, 6.07.

2-Tosyl-3,4-dihydro-1-(2H-naphthalenone) (16) . m.p. 142°C. ν_{max} (film) 1670, 1340, 1160 cm^{-1}. ^1H NMR : δ 2.45(s, 3H), 2.32-2.92 (m, 4H) 4.75(m, 1H) 7.50(m, 9H). M^+ 300. Anal Calcd for $C_{17}H_{16}O_3S$, C, 68.0; H, 5.33. Found, C, 68.04; H, 5.38.

1-Phynyl-2-tosyl-ethanone (17) . m.p. 90°C ν_{max} (film) 1685, 1320, 1150 cm^{-1}. ^1H NMR : δ 2.45 (s, 3H), 4.9(s, 2H) 7.42-7.96 (m, 9H). M^+ 274. Anal Calcd for $C_{15}H_{14}O_3S$, C, 65.69; H, 5.11. Found C, 65.71; H, 5.23.

1-p-bromophenyl-2-tosyl ethanone (18) . m.p. 120°C. ν_{max} (film) 1690, 1320, 1175 cm^{-1}. ^1H NMR : δ 2.45 (s, 3H), 5.1 (s, 2H) 7.44-8.02 (m,8H). M^+ 352. Anal Calcd for $C_{15}H_{13}O_3S$ Br, C, 51.13; H, 3.69. Found, C, 51.22; H, 3.71.

E-3-(p-toluenesulfonyl-2-propene)-1-ol (19) [3a,10]. m.p. 121°C. ν_{max} (KBr) 3500, 1620, 1300, 1150 cm^{-1}. ^1H NMR : δ 2.45 (s, 3H), 2.54 (brs, 1H) 4.40 (m, 2H) 6.60 (d of t, 1H, J_1=15 Hz, J_2=2Hz) 7.0 (d of t, 1H) 7.4-7.8 (m, 4H). M^+ 212, Anal Calcd for $C_{10}H_{12}O_3S$, C, 56.60, H, 5.66. Found, C, 56.62; H, 5.69.

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