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A Simple and Convenient Method for the Synthesis of Sulfones Using Polyethylene Glycols or Their Dialkyl Ethers as Solvents or Catalysts

Kazuaki SUKATA
Nihon Tokushu Kagaku Kogyo Co., Ltd., 3-36, Tohda-cho, Moriguchi, Osaka 570

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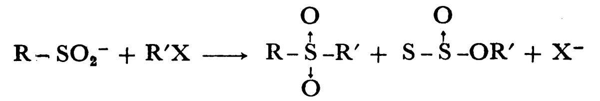
Synopsis. Various alkyl *p*-tolyl sulfones were prepared in good yields under mild conditions in the presence of polyethyene glycols or their dialkyl ethers as solvents or catalysts.

It has been reported[1] that the alkylation of sodium *p*-toluenesulfinate in methanol (MeOH) or *N, N*-dimethylformamide gives both the *p*-toluenesulfinic ester and the sulfone, and alkylation with hard alkylating agents gives predominantly the ester, whereas a soft alkylating agent gives predominantly the sulfone. This alkylation usually gives the sulfone only in moderate yields.[1]



$$R-SO_2^- + R'X \longrightarrow R-\overset{O}{\underset{O}{S}}-R' + S-\overset{O}{S}-OR' + X^-$$

Recently, Veenstra and Zwanenburg[2] have reported the reaction of tetrabutylammonium *p*-toluenesulfinate with alkyl halides as an improved method for the synthesis of sulfones. More recently, Manescalchi *et al.*[3] have reported a similar method using Amberlyst A-26, a macroreticular anion-exchange resin. In these methods, however, the tedious preparation of tetrabutylammonium *p*-toluenesulfinate or the sulfinate form of Amberlyst A-26 is required before reaction with the alkyl halide.

In this paper, a simpler and more convenient method for the synthesis of sulfones using polyethylene glycols (PEG) or their diethyl ethers is reported.

The reactions were carried out with sodium *p*-toluensulfinate monohydrate and various alkyl halides in PEG having an average molecular weight of 400 (PEG-400), PEG-400 diethyl ether (PEG-400-Et_2), or MeOH containing PEG-1000 or PEG-1000-Et_2 as a catalyst. Table 1 shows the results. In all cases, the sulfones were obtained in good to excellent yields. When PEG-400 was employed as a solvent, GLC showed that the product was almost entirely the sulfone because of the rapid hydrolysis of the ester. In the case of PEG-400-Et_2 or MeOH with a catalytic amount of PEG-1000 or PEG-1000-Et_2, however, GLC showed that a small amount of the ester remained under the experimental conditions used. These facts indicate that PEG is a good solvent for the alkylation of sulfinate anion to yield sulfones.

TABLE 1. REACTION OF $C_7H_7SO_2Na\cdot H_2O$ WITH ALKYL HALIDES[a]

Alkyl halide	Solvent	Catalyst[b]	Time h	Temp °C	Yield[c] %	Mp θ_m or Bp θ_b/°C (mmHg)	Lit Mp θ_m or Bp θ_b/°C (mmHg)
C_2H_5Br	PEG-400	—	3	60	89		
	PEG-400-Et_2	—	4	60	89	53—55	55—56[5]
	MeOH	A	7	reflux	80[d]	151—152(3)	
	MeOH	—	7	reflux	64[e]		
n-C_4H_9Br	PEG-400	—	3	60	90		
	PEG-400-Et_2	—	9	60	82[d]	143—144(1)	175—177(4)[6]
	MeOH	A	7	60	83[d]		
	MeOH	—	7	60	61[e]		
n-$C_8H_{17}Br$	PEG-400	—	4	60	94		
	PEG-400-Et_2	—	12	60	59[d]	40.0—40.5	[f]
	MeOH	A	7	60	80	150—151(0.12)	
	MeOH	—	7	60	56[d]		
$CH_2{=}CHCH_2Br$	PEG-400	—	1.5	60	95		
	PEG-400-Et_2	—	3	60	95	51—52	52—53[7]
	MeOH	A	3	60	89[d]	137(1)	
$PhCH_2Cl$[g]	PEG-400	—	2	60	94		
	MeOH	A	4	60	90	144—145	144—145[8]
$ClCH_2CN$	PEG-400	—	2	60	93		
	MeOH	B	4	60	83	147—148	145—146[10]
$BrCH_2Br$	PEG-400	—	6	60	73		
	PEG-400	—	4	80	89	87—88	90—92[9]

a) All reactions were carried out with $C_7H_7SO_2Na\cdot H_2O$ (0.05 mol) and alkyl halide (0.075 mol) in a solvent (20 ml) with or without a catalyst (0.005 mol). b) A: PEG-1000-Et_2, B: PEG-1000. c) Isolated yields. Unless otherwise noted, purities were >99% by GLC. d) Purities were 98% by GLC. e) Purities were 97% by GLC. f) See Experimental section. g) Forty milliliters of solvent were used.

Experimental

Materials. Methanol and PEG-400 (reagent grade, Kishida Kagaku Co., Ltd.) were dried with molecular sieves 4A. PEG-1000 (reagent grade, Kishida Kagaku Co., Ltd.) was used without further purification. PEG-400-Et_2 and PEG-1000-Et_2 were prepared according to the method previously reported.[4] Sodium *p*-toluenesulfinate ($C_7H_7SO_2Na$ nH_2O, $n \approx 1$) (reagent grade, Tokyo Kasei Kogyo Co., Ltd.) was used as obtained. The physical properties (bp or mp) of ethyl *p*-tolyl sulfone,[5] butyl *p*-tolyl sulfone,[6] allyl *p*-tolyl sulfone,[2,7] benzyl *p*-tolyl sulfone,[8] cyanomethyl *p*-tolyl sulfone,[2,10] and bromometyl *p*-tolyl sulfone[2,9] were in good agreement with those reported in the literature (Table 1) and satisfactory IR spectra for these compounds were obtained.

Typical Procedure for the Reaction of Sodium p-*Toluenesulfinate Monohydrate with Alkyl Halides. Bromomethyl* p-*Tolyl Sulfone*: A mixture of powdered sodium *p*-toluenesulfinate monohydrate (9.8 g, 0.05 mol) and dibromomethane (13.0 g, 0.075 mol) was stirred at 80 °C for 4 h in PEG-400 (20 ml). After removal of the excess dibromomethane, the reaction mixture was poured into water (300 ml). The precipitated white solid was collected and recrystallized from ethanol–water, giving 11.1 g (89%) of bromomethyl *p*-tolyl sulfone, mp 87—88 °C (lit,[9] mp 90—92 °C).

Butyl p-*Tolyl Sulfone*: A mixture of powdered sodium *p*-toluenesulfinate monohydrate (9.8 g, 0.05 mol), butyl bromide (10.3 g, 0.075 mol), MeOH (20 ml), and PEG-1000-Et_2 (5.3 g, 0.005 mol) was stirred at 60 °C for 7 h. The reaction mixture was diluted with water (200 ml) and extracted with benzene (20 ml × 3). The benzene layers were combined, washed with water, and dried. After removal of the benzene, the residual oil was distilled under reduced pressure, giving 8.8 g (83%) of butyl *p*-tolyl sulfone, bp 137—142 °C/1 mmHg (1 mmHg = 133.322 Pa) (lit,[6] bp 175—177 °C/4 mmHg). The purity was 98% by GLC.

Octyl p-*Tolyl Sulfone*: A mixture of powdered sodium *p*-toluenesulfinate monohydrate (9.8 g, 0.05 mol), octyl bromide (14.5 g, 0.075 mol), and PEG-400 (20 ml) was stirred at 60 °C for 3 h. After the reaction mixture had been treated according to the method for butyl *p*-tolyl sulfone, the residual oil was distilled under reduced pressure, giving 12.6 g (94%) of octyl *p*-tolyl sulfone (>99% pure), bp 175—178 °C/0.5 mmHg. Redistillation of the product gave pure octyl *p*-tolyl sulfone having bp 150—151 °C/0.12 mmHg, mp 40.0—40.5 °C; IR (neat) 1310, 1140 cm^{-1} ($-SO_2-$). Found: C, 66.90; H, 9.07; S, 11.93%. Calcd for $C_{15}H_{24}O_2S$: C, 67.12; H, 9.01; S, 11.94%.

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