Polymer Supported Reagents. The Use of Anion Exchange Resins in the Synthesis of Sulfones

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The alkylation of alkali metal salts of sulfinic acids is a widely used procedure for preparing sulfones[1], although it has been recognized that sulfinate esters can also be obtained, depending on the hard or soft alkylating agents employed[2]. This reaction is usually performed in refluxing alcohol or in dimethylformamide at room temperature, but it is quite slow and often produces only moderate yields of sulfones.

Recently the procedure has been modified by using tetrabutylammonium *p*-toluenesulfinate in the nucleophilic displacement reaction with organic halides[3]. The reaction thus proceeds in tetrahydrofuran at 20–40° in 2–4 h with satisfactory yields. However, the preparation of tetrabutylammonium *p*-toluenesulfinate from sodium *p*-toluenesulfinate and tetrabutylammonium bromide was not effective, since a two-fold excess of sodium *p*-toluenesulfinate was required and the reagent effectively used in the alkylation reaction was only 50 % pure.

As part of a program to demonstrate the applicability of polymer supported reagents in the organic synthesis[4–8], we wish now to report a more convenient synthesis of sulfones by the alkylation of benzenesulfinate anion supported on Amberlyst A-26, a macroreticular anion exchange resin containing quaternary ammonium groups.

We prepared reagent **1** by the exchange reaction of sodium benzenesulfinate with the resin in chloride form, or by neutralization of the resin in hydroxide form with benzenesulfinic acid.

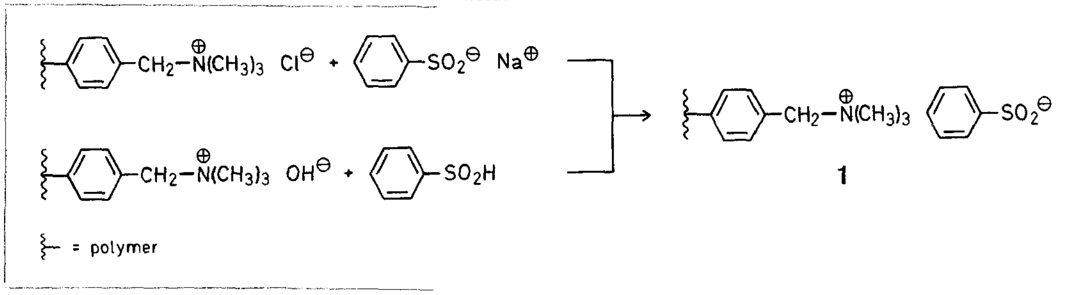

Table. Phenyl Sulfones **3** from Reagent **1** and Alkyl Halides **2**

Alkyl halide **2** R–X	Reaction time [h][a]	Yield [%] of **3**	m.p. or b.p./torr	Molecular formula[b] or Lit. m.p. or b.p./torr	^{1}H-N.M.R. (CDCl$_3$) δ [ppm]
H_3C–J	3	95	88°	88°[9]	3.1 (s, 3H); 7.6–8.2 (m, 5H_{arom})
n-C_3H_7–J	3	94	45°	46°[9]	0.95 (t, 3H); 1.4–2.1 (m, 2H); 2.95–3.2 (m, 2H); 7.5–8.1 (m, 5H_{arom})
n-C_6H_{13}–Br	3	92	170–175°/1	$C_{12}H_{18}O_2S$ (226.3)	0.85 (t, 3H); 1.1–2.1 (m, 8H); 3.0–3.3 (m, 2H); 7.5–8.2 (m, 5H_{arom})
n-C_8H_{17}–Br	3	92	175–180°/1	230°/19[10]	0.85 (t, 3H); 1.1–1.8 (m, 12H); 2.9–3.25 (m, 2H); 7.5–8.1 (m, 5H_{arom})
n-C_6H_{13}–CH(CH_3)–Br	3	60[c]	175–180°/1	$C_{14}H_{22}O_2S$ (254.3)	0.85 (t, 3H); 1.05–2.0 (m, 13H); 2.75–3.3 (m, 1H); 7.5–8.2 (m, 5H_{arom})
C_6H_5–CH_2–Cl	2	93	147°	146°[11]	4.3 (s, 2H); 6.9–8.1 (m, 10H_{arom})
$(H_3C)_2C{=}CH$–CH_2–Br	1.5	95	53°	54°[11]	1.2 (s, 3H); 1.7 (s, 3H); 3.8 (d, 2H); 5.25 (t, 1H); 7.5–8.2 (m, 5H_{arom})
(*E*)-C_2H_5OOC–$CH{=}C(CH_3)$–CH_2–Br	1.5	92	57°	57°[12]	1.25 (t, 3H); 2.25 (s, 3H); 3.9 (s, 2H); 4.15 (q, 2H); 5.6 (s, 1H); 7.5–8.1 (m, 5H_{arom})
(*E*)-H_3COOC–$C(CH_3){=}CH$–CH_2–Br	1.5	93	73°	$C_{12}H_{14}O_4S$ (254.2)	1.6 (s, 3H); 3.75 (s, 3H); 4.0 (d, 2H); 6.8 (t, 1H); 7.5–8.2 (m, 5H_{arom})
C_2H_5OOC–CH_2–Cl	2	91	47°	43°[13]	1.15 (t, 3H); 4.15 (q, 2H); 4.2 (s, 2H); 7.55–8.2 (m, 5H_{arom})
NC–CH_2–Cl	2	95	113°	114°[14]	4.15 (s, 2H); 7.5–8.3 (m, 5H_{arom})

[a] In refluxing benzene.

[b] The microanalyses for the new products were in satisfactory agreement with the calculated values (C ±0.1, H ±0.1, S ±0.15).

[c] In refluxing toluene.

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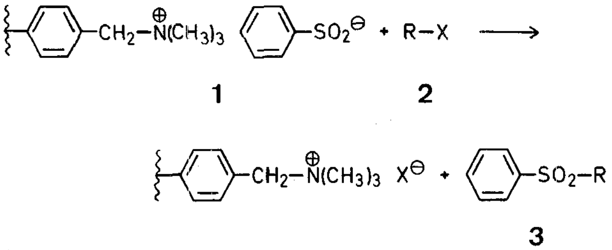
The alkylation reaction was then performed by a batch technique by stirring a slight excess of **1** with alkyl halides in refluxing benzene for 1.5–3 h. The reaction products **3** were isolated simply by filtering the resin and removing the solvent by distillation under reduced pressure.



= polymer

The yields with primary alkyl halides were always above 90 % and the crude products showed high purity on spectral analysis. The ^{1}H-N.M.R. spectrum of the crude product obtained from **1** and methyl iodide indicated the presence of the methyl ester of benzenesulfinic acid: the ratio of sulfone to ester was evaluated to be 97.5/2.5. The amount of the ester was not evaluated in all the other reaction products, but it was always very low, as demonstrated by the N.M.R. data of crude products. The sulfones **2** were obtained in pure state by crystallization, distillation, or column chromatography.

After the reaction the resins could be easily regenerated by washing with the appropriate reagents. We can conclude that the high effectiveness and the easy work-up make this procedure remarkably useful, introducing a significant improvement with respect to the usual methods.

Amberlyst A-26, Benzenesulfinate Form (1):
A 0.1 molar aqueous solution of sodium benzenesulfinate (Fluka) is slowly percolated through a column filled with Amberlyst A-26 (Rohm and Haas) in the chloride form, until a negative test for chloride ion in the eluate is obtained. The reagent **1** can be more quickly prepared using a system of two superimposed columns, the upper one filled with Amberlyst H-15 resin (16.6 g; $H^{\oplus}$ form, average capacity 4 meq/g) and the lower one with Amberlyst A-26 resin (20 g; $OH^{\ominus}$ form, average capacity 3.5 meq/g[5]). A slight excess of sodium benzenesulfinate (11.8 g; 72 mmol) dissolved in methanol (50 ml) is eluted through the system until an acidic reaction of the eluate is observed. The resins prepared by either of the methods are successively washed with water, acetone, and ether, and dried in vacuo at 50° for 5 h.

Preparation of *n*-Octyl Phenyl Sulfone; Typical Procedure:
Amberlyst A-26, benzenesulfinate form, (**1**; 11 g; 39 meq) and 1-bromooctane (5.8 g; 30 mmol) are vigorously stirred in refluxing benzene (30 ml) for 3 h. The resin is then filtered off, washed with dichloromethane (30 ml) and the solvent is removed in vacuo. Distillation of the crude product gives the sulfone; yield: 7.16 g (92 %); b.p. 175–180°/1 torr (Lit.[10] b.p. 230°/19 torr).

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