194 (12), 180 (58.5), 165 (22.1), 152 (29.8), 43 (100).

5,7-Dihydroxy-4-methylphthalide (1c). A solution of butyllithium (20 cm^3, 1.5 M in hexane) was added under stirring to a solution of 3-acetyl-4-(1-(methoxyccarbonyl)ethyl]-2,5-dihydrofuran-2-one (2.1 g, 0.01 mol) in 50 cm^3 of dry THF at −70 °C. The mixture was left to stand at this temperature for 3 h and then was allowed to reach ambient temperature. The mixture was shaken with dilute hydrochloric acid and extracted with diethyl ether. The organic extract was evaporated to dryness. The residue was chromatographed over silica gel (70:30 hexane–Et$_2$O) to give 0.45 g of 5,7-dihydroxy-4-methylphthalide (**1c**, 25% yield). Compound **1c** was identical with an authentic sample of 5,7-dihydroxy-4-methylphthalide:[12] mp 240 °C; IR (Njuol) $\nu_{\max}$ 3420, 3340, 1720, 1625 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 6.4 (s, 1 H), 5.2 (s, 2 H), 2.05 (s, 3 H); MS, m/e 180 (49), 151 (100), 122 (33).

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Registry No. **1a**, 24280-93-1; **1c**, 27979-57-3; **3**, 84280-59-1; **4**, 63285-91-6; **5**, 14337-43-0; **7a**, 84280-60-4; **7b**, 84280-61-5; **8**, 84280-62-6; **9**, 84280-63-7; **11**, 84280-64-8; **12a**, 84280-65-9; **12b**, 84280-66-0; methylketene diethyl acetal, 21504-43-8; diketene, 674-82-8.

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[12] We thank Prof. C. Scolastico for a sample of 5,7-dihydroxy-4-methylphthalide.

Nucleophilic Aromatic Substitution Reactions under Phase-Transfer Conditions. Synthesis of Alkyl Aryl Sulfides from Isomeric Dichlorobenzenes and Thiolates

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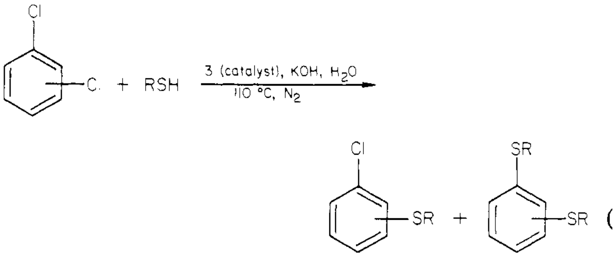
Nucleophilic aromatic substitutions (S$_N$Ar) of slightly activated aryl halides promoted by anions require drastic conditions,[1] even with dipolar aprotic solvents.[2] It is well-known that the conditions of phase-transfer catalysis (PTC) strongly accelerate anionic substitution reactions.[3] However, most of the reported examples deal with aliphatic displacements,[3] while only a few cases are described of S$_N$Ar reactions on activated substrates.[3c,4,5] The synthesis of 2- and 3-chlorophenyl methyl ethers from slightly activated 1,2- and 1,3-dichlorobenzene in the presence of 18-crown-6 in a PTC solid-liquid system has been also reported.[6]

We have found that S$_N$Ar reactions of dichlorobenzenes with powerful nucleophiles such as thiolates can be much more easily performed under the conditions of liquid-liquid PTC. Reactions were carried out, according to eq 1, by stirring at 110 °C under nitrogen a heterogeneous mixture of the substrate, dicyclohexano-18-crown-6 (**3**) as a catalyst, and the solution of the thiol in aqueous concentrated KOH. The reaction rate increases with the increase of the amount of KOH in the aqueous phase (Table I). This is likely related to the fact that, in the presence of highly concentrated alkaline solutions (60% KOH or 50% NaOH, w/w), anionic nucleophiles are transferred as nonhydrated species from the aqueous to the organic phase.[7]



1 **2** (1)

The reactivity of the first chlorine atom follows the order 1,2- > 1,3- > 1,4-dichlorobenzene in agreement with the prevalent influence of the −I activating effect of chlorine atoms. As expected, thiolates react according to the order primary alkyl > secondary alkyl > tertiary alkyl ≫ aryl. No cine-substitution product was observed, neither by NMR nor by GC analyses. As shown in Table I, the product distribution depends on the nature of both substrates and thiols. In particular, with secondary and tertiary thiolates, 1,2-dichlorobenzene gives only monosubstitution derivatives **1**, while with primary thiolates, **1** together with minor amounts of the disubstituted **2** are formed. Similar **1** to **2** ratios are obtained from 1,3-dichlorobenzene, independent of the thiolate.

In the case of 1,4-dichlorobenzene the selectivity of the reaction is noticeably reduced compared to that of the isomeric dichlorobenzenes. Moreover, the selectivity decreases in passing from primary to tertiary thiolates (Table I). Thiophenol is much less reactive than alkyl mercaptans, only a 21% conversion being reached after 75 h (Table I).

Experimental Section

General Methods. NMR spectra were recorded on a Varian EM-390 90-MHz spectrometer in CDCl$_3$ solutions with Me$_4$Si as an internal standard; IR spectra were measured as films or Nujol mulls on a Perkin-Elmer 377 grating spectrophotometer by using NaCl cells; GC data were obtained on a Varian 3700 gas chromatograph equipped with a 3% Carbowax 20M on Chromosorb W column and were evaluated with a Varian Model 401 data system by the internal standard method. Boiling points are uncorrected.

Materials. Thiols, dichlorobenzenes, **3**, and KOH were commercially available reagent grade products. The aqueous KOH–

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Table I. Synthesis of Alkyl Aryl Sulfides 1 and 2 under PTC Conditions at 110 °C

substrate[a] (1 mol)	thiol (2.5 mol)	aqueous KOH, % (w/w)	time, h	conversion,[b] %		isolated yield of 1, %
				1	2	
$o\text{-}Cl_2C_6H_4$	$n\text{-}C_4H_9SH$	60	14	92	5	88
	$i\text{-}C_3H_7SH$	60	16	93	0	89
		50	18	90	0	
		40	36	91	0	
		30	45	93	0	
		20	48	18	0	
		10	48	9	0	
		0	48	1	0	
	$t\text{-}C_4H_9SH$	60	75	94	0	84
	C_6H_5SH	60	75	21	0	
$m\text{-}Cl_2C_6H_4$	$n\text{-}C_4H_9SH$	60	24	87	6	81
	$i\text{-}C_3H_7SH$	60	24	86	6	79
	$t\text{-}C_4H_9SH$	60	125	86	12	73
$p\text{-}Cl_2C_6H_4$	$n\text{-}C_4H_9SH$	60	90	76	14	65
	$i\text{-}C_3H_7SH$	60	150	54	35	43
	$t\text{-}C_4H_9SH$	60	250	31	53	27

[a] In the presence of **3** (0.1 mol); no reaction occurred in the absence of the catalyst. [b] By GC analysis.

thiolate solutions were prepared by adding the thiol to the KOH solution under nitrogen. The KOH concentrations (in percent, w/w) were calculated on the amount of KOH left after complete salification of the thiol, thus representing the actual base concentration. A large excess of aqueous solution was used (100 mL of water/0.1 mol of substrate) to overcome stirring problems due to the precipitation of KCl in the course of the reaction.

Typical Procedure. Synthesis of Alkyl Chlorophenyl Sulfides (1). The dichlorobenzene (14.7 g, 0.1 mol) and **3** (3.7 g, 0.01 mol) were added to the solution of the thiol (0.25 mol) and KOH (16.4 g, 2.9 mol) in water (100 mL). The mixture was stirred under nitrogen at 110 °C (bath temperature) until the reaction was complete (by GC analysis). Pure **1** was obtained by extraction (ether) and fractional distillation. The reaction products were analyzed by NMR, GC, and IR, and their physical properties were identical with those of authentic samples prepared according to the literature.

Reaction Products 1. *n*-Butyl 2-chlorophenyl sulfide: bp 120–122 °C (12 mm); $n^{22}{}_D$ 1.5660; NMR δ 0.95 (t, 3 H), 1.2–1.9 (m, 4 H), 2.95 (t, 2 H), 6.9–7.5 (m, 4 H). Anal. Calcd for $C_{10}H_{13}ClS$: C, 59.83; H, 6.53. Found: C, 59.99; H, 6.56.

Isopropyl 2-chlorophenyl sulfide: bp 108–110 °C (16 mm) [lit.[2b] bp 113–114 °C (18 mm)]; $n^{24}{}_D$ 1.5685; NMR δ 1.25 (d, 6 H), 3–4 (septet, 1 H), 6.75–7.45 (m, 4 H).

***tert*-Butyl 2-chlorophenyl sulfide**: bp 109–111 °C (10 mm); $n^{25}{}_D$ 1.5510; NMR δ 1.3 (s, 9 H), 6.8–7.9 (m, 4 H). Anal. Calcd for $C_{10}H_{13}ClS$: C, 59.83; H, 6.53. Found: C, 59.71; H, 6.60.

***n*-Butyl 3-chlorophenyl sulfide**: bp 82–84 °C (0.4 mm); $n_D{}^{29}$ 1.5556; NMR δ 0.9 (t, 3 H), 1.15–1.9 (m, 4 H), 2.9 (t, 2 H), 6.9–7.2 (m, 3 H), 7.2–7.4 (m, 1 H). Anal. Calcd for $C_{10}H_{13}ClS$: C, 59.83; H, 6.53. Found: C, 59.89; H, 6.44.

Isopropyl 3-chlorophenyl sulfide: bp 49–51 °C (0.9 mm) [lit.[2b] bp 53–54 °C (1 mm)]; $n^{21}{}_D$ 1.5627; NMR δ 1.3 (d, 6 H), 3.4 (septet, 1 H), 6.9–7.2 (m, 3 H), 7.35–7.6 (m, 1 H).

***tert*-Butyl 3-chlorophenyl sulfide**: bp 99–101 °C (8 mm); $n^{29}{}_D$ 1.5440; NMR δ 1.35 (s, 9 H), 7.15–7.35 (m, 3 H), 7.4–7.65 (m, 1 H). Anal. Calcd for $C_{10}H_{13}ClS$: C, 59.83; H, 6.53. Found: C, 60.02; H, 6.65.

***n*-Butyl 4-chlorophenyl sulfide**: bp 138–140 °C (12 mm); $n^{22}{}_D$ 1.5618; NMR δ 0.95 (t, 3 H), 1.25–1.95 (m, 4 H), 3.0 (t, 2 H), 7.4 (s, 4 H). [Lit.[8] bp 136–137 °C (10 mm); $n^{20}{}_D$ 1.5623].

Isopropyl 4-chlorophenyl sulfide: bp 114–116 °C (14 mm) [lit.[2b] bp 117–118 °C (18 mm)]; $n^{21}{}_D$ 1.5623; NMR δ 1.3 (d, 6 H), 3.35 (septet, 1 H), 7.3 (s, 4 H).

***tert*-Butyl 4-chlorophenyl sulfide**: bp 77–79 °C (1 mm) [lit.[9] bp 74 °C (0.6 mm)]; $n^{27}{}_D$ 1.5401; NMR δ 1.3 (s, 9 H), 7.35 (s, 4 H).

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Registry No. *o*-**1** (R = $n\text{-}C_4H_9$), 84051-20-7; *o*-**1** (R = $i\text{-}C_3H_7$), 34560-82-2; *o*-**1** (R = $t\text{-}C_4H_9$), 84051-21-8; *o*-**1** (R = C_6H_5), 33667-82-2; *m*-**1** (R = $n\text{-}C_4H_9$), 84051-22-9; *m*-**1** (R = $i\text{-}C_3H_7$), 55698-06-1; *m*-**1** (R = $t\text{-}C_4H_9$), 49833-56-9; *p*-**1** (R = $n\text{-}C_4H_9$), 16155-34-3; *p*-**1** (R = $i\text{-}C_3H_7$), 7205-62-1; *p*-**1** (R = $t\text{-}C_4H_9$), 7205-65-4; *m*-**2** (R = $t\text{-}C_4H_9$), 25752-96-9; *p*-**2** (R = $n\text{-}C_4H_9$), 73732-39-5; *p*-**2** (R = $i\text{-}C_3H_7$), 70398-85-5; *p*-**2** (R = $t\text{-}C_4H_9$), 25752-95-8; $o\text{-}Cl_2C_6H_4$, 95-50-1; $m\text{-}Cl_2C_6H_4$, 541-73-1; $p\text{-}Cl_2C_6H_4$, 106-46-7; $n\text{-}C_4H_9SH$, 109-79-5; $i\text{-}C_3H_7SH$, 75-33-2; $t\text{-}C_4H_9SH$, 75-66-1; C_6H_5SH, 108-98-5.

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S_NAr Nucleophilic Substitutions of $Cr(CO)_3$-Complexed Aryl Halides with Thiolates under Phase-Transfer Conditions

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Nucleophilic substitution at unactivated aryl halides are known to occur with difficulty, unless special experimental conditions are adopted: high temperatures, very strong bases and nucleophiles, dipolar aprotic solvents, catalysis by transition-metal complexes.[1-4]

Aromatic compounds can be activated toward nucleophilic substitution by coordination of the arene ring with transition-metal residues.[5-8] Among the latter activating

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