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] % 1	conversion,[b] % 2	isolated yield of 1, %
o-$Cl_2C_6H_4$	n-C_4H_9SH	60	14	92	5	88
	i-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-C_4H_9SH	60	75	94	0	84
	C_6H_5SH	60	75	21	0	
m-$Cl_2C_6H_4$	n-C_4H_9SH	60	24	87	6	81
	i-C_3H_7SH	60	24	86	6	79
	t-C_4H_9SH	60	125	86	12	73
p-$Cl_2C_6H_4$	n-C_4H_9SH	60	90	76	14	65
	i-C_3H_7SH	60	150	54	35	43
	t-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-C_4H_9), 84051-20-7; o-1 (R = i-C_3H_7), 34560-82-2; o-1 (R = t-C_4H_9), 84051-21-8; o-1 (R = C_6H_5), 33667-82-2; m-1 (R = n-C_4H_9), 84051-22-9; m-1 (R = i-C_3H_7), 55698-06-1; m-1 (R = t-C_4H_9), 49833-56-9; p-1 (R = n-C_4H_9), 16155-34-3; p-1 (R = i-C_3H_7), 7205-62-1; p-1 (R = t-C_4H_9), 7205-65-4; m-2 (R = t-C_4H_9), 25752-96-9; p-2 (R = n-C_4H_9), 73732-39-5; p-2 (R = i-C_3H_7), 70398-85-5; p-2 (R = t-C_4H_9), 25752-95-8; o-$Cl_2C_6H_4$, 95-50-1; m-$Cl_2C_6H_4$, 541-73-1; p-$Cl_2C_6H_4$, 106-46-7; n-C_4H_9SH, 109-79-5; i-C_3H_7SH, 75-33-2; t-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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Table I[a]

Ar	X	R	NaOH, % concn	catalyst	time, h	temp, °C	isolated product	yield, %	mp, °C	bp, °C/torr
Ph	F	Me	50	TOAB[b]	0.1	rt[g]	1, 2	88	101[9]	
Ph	Cl	*n*-Bu	50	CTAB[c]	1.5	rt	2	90		120/15
Ph	F	*n*-Bu	50	CTAB[c]	0.5	rt	2	90		120/15
Ph	Cl	*i*-Pr	50	TOAB[b]	0.5	rt	1, 2	92	50	65/1[e]
Ph	Cl	*i*-Pr	50	CTAB[c]	2	rt	2	95		65/1
Ph	F	*i*-Pr	50	CTAB[c]	0.5	rt	2	95		65/1
Ph	Cl	*t*-Bu	50	CTAB[c]	2	45	1, 2	94	93[f]	73/5[e]
Ph	F	*t*-Bu	50	CTAB[c]	1	rt	1, 2	97	93[f]	73/5[e]
Ph	Cl	*t*-Bu	50	aliquat 336[d]	5	45	1, 2	95	93[f]	73/5[e]
Ph	F	*t*-Bu	50	aliquat 336[d]	0.5	45	1, 2	97	93[f]	73/5[e]
Ph	Cl	*t*-Bu	10	aliquat 336[d]	72	45	2	80		73/5
Ph	F	*t*-Bu	10	aliquat 336[d]	1	rt	2	>98		73/5
Ph	Cl	*t*-Bu	10	TOAB[b]	6	rt	2	>98		73/5
Ph	Cl	*t*-Bu	solid	aliquat 336[d]	0.75	45	2	>98		73/5
m-MePh	Cl	*t*-Bu	solid	aliquat 336[d]	6	60	2	>98		72/1.5
m-MePh	Cl	*t*-Bu	solid	TOAB[b]	0.5	60	2	>98		72/1.5
p-MePh	Cl	*t*-Bu	solid	aliquat 336[d]	6	60	2	>98		65/0.5

[a] Column headings refer to eq 1. [b] Tetraoctylammonium bromide. [c] Cetyltrimethylammonium bromide. [d] Tricaprylmethylammonium bromide. [e] For product 2. [f] For product 1. [g] Room temperature.

groups, $Cr(CO)_3$, when complexed with fluoro- and chlorobenzene, induces an effect similar in magnitude to that exerted by a *p*-nitro group[9] and nucleophilic substitution of $Cr(CO)_3$-complexed haloarenes can take place at moderate temperature, although in a number of cases it requires quite sophisticated reaction conditions or the use of Me_2SO or HMPA as solvent.

Phase-transfer catalysis coupled with $Cr(CO)_3$ activation appeared to us to be a very attractive combination to facilitate the reaction of haloarenes with nucleophiles because of the very simple conditions required and its well-documented potential in organic synthesis. Phase-transfer catalysis has never been applied to the study of S_NAr on (η^6-arene)metal complexes.[10] One of us[13] has shown that phase-transfer-induced nucleophilic substitution of unactivated haloarenes takes place only under rather severe conditions. We now report some results on nucleophilic substitution of $Cr(CO)_3$ complexed aryl halides with thiolates under phase-transfer conditions.

Complexed haloarenes and thiols, dissolved in benzene, were stirred under nitrogen with a 10–50% aqueous NaOH solution, or with solid ground NaOH, and variable amounts of a tetralkylammonium salt. The product was usually characterized after decomplexation. In some cases the $Cr(CO)_3$ complex could be isolated and purified. The

$$Cr(CO)_3ArX + RS^- \xrightarrow[\text{NaOH/catalyst}]{C_6H_6} \underset{\mathbf{1}}{Cr(CO)_3ArSR} \xrightarrow{I_2} \underset{\mathbf{2}}{ArSr} \quad (1)$$

nature and amount of the ammonium salt used, reaction conditions, and yields of products are summarized in Table I.

On the whole it appears that, qualitatively, fluoroarene complexes, are more reactive toward thiolates than are the corresponding chloro derivatives, as expected;[6] moreover, cetyltrimethylammonium bromide (CTAB) is a more effective catalyst than tricaprylmethylammonium bromide (aliquat) but less effective than tetraoctylammonium bromide (TOAB) in promoting nucleophilic substitution.[14]

The use of a 10% NaOH solution instead of a 50% one results, qualitatively, in a slower reaction, but yields are still very good with aliquat and especially with the highly lipophilic TOAB. With CTAB the reaction is very slow and workup is made difficult by the formation of a stable emulsion.[15] The nucleophilic substitution can be carried out more readily under solid–liquid phase-transfer conditions, using solid ground NaOH. In fact (chlorobenzene)chromium tricarbonyl reacts with 2-methyl-2-propanethiolate about 6 times more rapidly in the presence of solid NaOH than in the presence of 50% aqueous NaOH.

Under solid–liquid conditions, complexed *m*- and *p*-halotoluenes react with 2-methyl-2-propanethiolate, affording, in quantitative yield, the corresponding *m*- and *p*-tolyl *tert*-butyl sulfide, in accord with a S_NAr mechanism. Chromium carbonyl activated chlorotoluenes, as expected, react more slowly than (chlorobenzene)chromium tricarbonyl.

This and previous work[10] show the quite general and to some extent unexpected stability of (arene)$Cr(CO)_3$ complexes toward nondeoxygenated water and aqueous sodium hydroxide, supporting the potential in organic synthesis of the phase-transfer methodology coupled with $Cr(CO)_3$-induced activation.

Experimental Section

Melting points were taken on a Büchi apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 377 spectrophotometer. ^1H NMR spectra were obtained with a Varian EM-390 instrument in $CDCl_3$ solution at room temperature with Me_4Si as internal standard. Shifts are given as δ values. TLC were performed on Merck precoated silica gel 60 F 254 plates.

Materials. The following commercially available phase-transfer catalysts were employed: tetraoctylammonium bromide (TOAB); cetyltrimethylammonium bromide (CTAB); tricaprylmethylammonium bromide (aliquat 336).

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Chromium tricarbonyl complexed haloarenes were prepared following known procedures[16,17] and had been already described.[15,18]

General Procedure. $Cr(CO)_3$-complexed haloarenes (2,15 mmol) and thiols (2,37 mmol) were dissolved in benzene (25 mL) and stirred under nitrogen with a 10–50% NaOH solution (25 mL) or with solid ground NaOH (6.45 mmol) in the presence of a phase-transfer catalyst, whose molar ratio with respect to the substrate was 0.28 for TOAB, 0.37 for CTAB, and 0.56 (apparent:hygroscopic) for aliquat 336. The reaction progress was monitored by TLC (silica gel; eluant: Et_2O/light petroleum, 1/2). At the end of the reaction the organic layer was washed with water and dried over Na_2SO_4, and the solvent was removed at reduced pressure. The product was usually characterized after decomplexation by treatment of the crude chromium compound with iodine in Et_2O at 0 °C. The nature of the phase-transfer catalyst used in each reaction, reaction conditions, and yields of isolated products are summarized in Table I.

Uncomplexed Alkyl Aryl Sulfides. Compounds **2** were identified by comparison with authentic samples prepared according to literature procedures.

Tricarbonyl(isopropyl phenyl sulfide)chromium: mp 50 °C; IR ($CHCl_3$) 1970, 1890 cm^{-1} ($\nu_{C=O}$); ^1H NMR δ 1.35 (d, 6 H), 3.25 (m, 1 H), 5.25 (m, 5 H).

Anal. Calcd for $C_{12}H_{12}CrO_3S$: C, 49.99; H, 4.20. Found: C, 49.90; H, 4.40.

Tricarbonyl(*tert*-butyl phenyl sulfide)chromium: mp 93 °C; IR ($CHCl_3$) 2000, 1925 cm^{-1} ($\nu_{C=O}$); ^1H NMR δ 1.30 (s, 9 H), 5.25 (m, 3 H), 5.50 (m, 2 H).

Anal. Calcd for $C_{13}H_{14}CrO_3S$: C, 51.64; H, 4.69. Found: C, 51.48; H, 4.84.

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Registry No. 1 (Ar = Ph, R = *i*-Pr), 84029-36-7; 1 (Ar = Ph, R = *t*-Bu), 72068-09-8; $Cr(CO)_3PhF$, 12082-05-2; $Cr(CO)_3PhCl$, 12082-03-0; $Cr(CO)_3$-*m*-MePhCl, 33411-11-9; $Cr(CO)_3$-*p*-MePhCl, 12116-24-4; MeS^-, 17302-63-5; *n*-BuS^-, 20733-16-8; *i*-PrS^-, 20733-15-7; *t*-BuS^-, 20733-19-1; TOAB, 14866-33-2; CTAB, 57-09-0.

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Generation and Ring Opening of 2,3-Dilithio-1-(phenylsulfonyl)indole

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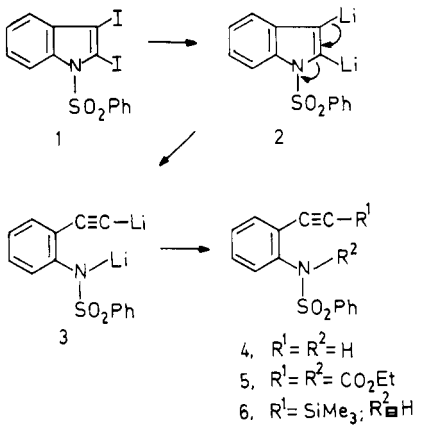
We recently reported[1] the generation of 3-lithio-1-(phenylsulfonyl)indole, a species which is stable at −100 °C but which cleanly rearranges to the more stable 2-lithio-1-(phenylsulfonyl)indole upon warming to room temperature, and we also discussed the possibility that this indole lithiation methodology could provide a synthetic equivalency for 2,3-dilithio-1-(phenylsulfonyl)indole (**2**). We now describe the apparent transient generation of **2** and its subsequent facile ring opening to lithium 2-(*N*-lithiophenylsulfonamido)phenylacetylide (**3**) at −100 °C.

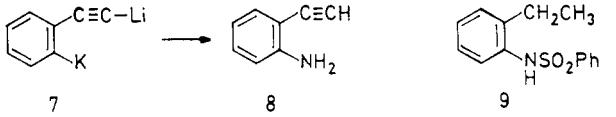
Treatment of 2,3-diiodo-1-(phenylsulfonyl)indole (**1**, which can be prepared from indole in 86% yield[1]) with 4 equiv[2] of *tert*-butyllithium [tetrahydrofuran (THF), −100 °C] results in the immediate formation of a yellow-orange color. After 3–5 min at −100 °C this solution is treated with various electrophiles (ammonium chloride, ethyl chloroformate, trimethylsilyl chloride) to give the products **4–6** in 66–82% yield (Scheme I).

Scheme I



Although we had hoped that the indole ring would retain its integrity in this reaction, it was clear from the IR and ^1H and ^{13}C NMR spectra of the products **4–6** that an acetylenic functionality was present. Thus, the IR spectrum of **4** shows a strong acetylenic C–H stretching absorption at 3315 cm^{-1}, and the IR spectra of **5** and **6** show C≡C absorption at 2210–2150 cm^{-1}.[3] The ^1H NMR spectrum of **4** displays the acetylenic proton at 3.38 ppm,[4] and the ^{13}C NMR spectra of **4–6** exhibit the expected[5] range of chemical shifts (78.4–102.2 ppm) for the acetylenic carbons.

Final structural proof was established both by an independent synthesis of **4** and by conversion of **4** to a known compound. Thus, the known[6] dimetalated phenylacetylide **7** is aminated with methoxylamine to give (2-amino-



phenyl)acetylene (**8**) in low yield. A Hinsberg reaction[7] on **8** gives a compound that is identical with **4** as obtained from **1**. In addition, catalytic hydrogenation of **4** gives the known[8] ethyl derivative **9**, which is identical with a sample prepared from 2-ethylaniline by a Hinsberg reaction. Thus, the structure of **4** is firmly secured as [2-(phenylsulfonamido)phenyl]acetylene.

We believe that this exceedingly rapid ring-opening reaction (observed even at −120 °C) involves the intermediacy of **2**, rather than cleavage of a monolithiated intermediate followed by the second halogen–metal interchange to give **3**. The aversion of both 2- and 3-lithio-1-(phenylsulfonyl)indole to undergo comparable ring-opening reactions,[1] even at higher temperatures, argues strongly against a stepwise process for the formation of **3**.

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