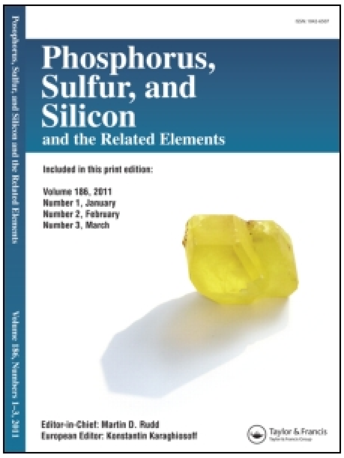

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ORTHO-LITHIATION OF PHENYLTHIOETHERS—AND SOME APPLICATIONS

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ORTHO-LITHIATION OF PHENYLTHIOETHERS—AND SOME APPLICATIONS

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A preparative procedure for the *ortho*-lithiation of phenylthioethers C_6H_5SR **1** is described. The preparations of 2-alkylthio-substituted benzoic acids **3**, benzophenones **5** and phenylphosphines **6** were carried out in isolated yields of 38–73%, depending on reaction and substituent. The procedure provides a simple route to dithiocatechol and trithiopyrogallol derivatives **7** and **8**.

The ring-lithiation step gives the best results for $R = t\text{-}C_4H_9$ (80–90%) and $R = i\text{-}C_3H_7$ (70–80%). $R = C_2H_5$ gave lower yields (ca. 45%), while $R = CH_3$ gave principally lithiation at alkyl carbon.

The reaction of *n*-butyllithium with phenylethers to yield principally ortho-substituted products is well known.[1] The analogous reaction with phenylthioethers **1** has also been investigated[2] on an analytical basis, but the results showed that reaction was slow, incomplete, gave a mixture of isomers and was clearly unsuitable for preparative purposes.

The presence of a thioether function *ortho* to other functional groups is necessary for the synthesis of a number of important classes of compounds, such as benzisothiazoles,[3,4] thiocoumarins and benzothiophenes,[4] cyclic sulfuranes,[5] and to accelerate the rate of homolysis[6] of the corresponding perbenzoates by a factor greater than 10^4.

A simple procedure for ortho-functionalization of the easily-obtained[7] phenylthioethers was therefore considered to be attractive and useful, and warranted a reinvestigation. The present paper describes our initial results, which show that the use of the co-reagent *N,N,N′,N′*-tetramethylethylenediamine, (TMEDA) is decisive and opens up the way for a versatile synthetic procedure which is by no means exhausted with the typical examples shown in the scheme.

EXPERIMENTAL:

1. 2-Alkyl(Aryl)thiophenyllithium

General procedure: Freshly distilled *N,N,N′,N′*-tetramethylethylenediamine (TMEDA), (55 ml, 364 mmol) was added dropwise over 1 hour to a stirred, cooled (10°C) solution of alkyl(aryl)thiobenzene[7] (320 mmol) and *n*-butyllithium **2** (300 mmol) in hexane (400 ml) under a nitrogen atmosphere. The resultant solution was stirred at 25°C for 2–3 hours. In the case of **1a** a white precipitate results and the further reactions were carried out on this suspension. In the remaining cases cloudy light-yellow solutions were obtained; in all cases the reaction mixtures were used without further delay.

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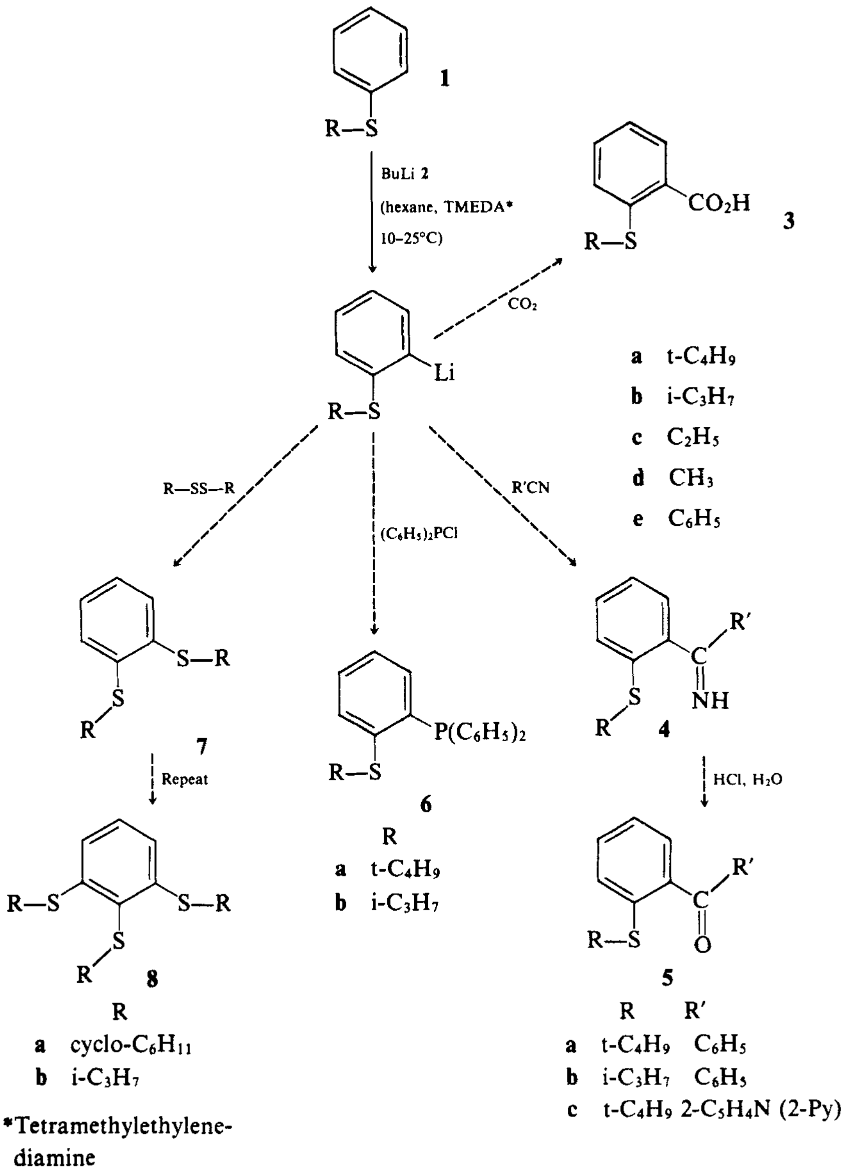

SCHEME

2. *2-(alkyl(aryl)thio)benzoic acids* 3

The hexane solution (suspension) obtained in 1. was added dropwise with shaking to finely divided dry CO_2 (100 g) at −180°C under N_2. The resulting mixture was left overnight, acidified with 2N HCl and the precipitate filtered off. Recrystallization was from hexane. Yields and data in Table I.

3. *2-(alkylthio)phenyl imines* 4

The hexane solution (suspension) obtained in 1. was stirred under N_2 at 0°C and the corresponding aromatic nitrile (330 mmol) added dropwise over 1 hour. The resulting brick-red suspension was stirred for

TABLE I

Yields, melting points and literature melting points for 2-(alkyl(aryl)thio)benzoic acids **3a**–**3e**

	R	yields %	m.p. (°C)	Lit.m.p. (°C)
a	t-C_4H_9	71–73	80	77–79[8]
b	i-C_3H_7	63–71	117	116–117[9]
c	C_2H_5	38–43	133–134	134[10]
d	CH_3	0[a]	—	—
e	C_6H_5	64	167–169	162–164[6]

[a] A 40% yield of (phenylthio)acetic acid (m.p. 62°C) was obtained as sole isolated product.

a further 12 hours at room temperature and then neutralized with dilute HCl. For **4** (a,b) the organic phase was separated, the aqueous layer extracted with ether (1 × 200 ml), the organic fractions combined, dried and fractionally distilled. For **4c**, the yellow-brown precipitated imine was filtered off, washed with water, dried and recrystallized from hexane or ethanol to give yellow crystals. Yields and data in Table II.

4. *2-(Alkylthio) phenyl ketones* 5

Concentrated HCl (10 g) was added carefully to a suspension of the corresponding imine **4** (62 mmol) in 60 ml 60% methanol (w.w.). The resultant reddish solution was heated vigorously under reflux for 3 h, cooled, added to 100 ml water and extracted with ether (4 × 100 ml). The ether extracts were combined, dried and the solvent removed. **5a** and **5c** were recrystallized (hexane); **5b** was fractionally distilled as a light yellow oil. Yields and data in Table II.

5. *2-(Alkylthio)phenyl diphenyl phosphines* 6

Chlorodiphenylphosphine (14 ml, 78 mmol) was added dropwise to the stirred hexane solution (suspension) obtained in 1. The mixture was stirred for a further 30 min and hydrolyzed with 300 ml 2% NaOH. The organic phase was taken up in ether, dried and fractionally distilled. Yields and data in Table III.

6. *1,2-Di(alkylthio)benzenes* 7 *and 1,2,3-tri(alkylthio)-benzenes* 8

Di-alkyldisulfide (260 mmol) was added dropwise to the cooled (10°C) stirred hexane solution (385 ml ≈ 220 mmol) obtained in 1. The mixture was stirred for a further 1 h at room temperature, then washed successively with 20% NaOH (2 × 200 ml) and water (1 × 100 ml). The organic phase was dried and fractionally distilled to give **7a** (Table III). The product **7**, subjected to the procedure 1. and 6. yielded the trithiopyrogallol derivative **8** (Table III).

TABLE II

Yields, melting points, boiling points and elemental analyses for 2-(alkylthio)phenyl imines **4** and -ketones **5**

			yield	m.p.	b.p.	Required			Found		
4	R	R′	%	(°C)	(°C/mm)	C	H	N	C	H	N
a	t-C_4H_9	C_6H_5	86	52–53	145/0.05	75.81	7.11	5.20	75.97	7.03	5.64
b	i-C_3H_7	C_6H_5	81	—	132/0.05	75.27	6.71	5.49	74.98	6.51	5.54
c	t-C_4H_9	2-C_5H_4N	53	104–105	—	71.09	6.71	10.36	71.16	6.78	10.37
5											
a	t-C_4H_9	C_6H_5	85	79–80	—	75.53	6.71	—	75.61	6.64	—
b	i-C_3H_7	C_6H_5	75	—	112–114/0.7	74.98	6.29	—	75.06	6.11	—
c	t-C_4H_9	2-C_5H_4N	68	95–96	—	70.83	6.32	5.16	70.67	6.24	5.28

TABLE III

Yields, melting points, boiling points and elemental analyses for the phosphines **6** and the phenylthioethers **7**, **8**

		yield	m.p.	b.p.	Required		Found	
6	R	%	(°C)	(°C/mm)	C	H	C	H
a	t-C_4H_9	61	97	192/0.04	75.39	6.61	75.79	6.72
b	i-C_3H_7	66	79	158/0.05	74.99	6.29	75.05	6.30
7								
a	cyclo-C_6H_{11}	64	—	174/0.1	70.55	8.55	70.22	8.34
b	i-C_3H_7	68	—	110/0.1	63.66	8.01	63.75	8.18
8								
a	cyclo-C_6H_{11}	37	95	—	68.51	8.62	68.26	8.50
b	i-C_3H_7	43	—	152/0.1	59.95	8.05	60.14	8.17

REFERENCES

1. G. Wittig, U. Pockels and H. Dröge, *Ber. Dtsch. Chem. Ges.*, **71**, 1903 (1938).
2. D. A. Shirley and B. J. Reeves, *J. Organometallic Chem.*, **1969**, 1. See also reference 9.
3. See A. J. Lawson, ***Phosphorus and Sulfur***, **12**, 357 (1982) and references therein, (following paper).
4. O. Meth-Cohn and B. Tarnowski, *Synthesis*, **1978**, 56, 58.
5. See J. C. Martin and T. M. Balthazor, *J. Amer. Chem. Soc.*, **99**, 152 (1977).
6. W. G. Bentrude and J. C. Martin, *J. Amer. Chem. Soc.*, **84**, 1561 (1962); D. L. Tuleen, W. G. Bentrude and J. C. Martin, *J. Amer. Chem. Soc.*, **85**, 1938 (1963).
7. V. N. Ipatieff, H. Pines and B. S. Friedman, *J. Amer. Chem. Soc.*, **60**, 2731 (1938).
8. F. M. Stojanovitch, R. G. Karmenko and J. L. Goldfarb, *Zh. Org. Khim.*, **1969**, 2005.
9. H. Gilman and F. J. Webb, *J. Amer. Chem. Soc.*, **71**, 4062 (1949).
10. J. J. Donleavy and J. English, *J. Amer. Chem. Soc.*, **62**, 220 (1940).