Selective *ortho*-Methylthiomethylation of Phenols with Dimethyl Sulphoxide and Thionyl Chloride

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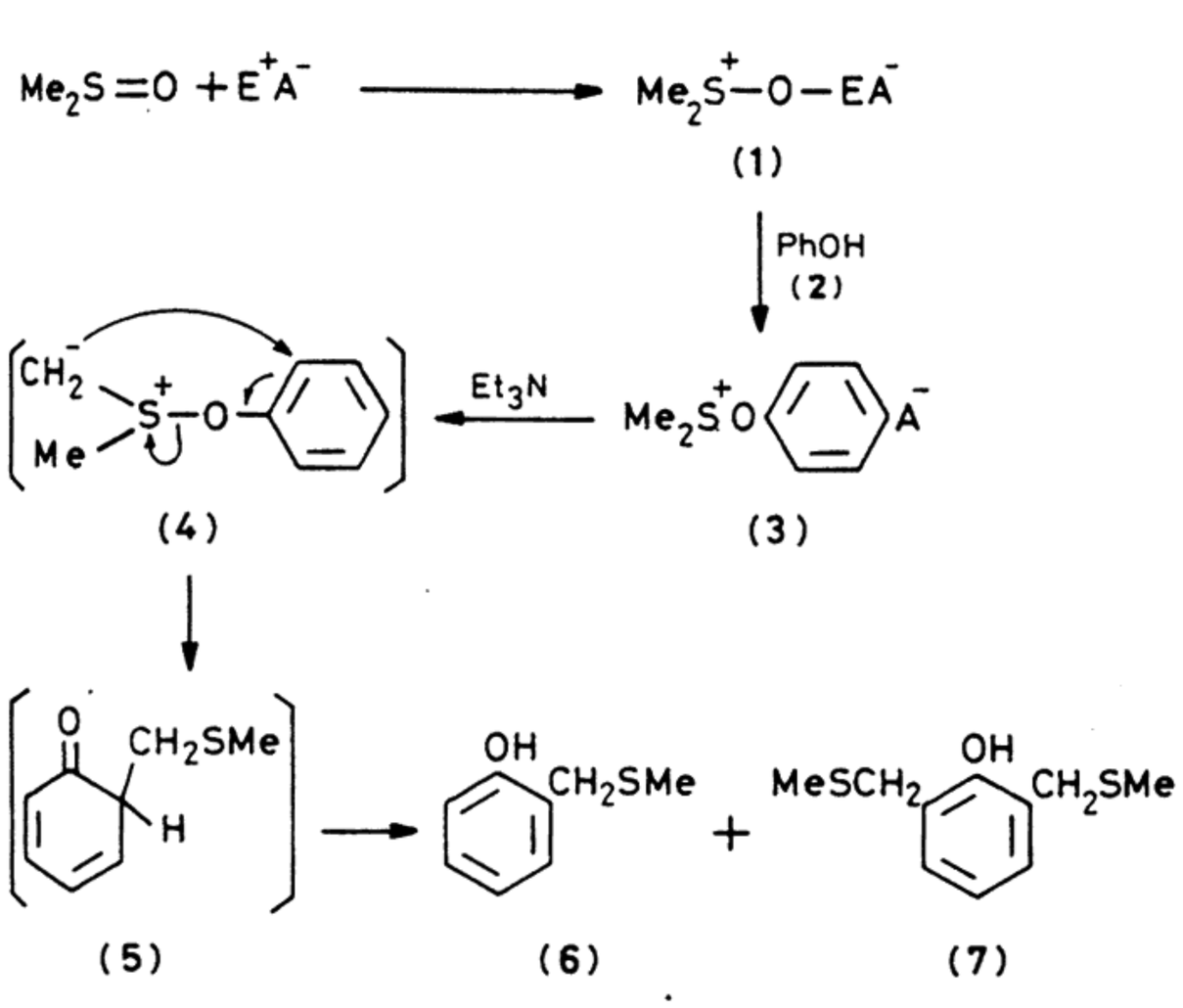
Thionyl chloride and phenyl chlorosulphinate have been shown to be useful activators for dimethyl sulphoxide in the selective preparation of *ortho*-methylthiomethylphenol *via* a [2,3]sigmatropic rearrangement. By this process, *ortho*-methylthiomethylated phenols having a variety of 2- or 4-substituents (Me, Cl, OMe, NO_2, and CO_2Me) have been prepared in good yields. In contrast, similar reactions of 3-substituted phenols were affected by the electronic characters of the substituents. With more electron-donating groups such as OH and OMe in the 3-position, none of the expected products were obtained, but in the case of other 3-substituted phenols, two possible rearrangement products were obtained in moderate yields.

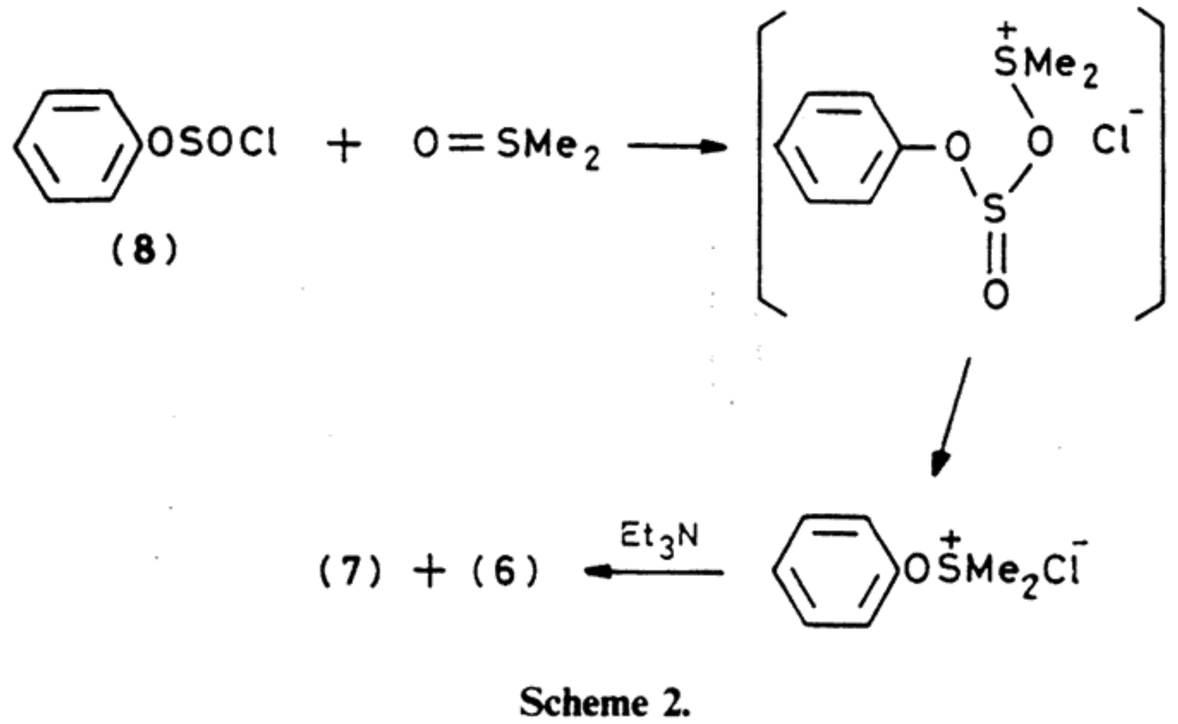
o-Alkylphenols are useful intermediates in organic syntheses and there are many methods [1] for the alkylation of phenol nuclei. In most cases, however, the products are mixtures of *o*- and *p*-substituted and polysubstituted phenols. The most effective procedure for selective *ortho*-alkylation of phenols seems to be that which involves a [2,3]sigmatropic rearrangement of a sulphonium ylide (**4**), the latter being generated *via* abstraction of a proton from a sulphonium salt (**3**).



Scheme 1.

Burden *et al.*[2] and Pfitzner *et al.*[3] reported *o*-methylthiomethylation of phenols using dimethyl sulphoxide (DMSO) in the presence of dicyclohexylcarbodi-imide (DCC) and a proton source. In other reports acetic anhydride,[4] trifluoroacetic anhydride,[5] and pyridine–sulphur trioxide[6] were used instead of DCC. *S,S*-Dimethylsulphilimines[7] and a combination of dimethyl sulphide and *N*-chlorosuccinimide[8] were also used for conversion of phenols into (**3**). Not only did the last-mentioned methods generally give unsatisfactory yields but, moreover, the alkylation of variously substituted phenols have not been studied systematically. Here, we report the selective *ortho*-substitution of phenols using sulphoxides activated by easily available electrophiles and the unexpected substituent effects of phenols in [2,3]sigmatropic rearrangements.

The most important feature of this route is the effective generation of the unstable sulphonium salt (**3**). Although the latter has been made by the reaction of phenol either with an activated sulphoxide (**1**), or an aza- or halogeno-sulphonium salt,[8,9] these reactions are reversible and hence tend not to go to completion. We thought that these drawbacks could be overcome by the use of appropriate electrophiles, derivable from phenol, as an activator of DMSO. We have, therefore, studied the reaction of phenyl chlorocarbonate[10] and phenyl chlorosulphinate[11] (**8**) with DMSO. The chlorosulphinate (**8**) was found to be a useful activator for the sulphoxide (Scheme 2).



Scheme 2.

DMSO was added to (**8**) in dichloromethane at −50 °C and then triethylamine was added at −40 °C; the mixture was then allowed to warm to room temperature to give 2-methylthiomethylphenol[2,3,5,6,8] (**6**) and 2,6-bis(methylthiomethyl)-phenol[2,3] (**7**) in 39 and 17% yields, respectively. The disubstituted product (**7**) seemed to arise from an exchange reaction between (**6**) and (**3**), followed by a second [2,3]sigmatropic rearrangement. The addition of phenol to the reaction mixture just before the addition of triethylamine was effective in suppressing the formation of (**7**) (see Table 1).

The sulphonium salt (**3**) is so unstable that it decomposes to phenol and chloromethyl methyl sulphide along with a small amount of (**6**) at higher temperature. Thus, a further key feature is the temperature at which the salt (**3**) is sufficiently stable and

Table 1. Effects of added phenol in the methylthiomethylation of phenol using (**8**) or (**9**)

Amounts of phenol added (equiv.)		Yields[a] of products (%)	
(**8**)	(**9**)	(**6**)	(**7**)
0		39	17
1		56	12
2		57	6
3		57	2
	1	32	32
	2	56	16
	3	55	10
	4	78[b]	5

[a] Based on (**8**) or (**9**). When (**8**) was used, the yields were determined by g.l.c.; in the case of (**9**), the yields were determined by isolated products. [b] Yield based on unrecovered phenol was 78%, too.

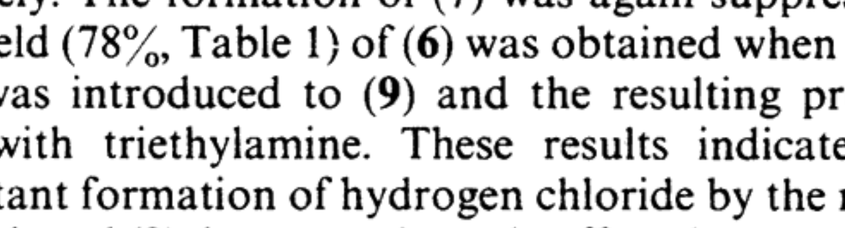
the rearrangement occurs at a reasonable rate. A high yield (57%, Table 1) of the product (**6**) was attained when triethylamine was introduced at a temperature below −40 °C.

Swern[12] reported that thionyl chloride and some other acid chlorides or anhydrides reacted easily with DMSO at a low temperature (−60 °C) to give activated DMSO (**1**). We now attempted the use of the salt (**9**), derivable from thionyl chloride, as the key material for the production of (**3**) in our reaction.

$$Me_2S{=}O + SOCl_2 \longrightarrow Me_2\overset{+}{S}{-}O\underset{\underset{O}{\|}}{S}Cl\ Cl^- \quad \text{or } Me_2\overset{+}{S}Cl\ Cl\underset{\underset{O}{\|}}{S}O^- \qquad (9)$$

Dimethyl sulphoxide (1.4 equiv.) was added to thionyl chloride (1 equiv.) in dichloromethane at —60 °C to generate (**9**); the phenol (**2**) (1 equiv.) was then allowed to react with (**9**) at −50 °C. Excess of triethylamine was added at −40 °C and the reaction mixture allowed gradually to warm to room temperature to give (**6**) and (**7**) in 32 and 32% yields, respectively. The formation of (**7**) was again suppressed and a higher yield (78%, Table 1) of (**6**) was obtained when 4 equiv. of phenol was introduced to (**9**) and the resulting product was treated with triethylamine. These results indicate that the concomitant formation of hydrogen chloride by the reaction of (**9**) with phenol (**2**) does not adversely affect the unstable salt (**3**) nor suppress the subsequent formation of the ylide (**4**), provided an excess of triethylamine is introduced to the reaction mixture.

Next, this procedure was applied to phenols having a variety of substituents in order to study substituent effects on the nucleophilic substitution reaction. When *ortho*-substituted phenols (**10a—e**) were used, exclusive formation of the corresponding 2-substituted 6-methylthiomethylphenols (**11a—e**) occurred, except in the case of *o*-nitrophenol (**10c**) where a small amount (11%) of *O*-methylthiomethyl ether was produced as a by-product (Scheme 3, Table 2). The reaction between *p*-substituted phenols (**12a—e**) and (**9**) gave the expected



(**10**) (**11**)

a; R = Me d; R = NO_2
b; R = Cl e; R = CO_2Me
c; R = OMe

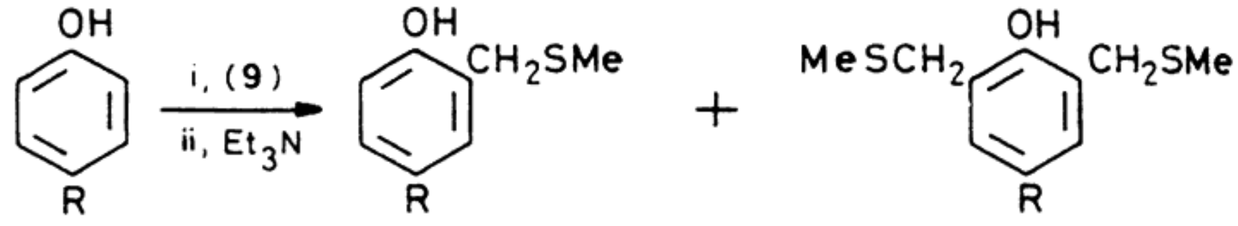
Scheme 3.

Table 2. *ortho*-Methylthiomethylation of *o*- and *p*-substituted phenols using (**9**)

			Products		
Phenols	Substituents R	Mono-sub'd.	Yield (%)[a]	Disub'd.	Yield (%)[a]
(**10a**)	Me	(**11a**)	78 (72)		
(**10b**)	Cl	(**11b**)	75 (63)		
(**10c**)	OMe	(**11c**)	74 (62)		
(**10d**)	NO_2[b]	(**11d**)	80 (82)		
(**10e**)	CO_2Me	(**11e**)	80 (48)		
(**12a**)	Me	(**13a**)	81 (77)	(**14a**)	7 (13)
(**12b**)	Cl	(**13b**)	75 (41)	(**14b**)	3 (3)
(**12c**)	OMe	(**13c**)	60 (55)	(**14c**)	3 (5)
(**12d**)	NO_2	(**13d**)	45 (24)	(**14d**)	5 (5)
(**12e**)	CO_2Me[c]	(**13e**)	62 (27)	(**14e**)	4 (4)

[a] Based on unrecovered phenol. Data in parentheses are based on the alkylating agent. [b] Methylthiomethyl 2-nitrophenyl ether was obtained in 11% yield. [c] Methyl *p*-(methylthiomethoxy)benzoate was obtained in 10% yield.

4-substituted 2-methylthiomethylphenols (**13a—e**) and a small amount of 4-substituted 2,6-bis(methylthiomethyl)phenols (**14a—e**) (Scheme 4). The yields are also summarized in Table 2.



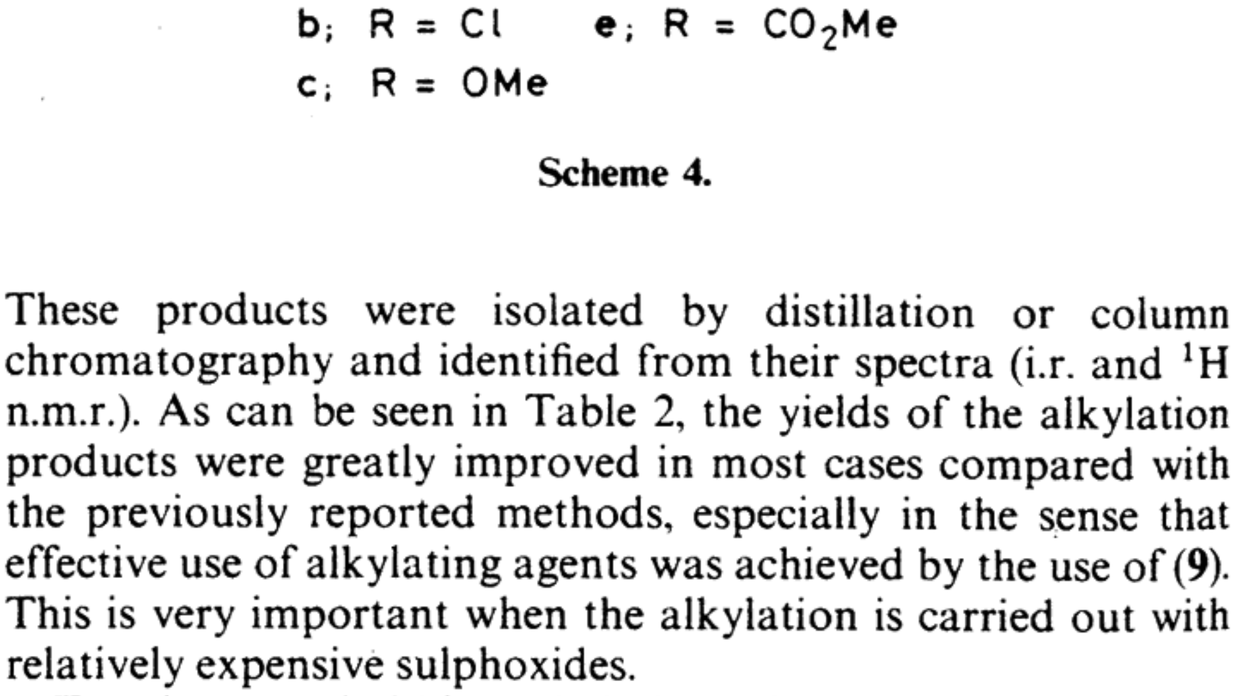
(**12**) (**13**) (**14**)

a; R = Me d; R = NO_2
b; R = Cl e; R = CO_2Me
c; R = OMe

Scheme 4.

These products were isolated by distillation or column chromatography and identified from their spectra (i.r. and ^1H n.m.r.). As can be seen in Table 2, the yields of the alkylation products were greatly improved in most cases compared with the previously reported methods, especially in the sense that effective use of alkylating agents was achieved by the use of (**9**). This is very important when the alkylation is carried out with relatively expensive sulphoxides.

For the *o*-methylthiomethylation of *m*-substituted phenols (**15**), the reaction was affected by the nature of the phenol

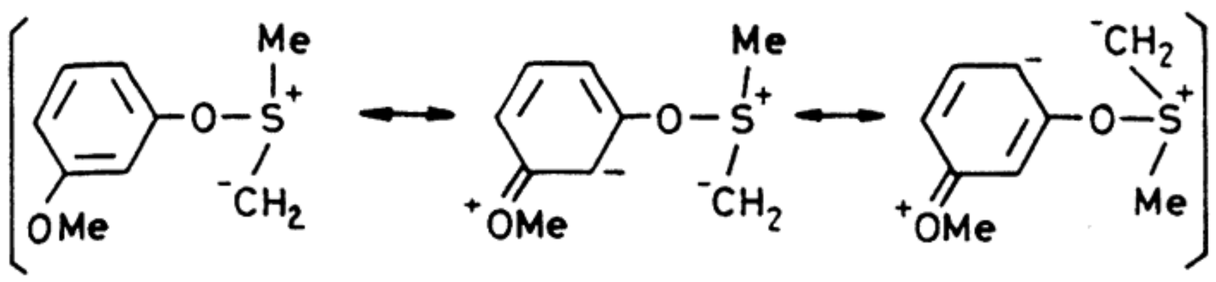


(**15**) (**16c—f**) (**17c—f**) (**18c,d,f**)

a; R = OH
b; R = OMe
c; R = Me
d; R = Cl
e; R = NO_2
f; R = CO_2Me

Scheme 5.

substituents. When the phenols (**15**), except for resorcinol (**15a**) and *m*-methoxyphenol (**15b**), were treated with (**9**) and triethylamine as described before, a mixture of two possible rearrangement products (**16c—f**) and (**17c—f**) were obtained (Scheme 5) accompanied by small amounts of dialkylated phenols (**18**). Since the substituents of (**15a**) and (**15b**) are strongly electron-donating, the carbanion of the phenoxysulphonium ylide could not attack the aromatic ring nucleophilically (Scheme 6). Table 3 summarizes the results



Scheme 6.

Table 3. *ortho*-Methylthiomethylation of *m*-substituted phenols using (**9**)

Phenols	Substituents R	Products (% Yield)[a] (**16**)	(**17**)	(**18**)
(**15a**)	OH			
(**15b**)	OMe			
(**15c**)	Me[b]	39 (37)	39 (37)	1 (3)
(**15d**)	Cl	36 (31)	29 (25)	4 (4)
(**15e**)	NO_2[c]	36 (14)	23 (9)	
(**15f**)	CO_2Me	32 (28)	21 (19)	2 (4)

[a] Based on unrecovered phenol. Data in parentheses are based on the alkylating agent. [b] The yields of the two isomers were determined by the ^1H n.m.r. integration of the mixture. [c] 1-Methylthiomethoxy-2-methylthiomethyl-3-nitrobenzene was obtained in 6% yield.

obtained in these reactions. Structural assignments for compounds (**16**) and (**17**) are based mainly on their ^1H n.m.r. spectra. In the aromatic region, compound (**16**) showed two doublets (4-H and 6-H) and one triplet (5-H), while compound (**17**) showed two doublets (3-H and 4-H) and one singlet (6-H). Further small *m*-splitting of 4-H and 6-H of (**16**) and 4-H and 6-H of (**17**) and *p*-splitting of 3-H and 6-H of (**17**) were also observed (Table 4).

Experimental

B.p.s and m.p.s are uncorrected. I.r. spectra were measured on either a Hitachi 215 or a Hitachi 260-50 spectrometer. ^1H N.m.r. spectra were obtained with a JEOL JNM-C-60M or a JEOL FT-90-Q with tetramethylsilane as an internal standard. Column chromatography was normally effected with Wakogel C-200 (Wako Pure Chemical Industries). Spectral data are summarized in Table 4. When excesses of phenols were used, yields were based on unrecovered phenols unless otherwise mentioned.

o-*Methylthiomethylation of the Phenol* (**2**) *using Phenyl Chlorosulphinate* (**8**).—DMSO (0.44 g, 5.6 mmol) in dichloromethane (5 ml) was added to a solution of (**8**)[13] (0.71 g, 4 mmol) in dichloromethane (20 ml) at −50 °C for 10 min under a dry nitrogen atmosphere. After the mixture had been stirred for 2 h at −50 °C, triethylamine (0.81 g, 8 mmol) was added to it. The solution was allowed to warm to room temperature and the reaction mixture was poured into 1M-hydrochloric acid. The organic layer was separated, and the aqueous solution was extracted with diethyl ether (3 × 30 ml). The combined organic layers were washed with brine (3 × 30 ml), dried ($MgSO_4$), and concentrated, and the residual oil was chromatographed on a column. Elution with ethyl acetate–hexane (3:97) gave 2,6-bis(methylthiomethyl)phenol (**7**) (72 mg, 17%). Further elution gave 2-methylthiomethylphenol (**6**) (0.24 g, 39%). Elution with ethyl acetate–hexane (1:9) gave the phenol (**2**) (0.124 g, 33%).

Table 4. Physical properties of *ortho*-methylthiomethylated phenols

Compds.	M.p. (°C)	I.r. ($\nu_{max.}$/cm^{-1})	SMe	$ArCH_2S$	^1H N.m.r. (δ, *J* in Hz; CCl_4 or $CDCl_3$) Aromatic	OH	Other
(**11e**)	Oil	3 150, 2 950, 2 900, 1 450, 760 (neat)	2.00	3.86	6.76 (1 H, t, *J* 7), 7.50 (1 H, dd, *J* 7 and 2), and 7.70 (1 H, dd, *J* 7 and 2)	7.30	3.96 (3 H, s)
(**14a**)	Oil	3 400, 2 920, 1 430, 780 (neat)	2.00	3.73	6.86 (2 H, s)	6.80	2.23 (3 H, s)
(**13e**)	63—64	3 350, 2 910, 1 440, 840 (KBr)	2.00	3.77	6.83 (1 H, d, *J* 7), 7.73 (1 H, s), and 7.80 (1 H, d, *J* 7)	7.43	3.87 (3 H, s)
(**14e**)	Oil	3 250, 2 950, 2 910, 1 430, 840 (CCl_4)	2.00	3.87	7.80 (2 H, s)	7.57	3.87 (3 H, s)
(**16c**) + (**17c**) (1:1)	Oil	3 400, 2 970 (CCl_4)	1.90, 1.96	3.63, 3.73	6.2—7.2 (4 H, m)[a]		2.23 (1.5 H, s) 2.30 (1.5 H, s)
(**18c**)	Oil	3 300, 2 900, 1 420, 805 (neat)	1.92, 1.99	3.68, 3.75	6.6 (1 H, d, *J* 7) and 6.87 (1 H, d, *J* 7)	6.73	2.33 (3 H, s)
(**16d**)	Oil	3 300, 2 950, 2 910, 1 420, 700 (CCl_4)	2.00	3.96	6.76 (1 H, dd, *J* 8 and 2), 6.92 (1 H, dd, *J* 8 and 2) and 7.08 (1 H, t, *J* 8)	6.53	
(**17d**)	Oil	3 300, 2 950, 2 920, 1 460, 860 (CCl_4)	1.95	3.70	6.78 (1 H, dd, *J* 8 and 2), 6.88 (1 H, d, *J* 2), and 6.96 (1 H, d, *J* 8)	6.65	
(**18d**)	Oil	3 300, 2 970, 2 950, 1 440, 875 (CCl_4)	1.96, 2.03	3.70, 3.96	6.93—7.13 (3 H, m)[a]		
(**16e**)	Oil	3 400, 2 980, 2 900, 1 420, 740 (neat)	2.08	4.03	7.16 (1 H, dd, *J* 8 and 2), 7.30 (1 H, t, *J* 8) and 7.46 (1 H, dd, *J* 8 and 2)	7.04	
(**17e**)	Oil	3 420, 2 980, 2 910, 1 430, 820 (neat)	2.02	3.84	7.28 (1 H, d, *J* 7), 7.73 (1 H, d, *J* 2), and 7.74 (1 H, dd, *J* 7 and 2)	7.04	
(**16f**)	74.5—75.5	3 400, 2 950, 2 900, 1 440, 760 (KBr)	2.00	4.13	6.96 (1 H, dd, *J* 7 and 2), 7.13 (1 H, t, *J* 7), and 7.36 (1 H, dd, *J* 7 and 2)	6.80	3.86 (3 H, s)
(**17f**)	68—69	3 400, 2 950, 2 910, 1 440, 800 (CCl_4)	2.00	3.73	7.13 (1 H, d, *J* 7), (7.50 1 H, d, *J* 7), and 7.57 (1 H, s)	6.83	3.86 (3 H, s)
(**18f**)	Oil	3 300, 2 950, 2 930, 1 440, 700 (CCl_4)	2.00	3.73, 4.16	7.00 (1 H, d, *J* 7) and 7.33 (1 H, d, *J* 7)	7.03	3.86 (3 H, s)

[a] Including OH.

Effects of added Phenol in the Methylthiomethylation of Phenol using (**8**).—DMSO (0.11 g, 1.4 mmol) was added to solution of (**8**) (0.18 g, 1 mmol) in dichloromethane (5 ml) of each of four reaction vessels at −50 °C under a dry nitrogen atmosphere. After each reaction mixture had been stirred for 2 h at −50 °C the following quantities of phenol were added to individual reaction mixtures: 0.09 g (1 mmol); 0.19 g (2 mmol); 0.28 g (3 mmol). Each reaction mixture was treated with triethylamine and allowed to warm to room temperature. The resulting mixtures were analysed by g.l.c. (column packed with silicone DC 200 coated on Chromosorb W) after work-up as described before. The results are shown in Table 1.

o-*Methylthiomethylation of Phenol using* (**9**).—*General procedure*. DMSO (0.44 g, 5.6 mmol) in dry dichloromethane (2 ml) was added dropwise to a solution of thionyl chloride (0.48 g, 4 mmol) in dry dichloromethane (15 ml) maintained at −60 °C under a dry nitrogen atmosphere, and the mixture was stirred for 20 min. To the solution was gradually added phenol (1.51 g, 16 mmol) in dry dichloromethane (5 ml) at −50 °C. The solution was stirred at −50 °C for 40 min. Triethylamine (2.4 g, 23.8 mmol) in dry dichloromethane (5 ml) was then added to the reaction mixture dropwise at −50 to −40 °C. The solution was allowed to warm to room temperature, and it was then poured into 1M-hydrochloric acid. The organic layer was separated and the aqueous solution was extracted with diethyl ether (3 × 40 ml). The combined organic layers were washed with brine (3 × 40 ml), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was column chromatographed as described before to give (**7**) (42 mg, 5%), (**6**) [0.48 g, 78% yield based on (**9**), and 78% yield, too, based on unrecovered phenol], and the recovered phenol (1.135 g). Using this procedure the following were prepared.

o-*Methylthiomethylation of* o-*cresol* (**10a**). After (**10a**) (1.73 g, 16 mmol) had been treated with (**9**) by the general procedure, the crude mixture was chromatographed on a column using ethyl acetate–hexane (5:95) as eluant to give 2-methyl-6-methylthiomethylphenol[2-5,7,8] (**11a**) (0.485 g, 77%) as a clear oil and recovered (**10a**) (1.325 g).

o-*Methylthiomethylation of* o-*chlorophenol* (**10b**). After (**10b**) (2.057 g, 16 mmol) had been treated with (**9**) by the general procedure, the resulting oil was distilled to give (**10b**) (1.625 g) and 2-chloro-6-methylthiomethylphenol[6] (**11b**) (0.476 g, 75%), b.p. 82—83 °C/0.9 mmHg (lit.,[6] 130—140 °C/1.2 mmHg).

o-*Methylthiomethylation of o-methoxyphenol* (**10c**). After (**10c**) (1.986 g, 16 mmol) had been treated with (**9**) by the general procedure, the resulting oil was distilled to give (**10c**) (1.571 g) and 2-methoxy-6-methylthiomethylphenol (**11c**) (0.475 g, 74%), b.p. 112—113 °C/0.9 mmHg (lit.,[6] 92—93 °C/3 × 10^{-2} mmHg).

o-*Methylthiomethylation of* o-*nitrophenol* (**10d**). After (**10d**) (2.225 g, 16 mmol) had been treated with (**9**) by the general procedure, the resulting mixture was chromatographed on a column using isopropyl ether–hexane (5:95) as eluant. The first fraction was methylthiomethyl 2-nitrophenyl ether[2] (11 mg). The second fraction was (**10d**) (1.656 g). The third fraction was 2-methylthiomethyl-6-nitrophenol (**11d**) (0.653 g, 80%),[2,8] m.p. 77—78 °C (lit.,[8] 77—78 °C).

o-*Methylthiomethylation of methyl* o-*hydroxybenzoate* (**10e**). After (**10e**) (2.434 g, 16 mmol) had been treated with (**9**) by the general procedure, the resulting mixture was chromatographed on a column using benzene–hexane (2:8). The first fraction was the ester (**10e**) (2.07 g). The second fraction was *methyl 2-hydroxy-3-methylthiomethylbenzoate* (**11e**) (0.407 g, 80%) (Found: C, 56.2; H, 5.7. $C_{10}H_{12}O_3S$ requires C, 56.58; H, 5.70%).

o-*Methylthiomethylation of* p-*crèsol* (**12a**). After (**12a**) (1.73 g, 16 mmol) had been treated with (**9**) by the general procedure, the resulting oil was chromatographed on a column using ethyl acetate–hexane (5:95) as eluant to afford 4-methyl-2,6-bis(methylthiomethyl)phenol (**14a**) (60 mg, 7%),[14] 4-methyl-2-methylthiomethylphenol[5,8,14] (**13a**) (0.518 g, 81%), and (**12a**) (1.32 g).

o-*Methylthiomethylation of* p-*chlorophenol* (**12b**). After (**12b**) (2.057 g, 16 mmol) had been treated with (**9**) by the general procedure, the resulting mixture was chromatographed on a column using benzene as eluant to give 4-chloro-2,6-bis(methylthiomethyl)phenol[6] (**14b**) (15 mg, 3%), m.p. 41—42 °C (lit.,[6] 41—43 °C). The second fraction was 4-chloro-2-methylthiomethylphenol[5,6,8] (**13b**) (0.31 g, 75%), m.p. 63—65 °C (lit.,[6] 63—65 °C). The third fraction was (**12b**) (1.774 g).

o-*Methylthiomethylation of* p-*methoxyphenol* (**12c**). After (**12c**) (1.986 g, 16 mmol) had been treated with (**9**) by the general procedure, the resulting mixture was chromatographed on a column using benzene as eluant to give 4-methoxy-2,6-bis(methylthiomethyl)phenol[6] (**14c**) (24 mg, 5%). Elution with ethyl acetate–benzene (2:98) gave 4-methoxy-2-methylthiomethylphenol[5,6,8] (**13c**) (0.405 g, 60%) and (**12c**) (1.527 g).

o-*Methylthiomethylation of* p-*nitrophenol* (**12d**). According to the general procedure. (**12d**) (1.606 g, 11.5 mmol) in dichloromethane (50 ml) was used. After work-up, the crude mixture was chromatographed on a column using dichloromethane as eluant. The first fraction was 2,6-bis(methylthiomethyl)-4-nitrophenol[2] (**14d**) (19 mg, 5%), m.p. 76—77 °C (lit.,[2] 76.5—77.5 °C). The second fraction was 2-methylthiomethyl-4-nitrophenol[2] (**13d**) (0.133 g, 45%), m.p. 125—126 °C (lit.,[2] 127.5—128.5 °C). The third fraction contained unchanged (**12d**) (1.40 g). Further elution with dichloromethane gave unidentified materials (80 mg).

Methylthiomethylation of methyl p-*hydroxybenzoate* (**12e**). According to the general procedure. (**12e**) (2.434 g, 16 mmol) in dichloromethane (50 ml) was used. After work-up, the resulting mixture was chromatographed on a column using dichloromethane–hexane (1:1). The first fraction contained *methyl* p-*methylthiomethoxybenzoate* (54 mg) as an oil; $\nu_{max.}$ 2 750 and 2 910 cm^{-1}; $\delta(CCl_4)$ 2.23 (3 H, s), 3.86 (3 H, s), 5.13 (2 H, s), 6.90 (2 H, d, *J* 7 Hz), and 7.90 (2 H, d, *J* 7 Hz). The second fraction contained *methyl 4-hydroxy-3,5-bis(methylthiomethyl)-benzoate* (**14e**) (21 mg, 4%) (Found: C, 53.1; H, 5.8. $C_{12}H_{16}O_3S_2$ requires C, 52.92; H, 5.92%). The third fraction contained *methyl 4-hydroxy-3-methylthiomethylbenzoate* (**13e**) (0.229 g, 62%) (Found: C, 56.4; H, 5.8. $C_{10}H_{12}O_3S$ requires C, 56.58; H, 5.70%). The fourth fraction contained unchanged (**12e**) (2.169 g).

o-*Methylthiomethylation of* m-*cresol* (**15c**). After (**15c**) (1.73 g, 16 mmol) had been treated with (**9**) by the general procedure, the crude mixture was chromatographed on a column using ethyl acetate–hexane (3:97) as eluant to afford 3-*methyl*-2,6-*bis(methylthiomethyl)phenol* (**18c**) (35 mg, 4%). Elution with ethyl acetate–hexane (6:94) gave an inseparable mixture (0.504 g, 78%) (*ca.* 1:1 by ^1H n.m.r. integration) of 3-methyl-2-methylthiomethylphenol (**16c**) and 5-methyl-2-methylthiomethylphenol (**17c**). Further elution afforded (**15c**) (1.32 g).

o-*Methylthiomethylation of* m-*chlorophenol* (**15d**). After (**15d**) (2.057 g, 16 mmol) had been treated with (**9**) by the general procedure, the resulting mixture was chromatographed on a column using benzene–hexane (1:1) as eluant. The first fraction was 3-*chloro*-2,6-*bis(methylthiomethyl)phenol* (**18d**) (35 mg, 4%) (Found: C, 48.5; H, 4.9. $C_{10}H_{13}ClOS_2$ requires C, 48.28; H, 5.26%). The second fraction was 5-*chloro*-2-*methylthiomethylphenol* (**17d**) (0.189 g, 29%) (Found: C, 50.8; H, 4.8. C_8H_9ClOS requires C, 50.92; H, 4.81%). The third fraction was 3-*chloro*-2-*methylthiomethylphenol* (**16d**) (0.234 g, 36%) (Found: C, 51.0; H, 5.0. C_8H_9ClOS requires C, 50.92; H, 4.81%). The fourth fraction was (**15d**) (1.614 g).

o-*Methylthiomethylation of* m-*nitrophenol* (**15e**). According to the general procedure. (**15e**) (2.226 g, 16 mmol) was used. After work-up, the resulting mixture was chromatographed on

a column using hexane–dichloromethane (1:5). The first fraction contained 1-*methylthiomethoxy*-2-*methylthiomethyl*-3-*nitrobenzene* (30 mg) as an oil; $\nu_{max.}$ 2 920 and 2 850 cm^{-1}; $\delta(CDCl_3)$ 2.13 (3 H, s), 2.16 (3 H, s), 3.57 (2 H, s), 5.29 (2 H, s), and 6.97—7.28 (3 H, m). The second fraction was 2-*methylthiomethyl*-3-*nitrophenol* (**16e**) (0.111 g, 36%) (Found: C, 48.2; H, 4.7. $C_8H_9NO_3S$ requires C, 48.23; H, 4.55%). The third fraction contained 2-*methylthiomethyl*-5-*nitrophenol* (**17e**) (72 mg, 23%) (Found: C, 48.3; H, 4.6. $C_8H_9NO_3S$ requires C, 48.23; H, 4.55%). The fourth fraction was unchanged (**15e**) (2.01 g).

o-*Methylthiomethylation of methyl* p-*hydroxybenzoate* (**15f**). After (**15f**) (2.434 g, 16 mmol) had been treated with (**9**) by the general procedure, the resulting mixture was chromatographed on a column using dichloromethane as eluant. The first fraction contained *methyl* 3-*hydroxy*-2,4-*bis*(*methylthiomethyl*)*benzoate* (**18f**) (19 mg, 2%) (Found: C, 53.0; H, 5.9. $C_{12}H_{16}O_3S_2$ requires C, 52.92; H, 5.92%). The second fraction contained *methyl* 3-*hydroxy*-2-*methylthiomethylbenzoate* (**16f**) (0.238 g, 32%) (Found: C, 56.2; H, 5.6. $C_{10}H_{12}O_3S$ requires C, 56.58; H, 5.70%). The third fraction contained *methyl* 3-*hydroxy*-4-*methylthiomethylbenzoate* (**17f**) (0.161 g, 21%) (Found: C, 56.3; H, 5.7. $C_{10}H_{12}O_3S$ requires C, 56.58; H, 5.70%). The fourth fraction contained unchanged ester (**15f**) (1.813 g).

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