Reaction of Dimethyl Sulfoxide–Trifluoroacetic Anhydride with Anilines, Phenols, and Thiophenols

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The reaction of dimethyl sulfoxide–trifluoroacetic anhydride complex with anilines, phenols, and thiophenols was studied, and the following results were obtained. (1) The yields of a methylthiomethylated product were improved with anilines. The reaction proceeded without significant amount of tar, the unreacted anilines being easily recovered. (2) Selective *ortho*-methylthiomethylation took place with phenols in good yields at lower temperature, *para*-methylthiomethylation occurring at higher temperature. (3) Methylthiomethylation took place with thiophenols on a sulfur atom of thiophenol at room temperature in a simple process.

Sulfides and sulfoxides are activated with electrophiles to produce the reactive sulfonium salts. These electrophiles include dicyclohexylcarbodiimide+acid,[1] acetic anhydride,[2] acetyl chloride,[3] phosphorus pentoxide, polyphosphoric acid,[4] sulfur trioxide–pyridine,[5] diphenylketene–*p*-tolylimine+acid,[6] *etc.*

By employing sulfides activated with chlorine or *N*-chlorosuccinimide, Corey and Kim[7] carried out the mild oxidation of aliphatic alcohols to ketones. Gassman and co-workers[8–10] described *ortho*-methylthiomethylation of anilines by using *N*-chloroanilines and dialkyl sulfide. However, *N*-chloroanilines with electron-donating groups are unstable and easily oxidized to tar. Thus the reaction does not proceed without disturbance even though the improved dimethyl sulfide–chlorine method[11] is employed. Similar difficulties arise with the *ortho*-methylthiomethylation of phenols.

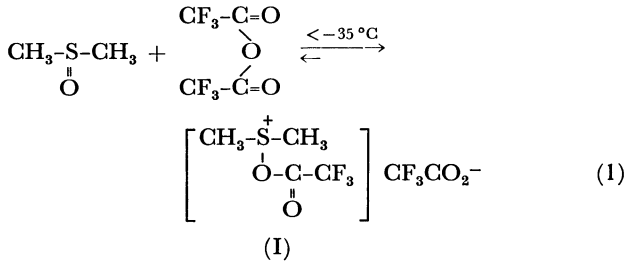
As for the reaction of activated sulfoxides, Claus and coworkers[12,13] reported that dimethyl sulfoxide and phosphorus pentoxide complex reacted with anilines to produce *N*-arylsulfimides. The dimethyl sulfoxide–phosphorus pentoxide system presented difficulties in purification of the product during the course of work-up. Swern and co-workers[14] also succeeded in preparing sulfimides by employing dimethyl sulfoxide–trifluoroacetic anhydride. Burdon and Moffatt[15,16] reported acid-catalyzed *ortho*-methylthiomethylation of phenols with dimethyl sulfoxide, dicyclohexylcarbodiimide, and anhydrous orthophosphoric acid. The yields were moderate, 1,3-benzoxathian and phenyldicyclohexyl urea being produced as by-products.

Dimethyl sulfoxide–trifluoroacetic anhydride system is expected to overcome these difficulties and improve the yields in alkylation of the anilines and the phenols owing to a good leaving group, *i.e.* trifluoroacetate.

No report has been found concerning the reaction of thiophenol with the activated sulfoxide and sulfide, except for the formation of diphenyl disulfide with dimethyl sulfide and dicyclohexylcarbodiimide.[15] The dimethyl sulfoxide–trifluoroacetic anhydride complex reacted with a variety of the substituted thiophenols to give methylthiomethyl phenyl sulfide in good yields.

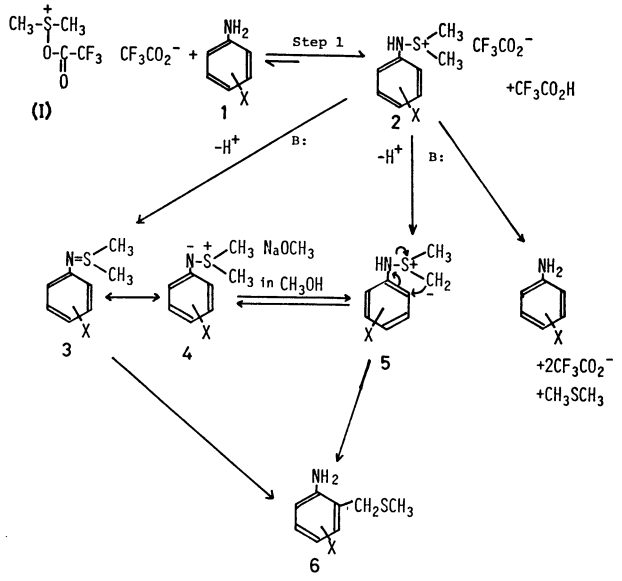
Results and Discussion

Trifluoroacetic anhydride (TFAA) reacts with dimethyl sulfoxide (DMSO) readily to afford the complex I at low temperature as formulated in Eq. 1. In methylene chloride as solvent, it appears as a white precipitate (see Experimental). Trifluoroacetoxyl group on the sulfur atom facilitates the substitution of sulfur atom being attacked by nucleophiles.



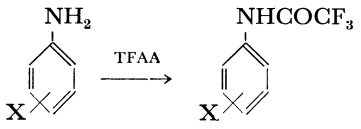
(I) (1)

ortho-*Methylthiomethylation of Aniline.* In general, the 'activated DMSO' reacts with a variety of anilines to afford azasulfonium compounds (**2**) followed by conversion into ylids (**5**) on treatment with base.[10] The ylid rearranges smoothly at lower temperature to the desired *o*-substituted aniline *via* Sommelet-Hauser type rearrangement as shown in Scheme 1. Alternatively, it may also be possible that the treatment of base leads to the abstraction of hydrogen on N atom of compound **2** to afford sulfimide (**3**), which rearranges to the corresponding product (**6**) in base. On the other hand, compound **2** is anticipated to decompose back to the starting aniline (**1**). If this process



Scheme 1.

is involved, a complete conversion can not be considered to be attained.



(2)

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Substituted anilines (X=NO_2, CN, CO_2CH_3, Cl, CH_3, OCH_3) were alkylated on the *ortho* position with 1.2 equivalent of the complex I. In each case, the reaction proceeded without significant amount of tar, the unreacted aniline being easily recovered as shown in Table 1.

TABLE 1. *ortho*-METHYLTHIOMETHYLATION OF *para*-SUBSTITUTED ANILINES

Compd	X	Yield (%)[a]		Recovered anilines (%)
		6	**7**	
1a	NO_2	55	5	40
1b	CN	52	2	46
1c	CO_2CH_3	49	—	33
1d	Cl	67	9	11
1e	H	54	1	45
1f	CH_3	45	16	33
1g	OCH_3	27	7	66

a) Isolated yield based on the starting anilines.

In the case of anilines substituted by the strong electron-withdrawing group (*i.e.* *p*-nitroaniline), sulfimide **3** is preferred to the ylid form, since the hydrogen of the amino group is prone to be abstrated rather than the methyl hydrogen, and required to be refluxed with triethylamine in dry toluene to cause *o*-alkylation. On the other hand, it is enough to keep the reaction mixture below room temperature in the case of the rearrangement of azasulfonium compounds derived from anilines substituted by electron-donating group (*i.e.* *p*-toluidine and *p*-anisidine).

Sodium methoxide in absolute methanol was employed in each rearrangement of the azasulfonium compounds. *N*-Trifluoroacetylation took place instead of the desired rearrangement, when the compound derived from *p*-anisidine was treated with triethylamine. Potassium *t*-butoxide in THF was examined in a similar procedure to give *N*-trifluoroacetylation product, but the yield of *o*-alkylation decreased to a few %. Methanol is presumed to facilitate the protonation and counter anion exchang[12] from **3** to **5** through structure **4**, and **5** rearranges spontaneously even at low temperature below −50 °C.

In step 1, trifluoroacetic acid is generated, and is thought to protonate the aniline, while the protonated aniline is considered not to attack complex I. Attempts were made to remove the acid generated. In the presence of one equivalent of 2,6-lutidine, *p*-chloroaniline was reacted with the complex followed by the usual procedure. GLC analysis shows the formation of *o*-substitution product (20%) and acylation product (27%), and recovery of unreacted aniline (30%), indicating that 2,6-lutidine was not effective. In the same manner, *p*-toluidine was reacted in the presence of potassium carbonate. GLC analysis suggests that acylation predominated. Two equivalent of *p*-chloroaniline to the complex I afforded *o*-substituted product in 45% yield, attempts being unsuccessful.

Trifluoroacetylation took place as the sole side reaction (Eq. 2). However, it was possible to depress it with a choice of solvent system. Trifluoroacetylation is more unfavorable than the alkylation of aniline in a less polar solvent, though the process of alkylation is complicated. Less polar solvent (toluene) was preferred to methylene chloride in the reaction of *p*-anisidine which has higher basicity; Methylene chloride–acetonitrile (1/1=v/v) solvent was preferred in the reaction of *p*-chloroaniline which is less basic (Table 2).

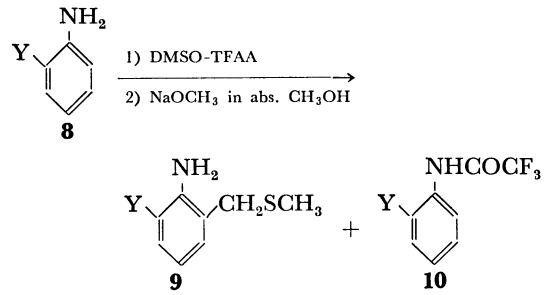
o-Monosubstituted anilines were also alkylated on the *ortho* position in a similar manner. Table 3 gives the yields of *o*-alkylation of the *o*-monosubstituted anilines. Methylene chloride–acetonitrile (1/1=v/v) was used as the solvent, toluene being used in the case of *o*-anisidine. *o*-Anisidine was alkylated in 52% yield in toluene as compared with 24% in methylene chloride.

TABLE 2.

Compd	X	Solvent	Yield(%)[a] of **6**	**7**/(Recovered aniline+**7**) ×100
1d	Cl	CH_2Cl_2	21	24
		CH_2Cl_2-CH_3CN[b]	67	25
		CH_3CN	40	29
1f	CH_3	CH_2Cl_2	39	15
		CH_2Cl_2-CH_3CN[b]	45	33
		CH_3CN	14	37
1g	OCH_3	Toluene	27	10
		CH_2Cl_2	23	9
		CH_2Cl_2-CH_3CN[b]	23	24

a) Isolated yield based on the starting anilines.
b) 1/1=v/v.

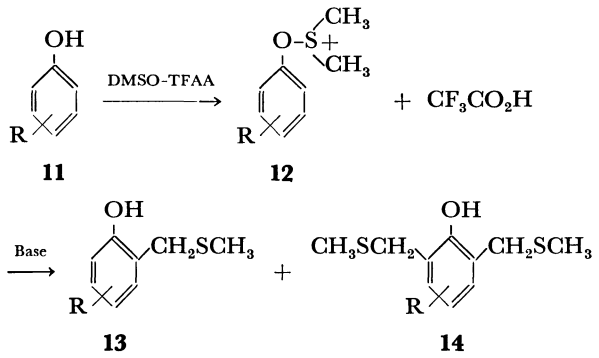
TABLE 3. *ortho*-METHYLTHIOMETHYLATION OF *ortho*-SUBSTITUTED ANILINES



Compd	Y	Yield (%)[a]		Recovered anilines (%)
		9	**10**	
8a	NO_2	41	8	40
8b	Cl	71	19	trace
8c	CH_3	48	15	25
8d	OCH_3	52	11	37

a) Isolated yield based on the starting anilines.

Methylthiomethylation of the Phenols. To a solution of the DMSO–TFAA complex formed below −60 °C was added the substituted phenol **11** to produce oxysulfonium compound **12**, followed by conversion into *ortho*-alkylated phenols **13** and **14** through the ylid intermediate on treatment with base. Scheme 2 shows the reaction path.



Scheme 2.

Various substituted phenols were alkylated as shown in Table 4, yields higher than those of the precedent works being marked.[15,20]

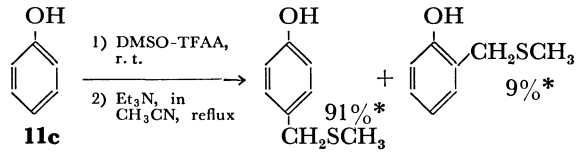
When the DMSO–TFAA complex and phenol were treated with sodium methoxide in absolute methanol, the desired product **13** was not obtained. Triethylamine was found to be the suitable base. In the reaction quenched 7 min after addition of the base, 0.5 equivalent of complex I to phenol marked a higher yield than one equivalent. This indicates that phenol was protonated and blocked by trifluoroacetic acid generated in the course of the reaction. It was thus necessary to eliminate the acid. 2,6-Lutidine, which has little nucleophilicity and is able to trap proton, was considered to be effective. Table 5 gives the yield from *o*-cresol and the effect of 2,6-lutidine. In the absence of triethylamine, 2,6-lutidine did not work as the base in the rearrangement, but a combination of 2,6-lutidine and triethylamine was recognized to be a good base. Optimum yield was attained in methylene chloride–hexane (1/1=v/v).

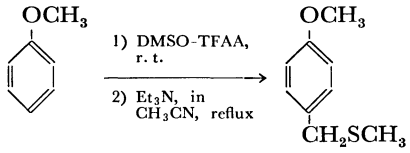
On the other hand, phenol reacted with DMSO–TFAA in acetonitrile at room temperature to produce viscous liquid instantaneously. NMR analysis (in $CDCl_3$) showed a singlet (6H) at δ 2.68 and a multiplet (4H) at δ 7.24—7.36. The liquid was refluxed with triethylamine in acetonitrile for 5 h to afford 4-methylthiomethylphenol in 23% yield (Eq. 3): NMR (CCl_4) δ=1.84 (s, 3), 3.44 (s, 2), and 6.44—7.08 ppm (q, 4). Anisol which also produced viscous liquid in a similar procedure was refluxed in acetonitrile with triethylamine to afford 4-methylthiomethylanisol (Eq. 4). The yield was low, but unreacted anisol was recovered: NMR (CCl_4) δ=1.88 (s, 3), 3.46 (s, 2), 3.64 (s, 3), 6.56—7.01 (q, 4).

Table 4. *ortho*-Methylthiomethylation of substituted phenols

Compd	R	Yield (%)[a]	
		13	**14**
11a	4-OCH_3	55	14
11b	4-CH_3	33	5
11c	H	39	—
11d	4-Cl	43	11
11e	2-CH_3	49[b]	
11f	2,4-CH_3	41	

a) Isolased yield based on TFAA.
b) Determined by GLPC.





Hirose and Ukai reported on the conversion of dimethyl-*p*-hydroxyphenylsulfonium perchlorate **17** into methyl *p*-hydroxyphenyl sulfide (**18**) by heating in an aqueous saturated potassium chloride solution.[17] The acetonitrile solution of DMSO–TFAA and phenol was refluxed in an aqueous saturated potassium chloride solution for 5 h. No methyl *p*-hydroxyphenyl sulfide was detected. Dimethyl-*p*-hydroxyphenylsulfonium perchlorate was prepared according to the method of Hirose and Ukai,[17] and treated with triethylamine in acetonitrile at room temperature. The sole product was identified with methyl *p*-hydroxyphenyl sulfide **18**. The results exclude the possibility of oxysulfonium intermediate **12** and dimethyl-*p*-hydroxyphenylsulfo-

* Yield was determined as cresol after desulfurization by Raney-Ni.

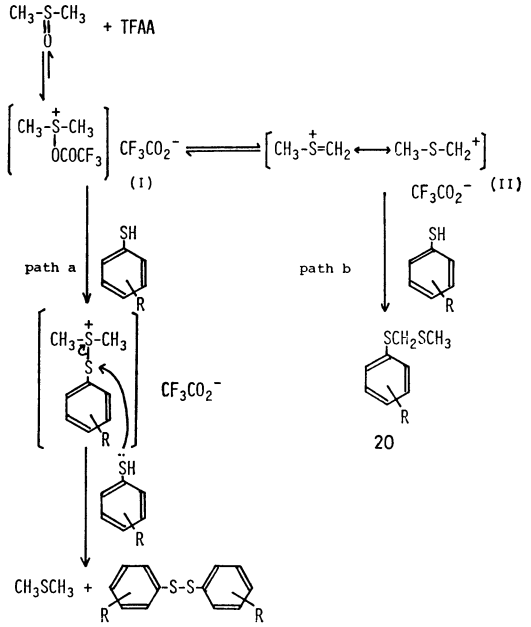
Table 5.

Compd	R	Reaction time (h)	Base	2,6-Lutidine (equiv)	Solvent	Yield (%) of **13**
11c	H	14	$NaOCH_3$	0	CH_2Cl_2	0
11e	2-CH_3	3	Et_3N	0	CH_2Cl_2	19
11e	2-CH_3	3	Et_3N	1.2	CH_2Cl_2	40
11e	2-CH_3	3	—	1.2	CH_2Cl_2	0
11e	2-CH_3	3	Et_3N	1.2	CH_2Cl_2–Hexane[a]	49

a) 1/1=v/v.

nium intermediate in the *para* alkylation reaction of phenol. It seems that methylmethylenesulfonium cation (Pummerer type intermediate) is the attacking species to phenol and anisol.

Methylthiomethylation on Sulfur Atom of Thiophenols. Complex I reacted with thiophenol below −50 °C under the usual conditions. Thiophenol was oxidized to give diphenyl disulfide, DMSO being reduced to dimethyl sulfide quantitatively. It is assumed that dimethylphenylthiosulfonium species was attacked by unreacted thiophenol along path a as shown in Scheme 3.

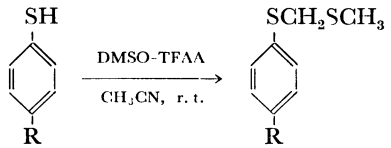


Scheme 3. Generation of the Pummere type intermediate.

On the other hand, complex I is expected to be transformed into carbonium ion following deprotonation (Pummerer type intermediate) (II). Trifluoroacetoxy anion (the counter anion) in the complex I has very weak nucleophilicity. Thus a certain nucleophile is considered to be able to trap this intermediate carbonium ion. *p*-Methylthiophenol gave methylthiomethyl *p*-methylphenyl sulfide **20** in good yield (59% isolated) and bis(*p*-methylphenyl) disulfide (21% yield) in a simple procedure: TFAA and thiophenols were added to an acetonitrile solution of DMSO successively at room temperature, and the reaction mixture was evaporated. The reaction was completed instantaneously, and dimethyl sulfide and trifluoroacetic acid formed were removed by evaporation of the solvent. No additional base was required. The yield decreased from 59 to 21% in the presence of triethylamine, because of the decomposition of complex I.

Several substituted thiophenols were alkylated (Table 6). DMSO–TFAA complex is the effective reagent for methylthiomethylation.

TABLE 6. METHYLTHIOMETHYLATION OF THIOPHENOL



19 **20**

Compd	R	Yield[a] of **20** (%)
19a	Cl	55
19b	H	59
19c	CH_3	59

a) Isolated yield by preparative thin layer chromatography.

Experimental

*Preparation of 4-Chloro-2-methylthiomethylaniline (**6d**) from* p-*Chloroaniline.* *(Procedure A)* Dimethyl sulfoxide (1.4 g, 18 mmol) was dissolved in 20 ml of dry methylene chloride–acetonitrile (1/1=v/v), and the solution was stirred with a magnetic stirrer under nitrogen atmosphere and cooled below −70 °C in a Dry Ice–acetone bath. Trifluoroacetic anhydride (TFAA, 2.5 g, 12 mmol) was added dropwise to the solution maintained below −30 °C. The reaction was exothermic and a white precipitate immediately appeared. To the solution was gradually added *p*-chloroaniline (1.28 g, 10 mmol) in 10 ml of acetonitrile. A white precipitate soon disappeared and the solution which became homogeneous was kept stirring for 5 h. Sodium methoxide (30 mmol) in 15 ml of absolute methanol was added to the reaction mixture dropwise below −50 °C. The solution was allowed to warm to room temperature and was kept overnight (*ca.* 12 h). The resulting mixture was diluted with 40 ml of 10% aqueous sodium hydroxide. The organic layer was separated, the aqueous phase extracted three times with 70 ml portions of methylene chloride, and the organic layers were combined with the original organic phase, dried over anhydrous magnesium sulfate, filtered, and concentrated *in vacuo* to yield yellow oil. The resulting oil was dissolved in 100 ml of acetonitrile with 5 ml of triethylamine, and refluxed for 15 h. The solution was evaporated in order to remove the solvent and triethylamine to give a brown oil. Column chromatography on silica gel gave acylated aniline, *p*-chloroaniline, and 4-chloro-2-methylthiomethylaniline: 1.27 g isolated (eluant: benzene–hexane=1/1, v/v); mp 79—80 °C (lit, mp 78—79 °C[12]); NMR (CCl_4) δ=2.00 (s, 3), 3.62 (s, 2), 4.07 (s, 2), 6.5—7.1 (m, 3) (identical with the lit[12]).

*Preparation of 4-Nitro-2-methylthiomethylaniline (**6a**) from* p-*Nitroaniline.* *(Procedure B)* DMSO (1.4 g, 18 mmol) in 90 ml of dry methylene chloride–acetonitrile (1/1=v/v) was stirred and kept below −70 °C in a Dry Ice–acetone bath under nitrogen atmosphere. TFAA (2.5 g, 12 mmol) was added dropwise to the solution maintained below −30 °C throughout the course of addition. No white precipitate appeared. To the solution was gradually added *p*-nitroaniline (1.38 g, 10 mmol) and DMSO (3 ml) dissolved in 20 ml of acetonitrile. It was kept stirring for 7 h, and sodium methoxide (50 mmol) in 25 ml of absolute methanol was added dropwise below −40 °C. The reaction mixture was allowed to warm to room temperature and kept overnight (10 h). After the usual workup, yellow crystals and oil were obtained. They were dissolved in 100 ml of dry toluene with 5 ml of triethylamine, and refluxed for two days. This solution was evaporated to give crude solid. Column chromatography on silica gel gave 4-nitro-2-methylthiomethylaniline: 0.99 g isolated (eluant: benzene); mp 75—76 °C (lit, mp 75—

77 °C[12]); NMR ($CDCl_3$) δ=2.06 (s, 3), 3.72 (s, 2), 4.92 (s, 2), 6.64—8.12 (m, 3) (identical with lit[12]). The crystals obtained before reflux were identified with *N*-nitrophenyl dimethyl sulfimide: mp 164—167 °C (lit, mp 166—167 °C[14]); NMR ($CDCl_3$) δ=2.72 (s, 3), 6.66—8.04 (q, 4) (identical with lit[14]).

*Preparation of 4-Methyl-2-methylthiomethylaniline (**6f**) from* p-*Toluidine. (Procedure C)* DMSO–TFAA complex was prepared in 20 ml of methylene chloride and acetonitrile from 18 mmol of DMSO and 12 mmol of TFAA as described in procedure A. *p*-Toluidine (1.07 g, 10 mmol) in 10 ml of acetonitrile was added dropwise below −50 °C. The solution was stirred for 3 h. Sodium methoxide (30 mmol) in absolute methanol 15 ml was added slowly, and the solution was kept overnight at room temperature (*ca.* 10 h). The usual work-up gave a dark oil. Column chromatography on silica gel gave 4-methyl-2-methylthiomethylaniline: 0.752 g isolated (eluant: benzene–hexane=1/1, v/v); mp 43—44 °C (lit, mp 42—45 °C[12]); NMR (CCl_4) δ=1.91 (s, 3), 2.21 (s, 3), 3.58 (s, 2), 3.79 (s, 2), 6.42—6.86 (m, 3) (identical with values in lit[12]).

*Preparation of 2-Methylthiomethylaniline (**6e**) from Aniline.* The reaction was carried out according to procedure A. Methylene chloride (20 ml) solution of the DMSO–TFAA complex (DMSO 36 mmol and TFAA 24 mmol) and 20 ml of methylene chloride solution of aniline (20 mmol) were employed. Column chromatography on silica gel gave 2-methylthiomethylaniline: 0.83 g isolated (eluant: benzene–hexane=1/1, v/v); NMR (CCl_4) δ=1.94 (s, 3), 3.64 (s, 2), 4.01 (s, 2) 6.60—7.12 (m, 4) (identical with lit[12]), and *N*-trifluoroacetylaniline **7e**: MS (20 eV), *m/e*, 189; NMR ($CDCl_3$) δ=7.14—7.50 (m, 5), 7.80 (s, 1); IR (KBr) 1710 cm^{-1}; mp 90.0—90.5 °C.

*Preparation of 4-Methoxy-2-methylthiomethylaniline (**6g**) from* p-*Anisidine.* The reaction was carried out according to procedure C. The DMSO–TFAA complex was prepared in dry toluene. Column chromatography on silica gel gave 4-methoxy-2-methylthiomethylaniline: 0.49 g (eluant: benzene–hexane); NMR (CCl_4) δ=1.92 (s, 3), 3.53 (s, 2), 3.63 (s, 3), 3.68 (s, 2), 6.46 (s, 3) (identical with lit[10]).

*Preparation of 4-Cyano-2-methylthiomethylaniline (**6b**) from* p-*Cyanoaniline.* The reaction was carried out according to procedure B. Column chromatography on silica gel gave 4-cyano-2-methylthiomethylaniline: 0.94 g isolated; mp 84—86 °C; NMR ($CDCl_3$) δ=2.00 (s, 3), 3.68 (s, 2), 4.7 (s, 2), 6.5—7.2 (m, 3) (identical with values in lit[18]).

*Preparation of 4-Carbomethoxy-2-methylthiomethylaniline (**6c**) from* p-*Carbomethoxyaniline.* The reaction was carried out according to procedure B. Column chromatography on silica gel gave starting aniline, acylated aniline, and 4-carbomethoxy-2-methylthiomethylaniline: 1.03 g isolated (eluant: benzene); mp 85—87 °C; NMR ($CDCl_3$) δ=2.00 (s, 3), 3.80 (s, 2), 3.82 (s, 3), 4.80 (s, 2), 7.4—8.0 (m, 3) (identical with values in lit[18]).

*Preparation of 6-Chloro-2-methylthiomethylaniline (**9b**) from* o-*Chloroaniline.* The reaction was carried out according to procedure A. The oil obtained after quenching with 10% aqueous sodium hydroxide was refluxed in 100 ml acetonitrile with 5 ml of triethylamine for 10 h. Column chromatography on silica gel gave 6-chloro-2-methylthiomethylaniline: 1.33 g isolated (eluant: benzene–hexane=1/1, v/v); NMR (CCl_4) δ=1.85 (s, 3), 3.57 (s, 2), 4.48 (s, 2), 6.51—7.18 (m, 4) (identical with values in lit[12]).

*Preparation of 6-Methoxy-2-methylthiomethylaniline (**9d**) from* o-*Anisidine.* DMSO (1.4 g) was dissolved in 100 ml of dry toluene, and the solution was cooled below −70 °C in a Dry Ice–acetone bath under nitrogen atmosphere. TFAA (2.5 g) was added. Methylene chloride solution of *o*-anisidine (10 mmol) was added dropwise. The precipitate soon disappeared, and the solution was kept standing for 5 h. Sodium methoxide (30 mmol) in 15 ml of methanol was added below −50 °C. The cooling bath was removed in order to warm the reaction mixture upto room temperature. After quenching with 10% aqueous sodium hydroxide, the reaction mixture was dissolved in 100 ml of acetonitrile and refluxed for several hours with 5 ml of triethylamine. Preparative thin layer chromatography (Merck Silica gel 60 PE_{254}) gave 6-methoxy-2-methylthiomethylaniline: 0.95 g isolated (eluant: benzene–hexane=1/1, v/v); NMR (CCl_4) δ=1.87 (s, 3), 3.57 (s, 2), 3.76 (s, 3), 4.04 (s, 2), 6.56—7.16 (m, 3); MS (20 eV), *m/e*, 183.

*Preparation of 6-Nitro-2-methylthiomethylaniline (**9a**) from* o-*Nitroaniline.* The reaction was carried out according to procedure B. Column chromatography on silica gel gave 6-nitro-2-methylthiomethylaniline: 0.812 g isolated (eluant: benzene–hexane=1/1, v/v); mp 80—82 °C; NMR ($CDCl_3$) δ=2.00 (s, 3), 3.70 (s, 2), 6.5—7.2 (m, 3), 8.0 (s, 2); MS (20 eV), *m/e*, 198, 151, and 105.

*Preparation of 6-Methyl-2-methylthiomethylaniline (**9c**) from* o-*Toluidine.* The reaction was carried out according to procedure A. Preparative thin layer chromatography (Merck Silica gel 60 PE_{254}) gave 6-methyl-2-methylthiomethylaniline: 0.802 g isolated (eluant: benzene–hexane=1/2, v/v); NMR (CCl_4) δ=1.86 (s, 3), 2.08 (s, 3), 3.53 (s, 2), 3.90 (s, 2), 6.56—7.16 (m, 3) (identical with values in lit[12]).

*Preparation of 2-Methylthiomethylphenol (**13c**) from Phenol. (General Procedure)* DMSO–TFAA complex was prepared from DMSO (28 mmol) and TFAA (14 mmol) in 10 ml of dry methylene chloride below −60 °C. White precipitate appeared immediately. Phenol (2.7 g, 29 mmol) and 2,6-lutidine (1.6 g 15 mmol) dissolved in 4.5 ml of DMSO and 10 ml of methylene chloride was added dropwise, and the solution was stirred for 3 h. After triethylamine (2 ml) had been added, the solution was allowed to warm up to room temperature overnight. The reaction mixture was poured into 70 ml of dil. hydrochloric acid, the organic layers were separated, and the aqueous phase was extracted three times with 50 ml portions of methylene chloride. The organic layers were combined, and dried over magnesium sulfate, filtered, and concentrated *in vacuo*. Column chromatography on silica gel gave 2-methylthiomethylphenol: 0.452 g isolated (eluant: benzene–hexane=1/1, v/v); NMR (CCl_4) δ=1.86 (s, 3), 3.58 (s, 2), 6.40—6.96 (m, 4) (identical with values in lit[19]); IR (neat), 3350 cm^{-1} (O–H).

*Preparation of 4-Methyl-2-methylthiomethylphenol (**13b**) from* p-*Cresol.* The reaction was carried out according to the general procedure. *p*-Cresol (0.99 g), DMSO (0.7 ml), and TFAA (1.04 g) were employed. The resulting oil was purified by preparative thin layer chromatography (Merck Silica gel 60 PF_{254}), which gave 0.28 g of mono substituted cresol and 0.06 g of disubstituted cresol (eluant: benzene–hexane=1/1, v/v). 4-methyl-2-methylthiomethylphenol: NMR (CCl_4) δ=1.88 (s, 3), 2.18 (s, 3), 3.58 (s, 2), 6.52 (m, 3) (identical with values in lit[20]); IR (neat), 3350 cm^{-1} (O–H) 4-methyl-2,6-bismethylthiomethylphenol: NMR (CCl_4) δ= 1.92 (s, 6), 2.20 (s, 3), 3.62 (s, 4), 6.78 (s, 2); IR (neat), 3300 cm^{-1} (O–H).

*Preparation of 4-Chloro-2-methylthiomethylphenol (**13d**) from* p-*Chlorophenol.* The reaction was carried out according to general procedure. DMSO (0.4 ml), TFAA (0.50 g), and *p*-chlorophenol (0.75 g) were employed. The resulting oil was separated by preparative thin layer chromatography (Merck Silica gel PF_{254}, eluant: benzene–hexane=1/1, v/v) to give 0.20 g of 4-chloro-2-methylthiomethylphenol:[21]

NMR (CCl_4) δ=1.96 (s, 3), 3.62 (s, 2), 6.96—7.20 (m, 3); IR (neat), 3310 cm^{-1} (O-H), and 0.06 g of 4-chloro-2,6-bis(methylthiomethyl)phenol: NMR (CCl_4) δ=1.92 (s, 6), 3.60 (s, 4), 6.96 (s, 2); IR (neat), 3290 cm^{-1} (O-H)

*Preparation of 4-Methoxy-2-methylthiomethylphenol (**13a**) from* p-*Methoxyphenol.* The reaction was carried out according to general procedure. DMSO (6 mmol), TFAA (2.3 mmol), and *p*-methoxyphenol (5 mmol) were employed. Preparative thin layer chromatography (Merck Silica gel 60 PF_{254}, eluant: benzene–hexane=1/1, v/v) gave 4-methoxy-2,6-bis(methylthiomethyl)phenol (0.08 g) and 4-methoxy-2-methylthiomethylphenol (0.23 g). Mono-alkylated product:[21] NMR (CCl_4) δ=1.94 (s, 3), 3.64 (s, 2), 3.68 (s, 3), 6.52—6.80 (m, 3); IR (neat), 3340 cm^{-1} (O-H) dialkylated product: NMR (CCl_4) δ=1.98 (s, 6), 3.68 (s, 4), 3.74 (s, 3), 6.60 (s, 2); IR (neat), 3340 cm^{-1} (O-H)

*Preparation of 2-Methyl-6-methylthiomethylphenol (**13e**) from* o-*Cresol.* The reaction was carried out according to general procedure. DMSO (10 mmol), TFAA (6 mmol), and *o*-cresol (5 mmol) were used. Column chromatography on silica gel (eluant: benzene–hexane=1/1, v/v) gave 6-methyl-2-methylthiomethylphenol (0.412 g):[20] NMR (CCl_4) δ=1.92 (s, 3), 2.24 (s, 3), 3.64 (s, 2), 6.56—7.00 (m, 3); IR (neat), 3360 cm^{-1} (O-H).

*Praparation of 2,4-Dimethyl-6-methylthiomethylphenol (**13f**) from 2,4-Xylenol.* According to the general procedure, 2,4-xylenol was converted into methylthiomethylated phenol. DMSO (20 mmol), TFAA (12 mmol), and 2,4-xylenol (10 mmol) were used. The resulting oil was separated by column chromatography on silica gel (eluant: benzene–hexane=1/1, v/v) to give 0.75 g of 4,6-dimethyl-2-methylthiomethylphenol:[2b] NMR (CCl_4) δ=1.88 (s, 3), 2.14 (s, 6), 3.60 (s, 2), 6.24—6.76 (m, 2); IR (neat), 3350 cm^{-1} (O-H).

*Reaction of Dimethyl-*p*-hydroxyphenylsulfonium Perchlorate with Triethylamine.* Dimethyl-*p*-hydroxyphenylsulfonium perchlorate was prepared by the method[17] of Hirose and Ukai; 78% yield, mp 158—159 °C (lit, mp 155—157 °C); NMR (CD_3CN–$CDCl_3$) δ=3.06 (s, 6), 7.00—7.75 (q, 4).

Triethylamine was added to 20 ml acetonitrile solution of dimethyl-*p*-hydroxyphenylsulfonium perchlorate at room temperature. White precipitates appeared instantaneously. After evaporation of the solvent, the reaction mixture was washed with 100 ml of water and extracted three times with 60 ml portions of chloroform. The organic phase was dried over anhydrous magnesium sulfate and concentrated *in vacuo* to yield white crystals which were identified with methyl *p*-hydroxyphenyl sulfide: mp 85—86 °C (lit, mp 86—87 °C[17]); NMR (CCl_4) δ=2.38 (s, 3), 4.18 (s, 1), 6.61—7.17 (q, 4).

*Preparation of Methylthiomethyl Phenyl Sulfide (**20b**) from Thiophenol. (General Procedure)* DMSO (10 mmol) wa dissolved in 10 ml of dry acetonitrile at room temperature. TFAA (2.1 g, 10 mmol) in 5 ml acetonitrile was added to the solution at room temperature with stirring. Thiophenol (10 mmol) was added. The reaction was completed instantaneously, and the reaction mixture was evaporated in order to remove the solvent. The resulting yellow liquid was separated by preparative thin layer chromatography (Merck Silica gel 60 PF_{254}, eluant: hexane) to give methylthiomethyl phenyl sulfide (1.0 g, 59% yield): NMR (CCl_4) δ=2.19 (s, 3), 3.95 (s, 2), 7.12—7.46 (m, 5); MS (20 eV), *m/e*, 170 and 61.

Preparation of Methylthiomethyl p-*Chlorophenyl Sulfide (**20c**) from* p-*Chlorothiophenol.* The reaction was carried out according to general procedure. Preparative thin layer chromatography (Merck Silica gel 60 PF_{254}, eluant: hexane) gave methylthiomethyl *p*-chlorophenyl sulfide: 0.94 g isolated: NMR (CCl_4) δ=2.18 (s, 3), 3.93 (s, 2), 7.30 (s, 4); MS (20 eV), *m/e*, 204 and 61.

Preparation of Methylthiomethyl p-*Methylphenyl Sulfide (**20c**) from* p-*Methylthiophenol.* The reaction was carried out according to general procedure. Preparative thin layer chromatography (Merck Silica gel 60 PF_{254}, eluant: hexane) gave methylthiomethyl *p*-methylphenyl sulfide: 1.1 g isolated; NMR (CCl_4) δ=2.16 (s, 3), 2.31 (s, 3), 3.82 (s, 2), 6.98—7.29 (q, 4); MS (20 eV), *m/e*, 184 and 61.

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