Reaction of Complex of Phenacyl Bromide and Silver Hexafluoroantimonate with Water. A mixture of phenacyl bromide (1 g, 5 mmol) and silver hexafluoroantimonate (1.8 g, 5 mmol) in anhydrous ether (15 mL) was heated to reflux for 2 h with vigorous stirring. To the reaction mixture was then added water (5 mL) and reflux and stirring were continued for 22 h. The reaction mixture was poured into water and extracted with benzene. The dried benzene extract gave only phenacyl bromide (883 mg, 88.3%).

Reaction of a Complex of Phenacyl Bromide and Silver Hexafluoroantimonate with Benzyl Alcohol. A mixture of phenacyl bromide (1 g, 5 mmol) and silver hexafluoroantimonate (1.8 g, 5 mmol) in anhydrous ether (15 mL) was heated to reflux for 2 h with vigorous stirring. To the reaction mixture was then added benzyl alcohol (5 mL) and reflux and stirring were continued for 22 h. The reaction mixture was poured into water and extracted with benzene. No benzaldehyde was detected on TLC, NMR, and IR.

Reaction of Benzylidenedibenzylhydrazine with $AgSbF_6$ in Wet Ether. A mixture of benzylidenedibenzylhydrazine (1.5 g, 5 mmol) and silver hexafluoroantimonate (1.8 g, 5 mmol) in wet ether[21] (15 mL) was heated to reflux for 24 h with vigorous stirring. The reaction mixture was poured into water and extracted with benzene. Removal of the solvent gave 1.3 g of an oily material which was shown to consist of starting material (89%) and benzaldehyde (11%) by NMR spectral examination.

Reaction of Phenylglyoxal with $AgSbF_6$ in Benzene. A mixture of freshly distilled phenylglyoxal (1.4 g, 10 mmol) and silver hexafluoroantimonate (3.5 g, 10 mmol) in anhydrous benzene was heated to reflux for 24 h with vigorous stirring. The reaction mixture was poured into water and extracted with benzene. The dried benzene extract was evaporated in vacuo and residue was chromatographed on 50 g of silica gel (60–200 mesh). Fractions were eluted rapidly with benzene to give benzil as a thick yellow oil whose IR spectrum and TLC retention time were identical to those of authentic sample; the infrared spectrum of the bis(2,4-dinitrophenylhydrazone), mp 285–290 °C (lit.[24] mp 317–318 °C), was identical to that of an authentic sample.

Acknowledgment. The generous support of this work by NIH under Grant GM 13689 is hereby gratefully acknowledged.

Registry No.—NDBA, 5336-53-8; *p*-bromobenzoic acid, 586-76-5; 4-bromobenzil, 39229-12-4; bibenzyl, 103-29-7; benzylidenedibenzylhydrazine, 21136-32-3; benzaldehyde, 100-52-7; diphenylmethane, 101-81-5; 1,1-dibenzylhydrazine, 5802-60-8; benzyl chloride, 100-44-7; phenylglyoxal, 1074-12-0.

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Nitro Displacement by Methanethiol Anion. Synthesis of Bis-, Tris-, Pentakis-, and Hexakis(methylthio)benzenes

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Bis- and tris(methylthio)benzenes have been synthesized by a facile process involving nitro displacement. Also prepared were pentakis- and hexakis(methylthio)benzene. The thioethers were readily oxidized to the corresponding sulfones in high yield.

Nucleophilic displacement of nitro groups either ortho of para to an electron pair stabilizing function is well documented. Our previous reports[1] have demonstrated the synthetic utility of nitro displacement ortho to cyano, carboxylic acid ester, and aldehyde functions by a variety of nucleophiles. Other workers[2] have reported nitro displacement involving activation by sulfone, carboxamide, ketone, and phenyl substituents, in addition to the three functions above. Reports also include displacements starting with 3-nitrophthalic anhydride[3] and *N*-substituted 3-nitrophthalimides.[4]

No examples were found for which the stabilization could be attributed to a thioether function. In fact, Miller[5] reported that *p*-methylthio showed only weak activation (similar to the heavier halogens) in rate studies involving methoxide displacement of chlorine activated by an *o*-nitro group. Also, Bordwell and Boutan[6] predicted only slight electron pair stabilization for an aromatic methylthio substituent based on acidity constants and spectral measurements. In contrast to these reports, we wish to describe several examples of facile nitro displacement by methanethiol anion where the activa-

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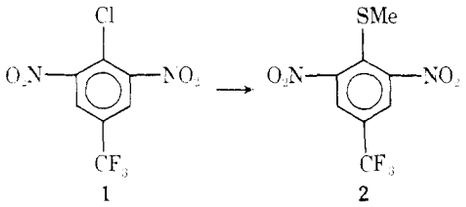
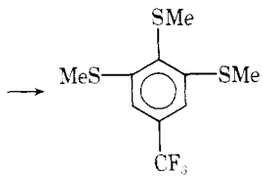
tion is due to an ortho (and in one case a para) methylthio function.

Results

Treatment of 4-chloro-3,5-dinitrobenzotrifluoride (**1**)[7] with methanethiol anion in aqueous alcohol gave the expected



1 **2**



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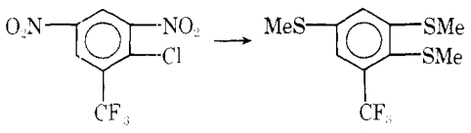
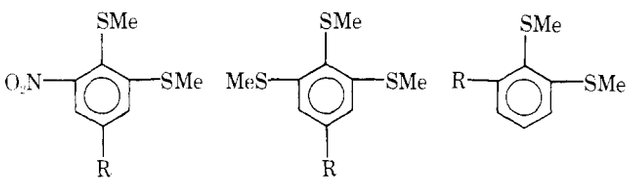


4 **5**

thioether **2** (67% yield). When **2** was allowed to react with excess methanethiol anion (lithium salt) in cold DMF (ice bath) for 1 h, the product obtained was 3,4,5-tris(methylthio)benzotrifluoride (**3**, 95%). Similar treatment of **1** yielded **3** directly (74%). The same reaction with 2-chloro-3,5-dinitrobenzotrifluoride (**4**)[8] gave 2,3,5-tris(methylthio)benzotrifluoride (**5**, 70%). The bis thioether **6a** (61%) could be obtained



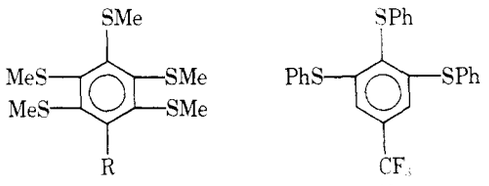
6a, R = CF_3
b, R = H
c, R = Me

7a, R = H
b, R = Me

8a, R = Cl
b, R = OMe

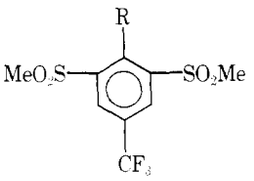
from **1** by lowering the reaction temperature to −20 °C, although some **3** was also present in the crude product. When 1-chloro-2,6-dinitrobenzene was subjected to the reaction conditions, the bis(thioether) **6b** was obtained cleanly in 79% yield after only 15 min at ice bath temperature. When the reaction was allowed to continued for 4.5 h at room temperature, the tris(thioether) **7a** (75%) was the isolated product. Similarly, from 4-chloro-3,5-dinitrotoluene[9] was obtained **6c** (78%) and **7b** (60%).

Treatment of 2,3-dichloro-1-nitrobenzene under the usual reaction conditions yielded 1-chloro-2,3-bis(methylthio)-benzene (**8a**, 73%). Similarly, 2-chloro-3-nitroanisole[10] gave 2,3-bis(methylthio)anisole (**8b**, 55%), although the reaction rate was slower (30 h at room temperature). When 1,3,5-trichloro-2,4-dinitrobenzene[11] was utilized as starting material, the product obtained was pentakis(methylthio)benzene (**9a**, 63%). Similar treatment of 1,3,4,5-tetrachloro-2,6-dinitrobenzene[12] yielded hexakis(methylthio)benzene (**9b**, 71%). The same compound was obtained likewise from 1,2,3,4-tetrachloro-5,6-dinitrobenzene[13] (57%), pentachloronitrobenzene (76%), and hexachlorobenzene (75%). The latter result is in contrast to the findings of Kulka,[14] who reported 1,4-bis and 1,2,4,5-tetrakis substitution in the reaction of hexachlorobenzene and ethanethiol anion.



9a, R = H
b, R = SMe

10

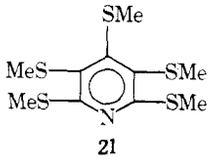


20a, R = OH
b, R = $NHCH_2CH_2NH_2$
c, R = $NHCH(CH_2CH_3)_2$

Displacement products were not obtained with a number of substrates. Although no attempts were made to isolate the desired product in these cases, TLC showed at least five major components, whereas the successful reactions described were essentially one component by TLC. For instance, both *o*- and *p*-chloronitrobenzene underwent chloride displacement at ice bath temperature, but complex mixtures were obtained when the reaction was brought to room temperature, apparently because of competing reactions involving reduction of the nitro group. Similar results were encountered with 2,4-dichloro-1-nitrobenzene, 2,4-dinitro-1-chlorobenzene, 2-chloro-3-nitrotoluene, and 2-chloro-5-nitrobenzotrifluoride. Picryl chloride, even at −60 °C, gave a complex mixture. In the case of compounds **3**, **5**, and **6a** through **8b**, the displaced nitro group (1 position) was always ortho (2 position) to a methylthio function and meta (3 position) to a substituent (nitro, trifluoromethyl, methylthio, chloro, or methoxyl) capable of withdrawing electrons by induction. All cases not meeting this criterion have given complex mixtures, except for the para displacement with compound **5**.

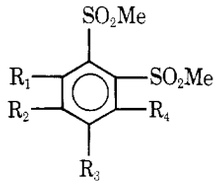
Treatment of **1** with benzenethiol anion at room temperature for 24 h gave 3,4,5-tris(phenylthio)benzotrifluoride (**10**, 50%). The longer reaction time and lower yield is probably due to steric hindrance. Other phenyl thioethers were not investigated. Most of the thioethers were readily oxidized to the corresponding sulfones by treatment with hydrogen peroxide in acetic acid. The yields were in the range of 80–95% and the products are summarized in Table I. Several nucleophilic displacements were examined utilizing the tris sulfonyl derivative **11**. Treatment with dipropylamine in hot Me_2SO produced the phenol **20a** (49%), apparently formed by reaction with water in the solvent. Condensation with the primary amines, ethylenediamine, and 3-aminopentane in alcohol gave the bis(sulfonyl)anilines **20b** (86%) and **20c** (90%), respectively. The NMR spectra of the latter three derivatives all showed singlet methylsulfonyl and aromatic proton signals, thus verifying the assigned symmetrical structures.

The scope of the nitro displacement reaction in heterocyclic systems was investigated for pyridine. Reaction of pentachloropyridine with methanethiol anion at room temperature for 48 h yielded pentakis(methylthio)pyridine (**21**) but only in 10% yield.



21

Table I. Synthesis of Methylsulfonylbenzenes



Compd[a]	Registry no.	Reactant	R_1	R_2	R_3	R_4	Mp, °C	Yield, %
11	65516-86-1	**3**	SO_2Me	H	CF_3	H	258–260	95
12	65516-87-2	**5**	CF_3	H	SO_2Me	H	279–281[b]	80
13	65516-88-3	**6b**	NO_2	H	H	H	237–239	90
14	65516-89-4	**6c**	NO_2	H	Me	H	256–258	93
15	65516-90-7	**7a**	SO_2Me	H	H	H	243–245	81
16	65516-91-8	**8a**	Cl	H	H	H	188–189	85
17	65516-92-9	**8b**	OMe	H	H	H	199–201	85
18	65516-84-9	**9a**	SO_2Me	SO_2Me	SO_2Me	H	>300	97
19	65516-25-8	**9b**	SO_2Me	SO_2Me	SO_2Me	SO_2Me	>300[c]	81

[a] Satisfactory analytical data (±0.4% for C, H, N, or S) were reported for all new compounds listed in the table. [b] Recrystallized from DMF–water. [c] Product triturated with hot DMF.

Discussion

From our observations it appears that the nitro displacement reactions described above occur by means of the classical addition–elimination mechanism of nucleophilic aromatic substitution.[15] The high yields and absence of side reactions, other than those leading to nitro group reduction, support this mechanism, although an alternate route involving radical anion intermediates cannot be ruled out. The reactions appeared to go equally well in the presence or absence of oxygen, but the slower reactions were carried out under nitrogen in order to prevent oxidation of the thiol.

The relative ease of nucleophilic displacement of the aromatic nitro group has been verified by numerous kinetic studies.[16] Also to be taken into consideration is the unusual nucleofuge–nucleophile relationship involving the nitro group and thiol anions. Bartoli and Todesco[17] recently examined the kinetics of the reaction of 1-X-2,4-dinitrobenzenes and benzenethiol anion in methanol at 25 °C. The relative rate of nitro displacement was 2000-times that of chlorine and 50-times that of fluorine. These differences were much larger than those found with other nucleophiles in the earlier kinetic studies. A similar observation was noted by Bunnett and Merritt,[18] who studied the kinetics of the same reaction at 0 °C and reported that nitro displacement was too fast for measurement, although rate constants were readily obtained for both chlorine and fluorine displacement. These authors concluded that the nitro group appears "to have an unusually high replaceability when the reagent is thiophenoxide ion". In our examples this unusual nucleofuge–nucleophile relationship apparently plays a major role, but it is probably not the complete explanation. For example, in the synthesis of compounds **7a–8b,** the only obvious activation of the nitro group must be attributed to an *o*-methylmercapto function. The requirement for a second electronegative substituent ortho to the methylmercapto group cannot be explained at this time, although effects on the reduction potential of the nitro group should be considered.

Our main interest in the reaction concerns the ease with which a seemingly unactivated nitro group can be converted to a thioether function and applications of the reaction to synthesis. Further examples of this utility are the subject of the following paper.

Experimental Section

All starting materials are commercially available except where literature references are given. Unless otherwise noted, cold solution refers to ice bath conditions. Lithium hydroxide was ground to a fine powder in order to facilitate solution. Addition of the lithium hydroxide was exothermic; in all cases the temperature was not allowed to exceed 15 °C during the addition. Excess reagent was utilized in all cases where molar equivalent is omitted. Alcohol refers to 95% ethanol. NMR spectral data are partial and only signals pertinent to the structural assignment are given. Melting points were determined on a Mel-Temp apparatus and are uncorrected.

α,α,α-Trifluoro-3,4,5-tris(methylthio)toluene (3). To a cold solution (under nitrogen) containing 5.4 g of 4-chloro-3,5-dinitrobenzotrifluoride[7] (20 mmol) and 7 mL of methanethiol in 100 mL of DMF was added portionwise 5 g of lithium hydroxide. The mixture was stirred in the cold for 0.5 h and poured into ice water. The solid was collected and crystallized from alcohol to yield 4.2 g (74%) of product: mp 140–141 °C; NMR ($CDCl_3$) δ 2.33 (s, 3 H). 2.43 (s, 6 H), and 6.99 (s, 2 H). Anal. Calcd for $C_{10}H_{11}F_3S_3$: C, 42.23; H, 3.90; S, 33.82. Found: C, 42.42; H, 4.05; S, 34.10.

α,α,α,-Trifluoro-4-(methylthio)-3,5-dinitrotoluene (2). To a cold solution of 5.4 g of 4-chloro-3,5-dinitrobenzotrifluoride[7] (20 mmol) and 2 mL of methanethiol in 75 mL of alcohol was added dropwise a solution of 1.2 g of potassium hydroxide in 15 mL of water. The mixture was stirred in the cold for 1 h and poured into ice water. The solid was collected and crystallized from alcohol to yield 3.8 g (67%) of product, mp 93–96 °C. Anal. Calcd for $C_8H_5F_3N_2O_4S$: C, 34.05; H, 1.79; N, 9.93; S, 11.36. Found: C, 34.20; H, 1.88; N, 9.82; S, 11.37.

Lithium hydroxide (8 g) was added portionwise to a cold mixture containing 11.3 g of **2** (40.1 mmol) and 15 mL of methanethiol in 150 mL of DMF. The solution was stirred in the cold for 1 h and poured into ice water. Crystallization from alcohol yielded 10.8 g (95%) of **3,** mp 140–141 °C.

α,α,α-Trifluoro-2,3,5-tris(methylthio)toluene (5). To a cold solution containing 5.4 g of 2-chloro-3,5-dinitrobenzotrifluoride[8] (20 mmol) and 7 mL of methanethiol in 100 mL of DMF was added portionwise 5 g of lithium hydroxide. The mixture was stirred in the cold for 2 h and at room temperature for 2 h. It was poured into ice water and the crude solid was collected and crystallized from alcohol to yield 4.1 g (70%) of product: mp 61–62 °C; NMR ($CDCl_3$) δ 2.33 (s, 3 H), 2.45 (s, 3 H), 2.52 (s, 3 H), 7.13 (d, 1 H), and 7.32 (d, 1 H). Anal. Calcd for $C_{10}H_{11}F_3S_3$: C, 42.23; H, 3.90; S, 33.82. Found: C, 42.48; H, 3.67; S, 33.90.

α,α,α-Trifluoro-3,4-bis(methylthio)-5-nitrotoluene (6a). A solution (under nitrogen) containing 8.4 g of 4-chloro-3,5-dinitrobenzotrifluoride[7] (31 mmol) and 4 mL of methanethiol in 125 mL of DMF was cooled to −20 °C (dry ice–alcohol). Lithium hydroxide (2 g) was added portionwise at a rate to keep the temperature below −10 °C. The mixture was stirred for 1 h while it slowly warmed to 0 °C and then the mixture was poured into ice water. The solid was collected and crystallized from alcohol to yield 5.3 g (61%) of product: mp 85–87 °C; NMR ($CDCl_3$) δ 2.48 (s, 3 H), 2.58 (s, 3 H), 7.48 (d, 1 H), and 7.60 (d, 1 H). Anal. Calcd for $C_9H_8F_3NO_2S_2$: C, 38.16; H, 2.85; N, 4.94; S, 22.64. Found: C, 38.40; H, 2.76; N, 5.07; S, 22.73.

General Procedure for Preparation of 6b and 6c. Lithium hydroxide (15 g) was added portionwise to a cold solution containing 60

mmol of the appropriate 1-chloro-2,6-dinitrobenzene and 20 mL of methanethiol in 100 mL of DMF. The mixture was stirred in the cold for 15 min and poured into ice water. The following were obtained after collection and crystallization from alcohol: **6b** (79%; mp 102–103 °C) and **6c** (78%; mp 109–110 °C). Anal. Calcd for $C_8H_9NO_2S_2$ (**6b**): C, 44.63; H, 4.21; N, 6.50; S, 29.79. Found: C, 44.77; H, 4.11; N, 6.47; S, 29.42. Calcd for $C_9H_{11}NO_2S_2$ (**6c**): C, 47.14; H, 4.84; N, 6.11; S, 27.96. Found: C, 47.43; H, 4.63; N, 6.13; S, 28.22.

General Procedure for Preparation of 7a and 7b. To a cold solution (under nitrogen) containing 20 mmol of the appropriate 1-chloro-2,6-dinitrobenzene and 10 mL of methanethiol in 80 mL of DMF was added portionwise 5 g of lithium hydroxide. The mixture was stirred in the cold for 15 min and at room temperature for 4.5 h for **7a** and 20 h for **7b**. It was then poured into ice water, and the solid was collected and crystallized from alcohol. The following were obtained: **7a** (75%; mp 111–113 °C; NMR ($CDCl_3$) δ 2.32 (s, 3 H) and 2.39 (s, 6 H)) and **7b** (60%; 156–158 °C). Anal. Calcd for $C_9H_{12}S_3$ (**7a**): C, 49.96; H, 5.59; S, 44.45. Found: C, 50.20; H, 5.37; S, 44.30. Calcd for $C_{10}H_{14}S_3$ (**7b**): C, 52.13; H, 6.12; S, 41.75. Found: C, 52.37; H, 6.22; S, 41.79.

1-Chloro-2,3-bis(methylthio)benzene (8a). To a cold mixture (under nitrogen) of 7.7 g of 2,3-dichloro-1-nitrobenzene (40.1 mmol) and 10 mL of methanethiol in 80 mL of DMF was added portionwise 5 g of lithium hydroxide. The mixture was stirred in the cold for 15 min and at room temperature for 30 min and poured into ice water. The solid was collected and crystallized from alcohol to yield 4.5 g of product, mp 71–72 °C. Concentration of the mother liquor yielded an additional 1.5 g of product: mp 71–72 °C; NMR ($CDCl_3$) δ 2.35 (s, 3 H) and 2.38 (s, 3 H). Anal. Calcd for $C_8H_9ClS_2$: C, 46.93; H, 4.43; Cl, 17.32; S, 31.32. Found: C, 47.11; H, 4.46; Cl, 17.52; S, 31.37.

1-Methoxy-2,3-bis(methylthio)benzene (8b). Lithium hydroxide (5 g) was added portionwise to a cold solution (under nitrogen) containing 3.7 g of 2-chloro-3-nitroanisole[10] (19.7 mmol) and 10 mL of methanethiol in 75 mL of DMF. The mixture was stirred in the cold for 15 min and at room temperature for 36 h. The mixture was then poured into ice water and the solid was collected and crystallized from alcohol–water to yield 2.2 g (55%) of product: mp 102–103 °C; NMR ($CDCl_3$) δ 2.33 (s, 3 H), 2.38 (s, 3 H), and 3.87 (s, 3 H). Anal. Calcd for $C_9H_{12}OS_2$: C, 54.00; H, 6.00; S, 32.00. Found: C, 53.82; H, 5.89; S, 31.70.

Pentakis(methylthio)benzene (9a). Lithium hydroxide (5 g) was added portionwise to a cold solution (under nitrogen) of 5.4 g of 2,4,6-trichloro-1,3-dinitrobenzene[11] (19.9 mmol) and 15 mL of methanethiol in 100 mL of DMF. The mixture was stirred in the cold for 1 h and at room temperature for 44 h. The mixture was then poured into ice water and the solid was collected and crystallized from alcohol to yield 3.9 g (63%) fo product: mp 103–105 °C; NMR ($CDCl_3$) δ 2.38 (s, 6 H), 2.44 (s, 6 H), and 2.53 (s, 3 H). Anal. Calcd for $C_{11}H_{16}S_5$: C, 42.82; H, 5.23; S, 51.96. Found: C, 43.07; H, 4.94; S, 52.26.

Hexakis(methylthio)benzene (9b). To a cold solution (under nitrogen) containing 1.7 g of 2,4,5,6-tetrachloro-1,3-dinitrobenzene[12] (5.6 mmol) and 10 mL of methanethiol in 75 mL of DMF was added portionwise 5 g of lithium hydroxide. The mixture was stirred in the cold for 30 min and at room temperature for 2 h. The mixture was then poured into ice water and the solid was collected and crystallized from alcohol to yield 1.4 g (71%) of product: mp 88–90 °C; NMR ($CDCl_3$) δ 2.52 (s). Anal. Calcd for $C_{12}H_{18}S_6$: C, 40.64; H, 5.12; S, 54.24. Found: C, 40.87; H, 5.27; S, 54.41.

Using the procedure above, 2.6 g of 3,4,5,6-tetrachloro-1,2-dinitrobenzene,[13] 15 mL of methanethiol, and 5 g of lithium hydroxide in 75 mL of DMF stirred in the cold for 30 min and at room temperature for 5 h yielded 1.7 g (57%) of **9b**; 5.9 g of pentachloronitrobenzene, 15 mL of methanethiol, and 5 g of lithium hydroxide in 75 mL of DMF stirred in the cold for 30 min and at room temperature for 5 h yielded 5.4 g (76%) of **9b**; 5.7 g of hexachlorobenzene, 15 mL of methanethiol, and 5 g of lithium hydroxide in 75 mL of DMF stirred in the cold for 1 h and at room temperature for 20 h yielded 5.3 g (75%) of **9b**.

α,α,α-Trifluoro-3,4,5-tris(phenylthio)toluene (10). To a solution (under nitrogen) containing 4.2 g of 4-chloro-3,5-dinitrobenzotrifluoride[7] (15 mmol) and 5.5 g of thiophenol (50 mmol) in 75 mL of DMF was added portionwise 5 g of lithium hydroxide. The mixture was stirred for 24 h and poured into ice water. The solution was extracted three times with ether and the combined extracts were washed with water. Evaporation of the solvent and crystallization from ether–hexane yielded 3.5 g (50%) of product, mp 72–74 °C. Anal. Calcd for $C_{25}H_{17}F_3S_3$: C, 63.81; H, 3.64; S, 20.44. Found: C, 63.52; H, 3.53; S, 20.64.

General Procedure for Preparation of Methylsulfonylbenzenes (11–19). A solution of the appropriate thioether (Table I) in 1 vol of 30% hydrogen peroxide and 2–3 vol of acetic acid was heated in an open flask at steam-bath temperature for the time shown. In most cases, the product crystallized and was collected and washed with cold alcohol. Otherwise, the mixture was diluted with water until the product crystallized. The following were obtained (reactant, mmol; mL of hydrogen peroxide;[19] reaction time): **11** (**3**, 21.1; 50/10; 2 h); **12** (**5**, 10.6; 25; 3 h); **13** (**6b**, 27.9; 40/20; 2 h); **14** (**6c**, 34.5; 50/25; 2 h); **15** (**7a**, 11.6; 15; 16 h); **16** (**8a**, 12.2; 15/7.5; 2 h); **17** (**8b**, 8.5; 15; 16 h); **18** (**9a**, 3.2; 25; 2 h); **19** (**9b**, 7.0; 20/20; 150 h). Yields and melting points are given in Table I.

α,α,α-Trifluoro-2,6-bis(methylsulfonyl)-p-cresol (20a). A solution of 3.8 g of **11** (10 mmol) and 10 mL of dipropylamine in 75 mL of Me_2SO was heated at 80 °C for 2 h. The solution was poured into ice water and then acidified with hydrochloric acid. The solid was collected to yield 1.4 g (49%): mp 226–228 °C; NMR (Me_2SO-d_6) δ 3.37 (s, 6 H) and 8.10 (s, 2 H). Anal. Calcd for $C_9H_9F_3O_5S_2$: C, 33.96; H, 2.85; S, 20.15. Found: C, 34.19; H, 2.84; S, 19.89.

***N*-[α,α,α-Trifluoro-2,6-bis(methylsulfonyl)-p-tolyl]ethylenediamine (20b).** A solution containing 3.8 g of **11** (10 mmol) and 10 mL of ethylenediamine in 10 mL of alcohol was stirred for 16 h. The mixture was cooled and the product was collected to yield 3.1 g (86%): mp 188–190 °C; NMR (Me_2SO-d_6) δ 3.38 (s, 6 H) and 8.64 (s, 2 H). Anal. Calcd for $C_{11}H_{15}F_3N_2O_4S_2$: C, 36.66; H, 4.20; N, 7.77; S, 17.79. Found: C, 36.95; H, 4.10; N, 7.79; S, 17.92.

***N*-(1-Ethylpropyl)-α,α,α-trifluoro-2,6-bis(methylsulfonyl)-p-toluidine (20c).** A mixture of 1.6 g of **11** (4.2 mmol) and 7 mL of 3-aminopentane in 75 mL of alcohol was heated to reflux for 48 h. The product crystallized from the cooled solution to yield 1.4 g (90%): mp 132–134 °C; NMR ($CDCl_3$) δ 3.12 (s, 6 H) and 8.35 (s, 2 H). Anal. Calcd for $C_{14}H_{20}F_3NO_4S_2$: C, 43.40; H, 5.20; N, 3.62; S, 16.55. Found: C, 43.61; H, 5.30; N, 3.89; S, 16.62.

Pentakis(methylthio)pyridine (21). To a cold solution containing 7.5 g of pentachloropyridine (30 mmol) and 20 mL of methanethiol in 75 mL of DMF was added portionwise 7 g of lithium hydroxide. The mixture was stirred in the cold for 1 h and at room temperature for 48 h. It was poured into ice water and the solid was collected and crystallized from alcohol to yield 0.9 g (10%) of product, mp 78–80 °C. Anal. Calcd for $C_{10}H_{15}NS_5$: C, 38.80; H, 4.88; N, 4.52; S, 51.79 Found: C, 38.57; H, 4.65; N, 4.56; S, 51.59.

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Registry No.—**1**, 393-75-9; **2**, 65516-76-9; **3**, 65516-85-0; **4**, 392-95-0; **5**, 65516-77-0; **6a**, 65516-78-1; **6b**, 65516-79-2; **6c**, 65516-80-5; **7a**, 65516-81-6; **7b**, 65516-82-7; **8a**, 65516-83-8; **8b**, 65516-73-6; **9a**, 65516-74-7; **9b**, 58468-22-7; **10**, 65516-68-9; **20a**, 65516-69-0; **20b**, 65516-70-3; **20c**, 65516-71-4; **21**, 65516-72-5; methanethiol anion, 17302-63-5; 1-chloro-2,6-dintrobenzene, 606-21-3; 4-chloro-3,5-dinitrotoluene, 5264-65-3; 2,3-dichloro-1-nitrobenzene, 3209-22-1; 2-chloro-3-nitroanisole, 3970-39-6; 2,4,5,6-tetrachloro-1,3-dinitrobenzene, 28073-03-2; 3,4,5,6-tetrachloro-1,2-dinitrobenzene, 781-15-7; pentachloronitrobenzene, 82-68-8; hexachlorobenzene, 118-74-1; ethylenediamine, 107-15-3; 3-aminopentane, 616-24-0; pentachloropyridine, 2176-62-7; 2,4,6-trichloro-1,3-dinitrobenzene, 6284-83-9.

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(19) Second number indicates volume of hydrogen peroxide added 1 h later.

Nitro Displacement by Methanethiol Anion. Synthesis of Bis-, Tris-, Tetrakis-, and Pentakis(methylthio)benzoic Acids and Related Derivatives

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3,4,5-Tris(methylthio)benzamide has been synthesized by a process involving nitro displacement with methanethiol anion. Similarly prepared were various bis-, tris-, and tetrakis(methylthio)benzoic acids and their *S*-methyl thioesters. Several of the thioethers were oxidized to the corresponding sulfones. Also prepared were 3,4,5-tris(methylthio)benzenesulfonamide, 3,4,5-tris(methylthio)phenylacetamide, and pentakis(methylthio)benzamide.

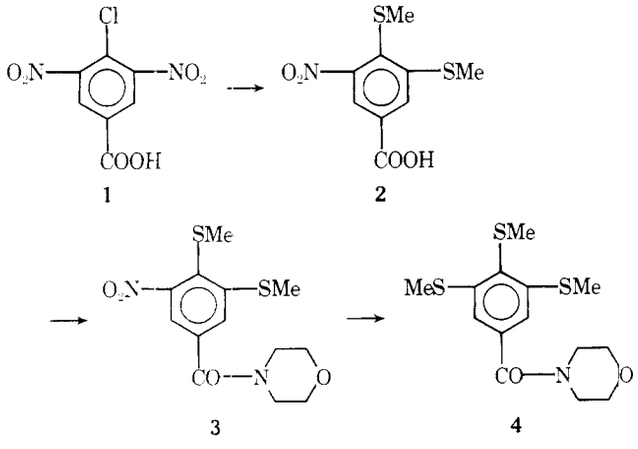
In a previous paper[1] we discussed the nucleophilic displacement of nitro groups, which were activated by *o*- or *p*-methylthio functions, with methanethiol anion. The objective of this work is to demonstrate the utility of this facile reaction for the preparation of bis-, tris-, tetrakis-, and pentakis(methylthio)benzoic acids (and their derivatives) and related benzenesulfonamides and phenylacetamides.

Results

Three general procedures were used for the synthesis of the benzoic acids. The first (Scheme I) involved treatment of 4-chloro-3,5-dinitrobenzoic acid (**1**) with excess methanethiol anion (lithium salt) in cold DMF for 0.5 h to yield 3,4-bis(methylthio)-5-nitrobenzoic acid (**2**, 80%). Attempted displacement of the second nitro group at elevated temperature and longer reaction time was unsuccessful. The benzoic acid **2** was converted to its morpholine amide **3** (81%), which readily underwent nitro displacement to give the tris(thioether) **4** (90%).

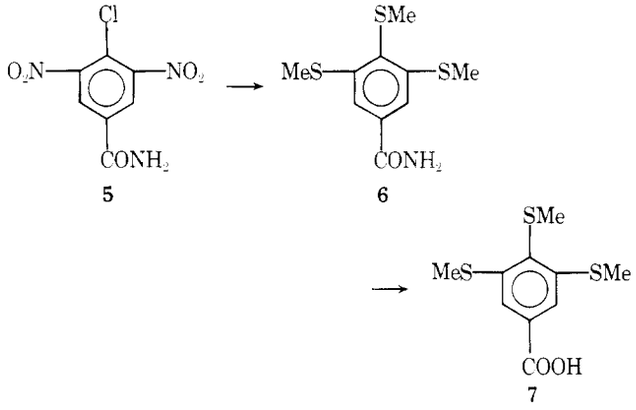
The second approach is illustrated in Scheme II. When 4-chloro-3,5-dinitrobenzamide (**5**) was allowed to react with excess methanethiol anion in DMF at room temperature for 1.5 h, 3,4,5-tris(methylthio)benzamide (**6**, 76%) was formed. This compound was hydrolyzed to yield 3,4,5-tris(methylthio)benzoic acid (**7**, 76%).

Scheme I



1 2 3 4

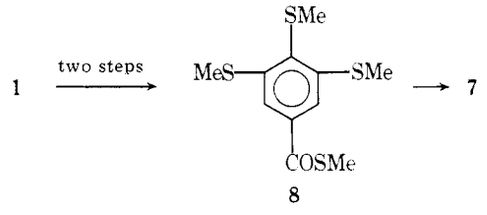
Scheme II



5 6

7

Scheme III



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The third procedure is shown in Scheme III. The benzoic acid **1** was first treated with a molar equivalent of 1,1′-carbonyldiimidazole in DMF at room temperature. The reaction mixture was then cooled and the intermediate was allowed to react with excess methanethiol anion. The isolated product was identified as the tris(methylthio) thioester **8** (71%). Hydrolysis of the ester yielded **7** (75%).

When the third procedure was utilized, the following thioesters were synthesized: **9a** (64% from 2-chloro-3-nitrobenzoic acid), **9b** (64% from 2-chloro-3,5-dinitrobenzoic acid), and **9c** (56% from 2,4-dichloro-3,5-dinitrobenzoic acid). Hydrolysis of these thioesters yielded the benzoic acids **10a** (87%), **10b** (93%), and **10c** (93%), respectively. Treatment of pentachlorobenzamide under the usual reaction conditions (Scheme II) for 27 h at room temperature yielded pentakis(methylthio)benzamide (**11**, 41%).

The thioethers were readily oxidized to the corresponding sulfones with hydrogen peroxide in acetic acid and these de-

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