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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.

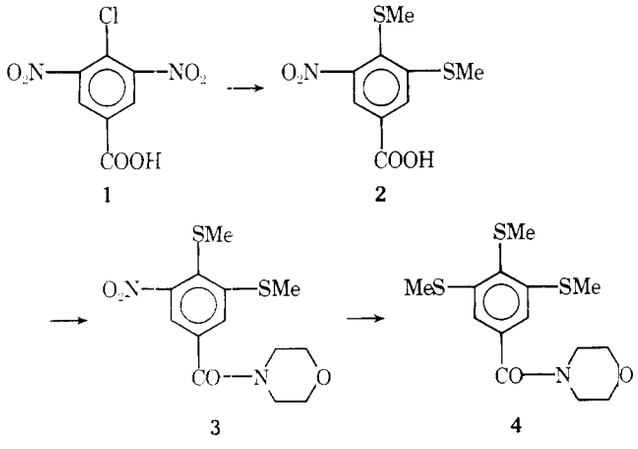
In a previous paper[1] we discussed the nucleophilic displacement of nitro groups, which were activated by *o*- or *p*-methylthio functions, with methanethiol anion. The objective of this work is to demonstrate the utility of this facile reaction for the preparation of bis-, tris-, tetrakis-, and pentakis(methylthio)benzoic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

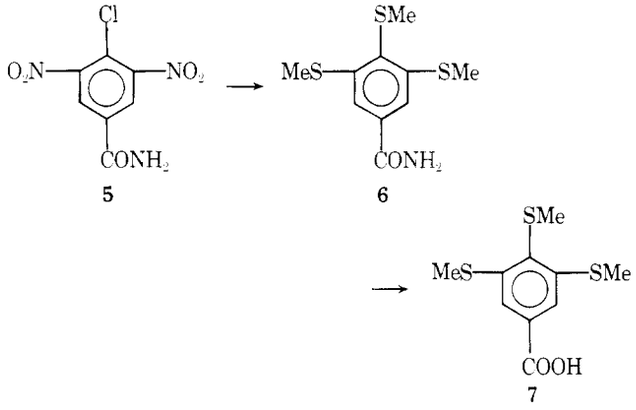
The second approach is illustrated in Scheme II. When 4-chloro-3,5-dinitrobenzamide (**5**) was allowed to react with excess methanethiol anion in DMF at room temperature for 1.5 h, 3,4,5-tris(methylthio)benzamide (**6**, 76%) was formed. This compound was hydrolyzed to yield 3,4,5-tris(methylthio)benzoic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

Scheme I



1 2 3 4

Scheme II



5 6

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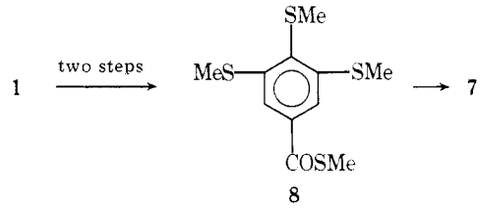
Scheme III



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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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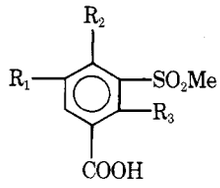
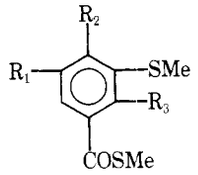
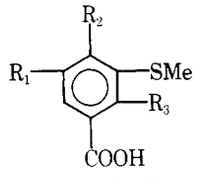
Table I. Synthesis of Methylsulfonylbenzoic Acids



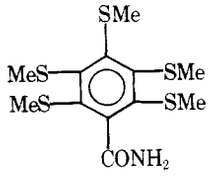
Compd	Reactant	R_1	R_2	R_3	Mp, °C	Yield, %
12a	**7**	SO_2Me	SO_2Me	H	287–293 dec	76
12b	**2**	NO_2	SO_2Me	H	270–280 dec	77
12c	**10a**	H	H	SO_2Me	225–227	26
12d	**10b**	SO_2Me	H	SO_2Me	274–277 dec	95
12e	**10c**	SO_2Me	SO_2Me	SO_2Me	247–250 dec	79



9a, $R_1 = R_2 = H$; $R_3 = SMe$
b, $R_2 = H$; $R_1 = R_3 = SMe$
c, $R_1 = R_2 = R_3 = SMe$

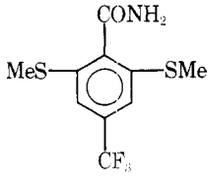


10a, $R_1 = R_2 = H$; $R_3 = SMe$
b, $R_2 = H$; $R_1 = R_3 = SMe$
c, $R_1 = R_2 = R_3 = SMe$



11

rivatives are summarized in Table I. Oxidation of **11** was accompanied by oxidative deamination followed by decarboxylation, and the product obtained was pentakis(methylsulfonyl)benzene (48%).[1] Oxidation of the bis(methylthio) derivative **13**, which was obtained from α,α,α-trifluoro-2,6-



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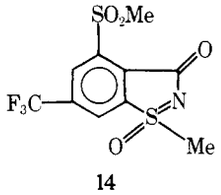
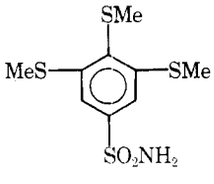


14

dinitro-*p*-toluamide by displacement with methanethiol anion in 80% yield, unexpectedly gave the 1,2-benzisothiazole-3-one 1-oxide **14** (73%). The synthesis of this ring system was first described by Stoss and Satzinger[2] using the reaction of *o*-(alkylsulfinyl)benzoic acid esters with hydrazoic acid.

4-Chloro-3,5-dinitrobenzenesulfonamide[3] was allowed to react with excess methanethiol anion at room temperature for 2 h, and the product obtained was the tris(methylthio) derivative **15** (71%). Oxidation of **15** with hydrogen peroxide in



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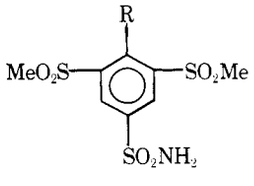
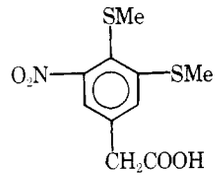


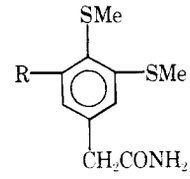
16a, R = SO_2Me
b, R = $NHCH(CH_2CH_3)_2$

acetic acid gave the tris(sulfone) **16a** (91%). Reaction of **16a** with 3-aminopentane in alcohol produced the aniline **16b** (72%). The NMR spectrum of **16b** showed a singlet aromatic proton signal and a singlet methylsulfonyl proton signal.

Still another example of the synthetic utility of the methanethiol anion displacement reaction involved treating 4-chloro-3,5-dinitrophenylacetic acid[4] under the usual reaction conditions (Scheme I). The product obtained was the bis(thioether) **17** (85%). As in the case of the related benzoic



17



18a, R = NO_2
b, R = SMe

acid derivative **2**, conditions could not be found for displacement of the second nitro group. The acid **17** was converted to its carboxamide **18a** (83%), which upon treatment with methanethiol anion gave the tris(thioether) **18b** (57%).

Discussion

The third method for the conversion of nitrobenzoic acids to the corresponding (methylthio)benzoic acid derivatives is probably the most general. It is possible that the use of an acid chloride, instead of the imidazole amide derivative, would yield the same thioester product, although this was not investigated.

The carboxylic acid or its derivative undoubtedly has a positive effect on the rate of displacement but, as was shown in the previous paper,[1] the same type of replacement reactions occurred in the presence of electron-donating substituents and the yields were similar. The same disadvantage noted in the previous examples was encountered with the benzoic acid derivatives. For example, treatment of 4-(methylthio)-3-nitrobenzamide or the corresponding morpholinamide with methanethiol anion under the usual conditions both led to the formation of complex mixtures. Thus, the requirement for an electronegative substituent in the position ortho to the methylthio function and meta to the nitro leaving group appears to be a general requirement for the displacement reaction.

With respect to the choice of the procedure to be used with a given substrate, no standard rules can be applied. For instance, treatment of the morpholinamide of 2-(methylthio)-3-nitrobenzoic acid with methanethiol anion, as in the first procedure, gave a complex mixture of products. However, the reaction of the free acid with methanethiol anion using the third procedure gave a 64% yield of the thioester **9a**.

Experimental Section

All starting materials are commercially available unless literature references are noted. Cold solution refers to ice bath conditions.

Lithium hydroxide was ground to a fine powder in order to facilitate solution. Since the addition of lithium hydroxide was exothermic, 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 structural assignment are given. Melting points were determined on a Mel-Temp apparatus and are uncorrected.

3,4-Bis(methylthio)-5-nitrobenzoic Acid (2). To a cold solution (under nitrogen) containing 7.4 g of 4-chloro-3,5-dinitrobenzoic acid (30 mmol) and 10 mL of methanethiol in 80 mL of DMF was added portionwise 10 g of lithium hydroxide. The mixture was stirred in the cold for 0.5 h and then poured into ice water and acidified with hydrochloric acid. The solid was collected and crystallized from alcohol to yield 6.2 g (80%) of product: mp 210–212 °C; NMR (Me_2SO-d_6) δ 2.44 (s, 3 H), 2.63 (s, 3 H), 7.92 (s, 1 H), and 8.00 (s, 1 H). Anal. Calcd for $C_9H_9NO_4S_2$: C, 41.69; H, 3.50; N, 5.40; S, 24.73. Found C, 41.46; H, 3.49; N, 5.53; S, 24.74.

4-[3,4-Bis(methylthio)-5-nitrobenzoyl]morpholine (3). 1,1′-Carbonyldiimidazole (5.8 g; 35.8 mmol) was added portionwise to a solution of 7.8 g of **2** (34.1 mmol) in 25 mL of DMF. The mixture was stirred at room temperature for 15 min, and then 5 mL of morpholine was added dropwise. The solution was stirred for 15 min and then poured into ice water. The solid was collected and crystallized from alcohol to yield 9.1 g (81%) of product, mp 179–180 °C. Anal. Calcd for $C_{13}H_{16}N_2O_4S_2$: C, 47.55; H, 4.91; N, 8.53; S, 19.53. Found: C, 47.81; H, 4.92; N, 8.50; S, 19.47.

4-[3,4,5-Tris(methylthio)benzoyl]morpholine (4). To a cold solution (under nitrogen) of 4.9 g of **3** (14.9 mmol) and 5 mL of methanethiol in 75 mL of DMF was added portionwise 3 g of lithium hydroxide. The mixture was stirred in the cold for 0.5 h and at room temperature for 1 h. The mixture was poured into ice water, and the solid was collected and crystallized from alcohol to yield 4.4 g (90%) of product: mp 113–114 °C; NMR ($CDCl_3$) δ 2.31 (s, 3 H), 2.38 (s, 6 H), and 6.84 (s, 2 H). Anal. Calcd for $C_{14}H_{19}NO_2S_3$: C, 51.03; H, 5.81; N, 4.25; S, 29.19. Found: C, 51.21; H, 5.95; N, 4.35; S, 28.97.

3,4,5-Tris(methylthio)benzamide (6). Lithium hydroxide (10 g) was added portionwise to a cold solution (under nitrogen) containing 9.8 g of 4-chloro-3,5-dinitrobenzamide (40 mmol) and 20 mL of methanethiol in 150 mL of DMF. The ice bath was removed and stirring was continued for 1.5 h. The mixture was poured into ice water, and the solid was collected and crystallized from alcohol to yield 7.9 g (76%) of product: mp 221–222 °C; NMR (Me_2SO-d_6) δ 2.32 (s, 3 H), 2.50 (s, 6 H), and 7.45 (s, 2 H). Anal. Calcd for $C_{10}H_{13}NOS_3$: C, 46.30; H, 5.05; N, 5.40; S, 37.08. Found: C, 46.13; H, 5.19; N, 5.38; S, 37.25.

3,4,5-Tris(methylthio)benzoic Acid (7). Potassium hydroxide (5 g) and 7.6 g of **6** (29.3 mmol) in 100 mL of alcohol was heated to reflux for 51 h. The mixture was poured into ice water and then acidified with hydrochloric acid. The solid was collected and crystallized from DMF–water to yield 5.8 g (76%) of product: mp 246–248 °C; NMR (Me_2SO-d_6) δ 2.30 (s, 3 H), 2.46 (s, 6 H), and 7.47 (s, 2 H). Anal. Calcd for $C_{10}H_{12}O_2S_3$: C, 46.13; H, 4.65; S, 36.94. Found: C, 46.33; H, 4.58; S, 36.82.

***S*-Methyl 3,4,5-Tris(methylthio)benzenecarbothioate (8).** To a solution containing 25 g of **1** (0.1 mol) in 125 mL of DMF was added portionwise 22.7 g of 1,1′-carbonyldiimidazole (0.14 mol). The mixture was stirred for 0.5 h and then cooled in an ice bath. Methanethiol (30 mL) was added to the solution (under nitrogen), and then 15 g of lithium hydroxide was added portionwise. The mixture was stirred in the cold for 0.5 h and at room temperature for 1 h. The mixture was then poured into ice water and the resulting solid was collected and crystallized from alcohol to yield 20.5 g (71%) of product: mp 121–123 °C; NMR ($CDCl_3$) δ 2.33 (s, 3 H), 2.45 (s, 9 H), and 7.36 (s, 2 H). Anal. Calcd for $C_{11}H_{14}OS_4$: C, 45.48; H, 4.86; S, 44.15. Found: C, 45.78; H, 4.75; S, 44.03.

3,4,5-Tris(methylthio)benzoic Acid (7). Potassium hydroxide (2 g) and 8 g of **8** (27.6 mmol) in 125 mL of alcohol was heated to reflux for 5 h. The solution was poured into ice water and then acidified with hydrochloric acid. The solid was collected and crystallized from alcohol to yield 5.4 g (75%) of product, mp 250–252 °C. The NMR spectrum was identical to that of **7** prepared above.

***S*-Methyl 2,3-Bis(methylthio)benzenecarbothioate (9a).** 1,1′-Carbonyldiimidazole (7.8 g; 48.1 mmol) was added portionwise to a solution of 8.1 g of 2-chloro-3-nitrobenzoic acid (40.2 mmol) in 80 mL of DMF. The mixture was stirred for 15 min and then cooled (under nitrogen) in an ice bath. Methanethiol (12 mL) was added and then 4 g of lithium hydroxide was added portionwise. The solution was stirred in the cold for 1 h and poured into ice water. The solid was collected and crystallized from alcohol–water to yield 6.3 g (64%) of product, mp 92–93 °C. Anal. Calcd for $C_{10}H_{12}OS_3$: C, 49.15; H, 4.95; S, 39.36. Found: C, 49.34; H, 4.91; S, 39.62.

***S*-Methyl 2,3,5-Tris(methylthio)benzenecarbothioate (9b).** To a solution containing 12.3 g of 2-chloro-3,5-dinitrobenzoic acid (49.9 mmol) in 120 mL of DMF was added portionwise 9.7 g of 1,1′-carbonyldiimidazole (59.9 mmol). The mixture was stirred for 15 min and then cooled (under nitrogen) in an ice bath. Methanethiol (12 mL) was added and then 5 g of lithium hydroxide was added portionwise. The mixture was allowed to warm to room temperature with stirring for 1.5 h. The product was isolated as in the case of **9a** to yield 9.3 g (64%), mp 123–124 °C. Anal. Calcd for $C_{11}H_{14}OS_4$: C, 45.48; H, 4.86; S, 44.15. Found: C, 45.67; H, 4.77; S, 44.43.

***S*-Methyl 2,3,4,5-Tetrakis(methylthio)benzenecarbothioate (9c).** 1,1′-Carbonyldiimidazole (13.6 g; 84 mmol) was added portionwise to a solution of 19.7 g of 2,4-dichloro-3,5-dinitrobenzoic acid (70.1 mmol) in 125 mL of DMF. The mixture was stirred for 15 min and then cooled (under nitrogen) in an ice bath. Methanethiol (30 mL) was added and then 15 g of lithium hydroxide was added portionwise. The solution was stirred in the cold for 0.5 h and at room temperature for 0.5 h. The product was isolated as in the case of **9a** to yield 13.2 g (56%); mp 93–94 °C. An analytical sample, mp 94–95 °C, was recrystallized. Anal. Calcd for $C_{12}H_{16}OS_5$: C, 42.82; H, 4.79; S, 47.63. Found: C, 43.11; H, 4.78; S, 47.89.

2,3-Bis(methylthio)benzoic Acid (10a). Potassium hydroxide (1 g) and 3 g of **9a** (12.3 mmol) in 50 mL of alcohol was refluxed for 3 h. The mixture was poured into ice water and then acidified with hydrochloric acid. The solid was collected and crystallized from alcohol–water to yield 2.3 g (87%) of product: mp 145–146 °C; NMR ($CDCl_3$) δ 2.45 (s, 6 H) and 7.40 (m, 3 H). Anal. Calcd for $C_9H_{10}O_2S_2$: C, 50.44; H, 4.70; S, 29.92. Found: C, 50.72; H, 4.84; S, 30.29.

2,3,5-Tris(methylthio)benzoic Acid (10b). Potassium hydroxide (1.5 g) and 6 g of **9b** (20.7 mmol) in 75 mL of alcohol was refluxed for 5.5 h. The product was isolated as in the case of **10a** to yield 5.0 g (93%): mp 146–147 °C; NMR ($CDCl_3$) δ 2.40 (s, 3 H), 2.43 (s, 3 H), 2.50 (s, 3 H), 7.10 (d, 1 H), and 7.43 (d, 1 H). Anal. Calcd for $C_{10}H_{12}O_2S_3$: C, 46.13; H, 4.65; S, 36.94. Found: C, 46.38; H, 4.56; S, 36.85.

2,3,4,5-Tetrakis(methylthio)benzoic Acid (10c). Potassium hydroxide (2 g) and 10 g of **9c** (29.8 mmol) in 125 mL of alcohol was refluxed for 5 h. The product was isolated as in the case of **10a** to yield 8.45 g (93%): mp 173–174 °C; NMR ($CDCl_3$) δ 2.48 (m, 12 H) and 7.50 (s, 1 H). Anal. Calcd for $C_{11}H_{14}O_2S_4$: C, 43.11; H, 4.60; S, 41.85. Found: C, 43.13; H, 4.61; S, 41.75.

2,3,4,5,6-Pentakis(methylthio)benzamide (11). To a cold solution (under nitrogen) containing 11.7 g of pentachlorobenzamide (39.9 mmol) and 20 mL of methanethiol in 120 mL of DMF was added portionwise 10 g of lithium hydroxide. The ice bath was removed and the mixture was stirred for 27 h. It was poured into ice water, and the resulting solid was collected and crystallized from Me_2SO–water to yield 5.7 g (41%) of product: mp 174–176 °C; NMR (Me_2NCHO-d_7) δ 2.46 (s, 6 H) and 2.55 (s, 9 H). Anal. Calcd for $C_{12}H_{17}NOS_5$: C, 40.99; H, 4.87; N, 3.98; S, 45.60. Found: C, 40.69; H, 4.63; N, 3.92; S, 45.75.

3,4,5-Tris(methylsulfonyl)benzoic Acid (12a). A solution of 2.4 g of **7** (9.2 mmol) in 15 mL of 30% hydrogen peroxide and 30 mL of acetic acid was heated in an open flask at steam-bath temperature for 1 h. More hydrogen peroxide (15 mL) was added and the mixture was heated for an additional 18 h. The solid residue was crystallized from DMF–water to yield 2.5 g (76%) of product, mp 287–293 °C dec. Anal. Calcd for $C_{10}H_{12}O_8S_3$: C, 33.70; H, 3.39; S, 26.99. Found: C, 33.50; H, 3.48; S, 27.23.

3,4-Bis(methylsulfonyl)-5-nitrobenzoic Acid (12b). A solution of 5 g of **2** (19.3 mmol) in 30 mL of 30% hydrogen peroxide and 60 mL of acetic acid was heated in an open flask at steam-bath temperature for 1 h. Hydrogen peroxide (15 mL) was added and heating was continued for 19 h. The solution was cooled to yield 4.8 g (77%) of product, mp 270–280 °C dec. Anal. Calcd for $C_9H_9NO_8S_2$: C, 33.44; H, 2.81; N, 4.33; S, 19.84. Found: C, 33.44; H, 2.81; N, 4.52; S, 20.13.

2,3-Bis(methylsulfonyl)benzoic Acid (12c). A solution of 3 g of **10a** (12.3 mmol) in 15 mL of 30% hydrogen peroxide and 30 mL of acetic acid was heated in an open flask at steam-bath temperature for 45 min. Hydrogen peroxide (15 mL) was added and heating was continued for 2 h. The mixture was filtered hot, cooled, and extracted twice with ethyl acetate. The combined organic extracts were washed three times with water, dried, and evaporated. The crude material was crystallized from ethyl acetate–hexane to yield 0.9 g (26%) of product, mp 225–227 °C. Anal. Calcd for $C_9H_{10}O_6S_2$: C, 38.84; H, 3.62; S, 23.04. Found: C, 38.55; H, 3.80; S, 22.83.

2,3,5-Tris(methylsulfonyl)benzoic Acid (12d). A solution containing 2.4 g of **10b** (9.2 mmol) in 10 mL of 30% hydrogen peroxide and 20 mL of acetic acid was heated in an open flask at steam-bath temperature for 1 h. Hydrogen peroxide (10 mL) was added and heating

was continued for 18 h. The solid residue was crystallized from water to yield 3.1 g (95%) of product, mp 274–277 °C dec. Anal. Calcd for $C_{10}H_{12}O_8S_3$: C, 33.70; H, 3.39; S, 26.99. Found: C, 33.91; H, 3.22; S, 27.29.

2,3,4,5-Tetrakis(methylsulfonyl)benzoic Acid (12e). A solution of 2.5 g of **10c** (8.2 mmol) in 15 mL of 30% hydrogen peroxide and 30 mL of acetic acid was heated in an open flask for 1 h. Hydrogen peroxide (15 mL) was added and heating was continued for 18 h. The solid residue was crystallized from water to yield 2.8 g (79%) of product, mp 247–250 °C dec. Anal. Calcd for $C_{11}H_{14}O_{10}S_4$: C, 30.41; H, 3.25; S, 29.52. Found: C, 30.66; H, 3.10; S, 29.72.

Oxidation of Pentakis(methylthio)benzamide. A solution containing 2.5 g of **11** (7.1 mmol) in 15 mL of 30% hydrogen peroxide and 30 mL of acetic acid was heated in an open flask for 1 h. Hydrogen peroxide (15 mL) was added and heating was continued for 1 h. The solution was cooled to yield 1.6 g (48%) of product, mp >350 °C. It was identified by microanalysis and NMR as pentakis(methylsulfonyl)-benzene.[1]

α,α,α-Trifluoro-2,6-dinitro-*p*-toluamide. A solution of 5.0 g of α,α,α-trifluoro-2,6-dinitro-*p*-tolunitrile[5] (19.2 mmol) in 10 mL of 80% sulfuric acid was heated at steam-bath temperature for 5 h and then poured into ice water. The product was collected and crystallized from alcohol to yield 3.6 g (68%) of product, mp 256–258 °C. Anal. Calcd for $C_8H_4F_3N_3O_5$: C, 34.42; H, 1.44; N, 15.09. Found: C, 34.65; H, 1.29; N, 14.86.

α,α,α-Trifluoro-2,6-bis(methylthio)-*p*-toluamide (13). To a cold solution (under nitrogen) of 11.1 g of α,α,α-trifluoro-2,6-dinitro-*p*-toluamide (39.8 mmol) and 10 mL of methanethiol in 120 mL of DMF was added portionwise 5 g of lithium hydroxide. The mixture was stirred in the cold for 0.5 h and then poured into ice water. The solid was collected and crystallized from alcohol to yield 9.0 g (80%) of product: mp 249–250 °C; NMR (Me_2SO-d_6) δ 2.50 (s, 6 H) and 7.39 (s, 2 H). Anal. Calcd for $C_{10}H_{10}F_3NOS_2$: C, 42.70; H, 3.58; N, 4.98. Found: C, 42.88; H, 3.73; N, 4.99.

1-Methyl-4-(methylsulfonyl)-6-(trifluoromethyl)-1*H*,3*H*-1,2-benzisothiazol-3-one 1-Oxide (14). A solution of 6.5 g of **13** (23.1 mmol) in 15 mL of 30% hydrogen peroxide and 30 mL of acetic acid was heated in an open flask at steam-bath temperature for 1 h. Hydrogen peroxide (15 mL) was added and heating was continued for 1 h. The mixture was cooled and the product was collected to yield 5.55 g (73%): mp 269–271 °C; NMR (Me_2SO-d_6) δ 3.62 (s, 3 H), 3.97 (s, 3 H), 8.60 (m, 1 H), and 9.35 (m, 1 H); IR (Nujol) 1698 cm^{-1}; MS 327 (M^+). Anal. Calcd for $C_{10}H_8F_3NO_4S_2$: C, 36.70; H, 2.45; N, 4.28; S, 19.57. Found: C, 36.69; H, 2.57; N, 4.31; S, 19.74.

3,4,5-Tris(methylthio)benzenesulfonamide (15). To a cold mixture (under nitrogen) containing 5.6 g of 4-chloro-3,5-dinitrobenzenesulfonamide[3] (19.9 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 15 min and at room temperature for 2 h. The mixture was poured into ice water which was then acidified with hydrochloric acid. The solid was collected and crystallized from DMF–water to yield 4.2 g (71%) of product: mp 260–262 °C; NMR (Me_2SO-d_6) δ 2.34 (s, 3 H), 2.56 (s, 6 H), and 7.37 (s, 2 H). Anal. Calcd for $C_9H_{13}NO_2S_4$: C, 36.59; H, 4.44; N, 4.74; S, 43.41. Found: C, 36.74; H, 4.69; N, 4.96; S, 43.62.

3,4,5-Tris(methylsulfonyl)benzenesulfonamide (16a). A solution of 6 g of **15** (20.3 mmol) in 50 mL of 30% hydrogen peroxide and 75 mL of acetic acid was heated in an open flask at steam-bath temperature for 3 h. The mixture was cooled and the product was collected to yield 7.1 g (91%) of product, mp 321–325 °C dec. Anal. Calcd for $C_9H_{13}NO_8S_4$: C, 27.61; H, 3.35; N, 3.58; S, 32.76. Found: C, 27.78; H, 3.35; N, 3.66; S, 32.65.

4-[(1-Ethylpropyl)amino]-3,5-bis(methylsulfonyl)benzenesulfonamide (16b). 3-Aminopentane (10 mL) and 2.6 g of **16a** (6.7 mmol) in 100 mL of alcohol was heated at reflux temperature for 18 h. The solution was cooled and the product was collected to yield 1.9 g (72%): mp 192–194 °C; NMR (Me_2SO-d_6) δ 3.38 (s, 6 H) and 8.50 (s, 2 H). Anal. Calcd for $C_{13}H_{22}N_2O_6S_3$: C, 39.18; H, 5.56; N, 7.03; S, 24.14. Found: C, 39.46; H, 5.35; N, 7.17; S, 23.91.

3,4-Bis(methylthio)-5-nitrophenylacetic Acid (17). To a cold solution (under nitrogen) containing 5.2 g of 4-chloro-3,5-dinitrophenylacetic acid[4] (20 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 1 h. It was poured into ice water, which was then acidified with hydrochloric acid. The solid was collected and crystallized from alcohol to yield 4.6 g (85%) of product, mp 165–168 °C. Anal. Calcd for $C_{10}H_{11}NO_4S_2$: C, 43.94; H, 4.06; N, 5.12; S, 23.46. Found: C, 43.97; H, 4.11; N, 5.35; S, 23.19.

3,4-Bis(methylthio)-5-nitrophenylacetamide (18a). 1,1′-Carbonyldiimidazole (3.3 g; 20 mmol) was added portionwise to a solution of 4.3 g of **17** (16 mmol) in 25 mL of DMF. The mixture was stirred for 10 min, and then 10 mL of concentrated ammonium hydroxide was added dropwise. The mixture was then stirred for 1 h and poured into ice water. The solid was collected and crystallized from alcohol to yield 3.6 g (83%) of product, mp 195–197 °C. Anal. Calcd for $C_{10}H_{12}N_2O_3S_2$: C, 44.10; H, 4.44; N, 10.29; S, 23.55. Found: C, 44.32; H, 4.53; N, 10.23; S, 23.80.

3,4,5-Tris(methylthio)phenylacetamide (18b). Lithium hydroxide (5 g) was added portionwise to a cold solution (under nitrogen) containing 7.5 g of **18a** (27 mmol) and 10 mL of methanethiol in 100 mL of DMF. The mixture was stirred in the cold for 15 min and at room temperature for 7 h and then poured into ice water. The solid was collected and crystallized from alcohol to yield 4.2 g (57%) of product: mp 178–180 °C; NMR (Me_2SOd_6) δ 2.26 (s, 3 H), 2.42 (s, 6 H), 3.47 (s, 2 H), and 6.93 (s, 2 H). Anal. Calcd for $C_{11}H_{15}NOS_3$: C, 48.32; H, 5.53; N, 5.12; S, 35.18. Found: C, 48.22; H, 5.31; N, 5.36; S, 35.03.

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Registry No.—**1,** 118-97-8; **2,** 65517-12-6; **3,** 65517-13-7; **4,** 65517-14-8; **5,** 20731-63-9; **6,** 65517-15-9; **7,** 65517-16-0; **8,** 65517-17-1; **9a,** 65517-18-2; **9b,** 65517-19-3; **9c,** 65517-20-6; **10a,** 65517-21-7; **10b,** 65517-22-8; **10c,** 65517-23-9; **11,** 65517-24-0; **12a,** 65517-25-1; **12b,** 65517-26-2; **12c,** 65517-00-2; **12d,** 65517-01-3; **12e,** 65517-02-4; **13,** 65517-03-5; **14,** 65517-04-6; **15,** 65517-05-7; **16a,** 65517-06-8; **16b,** 65517-07-9; **17,** 65517-08-0; **18a,** 65517-09-1; **18b,** 65517-10-4; 2-chloro-3,5-dinitrobenzoic acid, 2497-91-8; 2,4-dichloro-3,5-dinitrobenzoic acid, 52729-03-0; pentachlorobenzamide, 29956-85-2; pentakis(methylsufonyl)benzene, 65516-84-9; α,α,α-trifluoro-2,6-dinitro-*p*-toluamide, 65517-11-5; α,α,α-trifluoro-2,6-dinitro-*p*-tolunitride, 35213-02-6; 4-chloro-3,5-dinitrobenzenesulfonamide, 35168-73-1; 4-chloro-3,5-dinitrophenylacetic acid, 6093-34-1; 2-chloro-3-nitrobenzoic acid, 3970-35-2; methanethiol anion, 17302-63-5.

References and Notes

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