Anal. Calcd. for $C_{16}H_{26}Cl_2N_2O_2$: C, 55.00; H, 7.50; N, 8.02. Found: C, 54.73; H, 7.37; N, 8.08.

Ethyl 1-(N-methylbenzamido)cyclohexanecarboxylate (II. R = COC_6H_5; R′ = CH_3). To a stirred solution containing 9.2 g. of ethyl 1-(methylamino)cyclohexanecarboxylate, 50 ml. of chloroform, and 10 ml. of pyridine was added dropwise a solution of 10 g. of benzoyl chloride in 10 ml. of chloroform while the temperature was maintained at 10° by means of an ice bath. The solution was refluxed for 2 hr., the solvents were evaporated and the residue was taken up in benzene. The benzene solution was washed with successive portions of 3*N* hydrochloric acid, 20% potassium carbonate and water. The solvent was evaporated and the residue recrystallized from pentane, m.p. 62–63°, yield 6.8 g. (47%).

Anal. Calcd. for $C_{17}H_{23}NO_3$: C, 70.86; H, 8.01; N, 4.84. Found: C, 70.64; H, 7.97; N, 4.69.

General procedure for the preparation of aminocyclohexane cyano esters and aminocyclohexane diesters. A mixture consisting of molar quantities of II (R = H; R′ = H or CH_3), powdered anhydrous potassium carbonate and a cyano- or carbethoxyalkyl bromide was stirred and heated at 105° over a period of 3 days. Ice water (500 ml.) was added and the two layers were separated. The aqueous layer was extracted with three 500-ml. portions of ether and the extracts were combined with the original organic layer. The solution was dried and distilled. The following compounds were prepared by this method:

Ethyl 1-(3-cyanopropylamino)cyclohexanecarboxylate (II. R = H; R′ = $(CH_2)_3CN$), b.p. 136–139°/0.8 mm., n_D^{28} 1.4668, yield 76%.

Anal. Calcd. for $C_{13}H_{22}N_2O_2$: C, 65.51; H, 9.31; N, 11.76. Found: C, 65.40; H, 9.35; N, 11.47.

Ethyl 1-(3-carbethoxypropylamino)cyclohexanecarboxylate (II. R = H; R′ = $(CH_2)_3COOC_2H_5$), b.p. 104–106°/0.05 mm., n_D^{29} 1.4581, yield 87%. The base was converted into a hydrochloride, melting after a recrystallization from absolute ether at 140–142°.

Anal. Calcd. for $C_{15}H_{28}ClNO_4$: C, 55.97; H, 8.77; N, 4.35. Found: C, 55.87; H, 8.77; N, 4.32.

Ethyl 1-(3-cyanopropylmethylamino)cyclohexanecarboxylate (II. R = CH_3; R′ = $(CH_2)_3CN$), b.p. 122–125°/0.05 mm., n_D^{27} 1.4732, yield 65%.

Anal. Calcd. for $C_{14}H_{24}N_2O_2$: C, 66.63; H, 9.59; N, 11.10. Found: C, 66.37; H, 9.46; N, 11.13.

Ethyl 1-(carbethoxymethylmethylamino)cyclohexanecarboxylate (II. R = CH_3; R′ = $CH_2COOC_2H_5$), b.p. 108–109°/0.06 mm., n_D^{26} 1.4605, yield 93%.

Anal. Calcd. for $C_{14}H_{25}NO_4$: C, 61.96; H, 9.29; N, 5.16. Found: C, 62.25; H, 9.31; N, 5.34.

Ethyl 1-(3-carbethoxypropylmethylamino)cyclohexanecarboxylate (II. R = CH_3, R′ = $(CH_2)_3COOC_2H_5$), b.p. 125–130°/0.05 mm., n_D^{28} 1.4636, yield 97%.

Anal. Calcd. for $C_{16}H_{29}NO_4$: C, 64.18; H, 9.76; N, 4.68. Found: C, 64.00; H, 9.92; N, 4.52.

Ethyl 1-(N-3-carbethoxypropylbenzamido)cyclohexanecarboxylate (II. R = COC_6H_5; R′ = $(CH_2)_3COOC_2H_5$). A mixture consisting of 28.5 g. of ethyl 1-(3-carbethoxypropylamino)cyclohexanecarboxylate, 17 g. of benzoyl chloride, and 100 ml. of dry benzene was refluxed for 2 hr. Ethanol (20 ml.) was added and refluxing was continued for another 2 hr. The solution was washed with successive portions of 10% potassium hydroxide, 3*N* hydrochloric acid, and saturated potassium bicarbonate solution. After drying and removal of the solvent the residual viscous oil was distilled, b.p. 200–205°/0.05 mm., n_D^{30} 1.5122, yield 34 g. (78%).

Anal. Calcd. for $C_{22}H_{31}NO_5$: C, 67.84; H, 8.02; N, 3.60. Found: C, 67.88; H, 7.90; N, 3.72.

Ethyl 1-methyl-1-azaspiro[5.5]undecan-5-one-4-carboxylate (I, R = $COOC_2H_5$) *hydrochloride.* A suspension of 2.45 g. of sodium hydride in 35 ml. of dry benzene was flushed with nitrogen and a solution containing 13.5 g. of ethyl 1-(3-carbethoxypropylmethylamino)cyclohexanecarboxylate, 10 ml. of dry benzene, and 0.2 ml. of anhydrous ethanol was added. The reaction mixture was stirred and refluxed for 10 hr., cooled to 5°, and 6 ml. of glacial acetic acid and 5.5 ml. of water were added successively.

The suspension was filtered and the filtrate was evaporated to dryness under reduced pressure. The residue was dissolved in 200 ml. of ether and the solution was dried and saturated with gaseous hydrogen chloride. The precipitate was collected and recrystallized from ether-acetone (4:1), m.p. 177–178°, yield 11 g. (84%).

Anal. Calcd. for $C_{14}H_{24}ClNO_3$: C, 58.02; H, 8.35; N, 4.83. Found: C, 58.22; H, 8.32; N, 4.81.

1-Methyl-1-azaspiro[5.5]undecan-5-one (I. R = H) *hydrochloride.* A solution of 7.2 g. of ethyl 1-methyl-1-azaspiro [5.5]undecan-5-one-4-carboxylate hydrochloride in 40 ml. of 6*N* hydrochloric acid was refluxed for 2 hr. After cooling the solution was made basic with 20% potassium hydroxide. The resulting oil was extracted with several portions of ether and the extract was dried and distilled, b.p. 68–69°/0.06 mm., yield 3.8 g. (84%). The base was converted into its hydrochloride which melted after a recrystallization from ether-ethanol at 217–218°.

Anal. Calcd. for $C_{11}H_{20}ClNO$: C, 60.67; H, 9.26; N, 6.43. Found: C, 60.80; H, 9.11; N, 6.67.

1-Methyl-1-azaspiro[5.5]undecan-5-one (I. R = H) *methiodide.* A solution consisting of 8.4 g. of ethyl 1-methyl-1-azaspiro[5.5]undecan-5-one-4-carboxylate, 50 ml. of absolute ethanol, and 5 ml. of methyl iodide was refluxed for 2 hr. The solution was condensed to one-third of its original volume and 100 ml. of ether was added. The precipitate was filtered and recrystallized from acetone-ether, m.p. 99–102° dec., yield 4.6 g. (33%).

Anal. Calcd. for $C_{12}H_{22}INO$: C, 44.59; H, 6.86; N, 4.33. Found: C, 44.72; H, 7.15; N, 4.36.

1-(2-Hydroxyethylmethylamino)cyclohexanemethanol (III. X = OH). To a stirred suspension of 13.7 g. of lithium aluminum hydride in 600 ml. of ether was added dropwise a solution of 48 g. of ethyl 1-(carbethoxymethylmethylamino)-cyclohexanecarboxylate in 200 ml. of ether. The reaction mixture was refluxed for 12 hr. and the excess hydride destroyed by dropwise addition of 20% sodium hydroxide. The solution was filtered and distilled, b.p. 105–106°/0.03 mm., n_D^{26} 1.5013, yield 23.5 g. (71%).

Anal. Calcd. for $C_{10}H_{21}NO_2$: C, 64.13; H, 11.30; N, 7.48. Found: C, 63.93; H, 11.34; N, 7.66.

1-(2-Chloroethylmethylamino)-1-chloromethylcyclohexane (III. X = Cl) *hydrochloride.* A solution of 14 g. of the diol III (X = OH) in 25 ml. of dry benzene was saturated with gaseous hydrogen chloride, 23 g. of thionyl chloride was added and the mixture was stirred and heated at 55° over a period of 3 hr. The solvent was evaporated under reduced pressure and the residue was dissolved in 20 ml. of absolute ethanol. The solution was refluxed briefly and the solvent was evaporated. The solid residue was recrystallized from ethyl acetate and from benzene, m.p. 118–122°, yield 16.5 g. (85%).

Anal. Calcd. for $C_{10}H_{20}Cl_2N$: C, 46.08; H, 7.72; N, 5.38. Found: C, 45.95; H, 7.65; N, 5.64.

RESEARCH DIVISION
ETHICON, INC.
SOMERVILLE, N. J.

Synthesis of 3,3′-Thiobis(6-methylphenol)

FRANK J. KREYSA, THOMAS R. STEADMAN, AND ALIO J. BUSELLI

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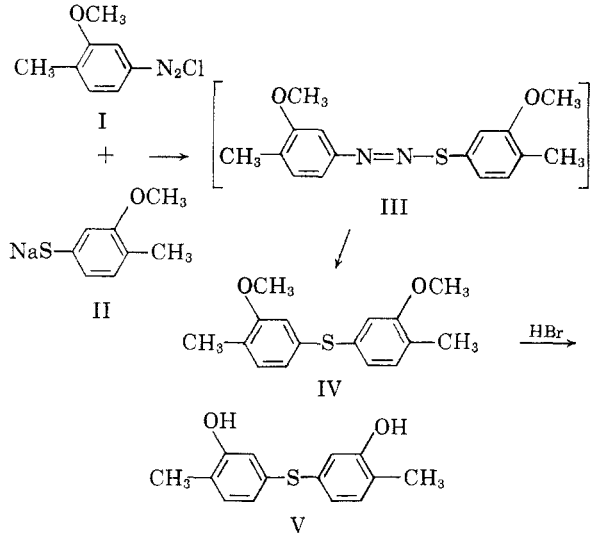
In the course of the synthesis of certain inhibitors and polymer stabilizers, we became interested in making diaryl sulfides with phenolic groups *meta* to

the sulfur bridge. Because suitable synthetic methods are not available, we have utilized an approach based on the diazotization and coupling of substituted anisidines rather than phenols.[1] The product is an ether which must be hydrolyzed to the desired *meta*-dihydroxydiaryl sulfide.

The outline of the experimental procedure for the preparation of 3,3′-thiobis(6-methylphenol) follows below:



The diazotized 4-methyl-*m*-anisidine (I) was prepared from 5-nitro-*o*-toluidine,[2] and the sodium salt of 3-methoxy 4-methylbenzenethiol (II) from 4-methyl-*m*-anisidine *via* the ethyl xanthate reaction.[3]

EXPERIMENTAL

3-Methoxy-4-methylbenzenethiol. The procedure was essentially the same as that reported for *m*-toluenethiol.[3] The product, obtained in 43.3% yield, was a colorless oil boiling at 145° at 1 mm. Its infrared spectrum showed the characteristic −SH group.

Anal. Calcd. for $C_8H_{10}OS$: C, 62.26; H, 6.55; S, 20.79. Found: C, 62.10; H, 6.07; S, 21.19.

3,3′-Thiobis(6-methylanisole) (IV). Diazotized 4-methyl-*m*-anisidine (11.2 g.) was slowly added to a warm (70°) alkaline solution of 10.0 g. of 3-methoxy-4-methylbenzenethiol. A yellow precipitate (III) formed which rapidly decomposed with the evolution of nitrogen (Caution!) and the formation of a brown oil. After the mixture had been kept at 70° for about 1 hr. it was steam distilled (to remove 4.2 g. of unchanged 3-methoxy-4-methylbenzenethiol), and then extracted with ether. The brown ether extract was washed with dilute sodium hydroxide, followed by water, and distilled *in vacuo*. The product (5.0 g.) came over at 165–205° at 0.2 mm.

Anal. Calcd. for $C_{16}H_{18}O_2S$: C, 70.00; H, 6.60; S, 11.67. Found: C, 70.51; H, 6.18; S, 11.25.

3,3′Thiobis(6-methylphenol) (V). To 22.5 g. of acetic anhydride was added, cautiously and with cooling, 9.0 g. of 48% hydrobromic acid, followed by 5.0 g. of 3,3′-thiobis(6-methoxyanisole). The mixture was then permitted to reflux for 6 hr.

After removing the excess hydrobromic and acetic acids *in vacuo*, the residual oil was stirred with 30 ml. of 10% sodium hydroxide solution for an hour at 95°. An ether extraction removed any unhydrolyzed methoxy compound; the alkaline residue was then acidified with 10 ml. of concd. hydrochloric acid and extracted with ether. The product (1.0 g.) distilled at 210–235° and 0.3 mm. in the atmosphere of nitrogen, and came over as a very viscous light amber oil. It solidified on standing and crystallized from petroleum ether (b.p. 30–60°) as white odorless solid, m.p. 85–87°.

Anal. Calcd. for $C_{14}H_{14}O_2S$: C, 68.26; H, 5.73; S, 13.02. Found: C, 68.19; H, 5.89, S, 12.79.

WASHINGTON RESEARCH CENTER
W. R. GRACE & CO.
CLARKSVILLE, MD.

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Homopiperazine and Its Derivatives. II.[1] A Convenient Synthesis of 1-Methylhomopiperazine

F. POPPELSDORF, R. C. MYERLY, AND R. B. CONROW

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1-Methylhomopiperazine is a pharmaceutical intermediate of interest inasmuch as several of its derivatives have recently been reported to have useful physiological activity.[2–4] It has been made by lithium aluminum hydride reduction of 1-methyl 5-homopiperazinone[2,5,6]; by the catalytic cyclodehydration of *N*-(2′-hydroxyethyl)-*N*-methyl-1,3-propanediamine[7]; and by the catalytic reductive cyclization of *N*- (or *N*′-) (2-cyanoethyl)-*N*-methylethylenediamine.[1] These preparative methods suffer from the disadvantage of mediocre yields or of being based on relatively inaccessible starting materials.

We present a simple and convenient synthesis of 1-methylhomopiperazine involving the reductive methylation of homopiperazine. Homopiperazine is now readily available by catalytic reductive cyclization of *N*-(2-cyanoethyl)ethylenediamine,[1] the addition product of ethylenediamine and acrylonitrile.

Treatment under pressure of a methanolic solution of homopiperazine with aqueous formaldehyde (1.11 molecular proportions), hydrogen, and Raney

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