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The Reaction of Dihalotetramethylbenzenes with Fuming Nitric Acid as a New Convenient Route to Some Dihalotrimethylbenzylic Compounds[1]

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Products obtained by the nitration of three isomeric dichloro and dibromotetramethylbenzenes with fuming nitric acid have been investigated. 3,6-Dihalo-1,2,4,5-tetramethylbenzene (dihalodurene) gave mainly 3,6-dihalo-2,4,5-trimethylbenzyl nitrate or 1,2-bis(nitrooxymethyl)-3,6-dihalo-4,5-dimethylbenzene, depending on the reaction temperature and the amount of nitrating agent. 4,6-Dihalo-1,2,3,5-tetramethylbenzene (dihaloisodurene) yielded a mixture of 3,5-dihalo-2,4,6-trimethylbenzyl nitrate and 2,6-dihalo-3,4,5-trimethylbenzyl nitrate, the latter in somewhat greater amount. 5,6-Dihalo-1,2,3,4-tetramethylbenzene (dihaloprehnitene) gave 5,6-dihalo-2,3,4-trimethylbenzyl nitrate as the sole nitrooxylation product. The reaction affords a new convenient route to precursors of various polysubstituted benzylic compounds hitherto not easily obtained by ordinary methods. Physical properties of some dihalotrimethylbenzylic compounds (chloride, nitrate, acetate, alcohol, and bisbenzyl ether) have been recorded.

On treatment with fuming nitric acid at low temperature, polyalkylbenzenes and their derivatives undergo side-chain nitrooxylation to give benzyl nitrates.[2-7] A noteworthy feature of this unusual reaction is that the product is usually composed of one isomer of specific orientation. Electron-withdrawing substituent brings about preferential side-chain nitrooxylation on the ortho methyl group, while the electron-releasing group is found to facilitate substitution on the meta methyl group. High positional selectivity, predominant substituent effect, and smooth occurrence of the reaction under mild conditions point to an ionic process.

From an interest in the anomalous nitration of polyalkylated aromatics, we investigated nitration of three isomeric dichloro and dibromotetramethylbenzenes with a view to obtaining further information on the general pattern of side-chain substitution in these systems, and clarifying the scope of synthetic utility of the reaction as a simple route to some polysubstituted benzylic compounds which are otherwise laborious to prepare.

Both dichlorotetramethylbenzenes and dibromotetramethylbenzenes react slowly with fuming nitric acid in dichloromethane at 0°C to give a pale yellow to light brown half-crystalline solid, mostly composed of dihalotrimethylbenzyl nitrates. The bromo compounds appear to be somewhat more reactive than the chloro compounds, and of the three isomeric dihalotetramethylbenzenes, 4,6-dihalo-1,2,3,5-tetramethylbenzene (dihaloisodurene) seems to be the most reactive.

1,2,4,5-Tetramethylbenzene (Durene) Series. 3,6-Dichloro-1,2,4,5-tetramethylbenzene (dichlorodurene) and 3,6-dibromo-1,2,4,5-tetramethylbenzene (dibromodurene) both reacted slowly with fuming nitric acid to give a crystalline solid, the major component of which was either dihalotrimethylbenzyl nitrate, or bis(nitrooxymethyl)dihalodimethylbenzene depending on the amount of nitric acid and the reaction temperature. With the use of three or four equivalent amounts of nitric acid at low temperature, the product was almost exclusively 3,6-dihalo-2,4,5-trimethylbenzyl nitrate. However, when dihalodurene was treated with a large excess of fuming nitric acid in an ice bath and the mixture was left standing for several hours, allowing the temperature of the system to gradually rise to room temperature, the product was a bis(nitrooxymethyl)dihalodimethylbenzene accompanied by some 5-nitro-3,6-dihalo-1,2,4-trimethylbenzene. If the reaction was allowed to proceed for a longer period, the latter compound constituted a significant portion of the product mixture. This product was no doubt derived from the initially formed benzyl nitrate through the replacement of the nitrooxymethyl group by the nitro group. Theoretically, three isomeric bis(nitrooxymethyl)dibromodimethyl-

1) The Reaction of Polysubstituted Aromatics. XXII. Part XXI: This Bulletin, **44**, 133 (1971).

2) L. I. Smith and S. A. Harris, *J. Amer. Chem. Soc.*, **57**, 1289 (1935); L. I. Smith and D. Tennenbaum, *ibid.*, **57**, 1293 (1935); L. I. Smith, F. L. Taylor, and I. M. Webster, *ibid.*, **59**, 1082 (1937); H. Suzuki and K. Nakamura, This Bulletin, **43**, 473 (1970).

3) L. I. Smith and J. W. Horner, *J. Amer. Chem. Soc.*, **62**, 1349 (1940); H. Suzuki, This Bulletin, **43**, 481 (1970).

4) H. Suzuki, This Bulletin., **43**, 879 (1970).

5) H. Suzuki, *Nippon Kagaku Zasshi*, **91**, 179 (1970).

6) K. Nakamura, This Bulletin., **44**, 133 (1971).

7) H. Suzuki and K. Nakamura, *ibid.*, **44**, 227 (1971).

benzenes can be derived from dibromodurene, and two of them, 1,3-bis(nitrooxymethyl)-2,5-dibromo-4,6-dimethylbenzene (I) and 1,4-bis(nitrooxymethyl)-2,5-dibromo-3,6-dimethylbenzene(II), were prepared from the corresponding bis(chloromethyl)benzenes by treatment with silver nitrate in hot acetonitrile. However, neither of these authentic specimens was found to be identical with the dinitrate obtained from dibromodurene. The bisnitrooxylated product is, therefore, most likely to be 1,2-bis(nitrooxymethyl)-3,6-dibromo-4,5-dimethylbenzene (III), although the authentic specimen is not available yet. This structural assignment is consistent with the observed directing effect of halogen atom and nitrooxymethyl group for the side-chain nitrooxylation of polymethylbenzene derivatives. The combined effect of the ortho/meta directing halogen[3] and the ortho directing nitrooxymethyl group[4] favors structure III over I and II.

Further nitrooxylation of bis(nitrooxymethyl)benzene could not be observed even by the action of a large excess of cold fuming nitric acid for a prolonged period. At somewhat higher temperature, the decomposition of the nitrate or the bis(nitrooxymethyl)-benzene into nitro or carbonyl compounds became prominent. No attempt has been made to identify them.

Chromatography of the crude nitration product on alumina requires some precaution since the active alumina converts the nitrate into bisbenzyl ether and benzyl alcohol during elution with benzene and ethanol. Dichlorotrimethylbenzyl nitrates were more readily decomposed than the bromo compounds. Light petroleum eluted unchanged material and benzyl nitrate, and the light petroleum - benzene mixture eluted bisbenzyl ether and nitro compound. Recovery of benzyl nitrates was usually unsatisfactory. Benzyl alcohol, bis(hydroxymethyl)benzene and unidentified carbonyl compounds were obtained from diethyl ether - ethanol eluates. The relative ratio of these products varied considerably depending on the activity of alumina and length of column.

1,2,3,5-Tetramethylbenzene (Isodurene) Series. 4,6-Dichloro-1,2,3,5-tetramethylbenzene (dichloroisodurene) and 4,6-dibromo-1,2,3,5-tetramethylbenzene (dibromoisodurene) reacted with fuming nitric acid more readily than durene analogs and gave a pale yellow pasty solid, PMR spectra of which showed two methylene peaks due to $-CH_2ONO_2$ at 4.24 and 4.48 τ with relative areas of 55 : 45 for chloro compound, and two peaks of relative intensity 66 : 34 at 4.12 and 4.43 τ for bromo derivative. These nitrates could be separated by fractional crystallization from ethanol. Direct comparison with the authentic specimens identified the benzyl nitrate with methylene proton absorption at higher field as 3,5-dihalo-2,4,6-trimethylbenzyl nitrate(IV), and another nitrate with lower field absorption as 2,6-dihalo-3,4,5-trimethylbenzyl nitrate(V). Attempted chromatographic separation of the product from dichloroisodurene on alumina resulted in nearly complete conversion of the nitrates to benzyl alcohol and bisbenzyl ether, but fairly selective decomposition occurred with the nitrates derived from dibromoisodurene. 2,6-dibromo-3,4,5-trimethylbenzylic product was adsorbed firmly on alumina and only a small portion was usually eluted as nitrate. 3,5-Dibromo-2,4,6-trimethylbenzylic compound was obtained mainly as bisbenzyl ether and alcohol. The structures of these bisbenzyl ethers were established by preparing authentic specimens from the corresponding alcohols. Under the conditions in which dihalodurenes were bisnitrooxylated, dihaloisodurenes were found to yield mononitrates together with a significant amount of nitro and carbonyl compounds.

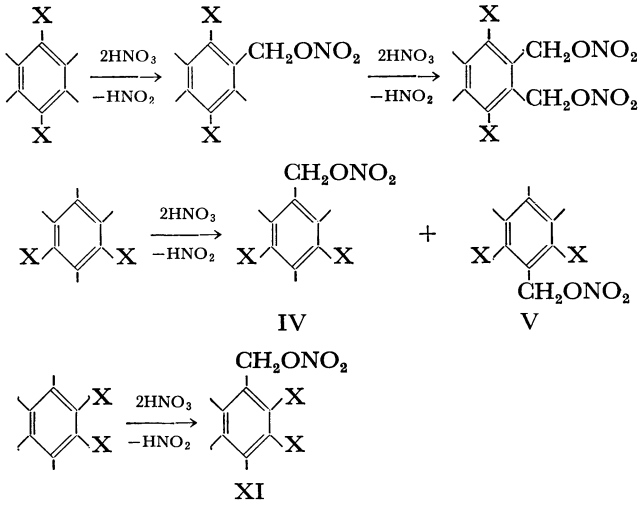

Fig. 1

Both nitrates IV and V derived from dihaloisodurene possess the methyl group at a position para to the nitrooxymethyl group (Fig. 1). The result is in line with the general observation that one of the main factors controlling the ease of side-chain nitrooxylation is the presence of the methyl group at a position para to the alkyl group to be nitrooxylated. This might indicate that the transition state of the anomalous substitution resembles a benzylic compound rather than a methylenecyclohexadiene, since the para methyl group is known to be more effective than halogen atom to delocalize the electron deficiency developed on the benzylic carbon atom during the reaction. The preferred formation of IV and V from dihaloisodurene may be explained as follows:

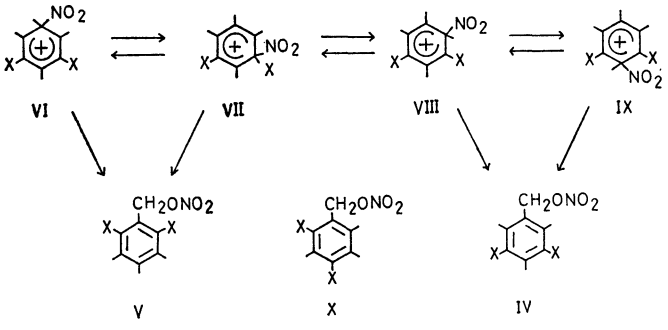

Fig. 2

Electrophilic attack of nitronium ion on dihaloisodurene would lead to an equilibrium mixture of four benzenonium ions VI—IX, in which VI and VII are supposed to predominate since three methyl groups can effectively contribute to the stabilization of these intermediates. Rearrangement of ions VI and VII according to the previously suggested mechanism,[6,7] which assumes migration of the nitro group from the attacking site to the α-carbon of the alkyl group from which the preferential proton removal takes place, will lead to V, because the proton release and subsequent migration of the nitro group would occur preferentially on the methyl group bonded to the more positively polarized ring carbon between two halogen atoms. Transformation of VI and VII into 4,6-dihalo-2,3,5-trimethylbenzyl nitrate(X) would be disfavored since the transition state can not be stabilized as effectively by the para halogen atom as by the para methyl group. On the other hand, less stable ions VIII and IX can be converted into IV more readily owing to the favorable orientation of substituent groups in the ring, the equilibrium being displaced in favor of these ions at the expence of the more stable ions VI and VII.

An alternative possibility may involve the ion-pair path; a proton is removed hyperconjugatively from the alkyl side-chain to form a sort of methylenecyclohexadiene or benzylic intermediate - nitrite ion pair, which will subsequently be converted into the nitrate. An increase in the formation of V relative to IV in going from chlorine to bromine is explained by the greater contribution of ions VI and VII in the equilibrium mixture as well as the easier migration of the nitro group due to the increased nuclear charge and bulkiness of bromine atom.

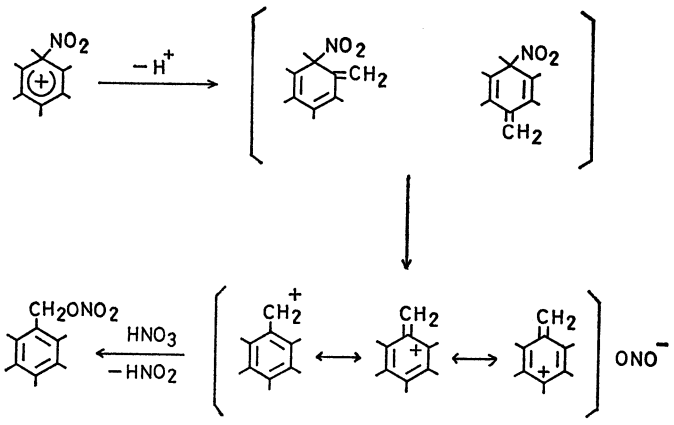

Fig. 3

1,2,3,4-Tetramethylbenzene (Prehnitene) Series. 5,6-Dihalo-1,2,3,4-tetramethylbenzene (dihaloprehnitene) was comparatively stable towards the action of cold nitrating agent, but slowly underwent side-chain nitrooxylation to give only one nitrate in good yield, which could be readily separated from the product mixture by fractional crystallization. The nitrate was identified as 5,6-dihalo-2,3,4-trimethylbenzyl nitrate(XI) by direct comparison with the authentic specimen prepared from 4,5-dihalo-1,2,3-trimethylbenzene through the ordinary sequence. Chromatographic behavior of the nitration product was similar to those obtained from dihaloisodurenes. Nitrate XI does not seem to undergo further nitrooxylation and is liable to suffer extensive decomposition by the action of a large excess of nitrating agent. The product mixture usually contains appreciable amounts of an unidentified crystalline solid which has absorption bands around 1610—1630 and 3400 cm^{-1}. Its structure has not been established yet. Formation of XI in preference to the isomeric 4,5-dihalo-2,3,6-trimethylbenzyl nitrate could be rationalized on the basis of a similar discussion as above.

The results indicate that the side-chain nitrooxylation of dihalotetramethylbenzenes with fuming nitric acid can provide a simple new method for the preparation of dihalotrimethylbenzylic compounds, some of which are laboriously obtained by the ordinary procedure.

Experimental

All melting points were determined with a hot-stage apparatus and are uncorrected. Infrared spectra were run as Nujol on a Jasco DS-402G spectrophotometer and only prominent peaks are recorded. PMR measurements were carried out on a Varian A-60A spectrometer and a JNM-3H spectrometer with carbon tetrachloride as solvent and tetramethylsilane as internal standard.

Dihalotetramethylbenzenes were prepared by halogenation of the corresponding hydrocarbons and purified through chromatography on alumina using light petroleum as eluant.

Authentic specimens of benzylic compounds were prepared essentially by the same sequence; chloride→nitrate, and chloride→acetate→alcohol→bisbenzyl ether. The general procedure is shown below with examples from the compounds of 3,5-dihalo-2,4,6-trimethylbenzylic series. Physical properties of some dihalotrimethylbenzylic compounds are summarized in Table 1.

3,5-Dibromo-2,4,6-trimethylbenzyl Chloride (XII). A crystal of iodine was added to a solution of 2,4,6-trimethylbenzyl chloride[8] (16.9 g) in carbon tetrachloride (50 m*l*), and bromine (*ca.* 33 g) was introduced dropwise at 0°C. The dibromobenzyl chloride soon began to separate from the mixture. The solvent was partly removed and the precipitate was recrystallized from light petroleum to give white needles (22.5 g, 69%), mp 125—127°C.

Found:C, 36.4; H, 3.3%. Calcd for $C_{10}H_{11}Br_2Cl$: C, 36.8; H, 3.4%.

Other dihalotrimethylbenzyl chlorides were similarly prepared by direct halogenation of the corresponding trimethylbenzyl chlorides. Yields varied from poor to moderate, depending on the structure of the chloride being halogenated. In some cases, a significant amount of unidentified higher halogenated products was formed as a by-product and its purification was tedious.

3,5-Dibromo-2,4,6-trimethylbenzyl Nitrate (XIII). A warm solution of silver nitrate (4.1 g) in acetonitrile (15 m*l*) was added all at once to a magnetically stirred solution of chloride XII (6.5 g) in acetonitrile (20 m*l*). The mixture was stirred for several hours, and silver chloride was filtered. After removal of the solvent in a vacuum, the residue was crystallized from light petroleum to give XIII (5.3 g), mp

8) R. C. Fuson and N. Rabjohn, "Organic Syntheses," Coll. Vol. III, 557 (1955).

Table 1. Physical properties of some dihalotrimethylbenzylic compounds

Compound		Mp (°C)	PMR spectra (τ) CH_2	PMR spectra (τ) CH_3	IR spectra[a] (cm^{-1})
3,6-Dihalo-2,4,5-trimethylbenzyl series					
Chloro	Alcohol	184—187	5.20	7.47 (1)[b] 7.57 (2)	717, 845, 998, 1041, 1187, 1208, 1270
	Chloride	94— 96	5.23	7.49 (1) 7.59 (2)	686, 723, 755, 843, 932, 1011, 1196, 1260
	Nitrate	80— 82	4.31	7.48 (1) 7.58 (2)	690, 752, 886, 975, 996, 1190, 1273* 1294, 1616, 1645*
	Bisbenzyl ether	222—223	5.24	7.59 (6)	718, 1002, 1073, 1089, 1191
Bromo	Alcohol	197—198	5.11	7.35 (1) 7.45 (2)	838, 992, 1041, 1175, 1282, 1314
	Chloride	118—119	5.16	7.38 (1) 7.48 (2)	676, 702, 747, 834, 923, 999, 1146, 1185, 1256
	Nitrate	97— 99	4.24	7.43 (1) 7.47 (2)	677, 756, 870, 963, 988, 1180, 1277, 1618, 1648*
	Bisbenzyl ether	240—241	5.39	7.32 (2) 7.54 (4)	724, 995, 1073, 1088, 1179
2,6-Dihalo-3,4,5-trimethylbenzyl series					
Chloro	Chloride	104—106	5.14	7.63 (2) 7.72 (1)	684, 704, 753, 905, 1019, 1172, 1260, 1299
	Nitrate	90— 91	4.27	7.62 (2) 7.68 (1)	703, 757, 867, 936, 969, 1271, 1629, 1643*
Bromo	Nitrate	111—112	4.13	7.56 (2) 7.63 (1)	699, 755, 867, 920, 973, 1273 1636
3,5-Dihalo-2,4,6-trimethylbenzyl series					
Chloro	Alcohol	193—194	5.24	7.43 (1) 7.48 (2)	817, 830, 992, 1027, 1168, 1208
	Acetate	102—103	4.89	7.52 (1) 7.61 (2) 8.00 ($COCH_3$)	707, 936, 956, 1023, 1175, 1215 1232, 1740
	Chloride	104—106	5.33	7.43 (2) 7.47 (1)	720, 796, 897, 978, 1012, 1176, 1255, 1302
	Nitrate	111—113	4.44	7.45 (1) 7.53 (2)	709, 755, 846, 893, 934, 966, 999, 1177, 1294, 1611
	Bisbenzyl ether	233—234	5.43	7.47 (2) 7.58 (4)	710, 942, 994, 1067, 1183, 1348
Bromo	Alcohol	205—206	5.17	7.28 (1) 7.44 (2)	805, 916, 978, 1005, 1024, 1159 1204
	Acetate	116—118	4.85	7.33 (1) 7.54 (2) 7.99 ($COCH_3$)	725, 920, 958, 1028, 1167, 1212 1233, 1742
	Chloride	125—127	5.39	7.35 (1) 7.50 (2)	678, 745, 888, 969, 987, 1019, 1163, 1255
	Nitrate	127—128	4.41	7.29 (1) 7.48 (2)	691, 755, 825, 885, 917, 964, 990, 1168, 1289, 1611
	Bisbenzyl ether	249—251	5.16	7.49 (6)	724, 929, 986, 1059, 1169, 1347
5,6-Dihalo-2,3,4-trimethylbenzyl series					
Chloro	Alcohol	193—194	5.18	7.57 (1) 7.62 (1) 7.74 (1)	916, 965, 1016, 1028, 1069, 1200
	Chloride	103—104	5.23	7.59 (1) 7.61 (1) 7.74 (1)	685, 753, 907, 942, 973, 1208 1260
	Nitrate	87— 90	4.32	7.58 (1) 7.67 (1) 7.75 (1)	699, 754, 890, 972, 1272*, 1298, 1612, 1645*
	Bisbenzyl ether	218—220	5.24	7.58 (2) 7.71 (2) 7.76 (2)	721, 917, 1009, 1061, 1088, 1206

Table 1. Continued

Compound		Mp (°C)	PMR spectra (τ) CH_2	PMR spectra (τ) CH_3	IR spectra[a] (cm^{-1})
5,6-Dihalo-2,3,4-trimethylbenzyl series					
Bromo	Alcohol	210—211	5.13	7.48 (1) 7.60 (1) 7.72 (1)	891, 951, 1019, 1028, 1065, 1192
	Chloride	127—128	5.15	7.49 (1) 7.62 (1) 7.73 (1)	748, 889, 925, 964, 1198, 1259
	Nitrate	98— 99	4.22	7.46 (1) 7.65 (1) 7.72 (1)	685, 755, 872, 963, 1278, 1634
	Bisbenzyl ether	263—264	5.12	7.49 (2) 7.68 (2) 7.74 (2)	722, 893, 1010, 1059, 1089, 1196

a) Principal peaks in the regions, 650—1350 and 1500—2000 cm^{-1}. Under certain conditions, benzyl nitrates show another asymmetric frequency band due to ONO_2 group in the 1640—1650 cm^{-1} region (indicated by asterisk). Appearance of this band is often accompanied by a small change in symmetric frequency in 1270—1290 cm^{-1} region.
b) Numerals in parentheses refer the number of methyl groups.

127—128°C.

Found: C, 33.9; H, 3.3%. Calcd for $C_{10}H_{11}Br_2NO_3$: C, 34.0; H, 3.1%.

Other dihalotrimethylbenzyl nitrates were prepared in a similar manner from the chlorides and recrystallized from light petroleum.

3,5-Dibromo-2,4,6-trimethylbenzyl Acetate (XIV). A mixture of chloride XII (9.8 g), silver acetate (5.2 g), and acetic acid (60 m*l*) was heated under gentle reflux for several hours. Silver chloride was filtered, and the reaction mixture was diluted with water to yield acetate as a white precipitate, which was recrystallized from light petroleum in the form of colorless needles (8.6 g), mp 116—118°C.

Found: C, 41.3; H, 3.9%. Calcd for $C_{12}H_{14}Br_2O_2$: C, 41.2; H, 4.0%.

A similar treatment of other dihalotrimethylbenzyl chlorides with silver acetate gave the corresponding acetates in high yields (75—89%).

3,5-Dibromo-2,4,6-trimethylbenzyl Alcohol (XV). Acetate XIV (3.5 g) was dissolved in a large volume of ethanol, to which was added an aqueous solution of sodium hydroxide (4 g). The mixture was gently refluxed for several hours and then poured into water to give XV (*ca.* 3 g), which was crystallized from boiling ethanol in the form of fine prisms, mp 205—206°C.

Other dihalotrimethylbenzyl alcohols were obtained similarly by analogous hydrolysis of the acetates using aqueous sodium hydroxide. Most dihalotrimethylbenzyl alcohols are only slightly soluble in light petroleum, carbon tetrachloride, benzene, and cold ethanol.

Attempt to prepare dibromotrimethylbenzyl alcohols by reducing dibromotrimethylbenzoic acids with lithium aluminum hydride in tetrahydrofuran proved unsatisfactory, since the bromine atom was partly or completely removed during the reduction.

Bis(3,5-dibromo-2,4,6-trimethylbenzyl) Ether (XVI). A mixture of XV and a catalytic amount of sulfamic acid was heated at 210—220°C in an oil bath. The alcohol melted to a pale yellow oil, and soon solidified to a white crystalline mass, which was taken up in a mixture of dichloromethane and ligroin and chromatographed on a short alumina column to remove any unchanged alcohol. Ether XVI crystallized from hot benzene as white needles and melted at 249—250°C. The yield was nearly quantitative.

Other bisbenzyl ethers were prepared in a similar way. The bromo alcohol needed somewhat higher temperature and longer heating than the chloro compound to complete the reaction.

2,6-Dimethyl-4-bromoaniline (XVII). 2,6-Dimethylaniline (12.1 g) was dissolved into a mixture of concentrated hydrochloric acid (30 m*l*) and water (220 m*l*), and the solution was cooled in an ice bath. A rapid stream of air saturated with bromine vapor was introduced with stirring until the solution assumed a distinctly yellow color. About 18—19 g of bromine was required. The bromoaniline hydrochloride came out of the solution as a white precipitate. The reaction mixture was made alkaline with aqueous sodium carbonate and the separated dark oil which soon solidified was filtered and recrystallized from ligroin to give large prisms (16.3 g, 82%), mp 50—51°C (lit,[9] 50—51°C). Acetanilide, mp 199—200°C (lit,[10] 198—200°C).

A similar treatment of 2,3-dimethylaniline gave 4,6-dibromo-2,3-dimethylaniline (mp 56—57°C) and unchanged starting material. The required monobromoaniline was obtained only in a small amount.

*2,5-Dibromo-*m*-xylene (XVIII).* A solution of XVII (20 g) in cold concentrated sulfuric acid (50 m*l*) was poured onto crushed ice (200 g) and diazotized with sodium nitrite (7.5 g). The resulting solution was filtered and the filtrate was added as rapidly as the foaming permitted to a boiling mixture of copper(I) bromide (7 g), cupper powder (*ca.* 1 g) and 47%-hydrobromic acid (80 m*l*). The separated black oil was removed by extraction with ether, washed with dilute aqueous sodium hydroxide and dried over anhydrous calcium chloride. The ethereal solution was distilled off to leave a dark oil, which on distillation under reduced pressure gave pale yellow oil (15 g, 57%), bp 120—121°C/15 mmHg (lit,[11] mp 28°C). Some 4-bromo-2,6-dimethylphenol (mp 79—80°C) was obtained as a by-product.

1,3-Bis(chloromethyl)-2,5-dibromo-4,6-dimethylbenzene (XIX).

9) E. Nölting, A. Braun, and G. Thesmar, *Ber.*, **34**, 2259 (1901).
10) E. G. Kleinschmidt and H. Braeuniger, *Pharmazie*, **1969**, 87.
11) J. J. Blanksma, *Rec. Trav. Chim. Pays-Bas*, **25**, 176 (1906).

A warm solution of XVIII (4 g) in chloromethyl methyl ether (*ca.* 5 g) was treated with 60%-fuming sulfuric acid (*ca.* 4—5 g) with vigorous stirring. The reaction proceeded with active liberation of heat and the mixture soon solidified into a black crystalline mass, which was washed with water, dissolved into a mixture of dichloromethane and ligroin, and freed from the polymeric substances through chromatography on a short alumina column. Removal of the solvent, followed by recrystallization of the product from carbon tetrachloride gave XIX (3.5 g, 64%) as long needles, mp 175—176°C.

Found: C, 33.0; H, 3.9%. Calcd for $C_{10}H_{10}Br_2Cl_2$: C, 33.3; H, 2.8%.

By a similar treatment, 2,5-dibromo-*p*-xylene gave *1,4-bis(chloromethyl)-2,5-dibromo-3,6-dimethylbenzene (XX)*, mp 213—215°C.

Found: C, 32.7; H, 2.8%. Calcd for $C_{10}H_{10}Br_2Cl_2$: C, 33.3; H, 2.8%.

1,3-Bis(nitrooxymethyl)-2,5-dibromo-4,6-dimethylbenzene(I). A warm solution of silver nitrate (2.1 g) in acetonitrile (10 m*l*) was added all at once with stirring to a hot solution of XIX (1.8 g) in acetonitrile (40 m*l*). The mixture was stirred with heating for several hours, and silver chloride was separated by filtration. Evaporation of the solvent *in vacuo*, followed by crystallization of the residue from hot ligroin gave white thin plates (2.5 g), mp 130—132°C. IR: 869, 971, 1179, 1278, 1620, and 1633 cm^{-1}, PMR: 7.36 (CH_3), and 4.25 τ (CH_2).

Found: C, 28.9; H, 2.5%. Calcd for $C_{10}H_{10}Br_2N_2O_6$: C, 29.0; H, 2.4%.

The above procedure applied to XX gave *1,4-bis(nitrooxymethyl)-2,5-dibromo-3,6-dimethylbenzene(II)*, mp 186—187°C, as white leaflets. IR: 876, 975, 1176, 1281, and 1628 cm^{-1}, PMR: 7.38 (CH_3) and 4.20 τ (CH_2).

Found: C, 29.0; H, 2.5%. Calcd for $C_{10}H_{10}Br_2N_2O_6$: C, 29.0; H, 2.4%.

General Procedure for Nitration of Dihalotetramethylbenzenes. A suspension of a dihalotetramethylbenzene (0.05 mol) in dichloromethane (50 m*l*) was vigorously stirred and fuming nitric acid ($d=1.50$) was added dropwise at 0°C over a period of 30 min. The solid part gradually dissolved giving a clear dark brown mixture, which was stirred for some hours and then quenched by being poured into ice water. The organic layer was throughly washed with aqueous sodium hydrogen carbonate and water. Evaporation of the solvent left a yellow to light brown pasty or half-crystalline solid, which was inspected by infrared, PMR, and thin-layer chromatography, and then subjected to chromatographic separation on alumina. Some nitrates were isolated by fractional crystallization of the product mixture from ethanol or ligroin.

Products were identified by elemental analyses, and by infrared and PMR spectra comparison or mixed melting as far as the authentic specimens were available. Typical examples of alumina chromatography are shown below for the nitration products from dibromotetramethylbenzenes.

i) A part (5 g) of light brown crystalline solid obtained from the nitration of dibromodurene (7.3 g) with fuming nitric acid (8 g) was placed on the top of alumina column and eluted with light petroleum to give unchanged starting material (1.2 g) and *3,6-dibromo-2,4,5-trimethylbenzyl nitrate* (0.5 g; Found: C, 33.9; H, 3.0; N, 4.0%. Calcd for $C_{10}H_{11}Br_2NO_3$: C, 34.0; H, 3.1; N, 4.0%). Elution with light petroleum-benzene gave *bis(3,6-dibromo-2,4,5-trimethylbenzyl) ether* (0.6 g; Found: C, 39.8; H, 3.3%. Calcd for $C_{20}H_{22}Br_4O$: C, 40.2; H, 3.7%); with ether-ethanol *3,6-dibromo-2,4,5-trimethylbenzyl alcohol* (1.3 g, Found: C, 39.1; H, 4.3%. Calcd for $C_{10}H_{14}Br_2O$: C, 38.7; H, 4.6%).

A similar treatment of the product (5 g) from the nitration with a large excess of fuming nitric acid at somewhat elevated temperature gave *3,6-dibromo-5-nitro-1,2,4-trimethylbenzene* (0.3 g, mp 198—200°C; Found: C, 33.9; H, 2.8%. Calcd for $C_9H_9Br_2NO_2$: C, 33.4; H, 2.8%) from light petroleum-benzene eluates; small amounts of bisbenzyl ether from benzene eluates; and finally *1,2-bis(hydroxymethyl)-3,6-dibromo-4,5-dimethylbenzene* (1.6 g, mp 225—226°C; Found: C, 37.1; H, 3.8%. Calcd for $C_{10}H_{12}Br_2O_2$: C, 37.0; H, 3.7%) from diethyl ether-ethanol eluates.

Direct crystallization of the latter nitration product from ethanol gave *1,2-bis(nitroxymethyl)-3,6-dibromo-4,5-dimethylbenzene* (mp 121—123°C) as white needles. IR: 847, 868, 940, 1180, 1274, 1280, 1629, and 1640 cm^{-1}, PMR: 7.41 (CH_3) and 4.23 τ (CH_2).

Found: C, 29.1; H, 2.7; N, 6.6%. Calcd for $C_{10}H_{10}Br_2N_2O_6$: C, 29.0; H, 2.4; N, 6.8%.

ii) A light yellow product (5 g) from the nitration of dibromoisodurene was chromatographed on alumina to give the recovered starting material (0.9 g) and *2,6-dibromo-3,4,5-trimethylbenzyl nitrate* (0.5 g, mp 111—112°C; Found: C, 34.3; H, 3.3%. Calcd for $C_{10}H_{11}Br_2NO_3$: C, 34.0; H, 3.1%) from light petroleum eluates. Light petroleum-benzene eluted a mixture of bisbenzyl ethers, most of which was composed of *bis(3,5-dibromo-2,4,6-trimethylbenzyl) ether* (0.3 g, Found: C, 40.6; H, 3.7%. Calcd for $C_{20}H_{22}Br_4O$: C, 40.2; H, 3.7%), and ether-ethanol eluted benzyl alcohol fraction, the major component of which was identified as *3,5-dibromo-2,4,6-trimethylbenzyl alcohol* (1.3 g, Found: C, 38.9; H, 4.2%. Calcd for $C_{10}H_{14}Br_2O$: C, 38.7; H, 4.6%). A greater part of 2,6-dibromo-3,4,5-trimethylbenzylic compounds was lost during elution.

iii) Chromatography of the nitration product from dibromoprehnitene (5 g) gave *5,6-dibromo-2,3,4-trimethylbenzyl nitrate* (0.7 g, Found: C, 34.0; H, 3.4; N, 3.9%. Calcd for $C_{10}H_{11}Br_2NO_3$: C, 34.0; H, 3.1; N, 4.0%) as colorless plates from light petroleum eluates; *bis(5,6-dibromo-2,3,4-trimethylbenzyl) ether* (0.2 g, Found: C, 39.7; H, 3.3%. Calcd for $C_{20}H_{22}Br_4O$: C, 40.2; H, 3.7%) from light petroleum-benzene eluates; an unidentified carbonyl compound from benzene-ether eluates (0.4 g, IR: 1625, 1735, and 3300—3400 cm^{-1}); and finally *5,6-dibromo-2,3,4-trimethylbenzyl alcohol* (1.2 g, Found: C, 39.0; H, 4.3%. Calcd for $C_{10}H_{14}Br_2O$: C, 38.7; H, 4.6%) from ethanol eluates.

By a similar treatment, the product (5 g) from dichloroprehnitene gave *5,6-dichloro*-2,3,4-*trimethylbenzyl nitrate* (0.5 g, Found: C, 45.2; H, 4.3%. Calcd for $C_{10}H_{11}Cl_2NO_3$: C, 45.5; H, 4.2%) and unchanged starting material (0.5 g) from light petroleum eluates. Light petroleum-benzene mixture eluted small amounts of nitro compound and *bis(5,6-dichloro*-2,3,4-*trimethylbenzyl) ether* (0.4 g, Found: C, 58.2; H, 5.5%. Calcd for $C_{20}H_{22}Cl_4O$: C, 57.2; H, 5.3%), and ether eluted an unidentified carbonyl compound (0.6 g, mp 178—179°C; Found: C, 60.8; H, 6.8%; IR: 3400, 1620, 1360, 1270, 1220, 1075, 1040, 1010, 900, 845, and 765 cm^{-1}). *5,6-Dichloro-2,3,4-trimethylbenzyl alcohol* (0.9 g, Found: C, 55.8; H, 5.8%. Calcd for $C_{10}H_{12}Cl_2O$: C, 54.8; H, 5.5%) was obtained as colorless plates from ethanol eluates.