The Preparation of Aromatic Amines with Sodium Amide in Liquid Ammonia

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A series of five compounds has been prepared and the reactions of these with sodium amide in liquid ammonia have been studied. Under these conditions, 2-bromo-3-methylanisole (I) gives no amine, 2-bromo-6-methylanisole (II) gives 4-methyl-m-anisidine in 30% yield, 2-bromo-4-methylanisole (III) yields over 50% of 6-methyl-m-anisidine, and 2-bromo-5-(trifluoromethyl)-anisole (IV) gives 5-(trifluoromethyl)-m-anisidine in 71% yield. Rather unexpectedly, 2-bromo-4-(trifluoromethyl)-anisole (V) leads to the formation of 5-(trifluoromethyl)-o-anisidine in 15–20% yield. These results indicate that, except in the case of V, substitution occurs only in the position adjacent to the halogen atom and that when this position is already occupied no reaction occurs.

Introduction

It has been reported recently that certain aryl halides will react with liquid ammonia solutions of sodium or potassium amide, or with lithium dialkylamides in ether solution, to give aromatic amines.[3–5] If the aryl halide contains an ether, sulfide, or dialkylamino group ortho to the halogen, it has been found that the entering amino or dialkylamino group does not take the position originally occupied by the halogen but rather that a meta-substituted product is formed.[6–8] This phenomenon is observed as well when the halogen is in a position ortho to a strong meta-directing group such as the trifluoromethyl.[9] The corresponding para halogen compounds react in a similar way, although the meta amine resulting appears to be formed in lower yields, and some of the amine resulting from direct replacement of the halogen atom can be isolated.[10]

The compounds previously studied provide no information regarding the possible mode of formation of the products. Thus, in the preparation of m-anisidine from o-bromoanisole, the final product gives no indication as to which of the positions meta to the methoxyl group, "a" or "b," has been substituted. None of the reported work has involved
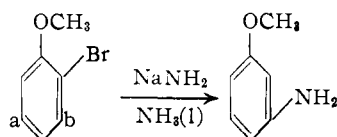
a compound in which both positions ortho to the halogen are occupied, nor indeed have any studies been made with compounds containing a third substituent in the ring. It was the purpose of this study to investigate compounds of this type in order to determine what effect, if any, a third group, located at various positions with respect to the halogen and "activating" group, would have upon this reaction. In addition, a non-reactive third group in the ring would serve as a reference point

(1) This paper was presented in part before the Division of Organic Chemistry at the Cleveland Meeting of the American Chemical Society, April, 1951.

(2) Abstracted from the Doctoral Dissertation of Walter E. Buting, Purdue University, 1951.

(3) H. Gilman and S. Avakian, This Journal, 67, 349 (1945).

(4) R. S. Urner and F. W. Bergstrom, ibid., 67, 2108 (1945).

(5) C. H. Horning and F. W. Bergstrom, ibid., 67, 2110 (1945).

(6) H. Gilman and J. F. Nobis, ibid., 67, 1479 (1945).

(7) H. Gilman, et al., ibid., 67, 2106 (1945).

(8) H. Gilman, R. H. Kyle and R. A. Benkeser, ibid., 68, 143 (1946).

(9) R. A. Benkeser and R. G. Severson, ibid. 71, 3838 (1949).

(10) H. Gilman and R. H. Kyle, ibid., 70, 3945 (1948).

which could prove useful in determining the exact position taken by the entering group.

It was felt that the answers to a few fundamental questions would provide a reasonable basis for predicting the results obtainable with a given compound. (1) Will the reaction proceed in the same way, $i.e.$, to give an amine substituted in the position meta to an "activating" group, if both positions ortho to the halogen are occupied? For example, would 2-bromo-3-methylanisole undergo reaction to form 5-methyl-m-anisidine? (2) If the reaction in the above case does not give a meta-substituted amine, will the halogen be replaced directly with the formation of an ortho-amine? (3) If two meta positions are available, can the amino group enter either of these, or does substitution occur exclusively in the position adjacent to the halogen atom? For example, would 2-bromo-6-methylanisole lead to the formation of both 2-methyl-m-anisidine and 4-methyl-m-anisidine, or would the latter compound alone result? (4) Is substitution made more difficult by the presence of a group adjacent to the meta position?

Accordingly, a series of five compounds was prepared and their reactions with sodium amide in liquid ammonia were studied. The compounds used were 2-bromo-3-methylanisole (I), 2-bromo-6-methylanisole (II), 2-bromo-4-methylanisole (III), 2-bromo-5-(trifluoromethyl)-anisole (IV) and 2-bromo-4-(trifluoromethyl)-anisole (V).
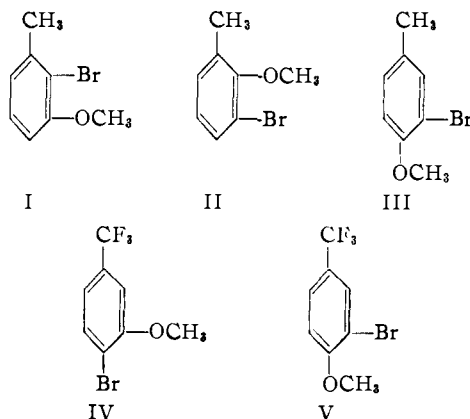
It is significant that in the numerous experiments carried out with I and sodium amide in liquid ammonia, most of the starting material was recovered unchanged. No acid-soluble organic material was obtained except for traces of a gummy substance which was insufficient in quantity to

permit identification. From this it would appear that in the formation of the meta-substituted amine, it is the position *adjacent* to the halogen atom which is involved, since the 5-position in this compound is not attacked. This view is supported by the fact that II undergoes reaction with sodium amide to give only 4-methyl-*m*-anisidine in 30% yield. The absence of any 2-methyl-*m*-anisidine as a reaction product confirms the belief that the position adjacent to that occupied by the halogen, is essential.

The absence of any basic material in the reaction of I indicates also that under the conditions studied, direct replacement of the halogen does not occur to any significant extent, and that where reaction to yield a meta-substituted amine is not possible, no reaction of any kind occurs. However, V leads to the formation of 5-(trifluoromethyl)-*o*-anisidine under these conditions, a product which can only be the result of a direct displacement of the halogen atom. In this compound, the halogen although ortho to the methoxyl group, is meta to the trifluoromethyl substituent. Benkeser and Severson[9] have reported that *m*-chlorobenzotrifluoride under these conditions gives *m*-(trifluoromethyl)-aniline. If the effect of the trifluoromethyl group upon this reaction is greater than that of the methoxyl group, the result observed is not entirely surprising.

In the reaction of III with sodium amide, 6-methyl-*m*-anisidine is obtained in yields ranging above 50%. Thus, it appears that the presence of a group adjacent to the meta position does not make entry into this position more difficult, at least in the case where this group is methyl.

The results with IV are those which might have been predicted on the basis of past observations. In this case, the bromine is not only ortho to the methoxyl group but also para to the trifluoromethyl substituent. Since either of these arrangements alone favors the formation of a meta amine, the excellent yield (71%) of 5-(trifluoromethyl)-*m*-anisidine is not unexpected.

Experimental

2-Bromo-*m*-cresol.—This compound was prepared by the bromination of *m*-cresol-4,6-disulfonic acid according to the method of Huston and Peterson.[11] An alternate method which was also used is described below.

A two-liter three-necked flask containing a solution of 108 g. (1.0 mole) of *m*-cresol in 540 cc. of carbon disulfide was cooled while 237.6 g. (2.04 moles) of chlorosulfonic acid was added at a rate such that the temperature did not exceed 35°. After all the chlorosulfonic acid had been added, the carbon disulfide was distilled from a steam-bath, and the thick paste which remained was heated on a boiling water-bath for two hours. The disulfonic acid so formed[12] was dissolved in 400 cc. of water and 500 cc. of carbon tetrachloride was added. Then 160 g. (1.0 mole) of bromine was added with stirring, the excess bromine dissolving in the carbon tetrachloride layer from which it was taken up as needed. The organic layer was drawn off and the aqueous layer was acidified with 400 cc. of concentrated sulfuric acid. The flask containing the acidified solution was heated in an oil-bath at 150–180° while superheated steam was passed in. The distillate was extracted with ether and the ether extract was dried over Drierite. After the ether was removed, the residue was distilled under vacuum to give 75 g. of a fraction boiling at 70–75° (4 mm.).

The fraction collected contained both 2- and 6-bromo-*m*-cresol.[13] After seeding with a crystal of 2-bromo-*m*-cresol, 30 g. (16%) of this isomer crystallized. Recrystallized from dilute ethanol, the compound melted at 61.5–62°.[11]

2-Bromo-3-methylanisole.—Methylation of 2-bromo-*m*-cresol was carried out by treating an alkaline solution of this compound with methyl sulfate. The product, after recrystallization from dilute ethanol, was a white solid melting at 41.5–42°.[11]

6-Bromo-*o*-cresol.—The method of Huston and Neeley[14] was employed without modification for this preparation. The fraction boiling at 55–57° (4 mm.) was collected.

2-Bromo-6-methylanisole.—A mixture of 65.5 g. (0.35 mole) of 6-bromo-*o*-cresol and 88.2 g. (0.7 mole) of practical methyl sulfate was cooled in an ice-bath while a solution of 58.8 g. (1.05 moles) of potassium hydroxide in 130 cc. of water was added as rapidly as possible. After being heated under reflux for four hours, the mixture was cooled and extracted with ether. The ether solution was dried, and the solvent was distilled from a steam-bath, leaving a residue of 55 g. (78%) of crude 2-bromo-6-methylanisole. This was rectified without decomposition through a three-foot Todd spiral-wire column at 754 mm. The fraction boiling at 215–216°, n^{20}D 1.5487, was collected. Since this compound has not been reported in the literature, its Grignard reagent was prepared and carbonated. After hydrolysis with dilute sulfuric acid, 2-methoxy-*m*-toluic acid, m.p. 83°,[15] was isolated.

Anal. Calcd. for C_8H_9OBr: C, 47.7; H, 4.48. Found: C, 47.65; H, 4.39.

2-Bromo-*p*-cresol.—This compound was prepared in 95% yield by diazotization and hydrolysis of 2-bromo-*p*-toluidine.[16]

2-Bromo-4-methylanisole.—Methylation of 2-bromo-*p*-cresol with dimethyl sulfate gave this compound, b.p. 126–127° at 25 mm.[16]

2-Bromo-5-(trifluoromethyl)-phenol.—The method of Mc-Bee and Rapkin[17] was used without modification for this preparation.

2-Bromo-5-(trifluoromethyl)-anisole.—Methylation of 2-bromo-5-(trifluoromethyl)-phenol with methyl sulfate and base gave this compound in 65% yield; b.p. 68–71° (4.5–5.0 mm.).[18]

3-Nitro-4-chlorobenzotrifluoride.—A mixture of 400 g. of fuming sulfuric acid (20–30% SO₃) and 200 g. of fuming nitric acid (sp. gr. 1.5) was agitated very vigorously while 54 g. (0.3 mole) of *p*-chlorobenzotrifluoride was added during an interval of about 30 minutes. The flask was heated cautiously on the steam-bath for 30 minutes after the addition was complete. The mixture was cooled, poured into a liter of crushed ice with vigorous stirring, and partially neutralized with ammonium hydroxide. The organic layer was separated, the aqueous portion was extracted with ether, and the combined organic fractions were dried over Drierite. After removal of the ether, the residue was distilled under vacuum to give 50 g. (75%) of 3-nitro-4-chlorobenzotrifluoride boiling at 92–93° (10 mm.).[19]

2-Nitro-4-(trifluoromethyl)-anisole.—A solution of sodium methoxide was prepared from 10 g. (0.435 g. atom) of sodium in 100 cc. of anhydrous methanol. This was added dropwise to a stirred solution of 99 g. (0.44 mole) of 3-nitro-4-chlorobenzotrifluoride in 100 cc. of anhydrous methanol. When the addition was completed, the mixture was heated on the steam-bath until the red color of the solution was replaced by a pale yellow. The mixture was cooled and filtered to remove sodium chloride, and the methanol was distilled from a steam-bath. The residue, upon cooling, solidified to yield, after recrystallization from petroleum ether

(11) R. C. Huston and W. J. Peterson, THIS JOURNAL, **55**, 3880 (1933).

(12) R. D. Haworth and A. Lapworth, *J. Chem. Soc.*, **125**, 1303 (1924).

(13) Huston and co-workers report without comment, conflicting constants: 80–85° (4 mm.)[11]; 60–70° (4 mm.) and 60–65° (4 mm.).[14] These have not been duplicated in our work, whereas the boiling point reported above has been duplicated repeatedly. The identity of our product was demonstrated by preparation of the Grignard reagent of the methyl ether and carbonation of this to the known 2-bromo-3-methoxybenzoic acid.

(14) R. C. Huston and A. Neeley, THIS JOURNAL, **57**, 2177 (1935).

(15) J. L. Simonsen, *J. Chem. Soc.*, **113**, 779 (1918).

(16) H. E. Ungnade and E. F. Orwoll, THIS JOURNAL, **65**, 1737 (1943).

(17) E. T. McBee and E. Rapkin, *ibid.*, **73**, 1325 (1951).

(18) E. T. McBee and E. Rapkin, *ibid.*, **73**, 2376 (1951).

(19) French Patent 745,293 (May 8, 1933); *C. A.*, **27**, 4414 (1933).

(b.p. 60–70°), 70 g. (72%) of 2-nitro-4-(trifluoromethyl)-anisole, m.p. 46–46.5°.[20]

5-(Trifluoromethyl)-o-anisidine.—A solution of 15 g. (0.068 mole) of 2-nitro-4-(trifluoromethyl)-anisole in 200 cc. of absolute ethanol was reduced catalytically to give a quantitative yield of the amine, m.p. 59.5°.[20]

2-Bromo-4-(trifluoromethyl)-anisole.—A mixture of 25 g. (0.13 mole) of 5-(trifluoromethyl)-o-anisidine and 39 cc. (0.325 mole) of 48% hydrobromic acid was cooled to 0°. After adding 20 cc. of water to make the mixture more fluid, a solution of 9 g. (0.13 mole) of sodium nitrite in 16 cc. of water was added rapidly, the temperature being maintained below 10° by the addition of ice to the mixture. The cold diazonium solution was added slowly to a boiling mixture of 10.4 cc. (0.078 mole) of 48% hydrobromic acid and 10.3 g. (0.072 mole) of freshly prepared cuprous bromide. After part of the diazonium solution had been added, steam was passed into the boiling mixture to aid in the steam distillation of the product, and the remaining diazonium solution was added. The distillate was extracted with ether, the ether extract was dried, and the solvent was evaporated. The residue was distilled under vacuum to yield 30 g. (90%) of 2-bromo-4-(trifluoromethyl)-anisole boiling at 90–92° (10 mm.); $n^{20}D$ 1.4968, d^{20}_4 1.6344. The structure of the product was verified by hydrolysis to the known 3-bromo-4-methoxybenzoic acid.

Anal. Calcd. for $C_8H_6OBrF_3$: C, 37.6; H, 2.35. Found: C, 37.69; H, 2.49.

Reactions with Sodium Amide in Liquid Ammonia.—All of the reactions with sodium amide were carried out under similar conditions. Experimental details for a typical reaction are given.

Reaction of 2-Bromo-4-methylanisole with Sodium Amide in Liquid Ammonia.—The reaction was carried out in a one-liter three-necked flask fitted with a mechanical stirrer and Dry Ice condenser. Sodium amide was prepared according to the method of Vaughn, Vogt and Nieuwland[21] from 5 g. (0.217 g. atom) of sodium in 500 cc. of liquid ammonia. When the formation of sodium amide was complete, 18 g. (0.09 mole) of 2-bromo-4-methylanisole was added over a period of 30 minutes from a dropping funnel. After stirring for an additional three hours, 11 g. (0.226 mole) of ammonium chloride was added to decompose the unreacted sodium amide. At this point 200 cc. of benzene was stirred into the mixture, whereupon the mass solidified and the ammonia was allowed to evaporate overnight. The benzene solution which remained was extracted with 10% hydrochloric acid after filtering to remove inorganic solids, and the acidic extract was made basic by the addition of ammonium hydroxide. Upon cooling this mixture, 6-methyl-m-anisidine separated and was removed by filtration. The filtrate was extracted with ether and the ether was evaporated, leaving a residue which solidified upon cooling. The solids were combined and dried to give 6.4 g. (56%) of crude amine melting at 40–42°. This after several recrystallizations from petroleum ether (b.p. 30–60°), melted at 42.5–43°.[22] The acetyl derivative was prepared and after recrystallization from water melted at 95.5–96°.[23] A mixed melting point with the acetyl derivative of an authentic sample of 6-methyl-m-anisidine, prepared as described below, was not depressed.

3-Nitro-p-toluidine was prepared by nitrating the salt of p-toluidine.[24]

3-Nitro-p-cresol, m.p. 77–7.5°,[24] was obtained by diazotization and hydrolysis of 3-nitro-p-toluidine.

3-Nitro-4-methylanisole resulted from the methylation of the corresponding cresol with dimethyl sulfate. The product was separated from the reaction mixture by steam distillation and was used without further purification for the next step.

6-Methyl-m-anisidine, m.p. 43°,[22] was prepared by the reduction with a Raney nickel catalyst of 3-nitro-4-methylanisole.

Reaction of 2-Bromo-3-methylanisole with Sodium Amide in Liquid Ammonia.—A number of attempts were made to obtain an amine from this reaction. The reaction time was varied from two to four hours, and the amount of starting material used ranged from 0.09 to 0.20 mole. However, in no case was there obtained sufficient basic material to permit purification and characterization. Starting material was recovered substantially unchanged except for slight amounts of discoloring impurities.

Reaction of 2-Bromo-6-methylanisole with Sodium Amide in Liquid Ammonia.—The experimental procedure employed was identical with that described for 2-bromo-4-methylanisole. Crude 4-methyl-m-anisidine, m.p. 53–55°, was obtained in 30% yield. Recrystallization from cyclohexane gave a pure product melting at 56°.[25] No other amine could be isolated from the reaction. The identity of the product was verified by a mixed melting point with an authentic sample whose preparation is described.

5-Nitro-o-cresol was prepared by diazotization and hydrolysis of 5-nitro-o-toluidine according to the procedure given in reference 26. The product after a single recrystallization from a mixture of benzene and ligroin melted at 115–116.5° and was used without further purification.

2-Methyl-5-nitroanisole was obtained in quantitative yield by methylation of 5-nitro-o-cresol. After recrystallization from dilute ethanol the product melted at 73°.[27]

4-Methyl-m-anisidine was obtained in quantitative yield by the reduction with a Raney nickel catalyst of 2-methyl-5-nitroanisole. After recrystallization from cyclohexane the amine melted at 56°.[25]

Reaction of 2-Bromo-5-(trifluoromethyl)-anisole with Sodium Amide in Liquid Ammonia.—The only variation from the procedure described was in the use of a reaction time of 3.5 hours. There was obtained 71% of crude 5-(trifluoromethyl)-m-anisidine melting at 45–47°. After recrystallization from petroleum ether (b.p. 30–60°), the product was in the form of long white needles, m.p. 48.5–49°. Identification was established by a mixed melting point with an authentic sample.

3,5-Dinitrobenzotrifluoride.—A mixture of 400 g. of fuming sulfuric acid (20–30% SO_3) and 200 g. of fuming nitric acid (sp. gr. 1.5) was stirred vigorously while 57.0 g. (0.3 mole) of m-nitrobenzotrifluoride was added from a dropping funnel. The mixture was slowly heated to 98° on a steam-bath and the temperature was maintained at 98° for four hours. The reaction mixture was then cooled and poured onto crushed ice. The white solid which separated was filtered from the solution and recrystallized from methanol. The pure product melted at 49–50°.[28] The yield was 60%.

3-Nitro-5-(trifluoromethyl)-aniline.—This material was obtained by selective reduction of 3,5-dinitrobenzotrifluoride with alcoholic ammonium sulfide.[28] The pure compound melts at 80.5–81.5°.

3-Nitro-5-(trifluoromethyl)-phenol.—Diazotization and hydrolysis of 3-nitro-5-(trifluoromethyl)-aniline produced this compound[29] which melted at 92–92.5° after recrystallization from petroleum ether (b.p. 60–70°).

3-Nitro-5-(trifluoromethyl)-anisole was obtained by methylation of the corresponding phenol. The pure product melts at 30.5–31°.

Anal. Calcd. for $C_8H_6O_3NF_3$: N, 6.3. Found: N, 6.5.

5-(Trifluoromethyl)-m-anisidine was obtained by low-pressure catalytic reduction of 3-nitro-5-(trifluoromethyl)-anisole. The product, after recrystallization from petroleum ether (b.p. 30–60°) melted at 48.5–49° and was identical with the product obtained from the reaction of 2-bromo-5-(trifluoromethyl)-anisole with sodium amide.

Anal. Calcd. for $C_8H_8ONF_3$: N, 7.3. Found: N, 7.1.

Reaction of 2-Bromo-4-(trifluoromethyl)-anisole with Sodium Amide in Liquid Ammonia.—The procedure used was exactly like the typical procedure described, with a reaction time of three hours. Yields of 15 and 20% of 5-(trifluoromethyl)-o-anisidine, m.p. 59.5°,[20] were obtained. A mixed melting point with an authentic sample, prepared as an in-

(20) J. H. Brown, C. W. Suckling and W. B. Whalley, *J. Chem. Soc.*, (Suppl. Issue No. 1), S95 (1949).

(21) T. H. Vaughan, R. R. Vogt and J. A. Nieuwland, THIS JOURNAL, **56**, 2120 (1934).

(22) I. Keimatsu and K. Yamaguchi, *J. Pharm. Soc. Japan*, **57**, 992 (1937).

(23) W. Kizhner and V. Krasnova, *Anilinokrasochnaya Prom.*, **3**, 179 (1933); *C. A.*, **27**, 5319 (1933).

(24) E. Nolting and A. Collin, *Ber.*, **17**, 263 (1884).

(25) F. Ullmann and R. Fitzenkam, *ibid.*, **38**, 3790 (1905).

(26) "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, 1941, pp. 404–405.

(27) F. Kaufler and F. Wenzel, *Ber.*, **34**, 2241 (1901).

(28) G. C. Finger and F. H. Reed, THIS JOURNAL, **66**, 1972 (1944).

(29) W. B. Whalley, *J. Chem. Soc.*, 3018 (1949).

termediate for the preparation of 2-bromo-4-(trifluoro-methyl)-anisole, was not depressed. Acetyl and benzoyl derivatives of both the reaction product and the authentic

sample were prepared and were identical. The acetyl derivative melted at 105°, the benzoyl derivative at 145°.

LAFAYETTE, INDIANA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ROCHESTER]

Maleic and Fumaric Dialdehydes, Δ⁴-Tetrahydrophthalaldehyde and Related Compounds[1]
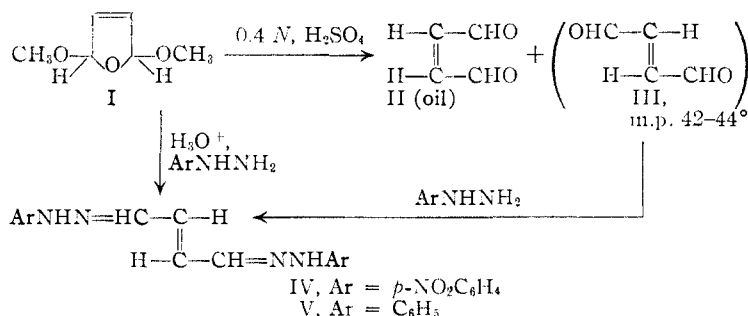
BY DUANE L. HUFFORD, D. S. TARBELL AND THOMAS R. KOSZALKA

A crystalline dialdehyde, believed to be fumaric dialdehyde, has been isolated from the acid hydrolysis of dimethoxydihydrofuran, and its infrared and ultraviolet absorption spectra have been determined; the compound yields the same carbonyl derivatives as the oily maleic dialdehyde, and both unsaturated dialdehydes add butadiene to form Δ⁴-tetrahydrophthalaldehyde. The latter has been reduced to hexahydrophthalaldehyde, and has been obtained in both the cis- and trans-form. Butadiene reacts with dimethoxydihydrofuran at 200° in the presence of a mole of water to form Δ⁴-tetrahydrophthalaldehyde. Maleic dialdehyde could not be condensed with methoxy- or hydroxyacetone to form tropolone, although small amounts of m-hydroxybenzaldehyde were isolated.

Recent work[2,3] on the synthesis of 4,5-benztropolone and its methyl ether, by the condensation of phthalaldehyde with hydroxyacetone and methoxyacetone, respectively, suggested an investigation of the general adaptibility of the reaction of 1,2-dialdehydes with methoxyacetone to form tropolones. We have therefore made a fairly detailed study of the preparation and properties of maleic dialdehyde.

The preparation of aqueous solutions of maleic dialdehyde has been mentioned several times,[4–7] and several derivatives have been prepared, but the compound itself has been isolated only as an impure yellow oil.[8,9]

We have found it convenient to isolate maleic dialdehyde (II) from the acid hydrolysis mixture of 2,5-dimethoxy-2,5-dihydrofuran (I) by partition chromatography of the mixture on silicic acid.
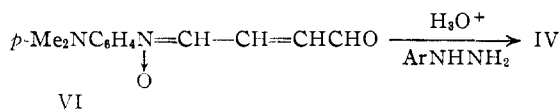

These mild conditions minimized decomposition of the aldehyde, and resulted, after vacuum distillation, in a yellow oil, consisting of maleic dialdehyde

mixed with unchanged dimethoxydihydrofuran. From this oil could be isolated, in some runs, up to 27% of yellow crystalline solid, m.p. 42–44°, which had the composition of maleic dialdehyde, and which formed the same carbonyl derivatives which were obtained directly from the dimethoxydihydrofuran by the action of aqueous acid and arylhydrazines. This yellow solid was first regarded[10] as crystalline maleic dialdehyde, but further work has brought us to the view that it is fumaric dialdehyde, formed from the oily maleic form in some runs by isomerization. Since the same arylhydrazones IV and V are formed from the furan I and the solid III, it must be concluded that isomerization has occurred in the first case, either during preparation or purification of the derivatives; identity of the derivatives was established by infrared spectra and mixed m.ps.

The reasons for regarding the crystalline dialdehyde as the trans-form are as follows. Treatment of the crystalline dialdehyde with hydrazine yielded only about 1% of pyridazine. The latter, identified as the chloroaurate, was formed in about 38% yield when the furan I was hydrolyzed with 0.4 N sulfuric acid and the resulting oily maleic dialdehyde was treated with hydrazine. Various modified procedures designed to decrease polymerization and favor the intramolecular reaction failed to form more than a trace of pyridazine from the crystalline dialdehyde.

Less convincing evidence for the configuration of the crystalline dialdehyde was afforded by the fact that the bis-p-nitrophenylhydrazone obtained from the nitrone VII, to which has been assigned the trans-configuration,[11] was found to be identical with the derivative IV obtained from the crystalline

(1) Aided by a grant from the National Cancer Institute.

(2) D. S. Tarbell, G. P. Scott and A. D. Kemp, THIS JOURNAL, 72, 379 (1950).

(3) D. S. Tarbell and J. C. Bill, ibid., 74, 1234 (1951).

(4) A. Wohl and E. Bernreuther, Ann., 481, 10 (1930).

(5) N. A. Preobrazhenskii, et al., J. Gen. Chem. (U. S. S. R.), 15, 952 (1945); C. A., 40, 6488 (1946).

(6) (a) N. Clauson-Kaas, et al., Kgl. Danske Videnskab. Selskab. Math.-Fys. Medd., 24, (6) (1947); C. A., 42, 1930 (1948); (b) Acta Chem. Scand., 1, 216, 379, 415 (1947); (c) ibid., 2, 109 (1948).

(7) C. Schöpf and W. Arnold, Ann., 558, 117 (1947).

(8) A. Wohl and B. Mylo, Ber., 45, 1746 (1912).

(9) D. G. Jones and Imperial Chemical Industries, British Patent, 603,422 (C. A., 43, 1808 (1949)), have reported the isolation of the compound as an oil, but give no analysis or description.

(10) D. L. Hufford and D. S. Tarbell, Abstracts of Papers, 119th Meeting of the American Chemical Society, April, 1951, p. 39 M.

(11) H. Schmid and E. Grob, Helv. Chim. Acta, 32, 79 (1949).