[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

RINGS THROUGH THE META AND PARA POSITIONS OF BENZENE. A STUDY OF CERTAIN ETHERS OF RESORCINOL AND META-AMINOPHENOL

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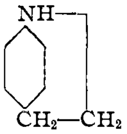
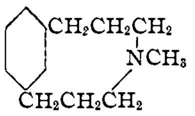
The formation and properties of rings combining the *meta* and *para* positions of benzene have been the subject of very little systematic study.[2] Rings through the *ortho* positions of benzene are very readily formed and offer a striking contrast to the comparatively rare *meta* and *para* rings. The assumption that *meta* and *para* ring structures exist in certain compounds has been made occasionally, but only in a few instances has the existence of such structures been proved with certainty.

It has been suggested that the non-formation of such rings is due to the great rigidity of the benzene nucleus[3] and to the unsymmetrical form which such rings would have to assume.[4] Mohr[5] has pointed out that the formation of rings in general should be a periodic function of the lengths of the chain to be converted to a ring. Finally, v. Braun has shown that one of the most important factors in the preparation of *meta* and *para* rings is the nature of the atoms in the chains to be closed.

The work in this field up to the present time has been very limited. V. Braun has succeeded in preparing a few of these rings and has established their constitution with practical certainty. These are represented by the following structures:



I



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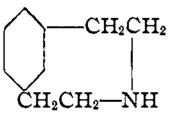

III

(I) was made merely by heating p-β-chloro-ethyl aniline;[6] however, p-tetrahydro-quinoline could not be obtained by heating p-γ-chloro-propyl aniline. II was formed by heating julolidine methochloride with sodium

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[1] This communication is an abstract of a thesis submitted by W. C. Wilson in partial fulfilment of the requirements for the degree of Doctor of Philosophy in Chemistry at the University of Illinois.

[2] A recent publication by Perkin and Titley, *J. Chem. Soc.*, **122**, 1562 (1922), indicates the intention of these authors to study systematically the formation of rings from *o*-, *m*- and *p*-phenylene-diacetic esters and analogous esters.

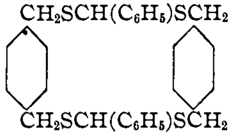
[3] V. Meyer, *Ber.*, **29**, 1414 (1896).

[4] R. Meyer, *Ann.*, **327**, 1 (1903).

[5] Mohr, *J. prakt. Chem.*, **98**, 349 (1918).

[6] V. Braun, *Ber.*, **45**, 1274, 2512 (1912).

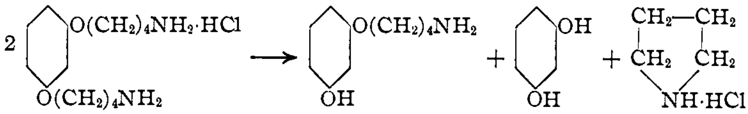
amalgam;[7] III by the reduction of *m*-xylylene dicyanide;[8] III is of particular interest because it may be converted by a Hofmann degradation of the corresponding quaternary ammonium hydroxide into a hydrocarbon which corresponds in structure to dihydro-naphthalene; the reduction of this latter hydrocarbon yields a saturated compound which corresponds to tetrahydro-naphthalene. Of more complex a character are the substances produced from *m*- and *p*-xylylene dihydrosulfides and aromatic aldehydes.[9] The constitution of the resulting compounds seems to be reasonably certain, since not only were complete analyses made, but also molecular-weight determinations.



All of the compounds just mentioned are quite normal as regards melting point and solubility, and resemble closely in properties the corresponding rings through the *ortho* positions of benzene whenever such rings are known.

In this investigation, unsuccessful attempts were made to close *meta* and *para* rings using various types of phenol ethers as starting materials. The formation of such rings which are similar to those already described by v. Braun except for the introduction of an oxygen atom, seemed a promising field for study, since the presence of a nitrogen or oxygen atom frequently favors ring formation. Moreover, the raw materials for the experiments were easily available.

As the reduction of *m*-xylylene dicyanide formed most readily a *meta* ring imine, an extension of this reaction to certain resorcinol ethers was first attempted. The abnormal difficulty in the reduction of resorcinol-bis (cyanomethyl) ether and in the formation of resorcinol-bis(β-cyano-ethyl) ether, made it necessary to limit the study to resorcinol-bis(γ-cyanopropyl) ether. When this last substance is reduced according to the method used for *m*-xylylene dicyanide, not a trace of ring compound is formed, but the corresponding diamine is obtained in excellent yields. Moreover, by distillation of the monohydrochloride of the diamine, no ring compound is produced. Instead, a decomposition takes place with the formation of resorcinol, resorcinol-mono-δ-aminobutyl ether and pyrrolidine.



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[7] v. Braun, *Ber.*, **51**, 1217 (1918); **52**, 2015 (1919).

[8] v. Braun, *ibid.*, **53**, 98 (1920).

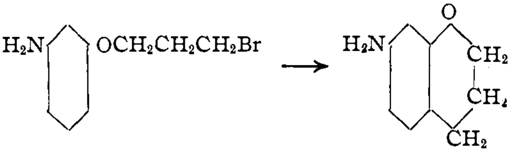
[9] Autenrieth and Beuttel, *ibid.*, **42**, 4352 (1909). See also Kotz and Sevin, *J. prakt. Chem.*, **64**, 526 (1901).

The question might be raised as to whether such a large ring as it was attempted to produce in this case could be formed. When it is considered that v. Braun,[7] by the heating of julolidine methochloride with sodium amalgam obtained a *meta* ring within 2 atoms as large as that which might have been produced in the above reaction, this objection seems to be invalid.

It was also impossible to obtain a ring compound by treating the resorcinol-bis(γ-iodopropyl) ether with 1 molecule of a primary amine. Under various conditions it was found that each iodine was always replaced by a NHR group.

Resorcinol-bis(γ-iodopropyl) ether and sodium, under a variety of conditions, gave no compounds having a ring structure. Very little reaction took place and that material which was changed, was converted into resorcinol-bis(*n*-propyl) ether. The reduction must be due to the action of the sodium on the dry ether used as a solvent. Durand has shown that such a reaction takes place with the evolution of hydrogen and formation of sodium alcoholate.[10]

V. Braun[6] was also able to convert, by heating, *p*-β-chloro-ethyl aniline into dihydro-*p*-indole. This same type of reaction was applied in this investigation to *p*- and *m*-aminophenol ethers. In no case, however, were the desired rings obtained. When *p*-aminophenol-β-bromo-ethyl ether was heated, no definite product could be isolated, whereas *m*-aminophenol-γ-bromopropyl ether did yield a product which was analyzed and gave a molecular weight which was correct for the *meta* ring. Further investigation, however, showed the compound to contain a primary amino group, thus indicating the structure to be either *m*-aminophenol allyl ether or *m*-aminochromane. The former was synthesized and proved not to be identical with it, so that the compound produced from *m*-aminophenyl-γ-bromopropyl ether was undoubtedly a chromane.



These experiments tend to confirm the previous observations of other investigators that a very definite kind and number of atoms are necessary for the formation of *meta* and *para* rings. It seems that if there is any other reaction which has the slightest tendency to take place in preference to the formation of *meta* and *para* rings, such a reaction will occur.

There have been described in the literature many substances which have been assigned simple ring structures connecting the *meta* and *para* positions of benzene, but which do not resemble in physical and chemical properties

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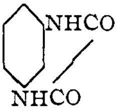
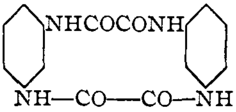
[10] Durand, *Compt. rend.*, **172,** 70 (1921).

the corresponding derivatives formed through the *ortho* positions. They are extremely insoluble, high-melting compounds, whereas the *ortho* derivatives are normal in this respect. Where hydrolysis is possible, the *meta* and *para* ring compounds hydrolyze much more readily than do the *ortho* derivatives. Among the numerous substances of this general type some of the more important may be mentioned: the condensation of *m*-phenylenediamine with oxalic acid[11] (Formula IV), with phosgene[12] (Formula V), or with carbon disulfide;[13] the condensation of resorcinol with phosgene[14] or with oxalic acid.[15] The corresponding *p*-phenylenediamine and hydroquinone derivatives were also made. Both iso- and terephthalic acid form anhydrides[16] entirely different in properties from *o*-phthalic anhydride. Only one conclusion can be drawn from these results, namely, that the structures of the *ortho* compounds are not analogous to those of the *meta* and *para* derivatives. It seems very likely that these insoluble compounds just mentioned do not possess simple formulas, but are dimolecular (VI).



IV

V



VI

It is not impossible that certain of the compounds are still more complex, or even consist of a mixture of several compounds of different molecular complexity, since in several instances the analyses do not indicate homogeneity. The dimolecular structures assigned to these compounds resemble closely the structures of the benzidine products described in the preceding paper,[17] and resemble them also in physical and chemical properties.

Experimental Part

Resorcinol-bis(β-bromo-ethyl) Ether, $C_6H_4(OCH_2CH_2Br)_2$.—In a 5-liter round-bottom flask fitted with a reflux condenser and mechanical stirrer, were placed 600 g. of ethylene bromide and 500 g. of absolute alcohol. To this mixture during the course of 4 hours was added in small portions a suspension of sodium resorcinate. This was made by dissolving 95 g. of sodium in 1 liter of absolute alcohol and adding with stirring to 1 liter of 95% alcohol containing 200 g. of resorcinol in solution. While the suspension was being added the mixture was kept boiling and was stirred during the entire period. After all of the sodium resorcinate had been added, the mixture was

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[11] Kluseman, *Ber.*, **7**, 1263 (1874).

[12] Michler and Zimmermann, *ibid.*, **14**, 2177 (1881). Lellmann and Würthner, *Ann.*, **228**, 225 (1885).

[13] Gucci, *Gazz. chim. ital.*, **17**, 524 (1887); **23**, [1] 298 (1893).

[14] (a) Birnbaum, Lurie, *Ber.*, **14**, 1754 (1881). (b) Bischoff, **35**, 3431 (1902).

[15] Ref. 14b, p. 3454.

[16] Bucher, This Journal, **30**, 1263 (1908); **31**, 1319 (1909).

[17] Adams, Bullock and Wilson, *Ibid.*, **45**, 521 (1923).

refluxed with stirring for 6 hours longer. The alcohol was distilled and the excess of ethylene bromide removed by distillation with steam. A pasty mass remaining in the flask was washed with water and then with 10% sodium hydroxide solution to remove unchanged resorcinol or any mono-ether.

The residue was distilled in a vacuum and the fraction boiling at 160–170° at 9 mm. collected. This was dissolved in hot alcohol, from which it separated upon cooling as waxy plates. When pure it melted sharply at 94.5–95° and boiled at 166–167° at 9 mm.

Analysis. Subs., 0.1676: AgBr, 0.1842. Calc. for $C_{10}H_{12}O_2Br_2$; Br, 49.4 Found: 49.9.

The mother liquors from the crystallization of the resorcinol-bis(β-bromo-ethyl) ether yielded, upon evaporation, a small amount of oil which was soluble in 20% sodium hydroxide and which reprecipitated upon the addition of hydrochloric acid. Upon distillation, a portion came over at 150–155° at 12 mm. This was not pure but gave an analysis about 2% low for resorcinol-mono-β-bromo-ethyl ether. It was contaminated with a small amount of resorcinol.

When resorcinol-bis(β-bromo-ethyl) ether was refluxed with sodium malonic ester, no condensation product was produced but most of the ether was decomposed with the formation of resorcinol.

Resorcinol-bis(γ-bromopropyl) Ether, $C_6H_4(OCH_2CH_2CH_2Br)_2$.—In a 5-liter flask fitted with a mechanical stirrer and reflux condenser were placed 220 g. of resorcinol, 1616 g. of trimethylene bromide, 1 liter of acetone, 250 cc. of water and 1 kg. of potassium carbonate. The mixture was refluxed with stirring on a steam-bath for 4 hours, after which an additional 350 g. of potassium carbonate was added and the stirring and refluxing were continued for 3 hours longer. The acetone was then distilled, agitation being continued to prevent bumping. About 800 to 900 cc. was recovered.

The residue was treated with enough water to dissolve the potassium bromide and carbonate. The under layer was separated and washed several times with water. It was then distilled, 100 cc. at a time, in a 200cc. Claisen flask. The trimethylene bromide was removed, using at first a water-pump vacuum; an oil pump was then used, and the resorcinol-bis(γ-bromopropyl) ether distilled at a pressure which was below 10 mm., for the product was rapidly and completely decomposed above 225–230° although it distilled at 215–220° at 10 mm. A low-boiling fraction, when purified, proved to be resorcinol-diallyl ether. Moreover, decomposition of the original product by superheating yielded large amounts of the diallyl derivative. The product when pure boiled at 204–206° at 6 mm. The yield of product varied from 150 to 200 g. From 700 to 800 g. of trimethylene bromide was recovered during the distillation. The distilled product, which solidified upon cooling, was crystallized twice from alcohol from which it formed pearly plates melting at 67°.

Analyses. Subs., 0.3270, 0.3566: 17.73, 19.26 cc. of 0.1050 *N* $AgNO_3$. Calc. for $C_{12}H_{16}O_2Br_2$: Br, 45.41. Found: 45.48, 45.37.

When the preparation of the resorcinol-bis(γ-bromopropyl) ether was attempted using trimethylene bromide and sodium resorcinate made from sodium, absolute alcohol and resorcinol, the reaction ran somewhat differently with the formation of 3 other products in addition to a certain amount of resorcinol-bis(γ-bromopropyl) ether, namely, resorcinol-γ-bromopropyl-allyl ether, $C_6H_4(OCH_2CH=CH_2)OCH_2CH_2CH_2Br$, resorinoldiallyl ether, $C_6H_4(OCH_2CH=CH_2)_2$, and in addition a substance which was probably γ-bromopropyloxyphenyl-allyloxyphenyl-trimethylene glycol, $BrCH_2CH_2CH_2OC_6H_4OCH_2CH_2CH_2OC_6H_4OCH_2CH=CH_2$.

In a 10-liter round-bottom flask fitted with a reflux condenser and a mechanical stirrer was placed 800 g. of trimethylene bromide and to this was added gradually a suspension of sodium resorcinate made by dissolving 50 g. of sodium in 500 cc. of absolute alcohol and adding 110 g. of resorcinol. The mixture was refluxed, stirred for 6 hours and filtered hot to remove the sodium bromide. Upon cooling, a white amorphous solid separated which was washed first with water, then with 10% sodium hydroxide, and again with water. It was then boiled with alcohol and filtered hot. Upon cooling the filtrate, crystals separated which after 5 crystallizations were pure and melted at 88–89°. This substance proved to be resorcinol-γ-bromopropyl-allyl ether.

Analyses. Subs., 0.3080: CO_2, 0.5994; H_2O, 0.1602. Subs., 0.2718: 9.6 cc. of 0.1050 N $AgNO_3$. Calc. for $C_{12}H_{15}O_2Br$: C, 53.13; H, 5.9; Br, 29.5. Found: C, 53.07; H, 5.8; Br, 29.62.

The alcohol-insoluble portion, after repeated washing with hot alcohol, was dissolved in benzene and treated with acetone until about $^2/_3$ of the product had separated. This was filtered and crystallized thrice from glacial acetic acid. The product was then washed with hot alcohol and dried. It formed a white amorphous powder melting at 119–120°. The analysis agreed with that of the γ-bromopropyloxyphenyl-allyloxyphenyl-trimethylene glycol.

Analyses. Subs., 0.5300: CO_2, 1.1670; H_2O, 0.2922. Subs., 0.4221: 9.30 cc. of 0.1050 N $AgNO_3$. Calc. for $C_{21}H_{25}O_4Br$: C, 59.86; H, 5.94; Br, 19.00. Found: C, 60.05; H, 6.12; Br, 18.51.

The alcoholic mother liquor from which the resorcinol-γ-bromopropyl-allyl ether was obtained, was evaporated to $^1/_2$ its volume and cooled. In this way a considerable portion of resorcinol-bis(γ-bromopropyl) ether was obtained. The mother liquors from this product were distilled and the main fraction boiling at 165–175° collected. Upon redistillation, a liquid boiling constantly at 156–158° at 12 mm. was produced; d_{20}^{20}, 1.1645; n_D^{20}, 1.5672. It was halogen-free and proved to be resorcinol-diallyl ether.

Analyses. Subs., 0.2756: CO_2, 0.7544; H_2O, 0.1916. Calc. for $C_{12}H_{14}O_2$: C, 75.78; H, 7.36. Found: C, 75.0; H, 7.7.

Resorcinol-bis(γ-Iodopropyl) Ether, $C_6H_4(OCH_2CH_2CH_2I)_2$.—One hundred g. of resorcinol-bis(γ-bromopropyl) ether was dissolved in 800 cc. of acetone, water was added until the solution just became turbid and then an additional amount of acetone sufficient to cause the solution to become clear. Two hundred g. of sodium iodide was then added and the flask allowed to stand. A reaction began immediately and the reaction mixture became warm. After standing overnight, the contents of the flask had become a thick solid. The crystals were filtered, about $^2/_3$ of the acetone was distilled, and the residue then cooled. A second crop of crystals were thus obtained which was added to the first crop, washed thoroughly with water to remove sodium bromide and iodide, and then recrystallized from acetone. The substance was obtained in nearly quantitative yields of soft white plates melting at 88–89°.

Analysis. Subs., 0.5730: 24.42 cc. of 0.1050 N $AgNO_3$. Calc. for $C_{12}H_{16}O_2I_2$: I, 56.9. Found: 56.7.

Upon treatment of this di-iodo compound with sodium malonic ester, there was obtained unchanged ether and, in addition, resorcinol-diallyl ether. No fraction could be isolated which contained the desired condensation product.

A solution of 30 g. of resorcinol-bis(γ-iodopropyl) ether was dissolved in 300 cc. of carefully dried ether and then treated with 4 g. of sodium cut into very thin slices. After every 4 days an additional 4 g. of sodium was added until a total of 12 g. had been used. At the end of 14 days the solution was poured off and the ether evaporated. A pasty mass remained which was dissolved in hot alcohol. Upon cooling the mixture, resorcinol-bis(γ-iodopropyl) ether separated and was filtered. The mother liquor was evaporated and then distilled. After the mixture was fractionated several times, there was obtained 3 cc. of a colorless liquid boiling at 120–125° at 11 mm.; n_D^{27}, 1.5126. It contained no halogen and proved by analysis to be resorcinol-bis(*n*-propyl) ether.

Analysis. Subs., 0.3880: CO_2, 1.0554; H_2O, 0.3264. Calc. for $C_{12}H_{18}O_2$: C, 74.22; H, 9.28. Found: C, 74.20; H, 9.35.

This substance was brominated by dissolving 2 g. in 10 cc. of glacial acetic acid, cooling to 0°, then adding 1.7 g. of bromine. The bromo substitution product, was shaken, when it crystallized in an almost quantitative yield. The product was washed with water and crystallized from hot alcohol. It formed in fine needles and melted at 81°. This substance proved to be identical with the bromine derivative of resorcinol-bis(*n*-propyl) ether made directly from resorcinol and *n*-propyl bromide.

Resorcinol-bis(*n*-propyl) Ether, $C_6H_4(OCH_2CH_2CH_3)_2$.—A mixture of 27.5 g. of resorcinol, 62 g. of *n*-propyl bromide, 90 g. of potassium carbonate, and 250 cc. of acetone was placed in a round-bottom flask and refluxed with stirring for 5 hours. The acetone was distilled and 500 cc. of water was added. The oily layer was drawn off and the aqueous solution extracted once with ether. The oil which was obtained from the ether was mixed with the main oily layer and fractionated. The product boiled at 127–128° at 12 mm.; d_{21}^{20}, 1.035; n_D^{33}, 1.5138. This substance was brominated as described for the product obtained by the action of sodium on resorcinol-bis(γ-iodopropyl) ether, and a product melting at 81° obtained. It proved to be identical with the monobromo derivative described above.

A reaction was carried out using sodium and resorcinol-bis(γ-iodopropyl) ether in hot toluene. Even under these conditions, however, there was obtained resorcinol-bis-(*n*-propyl) ether and resorcinol.

Finely divided silver did not react upon the di-iodo compound.

Resorcinol-bis-γ-(*n*-amylaminopropyl) Ether Dihydrochloride, $C_6H_4(OCH_2CH_2CH_2$-$NHC_5H_{11}.HCl)_2$.—A mixture of 60 g. of resorcinol-bis(γ-iodopropyl) ether and 10 g. of *n*-amyl amine in a 100cc. flask was heated with frequent shaking on a steam-bath at 95° for 1 hour, then in an oil-bath at 110° for 2 hours. The reaction mixture was allowed to stand overnight, when the contents had completely solidified. The solid was powdered and extracted with dil. hydrochloric acid. There remained after this treatment a residue of 25 g. of resorcinol-bis(γ-iodopropyl) ether. The aqueous hydrochloric acid extract was made alkaline with sodium hydroxide solution and extracted with ether. The ether was evaporated and the solid residue crystallized twice from a mixture of alcohol and hydrochloric acid (10 parts by volume of alcohol to 1 part of conc. hydrochloric acid). There were thus obtained white scales which darkened at 284° and melted at 287°. This proved to be the resorcinol-bis(γ-*n*-amyl aminopropyl) ether dihydrochloride.

Analyses. Subs., 0.3523: 15.32 cc. of 0.1050 *N* $AgNO_3$. Subs., 0.4064: 24.9 cc. of N_2 (29°, 746 mm.). Calc. for $C_{22}H_{42}O_2N_2Cl_2$: N, 6.41; Cl, 16.24. Found: N, 6.52; Cl, 16.19.

This compound was also made by dissolving 60 g. of the di-iodo compound and 11 g. of amyl amine in 300 cc. of toluene and heating to 100° with stirring for about 8 hours. The crystals of the amino-dihydro-iodide separated from the solution and could be filtered directly. There remained in the toluene about 20 g. of resorcinol-bis(γ-iodopropyl) ether.

An aqueous solution of the dihydrochloride, upon treatment with sodium hydroxide, yielded the free base. This was extracted with ether, the ether solution was dried and distilled and the residual base fractionated. It formed a pale yellow oil which boiled without decomposition at 249–252° at 10 mm.

Analysis. Subs., 0.7714: 34.1 cc. of N_2 (27°, 743 mm.). Calc. for $C_{22}H_{40}O_2N_2$: N, 7.76. Found: 7.88.

Resorcinol-bis(γ-cyanopropyl) Ether, $C_6H_4(OCH_2CH_2CH_2CN)_2$.—In a 2-liter round-bottom flask fitted with a reflux condenser was placed 450 cc. of 95% alcohol, 150 cc. of water, 50 g. of powdered sodium cyanide and 150 g. of resorcinol-bis(γ-iodopropyl) ether. The mixture was refluxed for 36 hours and the alcohol then distilled. The thick viscous liquid which remained was washed with water to remove sodium iodide and sodium cyanide, and then distilled under diminished pressure. The product when pure, boiled at 236–237° at 7 mm. and upon cooling, formed white, feather-like crystals melting at 31–32°; yield, about 60%.

Analysis. Subs., 0.3288: 33.5 cc. of N_2 (21°, 751 mm.). Calc. for $C_{14}H_{16}O_2N_2$: N, 11.47. Found: 11.45.

Resorcinol-bis(δ-aminobutyl) Ether, $C_6H_4(OCH_2CH_2CH_2CH_2NH_2)_2$.—In a 5-liter flask fitted with a reflux condenser and a mechanical stirrer, were placed 98 g. of resorcinol-bis-(γ-cyanopropyl) ether and 2112 g. of absolute alcohol. The solution was heated to boiling, the stirrer started and 150 g. of sodium was added in the course of about 20 minutes. When the sodium had all dissolved, a clear solution remained. It was cooled to 20° and 650 cc. of conc. hydrochloric acid was added slowly with stirring. The solution was again cooled to about 10° and the sodium chloride which precipitated was filtered. As the sodium chloride always included a certain amount of amine, it was dissolved in water, the aqueous solution made alkaline and extracted once with ether. The ether solution was added to the filtrate and the mixture made acid with hydrochloric acid. The alcohol and ether were distilled, and the residue which crystallized to a pasty mass, was washed once with benzene and then crystallized from dil. hydrochloric acid (1:2). The product separated as pearly plates, which after crystallization from a mixture of equal parts of benzene and alcohol melted at 248–249°; yield, 87 g. or 65%.

Analyses. Subs., 0.5043: 29.40 cc. of 0.1050 *N*, $AgNO_3$. Subs., 0.3494: 27.6 cc. of N_2 (23°, 751 mm.). Calc. for $C_{14}H_{26}O_2N_2Cl_2$: Cl, 21.8; N, 8.6. Found: Cl, 21.7; N, 8.8.

The mother liquors from the crystallization, upon evaporation, yielded a residue which after distillation proved to be unreduced cyanide.

The amine dihydrochloride just described was dissolved in alcohol and the calculated amount of powdered sodium hydroxide necessary to remove all the hydrogen chloride was added. The sodium chloride which precipitated was filtered and the alcohol evaporated. A brown oil remained, which distilled when pure at 208–209° at 7 mm.; d_{20}^{20}, 1.0589; n_D^{26}, 1.5315. It was colorless when first distilled, but slowly turned brown on standing.

Analysis. Subs., 0.3182: 32.4 cc. of N_2 (28°, 737 mm.). Calc. for $C_{14}H_{24}O_2N_2$: N, 11.1. Found: 11.0.

The monohydrochloride of this amine was prepared from the free base by dissolving 25 g. in 100 cc. of alcohol and adding 3.62 g. of hydrogen chloride dissolved in alcohol. After the solution had stood for a few minutes, prism-like crystals separated which melted at 233–234°.

Decomposition of Resorcinol-bis(δ-aminobutyl) Ether Hydrochloride by Heat.—For this experiment it was unnecessary to isolate the monohydrochloride as just described. The alcohol containing the crystals in suspension was placed in a Claisen flask arranged for distillation and the alcohol distilled. At this point the receiver was changed and the apparatus connected to a vacuum pump. There was inserted between the receiver and the vacuum pump first a flask containing solid sodium hydroxide and then a wash bottle containing conc. sulfuric acid. When the pressure reached 7 mm., the monohydrochloride was heated. The product melted and a vapor was given off so that the pressure rose for a short time to 15 mm. This vapor was absorbed by the sulfuric acid. When the pressure had again been reduced to 7 mm. a liquid began to distil at about 160° and the temperature gradually rose to 265°. At this point there remained practically no residue in the distilling flask. The sulfuric acid in the trap was carefully kept below 10°, and gradually made alkaline with sodium hydroxide. The alkaline solution which was thus obtained was distilled until the temperature of the distilling vapors reached 100°. The fraction which came over below this point was redistilled and 6 to 8 cc. of colorless liquid obtained which boiled between 85° and 95°. After it had been dried with sodium hydroxide and then with a little sodium, it distilled at 86–87.5°; d_{20}^{16}, 0.8620. It proved to be pyrrolidine, as shown by the formation of the chloroplatinate and picrate, both of which were identical with those obtained from pyrrolidine.

The distillate in the receiver was redistilled under a pressure of 7 mm. and 3 fractions were collected, at 145–155°, 190–230° and 240–265°. The lowest-boiling fraction crystallized upon cooling and after recrystallization from hot benzene, melted at 109–110° and proved to be resorcinol. The middle portion was refractionated and a product boiling at 210–211° at 7 mm. was obtained. This, upon cooling, crystallized to fine needles and proved to be pyrrolidine hydrochloride.

The third and largest portion was fractionated and a substance obtained which boiled 255–260° at 7 mm. It formed white crystals which were soluble in water. Upon treating the aqueous solution with alkali, a precipitate formed at the neutral point which redissolved upon addition of excess alkali. The solid (255–260° fraction) was purified for analysis by dissolving in warm alcohol, adding benzene slowly until a precipitate just began to appear, and then gradually cooling to 0°. The crystals when pure melted at 155–157°. Further purification was carried out by crystallization from absolute alcohol containing dry hydrogen chloride. A melting point of 159–161° was thus obtained. The substance proved to be resorcinol-mono-δ-aminobutyl ether hydrochloride.

Analyses. Subs., 0.3271, 0.3460: 14.47, 15.36 cc. of 0.1050 *N*, $AgNO_3$. Subs., 0.2645: CO_2, 0.5328; H_2O, 0.1711. Calc. for $C_{10}H_{16}O_2NCl$: C, 55.16; H, 7.36; Cl, 16.32. Found: C, 54.94; H, 7.19; Cl, 16.46, 16.52.

The amine hydrochloride was dissolved in alcohol and to it was added the calculated amount of sodium in alcohol that would just react with the hydrogen chloride. The sodium chloride was filtered from the alcohol solution and then the amine distilled. It boiled at 198–204° at 8 mm. and solidified to a white solid, which was crystallized from a mixture of benzene and alcohol (9:1). It melted at 119–119.5°.

Analysis. Subs., 0.3705: 26.8 cc. of N_2 (28°, 756.5 mm.). Calc. for $C_{10}H_{15}O_2N$: N, 7.73. Found: 7.96.

Resorcinol-bis(*p*-nitrobenzoyl-mono-δ-aminobutyl) Ether, $(p)NO_2C_6H_4CO_2C_6H_4OCH_2CH_2CH_2CH_2NHCOC_6H_4NO_2(p)$.—The amine just described was dissolved in 10% sodium hydroxide solution. Excess of *p*-nitrobenzoyl chloride was then added and the mixture shaken. A solid separated which was filtered, washed with 10% sodium hydroxide solution and water and then crystallized from 95% alcohol. It formed white needles melting at 123–124°.

Analysis. Subs., 0.3162: 26.2 cc. of N_2 (27°, 741 mm.). Calc. for $C_{24}H_{21}O_8N_3$: N, 8.77. Found: 9.02

Derivatives of Meta-Nitrophenol

***m*-Nitrophenol,** $NO_2C_6H_4OH$.—This was made by modification of the process described by Bantlin.[18] A suspension was made of 50 g. of *m*-nitro-aniline in 200 cc. of water to which 100 cc. of conc. sulfuric acid was added. The *m*-nitro-aniline was completely dissolved in the warm solution. This was poured with stirring into a mixture of 1 liter of water and 400 g. of cracked ice. A fine precipitate of *m*-nitro-aniline sulfate

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[18] Bantlin, *Ber.*, **11**, 2100 (1878). Henriques, *Ann.*, **215**, 323 (1882).

separated; this is quite essential if a good yield of the product is to be obtained. Four hundred g. more of cracked ice was now added to the suspension and when the temperature reached 0°, 26 g. of sodium nitrite in 200 cc. of water was added rapidly with vigorous stirring. More ice was added when necessary, to keep the temperature below 5°. In a few minutes, the solution darkened and all of the *m*-nitro-aniline had dissolved to form the diazonium salt.

The solution was filtered and diluted with 6 liters of dil. sulfuric acid (1:10). This was boiled until a clear solution resulted and filtered hot on a Büchner funnel, upon which was a layer of sand to prevent small amounts of tarry oil from being sucked through. The filtrate was cooled and extracted with ether until the aqueous solution no longer became red when made alkaline with sodium hydroxide. The ether was distilled and the yellow oil remaining was cooled. It formed a mass of yellow crystals. These were sucked dry, washed with benzene until they became a cream color, and then crystallized from dil. hydrochloric acid; yield, 70–75%.

_m_-Nitrophenyl-γ-bromopropyl Ether, $NO_2C_6H_4OCH_2CH_2CH_2Br$.—In a 1-liter round-bottom flask fitted with a reflux condenser was placed 50 g. of *m*-nitrophenol and 230 g. of trimethylene bromide in 400 cc. of alcohol. To this was added a solution of 8.3 g. of sodium in 100 cc. of absolute alcohol, and the mixture was refluxed on a steam-bath until it no longer reacted alkaline to litmus (about 4 hours). The sodium bromide which had separated was filtered, and the alcohol removed from the filtrate by distillation. The excess of trimethylene bromide was now distilled under diminished pressure, and the remaining oil washed with 10% sodium hydroxide and then with water. Upon purification, it boiled at 186–188° at 7 mm.; d^{20}_{20}, 1.513; n^{25}_{D}, 1.5700. The yield of the product which was a pale greenish-yellow oil, was about 70 g.

Analysis. Subs., 0.4316: 15.74 cc. of 0.1050 *N* $AgNO_3$. Calc. for $C_9H_{10}O_3NBr$: Br, 30.71. Found: 30.63.

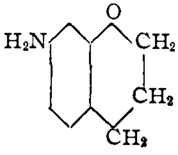
_m_-Aminophenyl-γ-bromopropyl Ether, $NH_2C_6H_4OCH_2CH_2CH_2Br$.—A solution was made of 120 g. of crystalline stannous chloride in 260 cc. of conc. hydrochloric acid and heated to 100°. Forty g. of *m*-nitrophenyl-bromopropyl ether was then added, a small portion at a time, as rapidly as it would dissolve. When it had all been added, the solution was cooled to 0°, thus causing the tin salt of the amine to crystallize. The crystals were filtered from the acid solution and sucked dry on a Büchner funnel.

The crystals were treated with 200 cc. of water, cooled to 0° and surrounded with a freezing mixture, and a 30% solution of sodium hydroxide was added with stirring until the stannic acid which at first precipitated, redissolved. Ether was added to dissolve the oil which separated, and the aqueous solution extracted two or three more times with ether. The ether solutions were mixed, washed with water and dried with anhydrous sodium sulfate.

The ether was distilled until 75 cc. of solution was left. Into this residual solution dry hydrogen chloride was passed until a precipitate no longer formed. The crystals were filtered, washed with ether and recrystallized from 1:1 hydrochloric acid. There was thus obtained 21 g. of white scales melting at 114–115°.

Analysis. Subs., 0.4201: 21.6 cc. of N (30°, 739 mm.). Calc. for $C_9H_{12}ONBr.HCl$: N, 5.26. Found: 5.49.

The Effect of Heat upon _m_-Aminophenyl-γ-bromopropyl Ether; 6 Amino-chromane,



—The free amine was obtained from the above mentioned hydrochloride by dissolving it in water, adding 10% sodium hydroxide solution, extracting with ether and then evaporating the ether. The amine was an unstable yellow oil which rapidly turned dark and became viscous on standing. It would not distil at 6 mm. It was found advantageous to prepare it from the hydrochloride just before using.

The free amine obtained from 50 g. of hydrochloride was dissolved in 600 cc. of benzene and the solution was refluxed for 8 hours. The solution turned very dark during this period. The benzene was distilled and there remained a black oil. Upon distilling this there was obtained about 12 g. of a brown oil boiling at 125–185° at 7 mm. This was dissolved in dil. hydrochloric acid, the solution extracted with ether, then the free amine liberated from the aqueous solution with sodium hydroxide and extracted with ether. The ether was evaporated and after three fractionations of the residue there was obtained about 3 g. of a pale yellow oil boiling at 140–142° at 7 mm.; d^{20}_{20}, 1.1549; n^{25}_{D}, 1.5944.

Analyses. Subs., 0.3150: 25.9 cc. of N_2 (25°, 755 mm.). Subs., 0.2401: CO_2, 0.6401; H_2O, 0.1712. Subs., 0.8010, 1.3631: 22 g. of C_6H_6; ΔT_f, 1.204°, 2.008°. Calc. for $C_9H_{11}ON$: C, 72.48; H, 7.38; N, 9.4; mol. wt., 149. Found: C, 72.41; H, 7.93; N, 9.2; mol. wt., 152, 154.

By dissolving the free amine in dry ether and adding dry hydrogen chloride, a hygroscopic hydrochloride was precipitated which started to decompose at 134° and melted at 158–160°.

By dissolving the product in alcohol and adding solid picric acid until the solution was no longer acid, a substance crystallized which on purification from 25% alcohol formed sulfur-yellow needles which darkened at 156–160° and melted with decomposition at 182–183°.

By adding the solution of chloroplatinic acid to an aqueous solution of the amine, a brown precipitate was formed which could be recrystallized from water. It formed brown crystals melting at 224–225°, and decomposing at 227°.

The acetyl derivative made by the action of the acetic anhydride upon the amine was an oil.

Benzene-sulfone-amide of the Amino-chromane, $C_6H_5SO_2NH(C_9H_9O)$.—The amine was added to a 10% sodium hydroxide solution and treated with excess of benzene-sulfonyl chloride. The reaction took place slowly and it was advisable to warm the mixture. After this had been shaken for 15 to 20 minutes, the benzene-sulfonyl chloride disappeared. The solution was filtered and the filtrate made acid with hydrochloric acid. A white precipitate formed which was crystallized from 50% alcohol. It formed long, white needles which melted at 148–148.5°.

Analyses. Subs., 0.3525: 16.2 cc. of N_2 (34°, 748 mm.). Subs., 0.3201: $BaSO_4$, 0.2611. Calc. for $C_{15}H_{15}O_3NS$: N, 4.84; S, 11.07. Found: N, 4.88; S, 11.21.

Diazotization of the Amino-chromane and Coupling with β-Naphthol.—The amino-chromane was diazotized in the usual way and coupled with β-naphthol in sodium hydroxide solution. A brilliant red color immediately developed and a solid separated. The solution was made slightly acid with hydrochloric acid and filtered. The red product which separated was only slightly soluble in cold 10% sodium hydroxide. It was crystallized twice from hot alcohol from which it separated as very fine plates. It was carefully dried in a vacuum before analysis.

Analysis. Subs., 0.2044: 17.0 cc. of N_2 (32°, 745 mm.). Calc. for $C_{19}H_{16}O_2N_2$: N, 9.21. Found: 8.92.

***m*-Nitrophenyl-allyl Ether, $NO_2C_6H_4OCH_2CH=CH_2$.**—In a 1-liter flask fitted with a reflux condenser were placed 60 g. of *m*-nitrophenol dissolved in 250 cc. of absolute alcohol and 54 g. of allyl bromide. To the solution was then added a solution of 10 g. of sodium dissolved in 250 cc. of absolute alcohol. The mixture was refluxed for 3 hours and the sodium bromide then filtered out while the mixture was still hot. As the solution proved to be alkaline, 2 g. more of allyl bromide was added and the solution was refluxed for another hour. Although the solution was, at the beginning, deep red, it finally became a pale straw color. The alcohol was distilled and the oil which remained was washed twice with 25 cc. portions of 10% sodium hydroxide solution and then with water. On distillation, there was obtained 61 g. of a pale yellow oil boiling constantly at 136–137° at 8 mm. The product, upon cooling, solidified into crystals melting at 31.5–32°.

Analysis. Subs., 0.3489: 24.6 cc. of N_2 (29°, 751.5 mm.). Calc. for $C_9H_9O_3N$: N, 7.76. Found: 7.72.

m-**Aminophenyl-allyl Ether,** $NH_2C_6H_4OCH_2CH=CH_2$.—To a solution of 190 g. of crystalline stannous chloride in 475 cc. of conc. hydrochloric acid, heated to 100°, was added 50 g. of *m*-nitrophenyl-allyl ether, a little at a time until all had dissolved. The solution was then cooled and while the temperature was kept below 20°, a solution of 30% sodium hydroxide was added until the stannic acid had just dissolved. The oil was extracted with ether, the ether evaporated and the residue fractionated. There was thus obtained 26 g. of a yellow oil boiling at 120–122° at 5 mm.; d_{20}^{20}, 1.0891; n_D^{25}, 1.5708.

Analysis. Subs., 0.2964: 25.8 cc. of N_2 (26°, 750 mm.). Calc. for $C_9H_{11}ON$: N, 9.40. Found: 9.63.

The hydrochloride was prepared by passing dry hydrogen chloride into a dry ether solution of the amine. It formed white crystals melting at 145–146°.

The acetyl derivative, formed upon treating the amine with acetic anhydride, was a colorless liquid.

A portion of the amine was added to a large excess of sodium hydroxide, benzenesulfonyl chloride was added, and the mixture was shaken. Heat was generated and within a very short time solution was complete. It was acidified and the white precipitate which formed was filtered. After two crystallizations from 25% alcohol white needles were obtained melting at 83–83.5°.

Derivatives of Para-Nitrophenol

p-**Nitrophenyl-β-bromo-ethyl Ether,** $NO_2C_6H_4OCH_2CH_2Br$.—A mixture of 1.5 gr. mol. of ethylene bromide and 1 gr. mol. of sodium *p*-nitrophenolate was mixed with about 600 cc. of water and the whole refluxed until practically all of the yellow color had disappeared from the water layer (30–40 hours). The mixture was then distilled with steam as long as any ethylene bromide came over. Upon cooling, the β-bromo-ethyl ether separated. It was filtered and crystallized from hot alcohol. It formed creamy-white plates which when pure melted at 64°.

Analysis. Subs., 0.2162: 0.1506: AgBr, 0.1642, 0.1144. Calc. for $C_8H_8O_3NBr$: Br, 32.5. Found: 32.3, 32.4.

p-**Aminophenyl-β-bromo-ethyl Ether,** $NH_2C_6H_4OCH_2CH_2Br$.—Four parts of crystalline stannous chloride were dissolved in 10 parts of conc. hydrochloric acid. The mixture was warmed to 60° and *p*-nitrophenyl-β-bromo ethyl ether added, a small portion at a time, as rapidly as it dissolved. The reaction was exothermic so that it was necessary to cool the mixture from time to time in order to keep the temperature at about 60°. As soon as no more nitro-ether dissolved, the mixture was diluted with a large volume of water, and hydrogen sulfide was passed in to precipitate the tin. The solution was then filtered and evaporated until crystals began to appear. As it cooled, long needles of *p*-aminophenyl-β-bromo-ethyl ether hydrochloride crystallized. It was purified by recrystallization from water, after which it melted at 196°.

To obtain the free base, the hydrochloride was dissolved in water and the solution cooled to 0°. Solid sodium hydroxide was then added until the solution became alkaline, as indicated by the change from a faint pink to a slightly blue color in the solution itself. The amine was filtered as rapidly as possible, washed with water, and dissolved in ether. The ether solution was filtered and evaporated until crystals began to appear. Upon the addition of petroleum ether at this point, practically all of the free amine crystallized. It could be recrystallized from a mixture of ether and petroleum ether and, when pure, formed small white plates which melted at 84°.

Analyses. Subs., 0.1976, 0.2321: AgBr, 0.1728, 0.2030. Calc. for $C_8H_{10}ONBr$: Br, 37.0. Found: 37.2, 37.2.

The decomposition of this substance by heat was attempted not only alone but in the presence of alcohol and benzene. In no case, however, was it possible to obtain a reaction product of reasonable purity.

Summary

An attempt has been made to produce ring structures through the *meta* and *para* positions of benzene by starting with various resorcinol ethers and with *m*- and *p*-aminophenol ethers. In no instance was a *meta* or *para* ring obtained such as might be expected from the reactions of compounds similar in structure except for the presence of the oxygen atom or atoms. Various types of decomposition occurred in each reaction, as given below.

(a) By the reduction of resorcinol-bis(γ-cyano-propyl) ether, there was obtained resorcinol bis(δ-aminobutyl) ether.

(b) Upon heating the monohydrochloride of resorcinol-bis(δ-aminobutyl) ether, there was obtained resorcinol, resorcinol mono-δ-amino-butyl ether and pyrrolidine.

(c) Resorcinol-bis(γ-iodopropyl) ether, upon treatment with sodium in dry ether, yielded unchanged material and a small amount of resorcinol-bis(*n*-propyl) ether.

(d) *p*-Aminophenyl-β-bromo-ethyl ether, when heated gave no definite product. *m*-Aminophenyl-γ-bromopropyl ether, when heated, gave the hydrobromide of 6-amino-chromane.

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