pared with the above samples and found to give no depressions in the melting points.

Bromo Compounds.—Using analogous methods the following compounds were prepared: **3-bromo-4-methoxy-4′-acetodiphenyl** (a), plates from methyl alcohol, m. p. 97–98°; **3-bromo-4-methoxy-4′-carboxydiphenyl** (b), needles from tetrachloroethane, m. p. 270–271°; methyl ester (c), long needles from alcohol, m. p. 148–149°.

Anal. Calcd. (a) C, 59.02; H, 4.30; (b) C, 54.72; H, 3.62; (c) C, 56.07; H, 4.08. Found: (a) C, 59.10; H, 4.63; (b) C, 54.66; H, 3.89; (c) C, 55.91; H, 3.95.

Condensation of *p*-Methoxydiphenyl with Acetyl Chloride.—The reaction of the ether (5 g.) and acetyl chloride (2.2 g.) in the presence of aluminum chloride (4 g.) was run in boiling carbon bisulfide, in tetrachloroethane at 0–20°, and in nitrobenzene at 0–20°. There was little difference in the total yield or the ratio of isomers in the three cases, although tetrachloroethane seemed to give slightly better results (65% yield) than the other solvents. A separation is easily accomplished with ether, which readily dissolves the low-melting isomer (VI) and leaves the other ketone (V) as a residue, and in each case the high-melting compound was found to comprise 65–75% of the total. This substance, **4-methoxy-4′-acetodiphenyl** (V), forms microcrystals from methyl alcohol, m. p. 153–154°. On oxidation with alkaline permanganate it gave an acid identical with III. **3-Aceto-4-methoxydiphenyl** (VI) was found in the ether mother liquor contaminated with unchanged *p*-methoxydiphenyl. It was easily separated from this substance and purified through the semicarbazone, which gives plates from alcohol. On hydrolysis with boiling 2 *N* hydrochloric acid the ketone was obtained and crystallized from dilute methyl alcohol; plates, m. p. 62–63°.

Anal. Calcd. for $C_{15}H_{14}O_2$: C, 79.61; H, 6.24. Found: (V) C, 79.65; H, 6.34; (VI) C, 79.66; H, 6.43.

Fries Rearrangement.—4-Acetoxydiphenyl (5 g.) was intimately mixed with aluminum chloride (3.5 g.) and carbon disulfide (20 cc.) and heated to evaporate the solvent. The residue was heated in a bath at 140° for thirty minutes and then decomposed with dilute hydrochloric acid and extracted with ether. The rearranged material was extracted from the washed solution with dilute alkali and recovered as a solid by acidification. **4-Hydroxy-4′-acetodiphenyl,** the less soluble isomer, was obtained by crystallization of the crude material to constant melting point from benzene; small needles, m. p. 206–207° (0.2 g.). It gave on methylation a product identical with the ether V described above. The material recovered from the benzene mother liquor was taken up in alcohol (50 cc.) and treated with an aqueous solution of semicarbazide hydrochloride (1.1 g.) and sodium acetate (0.8 g.). On standing yellow crystals of a semicarbazone separated (0.95 g.; m. p. >270°) and this was hydrolyzed with boiling 2 *N* hydrochloric acid. After crystallizing the recovered ketone from petroleum ether **3-aceto-4-hydroxydiphenyl** was obtained as small prisms, m. p. 61–62°, and on methylation it formed an ether, m. p. 62–63°, which did not depress the melting point of 3-aceto-4-methoxydiphenyl.

Anal. Calcd. for $C_{14}H_{12}O_2$: C, 79.21; H, 5.71. Found: (4′-isomer) C, 79.37; H, 6.01; (3-isomer) C, 79.19; H, 5.83.

Summary

In the Friedel and Crafts reaction with succinic anhydride and with acetyl chloride 4-methoxydiphenyl is substituted in both the 3- and the 4′-positions and solvents have little influence on the ratio of the isomers produced. The Fries rearrangement of 4-acetoxydiphenyl also proceeds in these two directions.

The closing of a six-membered ring at the 2-position of diphenyl is inhibited by a *m*-methoxyl group at position 4.

CONVERSE MEMORIAL LABORATORY
CAMBRIDGE, MASS.

RECEIVED JULY 6, 1936

[CONTRIBUTION FROM RÖHM AND HAAS COMPANY, INC.]

The Condensation of Phenols with Ethanolamine and Formaldehyde

BY HERMAN ALEXANDER BRUSON

It has been known for some time that amines catalyze the condensation between phenols and formaldehyde to form resins. The mechanism of this reaction is still obscure.

When phenols are condensed with molecular equivalents each of formaldehyde and secondary amines, such as dimethylamine or piperidine, tertiary amines are formed.[1]

Décombe has shown that the products thus obtained are, without doubt, *o*-hydroxybenzylamino derivatives.[2]

Morpholine is particularly prone to form well-defined, crystalline hydroxybenzylmorpholines with a variety of monohydric or polyhydric phenols and formaldehyde.[3]

In a study of this reaction with other amines, it has now been found that *β*-aminoethanol can be combined with formaldehyde and phenols to yield hydroxybenzylaminoethanols. The condensation is, however, complicated by the formation of resinous materials which in some cases form the main product. It has been found possible, by intro-

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(1) Bayer, German Patent 89,979, 92,309 (1895).

(2) J. Décombe, *Compt. rend.*, **196**, 866 (1933); **197**, 258 (1933).

(3) H. Bruson, U. S. Patent 2,040,039, 2,040,040 (1936).

ducing various orienting groups into the phenol nucleus and thereby decreasing the number of reactive available nuclear positions, to so arrest resin formation that the intermediate compounds can be isolated in pure crystalline form.

When phenol was mixed with a molecular equivalent quantity each of formaldehyde and ethanolamine, heat was evolved, and a sticky, sirupy mass was formed. After washing with water, this material formed a reddish, viscous, resinous material which was readily soluble in dilute hydrochloric acid or sodium hydroxide solution. It therefore contained an amino group and a free phenolic hydroxyl group. When heated to about 100°, it gradually hardened to a nitrogenous, pale reddish, resin which was still soluble in dilute acid, but which progressively became more and more insoluble as heating was continued. When two molecular equivalents of formaldehyde were used for the condensation, the product resinified faster to an infusible resin. At no stage was it possible to isolate therefrom any crystalline product.

The three isomeric cresols reacted in a similar manner to yield sticky, nitrogenous sirups or resins which could not be crystallized, nor could they be distilled, even in high vacuum, without decomposition.

However, the introduction of a phenyl group *ortho* to the phenolic hydroxyl group, led to the formation of a crystalline compound which could easily be separated from resinous by-products. *o*-Phenylphenol reacted with one mole equivalent each of formaldehyde and ethanolamine to yield a substance crystallizing in colorless needles melting at 116° and corresponding to the empirical formula $C_{15}H_{17}O_2N$. This compound was soluble in aqueous 10% sodium hydroxide solution or phosphoric acid solution, but was insoluble in sodium bicarbonate solution. From its empirical composition and chemical behavior, it would correspond to the probable formula $C_6H_5C_6H_3OHCH_2NHCH_2CH_2OH$ in which the entering group could be ortho or para to the phenolic hydroxyl group.

p-Phenylphenol, on the other hand, formed a crystalline compound containing less nitrogen than that called for by the above empirical formula. It was less soluble in acids or in sodium hydroxide solution and more soluble in alcohol than the *o*-phenyl compound. After repeated crystallizations from benzene, it melted at 102°. Assuming that it is not a mixture, its analysis approximates a possible formula $(C_6H_5C_6H_3OHCH_2)_2NCH_2CH_2OH$.

p-Cyclohexylphenol likewise formed a crystalline compound, m. p. 171°, which contained less nitrogen than that called for by a simple cyclohexylhydroxybenzylaminoethanol, and which approximates a possible structure analogous to the para-phenyl compound.

Well-defined crystalline reaction products were obtained from *p*-*t*-butylphenol, *p*-*t*-amylphenol, *p*-benzoylphenol, *p*-nitrophenol and 3-nitro-4-hydroxytoluene, the analysis and behavior of which indicated the presence of one $—CH_2NHCH_2CH_2OH$ group attached to the aromatic nucleus. In view of the blocking of the para positions in these phenols, the entering $—CH_2NHCH_2CH_2OH$ radical very probably enters the ortho position to the phenolic hydroxyl group. By using 2,4-dichlorophenol and 5-chloro-2-hydroxydiphenyl, which contain one very reactive free ortho position, the corresponding compounds containing the $—CH_2NHCH_2CH_2OH$ group undoubtedly ortho to the phenolic OH group, were obtained.

In the case of *o*-cyclohexylphenol, *p*-benzylphenol, *p*-α,α,γ,γ-tetramethylbutylphenol, *o*- and *p*-chlorophenols, oily, resinous materials were obtained. These products were soluble, however, for the most part in 10% phosphoric acid solution.

Resorcinol, upon treatment with one mole equivalent each of formaldehyde and ethanolamine, gave an amorphous water-insoluble powder which was soluble in dilute hydrochloric acid.

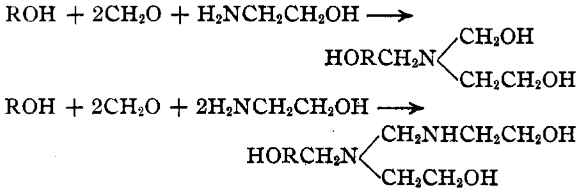
Attempts to introduce two hydroxyethyl aminomethyl groups into those phenols containing two free *ortho* positions to the hydroxyl group, led to the formation of viscous oils which could not be distilled without resinification.

The crystalline hydroxybenzylamino ethanols isolated, react further with formaldehyde to form resins. It is believed that the formaldehyde reacts with the imino group to form a methylol compound which is capable of further condensation with the components present. Various competing reactions may take place. These may be formulated as follows, where R is the phenolic nucleus

$$CH_2O + H_2NCH_2CH_2OH \longrightarrow HOCH_2NHCH_2CH_2OH \quad (A)$$

$$ROH + HOCH_2NHCH_2CH_2OH \longrightarrow HORCH_2NHCH_2CH_2OH \quad (B)$$

The formaldehyde and ethanolamine first combine with evolution of heat to form a methylol derivative (A), which then reacts with a mole of the phenol to form the hydroxyaralkylaminoethanol (B). This compound is usually the main product of the reaction, especially if care is taken to use only one molecular equivalent to each of the three components. If the phenol is suitably oriented, product (B) crystallizes out. However, side reactions also occur, especially if an excess of formaldehyde or of ethanolamine is present, so that a complex mixture of phenolic amino alcohols is formed, among which may be the following



$$ROH + 2CH_2O + H_2NCH_2CH_2OH \longrightarrow HORCH_2N\begin{cases} CH_2OH \\ CH_2CH_2OH \end{cases}$$

$$ROH + 2CH_2O + 2H_2NCH_2CH_2OH \longrightarrow HORCH_2N\begin{cases} CH_2NHCH_2CH_2OH \\ CH_2CH_2OH \end{cases}$$

These can, of course, again react with formaldehyde or with formaldehyde plus ethanolamine, and this can be kept up until all free molecular movement ceases and the end-product becomes a rigid, nitrogenous resin.

Experimental Part

Phenylhydroxybenzylaminoethanol.—(a) To a solution of 51 g. of *o*-phenylphenol (0.3 mol), 50 cc. of methanol, and 30 g. of aqueous 30% formaldehyde (0.3 mol), there was added, while shaking and cooling with tap water, 18.3 g. of β-aminoethanol. The clear, reddish solution was allowed to stand at room temperature (20–25°) for about sixty-five hours, during which time it solidified to a crystalline mass which contained a sticky, resinous material. The yield of the filtered, air-dried, crude crystalline product was 33 g. Upon recrystallization from 50 cc. of absolute ethyl alcohol, 19 g. of product were obtained in the form of colorless needles. The analytical sample melted at 116° (uncorr.) after three recrystallizations from alcohol.

Anal. Calcd. for $C_{15}H_{17}O_2N$: C, 74.03; H, 7.05; N, 5.76. Found: C, 73.72; H, 6.89; N, 5.51.

(b) The same product may be obtained in a much shorter time by the following procedure:

A solution of 60 g. of aqueous 30% formaldehyde (0.6 mole) was added slowly to 36.6 g. of β-aminoethanol (0.6 mole) while cooling and stirring the mixture. The clear solution was allowed to stand for about one hour until the odor of formaldehyde disappeared. It was then added to a solution of 102 g. of *o*-phenylphenol (0.6 mole) in 100 cc. of ethyl alcohol. The solution was boiled under reflux on a steam-bath for one and one-half hours, and allowed to stand overnight in an ice-box. The weight of colorless crystals obtained was 55 g. or 38%.

Condensation of *p*-Phenylphenol, Formaldehyde and Ethanolamine.—To a suspension of 34 g. of *p*-phenylphenol (0.2 mol) in 34 cc. of methanol, 12.2 g. of β-aminoethanol was added and the mixture warmed until it became clear. It was then cooled to 25° and 6 g. of powdered *p*-formaldehyde added. The mixture was shaken for about ten minutes, during which time the *p*-formaldehyde dissolved with heat evolution, the temperature reaching 40°. The clear solution thus obtained was then boiled for one hour under reflux on a steam-bath, cooled and poured slowly into 200 cc. of water with stirring. The white precipitate was filtered by suction, washed thoroughly with water and dried in the air. The somewhat yellowish powder thus obtained was recrystallized twice from benzene with chilling, using Norite to remove the yellow color, until a constant melting point of 102° was obtained; colorless crystals; very soluble in alcohol. Three separate preparations were analyzed in duplicate and averaged.

Anal. Calcd. for $C_{23}H_{27}O_3N$: C, 79.02; H, 6.40; N, 3.30. Found (1): C, 78.54; H, 6.98; N, 3.46. Found (2): C, 78.93; H, 6.92; N, 3.20. Found (3): C, 78.67; H, 6.88; N, 3.26.

***p*-Cyclohexylphenol, Formaldehyde, Ethanolamine Condensation.**—To a solution of 35.2 g. of *p*-cyclohexylphenol, 33 cc. of methanol and 12.2 g. of β-aminoethanol, there was added, with cooling and shaking, 20 g. of aqueous 30% formaldehyde solution. After standing at room temperature for one hour, the mixture was boiled for one and one-half hours under reflux on a steam-bath and placed in a refrigerator at 5° for several weeks. A small quantity (5 g.) of crystalline crusts separated, which were contaminated with a sticky sirup. The crystalline material was dried on porous tile and recrystallized from methanol to a constant melting point; colorless fine crystals, m. p. 170–171°. Four separate preparations were analyzed in duplicate and averaged.

Anal. Calcd. for $C_{15}H_{23}O_2N$: C, 72.23; H, 9.32; N, 5.62. $C_{28}H_{39}O_3N$: C, 76.83; H, 8.99; N, 3.20. Found (1): C, 76.27; H, 9.15; N, 3.21. Found (2): C, 76.71; H, 8.66; N, 3.26. Found (3): C, 76.94; H, 8.84; N, 3.27. Found (4): C, 76.38; H, 9.16; N, 3.38.

Chlorophenylphenol, Formaldehyde, Ethanolamine Condensation.—To a solution consisting of 20.5 g. of 5-chloro-2-hydroxydiphenyl, 27 cc. of methanol, and 10 g. of aqueous 30% formaldehyde, there was added, with cooling and shaking, 6.1 g. of ethanolamine. The mixture was then boiled under reflux for one and one-half hours on a steam-bath. The crystalline mass thus obtained was recrystallized from *n*-butanol. It separated in very fine colorless crystals, m. p. 182–183°; difficultly soluble in alcohol; readily soluble in 10% sodium hydroxide or hydrochloric acid solution.

Anal. Calcd. for $C_{15}H_{16}O_2NCl$: Cl, 12.77; N, 5.04. Found: Cl, 12.80; N, 4.81.

2-Hydroxy-3,5-dichlorobenzylaminoethanol.—To a solution of 16.3 g. of 2,4-dichlorophenol, 16 cc. of methanol, and 6.1 g. of ethanolamine, there was added 3 g. of *p*-formaldehyde. The mixture was shaken for fifteen minutes until the *p*-formaldehyde had dissolved, then boiled under reflux on the steam-bath. After about thirty minutes of boiling, a yellowish crystalline material began to separate. The mixture was cooled and filtered. The yellowish crystals (7 g.) were washed with a little methanol and recrystallized from *n*-butanol for analysis; colorless, fine white needles, m. p. 199–200°.

Anal. Calcd. for $C_9H_{11}O_2NCl_2$: Cl, 30.04; N, 5.93. Found: Cl, 29.80; N, 5.76.

2 - Hydroxy - 3 - nitro - 5 - methylbenzylaminoethanol.—A mixture of 15.3 g. of 3-nitro-4-hydroxytoluene, 20 cc. of methanol, 6.1 g. of ethanolamine and 3 g. of *p*-formaldehyde, was boiled under reflux for one hour. The clear red solution was cooled and scratched to induce crystallization. The yellow crystals were washed with a little methanol and recrystallized from butanol; yellow needles, m. p. 205–206°.

Anal. Calcd. for $C_{10}H_{14}O_4N_2$: C, 53.07; H, 6.24; N, 12.38. Found: C, 53.26; H, 6.36; N, 12.61.

***p*-*t*-Butylhydroxybenzylaminoethanol.**—To a solution consisting of 30 g. of *p*-*t*-butylphenol, 30 cc. of methanol and 12.2 g. of ethanolamine, there was added, with cooling and shaking, 6 g. of *p*-formaldehyde. After shaking until all heat evolution had ceased, the clear solution obtained was boiled for one hour under reflux on a steam-bath, and then placed in a refrigerator at 5° for several days, during which time it solidified to a colorless, crystalline mass; yield of crude air-dried crystals was 19 g. After recrystallization from methanol by repeated boiling and chilling, 5 g. of the analytically pure, colorless, crystalline product, m. p. 127–128°, was isolated.

Anal. Calcd. for $C_{13}H_{21}O_2N$: C, 69.99; H, 9.49; N, 6.27. Found: C, 69.91; H, 9.63; N, 6.17.

The product dissolved readily in 10% sodium hydroxide solution, as well as in 10% hydrochloric acid.

***p*-*t*-Amylhydroxybenzylaminoethanol.**—To a solution of 49.2 g. of *p*-*t*-amylphenol, 50 cc. of methanol, and 30 g. of aqueous 30% formaldehyde solution, there was added 18.3 g. of ethanolamine, while cooling with tap water and shaking. The solution was then boiled under reflux on a steam-bath for one and one-half hours. The oily layer which separated on cooling was run off and chilled to 0° to induce crystallization. The crystals were dried on porous tile to remove sticky, resinous material, and recrystallized from methanol to a constant melting point of 114° (uncorr.).

Anal. Calcd. for $C_{14}H_{23}O_2N$: C, 70.87; H, 9.77; N, 5.90. Found: C, 70.54; H, 9.44; N, 5.72.

***p*-Nitrohydroxybenzylaminoethanol.**—A solution of 20 g. of 30% formaldehyde and 12.2 g. of ethanolamine was added to a solution of 27.8 g. of *p*-nitrophenol in 30 cc. of methanol. A clear red solution was obtained. After standing for seven days at room temperature, there was no evidence of reaction. The solution was therefore boiled for one and one-half hours under reflux on a steam-bath. Upon cooling, yellow crystals slowly separated. Upon recrystallization from ethyl alcohol to a constant melting point, the product formed yellow needles melting at 195–196° (uncorr.).

Anal. Calcd. for $C_9H_{12}O_4N_2$: C, 50.91; H, 5.75; N, 13.20. Found: C, 50.81; H, 5.77; N, 12.86.

***p*-Benzoylhydroxybenzylaminoethanol.**—To a solution of 19.8 g. of *p*-benzoylphenol in 25 cc. of methanol, there was added a previously prepared solution made by mixing 10 g. of aqueous 30% formaldehyde with 6.1 g. of ethanolamine, with cooling. The mixture was allowed to stand for two hours at room temperature, and was then heated under reflux on a steam-bath for one and one-half hours. The solution thus obtained was allowed to stand at 5° for several days. The crystals which separated were dried on tile, washed with a little alcohol and recrystallized from alcohol to a constant melting point of 188–189°.

Anal. Calcd. for $C_{16}H_{17}O_3N$: C, 70.81; H, 6.32; N, 5.16. Found: C, 70.47; H, 6.38; N, 5.05.

The product was soluble in dilute oxalic or lactic acid. The above analyses were carried out by Dr. C. W. Nash of the Röhm and Haas Company.

Summary

The condensation of formaldehyde and β-aminoethanol with various phenols was investigated. Crystalline compounds were obtained from equimolecular mixtures of formaldehyde and ethanolamine with *o*-phenylphenol, *p*-*t*-butylphenol, *p*-*t*-amylphenol, *p*-nitrophenol, *p*-benzoylphenol, 5-chloro-2-hydroxydiphenyl, 2,4-dichlorophenol and 3-nitro-4-hydroxytoluene. These appear to be substituted hydroxybenzylaminoethanols; *i. e.*, phenols containing one $—CH_2NHCH_2CH_2OH$ group attached to the aromatic nucleus.

p-Phenylphenol and *p*-cyclohexylphenol gave compounds containing less nitrogen per mole of the phenol, indicating the presence of two phenolic nuclei in the products.

Resins containing nitrogen were obtained from phenol, the three cresols and resorcinol.

PHILADELPHIA, PENNA. RECEIVED MARCH 16, 1936