The crude product was purified by refluxing with 50 cc. of ether for one hour, then cooled in an ice-bath and filtered. The solid was washed with a little ice-cold ether and dried; m. p. 100.5–102°; 25 g., 77%.

Summary

The orientating effect of chlorine and bromine in the alpha position of acetophenone has been investigated and found to be slight in the case of nitration. *m*-Nitro-α-chloroacetophenone has been prepared in good yields by the direct nitration of α-chloroacetophenone.

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[CONTRIBUTION FROM THE GEORGE HERBERT JONES CHEMICAL LABORATORY OF THE UNIVERSITY OF CHICAGO, AND THE FERTILIZER AND FIXED NITROGEN INVESTIGATIONS DIVISION, BUREAU OF CHEMISTRY AND SOILS]

Factors Governing the Instability of a Carbon to Nitrogen Bond. I. The Instability of the Carbon to Nitrogen Bond in Substituted Methyl Amines[1]

BY M. S. KHARASCH AND LOUIS B. HOWARD

Introduction

In previous communications[2] has been discussed our hypothesis of the nature of the carbon-to-carbon bond in organic compounds. The extension of our concept to the problem of the stability or instability of the carbon-to-nitrogen bond in compounds of the type R-NH_2 is possible without further subsidiary hypotheses. The treatment of the subject matter is particularly simplified if one bears in mind that the bonding electrons of both carbon and nitrogen are in the L-shell, and that the NH_2 group acts as a strongly electronegative radical.[3]

Furthermore, from data available in the literature an exceedingly important deduction may be made, namely, the effects of attached radicals on the electronegativity of the nitrogen atom follow the same rules which have been evolved for the carbon atom; *i. e.*, strongly electronegative radicals attached to either carbon or nitrogen atoms decrease their electronegativity. It is quite evident, therefore, that in a group R_2N- if the radical R is strongly electronegative the group as a whole becomes weakly electronegative. The validity of this generalization is supported by the dissociation in inert solvents of some triarylmethyldiarylamines $(C_6H_5)_3C{=}N(C_6H_5)_2$ and tetraarylhydrazines studied by Wieland.[4] Thus, with the exception of tetrakis-(*p*-biphenyl)-hydrazine, the tendency toward dissociation of eight tetraarylhydrazines studied by Wieland and co-workers,[5] follows the order predictable upon the basis of the relative electronegativities of the radicals attached to the nitrogen atoms. The volumes or weights of the substituent groups appear to have as little significance as in the case of hexaarylethane dissociation.

Method of Study.—As a means of estimating the effects of different radicals on the stability of the carbon-to-amino bond, a study of the rate of hydrolysis of the amines in dilute acid at relatively low temperatures was made. We were cognizant of the difficulties involved in the interpretation of such results. The method, however, was considered adequate since we were trying to bring into relief factors of first magnitude.

Our study included the rate of hydrolysis of the following amines, using 0.05 *N* hydrochloric acid: (1) $(CH_3)_3CNH_2$, (2) $(CH_3)_2CH(C_6H_5)NH_2$, (3) $CH_3(C_6H_5)_2CHNH_2$, (4) $(C_6H_5)_3CNH_2$, (5) $(C_6H_5)CNHC_2H_5$.

Of these amines, 1, 2 and 3 were unaffected by 50 or 100 hours of heating at 100°. Triphenylmethylamine, on the other hand, was found to be hydrolyzed to the following extent:

Time in minutes	15	30	45	60	75	90
Hydrolyzed, %	22	40	58	70	80	85

With these facts as a background, the study of amines containing methyl substituents more electronegative than the phenyl radical appeared to be in order. The β-naphtholphenylmethylamine group readily suggested itself, for some of our other work had indicated that the β-naphthol group is very strongly electronegative.

In the case of those compounds it was thought

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(1) Abstracted from a dissertation submitted by Louis B. Howard to the Faculty of the Graduate School of the University of Chicago in March, 1931, in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

(2) For pertinent references consult the paper by Kharasch, Reinmuth and Mayo, *J. Chem. Ed.*, **11**, 82 (1934).

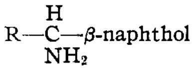
(3) Salt formation in general decreases tremendously the electronegative character of the amino group, and correspondingly the concomitant effect of that group on the other bonds in the molecule.

(4) Wieland, *Ann.*, **381**, 214 (1911).

(5) Wieland, "Die Hydrazine," Verlag von Ferdinand Enke, Stuttgart, 1913.

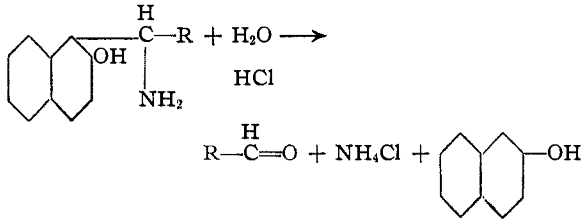
that the rate of elimination of NH_2 from the molecule would depend upon the electronegative character of the radical R.

A careful consideration of molecules of the type



$$R\text{—}\overset{H}{\underset{NH_2}{C}}\text{—}\beta\text{-naphthol}$$

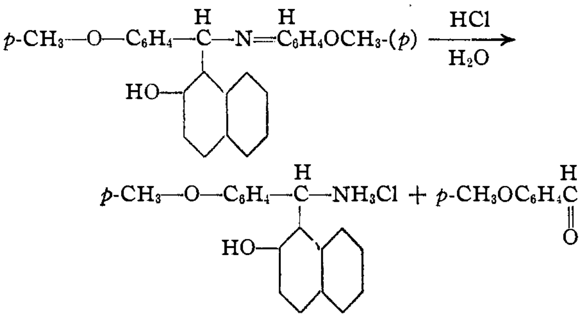
discloses the fact that when R is a strongly electronegative radical, all three of the groups joined to the methane carbon atom contribute to the instability of the substance. Potentially the molecule is susceptible to hydrolysis at three points; the bond involving the most electronegative group is, however, the most sensitive. Similarly greater stability of all bonds should be attained by decreasing the electronegativity of the radical R. These deductions were confirmed to a remarkable extent in the study of the hydrolysis of the compounds of this type in which R was, respectively: (1) $C_6H_5CH_2CH_2$-, (2) C_6H_5-, (3) $CH_3C_6H_4$- and (4) $CH_3OC_6H_4$-.



When R was $C_6H_5CH_2CH_2$- the compound could be refluxed with 0.05 *N* hydrochloric acid for five hours with only very slight hydrolysis, and from 3.0 g. of the amine hydrochloride, 2.6 g. was recovered unchanged. When R was C_6H_5- the compound was completely hydrolyzed under the same conditions in three hours, yielding benzaldehyde, β-naphthol, ammonium chloride, benzaldi-β-naphthol, and benzaldinaphthyl ether.[6]

With the *p*-tolyl radical in the role of R in the molecule β-$(C_{10}H_{10}OH)RCHNH_2$, the compound behaved very much like the corresponding phenyl derivative, except that the hydrolysis proceeded still faster. It was completed in about one hour and *p*-tolualdehyde, β-naphthol, ammonium chloride, and by-products corresponding in every way to the analogous benzalbi-β-naphthol and benzalbinaphthyl ether were obtained. These were not identified, however, for they were formed in extremely small amounts.

When the *p*-anisyl radical was introduced as R, the amine hydrochloride became so unstable that it could not be prepared by the usual method of treating the Schiff base with 20% hydrochloric acid. The only isolable products were the hydrolysis products of the amine, anisaldehyde, β-naphthol, ammonium chloride, and anisaldinaphthyl ether.



That these decompositions are not thermal but truly hydrolytic was shown by heating the hydrochloride of β-naphtholphenylmethylamine in toluene at 140° for eleven hours. The product was recovered unchanged. This compound was also unaffected by treatment with 20% hydrochloric acid at 100° for five hours. The stability of all these amine hydrochlorides (except the anisyl compound) toward 20% hydrochloric acid, and their instability toward 0.05 *N* hydrochloric acid is indeed a remarkable characteristic. It is attributable to two factors: (1) the insolubility of the amine hydrochloride in 20% hydrochloric acid; (2) the decrease in electronegativity of the amino group effected by salt formation.

In consideration of the weak basicities of these amines it seems probable that in 0.05 *N* hydrochloric acid small amounts exist in the form of free base.[7] In the case of the anisyl compound, however, the latter group exerts sufficient influence to predominate over the stabilizing effect of salt formation and the amine breaks down even in 20% hydrochloric acid.

Experimental Part

β-Naphthol-β-phenylethyl-methylamine.—A solution of 28.8 g. of β-naphthol dissolved in 60 cc. of alcohol was treated in the cold with 53.6 g. of hydrocinnamic aldehyde

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[6] The last two products are ascribable to condensation of hydrolysis products under the influence of hydrochloric acid. For many of the details of the experiment the reader is invited to consult the doctorate dissertation. This mechanism of many similar reactions is in our estimation more in agreement with the facts than the interpretation of Littman and Brode, THIS JOURNAL, **52**, 1655 (1930), and Dilthey and Steinborn, *J. prakt. Chem.*, **133**, 242 (1932); *cf.* Claisen, *Ann.*, **237**, 261 (1887); Hewitt and Turner, *Ber.*, **34**, 202 (1901).

[7] In conformity with this view the stronger base, 1-(α-dimethylaminobenzyl)-2-naphthol, shows about 50% less decomposition than Betti's base, when dissolved in 0.01 *N* hydrochloric acid and steam distilled for seventy-five minutes. The authors are indebted to Dr. Julius Porshe for determining the comparative rates of hydrolysis of these amines (doctorate dissertation, University of Chicago).

(b. p. 208–232°) and 40 cc. of saturated alcoholic ammonia. After standing for twenty-four hours the precipitate was collected on a filter and twice crystallized from a mixture of alcohol and benzene. The yield was 20 g. of a pure white substance; m. p. 103–122° (liquid crystals).

Anal. Calcd. for $C_{28}H_{27}OH$: C, 85.45; H, 6.93. Found: C, 85.33, 85.66; H, 6.94, 7.00.

The Schiff base thus obtained was treated with 200 cc. of 20% hydrochloric acid and steam distilled to remove the hydrocinnamic aldehyde. The solution was then chilled with ice and the resultant precipitate collected on a filter. It was crystallized from alcohol containing about 10% of concentrated hydrochloric acid. Eight grams of small colorless needles was thus obtained (m. p. 205–210°).

Anal. Calcd. for $C_{19}H_{20}ONCl$: Cl, 11.31. Found: Cl, 11.39 (Parr bomb).

The free base was obtained by working the salt into a paste with water, treating with an excess of cold 25% potassium hydroxide and extracting with ether. Concentration of the dried ether solution gave a white amorphous powder (m. p. 108°).

Anal. Calcd. for $C_{19}H_{19}ON$: N, 5.05. Found: N, 5.27.

β-Naphthol-*p*-tolyl-methylamine.—A solution of 21.6 g. of β-naphthol in 30 cc. of alcohol was treated in the cold with 36 g. of *p*-tolualdehyde and 30 cc. of saturated alcoholic ammonia. After twenty-four hours 47 g. (85% of calculated) of the crystalline Schiff base was collected on a filter. After two crystallizations from a mixture of alcohol and benzene a colorless product was obtained (m. p. 149°).

Anal. Calcd. for $C_{26}H_{23}ON$: C, 85.44; H, 6.35. Found: C, 85.48; H, 6.49, 6.48.

A mixture of 40 g. of Schiff base with 300 cc. of 20% hydrochloric acid was steam distilled until only a trace of *p*-tolualdehyde continued to pass over in the distillate. After cooling, the whole was filtered and 31 g. (92% of calculated) of the crude amine hydrochloride thus obtained. Crystallization from alcohol, containing about 10% of concentrated hydrochloric acid, gave pure white needles of the salt (m. p. 195–220° dec.).

Anal. Calcd. for $C_{18}H_{18}ONCl$: Cl, 11.83. Found: Cl, 11.73.

The free base, obtained in the same manner as the previous amine, was found to be a white solid which melted at 109.5°.

Anal. Calcd. for $C_{18}H_{17}ON$: N, 5.32. Found: N, 5.24.

Attempted Preparation of β-Naphthol-anisyl-methylamine.—A solution of 14 g. of β-naphthol in 20 cc. of alcohol was treated in the cold with 27 g. of anisaldehyde and 20 cc. of saturated alcoholic ammonia. After forty-eight hours the Schiff base was collected on a filter (42% yield) and crystallized from alcohol (m. p. 181°).

Anal. Calcd. for $C_{26}H_{26}O_3N$: C, 78.55; H, 5.84; N, 3.53. Found: C, 78.88; H, 5.95; N, 3.57.

The Schiff base was treated in the usual manner with four times its volume of 20% hydrochloric acid and steam distilled. A large amount of anisaldehyde passed over and a dark red precipitate formed. The precipitate was removed, first triturated with alcohol and then crystallized from it to yield very fine colorless crystals (m. p. 206°). This substance was found to be insoluble in water, dilute or concentrated sodium hydroxide either hot or cold, and difficultly soluble in benzene and alcohol. It contained neither halogen nor nitrogen.

Anal. Calcd. for $C_{26}H_{23}O_3$: C, 86.56; H, 5.19. Found: C, 86.30; H, 5.19, 5.08.

This substance was identified as an anisaldinaphthyl ether which has been prepared previously by Rogow.[8] Since it appeared highly probable that this compound was formed by a condensation of the hydrolysis products of the Schiff base, 7.2 g. of β-naphthol, 13.6 g. of anisaldehyde, and 2.7 g. of ammonium chloride were refluxed for one and one-half hours in 200 cc. of 20% hydrochloric acid. After standing overnight the mixture was steam distilled to remove the excess anisaldehyde. The almost black solid which formed was purified by the above-described procedure to give pure anisaldinaphthyl ether.

Hydrolysis of β-Naphthol-phenyl-methylamine.—(a) In a preliminary experiment, to determine the hydrolysis products, 28.5 g. (0.1 mole) of the amine hydrochloride was dissolved in a mixture of 150 cc. of 95% alcohol and 150 cc. of 0.05 *N* hydrochloric acid and refluxed for eighteen hours. The solution was concentrated *in vacuo.* Since the odor of benzaldehyde was detected in the distillate, the mixture was steam distilled for about three hours, during which time a considerable amount of benzaldehyde passed over. The solution was boiled and a brown colored residue collected on a filter. The residue was twice extracted with hot water, the extractions being added to the first filtrate. When the filtrate had become cold a large mass of white crystals separated. These were collected on a filter and identified as β-naphthol.

The steam distillate was extracted with ether, the ether solution dried over sodium sulfate, and allowed to evaporate. The residue was permitted to oxidize spontaneously in the air and was then crystallized from hot water (m. p. 121°). When mixed with known benzoic acid the melting point was unchanged.

The water insoluble brown colored precipitate (m. p. 178–182°) was identified as a mixture of benzal-di-β-naphthol[9] and the anhydride of benzaldi-β-naphthyl ether.

(b) 1.45 g. of the amine hydrochloride was heated in 50 cc. of distilled water at 100° for four hours and then steam distilled for fifteen minutes. The distillate contained benzaldehyde, which was extracted with ether, the ether evaporated, the residue allowed to oxidize in the air and identified as benzoic acid. The solution remaining behind was filtered hot to remove a light brown gummy mass (0.34 g.). Upon cooling the filtrate deposited white crystals which were identified as β-naphthol (m. p. 122°). The brown gummy mass after one crystallization from alcohol had m. p. 142–143°. It was found to contain nitrogen by a sodium fusion but no halogen by the Beilstein test. When mixed with some of the Schiff base $(C_6H_5)(\beta\text{-}C_{10}H_6OH)CHN{=}CHC_6H_5$ of m. p. 145° there was no depression of the melting point. The filtrate from

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(8) Rogow, *Ber.*, **33**, 3535 (1900).

(9) Hewitt and Turner, *ibid.*, **34**, 202 (1901).

the β-naphthol gave a precipitate of silver chloride with silver nitrate solution and when made strongly alkaline with sodium hydroxide and warmed, ammonia was evolved.

(c) Twenty grams of the amine hydrochloride moistened with a little alcohol was treated with 600 cc. of 2.5 *N* sodium hydroxide solution and steam distilled for about six hours until the distillate no longer evolved ammonia. Some benzaldehyde passed over in the distillate. The remaining solution was chilled and filtered to remove a yellowish insoluble solid which had formed. This solid was crystallized from alcohol to a nearly white material of m. p. 143–144°, which was proved to be the Schiff base. The alkaline filtrate was acidified with hydrochloric acid and cooled. A precipitate separated which after crystallization from water gave m. p. 118.5–119.5°, and was proved to be β-naphthol.

(d) 1.45 g. of the amine hydrochloride was refluxed for eleven hours in 50 cc. of toluene. The mixture was cooled and the solid collected on a filter. The weight and the m. p. of the substance (200–215°) proved conclusively that little or no hydrolysis took place during the heating.

(e) 1.45 g. of the amine hydrochloride was heated at 100° in 50 cc. of 20% hydrochloric acid for five hours. Upon cooling 1.40 g. of unchanged product was recovered (m. p. 200–215°).

Hydrolysis of β-Naphthol-β-phenylethyl-methylamine.—Three grams of the amine hydrochloride was refluxed in 90 cc. of 0.05 *N* hydrochloric acid for five hours. At the end of two hours of refluxing there was no apparent change, but after five hours the characteristic odor of hydrocinnamic aldehyde was noted. The mixture was steam distilled for thirty minutes. The solution was filtered hot and upon cooling deposited white crystals of the unchanged amine hydrochloride. The solution was cautiously evaporated and the residue crystallized from alcohol containing a little hydrochloric acid. In this manner 2.6 g. of the original material was recovered unchanged (m. p. 200–208°); original sample m. p. 205–210°.

Hydrolysis of β-Naphthol-*p*-tolyl-methylamine.—Five grams of the amine hydrochloride was refluxed for one hour with 150 cc. of 0.5 *N* hydrochloric acid and then steam distilled to remove the liberated aldehyde. The solution was filtered hot to remove a small globule of light brown material which upon crystallization from alcohol melted at 224°. The compound was probably *p*-tolyl-di-β-naphthol or the corresponding ether, formed as in the previous cases by condensation of the liberated aldehyde and β-naphthol. The filtrate upon cooling deposited a white solid which upon crystallization was proven to be β-naphthol. A small amount of the unhydrolyzed amine was also recovered from the filtrate.

Thermal Stability of Triphenyl-methylamine.—One gram of triphenylmethylamine dissolved in 35 cc. of pure dry xylene was heated in a sealed tube at 150° for twenty hours. The solution was then saturated with hydrogen chloride gas and 1.0 g. of the hydrochloride (calcd. 1.14 g.) was recovered. The salt was dissolved in water and the free base precipitated with ammonia, m. p. 104°. Another portion of 1.0 g. of the base dissolved in 25 cc. of xylene was heated in a sealed tube at 250° for twelve hours. The material was recovered unchanged as in the previous case, thus indicating complete thermal stability of the substance at these temperatures.

Summary

1. The general theory of the stability of carbon to carbon linkages has been extended to the stability of carbon to nitrogen linkages and given experimental confirmation in the case of certain amines.

2. Interesting cases of rupture of carbon to nitrogen and carbon to carbon linkages by mild hydrolysis conditions have been observed and a qualitative series arranged in the order of ease of rupture.

3. The following new compounds have been prepared: (1) $(C_6H_5CH_2CH_2)(\beta\text{-}C_{10}H_6OH)CH\text{-}N\text{-}CHCH_2CH_2C_6H_5$α-(β-naphthol)-γ-(phenyl)-propyl-γ-(phenyl)-γ-propylidene-amine; (2) $(C_6H_5CH_2CH_2)\text{-}(\beta\text{-}C_{10}H_6OH)CHNH_3Cl$ β-naphthol-phenylethyl-methylammonium chloride; (3) $(C_6H_5CH_2CH)(\beta\text{-}C_{10}H_6OH)CHNH_2$ β-naphthol-β-phenylethyl-methylamine; (4) $(p\text{-}CH_3C_6H_4)(\beta\text{-}C_{10}H_6OH)CHN{=}CHC_6H_4CH_3$ (*p*)-γ-(β-naphthol)-α-(*p*-tolyl)-methyl-(*p*-tolyl)-methylene-amine; (5) $(p\text{-}CH_3C_6H_4)(\beta\text{-}C_{10}H_6OH)CHNH_3Cl$ β-naphthol-*p*-tolyl-methylammonium chloride; (6) $(p\text{-}CH_3C_3H_4)(\beta\text{-}C_{10}H_6OH)CHNH_2$ β-naphthol-*p*-tolyl-methylamine; (7) $(p\text{-}CH_3OC_6H_4)(\beta\text{-}C_{10}H_6OH)CHN{=}CHC_6H_4OCH_3$ (*p*) - α-(β-naphthol)-α-(anisyl)-methyl-(anisyl)-methylene-amine.

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