hyde, and recrystallized in the same manner decomposed at 275–285°.

The acid was decarboxylated by heating it over a small free flame according to Dedichen[8] and the resulting 2-methylimidazole was recrystallized from benzene. The latter compound prepared from the acid from both sources melted at 134–136° and the mixed melting point was not depressed. Dedichen[8] reports the m. p. of 2-methylimidazole as 139°.

6-Methoxy-8-(4-diethylamino-1-methylbutylideneamino)-quinoline.—The Schiff base was used by Barber and Wragg in the preparation of tetrahydropamaquine but neither the method of synthesis nor physical constants of the compound are given by the British workers. A mixture of 157 g. (1 mole) of 1-diethylaminopentanone-4, 87 g. (0.5 mole) of 6-methoxy-8-aminoquinoline and 150 ml. of ethylbenzene was refluxed for one hundred hours in an apparatus equipped with a liquid separator from which the condensed reflux of ethylbenzene was returned to the reaction flask after passing through anhydrous potassium carbonate for removal of water. The bulk of the solvent was distilled off at atmospheric pressure in an atmosphere of nitrogen and 80 g. of the amino-ketone was then removed at water pump vacuum followed by 45 g. of unreacted 6-methoxy-8-aminoquinoline boiling at 175–185° (4 mm.). The crude Schiff base (85 g.) then distilled at 230–240° (4 mm.). Redistillation yielded 55 g. (35%) of orange oil boiling at 184–186° (0.4 mm.).

Anal. Calcd. for $C_{19}H_{27}ON_3$: C, 72.8; H, 8.7. Found: C, 72.8; H, 8.5.

6-Methoxy-8-(*p*-toluenesulfonylamido)-quinoline.—A mixture of 17.5 g. of 6-methoxy-8-aminoquinoline, 19 g. of *p*-toluenesulfonyl chloride and 100 ml. of 10% sodium hydroxide was shaken at room temperature until the acid chloride was all gone. The sulfonamide was recrystallized from isopropanol and melted at 133.5°.

Anal. Calcd. for $C_{17}H_{16}O_3N_2S$: C, 62.2; H, 4.9. Found: C, 62.0; H, 4.8.

6-Methoxy-8-(*p*-toluenesulfonylethylamido)-quinoline. To a stirred solution of 32.8 g. of the above tosyl compound in 350 ml. of absolute alcohol at 75–80° in a flask protected from atmospheric moisture was added a solution of 6.7 g. of potassium hydroxide in 150 ml. of absolute alcohol. After stirring the mixture for thirty minutes at 70–80° and then cooling, the crystalline potassium salt (90%) was filtered off and washed with absolute alcohol.

A stirred mixture of 18.3 g. of the above potassium salt, 8.3 g. of ethyl bromide (no reaction occurred when ethyl iodide was used) and 250 ml. of absolute alcohol was heated under reflux for twenty-four hours. After cooling the filtrate from the potassium bromide was evaporated to dryness. To the residue was added 250 ml. of 5% potassium hydroxide solution and this mixture was extracted with ether. After washing and drying the extract, evaporation of the ether left a yellow residue which was recrystallized from isopropanol or acetone. The substance melted at 125–126°.

Anal. Calcd. for $C_{19}H_{30}O_3NS$: C, 64.0; H, 5.7. Found: C, 64.0; H, 5.6.

6-Methoxy-8-ethylaminoquinoline.—A mixture of 1 g. of the above compound and 3 ml. of 96% sulfuric acid was heated with occasional stirring at 100° for ten minutes. After cooling and standing at room temperature for three hours, 20 ml. of 40% sodium hydroxide solution was added very cautiously. The mixture was extracted with benzene, yielding a yellow oil which gradually solidified. After recrystallization from *n*-heptane, the ethylaminoquinoline melted at 38–40°.

Anal. Calcd. for $C_{12}H_{14}ON_2$: C, 71.3; H, 7.0. Found: C, 71.0; H, 6.9.

Summary

1. Reductive amination of 1-diethylaminopentanone-4 with 6-methoxy-8-aminoquinoline with Raney nickel under various conditions leads to a mixture consisting of Plasmochin and 2-methyl-8-methoxy-5,6-dihydro-4-imidazo[ij]-quinoline as principal components.

2. A study of the oxidative degradation of 2-methyl-8-methoxy-5,6-dihydro-4-imidazo[ij]-quinoline has been made.

3. N,N-Diethylpropylamine and 6-methoxy-8-ethylaminoquinoline have been prepared.

NEW YORK 27, N. Y.
WYANDOTTE, MICH. RECEIVED MARCH 21, 1947

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF COLUMBIA UNIVERSITY]

The Reaction of *o*-Phenylenediamine and of 8-Amino-1,2,3,4-tetrahydroquinoline Derivatives with Carbonyl Compounds

BY ROBERT C. ELDERFIELD AND FRANK J. KREYSA

In the preceding paper[1] a study of the reductive amination of 1-diethylamino-pentanone-4 with 6-methoxy-8-aminoquinoline has been described. The major product of the reaction was 2-methyl-8-methoxy-5,6-dihydro-4-imidazo[ij]quinoline (I) and N,N-diethyl-*n*-propylamine was isolated from the products of the reaction. Since the formation of I obviously involves cleavage of a carbon–carbon bond under relatively mild conditions the reaction conditions under which imidazoles of the general type of I are formed from ketones have been the subject of further investigation.

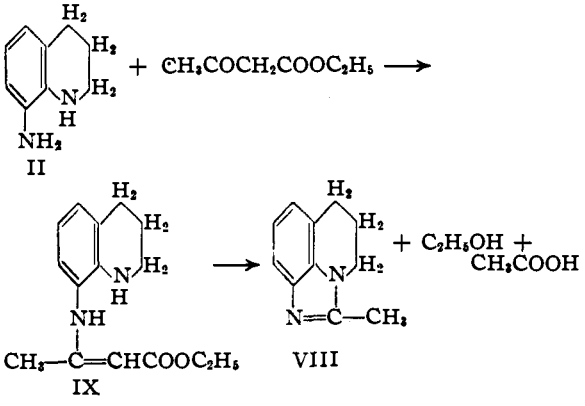
As pointed out by Hazlewood, Hughes and Lions[2] 8-amino-1,2,3,4-tetrahydroquinoline (II) can be regarded as a mono-N-alkyl-*o*-phenylenediamine and the same authors prepared imidazoles of the type of I by the action of acids on II under mild dehydrating conditions. Formation of the imidazole ring in this fashion is easily understood and obviously proceeds by intramolecular elimination of water from an enolic form of an N-acyl derivative of II (III) in accordance with the observations of Phillips[3] on the behavior of *o*-phenylenediamine itself under similar conditions. Whether the acyl derivatives of II involve the ring nitrogen or that of the primary amino group is irrelevant and cannot be stated with certainty at this time. As far as we are aware only three cases of the formation of a 2-substituted benzimidazole

(1) Elderfield, *et al.*, THIS JOURNAL, **70**, 40 (1948).

(2) Hazlewood, Hughes and Lions, *J. Proc. Roy. Soc. N. S. Wales*, **71**, 467 (1937–1938).

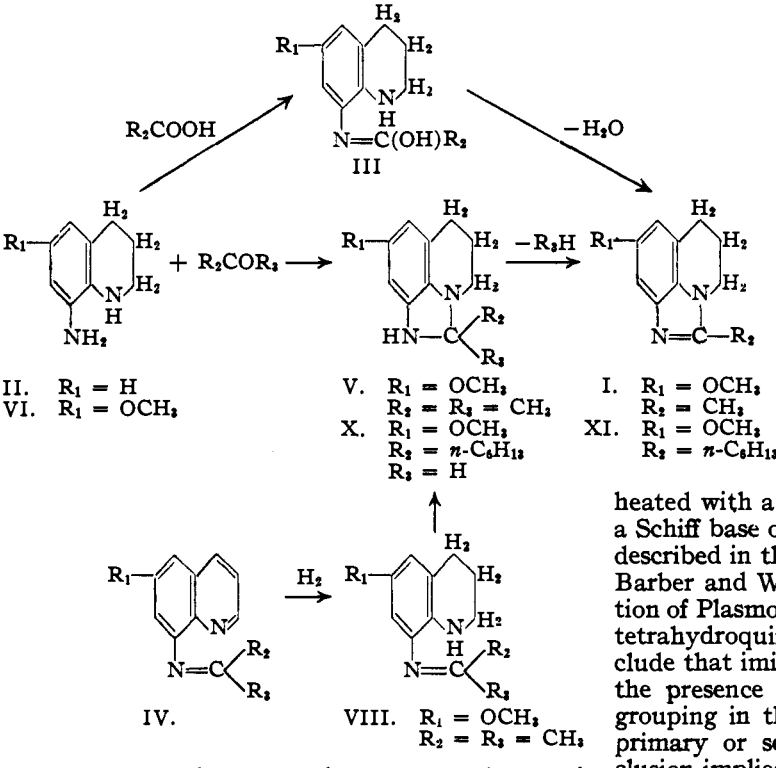
(3) Phillips, *J. Chem. Soc.*, **173**, 2395 (1928); see also McCoy and Day, THIS JOURNAL, **65**, 2159 (1943).

from the action of a ketone on *o*-phenylenediamine or its derivatives have been reported.[4] Hazlewood, Hughes and Lions[2] describe the formation of the imidazole, VIII, from II and ethyl acetoacetate and suggest the following sequence of reactions for the observed facts.



II

IX VIII



II. $R_1 = H$
VI. $R_1 = OCH_3$

V. $R_1 = OCH_3$, $R_2 = R_3 = CH_3$
X. $R_1 = OCH_3$, $R_2 = n\text{-}C_6H_{13}$, $R_3 = H$

I. $R_1 = OCH_3$, $R_2 = CH_3$
XI. $R_1 = OCH_3$, $R_2 = n\text{-}C_6H_{13}$

IV.

VIII. $R_1 = OCH_3$, $R_2 = R_3 = CH_3$

The formation of IX took place when a mixture of II and ethyl acetoacetate was allowed to stand at room temperature in the presence of a trace of hydrochloric acid and the crotonic ester, IX, on dropping into hot paraffin lost the elements of ethyl acetate to yield VIII. A similar reaction has been noted by Baxter and Spring,[5] who obtained 2-methylbenzimidazole instead of the expected 2-methyl-3-carbethoxyquinoxaline by merely warming *o*-phenylenediamine with ethyl α-chloroacetoacetate in alcoholic solution. Finally, Weil and Marcinkowska[6] describe the formation of 2-phenylbenzimidazole by heating *o*-phenylenediamine with dibenzoylphenylmethane in the presence of hydrochloric acid. Desoxybenzoin must have been eliminated at some stage of this reaction, although its isolation was not reported.

TABLE I

PRODUCTS FROM THE REACTION OF *o*-PHENYLENEDIAMINES WITH CARBONYL COMPOUNDS

Diamine	Carbonyl compd.	R_2 in the 2-position of the resulting imidazole
6-Methoxy-8-amino-tetrahydroquinoline	$CH_3CO(CH_2)_2N(C_2H_5)_2$	CH_3
	$CH_3COCH_2C_6H_5$	CH_3
	$CH_3CO(CH_2)_5CH_3$	CH_3
	$OCCH_2CH_2CH_2CH_2$	$CH_2CH_2CH_2CH_3$
	CH_3COCH_3	CH_3
	$n\text{-}C_6H_{13}CHO$	$n\text{-}C_6H_{13}$
o-Phenylenediamine	$CH_3COCH_2C_6H_5$	CH_3 and $CH_2C_6H_5$
	$CH_3CO(CH_2)_2N(C_2H_5)_2$	Product not isolated

Accordingly the action of representative simple ketones on 6-methoxy-8-amino-1,2,3,4-tetrahydroquinoline and on *o*-phenylenediamine has been investigated. The results are summarized in Table I. We suggest the sequence of reactions shown in formulas VI to I or IV to I as a tentative explanation for the observed results. Imidazole formation occurs when an 8-amino-1,2,3,4-tetrahydroquinoline is heated with a ketone (formulas VI to I), or where a Schiff base of an 8-aminoquinoline is reduced as described in the preceding paper (IV to I). Since Barber and Wragg[7] have shown that hydrogenation of Plasmochin yields an 8-alkylamino-1,2,3,4-tetrahydroquinoline and not an imidazole, we conclude that imidazole formation is contingent upon the presence in the molecule of an azomethine grouping in the proper spatial relationship to a primary or secondary amino group. This conclusion implies that on reduction of IV, the pyridine ring is saturated before any substantial reduction of the azomethine grouping has occurred.

Both reaction paths involve an intermediate for which we propose an imidazoline structure of the type of V. Barber and Wragg[7] have assigned structure V to the product arising from condensation of VI with acetone, and we have now shown that this condensation product does indeed give I

(4) An excellent review of the modes of formation of 2-substituted benzimidazoles is given by Wiedenhagen, *Ber.*, **69**, 2263 (1936).

(5) Baxter and Spring, *J. Chem. Soc.*, 229 (1945).

(6) Weil and Marcinkowska, *Roczniki Chem.*, **14**, 1312 (1934); *C. A.*, **29**, 6233 (1935).

(7) Barber and Wragg, *J. Chem. Soc.*, 610 (1946).

in good yield on heating at 250–300° for six hours. Structure V for the condensation product is confirmed by the close similarity of its ultraviolet absorption spectrum to that of VI. If the condensation product possessed the Schiff base structure, VII, the azomethine double bond in conjugation with the benzene ring should have caused a more profound change in absorption characteristics. Furthermore, the instability of the condensation product—alcoholic picric acid cleaves it to the picrate of VI–argues against the Schiff base structure.

The ready conversion of the imidazoline into the imidazole type is noteworthy. We assume that the gain in resonance stabilization[8] accompanying this aromatization provides the driving force for the direct elimination of the alkyl group and a hydrogen atom from the molecule. It is of

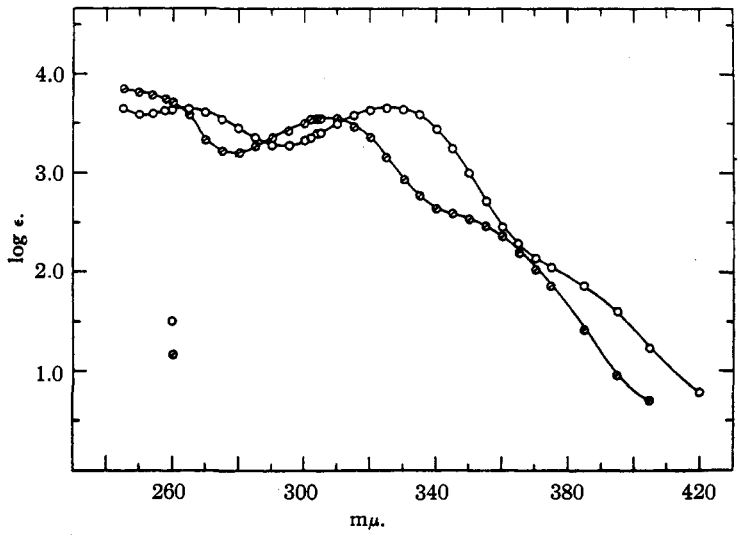


Fig. 1.—Ultraviolet absorption spectra: O, 6-methoxy-8-amino-1,2,3,4-tetrahydroquinoline; ⊖, the imidazoline, V; solvent, cyclohexane.

interest that the benzothiazolines resulting from the reaction of *o*-aminothiophenol and aldehydes or ketones, are relatively stable.[9] The principle of molecular symmetry suggests that the benzothiazoles conceivably can possess a lower level of resonance stabilization than the imidazoles, which would account for the greater reported stability of the thiazolines.

The factor determining which of the two substituents in structure V is eliminated, in the formation of the benzimidazole ring, appears to be connected with the degree of substitution on one of the nitrogens of the *o*-phenylenediamine derivative entering into the reaction. Thus in all cases examined in which an N-alkyl-*o*-phenylenediamine, typified by a tetrahydroquinoline derivative (VI), was one of the reactants, the other being a methyl ketone, the only imidazole emerging was the 2-methyl derivative, I, although the results obtained with acetophenone were obscure in the sense that a poor yield of I was obtained. On the other hand, in the reaction of *o*-phenylenediamine with methyl benzyl ketone and, presumably, with 1-diethylaminopentanone-4, elimination of the methyl group of the ketone occurred to a major extent. While it would be attractive to generalize on this point, no such generalization can be more than suggested at this time pending the outcome of further experiments currently in progress in these laboratories.

We have also investigated the reaction of a typical aliphatic aldehyde, *n*-heptaldehyde, on 6-methoxy-8-amino-1,2,3,4-tetrahydroquinoline (VI) and find that hydrogen is eliminated from the proposed intermediate, X, as readily as is a hydrocarbon residue when a ketone is employed with the formation of XI. The use of aldehydes in the synthesis of benzimidazoles from *o*-phenylenediamine has been recorded in the literature. Hinsberg and Koller[10] and Weil and Marcinkowska[6] obtained 2-phenylbenzimidazole from the action of benzaldehyde on *o*-phenylenediamine. As far as we are aware the only instance whereby a 2-substituted imidazole carrying an alkyl substituent has been obtained by this general method using an aliphatic aldehyde as one reactant is that reported by Weidenhagen.[4] In this case cupric salts were added to the reaction mixture which raises the possibility that the aldehyde used might be oxidized to the corresponding acid prior to condensation with *o*-phenylenediamine. Production of imidazoles from acids is a well known reaction. In the present work, such oxidation of the aldehyde to the acid was avoided by working in an atmosphere of nitrogen, a fact which would appear to establish beyond doubt that the imidazole results from the intermediate imidazoline by direct expulsion of hydrogen.

Experimental[11,12]

6-Methoxy-8-amino-1,2,3,4-tetrahydroquinoline.—The preparation of this compound has been described by Price and Herbrandson[13] by the reduction of 6-methoxy-8-aminoquinoline with stannous chloride (62%) or catalytically with copper chromium oxide (78%) and by Barber and Wragg[7] by reduction of the corresponding quinoline derivative catalytically with Raney nickel in dioxane (80%). None of the above workers report a yield or analysis of the free amine, but rather converted it directly into a suitable salt, on which the yield was based, because of the instability of the free amine. In the present work,

(8) Hückel, Datow and Simmersbach, *Z. physik. Chem.*, **A186**, 129 (1940); Jensen and Friediger, *Kgl. Danske Videnskab, Selskab, Math.-fys. Medd.*, **20**, No. 20, 1 (1943) [*C. A.*, **39**, 2068 (1945)].

(9) Lankelma and Sharnoff, THIS JOURNAL, **53**, 2654 (1931); **54**, 379 (1932).

(10) Hinsberg and Koller, *Ber.*, **29**, 1498 (1896).

(11) All melting points are corrected.

(12) The microanalyses reported were done by Miss Lois May of these laboratories.

(13) Price and Herbrandson, THIS JOURNAL, **68**, 910 (1946).

we have avoided catalytic reduction with nickel in dioxane, because of the inherent danger involved, and have used the sodium and alcohol method first used in the reduction of 8-aminoquinoline by Hazlewood, Hughes and Lions.[8]

To a refluxing solution of 30 g. of 6-methoxy-8-aminoquinoline (m. p. 48.5–49.5°) in 750 ml. of absolute alcohol (distilled from sodium and diethyl phthalate) protected with a calcium chloride tube was added, with stirring, 60 g. of sodium during the course of ninety minutes. Refluxing and stirring was continued for an additional ninety minutes. The flask was then equipped with a condenser set downward and about 250 ml. of alcohol was distilled off. To the contents of the flask 400 ml. of cold water was added and the alkaline solution was extracted with four 100-ml. portions of benzene. The combined extracts were dried with anhydrous potassium carbonate and concentrated in an atmosphere of nitrogen to about 200 ml. The resulting solution was washed with three 20-ml. portions of water and dried with potassium carbonate. After removal of the solvent, the dark, viscous red oil was distilled in an atmosphere of nitrogen at 0.65 mm. pressure. The main fraction, boiling at 148–150°, amounted to 28 g. (90%), of pure 6-methoxy-8-amino-1,2,3,4-tetrahydroquinoline and slowly crystallized as plates which melted at 44–45°. Barber and Wragg[7] give the melting point as 43–45°.

Reaction of 6-Methoxy-8-amino-1,2,3,4-tetrahydroquinoline (VI) with 1-Diethylaminopentanone-4.—A mixture of 18 g. of freshly distilled VI and 31 g. of 1-diethylaminopentanone-4 was heated in a flask equipped with an inside thermometer and a condenser set downward for distillation through the contents of which a stream of dry nitrogen furnished agitation. At an inside temperature of 200° a colorless distillate appeared. The inside temperature was slowly raised during six hours to 265° at which point the heating was interrupted.

The distillate (15–20 g.) was redistilled in an atmosphere of nitrogen. The fraction boiling at 105–115° (5–6 g.) was collected, followed by a second fraction boiling at about 200° which consisted of unreacted 4-diethylamino-1-methylbutylamine. The lower boiling fractions, which separated into two layers, were taken up in 75 ml. of ether and dried over anhydrous potassium carbonate. After removal of the solvent, the main fraction was distilled twice, with drying over potassium hydroxide after the first distillation, yielding 4 g. of material boiling at 111–112°.

Anal. Calcd. for $C_7H_{17}N$: C, 73.0; H, 14.9. Found: C, 73.2; H, 15.1.

The amine was identified as N,N-diethyl-*n*-propylamine by mixed melting points of its hydrochloride and methiodide with authentic samples.[1]

The residue in the original reaction flask solidified on cooling. It was triturated with 50 ml. of cold ether and the insoluble portion was recrystallized from heptane. The product was identified as 2-methyl-8-methoxy-5,6-dihydro-4-imidazo[ij]quinoline by mixed melting point with an authentic sample.[1]

Reaction of 6-Methoxy-8-amino-1,2,3,4-tetrahydroquinoline with Octanone-2.—A mixture of 5 g. of the tetrahydroquinoline and 5 g. of octanone-2 (b. p. 173–174°) was heated in an atmosphere of nitrogen for three hours at 150–250°. The distillate was discarded and the residue in the reaction flask was distilled *in vacuo* under nitrogen, the fraction boiling at 170–175° (0.6 mm.) being collected. This crystallized in the receiver and was identified as the imidazole, I, as in the preceding cases.

Reaction of 6-Methoxy-8-amino-1,2,3,4-tetrahydroquinoline with Methyl Benzyl Ketone.—A mixture of 18 g. of the tetrahydroquinoline and 27 g. of methyl benzyl ketone [b. p. 75° (3 mm.)] was heated in a flask equipped with a thermometer and a condenser set downward in an atmosphere of nitrogen from 150 to 250° during six hours. At 150° water separated in the reaction mixture and the color changed from dark red to a light orange red. During the course of the reaction about 10 ml. of distillate was collected. This was taken up in 20 ml. of ether, dried over anhydrous magnesium sulfate and again distilled. The fraction boiling at 110–111° (3 g.) was identified as toluene by oxidation to benzoic acid with potassium permanganate.[14]

The orange-red residue in the reaction flask was seeded with a crystal of the imidazole, I, and after refrigeration it crystallized for the most part. The crystalline material was isolated and identified as the imidazole, I, as previously described.

Thermal Decomposition of 2,2-Dimethyl-8-methoxy-1,2,5,6-tetrahydro-4-imidazo[ij]quinoline.—This compound was prepared according to Barber and Wragg,[7] whose results were duplicated. Although the substance melts at approximately the same temperature as the imidazole, I, it differs from the imidazole in its easy decomposition to 6-methoxy-8-amino-1,2,3,4-tetrahydroquinoline when warmed with an alcoholic solution of picric acid. The mixed melting point of the two substances is likewise depressed. The British authors report the m. p. of the picrate of the latter substance as 163–164°, whereas Price and Herbrandson[13] give 151.5–152°. This discrepancy has now been found to be due to the rate of heating. On rapid heating of the capillary, the m. p. of 163–164° is observed, whereas on slow heating (several minutes per degree) the decomposition point of 150–152° is observed.

When the acetone condensation product of the tetrahydroquinoline was heated at 250–300° for six hours in a stream of nitrogen, the residue, on distillation at 0.6 mm, yielded 78% of the imidazole, I, which was identified as in the preceding cases.

Reaction of 6-Methoxy-8-amino-1,2,3,4-tetrahydroquinoline with Cyclopentanone.—A mixture of 9 g. of the tetrahydroquinoline and 8.5 g. of cyclopentanone (b. p. 129–130°) was heated under nitrogen in a sealed tube for twenty-four hours at 265°. The black mixture was distilled *in vacuo* under nitrogen and a main fraction of 4 g. boiling at 210–220° (1.5 mm.) was collected. To the solution of this in hot absolute alcohol, 250 ml. of an alcoholic solution of picric acid was added. The yellow needles were recrystallized from alcohol and melted at 171.5–173°.

The picrate was then decomposed with warm potassium hydroxide solution and the liberated imidazole was extracted with ether and benzene. The free imidazole obtained on evaporation of the combined extracts was recrystallized first from ether and then from pentane and formed needles which melted at 60–61°.

Both the 2-*n*-butyl-8-methoxy-5,6-dihydro-4-imidazo-[ij]quinoline and its picrate obtained above were identified by mixed melting points with samples of the same substance prepared according to the general method of Hazlewood, Hughes and Lions[8] as follows.

A mixture of 1 g. of 6-methoxy-8-amino-1,2,3,4-tetrahydroquinoline and 5 ml. of *n*-valeric acid was refluxed in an atmosphere of nitrogen for two hours, after which 25 ml. of water and 25 ml. of ammonium hydroxide (d. 0.9) was added to the red mixture. The ammoniacal mixture was extracted with benzene. The crude imidazole from the extracts was purified by sublimation at 150–175° (0.3 mm.) and then was recrystallized twice from pentane. It melted at 60–61°.

Anal. Calcd. for $C_{15}H_{20}ON_2$: C, 73.7; H, 8.2. Found: C, 73.5; H, 8.0.

The picrate melted at 172–173° after crystallization from absolute alcohol.

Anal. Calcd. for $C_{21}H_{23}O_8N_5$: C, 53.3; H, 4.9. Found: C, 53.4; H, 4.8.

Reaction of 6-Methoxy-8-amino-1,2,3,4-tetrahydroquinoline with Acetophenone.—A mixture of 10 g. of 6-methoxy-8-amino-1,2,3,4-tetrahydroquinoline and 24 g. of acetophenone was heated in a distilling flask in an atmosphere of nitrogen for seven hours during which the temperature was raised from 150 to 265°. From the distillate from this reaction no benzene could be isolated. The reaction mixture was fractionally distilled under re-

(14) Shriner and Fuson, "The Systematic Identification of Organic Compounds," 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1940, p. 164.

duced pressure in an atmosphere of nitrogen. Unreacted acetophenone came over at 60–70° (3 mm.) followed by a fraction, a heavy red oil, (4 g.) boiling at 210–225° (1.5–2 mm.). A third fraction (4 g.) boiling at 225–250° (1.5–2 mm.) was a heavy red tar. The second fraction was dissolved in alcohol and treated with a saturated alcoholic solution of picric acid. The red picrate was recrystallized from boiling dioxane, washed with benzene and decomposed with 50% potassium hydroxide solution. The alkaline solution was extracted with benzene and the extract, after drying yielded a semi-solid which was sublimed at 185–235° (0.2 mm.). The sublimate was recrystallized from heptane and again converted to the picrate (0.1 g.). The picrate melted at 248–253° and did not depress the melting point of a known sample of the picrate of the imidazole, I.

Condensation of *n*-Heptaldehyde with 6-Methoxy-8-amino-1,2,3,4-tetrahydroquinoline.—A mixture of 18 g. of 6-methoxy-8-amino-1,2,3,4-tetrahydroquinoline and 23 g. of pure *n*-heptaldehyde was heated in an atmosphere of nitrogen at 150–250° for eight hours. The residue was distilled under reduced pressure, a main fraction (22 g.) boiling at 180–220° (0.3 mm.) being collected. After redistillation, the fraction boiling at 190–210° (0.35 mm.) (19 g.) consisting of a viscous yellow oil was treated with a saturated absolute alcoholic solution of an equal weight of picric acid. The yellow needles of the imidazole picrate were recrystallized from alcohol yielding 20 g. of material melting at 127°.

Anal. Calcd. for $C_{23}H_{27}O_8N_5$: C, 55.1; H, 5.4. Found: C, 55.1; H, 5.4.

The picrate was decomposed with 50% potassium hydroxide as before and the *n*-hexylimidazole derivative crystallized on refrigerating. It melted at 27°. The free base was very hygroscopic which prevented securing satisfactory analytical data. Both the above imidazole and its picrate were identified by mixed melting point with an authentic sample prepared from I and oenanthic acid.

Reaction of *o*-Phenylenediamine with Methylbenzyl Ketone.—A mixture of 10.8 g. of *o*-phenylenediamine and 27 g. of methyl benzyl ketone was heated in an atmosphere of nitrogen in a distilling flask at 200–250°. The distillate was dried over anhydrous magnesium sulfate and redistilled yielding a fraction (1.5 g.) boiling at 110–111° which was identified as toluene by oxidation to benzoic acid. The residue in the distilling flask was poured out while still molten and, after cooling, was rubbed up under ether. The ether insoluble portion was repeatedly recrystallized from 60% methanol–water yielding 8 g. of 2 benzylbenzimidazole melting at 186.5–187.5°. The picrate melted at 214–215° (dec.). Both substances were identified by mixed melting point with an authentic sample synthesized for the purpose. 2-Benzylbenzimidazole is reported as melting at 187° and its picrate at 214°.[15]

From the combined mother liquors of the above 2-benzylbenzimidazole about 1 g. of 2-methylbenzimidazole was obtained by taking advantage of the ready solubility of the latter as compared to the benzyl derivative in hot water. The methyl derivative melted at 175–176° after final recrystallization from benzene and was identified by mixed melting point with an authentic sample. It is reported as melting at 176° by Phillips[3] among other workers.

Reaction of *o*-Phenylenediamine with 1-Diethylaminopentanone-4.—When the reaction was carried out as in the preceding case, no 2-methylbenzimidazole could be isolated from the reaction mixture. On attempted distillation substantially complete decomposition occurred. The reaction was not investigated further.

Summary

1. Direct heating of *o*-phenylenediamine and a mono-N-alkyl derivative with representative aldehydes and ketones leads to 2-substituted benzimidazoles by elimination of one of the atoms or radicals of the carbonyl compound from the intermediate imidazoline.

2. A mechanism for the reaction is suggested.

(15) Walther and V. Pulawski, *J. prakt. Chem.*, [2] **59**, 253 (1899).

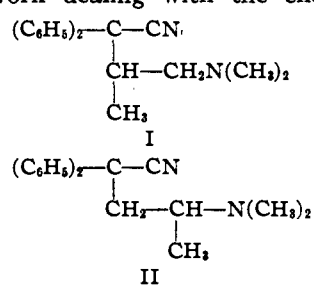
NEW YORK 27, N. Y. RECEIVED MARCH 21, 1947

[FROM THE DEPARTMENT OF ORGANIC CHEMISTRY, MEDICAL RESEARCH DIVISION, SHARP AND DOHME, INC.]

The Preparation and Rearrangements of 1,2-Dimethylaminochloropropanes

BY EVERETT M. SCHULTZ AND JAMES M. SPRAGUE

Recent work has shown that the chloroamine obtained from 1-dimethylamino-2-propanol reacts with diphenylacetonitrile in the presence of basic condensing agents to yield two isomeric nitriles, I and II.[1] The structures of these nitriles showed that a rearrangement had occurred, otherwise only the nitrile I should have resulted. In view of recent work dealing with the chemistry of chloroethylamines,[2] it seemed probable that, under the influence of the basic condensing agents, the chloroamine gave rise to an ethylenimonium ion which led to the isomeric nitriles on further reaction with diphenylacetonitrile. However, the possibility that the rearrangement occurred during the conversion of the aminoalcohol to the chloroamine was not excluded. More recently, Brode and Hill[3] have raised the question of the identity of the chloroamine employed in this reaction. These investigators failed to obtain different and distinct isomeric chloroamine bases from the treatment of 1-dimethylamino-2-propanol and 2-dimethylamino-1-propanol with thionyl chloride although apparently two distinct hydrochlorides were obtained. They conclude that the chloroamines rearranged, under the conditions used to isolate the bases from their salts,



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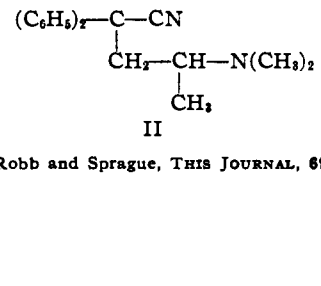

II

(1) Schultz, Robb and Sprague, THIS JOURNAL, **69**, 188 (1947); **69**, 2454 (1947).

(2) Golumbic, Fruton, Bergmann, *et al.*, *J. Org. Chem.*, **11**, 518-591 (1947).

(3) Brode and Hill, THIS JOURNAL, **69**, 724 (1947).