dropwise (90 min.) under nitrogen to a stirred slurry of 19.0 g. of lithium aluminum hydride in 100 ml. purified tetrahydrofuran and the resulting mixture refluxed for 45 hr. The excess of hydride was decomposed by cautious addition of a tetrahydrofuran–water mixture (1:1) to the cooled solution. After addition of an excess of dilute hydrochloric acid, the crude product, m.p. 84–95° (20.5 g.) was isolated and oxidized as reported[5] to yield 18.8 g. (91%) of crude II, m.p. 72–77°. Recrystallization from methanol (charcoal) gave, in two crops, 16.0 g. (77%) of II as yellow needles, m.p. 78–79°.

The trinitrobenzene complex of II was prepared and crystallized from absolute ethanol to give 1.74 g. (86%) of complex as yellow needles, m.p. 137.5–139.5°. Recrystallization from absolute ethanol gave the analytical sample, m.p. 138.8–140.4° corr.

Anal. Calcd. for $C_{21}H_{16}N_4O_6$: C, 60.0; H, 3.8. Found: C, 60.2; H, 3.5.

1,4,5,8-Tetramethylacridine, III. *A. From 1-(2,5)-Xylyl-4,7-dimethylisatin,* VII. A solution of 10.0 g. of VII in 150 ml. of water containing 20.0 g. of potassium hydroxide was refluxed for 305 hr. The cooled reaction mixture was acidified with ice and concentrated hydrochloric acid. The orange powder, obtained by filtration, was triturated with hot benzene and the residue dissolved in hot 10% potassium carbonate solution, treated with charcoal, and acidified with concentrated hydrochloric acid to yield 7.9 g. (79%) of 1,4,5,8-tetramethylacridine-9-carboxylic acid as an orange powder, m.p. 229–233° dec., sufficiently pure for the next step.

The methyl ester, m.p. 126.0–127.5° was prepared (diazomethane) in 91% yield. Two recrystallizations from alcohol gave the analytical sample, m.p. 127.2–128.3° corr.

Anal. Calcd. for $C_{19}H_{19}NO_2$: C, 77.8; H, 6.5; N, 4.8. Found: C, 77.6; H, 6.7; N, 5.0.

The crude acid, 7.8 g., was treated as above (II-A) to yield 6.2 g. (94%) of III as yellow needles, m.p. 187–189°. The analytical sample, m.p. 188.7–189.2° corr., was prepared by recrystallization from Skellysolve B followed by sublimation.

Anal. Calcd. for $C_{17}H_{17}N$: C, 86.8; H, 7.3; N, 6.0. Found: C, 86.7; H, 7.3; N, 6.2.

B. From 9-Chloro-1,4,5,8-tetramethylacridine, XI. *1. By reduction with Raney nickel and hydrogen.* XI was converted to III, m.p. 188–189°, in 76% yield as described above for the conversion of X to II.

2. By reduction with lithium aluminum hydride. Reduction of XI with lithium aluminum hydride as described above for II followed by oxidation[5] with potassium dichromate and sulfuric acid yielded III as yellow needles, m.p. 187.5–189.0°, in 74% yield.

The trinitrobenzene complex of III was prepared by mixing a hot solution of 1.20 g. of III in 20 ml. benzene and a hot solution of 1.10 g. of trinitrobenzene in 10 ml. of benzene and boiling for 5 min. Thorough chilling produced 2.10 g. (92%) of orange needles, m.p. 179–181°. Two recrystallizations from benzene gave the analytical sample, m.p. 180.6–182.0° corr.

Anal. Calcd. for $C_{23}H_{20}N_4O_6$: C, 61.6; H, 4.5; N, 12.6. Found: C, 61.9; H, 4.6; N, 12.5.

Heats of reaction of bases with boro trifluoride and diborane. The heats of reaction were app oximated by noting the temperature rise of 10.0 ml. of a dry thiophene-free benzene solution of 0.002 mole of the base at the same initial temperature when treated with an excess of boron trifluoride (from a cylinder) or diborane (generated by dropwise addition of a solution of sodium borohydride in redistilled diglyme to a solution of redistilled boron trifluoride etherate in redistilled diglyme). Nitrogen was used to sweep the system before and after each run. Two runs were made with each base and the results agreed to within 1°. The results are listed in Table I.

TABLE I

HEATS OF REACTION OF BASES

Compound	ΔT_{BF_3}, °	ΔT_{BH_3}, °
Benzene(blank run)	−0.5	1.9
Pyridine	9.3	5.4
2,4,6-Collidine	8.3	4.4
Acridine	7.9	4.5
4,5-Dimethylacridine, II	−0.4	0.1
1,4,5,8-Tetramethylacridine[a]	−0.7	...

[a] Concentration was only 0.001 mole/10 ml. because of low solubility in benzene.

COLUMBUS 10, OHIO

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

Condensation of *N*-Phenylbenzimidyl Chloride with Hydrogen Cyanide and Heterocyclic Bases

PAUL DAVIS AND WILLIAM E. McEWEN

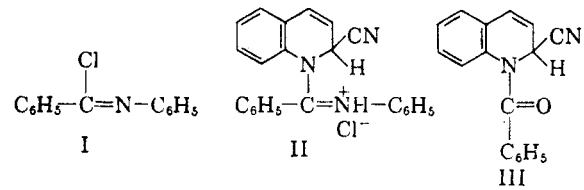
Received June 15, 1960

The hydrochlorides of 1-(α-phenyliminobenzyl)-1,2-dihydropicolinonitrile, 1-(α-phenyliminobenzyl)-1,2-dihydroquinaldonitrile and 2-(α-phenyliminobenzyl)-1,2-dihydroisoquinaldonitrile are obtained by reaction of *N*-phenylbenzimidyl chloride and hydrogen cyanide with pyridine, quinoline, and isoquinoline, respectively. The pyridine adduct gives benzaldehyde, aniline and picolinic acid on acid hydrolysis and the amide of picolinic acid on nitrobenzene oxidation. The quinoline adduct affords benzaldehyde, aniline, and quinaldic acid on acid hydrolysis, and quinaldonitrile is produced by nitrobenzene oxidation. The isoquinoline adduct behaves in an analogous manner, giving benzaldehyde, aniline, and isoquinaldic acid on acid hydrolysis and 1-cyanoisoquinoline on oxidation with nitrobenzene.

As part of an investigation of the effect of various amines on the preparation of *N*-phenylbenzimidyl cyanide, Mumm, Volquartz, and Hesse[1] found that a reaction of *N*-phenylbenzimidyl chloride (I) with anhydrous hydrogen cyanide in the presence of quinoline led to the formation of an addition compound, $C_{23}H_{18}N_3Cl$. This product was thought to be 1-(α-phenyliminobenzyl)-1,2-dihydroquinaldonitrile hydrochloride (II) in analogy

(1) O. Mumm, H. Volquartz, and H. Hesse, *Ber.*, **47**, 751 (1914).

with the structure of the compound, 1-benzoyl-1,2-dihydroquinaldonitrile (III), obtained by Reissert[2] from the reaction of benzoyl chloride with quinoline and potassium cyanide. The analogy was strengthened by the fact that the odor of benzaldehyde became apparent when the addition compound, $C_{23}H_{18}N_3Cl$, was heated in dilute hydrochloric acid solution. One of the most characteristic reactions of Reissert compounds is the formation of aldehydes on acid-catalyzed hydrolysis.[3]

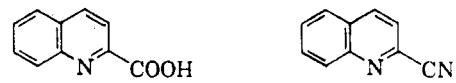


I II III

Pyridine was reported[1] to form an addition product, $C_{19}H_{16}N_3Cl$, by reaction with I and hydrogen cyanide, but its chemical properties were not investigated. Acridine was found not to undergo an analogous reaction, and no mention was made of the use of isoquinoline, even though the latter compound was known to form a Reissert compound.[2]

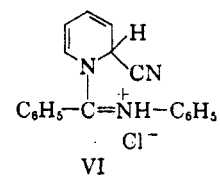
Inasmuch as the Reissert compounds have proved to be useful and versatile intermediates for the synthesis of a variety of quinoline and isoquinoline derivatives,[3,4-13] it was thought that the 1-(α-phenyliminobenzyl) analogs merited more intensive study. The method of Mumm, Volquartz, and Hesse[1] was used to prepare the quinoline adduct, $C_{23}H_{18}N_3Cl$, and the pyridine compound, $C_{19}H_{16}N_3Cl$. The yields, not previously reported,[1] were 70–78% and 76–79%, respectively. In addition, an isoquinoline adduct, $C_{23}H_{18}N_3Cl$, was prepared from *N*-phenylbenzimidyl chloride (I), isoquinoline and hydrogen cyanide in 78% yield.

That the quinoline adduct actually possessed the structure II, or that of a tautomer thereof, was shown both by acid-catalyzed hydrolysis and oxidation experiments. Hydrolysis with 20% hydrochloric acid for a prolonged period gave benzaldehyde in 87% yield and quinaldic acid (IV) in 95% yield. Aniline, also produced in the hydrolysis reaction, was isolated in 45% yield as the benzoyl derivative. When the adduct was heated in nitrobenzene solution, quinaldonitrile (V) was obtained in small yield.



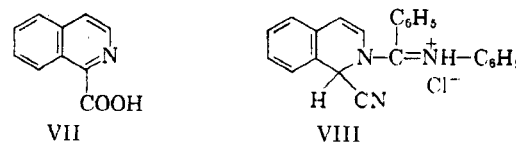
IV V

Because benzaldehyde, picolinic acid (2-pyridinecarboxylic acid), and aniline were obtained on acid-catalyzed hydrolysis of the pyridine adduct, $C_{19}H_{16}N_3Cl$, it was concluded that the latter compound was 1-(α-phenyliminobenzyl)-1,2-dihydropicolinonitrile hydrochloride (VI) or a tautomer thereof. Confirmation of this structure was obtained by oxidation of the adduct with nitrobenzene; 2-pyridinecarboxamide was obtained in this reaction.



VI

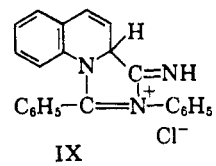
The newly prepared isoquinoline adduct, $C_{23}H_{18}N_3Cl$, gave benzaldehyde, aniline, and isoquinaldic acid (VII) on acid-catalyzed hydrolysis and isoquinaldonitrile on nitrobenzene oxidation. Hence, the new adduct has been assigned the structure of 2-(α-phenyliminobenzyl)-1,2-dihydroisoquinaldonitrile hydrochloride (VIII) or a tautomer thereof.



VII VIII

With regard to the fine structures of the three adducts, II, VI, VIII, there is evidence that these compounds, like the analogous Reissert compounds,[3] exist largely in the cyclic forms, IX, and the two analogous structures derived from VI and VIII. Specifically, the infrared spectra of all three compounds are rather similar, and, in particular, while all three lack absorption peaks in the region 2200–2400 cm.$^{-1}$, characteristic of a free cyano group, they do possess two absorption peaks each in the 1630–1660 cm.$^{-1}$ region. The latter absorption peaks are characteristic of the C=N group.

(2) A. Reissert, *Ber.*, **38**, 1603 (1905).
(3) W. E. McEwen and R. L. Cobb, *Chem. Revs.*, **55**, 511 (1955).
(4) R. L. Cobb and W. E. McEwen, *J. Am. Chem. Soc.*, **77**, 5042 (1955).
(5) A. P. Wolf, W. E. McEwen, and R. H. Glazier, *J. Am. Chem. Soc.*, **78**, 861 (1956).
(6) F. D. Popp and W. E. McEwen, *J. Am. Chem. Soc.*, **79**, 3773 (1957).
(7) L. R. Walters, N. T. Iyer, and W. E. McEwen, *J. Am. Chem. Soc.*, **80**, 1177 (1958).
(8) F. D. Popp and W. E. McEwen, *J. Am. Chem. Soc.*, **80**, 1181 (1958).
(9) N. C. Rose and W. E. McEwen, *J. Org. Chem.*, **23**, 337 (1958).
(10) N. C. Rose, L. R. Walters, and W. E. McEwen, *J. Org. Chem.*, **23**, 341 (1958).
(11) R. F. Collins and T. Henshall, *J. Am. Chem. Soc.*, **80**, 159 (1958).
(12) J. W. Davis, Jr., *J. Org. Chem.*, **24**, 1691 (1959).
(13) J. W. Davis, Jr., *J. Org. Chem.*, **25**, 376 (1960).



IX

Studies of the acid-catalyzed and base-catalyzed condensation reactions of the three adducts are in progress.

Acknowledgment. This investigation was supported in part by a research grant, E-1961, from the National Institute of Allergy and Infectious Diseases of the National Institutes of Health, Public Health Service.

EXPERIMENTAL[14]

N-Phenylbenzimidyl chloride (I). This compound was prepared by the method of Braun and Pinkernelle.[15]

2-(α-Phenyliminobenzyl)-1,2-dihydroisoquinaldonitrile hydrochloride (VIII). A solution of 4.8 ml. (0.12 mole) of liquid hydrogen cyanide and 17.0 g. (0.13 mole) of freshly distilled isoquinoline in 35 ml. of anhydrous ether was added to a cold solution of 32.3 g. (0.17 mole) of *N*-phenylbenzimidyl chloride (I) in anhydrous ether. An exothermic reaction took place, and the solution turned yellow-orange. A hard cake formed and, after a 24-hr. reaction period, this solid was collected by filtration and washed, first with anhydrous ether, then with anhydrous acetone. There was obtained 29.5 g. of yellow VIII, m.p. 277.0–278.5°. An additional 5.9 g. of the same material (total of 35.4 g., 78%) was obtained upon concentration of the mother liquor and wash solutions.

Anal. Calcd. for $C_{23}H_{18}N_3Cl.3/4H_2O$: C, 71.68; H, 5.10; N, 10.90; Cl, 9.20. Found: C, 71.67, 71.41; H, 4.57, 4.57; N, 11.10; Cl, 9.39.

The hydrochloride was readily converted to the picrate by treatment with ethanolic picric acid. After several recrystallizations from ethanol, the *picrate* had a m.p. of 225.5–226.0°.

Anal. Calcd. for $C_{29}H_{20}N_6O_7$: C, 61.70; H, 3.57; N, 14.89. Found: C, 61.75; H, 3.64; N, 15.13.

1-(α-Phenyliminobenzyl)-1,2-dihydroquinaldonitrile hydrochloride (II). This compound was obtained in 70–78% yields from *N*-phenylbenzimidyl chloride (I), hydrogen cyanide and quinoline by the method described in the literature[1] (essentially the same as that described above for the preparation of VIII). The bright yellow solid, II, had a m.p. of 269.5–270.5° (reported,[1] m.p. 272°).

1-(α-Phenyliminobenzyl)-1,2-dihydropicolinonitrile hydrochloride (VI). Prepared in 76–79% yields by the method of Mumm, Volquartz, and Hesse,[1] the bright yellow compound had a m.p. of 251.0–251.5° (reported,[1] m.p. 253°).

Acid-catalyzed hydrolysis of II. A mixture of 30.0 g. (0.081 mole) of 1-(α-phenyliminobenzyl)-1,2-dihydroquinaldonitrile hydrochloride (II) and 300 ml. of 20% hydrochloric acid was heated under reflux for 1 hr. The resulting red solution was then distilled with but partial takeoff during a period of 28 hr., 150 ml. of distillate being collected. Extraction of the distillate with ether gave 7.1 ml. (86.5%) of benzaldehyde.

The residual solution from the distillation was neutralized with saturated sodium bicarbonate solution, and a brown solid which had formed was removed by filtration. The filtrate was acidified by addition of acetic acid, then treated with an excess of a solution of copper sulfate. The copper quinaldate which had formed was collected by filtration, washed thoroughly with distilled water, and dried. There was obtained 15.5 g. (94.5%) of the salt. A sample was suspended in distilled water, treated with hydrogen sulfide, and filtered. Evaporation of the filtrate gave quinaldic acid (IV), m.p. 153.5–154.5° after recrystallization from benzene. A mixed melting point with authentic quinaldic acid showed no depression.

The filtrate from which the copper quinaldate had been removed was made alkaline and steam distilled. Benzoylation of the aniline so obtained gave 7.15 g. (45%) of benzanilide.

Acid-catalyzed hydrolysis of VI. The hydrolysis and workup were the same as in the previous experiment, and there was obtained benzaldehyde in 65% yield, copper picolinate in 71% yield and aniline, isolated as the benzoyl derivative, in 41% yield. The copper picolinate was decomposed with hydrogen sulfide to give picolinic acid, m.p. 136.5–138.0° after recrystallization from benzene. The infrared absorption spectrum was identical with that of a pure sample of picolinic acid prepared by the potassium permanganate oxidation of α-picoline, and a mixed melting point determination of the two samples showed no depression.

Acid-catalyzed hydrolysis of VIII. On a small scale experiment with VIII (0.0025 mole being used), carried out under the same conditions as described for the hydrolysis of II, benzaldehyde was isolated in 25% yield, copper isoquinaldate in 48% yield, and aniline in 25% yield. The isoquinaldic acid (VII) obtained by treatment of the copper salt with hydrogen sulfide had a m.p. of 157.0–159.0° after recrystallization from benzene and showed no depression in a mixed m.p. test with authentic isoquinaldic acid.

Oxidation of II *with nitrobenzene.* A solution of 10.0 g. (0.027 mole) of II in 50 ml. of nitrobenzene was heated under reflux for 6 hr. The nitrobenzene was distilled *in vacuo*, and the residue was steam distilled. Extraction of the steam distillate with ether gave 0.45 g. (11%) of quinaldonitrile (V), m.p. 88.0–89.5° after recrystallization from petroleum ether. A mixed melting point with authentic[16] V showed no depression.

Oxidation of VI *with nitrobenzene.* A solution of 10.0 g. (0.031 mole) of VI in 50 ml. of nitrobenzene was heated under reflux for 6 hr., and the solution was then distilled to dryness *in vacuo*. The distillate was extracted with 20% hydrochloric acid, the acid extract made alkaline by addition of sodium bicarbonate solution, and the alkaline solution extracted with ether. Distillation of the ether gave 2-pyridinecarboxamide (0.12 g., 3.2%), m.p. 101.5–102.5° after recrystallization from petroleum ether (reported,[17] m.p. 106.5°). No depression of the melting point was observed when this material was mixed with an authentic sample of 2-pyridinecarboxamide prepared by the method of Camps.[17] The infrared absorption spectra of the two samples were taken in chloroform solution and found to be identical.

Oxidation of VIII *with nitrobenzene.* A solution of 10.0 g. (0.027 mole) of VIII in 50 ml. of nitrobenzene was heated under reflux for 48 hr. A white solid subliming into the condenser was removed as it accumulated and recrystallized from petroleum ether. There was obtained 0.11 g. of isoquinaldonitrile, m.p. 90.0–90.5°. After distillation of nitrobenzene *in vacuo* and steam distillation of the residue, an additional 0.35 g. of isoquinaldonitrile was isolated from the steam distillate (total yield, 11%). A mixed melting point determination with authentic[18] isoquinaldonitrile showed no depression and the infrared spectra of the two samples, taken in chloroform solution, were identical.

LAWRENCE, KAN.

(14) All melting points are corrected. Analyses were performed by Weiler and Strauss, Oxford, England, and Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

(15) J. Braun and W. Pinkernelle, *Ber.*, **67**, 1218 (1934).

(16) A. Kaufmann and P. Dandliker, *Ber.*, **46**, 2924 (1914).

(17) R. Camps, *Arch. Pharm.*, **240**, 345 (1902).