vacuum. The remaining deep orange liquid (weight 18.8 g.) was dissolved in 40 ml. of absolute methanol, 0.1 g. of 5% palladium on activated carbon was added and the mixture was shaken under 45 lb. pressure of hydrogen. Sixteen hundredths mole of hydrogen was absorbed. The catalyst was removed by filtration and the methanol was removed by evaporation in a vacuum. The remaining liquid was distilled in a vacuum. The fraction boiling at 88–93° (0.1 mm.) was collected as β-(1-hydroxycyclohexyl)propionaldehyde diethylacetal. This fraction (17.2 g.) was redistilled and the fraction boiling at 90° (0.1 mm.) was collected as pure material, n_D^{21} 1.4560.

Anal. Calcd. for $C_{13}H_{26}O_3$: C, 67.83; H, 11.30. Found: C, 68.11; H, 11.65.

The 2,4-dinitrophenylhydrazone, after one recrystallization from aqueous ethanol, melted at 132.5°.

Anal. Calcd. for $C_{15}H_{20}N_4O_5$: C, 53.56; H, 5.99. Found: C, 53.29; H, 5.95.

The semicarbazone melted at 234°.

Lactone of β-(1-hydroxycyclohexyl)propionic acid. A solution containing 11.5 g. (0.05 mole) of β-(1-hydroxycyclohexyl)propionaldehyde diethylacetal in 60 ml. of ether was shaken periodically over a period of 1 hr. with 100 ml. of 3*N* sulfuric acid. Five g. (0.017 mole) of potassium dichromate in 200 ml. of water was added and the mixture was shaken vigorously and allowed to stand overnight. The ether layer was separated and the aqueous layer was extracted with three 50-ml. portions of ether. The combined ether extract was extracted with one 100-ml. and two 50-ml. portions of 15% potassium hydroxide. The potassium hydroxide extract was acidified and was extracted with three 25-ml. portions of ether. The combined ether extract was washed twice with 20-ml. portions of water and the ether extract was removed by evaporation in a vacuum. The lactone (4.4 g.) was obtained as a colorless liquid by distillation at 49° and 0.3 mm. pressure; sapon. equiv., 156 (calcd., 154); n_D^{30} 1.4772. The lactone crystallized upon standing in the refrigerator, m.p. 26°. A mixture of this material with an authentic specimen prepared by the procedure of Johnson and Hunt[7] melted at 26°.

The *amide* of β-(1-hydroxycyclohexyl) propionic acid was prepared by allowing 1.0 g. of the lactone to stand for 3 days in 10 ml. of water saturated with NH_3. After one crystallization from aqueous ethanol the amide melted at 144°. A mixture of this amide and an authentic specimen of the amide of β-(1-hydroxycyclohexyl)propionic acid melted at 144°.

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(7) W. S. Johnson and R. H. Hunt, *J. Am. Chem. Soc.*, **72**, 938 (1950).

Reduction and Benzylation by Means of Benzyl Alcohol. IV. 3-Benzylquinolines

MOSHE AVRAMOFF AND YAIR SPRINZAK

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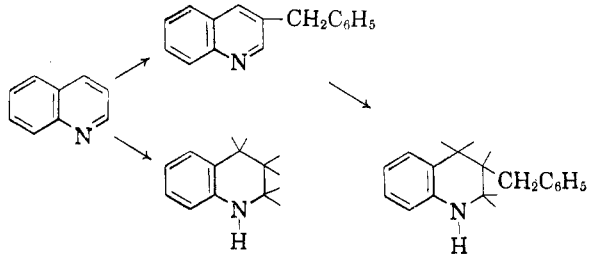
The preceding paper of this series[1] reported that quinoline is readily transformed into 3-benzyl-1,2,-3,4-tetrahydroquinoline on heating with benzyl alcoholic potassium hydroxide, and that the reaction proceeds through the formation of 3-benzylquinoline, isolable from the reaction mixture after a short reaction time; at the same time, part of the quinoline is reduced to 1,2,3,4-tetrahydroquinoline.



It was further pointed out that substituents in the α- and γ-positions of the pyridine ring ordinarily inhibit reduction and ring benzylation.

We wish to report here the results of experiments with quinolines substituted in the benzene ring, *viz.*, 6-methyl-, 8-methyl-, 6-phenyl-, 8-phenyl-, and 6-methoxyquinoline, performed in order to test the scope of the reaction, in particular with regard to the β-benzylation of the pyridine ring. The structures of the various benzylated products obtained were established by independent (Skraup) synthesis.

6-Methyl-, 8-methyl-, and 8-phenylquinoline furnished, upon heating with the reagent, all three types of products obtainable from unsubstituted quinoline, namely, the corresponding 1,2,3,4-tetrahydroquinolines (I, II, and III), 3-benzylquinolines (V, VI, and VIII), and 3-benzyl-1,2,3,4-tetrahydroquinolines (X, XI, and XIII). With 6-phenylquinoline only the benzylated compounds (VII and XII) could be isolated; the absence of 6-phenyl-1,2,3,4-tetrahydroquinoline may be due to its reported instability.[2] A marked difference was observed between the reactivities of the 6- and the 8-substituted compounds, the reduction of the benzylquinolines formed initially being apparently slower for the 8-isomers (Table I). A 36% yield of XI could be obtained, however, when VI was used as the starting material and the time of reaction extended to 42 hr.; even under these conditions 15% of the starting material was recovered.

TABLE I
PER CENT YIELDS OF SUBSTITUTED QUINOLINES

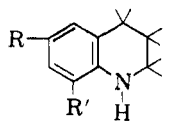
Substituent	Reaction Time, Hr.	Tetrahydroquinoline	Benzylquinoline	Benzyltetrahydroquinoline
6-Methyl	3	10	19	26
8-Methyl	5	14	34	3
6-Phenyl	2	—	5	43
8-Phenyl	2	17	20	17

While the main reaction observed with 6-methoxyquinoline was hydrolysis to 6-quinolinol, 6-methoxy-1,2,3,4-tetrahydroquinoline (thalline, IV),

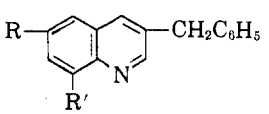
(1) M. Avramoff and Y. Sprinzak, *J. Am. Chem. Soc.*, **78**, 4090 (1956).

(2) W. La Coste and C. Sorger, *Ann.*, **230**, 1 (1885).

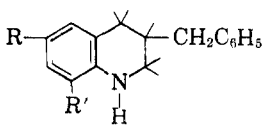
and 3-benzyl-6-methoxyquinoline (IX) were nevertheless isolated in low yields (3% and 5%, respectively).



I, R = CH_3, R′ = H
II, R = H, R′ = CH_3
III, R = H, R′ = C_6H_5
IV, R = CH_3O, R′ = H



V, R = CH_3, R′ = H
VI, R = H, R′ = CH_3
VII, R = C_6H_5, R′ = H
VIII, R = H, R′ = C_6H_5
IX, R = CH_3O, R′ = H



X, R = CH_3, R′ = H
XI, R = H, R′ = CH_3
XII, R = C_6H_5, R′ = H
XIII, R = H, R′ = C_6H_5

The preparation of 3-substituted quinolines usually meets with difficulties.[3] The *o*-aminobenzaldehydes required for the Friedländer synthesis are well known to be unstable.[4] On the other hand, the substituted isatins needed for the Pfitzinger modification of this method are either unknown or relatively inaccessible.[5] Recourse was therefore had to the Skraup method with the appropriate anilines on the one hand and 2-benzylglycerol-1,3-diethyl ether on the other, following Darzens' modification,[6] which employs 2-alkylglycerol-1,3-diethyl ethers as precursors of the requisite acrylaldehydes. Although the low volatility of the quinolines formed made their isolation by steam distillation impractical, fair yields of these compounds could nevertheless be obtained.

EXPERIMENTAL

The reaction of the various quinolines with benzyl alcoholic potassium hydroxide and the isolation of the reaction products were performed by the procedure described in the preceding paper.[1] All melting points are corrected.

Reaction with 6-methylquinoline. A mixture of 35.8 g. (0.25 mole) of 6-methylquinoline (City Chemical Corp., New York, N. Y.) and 250 ml. of benzyl alcoholic potassium hydroxide was refluxed for 3 hr. After the usual treatment the following fractions were collected: (*a*) 13.9 g., b.p. 155–175° (30 mm.); (*b*) 33.7 g., b.p. 150–165° (0.04 mm.). Fraction *a* was dissolved in 100 ml. of alcohol and treated with a solution of 20 g. of picric acid in 400 ml. of hot alcohol. Upon cooling, 6.2 g. of the picrate of the starting material, m.p. and mixed m.p. 237–240°, was collected by filtration. The residue left after the evaporation of the alcoholic mother liquor was washed with benzene and recrystallized from toluene to give 12 g. of a picrate melting at about 125–130°. Decomposition of this picrate gave 3.5 g. of *6-methyl-1,2,3,4-tetrahydroquinoline* (I), b.p. 159° (28 mm.); m.p. 36–37° (lit.[7] 37–38°); *N*-acetyl derivative,[7] b.p. 312–316° (lit.[7] 306–307°); *N*-benzoyl derivative,[8] m.p. 81°, from dilute alcohol (lit.[9] 78°).

Picrate, readily soluble in alcohol, yellow needles, m.p. 141° (from benzene).

Anal. Calcd. for $C_{16}H_{16}N_4O_7$: C, 51.06; H, 4.29. Found: C, 51.02; H, 4.57.

Fraction *b* was recrystallized from alcohol to give 15.2 g. of *3-benzyl-6-methyl-1,2,3,4-tetrahydroquinoline* (X), white plates, m.p. 91–92.5°.

Anal. Calcd. for $C_{17}H_{19}N$: C, 86.03; H, 8.07. Found: C, 86.18; H, 7.92.

Picrate, yellow needles, m.p. 150–151° (from benzene).

Anal. Calcd. for $C_{23}H_{22}N_4O_7$: C, 59.22; H, 4.75. Found: C, 59.73; H, 4.96.

The alcoholic mother liquor from the recrystallization of the base was treated with an alcoholic solution of 15 g. of picric acid. Recrystallization from xylene afforded 21.8 g. of *the picrate of 3-benzyl-6-methylquinoline* (V),[10] yellow needles, m.p. 197–198°.

Anal. Calcd. for $C_{23}H_{15}N_4O_7$: C, 59.74; H, 3.92. Found: C, 59.29; H, 3.86.

The base,[10] recovered from the picrate, crystallized from petroleum ether in white needles, m.p. 69–70°.

Anal. Calcd. for $C_{17}H_{15}N$: C, 87.51; H, 6.48. Found: C, 87.32; H, 6.07.

The same base was obtained by dehydrogenating X in the presence of 5% palladium on barium sulfate for 1 hr. at 250–300°.

Reaction of 8-methylquinoline. A mixture of 71.5 g. (0.5 mole) of 8-methylquinoline (City Chemical Corp., New York, N. Y.) and 500 ml. of benzyl alcoholic potassium hydroxide was refluxed for 5 hr. After the usual treatment the following fractions were collected: (*a*) 25 g. b.p. 155–175° (30 mm.); (*b*) 61.5 g., b.p. 155–170° (0.5 mm.). Fraction *a* was converted to the hydrochloride by treatment with concentrated hydrochloric acid and evaporation of the excess acid on a water bath *in vacuo*. Recrystallization from alcohol afforded 12.6 g. of *the hydrochloride of 8-methyl-1,2,3,4-tetrahydroquinoline* (II), m.p. 216–219° (lit.[11] 214°).

Anal. Calcd. for $C_{10}H_{14}ClN$: C, 65.33; H, 7.67; Cl, 19.3. Found: C, 65.31; H, 7.70; Cl, 19.2.

The recovered liquid base was converted to the *N*-benzoyl derivative,[8] m.p. 110° (lit.[12] 108°).

Fraction *b* was dissolved in alcohol and precipitated with an alcoholic solution of picric acid to afford 78.7 g. of *the picrate of 3-benzyl-8-methylquinoline* (VI),[10] yellow plates, m.p. 219–221° (from alcohol or xylene).

The base[10] obtained from the picrate boiled at 155–158° (0.1 mm.) and crystallized from petroleum ether in white plates, m.p. 61–62°.

Anal. Calcd. for $C_{17}H_{15}N$: C, 87.51; H, 6.48. Found: C, 87.58; H, 6.47.

Hydrochloride, white prisms, m.p. 210–213° (from concentrated hydrochloric acid or alcohol-ether).

Anal. Calcd. for $C_{17}H_{16}ClN$: Cl, 13.1. Found: Cl, 13.1.

The alcoholic mother liquor from the picrate of VI was evaporated and the residue was washed several times with benzene, decomposed with aqueous sodium hydroxide and

(3) See, *e.g.*, W. P. Utermohlen, Jr., *J. Org. Chem.*, **8**, 544 (1943).

(4) R. C. Elderfield, *Heterocyclic Compounds*, John Wiley and Sons, Inc., New York, N. Y., 1952, Vol. IV, p. 46.

(5) R. Bauer, *Ber.*, **40**, 2650 (1907); T. Sandmeyer, *Helv. Chim. Acta*, **2**, 234 (1919); H. Colombara, U. S. Patent **1,856,210** [*Chem. Abstr.*, **26**, 3522 (1932)].

(6) G. Darzens and M. Meyer, *Compt. rend.*, **198**, 1428 (1934).

(7) R. Escourrou, *Bull. soc. chim. France*, [5] **5**, 1184 (1938).

(8) R. L. Shriner and R. C. Fuson, *The Systematic Identification of Organic Compounds*, 3rd ed., John Wiley and Sons, Inc., New York, N. Y., 1948, p. 88.

(9) J. V. Braun, A. Grabowski, and G. Kirschbaum, *Ber.*, **46**, 1266 (1913).

(10) This compound gave no depression of melting point when mixed with the appropriate product of the Skraup synthesis, described below.

(11) E. Bamberger and P. Wulz, *Ber.*, **24**, 2055 (1891).

(12) J. V. Braun, W. Gmelin, and A. Schultheiss, *Ber.*, **56**, 1338 (1923).

extracted with ether. The base so recovered (about 7 g.) was converted to the *N*-benzoyl derivative.[8] Recrystallization from dilute alcohol and then from petroleum ether afforded 4.1 g. of *N-benzoyl-3-benzyl-8-methyl-1,2,3,4-tetrahydroquinoline*, white prisms, m.p. 98–98.5°.

Anal. Calcd. for $C_{24}H_{23}NO$: C, 84.42; H, 6.79. Found: C, 84.67; H, 6.65.

3-Benzyl-8-methyl-1,2,3,4-tetrahydroquinoline (XI) was obtained by refluxing its *N*-benzoyl derivative with 2*N* KOH in benzyl alcohol for 5 hr. It boiled at 205–207° (8 mm.) and crystallized from alcohol in white plates, m.p. 56–57°.

Anal. Calcd. for $C_{17}H_{19}N$: C, 86.03; H, 8.07. Found: C, 86.40; H, 7.88.

Picrate, readily soluble in alcohol, yellow prisms, m.p. 166.5° (from benzene).

Anal. Calcd. for $C_{23}H_{22}N_4O_7$: C, 59.22; H, 4.75. Found: C, 59.12; H, 4.53.

Reduction of 3-benzyl-8-methylquinoline. A mixture of 11.7 g. (0.05 mole) of VI and 50 ml. of reagent was refluxed for 42 hr. The residue left after the usual treatment and distillation of the benzyl alcohol was benzoylated.[8] The semisolid product was crystallized from 70% alcohol and then from 95% alcohol to give 6.1 g. of the *N*-benzoyl derivative of XI, m.p. 97–98°. Addition of water to the combined alcoholic mother liquors precipitated a colorless oil, which was separated and distilled to give 1.7 g. of the starting material, identified by its picrate.

Reaction with 6-phenylquinoline. A mixture of 5.1 g. (0.025 mole) of 6-phenylquinoline[13] (m.p. 109°) and 25 ml. of reagent was refluxed for 2 hr. After the usual treatment the fraction boiling at 160–220° (0.2 mm.) was collected. Recrystallization from propanol and from heptane afforded 3.2 g. of *3-benzyl-6-phenyl-1,2,3,4-tetrahydroquinoline* (XII), clusters of yellowish plates, m.p. 100°.

Anal. Calcd. for $C_{22}H_{21}N$: C, 88.25; H, 7.07. Found: C, 88.35; H, 6.95.

N-Benzoyl derivative,[8] white prisms, m.p. 129° (from alcohol).

Anal. Calcd. for $C_{29}H_{25}NO$: C, 86.32; H, 6.25. Found: C, 86.06; H, 6.18.

Dehydrogenation of the base in the presence of 5% palladium on charcoal at 300° afforded *3-benzyl-6-phenylquinoline* (VII),[10] white needles m.p. 134° (from heptane).

Anal. Calcd. for $C_{22}H_{17}N$: C, 89.46; H, 5.80. Found: C, 89.63; H, 5.71.

Picrate,[10] yellow plates, m.p. 257–259° (from dioxane or chlorobenzene).

Anal. Calcd. for $C_{28}H_{20}N_4O_7$: C, 64.12; H, 3.84. Found: C, 64.72; H, 4.18.

The mother liquors from the recrystallization of XII were evaporated and the residue was treated with picric acid to give 0.58 g. of the picrate of VII.

Reaction with 8-phenylquinoline. A mixture of 20.5 g. (0.1 mole) of 8-phenylquinoline[14] and 100 ml. of benzyl alcoholic potassium hydroxide was refluxed for 2 hr. After the usual treatment the following fractions were collected: (*a*) 10.2 g., b.p. 150–210° (4 mm.); (*b*) 17.9 g., b.p. 230–260° (4 mm.). Fraction *a* was converted in alcoholic solution to the picrate (7.2 g.), m.p. about 160° (from benzene or alcohol). The base recovered from this picrate is *8-phenyl-1,2,3,4-tetrahydroquinoline* (III), viscous oil, b.p. 160° (3 mm.).

Anal. Calcd. for $C_{15}H_{15}N$: C, 86.08; H, 7.22. Found: C, 85.97; H, 6.78.

(13) D. H. Hey and E. W. Walker, *J. Chem. Soc.*, 2213 (1948).

(14) C. E. Kaslov and M. Hayek [*J. Am. Chem. Soc.*, **73**, 4986 (1951)] describe this compound as liquid. Following their procedure, we have obtained it as a solid of m.p. 48–49° in accordance with F. W. Bergstrom [*J. Org. Chem.*, **3**, 424 (1939)]. Furthermore, its picrate (checked by analysis) melted at 156°, as compared with 200°, reported in reference 13.

In order to ascertain the structure of this base its ultraviolet absorption spectrum was compared with that of 3-benzyl-8-phenyl-1,2,3,4-tetrahydroquinoline, since it has been observed[15] that the introduction of a 3-benzyl group into a quinoline or a tetrahydroquinoline does not modify their spectra appreciably. 8-Phenyl-1,2,3,4-tetrahydroquinoline showed the following maxima: λ = 229, 290, 319 mμ (log ϵ = 4.31, 3.22, 3.58, respectively); 3-benzyl-8-phenyl-1,2,3,4-tetrahydroquinoline showed λ = 230, 288, 322 mμ (log ϵ = 4.31, 3.19, 3.60, respectively).[16]

N-Benzoyl derivative,[8] colorless cubes, m.p. 175–176° (from alcohol).

Anal. Calcd. for $C_{22}H_{19}NO$: C, 84.31; H, 6.11. Found: C, 84.40; H, 6.09.

Refluxing the *N*-benzoyl derivative with 2*N* KOH in benzyl alcohol for 5 hr. afforded the base, still in the form of a viscous oil.

Picrate, yellow prisms, m.p. 164–166° (from benzene).

Anal. Calcd. for $2C_{15}H_{15}N{\cdot}3C_6H_3N_3O_7$: C, 52.14; H, 3.55. Found: C, 52.61; H, 3.65.

Confirmation of this unusual ratio of picric acid to base was obtained by titrating the picric acid component in dimethylformamide solution with 0.1*N* sodium methoxide in methanol in the presence of Thymol Blue; the equivalent weight so obtained was 375, as compared with the calculated 367. The purity of the picric complex was further checked by successive recrystallizations from alcohol and from benzene, as well as by fractional crystallization from alcohol.

Fraction *b* was recrystallized from petroleum ether and then from alcohol to afford 6.0 g. of *3-benzyl-8-phenylquinoline* (VIII),[10] colorless plates, m.p. 120–122°.

Anal. Calcd. for $C_{22}H_{17}N$: C, 89.46; H, 5.80. Found: C, 89.76; H, 5.61.

Picrate,[10] green-yellow needles, m.p. 173–175° (from alcohol).

Anal. Calcd. for $C_{28}H_{20}N_4O_7$: C, 64.12; H, 3.84. Found: 64.38; H, 3.43.

The residue left after the evaporation of the hydrocarbon mother liquor was recrystallized twice from alcohol to afford 4.9 g. of *3-benzyl-8-phenyl-1,2,3,4-tetrahydroquinoline* (XIII), colorless plates, m.p. 69–70°.

Anal. Calcd. for $C_{22}H_{21}N$: C, 88.25; H, 7.07. Found: C, 87.98; H, 6.97.

Picrate, orange needles, m.p. 143–144° (from alcohol).

Anal. Calcd. for $C_{28}H_{24}N_4O_7$: C, 63.63; H, 4.58. Found: C, 63.91; H, 4.86.

N-Benzoyl derivative,[8] colorless plates, m.p. 146° (from alcohol).

Anal. Calcd. for $C_{29}H_{25}NO$: C, 86.32; H, 6.25. Found: C, 86.44; H, 6.20.

Reaction with 6-methoxyquinoline. A mixture of 8.0 g. (0.05 mole) of 6-methoxyquinoline (Eastman Kodak Co.) and 50 ml. of reagent was refluxed for 1 hr. After the usual treatment the ethereal and aqueous layers were worked up as follows:

The aqueous layer was acidified with an excess of concentrated hydrochloric acid and extracted with ether in order to remove the benzoic acid present. An excess of solid sodium hydrogen carbonate was then added and the precipitated phenol fraction filtered, dried, and recrystallized from xylene to give 3.1 g., m.p. 190–195°. It consisted mainly of 6-hydroxyquinoline, which, after separation by fractional sublimation, melted at 209–211° (lit.[17] 193°).

Anal. Calcd. for C_9H_7NO: C, 74.47; H, 4.86. Found: C, 75.07; H, 5.21.

The ethereal layer was evaporated and the residue fractionated to give (*a*), 1.95 g., b.p. 100–160° (4 mm.), and (*b*) 1.5 g., b.p. 170–210° (4 mm.). Fraction *a* was dissolved in alcohol and precipitated with picric acid to give 1.85 g.

(15) M. Avramoff and Y. Sprinzak, unpublished results.

(16) Measurements were made in ethanol solution.

(17) J. M. Heilbron, *Dictionary of Organic Compounds*, Eyre and Spottiswoode, London, 1936, Vol. II, p. 325.

of *6-methoxyquinoline picrate*, m.p. and mixed m.p. 220–222° (from xylene).

Anal. Calcd. for $C_{16}H_{12}N_4O_8$: C, 49.47; H, 3.12. Found: C, 49.88; H, 3.19.

The alcoholic mother liquor from the picrate was evaporated, the residue washed with benzene and recrystallized from toluene to yield 0.62 g. of the picrate of *6-methoxy-1,2,3,4-tetrahydroquinoline* (IV), m.p. 160–161° (lit.[18] 164–165°) (rapid heating).

Anal. Calcd. for $C_{16}H_{16}N_4O_8$: C, 48.98; H, 4.11. Found: C, 49.51; H, 4.37.

The recovered base melted at 42° (lit.[18] 42–43°).

Fraction *b* was dissolved in alcohol and treated with picric acid to afford 1.2 g. of *3-benzyl-6-methoxyquinoline* (IX) *picrate*,[10] yellow needles, m.p. 173–176° (from alcohol).

Anal. Calcd. for $C_{23}H_{18}N_4O_8$: C, 57.74; H, 3.79. Found: C, 58.00; H, 4.03.

The *base*[10] recovered from the picrate crystallized from petroleum ether in colorless plates, m.p. 106–107°.

Anal. Calcd. for $C_{17}H_{15}NO$: C, 81.90; H, 6.06. Found: C, 81.68; H, 5.51.

3-Benzylquinolines (Skraup method). 2-Benzylglycerol-1,3-diethyl ether (b.p. 160–163° at 25 mm.) was obtained in a 25% yield by treating diethoxyacetone with benzylmagnesium chloride.[19]

The general procedure consisted in heating 0.01 mole of the appropriate aniline, 0.75 ml. of concentrated sulfuric acid, 1.2 g. of finely powdered sodium *m*-nitrobenzenesulfonate and 2.4 g. of the ether at 130° for 8 hr. After cooling, 0.35 ml. of sulfuric acid was added and heating was continued for another 8 hr. This last operation was repeated once again. The cold reaction mixture was treated with water and an excess of sodium hydroxide and extracted several times with ether. A certain amount of insoluble resins was always present. The residue from the evaporation of the ethereal solution was fractionated to yield the corresponding crude 3-benzylquinoline, which was purified through its picrate. The per cent yields of pure products were the following: 3-benzylquinoline 22; 3-benzyl-6-methylquinoline 25; 3-benzyl-8-methylquinoline 24; 3-benzyl-6-phenylquinoline 20; 3-benzyl-8-phenylquinoline 8; 3-benzyl-6-methoxyquinoline 14.

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(18) N. H. Cromwell, J. A. Caughlan, and G. F. Gilbert, *J. Am. Chem. Soc.*, **66**, 401 (1944).

(19) G. Darzens and M. Meyer, *Compt. rend.*, **198**, 478 (1934).

Separation of Some Amaryllidaceae Alkaloids by Paper Chromatography

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The genus *Crinum* (N.O. *Amaryllidaceae*) comprises about 165 species, distributed mostly in the coastal tropical and subtropical regions of the world. The two most commonly met with in Western India are *C. asiaticum* L. and *C. latifolium* L. Both plants find a limited use in indigenous medicine as rubefacient and tonics.[1] In the past few years several authors, especially W. C. Wildman[2] and H. G. Boit,[3] have investigated several different *Amaryllidaceae* species and described a number of new alkaloids in addition to the already known ones which were isolated by H. Kondo and his school. During our investigation of some Indian medicinal plants our attention was called to the two *Crinum* species and in view of the rather scanty information available (the presence of lycorine in *Crinum asiaticum* L.[4,5] has been noted) we decided to reinvestigate the two species. The plant material which was available to us for investigation was limited in quantity and it soon became apparent that conventional isolation techniques would lead to separation of the major constituent only, leaving alkaloids present in small quantities undetected. We selected paper chromatography to determine qualitatively all the alkaloids present; the results of our investigation are reported below.

Under the term *Amaryllidaceae* alkaloids one includes a rather heterogeneous mixture of compounds with varying functional groupings which are difficult to separate in a single solvent system, but, using a partition first in a less polar solvent followed by chromatography in a more polar system, a good separation can be achieved. Thus, chromatography in benzene, followed by partition in butanol–acetic acid, combined with some specific color reactions and determination of the absorption in ultraviolet light can be used for a fairly rapid identification of alkaloids present in the crude basic fraction.

A literature survey failed to reveal any information pertaining to paper chromatography of *Amaryllidaceae* alkaloids and we found it necessary to establish first comparative data for a number of alkaloids made available to us. The observed data, average R_f values, color reactions and fluorescence under ultraviolet light, are listed in Table I. In a number of cases the alkaloids, after chromatography, were eluted from the paper and the ultraviolet absorption maxima were determined; the observed values were found to be in good agreement with those reported elsewhere. It will be noted also that most of the alkaloids gave almost identical colors with iodoplatinate solution and hence this reaction finds only a limited value for rapid spotting and determination of the R_f values.

(1) K. R. Kirtikar and B. D. Basu, *Indian Medicinal Plants*, Vol. IV, 2472, 2nd Ed., Allahabad, India.

(2) *Cf. inter al.*, *J. Am. Chem. Soc.*, **77**, 1248, 1253, 4807 (1955); **78**, 2899 (1956).

(3) *Ber.*, **87**, 624, 681, 1339, 1704 (1954).

(4) *The Wealth of India*, Council of Scientific and Industrial Research, New Delhi, 1950, Vol. 2, p. 367.

(5) For the alkaloids of other *Crinum* species see L. H. Mason, *et al.*, *J. Am. Chem. Soc.*, **77**, 1253 (1955) and H. G. Boit, *Ber.*, **87**, 1704 (1954); **88**, 1590 (1955).

(6) The alkaloid "crinidine," $C_{16}H_{17}NO_3$, m.p. 210°, described by H. G. Boit in *Ber.*, **87**, 1704 (1954) was shown to be identical with the alkaloid crinine isolated at an earlier date by W. C. Wildman and coworkers [*cf. J. Am. Chem. Soc.*, **78**, 4180, footnote 3 (1956)].