sium permanganate, 4.0 ml. of 10% aqueous sodium hydroxide, and 90 ml. of water was refluxed for 4 hr. with constant stirring. The product (0.23 g., 67%), isolated by usual means, melted at 210–225° (most at 220–225°). Trituration with hot benzene sharpened the melting point to 224–225.5°.

A sample of trimellitic acid (VI) was prepared by a similar oxidation of pseudocumene. It melted at 214–225° (most at 220–225°). There was no depression of the melting point of a mixture of this product with that obtained from V. Infrared spectra of the two samples of trimellitic acid were identical.

Hydrogenation of IV and of the acrylic acid adduct. These products were hydrogenated at 38 p.s.i. in acetic acid solution with Adam's catalyst. About 2 hr. was required for each hydrogenation. The product from IV was isolated in 90% yield; n_D^{30} 1.4750. The product from the acrylic acid adduct also was isolated in 90% yield; n_D^{30} 1.4780. Infrared spectra of the two products were identical.

Oxidation of the acrolein adduct. The acrolein adduct was oxidized with silver oxide.[20] The product was isolated by chromatographic method B.

Anal. Calcd. for $C_{21}H_{36}O_4$: C, 71.55; H, 10.29. Found: C, 71.38; H, 10.09.

The infrared spectrum of this product was identical with that of the acrylic acid adduct.

PEORIA, ILL.

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(20) R. R. Burtner and J. W. Cusic, *J. Am. Chem. Soc.*, **65**, 265 (1943).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, FLORIDA A. AND M. UNIVERSITY]

Bimolecular Compounds from Dissolving-Metal Reductions of *N*-Heterocyclics[1]

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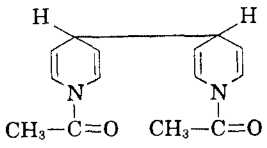
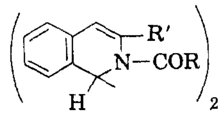
Isoquinoline and its 3-methyl homolog yield the corresponding diacyltetrahydrobiisoquinolines by reduction with zinc dust in either acetic anhydride or benzoyl chloride. Evidence is presented to establish that these dimeric compounds are derivatives of 1,1′-biisoquinoline. From a similar reduction of acridine, biacridanyl is obtained.

Pyridine was reported by Dimroth and Heene[2] to be reduced by zinc in acetic anhydride to 1,1′-diacetyl-1,4,1′,4′-tetrahydro-4,4′-bipyridine (I). When quinoline was reduced under the same conditions the product was assumed to be a bimolecular derivative analogous to I, but no analytical data were given for the product. We originally reinvestigated the zinc–acetic anhydride reduction of quinoline to determine whether the theoretical biquinoline compound was coupled at the 2- or 4- positions, but we were unable to isolate a product identifiable as a diacetyltetrahydrobiquinoline. The main reaction product was in amorphous organozinc complex or mixture.[3]

Quinoline, however, proved to be the anomalous case, for isoquinoline was reduced, like pyridine, to the expected 2,2′-diacetyl-1,2,1′,2′-tetrahydro-1,1′-biisoquinoline (IIa) in 18% yield. A similar compound (IIb) was obtained from 3-methylisoquinoline (1.4% yield), and by substituting benzoyl chloride for acetic anhydride a corresponding dibenzoyltetrahydrobiisoquinoline (IIc) was prepared from isoquinoline in 6% yield.





IIa R = CH_3, R′ = H
IIb R = CH_3, R′ = CH_3
IIc R = C_6H_5, R′ = H

It was postulated that the dimeric isoquinoline compounds should be 2,2′-diacyl-1,2,1′,2′-tetrahydro-1,1′-biisoquinolines (*cf.* II) on the basis that a proposed intermediate 2-acylisoquinolinium ion would bear the highest positive charge at the 1- position,[4] and nucleophilic attack by zinc would occur here.[5] Most of the work of structure determination was done with diacetyltetrahydrobiisoquinoline (IIa) and involved attempts to convert it to an aromatic species since a number of biisoquinolines are known. Air oxidation of the ethanolic solution was successful for degrading the pyridine dimer (I) to 4,4′-bipyridine, but when this method was applied to the isoquinoline analog the only product identifiable was isoquinoline. In other attempts iodine

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(1) We wish to acknowledge a Frederick Cottrell grant from the Research Corp.

(2) Dimroth and Heene, *Ber.*, **54**, 2934 (1921).

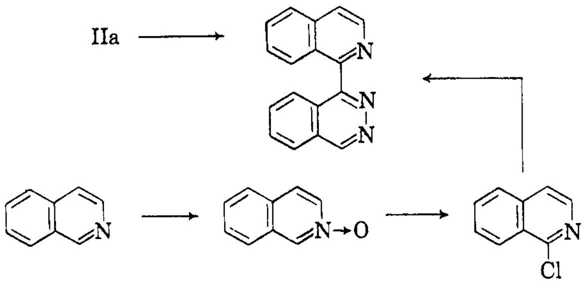
(3) Unpublished results, this laboratory.

(4) M. J. S. Dewar, in *Progress in Organic Chemistry* (J. W. Cook, Editor) Academic Press, Inc., New York, N. Y., 1953, Vol. II, p. 13.

(5) The question whether the actual coupling reaction involves ionic or free radical intermediates appears complicated in these heterogeneous systems and probably should be approached through the concept of the chemisorption of the organic cation on the metal surface, which, according to Brewster, *J. Am. Chem. Soc.*, **76**, 6361 (1954), may exist as a resonance hybrid of several ionic or radical forms with participation of the electrons of the metal undergoing oxidation. [*Cf.* also Fouad and Herringshaw, *J. Chem. Soc.*, 1207 (1954) and Morton and Lanpher, *J. Org. Chem.*, **21**, 93 (1956).] One observation that follows from this hypothesis is that proposals of one- or two-electron changes need not be a problem for metals for which extraordinary oxidation states would otherwise have to be postulated.

and potassium acetate in ethanol[6] and alcoholic potassium hydroxide were tried, but isoquinoline and unreacted IIa were recovered from the reaction mixture in each case. Although the details of the alkaline hydrolysis are not known, the cleavage of the carbon-carbon bond under these conditions appears comparable to the base-catalyzed hydrolysis of 2-benzoyl-1,2-dihydroisoquinaldonitrile[7] in which a cyanide ion is expelled.

Moreover, IIa proved very resistant to hydrolysis in dilute acid, but when 70% sulfuric acid was used 1,1′-biisoquinoline (III) was isolated from the acid-soluble fraction. The infrared spectrum of this product showed that the acetyl group had been lost and that oxidation had apparently occurred without disproportionation to a tetrahydroisoquinolylisoquinoline, for there was no evidence for a N—H bond. In order to confirm that the product was 1,1′-biisoquinoline an alternative synthesis that parallels that of Case[8] was carried out. Isoquinoline was converted to its *N*-oxide (IV) in 53% yield by the procedure developed by Ochai[9] for pyridine and quinoline; IV was treated with phosphoryl chloride to give 1-chloroisoquinoline,[10] and this latter compound was coupled in an Ullmann condensation to give III in 8% yield. The two biisoquinolines, one from the Ullmann condensation and the other from the degradation of IIa, proved identical from a mixture melting point determination.

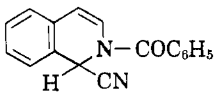


Additional evidence for the assignment of the 2-acyl-1,2-dihydroisoquinoline structures to these derivatives (II) was obtained by comparing the ultraviolet spectrum of dibenzoyltetrahydrobiisoquinoline (IIc) with that of 2-benzoyl-1,2-dihydroisoquinaldonitrile (V). Absorption maxima were found for IIc at 238 and 316 mμ (log ε 4.43 and 4.13) with minimum absorption at 230 and 287 mμ (log ε 4.42 and 3.42) and a shoulder at 260 mμ (log ε 4.34); by comparison V showed absorption maxima at 228, 292, and 302 mμ (log ε 4.34, 4.06, and 4.03) with minima at 217, 249, and 300 mμ (log ε 4.28, 3.64, and 4.02).[11] The other biisoquinolines (IIa and b) generally show absorption in the ultraviolet like V and 2-benzoyl-3-methyl-1,2-dihydroisoquinaldonitrile (see Experimental for details).

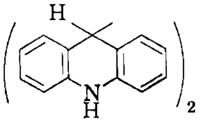
When acridine was heated with acetic anhydride and zinc dust in dimethylformamide, there remained mixed with the unreacted zinc a highly insoluble solid that was identified as 9,10,9′,10′-tetrahydro-9,9′-biacridine (biacridanyl, VI) rather than the acetylated derivative.[12] The biacridanyl was purified by recrystallization from dimethylformamide in which it was most soluble of the various solvents tried.

It has been shown that biacridanyl is capable of existing in two isomeric forms, one that melts at 247° and the other at 214°; the exact nature of this isomerism has not been established.[13] The biacridanyl obtained in this reaction melted at 247–248° under the conditions prescribed for the higher-melting isomer. Moreover, the biacridanyl showed no depression of melting point on admixture with an authentic sample of VI.[14] Although VI was practically insoluble in ethanol, a solution of the order of 10^{-5} molar was prepared; biacridanyl in this solution showed maximum absorption at 250 and 287 mμ. These compare favorably in the assignment of structure VI to the maxima reported for acridan[15] (9,10-dihydroacridine) which were found at 250 and 290 mμ.

Before we were aware that the reduced acridine product contained no *N*-acetyl groups we subjected it to prolonged acid hydrolysis in the attempt to prepare the free base. The products obtained from the acid treatment were acridine (64%) and unreacted biacridanyl (28%). These unusual results are explainable on the basis of the recorded observations that biacridanyl undergoes disproportionation, promoted by heat, to yield acridine and acridan, and acridan is easily oxidized by air in the presence of acids to acridine.[16]



V



VI

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[6] Doering and McEwen, *J. Am. Chem. Soc.*, **73**, 2104 (1951).

[7] Boekelheide and Ainsworth, *J. Am. Chem. Soc.*, **72**, 2134 (1950).

[8] Case, *J. Org. Chem.*, **17**, 471 (1952).

[9] Ochai, *J. Org. Chem.*, **18**, 534 (1953).

[10] Ikehara, *Pharm. Bull. (Japan)*, **2**, 114 (1954); *Chem. Abstr.*, **50**, 1014 (1956).

[11] The observed difference between the spectra of IIc and V may be due to the steric distortion of the benzoyl groups in the dimer.

[12] *Cf.* Massie and Kadaba, *J. Org. Chem.*, **21**, 347 (1956) who similarly report failure to isolate acetylated phenothiazine derivatives after treatment with water.

[13] (a) Lehmstedt and Hundertmark, *Ber.*, **63**, 1229 (1930). (b) Albert, *The Acridines*, E. Arnold and Co., London, 1951, p. 223.

[14] We kindly thank Dr. G. M. Badger who provided a generous sample of biacridanyl; *cf.* Badger and Sasse, *J. Chem. Soc.*, 616 (1956).

[15] Karyakin, Grigonovskii, and Yaroslavskii, *Doklady Akad. Nauk S.S.S.R.*, **67**, 679 (1949); *Chem. Abstr.*, **44**, 3999 (1950).

[16] See ref. 13b, p. 225 and p. 6.

EXPERIMENTAL[17]

2,2'-Diacetyl-1,2,1',2'-tetrahydro-1,1'-biisoquinoline (IIa). To a solution of 25 g. of isoquinoline in 110 ml. of acetic anhydride was added 20 g. of zinc dust in small portions over a period of 2 hr. with good stirring. The mixture was stirred for 2 hr. longer and filtered. The filtrate was treated with methanol, concentrated, and cooled overnight. The first crop of crystals was collected and washed with methanol; wt. 1.3 g.; m.p. 192–194°. Further batches of product crystallized slowly, bringing the yield of product to 3.5 g. The residue from the original reaction mixture was heated with 200 ml. of acetone, filtered hot, and the acetone was removed under reduced pressure leaving an oil. This was dissolved in methanol and on standing yielded 2.4 g. of the biisoquinoline product. Repeated recrystallizations from alcohol gave colorless prisms, m.p. 193–194°.

Anal. Calcd. for $C_{22}H_{20}N_2O_2$: C, 76.72; H, 5.85; N, 8.14; mol. wt. 344.4. Found: C, 76.90; H, 5.77; N, 7.93; mol. wt. (Rast) 331.

The ultraviolet spectrum of IIa in 95% ethanol had maxima at 229 mμ (log ϵ 4.20) and 305 mμ (log ϵ 4.01) and a minimum at 274 mμ (log ϵ 3.75).

Acid hydrolysis of IIa. To 2.0 g. of IIa was added a solution of 20 ml. of sulfuric acid and 15 ml. of water. The solid dissolved readily on heating the mixture, and it was refluxed 0.5 hr. The solution was added to 200 ml. of water, heated to boiling, and a solution of 2.8 g. of potassium dichromate in water was added. A solution of sodium sulfite was added after about a min., and the solution was made strongly basic. An odor like isoquinoline was noted at this point.

The cooled mixture was extracted several times with an ether-chloroform mixture. These extracts were evaporated leaving an oily semisolid. The residue was dissolved in benzene, and dilution with ligroin gave 0.2 g. of an amorphous solid, m.p. 190–205°. Evaporation of the benzene solution gave an oil which was triturated with ligroin and eventually yielded 0.1 g. of solid which was recrystallized from a large volume of ligroin. The product, m.p. 161–163°, was identified as 1,1'-biisoquinoline (lit.[8] 163°) by a mixture melting point with a sample prepared by the Ullmann condensation.

2,2'-Diacetyl-3,3'-dimethyl-1,2,1',2'-tetrahydro-1,1'-biisoquinoline (IIb). This compound was prepared in an analogous manner to IIa from 43 g. of 3-methylisoquinoline, 125 ml. of acetic anhydride, and 25 g. of zinc dust. After the unreacted zinc was removed the reaction mixture was digested in water to leave a heavy oil which was dissolved in ethanol. From this solution IIb was obtained, wt. 0.8 g., m.p. 181–183°; ultraviolet λ_{max} 225 mμ (log ϵ 4.46) and 288 mμ (log ϵ 4.24).

Anal. Calcd. for $C_{24}H_{24}N_2O_2$: C, 77.50; H, 6.46; N, 7.52. Found: C, 77.47; H, 6.45; N, 7.73.

2,2'-Dibenzoyl-1,2,1',2'-tetrahydro-1,1'-biisoquinoline (IIc). Isoquinoline, 20 g., was reduced with 13 g. of zinc dust in 29 g. of benzoyl chloride and 100 ml. of dimethylformamide by the procedure described for IIa. The reaction mixture was poured into water, and the residue was taken up in isopropyl alcohol. From this solution 5 g. of a golden powder, m.p. 173–175°, was first obtained. This material left an ash on combustion and was not investigated further.

The filtrate from the above was mixed with excess water, and a dark oil separated. The oil was changed to a gum by trituration with water, and when methanol was mixed with the residue a crystalline material remained undissolved. This was collected and washed with ether to give 1.0 g. of IIc, m.p. 209–228°. From the methanol solution 2.0 g. more of IIc was obtained. Recrystallization of IIc from a mixture of ethanol and chloroform gave colorless needles, m.p. 246–247°.

Anal. Calcd. for $C_{32}H_{24}N_2O_2$: C, 82.01; H, 5.16; N, 5.99; mol. wt. 468. Found: C, 82.04; H, 5.23; N, 6.15; mol. wt. (Rast) 462.

The ultraviolet spectrum of IIc has absorption maxima (log ϵ) at 238 mμ (4.43) and 316 mμ (4.13), with a shoulder at 260 mμ (4.16) and minima at 287 mμ (3.42) and 230 mμ (4.42).

9,10,9',10'-Tetrahydro-9,9'-biacridine (VI). To 20 g. of practical grade acridine in 125 ml. of acetic anhydride was added 13 g. of zinc dust in small portions. The mixture was stirred and refluxed during the addition of the zinc which required 1.5 hr. and then for 0.5 hr. longer. The reaction mixture was allowed to stand overnight and filtered to give a mixture of biacridine derivative and zinc residues. The solid product was washed with water to remove soluble zinc salts and gave 26 g. of crude material containing unreacted zinc. Attempts to recrystallize the crude product from ethanol, benzene, acetic acid, chloroform, or ligroin were unsuccessful. The product was slightly soluble in hot nitrobenzene, pyridine, and dimethylformamide. Several crystallizations from dimethylformamide gave biacridanyl (VI) as pale yellow prisms which placed in a bath preheated to 216° and heated at rate of 5° per minute[13] had a corrected m.p. 247–248°, and the melting point of this compound was not depressed when it was mixed with biacridanyl.[14]

Anal. Calcd. for $C_{26}H_{20}N_2$: N, 7.77. Found: N, 7.85.

Acid treatment of biacridanyl. A mixture of 500 mg. of biacridanyl and 50 ml. of 66% hydrochloric acid was refluxed 36 hr. Not all of the solid dissolved, and that remaining, 0.14 g., was collected and washed; m.p. 241–243° alone and mixed with biacridanyl. The yellow filtrate was neutralized to yield a copious white precipitate, 0.32 g. (64%), m.p. 109–110°; the mixture melting point with acridine was not depressed.

Spectra of the isoquinoline Reissert compounds. The ultraviolet absorption spectra for 2-benzoyl-1,2-dihydroisoquinaldonitrile (V)[18] and 2-benzoyl-3-methyl-1,2-dihydroisoquinaldonitrile (VII)[19] have not been recorded previously. The following data were found for ethanolic solutions: for V, λ_{max} (log ϵ) at 228 mμ (4.34), 292 mμ (4.06) and a shoulder at 302 mμ (4.03) with λ_{min} (log ϵ) at 217 mμ (4.28), 249 mμ (3.64), and an inflection at 300 mμ (4.02); for VII, λ_{max} (log ϵ) at 230 mμ (4.29), 278 mμ (3.98), and 305 mμ (3.95) with λ_{min} (log ϵ) at 218 mμ (4.21), 255 mμ (3.85), and 300 mμ (3.94).

TALLAHASSEE, FLA.

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[17] Melting points are corrected, the analyses are by Schwarzkopf Microanalytical Laboratory and the ultraviolet spectra were determined on a Beckman DR spectrophotometer.

[18] Reissert, *Ber.*, **38**, 1603 (1903).

[19] Elliott, *J. Am. Chem. Soc.*, **77**, 4408 (1955).