flask of the Brown hydrogenator along with the solvent and Norit A. Reduction was carried out for 1 hr. Isolation of the product in the manner described above gave crystalline material, which after three recrystallizations from benzene–hexane and one recrystallization from ethanol gave 232 mg. (19% yield) of pure white *cis,cis*-2,3-bis(*p*-methoxyphenyl)cyclopropane-1-carboxylic acid, m.p. 157–158°.

Anal. Calcd. for $C_{18}H_{18}O_4$: C, 72.46; H, 6.08; neut. equiv., 298.3. Found: C, 72.14; H, 6.45; neut. equiv., 298.

The n.m.r. spectrum determined in deuteriochloroform showed a symmetric multiplet at 2.88–3.40 (two sets of equivalent aromatic protons), a peak at 6.27 (aromatic methoxy protons), and a multiplet of eight peaks at 6.68–7.84 τ (cyclopropane protons of an A_2B system). The acyclic and cyclopropane protons were in the ratio of approximately 2:1, respectively.

Potentiometric Titrations of the 2,3-Diphenylcyclopropane-1-carboxylic Acids.—Identical weights, 100-mg. (0.42-mole) each, of *cis,cis-*, *cis,trans-*, and *trans,trans*-diphenylcyclopropane-1-carboxylic acids were dissolved in 25 ml. of absolute ethanol, and 25 ml. of distilled water was added. Each solution was titrated potentiometrically with 0.05 *N* sodium hydroxide in 50% by volume aqueous ethanol. The pH meter used was standardized against an aqueous buffer at pH 7.

From the curves obtained by plotting the pH of the solution *vs.* the volume of titrant, the pH at half-neutralization (4.20 ml. of titrant) was determined. Calculations gave the pK_a and K_a of the acids. The values were as follows.

cis,cis isomer: $pK_a = 6.69$; $K_a = 2.0 \times 10^{-7}$
cis,trans isomer: $pK_a = 6.03$; $K_a = 9.3 \times 10^{-7}$
trans,trans isomer: $pK_a = 5.68$; $K_a = 21.0 \times 10^{-7}$

The values given in the literature[4] are for the *trans,trans* isomer, $K_a = 17.1 \times 10^{-7}$; and for the *cis,trans* isomer, $K_a = 0.91 \times 10^{-7}$. We can offer no explanation for the discrepancy between the literature and our value in the latter case.

Acknowledgment.—We are grateful for a grant from the National Institutes of Health, AM-06466-01, which made this work possible. We wish to thank Professor F. Kaplan for advice and for interpretation of n.m.r. spectra.

Synthesis and Transformation Products of Compounds in the 1,3,4,5-Tetrahydro-5-oxobenz[*cd*]indole-3-carboxylic Acid Series

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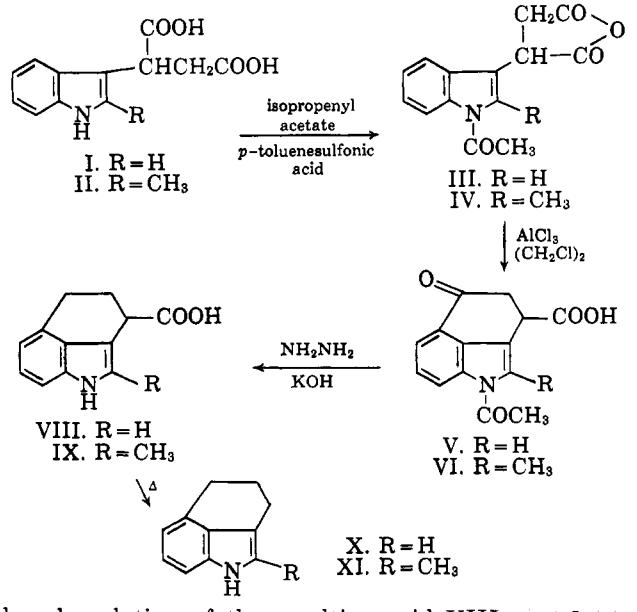
1-Acetyl-1,3,4,5-tetrahydro-5-oxobenz[*cd*]indole-3-carboxylic acid (V) was synthesized from 3-indolesuccinic acid (I) *via* 1-acetyl-3-indolesuccinic anhydride (III). The corresponding 2-methyl compound (VI) was prepared analogously from 2-methyl-3-indolesuccinic acid (II) *via* the anhydride IV. 1,3,4,5-Tetrahydrobenz[*cd*]-indole-3-carboxylic acid (VIII) and the corresponding 2-methyl compound (IX) were prepared by the Wolff–Kischner reduction of V and VI, respectively. Compound VIII was decarboxylated to the known 1,3,4,5-tetrahydrobenz[*cd*]indole (X), and IX to the corresponding 2-methyl derivative (XI). In the 2-methyl series, acid IX was converted to amides XV and XVI, which were reduced to amines XVII and XVIII, respectively. Acid IX afforded methyl ketone XIX which was converted to two isomers of 3-(1-aminoethyl)-1,3,4,5-tetrahydro-2-methylbenz[*cd*]indole (XXII) *via* reduction of oxime XX. An interesting fragmentation followed by reduction was observed in the case of oxime XX and also was applied to the oxime of indole-3-acetone.

Interest in the tetracyclic ergoline[1] system has been stimulated over the years by the potent physiological activity of compounds in this series. In the present paper we describe a method for the synthesis of 2-unsubstituted and 2-methyl-substituted tricyclic compounds in the 1,3,4,5-tetrahydrobenz[*cd*]indole series which is relatively simple, and which made possible the introduction of a carboxylic acid function in the hitherto inaccessible 3-position.

The synthesis of 1-acetyl-1,3,4,5-tetrahydro-5-oxobenz[*cd*]indole-3-carboxylic acid (V) was accomplished in two steps starting from 3-indolesuccinic acid (I). Reaction of I with isopropenyl acetate and *p*-toluenesulfonic acid brought about concomitant acetylation and anhydride formation, and led to 1-acetyl-3-indolesuccinic anhydride (III). Compound III underwent a facile cyclization in 1,2-dichloroethane with aluminum chloride to give the tricyclic N-acetyl keto acid V.

The ring structure of this cyclization product was proved by deacetylation and reduction of V with hydrazine[2] under mild conditions, followed by thermal decarboxylation of the resulting acid VIII to 1,3,4,5-tetrahydrobenz[*cd*]indole (X),[3] which was identical with an authentic sample.[4]



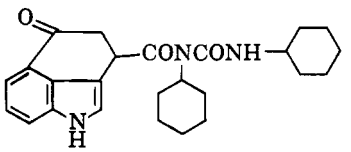
(1) For recent reviews on this subject, see D. F. Downing, *Quart. Rev.*, **16**, 133 (1962); R. Voigt, *Pharmazie*, **17**, 318 (1962); V. Erspamer in "Progress in Drug Research," Vol. 3, E. Jucker, Ed., Interscience, New York, N. Y., 1961, p. 269; J. H. Birkinshaw and C. E. Stickings in "Progress in the Chemistry of Organic Natural Products," Vol. 20, L. Zechmeister, Ed., Springer-Verlag, Vienna, 1962, p. 17. Subsequent papers include G. N. Walker and B. N. Weaver, *J. Org. Chem.*, **26**, 4441 (1961); J. A. Moore and M. Rahm, *ibid.*, **26**, 1109 (1961); C. A. Grob and O. Weissbach, *Helv. Chim. Acta*, **44**, 1736 (1961).

(2) Huang-Minlon, *J. Am. Chem. Soc.*, **68**, 2487 (1946).

(3) F. C. Uhle, *ibid.*, **71**, 761 (1949); J. A. Barltrop and D. A. H. Taylor, *J. Chem. Soc.*, 3403 (1954); F. C. Uhle, C. G. Vernick, and G. L. Schmir, *J. Am. Chem. Soc.*, **77**, 3334 (1955).

(4) We thank Dr. F. C. Uhle for sending us a sample of this material for comparison.

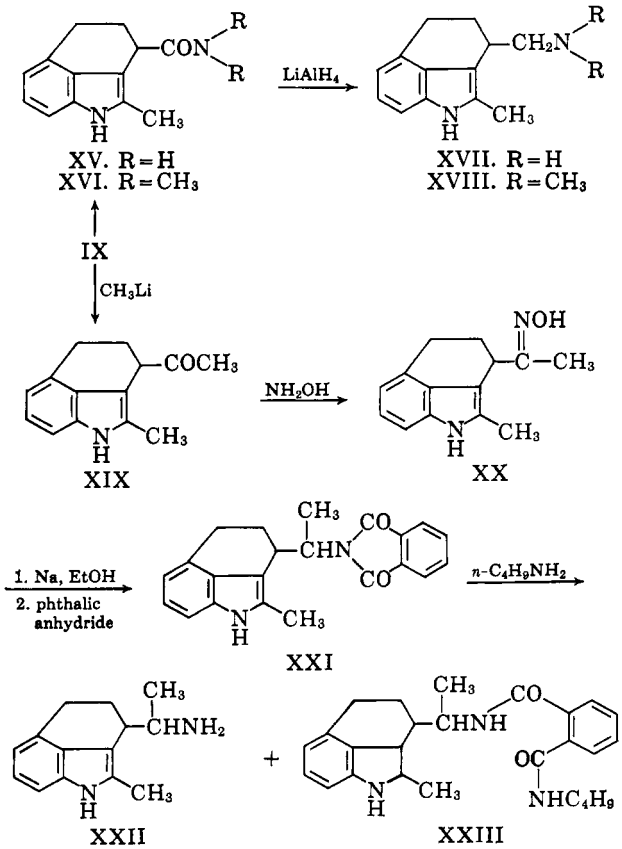
Acid V was best converted to the corresponding methyl ester VII by the oxalyl chloride procedure (see Experimental). An attempted esterification with methanol in presence of N,N′-dicyclohexylcarbodiimide led to addition product XII.[5,6]



XII

In the 2-methyl-1,3,4,5-tetrahydrobenz[*cd*]indole series the required starting material, 2-methyl-3-indolesuccinic acid (II), was prepared by condensation of 2-methylindole with maleic acid. The last two steps were analogous to those described above and led *via* anhydride IV to 1-acetyl-2-methyl-1,3,4,5-tetrahydro-5-oxobenz[*cd*]indole-3-carboxylic acid (VI). The assignment of structure to this compound is supported by the ultraviolet and infrared spectra (see Experimental). Additional evidence was provided by isolation of 2-methyl-1,3,4,5-tetrahydrobenz[*cd*]indole (XI) from the decarboxylation of acid IX, which in turn was obtained from VI by treatment with hydrazine. The ultraviolet and infrared spectra of XI were similar to those of the known compound X.

Several transformations of acid IX were carried out. Lithium aluminum hydride ($LiAlH_4$) reduction of

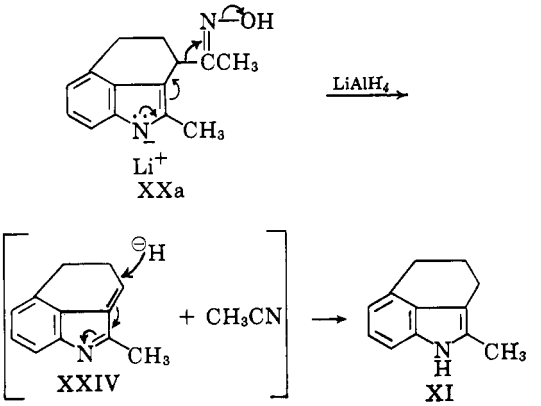


(5) The same type of adduct, namely phthaloyl-L-threonyl-N,N′-dicyclohexylurea, was isolated in addition to the desired peptide derivative from the reaction of phthaloyl-L-threonine with amino acid esters and N,N′-dicyclohexylcarbodiimide in dioxane or tetrahydrofuran by J. C. Sheehan, M. Goodman, and G. P. Hess, *J. Am. Chem. Soc.*, **78**, 1367 (1956).

(6) The ultraviolet spectrum of XII (see Experimental) is similar to that of 1,3,4,5-tetrahydro-5-oxobenz[*cd*]indole reported by C. A. Grob and J. Voltz, *Helv. Chim. Acta*, **33**, 1796 (1950).

methyl ester XIII, prepared from IX by the oxalyl chloride procedure, led to carbinol XIV. Compound IX also was converted *via* its acid chloride to amide XV and dimethyl amide XVI, which were in turn reduced with $LiAlH_4$ to amines XVII and XVIII, respectively.

Reaction of acid IX with methyllithium led to methyl ketone XIX which was converted to oxime XX. Reduction of XX with $LiAlH_4$ afforded a basic product, which appeared to be the hydroxylamine derived from XX, and a neutral compound (XI) which was identical with the decarboxylation product of acid IX. The formation of XI from XX can be rationalized in terms of a second-order Beckmann rearrangement,[7] and likely proceeds *via* the indolenine XXIV. The driving force for this reaction probably derives from negative charge on the indolic nitrogen in salt XXa. This type of



cleavage followed by reduction also was demonstrated to occur with the model oxime of indole-3-acetone, which on treatment with $LiAlH_4$ afforded a small yield of skatole along with the product of simple reduction, α-methyltryptamine.

The above fragmentation was circumvented by reduction of oxime XX with sodium and ethanol to give a mixture of two diastereoisomeric amines, which were separated by chromatography of their phthalimido derivatives (XXI). Treatment of each diastereoisomeric phthalimido compound (XXI) with butylamine produced the corresponding amines (XXII). The product of partial aminolysis (XXIII) was also isolated from the reaction of one of the phthalimido derivatives, and it was readily converted to the corresponding amine.

Experimental[8,9]

3-Indolesuccinic acid (I) was prepared as described previously[10] by condensation of indole-3-carboxaldehyde with ethyl cyanoace-

(7) For leading references on the second-order Beckmann rearrangement, see R. K. Hill, *J. Org. Chem.*, **27**, 29 (1962); J. P. Freeman, *J. Org. Chem.*, **26**, 3507 (1961).

(8) Melting points were taken in a capillary tube and are uncorrected. Ultraviolet spectra (recorded in mμ) were determined in 95% ethanol (unless otherwise specified) using a Cary spectrophotometer Model 14. Infrared spectra (recorded in cm.$^{-1}$) were determined in Nujol using a Perkin-Elmer recording infrared spectrophotometer Model 21. Skellysolve B is commercial hexane, b.p. 60–70°, made by Skelly Oil Co., Kansas City, Mo. Florisil is a magnesia-silica gel adsorbent manufactured by Floridin Co., Tallahassee, Fla.

(9) The author is indebted to Dr. R. W. Rinehart and his associates for microanalyses, to Betty F. Zimmer and Miss L. M. Pschigoda for ultraviolet and infrared spectra, and to Mr. L. G. Laurian for laboratory assistance.

(10) Y. G. Perron and W. F. Minor, *J. Org. Chem.*, **24**, 1165 (1959).

tate, followed by reaction with potassium cyanide, and then hydrolysis with potassium hydroxide.

1-Acetyl-3-indolesuccinic Anhydride (III).—A mixture of 3-indolesuccinic acid (I, 187 g., 0.8 mole), 1500 ml. of isopropenyl acetate, and 15 g. of *p*-toluenesulfonic acid was refluxed for 10 min. The condenser was then replaced by a 1 in. × 8 in. column packed with glass helices attached to a condenser set for distillation. The mixture was heated for 3 hr., and 300 ml. of distillate was collected. During the last 0.5 hr. the temperature of the oil bath was raised from 120 to 128°, and the boiling point of the distillate rose from 55–65 to 90°. The dark reaction mixture was evaporated at 40–50° *in vacuo* to dryness. The residue was dissolved in 400 ml. of acetic acid and 50 ml. of acetic anhydride and allowed to crystallize overnight. The resulting solid was filtered and washed with acetic acid followed by ether. This solid was refluxed with 2 l. of benzene and filtered. The insoluble product III amounted to 21.5 g. melting at 169–170° (first crop). The benzene filtrate was evaporated to *ca.* 1500 ml. and was allowed to crystallize overnight; this gave 62.7 g., m.p. 170–171° (second crop). The third crop of the same melting point amounted to 4.84 g. The total yield was 89.04 g. (44%). The analytical sample was prepared by recrystallization from benzene containing a little acetic anhydride (Darco-G-60) as pale yellow needles, m.p. 170–171°. Ultraviolet spectrum showed λ_{max} 239 mμ (ε 19,450); 260 (8800); sh 270 (7750); sh 280 (4700); 290 (7200); 298 (7700). Infrared spectrum showed 3120 (=CH) 1860, 1825, 1783, 1750 (anhydride); 1688 (acetyl); 1610, 1600, 1577, 1503, 1480 (C=C); 1395, 1360, 1260, 1217, 1065, 1010 (C–O/C–N); 767, 758, 728, 672 (ring) cm.$^{-1}$.

Anal. Calcd. for $C_{14}H_{11}NO_4$: C, 65.36; H, 4.31; N, 5.45. Found: C, 65.42; H, 4.17; N, 5.56.

1-Acetyl-1,3,4,5-tetrahydro-5-oxobenz[*cd*]indole-3-carboxylic Acid (V).—Aluminum chloride (136 g., 1.02 moles) was added in portions over a 10-min. period to a stirred solution of 1-acetyl-3-indolesuccinic anhydride (III, 88 g., 0.342 mole) in 1370 ml. of 1,2-dichloroethane. The mixture became warm and an oily complex separated. The mixture was refluxed on a steam bath for 15 min. It was then cooled in an ice bath; 300 g. of ice was added followed by a solution of concentrated hydrochloric acid (260 ml.) in 1370 ml. of water. The resulting suspension was stirred in the cold for at least 1 hr. until a precipitate resulted. It was then filtered, and the solid was dissolved in 1 l. of acetone. The solution was treated with 10 g. of Darco-G-60, filtered, and evaporated to *ca.* 100 ml. Methylene chloride (250 ml.) was added; the solution was evaporated to *ca.* 100 ml. and allowed to crystallize; 59.5 g. (68% yield), m.p. 172–173°, unchanged on recrystallization from water. Ultraviolet spectrum showed λ_{max} 226 mμ (ε 15,100); 257 (16,800); sh 292 (8700); 302.5 (10,750); 326 (3800). Infrared spectrum showed 3080, 2720, 2600 (acid OH); 1725, 1715, 1680, 1670, sh 1655 (C=O) cm.$^{-1}$.

Anal. Calcd. for $C_{14}H_{11}NO_4$: C, 65.36; H, 4.31; N, 5.45; $COCH_3$, 16.73. Found: C, 65.64; H, 4.48; N, 5.53; $COCH_3$, 17.47.

1,3,4,5-Tetrahydrobenz[*cd*]indole-3-carboxylic Acid (VIII).—Potassium hydroxide (8.18 g., 0.146 mole) was dissolved in 73.5 ml. of diethylene glycol by heating. The solution was cooled and 7.53 g. (0.0293 mole) of N-acetylketo acid V and 7.3 g. (0.146 mole) of 85% aqueous hydrazine hydrate were added. The solution was refluxed for 10 min. The condenser was then removed and the solution was evaporated until the inside temperature reached 190° and was then heated for 10 min. It was cooled and 200 ml. of water was added. The solution was extracted with ether (5 × 100 ml.). The aqueous layer was cooled in ice and acidified with 40 ml. of concentrated hydrochloric acid. The acidic solution was extracted with ether (5 × 200 ml.), the extracts were washed with water and treated with Nuchar C-190-N, and the resulting pale yellow solution was dried over sodium sulfate and evaporated to give 1.8 g. of a crude VIII as a yellow solid. Crystallization from chloroform afforded 0.45 g. (7.6% yield), m.p. 203° dec., unchanged on recrystallization from chloroform. Ultraviolet spectrum showed λ_{max} 223 mμ (ε 33,400); 274 (5750); 280 (5900); 291 (4560). Infrared spectrum showed 3390 (NH); 3000, 2700, 2620 (OH); 1688 (C=O); 1608, 1512 (C=C); 930–915 (OH deformation); 795, 785, 770, 765, 750, 710 (ring) cm.$^{-1}$.

Anal. Calcd. for $C_{12}H_{11}NO_2$: C, 71.62; H, 5.51; N, 6.96. Found: C, 71.66; H, 5.66; N, 7.22.

1,3,4,5-Tetrahydrobenz[*cd*]indole (X).—One hundred milligrams of acid VIII was heated at 210° for 5 min. The resulting brown oily distillate solidified. On sublimation at 60° (0.01 mm.) colorless crystals of X were obtained; 58 mg. (74% yield), m.p. 57–58,[3] unchanged after crystallization from petroleum ether (b.p. 30–60°). Ultraviolet spectrum showed λ_{max} 225 mμ (ε 34,450); 275 (5500); 281 (5700); 291 (4400). Infrared spectrum showed 3380 (NH); 3040 (=CH); 1613, 1602, 1552, 1506 (C=C); 800, 773, 750 (ring) cm.$^{-1}$.

Anal. Calcd. for $C_{11}H_{11}N$: C, 84.04; H, 7.05; N, 8.91. Found: C, 83.72; H, 7.15; N, 8.93.

This compound was found to be identical with an authentic sample[4] as determined by mixture melting point and comparison of ultraviolet and infrared spectra.

Methyl 1-Acetyl-1,3,4,5-tetrahydro-5-oxobenz[*cd*]indole-3-carboxylate (VII). A. With Diazomethane.—A solution of acid V (5.14 g., 0.02 mole) in methanol was added to an ethereal solution of diazomethane prepared from 11 g. (0.072 mole) of N-methyl-N-nitroso-N′-nitroguanidine while cooling in ice. The solution was evaporated to *ca.* 30 ml. and allowed to crystallize overnight. The crystals were filtered and washed with ether, 2.26 g., m.p. 121–123°. A second crop was collected from the filtrate to bring the total yield to 55%. A sample was recrystallized for analysis from methanol, m.p. 123–124°. Ultraviolet spectrum showed λ_{max} 226 mμ (ε 15,650); 256 (17,350); sh 292 (9250); 302 (11,200) sh 328 (3900). Infrared spectrum showed 1727, 1707, 1678 (C=O); 1606, 1576, 1498, 1483 (C=C) cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{13}NO_4$: C, 66.41; H, 4.83; N, 5.16. Found: C, 66.15; H, 4.39; N, 4.84.

B. With Oxalyl Chloride.—Oxalyl chloride (40 ml., 0.47 mole) was added during 15 min. to a suspension of acid V (10.30 g., 0.04 mole) in 400 ml. of benzene while stirring and refluxing. The mixture was refluxed for an additional 15 min., and the solution was allowed to stand at room temperature for 2 hr. It was then evaporated to dryness *in vacuo* at 50–60°. The residue was flushed twice with 50-ml. portions of benzene. The residue was suspended in 600 ml. of methanol, the suspension was refluxed for 15 min., and the resulting solution was evaporated to *ca.* 50 ml. *in vacuo*. The suspension was filtered and the product washed with cold methanol; 7.1 g., m.p. 121–122°. The second crop amounted to 1.09 g., m.p. 120–121°, yield 76%.

C. Attempted Esterification of V in Presence of N,N′-Dicyclohexylcarbodiimide.—N,N′-Dicyclohexylcarbodiimide (2.32 g., 0.0106 mole) was added to a solution of V in 50 ml. of methanol. The resulting suspension was stirred overnight after adding 25 ml. of methanol. The suspension was filtered to separate some N,N′-dicyclohexylurea. The filtrate was evaporated to dryness, and the residue was refluxed with 100 ml. of ether and filtered to separate a further crop of N,N′-dicyclohexylurea. The ethereal filtrate was evaporated to dryness, and the residue was crystallized from 10 ml. of methanol to give 1,3-dicyclohexyl-1-(1,3,4,5-tetrahydro-5-oxobenz[*cd*]indole-3-ylcarbonyl)urea (XII)[5] in two crops; 1.2 g., m.p. 219–221°. Recrystallization from methanol afforded needles melting at 219.5–220°. Ultraviolet spectrum showed λ_{max} 242 mμ (ε 16,800); 320 (4800); 360 (4250).[6] Infrared spectrum showed 3340, 3260 (NH); 3110; 3060 (=CH); 1680, 1650 (C=O) 1622; 1600, 1495 (C=C) 1525 (amide II) cm.$^{-1}$.

Anal. Calcd. for $C_{25}H_{31}N_3O_3$: C, 71.23; H, 7.41; N, 9.97. Found: C, 70.77; H, 7.47; N, 9.87; CH_3CO, 0.

2-Methyl-3-indolesuccinic Acid (II).—A mixture of 2-methylindole (131.17 g., 1.0 mole) and maleic acid (116.07 g., 1.0 mole) was well mixed and then heated on the steam bath. After 10 min. it melted and then started to solidify. The flask was quickly removed from the bath and a vigorous reaction ensued. It was allowed to stand for 0.5 hr. A solution of potassium hydroxide (113 g.) in 1800 ml. of water was added and the mixture heated on the steam bath with stirring for 40 min. The solution was cooled, decanted, and extracted with ether (4 × 200 ml., discarded). It was then treated with Nuchar C-190-N (10 g.) in the hot, filtered, cooled, acidified with concentrated hydrochloric acid (250 ml.) and allowed to crystallize overnight in the refrigerator. The precipitate was filtered and washed with cold water to give 126.3 g. of material melting at 210–211° dec. The filtrate was extracted with ether (4 × 500 ml.). The ethereal extracts were washed with saturated salt solution and evaporated to give a brown solid (10.5 g., m.p. 183–200°) which was crystallized from 175 ml. of acetonitrile to give 5.0 g. of material melting at 210–211° dec. The total yield was 53%. This compound was previously prepared by hydrolysis of the adduct obtained from 2-

methylindole and maleic anhydride, lit.[11a] m.p. 212° dec.; *cf.* also ref. 11b.

1-Acetyl-2-methyl-3-indolesuccinic Anhydride (IV).—A mixture of 233 g. (0.945 mole) of 2-methyl-3-indolesuccinic acid (II), isopropenyl acetate (1880 ml.), and *p*-toluenesulfonic acid monohydrate (18.8 g.) was refluxed for 20 min. The acetone was then distilled slowly over a period of 6 hr. through a glass helices-packed column. The distillation was allowed to proceed until the boiling point reached 95°. The solution was then evaporated to dryness and the resulting dark solid crystallized from 660 ml. of acetic acid and 130 ml. of acetic anhydride. After 2 days the dark crystals were filtered, washed with acetic acid and then with ether; 123.9 g. (52%), m.p. 185–186° dec.. This material was suitable for cyclization with aluminum chloride.

A sample was dissolved in benzene, filtered from the dark pigment, and allowed to crystallize; pale yellow plates, m.p. 189–191.5°. This material (0.8 g.) was recrystallized from 2.5 ml. of acetic acid and 0.5 ml. of acetic anhydride, m.p. 192–193° (sint. 189°). Ultraviolet spectrum showed λ_{max} 244 mμ (ε 15,450); f 264 (9750); f 272 (8700); f 276 (7950); 290 (5250); 298.5 (5250). Infrared spectrum showed 1858, 1775 (anhydride); 1687 (acetyl); 1605, 1580, 1475 sh (C=C); 1305, 1260, 1242, 1220, 1210, 1060, 1035, 1025, 1005, 995 (C–O/C–N); 842, 763, 750, 727, 680 (ring) cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{13}NO_4$: C, 66.41; H, 4.83; N, 5.16. Found: C, 66.67; H, 4.77; N, 5.26.

1-Acetyl-2-methyl-1,3,4,5-tetrahydro-5-oxobenz[*cd*]indole-3-carboxylic Acid (VI).—Anhydride IV (9.57 g., 0.035 mole) was dissolved in 176 ml. of hot 1,2-dichloroethane. The solution was cooled to room temperature with stirring to give a fine suspension. Aluminum chloride (23.5 g., 0.177 mole) was added all at once. The mixture warmed up slightly and after 5 min. was heated on the steam bath for 2 hr. It was cooled in ice; ice was added and then a solution of 27 ml. of concentrated hydrochloric acid in 142 ml. of water. The mixture was filtered and the precipitate was washed well with water. It was crystallized from acetone (Nuchar C-190-N) to give 5.6 g. of yellow needles, m.p. 215–217° dec. The second crop amounted to 1.6 g., m.p. 205–207° (75%). A sample was recrystallized for analysis from acetone, m.p. 212–216° dec. (sint. 207°). Ultraviolet spectrum showed λ_{max} 226.5 mμ (ε 17,850); 259 (15,250); f 292 (8700); f 303 (10,800); 341 (4150); in base: f 220 (16,500); 251 (17,500); f 272 (3300); 309 (4500); 360 (4050). Infrared spectrum showed 3090 sh, 3020 sh, 2700, 2690, 2510, 2340 (OH, acid); 1715, 1700, 1680 (C=O); 1655 sh, 1647, 1608, 1587, 1483 (C=C); 1320 (C–O); 790, 756 (ring) cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{13}NO_4$: C, 66.41; H, 4.83; N, 5.16; neut. equiv., 271. Found: C, 66.37; H, 4.74; N, 5.00; neut. equiv., 263.

The dinitrophenylhydrazone was crystallized from ethanol in the form of orange needles, m.p. 243–244° dec. (sint. 240°). Ultraviolet spectrum showed $\lambda_{max}^{CHCl_3}$ 264.5 mμ (ε 20,950); 307 (10,600); 394 (30,250).

Anal. Calcd. for $C_{21}H_{17}N_5O_7$: C, 55.87; H, 3.80; N, 15.52. Found: C, 55.65; H, 3.74; N, 15.73.

2-Methyl-1,3,4,5-tetrahydrobenz[*cd*]indole-3-carboxylic Acid (IX).—Potassium hydroxide (35.8 g., 0.64 mole) was dissolved in diethylene glycol (320 ml.). The solution was cooled to room temperature and 34.8 g. (0.128 mole) of VI was added followed by 38.4 g. (0.64 mole) of hydrazine hydrate (85%). The mixture was refluxed for 10 min. The inside temperature was then raised to 190° and the solution refluxed at that temperature for 10 min. The solution was cooled, 500 ml. of water was added, and the mixture extracted with ether (3 × 200 ml., discarded). The aqueous solution was cooled in ice and acidified with 140 ml. of concentrated hydrochloric acid. It was then extracted with ether (10 × 300 ml.). The ether extracts were washed with water, saturated salt solution, dried by passage through sodium sulfate, and evaporated to give a dark oil. The oil was dissolved in chloroform and treated with Nuchar C-190-N, and the solution was evaporated down to about 100 ml. and allowed to crystallize; yellow plates, 12.7 g., m.p. 173–174°. The second crop amounted to 1.45 g., m.p. 171–173° (51%). A sample was recrystallized for analysis from chloroform, m.p. 174–174.5°. Ultraviolet spectrum showed λ_{max} 226 mμ (ε 34,200); f 275 (7250); 279 (7350); f 290 (5350). Infrared spectrum showed 3340 (NH); 3100 sh, 3010 sh, 2720, 2630, 2600, 2540 (OH, acid); 1690 (C=O); 1620, 1608, 1573, 1505 (C=C); 1330, 1305, 1240, 1233 (C–O/C–N), 932 (OH, deformation); 785, 780, 763, 755, 747, 688 (ring) cm.$^{-1}$.

Anal. Calcd. for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09; N, 6.51. Found: C, 72.96; H, 6.04; N, 6.38.

Decarboxylation of IX to 2-Methyl-1,3,4,5-tetrahydrobenz[*cd*]-indole (XI).—Acid IX (0.3 g.) was heated in an oil bath at 220° for 5 min. The product was sublimed at 75–140° (0.1 mm.). The sublimate (0.2 g.) was dissolved in methylene chloride, and the solution was washed with 5% sodium hydroxide (2 × 10 ml.), water, and salt solution. The solution was dried by passage through sodium sulfate and evaporated. The product (60 mg.) was crystallized from Skellysolve B to give colorless crystals of XI melting at 74–75°. This compound was identical with the sample obtained by treatment of oxime XX with $LiAlH_4$ as shown by mixture melting point and comparison of ultraviolet and infrared spectra.

The basic extracts were acidified with 10% hydrochloric acid, extracted with methylene chloride, and worked up as usual. The product (0.13 g.) was crystallized from chloroform and melted at 171–172°. Mixture melting point with the starting material IX showed no depression.

2-Methyl-1,3,4,5-tetrahydrobenz[*cd*]indole-3-carboxylic Acid Chloride.—Acid IX (4.3 g., 0.02 mole) was dissolved in 200 ml. of hot benzene. The solution was cooled in ice, and oxalyl chloride (20 ml.) was added during 5 min. while swirling. The dark solution was allowed to stand at room temperature; gas evolution started after a few minutes. After 2 hr. the solution was evaporated at 40–45° *in vacuo*. Benzene (50 ml.) was added and the solution evaporated again to give the oily brown acid chloride which was used directly.

Methyl Ester of 2-Methyl-1,3,4,5-tetrahydrobenz[*cd*]indole-3-carboxylic Acid (XIII).—The acid chloride was prepared from 0.09 mole of the acid with oxalyl chloride in benzene as described above. The benzene solution was evaporated to dryness and 300 ml. of methanol was added. After the reaction subsided, the suspension was refluxed for 45 min. The mixture was allowed to crystallize overnight and afforded 17.34 g. in two crops. It was recrystallized from methanol (Darco G-60) to give 13.1 g. melting at 157–158°. The second crop amounted to 1.54 g., m.p. 156–157°, total yield 71%. The analytical sample melted at 156.5–157.5°. Ultraviolet spectrum showed λ_{max} 225 mμ (ε 35,450); f 274 (7300); 279 (7450); f 289 (5300). Infrared spectrum showed 3340 (NH); 1705 (C=O); 1627, 1612, 1582, 1510 (C=C); 1225 (C–O) cm.$^{-1}$.

Anal. Calcd. for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59; N, 6.11. Found: C, 73.29; H, 6.57; N, 6.06.

2-Methyl-1,3,4,5-tetrahydrobenz[*cd*]indole-3-methanol (XIV).—A solution of methyl ester XIII (6.9 g., 0.03 mole) in 100 ml. of tetrahydrofuran was added during 0.5 hr. to a solution of $LiAlH_4$ (7 g.) in 500 ml. of ether. The mixture was then refluxed for 3 hr. It was cooled in ice and decomposed with dilute sulfuric acid. The aqueous layer was extracted twice with ether and the combined ether layer was washed with sodium bicarbonate solution, and then with saturated salt solution, dried by passage through sodium sulfate, and evaporated to give 6.5 g. of a pale green oil. A sample was evaporatively distilled at 120–140° (0.05 mm.). Attempts to achieve crystallization were unsuccessful. Ultraviolet spectrum showed λ_{max} 227 mμ (ε 35,000); f 274 (7000); 279 (7100); f 290 (5200). Infrared spectrum showed ($CHCl_3$ mull) 3520, 3380, 3300 sh (OH/NH); 1625, 1610, 1580, 1505 (C=C); 1075, 1050, 1028 sh, 1022 (C–O) cm.$^{-1}$.

Anal. Calcd. for $C_{13}H_{15}NO$: C, 77.58; H, 7.51; N, 6.96. Found: C, 77.81; H, 7.21; N, 7.26.

2-Methyl-1,3,4,5-tetrahydrobenz[*cd*]indole-3-carboxamide (XV).—Fifty milliliters of aqueous ammonium hydroxide (29%) was added to the oily acid chloride (cooled in ice) prepared from 2.15 g. of acid IX (0.01 mole) by the oxalyl chloride procedure. An oily product separated which afforded a precipitate after it was scratched. The suspension was cooled in ice and filtered, and the solid was washed with cold water; 1.25 g. (59%), m.p. 210–212°. Crystallization from methanol–benzene (Nuchar C-190-N) afforded pale yellow leaflets melting at 213–215°. A sample was recrystallized for analysis from benzene containing a trace of methanol, m.p. 214–215.5°. Ultraviolet spectrum showed λ_{max} 224.5 mμ (ε 33,900); 274 (7200); 278 (7300); f 289 (5150). Infrared spectrum showed 3410, 3320, 3180 (NH); 1665 (C=O); 1642 (amide II); 1587 (C=C); 775, 752 (ring) cm.$^{-1}$.

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Anal. Calcd. for $C_{13}H_{14}N_2O$: C, 72.87; H, 6.59; N, 13.08. Found: C, 72.86; H, 6.67; N, 12.73.

2-Methyl-1,3,4,5-tetrahydro-3-aminomethylbenz[cd]indole Acetic Acid Salt (XVII).—A solution of amide XV (0.86 g., 4 mmoles) in 35 ml. of warm tetrahydrofuran (freshly distilled from $LiAlH_4$) was added during 5 min. with stirring to a solution of $LiAlH_4$ (1 g.) in 100 ml. of ether. The mixture was then refluxed for 5 hr. and allowed to stand for 2 days. It was cooled in ice and decomposed in succession with 1 ml. of water, 1 ml. of 15% sodium hydroxide solution, and 3 ml. of water. The suspension was filtered, the precipitate was washed well with ether, and the filtrate was evaporated to dryness at room temperature to give 0.83 g. of a yellow oil. It showed only a trace of residual amide band at 1670 cm.$^{-1}$. The oil (0.794 g.) was dissolved in 25 ml. of warm ether, and the solution was decanted from a small amount of undissolved amorphous material. A solution of acetic acid (0.36 g.) in 3 ml. of ether was added. The resulting precipitate was filtered and washed with ether; 0.9 g., m.p. 190–192.5° dec. (sint. 189°). It was dissolved in about 10 ml. of methanol, 40 ml. of ether was added, and crystallization allowed to proceed in the cold overnight; clusters of needles, 0.75 g., melting at 195–198° dec., darkening at 185°. Ultraviolet spectrum showed λ_{max} 226 mμ (ε 34,900); 274 (7250); 279 (7300); f 290 (5150). Infrared spectrum showed 3260 (NH); 3000, 2770, 2700, 2640, 2560, 2460, 2190 (salt); 1635, 1575 sh, 1560 sh, 1538, 1415 (COO^-/C=C); 735, 680 (ring) cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{20}N_2O_2$: C, 69.20; H, 7.74; N, 10.76. Found: C, 68.89; H, 7.44; N, 10.49.

2-Methyl-1,3,4,5-tetrahydrobenz[cd]indole-N,N-dimethyl-3-carboxamide (XVI).—Fifty milliliters of aqueous dimethylamine (40%) was added to the oily acid chloride (cooled in ice) prepared from 2.15 g. of acid IX (0.01 mole) by the oxalyl chloride procedure. The resulting suspension was stirred for a few minutes. It was then cooled in ice and filtered, and the precipitate was washed with cold water; 2.15 g. (89%), m.p. 231–233°. Crystallization from methanol (Nuchar C-190-N) gave pale yellow plates, m.p. 232.5–234° (darkening at 220°), unchanged on added recrystallization. Ultraviolet spectrum showed λ_{max} 227 mμ (ε 62,800); f 274 (6750); 280 (6950); f 290 (5100). Infrared spectrum showed 3190 (NH); 1620 sh, 1612 (C=O); 1578, 1500 (C=C); 757, 745, 723 (ring) cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{18}N_2O$: C, 74.35; H, 7.49; N, 11.56. Found: C, 73.96; H, 7.73; N, 11.83.

2-Methyl-1,3,4,5-tetrahydro-N,N-dimethyl-3-aminomethylbenz[cd]indole (XVIII).—A solution of dimethylamide XVI (1.55 g.; 6.4 mmoles) in 100 ml. of hot tetrahydrofuran (freshly distilled from $LiAlH_4$) was added to a solution of $LiAlH_4$ (2 g.) in 150 ml. of ether so that mild reflux resulted. The mixture was then refluxed for 6 hr. and allowed to stand overnight. It was decomposed in succession with 2 ml. of water, 2 ml. of 15% sodium hydroxide solution, and 6 ml. of water. The suspension was filtered, the cake washed with ether, and the filtrate evaporated to dryness *in vacuo* to give 1.48 g. (quantitative yield) of a solid melting at 111.5–113.5° (it showed no residual amide band in the infrared). A sample was crystallized for analysis from Skellysolve B; prisms, m.p. 113.5–115°. Ultraviolet spectrum showed λ_{max} 227 mμ (ε 32,150); f 274 (6900); 280 (6950); f 290 (5100). Infrared spectrum showed 3140 (NH); 2780, 2740 sh, 2700 (tert. amine); 1623, 1606, 1575, 1507, 1495 sh (C=C); 860, 846, 800, 780, 738 (ring) cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{20}N_2$: C, 78.90; H, 8.83; N, 12.27. Found: C, 78.59; H, 8.57; N, 12.43.

2-Methyl-3-acetyl-1,3,4,5-tetrahydrobenz[cd]indole (XIX).—A solution of methyllithium[12] containing 0.015 equiv. of the reagent in 23 ml. of ether was added during 10 min. to a solution of acid IX (1.08 g., 5 mmoles) dissolved in 50 ml. of ether under nitrogen at room temperature. Immediate precipitation occurred accompanied by mild reflux. The mixture was then refluxed for 35 min. It was cooled in ice, 50 ml. of water was added, and the ether layer was separated. The aqueous solution was extracted twice with ether. The combined ether solution was washed twice with saturated salt solution, dried by passage through sodium sulfate, and evaporated to give 0.34 g. of a viscous oil. Crystallization from ether–Skellysolve B afforded 0.24 g. (22%) of prisms, m.p. 96.5–97.5°. Recrystallization (Nuchar C-190-N) gave raised m.p. 97–98°. Ultraviolet spectrum showed λ_{max} 225 mμ (ε 35,200); 274 (7450); f 280 (7400); f 289 (5300). Infrared spectrum showed 3320 (NH); 1688 (C=O); 1620, 1608, 1575 (C=C) cm.$^{-1}$.

Anal. Calcd. for $C_{14}H_{15}NO$: C, 78.84; H, 7.09; N, 6.57. Found: C, 79.20; H, 7.00; N, 6.66.

The aqueous solution was cooled in ice, acidified with concentrated hydrochloric acid, and extracted with ether. Work-up in the usual way afforded 0.8 g. (73% recovery) of the starting acid which melted at 170–173°.

Oxime of 2-Methyl-3-acetyl-1,3,4,5-tetrahydrobenz[cd]indole (XX).—A solution of ketone XIX (6.3 g., 0.0296 mole) in 40 ml. of 95% ethanol was added to a solution of hydroxylamine hydrochloride (10.4 g., 0.15 mole) and sodium acetate (18.5 g., 0.225 mole) in 40 ml. of water. The mixture was refluxed for 1 hr., and the resulting yellow solution was evaporated until an oily product separated. Water (50 ml.) was added and the mixture was cooled and filtered to give 6.38 g. (94.5%) of oxime mixture, m.p. 163–171° (sint. 145°). One crystallization from benzene–petroleum ether (b.p. 30–60°) gave clusters melting at 167–174° (sint. 154°). Ultraviolet spectrum showed λ_{max} 227 (mμ ε 36,150); 274 (7100); 280 (7200); f 290 (5100). Infrared spectrum showed 3350 (NH); 3200 (OH); 1660 (w) (C=N); 1605, 1570, 1505 (C=C); 963, 940, 906, 860 (=N—OH) cm.$^{-1}$.

Anal. Calcd. for $C_{14}H_{16}N_2O$: C, 73.65; H, 7.06; N, 12.27. Found: C, 73.55; H, 7.36; N, 12.63.

Reduction of Oxime XX with $LiAlH_4$.—A solution of oxime XX (5.88 g., 0.0258 mole) in 175 ml. of ether was added during 15 min. to $LiAlH_4$ (9.8 g., 0.258 mole) in 500 ml. of ether. The suspension was stirred and refluxed for 7.5 hr. and allowed to stand for 2 days. The mixture was worked up as described below and separated into basic and neutral fractions. Analytical results and ultraviolet spectrum indicated that the basic fraction (2.15 g.) was impure hydroxylamine derivative of the starting material. Papergram analysis of the neutral fraction (2.51 g.) showed the presence of the starting oxime. A solution of the two fractions (4.06 g.) in 100 ml. of tetrahydrofuran was added during 15 min. to a solution of $LiAlH_4$ (10 g.) in 500 ml. of tetrahydrofuran under nitrogen. The resulting cloudy solution was stirred and refluxed for 16 hr. It was then decomposed in succession with 10 ml. of water, 10 ml. of 15% sodium hydroxide, and 30 ml. of water. The mixture was filtered, and the filtrate was evaporated to *ca.* 10 ml. and diluted with 100 ml. of ether. The ethereal solution was extracted three times with 10% hydrochloric acid (total, 75 ml.). The acidic extracts were washed once with ether, and then treated with 15% sodium hydroxide. The resulting yellow oil was extracted with ether. The ether layer was washed with water, saturated salt solution, dried by passage through sodium sulfate, and evaporated to give a 2.78 g. of a foamy powder, m.p. 85–95° (efferv.). Ultraviolet spectrum showed λ_{max} 225 mμ (ε 30,200); f 275 (6070); 280 (6170); f 289 (4520).

Anal. Calcd. for the hydroxylamine, $C_{14}H_{18}N_2O$: C, 73.01; H, 7.88; N, 12.17. Found: C, 73.40; H, 8.35; N, 11.74.

The neutral ethereal fraction was worked up as usual to give a greenish oil (0.78 g.) which slowly crystallized. It was dissolved in 10 ml. of ether and treated twice with Nuchar C-190-N to give a pale yellow solution. It was evaporated to a small volume; Skellysolve B was added and the solution evaporated to about 5 ml. and cooled in Dry Ice to give oily crystals. On warming cautiously in Skellysolve B the crystals dissolved leaving the impure gum behind. The solution was allowed to crystallize to give pale yellow plates of XI (0.33 g.), m.p. 74.5–75.5°. It was sublimed at 70° (0.05 mm.) to give prisms melting at 73–74°, unchanged on recrystallization from Skellysolve B. Ultraviolet spectrum showed λ_{max} 230 mμ (ε 33,100); f 275 (6500); 281.5 (6800); f 291 (5050). Infrared spectrum showed 3350 (NH); 1602, 1575, 1502 (C=C) cm.$^{-1}$.

Anal. Calcd. for $C_{12}H_{13}N$: C, 84.17; H, 7.65; N, 8.18. Found: C, 84.16; H, 7.64; N, 7.90.

Oxime of Indole-3-acetone.—A solution of 10.6 g. (0.0614 mole) of indole-3-acetone[13] and hydroxylamine (prepared from 21.6 g. or 0.31 mole of hydroxylamine hydrochloride and 37.7 g. or 0.46 mole of sodium acetate) in 50 ml. of 95% ethanol and 83 ml. of water was refluxed for 45 min. The initial yellow solution turned brown. The solution was evaporated until it became cloudy, 150 ml. of water was added, and the brown oil was extracted with ether and chloroform. The organic layer was washed with water, sodium bicarbonate solution, then with

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(13) J. B. Brown, H. B. Henbest, and E. R. H. Jones, *J. Chem. Soc.*, 3172 (1952).

water, and saturated salt solution, dried over sodium sulfate, and evaporated to give 11.6 g. (quantitative yield) of a brown oil which could not be crystallized. Infrared showed no residual carbonyl absorption. Ultraviolet spectrum showed λ_{max} 221 mμ (ε 33,950); 274 (6000); 280 (6300); 289 (5400).

Reduction of the Oxime of Indole-3-acetone with $LiAlH_4$.—A solution of the oxime (11.5 g., 0.061 mole) in 100 ml. of tetrahydrofuran was added at room temperature during 5 min. to a solution of $LiAlH_4$ (23.2 g., 0.61 mole) in 1 l. of tetrahydrofuran. The mixture was then refluxed under nitrogen for 20 hr. It was cooled in ice and decomposed in succession with 23 ml. of water, 23 ml. of 15% sodium hydroxide, and 70 ml. of water. The suspension was filtered, the cake was washed with ether, and the combined filtrate was evaporated to about 20 ml. and diluted with 250 ml. of ether. The ether solution was extracted five times with 10% hydrochloric acid (total 125 ml.). The acid extracts were washed once with ether and then treated in the cold with 15% sodium hydroxide. The product was extracted with ether and worked up as usual to give 7.92 g. of a brown oil which solidified overnight. Direct crystallization proved difficult. Therefore, 1 g. of the crude solid was distilled from an oil-jacketed flask at 140–170° (outside *T*., 0.1 mm.) to give 0.5 g. of a yellow oil which solidified, m.p. 99–102°. It was crystallized from benzene–petroleum ether (b.p. 30–60°) to give clusters of needles, m.p. 104–105.5°. This product was identical with an authentic sample of α-methyltryptamine[14] (by infrared and mixture melting point).

The neutral ether solution was worked up to give 0.7 g. of a brown solid. It was sublimed at 70–75° (0.1 mm.) and afforded 0.5 g. of a white crystalline sublimate, m.p. 98.5–99°, which was identical with skatole (by infrared and ultraviolet spectra and mixture melting point).

Reduction of Oxime XX with Sodium and Ethanol.—Sodium (78 g.) was added during 20 min. to a refluxing solution of the oxime (12.1 g., 0.053 mole) in 800 ml. of absolute ethanol without external heating. The solution was then refluxed for 1 hr. The resulting brown solution was cooled in ice, 800 ml. of water was added, and the solution was evaporated *in vacuo* until about 800 ml. of distillate was collected and an oil separated. The mixture was extracted with ether and the ethereal layer washed with water and then extracted six times with a total of 175 ml. of 10% hydrochloric acid. The acidic extracts were washed once with ether and treated with 15% sodium hydroxide. The resulting oil was extracted with ether and worked up as usual to give 9.88 g. of crude amine XXII as an oily brown solid. The neutral ethereal solution was worked up in the usual way to give 1.873 g. of brown residue which was shown by papergram to be the impure oxime.

Phthalimido Derivatives XXI.—A mixture of phthalic anhydride (7.8 g., 0.0526 mole) and the crude amine from sodium–ethanol reduction (7.53 g., 0.0352 mole) was heated in an oil bath. The temperature was raised to 210° during 15 min. and then kept at 210–220° for 15 min. The mixture was allowed to cool, 350 ml. of absolute ethanol was added, and the mixture was refluxed for 1 hr. and 40 min. It was evaporated *in vacuo* to a small volume, diluted with 250 ml. of ethyl acetate, and washed three times with dilute sodium bicarbonate solution. The bicarbonate washes were re-extracted once with ethyl acetate and the combined organic layer was filtered, washed with water, then twice with 10% hydrochloric acid followed by saturated salt solution. It was dried over sodium sulfate and evaporated to give 11.5 g. of a brown solid.

The solid was dissolved in 100 ml. of benzene and chromatographed on 1,150 g. of Florisil. Elution with 6% acetone–Skellysolve B (8 l.) gave 124.3 mg. (discarded). Further elution (10 l.) gave a total of 7.07 g. of product with varying m.p. 184 to 187°. It was crystallized from methanol (Darco G-60) to give isomer A of XXI; 3.32 g. of yellow clusters, m.p. 180–181°. The second crop amounted to 0.48 g., m.p. 179–180°. The analytical sample melted at 182–182.5° (from methanol). Ultraviolet spectrum showed λ_{max} 222 mμ (ε 71,850); f 242 (11,400); 275 (9150); 279 (9250); 290 (7250). Infrared spectrum showed 3400, 3360 (NH); 1768, 1700 (C=O); 1622 sh, 1615, 1575, 1508 (C=C) cm.$^{-1}$.

Anal. Calcd. for $C_{22}H_{20}N_2O_2$: C, 76.72; H, 5.85; N, 8.13. Found: C, 77.01; H, 5.94; N, 8.10.

Further elution (18 l.) gave 5.3-g. total of product melting from 166 to 170°. Crystallization from methanol afforded isomer B of XXI; 2.08 g. of yellow rods, m.p. 169–170°. The second crop (0.46 g.) melted at 167–168°. Ultraviolet spectrum showed λ_{max} 225 mμ (ε 71,250); f 240 (12,800); 275 (8050); 280 (8150); f 289 (6600). Infrared spectrum showed 3350 (NH); 1771, 1695 (C=O); 1615, 1605 sh, 1579, 1510 (C=C) cm.$^{-1}$.

Anal. Calcd. for $C_{22}H_{20}N_2O_2$: C, 76.72; H, 5.85; N, 8.13. Found: C, 76.92; H, 5.98; N, 8.17.

Cleavage of XXI Isomer A to XXII Isomer A.—A solution of XXI (isomer A, m.p. 180–181°, 3.8 g., 0.011 mole) in 100 ml. methanol and 11 ml. of butylamine[15] was refluxed for 20.5 hr. under nitrogen. It was evaporated to dryness *in vacuo* to give a pale yellow gum. Water (50 ml.) and ether (50 ml.) were added, and the mixture was stirred until a fine suspension resulted. Filtration (filtrate worked up below) gave 2.65 g. of a colorless precipitate, m.p. 209–213° (sint. 155°). Crystallization from aqueous methanol afforded colorless needles of partial product of aminolysis, N-butyl-N′-[1-(1,3,4,5-tetrahydro-2-methylbenz[*cd*]-indole-3-yl)ethyl]phthalamide (XXIII), m.p. 217–218°, unchanged on further crystallization. Ultraviolet spectrum showed λ_{max} 227 mμ (ε 45,950); 273.5 (8400); f 278 (8200); f 290 (5550). Infrared spectrum showed 3350, 3260, 3180 (NH); 3030 (=CH); 1625 (C=O); 1600, 1580, 1507 sh, 1480 sh (C=C); 1560 sh (amide II) cm.$^{-1}$.

Anal. Calcd. for $C_{26}H_{31}N_3O_2$: C, 74.79; H, 7.48; N, 10.06. Found: C, 74.68; H, 7.59; N, 10.15.

The above filtrate was separated into layers, and the aqueous layer was extracted once with ether. The ether extracts were washed four times with 10% hydrochloric acid (85 ml.) and treated with 15% sodium hydroxide. The product was extracted three times with ether and worked up as usual to give 1.05 g. (45% yield) of a pale yellow oil. Crystallization from benzene–petroleum ether (b.p. 30–60°) gave XXII isomer A, m.p. 123–125° (0.91 g.). Recrystallization from ether–Skellysolve B gave raised m.p. 126–127°. Ultraviolet spectrum showed λ_{max} 228 mμ (ε 35,050); f 275 (7050); 280 (7150); f 290 (5200). Infrared spectrum showed 3130, 3020 (NH); 1620, 1597, 1575 (C=C/NH def.) cm.$^{-1}$.

Anal. Calcd. for $C_{14}H_{18}N_2$: C, 78.46; H, 8.47; N, 13.07. Found: C, 78.23; H, 8.45; N, 13.03.

The neutral ether fraction was worked up to give 1.19 g. of a gummy solid which was crystallized from benzene to give solvated N,N′-dibutyl phthalamide, m.p. 92–96°[15,16] (by C, H, N analyses) identical by infrared with the sample obtained below.

Cleavage of XXIII to XXII Isomer A.—A solution of XXIII (2.45 g., 5.9 mmoles) in 50 ml. of ethanol and 17 ml. of butylamine was refluxed under nitrogen for 22.5 hr. The solution was evaporated to dryness *in vacuo* to give a gum. Water and ether were added (50 ml. of each) and the mixture was stirred. A solution resulted at first and then a white precipitate separated. The suspension was filtered to give 0.9 g. of solid, m.p. 105–110°, which was not investigated further. The filtrate was separated into layers, and the ether layer was washed four times with 10% hydrochloric acid (total 100 ml.). The acidic extract was washed with ether and then treated with potassium hydroxide. The product was extracted with ether and worked up as usual to give 0.81 g. of crude XXII isomer A. It was triturated with ether–petroleum ether (b.p. 30–60°) to give 0.588 g., m.p. 126–127°.

Cleavage of XXI Isomer B to XXII Isomer B.—A solution of XXI (isomer B, m.p. 169–170°, 2.54 g. or 7.4 mmoles) in 63 ml. of ethanol and 22 ml. of butylamine was refluxed for 72 hr. under nitrogen. The pale yellow solution was evaporated to dryness *in vacuo*. Ether (100 ml.) and 10% hydrochloric acid (100 ml.) was added, and the mixture was stirred for about 1 hr. to give an almost complete solution. The layers were separated and the aqueous was extracted with ether. The acidic solution was cooled and treated with 30% potassium hydroxide. The resulting product was extracted with benzene and worked up as usual to give 1.58 g. of a pale yellow oil. It was crystallized from benzene–petroleum ether (b.p. 30–60°) to give 0.13 g. of N,N′-dibutylphthalamide melting at 115–116°[15,16] identical by infrared with the sample obtained previously. The filtrate was evaporated to dryness, the residue was dissolved in ether, and the same acid extraction procedure was followed as above, the only difference being that ethyl acetate was used to extract neutral material from the acidic layer. The product amounted to 1.04 g.

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and showed no residual amide in the infrared. It was crystallized from ether–Skellysolve B to give 0.82 g. of XXII isomer B, m.p. 101–102.5°, unchanged on further recrystallization. Ultraviolet spectrum showed λ_{max} 227 mμ (ε 35,400); 274 (6950); 279 (7050); f 289 (5000). Infrared spectrum showed 3160, 3100, 3050 (NH); 1623, 1603, 1585, 1510 (C=C/NH def.) cm.$^{-1}$.

Anal. Calcd. for $C_{14}H_{18}N_2$: C, 78.46; H, 8.47; N, 13.07. Found: C, 78.52; H, 8.69; N, 12.87.

Copper-Catalyzed Reactions of Benzoyl Peroxide with Norbornadiene Derivatives[1,2]

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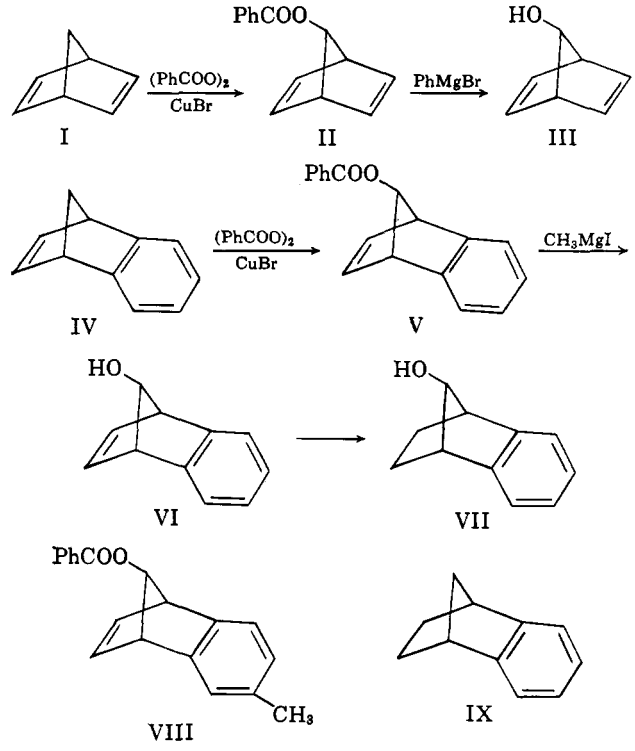
The copper-catalyzed reactions of benzoyl peroxide with norbornadiene or benzonorbornadiene derivatives have been shown to give the stereospecific 7-benzoyloxy derivatives. It has proved to be a much improved method for use in syntheses than others reported hitherto. A rational mechanism involves addition of PhCOO· to the olefinic double bond, oxidation of the adduct radical into the carbonium ion intermediate, the Wagner–Meerwein rearrangement, and proton loss to form a double bond. In addition, bis(*p*-chlorobenzoyl) peroxide has proved to give the best yield of the desired esters.

The chemistry of 7-substituted bicyclo[2.2.1]heptanes has been of considerable interest in recent years, particularly in connection with the behavior in solvolytic displacement reactions. Aside from the saturated parent compounds many unsaturated and aromatic variants have been investigated.[3] Until very recently, however, the preparations of these compounds required a long and arduous route. The formation of 7-*t*-butoxynorbornadiene by the reaction of *t*-butyl perbenzoate and norbornadiene found by Story[4] has provided a facile path to this series of compounds. However, a weak point in this reaction may be that one can not control the stereochemistry of the 7-alcohol or other derivatives which are obtained from the replacement of *t*-butyloxy group *via* 7-norbornadienyl cation.[4]

In connection with another investigation,[5] it became necessary to prepare these kinds of alcohols which had a desired stereochemistry. In a previous communication,[6] we reported that the copper-catalyzed reaction of benzoyl peroxide with norbornadiene derivatives had proved to be a much improved method for use in syntheses and also satisfactory for the above requirement. This paper deals with further improvements of our method and with detailed investigations of the reaction mechanism.

CHART I



Results and Discussion

The reaction of norbornadiene (I) with benzoyl peroxide in the presence of cuprous bromide gave a 35% yield of 7-benzoyloxynorbornadiene (II) from the peroxide as the sole substitution product. The hydrolysis of II with phenylmagnesium bromide[7] yielded 7-norbornadienol (III) almost quantitatively, whose structure was identified by independent synthesis.[4] In order to elucidate the stereochemistry of this reaction, the same procedure was applied for benzonorbornadiene (IV), which is readily obtainable by the cycloaddition of benzyne with cyclopentadiene.[8] *anti*-7-Benzoyloxybenzonorbornadiene (V) was obtained in about 40% yield. The structure of V was established by hydrolysis with methylmagnesium iodide to *anti*-7-benzonorbornadienol (VI), then catalytic reduction to *anti*-7-benzonorborneol (VII), which was confirmed by independent synthesis.[3b] The *syn*-benzoyloxy-substituted product has not been obtained under a variety of reaction conditions. Applications of the above reaction to some benzonorbornadienes having substituents on the benzene ring were also successful,

(1) Part IV of a series on bicyclic systems; Part III, *Bull. Chem. Soc. Japan*, **37**, 40 (1964).

(2) Presented, in part, at the 16th Annual Meeting of the Chemical Society of Japan, Tokyo, March, 1963.

(3) (a) S. Winstein and C. Ordronneau, *J. Am. Chem. Soc.*, **82**, 2084 (1960), and references therein; (b) P. D. Bartlett and W. P. Giddings, *ibid.*, **82**, 1240 (1960); (c) E. E. van Tamelen and C. I. Judd, *ibid.*, **80**, 6305 (1958).

(4) P. R. Story, *ibid.*, **82**, 2085 (1960); P. R. Story, *J. Org. Chem.*, **26**, 287 (1961).

(5) H. Tanida, *J. Am. Chem. Soc.*, **85**, 1703 (1963).

(6) H. Tanida and T. Tsuji, *Chem. Ind.* (London), 211 (1963).

(7) Phenylmagnesium bromide was better than methylmagnesium iodide previously used (refer to ref. 6), because III was more easily distilled, leaving trityl alcohol.

(8) G. Wittig and E. Knauss, *Ber.*, **91**, 895 (1958).