The Synthesis of 3,4,4a,9a-Tetrahydro-2(1*H*)-carbazolones

Raymond R. Wittekind and Sam Lazarus (1)

Department of Organic Chemistry, Warner-Lambert Research Institute

Cyclization of 4-(1-methylindol-3-yl)-2-butanone and the corresponding 1-benzyl analog in trifluoroacetic acid furnishes 9-methyl- and 9-benzyl-3,4,4a,9a-tetrahydro-2(1*H*)-carbazolone, respectively. Under the same conditions, 4-(indol-3-yl)-2-butanone gives the dimer, 3-(3-oxobutyl)-2-[3-(3-oxobutyl)-2-indolinyl]indole. When boron trifluoride etherate is used instead of trifluoroacetic acid, the desired 3,4,4a,9a-tetrahydro-2(1*H*)-carbazolone is obtained. The determination of the structure of the tetrahydrocarbazolones is described and the stereochemistry of the ring fusion is discussed.

The acid-catalyzed annelation of 1,3-dimethylindole (**1a**) with 3-methyl-2-cyclohexen-1-one (**2**) and with 4-methyl-3-penten-2-one (**4**) was reported by Robinson and co-workers (2) to give the tetrahydro-2(1*H*)-carbazolones **3** and **5**, respectively. The gross structure, but not the stereochemistry, of **5** was subsequently established (3). We envisioned the use of this process for the preparation of the tetrahydro-2(1*H*)-carbazolones **10a-10c**, precursors of the unknown (4) dihydro-2(1*H*)-carbazolones **11a-11c**, which were required for elaboration of potential cardiovascular agents. While this work was in progress, Teuber and Cornelius (5) described an efficient synthesis of 3,4-dihydrocarbazol-2(1*H*)-one (**11c**) by Birch reduction of 2-methoxycarbazole (**13c**). Nevertheless, the paucity of information concerning the synthesis of 3,4,4a,9a-tetrahydrocarbazol-2(1*H*)-ones prompts us to report the

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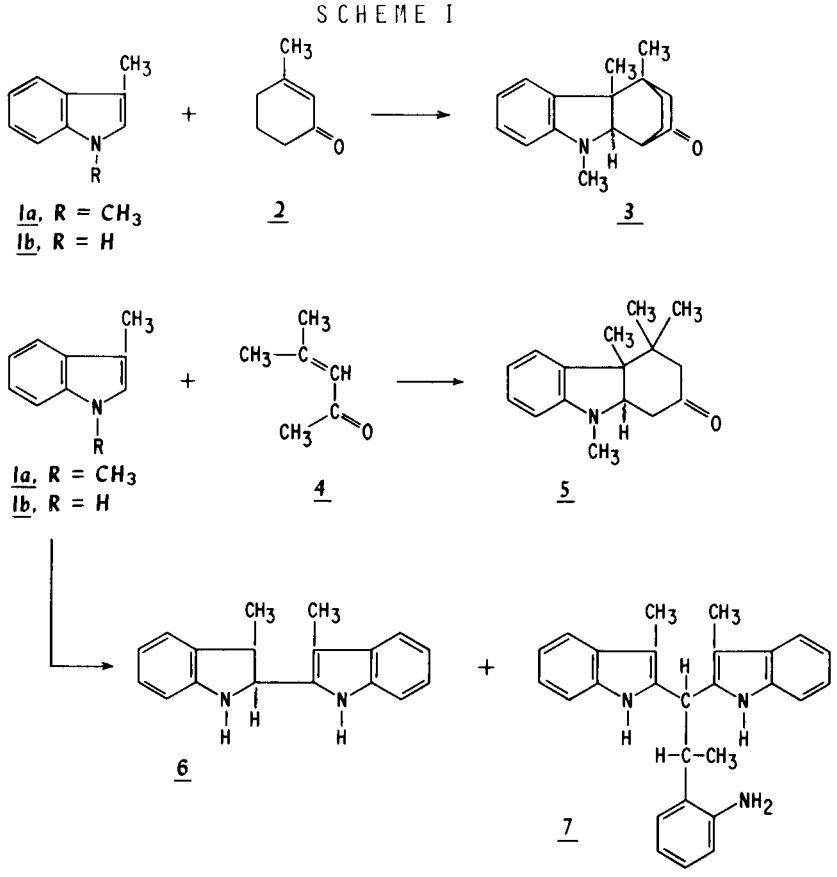
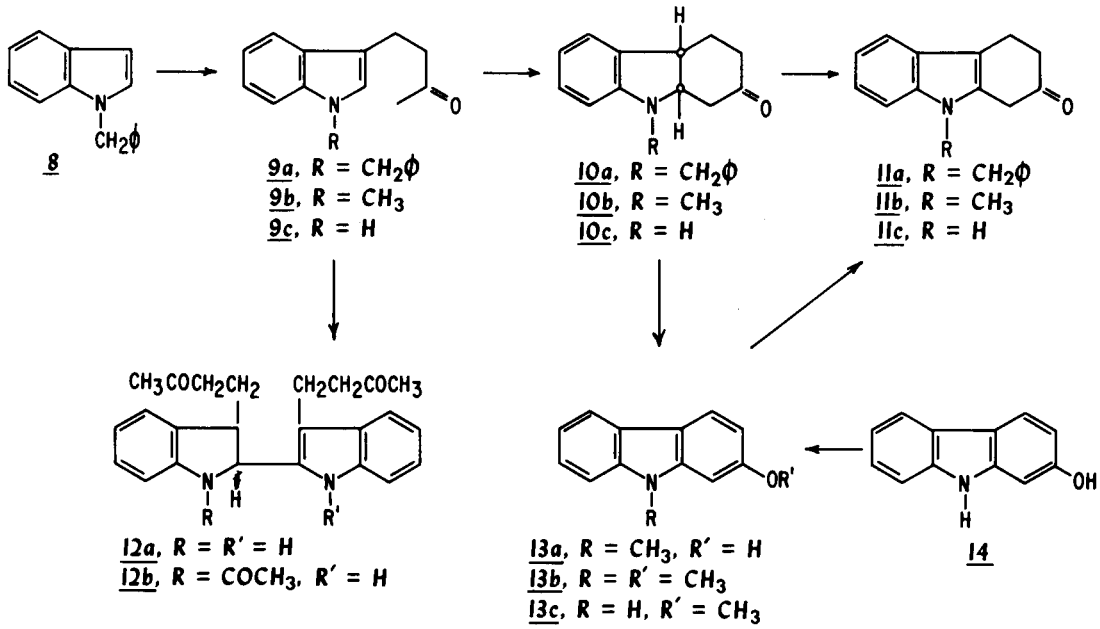


SCHEME I (CONTINUED)



results of our efforts in this area.

Attempted preparation of 1-benzyl-3,4,4a,9a-tetrahydrocarbazol-2(1*H*)-one (**10a**) by treatment of 1-benzylindole (**8**) (6) with methyl vinyl ketone in the presence of ethanolic hydrochloric acid according to the procedure of Robinson (2), gave an inseparable complex mixture according to thin-layer chromatography. Similar results were obtained when the 1-benzyl- (**9a**) and 1-methylindolylbutanones (**9b**) (7) were subjected to these reaction conditions. However, when a dilute solution of **9b** and trifluoroacetic acid (8) was allowed to stand at room temperature for two days, the desired tetrahydrocarbazolone **10b** was isolated in 28% yield.

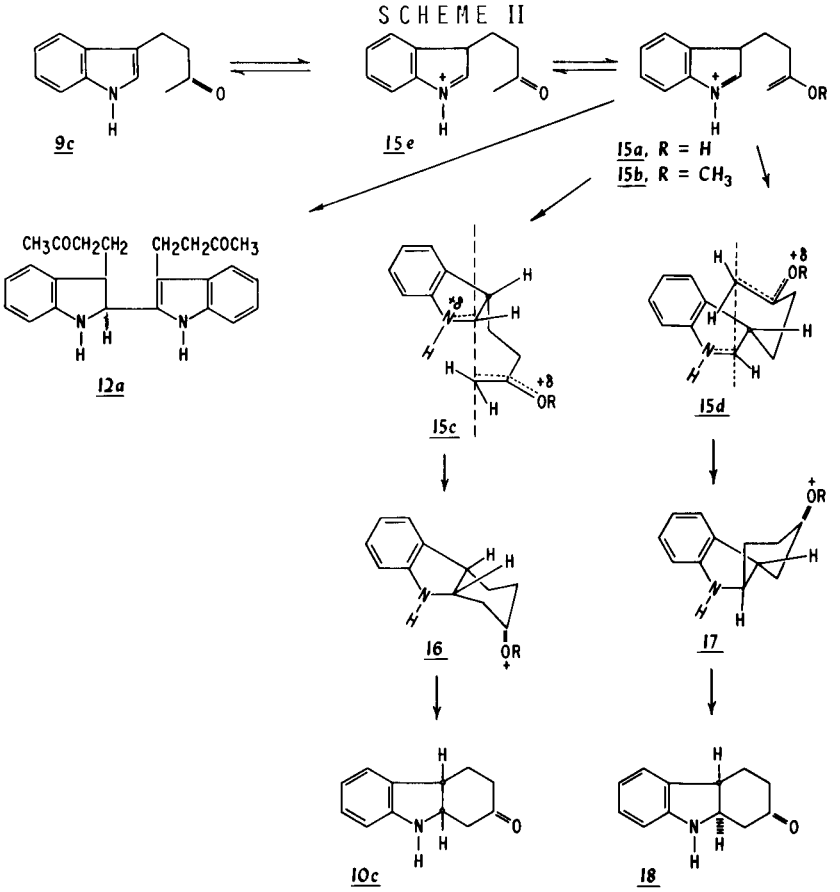
The structure of **10b**, the ultraviolet spectrum of which exhibited maxima at 254 mμ (ε, 8,240) and 301 (3,060), characteristic of the indoline system (9), was confirmed chemically. Dehydrogenation of **10b** with 10% palladium-on-carbon in boiling xylene (10) afforded 2-hydroxy-9-methylcarbazole (**13a**) (11) which was converted to 2-methoxy-9-methylcarbazole (**13b**) (12), identical with an authentic sample prepared by the methylation of 2-hydroxycarbazole (**14**).

Similarly, dissolution of **9a** in trifluoroacetic acid for two days afforded the 1-benzyltetrahydrocarbazolone **10a**, characterized by elemental analysis and infrared, ultraviolet and proton magnetic resonance spectroscopy.

Interestingly, when the indolylbutanone **9c** (13) was allowed to stand in trifluoroacetic acid at -5° for sixteen hours, a dimeric product, characterized as a *N*-monoacetate and a hydrochloride, was isolated in 70% yield instead of the desired tetrahydrocarbazolone **10c**. The dimer, the molecular weight of which was determined by mass spectrometry, was assigned structure **12a** by analogy with the dimerization of 3-methylindole (**1b**) to the indolinylindole **6** (14). The infrared spectrum of the dimer **12a**, which exhibited an absorption band at 1710 cm^{-1}, indicative of a saturated carbonyl group, and the proton magnetic resonance spectrum, which showed singlets at δ 1.88 and 1.92 p.p.m. and a multiplet between δ 2.0 and 3.3 p.p.m., established the presence of two dissimilar butan-2-one systems. The similarity between these spectra, including the ultraviolet spectrum, and those of diskatole (**6**), prepared by the dissolution of skatole (**1b**) in trifluoroacetic acid (15) supported the initial structural assignment.

These results are explicable in terms of the mechanism outlined in Scheme II. Protonation of the indole **9c** at the 3-position (16) and acid-catalyzed enolization of the methyl ketone moiety result in an equilibrium formation of the iminium ketone **15e** and the iminium enol **15a**. Internal nucleophilic attack by the enol on the iminium group of **15a** furnishes the tetrahydrocarbazole **10c** whereas external nucleophilic attack by the 2-position (14)

SCHEME II



of the unprotonated indole **9c** on the iminium function of **15e** and/or **15a** affords the dimer **12a**. Since 1-methylindole is less nucleophilic and dimerizes less readily than indole (17), internal attack predominates (18) when the indole nitrogen bears an alkyl substituent and external attack is favored when it is unsubstituted.

This mechanism suggests that reaction conditions resulting in the displacement of the equilibrium toward the enol **15a** would decrease dimerization and possibly favor tetrahydrocarbazole formation. Thus, a solution of the butanone **9c**, boron trifluoride etherate and methanol, a reaction medium expected to produce the intermediate enol ether **15b**, was allowed to stand at room temperature for three days. From this reaction, the desired tetrahydrocarbazolone **10c**, characterized by elemental analysis and infrared, ultraviolet, proton magnetic resonance and mass spectroscopy, was obtained in 21% yield (18).

Reductive alkylation (19) of the carbazolone **10c** with formaldehyde and with benzaldehyde afforded the *N*-methyl **10b** and *N*-benzyl **10a** derivatives, respectively. Hence the three carbazolones **10a-10c** belong to the same stereochemical series.

The likely stereochemical course of the cyclization of the indolylbutanones **9a-9c** to the tetrahydrocarbazolones **10a-10c** is predictable on the basis of the principle of induced asymmetric synthesis (20) which states that the lower energy transition state for bond formation between two trigonal carbon atoms is that in which the perpendiculars to the planes of the centers involved are co-linear. Dreiding models show clearly that this geometrical condition is satisfied in the transition state **15c** (obtained by addition of one terminus of the enol to that face of the indolenine to which the butanone chain is attached) leading to the *cis*-isomer **10c** without strain whereas this requirement is satisfied in the transition state **15d** (obtained by addition of the enol to the opposite face of the indolenine) leading to the *trans*-isomer **18** only with considerable bond and angle strain.

In accordance with this prediction, the stereochemistry (21) of the ring-fusion of the tetrahydrocarbazolone **10b** and therefore also of **10a** and **10c** was shown to be *cis* by proton magnetic resonance spectroscopy. The 100 MHz spectrum (deuteriochloroform) of **10b** at 25° exhibited a broad doublet and three complex multiplets. At 0° the complexity of the multiplets changed and an unsummetrical triplet appeared in the region of the original doublet. Additional changes occurred as the temperature was lowered and the spectrum was not stabilized at the lowest

observable temperature (-60°). Since the proton magnetic resonance spectrum of *N*-methylpyrrolidine is temperature invariant to -90° (22), the observed spectral changes can not be due to restricted nitrogen inversion. Thus, we ascribe them to variations in conformational population; such variations being possible in a mobile *cis*-fused 1-azahydrindane system but not in the rigid *trans*-fused epimer (23).

EXPERIMENTAL (24)

4-(1-Benzylindol-3-yl)-2-butanone (**9a**). A. Addition of 3-Buten-2-one to 1-Benzylindole (**8**).

A solution of 1-benzylindole (**8**) (65.7 g., 0.318 mole), 3-buten-2-one (66.6 g., 0.951 mole), acetic anhydride (110 ml.) and glacial acetic acid (330 ml.) was heated under reflux for 30 minutes and allowed to stand at room temperature for 18 hours. Distillation of the residue, obtained by concentration of the reaction mixture under reduced pressure gave 59.6 g. of a viscous oil, b.p. 202.0-210.0° (0.15-0.20 mm.), which solidified on standing. Recrystallization from 2-propanol afforded 50.0 g. (56.8%) of the butanone (**9a**), m.p. 72.0-73.0°; γ max (chloroform) 1710 (C=O) cm^{-1}; λ max 224 mμ (ε, 36,300), 288 (6,200); δ 2.05 (singlet, 3H, CH_3-), 2.89 (A_2B_2, 4H, $-CH_2CH_2-$), 5.19 (singlet, 2H, $-CH_2-$), 6.88 (singlet, 1H, indole C-H), 7.02-7.75 (multiplet, 9H, aromatic) p.p.m.

Anal. Calcd. for $C_{19}H_{19}NO$: C, 82.27; H, 6.90; N, 5.05. Found: C, 82.09; H, 7.13; N, 4.95.

B. Benzylation of 4-(Indol-3-yl)-2-butanone (**9c**).

A solution of 4-(indol-3-yl)-2-butanone (**9c**) (10.0 g., 0.0535 mole), benzyl chloride (7.6 g., 0.059 mole) and dimethylformamide (50 ml.) was added dropwise, over twenty-five minutes, with stirring at 0° to a suspension of 53% sodium hydride-oil (2.8 g., 0.056 mole) and dimethylformamide (30 ml.). After the addition was complete, the mixture was stirred at 0° for fifteen minutes. 2-Propanol (10 ml.) was added and the reaction mixture was concentrated under reduced pressure. The residue was dissolved in benzene and the solution was washed thoroughly with water, dried over anhydrous sodium sulfate, filtered and evaporated. Distillation of the residual oil from an oil-jacketed flask followed by recrystallization of the solidified distillate from absolute ethanol gave 7.4 g. (51%) of the indolylbutanone **9a**, m.p. 71.5-73.0° alone or admixed with a sample prepared by Method A.

The spectra (infrared and ultraviolet) and chromatograms (thin-layer and gas-liquid) of the two samples were identical.

9-Methyl-3,4,4a,9a-tetrahydro-2(1*H*)-carbazolone (**10b**). A. Cyclization of 4-(1-Methylindol-3-yl)-2-butanone (**9b**) with Trifluoroacetic Acid.

A solution of the butanone (**9b**) (30.0 g., 0.149 mole) and freshly distilled trifluoroacetic acid (350 ml.) was allowed to stand at room temperature for two days. The reaction mixture was poured onto ice containing 50% potassium hydroxide solution (600 ml.) and extracted with methylene chloride. The organic extracts were dried over anhydrous potassium carbonate, filtered and concentrated *in vacuo*. The residual oil was dissolved in benzene and extracted with 2 *N* hydrochloric acid. The combined aqueous extracts were cooled in an ice-bath, basified with 20% potassium hydroxide and extracted with methylene chloride. The organic extracts were washed with saturated sodium chloride solution, dried over anhydrous potassium carbonate and filtered. Recrystallization of the residual solid, obtained by concentration of the filtrate, from cyclohexane furnished 8.52 g. (28.4%) of the carbazolone (**10b**), m.p. 65.5-66.5°.

An analytical sample, obtained by sublimation at 50° (0.08 mm.) had m.p. 65.6-66.5°; γ max (chloroform) 1710, 1720 (C=O) cm^{-1}; λ max 254 mμ (ε, 8,240), 301 (3,060); δ 2.64 (singlet, 3H, CH_3-), 6.3-7.2 (multiplet, 4H, aromatic) p.p.m.

Anal. Calcd. for $C_{13}H_{15}NO$: C, 77.58; H, 7.51; N, 6.96; mol. wt. 201. Found: C, 77.75; H, 7.74; N, 7.06; mol. wt. (mass spectrometry) 201.

The gas-liquid chromatogram (2% XE-60-on-Gas-Chrom Z 80/100, column temperature 180°, flame detector) showed one symmetrical band.

The 2,4-dinitrophenylhydrazone of **10b** had m.p. 190.0-190.5°; γ max (Nujol) 3300, 3100 (NH), 1620 (C=N), 1537, 1335 (NO_2) cm^{-1}; λ max 230 mμ (ε, 20,800), 257 (21,700), 361 (24,200).

Anal. Calcd. for $C_{19}H_{19}N_5O_4$: C, 59.83; H, 5.02; N, 18.39. Found: C, 59.61; H, 5.09; N, 18.12.

B. Methylation of 3,4,4a,9a-tetrahydro-2(1*H*)-carbazolone (**10c**).

A mixture of 1.87 g. (0.0100 mole) of the carbazolone (**10c**), the gas-liquid chromatogram (2% XE-60-on-Gas-Chrom Z 80/100, column temperature 180°, flame detector) of which showed one symmetrical band, 38.7% formalin (1.2 ml., 0.012 mole), 10% palladium-on-carbon (0.5 g.) and absolute ethanol (50 ml.) was shaken on a Parr pressure reaction apparatus at room temperature and an initial pressure of 20 p.s.i. After three days the theoretical quantity of hydrogen was absorbed and there was no additional uptake. The catalyst was collected, washed with absolute ethanol and the filtrate was evaporated under reduced pressure; yield 1.85 g. of a colorless oil, the gas-liquid chromatogram (2% XE-60-on gas-Chrom Z 80/100, column temperature 180°, flame detector) of which indicated the presence of 60% of the *N*-methyl derivative (**10b**). Sublimation of the residue at 65° (0.06 mm.) afforded 0.65 g. (32%) of **10b**, m.p. 65.0-66.5°.

A sample, recrystallized from cyclohexane, had m.p. 66.0-66.5, along or admixed with a sample prepared by method A. The infrared and ultraviolet spectra of the 9-methylcarbazolones, prepared by methods A and B, were superimposable. The thin-layer and gas-liquid chromatograms were identical.

9-benzyl-3,4,4a,9a-tetrahydro-2(1H)-carbazolone (**10a**). A. Cyclization of 4-(1-Benzylindol-3-yl)-2-butanone (**9a**).

A solution of the butanone (**9a**) (50.0 g., 0.180 mole) and freshly distilled trifluoroacetic acid (1.5 l.) was allowed to stand at room temperature for two days. The reaction mixture was poured onto ice-water (*ca.* 10 l.) containing 880 g. of 85% potassium hydroxide and extracted with methylene chloride. The organic extracts were washed with saturated sodium chloride solution, dried over anhydrous potassium carbonate, filtered and evaporated. Two recrystallizations of the solid residue from absolute ethanol afforded 10.5 g. (21.0%) of the carbazolone (**10a**), m.p. 118.0-119.0°; γ max (chloroform), 1710 (C=O) cm^{-1}; λ max 254 mμ (ε, 9,720), 303 (3,220); δ 6.3-7.3 (multiplet, 9H, aromatic) p.p.m.

Anal. Calcd. for $C_{19}H_{19}NO$: C, 82.27; H, 6.90; N, 5.05. Found: C, 82.21; H, 7.00; N, 4.94.

B. Benzylation of 3,4,4a,9a-Tetrahydro-2(1*H*)-carbazolone (**10c**).

A mixture of 0.15 g. (0.83 millimoles) of the carbazolone (**10c**), the gas-liquid chromatogram (2% XE-60-on-Gas-Chrom Z 80/100, column temperature 185°, flame detector) of which exhibited one symmetrical peak, freshly distilled benzaldehyde (1.3 g., 12 millimoles), 10% palladium-on-carbon (45 mg.) and

absolute ethanol (10 ml.) was shaken on a Parr pressure reaction apparatus at room temperature and an initial pressure of 41 p.s.i. for 20 minutes. The catalyst was collected, washed with absolute ethanol, and the filtrate was concentrated under reduced pressure. Trituration of the residual oil (0.2 g.), the gas-liquid chromatogram (2% XE-60-on-Gas-Chrom ℣ 80/100, column temperature 185°, flame detector) of which indicated the presence of 80% of **10a**, with ether followed by recrystallization from absolute ethanol afforded 0.06 g. (27%) of the carbazolone (**10a**), m.p. 118.0-118.5°, alone or admixed with a sample prepared by method A. The infrared spectra, the thin-layer chromatoplates and the gas-liquid chromatograms of the two samples were identical.

3,4,4a,9a-Tetrahydro-2(1*H*)-carbazolone (**10c**).

A solution of the butanone (**9c**) (57.0 g., 0.305 mole), freshly distilled boron trifluoride etherate (1.2 l.) and methanol (6 l.) was allowed to stand at room temperature for three days. The reaction mixture was cooled in an ice-bath. Fifty percent sodium hydroxide solution (500 ml.) was added slowly, with stirring, and the resultant solid was collected and washed with methanol. The filtrate, cooled in an ice-bath, was acidified with 1 *N* hydrochloric acid and extracted with benzene. The aqueous phase was cooled in an ice-bath, basified with 50% sodium hydroxide solution and extracted with methylene chloride. The organic extracts were washed with saturated sodium chloride solution, dried over anhydrous potassium carbonate and filtered. Distillation of the residual oil (28 g.), obtained by evaporation of the filtrate under reduced pressure, from an oil-jacketed flask at 170° (bath temperature, 0.1 mm.) afforded 17.9 g. of a yellow oil which solidified on standing. Recrystallization from 2-propanol gave 12.2 g. (21.4%) of the carbazolone (**10c**), m.p. 87.0-88.0°.

An analytical sample, prepared by sublimation at 78.0-85.0° (0.1 mm.) had m.p. 87.0-88.0°; γ max (dichloromethane) 3400 (NH), 1715 (C=O) cm^{-1}; λ max 246 mμ (ε, 7,300), 298 (2,980); δ 3.97 (deuterium oxide-exchangeable singlet, 1H, -NH-), 6.5-7.3 (multiplet, 4H, aromatic) p.p.m.

Anal. Calcd. for $C_{12}H_{13}NO$: C, 76.97; H, 7.00; N, 7.48; mol. wt. 187. Found: C, 77.15; H, 7.27; N, 7.25; mol. wt. 187 (mass spectrometry).

The gas-liquid chromatogram (2% XE-60-on-Gas-Chrom ℣ 80/100, column temperature 180°, flame detector) showed one symmetrical band.

2-Hydroxy-9-methylcarbazole (**13a**).

A mixture of 9-methyl-3,4,4a,9a-tetrahydro-2(1*H*)-carbazolone (**10b**) (0.75 g., 3.7 millimoles), 10% palladium-on-carbon (0.75 g.) and xylene (45 ml.) was heated under reflux for one hour. The catalyst was collected on a filter and the filtrate was evaporated under reduced pressure. The residue was dissolved in ether and the ether and the ethereal solution was washed with 1 *N* potassium hydroxide solution. The combined aqueous washings were cooled in an ice-bath, acidified with 1 *N* hydrochloric acid and extracted with methylene chloride. The organic extracts were dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. Recrystallization of the residual solid from benzene gave 0.30 g. (41%) of the hydroxycarbazole (**13a**) m.p. 166.5-167.5° (lit. (11) m.p. 167.0-168.0°).

2-Methoxy-9-methylcarbazole (**13b**). A. Methylation of 2-Hydroxy-9-methylcarbazole (**13a**).

A solution of the hydroxycarbazole (**13a**) (0.065 g., 0.33 millimoles), 1 *N* potassium hydroxide solution (2 ml.), dimethyl sulfate (2 ml., 2.7 g., 21 millimoles) and methanol (5 ml.) was stirred at room temperature for 16 hours. The resultant precipitate was collected on a filter, washed with methanol, dried at 0.1 mm. and sublimed at 90° (0.08 mm.); yield 0.053 g. (79%) of the carbazole (**13b**), m.p. 97.5-98.5° (lit. (12) m.p. 104°) alone or admixed with a sample prepared by method B.

B. Methylation of 2-Hydroxycarbazole (**14**).

A solution of 2-hydroxycarbazole (**14**) (2.0 g., 0.011 mole) and dimethylformamide (10 ml.) was added dropwise, with stirring to a slurry of 50% sodium hydroxide-oil (1.5 g., 0.031 mole) and dimethylformamide (25 ml.) over fifteen minutes. After the addition was complete, the reaction mixture was stirred for one hour and then a solution of methyl iodide (4.4 g., 0.031 mole) and dimethylformamide (10 ml.) was added. The reaction mixture was stirred at room temperature for three hours. 2-Propanol (10 ml.) was added. The mixture was poured through a filter, water was added to the filtrate, and the suspension was extracted with benzene. The organic extracts were washed with water, dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. Recrystallization of the residue from methanol afforded 1.6 g. (69%) of (**13b**), m.p. 96.0-97.0°.

An analytical sample, prepared by repeated recrystallization from methanol, had m.p. 97.0-98.0° (lit. (12) m.p. 104°); γ max (chloroform) 1630, 1604, 1580, 1502 (aromatic) cm^{-1}; λ max 238 mμ (ε, 54,000), 261 (22,800), 302 (16,900).

Anal. Calcd. for $C_{14}H_{13}NO$: C, 79.59; H, 6.20; N, 6.63. Found: C, 79.68; H, 6.18; N, 6.87.

The infrared and ultraviolet spectra of the samples prepared by methods A and B were superimposable. The thin-layer chromatoplates were identical.

3-(3-Oxobutyl)-2-[3-(3-oxobutyl)-2-indolinyl]indole (**12a**).

A solution of the indolylbutanone (**9c**) (40.0 g., 0.214 mole) and freshly distilled trifluoroacetic acid (600 ml.) was allowed to stand at −5° overnight. The reaction mixture was poured onto ice containing 400 g. of sodium hydroxide and extracted with methylene chloride. The organic extracts were washed with saturated sodium chloride solution, dried over anhydrous potassium carbonate, filtered and evaporated under reduced pressure. Three recrystallizations of the residue from absolute ethanol gave 27.0 g. (69.6%) of the indolinylindole (**12a**), m.p. 118.5-120°.

A sample repeatedly recrystallized from absolute ethanol for analysis had m.p. 120.0-120.5°; γ max (chloroform) 3420 (indole NH), 3350 (indoline NH), 1710 (C=O) cm^{-1}; λ max 225 mμ (ε, 39,800), 285 (12,400), 293 (11,800); δ 1.88, 1.98 (singlets, 6H, CH_3-), 4.31 (deuterium oxide-exchangeable broad singlet, 1H, indoline NH), 4.91 (doublet, J = 9 c.p.s., 1H, indoline C_2-H), 6.5-7.5 (multiplet, 8H, aromatic), 8.56 (deuterium oxide-exchangeable singlet, 1H, indole NH) p.p.m.

Anal. Calcd. for $C_{24}H_{26}N_2O_2$: C, 76.97; H, 7.00; N, 7.48; mol. wt. 374. Found: C, 76.99; H, 6.84; N, 7.21; mol. wt. 391 (isothermal distillation in methylene bromide); 374 (mass spectrometry).

The acetyl derivative (**12b**), prepared by treatment of (**12a**) with acetyl chloride and pyridine, had m.p. 165.5-166.5°; γ max (dichloromethane) 3400 (indole NH), 1708 (ketone C=O), 1655 (amide C=O), 1655 (amide C=O), 1595 (aromatic) cm^{-1}; λ max 222 mμ (ε, 45,400), 255 (16,700); δ 2.10 (singlet, *ca.* 9H, CH_3-), 5.55 (doublet, J = 2 c.p.s., indole C_2-H), 7.0-7.2 (multiplet, 8H, aromatic), 8.14 (deuterium oxide-exchangeable singlet, 1H, indole-NH-) p.p.m.

Anal. Calcd. for $C_{26}H_{28}N_2O_3$: C, 74.97; H, 6.78; N, 6.73. Found: C, 74.85; H, 6.74; N, 6.87.

The hydrochloride of **12a** had m.p. 158.0-160.0°; λ max

(Nujol) 3200 (indole NH), 1710 (C=O) cm^{-1}; λ max 225 mμ (ε, 38,200), 285 (12,200), 293 (11,400).

Anal. Calcd. for $C_{24}H_{27}ClN_2O_2$: C, 70.15; H, 6.62; Cl, 8.61; N, 6.81. Found: C, 70.07; H, 6.53; Cl, 8.59; N, 7.05.

2-(3-Methyl-2-indolinyl)-3-methylindole (**6**) and 2,2'-[2-*o*-Aminophenylpropylidene]di[3-methylindole] (**7**).

A solution of 3-methylindole (**1b**) (50.0 g., 0.382 mole) and trifluoroacetic acid (500 ml.) was allowed to stand at −15° for 18 hours. The reaction mixture was concentrated under reduced pressure. The residue was poured onto ice containing excess potassium hydroxide and extracted with methylene chloride. The organic extracts were washed with saturated sodium chloride solution, dried over anhydrous sodium sulfate, filtered and evaporated. The residue (51 g.) was dissolved in benzene (400 ml.) and the solution was shaken with four one liter portions of 0.08 *N* hydrochloric acid. The precipitate, which formed during the second washing, was collected and partitioned between excess potassium hydroxide solution and methylene chloride. The organic extract was dried over anhydrous potassium carbonate, filtered and evaporated under reduced pressure. Two recrystallizations of the residue (26 g.) from anhydrous ether - Skelly B (1:6) afforded 10.8 g. (21.6%) of the trimer (**7**), m.p. 183.0-184.0°; γ max (dichloromethane) 3440 (indole NH), 3350, 3200 (NH_2), 1620 (NH_2), 1495, 1590 (aromatic) cm^{-1}; λ max 224 mμ (ε, 68,000), 293 (22,400); δ 1.22 (doublet (J = 7 c.p.s.) 3H, CH_3-), 1.96 (singlet, 3H, CH_3-), 2.43 (singlet, 3H, CH_3-), 3.30 (deuterium oxide-exchangeable broad singlet, 2H, NH_2-), 4.75 (doublet (J = 10 c.p.s.), 1H, –CH), 6.5-7.7 (multiplet, 12H, aromatic), 7.96 (deuterium oxide-exchangeable broad singlet, 1H, indole NH) p.p.m.

Anal. Calcd. for $C_{27}H_{27}N_3$: C, 82.40; H, 6.92; N, 10.68; mol. wt. 393. Found: C, 82.69; H, 6.95; N, 10.92; mol. wt. 393 (mass spectrometry).

The combined organic phase was washed with 10% potassium hydroxide solution until the washings were basic, saturated sodium chloride solution, dried over anhydrous potassium carbonate and filtered. Recrystallization of the residue (23 g.) from cyclohexane gave 11.0 g. (21.2%) of the dimer (**6**), m.p. 124.5-125.5°.

An analytical sample, obtained by two recrystallizations from cyclohexane, had m.p. 125.5-126.0°, (lit. (14) m.p. 125.0-127.0°); γ max (dichloromethane) 3450 (indole NH), 3380 (indoline NH), 1610, 1600 (aromatic) cm^{-1}; λ max 228 mμ (ε, 39,600), 285 (12,300), 293 (11,600); δ 1.27 (doublet (J = 7 c.p.s.), 3H, CH_3-), 2.50 (singlet, 3H, CH_3-), 3.83 (deuterium oxide-exchangeable broad singlet, 1H, indoline NH), 6.6-7.7 (multiplet, 8H, aromatic). 8.22 (deuterium oxide-exchangeable broad singlet, 1H, indole NH) p.p.m.

Anal. Calcd. for $C_{18}H_{18}N_2$: C, 82.40; H, 6.92; N, 10.68. Found: C, 82.29; H, 7.13; N, 10.92.

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