The Dimerization of 2-Vinylindoles and Their Alcohol Precursors[1]

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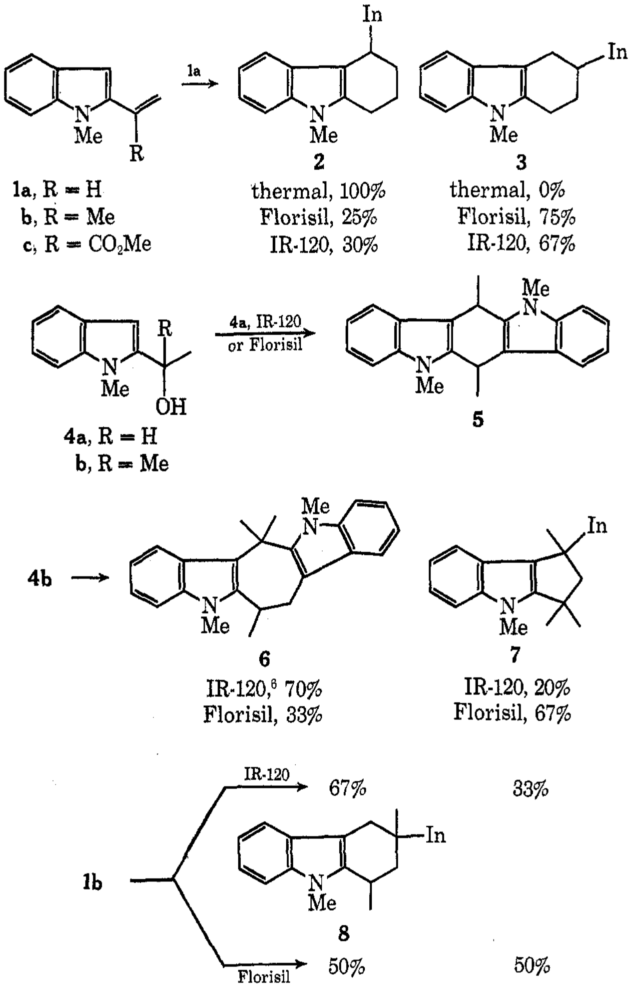
The dimerization of a select pair of 2-vinylindoles and 2-(α-hydroxyalkyl)indoles was investigated. The structures of the dimeric species are elucidated.

Since 2- and 4-vinylpyridines are well known[3] to function as electrophilic olefins, the corresponding reaction with 2-vinylindoles might be expected to behave in a similar fashion under the influence of acid catalysis. Prior to our utilization of 1-methyl-2-(α-carbomethoxyvinyl)indole (**1c**) in alkaloid synthesis,[4] we had occasion to explore the reactivity of four indolic compounds which were devoid of electron-withdrawing groups, *i.e.*, carbomethoxyl. The dimers formed from 1-methyl-2-vinylindole (**1a**), 1-methyl-2-isopropenylindole (**1b**), 1-methyl-2-(α-hydroxyethyl)indole (**4a**), and 1-methyl-2-(α-hydroxyisopropyl)indole (**4b**) under either acid and/or thermal conditions are outlined in Scheme I.[5,6]

Scheme I[5]



Attempted distillation of 1-methyl-2-vinylindole (**1a**), prepared from 1-methyl-2-formylindole[7] and methylene triphenylphosphine, produced a viscous oil from which could be isolated dimer **2**. A more efficient means of effecting this transformation was achieved by refluxing the vinylindole in toluene for 30 hr. The structural assignment was made on the basis of the similarity in chemical shift and multiplicity of the high-field portion of its nuclear magnetic resonance spectrum with that of the thermal dimers of 2-vinylfuran,[8] 2-vinylthiophene,[9] and styrene.[10] The mass spectrum provided confirmatory evidence for this assignment since a metastable peak[11] at *m/e* 260.5 ($286^2/314$) can be derived from the daughter ion (*m/e* 286) and the molecular ion (*m/e* 314). The alternate assignment **3** (*vide infra*) would have been expected to yield a metastable at *m/e* 78.5 ($157^2/314$) (Scheme II).

Exposure of vinylindole **1a** in benzene solution to Florisil[12] overnight promoted self-condensation. Under these conditions, dimers **2** and **3** were obtained in a 1:3 ratio, respectively. The assignment of structure **3** to the major component followed from both its nuclear magnetic resonance spectrum and mass spectrum, the latter displaying the second fragmentation pattern[13] in Scheme II. When the experiment was conducted in the absence of Florisil, only recovered starting material was obtained, indicating the reaction to be catalyzed by Florisil. Consequently, the appearance of **2** in the thermal reaction presumably arises *via* a radical pathway,[8-10] whereas dimers **2** and **3** are formed by an ionic route in the presence of Florisil.

A similar ratio of products was obtained by refluxing an ethanol solution of the vinylindole **1a** in the presence of Amberlite IR-120 sulfonic acid resin. The possibility of the reversible formation of dimers **2** and **3** was eliminated when either dimer was recovered unchanged when subjected to the conditions of IR-120 resin or Florisil.

When an attempt was made to prepare vinylindole **1a** by the dehydration of alcohol **4a**, the sole product of undefined stereochemistry was dimer **5**.

These data reflect the propensity of vinylindole **1a** to give rise to its 3-protonated species **9** as a reactive intermediate, whereas the alcohol produces the cation

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[1] Taken in part from the Ph.D. thesis of E. B. S., Yale University, 1970.

[2] National Institutes of Health Predoctoral Fellow, 1966–1969.

[3] W. v. E. Doering and R. A. N. Weil, *J. Amer. Chem. Soc.*, **69**, 2641 (1947); G. Singerman and S. Danishefsky, *Tetrahedron Lett.*, 2249 (1964).

[4] F. E. Ziegler and E. B. Spitzner, *J. Amer. Chem. Soc.*, **92**, 3492 (1970).

[5] Percentages indicated represent relative amounts of products present in the crude reaction mixture as determined by the nuclear magnetic resonance spectrum. Throughout the text, In = 2-(1-methylindolyl).

[6] The mixture of the IR-120 resin and Florisil contained 10% of vinylindole **1b**.

[7] K. Hoffman, A. Rossi, and J. Kebrle, German Patent 1,093,365 (1958); *Chem. Abstr.*, **56**, 4735*f* (1962).

[8] C. A. Aso, T. Kunitake, and Y. Yanaka, *Bull. Chem. Soc. Jap.*, **38**, 675 (1965).

[9] C. A. Aso, T. Kunitake, M. Shinsenji, and H. Miyakazi, *J. Polym. Sci., Part A-1*, **7**, 1497 (1969).

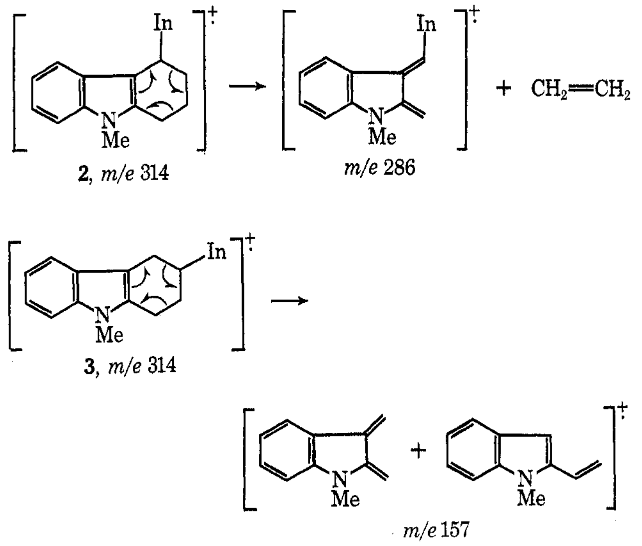
[10] F. R. Mayo, *J. Amer. Chem. Soc.*, **90**, 1289 (1968).

[11] For a discussion of metastable peaks, see K. Biemann, "Mass Spectrometry," McGraw-Hill, New York, N. Y., 1962.

[12] Florisil is a magnesium silicate chromatographic adsorbent available from Fisher Scientific Co.

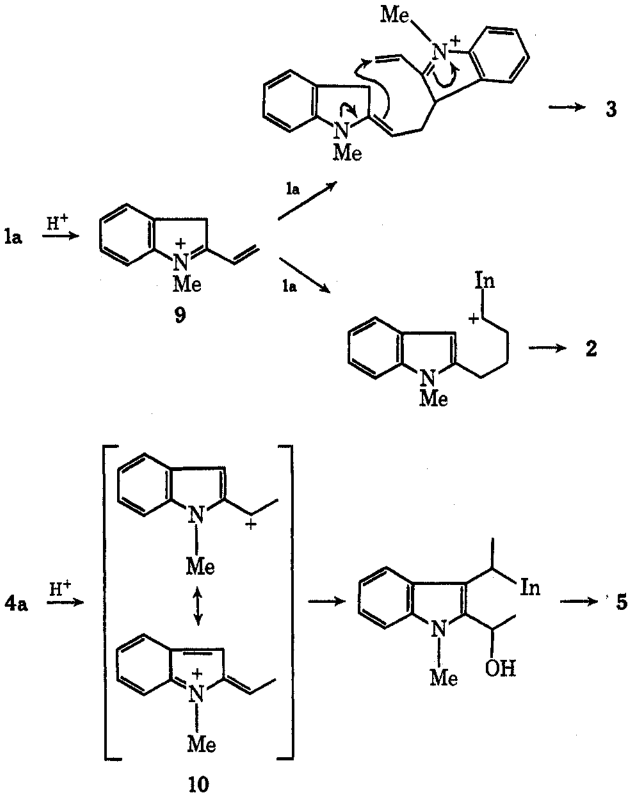
[13] Although the peak, *m/e* 157, can be attributed to a doubly charged species derived from the molecular ion, at least some of the peak must be due to fragments in light of the metastable peak.

Scheme II



10[14] (2-β protonated **1a**) which leads to its discrete product (Scheme III).

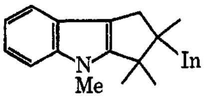
Scheme III



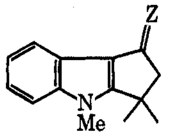
In contrast to the thermal instability of 1-methyl-2-vinylindole, 1-methyl-2-isopropenylindole was capable of distillation. In addition, it was stable in refluxing ethylene glycol and could be chromatographed on Florisil. However, prolonged exposure of a benzene solution of vinylindole **1b** to Florisil provided a 1:1 mixture of dimers **7** and **8**. The structure of **8**, a single diastereomer, was dictated by its nuclear magnetic resonance spectrum which showed an AB pattern consisting of a one-proton doublet at δ 2.77 (J = 14 Hz), discernible in a three-proton signal (δ 2.50–3.00), and a partly hidden one-proton doublet at δ 3.54 (J = 14 Hz). Irradiation of either member of the AB pattern caused the other to collapse to a singlet. In addition, irradiation of the high-field side of the multiplet at δ 2.50–3.00 containing the C-1 proton and one of the C-2 protons caused collapse of a three-proton methyl doublet at δ 1.34 and a one-proton doublet of doublets centered at δ 1.78 to singlets. This clearly ruled out the possibility of the alternate mode of dimerization having the quaternary methyl and indole moiety at C-4.

The mass spectrometric fragmentation of dimer **8** was reminiscent of dimer **3** in that the parent ion *m/e* 342 gave rise to a base daughter peak *m/e* 171 in conjunction with the accompanying metastable peak at *m/e* 85.5 ($171^2/342$).

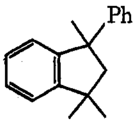
The second dimer revealed five three-proton singlets at δ 1.38, 1.49, 1.88, 3.57, and 3.65, an AB quartet, the halves centered at δ 2.55 and 2.90 (J = 13 Hz), and a one-proton singlet at δ 6.23 as the most salient features of its nuclear magnetic resonance spectrum. A ready distinction between structures **7** and **11** could not be made without knowing the chemical shifts of the AB quartets of at least one of these structural types. To this end, indole **12a** was prepared by the reaction of



11



12a, Z = O
b, Z = H₂
c, Z = D₂



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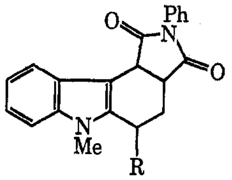

14a, R = H
b, R = Me

α-methylphenylhydrazine and methyl 3,3-dimethyllevulinate in the presence of polyphosphoric acid,[15] effecting indolization and cycloacylation in one operation. Hydrogenolysis with lithium aluminum hydride–aluminum chloride[16] provided indole **12b** (*m/e* 199) whose nuclear magnetic resonance spectrum displayed the vicinal methylene protons as a centrosymmetric A_2B_2 multiplet with the halves centered at δ 2.31 and 2.88. When the reduction was effected with lithium aluminum deuteride–aluminum chloride, the dideuterated species **12c** (*m/e* 201) was produced which showed a broad two-proton singlet at δ 2.31 confirming that the high-field portion of the A_2B_2 pattern could be assigned to the homobenzylic methylene. These values are in accord with the assignment of structure **7** to this dimer. An identical substitution pattern is observed in the dimer **13** obtained from the acid-catalyzed dimerization of

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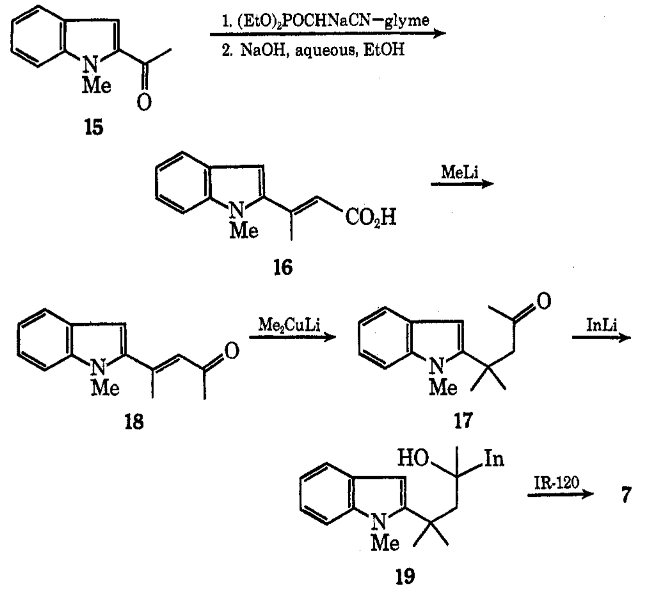
(14) G. Büchi, R. E. Manning, and S. A. Monti, *J. Amer. Chem. Soc.*, **86**, 4631 (1964).

(15) H. M. Kissman, D. W. Farnsworth, and B. Witkop, *ibid.*, **74**, 3948 (1952).

(16) K. T. Potts and P. R. Liljegren, *J. Org. Chem.*, **28**, 3202 (1963).

phenyldimethylcarbinol.[17] Independent evidence for structure **7** was obtained by the synthetic route outlined in Scheme IV.

Scheme IV

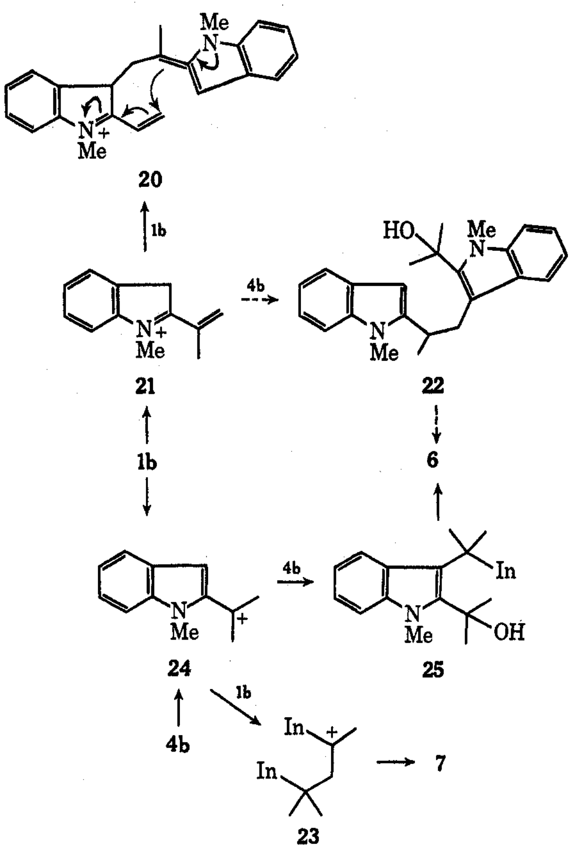


When either the vinylindole **1b** or tertiary alcohol **4b** was refluxed in 95% ethanol containing Amberlite IR-120 resin, a nearly identical mixture of two compounds was obtained with a new dimer **6** predominating over dimer **7**. The structure of the new dimer was based upon its nuclear magnetic spectrum which revealed a three-proton doublet at δ 1.13 (J = 7 Hz), a six-proton singlet, δ 2.16, and a one-proton multiplet centered at δ 3.45 in addition to other signals. Irradiation at δ 3.45 caused the high-field multiplet to collapse to a singlet. This data along with the lack of any indole C_3-H signal argued for structure **6** to be assigned to the second dimer. Finally, subjection of alcohol **4b** to Florisil conditions produced the same two dimeric species as did the IR-120 resin; however, the product distributions were essentially reversed.

The thermal reactivity of both vinylindoles is reflected in their ability to undergo Diels–Alder reactions with *N*-phenylmaleimide.[18] Whereas 1-methyl-2-vinyl indole formed adduct **14a** in 1 day at room temperature, upward to 1 week was required to prepare adduct **14b** from vinylindole **2b**.

Some general mechanistic considerations can be gleaned from these data (Scheme V). The striking fact is that dimer **8** is formed from olefin **1b** under Florisil catalysis without the formation of dimer **6** which is derived under the same conditions from alcohol **4b**. This observation points out the essential dehydrating nature of the Florisil medium and the hydrating conditions used with IR-120 resin. Although both systems are capable of producing cations **21** and **24**, the Florisil–benzene favors vinylindole **1b** as the second reactive species, whereas IR-120–alcohol favors alcohol **4b** (or its ethyl ether). In addition, the similarity of product distribution in treating either the olefin or alcohol with IR-120 resin indicates that the same reactive intermediates are formed in both experiments. The reversal of yields in treating alcohol **4b** with Florisil–benzene reflects the higher concentration of **1b** relative to the IR-120–ethanol conditions. Although dimer **6** can be formally derived by two different pathways while dimer **8** can only be formed by one route, it is likely that dimer **6** is formed *via* intermediate **25** since **22** has the same substitution pattern as intermediate **20** and could lead to dimer **8**.

Scheme V



Experimental Section

Melting points were obtained on a Fisher-Johns apparatus and are corrected. Microanalyses were performed by Galbraith Laboratories and Bernhardt Microanalytische Laboratorium. Infrared spectra were determined on a Perkin-Elmer Model 421 or 237B spectrometer. Nuclear magnetic resonance spectra were obtained with Varian Model A-60, A-60A, or HA-100 spectrometers. Chemical shifts are reported in δ units using tetramethylsilane as internal reference. Ultraviolet spectra were recorded on a Bausch and Lomb Spectronic 505 or a Cary 11S recording spectrometer. Absorptions are reported as λ_{max} (ϵ) in nanometer units. Mass spectra were obtained on an AEI MS-9 spectrometer or a Hitachi RMU-6.

Except where noted, solvents were reagent grade and were used as received. Analytical thin layer plates were run using 3:1 benzene–hexane as the moving phase unless otherwise noted. In all work-up procedures the drying process involved treatment with anhydrous magnesium sulfate and filtering prior to evaporation.

1-Methyl-2-vinylindole (1a).—In a three-necked flask fitted with a serum cap, addition funnel, and reflux condenser was placed 14.68 g (0.0512 mol) of methyltriphenylphosphonium bromide and 250 ml of dry ether. To this stirred suspension, under nitrogen, 22.0 ml (0.0343 mol) of 1.56 *M* *n*-butyllithium in hexane was added by a syringe and the mixture was refluxed for 2 hr. A solution of 4.00 g (0.0252 mol) of 1-methyl-2-formyl-

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[17] A. Dierichs and E. Preu, *Chem. Ber.*, **90**, 1208 (1957); N. G. Polyanski, S. M. Markevich, N. L. Potudina, and A. N. Burova, *Neftekhimiya*, **2**, 348 (1962); *Chem. Abstr.*, **58**, 8938 (1963).

[18] D. Beck and K. Schenker, *Helv. Chem. Acta*, **51**, 260, 264 (1968).

indole[19] in 100 ml of dry ether was then added at room temperature and refluxing was continued for 2 hr. After being cooled in an ice bath, saturated sodium sulfate solution was added and the ether layer was separated, washed four to five times with cold water, dried, and evaporated at room temperature. The residue was thoroughly washed with petroleum ether (bp 30–60°) and the combined washes were evaporated. The petroleum ether wash was repeated and evaporation gave 2.54 g (64%) of a clear yellow liquid whose spectral properties were in accord with the desired product: nmr (CDCl$_3$) δ 3.50 (3 H, s), 5.24 (1 H, dd, J = 11 and 2 Hz), 5.69 (1 H, dd, J = 17.5 and 2 Hz), 6.62 (1 H, s), 6.68 (1 H, dd, J = 17.5 and 11 Hz), and 6.90–7.80 (4 H, m); uv λ_{max} (EtOH) 228 nm (ϵ 25,700) and 305 (13,700).

Anal. Calcd for $C_{11}H_{11}N$: C, 84.04; H, 7.05; N, 8.91. Found: C, 84.04; H, 6.99; N, 8.81.

Thermal Dimerization of 1-Methyl-2-vinylindole. 9-Methyl-1,2,3,4-tetrahydro-4-[2′-(1′-methylindolyl)]carbazole (2).—A solution of 0.50 g (3.18 mmol) of vinylindole **1a** in 8 ml of toluene was refluxed under nitrogen for 30 hr. Evaporation of the solvent gave an orange oil which afforded 0.364 g (73%) of a tan solid from benzene–methanol. Chromatography on a short Florisil column with benzene and trituration of the residual pale green oil (0.349 g) with ether gave a light tan solid, mp 140–145°. Two recrystallizations from ether failed to improve the purity, but recrystallization from benzene–methanol gave a white solid material: mp 142–144°; nmr (CDCl$_3$) δ 1.56–2.92 (6 H, m), 3.53 (3 H, s), 3.62 (3 H, s), 4.28–4.60 (1 H, m), 6.10 (1 H, s), and 6.68–7.60 (8 H, m); uv λ_{max} (MeOH) 225 nm (ϵ 66,500), 286 (14,400); mass spectrum (70 eV) *m/e* (rel intensity) 314 (34), 158 (21.5), 157 (100), 156 (16), and 78.5 (metastable).

Anal. Calcd for $C_{22}H_{22}N_2$: C, 84.04; H, 7.05; N, 8.91. Found: C, 83.77; H, 7.40; N, 8.88.

Reaction of 1-Methyl-2-vinylindole with Florisil. 9-Methyl-1,2,3,4-tetrahydro-3-[2′-(1′-methylindolyl)]carbazole (3).—A slurry of 0.351 g (2.17 mmol) of vinylindole **1a** and 20 g of Florisil in 40 ml of benzene was stirred at room temperature overnight. The mixture was filtered and, after thoroughly washing the dark red-brown Florisil with hot benzene, the combined benzene solutions were evaporated to give 0.294 g of a yellow oil which showed two spots on an analytical thin layer plate. The nmr spectrum indicated that the mixture consisted of dimer **2** (smaller R_f) and an isomeric dimer in a 1:3 ratio. Chromatography on Florisil with 1:1 benzene–petroleum ether gave 0.196 g (56%) of a white solid, mp 130–144°. Recrystallization from benzene–methanol afforded 0.108 g of white prisms: mp 153–153.5°; nmr (CDCl$_3$) δ 2.09–3.58 (7 H, m), 3.62 (3 H, s), 3.74 (3 H, s), 6.38 (1 H, s), and 6.90–7.80 (8 H, m); uv λ_{max} (MeOH) 227 nm (ϵ 68,000), 283 (17,500), and 290 (15,900); mass spectrum (70 eV) *m/e* (rel intensity) 315 (29), 314 (100), 286 (46), 285 (52), 271 (29), 270 (25), 260.5 (metastable), 183 (46), and 157 (27).

Anal. Calcd for $C_{22}H_{22}N_2$: C, 84.04; H, 7.05; N, 8.91. Found: C, 83.78; H, 7.01; N, 9.33.

1-Methyl-2-(α-hydroxyethyl)indole (4a).—A mixture of 1.0 g (5.8 mmol) of 1-methyl-2-acetylindole[20] and 0.50 g (13.2 mmol) of sodium borohydride in 40 ml of ethanol containing 2 ml of 10% aqueous sodium hydroxide was stirred at 0° for 2 hr. Addition of water, ether extraction, and evaporation of the dried ether solution led to a pale green oil which upon standing with a small amount of benzene in a freezer overnight gave 0.93 g of solid material. Recrystallization from ether–petroleum ether gave 0.86 g (86%) of white needles: mp 56.5–57.5°; nmr (CDCl$_3$) δ 1.55 (3 H, d, J = Hz), 1.97 (1 H, s), 3.60 (3 H, s), 5.81 (1 H, q, J = 7 Hz), 6.35 (1 H, s), and 6.85–7.70 (4 H, m); ir (CHCl$_3$) 3650 cm^{-1}.

Anal. Calcd for $C_{11}H_{13}NO$: C, 75.40; H, 7.48; N, 7.99. Found: C, 75.08; H, 7.44; N, 7.92.

Reaction of Alcohol 4a with Amberlite IR-120 Ion Exchange Resin. 5,6,11,12-Tetramethyl-6,12-dihydroindole[3,2-*b*]carbazole (5).—A mixture of 0.50 g (2.86 mmol) of alcohol **4a** and 0.525 g of Amberlite IR-120 ion exchange resin in 6 ml of 95% ethanol was refluxed overnight under nitrogen. Benzene was added and the dried solution was evaporated to yield 0.465 g of a tacky, pale green gum. Chromatography on Florisil with 1:1 benzene–petroleum ether followed by recrystallization of the residue from benzene–methanol gave 0.267 g (55%) of pale green solid. Several recrystallizations from benzene–methanol led to a semipure material (mp 235–255°), but sublimation [180–200° (1 μ)] gave a pale yellow solid: mp 262–264°; nmr (CDCl$_3$) δ 1.63 (3 H, d, J = 7 Hz), 3.79 (3 H, s), 4.47 (1 H, q, J = 7 Hz), and 6.91–7.80 (4 H, m); uv λ_{max} (MeOH) 233 nm (ϵ 77,000), 286 (13,600), and 294 (13,300); mass spectrum (70 eV) *m/e* (rel intensity) 314 (41), 299 (80), 285 (24), 284 (100), 269 (23), 254 (7), 157 (7), and 142 (33).

Anal. Calcd for $C_{22}H_{22}N_2$: C, 84.04; H, 7.05; N; 8.91. Found: C, 84.25; H, 6.89; N, 9.00.

1-Methyl-2-isopropenylindole (1b).—The procedure was the same as was used for the preparation of 1-methyl-2-vinylindole (**1a**). From 4.32 g (0.025 mol) of 1-methyl-2-acetylindole the work-up gave 5.03 g of an orange oil. Chromatography on a short Florisil column with petroleum ether afforded 3.35 g (78%) of a colorless liquid: bp 95° (0.07 mm); nmr (CDCl$_3$) δ 2.13 (3 H, s), 5.06 (1 H, s), 5.22 (1 H, s), 6.35 (1, H, s), and 6.85–7.60 (4 H, m); uv λ_{max} (EtOH) 226 nm (ϵ 25,200) and 295 (15,800).

Anal. Calcd for $C_{12}H_{13}N$: C, 84.17; H, 7.65; N, 8.18. Found: C, 83.67; H, 8.00; N, 8.23.

1-Methyl-2-(α-hydroxylisopropyl)indole (4b).—To a solution of 4.0 g (0.021 mol) of 1-methyl-2-acetylindole in 100 ml of dry ether was added 50 ml (0.024 mol) of 0.48 *M* methylmagnesium bromide in ether. After the addition was completed, the mixture was stirred for 10 min at room temperature and then decomposed with saturated sodium sulfate solution. The ether was decanted and, after thoroughly washing the residual salts with ether, the combined ether solutions were dried and evaporated. Trituration of the resulting oil with ether–petroleum ether gave 3.1 g (78%) of a white solid. Recrystallization from petroleum ether provided silky white crystals: mp 90–91°; nmr (CDCl$_3$) δ 1.52 (6 H, s), 3.71 (3 H, s), 6.09 (1 H, s), and 6.80–7.80 (4 H, m).

Anal. Calcd for $C_{12}H_{15}NO$: C, 76.15; H, 7.99; N, 7.40. Found: C, 76.36; H, 8.12; N, 7.51.

Reaction of Alcohol 4b with Amberlite IR-120. 5,6,6,11,12-Pentamethyl-5,11,12,13-tetrahydro-6*H*-indolo[3,2-*c*]cyclohept[*b*]-indole (6).—A mixture of 0.20 g (1.06 mmol) of alcohol **4b** and 0.225 g of Amberlite IR-120 ion exchange resin in 5 ml of 95% ethanol were refluxed overnight under nitrogen. Benzene was added and evaporation of the dried solution gave 0.156 g of a yellow oil whose thin layer chromatogram showed three spots of almost identical R_f. The nmr spectrum of the crude material indicated a 1:2:7 mixture of vinylindole **1b**, dimer **7**, and dimer **6**, respectively; crystallization from benzene–methanol afforded 0.046 g (25%) of a tan solid, mp 236–241°. Chromatography on a short Florisil column with benzene and trituration of the residue with petroleum ether gave 0.028 g of white solid. Recrystallization from benzene–methanol gave colorless prisms: mp 247–248°; nmr (CDCl$_3$) δ 1.13 (3 H, d, J = 7 Hz), 2.16 (6 H, s), 3.23 (2 H, m), 3.33–3.56 (1 H, m), 3.67 (3 H, s), 3.94 (3 H, s), and 6.90–8.00 (8 H, m); uv λ_{max} (EtOH) 232 nm (ϵ 72,000), 287 (15,300), and 294 (14,300); mass spectrum (70 eV) *m/e* (rel intensity) 342 (39), 328 (48), 327 (100), 312 (7), 297 (24), 282 (8), 163 (24), and 156 (37).

Anal. Calcd for $C_{24}H_{26}N_2$: C, 84.17; H, 7.15; N, 8.18. Found: C, 84.09; H, 7.91; N, 8.19.

Reaction of Alcohol 4b with Florisil. 1,3,3,4-Tetramethyl-1-[2′-(1′-methylindolyl)]-1,2,3,4-tetrahydrocyclopent[*b*]indole (7).—A slurry of 0.200 g (1.06 mmol) of alcohol **4b** and 12 g of Florisil in 25 ml of benzene was stirred at room temperature overnight. The benzene was decanted and, after thoroughly extracting the blue-black Florisil with hot chloroform, the combined organic solutions were evaporated to give an oil whose nmr spectrum indicated a 2:1 mixture of dimers **7** and **6**, respectively. Chromatography on a short Florisil column with benzene and low temperature crystallization of the residue from ether–petroleum ether afforded 0.079 g (43%) of a solid material, mp 137–147°. Sublimation [145–150° (1 μ)] and two recrystallizations from ethanol gave 0.031 g of white needles: mp 160–162°; nmr (CDCl$_3$) δ 1.38 (3 H, s), 1.49 (3 H, s), 1.88 (3 H, s), 2.90 (1 H, d, J = 13 Hz), 2.55 (1 H, d, J = 13 Hz), 3.57 (3 H, s), 3.65 (3 H, s), 6.23 (1 H, s), and 6.70–7.50 (8 H, m); uv λ_{max} (EtOH) 299 nm (ϵ 64,000), 279.5 (16,400), 285 (18,200), and 293 (16,400); mass spectrum (70 eV) *m/e* (rel intensity) 342 (66), 328 (64), 327 (100), 312 (9), 297 (12), 282 (5.5), 196 (32), and 156 (40).

Anal. Calcd for $C_{24}H_{26}N_2$: C, 84.17; H, 7.65; N, 8.18. Found: C, 83.82; H, 8.02; N, 8.22.

Reaction of 1-Methyl-2-isopropenylindole (1b) with Florisil. 1,3,9-Trimethyl-1,2,3,4-tetrahydro-3-[2′-(1′-methylindolyl)]-carbazole (8).—A slurry of 1.00 g (5.51 mmol) of vinylindole **1b**

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(19) K. Hoffman, A. Rossi, and J. Kebrle, German Patent 1,093,365 (1958); *Chem. Abstr.*, **56**, 4735*f* (1962).

(20) O. Diels and A. Kollisch, *Chem. Ber.*, **44**, 266 (1911).

and 50 g of Florisil in 100 ml of benzene was stirred at room temperature for 5 days. The mixture was filtered and, after thorough washing of the dark brown Florisil with hot chloroform, the combined solutions were evaporated to give 0.927 g of a brown oil which showed two spots on an analytical thin layer plate. The nmr spectrum of the crude residue indicated a 1:1 mixture of dimers **8** (smaller R_f) and **7**. Trituration of the residue with benzene–methanol gave 0.189 g of a white solid, mp 204–207°.

The filtrate was concentrated and chromatographed on a short Florisil column. Elution with hexane removed the nonindolic material; elution with 1:3 benzene–hexane (fraction 2) afforded 0.381 g of a viscous oil. Trituration with ethanol gave 0.173 g of a pale yellow solid (mp 120–160°) which partially dissolved in benzene leaving 0.014 g of a white solid, mp 196–200°. Elution with 1:1 benzene–hexane (fraction 3) then gave 0.159 g of an orange liquid from which 0.013 g of solid, mp 203–205°, was obtained by trituration with ethanol. The solids were combined (0.216 g, 22%) and recrystallized from a minimal amount of benzene to give 0.163 g of chunky white crystals, mp 207–209°. Another recrystallization afforded analytically pure material: mp 207.5–208.5°; nmr (CDCl$_3$) δ 1.34 (3 H, d, J = 6 Hz), 1.56 (3 H, s), 1.78 (1 H, dd, J = 12 and 16 Hz), 2.50–3.00 (3 H, m), 3.45 (3 H, s), 3.54 (1 H, d, J = 14 Hz), 3.82 (3 H, s), 6.02 (1 H, s), and 6.70–7.70 (8 H, m); uv λ_{max} (EtOH) 232 nm (ϵ 55,000), 286 (14,200), and 292 (14,200); mass spectrum (70 eV) m/e (rel intensity) 342 (15), 327 (1), 171 (100), and 85.5 (metastable).

Anal. Calcd for $C_{24}H_{26}N_2$: C, 84.17; H, 7.65; N, 8.18. Found: C, 84.09; H, 7.70; N, 8.08.

The mother liquors from fractions 2 and 3 were concentrated and crystallized from ethanol to give a total of 0.144 g of white solid, mp 145–60°. This material was sublimed [145–150° (1 μ)] and twice recrystallized from ethanol to give 0.010 g of clear needle-like crystals, mp 160.5–162°, identical in all respects with dimer **7**.

3,3,4-Trimethyl-1,2,3,4-tetrahydrocyclopent[*b*]indol-1-one (12a).—In a 50-ml flask was placed 1.06 g (6.71 mmol) of methyl 3,3-dimethyllevulinate (prepared from the acid[21] by reaction with excess diazomethane) and 0.99 g (7.39 mmol) of α-methylphenylhydrazine. To this mixture was added, with stirring, 4.0 g of polyphosphoric acid and, after the initial exothermic reaction had subsided (the temperature rising to 75–80°), the mixture was heated at 125–130° for 2 hr. After cooling to room temperature, the residual hard mass was carefully dissolved in water with cooling and the solution was thoroughly extracted with methylene chloride. The extracts were washed with dilute base and water, dried, and evaporated to give 0.79 g of a dark brown solid. Chromatography on Florisil with 9:1 benzene–ether and crystallization of the residue from benzene–hexane afforded 0.38 g (27%) of light gray flakes, mp 150–153°. Recrystallization from benzene–hexane gave white flakes: mp 154.4–155.5°; nmr (CDCl$_3$) δ 1.58 (6 H, s), 2.88 (2 H, s), 3.83 (3 H, s), 7.15–8.10 (4 H, m); ir (CHCl$_3$) 1680 cm^{-1}.

Anal. Calcd for $C_{14}H_{15}NO$: C, 78.84; H, 7.09; N, 6.57. Found: C, 78.04; H, 6.81; N, 6.34.

3,3,4-Trimethyl-1,2,3,4-tetrahydrocyclopent[*b*]indole (12b).—In a three-necked flask fitted with addition funnel and reflux condenser was placed 0.18 g (4.70 mmol) of lithium aluminum hydride, 0.47 g (3.52 mmol) of aluminum chloride, and 5 ml of dry tetrahydrofuran. To this stirred suspension, under nitrogen, a solution of 0.100 g (4.70 mmol) of ketone **12a** and 0.14 g (1.04 mmol) of aluminum chloride in 15 ml of dry tetrahydrofuran was added dropwise and the mixture refluxed overnight. After cooling to 0°, the mixture was carefully decomposed with saturated sodium sulfate solution and extracted with benzene. The extracts were washed with water, dried, and evaporated to give a clear oil which solidified on standing. Chromatography on a short Florisil column with benzene followed by sublimation [50° (0.5 μ)] of the residue gave 0.035 g (37%) of clear flakes: mp 74–75°; nmr (CDCl$_3$) δ 1.38 (6 H, s), 2.13–2.95 (4 H, m, A_2B_2), 3.67 (3 H, s), 6.90–7.60 (4 H, m); mass spectrum (70 eV) m/e (rel intensity) 199 (62), 185 (34), 184 (100), 169 (21), and 168 (28).

Anal. Calcd for $C_{14}H_{17}N$: C, 84.37; H, 8.60; N, 7.03. Found: C, 84.43; H, 8.68; N, 6.98.

1,1-Dideuterio-3,3,4-trimethyl-1,2,3,4-tetrahydrocyclopent[*b*]-indole (12c).—Ketone **12a** (0.200 g, 0.94 mmol) was reduced with lithium aluminum deuteride as described above. The residue from benzene extraction (0.18 g) was purified by low temperature crystallization from methanol and the product (0.101 g, 54%) was obtained as clear flakes: mp 74.5–75.5°; nmr (CDCl$_3$) δ 1.39 (6 H, s), 2.31 (2 H, s), 3.69 (3 H, s), 6.90–7.60 (4 H, m); mass spectrum (70 eV) m/e (rel intensity) 201 (31), 186 (100), 171 (8), and 170 (11).

Reaction of 1-Methyl-2-vinylindole with *N*-Phenylmaleimide. 6-Methyl-2-phenyl-1,3-dioxo-2,3,3a,4,5,10c-hexahydro[1*H*]-pyrrolo[3,4-*c*]carbazole (14a).—A mixture of 0.25 g (1.59 mmol) of vinylindole **1a** and 0.25 g (1.45 mmol) of *N*-phenylmaleimide in 5 ml of benzene was stirred under nitrogen at room temperature for 30 hr. After 16 hr the clear yellow solution had become milky white with precipitated solid. The precipitate was filtered, washed with benzene, and air-dried to give 0.292 g (61%) of a white solid, mp 188–188.5°. Recrystallization from benzene–hexane gave analytically pure material: mp 189–190°; nmr (CDCl$_3$) δ 1.33–1.92 (4 H, m), 3.26–3.54 (1 H, m), 3.58 (3 H, s), 4.41 (1 H, d, J = 7.5 Hz), and 7.00–8.17 (9 H, m); ir (CHCl$_3$) 1710 cm^{-1}; mass spectrum (70 eV) m/e (rel intensity) 331 (49), 330 (100), 210 (23), 184 (26), 183 (100), 182 (100), 181 (33), 168 (20), and 167 (64).

Anal. Calcd for $C_{21}H_{18}N_2O_2$: C, 76.34; H, 5.49; N, 8.48. Found: C, 76.58; H, 5.80; N, 8.14.

Reaction of 1-Methyl-2-isopropenylindole with *N*-Phenylmaleimide. 5,6-Dimethyl-2-phenyl-1,3-dioxo-2,3,3a,4,5,10c-hexahydro[1*H*]pyrrolo[3,4-*c*]carbazole (14b).—A mixture of 0.25 g (1.46 mmol) of vinylindole **1b** and 0.25 g (1.45 mmol) of *N*-phenylmaleimide in 10 ml of benzene was stirred, under nitrogen, at room temperature for 7 days. Hexane was added and 0.32 g of a yellow-orange solid was collected. Recrystallization from benzene–hexane afforded 0.047 g (9%) of white prisms: mp 209–213.5° (another recrystallization raised the melting point to 210.5–212°); nmr (CDCl$_3$) δ 1.23 (3 H, d, J = 9 Hz), 1.80–3.60 (3 H, m), 3.61 (3 H, s), 4.44 (1 H, d, J = 9 Hz), and 6.80–8.20 (9 H, m); ir (CDCl$_3$) 1710 cm^{-1}; mass spectrum (70 eV) m/e (rel intensity) 344 (6), 343 (26), 342 (100), 208 (17), 197 (16), 182 (53), and 167 (26).

Anal. Calcd for $C_{22}H_{20}N_2O_2$: C, 76.72; H, 5.85; N, 8.13. Found: C, 76.65; H, 6.10; N, 7.90.

3-[2′-(1′-Methylindolyl)]but-2-enoic Acid (16).—In a 1-l. three-necked flask fitted with a thermometer, addition funnel, and reflux condenser was placed 2.64 g (0.055 mol) of 50% sodium hydride suspension and 100 ml of dry 1,2-dimethoxyethane (glyme). To this stirred suspension, under nitrogen, a solution of 10.7 g (0.06 mol) of diethyl cyanomethylphosphonate in 50 ml of dry glyme was added so as to keep the temperature below 10° with the aid of external cooling. After being stirred at room temperature until hydrogen evolution ceased (approximately 1.5 hr), the mixture was cooled below 10° while a solution of 8.65 g (0.05 mol) of 1-methyl-2-acetylindole in 100 ml of dry glyme was added. The mixture was stirred at room temperature for 2 hr, decomposed with saturated sodium sulfate solution, and extracted with ether. The combined extracts were then washed with water, dried, and evaporated.

The residue was dissolved in 100 ml of ethanol, 25% aqueous sodium hydroxide solution was added until two layers remained, and the mixture was refluxed, under nitrogen, overnight. Following separation of the layers, the organic layer was washed with 10% sodium hydroxide solution and the combined aqueous solutions were washed twice with ether and then acidified with cold concentrated hydrochloric acid. The acid solution was extracted with ether and the combined extracts were dried and evaporated to give 8.0 g of an orange solid (after drying in a vacuum desiccator). Recrystallization from ether–petroleum ether followed by sublimation [110–125° (0.02 mm)] afforded 5.25 g (50%) of yellow needles, mp 146–149°. Sublimation of the material which was recrystallized several times from ether–petroleum ether gave pale yellow needles: mp 150.5–151.5°; nmr (CDCl$_3$) δ 2.61 (3 H, s), 3.74 (3 H, s), 5.98 (1 H, s), 6.62 (1 H, s), 6.90–7.70 (4 H, m), and 11.03 (1 H, s); ir (CHCl$_3$) 3500–2500 (broad OH), 1695, and 1610 cm^{-1}.

Anal. Calcd for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09; N, 6.51. Found: C, 72.78; H, 5.82; N, 6.16.

Evaporation of the ether solution containing the neutral material from the hydrolysis gave an oil which crystallized on trituration with ether. This material, the amide of the acid, was twice recrystallized from methylene chloride–ether to give 0.200 g of a fluffy white solid: mp 137–138°; nmr (CDCl$_3$) δ 2.53 (3 H, d, J = 1.5 Hz), 3.68 (3 H, s), 5.76 (2 H, broad s), 5.93 (1 H, d, J = 1.5 Hz), 6.55 (1 H, s), and 6.90–7.80 (4 H, m).

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(21) N. R. Easton and R. D. Dillard, *J. Org. Chem.*, **27**, 3602 (1962).

When the reaction was run using 0.865 g (5.0 mmol) of 1-methyl-2-acetylindole and the crude residue washed several times with petroleum ether to remove the mineral oil, 0.959 g (98%) of the nitrile was obtained as a light orange oil: nmr ($CDCl_3$) δ 2.46 (3 H, s), 3.67 (3 H, s), 5.36 (1 H, s), 6.68 (1 H, s), and 6.90–7.80 (4 H, m); ir ($CHCl_3$) 2220 (conjugated CN) and 1655 cm^{-1}.

4-[2'-(1'-Methylindolyl)]pent-3-en-2-one (18).—In a 250-ml three-necked flask fitted with a serum cap, an addition funnel, and a reflux condenser was placed 5.0 g (0.023 mol) of butenoic acid **16** and 125 ml of dry ether. To this stirred solution, under nitrogen, 26.0 ml (0.061 mol) of 2.35 *M* methyllithium in ether was added by a syringe so as to maintain a gentle reflux. The mixture was stirred at room temperature for 45 min and then poured into a cold, saturated solution of ammonium chloride. After separating the ether layer, the aqueous layer was washed with ether and the combined organic solutions were washed with 10% aqueous sodium hydroxide and water, dried, and evaporated to give 4.61 g (93%) of an orange oil which showed essentially one spot on an analytical thin layer plate (4:1 benzene–ethyl acetate). The material was passed through a short Florisil column with benzene prior to use: nmr ($CDCl_3$) δ 2.11 (3 H, s), 2.43 (3 H, s), 3.52 (3 H, s), 6.14 (1 H, s), 6.42 (1 H, s), and 6.70–7.50 (4 H, m); ir ($CHCl_3$) 1675 (conjugated C=O), and 1590 cm^{-1}.

4-Methyl-4-[2'-(1-methylindolyl)]pentan-2-one (17).—A solution of lithium dimethylcopper(I) was prepared under nitrogen by adding 19.2 ml (0.045 mol) of 2.35 *M* methyllithium in ether *via* a syringe to a suspension of 4.28 g (0.0224 mol) of copper(I) iodide in 75 ml of dry ether at 0°. To the cold stirred suspension a solution of 2.39 g (0.011 mol) of pentenone **18** in 80 ml of dry ether was added and the mixture was stirred at 0° for an additional 30 min. The mixture was poured into an aqueous ammonium chloride solution and, after the ether layer separated, the aqueous layer was extracted with ether and the combined organic solutions were washed with water, dried, and evaporated to give 2.28 g (89%) of an orange liquid. The crude product showed essentially one spot (R_f considerably larger than that of the starting material) on an analytical thin layer plate (4:1 benzene-ethyl acetate). The nmr spectrum indicated that the only contaminants were those present in the starting material, *i.e.*, no 1,2 addition had occurred. The liquid was chromatographed on Florisil first with petroleum ether to remove impurities and then with benzene. Evaporation of the benzene solvent led to a pale yellow liquid whose spectra were in accord with the desired product: nmr ($CDCl_3$) δ 1.51 (6 H, s), 1.78 (3 H, s), 2.80 (2 H, s), 3.81 (3 H, s), 6.30 (1 H, s), and 6.90–7.70 (4 H, m); ir ($CHCl_3$) 1700 cm^{-1}.

Preparation of the oxime in the usual fashion gave white prisms from ethanol, mp 161–163°.

Anal. Calcd for $C_{15}H_{20}N_2O$: C, 73.73; H, 8.25; N, 11.47. Found: C, 73.77; H, 7.85; N, 11.53.

4-Methyl-2,4-di[2'-(1'-methylindolyl)]pentan-2-ol (19).—In a three-necked flask fitted with a serum cap, an addition funnel, and a reflux condenser was placed 2.06 g (0.016 mol) of 1-methylindole[22] in 40 ml of dry ether. To the stirred solution, under nitrogen, 10.0 ml (0.0156 mol) of 1.56 *M* *n*-butyllithium in hexane was added *via* a syringe and the mixture was then refluxed for 6 hr. After cooling to room temperature, a solution of 1.20 g (0.0052 mol) of ketone **17** in 20 ml of ether was added and the mixture was then refluxed for 3 hr. The solution was cooled and, after decomposing with saturated sodium sulfate solution, the ether layer was separated, the aqueous layer was extracted with ether, and the combined ether solutions were washed with water, dried, and evaporated. The residue was chromatographed on Florisil, first with petroleum ether to remove excess 1-methylindole and then with benzene. Evaporation of solvent gave 1.46 g (77%) of an orange glass which showed one major spot on an analytical thin layer plate. The crude alcohol could not be crystallized, sublimed, or chromatographed without extensive decomposition and was used in the subsequent reaction without further purification: nmr ($CDCl_3$) δ 1.27 (3 H, s), 1.34 (3 H, s), 1.43 (3 H, s), 2.52 (2 H, s), 2.72 (1 H, s), 3.84 (3 H, s), 3.90 (3 H, s), 6.23 (1 H, s), 6.28 (1 H, s), and 6.80–7.70 (8 H, m).

1,3,3,4-Tetramethyl-1-[2'-(1'-methylindolyl)]-1,2,3,4-tetrahydrocyclopent[*b*]indole (7) from Alcohol 19.—A mixture of 0.273 g (0.769 mmol) of alcohol **19** and 0.30 g of Amberlite IR-120 ion exchange resin in 10 ml of 95% ethanol was refluxed, under nitrogen, overnight. After cooling benzene was added and the mixture was dried and evaporated to give 0.246 g of a dark brown oil. Chromatography on Florisil with benzene afforded 0.201 g of an oil which on standing with ether–petroleum ether gave 0.042 g (16%) of a white solid, mp 159–161°, identical with dimer **7** on the basis of their mixture melting point and identical nmr spectra.

Registry No.—**1a**, 29124-06-9; **1b**, 29124-07-0; **2**, 29124-08-1; **3**, 29124-09-2; **4a**, 29124-10-5; **4b**, 29124-11-6; **5**, 29124-12-7; **6**, 29124-13-8; **7**, 29199-39-1; **8**, 29124-14-9; **12a**, 29124-15-0; **12b**, 29124-16-1; **12c**, 29124-17-2; **14a**, 29124-18-3; **14b**, 29124-19-4; **16**, 29124-20-7; **16** amide, 29124-21-8; **16** nitrile, 29124-22-9; **17**, 29199-40-4; **17** oxime, 29124-23-0; **18**, 29124-24-1; **19**, 29125-25-2.

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[22] K. T. Potts and J. E. Saxton, *J. Chem. Soc.*, **2641** (1954); W. E. Noland, W. C. Kuryla, and R. F. Lange, *J. Amer. Chem. Soc.*, **81**, 6010 (1959).