References and Notes

(1) (a) For preliminary communications on some of this work see R. A. Abramovitch, C. I. Azogu, and I. T. McMaster, *J. Am. Chem. Soc.*, **91**, 1219 (1969). R. A. Abramovitch and D. P. Vanderpool, *J. Chem. Soc., Chem. Commun.*, 18 (1977). (b) Present address: Department of Chemistry and Geology, Clemson University, Clemson, S.C. 29631.
(2) R. A. Abramovitch, T. Chellathurai, I. T. McMaster, T. Takaya, C. I. Azogu, and D. P. Vanderpool, *J. Org. Chem.*, **42**, 2914 (1977).
(3) R. A. Abramovitch, T. Chellathurai, W. D. Holcomb, I. T. McMaster, and D. P. Vanderpool, *J. Org. Chem.*, **42**, 2920 (1977).
(4) See, for example, I. M. McRobbie, O. Meth-Cohn, and H. Suschitzky, *J. Chem. Res. (S)*, 17 (1977), and references cited therein.
(5) If sulfur participation were involved the thermolysis would be expected to take place at a temperature below that (~130–150 °C) at which unassisted decomposition takes place. The nitrene would be by-passed and hence, also, formation of **7** and **8**, unless assisted and unassisted decompositions are delicately balanced. Formation of **10** rather than the sulfur analogue of **4** can be explained by the superior nucleophilicity of sulfur compared with the benzene ring toward the electrophilic singlet sulfonylnitrene.
(6) R. A. Abramovitch and R. G. Sutherland, *Fortschr. Chem. Forsch.*, **16**, 1 (1970).
(7) D. S. Breslow, M. F. Sloan, N. R. Newburg, and W. B. Renfrow, *J. Am. Chem. Soc.*, **91**, 2273 (1969).
(8) D. H. Hey and R. D. Mulley, *J. Chem. Soc.*, 2276 (1953).
(9) R. A. Abramovitch, E. M. Smith, B. Purtschert, P. C. Srinivasan, and G. M. Singer, *J. Chem. Soc. Perkin Trans. 1*, 2590 (1974).
(10) H. Watanabe, R. L. Gay, and C. R. Hauser, *J. Org. Chem.*, **33**, 900 (1968).
(11) J. I. G. Cadogan, *Acc. Chem. Res.*, **5**, 303 (1972).
(12) M. D. Sohon, *Am. Chem. J.*, **20**, 257 (1898).
(13) T. Cohen and J. Lipowitz, *J. Am. Chem. Soc.*, **86**, 5611 (1964).
(14) (a) G. Hafelinger in "The Chemistry of Amidines and Imidates", S. Patai, Ed., Wiley, New York, N.Y., 1975, pp 48–53; (b) D. Y. Curtin and L. L. Miller, *J. Am. Chem. Soc.*, **89**, 637 (1967).
(15) M. S. Ao and E. M. Burgess, *J. Am. Chem. Soc.*, **93**, 5298 (1971).
(16) Thermolysis of tertiary alkyl azides has been shown to involve the intermediacy of alkylnitrenes [R. A. Abramovitch and E. P. Kyba, *J. Am. Chem. Soc.*, **96**, 480 (1974)].
(17) R. A. Abramovitch, *Chem. Soc., Spec. Publ.*, **No. 24**, 323 (1970).
(18) J. H. Hall, F. E. Behr, and R. L. Reed, *J. Am. Chem. Soc.*, **94**, 4952 (1972).
(19) W. D. Emmons in "Heterocyclic Compounds with Three and Four Membered Rings", Part 1, A. Weissberger, Ed., Interscience, New York, N.Y., 1964, p 624.
(20) M. Ahmed and J. M. Vernon, *J. Chem. Soc., Perkin Trans. 1*, 2048 (1975).
(21) M. Renson, *Bull. Soc. Chim. Belg.*, **70**, 77 (1961).
(22) J. F. King, A. Hawson, B. L. Huston, L. J. Danks, and J. Komery, *Can. J. Chem.*, **49**, 943 (1971).
(23) K. A. Freeman and C. D. Ritchie, *J. Assoc. Off. Agric. Chem.*, **40**, 1108 (1957); *Chem. Abstr.*, **52**, 6067a (1958).
(24) H. Watanabe, C.-L. Mao, I. T. Barnish, and C. R. Hauser, *J. Org. Chem.*, **34**, 919 (1969).
(25) A. J. Neale, T. J. Rawlings, and E. B. McCall, *Tetrahedron*, **21**, 1299 (1965).
(26) F. Ullmann and G. Pasdemadjian, *Ber.*, **34**, 1150 (1901).
(27) H. Gilman and D. L. Esmay, *J. Am. Chem. Soc.*, **74**, 2021 (1952).
(28) J. B. Wright, *J. Heterocycl. Chem.*, **5**, 453 (1968).
(29) H. Meerwein, G. Dittmar, R. Goellner, K. Haffner, F. Mensch, and O. Steinfort, *Chem. Ber.*, **90**, 841 (1957).
(30) H. J. Scheifele, Jr., and D. F. de Tar, "Organic Syntheses", Collect. Vol. IV, Wiley, New York, N.Y., 1963, p 35.
(31) C. Krannich, *Ber.*, **33**, 3485 (1900).
(32) H. T. Clarke and E. E. Dreger, "Organic Syntheses", Collect. Vol. I, Wiley, New York, N.Y., 1958, p 495.
(33) R. Hayduck, *Justus Liebigs Ann. Chem.*, **174**, 350 (1874).
(34) D. A. Denton and H. Suschitsky, *J. Chem. Soc.*, 4741 (1963).
(35) To convert any disulfides and/or thiosulfonates to the corresponding sulfonic acid: H. V. Daeniker and J. Druey, *Helv. Chim. Acta*, **40**, 2148 (1957).

Addition and Annulation Reactions between Indoles and α,β-Unsaturated Ketones

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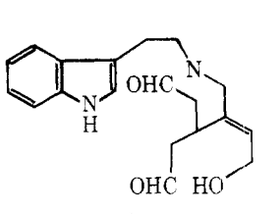
The structure of the addition product formed by acid-catalyzed reaction between 1,3-dimethylindole and mesityl oxide is shown to be **12**. Analogous products are formed with methyl vinyl ketone and benzalacetone as annulating agents. The reactions between methyl vinyl ketone and indole, 1,2-dimethylindole, and 3-methylindole are compared with these and with cyclization steps in the syntheses of the alkaloids villalstonine and vindorosine.

In a planned synthesis of strychnine Robinson and Saxton envisaged[1] the conversion of the dialdehyde **1** by a combination of Mannich and aldol-type condensations into the Wieland–Gumlich aldehyde **2**, already known to be convertible into strychnine. The conversion **1** → **2** would have exemplified the concept of annulation utilizing electrophilic addition reactions of indoles. Subsequently, this concept has been realized in Büchi's synthesis of vindorosine,[2] in which a key step is the cyclization of the *N*-acetylenone **3** with boron trifluoride etherate into the indoline **4**, and by our biomimetic synthesis of villalstonine (**5**) from macroline (**6**) and pleio-



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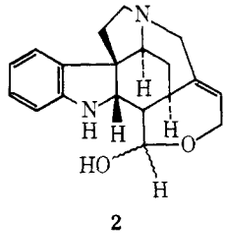

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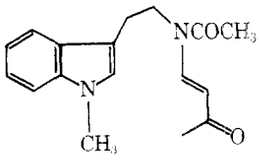

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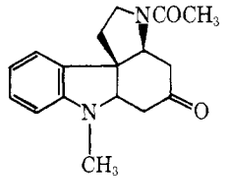

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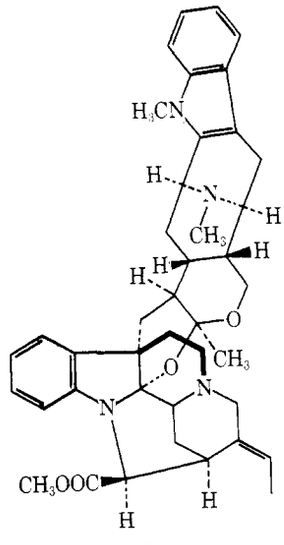

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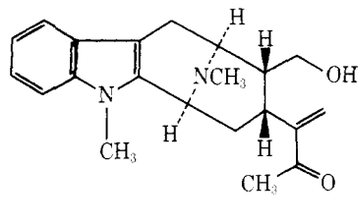

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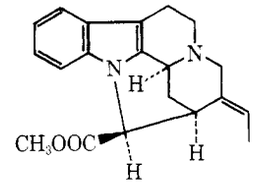

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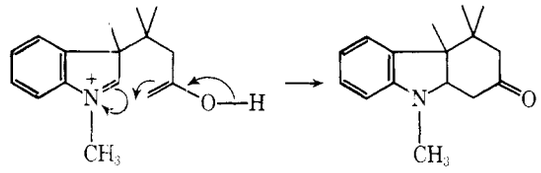
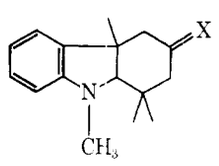
carpamine (7) with 0.2 N aqueous hydrochloric acid.[3] In these examples, a carbocyclic and two heterocyclic rings, respectively, are generated. In view of a surprising lack of general information on the scope and limitations of these potentially useful annulation reactions of indoles, and to compare them with the villalstonine synthesis, we have studied model reactions between indoles and enones.

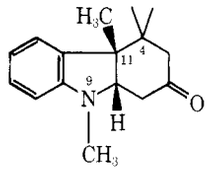
Cockerill, Robinson, and Saxton[4] had reported that 1,3-dimethylindole reacts with mesityl oxide in aqueous ethanolic hydrogen chloride to give the adduct $C_{10}H_{21}NO$. On the basis of color tests and reasoning by analogy they assigned structure **9** to this compound. This would presumably arise by cyclization of an intermediate **8**, which would be analogous to that involved in the vindorosine annulation **3** → **4**.[2] In 1958 Noland and D. N. Robinson proposed structure **10** for this adduct,[5]



8 **9**



10, X = O
11, X = H_2

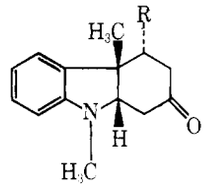


12

but this proposal was refuted in 1960 by B. Robinson and Smith,[6] who established the nonidentity of the deoxydihydro derivative of the adduct with compound **11** synthesized independently. We have, therefore, first reinvestigated this reaction and have established the validity of Cockerill, Robinson, and Saxton's original structure proposal.[4] Further, the stereochemistry shown in **12** has been determined. In the NMR spectrum, 3 H singlets at δ 0.82, 1.06, 1.46, and 2.64 are assigned to the two 4-methyl, the 11-methyl, and the 9-methyl groups, respectively. The aromatic protons give a 4 H multiplet centered at δ 6.9. The ring junction methine proton gives rise to a triplet-like doublet of doublets at δ 3.36 (J, $J \sim 4$ Hz), split by the two adjacent methylene protons, whose absorption is partly obscured by that of the N-methyl group, but appears like a doublet (J = 4 Hz). The remaining isolated pair of methylene hydrogens gives rise to an AB pattern centered at δ 2.26 (J_{AB} = 15 Hz, $\Delta\nu$ = 8 Hz).

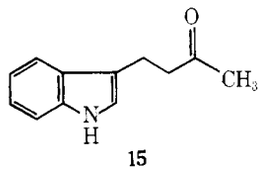
These spectral data clearly establish the gross structure **12** for this adduct, whose mode of formation is analogous to that of **4** from **3**.[2] Because **4** is a β,β′-diamino ketone, two of the three chiral centers generated are epimerizable and the stereoisomer obtained is the thermodynamically most stable one. One chiral center in **12** is similarly epimerizable, and the stereochemistry in this less constrained compound was therefore of interest. If the aliphatic rings were trans fused, models would suggest one possible pseudo-chair and two pseudo-boat conformations for the cyclohexanone ring. These would be expected to lead to ABX (J_{AB} ca. 15 Hz, $J_{AX} = J_{BX}$) patterns from the ring junction methine and adjacent methylene protons. These possibilities are clearly ruled out by the data given above, which are in accord with a cis fusion. Similar inferences have been made for other comparably generated ring systems by Stevens and his co-workers.[7] A preliminary x-ray crystallographic investigation of **12** is in accord with these stereochemical assignments, although the crystal structure has not yielded to satisfactory refinement below R = 0.14.[8]

The reaction can be extended to other α,β-unsaturated ketones; methyl vinyl ketone and benzalacetone with 1,3-dimethylindole give, respectively, adducts **13** and **14** as predominant reaction products. The structures are assigned on the basis of the closely analogous IR and NMR spectra to those of **12** (see Experimental Section). The pseudoequatorial configuration for the phenyl group in **14** is also assigned on the basis of NMR evidence. First, two of the aromatic protons are markedly shielded, in particular the 5 proton of the dihydroindole ring, which gives rise to a signal at ca. δ 5.8. This arises from mutual shielding of the two aromatic rings, possible only if the phenyl substituent is pseudoequatorial. The ring junction methine hydrogen gives rise to a triplet-like doublet of doublets at δ 3.52 (both J = 3 Hz). The proton adjacent to the phenyl ring gives rise to a clear doublet of doublets (J = 13, 4 Hz) centered at δ 3.28, which shows the phenyl ring to be pseudoequatorial; if it were pseudoaxial the pseudoequatorial hydrogen would, from Dreiding models, have approximately equal dihedral angles of ca. 45° with each neighboring methylene proton and would be expected to give rise to a second triplet-like doublet of doublets having J values of ca. 3 Hz.



13, R = H
14, R = C_6H_5

These reactions can be compared with some described by Szmuszkovicz.[9] Indole was reported to react with methyl vinyl ketone in acetic acid with or without added acetic anhydride to give the 3-substituted adduct **15**, but skatole (3-methylindole) with methyl vinyl ketone in acetic acid–acetic anhydride was said to give the 2-substituted adduct **16**;[9] no tetrahydrocarbazole analogous to **12** was obtained. Since the analytical and spectral data quoted in support of structure **16** are equivocal, we repeated the condensation. We obtained, as well as much recovered skatole, an oil having the same infrared spectral characteristics as reported by Szmuszkovicz,[9] but TLC of this substance showed it to contain at least seven compounds. The major product, isolated by preparative TLC, was an oily ketone, $C_{17}H_{19}NO$. A methyl ketone was inferred from the infrared (ν_{max} 1715 cm^{-1}) and NMR (δ 2.33, 3 H, s) spectra. The low-field NMR spectrum showed, as well as the four indolic protons, two coupled 1 H doublets at δ 6.60 and 6.10 (J = 6 Hz each). The spectrum also showed two other methyl group signals at δ 1.83 and 1.53. The base peak ion in the mass spectrum had formula $C_{13}H_{12}N$ and is believed to arise from the molecular ion by loss of C_4H_7O. These data taken together are consonant with structures **17** or **18** for this compound, although a distinction between the two is certainly not possible from the data at hand. The ultraviolet spectrum [λ_{max} 215 nm (ε 9200), 232 sh (8100), 252 sh (3500), 315 (3700)] is not easily correlated with spectra of model compounds (cf. ref 10); the rigid planar structures of **17** and **18** and the sub-



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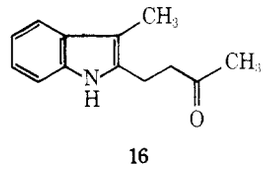

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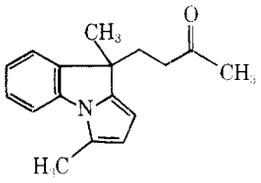
stitution patterns of the chromophoric groups prevent empirical comparison with other systems known to us. The compound must arise from 1 mol of skatole and 2 of the enone; various pathways can be envisaged for generating structures **17** and **18**.



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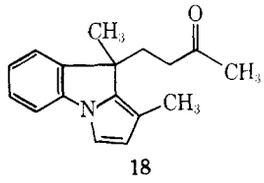

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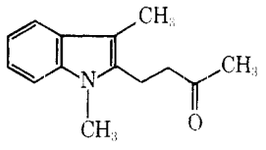
When 1,3-dimethylindole was treated with methyl vinyl ketone in acetic acid–acetic anhydride, one product, in addition to recovered starting material, was obtained. This compound, mp 72 °C, had molecular formula $C_{14}H_{17}NO$ and from examination of its spectra could be assigned structure **19**. The



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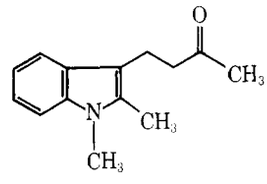

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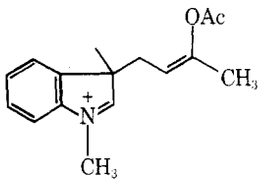
infrared spectrum shows a nonconjugated carbonyl group (ν_{max} 1715 cm^{-1}), which is assigned to a methyl ketone function from the 3 H methyl singlet at δ 2.10 in the NMR spectrum. The indolic *N*-methyl signal falls at δ 3.61 and the 3-methyl group at δ 2.25. The four methylene protons give a complex, extensive, and almost symmetrical multiplet centered at δ 2.8. These data are comparable with, but distinct from, those reported[11] for the isomer **20**; this compound was prepared in high yield from 1,2-dimethylindole and methyl vinyl ketone in acetic acid–acetic anhydride.[11] These results show that the thermodynamically most stable stereoisomers of hexahydrocarbazoles can readily be prepared from 1,3-disubstituted indoles and enones under acidic conditions in the absence of acylating agents such as acetic anhydride.

The reactions considered in this work can be interpreted together as follows. The annulation reactions, which take place in acidic alcohol solutions, involve intermediates such as **8**. In these reactions the initial electrophilic attack at C-3 of the indole is followed by ketonization, re-enolization, and ring closure (**8** → **9**). The reaction of 1,3-dimethylindole and methyl vinyl ketone in acetic acid–acetic anhydride presumably involves the acylation of an intermediate enol to give **21**, which may either revert to starting material or else undergo rearrangement by migration of an alkyl substituent from the indolic 3 position; in **21** migration of the allylic ester chain would preempt that of the methyl group (see ref 12). We may assume that in the former case (annulation in acidic alcohol solution) tautomerization of the initially produced enol to the isomeric enol which cyclizes is fast compared to alkyl group shift, and in the latter case (2 substitution in acetic acid–acetic anhydride) alkyl group migration is the faster process. The villalstonine annulation may be seen in this light; the initially produced iminium ion **22** is trapped by the hemiacetal OH group faster than alkyl group migration can take place. Note that 1,2-dimethylindole, however,[11] reacts with methyl vinyl ketone in acetic acid–acetic anhydride to give the simple 3-alkylated indole; here, the initial ion resulting from electrophilic attack at the unsubstituted 3 position loses the 3 proton and re-aromatizes with great rapidity, excluding alternative pathways. Skatole, a 3-substituted but N-unalkylated indole, undergoes complex reactions involving both N- and C-alkyl-



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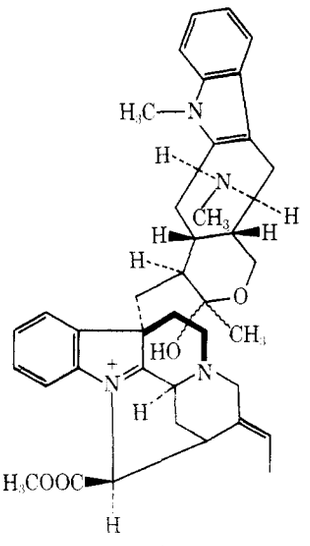

22

ation by the enone. In the cases of the simpler indoles, it appears that the reactions with enones, analyzed by modern separation techniques, may be much more diverse than has been recognized hitherto and would repay further investigation as a means of entry to novel indolic and other heterocyclic systems.

Experimental Section

Microanalyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Mich. Melting points were taken in a Thomas-Hoover capillary apparatus and are uncorrected. Nuclear magnetic resonance spectra were recorded on a Varian T-60 spectrometer. Infrared spectra were taken on a Perkin-Elmer 567 instrument. Analytical TLC plates used were Eastman UV-active 2-mm and 0.5-mm silica gel on glass. The indicator was a saturated solution of cerium(IV) sulfate in 50% aqueous sulfuric acid.

Condensation of 1,3-Dimethylindole and Mesityl Oxide. A mixture of 1,3-dimethylindole (0.40 g, 2.81 mmol), ethanol (1.65 mL), and water (0.35 mL) was stirred while concentrated sulfuric acid (1.0 mL) was added quickly. The temperature rose to 70 °C. More sulfuric acid (0.5 mL) was added, followed immediately by mesityl oxide (0.50 g, 5.1 mmol). After stirring for 5 min, the mixture was heated to 93 °C, and stirring was continued a further 5 min. The reaction mixture was made alkaline with concentrated ammonia and evaporated to dryness under reduced pressure. The residue was taken up in dichloromethane, the insoluble inorganic salts were filtered off by suction, and the dichloromethane solution was reduced in volume under reduced pressure. Preparative TLC (silica gel, benzene) of the residue gave two components. A faster moving minor component degraded rapidly on exposure to air, but the slower moving major component slowly crystallized to greenish-white needles on evaporation of the extracting solvent (ethanol). The product was purified by sublimation (80 °C, 0.03 mm), giving 0.421 g (61%) of off-white needles, mp 90 °C. Recrystallization from cyclohexane gave white rectangular prisms of 1,2,3,4,10,11-hexahydro-4,4,9,11-tetramethyl-2-oxocarbazole (**12**): mp 92–95 °C (lit.[4] 96–97 °C); NMR δ ($CDCl_3$) 0.82 (s, 3 H), 1.06 (s, 3 H), 1.46 (s, 3 H), 2.26 (dd, J = 14, 16 Hz, 2 H), 2.64 (s, 3 H), 2.72 (d, J = 4 Hz, 2 H), 3.36 (t, J = 4 Hz, 1 H), 7.32–6.46 (m, 4 H); IR (KBr) ν 2980, 2940, 2900, 2865, 2840, 2810, weak overtones at 1920 and 1882, 1705, 1591, 1481, 1450, with strongest bands below 1400 at 1350, 1292, 1020, 790, 744 cm^{-1}.

The product was also prepared several times by using a saturated HCl solution to catalyze the reaction, as recommended by Cockerill, Robinson, and Saxton.[4] The highest yield obtained was 30% of theory.

An attempt to catalyze the reaction with BF_3·Et_2O was unsuccessful.

Condensation of 1,3-Dimethylindole and Methyl Vinyl Ketone. To a solution of 1,3-dimethylindole (0.40 g, 2.81 mmol) in 83% aqueous ethanol (2 mL) was added quickly concentrated sulfuric acid (1.5 mL, temperature reached 70 °C) followed immediately by 3-buten-2-one (0.36 g, 5.1 mmol). The mixture was stirred 5 min without further heating and then made basic with concentrated ammonia. The mixture was concentrated to dryness under reduced pressure, and the product was taken up in dichloromethane. This solution was dried

(Na_2CO_3) and filtered. TLC (silica gel, benzene) showed nearly complete disappearance of 1,3-dimethylindole (R_f 0.58) and formation of two new compounds, the major component having an R_f of 0.37 (color with cerium(IV) reagent, red). Preparative TLC (silica gel, benzene) allowed separation of the desired product, pure by TLC, as a golden oil: NMR δ ($CDCl_3$) 1.42 (s, 3 H), 1.70–2.23 (complex, 4 H), 2.64 (d, J = 3 Hz, 2 H), 3.34 (t, J = 3 Hz, 1 H), 7.22–6.26 (complex multiplet, 4 H); IR (neat) ν (major features) 3040, 3020, 2950, 2920, 2860, 2805, 1713, 1600, 1485, 1295, 1192, 1105, 1015, 948, 743 cm^{-1}. Kugelrohr distillation (twice at 1 mm, 120–130 °C) yielded 163 mg (27%) of analytically pure 1,2,3,4,10,11-hexahydro-9,11-dimethyl-2-oxocarbazole (**13**). Anal. Calcd for $C_{14}H_{17}NO$: C, 78.10; H, 7.96; N, 6.51. Found: C, 78.12; H, 7.98; N, 6.42.

Condensation of 1,3-Dimethylindole with Benzalacetone. To 1,3-dimethylindole (0.81 g, 5.7 mmol) in ethanol (3.30 mL) and water (0.70 mL) was added concentrated sulfuric acid (ca. 2 mL, continuous stirring) followed immediately by benzalacetone (0.78 g, 5.3 mmol). After stirring for 10 min, the reaction mixture was made basic with concentrated aqueous ammonia and evaporated to dryness under reduced pressure, and the residue taken up in dichloromethane. Preparative TLC (silica gel, benzene) gave as the major component a brown oil. Purification by Kugelrohr distillation (1 mm, 140–160 °C) gave a highly viscous golden oil (452 mg, 29%). Preparative TLC (silica gel, benzene) of this showed three components: R_f 0.10 (color with Ce(IV), red), R_f 0.19 (colorless, turns grey on standing), and R_f 0.63 (1,3-dimethylindole; colorless, turns gray on standing). Extraction of the band at R_f 0.10 gave 302 mg of a crystalline material, still contaminated owing to overlap with the band at R_f 0.19. Recrystallization from cyclohexane[9] gave **14** as a white crystalline material, nearly pure (TLC): mp 125–139 °C; R_f 0.17; NMR δ ($CDCl_3$) 1.45 (s, 3 H), 2.66 (s, 3 H), 2.00–3.40 (complex, 5 H), 3.52 (dd, J = 3 Hz, 1 H), 5.70–5.84 (complex, 1 H), 6.34–7.34 (complex, 8 H). Two small absorptions at δ 1.32 and 2.74, much larger in the crude substance, are apparent singlets associated with the major impurity and were seen to decrease in intensity at each successive stage of purification. Final purification by sublimation (0.10 mm, 109–111 °C) gave white crystals, mp 122–134 °C, pure by TLC; IR (film) ν (major features) 3020, 2950, 2859, 2800, 1713, 1600, 1480, 1450, 1293, 1020, 750, 700 cm^{-1}. Anal. Calcd for $C_{20}H_{21}NO$: C, 82.44; H, 7.26; N, 4.81. Found: C, 82.41; H, 7.19; N, 4.77.

Reaction of 3-Methylindole with Methyl Vinyl Ketone in Acetic Acid–Acetic Anhydride. 3-Methylindole (655 mg, 5 mmol) was dissolved in a solution of glacial acetic acid (9.2 mL) containing acetic anhydride (3.1 mL). To this solution was added methyl vinyl ketone (700 mg, 10 mmol), and the reaction mixture was heated on the steam bath for 0.5 h. Water (50 mL) was then added and the solution heated for an additional 0.5 h. The reaction mixture was then neutralized with saturated sodium carbonate solution and extracted with chloroform (3 × 10 mL). The chloroform extracts were dried over anhydrous sodium carbonate, concentrated to a small volume under reduced pressure, and distilled. The major products were unreacted 3-methylindole and a small amount of a new product (75 mg), bp 170–200 °C (0.1 mm). This product was chromatographed on a silica gel preparative plate (0.25 mm, benzene) to yield 50 mg of an oil (pure by TLC) which had the following properties: UV (EtOH) λ_{max} 215 nm (ε 9200), 232 sh (8100), 252 sh (3500), 315 (3750); IR (neat) 3030, 2920, 1715 broad, 1455, 1345, 750 cm^{-1}; NMR ($CDCl_3$) δ 7.6–6.95 (4 H, m, aromatic protons), 6.60–6.10 (2 H, dd, J = 6 Hz), 2.33 (3 H, s), 1.83 (3 H, s, CH_3), 1.58 (3 H, s, CH_3); mass spectrum, m/e 253 (M^+), 182 (100); high-resolution mass spectrum, M^+ 253.147 (calcd for $C_{17}H_{19}NO$, 253.146), 182.097 (calcd for $C_{13}H_{12}N$, 182.096).

Preparation of 1,3-Dimethyl-2-(3′-oxobutyl)indole (19). 1,3-Dimethylindole (5 g, 35 mmol) was dissolved in a solution of glacial acetic acid (23 mL) containing acetic anhydride (8 mL). To this solution was added methyl vinyl ketone (7 g, 0.1 mmol). The solution was heated on the steam bath for 0.5 h, water (100 mL) added, and the solution heated for an additional 0.5 h. The reaction mixture was then neutralized with saturated sodium carbonate solution and extracted with chloroform (3 × 50 mL). The chloroform solution was dried over anhydrous sodium carbonate and concentrated to a small volume under reduced pressure. Distillation of the residue at 170 °C (0.01 mm) produced a yellow oil (1.2 g) slightly contaminated with impurities. Chromatography of this oil on silica gel preparative plates (0.5 mm, benzene) followed by excision of the major band produced 1 g of a yellow oil, substantially pure. Kugelrohr distillation at 140 °C (0.25 mm) produced a yellow oil which recrystallized on standing: mp 72 °C; IR (film) 2920, 1715, 1475, 1370, 1170, 1015, 745 cm^{-1}; NMR ($CDCl_3$) δ 7.5–6.90 (4 H, m, aromatic protons), 3.61 (3 H, s, NCH_3), 3.2–2.2 (4 H, m, $-CH_2CH_2$), 2.25 (3 H, s, indole 3 -CH_3), 2.10 (3 H, s, $COCH_3$). Anal. Calcd for $C_{14}H_{17}NO$: C, 78.10; H, 7.95; N, 6.50. Found: C, 78.06; H, 8.04; N, 6.53.

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Registry No.—**12,** 64884-70-4; **13,** 64884-71-5; **14,** 64884-72-6; **17/18,** 64885-16-1; **19,** 64884-73-7; 1,3-dimethylindole, 875-30-9; mesityl oxide, 141-79-7; 3-buten-2-one, 78-94-4; benzalacetone, 122-57-6; 3-methylindole, 83-34-1.

References and Notes

(1) R. Robinson and J. E. Saxton, *J. Chem. Soc.*, 2596 (1953).
(2) G. Büchi, K. E. Matsumoto, and H. Nishimura, *J. Am. Chem. Soc.*, **93,** 3299 (1971).
(3) D. E. Burke, J. M. Cook, and P. W. Le Quesne, *J. Am. Chem. Soc.*, **95,** 546 (1973).
(4) D. A. Cockerill, R. Robinson, and J. E. Saxton, *J. Chem. Soc.*, 4369 (1955).
(5) W. E. Noland and D. N. Robinson, *Tetrahedron*, **3,** 68 (1958).
(6) B. Robinson and G. F. Smith, *J. Chem. Soc.*, 4574 (1960).
(7) R. V. Stevens, L. E. DuPree, Jr., and P. L. Lowenstein, *J. Org. Chem.*, **37,** 977 (1972); R. V. Stevens, P. M. Lesko, and R. Lapalme, *ibid.*, **40,** 3495 (1975).
(8) Professor T. Brennan, Northeastern University, personal communication.
(9) J. Szmuszkovicz, *J. Am. Chem. Soc.*, **79,** 2819 (1957).
(10) Y. Chiang, R. L. Hinman, S. Theodoropulos, and E. B. Whipple, *Tetrahedron*, **23,** 745 (1967).
(11) R. L. Garnick and P. W. Le Quesne, *J. Am. Chem. Soc.*, submitted for publication.
(12) For chemical and isotopic studies of these reactions, see A. H. Jackson and A. E. Smith, *Tetrahedron*, **21,** 989 (1965); A. H. Jackson and P. Smith, *Chem. Commun.*, 264 (1967); A. H. Jackson, B. Naidoo, and P. Smith, *Tetrahedron*, **24,** 6119 (1968).