[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE UPJOHN CO.]

The Reaction of 3-Acylindoles with Grignard Reagents

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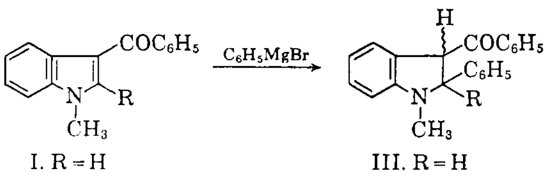
Reaction of 1-methyl- and 1,2-dimethyl-3-benzoylindole (I and II) with phenylmagnesium bromide gives 1-methyl- and 1,2-dimethyl-2-phenyl-3-benzoylindoline (III and IV), respectively. The structure of III has been proved by dehydrogenation to be 1-methyl-2-phenyl-3-benzoylindole which was also synthesized by an unequivocal method. Reaction of II with phenyllithium led to IV, 1,2-dimethyl-3-(methoxydiphenylmethyl)indole (V) and VII of unknown structure. 3-Benzoylindole and phenylmagnesium bromide gave 3-diphenylmethylene-3*H*-indole (VIII) while 1,2-dimethyl-3-acetylindole with the same reagent afforded 1,2-dimethyl-3-(α-methylenebenzyl)indole (IX). Structure X—3-(hydroxydiphenylmethyl)-1-methyl-α,α-diphenylindole-2-ethanol—is advanced for the condensation product which resulted from the reaction of the lithium derivative of 1,2-dimethylindole with benzophenone, and structure XII—1,1,3,3-tetraphenylpyrano[4,3-*b*]indole—for the product obtained by treatment of X with acid.

The present study was undertaken in order to synthesize indoles bearing a phenyl (or diphenyl)-hydroxymethyl substituent at position 3.



I. R = H
II. R = CH_3

III. R = H
IV. R = CH_3

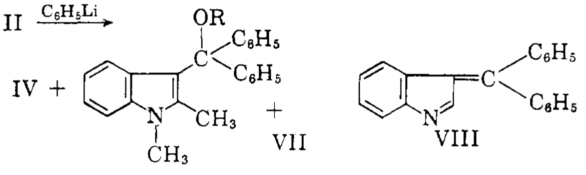
Condensation of 1-methyl-3-benzoylindole (I) (C═O band at 1620 cm.$^{-1}$) with phenylmagnesium bromide afforded 1-methyl-2-phenyl-3-benzoylindoline (III) instead of the expected tertiary carbinol. The structure of the indoline is supported by the characteristic ultraviolet spectrum (λ_{max} 248, plateau 288)[1] and the shift of the C═O band to 1678 cm.$^{-1}$.[2] Dehydrogenation of III with palladium gave 1-methyl-2-phenyl-3-benzoylindole, identical with an authentic sample prepared from 2-phenylindole by reaction with dimethylbenzamide and phosphorus oxychloride,[7] followed by alkylation with dimethyl sulfate.

Similarly 1,2-dimethyl-3-benzoylindole (II) gave 1,2-dimethyl-2-phenyl-3-benzoylindoline (IV).

Molecular models of I and II show considerable steric crowding of the carbonyl especially by the hydrogen atom at C-4. However, C-2 is relatively unhindered even when substituted by a methyl group. Thus, with phenylmagnesium bromide, 1,4-addition predominates.

Since phenyllithium is reported[3] to give 1,2- in preference to 1,4-addition, the reaction 1,2-dimethyl-3-benzoylindole (II) with this reagent was carried out. A mixture of three compounds was obtained. The first product was identical with 1,2-dimethyl-2-phenyl-3-benzoylindoline (IV). Structure V is proposed for the second product on the basis of ultraviolet and infrared spectra and the presence of a methoxyl group. Methyl ether formation very likely occurred during chromatography since the acetone used contained 0.05% methanol. Elucidation of the structure of the third product (VII) will be the subject of a future publication.

When this reaction was repeated using methanol-free acetone during chromatography and avoiding methanol during crystallization, 1,2-dimethyl-α,α-diphenylindole-3-methanol (VI) was obtained. Compound VI was unstable and started to decompose after a few days. Therefore, we did not have the opportunity to attempt the conversion of VI to V.



V. R = OCH_3
VI. R = H

The reaction of 3-benzoylindole with phenylmagnesium bromide gave a poor yield of a red compound the properties of which are consistent with 3-diphenylmethylene-3*H*-indole (VIII).[4]

The condensation of 1,2-dimethyl-3-acetylindole with phenylmagnesium bromide afforded a 30% yield of 1,2-dimethyl-3-(α-methylenebenzyl)indole

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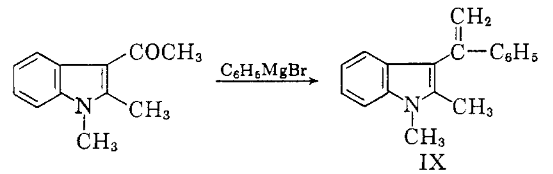
(1) *Cf.*, *e.g.*, deacetylspermostrychnine (data approximated from a curve): λ_{max} 250 (8000); 300 (4200), F. A. L. Anet and R. Robinson, *J. Chem. Soc.*, 2253 (1955); Ajmaline: λ_{max} 248 (8730); 292 (3070), and Ajmalidine: λ_{max} 248 (8420); 294 (2880), *Physical Data of Indole and Dihydroindole Alkaloids*, Lilly Research Laboratories (1960); Sandwicine: λ_{max} 246 (8130); 292 (2880), and Dihydrosandwicine: λ_{max} 246 (7940); 288 (2820), M. Gorman, *Tetrahedron*, 1, 328 (1957).

(2) It is possible to predict the stereochemistry of III and IV on the basis of the work of H. E. Zimmerman and T. W. Cutshall, *J. Am. Chem. Soc.*, **81**, 4305 (1959) and references therein, but we made no attempt to prove it experimentally.

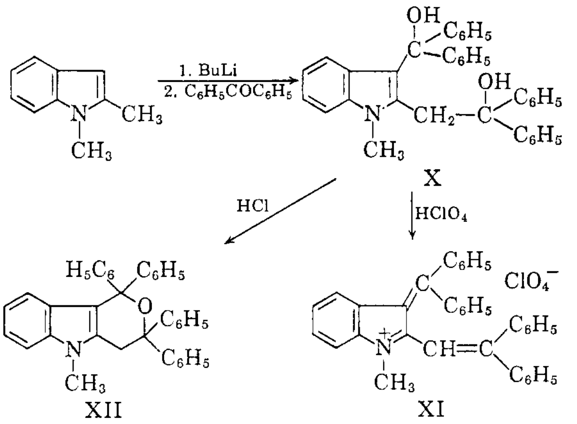
(3) M. S. Kharash and O. Reinmuth, *Grignard Reactions of Nonmetallic Substances*, Prentice Hall, New York, 1954, p. 223, and, *e.g.*, H. E. Zaugg, R. J. Michaels, and R. W. DeNet, *J. Org. Chem.*, **23**, 847 (1958), and ref. 3 cited therein.

(4) For a discussion of this class of compounds, *Heterocyclic Compounds*, Vol. 3, R. C. Elderfield, ed., J. Wiley and Sons, Inc., New York, 1952, p. 74.



(IX) which was also obtained in 6.4% yield with phenyllithium.

When 1,2-dimethylindole was treated with butyllithium and then condensed with benzophenone, a product resulted which clearly contained two units of benzophenone for one of the indole. The physical properties and the anticipated mode of reaction indicated structure X for this product.



Compound X could be titrated with perchloric acid in acetic acid giving rise to a deep red solution most likely due to structure XI.

When compound X was treated with an excess of hydrogen chloride the initially formed red solution afforded a colorless crystalline compound for which structure XII is proposed.

EXPERIMENTAL[5,6]

3-Benzoylindole was prepared as described previously[7]; m.p. 240–241.5°, yellow crystals (from acetone).[8] Ultraviolet spectrum showed λ_{max} 208 (39,025); 247 (14,750); pl 266 (10,325); 312 (11,900); in alkali: 211 (27,875); 248 (13,350); 270 (10,625); 314 (10,250). Infrared spectrum showed NH: 3100; C=O: 1600; C=C: 1580 sh, 1520, 1495; amide II: 1570; ring: 890, 867, 800, 790, 765, 755, 743, 710, 694.

1-Methyl-3-benzoylindole (I). A solution of potassium hydroxide (268 g.) in 1200 ml. of water was added to a solution of 3-benzoylindole (53.1 g., 0.24 mole) in 3300 ml. of acetone. Dimethyl sulfate (228 ml.) was added during 15 min. and the mixture was then stirred for 30 min. Acetone was then evaporated *in vacuo* at 50°. The resulting yellow precipitate was filtered, washed with water, and crystallized from 150 ml. of methanol to give colorless prisms; 50.8 g., m.p. 116–118.5°. The second crop amounted to 1.8 g. (yield: 93.2%). Ultraviolet spectrum showed λ_{max} 211 (37,500); 250 (15,775); f 272 (9425); 317 (16,050). No change in alkali. Infrared spectrum showed C=O: 1620; C=C: 1603 sh, 1575, 1525, 1485 sh; ring: 870, 795, 712, 688, 658.

Anal. Calcd. for $C_{16}H_{13}NO$: C, 81.68; H, 5.57; N, 5.95. Found: C, 81.98; H, 5.50; N, 5.80.

1-Methyl-2-phenyl-3-benzoylindoline (III). A solution of phenylmagnesium bromide (0.532 mole) in 700 ml. of ether was added under nitrogen during 20 min. to a solution of 1-methyl-3-benzoylindole (62.5 g., 0.266 mole) in 535 ml. of benzene and 1600 ml. of ether. The mixture was refluxed for 1 hr. and 45 min. It was then cooled in ice and decomposed with a solution of ammonium chloride (74.5 g.) in 650 ml. of water. The aqueous layer was extracted with ether (2 × 100 ml.). The combined organic solution was washed with dilute sodium thiosulfate solution, then with saturated salt solution, dried through sodium sulfate, and evaporated *in vacuo*[9] to give 100.7 g. of a yellow solid. It was crystallized from 100 ml. of methanol to give yellow needles melting at 116.5–120° (48.38 g.). The second crop melted at 117–119° (13.07 g.) and the third at 116–119° (2.71 g.). Yield: 77.6%.

A sample was sublimed at 115–120° (0.05 mm.) and then crystallized for analysis, m.p. 115.5–116°. Ultraviolet spectrum showed λ_{max} 248 (20,425); pl 288 (3725). Infrared spectrum showed C=O: 1678, 1645 sh; C=C: 1600, 1580 sh, 1495; C=N: 1253, 1210, 1155, 1020, 1010 sh; ring: 745, 732, 692, 675.

Anal. Calcd. for $C_{22}H_{19}NO$: C, 84.31; H, 6.11; N, 4.47. Found: C, 83.98; H, 5.73; N, 4.42.

Dehydrogenation of III to 1-methyl-2-phenyl-3-benzoylindole. A. *With palladium.* A mixture of 1-methyl-2-phenyl-3-benzoylindoline (1.0 g.), 10% palladium on carbon (0.6 g.) and 15 ml. of *p*-cymene was refluxed with stirring for 3 hr. and 40 min. It was then cooled, filtered, and the catalyst washed with benzene. The colorless filtrate was evaporated to dryness *in vacuo* to give an oil. It was dissolved in 2 ml. of methanol and allowed to stand overnight. The oily crystals were washed with petroleum ether (b.p. 30–60°) until free of oil to give 0.33 g. (33.2% yield) of the colorless indole melting at 125–127° (s119°). Crystallization from methanol gave plates, m.p. 129.5–131°.[10] Ultraviolet spectrum showed λ_{max} 210 (40,100); f 224 (27,700); 258 (17,100); f 280 (14,000); 325 (9,940). Infrared spectrum showed C=O: 1613; C=C: 1578, 1535 sh, 1525, 1491; ring: 880, 753, 720, 685.

Anal. Calcd. for $C_{22}H_{17}NO$: C, 84.86; H, 5.50; N, 4.50. Found: C, 84.92; H, 5.62; N, 4.16.

B. *With Magnesol.* 1-Methyl-2-phenyl-3-benzoylindoline (0.2 g.) was dissolved in 200 ml. of petroleum ether (b.p. 30–60°) and filtered through a layer of Magnesol (7 g.) whereupon it was absorbed quantitatively to give a yellow layer. The Magnesol was allowed to stand at room temperature for 72 hr. The brown cake was extracted with 100 ml. of acetone and evaporated *in vacuo* to give 0.138 g. of yellow gum. Crystallization from methanol gave 68.3 mg. melting

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(5) Melting points were taken in a capillary tube and are uncorrected. Ultraviolet spectra (recorded in mμ) were determined in 95% ethanol using a Cary spectrophotometer Model 14. Infrared spectra (recorded in cm.$^{-1}$) were determined in Nujol using a Perkin-Elmer recording infrared spectrophotometer Model 21. Skellysolve B is commercial hexane, b.p. 60–70°, made by Skelly Oil Co., Kansas City, Mo. Florisil is a magnesia–silica gel adsorbent, and Florex is natural Florida fullers earth; both are manufactured by Floridin Co., Tallahassee, Fla. Magnesol is magnesium silicate formerly manufactured by Westvaco-Chlor-Alkali Division, Food, Machinery and Chemical Corp., New York.

(6) The author is indebted to Professors D. J. Cram, M. S. Newman, and E. vanTamelen for stimulating discussions, to Mr. W. A. Struck and his associates for microanalyses, to Mr. M. F. Grostic and Mr. J. E. Stafford for infrared and ultraviolet data, and to Mr. L. G. Laurian for laboratory assistance.

(7) W. C. Anthony, *J. Org. Chem.*, **25**, 2079 (1960).

(8) Oddo and Sessa reported 3-benzoylindole as a red compound melting at *ca.* 170°, Beilstein, **21**, 318.

(9) This type of work-up was used throughout the experimental.

(10) W. Borsche and A. Klein, *Ann.* **548**, 64 (1941) prepared this compound by the reaction of 1-methyl-2-phenyl-3-indolecarboxylic acid chloride with aluminum chloride and benzene; m.p. 130°.

at 121–126°. Further recrystallization afforded 35.3 mg., m.p. 130–131°. This compound was identical with the sample obtained by palladium-on-charcoal dehydrogenation (mixed m.p., infrared, ultraviolet).

2-Methyl-3-benzoylindole. 2-Methylindole (53.1 g., 0.406 mole) was added with stirring to a solution containing 132 g. (0.886 mole) of *N,N*-dimethylbenzamide and 84.9 g. (0.554) mole) of phosphorus oxychloride. The resulting yellow solution was heated on the steam bath until the internal temperature reached 45°. When the temperature rose to 80°, ice bath cooling was applied. The temperature rose to 145° and then it fell to 100°; the mixture was heated on the steam bath for 2 hr. The deep brown solution was cooled to room temperature and a solution of sodium hydroxide (145 g.) in 1305 ml. of water was added during 45 minutes. The temperature was kept below 40° by ice cooling. A heavy orange oil resulted. Water (400 ml.) was added and stirring was continued for 45 min. whereupon a precipitate was obtained. It was filtered and washed well with water. The yellow solid was crystallized from *ca.* 800 ml. of ethanol, filtered, and washed with ether to give almost colorless plates (72 g.) melting at 164.5–166.5° (possibly ether solvate). The second crop amounted to 8.06 g. melting at 185.5–186.5°. The third crop, 1.38 g., m.p. 186–187°. The three crops were combined and recrystallized from 500 ml. of ethanol to give 76.4 g. (80% yield) melting at 185–186°.

The analytical sample was prepared in ethanol as colorless needles, m.p. 185–186°. Ultraviolet spectrum showed λ_{max} 211 (40,825); 246 (15,000); 272 (8825); 318 (9150). No change in alkali. Infrared spectrum showed NH: 3150, 3120 sh, 3080 sh; C=O: 1595, 1580 sh; C=C: 1565, 1525 sh, 1490; C—N: 1220, 1205 sh; ring: 757, 740, 720, 695.

Anal. Calcd. for $C_{16}H_{13}NO$: C, 81.68; H, 5.57; N, 5.95. Found: C, 81.63; H, 5.69; N, 5.96.

1,2-Dimethyl-3-benzoylindole (II). A solution of potassium hydroxide (299 g.) in 1340 ml. of water was added to a solution of 2-methyl-3-benzoylindole in 2680 ml. of acetone. Two layers resulted. Dimethyl sulfate (254 ml.) was added during 10 min. to the well stirred mixture, and stirring was continued for 1 hr. Most of the acetone was evaporated *in vacuo* at 50°. The resulting precipitate was filtered and washed with water. It was crystallized from *ca.* 500 ml. of methanol to give 60 g. melting at 139–140°. Recrystallization did not alter the melting point. Ultraviolet spectrum showed λ_{max} 213 (37,825); 247 (14,125); pl 272 (8675); f 284 (7200); 332 (9875). No change in alkali. Infrared spectrum showed C=O: 1612, 1600 sh; C=C: 1574, 1520, 1470; C—N: 1225, 1170, 1055, 1015; ring: 747, 720, 692.

Anal. Calcd. for $C_{17}H_{15}NO$: C, 81.90; H, 6.06; N, 5.62. Found: C, 81.79; H, 5.96; N, 5.52.

1,2-Dimethyl-2-phenyl-3-benzoylindoline (IV). Phenylmagnesium bromide (0.1 mole) in 150 ml. of ether was added during 15 min. under nitrogen with stirring to a solution of 1,2-dimethyl-3-benzoylindole (12.5 g., 0.05 mole) in 200 ml. of benzene. The mixture was refluxed for 3 hr. and worked up as before[9] to give 18.6 g. of a dark brown oil. The oil was refluxed with 50 ml. of petroleum ether (b.p. 30–60°) to give 11 g. of insoluble residue (A). The petroleum-ether solution was passed through a column of Florex (7.5 g.) and the resulting pale yellow solution was evaporated to give 4.0 g. of an oil (B).

The solid A (10.8 g.) was dissolved in 50 ml. of benzene and chromatographed on 1080 g. of Florisil. Elution with 1.5 l. of 2% acetone–Skellysolve B gave 0.19 g. of diphenyl. Further elution with 3% acetone–Skellysolve B gave 7.54 g. of a product which was crystallized from petroleum ether (30–60°) to give a total of 1.7 g. of yellow rods melting in the range of 135–140°.

The analytical sample was prepared from ether–petroleum ether (b.p. 30–60°), m.p. 139–140°. Ultraviolet spectrum showed λ_{max} 249 (23,200); 294 (3500). Infrared spectrum showed C=O: 1678; C=C: 1603, 1580, 1498; ring: 857, 848, 840, 832, 753, 736, 724, 713, 695, 683.

Anal. Calcd. for $C_{23}H_{21}NO$: C, 84.37; H, 6.47; N, 4.28; neut. equiv. 327.41. Found: C, 84.20; H, 6.25; N, 4.37; neut. equiv. ($HOAc–HClO_4$): 343.

The oil B (4 g.) was dissolved in 20 ml. of benzene and chromatographed on 400 g. of Florisil in the same manner as described above to give 0.8 g. of material melting at 135–139°. Total amount of product: 2.5 g. (15.4% yield).

Condensation of 1,2-dimethyl-3-benzoylindole with phenyllithium. A solution of phenyllithium was prepared from 2.94 g. (0.42 g.-atom) of lithium and 31.4 g. (0.2 mole) of bromobenzene in 150 ml. of ether. A solution of 1,2-dimethyl-3-benzoylindole (24.9 g., 0.1 mole) in 200 ml. of benzene was added under nitrogen during 30 min. with stirring. The resulting brown solution was refluxed for 3 hr. and worked up as before[9] to give an oily solid. Trituration with ether afforded 3.1 g. of an orange solid melting at 282–292°. Crystallization from dimethylformamide afforded yellow crystals of VII melting at 295–297.5°.

Since infrared indicated residual dimethylformamide, the compound was sublimed at 270° (0.1 mm.) to give yellow prisms, m.p. 287–290°. Ultraviolet spectrum showed sh 288 (5900); sh 296 (6100); broad max. 350 (7800). Infrared spectrum showed C=C: 1600, 1582, 1565, 1530, 1495; ring: 785, 765, 757, 735, 715, 695.

Anal. Calcd. for $C_{23}H_{19}N$: C, 89.28; H, 6.19; N, 4.53; N—CH_3, 4.9. Found: C, 89.15; H, 6.26; N, 4.52; N—CH_3, 4.7.

The original ethereal filtrate was evaporated to dryness and the residue (34 g.) was dissolved in benzene and chromatographed on 3400 g. of Florisil.

Elution with 10 l. of 3% acetone–Skellysolve B gave 1.07 g. diphenyl. Further elution with 7 l. of the same solvent gave 4.90 g. of material which on crystallization from methanol afforded 0.38 g. melting at 128–134°. Recrystallization gave pale yellow rods, m.p. 138–139°. This compound was identical to 1,2-dimethyl-2-phenyl-3-benzoylindoline (IV) prepared previously by the condensation of 1,2-dimethyl-3-benzoylindole with phenylmagnesium bromide (confirmed by analyses, infrared and ultraviolet spectra).

Further elution with 8 l. of the same solvent gave 2.72 g. of solid which on trituration with ether gave a solid melting at 285–290°. It was identical (mixed m.p.) with VII. Further elution with 4 l. gave fractions (2.705 g.) which were discarded. Elution with 17 l. gave 8.62 g. of an oil which solidified after standing for about one week. On trituration with ether–petroleum ether (30–60°) in 1:1 ratio 3.6 g. of V was obtained, m.p. 131.5–134°. It was dissolved in 50 ml. of ether and 50 ml. of methanol and concentrated until crystallization began. Pale yellow needles were obtained; 3.3 g., m.p. 139–140°. Further recrystallization raised the m.p. to 139.5–140.5°. Ultraviolet spectrum showed λ_{max} 200 (40,500); f 276 (6850); 284 (7700); 292 (7250). Infrared spectrum showed C=C: 1605, 1597, 1585, 1532, 1510 sh., 1505 sh, 1492 sh; C—O: 1075, 1053, 1027; ring: 880, 767, 735, 703, 687, 670.

Anal. Calcd. for $C_{24}H_{23}NO$: C, 84.42; H, 6.79; N, 4.10; OCH_3, 9.00. Found: C, 84.63; H, 6.87; N, 4.03; OCH_3 (gravimetric), 9.77.

Preparation of 1,2-dimethyl-α,α-diphenylindole-3-methanol (VI). This reaction was repeated on the same scale as described above but methanol free acetone (purified by boiling with potassium permanganate) was employed for chromatography. Diphenyl was eluted with Skellysolve B and compound VII with 2% and 3% acetone–Skellysolve B. Elution with 5% acetone–Skellysolve B (32 l.) gave 11.86 g. of an oil which was dissolved in 20 ml. of benzene and rechromatographed on 120 g. of Florisil. Elution with 230 ml. of Skellysolve B gave fractions which were discarded. Further elution with 6.2 l. of Skellysolve B gave 3.1 g. of a yellow solid which could not be crystallized; m.p. 70–80°. Ultraviolet spectrum showed λ_{max} 216 (33,100); f 244 (11,350); f 256 (8500); f 264 (8000); 275 (7900); 284 (7800); 292 (6750); 330 impurity (2450). Infrared spectrum showed OH: 3540, 3450; impurity: 1650W; C=C: 1610, 1600, 1575, 1530, 1495 sh; C—O: 1053, 1025, 998; ring: 755 sh, 735, 692.

Anal. Calcd. for $C_{23}H_{21}NO$: C, 84.37; H, 6.47; N, 4.28. Found: C, 84.15; H, 6.45; N, 4.03; OCH_3, 0.

Condensation of 3-benzoylindole with phenylmagnesium bromide. A warm solution of 3-benzoylindole[7] (8.35 g., 0.376 mole) in 200 ml. of tetrahydrofuran was added during 10 min. to phenylmagnesium bromide prepared from magnesium (2.9 g., 0.119 g.-atom) and bromobenzene (17.7 g., 0.113 mole) in 100 ml. of ether. The dark brown solution was refluxed for 3.5 hr. It was then allowed to stand overnight and worked up as before.[9] The resulting brown oil (13.3 g.) showed a band at 1600 cm.$^{-1}$ (m) probably due to the starting material. Therefore the oil was dissolved in 150 ml. of benzene and added to the Grignard reagent prepared from magnesium 4.86 g., 0.2 g.-atom) and bromobenzene (29 g., 0.19 mole) in 200 ml. of ether. Ether was evaporated and the resulting benzene solution refluxed for 16.5 hr. The mixture was worked as above. The resulting brown oil (14.5 g.) showed a strong band at 1602 cm.$^{-1}$ The oil was dissolved in 35 ml. of benzene and was chromatographed on 420 g. of Florisil.

Elution with Skellysolve B (2 l.) gave 2.19 g. of diphenyl. Elution with 1% acetone–Skellysolve B (4750 ml.) gave 5.613 g. which was rechromatographed to give 0.70 g. of the same material as obtained below. Elution with 3% acetone–Skellysolve B (2.5 l.) gave 1.19 g. which was crystallized from methanol to give dark red needles of 3-diphenylmethylene-3*H*-indole (VIII), m.p. 215–217° (s 212°). The analytical sample was prepared from ether, m.p. 220–221°. Ultraviolet spectrum showed λ_{max} f 228 (14,000); 269 (21,000); 390 (9800). Infrared spectrum showed =CH: 3040; C=N and C=C: 1588, 1573, 1547, 1500.

Anal. Calcd. for $C_{21}H_{15}N$: C, 89.65; H, 5.37; N, 4.98. Found: C, 89.97; H, 5.44; N, 4.16.

Synthesis of 1,2-dimethyl-3-(α-methylenebenzyl)indole (IX). A. *Condensation of 1,2-dimethyl-3-acetylindole with phenylmagnesium bromide.* A solution of phenylmagnesium bromide (0.2 mole in 66 ml. of ether) was added with stirring during 25 min. to a solution of 1,2-dimethyl-3-acetylindole (18.72 g.; 0.1 mole) in 200 ml. of benzene without cooling. The mixture was refluxed for 2.5 hr. and worked up as before[9] but using methylene chloride for extraction. The resulting brown oil (25 g.) was extracted with boiling petroleum ether (b.p. 30–60°). The undissolved material (*ca.* 2 g.) was discarded and the solution was evaporated to dryness and then distilled from an oil-jacketed flask at 0.05 mm.

The fraction, b.p. 155–200° (12.75 g.), was triturated with petroleum ether (b.p. 30–60°) to give a solid which was crystallized from the same solvent and afforded two crops (total 7.51 g.; 30.3% yield) of yellow crystals melting at 81.5–82°.

This compound was identical with IX prepared by the phenyllithium reaction described below (mixed m.p. determination).

B. *Condensation of 1,2-dimethyl-3-acetylindole with phenyllithium.* A solution of 1,2-dimethyl-3-acetylindole (18.72 g.; 0.1 mole) in 200 ml. of benzene was added during 30 min. under nitrogen with stirring to a solution of phenyllithium prepared from bromobenzene (31.4 g.; 0.2 mole) and lithium (2.94 g.; 0.42 g.-atom). The resulting brown solution was refluxed for 2 hr. and worked up as before[9] to give 29.7 g. of an oil. It was dissolved in minimum of benzene and chromatographed on 2970 g. of Florisil.

Elution with 5 l. of Skellysolve B and 9 l. of 1% acetone–Skellysolve B gave 2.47 g. of material which was discarded. Further elution with 5% acetone–Skellysolve B (4 l.) gave 5.55 g. of a solid which was crystallized from petroleum ether (b.p. 30–60°) to give 1.58 g. (6.4% yield) of IX as small colorless prisms in two crops; m.p. 79.5–80°.

A sample was recrystallized for analysis from petroleum ether (b.p. 30–60°), m.p. 79.5–80°. Ultraviolet spectrum showed λ_{max} 227 (37,800); 285 (9200); f 290 (9100). Infrared spectrum showed C=C: 1610, 1605, 1575, 1535, 1495; methylene: 895; ring: 783, 766, 747, 720, 698.

Anal. Calcd. for $C_{18}H_{17}N$: C, 87.41; H, 6.93; N, 5.66. Found: C, 87.46; H, 6.99; N, 5.48.

Condensation of lithium-1,2-dimethylindole with benzophenone. A solution of butyllithium (24.8 g., 0.4 mole) in 616 ml. of hexane was added during 20 min. under nitrogen with stirring to a solution of 1,2-dimethylindole (58.0 g., 0.4 mole) in 600 ml. of ether. The solution was refluxed for 3 hr. It was cooled to room temperature and a solution of benzophenone (72.8 g., 0.4 mole) in 600 ml. was added during 25 min. The resulting dark solution was refluxed for 2.5 hr. and worked up as before[9] to give 135.6 g. of an oil. Trituration with hot Skellysolve B (200 ml.) afforded X as a yellow solid melting at 187.5–190° (31.22 g. or 30% yield).

The product was crystallized from benzene–Skellysolve B; clusters of colorless needles, m.p. 193.5–194.5° (immersed at 165°). Ultraviolet spectrum showed λ_{max} f 258 (6050); 288 (9500); f 292 (9400). Infrared spectrum showed OH: 3400, 3240 sh, 3160; C=C: 1605, 1587, 1575 sh, 1525 sh, 1497 sh, 1490; aromatic: 783, 777, 760, 752, 732, 700, 662, 648.

Anal. Calcd. for $C_{36}H_{31}NO_2$: C, 84.84; H, 6.13; N, 2.75; act. H, 2; N.E., 509.62. Found: C, 84.95; H, 6.20; N, 2.80; act. H, 1.78; N.E. (HOAc–$HClO_4$), 498.

Conversion of X → XII. One gram of X was dissolved in 10 ml. of benzene and the solution was treated with 15 ml. of saturated ethereal hydrogen chloride solution. The solution turned red and an oil settled out. The mixture was evaporated *in vacuo* at room temperature and the residue was kept *in vacuo* overnight. The resulting oily red solid was dissolved in *ca.* 5 ml. of acetone. Crystallization started in about 2 minutes and was allowed to proceed for 0.5 hr. The product 5-methyl-1,1,3,3-tetraphenylpyrano[4,3-*b*]indole (XII), was filtered and washed with minimum of cold acetone; 0.35 g. (33% yield), m.p. 213–214°. Recrystallization from benzene-petroleum ether (b.p. 30–60°) afforded leaflets, m.p. 213-214.5° (dec.). Ultraviolet spectrum showed f 220 (42,700); f 270 (6450); f 278 (7750); λ_{max} 285 (8550); 293 (8200); f 300 (4850). In acid (the compound was dissolved in ethanol and made up to 3*N* sulfuric acid): f 232 (24,450); 259 (10-800); 272 (10, 100); f 292 (7250); 328 (4900); plateau 344 (4550); 455 (6450). Infrared spectrum showed: No OH; =CH: 3030; C=C: 1618, 1600, 1568, 1496; C—O: 1060, 1045, 1015, 986; ring: 779, 757, 745, 728, 707, 693.

XII did not take up hydrogen in either ethanol (35 min.) or acetic acid (30 min.) in presence of 30% palladium on carbon.

Anal. Calcd. for $C_{36}H_{29}NO$: C, 87.95; H, 5.94; N, 2.85. Found: C, 87.96; H, 6.07; N, 2.94; active H: 0.07.

When this reaction was repeated on a larger scale (16.2 g. of X) the yield of XII was 20%.

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