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Structure Elucidation of Some Products Obtained by Acid-Catalyzed Condensation of Indole with Acetone

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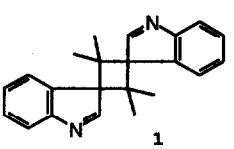
Abstract: Acid-induced condensation reactions between indole and acetone have been investigated under different reaction conditions. The structures of the 2:2 condensation products have been elucidated and supported by independent syntheses. A new acid-induced annulation reaction has been utilized in the preparation of cyclopentano[*b*]indoles.

Condensations of indoles and carbonyl compounds yield a wide variety of products[1-10], albeit several of the structures originally suggested have later been shown to be incorrect. For example, the structure of a 2:2 product from acetone and 2-methylindole was at first[11] suggested to be **1**, but in fact, the correct structure is **2b**, as shown by Noland[3] (*cf.* **Scheme I**). The intermediates such as the indolenine **3** and the vinylindole **4** can be isolated in certain cases[12].



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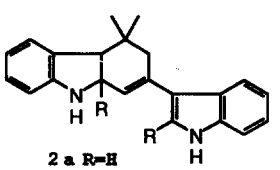
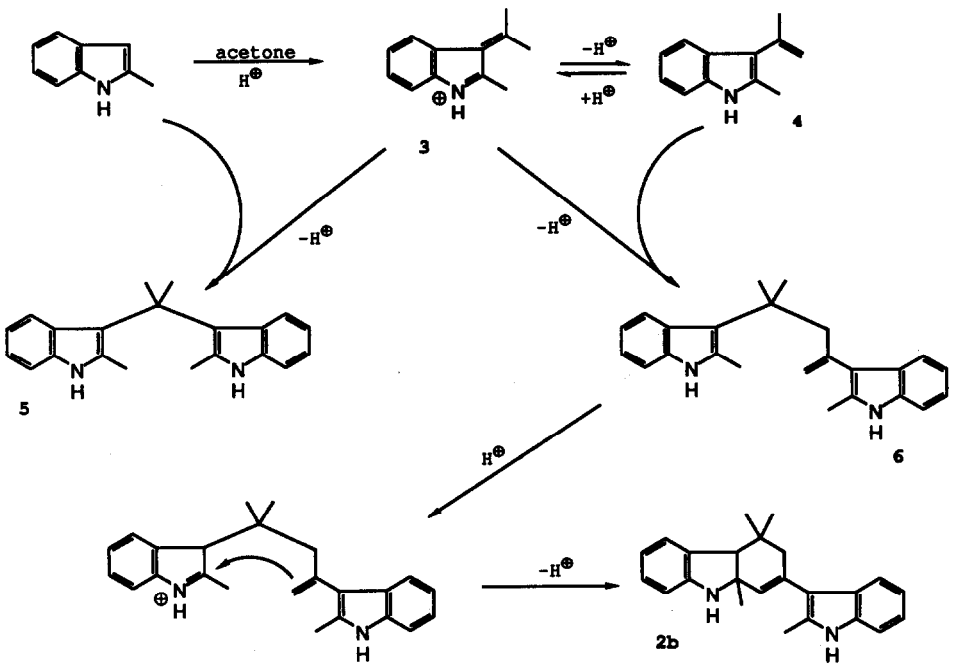
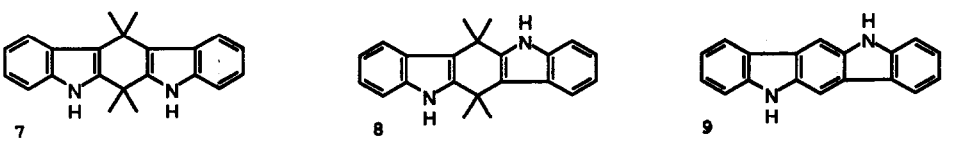


2 a R=H
b R=CH_3

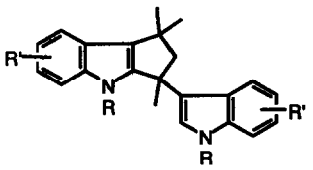


Scheme I

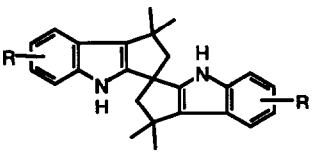
The product pattern from condensations of indole and acetone in ethanolic hydrochloric acid is complex,[13] and in several comprehensive studies[1-3] Noland isolated two 2:2 ($C_{22}H_{22}N_2$) condensation products as well as three 2:3 ($C_{25}H_{26}N_2$) products. Complicated chromatographic separations were sometimes necessary. One of the 2:2 condensation products was correctly assigned[3], (structure **2a**), but the second one, usually obtained in modest yield by condensation of indole and acetone using maleic acid as a catalyst[4], was at the time considered to be 6,12–dihydro-6,6,12,12-tetramethyl-indolo[2,3–*b*]carbazole (**7**).



A more likely candidate would be the isomer 6,12-dihydro-6,6,12,12-tetramethyl-indolo[3,2–*b*]carbazole (**8**) in view of the facile transformation of 3,3'-diindolylmethane into indolo[3,2-*b*]carbazole (**9**) demonstrated by Bergman[14,15]. However, after inspection of the ^{1}H NMR spectrum both alternatives could be immediately rejected.

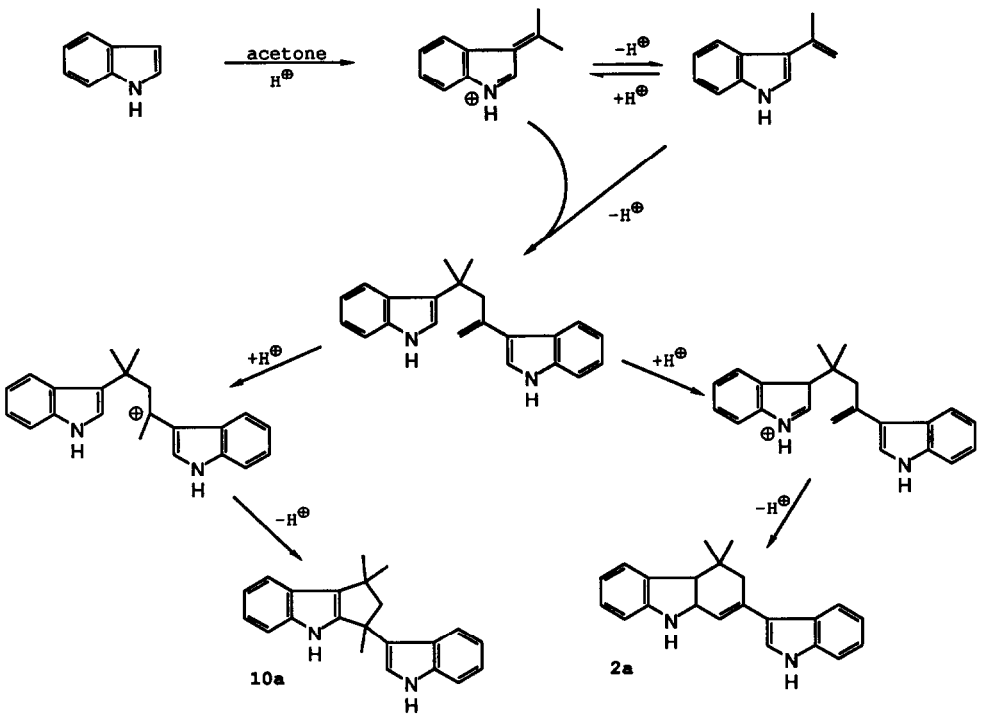


10 a R=H, R'=H
b R=CH_3, R'=H
c R=$SO_2C_6H_5$, R'=H
d R=H, R'=7-CH_3
e R=H, R'=5-Br

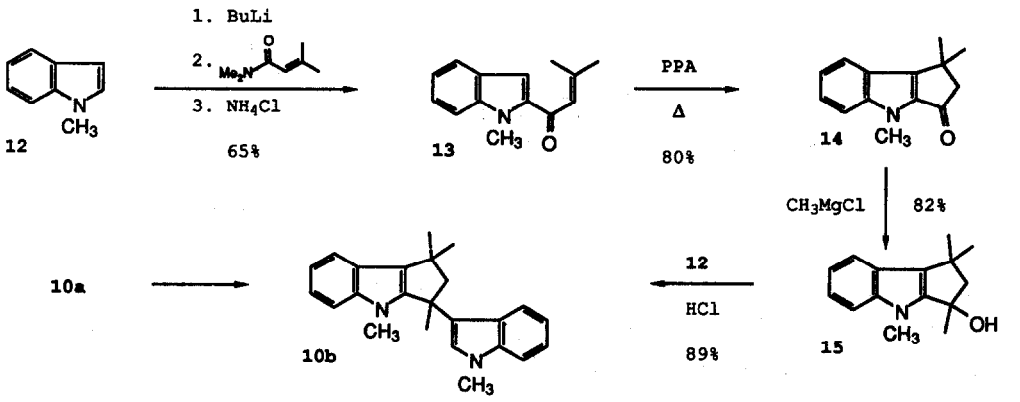


11 a R=H
b R=7-CH_3
c R=5-Br

Based on the analysis showed in **Scheme II**, structure **10a** was suggested[16]. Simultaneously[16] one of the 2:3 condensation products was suggested to have the spiro structure **11a** rather than the one previously[3] suggested.

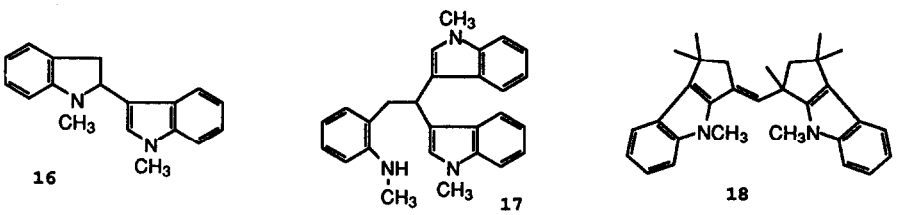


Scheme II



Scheme III

The proposed structure **10a** has now been proven to be correct through an independent synthesis (**Scheme III**), which in the key step (**13** → **14**) involves an acid-induced annulation recently developed[17] by Bergman and Venemalm. In the final step the tertiary alcohol **15** (on condensation with equimolar amounts of *N*-methylindole (**12**) in dilute methanolic hydrochloric acid) was converted to **10b** in 89 % yield. A by-product with the unusual structure **18**, *i. e.* a dimer of **16**, was isolated in 5% yield.[18] The condensation with *N*-methylindole is faster than the acid induced oligomerization of **12** since the reaction yielded neither the dimer **16** nor the trimer **17**.



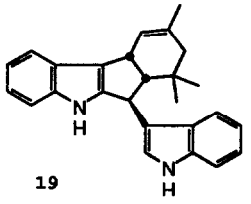
The final correlation between **10a** and **10b** was obtained simply by methylation of the anion of **10a** with methyl iodide. Treatment of the anion of **10a** with benzenesulfonyl chloride gave **10c**, thereby proving the structure of a product recently[19] obtained by interaction of 3–isopropenyl-*N*-benzensulfonylindole with $AlCl_3$.

The fact that the acetone-indole 2:2 dimer **10a** can be considered[20] as a simplified analog of the recently isolated[21a] and synthesized[21b-24] indole alkaloid yuehchukene (**19**) has inspired some efforts to develop a cleaner and higher-yielding route to **10a**. For instance, it was found that treatment of indole with trifluoroacetic acid in refluxing acetone gave **10a** in 70% yield.

Substituted derivatives of **10a** like 5,5'-dibromo and 7,7'-dimethyl can be similarly prepared. In all these condensations 3,3'-diindolyl dimethylmethanes (readily isolable) are rapidly formed and then slowly (particularly for the bromo-substituted derivative) converted into **10a** (or its derivatives). In separate experiments it was also confirmed that pre-prepared 3,3'-diindolyl dimethylmethanes could likewise serve as starting materials for products of type **10**.

As mentioned above, one of the originally suggested and rejected structures for the 2:2 condensation products was the indolo[2,3-*b*]carbazole **7**. This compound has now been prepared in 15% yield by a double Fischer indolization (induced by PPA at 120°C) of the bis-phenylhydrazone of 2,2,5,5-tetramethylcyclohexane-1,3-dione. Compound **7** was found to be completely absent in the reaction mixtures from acid-induced condensations of indole and acetone. Thus, the maleic acid-induced condensation between indole and acetone, reported to give a 54% yield of **7**[4], was repeated in our laboratory and gave **10a** (27%) and **11a** (28%) but not a trace of **7**.

In view of the strong interaction[25,26] of indolo[3,2-*b*]carbazole (**9**) and some of its derivatives with the TCDD-receptor, synthesis and investigation of 6,12-dihydroindolo-[3,2–*b*]carbazoles is highly desirable. In fact, in an attempt to synthesize **8**, ethyl indole-2-carboxylate was converted to 2-(α-hydroxy-isopropyl)-indole (**20a**) in good yield by treatment with excess methyl lithium. However, acid-induced dimerization of **20a** gave the 7-membered ring compound **21a** and not **8**. This was indicated by NMR spectral data. The structure of **21a** was ultimately proven by methylation to **21b**, which had previously been synthesized[27] by Ziegler.



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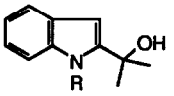
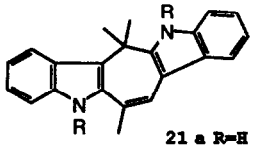
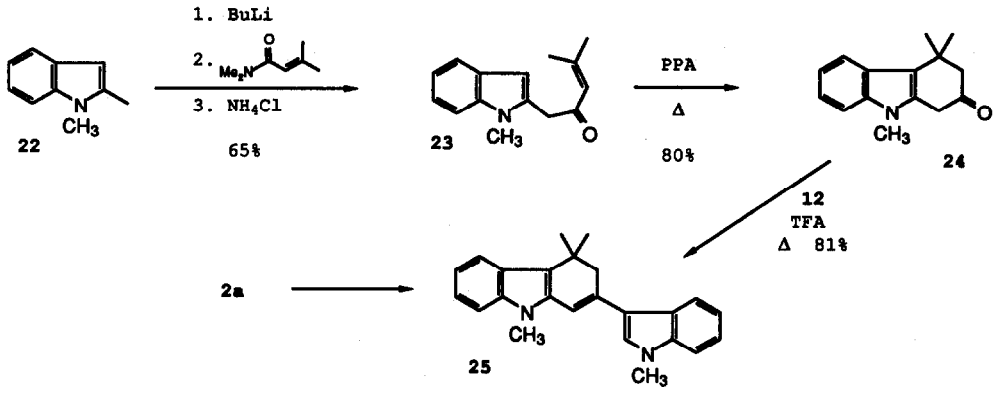


20 a R=H
b R=CH_3



21 a R=H
b R=CH_3

In another attempt to synthesize **8** the bis-phenylhydrazone of 2,2,5,5-tetramethylcyclo-hexane-1,4-dione was treated with PPA and PPSE (polyphosphoric acid trimethylsilyl ester) in order to induce a double Fischer indolization. These attempts were, however, unsuccessful.



Scheme IV

The structure of the second 2:2 dimer **2a** which previously[12] was strongly supported by spectral and mechanistic evidence has now been corroborated by an independent synthesis outlined in **Scheme IV**. The first step of the reaction involves a selective deprotonation of the methyl group in 2-position of 1,2-dimethylindole (**22**). In the crucial step the α,β-unsaturated ketone **23** is cyclized to the tetrahydrocarbazole **24**, which is then subsequently condensed with 1-methylindole to give **25**. This product is also readily obtained from the 2:2 condensation product **2a** by dehydrogenation and methylation[3].

Acknowledgements.

We are grateful to Professor W.E. Noland, University of Minnesota, Minneapolis, for valuable discussions, submission of samples and unpublished data.

Thanks are also due to Professor F.E. Ziegler, Yale University, New Haven, Connecticut, and Professor U. Pindur, University of Mainz, FRG, for submission of samples.

Experimental Section.

Melting points were determined on a Reichert WME Kofler hot stage and are uncorrected. NMR spectra were recorded on a Bruker WP-200 or on a Bruker AM 400. Chemical shifts are reported relative to tetramethylsilane. IR were obtained using a Perkin Elmer 257 or a Perkin Elmer 1710 IR FT instrument. MS (70 eV) were obtained with a LKB-9000 or a Finnigan 4500 spectrometer.

TFA-catalyzed condensation of indole and acetone at reflux.

Trifluoroacetic acid (1.5 mL) was added to a solution of indole (1.17 g, 10 mmol) in acetone (20 mL) and the mixture was refluxed for 2.5 h. After cooling to room temperature, ether (50 mL) was added and the mixture was washed with sodium bicarbonate (aq., sat., 2×20 mL), dried ($MgSO_4$) and evaporated to dryness. Flash cromatography (hexane/ether, 70/30) yielded in the first fraction 0.22 g (12%) of **11a**, mp 255-257°C (lit.[13b] 248°C).

^1H NMR (200M Hz, $CDCl_3$): δ 1.50(s, 6H), 1.58(s, 6H), 2.61(d, 2H, J=13.1 Hz), 2.78(d, 2H, J=13.1 Hz), 7.1-7.5(m, 10H) ppm.

IR (KBr): 3454, 3399, 3055, 2952, 1455, 1293, 749, 726 cm^{-1}.

Later fractions yielded 1.10 g(70%) of 1,1,3-Trimethyl-3-(3-indolyl)-1,2,3,4-tetrahydrocyclopent[b]indole (**10a**), mp 175-177°C (benzene/pentane).

^1H NMR (200 M Hz, $CDCl_3$): δ 1.48(s, 3H), 1.53(s, 3H), 1.87(s, 3H), 2.46(d, 1H, J=12.9 Hz), 2.90(d, 1H, J=12.9 Hz), 6.9–7.8(m, 11H) ppm.

IR (KBr): 3400, 2960, 1455, 1415, 1335, 1100, 1010, 745 cm^{-1}.

MS m/z: 314(M^+) 299, 297(100), 284, 283, 182, 148.

Methylation of 10a.

Compound **10a** (314 mg, 1 mmol) was dissolved in dry DMF (5 mL) and treated with NaH (50 mg, 2 mmol) under N_2 at room temperature. After 30 min. methyl iodide (400 mg) was added and the mixture was stirred for 4 h at room temperature before trituration with ice/water. The mixture was extracted with ether (3×5 mL) and the combined organic phases washed with water, dried ($MgSO_4$) and evaporated. The residue was crystallized from pentane giving **10b** in 85% yield, mp. 177–178°C.

^1H NMR (200 M Hz, $CDCl_3$): δ 1.48(s, 3H), 1.53(s, 3H), 1.88(s, 3H), 2.43(d, 1H, J=13 Hz), 2.90(d, 1H, J=13 Hz), 3.30(s, 3H) 3.74(s, 3H), 6.84(2, 1H), 6.9-7.6(m, 8H) ppm.

Benzensulfonylation of 10a.

A solution of **10a** (314 mg, 1.0 mmol) in dry ether (1mL) was added to a solution of NaH (55 mg, 2.2 mmol) in dry DMSO (4mL). After complete addition, the mixture was stirred for 30 min, whereupon benzenesulfonyl chloride (371 mg, 2.2 mmol) was added dropwise. The reaction mixture was stirred for 30 min, poured into water, and extracted with methylene chloride (2×20 mL). The combined organic phases were washed with sodium bicarbonate (aq., sat., 20 mL), water (20mL), brine (20mL), dried ($MgSO_4$) and evaporated to dryness. The solid residue was triturated with ether and the colorless crystals formed were collected. Yield: 400 mg (67%) of **10c**, mp 225-226°C (lit.[19] mp 255°C).

^1H NMR (400 M Hz, $CDCl_3$): δ 1.49(s, 3H), 1.53(s, 3H), 2.09(s, 3H), 2.35(d, 1H, J=13.5 Hz), 2.88(d, 1H, J=13.5 Hz), 6.5-8.1(m, 19H) ppm.

IR (KBr): 3056, 2960, 1446, 1377, 1370, 1185, 1172, 1132, 1091, 749, 725, 686, 638, 590, 575 cm^{-1}.

A sample kindly provided by Professor U. Pindur was identical with our product.

TFA-catalyzed condensation of 7-methylindole and acetone at room temperature.

Trifluoroacetic acid (1.5 mL) was added to a solution of 7-methylindole (1.31g, 10 mmol) in acetone (20 mL).The mixture was allowed to stand over night, ether (50 mL) was added and the mixture was washed with sodium bicarbonate (aq., sat., 2×20 mL), dried ($MgSO_4$) and evaporated to dryness. Flash chromatography (hexane/ether, 70/30) yielded 1.13 g (75%) of 2,2-bis-(7-methyl-3-indolyl)-propane as an amorphous solid, which could be crystallized from benzene/pentane, mp 166-167°C.

^1H NMR (200 M Hz, $CDCl_3$): δ 1.91(s, 6H), 2.44(s, 6H), 6.8-7.3(m, 8H), 7.8(br., 2H) ppm.

IR(KBr): 3418, 3050, 2967, 1614, 1431, 1105, 784, 749 cm^{-1}.

TFA-catalyzed condensation of 7-methylindole and acetone at reflux.

Trifluoroacetic acid (1.5 mL) was added to a solution of 7-methylindole (1.31 g, 10 mmol) in acetone (20 mL) and the mixture was refluxed for 2.5 h. After cooling to room temperature, ether (50 mL) was added and the mixture was washed with sodium bicarbonate (aq., sat., 2×20 mL), dried ($MgSO_4$) and evaporated to dryness.

Flash cromatography (hexane/ether, 70/30) yielded in the first fraction 0.47g (25%) of **11b**, mp 301-303°C.

^1H NMR (200 M Hz, $CDCl_3$): δ 1.50(s, 6H), 2.38(s, 6H), 2.62(d, 2H, J=13.1 Hz), 2.80(d, 2H, J=13.1 Hz), 7.0-7.5(m, 8H) ppm.

IR(KBr): 3468, 3451, 3022, 2948, 1452, 1300, 782, 747 cm^{-1}.

Later fractions yielded 1.23 g (72%) of **10d**, mp 168-170°C (benzene/pentane).

^1H NMR (200 M Hz, $CDCl_3$): δ 1.48(s, 3H), 1.53(s, 3H), 1.86(s, 3H), 2.37(s, 3H), 2.47(s, 3H), 2.46(d, 1H, J=13.0 Hz), 2.92(d, 1H, J=13.0 Hz), 6.9-7.9(m, 9H)ppm.

IR(KBr): 3424, 3050, 2952, 1616, 1456, 1430, 1108, 782, 751 cm^{-1}.

TFA-catalyzed condensation of 5-bromoindole and acetone at room temperature.

Trifluoroacetic acid (1.5 mL) was added to a solution of 5-bromoindole (1.97 g, 10 mmol) in acetone (20 mL).The mixture was allowed to stand over night, ether (50 mL) was added and the mixture was washed with sodium bicarbonate (aq., sat., 2×20 mL), dried ($MgSO_4$) and evaporated to dryness. Flash chromatography (hexane/ether, 70/30) yielded 1.85 g (85%) of 2,2-bis-(5-bromo-3-indolyl)-propane as an amorphous solid, which was recrystallized from benzene/pentane, mp 165-166°C.

^1H NMR (200 M Hz, $CDCl_3$): δ 1.85(s, 6H), 7.1-7.4(m, 8H), 8.0(br., 2H) ppm.

IR(KBr): 3422, 3125, 2964, 1459, 1099, 796, 582 cm^{-1}.

TFA-catalyzed condensation of 5-bromoindole and acetone at reflux.

Trifluoroacetic acid (0.75 mL) was added to a solution of 5-bromoindole (0.98 g, 5 mmol) in acetone (10 mL) and the mixture was refluxed for 21 h. After cooling to room temperature, ether (25 mL) was added and the mixture was washed with sodium bicarbonate (aq., sat., 2×10 mL), dried ($MgSO_4$) and evaporated to dryness.

Flash cromatography (hexane/ether, 70/30) yielded in the first fraction 0.125 g (10%) of **11c**, mp 290-293°C (benzene/pentane).

^1H NMR (200 M Hz, $CDCl_3$): δ 1.47(s, 6H), 1.54(s, 6H), 2.60(d, 2H, J=13.2 Hz), 2.76(d, 2H, J=13.2 Hz), 7.1-7.7(m, 8H) ppm.

IR(KBr): 3419, 3070, 2952, 1435, 1287, 789 cm^{-1}.

Later fractions yielded 0.91 g(77%) of **10e**, mp 200-203°C (benzene/pentane).

^1H NMR (200 M Hz, $CDCl_3$): δ 1.41(s, 3H), 1.51(s, 3H), 1.82(s, 3H), 2.50(d, 1H, J=13.0 Hz), 2.87(d, 1H, J=13.0 Hz), 6.9-7.7(m, 7H), 8.0(br., 2H) ppm.

IR(KBr): 3418, 3372, 3074, 2955, 1455, 1287, 796, 585 cm^{-1}.

1-Methyl-2-(2-isopentenoyl)-indole 13

Butyl lithium (11.0 mL, 10 M in hexane) was added to a stirred solution of *N*-methylindole (13.1 g, 0.1 mol) in dry ether (230 mL) at 20°C under N_2. After complete

addition the mixture was refluxed for 5h. After cooling to -7°C, *N,N*-dimethylisopentenoylamide (14.0 g, 0.11 mol) was added dropwise at such a rate that the temperature did not exceed 0°C. The mixture was allowed to stand for 2h at -7°C, and then was rapidly hydrolyzed with NH_4Cl (150 mL, aq, satd). The organic layer was separated, washed with water, dried ($MgSO_4$) and evaporated *in vacuo* to give a crystalline, yellow residue. Trituration with light petroleum (bp 40–60°C) gave 13.9 g (65%) of **13** as whitish crystals, mp 118–120°C.

^1H NMR (200 M Hz, $CDCl_3$): δ 2.02(d, 3H, J=1.2 Hz), 2.25(d, 3H, J=1.2 Hz), 4.10(s, 3H), 6.79(m, 1H), 7.1–7.7(m, 5H) ppm.

IR (KBr): 3050, 2940, 1650, 1610, 1510, 1450, 1370, 1220, 1010, 760, 750 cm^{-1}.

1,1,4-Trimethylcyclopent[b]indole-3(2H)-one 14

Compound **13** (1.0 g, 4.7 mmol) was heated in PPA (20 mL) at 120°C for 3 min. with stirring. The mixture was poured into ammonia/ice (75 ml) and the precipitate which formed was collected, dried and crystallized from light petroleum (bp 40–60°C), yielding 0.80 g (80%) of white needles, mp 100–102°C.

^1H NMR (200 M Hz, $CDCl_3$): δ 1.55(s, 6H), 2.84(s, 2H), 3.90(s, 3H), 7.2–8.1(m, 4H) ppm.

IR (KBr): 3050, 2950, 1680, 1620, 1490, 1410, 1200, 760, 740 cm^{-1}.

3-Hydroxy-1,1,3,4-tetramethylcyclopent[b]indole 15

To a stirred solution of **14** (0.84 g, 3.9 mmol) in dry ether (20 mL), methyl magnesium chloride (1.44 mL, 3M in THF) was added dropwise. After the addition was complete the mixture was allowed to stand for an additional hour and was then quenched with NH_4Cl (5 mL, aq, satd). The organic layer was separated, washed with brine, dried ($MgSO_4$) and evaporated *in vacuo* to give a crystalline residue. Flash cromatography (light petroleum/EtOAc, 80/20) and evaporation of the solvent yielded 0.74 g (82%) of colorless prisms, mp 105-131°C (dec.).

^1H NMR (200 M Hz, $CDCl_3$): δ 1.41(s, 3H), 1.50(s, 3H), 1.71(s, 3H), 1.79(s, 1H), 2.46(d, 1H, J=13.8 Hz), 2.56(d, 1H, J=13.8 Hz), 3.78(s, 3H), 7.0–7.6(m, 4H) ppm.

IR (KBr): 3440, 3060, 2960, 1610, 1460, 1380, 740 cm^{-1}.

The compound slowly decomposed on standing.

3-(1-Methylindolyl)-1,1,3,4-tetramethylcyclopent[b]indole 10b

HCl (1 drop, aq, conc) was added with stirring to a mixture of **15** (0.458 g, 2.0 mmol) and 1-methylindole (**12**, 0.262 g, 2.0 mmol) in methanol (8 mL). An intense emerald-green color was immediately observed. After one minute a white precipitate appeared. After 30 min. the precipitate was collected and washed with methanol, yielding 0.609g (89%) of white crystals. Recrystallization from ethanol gave white needles, mp 177-178°C.

This product was identical in all respects with the product obtained by methylation of **10a** as described above.

To the mother liquid was added ether (20mL) and the mixture was washed with sodium bicarbonate (aq., sat., 2×5mL), dried ($MgSO_4$) and evaporated to dryness. Flash chromatography (hexane/ether, 90/10) yielded 22 mg(5%) of **18**, mp 147-150°C (methanol).

^{1}H NMR(200 M Hz, $CDCl_3$): δ 1.24(s, 3H), 1.30(s, 3H), 1.48(s, 3H), 1.51(s, 3H), 1.62(s, 3H), 2.23(dd, 1H, J=16.3 Hz, J=2.2 Hz), 2.41(d, 1H, J=13.1 Hz), 2.63(dd, 1H, J=16.3 Hz, J=2.4 Hz), 2.67(d, 1H, J=13.0 Hz), 3.64(s, 3H), 3.84(s, 3H), 6.06(t, 1H, J=2.3 Hz), 7.0-7.6(m, 8H) ppm.

^{13}C NMR(100 M Hz, $CDCl_3$): δ q:29.15, 29.35, 29.79, 30.14, 30.42, 30.73, 30.98; t:50.20, 63.82; d:109.41, 109.46, 118.22, 118.78, 118.92, 119.13, 120.05, 121.75, 125.50; s:38.15, 38.35, 44.16, 122.49, 123.10, 124.84, 132.97, 135.00, 141.39, 141.54, 143.06, 147.81 ppm.

IR(KBr): 3053, 2952, 1641, 1611, 1470, 736, 725 cm^{-1}.

MS m/z: 422(M^+), 407, 212, 196, 181, 141.

Acid-catalyzed dimerization of 15.

To a solution of **15** (229 mg, 1.0 mmol) in methanol (3mL), HCl (1 drop, aq., conc.) was added under stirring at room temperature. The color turned immediately emerald-green, as in the previous reaction. The mixture was stirred for 30 min., ether (20mL) was added and the mixture was washed with sodium bicarbonate (aq., sat., 2×5mL), dried ($MgSO_4$) and evaporated to dryness. Flash chromatography (hexane/ether, 90/10) yielded 125 mg(59%) of **18**.

2,2,5,5-Tetramethyl-cyclohexane-1,3-dione

Dimedone (17.5 g, 0.125 mol) was added to a stirred slurry of NaH (3.6 g, 0.15 mol) in DMSO (150 mL) at room temperature. After 1h methyl iodide (20.0 g, 0.14 mol) was added to the cooled solution during 20 min. After 1h NaH (3.6 g, 0.15 mol) was added, followed (after

20 min.) by methyl iodide (20.0 g, 0.14 mol). After stirring for 1h, another aliquot of methyl iodide (20.0 g, 0.14 mol) was added. After standing overnight, the mixture was diluted with ether (150 mL). The precipitated salt was collected and the crystals washed with ether. The combined ether extracts were evaporated and the residue was poured into ice/water. The precipitated crystals were collected, washed with water and dried. Yield 19.75 g (94%) of white crystals, mp 95-96°C (lit.[28] 96-97°C).

2,2,5,5-Tetramethylcyclohexanedione 1,3-bis-phenylhydrazone

Acetic acid (0.25 mL) was added to a solution of 2,2,5,5-tetramethyl-cyclohexane-1,3-dione (1.05 g, 6.25 mmol) and phenyl hydrazine (1.35 g, 12.5 mmol) in absolute ethanol (15 mL) and the mixture was refluxed for 3h. The reaction mixture was allowed to cool and the solution was concentrated. after 1h in the refrigator the crystals were collected, washed with a small amount of cold ethanol and dried. Yield 1.52 g (70%) of white needles, mp 163°C (lit.[29] 147°C).
^{1}H NMR (200 M Hz, $CDCl_3$): δ 1.02(s, 6H), 1.49(s, 6H), 2.33(s, 4H), 6.8-7.3(m, 10H) ppm.

6,12-dihydro-6,6,12,12-tetramethylindolo[2,3-b]carbazole 7

2,2,5,5-Tetramethylcyclohexanedione 1,3-bis-phenylhydrazone (0.75 g, 2.15 mmol) was added to PPA (25 mL) and the mixture was heated while stirring under N_2 for 3h at 120°C. The reaction mixture was then allowed to cool and poured into ice/water (150 mL) and extracted with methylene chloride. The organic layer was separated and washed with $NaHCO_3$ (aq, satd), water and brine. After drying ($MgSO_4$) the organic layer was evaporated which gave a solid residue. Flash cromatography (CH_2Cl_2) gave 100 mg (15%) of a white powder, mp 317-320°C.
^{1}H NMR (400 M Hz, $CDCl_3$): δ 1.70(s, 6H), 1.97(s, 6H), 7.1–7.2(m, 4H), 7.4(m, 2H), 7.83(b, 2H), 7.9(m, 2H) ppm.
^{13}C NMR (100 M Hz, $CDCl_3$): δ 29.3, 30.1, 33.1, 34.1, 111.0, 118.1, 119.2, 120.6, 121.3, 125.5, 136.9, 137.3 ppm.
IR (KBr): 3450, 3408, 3052, 2960, 1461, 1313, 749, 719 cm^{-1}.
MS m/z: 314(M^+), 299(100), 284, 142.

2,2,5,5-Tetramethylcyclohexanedione-1,4-bis-phenylhydrazone

Acetic acid (1 drop) was added to a solution of 2,2,5,5-tetramethylcyclohexane-1,4-dione[30] (107 mg, 0.64 mmol) and phenylhydrazine (138 mg, 1.27 mmol) in absolute ethanol (2.5 mL). The reaction mixture was refluxed for 3h and allowed to cool. After 1h in the refrigerator the

crystals were filtered and washed with a small amount of cold ethanol and dried. Yield 122 mg (55%) of white needles, mp 192–193°C.

^{1}H NMR (200 M Hz, $CDCl_3$): δ 1.26(s, 12H), 2.40(s, 4H), 6.8-7.3(m, 10H) ppm.

2-(α-Hydroxyisopropyl)-indole 20a

Methyl lithium (40 mL, 1.5 M in ether) was added to a stirred solution of ethyl indole-2-carboxylate (3.78 g, 20 mmol) in dry THF (50 mL) at –70°C. After complete addition the mixture was stirred for 30 min. at this temperature and then quenched by addition of water (30 mL). Following evaporation of the organic solvents the residue was extracted with ether, dried ($MgSO_4$) and evaporated to yield 2.48 g (71%) of a white solid, mp 108–110°C.

^{1}H NMR (200 M Hz, $CDCl_3$): δ 1.56(s, 6H), 2.44(s, 1H), 6.22(dd, 1H, J_1=0.88 Hz, J_2=1.17 Hz), 7.0-7.24(m, 3H), 7.52(d, 1H, J=7 Hz), 8.55(br, 1H) ppm.

^{13}C NMR (50 M Hz, $CDCl_3$): δ q: 31; d: 97, 110.6, 119.5, 120.1, 121.5; s: 69.7, 128.1, 135.2, 145.2 ppm.

IR (KBr): 3500, 3300, 2980, 1460, 1385, 1370, 1325, 1295, 1255, 1160, 1135, 945 cm^{-1}.

MS m/z: 175(M^+), 160, 157(100), 156, 142.

6,6,12-Trimethyl-5,11,12,13-tetrahydro-6H-indolo[3,2-c]cyclohept[b]indole 21a

Hydrochloric acid (2 mL, aq, conc.) was added to a stirred solution of 2-(α-hydroxyisopropyl)-indole (175 mg, 1 mmol) in methanol (5 mL) at 25°C. The precipitate formed was collected after 10 min., washed with methanol and dried to yield 135 mg (86%) as a white solid, mp>300°C.

^{1}H NMR ($CDCl_3$): δ 1.17(d, 3H, J=6.8 Hz), 1.85(s, 3H), 3.0-3.2(m, 2H), 3.34-3.47(m, 1H), 6.90-6.98(m, 4H), 7.27-7.36(m, 2H), 7.44(d, 1H, J=7.2 Hz), 7.77(d, 1H, J=7.5 Hz), 10.6(br, 2H), ppm.

^{13}C NMR ($CDCl_3$): δ q: 20.7, 29.3, 31.6; t: 29.4; d: 32.9, 110.1, 110.5, 116.9, 117.4, 117.5, 119.3, 119.7, 120.3; s: 38.0, 105.6, 113.1, 126.7, 128.6, 134.5, 134.7, 139.3, 141.9 ppm.

IR (KBr): 3410, 3380, 2960, 1460, 1430, 1340, 1320, 1300, 1230, 750 cm^{-1}.

MS m/z: 314(M^+), 299, 283, 149.5, 142.

Methylation of 21a.

Sodium hydride (12 mg, 0.5 mmol) was added to a stirred solution of compound **21a** (62.8 mg, 0.2 mmol) in dry DMF (2.5 mL) at 30°C under N_2. After a stirring period of 45 min., methyl iodide (71 mg, 0.05 mmol) in dry DMF (0.5 mL) was added. The solution was stirred

for 2 h at 30°C and then 1 h at 40°C, and then the reaction mixture was poured into water. The precipitate was collected, yielding 62 mg (90%) of **21b** as a white solid, mp 247-248°C (lit.[27] 247-248°C).

A sample kindly provided by Professor F.E. Ziegler was identical to our product.

1-(1-Methyl-2-indolyl)-4-methyl-3-penten-2-one 23

Butyl lithium (8.4 mL, 2.5M in hexane) was added to a stirred solution of 1,2–dimethylindole (**22**, 2.90 g, 20 mmol) in dry ether (60 mL) under N_2. The mixture was refluxed for 3h, then cooled to –15°C. *N,N*-Dimethylisopentenoyl amide (2.68 g, 21 mmol) was added dropwise at such a rate that the temperature did not exceed –10°C. After complete addition the mixture was kept at –15°C for 3h. The mixture was then rapidly poured into NH_4Cl (100 mL, aq, satd), the organic layer was separated, washed with brine, dried ($MgSO_4$) and evaporated *in vacuo* to give a red oil. Flash cromatography (light petroleum/EtOAc, 90/10) gave compound **23** as a light yellow oil, yield 2.0 g (44%) which crystallized in the refrigerator, mp 23°C.

^{1}H NMR (200 M Hz, $CDCl_3$): δ 1.84(s, 3H), 2.15(s, 3H), 3.63(s, 3H), 3.83(s, 2H), 6.15(s, 1H), 6.38(s, 1H), 7.0–7.6(m, 4H) ppm.

The compound slowly decomposed on standing.

1,2,3,4-Tetrahydro-4,4,9-trimethylcarbazol-2-one 24

Compound **23** (0.75 g, 3.3 mmol) was stirred in PPA (20 mL) at 100°C for 5 min. This mixture was then quenched with ammonia/ice (50 mL). The precipitate that formed was collected and subjected to flash chromatography (light petroleum/EtOAc, 80/20) yielding 0.60 g (80%) of white needles, mp 139–142°C.

^{1}H NMR (200 M Hz, $CDCl_3$): δ 1.51(s, 6H), 2.65(s, 2H), 3.59(s, 2H), 3.60(s, 3H), 7.1–7.8(m, 4H) ppm.

IR (KBr): 3060, 2960, 1720, 1620, 1470, 1370, 1230, 760, 740 cm^{-1}.

3,4-Dihydro-2-(1-methyl-3-indolyl)-4,4,9-trimethylcarbazole 25

Trifluoroacetic acid (0.171 g, 1.5 mmol) was added to a solution of **24** (0.226 g, 1.0 mmol) and *N*-methylindole (0.144 g, 1.1 mmol) in CH_3CN (5 mL) and the mixture was refluxed overnight. After cooling to room temperature, methanol was added, resulting in the formation of a crystalline precipitate, which was collected, washed with methanol and dried, yielding

0.28 g (82%) of yellow needles, mp 219–221°C.

^{1}H NMR (200 M Hz, $CDCl_3$): δ 1.49(s, 6H), 2.75(d, 2H, J=1.0 Hz), 3.78(s, 3H), 3.82(s, 3H), 7.0–8.1(m, 9H) ppm.

IR (KBr): 3040, 2960, 1620, 1470, 1370, 1230, 740, 730 cm^{-1}.

MS m/z: 340(M^+), 325(100), 310, 295.

This product was identical in all respects with the second 2:2 adduct obtained from the acid catalyzed condensation between *N*-methylindole and acetone[3].

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