

SYNTHESIS OF CARBAZOLES BY CYCLIZATIVE
CONDENSATION OF THE METHYL GROUP OF 2-METHYLINDOLES^{1,2}

Wayland E. Noland and James Elver Johnson

School of Chemistry, University of Minnesota, Minneapolis 14, Minnesota

(Received 27 April 1962; in revised form 25 May 1962)

AN example of cyclizative condensation of the 2-methyl group of a 2-methylindole has been described by Szmuszkovicz³, in which 2-methylcarbazole was obtained in 11 per cent yield by heating 2-methylindole and methyl vinyl ketone at a final temperature of 280-290° for 20 hr. Ireland⁴ has reported a similar reaction with 1-methyl-2-alkylpyrrolines, in which, for example, addition of 1,2-dimethylpyrrolidine to methyl vinyl ketone is accompanied by cyclization in 35 per cent yield to 1,6-dimethyl-2,3,4,5-tetrahydroindole, which was subsequently dehydrogenated with palladium on carbon in 80 per cent yield to 1,6-dimethylindole.

We have found that addition of 2-methylindole derivatives to α -hydroxy-methylene ketones, followed by cyclizative condensation of the 2-methyl group, is an effective and fairly general method of carbazole synthesis, as

¹ This is Paper V in the series "Cyclizative Condensations of Indoles"; for Paper IV see W.E. Noland and M.R. Venkiteswaran, J. Org. Chem. **26**, 4263 (1961). It is a pleasure to acknowledge support of part of this research from the National Science Foundation Undergraduate Research Participation Program, Grant No. G-11896 (J.E.J., June 15-Aug. 31, 1960), and from the U.S. Public Health Service, National Cancer Institute, Research Grant CY-4073 (J.E.J., Sept. 1, 1960-May 31, 1961). Another part of this work is from the senior thesis research of James Elver Johnson, 1960-61. Melting points were determined on calibrated hot stages unless otherwise stated.

² Part of this work was presented by W.E. Noland, J.E. Johnson, D.N. Robinson and J.A. Elberling, as Paper 184 before the Organic Division at the 140th National Meeting of the American Chemical Society, Chicago, Ill., Sept. 8, 1961, Abstracts, p. 97Q.

³ J. Szmuszkovicz, J. Amer. Chem. Soc. **79**, 2819 (1957).

⁴ R.E. Ireland, Chem. & Ind. 979 (1958).

aromatization is effected entirely by dehydration, rather than requiring as a final step a "spontaneous" dehydrogenation of a dihydrocarbazole. For example, refluxing of an equimolar (0.03 mole) solution of 2-methylindole and 2-hydroxymethylencyclohexanone⁵ in acetic acid (20 cc) for 2 hr gave in 38 per cent yield 7,8,9,10-tetrahydro-5H-benz[b]carbazole (Ia), colorless crystals (from methanol-water), m.p. 215-217° (sealed capillary), ν_{NH} 3400 ms cm^{-1} in Nujol (Found: C, 86.50; H, 6.80; N, 6.37. $\text{C}_{16}\text{H}_{15}\text{N}$ (221.29) requires: C, 86.84; H, 6.83; N, 6.33 per cent). Similarly prepared were the 8-methyl derivative (Ib, 55 per cent), colorless needles (from ethanol-water), m.p. 201-204°, ν_{NH} 3400 ms cm^{-1} in Nujol (Found: C, 86.63; H, 7.40; N, 6.09. $\text{C}_{17}\text{H}_{17}\text{N}$ (235.31) requires: C, 86.77; H, 7.28; N, 5.95 per cent); and its 9-methyl isomer (Ic, 30 per cent), colorless crystals (from ethanol-water), m.p. 196-198°, ν_{NH} 3380 ms cm^{-1} in Nujol (Found: C, 86.96; H, 7.19; N, 6.18 per cent); as well as 1,2,3,4,5,7-hexahydrocyclohept[b]carbazole (77 per cent), colorless crystals (from ethanol), m.p. 237-238° (sealed capillary), ν_{NH} 3390 m cm^{-1} in Nujol (Found: C, 86.74; H, 7.30; N, 6.06. $\text{C}_{17}\text{H}_{17}\text{N}$ (235.31) requires: C, 86.77; H, 7.28; N, 5.95 per cent); and (from hydroxymethylene- β -tetralone⁶) 5,6-dihydro-8H-naphtho [1,2-b]carbazole (19 per cent), yellow crystals (after vacuum sublimation), m.p. (softens ~ 340°) 378-390° (sealed capillary), ν_{NH} 3390 ms cm^{-1} in Nujol and in halocarbon oil (Found: C, 89.26; H, 5.64; N, 5.41. $\text{C}_{20}\text{H}_{15}\text{N}$ (269.33) requires: C, 89.18; H, 5.61; N, 5.20 per cent); and 2,3-dimethylcarbazole (30 per cent), colorless crystals (from ethanol-water), m.p. 250-253° (sealed capillary) (reported m.p. 250-252°,⁷ 251-253°⁸), ν_{NH} 3350 ms cm^{-1}

⁵ C. Ainsworth, Org. Synth. **39**, 27 (1959), Method 1.

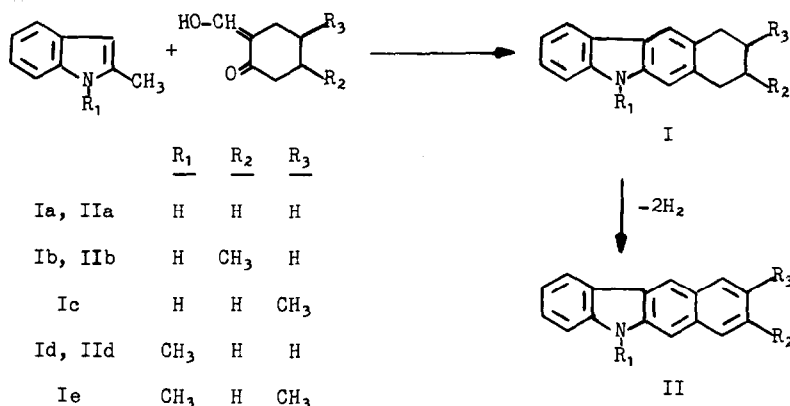
⁶ W.E. Noland and J.E. Johnson, unpublished work, University of Minnesota (1961).

⁷ G. Anderson and N. Campbell, J. Chem. Soc. 2855 (1950).

⁸ N. Campbell and E.B. McCall, J. Chem. Soc. 2870 (1950).

in Nujol (Found: C, 86.32; H, 6.99; N, 7.35. Calc. for $C_{14}H_{13}N$ (195.25): C, 86.11; H, 6.71; N, 7.17 per cent).

1-Alkyl-2-methylindoles are also suitable precursors for the carbazole synthesis, as illustrated by the preparation in a similar manner from 1,2-dimethylindole of 5-methyl-7,8,9,10-tetrahydrobenz[b]carbazole (Id, 32 per cent), colorless needles (from acetone-water), m.p. 87-88° (Found: C, 87.02; H, 7.14; N, 5.99. $C_{17}H_{17}N$ (235.31) requires: C, 86.77; H, 7.28; N, 5.95 per cent); and its 9-methyl derivative (Ie, 40 per cent), colorless needles (from ethanol-water), m.p. 104-106° (Found: C, 86.68; H, 7.97; N, 5.79. $C_{18}H_{19}N$ (249.34) requires: C, 86.70; H, 7.68; N, 5.62 per cent).



The carbazole synthesis can serve as a synthetic route to fully aromatic 5H-benz[b]carbazoles (II), as illustrated by dehydrogenation with chloranil (2 moles) in refluxing xylene of Ia to 5H-benz[b]carbazole⁹ (IIa, 92 per cent), colorless plates (from benzene), m.p. 340-345°, ν_{NH} 3400 cm^{-1} in Nujol, identical, as shown by mixed melting point and infrared (Nujol) com-

^{9a} C. Graebe and W. Knecht, *Ber. Dtsch. Chem. Ges.* **12**, 341, 2242 (1879); *Liebigs Ann.* **202**, 1 (1880); E. H. T. Bucherer and E. F. Sonnenburg, *J. Prakt. Chem.* [2] **81**, 1 (1910); G. N. P. Buu-Hoi, N. Hoan and N. H. Khôi, *J. Org. Chem.* **15**, 131 (1950); R. Huisgen and G. Sorge, *Liebigs Ann.* **566**, 162 (1950); G. N. P. Buu-Hoi, P. Jacquignon and D. Lavit, *J. Chem. Soc.* 2593 (1956); H. M. Grotta, C. J. Riggle and A. E. Bearse, *J. Org. Chem.* **26**, 1509 (1961).

parison with a recrystallized authentic sample purchased from the Aldrich Chemical Co.; and by dehydrogenation with 10 per cent palladium on carbon in refluxing decalin of Ib to 8-methyl-5H-benz[b]carbazole (IIb, 72 per cent), colorless plates (from benzene), m.p. 350-354° (reported m.p. 343°^{9a}), ν_{NH} 3400 cm^{-1} in Nujol (Found: C, 88.25; H, 5.54; N, 6.14. $\text{C}_{17}\text{H}_{13}\text{N}$ (231.28) requires: C, 88.28; H, 5.67; N, 6.06 per cent); and of its isomer Id to 5-methyl-5H-benz[b]carbazole (IIc, 75 per cent), colorless plates (from methanol), m.p. 139-140° (Found: C, 88.15; H, 5.65; N, 5.88 per cent). The sample of IIc was identical, as shown by mixed melting point and infrared comparison (except for a very weak NH band at 3390 cm^{-1} in the spectrum of the latter sample), with a sample prepared in 23 per cent yield by methylation of Ia with methyl iodide and sodamide in liquid ammonia.

The carbazole nature of all the cyclizative condensation products and their dehydrogenated derivatives is shown clearly by their carbazole type of ultraviolet spectra.

In the majority of cases in which our carbazole synthesis from α -hydroxymethylene ketones and 2-methylindole fails, unreactive conjugated 3-vinylindoles¹⁰ are formed,⁶ including with 4,4-dimethoxy-2-butanone,² 2-hydroxymethylene-3-pentanone,⁶ 2-hydroxymethylenecyclopentanone,⁶ 2-hydroxymethylenecyclooctanone,⁶ β -hydroxymethylene- α -tetralone,⁶ and (25 per cent yield) with 2-hydroxymethylenecyclohexanone and 1,2-dimethylindole after only 1 hr of refluxing in acetic acid.² Hydrogenation of the vinylindole, 4-(2-methyl-3-indolyl)-3-butene-2-one (obtained in 36 per cent yield from the condensation of 2-methylindole and 4,4-dimethoxy-2-butanone), over Raney nickel at 2 atm in ethanol solution was accompanied by cyclization and dehydrogenation, thus providing an alternate route to 2-methylcarbazole (8 per cent), m.p. 260-263° (reported m.p. 261.5-262.5°³).²

¹⁰ W.E. Noland and D.N. Robinson, *J. Org. Chem.* 22, 1134 (1957); Donald N. Robinson, Ph.D. thesis, University of Minnesota (March 1959), *Diss. Abstr.* 21, 50 (1960).