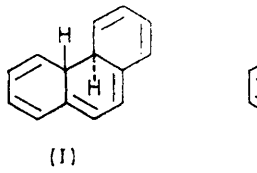
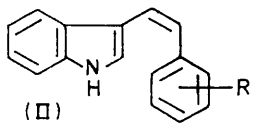
Photocyclisation of Styrylindoles. Synthesis of 1-, 2-, 3- and 4-Methyl-11*H*-benzo[*a*]carbazoles

By **William Carruthers** * and **Nigel Evans**, Chemistry Department, The University, Exeter EX4 4QD

11*H*-Benzo[*a*]carbazole and the 1-, 2-, 3-, and 4-methyl derivatives have been obtained by photocyclisation of the appropriate 3-styrylindoles. The 1- and 4-methyl compounds can be distinguished by the chemical shifts of the methyl protons. A convenient route to 3-styrylindoles is described.

PHOTOCYCLISATION of stilbene and stilbene analogues in the presence of a suitable oxidant has been used to prepare a variety of polycyclic aromatic hydrocarbon and heterocyclic systems.[1] The reaction is thought to proceed by cyclisation of the *cis*-stilbene in its lowest excited singlet state to a dihydrophenanthrene (I), which undergoes hydrogen abstraction by the oxidant to give the aromatic compound. We find that 3-styrylindoles (II; R = H or Me) are converted into 11*H*-benzo[*a*]-carbazoles by this route, and we report the preparation of the 1-, 2-, 3-, and 4-methyl derivatives (III; R = Me), which were required in connection with another investigation.[2]


(I)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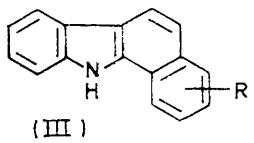
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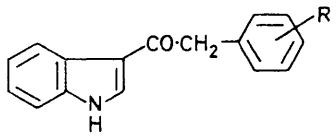
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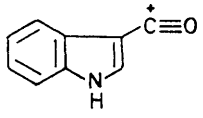
(V)

Irradiation through Pyrex of a solution of 3-styryl-indole (II; R = H) in benzene with light from a medium-pressure mercury lamp and purification of the product by chromatography gave 11*H*-benzo[*a*]carbazole in 25% yield. Under the same conditions *o*-, *m*-, and *p*-methylstyrylindoles gave the corresponding methyl-benzocarbazoles. With the *para*-isomer 2-methylbenzo-carbazole was obtained in 17% yield. The *o*-methyl compound yielded mainly the expected 4-methyl-11*H*-benzo[*a*]carbazole, but g.l.c. of the crude product showed that the parent benzocarbazole, formed by displacement of the methyl group, accounted for about 4% of the product. Ejection of methyl substituents during photocyclisation of stilbenes has been noted before.[3] With *m*-methylstyrylindole two modes of cyclisation are possible, and a mixture of approximately equal amounts of 1- and 3-methylbenzo[*a*]carbazole was formed on irradiation. The pure compounds were isolated by chromatography on alumina and identified through their n.m.r. spectra (see Table 1). In the spectrum of the 1-methyl derivative, in which the substituent lies in the deshielding zone of two aromatic nuclei, the signal due to the methyl protons occurs at an abnormally low field. A similar but smaller downfield shift is noticeable in the spectrum of the 4-methyl compound. Precedent for these effects is found in the n.m.r. spectra of certain methylphenanthrenes and methylbenz[*a*]anthracenes.[4] 1-Methylbenzo[*a*]carbazole is distinguished also by a comparatively short retention time on g.l.c. (see Table 1); curiously this is the reverse of the situation with the related methylbenzo[*a*]fluorenes and methyl-11-thiabenzo[*a*]fluorenes, where the 1-methyl derivatives have longer retention times than the 2-, 3-, and 4-isomers.[5]

TABLE 1

	Chemical shifts * (τ) of protons in methylbenzo[*a*]carbazoles			G.l.c. retention times † (min)
	Aromatic	NH	Me	11*H*-Benzo[*a*]carbazole 7·0
1-Me	1·72—2·71	0·80	6·9	8·9
2-Me	1·80—2·80	1·34	7·41	9·8
3-Me	1·84—2·79	1·32	7·45	10·0
4-Me	1·79—3·00	1·26	7·21	9·3

* Recorded with a JEOL MH-100 spectrometer (100 MHz) for 2% solutions (w/w) in deuteriochloroform containing tetramethylsilane as internal reference. † 5 ft 3% SE 30 on Chromosorb W at 210 °C; Pye 104 instrument with hydrogen flame detector and nitrogen as carrier gas.

The yields of cyclised products from the irradiation of styrylindoles are, in general, considerably lower than those obtained in many other related photocyclisations,[1] presumably because of the reactivity of the indole nucleus. Irradiation in the presence of oxygen or iodine, techniques commonly employed in other cases, led to drastically reduced yields in the present experiments, in line with an earlier report[6] that 2-styryl-pyrrole gives no cyclised product on irradiation in the presence of oxygen.

The styrylindoles used were prepared from the corresponding 3-arylacetylindoles (IV), which were

[1] *Cf.* E. V. Blackburn and C. J. Timmons, *Quart. Rev.*, 1969, **23**, 482.

[2] *Cf.* W. Carruthers, *J. Chem. Soc.* (*C*), 1968, 2244.

[3] *E.g.*, W. Carruthers and H. N. M. Stewart, *J. Chem. Soc.*, 1965, 6221, 1967, 556; G. M. Badger, R. J. Drewer and G. E. Lewis, *Austral. J. Chem.*, 1963, **16**, 1042; 1964, **17**, 1036.

[4] K. D. Bartle and J. A. S. Smith, *Spectrochim. Acta*, 1967, **23A**, 1689; R. J. Oudette and B. G. Van Leuwen, *J. Org. Chem.*, 1969, **34**, 62.

[5] W. Carruthers and H. N. M. Stewart, *J. Chem. Soc.* (*C*), 1967, 556, 560.

[6] C. E. Loader and C. J. Timmons, *J. Chem. Soc.* (*C*), 1967, 1677.

themselves obtained from the 3-arylacetyl chloride and indol-1-ylmagnesium bromide.[7] The mass spectra of these derivatives showed the fragmentation pattern found for other 3-acylindoles,[8] with a base peak at *m/e* 144 due to the ion (V), and other comparatively strong peaks at *m/e* 116 and 89. Reduction of the arylacetyl compounds with sodium borohydride in diethylene glycol, or in methanol containing some sodium hydroxide, gave the corresponding carbinols. (Attempted reduction with sodium borohydride in methanol led to a vigorous exothermic reaction, presumably involving the NH group and the solvent, from which only starting material was recovered.) Dehydration of the carbinols with ethyl chloroformate in pyridine[9] gave the crystalline *trans*-styrylindoles.

An alternative route to the styrylindoles appeared to lie in the reaction of indole-3-carbaldehyde with the appropriate Wittig reagent. Reaction under the usual conditions, however, using 1 mol. equiv. of the phosphorane, gave only poor yields of styrylindoles, presumably because of deactivation of the carbonyl group by interaction with the nitrogen of the indole nucleus. While the work was in progress it was reported[10] that 3-styrylindole can be obtained in reasonable yield by reaction of indole-3-carbaldehyde with a large excess of the Wittig reagent and an extended reaction time. We have confirmed this, but the method is not so convenient as that described above, because of the large amounts of triphenylphosphine oxide produced, from which the product has to be separated.

EXPERIMENTAL

U.v. spectra were measured with a Unicam SP 800 spectrometer for solutions in methanol, unless otherwise stated. Routine i.r. spectra were measured with a Perkin-Elmer Infracord and high resolution spectra with a Hilger-Watts H 900 instrument. Mass spectra were recorded with a Hitachi RMU 60 instrument and ^{1}H n.m.r. spectra with a Perkin-Elmer R10 spectrometer at 60 MHz or a JEOL MH-100 instrument at 100 MHz, for solutions in deuteriochloroform, with tetramethylsilane as internal reference. G.l.c. experiments were run on a Pye 104 instrument at 210 °C (5 ft columns of 3% SE 30 on Chromosorb W). Light petroleum refers to the fraction b.p. 60—80 °C unless otherwise stated.

3-Phenylacetylindole (IV; R = H).—A solution of indole (12·8 g) in ether (50 ml) was added slowly to a solution of ethylmagnesium bromide [from ethyl bromide (9 ml) and magnesium (3 g)] in ether (80 ml). The mixture was boiled for 30 min, then cooled to 0 °C, and a solution of phenylacetyl chloride (17 g) in ether (100 ml) was added with vigorous stirring. A sticky brown gum separated. The mixture was boiled for 1 h, aqueous ammonium chloride was added, and the mixture was stirred vigorously. The white precipitate of 3-phenylacetylindole (4·1 g) was filtered off and washed with ether. The combined ether layers were washed with water and evaporated, and the oily residue (14 g) (which contained some 1,3-bisphenylacetylindole) was boiled with aqueous sodium hydroxide (10%; 35 ml) and methanol (140 ml) for 10 min. The neutral product gave a further 4·5 g of the 3-phenylacetyl compound. Crystallisation of the combined product from ethanol–benzene gave *3-phenylacetylindole* (7·5 g) as fluffy needles, m.p. 206—207 °C (Found: C, 81·6; H, 5·5; N, 5·6%; M^+, 235. $C_{16}H_{13}NO$ requires C, 81·7; H, 5·6; N, 5·95%; *M*, 235).

3-Styrylindole (II; R = H).—A mixture of sodium borohydride (5·2 g) and 3-phenylacetylindole (5·0 g) in diethylene glycol (125 ml) was stirred at room temperature for 12 h, diluted with saturated brine, and extracted with ether. 3-(1-Hydroxy-2-phenylethyl)indole formed flakes, m.p. 112—114 °C (4·3 g), $\nu_{max.}$ (KBr) 3500 and 3285 cm^{-1}; M^+ 237. This material (2·0 g) in pyridine (30 ml) was treated with ethyl chloroformate (7 ml) at 0 °C for 2 h, then overnight at room temperature. trans-3-*Styrylindole* (1·45 g) was obtained as platelets, m.p. 196—197 °C (from benzene–light petroleum) (Found: C, 87·5; H, 6·3; N, 6·2%; M^+ 219. $C_{16}H_{13}N$ requires C, 87·6; H, 6·0; N, 6·4%; *M*, 219); $\nu_{max.}$ (KBr) 3395, 966, and 958 cm^{-1}; $\lambda_{max.}$ 235, 284, and 326 nm (log ε 4·34, 4·08, and 4·41). *trans-o-*, *m-*, and *p*-Methylstyrylindoles (II; R = Me) were prepared in the same way from the appropriate tolylacetylindoles; m.p.s and analytical data are recorded in Table 2.

TABLE 2

Compound	M.p. (°C)	C(%)	H(%)	N(%)
3-Tolylacetylindole				
o-	218—219	82·0	6·2	5·6 *
m-	180—181	82·1	6·1	5·5
p-	207—208	81·7	5·95	5·6
trans-3-Styrylindole				
o-Methyl	142—143	88·0	6·3	6·2 †
m-Methyl	185—186	87·8	6·3	6·1
p-Methyl	215—216	87·6	6·4	5·9

* $C_{17}H_{15}NO$ requires C, 81·9; H, 6·1; N, 5·6%. † $C_{17}H_{15}N$ requires C, 87·5; H, 6·5; N, 6·0%.

TABLE 3

U.v. data [$\lambda_{max.}$/nm (log ε)] of methyl-11*H*-benzo[*a*]-carbazoles

1-Methyl	235 (4·38), 243infl (4·42), 253 (4·52), 2·68 (4·33), 275 (4·51), 397 (4·21), 306infl (4·19), 325 (3·63), 341 (3·71), 358 (3·85)
2-Methyl	228 (4·36), 245 (4·45), 246·5 (4·44), 253 (4·55), 257infl (4·47), 269infl (4·29), 279 (4·53), 298 (4·17), 305 (4·19), 322 (3·60), 339 (3·59), 356 (3·62)
3-Methyl	228 (4·32), 243 (4·34), 251·5 (4·41), 256 (4·40), 280 (4·45), 301 (4·07), 307 (4·09), 322 (3·57), 330infl (3·40), 338 (3·56), 346 (3·25), 355 (3·65)
4-Methyl	243·5 (4·58), 248·5 (4·58), 252 (4·66), 270infl (4·39), 279 (4·63), 298infl (4·29), 306 (4·31), 323 (3·79), 339 (3·79), 356 (3·86)

Photocyclisation of 3-Styrylindoles.—The light source was a Hanovia 125 W medium-pressure mercury vapour lamp fitted with a Pyrex filter; irradiations through silica proceeded more rapidly but gave a less pure product. A stirred solution of the styrylindole ($3·0 \times 10^{-3}$ mol dm^{-3}) in dry benzene was irradiated under air at room temperature until the u.v. absorption of the styrylindole had been replaced by that of 11*H*-benzo[*a*]carbazole (10—20 h for 200 ml solution). The crude product was chromatographed on silica gel coated with 5% silver nitrate. Elution

[7] T. E. Young and M. F. Mizianty, *J. Medicin. Chem.*, 1966, **9**, 635.

[8] N. S. Vul'fson, V. I. Zaretskii, A. V. Kisin, N. N. Suvorov, and Zh. D. Ovchinnikova, *Khim. geterotsikl. Soedinenii*, 1957, **3**, 502; J. C. Powers, *J. Org. Chem.*, 1968, **33**, 2044.

[9] J. Szmuszkovicz, *J. Amer. Chem. Soc.*, 1960, **82**, 1180.

[10] N. N. Suvorov, I. A. Orlova, and K. F. Turchin, *Khim. geterotsikl. Soedinenii*, 1969, **5**, 250.

with benzene–light petroleum (1 : 1) gave the product free from starting material. From 3-styrylindole itself 11*H*-benzo[*a*]carbazole was obtained (25%), m.p. 226—228 °C (lit.,[11] 227—228 °C), M^+ 217; u.v. spectrum identical with that reported.[11] Similarly 3-(*p*-methylstyryl)indole gave 2-*methyl*-11H-*benzo*[a]*carbazole* (17%) as needles (from cyclohexane), m.p. 208 °C (Found: M^+, 231·1046. $C_{17}H_{13}N$ requires M, 231·1048); for u.v. maxima see Table 3. 3-(*o*-Methylstyryl)indole gave a mixture of 4-*methyl*-11H-*benzo*[a]*carbazole* and benzo[*a*]carbazole in the ratio 96 : 4 (g.l.c.), from which the methyl compound was isolated (16%) by crystallisation from benzene–light petroleum as needles, m.p. 262—263 °C (decomp.) (Found: M^+, 231·1039. $C_{17}H_{13}N$ requires M, 231·1048). From 3-(*m*-methylstyryl)-indole a mixture of 1- and 3-methyl-11*H*-benzo[*a*]carbazoles was formed (total yield 15%) in the ratio 44 : 56 (g.l.c.). Chromatography on neutral alumina (grade I) and elution with benzene–light petroleum (1 : 3) gave first 1-*methyl*-11H-*benzo*[a]*carbazole* as needles, m.p. 138—139 °C (Found: M^+, 231·1053. $C_{17}H_{13}N$ requires M, 231·1048), then the 3-*methyl isomer*, m.p. 228—229 °C (from benzene) (Found: M^+, 231·1048. $C_{17}H_{13}N$ requires M, 231·1048); for u.v. data see Table 3.

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[11] G. R. Clemo and D. G. Felton, *J. Chem. Soc.*, 1952, 1658.