Thermal Cyclisation of Diphenylamine to Carbazole: Synthesis of the Natural Product Glycozolidine

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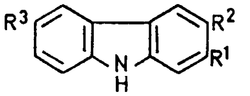
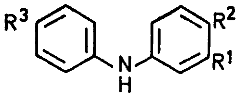
Summary Iodine-catalysed cyclisation at 350 °C of diphenylamine to carbazole has been used to synthesise glycozolidine (VI), a natural product from *Glycosmis pentaphylla* (Retz.) D.C.

Diphenylamine (I) is known to cyclise to carbazole (II) at red heat in the vapour state. There has recently been interest in this transformation using photolytic methods.[1-3] It has been shown that the photocyclisation involves hydrogen abstraction through a transient polar ring-closed intermediate.[3] Hydrogen abstraction from paraffins at 550 °C with elemental iodine resulting in the aromatisation of hydrocarbons has been reported.[4,5] We now report the convenient thermal cyclisation of diphenylamine to carbazole at 350 °C in the presence of elemental iodine.



(II) $R^1=R^2=R^3=H$
(IV) $R^1=R^3=H, R^2=Me$
(VI) $R^1=OMe, R^2=Me, R^3=OMe$



(I) $R^1=R^2=R^3=H$
(III) $R^1=R^3=H, R^2=Me$
(V) $R^1=OMe, R^2=Me, R^3=OMe$

Diphenylamine was heated at 350 °C in a sealed tube for 2 h in the presence of catalytic amounts of elemental iodine. Spectral examination of the reaction product after removal of iodine showed absence of the characteristic u.v. absorption maximum for diphenylamine [λ_{max} (EtOH) 285 nm]. The product on purification over alumina gave carbazole (II) [mixed m.p. 225 °C, lit. 225 °C, λ_{max} 233 ($\log \epsilon$ 4·5), 257 (4·18), 293 nm (4·10), ν_{max} (Nujol) 3480, 1610, 1505, and 935 cm^{-1}]. Similar methods were used to obtain 3-methylcarbazole (IV), m.p. 208 °C (lit. 208 °C) from the corresponding diphenylamine derivative (III) The yields obtained in all cases were *ca.* 45%.

The second carbazole alkaloid of *Glycosmis pentaphylla* (Retz.) D.C.[6,7] was assigned structure (VI), 2,6-dimethoxy-3-methylcarbazole.[8] (VI) was also isolated from the mixture of reaction products obtained by heating the diphenylamine derivative (V) by the method described above. (V) [m.p. 85 °C, λ_{max} (EtOH) 283 ($\log \epsilon$ 4·23), 240 nm (3·92)] was prepared by heating 3-methoxy-4-methylaniline hydrochloride with *p*-anisidine at 270 °C for 4 h. The n.m.r. data (60 MHz in $CDCl_3$) for (VI) confirmed the structure assigned. The signals for 4-H and 5-H (δ 7·17—7·45)[9] were not *ortho*-coupled. The shielded proton signal (δ 6·52) for 1-H was in conformity with the substitution pattern of (VI). There were also signals for –NH– (δ 7·65), two Ar–OCH_3 (δ 3·9 and 3·77), Ar–CH_3 (δ 2·35), and two Ar–H (δ 6·92—7·02).

The compound was identical (i.r., u.v., mixed m.p.) with authentic specimens (natural and synthetic).

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