The Protoberberine→Spirobenzylisoquinoline→Dibenzocyclopent[*b*]azepine Rearrangement

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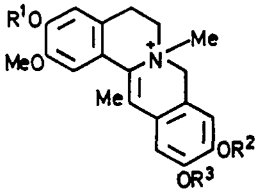
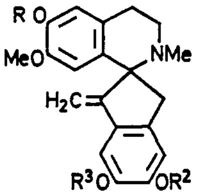
Summary Base-catalysed rearrangement of the monophenolic dihydroprotoberberine salts (5) and (7) leads to the spirobenzylisoquinolines (6) and (8) respectively, while rearrangement of the salt (9) furnishes the dibenzocyclopent[*b*]azepine (14).

IT has been demonstrated that base-catalysed rearrangement of the diphenolic dihydroprotoberberine salt (1) yields the spirobenzylisoquinoline (2).[1] In a later study it was shown that the two phenolic groups need not be in the same ring for the rearrangement to occur. Specifically, diphenol (3) was shown to rearrange in base to the spirobenzylisoquinoline (4).[2]

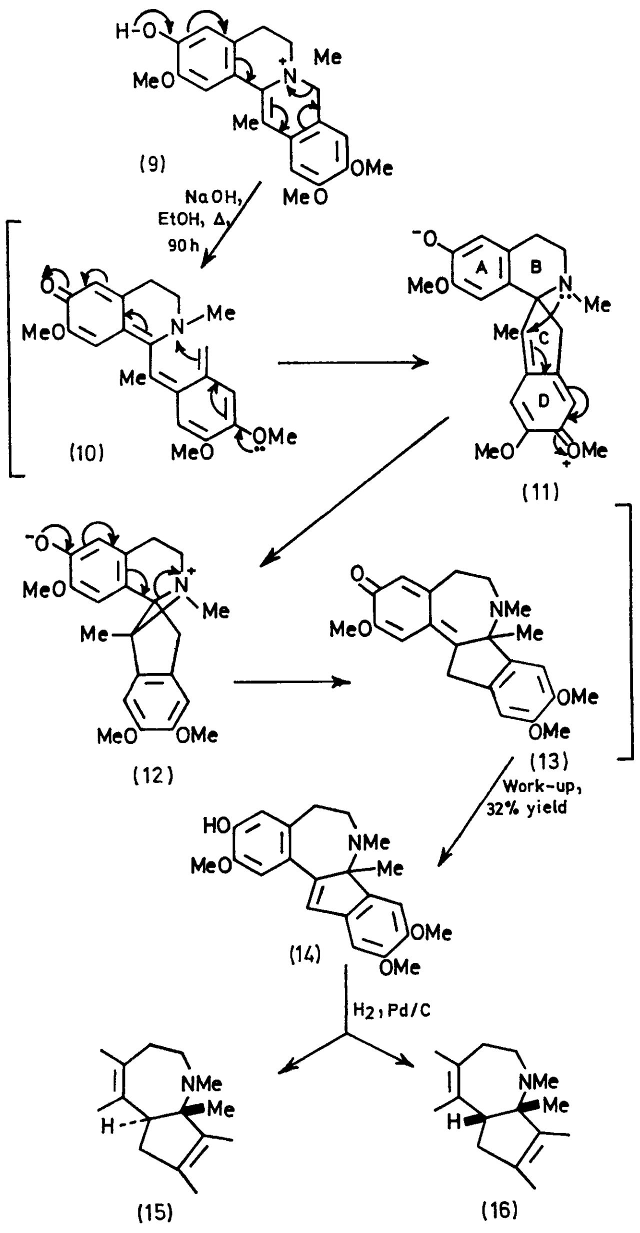
We were now interested in finding out if rearrangement could occur with only one phenolic group present. Treatment of the monophenol (5), $C_{22}H_{26}O_4N^+Br^-$, m.p. 216—218° decomp., with base was indeed found to give the spirobenzylisoquinoline (6), $C_{22}H_{25}O_4N$, m.p. 125—127°. Similarly, but less readily, monophenol (7), $C_{22}H_{26}O_4N^+Br^-$, m.p. 183—186° decomp., afforded the amorphous spirobenzylisoquinoline (8), $C_{22}H_{25}O_4N$.



(1) R^1 = Me, R^2 = R^3 = H
(3) R^1 = R^2 = H, R^3 = Me
(5) R^1 = R^2 = Me, R^3 = H
(7) R^1 = R^3 = Me, R^2 = H

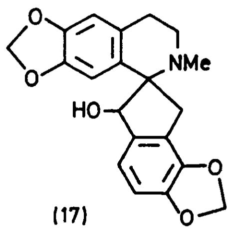


(2) R^1 = Me, R^2 = R^3 = H
(4) R^1 = R^2 = H, R^3 = Me
(6) R^1 = R^2 = Me, R^3 = H
(8) R^1 = R^3 = Me, R^2 = H

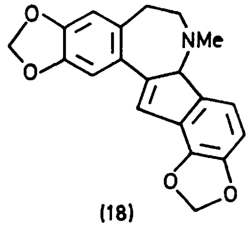


Interestingly enough, monophenol (9),[3] $C_{22}H_{26}O_4N^+Br^-$, m.p. 177—180° decomp., when treated with base did not yield a spirobenzylisoquinoline, but furnished instead the olefinic dibenzocyclopent[*b*]azepine (14), $C_{22}H_{25}O_4N$, m.p. 190—192°, which was reduced catalytically to a mixture of diastereoisomeric amines (15) and (16); isomer A, $C_{22}H_{27}O_4N$, m.p. 192—194° decomp., λ_{max} (EtOH) 232 and 285 nm (log ϵ 4·12 and 3·88), n.m.r. δ 1·53 (s, 3H, C–CH_3), and isomer B, $C_{22}H_{27}O_4N$, m.p. 197—198° decomp., λ_{max} (EtOH) 230sh and 286 nm (log ϵ 4·21 and 4·00), n.m.r. δ 1·64 (s, 3H, C-CH_3). In this reaction sequence, cyclization of the quinone methide (10) leads to the spirobenzylisoquinoline intermediate (11) which possesses a net positive charge spread between rings C and D. This charge induces formation of the aziridinium ion (12) which can readily be transformed into product (14). A net positive charge is lacking in rings C and D of the spirobenzylisoquinoline intermediates involved in the rearrangements of salts (1), (3), (5), and (7).

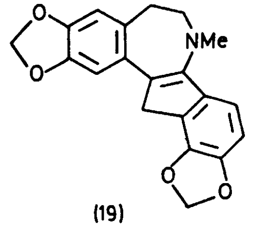
The dehydration of the spirobenzylisoquinoline (17) to the olefinic dibenzocyclopent[*b*]azepines (18) and (19) under ionic conditions has recently been reported.[4] Although no mechanism was offered, it is logical to assume that an aziridinium ion is involved in this transformation.



(17)



(18)



(19)

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[1] M. Shamma and C. D. Jones, *J. Amer. Chem. Soc.*, 1969, **91**, 4009; 1970, **92**, 4943.

[2] M. Shamma and J. F. Nugent, *Tetrahedron Letters*, 1970, 2625.

[3] The syntheses of monophenols (5), (7), and (9) do not involve any drastic departures from the similar preparations already described in ref. 1, and will be given in detail in a later paper. Acceptable elemental analyses and/or high-resolution mass spectra, and other spectroscopic data, were obtained for all compounds described.

[4] H. Irie, S. Tani, and H. Yamane, *Chem. Comm.*, 1970, 1713.