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A NEW DEGRADATION OF THEBAINE TO MORPHINANDIENONE DERIVATIVES

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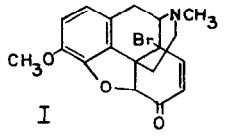
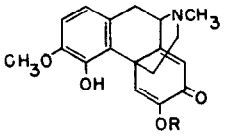
In the course of other work we have encountered an interesting conversion of 14-bromocodeinone (I), easily available in a single step from thebaine[1], into a new substance which proved to be the parent diketone of salutaridine (III), an important biosynthetic precursor of thebaine.[2] Thus, although 14-bromocodeinone has been reported to be insoluble in alkali[1a], we find that it dissolves readily in Claisen's alkali and that neutralization of the solution gives in fair yield the enolic diketone II, m.p. 220 - 225° dec, $[\alpha]_D^{22}$ + 130° (C 1.09, $CHCl_3$); methiodide, m.p. 164 - 166° dec, which we have called 6-0-demethylsalutaridine.



I



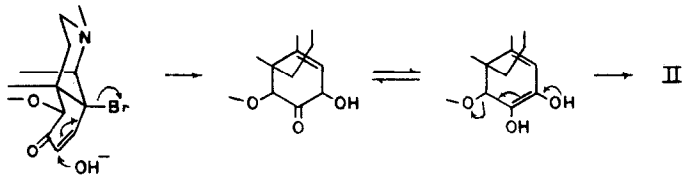
II R=H

III R=OCH3

The structure of II is clearly defined by its spectral characteristics, particularly its uv spectrum (λ_{max}^{etOH} 240 nm (ε 20,000), sh 280 nm (ε6000) which agrees well with that of salutaridine.[2] The ir spectrum (broad peak 1640 cm^{-1}, shoulders 1670, 1620 and 1600 cm^{-1}, Nujol) also is in accord with a cyclohexadienone structure. The substance also exhibits a molecular ion peak at m/e 313 in its mass spectrum. The most distinctive feature of the nmr spectrum of 6-0-demethylsalutaridine is a sharp singlet at 7.88 δ ($CDCl_3$) assignable to the C_5-H (the C_5-H of salutaridine appears at 7.56 δ); the other assignable absorptions (2.45δ, N-CH_3; 3.87δ, O-CH_3; 6.71 and 6.74δ, aromatic H; 6.43 δ, C_8-H)are very close to those of salutaridine.

Finally, methylation with diazomethane yields salutaridine[3] as the predominant product along with a trace of what is thought to be o-methylsalutaridine.

The following reaction sequence appears to account for the production of 6-O-demethylsalutaridine:



In particular, the geometrical requirements of the SN_2' displacement[4] of bromine by hydroxyl are unusually well-met by this system in which the ordinary reactions of tertiary halides are at least partially suppressed by geometrical constraints.

This facile series of reactions provides a simple entry into the morphinandienone alkaloid series of which the number of examples continues to grow. We are at present investigating certain of the rearrangements undergone by this system.

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1. a) M. Freund, Chem. Ber., 39, 844 (1906); b) H. Conroy, J. Am. Chem. Soc., 77, 5960 (1955).
2. D. H. R. Barton, G. W. Kirby, W. Steglich, G. M. Thomas, A. R. Battersby, T. A. Dobson and H. Ramuz, J. Chem. Soc., 1965, 2423. In this paper the conversion of thebaine to salutaridine by another route is described and the isolation of salutaridine from Croton salutaris by R. A. Barnes is referred to. Salutaridine has also been isolated from C. Balsamifera Jacq. by C. Chambers, L. J. Haynes and K. L. Stuart. (Chem. Comm., 1966, 449) and its enantiomer sinoacutine has been isolated from Sinomenium acutum by H. Chu, S. Y. Lo and Y. L. Chow (Acta. Chimica. Sinica., 30, 265 (1964), Chem. Abstr., 61, 12037h (1964).
3. Identical in all respects with a sample graciously supplied by Professor D. H. R. Barton.
4. The formation of 7-methoxyneopine by SN_2' displacement of bromine from 14-bromocodeine has been reported by Okuda, et al. Chem. Pharm. Bull. (Japan) 16 (6) 1124 (1968) and Conroy[1b] had suggested that the conversion of 14-bromocodeine to neopine by sodium borohydride might be the result of an SN_2' displacement.