Orientalinone, Dihydro-orientalinone, and Salutaridine from *Papaver orientale*: Related Tracer Experiments

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IT has been suggested[1] that (+)-isothebaine (III) is formed by dienol–benzene rearrangement of the dienol derived from (−)-orientalinone (II), this in turn being generated by phenol oxidation[2] of orientaline (I). Supporting evidence came from the incorporation of (±)-[*O*-methyl, 3-^{14}C]orientaline (as I) into isothebaine without change of the ^{14}C-ratio.[3]

In order to demonstrate the intermediacy of the dienone (II) the following experiments were carried out.

(a) The alkaloids from the foregoing feeding experiment, after extracting the isothebaine, were diluted with synthetic[4] (±)-orientalinone (as II) which was then re-isolated and rigorously purified. The activity of the dienone so obtained corresponded to an incorporation into orientalinone (II) of 0·02% of the (±)-orientaline fed.

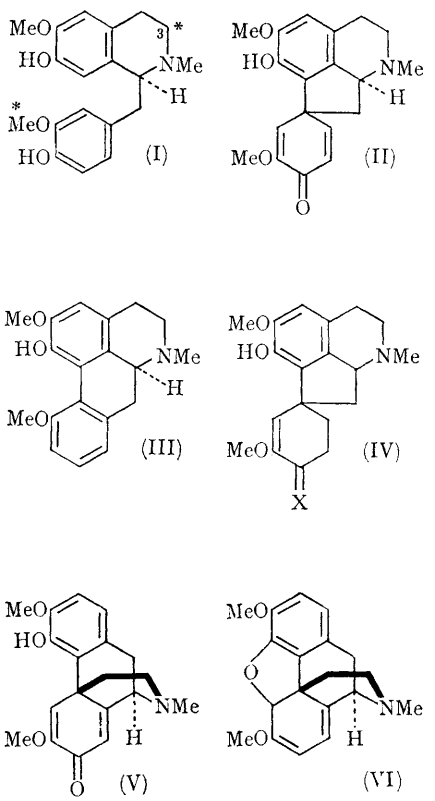
(b) (±)-[*N*-methyl-^{3}H]Orientalinone (as II) prepared by oxidation[4] of (±)-[*N*-methyl-^{3}H]orientaline was administered to *P. orientale* plants; the isolated isothebaine (2·1% incorpn.) was shown to be labelled solely at the *N*-methyl group (Herzig–Meyer).

(c) The alkaloids from *ca.* 100 large *P. orientale* plants were separated by countercurrent distribution and chromatography to yield three alkaloids in addition to the four previously isolated from this plant.[5] One (50 mg.) was shown by complete chemical and physical study to be identical with synthetic (−)-orientalinone[4] (II).

The foregoing results together with the earlier ones[3] constitute powerful evidence for the steps (I) → (II) → (III) in *P. orientale*.

The second alkaloid (29 mg.) was similarly proved to be (+)-salutaridine (V) by comparison with partially synthetic material.[6] This substance has been shown to be the precursor of thebaine (VI) by tracer experiments of *P. somniferum*.[6] Since thebaine accompanies isothebaine in *P. orientale*,[5] it is particularly significant that (−)-orientalinone (II) and (+)-salutaridine (V) can both be isolated from this plant and that they have the absolute configurations corresponding, respectively, to those of (+)-isothebaine (III) and (−)-thebaine (VI). The same dienones have also been isolated independently from *P. bracteatum*.[7]

The mass spectrum of the third alkaloid (59 mg.) $[\alpha]_D$ + 50° ($CHCl_3$), was very similar to that of orientalinone (II) save that the prominent peaks (at M^+ −1, −15, −29, −31, and −43) were shifted two units higher (M+ 329), $C_{19}H_{23}NO_4$. Also



the alkaloid was clearly an $\alpha\beta$-unsaturated ketone (ν_{max} 1680, 1625 cm.$^{-1}$) so that a dihydro-orientalinone structure (*e.g.*, IV, X = O) was probable. In agreement with this, the n.m.r. spectrum showed two *O*-methyl groups (τ 6·22 and 6·46), one *N*-methyl group (τ 7·65), one aryl proton (singlet, τ 3·52) and a singlet at τ 4·36 (1H, olefinic; *cf.* spectrum of orientalinone[4]). Borohydride reduction of orientalinone (II) can yield epimeric dihydro-orientalinols (IV, X = H, OH) and these

two products are identical (chromatography, infrared and mass spectra) with the pair produced by reduction of the new alkaloid under the same conditions. These results establish its constitution as (+)-dihydro-orientalinone (IV, X = O) which stands structurally in the same relation to orientalinone (II) as does linearisine to *N*-methylcrotonosine.[8]

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