Structure of the Products of the Photochemical Rearrangement of the Adduct of Thebaine with Dimethyl Acetylenedicarboxylate

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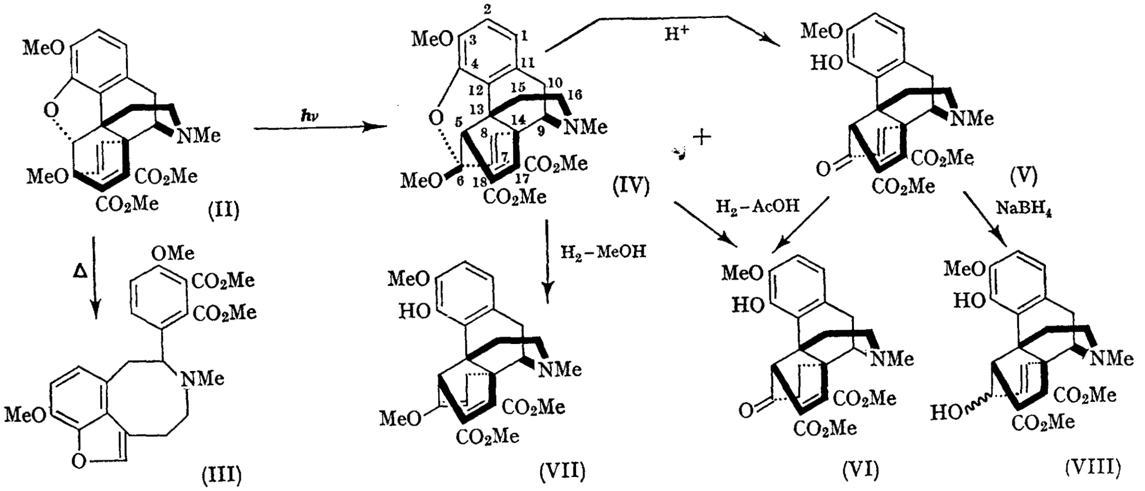
THERE appears to have been no systematic study of the photochemistry of the morphine series. Recently, Barneis *et al.*[1] reported a study of photochemically induced rearrangements of thebainequinone and thebainehydroquinone, which possess the enedione or the hydroquinone system within the morphine skeleton (I). We now report the isolation and proof of the structures of photochemically induced rearrangements of the adduct (II), which possesses the bicyclo[2,2,2]octadiene system within the morphine skeleton. In 1963, a novel thermal rearrangement product of the adduct (II) was assigned a benzazocine structure (III).[2]

Irradiation of a 90% water–dioxan solution of (II), in a Pyrex vessel under nitrogen using a high-pressure, mercury lamp, gave (IV) (82%), pale yellow prisms, m.p. 184°, $C_{25}H_{27}NO_7$, M^+, 453 (mass spectrometry), 458 (osmometry in chloroform), ν_{max} (KBr) cm.$^{-1}$ 1730s, 1712,wsh,



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(conjugated diesters) and 1620m (double bonds), and (V) (low yield), yellow prisms, m.p. 270—272° (decomp.), $C_{24}H_{25}NO_7$, M^+,439 (mass spectrometry, ν_{max} (KBr) cm.$^{-1}$ 3445s (hydroxyl), 1730s (conj. diesters), 1695s (conjugated ketone), and 1635m (double bonds). In (IV), olefinic protons are at 6·24 (1H, doublet, $J = 9\cdot5$c./sec.) and 4·98 ppm (1H, doublet of doublets, $J = 9\cdot5$ and 2·5c./sec.), which shows that disposition of the C-5 and C-7 hydrogen atoms is such as to permit long-range coupling by Dreiding models; (IV) lacked absorption for the proton adjacent to oxygen by the n.m.r. Compound (IV) is nonphenolic, but differs from adduct (II) in being sensitive to acid hydrolysis. Colour reactions for the hydrolysis product (immediate red precipitates with *p*-nitrobenzenediazonium fluoroborate, a blue-green colour with Gibbs' reagent, and yellow precipitates with 2,4-dinitrophenylhydrazine) were characteristic of the phenolic ketone. The hydrolysis product, m.p. 270—272° (decomp.), thus obtained from (IV), and compound (V) have identical analytical values, i.r., u.v., and n.m.r. spectra. Olefinic protons for (V) appeared at 6·95 (1H, doublet, $J = 10$c./sec.) and 5·36 p.p.m. (1H, doublet of doublets, $J = 10$ and 2c./sec.); it is probable that anisotropy of the conjugated carbonyl group accounts for the displacement to low-field side of one of the two protons in the AB-type. The ultraviolet spectra showed maxima at 239 (shoulder) and 280 mμ in (IV), and at 280 and 328 mμ in (V), and the last band can be assigned only to an $\alpha\beta$-unsaturated ketone. Catalytic hydrogenation of (IV) with PtO_2 in acetic acid gave the phenolic dihydro-compound (VI), $C_{24}H_{27}NO_7$, m.p. 200—205° (no olefinic protons by n.m.r.), and showed a strong broad absorption at 1730—1710 cm.$^{-1}$ (five-membered conjugated diesters and six-membered saturated ketone; no absorption for $\alpha\beta$-unsaturated ketone), which was also obtained by hydrogenation of (V). Reduction of (V) with sodium borohydride in methanol yielded (VIII), $C_{24}H_{27}NO_7$, m.p. 209—211° (decomp.). Catalytic hydrogenation of (IV) with PtO_2 in methanol gave the phenolic compound (VII), $C_{25}H_{29}NO_7$, m.p. 231—234°, which showed one olefinic proton as a pattern centred at 5·80 p.p.m. and two methoxy- and two methyl ester groups at 3·81 (3H), 3·78 (3H), and 3·68 (3H $\times$ 2) p.p.m. in the n.m.r. spectrum. These data suggest that one of the two double bonds in (IV) is part of an allylic ether system which could suffer 1:4-reduction to give the phenolic compound (VII). As a result, it was suggested that (IV) contained the mixed acetal of an $\alpha\beta$-unsaturated ketone, and (V) had an $\alpha\beta$-unsaturated, six-membered ring ketone in the molecule. Furthermore, the methoxy- and methyl ester groups appeared at 3·85 (3H), 3·81 (3H), 3·80 (3H) and 3·52 (3H) in (IV), and at 3·89 (3H), 3·80 (3H) and 3·78 (3H) in (V), respectively. The shifts of the infrared frequencies of the carbonyl groups of (IV) from that of (II) (1720 cm.$^{-1}$) suggest the presence of conjugated diester groups in a five-membered ring. Therefore, the novel photochemical rearrangement products were assigned 17,18-bis-(methoxycarbonyl)-4(*O*)-6-dehydro-5,14-etheno-6-methylthebainol (IV) and 17,18-bis-(methoxycarbonyl)-5,14-ethenothebainone (V).[3]

Compound (IV) has weak analgetic effects (ED_{50} 46·2 mg./kg. compared to 7·0 mg./kg. for codeine in mice) but the adduct (II) exhibited no activity.

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[1] Z. J. Barneis and D. M. S. Wheeler, *Tetrahedron Letters*, 1965, **275**.

[2] H. Rapoport and P. Sheldrick, *J. Amer. Chem. Soc.*, 1963, **85**, 1636.

[3] The structure assigned to (IV) shows a skeletal resemblance to that proposed for isonepenthone and isothevinone; K. W. Bentley and J. C. Ball, *J. Org. Chem.*, 1958, **23**, 1725; K. W. Bentley, D. H. Hardy, H. P. Crocker, D. I. Haddlesey, and P. A. Mayor, *J. Amer. Chem. Soc.*, 1967, **89**, 3312.