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ISOLATION AND STRUCTURE OF PHOTOTHEBAINEHYDROQUINONE

Z. J. Barneis and D. M. S. Wheeler
Department of Chemistry, University of Nebraska,
Lincoln, Nebraska 68508*

and

T. H. Kinstle
Department of Chemistry, University of Illinois,
Urbana, Illinois 61803

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Although there have been scattered accounts of the effect of light on morphine and some of its derivatives (1), there appears to have been no systematic study of the photochemistry of this series of compounds. We now report the isolation and characterization of a photo product related to thebaine.

Irradiation of solutions of thebainequinone (I) (λ_{max} 289 mμ, $\mathcal{E}$ 3500) (2) or thebainehydroquinone (IIa) (λ_{max} 310 mμ, ϵ 5600) (2) in dioxane in a nitrogen atmosphere with light from a high pressure mercury lamp, gave photothebainehydroquinone (m.p. 156-157°, λ_{max} 309 mμ, $\mathcal{E}$ 11,000, $C_{50}H_{50}O_{10}N_2$, molecular

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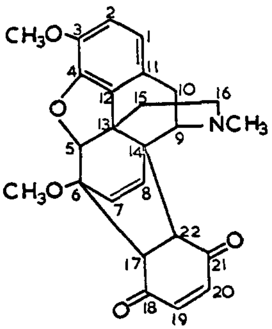
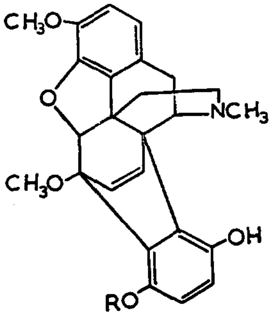
*This work was started in the Department of Chemistry, University of South Carolina, Columbia, South Carolina. Portion of it was done while one of us (D.M.S.W.) was at the University of Illinois (summer 1964).

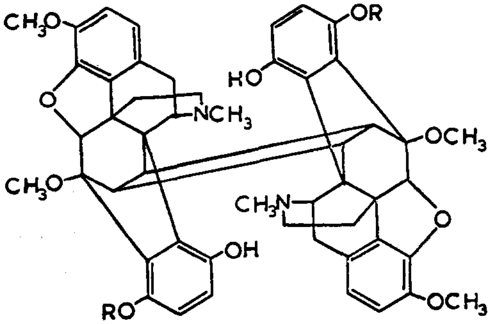


I



IIa R= H

IIb R= $\underset{\overset{\|}{O}}{C}-CH_3$



IIIa R=H

IIIb R= $\underset{\overset{\|}{O}}{C}-CH_3$

weight found (isothermal distillation method) 836 and 842, required 838; for dihydrochloride found: C, 66.57; H, 5.91; O, 17.04; N, 3.00; Cl, 7.57. $C_{50}H_{50}O_{10}N_2 \cdot 2HCl$ requires: C, 65.91; H, 5.71; O, 17.54; N, 3.08; Cl, 7.80%.) in yields of up to 65%. The course of this reaction was followed by analyzing samples from the reaction by thin-layer chromatography. No trace of the starting compounds could be detected after 8 hours reaction time. The formation of photothebainehydroquinone started immediately and its concentration reached a maximum after 10 hours; it then decomposed to at least 2 further products. (This has been confirmed by irradiation of photothebainehydroquinone).

The ultraviolet spectrum, analysis and molecular weight determinations of photothebainehydroquinone suggest that it is a dimer IIIa of IIa through the C_{7-8} double bonds. A study of the nuclear magnetic resonance spectra* of IIa, IIIa and other related compounds supports this structure. The major difference between the spectra of IIa and IIIa is that the signals for the C_7 and C_8 vinyl protons ($\delta = 5.5$-6.5) in the spectrum of IIa no longer appear in that of IIIa. Instead the integration indicates the presence of signals corresponding to 2 protons (based on the monomer) about $\delta = 2.0$-3.0, a region in which the peaks for cyclobutane protons would be expected. In the spectra of I and IIa the signal corresponding to the proton at C_5 ($\delta = 4.7$-4.8) is split by one of the vinyl protons at C_7 and C_8. In agreement with Rapoport and Sheldrick (3), who suggested that this splitting is characteristic of the Diels-Alder adducts of

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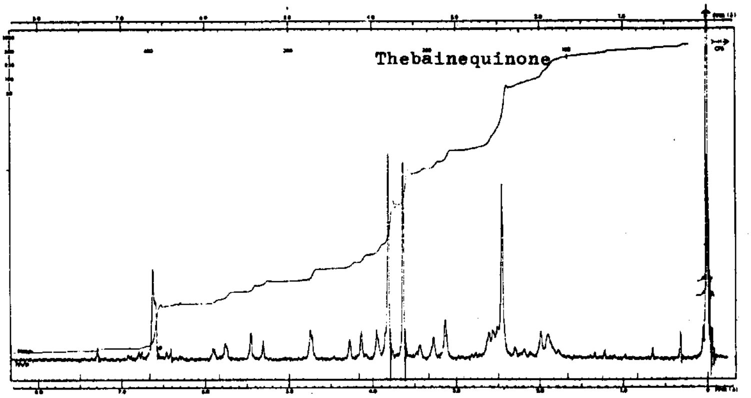
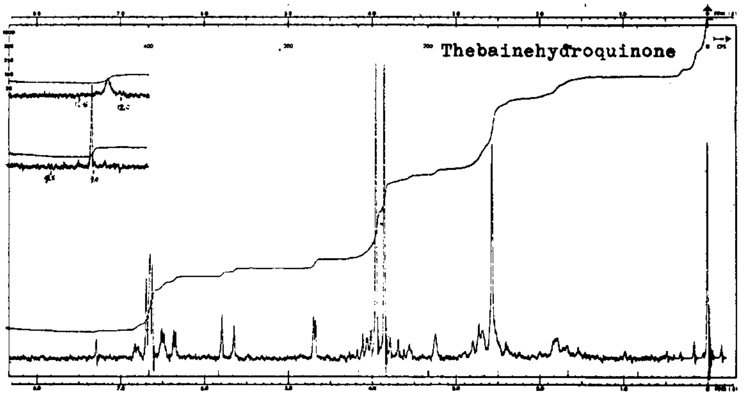
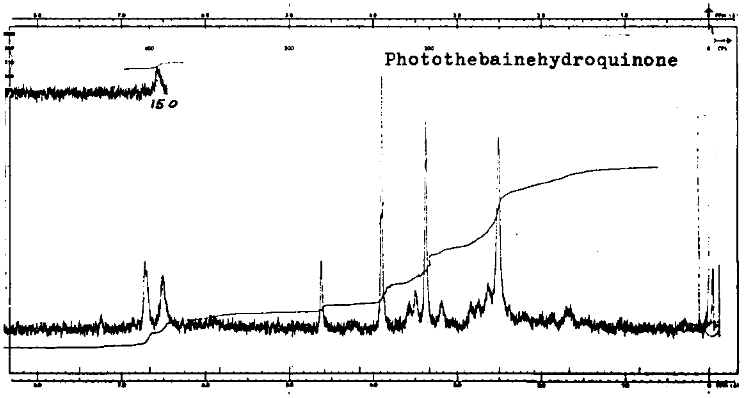
*The spectra reported in this communication were run in $CDCl_3$ solutions.


Thebainequinone


Thebainehydroquinone


Photothebainehydroquinone
150

thebaine, we believe that the C_7 proton is involved. The splitting no longer appears in the photocompound. Two of the hydroxyl protons (based on dimer) in the photocompound are involved in strong hydrogen bonds; their n.m.r. signal appears at $\delta = 15.0$.[*] In accord with this the photocompound has a broad low-intensity infrared absorption band centered at 1885 cm.$^{-1}$ (*cf.* 4). It forms a diacetate (IIIb) (m.p. 249°; Found: C, 69.91; H, 6.09; O, 21.18; N, 3.14. $C_{54}H_{54}O_{12}N_2$ requires C, 70.27; H, 5.90; O, 20.80; N, 3.04%), which also has a signal corresponding to two protons (based on dimer) at $\delta = 15.0$ and absorbs in the infrared at 1850-1800 cm.$^{-1}$

The assignment of structures IIIa and IIIb is confirmed by a study of their mass spectra.[+] Above m/e 200 the spectra closely resemble those of the corresponding monomeric compounds IIa and IIb (5), thus showing that skeletal rearrangements did not occur during the photochemical reaction. There are no peaks at m/e higher than the molecular weight of the monomer; this is not unexpected: the dimers are much less volatile than the monomers and must be heated strongly before a spectrum appears; under these conditions they dissociate to the corresponding monomers. It is not known whether the reversal to monomer is an electron impact or thermal phenomenon. The differences below m/e 200 between the spectra of IIIa and IIIb and their corresponding monomers are due perhaps to partial pyrolysis of IIa and IIb which results from the necessarily strong heating of IIIa and IIIb.

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[*] The corresponding signal in IIa appears at $\delta = 12.1$

[+] Detailed accounts of the mass spectra of these compounds and others in the morphine series will appear shortly.

While the details of the mechanism of the conversion of I or IIa to IIIa have still to be worked out (cf. 6), it seems clear that the reaction must involve an intramolecular sensitization of the C_7-C_8 double bond in I and IIa by the enedione or the hydroquinone system. Further, the observation that both I and IIa give IIIa suggests that the monomers are interconverted photochemically.

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