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CONCENTRATION DEPENDENT PHOTOXIDATION OF 13-HYDROXYBERBERINIUM PHENOLBETAINE AND FORMATION OF STABLE EPIDIOXY COMPOUND

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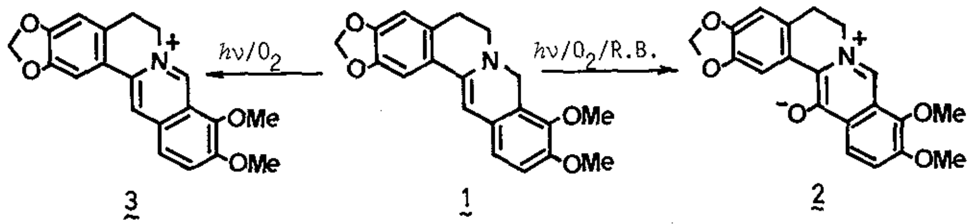
Irradiation of an oxygenated solution of 13-hydroxyberberinium phenolbetaine 2 in over 0.1% concentrations gave a stable epidioxy derivative, 8,13a-epidioxy-2,3-methylenedioxy-9,10-dimethoxy-13-oxo-dibenzo[a,g]quinolizidine 4 in 42% yield. Contrast to it, in a below 0.01% solution photoxidation of 2 gave berberal 5 in 56% yield.

The reactions are interpreted as occurring by initial addition of singlet oxygen to give a peroxide intermediate A which subsequently gave 4 and 5 *via* the 1,2-dioxetane B depending upon concentrations of A, respectively.

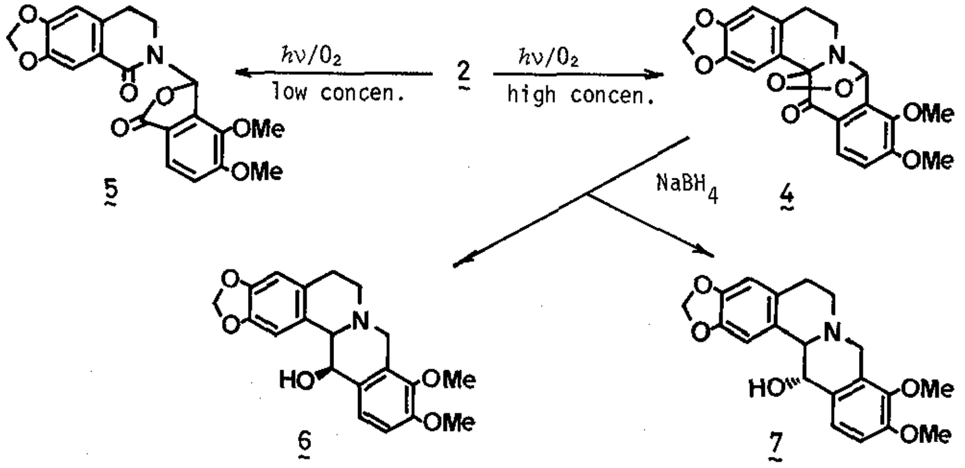
As has been expected from our current investigations[1-3], an analog dihydroberberine[4] 1 was smoothly converted to 13-hydroxyberberinium phenolbetaine[5] 2 by dye-sensitized (Rose Bengal) photoxidation in 80% yield. On the other hand, photoxidation of 1 in the absence of the sensitizer afforded berberine 3 in 70% yield with minor formation of the phenolbetaine 2 in 8% yeild (Scheme 1).

Further irradiation of 2 in the presence of oxygen resulted either an



Scheme 1

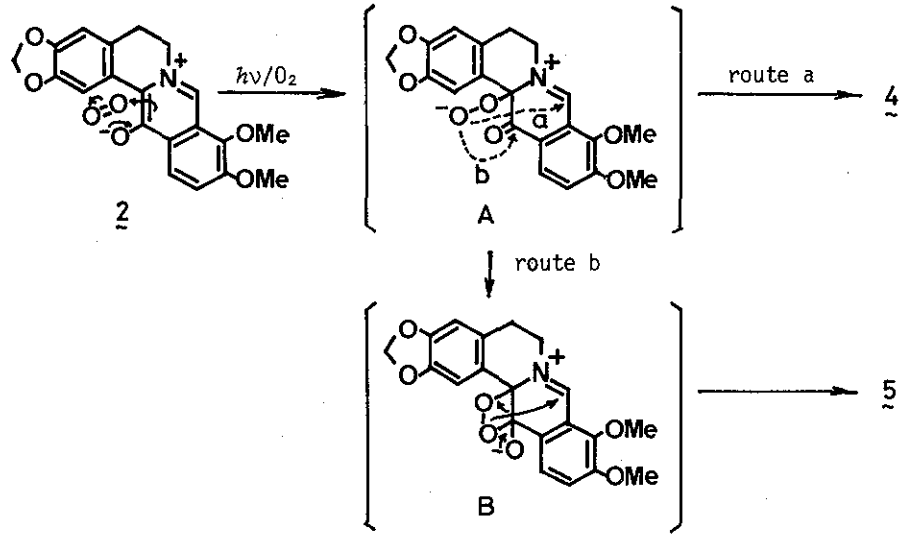
epidioxy compound 4 or *berberal* 5 depending upon the concentration of the solution. A solution of 2 (over 0.1%) in methanol was exposed to sun-light (of winter in Sendai) in the presence of oxygen to yield a tertiary base 4, mp 100.5-101.5°, in 42% yield. The compound 4 had the molecular formula $C_{20}H_{17}O_7N$ on the basis of elemental analysis[6] and mass spectral results (m/e 383, M^+). The IR spectrum of 4 displayed the absorption of a conjugated carbonyl group at 1690 cm^{-1} and lacked that of a hydroxyl group. The UV spectrum showed absorption maxima at 226 (log ε 4.49), 269 (4.04) and 309 nm (3.93). The NMR spectrum (in d_6-acetone) of 4 revealed the presence of a couple of methylene groups, two methoxyls, a methylenedioxy, a methin proton, and four aromatic ring protons at 2.80 (2H, m), 3.25 (2H, m), 3.88 (3H, s), 3.98 (3H, s), 6.01 (2H, s), 6.54 (1H, s), 6.71 (1H, s), 6.82 (1H, s), 7.20 (1H, d, J=8.5 Hz), and 7.75 (1H, d, J=8.5 Hz), respectively. The highly deshielded singlet appearing at 6.54 ppm was consistent with the chemical shift of the proton on the carbon bearing the oxygen and nitrogen atoms. Treatment of 4 with $NaBH_4$ in methanol gave a mixture of *dl*-ophiocarpine[5] 6 and *dl*-13-*epi*-ophiocarpine 7, mp 184-186° (lit.[7] mp 176°), in 72% and 8% yield, respectively. The spectral results of 7 were shown as follows; IR (KBr) cm^{-1}: 3300 (-OH), 2740 and 2780 (Bohlmann band). NMR ($CDCl_3$) δ (ppm): 2.26 (1H, br. s, -O$\underline{H}$), 2.75 (2H, m, $-CH_2-\underline{CH_2}N<$), 3.12 (2H, m, $-\underline{CH_2}-CH_2N<$), 3.48 (1H, d, J=8.5 Hz, Ar-CH-N<), 3.66 (1H, d, J=16 Hz, Ar-CHH-N<), 3.88 (3H, s, -OCH$_3$), 3.90 (3H, s, -OCH$_3$), 4.13 (1H, d, J=16 Hz, Ar-CHH-N<), 4.70 (1H, br. d, J=8.5 Hz, Ar-CH-OH), 5.96 (2H, s, -OCH$_2$O-), 6.64 (1H, s, Ar-H), 6.90 (1H, d, J=8 Hz, Ar-H), 7.29 (1H, d, J=8 Hz, Ar-H), 7.45 (1H, s, Ar-H). MS (m/e): 355 (M^+). Based on these findings compound 4 is best represented by the structure 8,13a-epidioxy-2,3-methylenedioxy-9,10-dimethoxy-13-oxo-dibenzo [a,g]quinolizidine.



Scheme 2

In the more dilute solutions serious difference was observed. When a methanol solution (below 0.01%) of 2 was irradiated in the same fashion, berberal 5, $C_{20}H_{17}O_7N$, mp 153-155° (lit.[8] mp 148-150°) was obtained in 56% yield. The spectral data of 5 were shown as follows; IR (KBr) cm^{-1}: 1760 (lactone), 1650 (amide). NMR (d_6-benzene) δ (ppm): 2.25 (2H, t, J=7 Hz, -CH$_2$-CH$_2$N<), 2.59 (1H, dd, J_1=7 Hz, J_2=14 Hz, -CHH-CH$_2$N<), 2.86 (1H, dd, J_1=7 Hz, J_2=14 Hz, -CHH-CH$_2$N<), 3.35 (3H, s, -OCH$_3$), 3.61 (3H, s, -OCH$_3$), 5.37 (2H, s, -OCH$_2$O-), 6.13 (1H, s, -CO-O-CH-N<), 6.50 (1H, d, J=8 Hz, Ar-H), 7.43 (1H, d, J=8 Hz, Ar-H), 7.73 (1H, s, Ar-H), 7.82 (1H, s, Ar-H).

UV (MeOH) nm (log ε): 223 (4.56), 265 (4.09), 305 (3.83). MS (m/e): 383 (M^+), 193, 190.



Scheme 3

Although a little work has been reported concerning the influence of the concentration on photoxidation[9], we postulated a provisional reaction mechanism as follows. The photoxidation of 2 might start by addition of singlet oxygen to form the dipolar intermediate A[10]. In dilute solutions A could exist in the state of separated ion pair which facilitates the subsequent formation of the 1,2-dioxetane intermediate[11] B and cleavage between the C^{13a}-C^{13} bond followed by concomitant cyclization gives berberal 5 (route b in Scheme 3). On the other hand, in case when the photoxidation is carried out in a more concentrated solution, a simple cyclization is favored to yield the epidioxy compound 4 (route a in Scheme 3).

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