HETEROCYCLES, Vol 19, No 11, 1982

A PHOTOCHEMICAL CONVERSION OF A SPIROBENZYLISOQUINOLINE INTO A SECOBERBINE

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Abstract: Oxidative photolysis of the spirobenzylisoquinoline alkaloid (-)-fumaricine (1) provides the secoberbine (±)-2.

The isoquinoline alkaloids fall within several main groups, and one of the more interesting features of isoquinoline natural products chemistry in recent years has been the large number of in vitro transformations that have been carried out interrelating these different categories. An exception to this trend has been the spirobenzylisoquinolines which, although numbering almost thirty naturally occurring bases, have so far been converted in the laboratory only into isoquinolones and indenobenzazepines.[3] We describe here the transformation of a spirobenzylisoquinoline into a secoberbine.

Photo irradiation of an ethanolic solution of the spirobenzylisoquinoline (-)-fumaricine (1) using a Hanau low pressure TNN 15/32 mercury lamp equipped with a quartz filter for six hours, while continuously passing a stream of air, afforded in 4% yield the colorless, optically inactive, secoberbine 2, $C_{21}H_{21}O_7N$, mp 267° C (ethanol).

The 200 MHz $CDCl_3$ NMR spectrum of secoberbine 2 has been summarized around expression 2. Of particular significance is the one-proton singlet at δ 5.93 assigned to H-8 which is both benzylic and alpha to two oxygen atoms.[4] There is also a fairly large difference in chemical shifts between the aromatic H-11 and H-12, which appear as doublets at δ 6.93 and 7.77, respectively, reflecting conjugation with a carbonyl group.

The IR spectrum, obtained as a KBr disc, exhibits a conjugated ketone absorption at 1700 cm^{-1}. The UV spectrum, λ max MeOH 233, 287 and 312 nm (log ε 4.29, 4.03 and 3.89), shows essentially no change upon addition of hydroxylic base. In dilute hydrochloric acid, however, a small bathochromic shift is realized, λ max MeOH-HCl 235, 287 and 320 nm (log ε 4.30, 3.98

and 4.00). The aforementioned UV spectrum in methanol is particularly significant since it helps eliminate from consideration alternate structure 3 in which the methylenedioxy substituent is located at C-11 and C-12. Such a species would evidence a spectrum incorporating a maximum between 260 and 263 nm,[3,5] a feature which is conspicuously absent in the spectrum of the isolated product 2.[6]

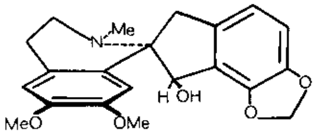
Treatment of 2 with sodium borohydride in ethanol and chloroform (5:1 v/v) led to reduction of the ketone function and formation of the amorphous dihydro derivative 4, $C_{21}H_{23}O_7N$. The 200 MHz $CDCl_3$ NMR spectrum for this compound has been outlined around expression 4. Salient features are the doublet of doublets at δ 6.86 and 7.12 (J = 7.9 Hz) representing H-11 and H-12, as well as the one-proton singlets at 5.51 (H-13) and 5.78 (H-8). Consonant with the absence of extensive conjugation in derivative 4, the UV spectrum shows a simple absorption pattern with λ max MeOH 209 and 287 nm (log ε 4.56 and 3.86).[7]

Finally, acetylation of 4 using acetic anhydride in pyridine at room temperature led to amorphous monoacetyl derivative 5, $C_{23}H_{25}O_8N$, λ max MeOH 209, 232 sh and 287 nm (log ε 4.67, 4.21 and 3.98), ν max KBr 1740 cm^{-1}, whose NMR spectrum again in $CDCl_3$ solution includes a 3-proton singlet at δ 1.89 due to the acetyl methyl, another 3-proton singlet at 2.38 representing the N-methyl group, two 3-proton singlets at 3.88 and 3.90 for the two methoxyls, and a 1-proton singlet at 5.72 representing H-8. The two methylenedioxy protons appear as a close doublet of doublets at δ 5.97 and 6.02 (J_{gem} = 1.5 Hz), while the four aromatic protons and H-13 form a complex absorption pattern between 6.71 and 6.96.[8,9]

A possible mechanism for the formation of photo product 2 would involve initial oxidative fission of the C-8 to C-14 bond of (-)-fumaricine (1) to furnish iminium salt 6 which could readily isomerize to enamine 7. Further oxidation would then lead to keto iminium salt 8 which can hydrate and cyclize to 2.

The racemic photo product 2 should be compared with, and is structurally close to, the secoberbine alkaloids (±)-hypecorine (9) and (±)-hypecorinine (10). It is also worth pointing out that even though two diastereomers are possible for a structure of type 2, only one was actually obtained.

ACKNOWLEDGMENT: M.S. was supported by grant CA-11450 from the National Cancer Institute, National Institutes of Health, USPHS, DHHS.



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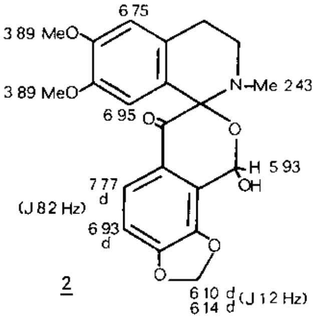

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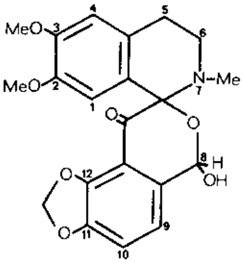

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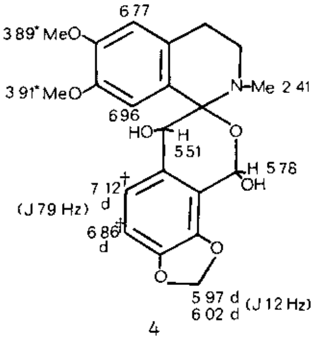

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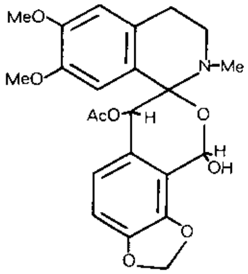

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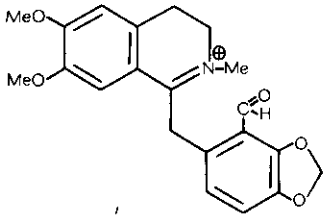

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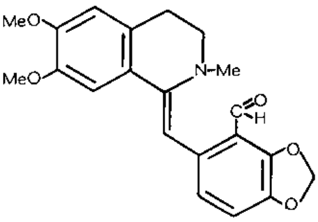

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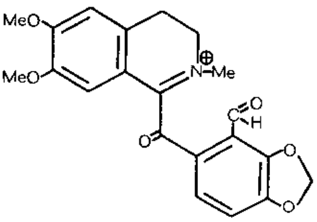

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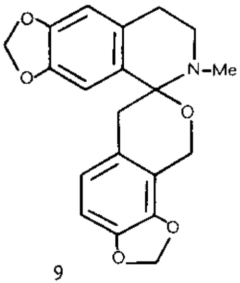

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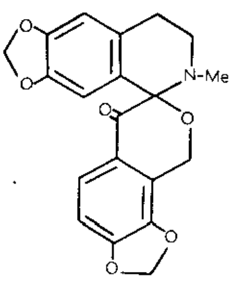

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REFERENCES AND FOOTNOTES

1. Permanent address: Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Ege University, Inciralti, Izmir, Turkey.
2. Permanent address: Department of Chemistry and Biochemistry, High Medical Institute, Plovdiv, Bulgaria.
3. G. Blaskó, S.F. Hussain and M. Shamma, J. Am. Chem. Soc., 104, 1599 (1982); and G. Blaskó, N. Murugesan, S.F. Hussain, R.D. Minard and M. Shamma, Tetrahedron Lett., 22, 3135 (1981).
4. The chemical shift of H-8 (δ 5.93) for compound 2 compares well with the shift value of δ 6.08 for H-14 in the rhoeadine alkaloid (+)-glaucamine which bears a similar benzylic hemiacetal linkage, see G. Sariyar and J.D. Phillipson, Phytochem., 19, 2189 (1980).
5. R.M. Preisner and M. Shamma, J. Natural Products, 43, 305 (1980).
6. The mass spectrum of 2 incorporates peaks m/z 382 $(M - 17)^+$ (7), 381 $(M - 18)^+$ (29), 336 (4), 204 (42), 190 (100), and 162 (10).
7. The mass spectrum of 4 has peaks m/z 384 $(M - 17)^+$ (2), 383 (9), 382 (8), 336 (3), 220 (3), 204 (22), 192 (100), 177 (9), 163 (11), and 149 (7).
8. The mass spectrum of 5 presents peaks m/z 426 $(M - 17)^+$ (11), 425 (44), 382 (43), 366 (100), 352 (23), 336 (32), 322 (13), 306 (12), 264 (41), 234 (34), 222 (63), 204 (65), and 192 (58).
9. Elemental analyses are by high and low resolution mass spectroscopy. NMR chemical shift values with identical superscripts are interchangeable.

Received, 19th July, 1982