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THE PHOTOLYSIS OF ENAMINE N-METHO SALTS

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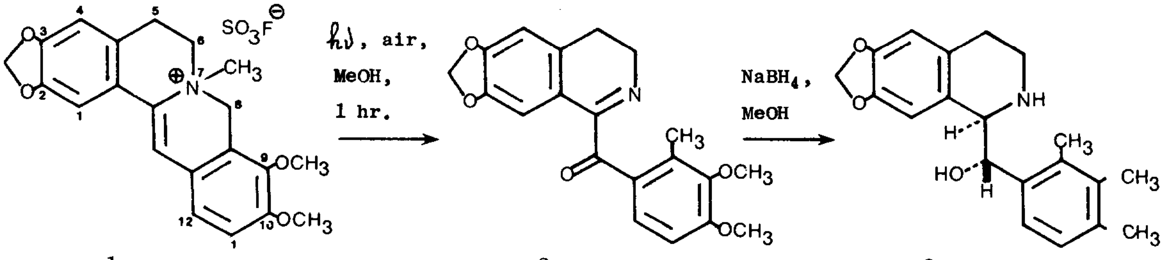
As part of a systematic study of the photolysis of enamines within the framework of protoberberine chemistry, we had occassion to subject a methanolic solution of the known N-methyl dihydroberberine salt 1[1] to sunlight for one hour. The product, isolated in 27% yield, proved to be the crystalline 1-(2′-methyl-3′,4′-dimethoxybenzoyl)-6,7-methylenedioxy-3,4-dihydroisoquinoline (2), $C_{20}H_{19}NO_5$, mp 107-110° (EtOH), $\nu_{max}^{CHCl_3}$ 1660 cm^{-1}, while the starting material 1 could be recovered in 55% yield. For the purpose of characterization, the imino ketone 2 was reduced with sodium borohydride to the amino alcohol 3, $C_{20}H_{23}NO_5$, mp 101-103° ($CHCl_3$-acetone).

In contrast, the analogous 13-methylated salt 4[2] when submitted to sunlight under identical conditions, cleanly afforded, together with approximately 50% of the starting material, a 36% yield of the amorphous spirobenzylisoquinoline 5, $C_{22}H_{23}NO_4$, λ_{max}^{EtOH} 244, 284 and 296 nm (log ϵ 4.01, 4.15 and 4.14), pmr $CDCl_3$ δ2.15 (3H, s, N-CH_3), δ4.98 and 5.67 (2x1H, 2s, $H_2C{=}C<$).

The conversion of a 13-methylated dihydroisoquinoline salt to a spirobenzylisoquinoline had previously been achieved through the intermediacy of a quinone methide when at least one phenolic function was present in the starting material.[3] The attractiveness of the present highly directed photorearrangement to a spirobenzylisoquinoline is enhanced by the greater availability of the non-phenolic substrate salt, since it is derived from commercially available berberine.



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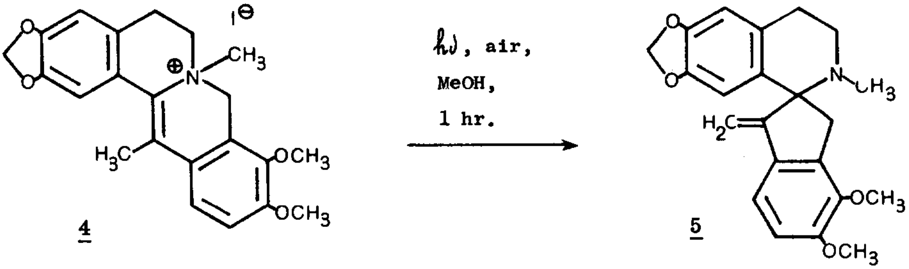
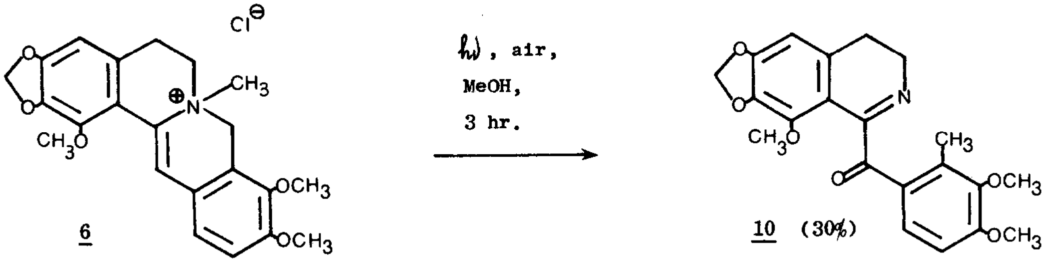
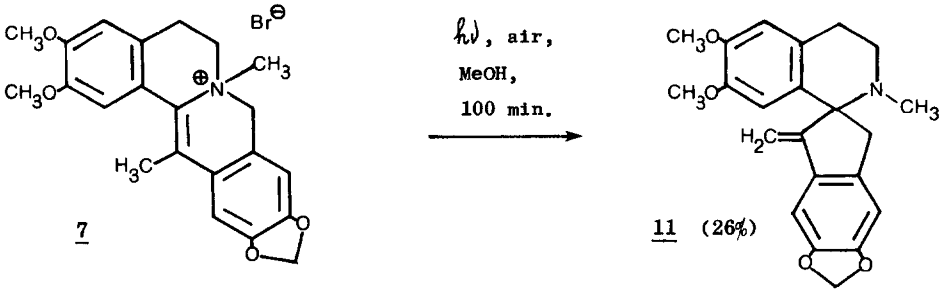
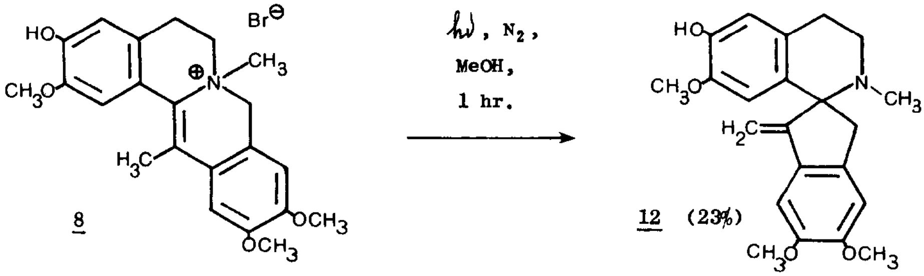
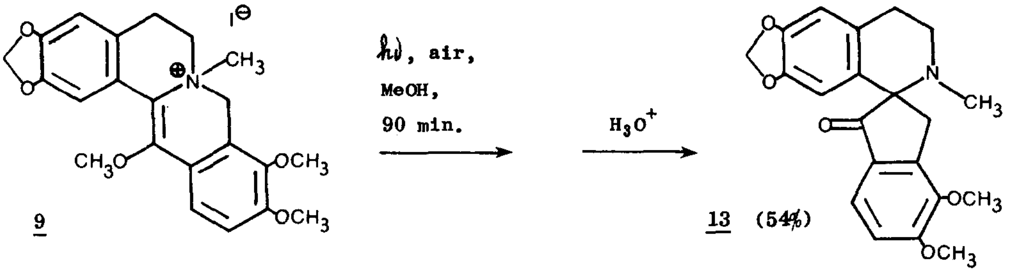


In order to define the scope of the above two light catalyzed transformations, the enamine salt <u>6</u>, as well as the C-13 substituted analogs <u>7</u>, <u>8</u>, and <u>9</u>, were placed in sunlight. In analogy with the two model cases, enamine salt <u>6</u>, mp 131-133° ($CHCl_3$-ether), derived from narcotine, provided a 30% yield of the amorphous imino ketone <u>10</u>, $C_{21}H_{21}NO_6$, $\nu_{max}^{CHCl_3}$ 1669 cm^{-1}, while salts <u>7</u>, <u>8</u>, and <u>9</u>, led to the amorphous spirobenzylisoquinolines <u>11</u>,[4] and <u>12</u>, $C_{22}H_{25}NO_4$, and the crystalline <u>13</u>,[5] respectively, the latter obtained in a remarkable 54% yield.

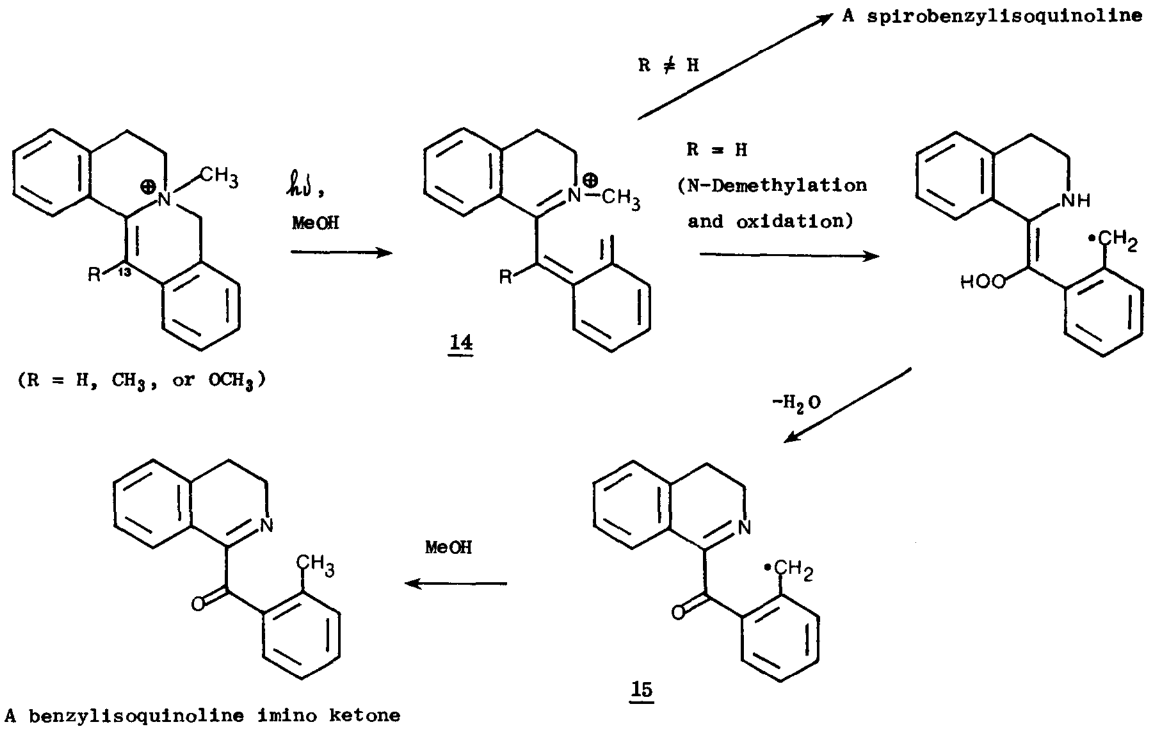






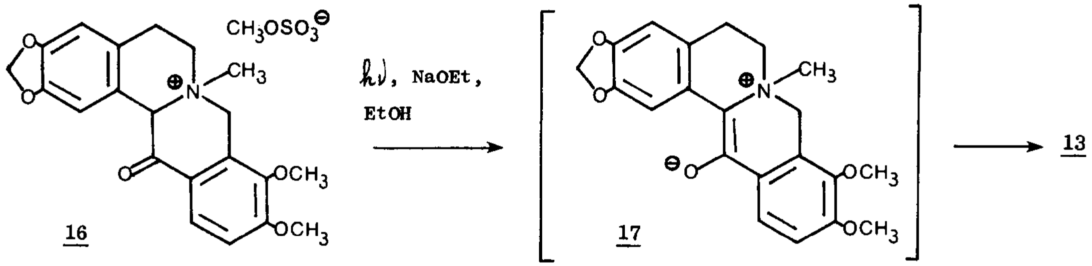


A mechanism which explains the formation of both benzylisoquinoline imino ketone and spirobenzylisoquinoline proceeds through the intermediacy of the *o*-quinodimethide 14 as shown below:



The generalization can thus be drawn that *N-metho protoberberine enamine salts unsubstituted at C-13 when subjected to sunlight will undergo N-demethylation and oxidation to provide the corresponding benzylisoquinoline imino ketones. The C-13 substituted enamine salts, on the other hand, will furnish spirobenzylisoquinolines.* The fact that the C-1 methoxylated salt 6 is converted to an imino ketone indicates that steric crowding, which should favor a conformation of the intermediate 14 favorable for spirobenzylisoquinoline formation, is not a dominant factor.

Photolysis of the N-metho amino ketone salt 16 has previously been shown to supply the spirobenzylisoquinoline 13.[5] This reaction has been correctly assumed to proceed through the intermediacy of the corresponding enamine salt 17, so that it constitutes yet another example of the photolytic rearrangement of a 13-substituted salt to a spirobenzylisoquinoline.



Important corollaries may be derived from this study. It is conceivable that the spirobenzylisoquinoline alkaloids, so far found solely within the Fumariaceae, may arise in nature by a similar rearrangement of dihydroprotoberberine enamine salts. Thus, the presence of phenolic groups in the precursors may very well not be an absolute requirement as previously assumed.[3] Furthermore, intermediates 14 (R = H) and 15 could be implicated in the formation of the secoberbines[6] which occur predominantly among the Fumariaceae and the botanically proximate Papaveraceae.

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