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OXIDATION OF APORPHINES BY TRIPLET BENZOPHENONE[1]

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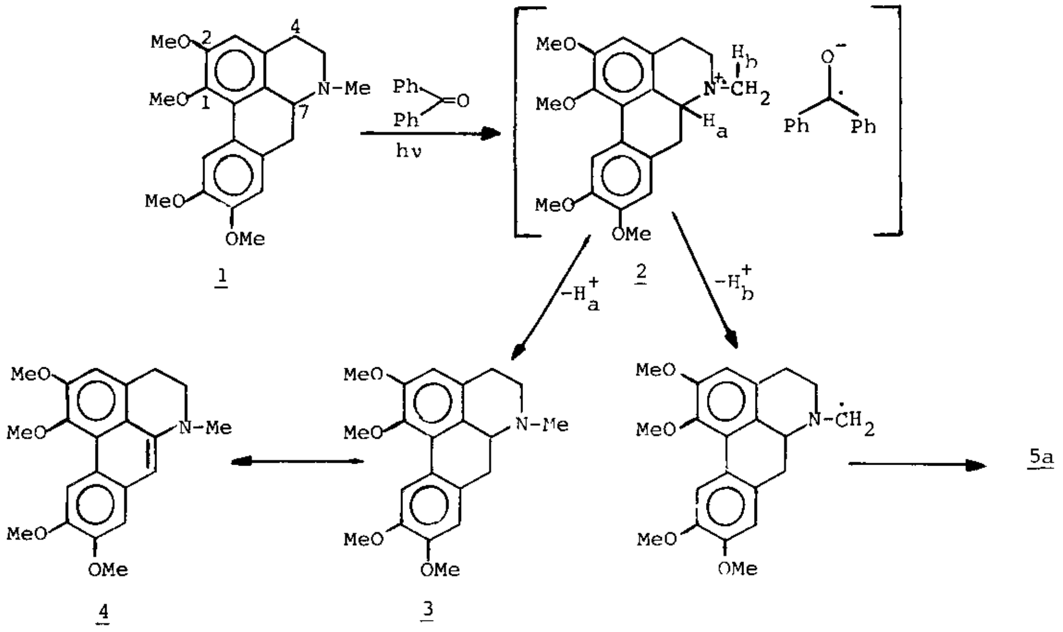
Abstract.- A mild and efficient method to dehydrogenate nonphenolic and phenolic aporphine and noraporphine alkaloids is described. It is based on the photoreduction of benzophenone by amines.

Continuing with our studies on the oxidation of aporphine alkaloids[3,4], we would like to report the results of the oxidation of a number of aporphines induced by triplet benzophenone. According to the generally accepted mechanism for the photoreduction of aromatic ketones by amines[5], two different pathways for the initially formed aminium radical(2) are likely to occur (scheme 1).

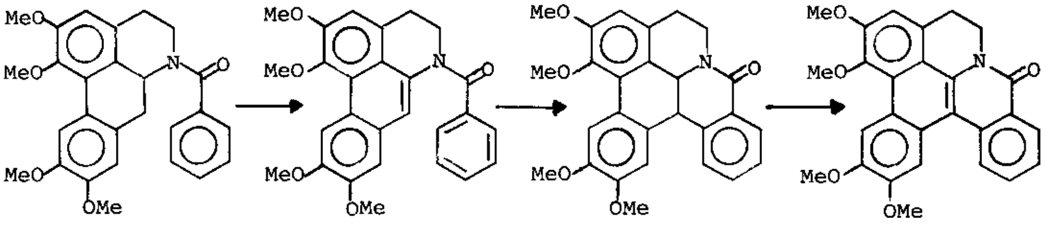


SCHEME 1

Cohen et al.[6] reported that cleavage at the least substituted carbon generally predominates, although some exceptions have also been observed[7]. Therefore, we hoped to convert aporphines into N-noraporphines (5a) by photooxidation, a process difficult to be achieved by conventional means[8]. However, when a pyridine/water solution of benzophenone and (+)glaucine (1)[9] was irradiated with a medium pressure mercury lamp for 45 mins. until almost complete disappearance of the starting material (1)(by tlc), a crystalline precipitate of benzopinacol was isolated together with a single basic product (75% yield), identified as dehydroglaucine (4).

At the present time the transformation of aporphines to the corresponding dehydroaporphines are the chemical oxidation with iodine^{10} or the direct dehydrogenation with Pd/C^{11}. However, these methods are limited to the nonphenolic aporphines, since noraporphines with iodine are oxidized all the way to the corresponding oxoaporphines and phenolic aporphines give essentially quinones^{10}. The milder reaction conditions used in the above described photodehydrogenation might overcome these limitations and therefore would be an alternative of wider application.

Thus, when benzophenone was irradiated in the presence of norglaucine hydrobromide (5a), dehydronorglaucine (6a) resulted in a high yield, although its instability precluded its isolation in more than 50% yield (mp 177ºC from ethyl ether)^{12}. Treatment of (6a) with ethyl chloroformate or oxalyl chloride gave in a quantitative yield the known urethane (6b)^{12} and the isatine (7)^{13}, respectively. To prevent the extended decomposition observed during work-up, norglaucine (5a) was converted to its N-benzoylderivative(8)by treatment with benzoyl chloride. When the photochemical dehydrogenation was then attempted on N-benzoylnorglaucine (8)a single product (10)resulted (by tlc) which was isolated in 72% yield (mp 171-73ºC from EtOH)^{13}. The formation of (10) can be rationalized as the result of initial dehydrogenation of (8) to the corresponding enamide (9), which in turn suffers the well known photochemical electrocyclization ^{14} followed by a second dehydrogenation (scheme 2).



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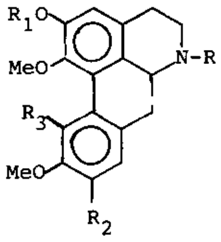
SCHEME 2

Similar dehydrogenation of the phenolic aporphine (+)boldine (5b) until complete disappearance of the starting material (tlc) produced a single product with identical characteristics of dehydroaporphines (UV),which rapidly decomposes during work-up. However, dehydrogenation of (+)boldine diacetate (5c) under the same conditions allowed the isolation of dehydroboldine diacetate (6c) in 50% yield (mp 123ºC from MeOH)^{13}.

When we attempted the dehydrogenation of O,O-dimethylcorytuberine (5d) , a 1,2,10,11-substituted aporphine, under the classical methods (I_2 or Pd/C) a poor yield of the corresponding dehydroaporphine (6d) was obtained conversely to 1,2,9,10-substituted aporphines^{10,11}. However, the photochemical dehydrogenation was also found advantageous in this case giving a 70% yield of the corresponding dehydroderivative (6d).



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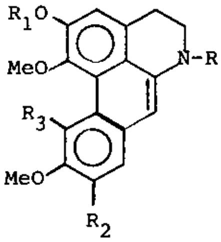

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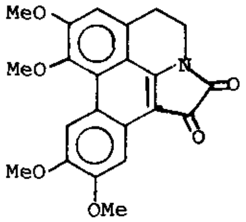

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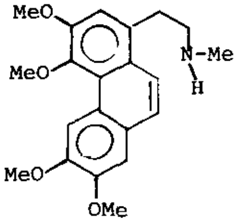

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a) R_1=Me; R_2=OMe; R_3=R=H.
b) R_1=R_3=H; R=Me; R_2=OH.
c) R_1=$COCH_3$;R=Me;R_2=OAc;R_3=H.
d) R_1=R=Me; R_2=H; R_3=OMe.

a) R_1=Me; R_2=OMe; R_3=R=H.
b) R_1=Me;R_2=OMe;R_3=H;R=CO_2Et.
c) R_1=COMe;R=Me;R_2=OAc;R_3=H.
d) R_1=R=Me; R_2=H; R_3=OMe.

Analogous results have also been found using fluorenone as oxidant, although the irradiation times were longer.

The previous results can be easily explained following the recent work by Cohen et al.[15] where they have shown that the primary reaction of benzophenone triplet with aliphatic amines gives benzophenone ketyl radical with a quantum yield close to 1.0. Accordingly, the tertiary benzylic hydrogen H-7 of the aporphine skeleton should be the most easily abstracted resulting in the intermediate (3) (scheme 1), which subsequently gives (4).

Since colorants such as eosine and methylene blue have also been proved to produce the photochemical N-demethylation of amines[16], we then tried the photooxidation of glaucine (1) by an equimolar amount of eosine (N_2, MeOH). Unexpectedly a 54% yield of the phenanthrene (11)[17] together with a 27% yield of dehydroglaucine (4) were obtained. A photoHofmann elimination can be invoked to explain the formation of the phenanthrene (11). Other processes, different than α-proton transfer, have also been observed from the aminium radical generated by charge trasfer interaction[18].

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