A NOVEL CLEAVAGE OF THE METHYLENEDIOXY GROUP DURING THE PHOTOCHEMICAL SYNTHESIS OF APORPHINES

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Irradiation of 1-(2-bromo-5-hydroxybenzyl)-1,2,3,4-tetrahydro-2-methyl-6,7-methylenedioxyisoquinoline (1) in 2% aqueous sodium hydroxide solution gives (±)-roemeroline (2) and 2,9-dihydroxyaporphine (3). Similarly 1-(2-bromo-5-hydroxy-4-methoxybenzyl)-1,2,3,4-tetrahydro-2-methyl-6,7-methylenedioxyisoquinoline (5) leads to (±)-cassythicine (6) and 2,9-dihydroxy-10-methoxyaporphine (7). These are the first examples of the cleavage of methylenedioxy groups during photolysis in an alkaline medium.

We wish to report the cleavage of a methylenedioxy group to give a monophenol during aporphine synthesis by photolysis. Irradiation of 1-(2-bromo-5-hydroxybenzyl)-1,2,3,4-tetrahydro-2-methyl-6,7-methylenedioxyisoquinoline (1) (1 g) in 2% sodium hydroxide solution using a Hanovia mercury lamp with a pyrex filter gave, apart from the recovered starting material, two products A and B, both of which were identified as aporphines.

Compound A (150 mg), mp. 218-220° (methanol) exhibits a bathochromic alkaline shift in its uv spectrum characteristic of 9-hydroxyaporphines,[1] λ_{max} (EtOH) 240 (sh) and 280 nm (log ε 4.13

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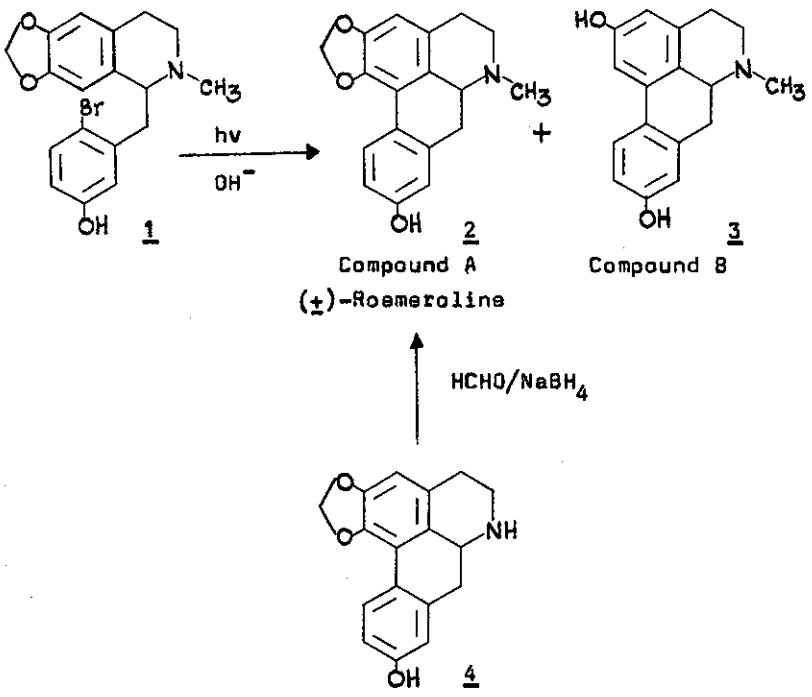
and 4.29), λ_{max} (EtOH+NaOH) 315 nm (log ε 4.40). The mass and nmr spectra are consistent with an aporphine structure,[2,3] m/e 295 (M^+), 294 $(M-1)^+$, 252 $(M-43)^+$; nmr (DMSO-d_6) δ 2.49 (3H, s, N-CH_3), 6.04 and 6.17 (2H, 2d, OCH_2O), 6.63 (1H, s, H-3), 6.75-6.97 (2H, H-8 and 10), 7.97 (1H, d, H-11), 9.75 (1H, OH, exchangeable with D_2O). The material was found to be identical (ir in KBr and Mass spectra) with (±)-roemeroline (2) obtained from (±)-anolobine[4] (4) by reductive methylation.

Scheme 1

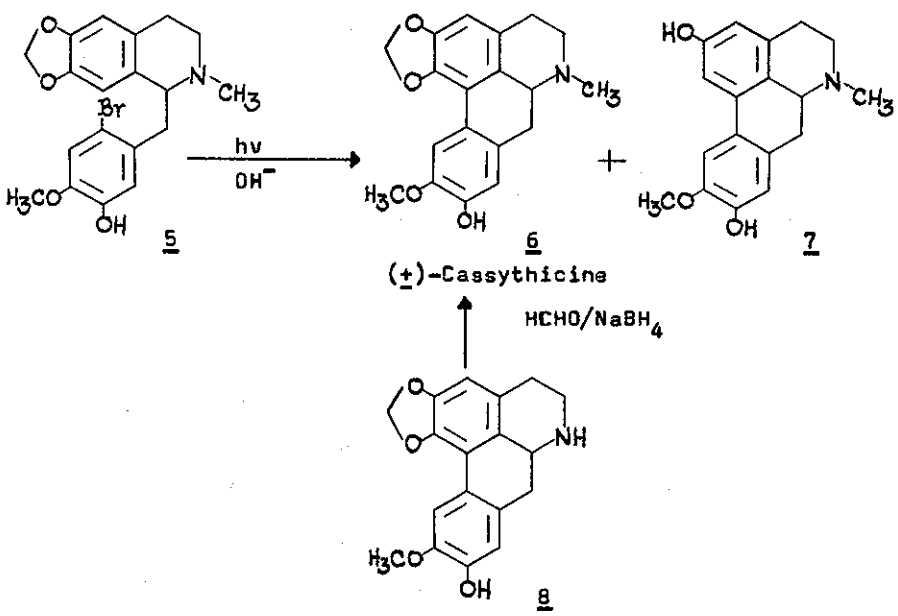


Compound B (125 mg), mp. 188°(methanol) was assigned structure 3 based on spectral data. The uv spectrum is suggestive of a phenolic aporphine, λ_{max} (EtOH) 277, 302 and 310-315 (sh) nm (log ε 4.06, 3.93 and 3.90), λ_{max} (EtOH+NaOH) 291, 318 and 325 (sh) nm (log 4.01, 4.12 and 4.11). The ir spectrum shows no bands characteristic of a methylenedioxy group. The nmr spectrum is conspicuous by the absence of the doublets at δ 6.04 and 6.17 present in (±)-roemeroline (2) which is characteristic of a $C_{1,2}$-methylenedioxy group[3]; nmr ($CDCl_3$) δ 2.50 (3H, s, N-CH_3), 6.70-7.00 (3H, aromatic), 7.50 (1H, s, H-1), 8.35 (1H, d, H-11), 9.37 (2H, 2 x OH, exchangeable with D_2O). By analogy with the published nmr chemical shifts of the aromatic protons of aporphines,[5] the signal at δ 8.35 was assigned to H-11 and that at δ 7.50 to H-1. Since there are two phenolic groups in compound B and one of which is at C_9, the other could arise only by the photolytic cleavage of the 1,2-methylenedioxy group. The OH could then occupy position 1 or 2; the OH could only be at C_2 since the signal at δ 7.50 is assigned a H-1. Thus compound B is 2,9-dihydroxy-aporphine (3) and this structure is supported by its mass spectrum, m/e 267 (M^+), 266 $(M-1)^+$, 224 $(M-43)^+$.

Similar results were obtained during the irradiation of 1-(2-bromo-5-hydroxy-4-methoxybenzyl)-1,2,3,4-tetrahydro-2-methyl-6,7-methylenedioxyisoquinoline (5) (1 g) in 2% sodium hydroxide solution. Again two products were obtained, one of which (200 mg), mp. 117° (methanol) was identified as (±)-cassythicine[6] (6) on the basis of spectral data and comparison with N-methylactinodaphnine obtained from actinodaphnine (8) by reductive methylation. The other product (70 mg),

mp. 201° (methanol) was assigned structure 7 because of its mass spectrum m/e 297 (M^+), 296 $(M-1)^+$, 254 $(M-43)^+$ and by analogy with compound 3 obtained during the synthesis of (±)-roemeroline (2).

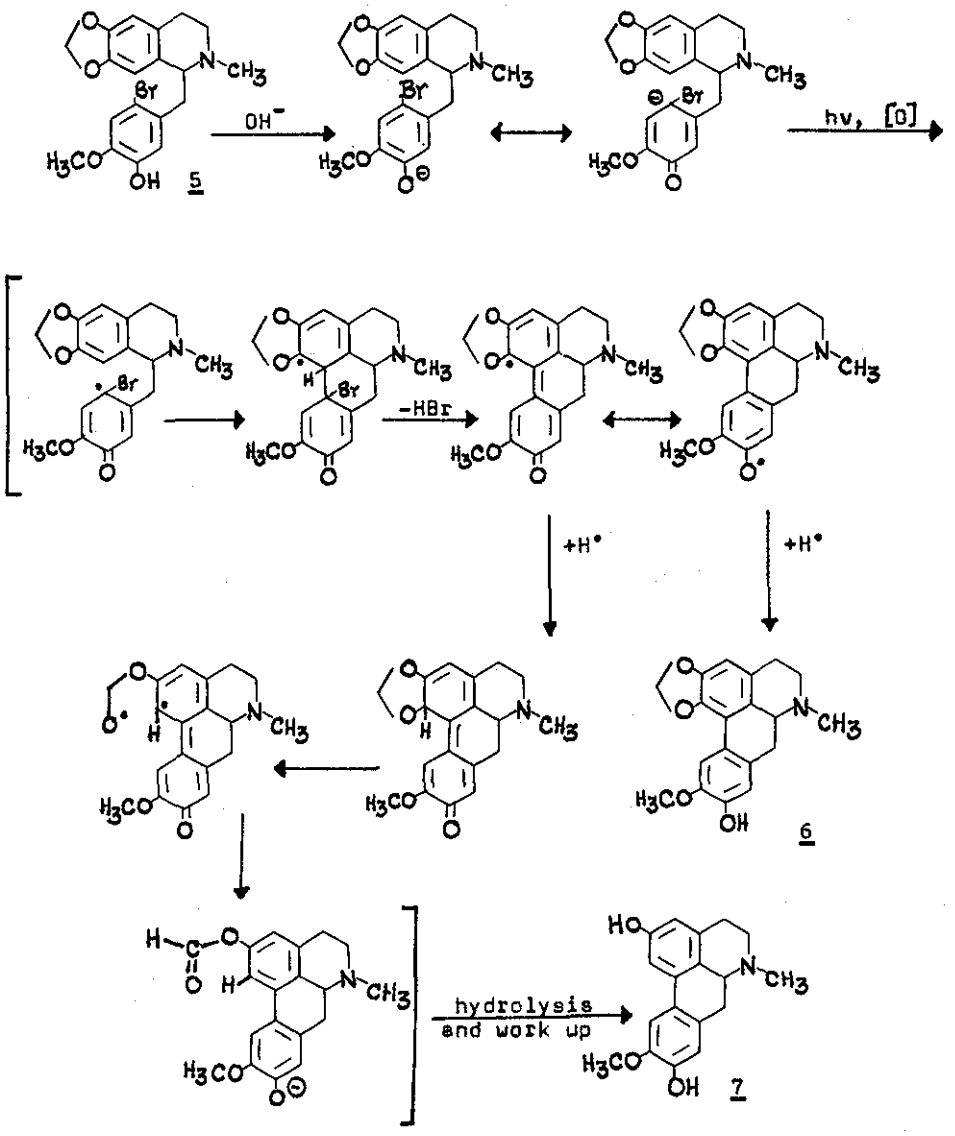
Scheme 2



The present cleavage of the methylenedioxy group during the synthesis of aporphines was observed only during the irradiation under alkaline conditions. When irradiations were carried out in neutral or acid solutions (pH 2.5) only the expected aporphines 2 and 6 were formed in the above two cases. There was no trace of the cleaved product. This is the first instance where the cleavage of the methylenedioxy group has been observed during photolysis under alkaline conditions, though such a cleavage in an aporphine using sodium and liquid ammonia had earlier been reported.[7]

A possible rationalisation for this cleavage assuming a free radical mechanism is shown below (cf. ref.8).

Scheme 3



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