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SMILES REARRANGEMENT IN PROTOBERBERINIUM SALT

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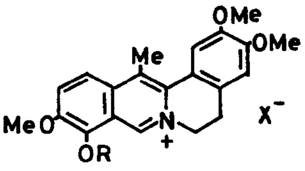
In an attempted synthesis of 9-(2-aminoethoxy)-13-methyl-2,3,10-trimethoxy-5,6-dihydrodibenzo[a,g]quinolizinium bromide(1) as a series of dehydrocorydaline(2) derivatives[1], it became apparent that the target(1) had not been obtained by hydrazinolysis of a phthalimido derivative(3).

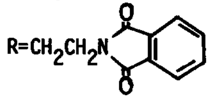
On treatment with sodium hydroxide, 9-desmethyldehydrocorydaline(4)[1] gave a phenolbetaine (5)[2], mp >260°(dec) λ_{max}^{EtOH} 238 nm(log ε, 4.47), 279(4.41), 384(4.10), 502(3.81), which was led to 3, mp 163-165°(dec) by refluxing with β-bromoethylphthalimide in dioxane. Hydrazinolysis of 3 with hydrazine hydrate and hydrobromic acid gave almost quantitatively an unexpected product, mp 233-236°(dec), which proved to be 9-(2-hydroxyethyl)amino-13-methyl-2,3,10-trimethoxy-5,6-dihydrodibenzo[a,g]quinolizinium bromide(6) on the basis of the following evidences.

On $NaBH_4$-MeOH reduction, 6 gave 7, oil, 2HCl salt mp 195-197°, whose mass spectrum



1 $R=CH_2CH_2NH_2$, X=Br

2 R=Me, X=Cl



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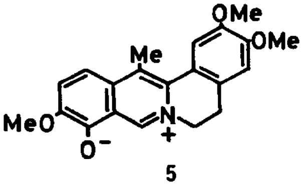
4 R=H, X=Cl



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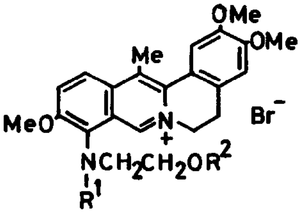
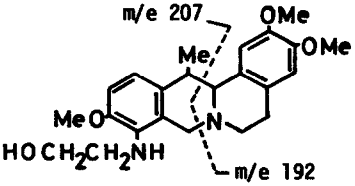


6 $R^1=R^2=H$

8 $R^1=H$, $R^2=COCH_3$

9 $R^1=R^2=COCH_3$

10 $R^1=COCH_3$, $R^2=H$



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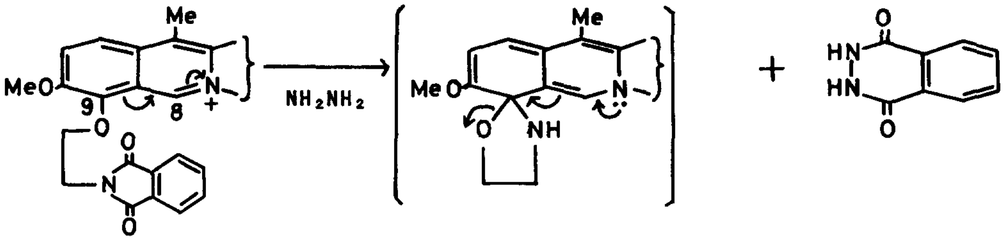
exhibited intense ion peaks at m/e 398(M^+), 353($M-CH_2CH_2OH$), 207(base peak), 192 and 176. Acetylation of 6 with acetic anhydride-pyridine at room temperature afforded an O-acetate(8), mp 173-175°(dec) $\nu_{C=O}$ 1740 cm^{-1}. On refluxing with acetic anhydride, 6 gave an O,N-diacetate(9) mp 204-205°(dec) $\nu_{C=O}$ 1665 and 1735 cm^{-1}, which was partially hydrolyzed to give a N-acetate (10), mp 245-250°(dec), $\nu_{C=O}$ 1660 cm^{-1}, during the course of several recrystallization from ethanol. Absorption spectra of 6, λ_{max}^{EtOH} 232 nm(log ε, 4.50), 283(4.47), 346(4.17), 480(3.86), and 8, λ_{max}^{EtOH} 232(4.52), 283(4.49), 346(4.22), 479(3.85) showing bathochromic shifts in comparison with those of 2, λ_{max}^{EtOH} 231(4.46), 267(4.52), 340(4.43), 425(3.81), and 9, λ_{max}^{EtOH} 232 (4.46), 263(4.46), 339(4.42), 420(3.72), indicated the presence of NH-chromophore at the C_9-position. The unexpected product 6 was interpreted by a process in terms of the Smiles rearrangement[3,4] via an intermediate 11. The C_9-position of protoberberinium salt is activated by the suitably located $C_8=\overset{+}{N}=$ group. This is the first example of the Smiles rearrangement in protoberberinium salts.



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This finding has an important implication for a facile nucleophilic substitution reaction at the C_9-alkoxyl group of protoberberinium salts with primary amines, and a novel amination based on this consideration is reported in the accompanying communication[5].

References

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