Fragmentation of Laudanosine by Single Electron Transfer Reactions

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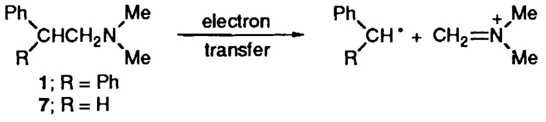
The radical cation of laudanosine, formed by a photoinduced electron transfer reaction or by oxidation with a tris(4-bromophenyl)aminium salt, undergoes cleavage of a C–C bond similar to the mass spectrometric fragmentation induced by electron ionization.

Recently C–C bond cleavage reactions by photoinduced electron transfer have attracted considerable interest.[1] For instance Arnold discussed C–C bond cleavage of the radical cations of phenylethyl ethers,[2] while Whitten *et al.* examined photoinduced electron transfer fragmentation of β-amino alcohols in detail.[3] On the other hand, C–C bond cleavage reactions with various one-electron reagents have been reported.[4] We have also investigated the cleavage of a C–C bond in the radical cation of *N*,*N*-dimethyl-2,2-diphenylethylamine (**1**), and shown that the fragmentation is in a way similar to that occurring in electron ionization mass spectrometry, as shown in Scheme 1.[5] Now, we demonstrate that this fragmentation is generally applicable to compounds having a similar Ar–C–C–N moiety. This paper deals with the fragmentation of the radical cation of laudanosine, an isoquinoline alkaloid, in solution by photoinduced electron transfer and by single electron transfer with an aminium salt, and in the gas phase by electron ionization mass spectrometry.



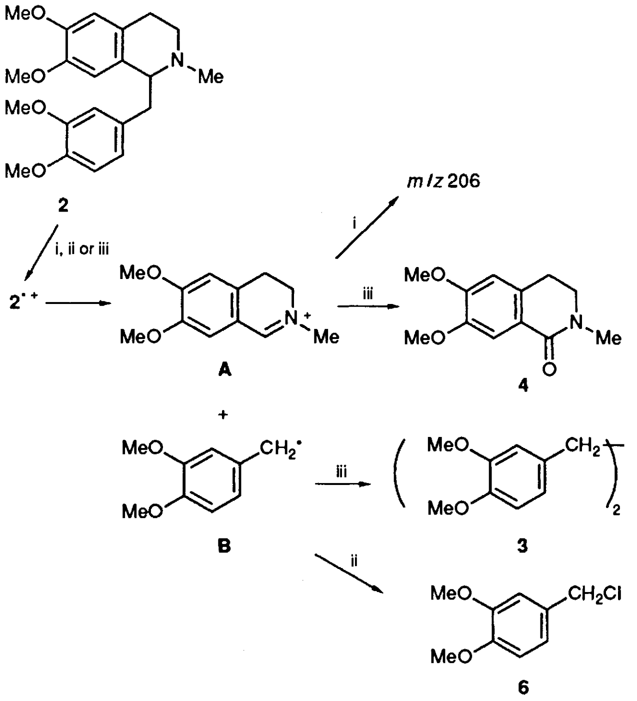
Scheme 1

Irradiation (λ > 360 nm) of laudanosine (**2**; 0.13 mol) in the presence of 9,10-dicyanoanthracene (DCA; 0.01 mol) in wet acetonitrile at room temperature with a 450 W high pressure mercury arc for 5 h gave 1,2-bis(3,4-dimethoxyphenyl) ethane (**3**; 46%) and 5,6-dimethoxy-*N*-methyl-1,2,3,4-tetrahydroisoquinolin-1-one (**4**; 7%), while similar irradiation with a large amount of DCA (0.1 mol) under reflux for 3 h gave only traces of **3**, but gave **4** in 20% yield. Since the fluorescence of DCA was quenched by **2** and a k_q of 1.6×10^{10} dm^3 mol^{-1} s^{-1} was obtained from the Stern–Volmer plot, the initial step of the reaction must be electron transfer from **2** to DCA to give a radical cation–radical anion pair. The former ($\mathbf{2}^{\bullet +}$) may fragment to give cation **A** and radical **B**. The final products (**3** and **4**) must be derived from these unstable intermediates.

On the other hand, the thermal reaction of **2** with tris(4-bromophenyl)aminium hexachloroantimonate (**5**; one equivalent) in acetonitrile takes place smoothly to give 3,4-dimethoxybenzyl chloride (**6**) in 63% yield, together with a small amount of 3,4-dimethoxybenzaldehyde and 3,4-dimethoxytoluene. The formation of **6** is accounted for in terms of the fragmentation of the radical cation initially formed by electron transfer[6] from **2** to **5**, followed by cleavage of the C–C bond to give the radical **B**. This radical may abstract a chlorine atom from the hexachloroantimonate anion to give the final product **6**. Other products are also explained by the abstraction of a hydrogen atom or trapping of an oxygen molecule by the radical **B**.

In the gas phase reaction the mass spectrum of **2** exhibits an ion at *m*/*z* 206 as the base peak and a very small molecular ion at *m*/*z* 357, typical mass spectrometric behaviour of an isoquinoline alkaloid.[7] This fragmentation is accounted for in terms of α-cleavage of nitrogen in the molecular ion, in which charge is localized on the nitrogen atom, under electron ionization.[8]

Thus we conclude that the three reactions represented in Scheme 2 indicate that radical cations produced *via* different routes undergo cleavage of the same C–C bond to give cation **A** and radical **B** which then react in different ways according to the reaction conditions.



Scheme 2 *Reagents and conditions:* i, electron ionization (MS); ii, $(BrC_6H_4)_3NSbCl_6$ (**5**); iii, *hν*, 9,10-dicyanoanthracene

Although *N*,*N*-dimethyl-2,2-diphenylethylamine (**1**) fragments in ways similar to that described here,[5] we found that *N*,*N*-dimethyl-2-phenylethylamine (**7**) did not undergo the single electron transfer reactions smoothly. The mass spectrum of **7** exhibits a base peak at *m*/*z* 58, which indicates that α-cleavage of the nitrogen radical cation takes place. The thermal oxidation of **7** with **5** gives benzyl chloride in 12% yield indicating that the fragmentation of the radical cation proceeds only partially, while a similar photochemical reaction of **7** in the presence of DCA gives mainly a cyanated derivative of **7**, but no fragmentation products were detected. Since the fluorescence of DCA was quenched by **7** with a k_q value of 1.9×10^{10} dm^3 mol^{-1} s^{-1}, single electron transfer from **7** to DCA must take place. These reactions may indicate that the formation of the diphenylmethyl radical is energetically favourable enough for the C–C bond cleavage of the radical cation, but that of the benzyl radical is not. In the case of laudanosine the single electron transfer reactions give the dimethoxybenzyl radical smoothly indicating that the methoxy-substituted benzyl radical lowers the activation energy of the C–C bond cleavage step in this series of reactions considerably.

Acknowledgements

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