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Functional group interactions in the fragmentation of protonated and methylated succinic acid derivatives

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Abstract

The methane chemical ionization (CI) mass spectra of succinic acid monoamide and monomethyl succinate have been determined. In addition, the unimolecular metastable ion fragmentation reactions and low-energy collision-induced dissociation reactions of the MH^+ and $M.CH_3^+$ ions of these compounds have been determined. In the CH_4 CI mass spectra extensive fragmentation of the MH^+ ions is observed, indicative of functional group interactions. An important fragmentation reaction for the protonated monoamide involves formation of NH_4^+ and it is suggested that this occurs through the intermediacy of a protonated succinic anhydride/ammonia ion-neutral complex. The $[MH–H_2O]^+$ and $[MH–CH_3OH]^+$ fragment ions formed in the CH_4 CI of monomethyl succinate give collision-induced dissociation (CID) spectra which are in agreement with the spectra obtained for methylated and protonated succinic anhydride, respectively; these results strongly support the suggestions that the formation of stable cationated cyclic anhydride structures are one of the factors which result in extensive fragmentation of protonated and cationated dicarboxylic acid derivatives. The $M.CH_3^+$ adduct of succinic acid monoamide gives a CID spectrum which is distinctly different from that obtained for the protonated monomethyl ester of succinic acid monoamide. This result indicates that little addition of CH_3^+ to the free COOH group of the monoamide occurs. The CID spectrum of the $M.CH_3^+$ adduct of monomethyl succinate also shows substantial differences from the CID mass spectrum of protonated dimethyl succinate. (Int J Mass Spectrom 179/180 (1998) 15–25) © 1998 Elsevier Science B.V.

Keywords: Succinic acid derivatives; Fragmentation mechanisms; Collision-induced dissociation (CID); Chemical ionization; Ion structures

1. Introduction

Protonation of carboxylic acids by gaseous Brønsted acids leads to elimination of H_2O from the MH^+ ion [1–4], whereas protonation of methyl esters leads to elimination of CH_3OH from MH^+ [1,4–6]. In both cases the elimination reaction is enhanced in dicarboxylic acids or esters when the two carboxyl functions can interact with each other [1,4,7]. The thermochemically favoured site of protonation in carboxylic compounds is the carbonyl oxygen [8]. For monocarboxylic compounds or olefinic dicarboxylic compounds with a *trans* configuration, elimination of H_2O or CH_3OH requires a symmetry-forbidden 1,3–H migration, a reaction with a high energy barrier [3]. Interaction of two carboxyl functions provides an alternative mode of hydrogen migration, as shown in

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Dedicated to Professor Fulvio Cacace in recognition of his outstanding contributions for many decades to gas-phase ion chemistry and physics.

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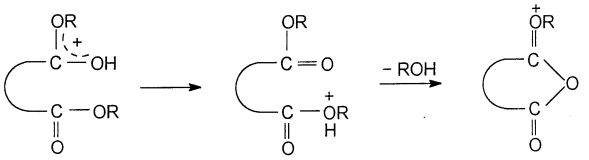


Scheme 1.

Scheme 1, which is not symmetry-forbidden and, thus, is of lower energy requirement; in addition, it is believed [1,9] that cyclization to a more stable cationated anhydride structure also occurs, further lowering the energy barrier, although little direct evidence for such cyclic structures has been presented. Recent work from this laboratory [10] on the fragmentation of diethyl succinate and diethyl glutarate has presented evidence that the $[MH–C_2H_5OH]^+$ ions have ethyl-cationated cyclic anhydride structures, at least for those ions undergoing fragmentation on the metastable ion time scale.

With the exception of the study of the fragmentation of protonated methyl ethyl diesters of 2-*t*-butylmaleic and 2-*t*-butylsuccinic acids by Mandelbaum and co-workers [11], studies of functional group interactions in dicarboxylates have been limited to the diacids or diesters where the two ester functions are identical. In the present work we have studied the fragmentation reactions of the protonated and methylated monoamide and monomethyl ester of succinic acid. It was initially hoped that the study of such bifunctional compounds might provide information as to the initial site of proton or methyl cation attachment. Although this hope has been realized to some extent for methyl cation attachment, the high mobility of the proton precludes obtaining information as to the initial site of proton attachment. However, the results obtained do provide substantial information concerning functional group interactions and the role of cyclic cationated structures in the fragmentation reactions of dicarboxylate derivatives.

2. Experimental

All chemical ionization (CI) mass spectra were acquired on a HP5988A quadrupole mass spectrometer (Hewlett-Packard, Palo Alto, CA) with methane as the reagent gas at a source pressure of 0.5 Torr and a source temperature of 150 °C. Metastable ion studies and low-energy collision-induced dissociation (CID) studies were carried out using a VG Analytical hybrid BEqQ mass spectrometer (VG Analytical, Wythenshawe, Manchester, UK), which has been described in detail previously [12]. In the metastable ion studies, the appropriate ion beam was mass-selected by the double-focusing BE stage at 6 keV ion energy, decelerated to ~20 eV kinetic energy, and introduced into the rf-only quadrupole cell, *q*, in the

Table 1
CH_4 CI mass spectra (MS) and metastable ion mass spectra (MI) of MH^+

	m/z (relative intensity, % of base peak)				
Compound	MH^+	$[MH–H_2O]^+$	$[MH–NH_3]^+$	$[MH–MeOH]^+$	NH_4^+
1 MS	118 (71)	100 (100)	101 (14)		
1 MI		100 (100)	101 (2)		18 (31)
2 MS	133 (20)	115 (100)		101 (28)	
1 MI		115 (100)			

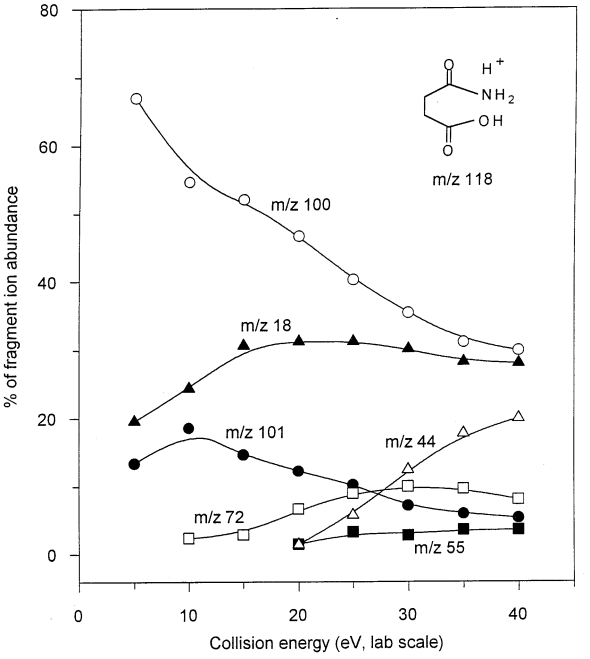
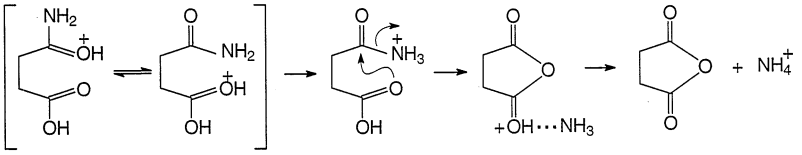


Fig. 1. Breakdown graph for protonated succinic acid monoamide.



Scheme 2.

absence of collision gas. The ionic products of unimolecular fragmentation in the cell were analyzed by scanning the mass-analyzing quadrupole *Q*. Low-energy CID experiments were carried out in the same fashion but with the addition of N_2 as a collision gas to the quadrupole collision cell *q* at a pressure of 1–2 $\times$ 10^{-7} Torr as read by the ionization gauge attached to the pumping line for the quadrupole section. The collision energy typically was varied from 5–45 eV (laboratory scale) in the CID studies. In MS/MS/MS experiments the initial precursor was mass-selected by the magnetic sector and underwent either unimolecular or collision-induced dissociation in the region before the electric sector. The desired product of this fragmentation was selected according to its kinetic energy by the electric sector, decelerated to 40 eV kinetic energy and introduced into the quadrupole collision cell *q* where it underwent CID

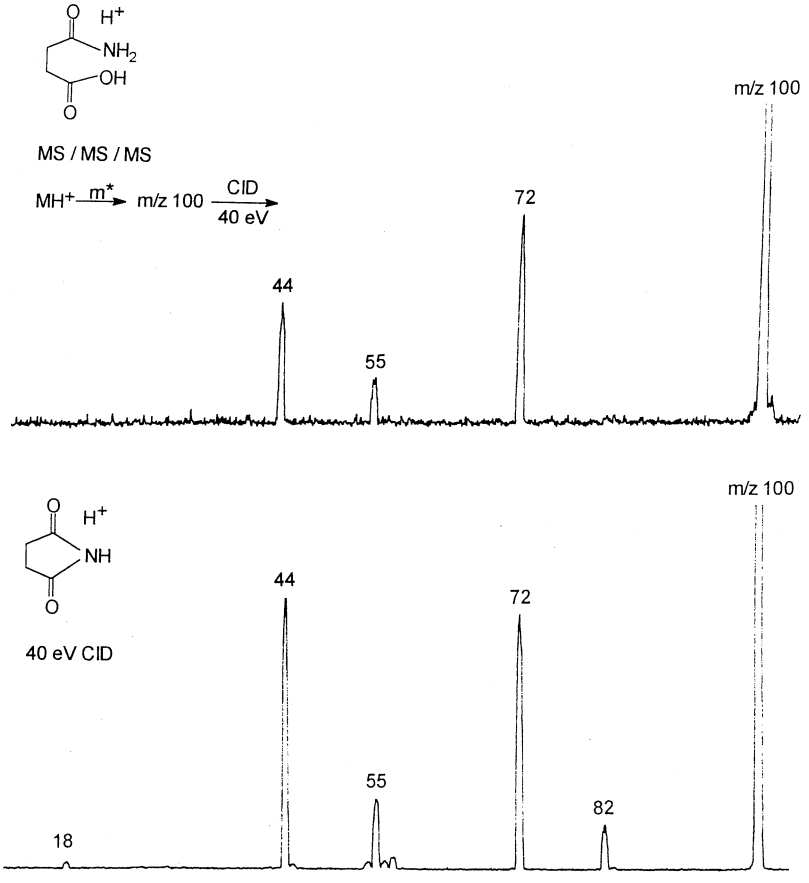
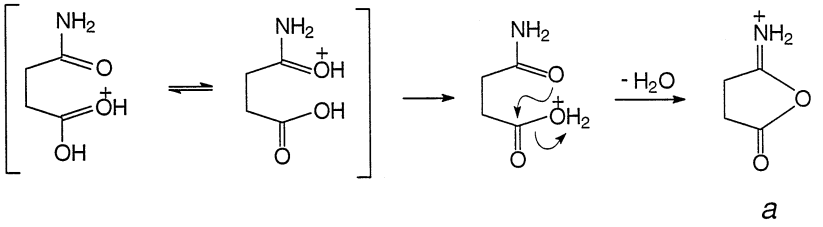


Fig. 2. 40 eV CID spectra of *m*/*z* 100 derived from unimolecular decomposition of protonated succinic acid monoamide and from protonation of succinimide.



Scheme 3.

with the products being analyzed by the final quadrupole *Q*. In both the metastable and CID studies approximately 20–40 2 s scans were accumulated on a multichannel signal averager to improve the signal-to-noise ratio.

The ion source of the ZAB was operated in the CI

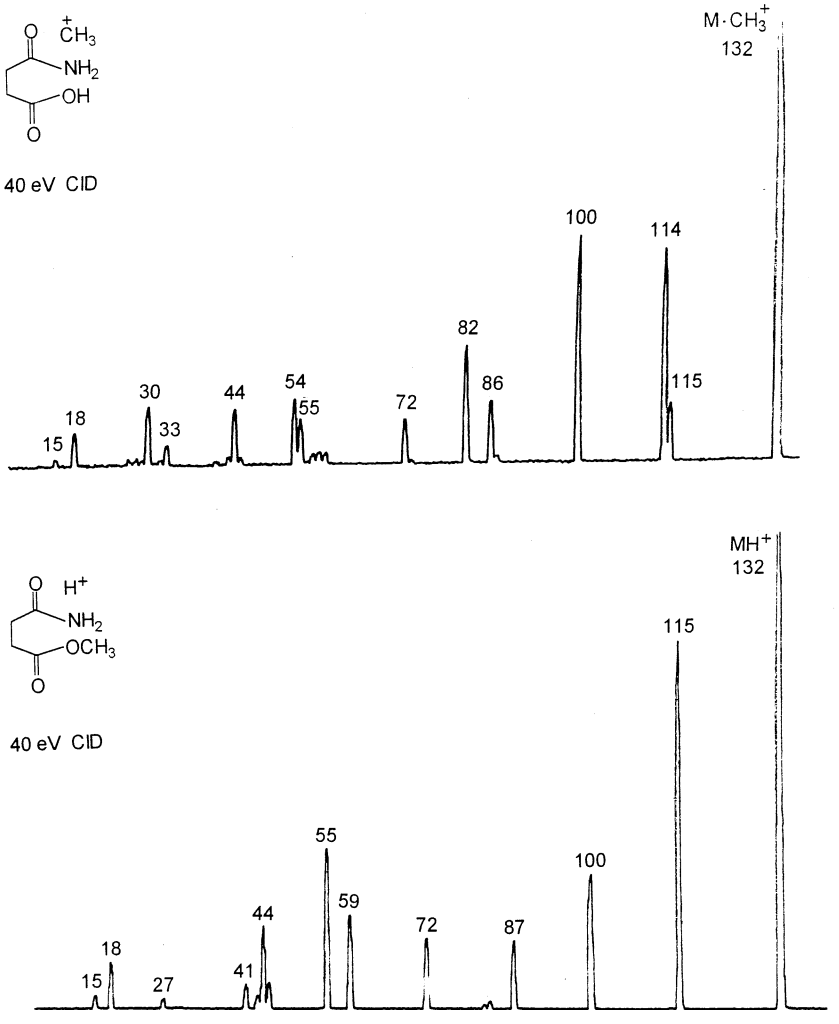
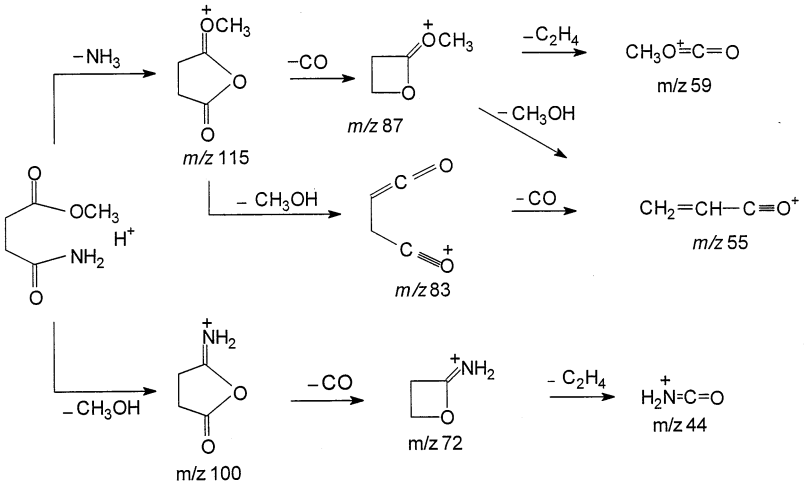


Fig. 3. 40 eV CID spectra of methylated succinic acid monoamide and protonated methyl succinamate.



Scheme 4.

mode at a temperature of 200 °C. Methane was used as the reagent gas to produce MH^+ ions. Where it was desired to produce MD^+ ions, CD_4 or $(CD_3)_2CO$ was used as reagent gas. The use of CH_3OD as reagent gas resulted in H/D exchange of the labile hydrogens of the analyte and production of the MD^+ ion of the exchanged species [13]. The methyl-cationated species were obtained using CH_3I/CH_4 as the CI reagent [14] or, when CD_3^+ adducts were required, CD_3I/CD_4 was used.

The reaction of succinic anhydride with aqueous ammonia gave rise to the monoamide; the monomethyl ester was obtained by methanolysis of the anhydride. The methyl ester of the monoamide and dimethyl succinate were prepared by esterification of the monoamide and the monoester, respectively, with acidic methanol. Purification was by recrystallization. Succinic acid, succinimide, and succinic anhydride were used as commercially available.

3. Results and discussion

The CH_4 CI mass spectra of succinic acid monoamide (**1**) and monomethyl succinate (**2**) are presented in Table 1 along with the metastable ion mass spectra of the respective MH^+ ions. As expected, extensive fragmentation of MH^+ is observed in the CI mass spectra since the two functional groups can interact, the major fragmentation reaction in both cases involving elimination of H_2O. Indeed, for the monoester this is the only fragmentation reaction observed in the metastable ion mass spectrum of MH^+. The metastable ion mass spectrum of the protonated monoamide also shows dominant elimination of H_2O with very minor elimination of NH_3. An interesting observation is the formation of NH_4^+ in significant amounts in the metastable ion mass spectrum of the amide; this product could not be detected in the CH_4 CI mass spectrum because of interference from the reagent gas ion signals. The breakdown graph, expressing the energy dependence of the fragmentation reactions, for the protonated monoamide is shown in Fig. 1. The ammonium ion (m/z 18) remains a significant product at all collision energies. The formation of NH_4^+ is best rationalized by the sequence shown in Scheme 2 involving initial formation of a protonated succinic anhydride/ammonia complex within which proton transfer occurs to form the ammonium ion because the proton affinity of ammonia (204 kcal mol^{-1} [15]) is greater than that of succinic anhydride (192 kcal mol^{-1} [16]).

Fig. 2 compares the 40 eV CID mass spectrum of the $[MH–H_2O]^+$ (m/z 100) ion formed in metastable ion decomposition of the protonated monoamide with

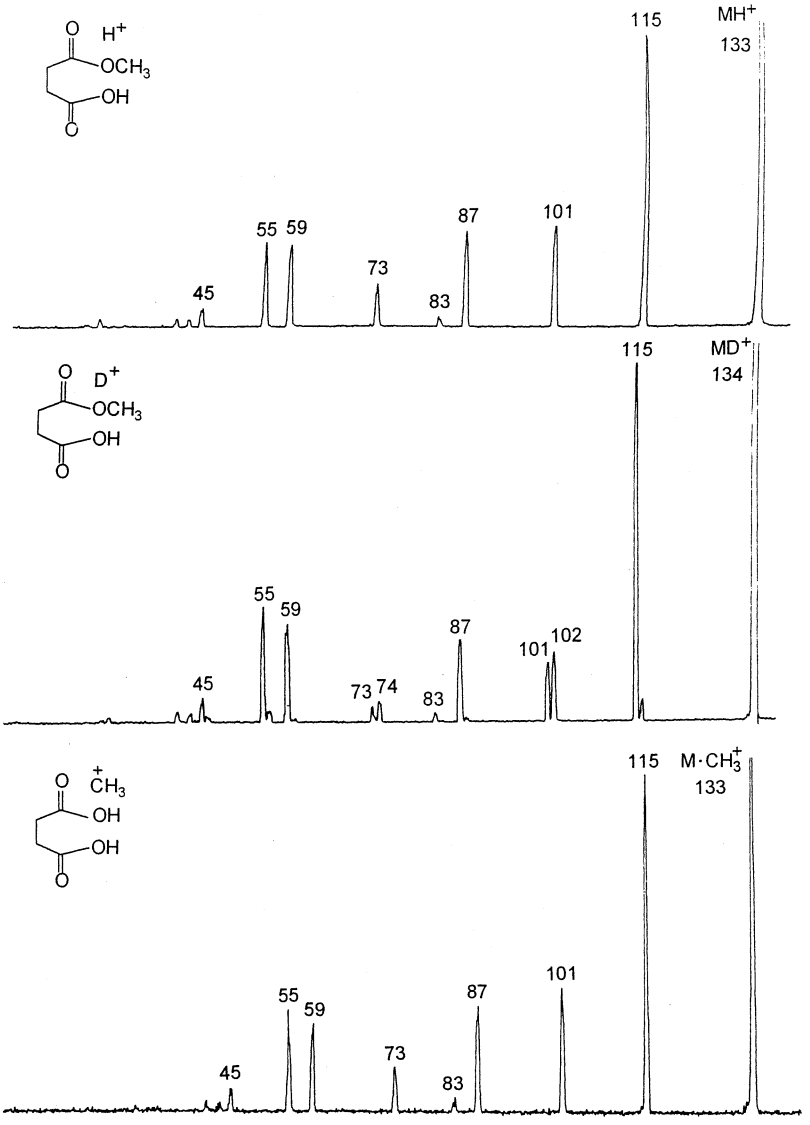


Fig. 4. Comparison of 40 eV CID mass spectra of MH^+ and MD^+ of monomethyl succinate and methylated succinic acid.

the 40 eV CID mass spectrum of protonated succinimide. Although the two CID mass spectra show some similarities, the most noticeable difference is the ion signal at *m*/*z* 82 for the protonated imide which is not seen for the $[MH–H_2O]^+$ ion derived from the protonated monamide. It is well known [17–19] that amides preferentially undergo protonation at the carbonyl oxygen and one would expect, by analogy, that succinimide also would be protonated at a carbonyl oxygen. By contrast, cyclization accompanying loss of water from the protonated monamide would lead straightforwardly either to N-protonated succinimide or to structure **a** of Scheme 3. The differences observed in the CID spectra indicate that whichever of these structures is formed, it does not readily isomerize to O-protonated succinimide.

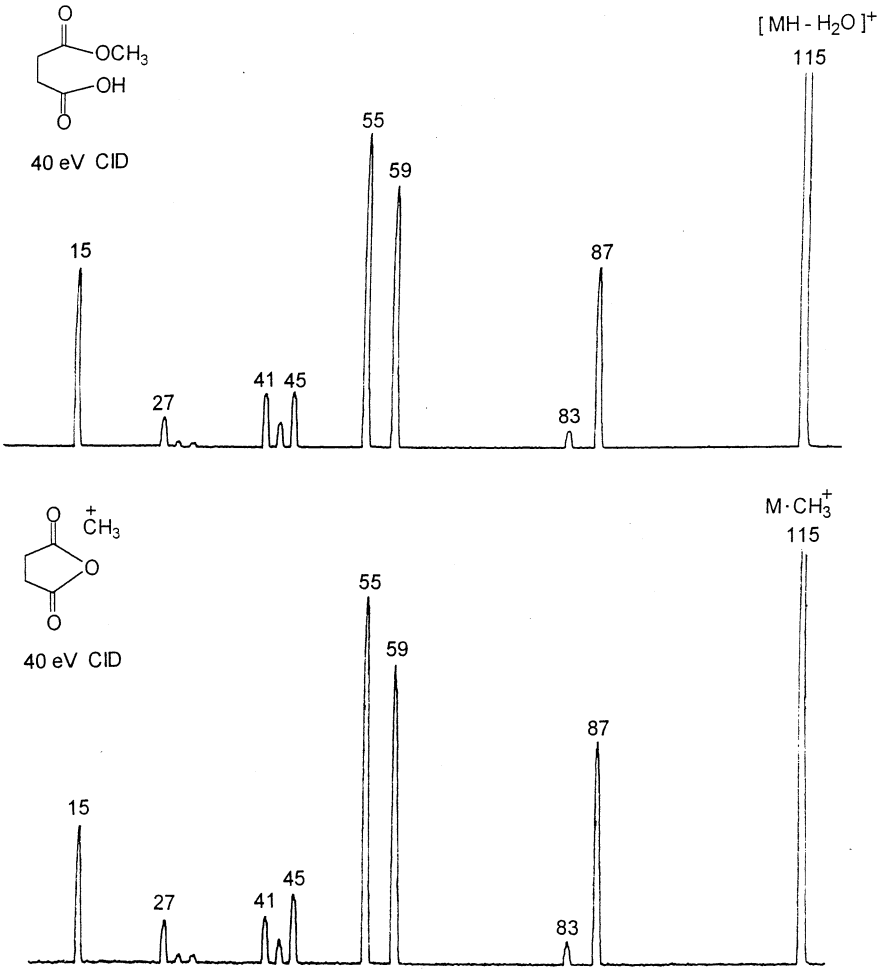


Fig. 5. Comparison of 40 eV CID mass spectra of *m*/*z* 115 derived from protonated monomethyl succinate and methylation of succinic anhydride.

The CD_3^+ adduct of succinic acid monoamide fragments in metastable ion decomposition by loss of CD_3OH, H_2O and NH_3 with relative intensities 100: 71:14. By contrast, protonated methyl succinamate showed metastable loss of CH_3OH and NH_3 in the ratio 100:27. Fig. 3 compares the 40 eV CID mass spectrum of the CH_3^+ adduct of the monoamide with the 40 eV CID mass spectrum of protonated methyl succinamate. The spectra are distinctly different, indicating that, for the monoamide, the methyl cation does not add to the COOH function to a significant extent but rather adds either to the carbonyl oxygen or the nitrogen of the $CONH_2$ function, more likely the former. If the methyl cation added to the nitrogen one might have expected to see loss of methyl amine from the adduct but this is not observed. Metastable ion fragmentation of the protonated methyl succinamate shows more facile loss of CH_3OH than NH_3 in agreement with earlier studies [9,20–22] of the ease of loss of neutral molecules from protonated species. However, as shown, ammonia loss is of greater importance in the CID spectrum, presumably reflecting entropic effects on the rates of the two fragmentation reactions. The fragmentation of protonated

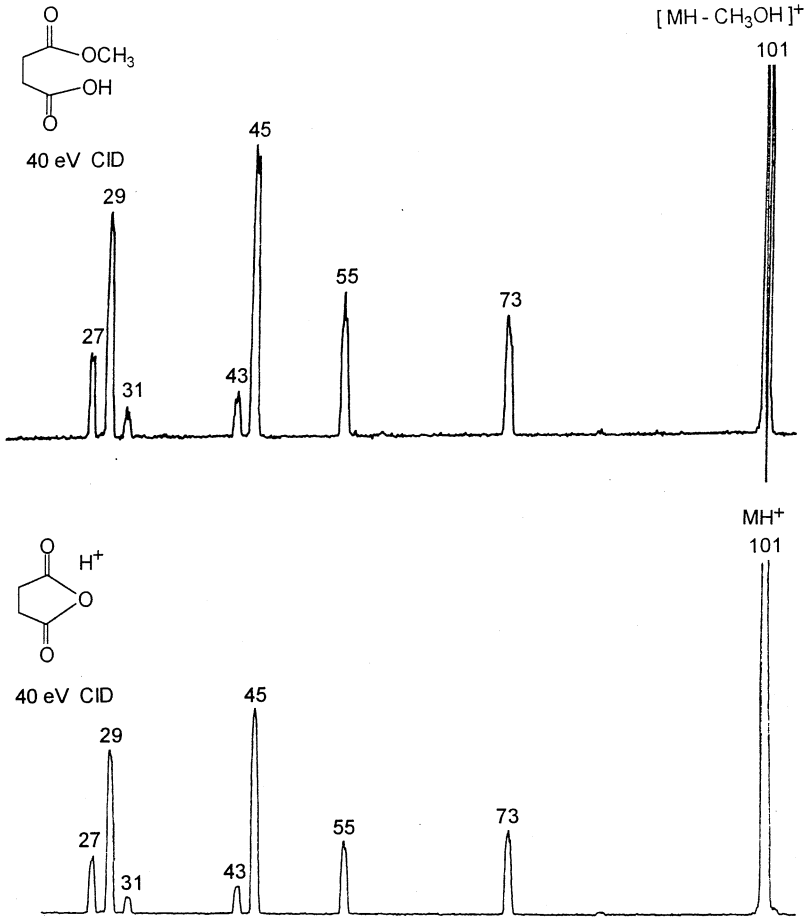
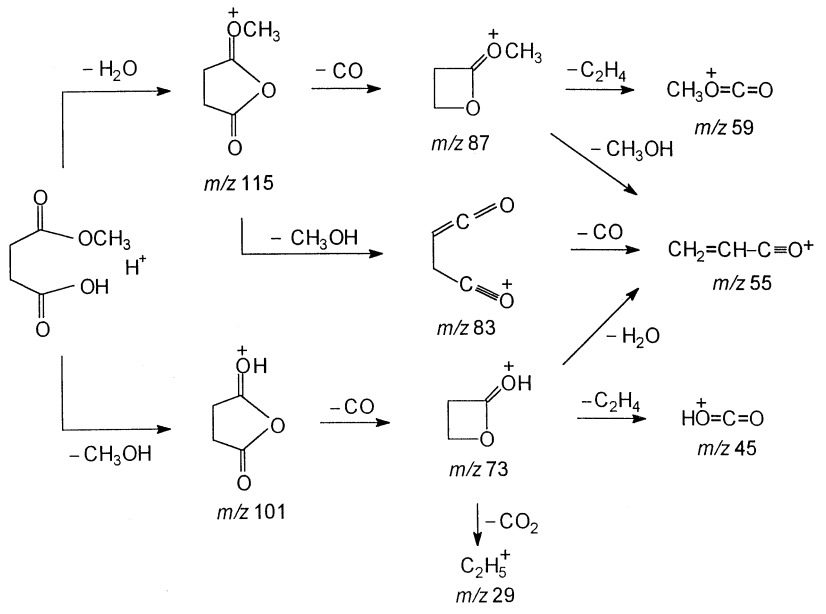


Fig. 6. Comparison of 40 eV CID mass spectra of *m*/*z* 101 derived from protonated monomethyl succinate and protonation of succinic anhydride.

methyl succinamate is rationalized by the sequences shown in Scheme 4.

Although metastable ion decomposition of protonated monomethyl succinate involves only loss of H_2O (Table 1), loss of CH_3OH is observed in both the CI mass spectrum (Table 1) and the CID mass spectrum. Fig. 4 presents the 40 eV CID mass spectra of the MH^+ and MD^+ ions of monomethyl succinate. The spectrum of the MD^+ ion shows that loss of water involves largely, but not exclusively, the added proton/deuteron to give *m*/*z* 115, whereas the essentially equal intensities of *m*/*z* 101 and *m*/*z* 102 show that CH_3OH and CH_3OD are lost with equal probability from MD^+. The thermochemically favoured site of protonation of the monomethyl ester should be the carbonyl oxygen of the carbomethoxy group, since the proton affinities of esters are greater than the proton affinities of the corresponding carboxylic acids [9]; in addition, it is known [8] that, in acids and esters, the proton affinity of the carbonyl oxygen is greater than that of the hydroxyl or alkoxyl oxygen. If D^+ addition occurs at this thermochemically favoured site and is followed by 1,2-elimination of methanol, one would expect *m*/*z* 101 ($-CH_3OD$) to be greater than *m*/*z* 102 ($-CH_3OH$). Similarly, D^+ addition to the methoxy oxygen would lead to enhanced elimination of CH_3OD. Consequently, one can conclude that, if protonation does occur at the carbomethoxy group, there is a 1,6-proton/deuteron shift (from C═O to C═O) prior to fragmentation, thus making the H and



Scheme 5.

D equivalent. Alternatively, it is possible that the chemical ionization step is kinetically controlled and that protonation of the COOH group is favoured kinetically, again making the H and D equivalent. The bottom panel of Fig. 4 shows the 40 eV CID mass spectrum of methyl-cationated succinic acid. The spectrum is essentially identical to that of protonated monomethyl succinate; this is to be expected given the mobility of the protons in these systems. Isbell and Brodbelt [23] have studied the low-energy CID of protonated monomethyl succinate and methylated succinic acid in a quadrupole ion trap mass spectrometer. For the former they reported loss of H_2O (100%) and loss of H_2O + CO (15%) while for the latter they observed loss of H_2O only. Clearly, their results correspond to very low energy collisional activation.

The *m*/*z* 115 ($[MH–H_2O]^+$) and *m*/*z* 101 ($[MH–CH_3OH]^+$) ions were of sufficient abundance in the CH_4 CI mass spectrum of the monoester to obtain their CID mass spectra. Fig. 5 compares the 40 eV CID mass spectrum of the *m*/*z* 115 ion with that of methylated succinic anhydride while Fig. 6 compares the CID mass spectrum of the *m*/*z* 101 ion with that of protonated succinic anhydride. In both cases the spectra for the fragment ion derived from the monomethyl ester are in good agreement with the spectra obtained for the cationated succinic anhydride, providing strong evidence for cyclization to an anhydride structure as one of the factors leading to facile fragmentation of protonated dicarboxylic acid derivatives. The $[MH–H_2O]^+$ ion signal observed [10] in the metastable ion spectrum of protonated succinic anhydride is of extremely low abundance in the CID mass spectrum. The major fragmentation route of both methyl-cationated succinic anhydride (*m*/*z* 115) and protonated succinic anhydride (*m*/*z* 101) involves loss of CO. We propose (Scheme 5) that this CO loss is accompanied by rearrangement to give methylated and protonated β-propiolactone, respectively.

The CD_3^+ adduct of monomethyl succinate fragments on the metastable ion time scale by elimination of CD_3OH and CH_3OH in approximately a 1:1 ratio, indicating that the two methyl groups have become equivalent. Isbell and Brodbelt [23] have observed only loss of CH_3OH from methylated monomethyl succinate in low energy CID in a quadrupole ion trap mass spectrometer. Fig. 7 compares the 40 eV CID

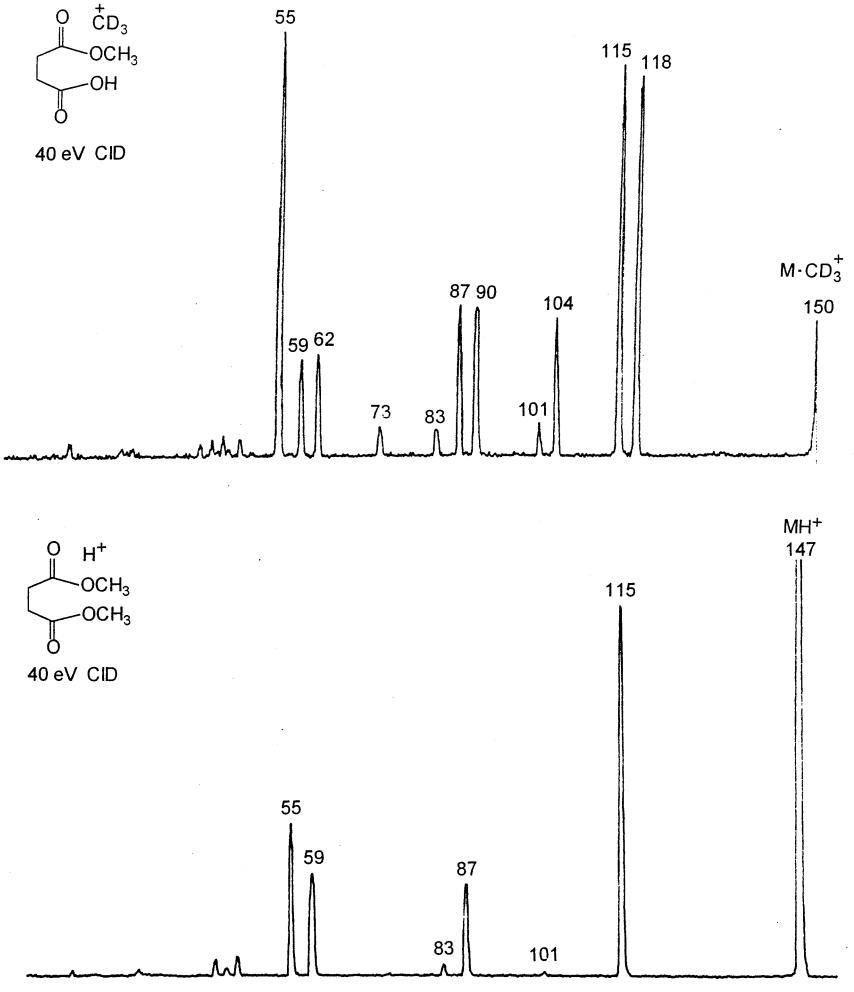
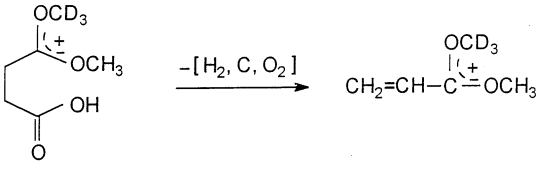


Fig. 7. 40 eV CID mass spectra of CD_3^+ adduct of monomethyl succinate and protonated dimethyl succinate.

mass spectrum of the CD_3^+ adduct of monomethyl succinate with the 40 eV CID mass spectrum of protonated dimethyl succinate. Although there are many similarities in the CID mass spectra, the spectrum of the CD_3^+ adduct of the mono ester shows significant ion signals at *m*/*z* 73, 101, and 104 which totally are not observed in the CID mass spectrum of protonated dimethyl succinate. The ion signal at *m*/*z* 101 results from elimination of CD_3OCH_3 from $M.CD_3^+$ whereas *m*/*z* 73 results from subsequent elimination of CO from the *m*/*z* 101 ion; these fragments are most readily interpreted in terms of CD_3^+ addition to the methoxy oxygen of the mono ester. The ion signal at *m*/*z* 104 is surprising and corresponds to elimination of [H_2, C, O_2] from $M.CD_3^+$. It is not known whether this fragmentation reaction involves the loss of H_2O + CO (no signal is observed corresponding to loss of either separately) or loss of HCOOH (formic acid). Regardless of the exact



Scheme 6.

mechanism, this ionic product is most readily rationalized in terms of addition of CD_3^+ to the carbonyl oxygen of the carbomethoxy group and fragmentation to form the CD_3^+ adduct of methyl acrylate (Scheme 6). A similar loss of [H_2, C, O_2] from the M.CH_3^+ of succinic acid monoamide gives *m*/*z* 86 (Fig. 3) supporting the conclusion that the methyl cation adds to the carbonyl oxygen of the amide group.

4. Conclusions

Protonated succinic acid monoamide and monomethyl succinate show extensive fragmentation under CH_4CI conditions, consistent with functional group interaction as outlined in Scheme 1. A significant fragmentation channel for the protonated monoamide involves formation of NH_4^+, presumably through the intermediate formation of a protonated succinic anhydride-ammonia ion/neutral complex within which proton transfer to ammonia takes place. The ion formed by loss of H_2O from the protonated amide yields a CID spectrum which differs from that of protonated succinimide; it is suggested that the ion produced by fragmentation of the protonated amide is N-protonated succinimide although that produced by protonation of succinimide is the O-protonated species. The M.CH_3^+ adduct of the monoamide yields a distinctly different CID spectrum than the protonated monomethyl ester of succinimide, indicating that CH_3^+ addition does not occur to a significant extent at the COOH group of the monoamide.

The $[MH–H_2O]^+$ and $[MH–CH_3OH]^+$ ions observed in the CH_4 CI mass spectrum of monomethyl succinate give CID spectra in agreement with the CID spectra of methylated succinic anhydride and protonated succinic anhydride, respectively. This result provides strong support for the proposal that the fragmentation of protonated and cationated succinic acid derivatives is promoted, in part, by formation of cationated cyclic anhydride structures.

Acknowledgement

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