Search for charge-remote reactions of even-electron organic negative ions in the gas phase. Anions derived from disubstituted adamantanes

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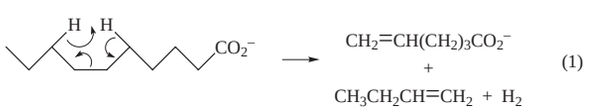
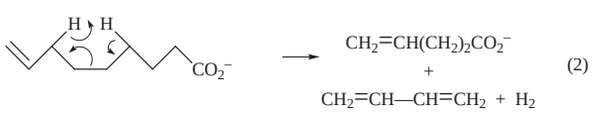
The collision induced decompositions of 3-substituted adamantanecarboxylate anions have been studied with a view to uncover charge-remote fragmentations of the 3-substituent. The 3-substituent is chosen so that it cannot approach the anion site and therefore any fragmentations of that substituent should proceed independently of the charged centre. (i) Charge-remote radical losses are observed from a 3-$CH(Et)_2$ substituent [*e.g.* Et$^{\bullet}$ and $^{\bullet}CH(Et)_2$ losses], but the classical Adams–Gross charge remote loss of an ethene plus dihydrogen is not observed. (ii) Charge-remote loss of MeOD is observed from a 3-$C(CD_3)_2(OMe)$ substituent together with a number of charge-remote radical losses [*e.g.* Me$^{\bullet}$, MeO$^{\bullet}$ and $^{\bullet}C(CD_3)_2(OMe)$]. (iii) The 3-substituent $C(CD_3)_2$ (OCH=O) undergoes charge-remote loss of HCO_2D for both the carboxylate anion and its corresponding cation, a neutral reaction analogous to both the McLafferty rearrangement of radical cations and the Norrish II diradical rearrangement of aliphatic ketones. (iv) The charge-remote radical losses of MeO$^{\bullet}$ and $^{\bullet}CO_2Me$ occur from a 3-CO_2Me substituent.

Introduction

A charge-remote reaction is one which is uninfluenced by the charged centre and occurs remote from that centre. Fragmentations of even-electron organic negative ions in the gas phase generally involve the loss of even-electron neutrals, with cleavages involving loss of radicals being less common.[1,2] A number of examples of charge-remote losses of radicals have been documented:[3,4] in these cases, stable distonic radical anions are produced. The situation concerning the complementary neutral loss is not so straightforward however. The classical example of a charge-remote negative ion reaction is the six-centre process shown in eqn. (1) proposed by Adams and Gross,[5,6] with this



(1)



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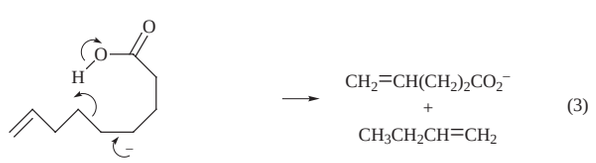
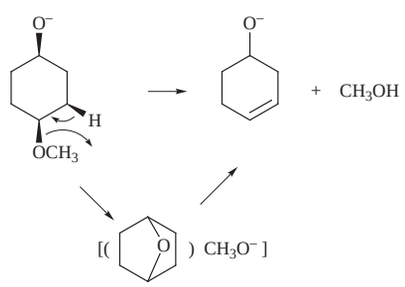


(3)

process having a significant barrier to the transition state.[7] The mechanism has been questioned,[8] but has been supported by the identification of neutral alk-1-enes by neutral fragment reionization mass spectrometric (N_fRMS) studies.[9] A recent study of a cognate system has supported the operation of the charge-remote process shown in eqn. (2) (which has a computed barrier of some 370 kJ mol^{-1}), but shown that (i) the process is preceded or accompanied by hydrogen scrambling along the carbon chain, and (ii) the alternative anionic process (3) [which has a lower overall activation barrier than that of eqn. (2) (including the proton transfer from the carboxylate anion to form the precursor anion)], does not occur because the precursor anion, although formed, undergoes competing (and preferential) proton transfer to form a more stable anion.[10]

We have since designed a number of other systems which we believed might undergo charge-remote reactions.[4,11,12] None of these showed any evidence of such processes: there was always a more kinetically favoured process directed from the anion centre. A recent example involves the loss of methanol from $(M - H)^-$ ions of the geometrical isomers of 4-methoxycyclohexanol.[12] There is no evidence for the operation of the charge-remote reaction shown in Scheme 1 (which has a computed



A

Scheme 1

barrier of some 290 kJ mol^{-1}). Instead, the cyclization process shown in Scheme 1 results in the loss of methanol through **A**, even though the initial cyclization to **A** is unfavourable because of the *cis* orientation of the two interacting substituents.

We have concluded, from currently available results, that charge-remote processes are only likely to occur when there is no suitable and lower energy decomposition channel directed by the anionic centre. Yet it is not always an easy undertaking to differentiate, by experimental means, a charge-remote process from one that is initiated from the charged anionic centre. On occasions, neither heavy atom labelling, nor N_fRMS (neutral) studies can resolve the issue. In addition, there is the problem with conformationally mobile systems [like those illustrated in eqns. (1) and (2)], that the charged centre is able to approach the reacting centre and may have some electronic influence on that reaction (like, for example, a counter ion in a condensed phase reaction), without necessarily inducing a specific anionic reaction (*e.g.* like deprotonation, nucleophilic substitution or an anion induced elimination). The reaction shown in eqn. (2) is illustrative of such a problem: in conformation **B**, the carboxylate anion could assist anchimerically with the dissociation by making the adjacent H more acidic.

In the present study we have overcome the mobility problem outlined above. A number of 1,3-disubstituted adamantane systems have been synthesized in which the anion centre cannot approach close enough to the other substituent to be directly

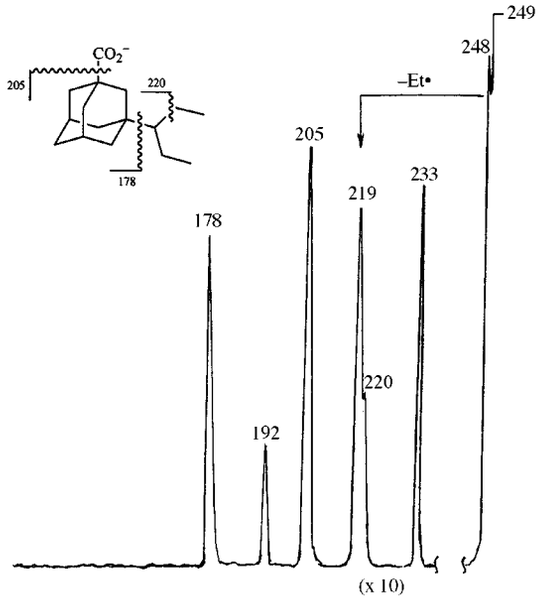
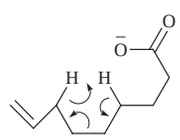


Fig. 1 Collisional activation mass spectrum (MS/MS) of the 3-(3-pentyl)adamantane-1-carboxylate anion. VG ZAB 2HF mass spectrometer. See Experimental section for experimental details.



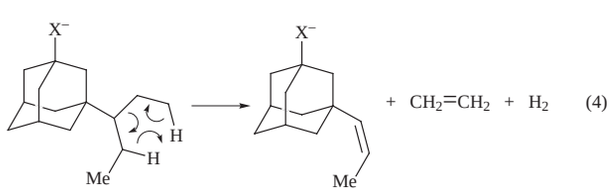
B

involved in any fragmentation of that substituent. The substituents have been designed so that the possibility of even-electron neutral loss by charge-remote fragmentation may be probed.

Results and discussion

Adams and Gross charge-remote reaction

The first reaction that we wished to study was one analogous to those shown in eqns. (1) and (2), but utilizing a 1,3-disubstituted adamantane where the anion centre and the alkyl (reaction) centre occupy the 1 and 3 positions respectively. The two substituents must not be able to interact through bonds or through space and the adamantane skeleton must neither rupture nor rearrange under the reaction conditions. The reaction sequence is shown in eqn. (4). The substituent X needs to



have a high electron affinity but cannot be directly adjacent to the adamantane ring (*e.g.* like O, S or NH), since fragmentation through such an anionic site could in principle rupture the adamantane skeleton. We have investigated the use of each of the three functional groups $-CH_2O^-$, $-(CO-CH_2)^-$ and $-CO_2^-$: all give similar results but of the three, 3-substituted adamantane-1-carboxylate anions give the most intense spectra. We therefore use the carboxylate group as the anion site for three of the systems described in this paper. The prerequisite that the 3-alkyl group may not approach the carboxylate anion centre restricts the choice of substituent: the symmetrical 3-pentyl substituent was chosen for this study.

The collision induced dissociation mass spectrum of the $(M - H)^-$ ion of 3-(3-pentyl)adamantane-1-carboxylic acid is shown in Fig. 1. B^2/E Linked scans were used to identify the

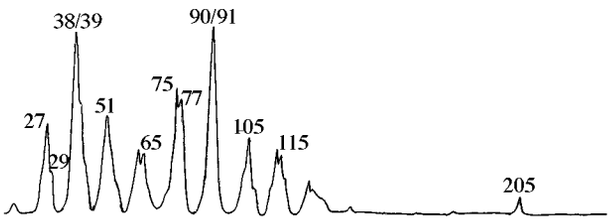


Fig. 2 $^-N_fR^+$ spectrum of neutrals formed from the 3-(3-pentyl)-adamantane-1-carboxylate anion. VG Autospec mass spectrometer. See Experimental section for experimental details.

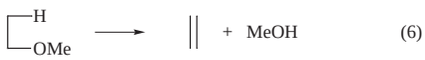
precursor ions of all source formed daughter ions. Although there is a peak corresponding to $[(M - H)^- - 30]^-$ (*m*/*z* 219), this process does not correspond to the charge-remote neutral process shown in eqn. (4). A B^2/E linked scan shows that *m*/*z* 219 is formed exclusively by sequential radical cleavages, *i.e.* $[(M - H)^- - H^\bullet] - C_2H_5^\bullet$. Other processes shown in Fig. 1 also involve charge-remote radical cleavages, *i.e.* $[(M - H)^- - H^\bullet]^{\bullet -}$, $\{[(M - H)^- - H^\bullet] - CH_3^\bullet\}$ and $[(M - H)^- - C_5H_{11}^\bullet]$. The radical losses are more energetically favourable than the charge-remote reaction shown in eqn. (4) {ΔH [for eqn. (4)] is 210 kJ mol^{-1} and the barrier is calculated[10] to be near 370 kJ mol^{-1}}. For example (i) homolytic H-cleavage of the 3-substituent gives a stable tertiary radical and (ii) the process shown in eqn. (5) is endothermic only by 70 kJ mol^{-1}.†,[13]

$$(R)^-{-}C^\bullet(Et)_2 \longrightarrow (R)^-{-}C(Et){=}CH_2 + CH_3^\bullet \qquad (5)$$

We have also attempted to identify the neutrals formed by the processes shown in Fig. 1 using neutral fragment reionization mass spectrometry. The $^-N_fR^+$ method used has been described in full.[10] The composite $^-N_fR^+$ spectrum is shown in Fig. 2. Although the use of the carboxylate anion is advantageous for the study of the anionic fragments (*e.g.* Fig. 1), it is not a good choice for an $^-N_fR^+$ study (*i.e.* the complementary neutral fragments) because the resultant positive ion spectrum is dominated by the reionization products of the largest neutral loss (205 Da) which is coproduced with the CO_2 ion. The spectrum is consistent with the formation of $Et^\bullet$ but is inconclusive concerning the presence of C_2H_4 [required by the process shown in eqn. (4)].

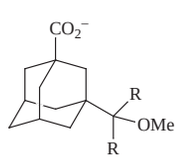
Charge-remote loss of methanol

The retro process shown in eqn. (6) is endothermic (ΔH = 67 kJ



(6)

mol^{-1})[13] and has a computed (AM1) barrier of 280 kJ mol^{-1}.[12] We have searched earlier for a charge-remote reaction of this type without success,[12] and here we use 3-disubstituted adamantane-1-carboxylate anions **1** (R = Me and CD_3) to



1 R = CH_3 or CD_3

† We attempted to synthesize the 3-$CH(C_2D_5)_2$ labelled derivative of adamantane-1-carboxylic acid in order to determine the position of $H^\bullet$ loss from the $(M - H)^-$ ion shown in Fig. 1. The method used was the same as that used for the synthesis of 3-(3-pentyl)adamantane-1-carboxylic acid (see Experimental section) except that [$^2H_5$]ethyl iodide was used (*cf.* refs. 14 and 15). During the second step {heating 3-(1-adamantyl)-1,1,1,2,2,4,4,5,5,5-[$^2H_{10}$]pentan-3-ol with trifluoroacetic acid to yield the expected 3-(1-hydroxy-3-adamantyl)-1,1,1,2,2,4,4,5,5,5-[$^2H_{10}$]pentane}, significant loss of and scrambling of labels occurred (use of CF_3CO_2D will result in an increase in and scrambling of the label).[14,15]

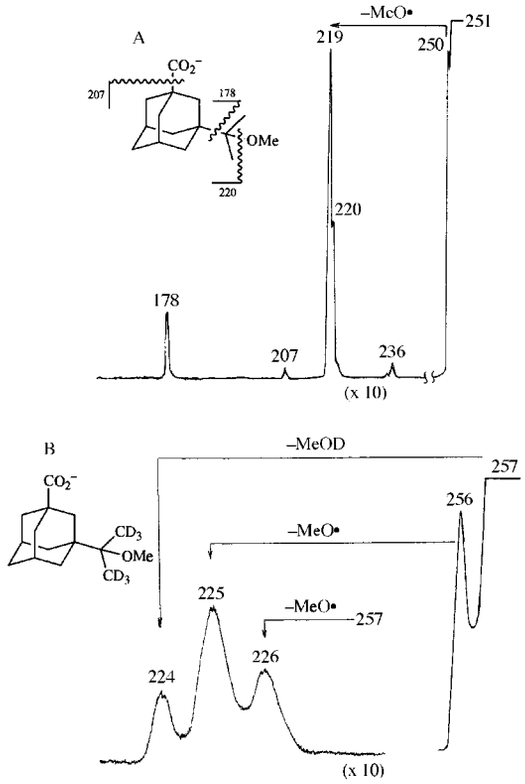
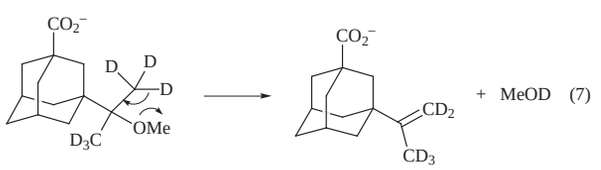


Fig. 3 (A) Collisional activation mass spectrum (MS/MS) of the 3-(2-methoxypropyl)adamantane-1-carboxylate anion, and (B) the partial B/E mass spectrum of the 3-(2-methoxy-2-[$^2H_6$]propyl)-adamantane-1-carboxylate anion. VG ZAB 2HF instrument.



probe this process further. The collision induced dissociation spectra of these anions are recorded in Fig. 3: the reaction of interest is summarized in eqn. (7).

Fig. 3A is the full spectrum (MS/MS) of **1** (R = CH_3), while Fig. 3B shows the partial B/E spectrum of **1** (R = CD_3) (the B/E spectrum gives better resolution of products than the corresponding MS/MS data). B^2/E Linked scanning was performed in order to determine the immediate precursors of all source formed daughter ions. Decomposition pathways are indicated by schematic arrows in Fig. 3A and B.

B^2/E Linked scanning indicates that the $[(M - H)^- - 32]$ peak is formed by two processes, *viz*. $[(M - H)^- -$ MeOH] and $\{[(M - H)^- - H^\bullet] - MeO^\bullet\}$. These data cannot be used to indicate the relative proportions of the two processes. The spectrum of the labelled derivative confirms the operation of the charge-remote process shown in eqn. (7), *i.e.* $[(M - H)^- -$ MeOD]. The peak resulting from this process is less pronounced than those resulting from reaction sequences involving charge-remote radical losses, *i.e.* $[(M - H)^- - H^\bullet]$, $[(M - H)^- - MeO^\bullet]$, $\{[(M - H)^- - H^\bullet] - MeO^\bullet\}$ and $[(M - H)^- - {}^\bullet C(CD_3)_2(OMe)]$. The $^-N_fR^+$ spectrum of neutrals from **1** (R = CH_3) is inconclusive concerning the formation of MeOH. There is no peak corresponding to $MeOH^{\bullet+}$, but there is a very small peak (0.5% relative abundance) originating from $MeO^\bullet$.‡ The major contributor to the $^-N_fR^+$ spectrum is again

‡ The conventional positive ion spectrum of methanol gives an $(M - H)^+$ ion of higher abundance than that of the $M^{\bullet+}$ ion.[16] Given the very small abundance of *m/z* 31 (which can arise directly from $MeO^\bullet$ and indirectly from $MeOH^{\bullet+}$) in the $^-N_fR^+$ spectrum, any peak at *m/z* 32 will be lost in baseline noise.

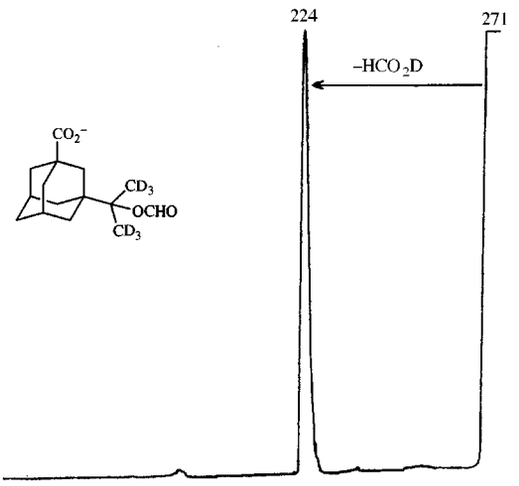
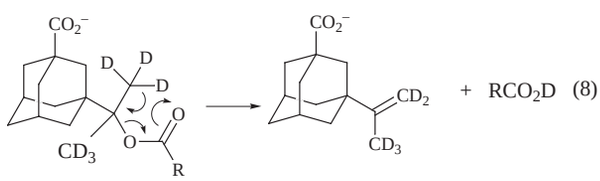


Fig. 4 Collisional activation mass spectrum (MS/MS) of the 3-(2-formyloxy-2-[$^2H_6$]propyl)adamantane-1-carboxylate anion. VG ZAB 2HF mass spectrometer.

the heaviest neutral loss, *viz*. fragment $[(M - H)^- - CO_2]$ which is cogenerated with $CO_2^{\bullet-}$.

Charge-remote loss of formic acid. A neutral process analogous to the Norrish type II and McLafferty rearrangements

When cyclohexyl acetate is heated to 160 °C in solution, cyclohexene and acetic acid are formed in high yield.[17] The reaction is only slightly endothermic [$\Delta G = +18$ kJ mol^{-1}][13] and the barrier is calculated [at the MP4 (SDTQ)/6-31G* level for the model system ethyl formate] to be near 220 kJ mol^{-1}.[18] This should be a good candidate for a charge-remote reaction in an anionic system. We chose to study a formate ester (**2**, R = H): the expected reaction is summarized in eqn. (8), and shows



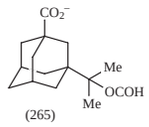
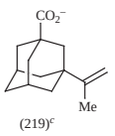
2 R = H or Me

similarities to both the McLafferty rearrangement of radical cations,[19] and to the photochemical Norrish type II radical rearrangement of ketones.[20]

The negative ion spectrum of the labelled formate [**2**, R = H] is shown in Fig. 4 (for a communication see ref. 21). The negative ion spectrum shows only the loss of HCO_2D, and a B^2/E linked scan experiment on source formed *m/z* 224, which confirms that it is formed exclusively from the $(M - H)^-$ ion (*m/z* 271). The collisional activation and charge reversal spectra of the $[(M - H)^- - HCO_2H]$ product ion from unlabelled **2** (R = H) are compared with that of the independently synthesized propenyl anion in Table 1. These data are in accord with the structure of the product anion shown in eqn. (8). In addition, the $^-N_fR^+$ spectrum of the unlabelled analogue of **2** (R = H) has been measured to confirm that neutral formic acid is eliminated from the parent anion. The low mass end of the $^-N_fR^+$ spectrum is shown in Fig. 5. The spectrum is complex, but there is an unresolved peak corresponding to *m/z* 46 ($HCO_2H^{\bullet+}$). These data, collectively, support the occurrence of the charge-remote process shown in eqn. (8).

We have also investigated the decompositions of **2** (R = CH_3). A molecular model indicates that in this case the acetate methyl group can now approach the carboxylate anion centre. Even so, the only fragmentation observed is loss of CH_3CO_2D: there are no fragmentations resulting from proton transfer between CO_2^-

Table 1 Product ion studies

Parent ion	Product ion	Mode	Spectrum-CA [*m/z* (loss) abundance] CR [*m/z* (abundance)]
 (265)	$-HCO_2H$ (219)	CA	218 ($H^{\bullet}$) 100, 178 ($C_3H_5^{\bullet}$) 2
		CR [a]	175 (80), 131/130 [b] (30), 118/117 [b] (35), 105 (38), 91 (100), 79 (75), 77 (77), 65 (15), 51 (11), 39 (12)
 (219) [c]		CA	218 ($H^{\bullet}$) 100, 178 ($C_3H_5^{\bullet}$) 3
		CR	175 (100), 131/130 [b] (25), 118/117 [b] (28), 105 (32), 91 (73), 79 (56), 77 (54), 65 (12), 51 (8), 39 (9)

[a] Peaks are not resolved. [b] This spectrum is weak because the source formed daughter ion *m/z* 219 is not abundant. The spectra of this *m/z* 219 ion and that of the standard were measured using the same collision gas pressure: the two spectra are characteristic and visually very similar. The difference lies in the relative abundances of the peaks due to product cations *m/z* 175. The difference is almost certainly due to the low abundance of the precursor *m/z* 219, compared with the pronounced parent peak at *m/z* 219 from the standard (abundances of peaks in CR spectra are very dependent on the concentration of the parent anion, and on the collision gas pressure). [c] Prepared by the S_N2 reaction between HO^- and the neutral methoxycarbonyl derivative.

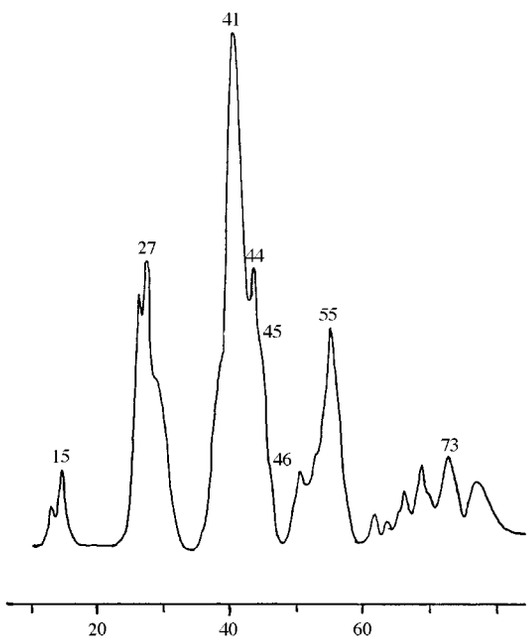


Fig. 5 Low mass region of the $^-N_fR^+$ spectrum of neutrals from the 3-(2-formyloxy-2-propyl)adamantane carboxylate anion. VG Autospec mass spectrometer.

and CH_3 (a simple ester enolate $^-CH_2CO_2R$ should lose CH_2=C=O to yield RO^-).[22] The $^-N_fR^+$ spectrum in this case is inconclusive: any peaks at *m/z* 61 ($CH_3CO_2D^{\bullet +}$) and 43 (CH_3CO^+) (*cf.* ref. 23) are masked by peaks centred on *m/z* 62/63 and 41–44 {decomposition products of the ionized neutrals from $[(M - H)^- - CO_2]$ (*cf.* Fig. 2)}.

If the reaction of **2** (R = H) [shown in eqn. (8)], is really uninfluenced by the anionic centre, then it should also operate for the cognate species containing a carboxylate cation centre, provided that there is no low energy positive ion fragmentation which occurs in preference to the charge-remote reaction. A carboxylate cation cannot be formed by conventional ionization procedures, but is accessible by charge reversal [24] of a carboxylate anion. The charge reversal spectrum of the deuterium labelled formate substituted adamantanecarboxylate anion is shown in Fig. 6. The formation of an $[(M - H)^+ - HCO_2D]$ ion {together with a base peak formed by the sequence $[(M - H)^+ - (CO_2 + HCO_2D)]$: the sequence of CO_2 and HCO_2D loss are not known} confirms the operation of the charge-remote process for both negatively and positively charged carboxylate species **2** (R = H).

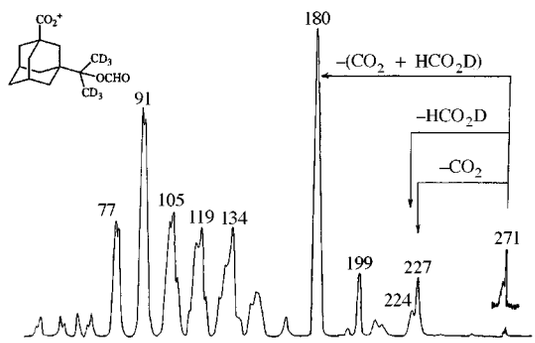
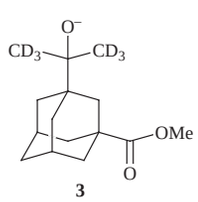


Fig. 6 Charge reversal (positive ion) mass spectrum of the 3-(2-formyloxy-2-[$^2H_6$]propyl)adamantane-1-carboxylate anion. For experimental conditions see Experimental section.

Charge-remote radical losses of a simple ester

Finally, we have investigated an anion derived from a 1,3-disubstituted adamantane which should undergo simple fragmentations through the anionic centre, and where charge-remote reactions were not anticipated. The collisional activation mass spectrum of anion **3** is recorded in Fig. 7: the



3

$(M - H)^-$ ion should undergo pronounced loss of CD_4 by the characteristic fragmentation of an alkoxide.[25]

The spectrum shown in Fig. 7 does show that major cleavages are initiated from the anion centre, *i.e.* abundant peaks are formed by the competitive loss of CD_4 and CD_3COCD_3. But it also shows two charge-remote radical cleavages of the methyl ester group, *viz*. loss of $MeO^{\bullet}$ and $MeOCO^{\bullet}$ from the $(M - H)^-$ ion. The charge-remote radical losses do not conform to negative ion cleavages of a simple methyl ester [*i.e.* $(M - H)^- - Me^{\bullet} - CO_2$],[26] but are similar to the analogous positive ion cleavages [*i.e.* $M^{\bullet +} - MeO^{\bullet} - CO$].[27]

Conclusions

We have shown for 3-substituted adamantane carboxylate anions that (i) the Adams and Gross charge-remote neutral

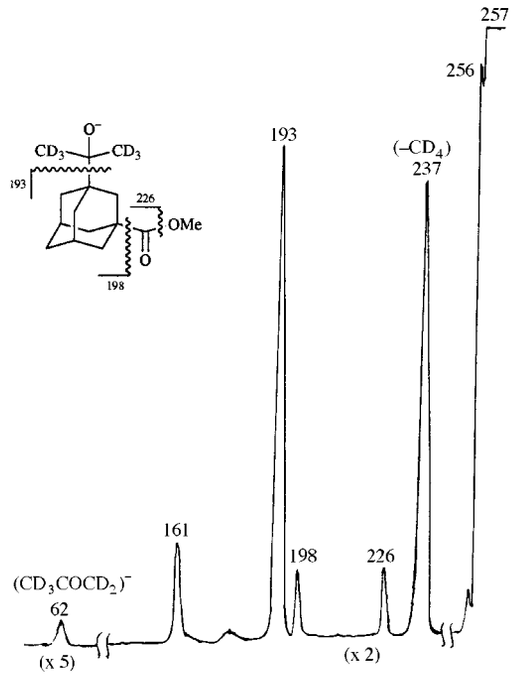


Fig. 7 Collisional activation mass spectrum of the $(M - H)^-$ ion from methyl 3-(2-hydroxy-2-[$^2H_6$]propyl)adamantane-1-carboxylate. VG ZAB 2HF instrument.

process [eqn. (4): compare with eqns. (1) and (2)] does not occur; in this case charge-remote radical cleavages are more energetically favourable, (ii) charge-remote loss of methanol from **1** [eqn. (8): compare with eqn. (6)] co-occurs with a number of charge-remote radical losses, (iii) the charge-remote loss of formic acid [eqn. (8) (R = H)] is facile and produces the major fragment anion in the spectrum. The same process occurs from the cognate carboxylate cation. In addition, the charge-remote radical cleavages of a methyl ester group involve the loss of MeO$^\bullet$ and MeOCO$^\bullet$.

Experimental

Mass spectrometric methods

Collisional activation (CID) mass spectra (MS/MS) were determined with a VG ZAB 2HF mass spectrometer.[28] Full operating details have been reported.[29] Specific details are as follows: the chemical ionization slit was used in the chemical ionization source, the ionizing energy was 70 eV, the ion source temperature was 100 °C, and the accelerating voltage was 7 kV. Samples were introduced into the source *via* the direct probe with no heating [measured pressure of sample 1×10^{-6} Torr (1 Torr = 133.322 Pa)]. Deprotonation was effected using HO^- (from H_2O) or DO^- (from D_2O) for deuterium labelled derivatives. The measured pressure of H_2O or D_2O was 1×10^{-5} Torr. The estimated source pressure was 10^{-1} Torr. Argon was used in the second collision cell (measured pressure, outside the cell, 2×10^{-7} Torr), giving a 10% reduction in the main beam, equivalent to single collision conditions.

Charge-reversal (positive ion) mass spectra[24] of negative ions were measured as described above except that the electric sector potential was reversed in order to allow the transmission of positive ions.

The N_fRMS-type experiments were conducted with an E_1BE_2 tandem mass spectrometer (VG AutoSpec at Akron) that has previously been described.[30] This instrument houses two collision cells (C-1 and C-2) and an intermediate deflector in the interface region between E_1B and E_2. The carboxylate anions $(M - H)^-$ acid were formed by FAB ionization, using a 20 keV Cs^+ ion gun and triethanolamine as the matrix. The $(M - H)^-$ precursor anions were accelerated to 8 keV, selected by E_1B and dissociated with He in C-1. CID coproduces ionic and neutral fragments. After exiting C-1, the ionic fragments and any undissociated $(M - H)^-$ ions were deflected from the beam path, and the remaining neutral losses were post-ionized in C-2 by collision induced dissociative ionization with O_2.[29] The newly formed cations were mass-analysed by E_2 and recorded in the neutral fragment-reionisation, $^-N_fR^+$, spectrum.[9,31] The superscripts beside N and R in the N_fR notation designate the charge of the precursor ion (from which the neutrals are eliminated) and the charges of the ultimate product ions (to which the neutrals are reionized), respectively.[32]

Syntheses of unlabelled and labelled precursor molecules

All ^1H NMR spectra were measured in $CDCl_3$ using a Bruker 200 MHz NMR spectrometer. Mass measurements were measured with a Kratos Concept ISQ mass spectrometer on $M^{\bullet+}$ ions formed by electron impact, or MH^+ ions formed by liquid secondary ion mass spectrometry, with *m*-nitrobenzyl alcohol as the liquid matrix, and 10 kV Cs^+ ions as the primary beam (courtesy of Dr N. Davies of the University of Tasmania). Incorporation of label was determined by examination of $(M - H)^-$ ions in negative ion mass spectra using the VG ZAB 2HF instrument.

Methyl 3-(2-hydroxy-2-propyl)adamantane-1-carboxylate. Methyl magnesium iodide [from methyl iodide (2.4 g) and Mg (0.4 g)] was added at 20 °C and over 30 min to dimethyl adamantane-1,3-dicarboxylate (2 g) in anhydrous diethyl ether (40 cm^3). The reaction mixture was allowed to stir at 20 °C for 18 h, heated at reflux for 1 h, cooled to 0 °C, and aqueous ammonium chloride (saturated, 20 cm^3) was added. The layers were separated, the aqueous layer extracted with diethyl ether (2×20 cm^3), the organic extracts combined, dried ($MgSO_4$), the solvent removed *in vacuo*, and the residue distilled to give methyl 3-(2-hydroxy-2-propyl)adamantane-1-carboxylate as a colourless liquid (1.9 g, yield 92%, bp 133–136 °C/0.1 mmHg). $MH^+ = 253.1794$, $C_{15}H_{25}O_3$ requires 253.1797. δ_H 3.6 (s, 3H), 2.15 (br s, 2H), 1.55–1.9 (m, 13H), 1.1 (s, 6H).

Methyl 3-(2-hydroxy-2-[$^2H_6$]propyl)adamantane-1-carboxylate. Prepared as for the unlabelled compound (above), but using [$^2H_3$]methyl iodide. $D_6 = 99\%$.

3-(2-Methoxy-2-propyl)adamantane-1-carboxylic acid. A mixture of methyl 3-(2-hydroxy-2-propyl)adamantane-1-carboxylate (2.0 g) and acetic anhydride (20 cm^3) was heated under reflux for 96 h, cooled to 20 °C, and poured into ice (200 g) and extracted with diethyl ether (2×30 cm^3). The ethereal layer was washed with aqueous sodium hydrogen carbonate (saturated) until the evolution of CO_2 ceased, dried ($MgSO_4$), the solvent removed *in vacuo*, and the residue distilled to yield methyl 3-(propen-2-yl)adamantane-1-carboxylate (1.4 g, yield 70%; bp 92–96 °C/0.5 mmHg). $MH^+ = 235.1684$, $C_{15}H_{23}O_2$ requires 235.1692. δ_H 4.7 (m, 2H), 3.6 (s, 3H), 2.2 (br s, 2H), 1.5–1.8 (m, 12H).

Mercuric acetate (2.5 g) was added to the substituted prop-1-ene (1.4 g) in anhydrous methanol (30 cm^3), the mixture was allowed to stir for 1 h at 20 °C, cooled to 0 °C, then aqueous sodium hydroxide (6 M, 10 cm^3) followed by sodium borohydride (0.6 g) in aqueous sodium hydroxide (3 M, 8 cm^3) was added. The mixture was allowed to stir at 20 °C for 12 h, filtered through Celite, and heated under reflux for 2 h. The methanol was removed *in vacuo*, water (50 cm^3) was added to the residue, aqueous hydrogen chloride (2 M) was added until the pH was 2, the mixture extracted with diethyl ether (2×25 cm^3), the ether layer was extracted with aqueous sodium hydrogen carbonate (saturated, 2×25 cm^3), and aqueous hydrogen chloride (2 M) was added to the aqueous layer until the pH was 2. The precipitate was filtered and dried giving 3-(2-methoxy-2-propyl)adamantane-1-carboxylic acid (0.8 g, 44% yield) as a colourless powder, mp 85–88 °C. $MH^+ = 253.1805$, $C_{15}H_{25}O_3$

requires 253.1803. δ_H 9.0 (br s, 1H), 3.15 (s, 3H), 2.15 (br s, 2H), 1.4–1.85 (m, 12H), 1.0 (s, 6H).

3-(2-Methoxy-2-[$^2H_6$]propyl)adamantane-1-carboxylic acid. This was made by the route outlined above but from methyl 3-(2-hydroxy-2-[$^2H_6$]propyl)adamantane-1-carboxylate. D_6 = 99%.

3-(3-Pentyl)adamantane-1-carboxylic acid. (a) 3-(1-*Adamantyl*)*pentan*-3-*ol*.—This was made by a method similar to that used for the synthesis of methyl 3-(2-hydroxy-2-propyl)adamantane-1-carboxylate (see above), except that ethyl magnesium bromide was used. Yield 85%, bp 148–153 °C/0.1 mmHg. δ_H 2.2 (br s, 3H), 1.65–1.8 (m, 13H), 1.55 (q, 4H), 0.85 (t, 6H).

(b) 3-(1-*Hydroxy*-3-*adamantyl*)*pentane*.—This procedure involves a known rearrangement.[15] A mixture of 3-(1-adamantyl)pentan-3-ol (2 g) and trifluoroacetic acid (10 cm^3) was heated at 60 °C for 2 h, cooled to 0 °C, aqueous sodium carbonate (saturated, 20 cm^3) was added, the mixture heated at reflux for 2 h, cooled to 20 °C and extracted with diethyl ether (2 × 25 cm^3). The solvent was removed *in vacuo*, and the residue purified by flash chromatography over silica eluting with hexane–diethyl ether (2:1) to give 3-(1-*hydroxy*-3-*adamantyl*)-*pentane* as a colourless liquid (1.2 g, 60% yield). δ_H 2.1 (br s, 2H), 1.4–1.9 (m, 15H), 0.8 (t, 6H).

(c) 3-(3-*Pentyl*)*adamantane*-1-*carboxylic acid*.—This procedure involves a known rearrangement.[15] 3-(1-Hydroxy-3-adamantyl)pentane (1.0 g) was dissolved in sulfuric acid (concentrated, 5 cm^3) at 0 °C, and anhydrous formic acid (0.25 cm^3) was added dropwise with the temperature kept below 5 °C. The mixture was stirred at 0 °C for 2 h, then at 20 °C for 48 h, and poured onto crushed ice (100 g). Filtration of the mixture gave a pale solid which was dissolved in aqueous sodium hydrogen carbonate (saturated, 25 cm^3). Addition of aqueous hydrogen chloride (10%) until the mixture was just acidic gave a precipitate, which when filtered and dried gave 3-(3-*pentyl*)-*adamantane*-1-*carboxylic acid* (0.5 g, 45% yield), mp 121–123 °C. MH^+ = 251.2024, $C_{16}H_{27}O_2$ requires 251.2021. δ_H 8.9 (br s, 1H), 2.2 (br s, 2H), 0.8–1.9 (m, 21H).

Methyl 3-(2-formyloxy-2-propyl)adamantane-1-carboxylate. Prepared by formylation of methyl 3-(2-hydroxy-2-propyl)-adamantane-1-carboxylate using acetic formic anhydride.[33] Yield 58%. MH^+ = 279.1591, $C_{15}H_{23}O_4$ requires 279.1596. δ_H 3.6 (s, 3H), 2.15 (br s, 2H), 1.4–1.8 (m, 12H), 1.05 (s, 6H).

Methyl 3-(2-formyloxy-2-[$^2H_6$]propyl)adamantane-1-carboxylate. Prepared by formylation of methyl 3-(2-hydroxy-2-[$^2H_6$]propyl)adamantane-1-carboxylate using acetic formic anhydride.[33] Yield 55%. D_6 = 99%.

Methyl 3-(2-acetyloxy-2-propyl)adamantane-1-carboxylate. A mixture of methyl 3-(2-hydroxy-2-propyl)adamantane-1-carboxylate (1.0 g) and acetic anhydride (20 cm^3) was heated at 120 °C for 1 h, cooled to 20 °C, poured onto ice (200 g) and extracted with diethyl ether (2 × 50 cm^3). The organic layer was washed with aqueous sodium hydrogen carbonate (saturated) until evolution of CO_2 ceased, dried ($MgSO_4$), the solvent removed *in vacuo*, and the residue distilled to give methyl 3-(2-acetyloxy-2-propyl)adamantane-1-carboxylate; bp 105–108 °C/0.1 mmHg (0.7 g, 65% yield). Gives neither $M^{\cdot+}$ by electron impact nor MH^+ by FABMS. δ_H 3.6 (s, 3H), 2.2 (s, 3H), 1.4–1.8 (m, 12H), 1.05 (s, 6H).

Methyl 3-(2-acetyl-2-[$^2H_6$]propyl)adamantane-1-carboxylate. Prepared from acetic anhydride and methyl 3-(2-hydroxy-2-[$^2H_6$]propyl)adamantane-1-carboxylate by the method outlined above. Yield 60%. D_6 = 99%.

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