Carbanion Rearrangements. Collision-induced Dissociations of Tertiary Carbanions derived from Alkyl Esters

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The collisional activation mass spectra of enolates $R^1R^2\bar{C}CO_2R^3$ (R^1, R^2, and R^3 are alkyl) show a variety of competitive fragmentations including the losses of H_2, $R^{3\cdot}$, (R^3O − H), and (R^3O + H) together with the formation of R^3O^- and $R^1C{\equiv}CO^-$. Deuterium labelling has been used to aid elucidation of mechanistic pathways. In one case, the elimination of R^3OH from $Et_2\bar{C}CO_2R^3$, the reaction involves prior hydrogen rearrangement before elimination of the alcohol.

Collision-induced dissociations of negative ions may be used to provide structural information on unidentified compounds,[1,2] and also to obtain fundamental information concerning ion behaviour.[1,3] Enolate negative ions may be produced from alkyl carbonyl compounds by reaction of HO^- in the chemical ionisation source of a mass spectrometer.[4] Collision-induced fragmentations of enolate anions have been studied in several laboratories.[5–12] Collision-induced dissociations of enolate ions of simple esters have been measured by Hunt[7] in a triple quadrupole instrument and, more recently by Squires[12] using an FT ICR instrument. The low-energy decompositions of primary (R^2 = H) and secondary (R^2 = alkyl) carbanions from esters are considered[12] to proceed by pathways *a* and *b* (Scheme);† the only tertiary carbanion studied is reported to decompose through channel *c*.

$$^{-}O\text{–}C{\equiv}CR^1 + R^2OH \xleftarrow{a} R^1\bar{C}H\text{–}C(O)\text{–}OR^2 \xrightarrow{b} R^2O^- + O{=}C{=}CHR^1$$

$$Me_2\bar{C}\text{–}C(O)\text{–}OMe \xrightarrow{c} MeO^- + O{=}C{=}CMe_2$$

Scheme.

Our studies of collisional activation (c.a.) mass spectra of enolate ions derived from ^2H- and ^{13}C-labelled ketones have shown that the mechanisms are more complex than those suggested in the original study.[7] We expected, therefore, that the collision-induced dissociations of ester tertiary carbanions (such as process *c*, Scheme) would also be complex, and in this paper we demonstrate that to be the case.

Results and Discussion

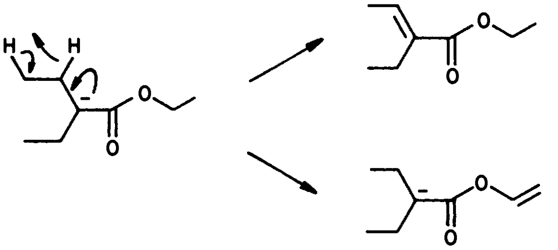
All c.a. mass spectra reported in this paper were measured with a Vacuum Generators ZAB 2HF mass spectrometer operating in the chemical ionisation mode at 70 eV (accelerating voltage 8 kV). Water was used to produce HO^- reagent ions,[9,13,14] and helium was used as collision gas in the second collision cell. Full details are provided in the Experimental section. The compounds used in this study, together with the c.a. mass spectra of their enolate ions, are listed in the Table. Representative spectra are shown in Figures 1 and 2.

We have determined the c.a. mass spectra of several simple esters which yield primary and secondary carbanions, and we confirm the major processes to be those shown in sequences *a* and *b* (Scheme). However, the c.a. mass spectra of the tertiary carbanions derived from compounds (**1**)—(**22**) show a variety of complex fragmentations. We have chosen to study symmetrical esters in detail since the presence of symmetrical substituents $CHMe_2$ and $CHEt_2$ allows the study of intramolecular isotope effects.

$$R^1R^2\bar{C}\text{–}C(O)\text{–}OR^3 \longrightarrow R^3O^- + R^1R^2C{=}C{=}O \quad (1)$$

$$\longrightarrow R^1R^2\bar{C}\text{–}C(O)\text{–}\dot{O} + R^{3\cdot} \quad (2)$$

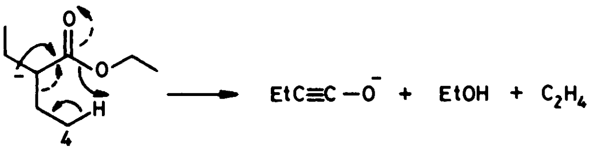
The major fragmentation observed in all spectra is the formation of the appropriate alkoxide negative ion [sequence (1); *cf.* process *c* (Scheme)[12]]. *This process is entirely unimolecular; all other processes are mainly collision-induced but have minor unimolecular contributions* (see *e.g.* legend to Figure 2). A second process involves elimination of the alkoxide alkyl group R^3 [sequence (2)]. This process occurs with considerable kinetic energy release; thus the reaction has appreciable reverse activation energy. In the case of the loss of $Et^\cdot$ shown in Figure 2, the width of the product peak at half-height is 105 V, corresponding to an energy release of 0.53 eV. In contrast, other peaks shown in Figures 1 and 2 are narrow, corresponding to small kinetic energy releases, *e.g.* EtO^- (Figure 2), 0.026 eV.



(3)

(4)

The various losses of H_2 can be complex. In the case of $Et_2\bar{C}CO_2Et$, the major loss is that shown in sequence (3). This is a characteristic reaction of both carbanion[9–11] and alkoxide systems[15,16] and proceeds in a stepwise fashion through a solvated hydride ion intermediate. The minor loss is shown in sequence (4). When R^1 and/or R^2 is ethyl, and R^3 is methyl, $H^\cdot$ loss is more pronounced than loss of H_2. Loss of $H^\cdot$ is observed in spectra from compounds (**1**)—(**7**): its genesis has not been studied by deuterium labelling.



(5)

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† Squires[12] suggests the product ion of sequence *a* to be a deprotonated ketene $R\text{–}\bar{C}{=}C{=}O$. *Ab initio* calculations[11] indicate the structure $R\text{–}C{\equiv}C\text{–}O^-$.

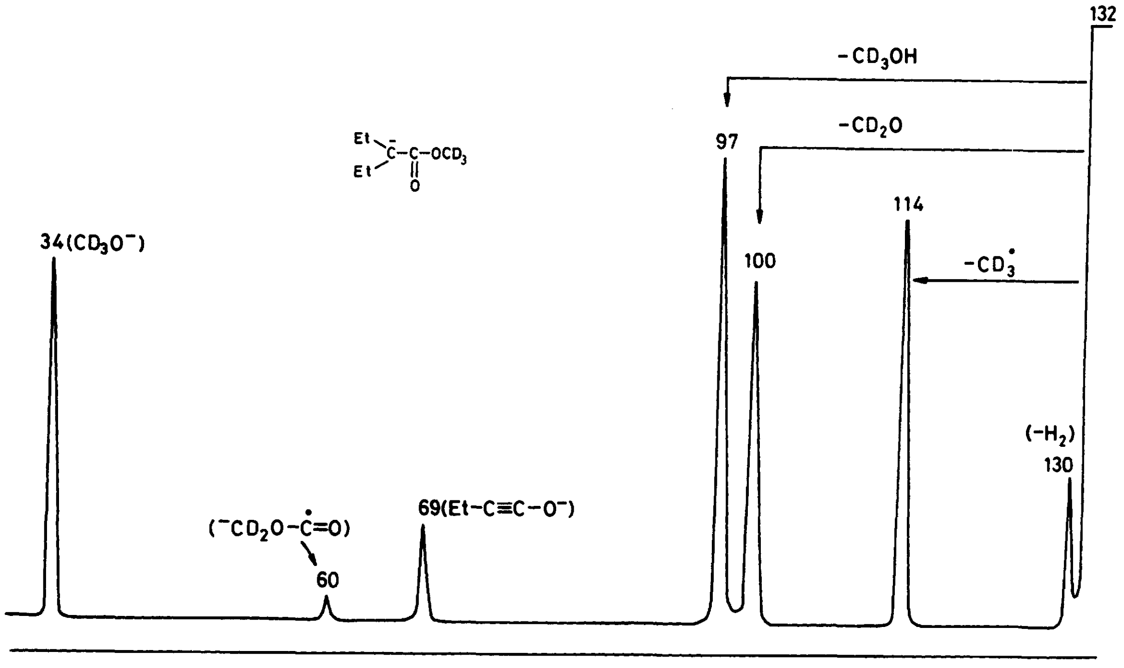


Figure 1. C.a. mass spectrum of the enolate ion of $Et_2CHCO_2CD_3$; conditions as in Experimental section

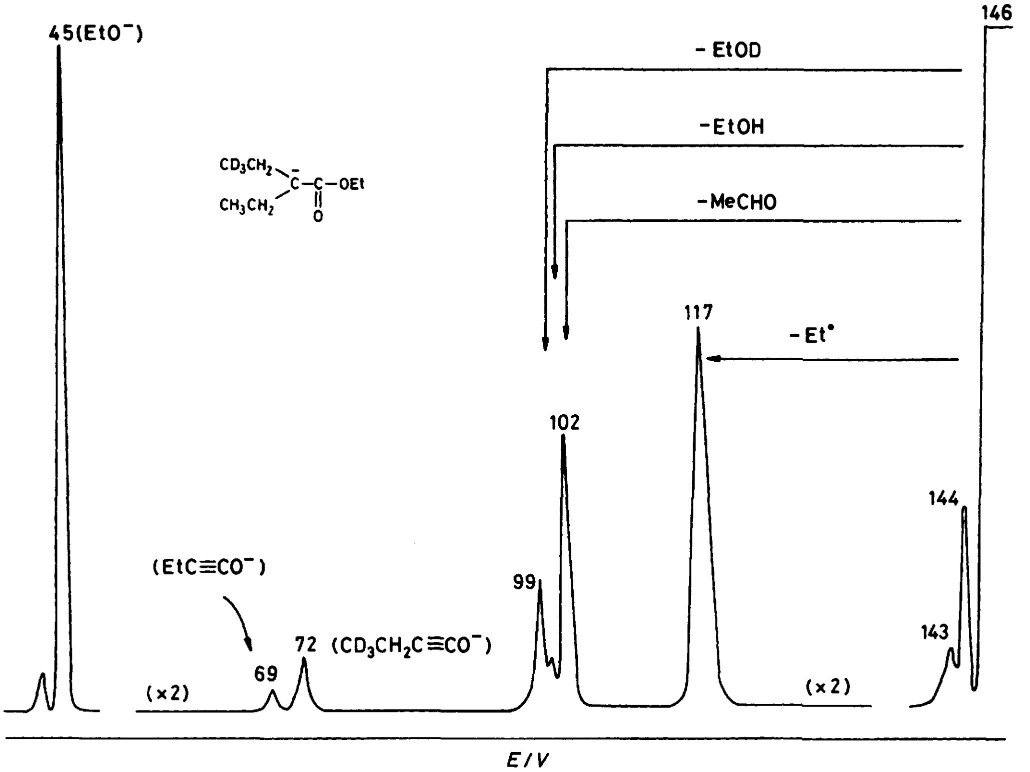
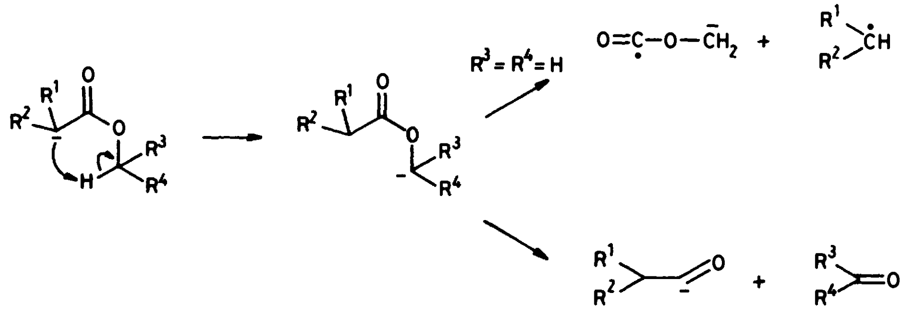


Figure 2. C.a. mass spectrum of the enolate ion of $CD_3CH_2(Et)CHCO_2Et$. Kinetic energy release values (calculated from the widths in volts of product peaks) as follows (in eV): *m/z* 117, 0.532; *m/z* 102, 0.089; *m/z* 99, 0.034; *m/z* 72, 0.015; and *m/z* 45, 0.026. When a voltage of 1 kV is applied to the collison cell, all peaks (except EtO^-) were split, with the major component in each case having moved from its original position. Thus EtO^- is produced by a unimolecular process; all other processes are mainly collision-induced with minor unimolecular components

Table. Collision activation mass spectra of enolate ions derived from the esters (**1**)—(**22**)

$R^1R^2CH-C(O)-OR^3$

Compd.	R^1	R^2	R^3	% Relative abundance										
				$-H$	$-H_2$	$-HD$	$-R^{3\bullet}$	$-(R^3O-H)$	$-(R^3O-D)$	$-(R^3O + H)$	$-(R^3O + D)$	$R^1C{\equiv}CO^-$	$R^2C{\equiv}CO^-$	R^3O^-
(**1**)	Me	Me	Me	8	2		25	61		88				100
(**2**)	Me	Me	Et	8	6		18	20		6				100
(**3**)	CD_3	Me	Et	7	7		29	22		7.1	2.6			100
(**4**)	Me	Me	Pr	10	6		8	8		4				100
(**5**)	Me	Me	Pr^i	6	4		11	3		2				100
(**6**)	Me	Me	Bu^t	1	2		5	—		2				100
(**7**)	Et	Me	Et	5	8		25	65		100				65
(**8**)	Et	Me	Pr	5	5		8	8		52				100
(**9**)	Et	Et	Me		32		14	100		63		32		91
(**10**)	Et	Et	CD_3		31		18		78	100		21		78
(**11**)	Et	Et	Et		6		22	25		13		3		100
(**12**)	Et	Et	CH_2CD_3		7	2	18	25		21		4		100
(**13**)	Et	Et	CD_2Me		8	3	21	14	19	17		5		100
(**14**)	Et	Et	CHDMe		9	3	24	26	7	22		4		100
(**15**)	CD_3CH_2	CD_3CH_2	Et		3	4	22	11			18	3		100
(**16**)	CD_3CH_2	Et	Et		6	2	20	18		1.6	9.0	2.4	1.2	100
(**17**)	$MeCD_2$	$MeCD_2$	Et		3	5	19	24		4		3		100
(**18**)	$MeCD_2$	Et	Et		6	3	18	21		5		2	2	100
(**19**)	Et	Et	Pr		5		8	10		6		2		100
(**20**)	Et	Et	Pr^i		3		10	14		9		2		100
(**21**)	Et	Et	$CH(CD_3)_2$		5		10	17		5		2		100
(**22**)	CD_3CH_2	Et	Pr^i		5	2.5	26	18		1.5	8	1	2.5	100



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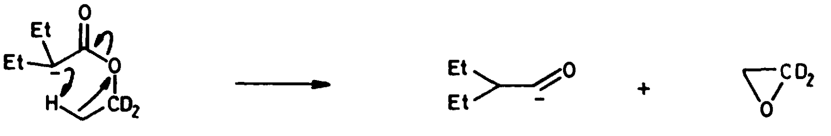
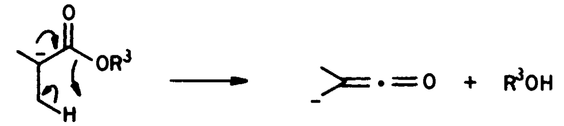
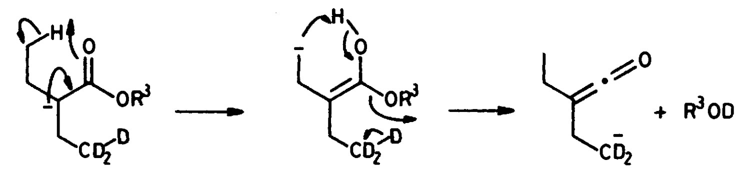
(7)



(8)



(9)



(10)

The formation of R^{1}C≡CO$^-$ occurs only when R^1 and R^2 are ethyl; the reaction involves elimination of R^{3}OH and C_2H_4. In the case of Et$_2\bar{C}$CO$_2$Et we represent the process by sequence (5). The formulation of this reaction as an elimination (rather than an internal S_N2 process) is supported by the operation of a primary deuterium isotope effect of 2.0 at position 4 [see *e.g.* Figure 2 and sequence (5)].

The most unusual reactions are those which involve hydrogen transfer from and to the alkoxy group. In the case of primary or secondary carbanions, ready elimination of an alcohol may occur as shown in sequence *a* (Scheme). This reaction is blocked for tertiary carbanions and alternative decomposition channels are observed. Two of these are shown in sequences (6) and (7). Reaction (6) is *only* observed when R^3 = R^4 = H, *i.e.* for methyl esters. An example is shown in Figure 1. Reaction (7) involves transfer of the α-hydrogen atom of the alkoxide group, resulting in elimination of either an aldehyde or a ketone as appropriate. A pronounced deuterium isotope effect is observed for this reaction. While Et$_2\bar{C}$CO$_2$CH$_2$CD$_3$ *specifically* eliminates CD$_3$CHO, Et$_2\bar{C}$CO$_2$CHDMe eliminates MeCHO and MeCDO in ratio 3.7:1, *i.e.* ^{1}H/^{2}H = 3.7. The isotope effect is so marked that elimination of MeCDO from Et$_2\bar{C}$CO$_2$CD$_2$Me is a minor process; the major channel is loss of C_2H_2DO which we represent by sequence (8). This is the first example we have seen of a deuterium-labelled negative ion fragmenting through a decomposition channel not followed by the unlabelled analogue.

The final reaction, loss of R^{3}OH, demonstrates the importance of labelling in studies of this type. When R^1 = R^2 = Me, loss of R^{3}OH occurs as shown in sequence (9). A large deuterium isotope effect (^{1}H/^{2}H = 2.7) is exhibited by the spectrum of Me(CD$_3$)$\bar{C}$CO$_2$Et. However when R^1 = R^2 = Et, a very different scenario is apparent. The spectra (Table) of (CD$_3$CH$_2$)$_2\bar{C}$CO$_2$Et and (MeCD$_2$)$_2\bar{C}$CO$_2$Et show losses of EtOD and EtOH, respectively, *i.e. specific* loss of H (or D) from the terminal positions. Thus no fragmentation analogous to that shown in sequence (9) occurs for this system. Even more unusual is the observation that (CD$_3$CH$_2$)(Et)$\bar{C}$CO$_2$R^3 (R^3 = Et or Pr^i) shows *apparent* reverse deuterium isotope effects, *i.e.* R^{3}OD:R^{3}OH = 5.6:1 and 5.3:1 for R^3 = Et and Pr^i, respectively (see Table). We conclude that this can only be due to a hydrogen rearrangement which *precedes* the loss of the alkanol. Following sequence (10), we suggest that the initial H transfer has a large primary deuterium isotope effect, which ensures that R^{3}OD is lost preferentially in the ensuing steps.

In conclusion, we have shown that tertiary carbanions derived from alkyl esters have characteristic reactions which depend upon the nature of the alkyl substituents attached to the ester function.

Experimental

C.a. mass spectra were recorded with a Vacuum Generators ZAB 2HF mass spectrometer. All slits were fully open to obtain maximum sensitivity and to minimise energy-resolution effects.[17] The chemical ionisation slit was used in the ion source (ionising energy 70 eV, trap current 100 μA, ion source temperature 200 °C, accelerating voltage 8 kV). The enolate ions were generated by ^{1}H abstraction from compounds (**1**)—(**22**) by HO$^-$ (or H$^-$ and O$^{-\bullet}$) reactant ions.[9,13,14] Reactant negative ions were produced by the action of 70 eV electrons on H_2O. The indicated source ion gauge pressure (of H_2O) was *ca.* 2×10^{-6} Torr. The substrate pressure was typically 2×10^{-7} Torr. The estimated total source pressure is 2×10^{-2} Torr. The pressure of He in the second cell was 2×10^{-7} Torr, measured by an ion gauge situated between the electric sector and the second collision cell. This produced a decrease in the main beam signal of *ca.* 10% and thus corresponded to essentially single collision conditions. Isotope effects quoted in the discussion are averages of six individual scans.

All unlabelled compounds used were known previously and were prepared by esterification of the appropriate carboxylic acids by a standard procedure.[18]

Labelled Compounds: General.—[$^2H_3$]Methyl 2-ethylbutanoate (**10**) ($^2H_3$ 99%), [1-$^2H_1$]ethyl 2-ethylbutanoate (**14**) ($^2H_1$ 99%), [1-$^2H_2$]ethyl 2-ethylbutanoate (**13**) ($^2H_2$ 99%), [2-$^2H_3$]ethyl 2-ethylbutanoate (**12**) ($^2H_3$ 99%), and [1,1,1,3,3,3-$^2H_6$]propan-2-yl 2-ethylbutanoate (**21**) ($^2H_6$ 99%) were prepared from 2-ethylbutanoyl chloride by a standard procedure.[18] The labelled precursors used were [1-$^2H_1$]ethanol,[16] [1,1-$^2H_2$]ethanol,[16] [2,2,2-$^2H_3$]ethanol,[16] [1,1,1,3,3,3-$^2H_6$]propan-2-ol,[16] and [$^2H_4$]methanol, which was a commercial product.

Ethyl 2-([1,1-$^2H_2$]ethyl)[3,3-$^2H_2$]butanoate (**17**) ($^2H_4$ 98%) and ethyl 2-([2,2,2-$^2H_3$]ethyl)[4,4,4-$^2H_3$]butanoate (**15**) ($^2H_6$ 98%) were prepared from 1-iodo[1,1-$^2H_2$]ethane and 1-iodo-[2,2,2-$^2H_3$]ethane by the following method.

Ethyl 2-Ethylbutanoates (**15**) *and* (**17**).—(a) *Diethyl ethylmalonate.* Diethyl malonate (0.48 g) was added dropwise to a stirred solution of potassium t-butoxide (8 cm^3), and the resultant mixture was stirred for 15 min at 20 °C. The appropriate iodoethane (0.51 g) was added dropwise, and the mixture heated under reflux for 4 h; excess of t-butyl alcohol was removed by distillation, and water (10 cm^3) was added to the residue, which was extracted with diethyl ether (3 × 10 cm^3). The organic layer was washed with water (10 cm^3), aqueous sodium hydrogen sulphite (5%; 10 cm^3), water (10 cm^3), and saturated aqueous sodium chloride (10 cm^3), dried (Na_2SO_4), and distilled to yield the required labelled diethyl ethylmalonate. The yields were in the range 95—96%.

(b) *Diethyl diethylmalonate.* The diethyl ethylmalonate was treated as in (a) to yield the doubly labelled diethyl diethylmalonate. The yields were in the range 90—95%.

(c) *Ethyl 2-ethylbutanoate.* A mixture of the foregoing ester (0.5 g), dimethyl sulphoxide (11 cm^3), water (1.0 g), and lithium chloride (0.24 g) was heated under reflux for 12 h, poured into aqueous sodium chloride (saturated; 15 cm^3), and extracted with hexane (3 × 10 cm^3). The organic extract was washed with water (10 cm^3), and dried (Na_2SO_4). The solvent was evaporated off, and the residue distilled to yield the corresponding ethyl 2-ethylbutanoate. Yields were in the range 90—95%.

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