Carbanion Rearrangements. Collision-induced Dissociations of Enolate Ions derived from 3-Ethylpentan-2-one

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Reaction of HO^- with $MeCOCHEt_2$ produces two enolate ions, $MeCO\bar{C}Et_2$ and $^-CH_2COCHEt_2$. The primary carbanion competitively eliminates C_2H_4 and C_4H_8, and forms C_2HO^-. The elimination of C_2H_4 is a stepwise reaction proceeding through a six-membered transition state; the first step (deprotonation) is rate-determining. The loss of C_4H_8 is a rearrangement reaction $^-CH_2COCHEt_2 \xrightarrow{a} {}^-CH_2COMe + EtCH{=}CH_2$. The tertiary carbanion competitively eliminates H_2, CH_4, and C_3H_8. The losses of CH_4 and C_3H_8 are stepwise processes occurring through six- and five-membered transition states, respectively. A double isotope fractionation experiment (^2H, ^{13}C) shows that both steps of the CH_4 elimination are rate-determining.

In the past five years there have been significant advances in the analytical application of negative ion chemical ionisation and fast atom bombardment.[1] These 'soft ionisation' techniques give molecular weight information, but since the $(M - H^+)$ ions fragment little, fragment ions which in principle could yield structural information are often absent in the spectra. Collision-induced dissociations of polyatomic negative ions can often provide this structural information.[1,2] In addition, fundamental information concerning ion behaviour may be obtained from such studies.[1,3]

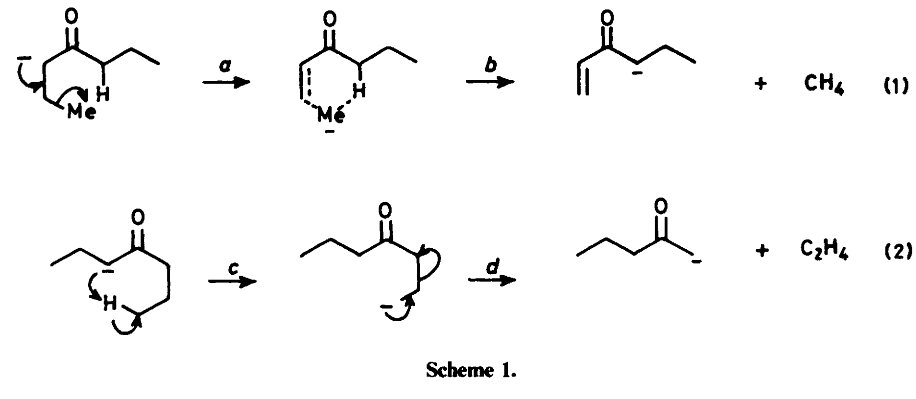
Enolate negative ions may be produced from alkyl ketones with HO^- in a chemical ionisation source.[4] Collision-induced fragmentations of such enolate ions have been explored in several laboratories.[5-10] In our last paper[10] we studied the collision-induced dissociations of the enolate ion of heptan-4-one using ^2H and ^{13}C labelling. This system was chosen for study since it can only form one carbanion (a secondary carbanion), and the symmetry of the molecule allows the measurement of intramolecular isotope effects. The losses of methane and ethene are the major decompositions channels of the heptan-4-one enolate ion and the reaction pathways are shown in sequences (1) and (2) in Scheme 1. In the stepwise process (1), steps *a* and *b* are both rate-determining, while in reaction (2), step *c* is rate-determining.

In this paper, we report the results of a study of 3-ethylpentan-2-one, a system which can form two carbanions, a primary and a tertiary. As was the case with heptan-4-one, 3-ethylpentan-2-one is symmetrical, thus allowing the determination of intramolecular isotope effects. We identify the decompositions of each carbanion, and use ^2H and ^{13}C labelling when appropriate, to determine the mechanism of each reaction.

Results and Discussion

Collisional activation (c.a.) mass spectra reported in this paper were measured with a Vacuum Generators ZAB 2HF mass spectrometer operating at 70 eV in the negative chemical ionisation mode (accelerating voltage 8 kV). Water was used to produce HO^- reactant ions,[11,12] and helium was used as collision gas. Full details are provided in the Experimental section. Compounds **(1)**—**(11)** were used; the major features of the c.a. spectra of their enolate anions are listed in Tables 1 and 2. The most visually informative spectrum is that of **(11)**: its spectrum is shown in the Figure. The data in Tables 1 and the Figure demonstrate a number of specific processes: *no carbon or hydrogen scrambling accompanies or precedes any decomposition.* The tertiary carbanion competitively eliminates H_2, CH_4, C_3H_8, whereas the primary carbanion eliminates C_2H_4 and C_4H_8 and forms C_2HO^-.

$CH_3COCH(C_2H_5)_2$	**(1)**	$CD_3COCD(C_2H_5)_2$	**(6)**
$CH_3COCH(^{13}CH_2CH_3)_2$	**(2)**	$CH_3COCH(CD_2CH_3)_2$	**(7)**
$CH_3COCH(^{13}CH_2CH_3)(C_2H_5)$	**(3)**	$CH_3COCH(CD_2CH_3)(C_2H_5)$	**(8)**
$CH_3COCH(CH_2{}^{13}CH_3)_2$	**(4)**	$CH_3COCH(CH_2CD_3)_2$	**(9)**
$CH_3COCH(CH_2{}^{13}CH_3)(C_2H_5)$	**(5)**	$CH_3COCH(CH_2CD_3)(C_2H_5)$	**(10)**
		$CH_3COCH(CD_2CD_3)(CH_2CH_3)$	**(11)**



Scheme 1.

Table 1. C.a. mass spectra of enolate anions derived from compounds (1)—(11); (I)—(XI) losses of H$^\cdot$, H_2, CH_4, and C_2H_4

	% Relative abundance													
	Loss of					Loss of					Loss of			
Compd.	H$^\cdot$	D$^\cdot$	H_2	HD	D_2	CH_4	$^{13}CH_4$	$^{13}CH_3D$	CD_3H	CH_3D	C_2H_4	$^{12}C^{13}CH_4$	$C_2H_2D_2$	C_2D_4
(1)	16		12			39					100			
(2)	15		11			37						100		
(3)	30		21			70					100	100		
(4)	16		14				38					100		
(5)	32		18			38	35				106	100		
(6)		17[a]	17[a]							22	100			
(7)	15			8		37							100	
(8)	30			10	3	71					102		100	
(9)	15			6					31				100	
(10)	22		8	3		31			24		100		58	
(11)	26		12		3	35			25		100			57

[a] Involves loss of 2 a.m.u.

Table 2. C.a. mass spectra of enolate anions derived from compounds (1)—(11); loss of C_3H_8 and formation of $C_2H_5O^-$ and C_2HO^-

	% Relative abundance												
	Loss of							Formation of				Formation of	
Compd.	C_3H_8	$^{12}C_2{}^{13}CH_8$	$^{12}C^{13}C_2H_8$	$C_3H_6D_2$	$C_3H_5D_3$	$C_3H_3D_5$	$C_3H_2D_6$	$C_2H_5O^-$	$^{12}C^{13}CH_5O^-$	$C_2H_3D_2O^-$	$C_2H_2D_3O^-$	C_2HO^-	C_2DO^-
(1)	9							3				7	
(2)		8						4				7	
(3)	4.07	3.99						4				8	
(4)			10						4			7	
(5)		10						2.05	1.92			8	
(6)										4			6
(7)	11			11				3				7	
(8)				6.7				6				10	
(9)	8.3						8				3	8	
(10)					10			2.0			1.4	10	
(11)					11	7.5		3.0			2.1	13	

(A) *Fragmentations of the Tertiary Carbanion.*—The elimination of H_2 involves hydrogen atoms at the 4- and 5-position; this process occurs also for heptan-4-one and is directly analogous to the stepwise 1,2-elimination of H_2 from alkoxides.[13,14] The latter fragmentation is thought to proceed through a solvated hydride ion intermediate. The fragmentation from 3-ethylpentan-2-one is represented in sequence (3), Scheme 2.*

The loss of C_3H_8 is a minor process, but its mechanism is interesting. The fragmentation involves loss of CH_3 and C_2H_5 from the two ethyl substituents. The mechanism must involve initial formation of an incipient anion, and we suggest reaction sequence (4) (Scheme 2). Isotope effects [measured from the spectra of (**3**), (**5**), (**8**), and (**11**)] for this process are drawn alongside formula (**12**) in Scheme 2.

The loss of CH_4 is specific and is directly analogous to the reaction described in sequence (1). The terminal methyl of the ethyl group is eliminated with H at C-1. Measured isotope effects are listed alongside formula (**13**). The isotope effect $^1H/^2H$ at position 1 was obtained in the following manner. Partial exchange of 3-ethylpentan-2-one with 0.1N-NaOD/D_2O for 10 min at 20 °C gave $D_1 = 15$, $D_2 = 46$, $D_3 = 30$, and $D_4 = 9\%$. Measurement of the appropriate losses of CH_4 and CH_3D from the enolates $CHD_2CO\bar{C}Et_2$ and $CH_2DCO\bar{C}Et_2$ gave an average value (statistically corrected) for $^1H/^2H$ of 2.5. The observed isotope effects can be interpreted in one of two ways: either the reaction is concerted, or it is stepwise with two kinetically significant steps [*cf.* sequence (1)].

In order to differentiate between these two possibilities, we need to carry out a double isotope fractionation experiment of the type proposed by Belasco, Albery, and Knowles,[15] and described in detail in our heptan-4-one paper.[10] *In this case*, the primary ^{13}C isotope effect at C-5 is 1.09 and the ^2H isotope effect at position 1 is 2.5. The $^{12}C/^{13}C$ ratios need to be compared for the appropriate losses from the enolate ions $MeCO\bar{C}(CH_2{}^{13}CH_2)(C_2H_5)$ and $CD_3CO\bar{C}(CH_2{}^{13}CH_3)(C_2H_5)$. If the reaction is stepwise, the activation energy for the second process in the latter ion will increase (*i.e.* for the removal of D^+ from the CD_3 group), and the kinetic significance of the first step will decrease, *i.e.* $^{12}C/^{13}C$ will decrease. If the reaction is concerted, the ^{13}C isotope effect will be the same in both cases. The compound $CD_3COCD(CH_2{}^{13}CH_3)(C_2H_5)$ was made by reaction of (**5**) with NaOD–D_2O, and the ratio of loss of $^{12}CH_3D$ to lots of $^{13}CH_3D$ is exactly 1:1, *i.e.* $^{12}C/^{13}C = 1.00$. *The reaction is therefore stepwise with two kinetically significant steps*; and exactly analogous to sequence (1).

(B) *Fragmentation of the Primary Carbanion.*—The formation of RC_2O^- (R = alkyl, aryl, or H) is a characteristic reaction of enolate ions;[5,6,9,10] the overall reaction in this case is shown in sequence (5). The product ion is H–C≡C–O$^-$ and not $^-$HC=-

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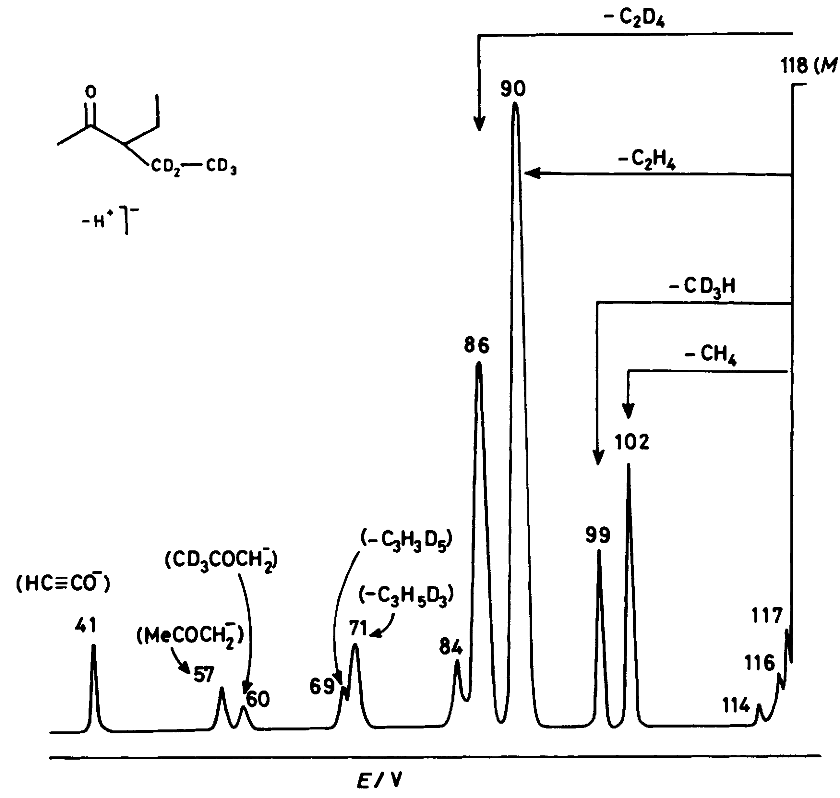
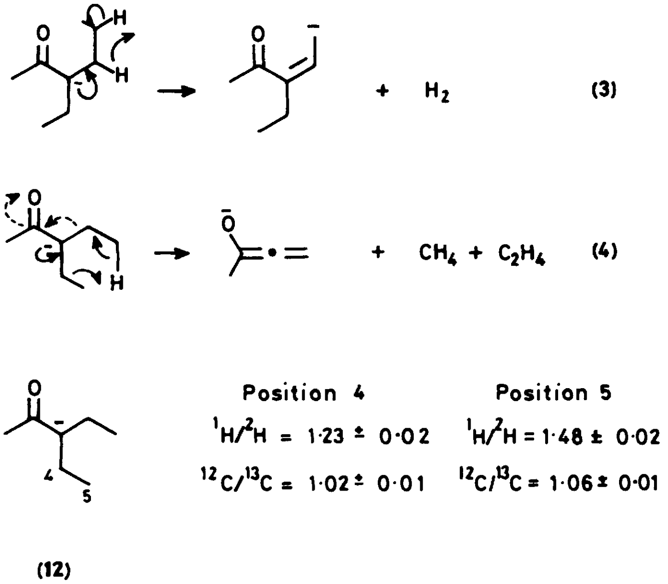
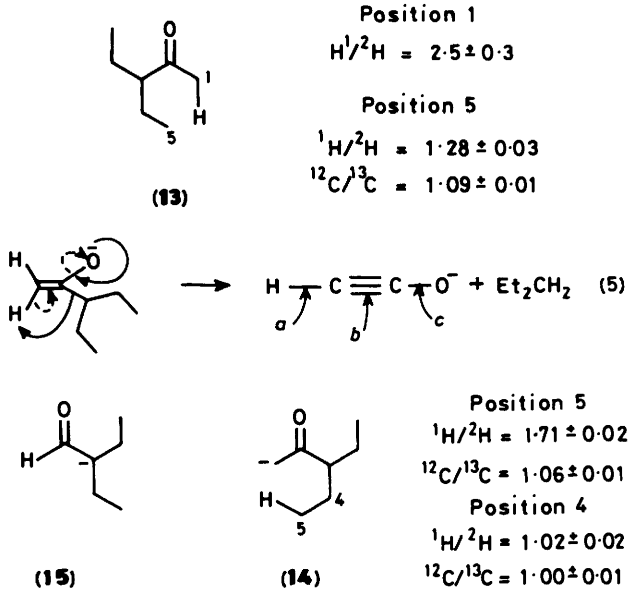
* The loss of H$^\cdot$ occurs from positions 1 and/or 3, and can therefore come from either enolate ion to form $^-CH_2CO\dot{C}(Et)_2$ or $^\cdot CH_2CO\bar{C}(Et)_2$.



C.a. mass spectrum of the enolate anion of (**11**); for conditions see Experimental section



Scheme 2.



Scheme 3.

C=O as suggested by Squires[16] in his study of ester enolate ions.*

The major fragmentation of the 3-ethylpentan-2-one enolate is loss of C_2H_4. This fragmentation is specifically that of the primary enolate (**14**), since the corresponding enolate ion (**15**) from 2-ethylbutanal does not lose C_2H_4.† The data listed in Table 2 together with isotope effects [from (**2**), (**5**), (**8**), and (**10**)] drawn alongside (**14**) (Scheme 3) demonstrate that this process is directly analogous to that shown in sequence (2), *with the first step rate-determining.*

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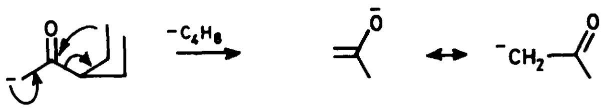
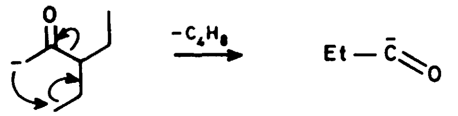
* An *ab initio* calculation[17] on the deprotonation of ketene shows the product ion to be ˙H–C≡C–O⁻, with bond lengths [see sequence (5)] *a* = 1.05, *b* = 1.22, and *c* = 1.25 Å (6-31G).

† The c.a. mass spectrum of $HC(O)\bar{C}Et_2$ shows fragments as follows: *m/z* 97 ($-H_2$, 91%), 83 ($-CH_4$, 100%), 55 ($-C_3H_8$, 14%), and 43 ($-C_4H_8$, 10%).



(6)



(7)

The final, and most unusual, fragmentation involves elmination of C_4H_8 to form an ion $C_3H_5O^-$. The ion contains CH_2 from position 1 together with CH_3 from position 5. The primary $^{12}C/^{13}C$ and secondary $^{1}H/^{2}H$ ratios for the methyl transfer are 1.07 ± 0.01 and 1.28 ± 0.02, respectively. Two mechanisms, shown in sequences (6) and (7), are possible. We have shown that enolate ions may be identified by their charge-reversal spectra.[18] For example, ions $RCOCH_2^-$ on reaction with helium yield RCO^+ plus CH_2.[10] The charge-reversal spectrum of the product ion from 3-ethylpentan-2-one shows loss of CH_2. In addition, both the charge-reversal spectrum and the c.a. mass spectrum are identical with those of the acetone enolate anion. We suggest that the rearrangement reaction proceeds as shown in sequence (6).

In conclusion, we have shown that proton abstraction from 3-ethylpentan-2-one yields two enolate ions, both of which may be identified by characteristic fragmentations.

Experimental

Collision activation and charge-reversal mass spectra were recorded with a Vacuum Generators ZAB 2HF mass spectrometer. All slits were open to obtain maximum sensitivity and to minimise energy resolution effects.[19] The chemical ionisation slit was used in the source. Ionising energy was 70 eV, trap current 100 A, ion source temperature 200 °C, and accelerating voltage 8 kV. The enolate ions of 3-ethylpentan-2-one and the labelled derivatives were generated by H abstraction with HO^- (or H^- or $O^{-\cdot}$) reactant ions, produced by the action of 70 eV electrons on H_2O.[20,21] The indicated source ion gauge pressure (of H_2O) was 5×10^{-6} Torr. The ethylpentan-2-one pressure was typically 2×10^{-6} Torr. The estimated total pressure within the source is 2×10^{-2} Torr. The pressure of helium in the second collision 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 effect values quoted in the discussion are averages of six individual scans.

3-Ethylpentan-2-one.—Hydrolysis of ethyl α,α-diethylacetoacetate with aqueous potassium hydroxide gave 3-ethylpentan-2-one as a colourless liquid in 36% yield.[22,23]

Labelled Compounds: General.—All labelled 3-ethylpentan-2-ones were formed from the appropriate alkyl iodide and ethyl acetoacetate. Alkyl iodides used were commercial products, *viz.* $CH_3{}^{13}CH_2I$ (^{13}C 91%), $^{13}CH_3CH_2I$ (^{13}C 91%), CH_3CD_2I ($^{2}H_2$ 99%), CD_3CH_2I ($^{2}H_3$ 99%), and CD_3CD_2I ($^{2}H_5$ 99%). The labelled products were first distilled at 70—75 °C and 10 mmHg using a small glass T-tube, then separated by g.l.c. on 20% SE 30 on Chromosorb AW (60—80 mesh) (6 mm × 3 m glass column; N_2 flow 40 ml min^{-1} at 170 °C; retention time 5.0 min under these conditions). The purity of products was checked by ^{1}H or ^{13}C n.m.r. (as appropriate), and the percentage incorporation of label was determined by positive-ion mass spectrometry. The overall yields from ethyl acetoacetate were typically 30—35% after purification.

The following synthesis is typical.

3-([1-^{13}C$_1$]*Ethyl*)[4-^{13}C$_1$]*pentan-2-one* (**2**).—(a) *Ethyl* α-([1-^{13}C$_1$]*ethyl*)*acetoacetate.* Potassium (59 mg) was added to anhydrous t-butyl alcohol (4 cm^3) at 20 °C and under nitrogen, and the mixture was stirred for 20 min. Ethyl acetoacetate (195 mg) was then added, the mixture was stirred at 20 °C for 15 min, and then [1-^{13}C$_1$]ethyl iodide (135 μl) was added. The mixture was heated under reflux for 5 h, then the t-butyl alcohol was removed *in vacuo*. The residue was poured onto water (10 cm^3) and extracted with diethyl ether (3 × 5 cm^3). The organic extract was washed with aqueous sodium hydrogen sulphite (saturated; 10 cm^3), water (10 cm^3), and aqueous sodium chloride (saturated; 10 cm^3), and dried ($MgSO_4$). Removal of the solvent followed by distillation in a small T-tube (75 °C and 10 mmHg) gave ethyl α-([1-^{13}C$_1$]ethyl)acetoacetate as a colourless oil (232 mg, 97%; ^{13}C 91%).

(b) *Ethyl* α,α-*di*([1-^{13}C$_1$]*ethyl*)*acetoacetate.* This compound was produced as described in (a), but from ethyl α-([1-^{13}C$_1$]ethyl)acetoacetate (232 mg) and [1-^{13}C$_1$]ethyl iodide (135 μl); yield 258.5 mg (94%).

(c) 3-([1-^{13}C$_1$]*Ethyl*)[4-^{13}C$_1$]*pentan-2-one* (**2**). A mixture of ethyl α-([1-^{13}C$_1$]ethyl)acetoacetate (258.5 mg), methanol (2 cm^3), water (0.35 cm^3), and potassium hydroxide (133 mg) was heated under reflux for 4 h. More potassium hydroxide (141.5 mg) and water (0.2 cm^3) were added and the mixture was stirred at reflux for a further 8 h. It was then poured into water (10 cm^3) and extracted with diethyl ether (3 × 5 cm^3). The organic extract was washed with water (2 × 10 cm^3) and aqueous sodium chloride (saturated; 15 cm^3), and dried ($MgSO_4$), and the solvent was removed by fractionation. Purification (as before) gave 3-([1-^{13}C$_1$]ethyl)[4-^{13}C$_1$]pentan-2-one as a colourless liquid (49.5 mg, 31%; $^{13}C_2$ 82%).

Compounds (**3**)—(**5**) and (**7**)—(**11**) were made similarly. In the case of those compounds which contain only one labelled alkyl group [(**3**), (**5**), (**8**), (**10**), and (**11**)], the labelled alkyl iodide was added in step (c), and ethyl iodide was added in step (a).

3-Ethyl[1,1,1,3-^{2}H$_4$]*pentan-2-one* (**6**).—This compound was prepared in quantitative yield by stirring a mixture of 3-ethylpentan-2-one (1 g) and sodium deuterioxide (1N in D_2O; 10 cm^3) at 20 °C for 2 h ($^{2}H_4$ 99%).

Acknowledgements

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