Do carbanions undergo 1,2 hydrogen transfers in the gas phase?

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Certain anions X–$^-$CH–CH$_2$–Y and X–CH$_2$–$^-$CH–Y interconvert under collisional activation conditions in the gas phase. Experiments designed to probe the mechanism(s) of particular interconversions suggest (i) that the ions MeO–CH$_2$–$^-$CH–CN and MeO–$^-$CH–CH$_2$–CN interconvert *via* 1,2 H transfer processes, and (ii) when X = Ph and Y = CO$_2$Me or CN, deuterium labelling and fragmentation data indicate that equilibration of Ph–$^-$CHCH$_2$Y and PhCH$_2$–$^-$CHY occurs, at least in part, by proton transfer to and from the phenyl ring.

Introduction

The basic fragmentations of (M − H)$^-$ ions derived from organic molecules are often simple, and have been reviewed.[1] In certain cases fragmentation through the initially formed anion is energetically unfavourable. In such a situation, the first formed anion may either (i) undergo proton transfer to form another anion which may fragment simply, or (ii) undergo skeletal rearrangement prior to or during fragmentation (for a review of rearrangement processes see ref. 2). Alternatively, a charge remote process (*i.e.* a reaction which proceeds remote from and uninfluenced by the negatively charged centre) may occur.[3,4]

We have recently been investigating rearrangements of (M − H)$^-$ ions from organic systems.[2] A number of these reactions are formally classified as 1,2-rearrangements, *i.e.* a rearrangement where an incipient anion migrates to a directly adjacent position. In some cases the 1,2 rearrangement reaction is stepwise, proceeding through an intermediate anion–neutral (or radical–radical anion) complex; for example, the Wittig rearrangement[5] and the negative ion Beckmann rearrangement.[6] In other cases (although we favour stepwise processes) the possibility of concerted mechanisms cannot be discounted on available evidence; for example the negative ion pinacol rearrangement,[7] and the acyloin,[8] Stephens,[9] Lossen[10] and Wolff rearrangements.[11]

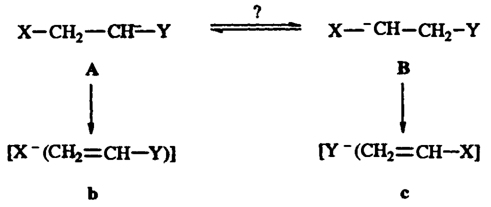
What is the situation with respect to the analogous 1,2 hydrogen (H) shift in carbanion systems? Concerted 1,2 H transfer in carbanions is considered to be forbidden because of orbital symmetry constraints: there are no recorded examples in the condensed phase of 1,2 H migration along a carbon chain in carbanions.[12] In the prototypical case of the ethyl anion, the concerted and degenerate 1,2 H shift is calculated to have a barrier of 202 kJ mol^{-1};[13] however this cannot be checked experimentally since the ethyl radical is calculated to have an electron affinity of −83 kJ mol^{-1} [14] and the ethyl anion is thus unstable with respect to its radical. Whether this reaction should be formally classified to involve hydride or proton movement is unclear. We will call such a reaction a concerted 1,2 H shift.

We have already studied a number of specific systems in this context. For example, (i) the acetyl anion, on collision activation, converts to the acetaldehyde enolate ion, but the process is stepwise, proceeding through an intermediate ion complex **a** as shown in reaction sequence (1),[15] (ii) theoretical calculations show that the anion HO–$^-$C=O may, in principle, transform in concerted fashion to the formate anion HCO$_2$$^-$ (barrier 122 kJ mol^{-1}): experimentally this process is not observed because HO–$^-$C=O has a more facile decomposition channel to HO$^-$ and CO[16] and (iii) the homoenolate to enolate rearrangement shown in reaction sequence (2) occurs by a stepwise procedure involving the two proton transfers shown.[17]

$$\text{Me–}^-\text{C=O} \longrightarrow \underset{\textbf{a}}{[(\text{CH}_2\text{=C=O})\text{H}^-]} \longrightarrow \text{CH}_2\text{=CH–O}^- \quad (1)$$

$$\text{Ph–CO–CH}_2\text{–CH}_2{}^- \longrightarrow (\text{C}_6\text{H}_4)^-\text{–CO–CH}_2\text{–CH}_3 \longrightarrow \text{Ph–CO–}^-\text{CH–CH}_3 \quad (2)$$

In summary, (i) theoretical evidence indicates that concerted 1,2 H transfers through three-membered transition states should be high energy processes,[13] and (ii) there is no experimental evidence (to date) to indicate the operation of concerted 1,2 H transfers, although the operation of a stepwise 1,2 hydride process has been confirmed [*cf.* reaction (1)].



Scheme 1

This paper describes attempts to (i) determine whether collisional activated systems X–$^-$CH–CH$_2$–Y and X–CH$_2$–$^-$CH–Y are interconvertible in the gas phase and (ii) if they are, to ascertain the mechanism(s) of the interconversion(s). Using Scheme 1 as an illustration, the procedure to be adopted is as follows. The individual ions **A** and **B**, upon collisional activation, should undergo characteristic fragmentation through ion complexes **b** and **c** respectively. Any competing conversion of **A** to **B** will be detected by the identification of fragmentations of **B** in the mass spectrum of **A**.

Results and discussion

It is necessary to choose systems which can be probed by the application of characteristic fragmentations of the two possible ion complexes **b** and **c** (Scheme 1). If a system cannot fragment through **b** and **c**, or undergoes a fragmentation which could occur from either **b** or **c**, then it is not appropriate for our purposes. An example of such a scenario is when either X or Y is Cl, Br or I: in such cases α-cleavage to the anion centre could occur to form the halide anion simply because of the ease of dissociation of the C$^-$–halogen bond and of the high electron affinity of the halide radical, *i.e.* X–CH$_2$–$^-$CH–Y could form Y$^-$ and XCH$_2$CH:, as well as the expected products X$^-$ and CH$_2$=CHY. We considered it likely that carbanions derived from (i) MeOCH$_2$CH$_2$OCD$_3$, (ii) MeOCH$_2$CH$_2$CN and (iii) some phenyl derivatives (*e.g.* $PhCH_2CH_2CO_2Me$, $PhCH_2CH_2CN$ and $PhCH_2CH_2OMe$) would be suitable candidates for study provided that α cleavage to a carbanion site does not compete with those processes (outlined in Scheme 1) that we intend to use as probes to test for interconversion of the two possible carbanions.

We have used GAUSSIAN 92[18] *ab initio* calculations at the RMP3/6-311++G(D,P)//RHF/6-311++G(D,P) level to explore the ease of formation of MeO^- and CN^- by elimination (*cf.* Scheme 1) and α-cleavage processes from the model systems $^-CH_2CH_2R$ and $CH_3{}^-CHR$ (R = OMe or CN). Methoxide formation is depicted in Fig. 1; all energies (in kJ mol^{-1}) are indicated relative to $^-CH_2CH_2OMe$ (considered as 0 kJ mol^{-1}). The precursor $^-CH_2CH_2OMe$ undergoes facile elimination to C_2H_4 and MeO^- in an exothermic reaction (−10.2 kJ mol^{-1}) over a modest barrier (13.0 kJ mol^{-1}). In contrast, the α-cleavage of the isomer $CH_3{}^-CHOMe$ to yield MeO^- and CH_3CH is endothermic by 280 kJ mol^{-1}. The nitrile system is similar overall. The elimination reaction $^-CH_2CH_2CN \longrightarrow C_2H_4 + CN^-$ has a barrier of 35 kJ mol^{-1} but is exothermic by 78 kJ mol^{-1}. The competing α-cleavage reaction ($CH_3{}^-CHCN \longrightarrow CN^- + CH_3CH$) is endothermic by 327 kJ mol^{-1}. [The following relative energies were obtained for the nitrile systems (kJ mol^{-1}): (i) α-cleavage; $CH_3{}^-CHCN$ (0), (CN^- + CH_3CH) (+327), (ii) elimination; $^-CH_2CH_2CN$ (+89.4), saddle point ($CH_2{=}CH_2\cdots{}^-CN$) (+124)† and (CN^- + CH_2CH_2) (+10.2).] These calculations indicate that the elimination process will occur in both cases to the exclusion of the α-cleavage, and thus support the strategy proposed above (see also Scheme 1).

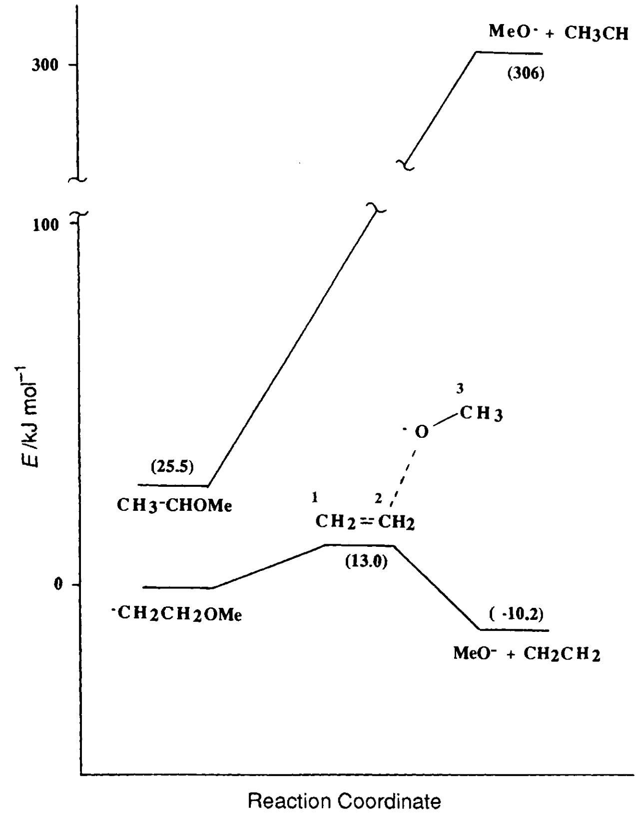
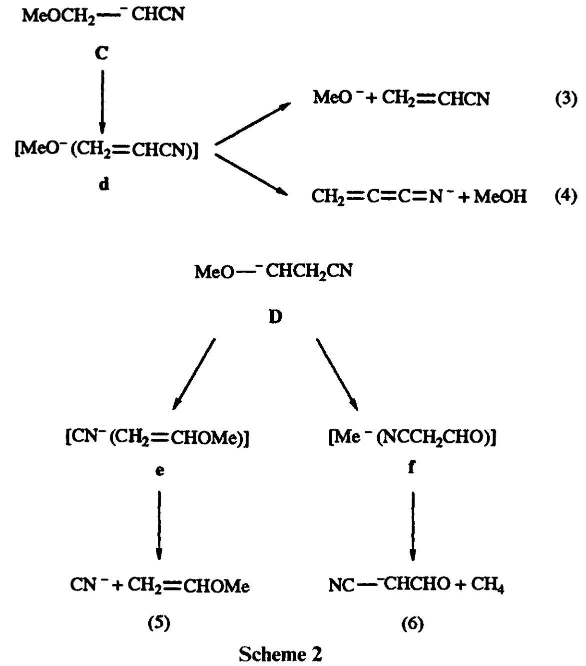


Fig. 1 *Ab initio* calculations for the formation of MeO^- from both $^-CH_2CH_2OMe$ and $CH_3{}^-CHOMe$. Energies in kJ mol^{-1} using $^-CH_2CH_2OMe$ as reference at 0 kJ mol^{-1}. The optimisation used the Berny procedure at RHF-311++G (D,P), GAUSSIAN 92.[18] The correctness of geometries was confirmed by the lack of negative analytical computed harmonic vibration frequencies. The post Hartree–Fock energies were calculated at RMP3/6-311++G (D,P)//RHF/6-311++G (D,P) level of theory. Geometry of transition state: bond lengths, C_1–C_2 = 1.393, C_2–O = 1.789, O–C_3 = 1.354 Å. Angles, C_1C_2O = 117.5 and C_2OC_3 = 111.8°.

Attempted formation of $MeO{-}CH_2{-}{}^-CH{-}OCD_3$

The prototypical system to study is $MeO{-}CH_2{-}{}^-CH{-}OCD_3$. This ion is the E_{1cb} intermediate in the elimination reaction which should yield MeO^- and $CD_3OCH{=}CH_2$.[19] Any formation of CD_3O^- from this anion would indicate a 1,2 H rearrangement. We were not able to detect an $(M - H)^-$ ion when 1,2-dimethoxyethane was allowed to react with either HO^- or $NH_2{}^-$ in the ion source of our VG ZAB 2HF mass spectrometer: the only ionic product was MeO^-. Thus we attempted to form the anion using an indirect approach. There are three established procedures that have been used for the formation of elusive anions, *viz.* loss of CO_2 from $RCO_2{}^-$, loss of CH_2O from RCH_2O^-, and S_N2(Si) nucleophilic displacement on Me_3SiR.[20] The last of these procedures is often the method of choice, thus we prepared $MeO{-}CH_2{-}CH(SiMe_3){-}OCD_3$. The reaction of this derivative with either HO^- or $NH_2{}^-$ forms a deprotonated species, but the S_N2(Si) product $MeO{-}CH_2{-}{}^-CH{-}OCD_3$ was not detected. However, the presence of a major peak corresponding to MeO^- in the mass spectrum suggests that the reaction does occur, but that the intermediate is not stable.

Interconversion of $MeO{-}{}^-CH{-}CH_2{-}CN$ and $MeO{-}CH_2{-}{}^-CH{-}CN$



Scheme 2

Deprotonation of $MeOCH_2CH_2CN$ with HO^- should exclusively form the enolate ion **C** [rather than **D** (Scheme 2)] because of the considerable difference in acidity of the hydrogens of the two CH_2 groups (the ΔG°_{acid} values of the model compounds MeCN and MeOMe are 1530[21] and 1666 kJ mol^{-1} [22] respectively). However the spectrum (Fig. 2) of the $(M - H)^-$ ion shows fragmentations of both **C** and **D**, indicating the possibility of partial conversion of **C** to **D** during collisional activation. The fragmentations of these ions are simple and are summarised in Scheme 2. Ion **C** fragments through **d** as shown in reactions (3) and (4). In contrast, **D** may form two ion complexes, *viz.* (i) **e**, which simply falls apart to give CN^- [reaction (5)] and (ii) **f**, in which the bound and transient methyl anion readily deprotonates the neutral to form the enolate ion [reaction (6)].

In order to confirm the interconversion of the two isomeric

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† Geometry of transition state $^1CH_2{=}^2CH_2\cdots{}^3CN^-$. Bond lengths, C_1–C_2 = 1.425, C_2–C_3 = 1.860 and C_3–N = 1.145 Å. Angles, C_1–C_2–C_3 = 119.2, C_2–C_3–N = 174.9°.

Table 1 Mass spectrum of the $(M - D)^-$ ion from $MeOCH_2CD_2CN$

Precursor ion (*m*/*z*)	Spectrum [*m*/*z* (loss or formation) relative abundance]
$[MeOCH_2-^-CDCN]$ (85)	84 ($H^\cdot$) 8, 83 ($D^\cdot$) 3, 69 (CH_4) 1.0, 68 (CH_3D) 0.7, 53 (MeOH) 5, 52 (MeOD) 100, 31 (MeO^-) 3, 26 (CN^-) 6

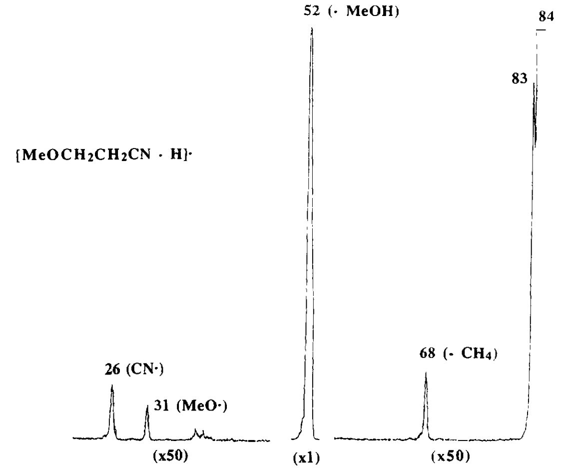


Fig. 2 MS–MS data for $(MeOCH_2CH_2CN - H)^-$. For experimental conditions see Experimental section.

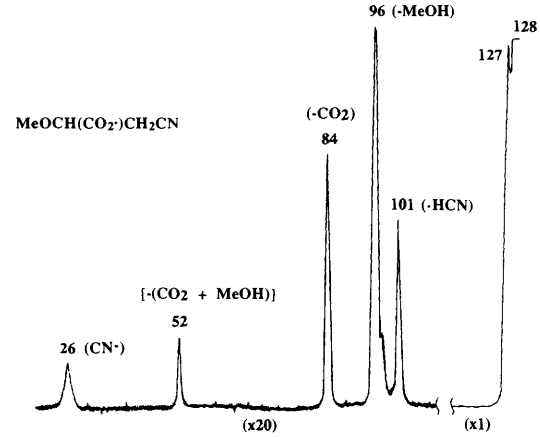


Fig. 3 MS–MS data for $MeOCH(CO_2^-)CH_2CN$

anions we need to independently synthesise **C** and **D** or deuteriated derivatives of these ions. The first of these tasks is straightforward, since the labelled derivative $MeOCH_2CD_2CN$ exclusively forms an $(M - D)^-$ ion when allowed to react with DO^-. The mass spectrum of the $(M - D)^-$ ion (Table 1) shows major fragmentation in accord with the pathways shown in reactions (3) and (4). However, it also shows the formation of CN^- [*cf.* reaction (5)] and this, together with the losses of CH_4 and CH_3D [*cf.* reaction (6)], is consistent with fragmentation of the rearranged species $MeO-^-CHCHDCN$.

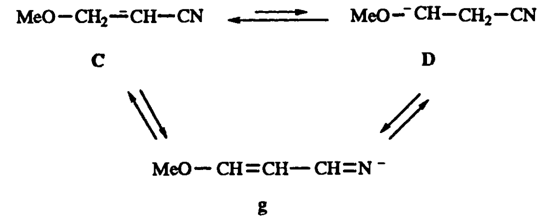
$$MeO\text{-}CH(CO_2^-)\text{-}CH_2\text{-}CN \longrightarrow MeO\text{-}^-CH\text{-}CH_2\text{-}CN + CO_2 \quad (7)$$

The synthesis of **D** is a more complex problem, since it cannot be formed by direct deprotonation. It was prepared by decarboxylation of the carboxylate ion as shown in reaction (7). The tandem (MS–MS) spectrum of the carboxylate species is shown in Fig. 3. The target ion *m*/*z* 84 ('**D**') is present in this spectrum. If some **D** ions interconvert to **C** during collisional activation, then *m*/*z* 84 must fragment by loss of methanol [reaction (4), Scheme 2]. Unfortunately, *m*/*z* 84 is not detected in the ion source which means we cannot obtain its tandem MS–MS data. Thus we were limited to the MS–MS–MS procedure (see Experimental section). An MS–MS–MS experiment using collision gas in both collision cells of the VG ZAB instrument identifies the operation of fragmentation sequence $MeO\text{-}CH(CO_2^-)\text{-}CH_2\text{-}CN$ (*m*/*z* 128) to *m*/*z* 84 ($128 - CO_2$) to *m*/*z* 52 [84 − MeOH], thus confirming the conversion of some **D** ions to **C** ions.

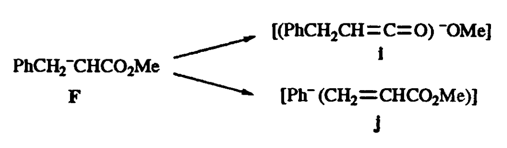
The experiments described above show that **C** and **D** do interconvert on collisional activation. This is an interesting result, particularly the conversion of the more stable **C** to **D** (*cf.* ΔG°_{acid} values listed above), which would be expected to be energetically unfavourable with respect to the simple fragmentations of **C** and **D** (see Scheme 2). We believe this interconversion involves a 1,2 H transfer (Scheme 3). The alternative possibility of a two H transfer process (**C** to **g** to **D**) is energetically unfavourable in comparison (the process involves a 1,3 as well as a 1,2 H transfer).

Fragmentations of $(PhCH_2CH_2Y - H)^-$ ions

Methyl 3-phenylpropionate can be deprotonated at either the benzylic or enolate positions by HO^- to form both **E** and **F** (Scheme 4). The spectrum shown in Fig. 4 shows fragmentations of both **E** and **F**. The benzyl anion **E** cleaves to form ion complex **h**, which fragments characteristically to form competitively $^-CO_2Me$ and eliminate both CO and HCO_2Me.[23,24] The enolate anion **F** may fragment through (i) **i** to form MeO^- and eliminate MeOH,‡,[23] or (ii) **j** to form Ph^- (*cf.* ref. 23). The question is whether **E** and **F** interconvert on collisional activation, and if so by what mechanism.



Scheme 3



Scheme 4

The various spectra of four deuteriated derivatives of methyl 3-phenylpropionate are recorded in Table 2. These spectra clearly show that (i) deprotonation occurs at both CH_2 positions, but not on the phenyl ring, (ii) **E** fragments preferentially through **h** and **F** fragments preferentially through **i** and **j** and (iii) there is significant interconversion of **E** and **F** on collisional activation. As an illustration of the latter scenario, the spectrum of the isomer $PhCH_2{}^-CDCO_2Me$ shows a number of fragmentations which can only originate from a

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‡ It is possible that the formation of MeO^- (and the loss of MeOH) could arise from **E** by a cyclisation process to form ion complex $[(Ph\text{-}cyclo\text{-}C_3H_3O)\text{-}^-OMe]$. We cannot completely exclude this possibility, but regard it as less likely than that proceeding from **F** through **i**.

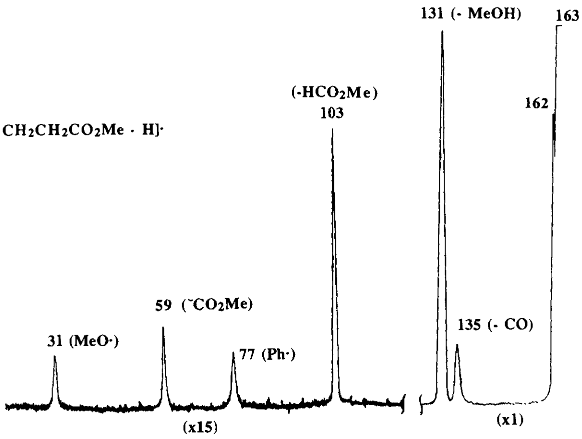


Fig. 4 MS–MS data for the $(M - H)^-$ ion(s) of methyl 3-phenylpropanoate

benzylic anion, *i.e.* the formation of $^-CO_2Me$ and the accompanying elimination of CO, HCO_2Me and DCO_2Me (*cf.* **E** to **h**, Scheme 4). The two most likely equilibration mechanisms involve either 1,2 H shifts, or proton transfers as shown in reaction sequence (8). The labelling data do not provide information which either substantiate or eliminate the possibility of the operation of a 1,2 H transfer process preceding major fragmentation. However, there is a minor process for which the labelling data do provide a definitive answer. Specifically, the $(M - D)^-$ ion of $PhCH_2CD_2CO_2Me$ (*i.e.* $PhCH_2{}^-CDCO_2Me$) forms mainly $C_6H_5{}^-$, whereas the corresponding $(M - H)^-$ ion ($Ph\text{–}{}^-CHCD_2CO_2Me$) yields mainly $C_6H_4D^-$. The formation of Ph^- is a reaction of the enolate ion, and in the latter instance, production of this ion from the initial benzyl anion involves deuterium transfer into the phenyl ring. This is in accord with the proton transfer mechanism shown in reaction sequence (8).

$$Ph - {}^-CHCH_2CO_2Me \longrightarrow (C_6H_4)^-\text{–}CH_2CH_2CO_2Me \longrightarrow PhCH_2\text{–}{}^-CHCO_2Me \quad (8)$$

Deprotonation of $PhCH_2CH_2CN$ with HO^- forms both **G** and **H** (Scheme 5), and the resulting collision induced spectrum (Fig. 5) shows fragmentation of both ions. The benzylic anion **G** fragments through **k** [reactions (9) and (10)], while **H** fragments through **l** reactions (11) and (12)]. The spectra of a labelled derivative are recorded in Table 2, and suggest that **G** and **H** interconvert upon collisional activation and that the interconversion involves proton transfer to the benzene ring by a mechanism analogous to that shown in reaction (8). As an illustration, the data in Table 2 show that the initially formed ion $Ph\text{–}{}^-CHCD_2CN$ (i) fragments to give both $C_6H_4D^-$ and $C_6H_3D_2{}^-$ [*cf.* reaction (11)] and (ii) eliminates both C_6H_5D and $C_6H_4D_2$ [*cf.* reaction (12)].

$$PhCD_2\text{–}{}^-CHOMe \longrightarrow Ph\text{–}{}^-CDCH_2OCH_2D \longrightarrow CH_2DO^- + PhCD{=}CH_2 \quad (13)$$

The spectra of deprotonated $PhCH_2CH_2OMe$ and of several deuteriated derivatives are listed in Table 2. Deprotonation occurs only at CH_2 positions: no deprotonation of the phenyl ring is observed. The major fragmentation process involves formation of MeO^-: presumably a simple elimination reaction of the benzylic anion $Ph\text{–}{}^-CHCH_2OMe$. The spectrum of the ion $PhCH_2\text{–}{}^-CDOMe$ also shows MeO^- as the base peak, thus indicating isomerisation to $Ph^-CHCHDOMe$. Due to the nature of the process, it is not possible to determine whether the equilibration involves 1,2 H or sequential proton transfer [*cf.* reaction sequence (8)]. However, this equilibration competes with, or involves, a most unusual proton transfer between the benzylic and methyl positions. This can be seen in the spectrum of $PhCD_2\text{–}{}^-CHOMe$, which shows CH_2DO^- [see reaction (13)] as a major ion. The sequence of this H/D transfer is not known, but it is an energetically unfavourable process since the difference in $\Delta G°_{acid}$ values for $PhCH_2R$ and $ROCH_3$ is 113 kJ mol^{-1}.[21,22] We are aware of only one other reported transfer of a proton from a methoxy group and that is for deprotonated anisole, in which *ortho* and methyl hydrogens partially equilibrate upon collisional activation of the parent anion.[24]

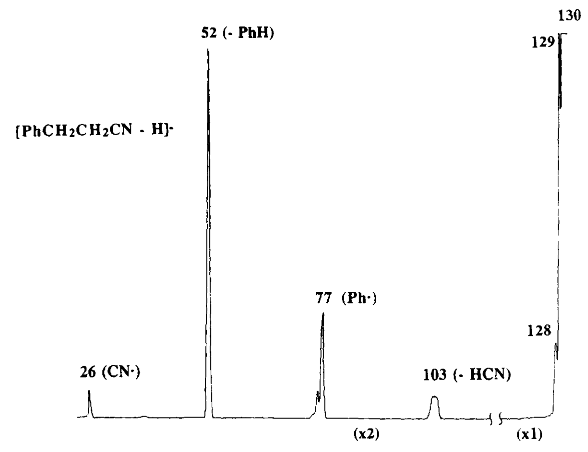
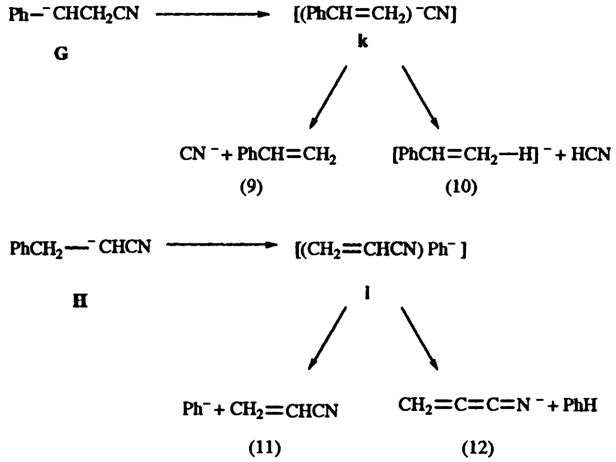


Fig. 5 MS–MS data for the $(M - H)^-$ ions from $PhCH_2CH_2CN$



Scheme 5

In conclusion, the two possible carbanions derived formally by deprotonation of suitable unsymmetrically disubstituted ethanes can interconvert under conditions of collisional activation in the gas phase. We have evidence of 1,2 H transfer in only one interconverting system. In general, it appears that 1,2 H rearrangement is energetically unfavourable in comparison to other (fragmentation) processes. In particular, (i) the simplest system $MeO\text{–}CH_2\text{–}{}^-CH\text{–}OCD_3$ is unstable with respect to elimination (to form MeO^-) under the reaction conditions. However, given the instability of the precursor anion, it seems unlikely that 1,2 H transfer could compete with elimination in this case. (ii) Interconversion of ions $MeO\text{–}{}^-CHCH_2CN$ and $MeOCH_2\text{–}{}^-CHCN$ does occur, but this interconversion, which we believe to involve 1,2 H transfer, competes unfavourably with simple cleavage of the individual carbanions. (iii) Energised $Ph\text{–}{}^-CHCH_2Y$ and $PhCH_2\text{–}{}^-CHY$ also interconvert, but the occurrence of sequential proton transfer reactions suggest that 1,2 H transfers are not energetically favourable in such systems. For example, interconversion of the two anions Ph^-CHCH_2Y and $PhCH_2\text{-}{}^-CHY$ (Y = CO_2Me or CN) proceeds, at least in part, by stepwise processes in which the first step involves transfer of a phenyl proton to the initial deprotonation site.

Table 2 Mass spectra (CID MS–MS) of $(M - H)^-$ [and $(M - D)^-$ as appropriate] ions from $PhCH_2CH_2Y$ and deuterium labelled derivatives

Precursor ion (*m*/*z*)	Spectrum [*m*/*z* (loss or formation) relative abundance]
$[PhCH_2CH_2CO_2Me - H]^-$ (163)	See Fig. 4
$[PhCH_2CH_2CO_2CD_3 - H]^-$ (166)	165 ($H^{\bullet}$) 98, 138 (CO) 10, 131 (CD_3OH) 100, 103 (HCO_2CD_3) 8, 62 ($CD_3O{-}^{-}C{=}O$) 3, 77 (Ph^-) 3, 34 (CD_3O^-) 2
$[PhCH_2CD_2CO_2Me - H]^-$ (165)	164, 163[a] ($H^{\bullet}$, $D^{\bullet}$) 65, 137 (CO) 14, 133 (MeOH) 31, 132 (MeOD) 100, 105 (HCO_2Me) 13, 104 (DCO_2Me) 15, 78 ($C_6H_4D^-$) 1, 77 ($C_6H_5^-$) 2, 59 ($MeO{-}^{-}C{=}O$) 6, 31 (MeO^-) 2
$[PhCH_2{-}^{-}CDCO_2Me]$ (164)	163 ($H^{\bullet}$) 90, 162 ($D^{\bullet}$) < 15[a], 136 (CO) 1, 132 (MeOH) 45, 131 (MeOD) 100, 104 (HCO_2Me) 2, 103 (DCO_2Me) 1, 77 (Ph^-) 7, 59 ($MeO{-}^{-}C{=}O$) 0.5, 31 (MeO^-) 7
$[C_6D_5CH_2CH_2CO_2Me - H]^-$ (168)[b]	167, 166[a] ($H^{\bullet}$, $D^{\bullet}$) 70, 140 (CO) 8, 136 (MeOH) 100, 108 (HCO_2Me) 13, 82 ($C_6D_5^-$) 2, 59 ($MeO{-}^{-}C{=}O$) 5, 31 (MeO^-) 4
$[C_6D_5{-}^{-}CHCD_2CO_2Me]$ (170)	169, 168[a] ($H^{\bullet}$, $D^{\bullet}$) 65, 142 (CO) 7, 138 (MeOH) 49, 137 (MeOD) 100, 110 (HCO_2Me) 12, 109 (DCO_2Me) 8, 82 ($C_6D_5^-$) 1, 81 ($C_6D_4H^-$) 0.5, 59 ($MeO{-}^{-}C{=}O$) 2, 31 (MeO^-) 6
$[C_6D_5CH_2CD_2CO_2Me - D]^-$ (169)	168, 167[a] ($H^{\bullet}$, $D^{\bullet}$) 58, 137 (MeOH) 100, 136 (MeOD) 65, 109 (HCO_2Me) 2, 108 (DCO_2Me) 4, 82 ($C_6D_5^-$) 2, 59 ($MeO{-}^{-}C{=}O$) 0.3, 31 (MeO^-) 2
$[PhCH_2CH_2CN - H]^-$ (130)	See Fig. 5
$[PhCH_2CD_2CN - H]^-$ (132)	131 ($H^{\bullet}$) 89, 130 (H_2,$D^{\bullet}$) 28, 105 (HCN) 8, 104 (DCN) 6, 53 (C_6H_5D) 55, 52 ($C_6H_4D_2$) 100, 26 (CN^-) 32
$[PhCH_2{-}^{-}CDCN]$ (131)	130 ($H^{\bullet}$) 95, 129 (H_2,$D^{\bullet}$) 45, 104 (HCN) 10, 103 (DCN) 3, 78 ($C_6H_4D^-$) 32, 77 (Ph^-) 34, 53 (PhH) 21, 52 (PhD) 100, 26 (CN^-) 8
$[PhCH_2CH_2OMe - H]^-$ (135)	134 ($H^{\bullet}$) 35, 31 (MeO^-) 100
$[C_6D_5CH_2CH_2OMe - H]^-$ (140)[b]	139 ($H^{\bullet}$) 22, 138 ($D^{\bullet}$) < 10[a], 31 (MeO^-) 100
$[PhCH_2CD_2OMe - H]^-$ (137)	136 ($H^{\bullet}$) 30, 135 ($D^{\bullet}$) < 10[a], 31 (MeO^-) 100
$[PhCH_2{-}^{-}CDOMe]$ (136)	135 ($H^{\bullet}$) 25, 134 ($D^{\bullet}$) < 5[a], 31 (MeO^-) 100
$[PhCD_2CH_2OMe - H]^-$ (137)	136, 135 ($H^{\bullet}$, $D^{\bullet}$) 40[a], 32 (CH_2DO^-) 100, 31 (MeO^-) 11
$[Ph{-}^{-}CDCH_2OMe]$ (136)	135 ($H^{\bullet}$) 30, 134 ($D^{\bullet}$) < 10[a], 32 (CH_2DO^-) 22, 31 (MeO^-) 100

[a] Peaks are not fully resolved. [b] Exclusive loss of H^+—no $(M - D)^-$ ion is detected.

Experimental

Collisional activation mass spectra (MS–MS) were determined with a VG ZAB 2HF[25] instrument. Full experimental details have been reported previously.[26] Specific details were as follows: a chemical ionisation slit was used in the ion source, the ionising energy was 70 eV, the ion source temperature was 150 °C (unless indicated to the contrary), and the accelerating voltage was 7 kV. Liquids were introduced through the septum inlet at 100 °C; solids *via* the direct probe using no heating [source pressure of sample 5×10^{-7} Torr (1 Torr is *ca.* 133.2 Pa)]. Deprotonation was effected using HO^- (from H_2O, measured source pressure of $H_2O = 1 \times 10^{-5}$ Torr) or DO^- as appropriate for labelled compounds, unless indicated to the contrary in the text. The estimated total 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.

The MS3 (MS–MS–MS) experiment, m_1^- to m_2^- to m_3^-, was carried out as follows. Both collision cells contained argon (measured pressure 1×10^{-6} Torr). The magnet was set at allow transmission of m_2^- [m_2^2/m_1], and the electric sector then used to detect the product ion of the decomposition m_2^- to m_3^-.

1,2-Dimethoxyethane and 1,2-dimethylaminoethane were commercial products. The following unlabelled compounds were prepared by reported procedures: methyl 3-phenylpropanoate,[27] 3-phenylpropanenitrile,[28] methyl 2-phenylethyl ether,[29] 3-methoxypropanenitrile.[30]

3-Cyano-2-methoxypropionic acid

Methyl 3-cyano-2-hydroxypropanoate[31] was methylated (sodium hydride–methyl iodide in tetrahydrofuran)[29] to yield methyl 3-cyano-2-methoxypropanoate (62% yield), which was hydrolysed [refluxing in methanol containing sodium methoxide (5%) for 12 h] to yield 3-cyano-2-methoxypropionic acid as an oil (yield 41%) (Found M^+, 129.0425. $C_5H_7NO_3$ requires *M*, 129.0426); $\delta_H(CDCl_3$; 200 MHz) 2.8 (2 H, dd), 3.5 (3 H, s) and 4.0 (1 H, m).

Preparation of labelled compounds

The following labelled compounds were prepared as follows.

1-Methoxy-2-([$^2H_3$]methoxy)-2-trimethylsilylethane. This compound was prepared from {([$^2H_3$]methoxy)methyl}trimethylsilane[32] by lithiation followed by alkylation with chloromethyl ether (at −78 °C)[33] (55% yield, $^2H_3 = 99\%$).

[$^2H_3$]Methyl 3-phenylpropanoate. This compound was made by the treatment of 3-phenylpropionyl chloride with [$^2H_4$]methanol (87% yield, $^2H_3 > 99\%$).

Methyl 3-phenyl[2,2-$^2H_2$]propanoate. This compound was prepared by three exchanges of the (initially) unlabelled material with NaOMe–MeOD (*cf.* ref. 34) ($^2H_2 = 98\%$).

Methyl 3-([$^2H_5$]phenyl)propanoate. Reaction between [$^2H_5$]phenyl magnesium bromide and oxetane using a standard procedure[35] gave 3-([$^2H_5$]phenyl)propanol in 85% yield. The labelled propanol was oxidised (with acidic chromium trioxide)[36] to 3-([$^2H_5$]phenyl)propanoic acid (65% yield), which was esterified (by refluxing with acidified methanol)[37] to yield methyl 3-([$^2H_5$]phenyl)propanoate (90% yield, $^2H_5 = 99\%$).

Methyl 3-([$^2H_5$]phenyl)[2,2-$^2H_2$]propanoate. This compound was prepared by three exchanges of methyl 3-([$^2H_5$]phenyl)propanoate with NaOMe–MeOD (*cf.* ref. 34) ($^2H_7 > 98\%$).

3-Phenyl[2,2-$^2H_2$]propanenitrile. This compound was prepared by a reported procedure ($^2H_2 > 99\%$).[38]

Methyl 2-([$^2H_5$]phenyl)ethyl ether. [$^2H_5$]Bromobenzene was converted[39] into 2-([$^2H_5$]phenyl)ethanol, which was methylated[29] to give the required product (overall 50% yield, $^2H_5$ > 99%).

Methyl 2-phenyl[2,2-$^2H_2$]ethyl ether. Three exchanges of methyl phenylacetate with NaOMe–MeOD[34] gave methyl phenyl[2,2-$^2H_2$]acetate (quantitative yield, $^2H_2$ = 98%), which was reduced[40] with lithium aluminium hydride to produce 2-phenyl[2,2-$^2H_2$]ethanol (68% yield, $^2H_2$ = 98%), which was then methylated[29] to form methyl 2-phenyl[2,2-$^2H_2$]ethyl ether (70% yield, $^2H_2$ = 98%).

Methyl 2-phenyl[1,1-$^2H_2$]ethyl ether. This compound was prepared by a standard procedure[29] (55% yield, $^2H_2$ = 99%).

3-Methoxy[2,2-$^2H_2$]propanenitrile. Butyllithium in light petroleum [40–50 °C, 1.4 mol dm^{-3} (4 cm^3)] was added to diisopropylamine (0.7 cm^3) in anhydrous tetrahydrofuran (5 cm^3) at −78 °C under nitrogen. The mixture was stirred for 10 min, [$^2H_3$]acetonitrile (0.16 g) in tetrahydrofuran (5 cm^3) was added, the mixture stirred at −78 °C (under nitrogen) for 5 min, and added to a solution of chloromethyl methyl ether (0.5 g) in tetrahydrofuran (10 cm^3). The mixture was stirred at −78 °C for 1 h, the temperature allowed to rise to room temperature (20 °C) and stirred at that temperature for 1 h, aqueous hydrogen chloride (10%, 10 cm^3) was added, the mixture extracted with dichloromethane (3 × 10 cm^3), the organic layer separated, washed with water (10 cm^3) and aqueous sodium chloride (saturated, 10 cm^3), and dried (Na_2SO_4). Removal of the solvent *in vacuo* followed by vacuum distillation gave 3-methoxy[2,2-$^2H_2$]propanenitrile [bp 43–45 °C/14 mmHg, 0.3 g (79%), $^2H_2$ 98%].

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