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Site-specific hydrogen exchange and hydrogen transfer processes preceding the fragmentation of long-lived radical cations of ethyl dihydrocinnamate and related arylalkanoates

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ABSTRACT

An electron ionisation study on the fragmentation of metastable molecular radical cations of ethyl 3-phenylpropanoate (ethyl dihydrocinnamate) and related arylalkanoic acid esters was performed by mass-analysed ion kinetic energy (MIKE) spectrometry. Six deuterium-labelled isotopomers of ethyl dihydrocinnamate were synthesised and studied by MIKE spectrometry. The fragmentation leading to ions $C_7H_7O^+$ (*m*/*z* 107) involving migration of the alkoxycarbonyl group was also observed in the 70-eV mass spectra of related alkyl dihydrocinnamates, but it was found to be a high-energy process that does not compete at low energies in metastable molecular ions. Instead, the metastable ions of ethyl dihydrocinnamate undergo competing losses of carbon monoxide, ethanol and the combined loss of these neutral fragments, giving ionised styrene, $C_8H_8^{\bullet+}$ (*m*/*z* 104). A highly specific H/D interchange involving the four hydrogen atoms at the benzylic α- and *ortho*-positions was found to precede the losses of ethanol and [ethanol + CO]. This represents another striking case of complete 4H – scrambling that enables the molecular ion to fully equilibrate the interchanging hydrogen atoms prior to fragmentation. A mechanism rationalising these observations and extending previously suggested mechanisms is proposed involving a series of distonic ions and the intermediacy of an ion/neutral complex. The metastable ions of the related esters exhibit in part similar fragmentation behaviour, but the McLafferty reaction turns out to be more favourable with higher alkyl dihydrocinnamates. For example, *n*-propyl 3-phenylpropanoate and isopropyl 3-phenylpropanoate react through highly distinct fragmentation channels.

1. Introduction

Since the beginnings of organic mass spectrometry more than half a century ago it has been known that hydrogen migration processes play a major role within the gaseous molecular ions of organic compounds [1–3]. The McLafferty reaction is the outstanding example for processes involving hydrogen rearrangement as the crucial step [2,4,5]. Hydrogen shifts are known to be the initial steps in many other important mass spectrometric fragmentation reactions, among which the ring expansion reactions of toluene radical cations, $C_7H_8^{\bullet+}$, and the products of primary fragmentation, $C_7H_7^+$, discovered by Meyerson et al. [6,7], are the best-known examples with which the typical organic chemist is usually familiar [8,9]. Since the advent of chemical ionisation [10], the realm of intramolecular (and intermolecular) hydrogen rearrangements inevitably included proton and hydride shifts, as demonstrated in great detail by Harrison et al. for protonated alkylbenzenes and other arylaliphatic compounds [11–13]. Nowadays, a vast amount of knowledge has been accumulated which has rendered the gas-phase ion chemistry of ions a well-rationalised subfield of organic and physical organic chemistry. Hydrogen rearrangements and hydrogen exchange ("scrambling") processes represent almost ubiquitous steps of the fragmentation scenario – be it of small organic [14] or large bioorganic ions [15]. Nevertheless, not all facets of this theme are understood completely and surprising fragmentation behaviour of gaseous ions can be encountered and initiate in-depth research. The present contribution is aimed at highlighting new facets of apparently well-established fragmentation reactions, namely, those of the molecular radical cations of ethyl dihydrocinnamate [16] and a number of related arylaliphatic esters.

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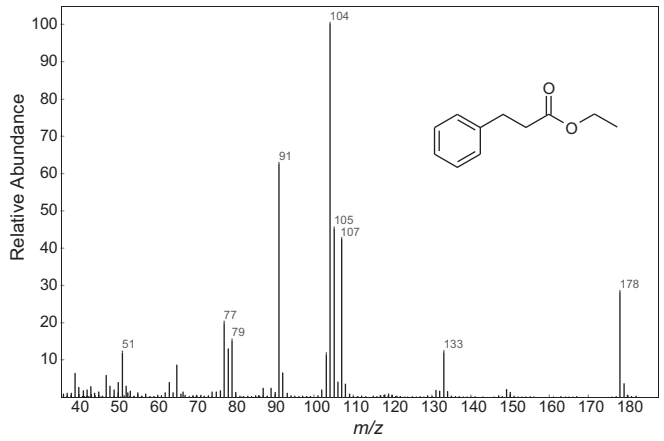


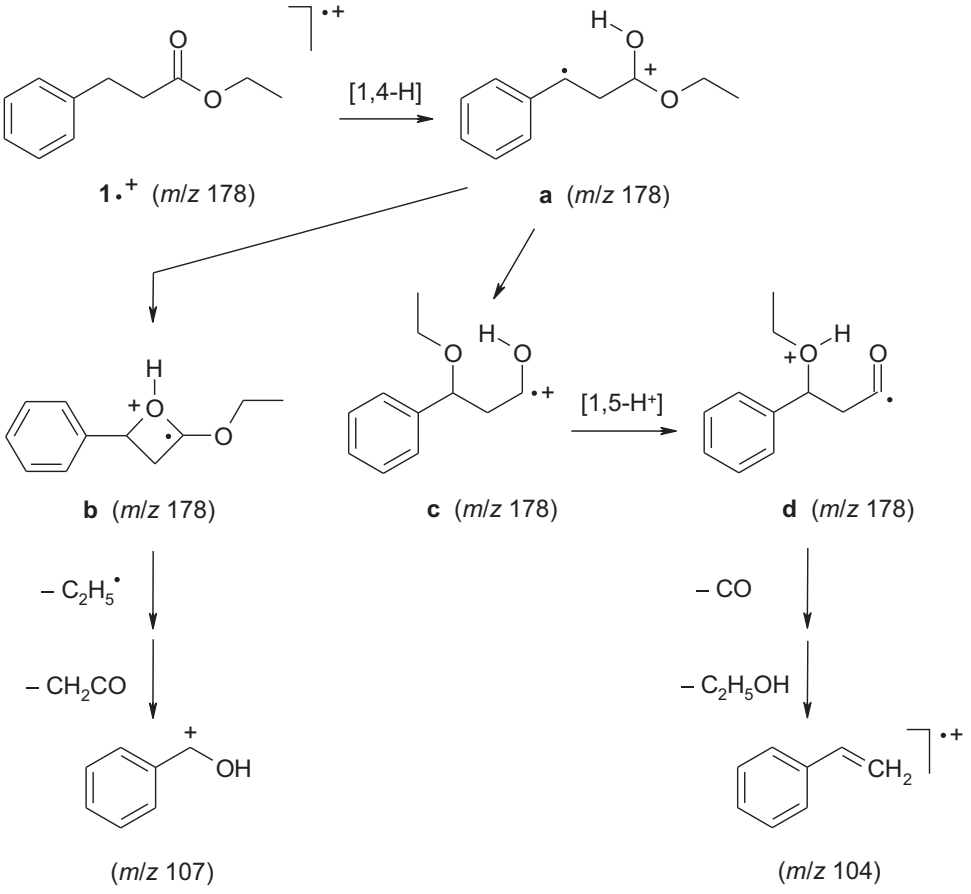
Fig. 1. EI mass spectrum (70 eV) of ethyl dihydrocinnamate (**1**).

2. Results and discussion

The standard EI mass spectrum of ethyl dihydrocinnamate **1** (Fig. 1) shows, besides the molecular ion peak at *m*/*z* 178, prominent peaks for ions $[M - OC_2H_5]^+$ (*m*/*z* 133), $C_7H_7O^+$ (*m*/*z* 107), $C_8H_9^+$ (*m*/*z* 105), $C_8H_8^{+\bullet}$ (*m*/*z* 104) and $C_7H_7^+$ (*m*/*z* 91), among others. The oxygen-containing fragment ion with *m*/*z* 107 occurring at 40–45% abundance relative to that of the most abundant $C_8H_8^{+\bullet}$ ion intrigued a number of scientists since the formation of a new C–O bond must be involved [16–18]. An early mechanistic suggestion [18a] included the migration of the carbonyl oxygen to one of the *ortho* positions of the benzene ring to give the *ortho*-hydroxybenzyl cation. Similar oxygen migration had previously been proposed for related derivatives of dihydrocinnamic acid [17]. However, Nibbering et al. [16] then demonstrated that the carbonyl oxygen was bound to the benzylic carbon atom prior to the overall loss of the constituents of $[C_4,H_7,O_2]$, suggesting the formation of the α-hydroxybenzyl ion (protonated benzyldehyde). Formation of the $C_6H_5CHOH^+$ ion was rationalised by sequential losses of an ethyl radical and ketene (Scheme 1) [16,18b].

The crucial step of this unusual reaction sequence was suggested to be a 1,4-H transfer from the benzylic methylene group to the carbonyl oxygen, giving rise to the distonic ion **a**. In fact, such β-H migrations are known to dominate fragmentation when γ-H transfer cannot take place [19–23] and to induce deep-seated skeletal rearrangement [22,23]. Even more generally, β-H transfer can compete with the well-known γ-H transfer representing the first step of the McLafferty reaction, as well as with an H transfer step from the δ position and from even more remote positions of the alkyl chain, if available [24]. Nibbering et al. [16] also postulated a fragmentation mechanism for ethyl dihydrocinnamate ions $\mathbf{1}^{\bullet+}$ that leads to the $C_8H_8^{+\bullet}$ ion which gives rise to the base peak at *m*/*z* 104 in the EI mass spectrum. The distonic ion **a**, undoubtedly being a very stable isomer of the molecular ion $\mathbf{1}^{\bullet+}$ (vide infra) was suggested as the first intermediate of both fragmentation channels, $\mathbf{1}^{\bullet+} \rightarrow C_7H_7O^+$ and $\mathbf{1}^{\bullet+} \rightarrow C_8H_8^{\bullet+}$. The latter ions were proposed to have the structure of ionised styrene and to be generated after multistep isomerisation and sequential losses of carbon monoxide and ethanol (Scheme 1).

As noted above, both fragmentation channels were found to compete efficiently within the time scale of an EI source ($\tau < 1$ μs), comprising the fragmentation of highly excited, short-lived molecular ions. However, this does not hold true for the much less excited,



Scheme 1. Major fragmentation reactions of ethyl dihydrocinnamate (**1**) occurring in the EI source (70 eV) and mechanism according to Nibbering et al. [16].

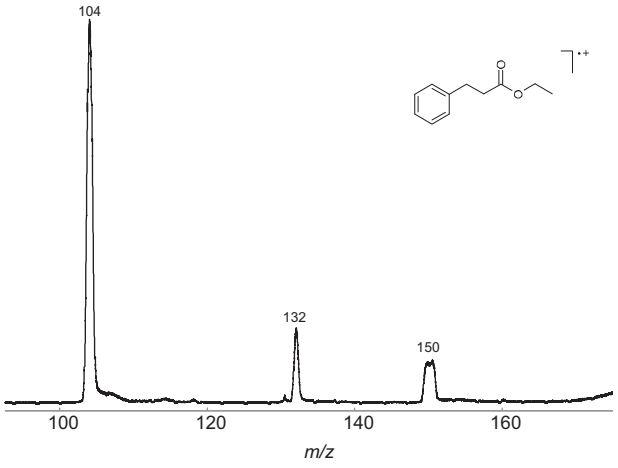


Fig. 2. EI-MIKE spectrum (70 eV) of the metastable radical cations $\mathbf{1}^{\bullet+}$ (m/z 178). The mass range < m/z 95 is void of signals and has been omitted for clarity.

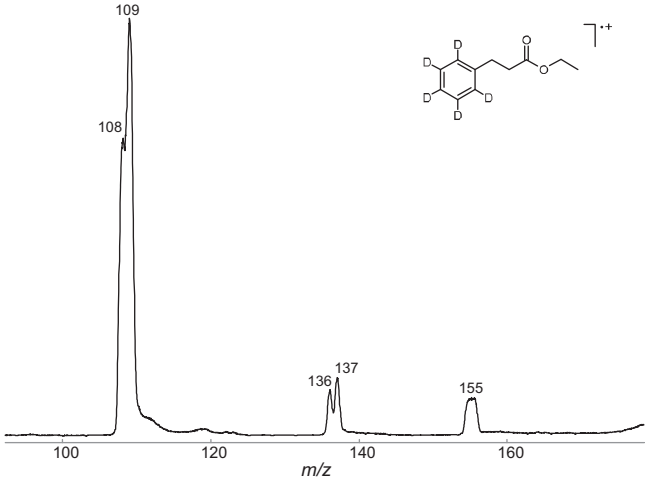


Fig. 4. EI MIKE spectrum (70 eV) of the radical cations $\mathbf{1d}^{\bullet+}$ (m/z 183). The mass range < m/z 95 is void of signals and has been omitted for clarity.

long-lived molecular ions of **1** that fragment in the field-free regions of a sector-field mass spectrometer ($\tau \approx 10$–$30\ \mu s$). This is evident from the mass-analysed ion kinetic energy (MIKE) spectrum of *metastable* ions $\mathbf{1}^{\bullet+}$ (Fig. 2), which lacks a peak for the fragment ion $C_7H_7O^+$ (m/z 107). Rather, a broadened, flat-topped signal at m/z 150 was observed for the expulsion of carbon monoxide, along with a Gaussian-shaped signal for the loss of ethanol at m/z 132, both in moderate relative amounts as compared to the dominating peak at m/z 104. Obviously, under relatively low-energy conditions, the formation of the radical cation $C_8H_8^{\bullet+}$ remains the preponderant fragmentation process.

Notably, there is no signal indicating the loss of an ethyl radical from any form of (isomerised) molecular ions. The presence of the corresponding fragment ions, $C_9H_9O_2^+$ (m/z 149), would be clearly visible in spite of the flat-topped peak for the loss of CO at m/z 150. Moreover, loss of ketene is not observed. Most interestingly, however, the MIKE spectrum of ions $\mathbf{1}^{\bullet+}$ also lacks a peak for the $C_7H_7O^+$ ions (m/z 107). Thus, the intriguing fragmentation $\mathbf{1}^{\bullet+} \rightarrow C_7H_7O^+$ has to be considered a high-energy process as compared to the fragmentation $\mathbf{1}^{\bullet+} \rightarrow C_8H_8^{\bullet+}$. As far as the metastable ions $\mathbf{1}^{\bullet+}$ are concerned, the styrene radical cation may be formed by both of the sequences $\mathbf{1}^{\bullet+} \rightarrow [\mathbf{1} - CO]^{\bullet+} \rightarrow [\mathbf{1} - CO - C_2H_5OH]^{\bullet+}$ and $\mathbf{1}^{\bullet+} \rightarrow [\mathbf{1} - C_2H_5OH]^{\bullet+} \rightarrow [\mathbf{1} - C_2H_5OH - CO]^{\bullet+}$ within the same field-free region of the sector-field mass spectrometer.

In order to gain more insight into the mechanistic course of the fragmentation, we synthesised a number of deuterium labelled analogues of **1** (Fig. 3). The fragmentation of the corresponding metastable ions $\mathbf{1a}^{\bullet+}$–$\mathbf{1f}^{\bullet+}$ is shown in Table 1. The loss of CO is clearly confirmed by the fact that all of the MIKE spectra contain the flat-topped peak at 28 u below the mass of the individual molecular ion peak. Hence, the data strictly exclude the elimination of ethene from the metastable ions $\mathbf{1}^{\bullet+}$. Beyond the CO loss, the MIKE spectra can be interpreted in a straightforward way as well. Thus, the [*ethyl*-D_5]-labelled isotopomer $\mathbf{1a}^{\bullet+}$ exclusively undergoes the loss of C_2D_5OH (51 u) and the combined losses of [CO + C_2D_5OH] (79 u), giving rise to the fragment ions with m/z 132 and m/z 104, respectively. The MIKE spectrum of the [2,2-D_2]-labelled analogue $\mathbf{1b}^{\bullet+}$ clearly shows shifts by two mass units for all fragmentation routes. In particular, the exclusive formation of the ions with m/z 134 and m/z 106, generated by elimination of C_2H_5OH (46 u) and [CO + C_2H_5OH] (74 u), respectively, suggests complete retention of the label in the ionic fragments. The same holds true for the [*phenyl*-3,4,5-D_3]-labelled isotopomer $\mathbf{1f}^{\bullet+}$, as shown by the likewise exclusive losses of C_2H_5OH and the combined losses of [CO + C_2H_5OH] generating the fragment ions with m/z 135 and m/z 107, respectively.

By contrast, the MIKE spectra of the isotopomeric ions $\mathbf{1c}^{\bullet+}$, $\mathbf{1d}^{\bullet+}$ and $\mathbf{1e}^{\bullet+}$ reveal that intramolecular hydrogen exchange processes occur prior to fragmentation. For example, the MIKE spectrum of the [*phenyl*-D_5]-labelled molecular ion $\mathbf{1d}^{\bullet+}$ (Fig. 3) exhibits the loss of singly deuterated ethanol along with that of the unlabelled alcohol. This indicates that the hydrogen transferred during the loss of ethanol originates in part from the aromatic ring. The combined losses of carbon monoxide and ethanol show the same behaviour. A similar peak splitting is observed in the MIKE

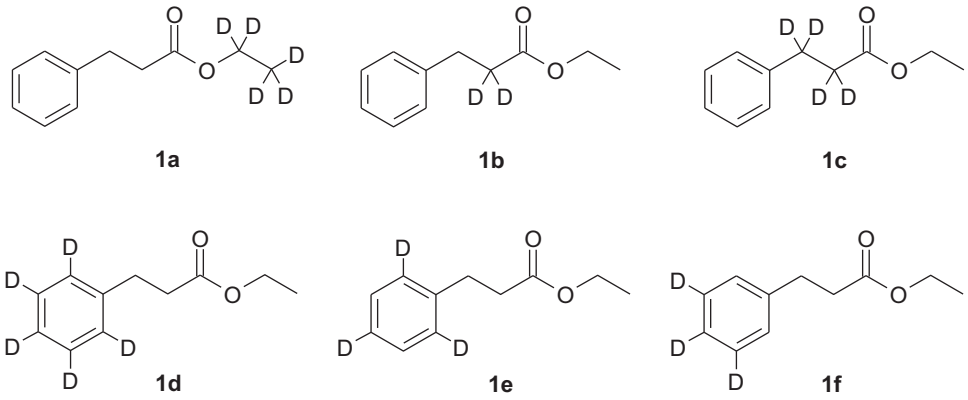


Fig. 3. Deuterium-labelled ethyl dihydrocinnamates.

Table 1
Fragmentation of the metastable radical cations of ethyl dihydrocinnamate (**1**) and its labelled analogues **1a**–**1f** (MIKE spectra, 70 eV).

Radical cation (label)	*m/z*	Loss of CO *m/z* (%)[a]	Loss of ethanol *m/z* (%)[a]	Loss of [CO + ethanol] *m/z* (%)[b]
1$^{\bullet+}$ (D_0)	178	150 (14)	132 (11)	104 (75)
1a$^{\bullet+}$ (D_5-ethyl)	183	155 (10)	132 (12)	104 (78)
1b$^{\bullet+}$ (2,2-D_2)	180	152 (14)	134 (6.3)	106 (80)
1c$^{\bullet+}$ (2,2,3,3-D_4)	182	154 (9.5)	136 (3.4)[c]	108 (52.2)[c]
			135 (2.7)[d]	107 (32.2)[d]
1d$^{\bullet+}$ (D_5-phenyl)	183	155 (7.5)	137 (5.2)[c]	109 (48.6)[c]
			136 (4.1)[d]	108 (34.7)[d]
1e$^{\bullet+}$ (2,4,6-D_3-phenyl)	181	153 (8.6)	135 (5.0)[c]	107 (48.8)[c]
			134 (3.8)[d]	106 (33.8)[d]
1f$^{\bullet+}$ (3,4,5-D_3-phenyl)	181	153 (10)	135 (10)	107 (80)

[a] Estimated error limits of relative ion abundances ± 5% (rel.).
[b] Estimated error limits of relative ion abundances ± 2% (rel.).
[c] Loss of C_2H_5OH or combined losses of [C_2H_5OH + CO], respectively.
[d] Loss of C_2H_5OD or combined losses of [C_2H_5OD + CO], respectively.

spectra of the isotopomers **1c**$^{\bullet+}$ and **1e**$^{\bullet+}$. In all three of these cases, C_2H_5OH (46 u) and C_2H_5OD (47 u) are eliminated in a ratio of about 56:44. In particular, the [2,2,3,3-D_4]-labelled ion **1c**$^{\bullet+}$ gives the fragment ions with *m/z* 136 and *m/z* 135 in a ratio of 55:45, and ion **1d**$^{\bullet+}$ and the [*phenyl*-2,4,6-D_3]-labelled analogue **1e**$^{\bullet+}$ give the respective fragment ions in a ratio of ca. 56:44 (Figs. 4 and 5). Moreover, the combined losses of carbon monoxide and ethanol occur in similar relative amounts. Ion **1c**$^{\bullet+}$ eliminates the masses of [CO + C_2H_5OH] (74 u) and [CO + C_2H_5OD] (75 u) in the ratio of 62:38 and ions **1d**$^{\bullet+}$ and **1e**$^{\bullet+}$ give similar ratios (ca. 58:42, see Table 1). Although an error limit of ca. ±3% has to be considered for these ratios, it appears likely that the isotope branching is identical within each individual fragmentation channel and very similar when both channels are compared. In fact, this finding suggests that a kinetic isotope effect operates in the rate-determining H-transfer step preceding not only the elimination of ethanol but also the expulsion of carbon monoxide and the sequential losses of both neutral fragments from the molecular ions **1**$^{\bullet+}$.

The data obtained from the MIKE spectra of the various deuterium-labelled ethyl dihydrocinnamates allow us to draw a relatively simple mechanistic picture for the fragmentation of the long-lived, metastable molecular ions **1**$^{\bullet+}$ (Scheme 2). As suggested earlier [16], the 1,4-transfer of a hydrogen atom from the benzylic methylene group to the carbonyl oxygen atom is the first mechanistic step, giving the stable distonic ion **a**. The [1,4-H] transfer is a kinetically and, because of the benzylic activation of the C–H donor bonds, energetically favourable isomerisation step that is known to be ubiquitous [19–23]. It may be pointed out that the intermediate ion **a** can be estimated to be 20–30 kJ mol^{-1} more stable than the molecular ion **1**$^{\bullet+}$ [25–27]. It can be assumed that, in general, the long-lived metastable ions of alkyl and aryl dihydrocinnamates, such as **1**–**5** and **8**, and even of the higher homologues (e.g., **6**, see Fig. 6 and below), predominantly exist as distonic ions bearing a benzylic radical moiety and a protonated-ester functionality – owing to the considerable hydrogen atom affinity of the radical-cationic ester group [28]. Moreover, it can be safely assumed that the transfer of a benzylic hydrogen atom in ion **1**$^{\bullet+}$ to the alkoxy oxygen atom leading to ion **f** is much more energetically demanding. This corresponds to the fact that the alkoxy oxygen atom of esters and acids is much less basic than the carbonyl oxygen. As a consequence, formation of intermediate **f** has to be considered the rate-determining step of the elimination of ethanol giving fragment ions **h** (*m/z* 132).

In line with these considerations, the MIKE spectra of the labelled ethyl dihydrocinnamates **1c**$^{\bullet+}$, **1d**$^{\bullet+}$ and **1e**$^{\bullet+}$ reveal not only that the [1,4-H] transfer step **1**$^{\bullet+}$ → **a** is reversible but that it specifically involves the two hydrogen atoms originating from the *ortho*-positions of the phenyl ring and those of the benzylic methylene group in an overall four-hydrogen exchange process that precedes fragmentation. This follows from the finding that the MIKE spectra of these three isotopomers are identical within the limits of experimental error. Complementarily, the MIKE spectrum of isotopomer **1f**$^{\bullet+}$, in particular, confirms that the hydrogen atoms from the *meta*- and *para*-positions of the aromatic ring are not involved. It follows that ion **1**$^{\bullet+}$ not only isomerises to the distonic ion **a** but also to the tautomeric isotoluene-type ion **e**. The fact that the *meta*- and *para*-hydrogen atoms are not involved in the hydrogen exchange indicates that hydrogen ring walk in the isotoluene-type ion **e** does not occur. Finally, it is obvious that the hydrogen atoms of the α-methylene group and of the ethyl group do not participate in the exchange process, as might have been expected.

Interestingly, the loss of [D_1]-ethanol, – reasonably assumed to be CH_3CH_2OD – falls short as compared to that of [D_0]-ethanol

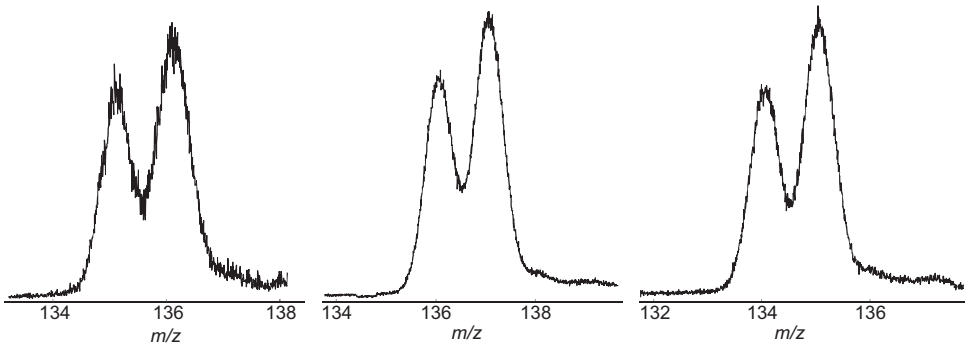
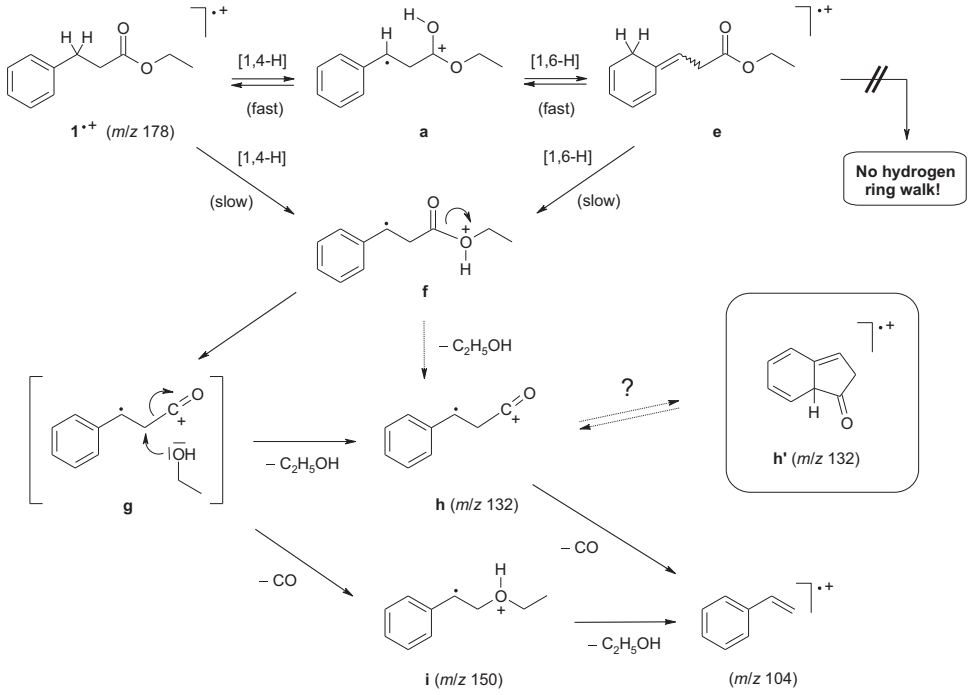


Fig. 5. Partial EI MIKE spectra (70 eV) of the metastable radical cations **1c**$^{\bullet+}$ (*m/z* 182, left), **1d**$^{\bullet+}$ (*m/z* 183, middle) and **1e**$^{\bullet+}$ (*m/z* 181, right) in the mass range showing the losses of C_2H_5OD and C_2H_5OH.



Scheme 2. Hydrogen exchange and proposed fragmentation of the metastable molecular ions $\mathbf{1}^{\bullet+}$.

with a ratio of 44:56 (within narrow error limits) for all of the three isotopomers $\mathbf{1c}^{\bullet+}$, $\mathbf{1d}^{\bullet+}$ and $\mathbf{1e}^{\bullet+}$. This unequivocally demonstrates that the four-hydrogen exchange involving the benzylic α- and *ortho*-positions has reached an equilibrium ("complete 4H-scrambling" [14]) and that a kinetic isotope effect of $k_H/k_D = 1.27$ operates in the rate-determining step, namely, the transfer of one of these four hydrogen atoms to the alkoxy oxygen atom leading to the loss of ethanol. Whether ion **f** is formed by [1,4-H] transfer from ion $\mathbf{1}^{\bullet+}$ or by [1,6-H] transfer from ion **e**, or by both pathways, cannot be answered on the basis of the present results. In any case, these H transfer steps have to be slower with respect to the [1,4-H]- and [1,6-H]-transfer involving ion **a** as the central intermediate. As mentioned above, the combined losses of carbon monoxide and ethanol are also subject to a kinetic isotope effect. The ratios observed for ions $\mathbf{1c}^{\bullet+}$, $\mathbf{1d}^{\bullet+}$ and $\mathbf{1e}^{\bullet+}$, $[C_2H_5OD + CO]$: $[C_2H_5OH + CO] \approx 40{:}60$, yield a slightly increased kinetic isotope effect, $k_H/k_D = 1.50$. This may indicate that, unexpectedly, the combined loss of the two neutrals is energetically less demanding than the simple loss of the alcohol and that both pathways leading to ion $C_8H_8^{\bullet+}$ may be pursued.

As depicted in Scheme 2, loss of ethanol can take place directly from ion **f** but also via an ion/neutral complex **g**, consisting of ion **f** and ethanol. In both cases, the distonic ion **h** (*m*/*z* 132) would be formed. This ion may lose carbon monoxide to give ionised styrene, $C_8H_8^{\bullet+}$ (*m*/*z* 105), as the final product of fragmentation. We also speculate that ion **h** may preferably exist as a ring-closed isomer, **h**′, representing another isotoluene derivative (vide infra). An alternative fragmentation route may be envisioned, starting from

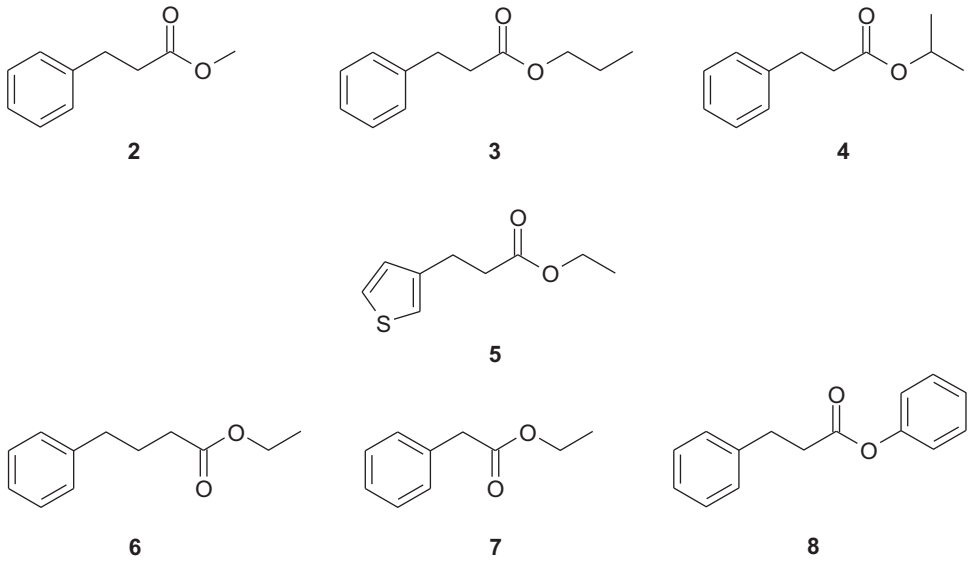


Fig. 6. Analogues **2**–**8** of ethyl dihydrocinnamate (**1**).

the ion/neutral complex **g**, which could undergo an intra-complex, S_N2-type replacement reaction to release carbon monoxide and form ion **i** (*m*/*z* 150). This could rationalise the observation of a flat-topped peak in the MIKE spectrum of ion $\mathbf{1}^{\bullet+}$, which indicates the release of kinetic energy during the expulsion of CO and the existence of a substantial reverse activation energy barrier for CO loss. Ion **i** represents another distonic ion from which ethanol could eventually be lost by a simple, albeit heterolytic, C–O bond cleavage giving the final fragment ions, $C_8H_8^{\bullet+}$. Whatever the true details of the fragmentation may be, it is evident that a complete hydrogen scrambling precedes the fragmentation of the metastable molecular ions of ethyl dihydrocinnamate, which specifically involves the benzylic α- and *ortho*-H atoms. Hydrogen transfer to the alkoxy group is the rate-determining step of the fragmentation leading to ionised styrene, $C_8H_8^{\bullet+}$ (*m*/*z* 104), as the final fragment ion. Formation of ions $C_7H_7O^+$ (*m*/*z* 107), to which the structure of protonated benzyldehyde has been assigned [16], cannot compete with the low-energy isomerisation and fragmentation reactions discussed here for the metastable ions. The finding that ion $C_7H_7O^+$ is formed by a high-energy process is in line with the absence of H/D exchange in the short-lived molecular deuterium-labelled ions $\mathbf{1a}^{\bullet+}$–$\mathbf{1f}^{\bullet+}$ (see standard EI-MS data in Section 4).

The mechanistic scenario depicted here has parallels to previously investigated isomerisation and fragmentation behaviour of arylalphatic compounds under EI conditions. In particular, the complete 4H-scrambling in ion $\mathbf{1}^{\bullet+}$, or variations of this process, was found to precede the fragmentation of the radical cations of 1,3-diphenylpropane [29], 2-benzylindanes [30] and related hydrocarbons [14,31,32], as well as of those of 2-phenylethanol and a number of ω-functionalised phenylpropanes [33–36]. In particular, it has been demonstrated earlier that a complete 4H-scrambling requires a minimum of about eight H transfer cycles, as shown in detail for the case of 2-benzylindanes [14,30].

Some homologues and analogues of ethyl dihydrocinnamate **1** were also studied with respect to their fragmentation under electron ionisation. The structures of these compounds are displayed in Fig. 6. Initially, we considered the appearance of the intriguing ion $C_7H_7O^+$ (*m*/*z* 107) in the cases of the dihydrocinnamates **2**–**4** and **6**–**8** or the analogous fragment ion in the case of the thienylpropanoate **5**. The standard EI mass spectra of the 3-arylpropanoates **3**–**5** were found to exhibit the *m*/*z* 107 peak, or the corresponding *m*/*z* 113 peak in the case of the thiophene analogue, in considerable intensity (28–43%) and similar to the spectrum of ester **1** (Table 2). The methyl ester **2** is an obvious exception as in this case the $C_7H_7O^+$ ion is formed in much lower relative abundance. This may be attributed to the somewhat increased energy requirements for the loss of $CH_3^{\bullet}$ as compared to that of $C_2H_5^{\bullet}$, in line with the rearrangement mechanism suggested by Nibbering et al. [16], which includes the consecutive loss of the alcoholic alkyl group and ketene (Scheme 1). In further agreement with that mechanism, neither the molecular ions of ethyl phenylbutyrate **6** nor those of ethyl phenylacetate **7** undergo the rearrangement reaction generating the $C_7H_7O^+$ fragment, nor does the phenyl ester **8** undergo this reaction. In the latter case, loss of $C_6H_5^{\bullet}$ is energetically unfavourable. Notably, the MIKE spectra of the low-energy ions $\mathbf{2}^{\bullet+}$–$\mathbf{4}^{\bullet+}$ and $\mathbf{5}^{\bullet+}$ do not exhibit a peak for ions $C_7H_7O^+$ (*m*/*z* 107) or $C_5H_5OS^+$ (*m*/*z* 113), respectively, and neither do those of ions $\mathbf{6}^{\bullet+}$–$\mathbf{8}^{\bullet+}$ (vide infra). This parallels the fragmentation behaviour of the metastable ions $\mathbf{1}^{\bullet+}$. Again, as mentioned above for the latter ions, the rearrangement reactions that give rise to the benzylic C–O bond proceed through a high-energy channel that is not accessible for metastable ions.

The MIKE spectra of the molecular ions $\mathbf{2}^{\bullet+}$–$\mathbf{8}^{\bullet+}$ were examined more closely in order to check how far the rather specific fragmentation of the long-lived molecular ions of ethyl dihydrocinnamate, $\mathbf{1}^{\bullet+}$, is carried on when some structural elements are changed. The

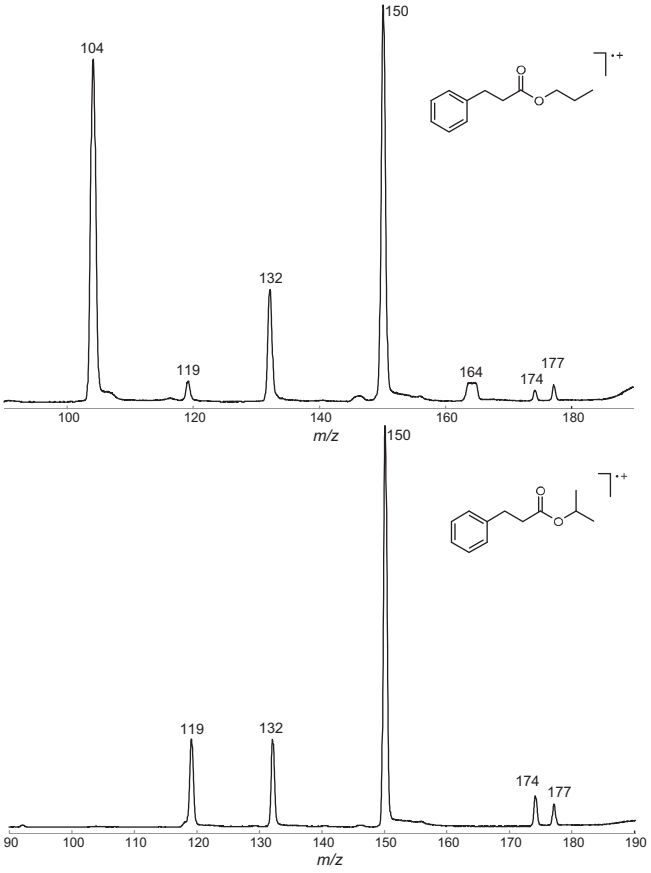


Fig. 7. MIKE spectra (70 eV) of the molecular ions of *n*-propyl dihydrocinnamate (**3**, top) and isopropyl dihydrocinnamate (**4**, bottom). The molecular ion peaks (*m*/*z* 192) and the void range < *m*/*z* 80 have been omitted for clarity.

complete MIKE spectral data are collected in Table 3 but we will focus the discussion on the major fragmentation routes only. The metastable ions $\mathbf{2}^{\bullet+}$ generated from the methyl ester behave very similar to the higher homologue. Expulsion of carbon monoxide is somewhat more pronounced at the expense of the combined loss of methanol and CO but the number and relative weight of the fragmentation channels remain unchanged. However, in the case of the higher homologue, metastable ions $\mathbf{3}^{\bullet+}$ generated from *n*-propyl dihydrocinnamate, a new major fragmentation path is opened, viz., loss of propene yielding a fragment ion with *m*/*z* 150 (Scheme 3). Obviously, the McLafferty reaction occurring with the alcoholic chain of ions $\mathbf{3}^{\bullet+}$ is much more favourable than in ions $\mathbf{1}^{\bullet+}$ due to the slightly activated secondary C–H bond at the γ-position of the alkoxy residue. Thus, in the case of ions $\mathbf{3}^{\bullet+}$, there is a balanced competition between the rearrangement of a hydrogen atom from the benzylic β-CH_2 group as the initial step leading to the loss of the alcohol and/or CO, on the one side, and the rearrangement of a hydrogen atom from the alkoxylic γ-CH_2 group as the initial step of the McLafferty reaction, on the other side (Scheme 3). This trend carries on with the metastable ions $\mathbf{4}^{\bullet+}$ generated from isopropyl dihydrocinnamate (see Fig. 7). These ions do undergo elimination of isopropanol but to a minor extent only, and CO loss and the combined loss of CO and isopropanol are virtually absent. By contrast, the McLafferty reaction is by far the dominant fragmentation channel here. Obviously, the entropic advantage of six (albeit primary) hydrogen donor bonds at the γ-positions of the isopropoxy group and the slightly weaker C–O bond enable ions $\mathbf{4}^{\bullet+}$ to circumvent the CO loss channels. Nevertheless, both long-lived ions $\mathbf{3}^{\bullet+}$ and $\mathbf{4}^{\bullet+}$ undergo skeletal isomerisation reactions leading to minor loss of water along with loss of a methyl radical. Similarly, the

Table 2
Relative abundances[a] of selected ions in the EI (70 eV) mass spectra and of the *m/z* 107 ions in the EI-MIKE spectra of esters **1**–**8**.

Compound	1	2	3	4	5[b]	6	7	8
EI-MS *m/z* 91% B	64	61[b]	85	100	100	100	100	100
EI-MS *m/z* 104% B	100	100	100	92	67	79	0.5	18[c]
EI-MS *m/z* 105% B	45	37	49	59	23	29	2	96
EI-MS *m/z* 107% B	41	4.5	43	28	34	0[d]	0	0
EI-MIKES *m/z* 107% B	<0.5	<0.5	≤1	0	<0.5	0	0	0
EI-MS $M^{\bullet+}$	27	31	31	15	33	22	16	8

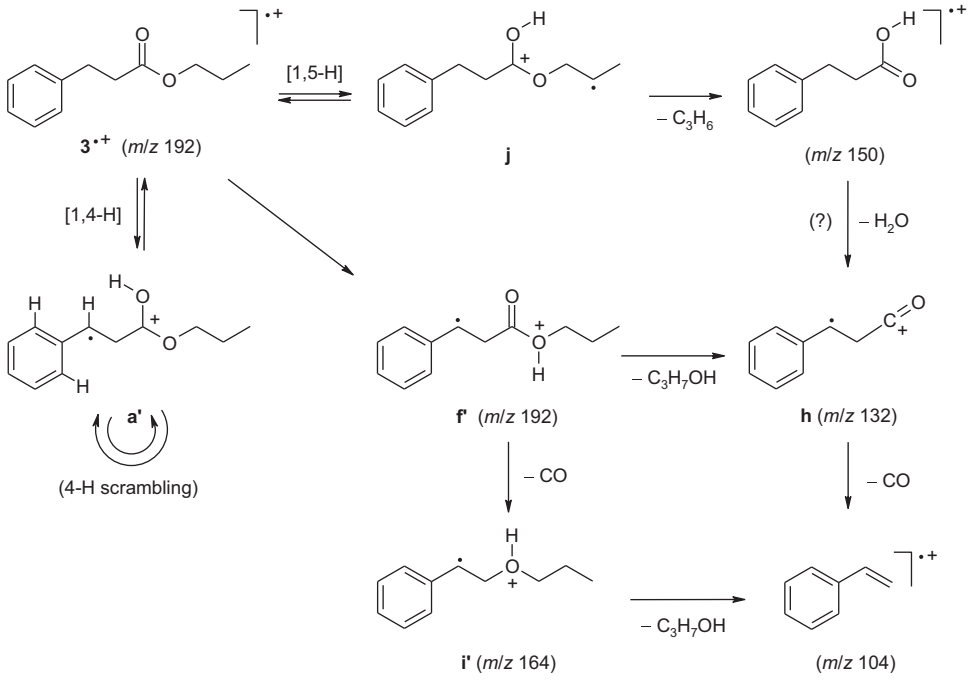
[a] Values are not corrected for isotopic contributions.
[b] The fragment-ion *m/z* values for 3-thienylpropanoate **5** shift to *m/z* 97, 110, 111, and 113, respectively.
[c] The fragment ion with *m/z* 103 appears with 12% B.
[d] The fragment ion with *m/z* 121 (=107 + 14) for 4-phenylbutyrate **6** appears with ca. 1% B.

Table 3
Fragmentation of the metastable radical cations of esters **2**–**8** (MIKE spectra, 70 eV).[a]

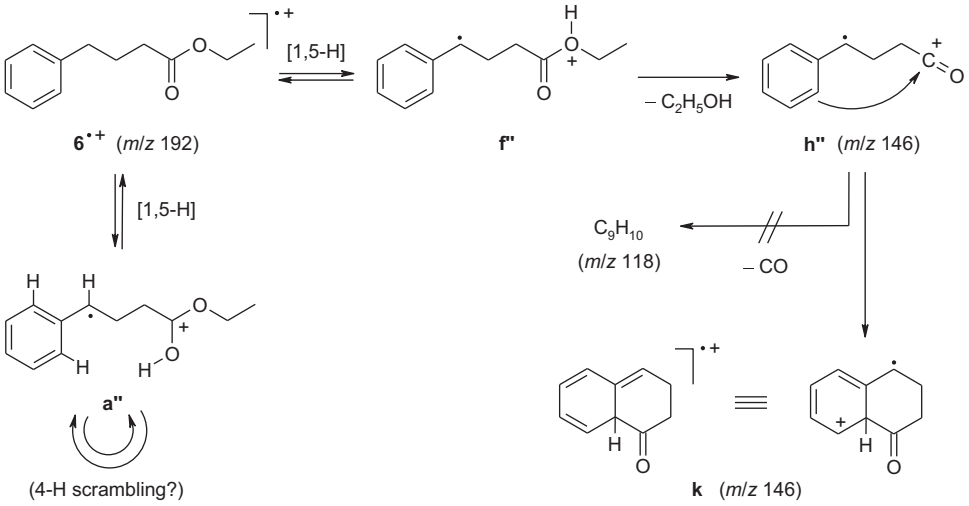
Radical cation	*m/z*	Loss of CO *m/z* (%)	Alcohol loss *m/z* (%)	Loss of [CO + alcohol] *m/z* (%)	Alkene loss *m/z* (%)	Other fragmentation channels *m/z* (%)
2$^{\bullet+}$	164	136 (26)[b]	132 (16)	104 (58)	–	91 (≤1)
3$^{\bullet+}$	192	164 (4.3)[b]	132 (11)	104 (42)	150 (39)	177 (1.1, $[M - CH_3]^+$) 174 (0.7, $[M - H_2O]^{\bullet+}$) 119 (2.0)
4$^{\bullet+}$	192	–	132 (13)	104 (≤0.1)	150 (65)	177 (3.1, $[M - CH_3]^+$) 174 (4.6, $[M - H_2O]^{\bullet+}$) 119 (14)
5$^{\bullet+}$	184	156 (5.3)	138 (0.3)	110 (77)	[c]	140 (0.3, $[M - C_2H_4O]^{\bullet+}$) 97 (17, $C_5H_5S^+$)
6$^{\bullet+}$	192	–	146 (100)	118 (0.2)	–	104 (≤0.1)
7$^{\bullet+}$	164	[d]	118 (0.5)	–	136 (32)[d]	120 (28, $[M - C_2H_4O]^{\bullet+}$) 105 (4.6), 92 (6), 91 (29)
8$^{\bullet+}$	226	–	–	104 (≤0.2)	–	208 (12.4, $[M - H_2O]^{\bullet+}$) 180 (0.9), 167 (1.6), 133 (81), 94 (4.5, $C_6H_6O^{\bullet+}$)

[a] Estimated error limits of relative ion abundances ± 5% (rel.).
[b] Broad and dished-topped peak.
[c] No indication of C_2H_4 loss along with the CO loss.
[d] The signal at *m/z* 136 has Gaussian shape; thus C_2H_4 instead of CO loss is assumed.

origin and composition of ions with *m/z* 119 (loss of 73 u in total) is unclear and indicates the occurrence of competing rearrangement processes. The fragmentation of metastable ions **5**$^{\bullet+}$ generated from ethyl thienylpropanoate is more similar to that the homocyclic ethyl ester analogue **1**$^{\bullet+}$ and the combined losses of ethanol and carbon monoxide strongly dominate in this case as well. In analogy to the homocyclic ions forming ionised styrene, $C_6H_5CHCH_2^{\bullet+}$ (*m/z* 104), as shown in Scheme 1, the ions resulting from the combined



Scheme 3. Competing fragmentation channels of the metastable molecular ions of *n*-propyl dihydrocinnamate **3**$^{\bullet+}$.



Scheme 4. Competing fragmentation channels of the metastable molecular ions of ethyl 4-phenylbutanoate **6**•+.

losses of CO and ethanol are assumed to have the structure of 2-vinylthiophene, $(C_4H_3S)CHCH_2^{\bullet+}$ (*m*/*z* 110). Whereas the $C_7H_7^+$ fragment ion (*m*/*z* 91) is not formed from any of the ions **1**•+–**4**•+, the more electron-rich thiophene core enables the cleavage of the "benzylic" C–C bond to give ions $C_5H_5S^+$ (*m*/*z* 97).

Remarkably, the metastable molecular ions of ethyl phenylbutyrate, **6**•+, reveal an extremely simple fragmentation behaviour (Scheme 4), as may have been expected. Here, all of the imaginable McLafferty reaction channels cannot compete with the simple loss of ethanol. We did not perform any labelling experiments in this case but we feel that a detailed analysis of the fragmentation of metastable ions **6**•+, including isotope labelling, would be very mechanistically interesting. As there is no loss of CO and no indication of any other C–C bond cleavage in these long-lived ions, we suggest the mechanism depicted in Scheme 4. The γ-hydrogen transfer from the benzylic methylene group to the carbonyl oxygen atom is assumed to be a hidden process as the C_α–C_β bond does not dissociate. However, transfer of a γ-hydrogen atom to the alcohol oxygen atom obviously represents a viable fragmentation channel. The distonic acyl cation, $C_6H_6(CH_2)_3CO^+$, (**h**″, *m*/*z* 142) generated in this way is likely to undergo a facile ring electrophilic attack at the benzyl radical moiety to form an ionised tautomer, **k**, of tetralone, in analogy to ion **h**′ (Scheme 2). To our knowledge, such ions have not been studied although they are reminiscent of the 5-methylenecyclohexa-1,3-diene radical ions generated by the McLafferty reaction of alkylbenzenes under EI conditions [29–32].

Finally, the fragmentation of the metastable ions of ethyl phenylacetate, **7**•+, and phenyl 3-phenylpropanoate, **8**•+, does not show any direct parallel to that of the ions discussed above. Neither the loss of ethanol nor of CO is observed in the MIKE spectra of these ions, but the McLafferty reaction of ion **7**•+ gives rise to the elimination of C_2H_4. Notably, a Gaussian-shaped $[M-28]^{\bullet+}$ peak appears in the MIKE spectrum of **7**•+, suggesting the elimination of C_2H_4, instead of a flat-topped one observed for the expulsion of CO in most of the previous cases. It is obvious that the benzylic methylene group cannot act as a hydrogen atom donor. Instead, moderate loss of acetaldehyde occurs ($[M-C_2H_4O]^{\bullet+}$, *m*/*z* 120), as does the anticipated benzylic cleavage giving rise to ions $C_7H_7^+$ (*m*/*z* 91). The very last case studied here are the metastable molecular ions of phenyl dihydrocinnamate, **8**•+. These ions do not show any of the major fragmentation paths of the analogous alkyl esters. Besides a minor loss of water, again pointing to deep-seated rearrangement processes, α-cleavage of the ester functionality is the principal fragmentation reaction, giving rise to ions $[M-C_6H_5O]^+$ with *m*/*z* 133. Nevertheless, the occurrence of a hydrogen transfer from the benzylic methylene group to the phenoxy residue – probably with a preceding but hidden hydrogen exchange involving the two *ortho*-positions of the aromatic ring – is indicated by the formation of ionised phenol, $C_6H_6O^{\bullet+}$ (*m*/*z* 94), in minor relative abundance.

3. Conclusion

Further insights into the EI-induced fragmentation of the radical cations of ethyl 3-phenylpropanoate (ethyl dihydrocinnamate) and related esters have been gained by studying their mass-analysed ion kinetic energy (MIKE) spectra. The complete scrambling involving the four hydrogen atoms at the benzylic methylene and the benzylic *ortho*-positions has been found to precede the fragmentation of the metastable ions of ethyl 3-phenylpropanoate. At least eight transfer cycles take place prior to the rate-determining hydrogen transfer giving rise to fragmentation. While this process is assumed to be a general feature of homologous and analogous dihydrocinnamates, the fragmentation of the metastable ions of related arylalkyl esters bearing modified alcohol and/or acid moieties differs markedly from that of the title compound. The long-known oxygen rearrangement giving rise to ions $C_7H_7O^+$ (*m*/*z* 107) in the EI mass spectrum of ethyl dihydrocinnamate was found to occur also with most of the other esters studied here, but MIKE spectrometry clearly revealed that this process is a high-energy reaction in all cases occurring without hydrogen scrambling.

4. Experimental

4.1. Mass spectrometry

All measurements were carried out on a double-focusing instrument, AutoSpec (Fisons, Manchester, UK) with a three-sector, EBE geometry. The compounds were introduced into the EI source via the direct insertion probe. The electron energy was set at 70 eV, the trap current at 400 μA, the accelerating voltage at 8000 V, and the source temperature at ca. 200 °C. Fragmentation of the metastable ions in the third field-free region was registered by selecting the precursor ion by the magnetic field and scanning the field of the second electrostatic analyser. The MIKE spectra are representative examples for several independent measurements and averaged from at least ten consecutive scans.

4.2. Synthesis: General

^{1}H NMR spectra were measured at 300 MHz, 400 MHz or 500 MHz ($CDCl_3$/TMS) on a Bruker AM 300 instrument, JEOL ECX-300, Bruker AVIII 400, and a Bruker DRX 500 instrument, respectively. Standard EI mass spectra were obtained as described above. Deuterium contents were evaluated from the EI mass spectrometric data after correction for naturally occurring ^{13}C. IR spectra were recorded on a Nicolet Avatar 360 Fourier transform-infrared spectrometer. GC/MS data was collected on Agilent 6890/5973 gas chromatograph/mass spectrometer. All distillations were performed using a Büchi GKR 50 kugelrohr apparatus. TLC: Silica (Kieselgel 60) on aluminium foil with fluorescence indicator F_{254}, thickness 0.2 mm (Merck). Microwave reactions were run in a CEM Discovery Microwave Reactor.

General esterification procedure. To the mixture of the carboxylic acid in excess alcohol was added 0.1 mL of concentrated sulphuric acid. The mixture was heated to reflux with stirring. After 12 h the reaction was cooled to room temperature and transferred to a separatory funnel. Saturated aqueous sodium bicarbonate was added and the desired product was extracted with diethyl ether. The combined organic layers were collected and dried over anhydrous magnesium sulphate, filtered, and concentrated under reduced pressure.

Ethyl 3-phenylpropanoate (1). The parent ester was prepared from dihydrocinnamic acid (496 mg, 3.30 mmol) and absolute ethanol (7.89 g, 171 mmol) to produce **1** as an oil. IR (neat, cm^{-1}): 1735 (C=O). ^{1}H ($CDCl_3$, 500 MHz): δ 1.23 (t, J = 7.2 Hz, 3H), 2.61 (t, J = 7.8 Hz, 2H), 2.95 (t, J = 7.9 Hz, 2H), 4.13 (q, J = 7.2 Hz, 2H), 7.20 (m, 3H), 7.28 (t, J = 7.6 Hz, 2H). MS (EI, 70 eV): m/z (%) 178 (27), 150 (4), 149 (2), 133 (13), 107 (41), 105 (45), 104 (100), 103 (11), 91 (64), 79 (15), 78 (13), 77 (19), 65 (9), 63 (4), 51 (11), 50 (4), 43 (5), 41 (2), and 39 (8).

[D$_5$]Ethyl 3-phenylpropanoate (1a). The [*ethyl*-d$_5$]-labelled ester **1a** was prepared from dihydrocinnamic acid (509 mg, 3.39 mmol) and perdeuterated ethanol (820 mg, 16.0 mmol) to yield an oil. IR (neat, cm^{-1}): 1730 (C=O). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.65 (t, 2H), 3.00 (t, 2H), 7.25 (m, 5H). MS (EI, 70 eV): m/z (%) 183 (28.3, [D$_5$]-M$^{\bullet+}$), 182 (2.0, [D$_4$]-M$^{\bullet+}$), 181 (0.4, [D$_3$]-M$^{\bullet+}$), 133 (9.7), 132 (1.6), 107 (44), 106 (5.5), 105 (46), 104 (100), 103 (10), 92 (13.3), 91 (43.7). D content: 98.2% (EI-MS).

Ethyl [2,2-D$_2$]-3-phenylpropanoate (1b). The [2,2-d$_2$]-labelled ester **1b** was generated from ester **1** in low yield by H/D exchange under basic conditions. A solution of sodium ethoxide in [*O*-D]ethanol was prepared by reaction of sodium metal (50 mg, 2.2 mmol) in [*O*-D]ethanol (2.0 mL). Ethyl 3-phenylpropanoate (180 mg, 1.0 mmol) was added to the solution at ambient temperature and the mixture was stirred overnight. The mixture was diluted with diethyl ether and the precipitate was filtered off. The filtrate was concentrated under reduced pressure and the residual liquid was analysed. ^{1}H ($CDCl_3$, 500 MHz): δ 1.23 (t, 3H), 2.60 (m, ca. 0.25 H), 2.92 (br s, 2H), 4.10 (q, 2H), 7.20 (m, 3H), 7.26 (m, 2H). GC/MS (EI, 70 eV): m/z (%) 180 (22, [D$_2$]-M$^{\bullet+}$), 179 (11, [D$_1$]-M$^{\bullet+}$), 135 (6), 134 (3), 108 (8), 107 (75), 106 (100), 105 (54), 104 (16), 91 (64). D content: 83% (EI-MS) or 84% (^{1}H NMR).

Ethyl [2,2,3,3-D$_4$]-3-phenylpropanoate (1c). The [2,2,3,3-D$_4$]-labelled ester **1c** was prepared from commercial ethyl phenylpropiolate by catalytic deuteration with deuterium gas. A solution of ethyl phenylpropiolate (260 mg, 1.49 mmol) in ethyl acetate (3.0 mL) containing suspended palladium-on-charcoal (50 mg, 10% Pd) was stirred under deuterium gas at ambient temperature and pressure for 2 h. After purging with argon the catalyst was filtered off and the solvent was removed under reduced pressure to give an almost colourless oil (150 mg, 55%). ^{1}H ($CDCl_3$, 500 MHz): δ 1.22 (t, 3H), 2.60 (br m, ca. 0.13 H), 2.92 (br m, ca. 0.29 H), 4.12 (q, 2H), 7.20 (m, 3H), 7.26 (m, 2H). MS (EI, 70 eV): m/z (%) 182 (34.7, [D$_4$]-M$^{\bullet+}$), 181 (17.6, [D$_3$]-M$^{\bullet+}$), 180 (3.9, [D$_2$]-M$^{\bullet+}$), 179 (0.7, [D$_1$]-M$^{\bullet+}$), 137 (15), 136 (9), 135 (3), 134 (2), 109.096 (42, $C_8H_5D_4^+$), 109.062 (62, $C_7H_5D_2O^+$), 108 (82), 107 (100), 106 (38), 105 (11), 104 (3), 94 (9), 93 (80), 92 (40), 91 (9). D content: 88% (EI-MS) or 89% (^{1}H NMR).

Ethyl 3-([D$_5$]phenyl)propanoate (1d). The [*phenyl*-D$_5$]-labelled ester **1d** was prepared in a two-step procedure starting with a Heck coupling. A 10 mL oven-dried microwave vessel was charged under N_2 with 10 mg (0.044 mmol) of palladium acetate, 17 mg (0.064 mmol) of triphenylphosphine, 500 mg (3.2 mmol) of [D$_5$]bromobenzene, 400 mg (0.43 mL, 4.0 mmol) of ethyl acrylate, and 1.0 mL of anhydrous triethylamine. The vessel was capped and heated under microwave irradiation, with stirring, for 40 min at 120 °C. Upon completion the reaction mixture was diluted with dichloromethane, transferred into a separatory funnel and neutralised with 200 mL of 10% HCl (4 × 50 mL portions). The organic layer was then collected, dried with anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. The crude mixture was purified by passing it through a pad of silica gel using hexanes as the eluent. The organic layer was concentrated under reduced pressure to yield an oil. IR (neat, cm^{-1}) 1700 (C=O). ^{1}H ($CDCl_3$, 400 MHz): δ 1.36 (t, 3H), 4.28 (q, 2H), 6.45 (d, 1H), 7.71 (d, 1H) GC/MS (EI): m/z 81, 96, 107, 108, 109, 112, 136, 153, 181. Catalytic hydrogenation of the [*phenyl*-D$_5$]cinnamate was accomplished under hydrogen gas by use of palladium-on-carbon with anhydrous tetrahydrofuran as the solvent, to yield **1d** as an oil. IR (neat, cm^{-1}): 2275 (C–D), 1730 (C=O). ^{1}H ($CDCl_3$, 400 MHz): δ 1.25 (t, 3H), 2.64 (t, 2H), 2.97 (t, 2H), 4.14 (q, 2H). MS (EI, 70 eV): m/z (%) 183 (42.8, [D$_5$]-M$^{\bullet+}$), 182 (1.9, [D$_4$]-M$^{\bullet+}$), 138 (17), 137 (1.9), 136 (1.5), 112 (60), 111 (8.3), 110 (67), 109 (100), 108 (48), 107 (12), 106 (3.6), 105 (5.2), 104 (8.9), 97 (7.8), 96 (81), 95 (13.6), 94 (1.8), 93 (1.6), 92 (1.5), 91 (6.0). D content: 99% (EI-MS).

Ethyl 3-([2,4,6-D$_3$]phenyl)propanoate (1e). The [*phenyl*-2,4,6-D$_3$]-labelled ester **1e** was also prepared by Heck coupling using the above reaction conditions starting with [2,4,6–D$_3$]bromobenzene. IR (neat, cm^{-1}): 1713 (C=O). ^{1}H ($CDCl_3$, 400 MHz): δ 1.36 (t, 3H), 4.28 (q, 2H), 6.45 (d, 1H), 7.40 (s, 2H), 7.70 (d, 1H). GC/MS (EI): m/z 79, 80, 94, 106, 134, 151, 179. Catalytic hydrogenation of the [*phenyl*-2,4,6-d$_3$]cinnamate was accomplished under hydrogen gas by use of palladium-on-carbon with anhydrous tetrahydrofuran as the solvent, to yield **1e** as an oil. IR (neat, cm^{-1}): 1735 (C=O). ^{1}H ($CDCl_3$, 400 MHz): δ 1.25 (t, 3H), 2.64 (t, 2H), 2.97 (t, 2H), 4.14 (q, 2H), 7.30 (s, 2H). MS (EI, 70 eV): m/z (%) 181 (44.4, [D$_3$]-M$^{\bullet+}$), 180 (1.6, [D$_2$]-M$^{\bullet+}$), 136 (17), 135 (1.8), 110 (57), 109 (7), 108 (62), 107 (100), 106 (47), 105 (17), 95 (7.5), 94 (76), 93 (9.4), 92 (3.2). D content: 99% (EI-MS).

Ethyl 3-([3,4,5-D$_3$])phenylpropanoate (1f). A Heck coupling starting with [3,4,5-D$_3$]bromobenzene [29,37] afforded ethyl [*phenyl*-3,4,5-D$_3$]-cinnamate as an oil. IR (neat, cm^{-1}): 2280, 2260 (C–D), 1735 (C=O). GC/MS (EI): m/z 79, 94, 106, 134, 151, 179. ^{1}H ($CDCl_3$, 300 MHz): δ 1.34 (t, 3H), 4.26 (q, 2H), 6.46 (d, 1H), 7.52 (s, 2H), 7.68 (d, 1H). Catalytic hydrogenation of the deuterated cinnamate ester using palladium-on-carbon with ethanol as the solvent gave **1f** as an oil. IR (neat, cm^{-1}): 2285, 2265 (C–D), 1710 (C=O). ^{1}H ($CDCl_3$, 300 MHz): δ 1.23 (t, 3H), 2.6 (t, 2H), 2.95 (t, 2H), 4.13 (q, 2H), 7.20 (s, 2H). MS (EI, 70 eV): m/z (%) 181 (30.9, [D$_3$]-M$^{\bullet+}$), 180 (3.1, [D$_2$]-M$^{\bullet+}$), 136 (13), 135 (2.6), 134 (2.4), 110 (43), 109 (8.0), 108 (48), 107 (100), 106 (23), 105 (6.4), 95 (5.7), 94 (59), 93 (9.5), 92 (1.6). D content: 97% (EI-MS).

Methyl 3-phenylpropanoate (2). The general esterification procedure was followed using dihydrocinnamic acid (522 mg, 3.68 mmol) and methanol (7.92 g, 247 mmol). IR (neat, cm^{-1}): 1738 (C=O). ^{1}H ($CDCl_3$, 400 MHz): δ 2.65 (t, 2H), 2.97 (t, 2H), 3.69 (s, 3H), 7.19–7.25 (m, 3H), 7.27–7.33 (m, 2H). MS (EI, 70 eV): m/z (%) 164 (31), 133 (10), 132 (1), 131 (3), 107 (5), 105 (37), 104 (100), 103

(11), 91 (61), 79 (10), 78 (12), 77 (16), 65 (9), 63 (4), 51 (11), and 39 (9).

***n*-Propyl 3-phenylpropanoate (3).** The general esterification procedure was followed using dihydrocinnamic acid (502 mg, 3.34 mmol) and *n*-propanol (8.03 g, 134 mmol). IR (neat, cm^{-1}): 1733 (C=O). ^1H ($CDCl_3$, 400 MHz): δ 0.93 (t, 3H), 1.64 (sextet, 2H), 2.65 (t, 2H), 2.97 (t, 2H), 4.04 (t, 2H), 7.19–7.23 (m, 3H), 7.27–7.33 (m, 2H). MS (EI, 70 eV): *m*/*z* (%) 192 (31), 150 (12), 149 (4), 133 (24), 132 (2), 107 (43), 105 (50), 104 (100), 103 (11), 91 (85), 79 (14), 78 (14), 77 (19), 65 (9), 63 (4), 51 (11), 43 (16), 41 (11), and 39 (9).

Isopropyl 3-phenylpropanoate (4). The general esterification procedure was followed using dihydrocinnamic acid (508 mg, 3.38 mmol) and isopropyl alcohol (7.86 g, 131 mmol). IR (neat, cm^{-1}): 1732 (C=O). ^1H ($CDCl_3$, 400 MHz): δ 1.22 (d, 6H), 2.60 (t, 2H), 2.96 (t, 2H), 5.01 (septet, 1H), 7.18–7.23 (m, 3H), 7.26–7.32 (m, 2H). MS (EI, 70 eV): *m*/*z* (%) 192 (16), 150 (48), 149 (3), 133 (26), 132 (4), 107 (28), 105 (59), 104 (92), 103 (12), 91 (100), 79 (13), 78 (16), 77 (21), 65 (9), 63 (4), 51 (12), 43 (34), 41 (14), and 39 (12).

Ethyl 3-(3-thienyl)propanoate (5). The general esterification procedure was followed using 3-(3-thienyl)propanoic acid (1.72 g, 11 mmol) and absolute ethanol (0.75 g, 16.5 mmol). IR (neat, cm^{-1}): 1730 (C=O). ^1H ($CDCl_3$, 400 MHz): δ 1.26 (t, 3H), 2.69 (t, 2H), 3.18 (t, 2H), 4.16 (q, 2H), 6.84 (d, 1H), 6.93 (t, 1H), 7.15 (d, 1H). MS (EI, 70 eV): m/z (%) 184 (32), 156 (3), 155 (11), 139 (9), 113 (35), 111 (32), 110 (67), 109 (5), 107 (3), 105 (3), 104 (6), 97 (100), 91 (6), 85 (5), 84 (5), 78 (4), 77 (8), 71 (3), 69 (4), 67 (5), 66 (3), 65 (5), 63 (2), 58 (4), 57 (2), 53 (7), 51 (5), 50 (2), 45 (16), 43 (2), 42 (2), 41 (3), and 39 (12).

Ethyl 4-phenylbutanoate (6). The general esterification procedure was followed using 4-phenylbutanoic acid (495 mg, 3.01 mmol) and absolute ethanol (7.89 g, 171 mmol). IR (neat, cm^{-1}): 1732 (C=O). ^1H ($CDCl_3$, 400 MHz): δ 1.27 (t, 3H), 1.97 (quintet, 2H), 2.33 (t, 2H), 2.67 (t, 2H), 4.13 (q, 2H), 7.17–7.23 (m, 3H), 7.26–7.33 (m, 2H). MS (EI, 70 eV): *m*/*z* (%) 192 (22), 147 (49), 146 (33), 118 (4), 117 (18), 116 (2), 115 (7), 105 (29), 104 (79), 103 (7), 92 (9), 91 (100), 90 (3), 89 (7), 88 (55), 79 (4), 78 (8), 77 (10), 74 (9), 70 (15), 65 (25), 63 (7), 61 (24), 59 (38), 51 (10), 50 (3), 45 (7), 43 (8), 42 (4), 41 (10), and 39 (14).

Ethyl phenylacetate (7). The general esterification procedure was followed using phenylacetic acid (509 mg, 3.74 mmol) and absolute ethanol (7.89 g, 171 mmol). IR (neat, cm^{-1}): 1732 (C=O). ^1H ($CDCl_3$, 400 MHz): δ 1.25 (t, 3H), 3.63 (s, 2H), 4.16 (q, 2H), 7.25–7.37 (m, 5H). MS (EI, 70 eV): *m*/*z* (%) 164 (16), 119 (2), 105 (2), 92 (12), 91 (100), 90 (3), 89 (4), 65 (13), 63 (4), 51 (3), 43 (4), 41 (2), and 39 (6).

Phenyl 3-phenylpropanoate (8). The general esterification procedure was followed using dihydrocinnamic acid (500 mg, 3.33 mmol) and phenol (5.10 g, 54.2 mmol). IR (neat, cm^{-1}): 1756 (C=O). ^1H ($CDCl_3$, 400 MHz): δ 2.91 (t, 2H), 3.10 (t, 2H), 7.20–7.40 (m, 10H). MS (EI, 70 eV): *m*/*z* (%) 226 (7), 133 (57), 132 (14), 131 (11), 121 (6), 105 (96), 104 (19), 103 (12), 94 (67), 92 (3), 91 (100), 89 (3), 79 (11), 78 (9), 77 (25), 66 (11), 65 (30), 64 (3), 63 (8), 62 (2), 55 (4), 52 (3), 51 (15), 50 (5), 41 (2), 40 (4), and 39 (24).

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.ijms.2012.01.005.

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