Tetrahedron Vol. 30, pp. 2797 to 2799. Pergamon Press 1974. Printed in Great Britain

ELECTRON-IMPACT INDUCED FRAGMENTATION OF LABELED 3-(*m*-NITROBENZOYL)-2-METHYLPROPANOIC ACIDS

EVIDENCE FOR A STEPWISE McLAFFERTY REARRANGEMENT

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(*Received in the UK* 28 *December* 1973; *Accepted for publication* 25 *February* 1974)

Abstract—The mass spectra of deuterium and ^{18}O labeled 3-(*m*-nitrobenzoyl)-2-methylpropanoic acid reveal that the McLafferty rearrangement and the rearrangement process leading to protonated *m*-nitrobenzoic acid do not take place via a common intermediate. H–D exchange phenomena point to a stepwise McLafferty rearrangement.

Recently, a remarkable rearrangement upon electron-impact of 3-aroyl-2-methylpropanoic acids has been observed:[1]

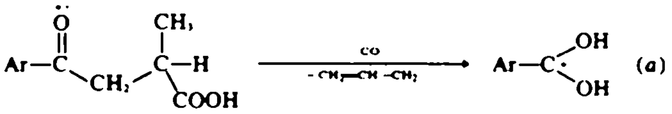


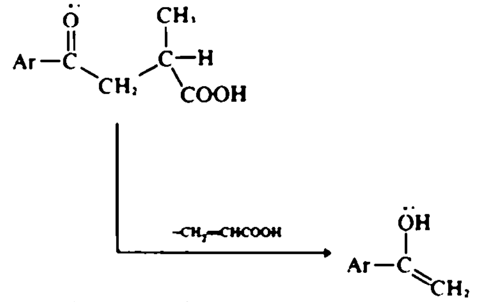
Table 1. Mass spectral data[a] of labeled 3 - (*m* - nitrobenzoyl) - 2 - methyl propanoic acids (Ar = *m*-$O_2NC_6H_4$)

No	Ar–CO–CH₂–R R =	Relative intensities and isotopic compositions[b] $[M]^{+\cdot}$	$\left[ArC\begin{smallmatrix}OH\\OH\end{smallmatrix}\right]^{+}$ (*a*)	$\left[ArC\begin{smallmatrix}OH\\CH_2\end{smallmatrix}\right]^{+\cdot}$ (*b*)
1	$-C(CH_3)(H)COOH$	6	13·9	25·2
2	$-C(CD_3)(H)COOH$	5	13·9 $\begin{cases}D_0 & 6\\ D_1 & 91\\ D_2 & 3\end{cases}$	19·5 $\begin{cases}D_0 & 41\\ D_1 & 58\\ D_2 & 1\end{cases}$
3	$-C(CH_3)(H)COOD$	7	13·1 $\begin{cases}D_0 & 19\\ D_1 & 81\\ D_2 & 0\end{cases}$	25·9 $\begin{cases}D_0 & 51\\ D_1 & 47\\ D_2 & 2\end{cases}$
4	$-C(CH_3)(H)CO^{18}OH$	5	13·0 $\begin{cases}^{18}O_0 & 52\\ ^{18}O_1 & 48\end{cases}$	25·5 $\begin{cases}^{18}O_0 & 100\\ ^{18}O_1 & 0\end{cases}$

[a] Mean values from 5–6 measurements corrected for isotopic content as calculated from the molecular ion region. m/e values: $M^{+\cdot}$, 237; *a*, 168; *b*, 165 (unlabeled species).

[b] Base peak at m/e 150, $(ArCO)^+$. Rel. int. ±0·2% (absolute), except for 3 (±1% due to the large corrections made for the isotopic content). Isotopic comp. ±2% (absolute) for 2 and 4, and ±5% for 3.

The formation of the protonated benzoic acid (*a*) involves both γ-H and -OH migration (γ with respect to the aroyl group), followed by loss of carbon monoxide and allyl radical, respectively. If γ-H transfer is the first step of this rearrangement process, this would imply directly that the McLafferty rearrangement:



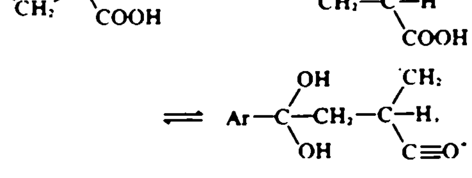
(*b*)

occurs in a stepwise fashion.

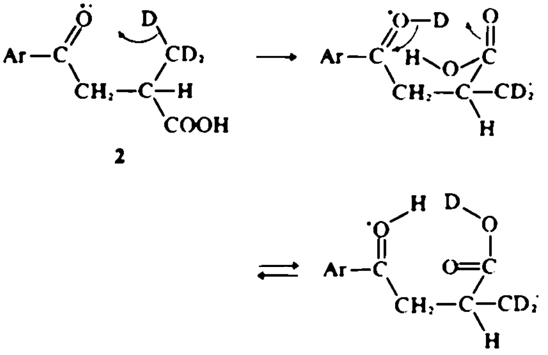
In order to obtain additional information concerning the above-mentioned rearrangement processes, we have undertaken a more detailed study of deuterium and ^{18}O labeled 3-(*m*-nitrobenzoyl)-2-methyl-propanoic acid ($Ar = m\text{-}O_2NC_6H_4$). The mass spectral data are summarized in Table 1.

First, the data show considerable H-D scrambling in *b* (2 and 3), whereas in *a* the scrambling is much less. Secondly, an isotope effect is operating on the McLafferty rearrangement of 2 (decreased intensity of *b*). Scrambling in the molecular ion before rearrangement cannot account for the isotopic compositions of *b* in 2 and 3. Furthermore, the data for *a* show that such scrambling if any is limited. On the other hand, the scrambling in *b* may be explained if (i) the McLafferty rearrangement is not site-specific, *i.e.* the H transferred originates in part from the OH group; (ii) scrambling takes place after the rearrangement, involving the originally transferred H and the H of the OH group. The value of the aforementioned isotope effect (expressed as k_H/k_D) depends on the mechanism. From the data for 1 and 2 values of 1·50 and 1·29 are obtained for (i) and (ii), respectively. The methyl esters of 1 and 2 reveal $k_H/k_D = 1{\cdot}26$ for the McLafferty rearrangement. In addition, the isotopic compositions of *b* in 2 and 3 are much better explained by (ii). Consequently, the scrambling in *b* is caused at least partly by scrambling after H transfer, *i.e.* the McLafferty rearrangement has to be interpreted as a 2-step process. This observation agrees with some recent data from other systems.[2]

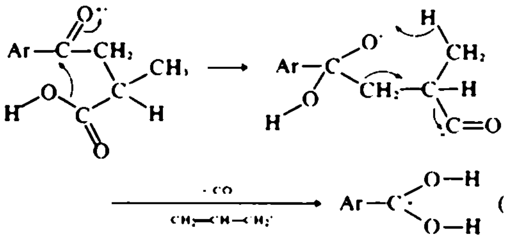
As the absence of ^{18}O in *b* (4) rules out any interconversion of OH according to:



which would be an attractive unifying mechanism for the rearrangement processes leading to both *a* and *b*, the H-D scrambling may be pictured in the following way:



With respect to the rearrangement process to *a* our present data prove the origin of the atoms transferred. Since no isotope effect for this process is observed OH migration will preceed the H transfer, which is in contrast to the assumption made earlier.[1] Together with our former observations,[1] the formation of *a* can be described with the following scheme:



(*a*)

Molecular models show that migration of OH and H cannot occur at the same time. The loss of carbon monoxide and allyl radical takes place both in one and in two steps as proved by the appropriate metastable transitions.

EXPERIMENTAL

The mass spectra were determined on a Varian-MAT SM-1 mass spectrometer operating at 70 eV, by using a direct insertion probe.

Trideuteriomethyl bromide (97% D_3) was purchased from Fluka A. G., water-^{18}O (72% ^{18}O) from Rohstoff-Einfuhr. The methyl ester of 2 was obtained with diazomethane.

3 - (*m* - *Nitrobenzoyl*) - 2 - *trideuteriomethylpropanoic acid* (2). $CD_3CH(COOEt)_2$ (5) was prepared from trideuteriomethyl bromide (18 g, 0·18 mole) and diethyl malonate (30 g, 0·16 mole) using the procedure of Cox and Elvain,[3] yield: 20 g (70%) of 5, b.p. 97°/22 mm. Reaction of the sodium derivative of 5 (10·5 g, 0·053 mole) with phenacyl bromide (10·6 g, 0·053 mole) in boiling ether (175 ml) for 2 h[4] yielded 7·7 g (49%) of diethyl phenacyltrideuteriomethylmalonate (6), b.p. 155°/1·3 mm. Saponifi-

cation of **6**,[4] followed by decarboxylation as described for the preparation of 2 - methyl - 4 - phenylbutanoic acid,[5] yielded 1·0 g (16%) of 3 - benzoyl - 2 - trideuteriomethylpropanoic acid, m.p. 139–140° (CCl_4). Nitration[1] of this compound (0·25 g, 1·3 mmole) with a mixture of 0·35 ml HNO_3 (1·52) and 1·65 ml H_2SO_4 (1·84) at 0° for 20 min yielded 0·16 g (50%) of **2**, m.p. 176–178° (EtOAc/PE 60–80), isotopic content 97% D_3, 3% D_2.

3 - (*m* - *Nitrobenzoyl*) - 2 - *methylpropanoic acid* - O - D (**3**) was obtained by dissolving **1** (10 mg) in MeOD (1 ml) followed by evaporating the solvent under vacuum. Isotopic content 43% D_0, 51% D_1, 5% D_2, 1% D_3.

3 - (*m* - *Nitrobenzoyl*) - 2 - *methylpropanoic acid*-^{18}O (**4**) was obtained by reflux of **1** (10 mg) in a mixture of dioxan (0·5 ml), toluene (0·5 ml), water-^{18}O (0·1 g) and H_2SO_4 (1·84, 0·1 g) for 5 days. The resulting mixture was chromatographied over silica (EtOAc), treated with water and the ppt filtered off. Isotopic content 45% $^{18}O_1$, 11% $^{18}O_2$.

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[4] *cf* F. G. Baddar, L. S. El-Assal, and A. Habashi, *J. Chem. Soc.* 1690 (1957), synthesis of 3 - (*o* - methoxybenzoyl) - 2 - methylpropanoic acid.

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