Rearrangements and Isomerism in the Molecular Ion of *o*-Methoxybenzoic Acid

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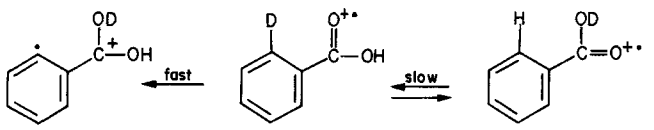
The molecular ion of *o*-methoxy-d_3-benzoic acid can undergo three different rearrangements and hydrogen/deuterium exchange between the functional groups. This can result in 14 isomers of the molecular ion before it decomposes giving fragments at *m/z* 105, 106, 107 and 108. Three types of isomer have been identified.

INTRODUCTION

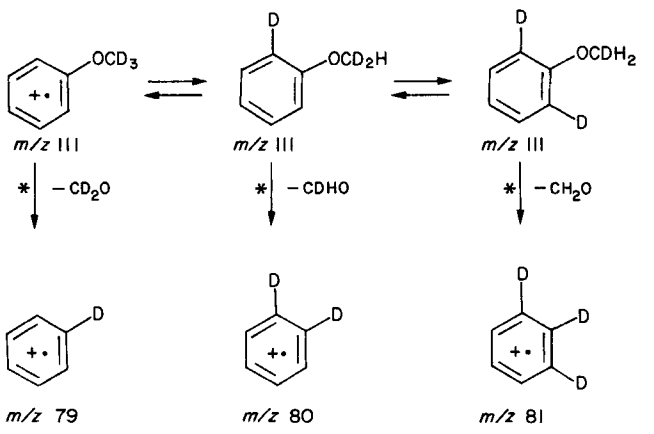
Deuterium labelling studies on benzoic acid[1,2] have shown that hydrogens from the *ortho* positions of the ring can exchange with those of the carboxyl group as shown in Scheme 1, and that there is both a fast non-reversible reaction and a slow reversible one. We refer later to this reaction as a Type 1 rearrangement (Scheme 1).



Type 1 rearrangement

Scheme 1.

Deuterium labelling of anisole has shown that hydrogens from the ring can exchange with those of the methoxyl group before the elements of formaldehyde are lost.[3] Presumably the *ortho* positions are involved but the reverse transfer using ring-labelled anisole, as was the case with benzoic acid,[1] does not appear to have been studied. We refer later to this reaction sequence as a Type 2 rearrangement (Scheme 2).



Type 2 rearrangement

Scheme 2.

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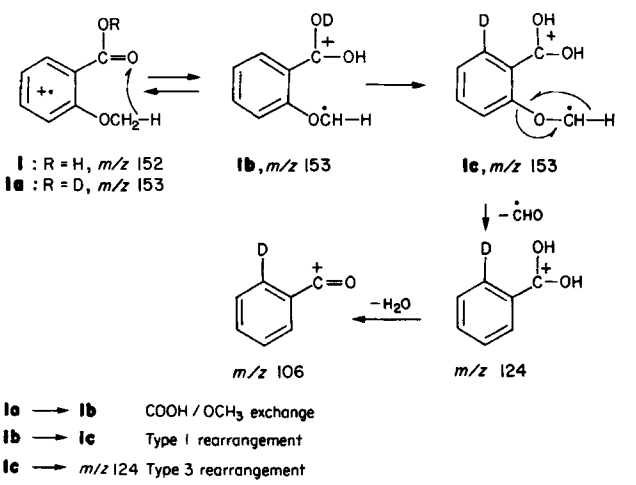
Ramana and Sundaram[4] recently reported a study of *o*-methoxybenzoic acid (**1**) in which they observed formation of an intense $[M-CHO]^+$ ion (50%). They explained its formation as the result of hydrogen transfer from the methoxyl to the carboxyl group followed by loss of a formyl radical, a Type 3 rearrangement (Scheme 3).



Ia : R = H, *m/z* 152
Ia : R = D, *m/z* 153
Ib, *m/z* 153
Ic, *m/z* 153

Ia → **Ib** COOH / OCH_3 exchange
Ib → **Ic** Type 1 rearrangement
Ic → *m/z* 124 Type 3 rearrangement

Scheme 3.

The $[M-CHO]^+$ ion was partly shifted to *m/z* 124 in the spectrum of *o*-$CH_3OC_6H_4COOD$ (**1a**) and this was attributed to exchange between the carboxyl deuterium and the *ortho* hydrogen atom, a Type 1 rearrangement, which resulted in the formation of a significant ion at *m/z* 106 (48%).

Because the deuterium in —COOD can back-exchange with adsorbed water in the ion source, we chose to study *o*-methoxy-d_3-benzoic acid (**2**) and for comparison the *meta* (**3**) and *para* (**4**) isomers.

RESULTS AND DISCUSSION

The 70 eV mass spectra of **2**, **3** and **4** are given in Table 1 and the 10 eV spectra in Table 2. In the spectrum of each isomer, the $[M-H]^+$ peak is negligible and there is no $[M-D]^+$ peak. Peaks at *m/z* 138

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Table 1. 70 eV mass spectra of the methoxy-d_3-benzoic acids[a]

m/z	2[b]	3	4
155	100	100	100
154	2	1	1
138	46	37	98
137	10	—	—
126	16	—	—
125	42	—	—
108	6	—	—
107	13	—	—
106	96	9	2
105	41	—	—
92	57	20	23
81	37	20	12
79	21	6	6
78	69	18	20
64	33	19	17
63	46	26	23

[a] Only the six most intense peaks are listed together with smaller peaks of significance. Complete spectra are available on request
[b] Metastable transitions of significance in the spectrum of **2**:
m^*/z 102.4 ≡ $[155]^+ \rightarrow [126]^+ + 29$;
m^*/z 100.8 ≡ $[155]^+ \rightarrow [125]^+ + 30$;
m^*/z 91.9 ≡ $[126]^+ \rightarrow [107]^+ + 19$;
m^*/z 91.6 ≡ $[125]^+ \rightarrow [107]^+ + 18$.

and 137 in the spectrum of **2** are due to $[M-OH]^+$ and $[M-OD]^+$; the former is the result of simple α-cleavage in the —COOH group and is much more intense than $[M-OD]^+$, formation of which requires H/D exchange before cleavage. In **3** and **4** there is no simple route to H/D exchange and $[M-OD]^+$ is absent. The weak peak at *m/z* 136 in the spectrum of **2** corresponds to loss of HOD from the molecular ion, and is of similar intensity to $[M-H_2O]^{+\cdot}$ in the spectrum of **1a**.[4] Peaks at *m/z* 126 and 125 in the spectrum of **2** are formed by losses of ĊHO and ĊDO from the molecular ion, a Type 3 rearrangement for which metastable ions are observed.

A peak at *m/z* 106 is observed in the spectra of all three isomers but is intense (96%) only in that of **2**, where it is formed (mainly at least) by a Type 3 rearrangement, because of the proximity of the carboxyl and methoxyl groups. This is not the case in **3** and **4** and only a weak *m/z* 106 ion is formed by ȮH loss and a Type 2 rearrangement. In **3**, where resonance interaction between the functional groups cannot occur, the intensity of *m/z* 106 is 9%; in **4** it is even less.

Table 2. 10 eV mass spectra of the methoxy-d_3-benzoic acids[a]

m/z	2	3	4
55	100.0	100.0	100.0
154	1.5	1.4	1.4
138	7.2	1.4	2.2
136	1.2	—	—
126	4.9	—	—
125	13.5	—	—
106	5.1	—	—
105	2.1	—	—
92	1.9	—	—

[a] Determined at the same repeller potential as the 70 eV spectra.

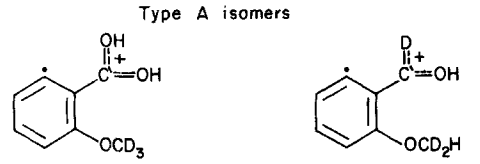
In the spectrum of **2** the intensity of *m/z* 107 (13%) is significantly higher than that calculated for the natural isotope peak of *m/z* 106, (7.4%), while *m/z* 105 is also intense (41%). The appearance of these peaks can be explained by H/D exchanges between carboxyl and methoxyl groups (via the reversible reaction preceding Type 3 rearrangement) together with exchanges between the two functional groups and their *ortho* ring hydrogen atoms (rearrangement Types 1 and 2), and finally decomposition by the sequence of Type 3 rearrangement.

Isomerism in the molecular ion

Exchange between the carboxyl and methoxyl groups can form two Type A isomers **2** and **2a** in which the positions of the charge and of the free electron are unspecified. Transfer of a hydrogen atom from the *ortho* position to the carboxyl group leaves the unpaired electron at the *ortho* position and the charge

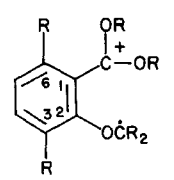
2, *m/z* 155 **2a**, *m/z* 155

Type A isomers

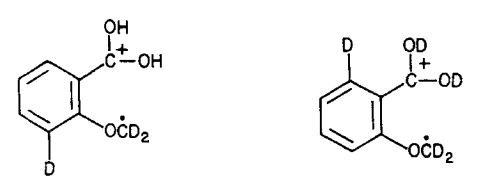


2b, *m/z* 155 **2c**, *m/z* 155

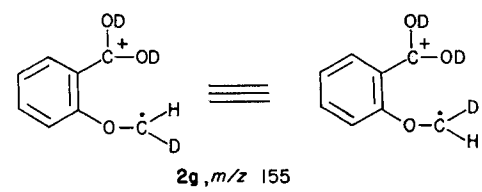
Type B isomers



2d : 3 R = H, 3 R = D, *m/z* 155

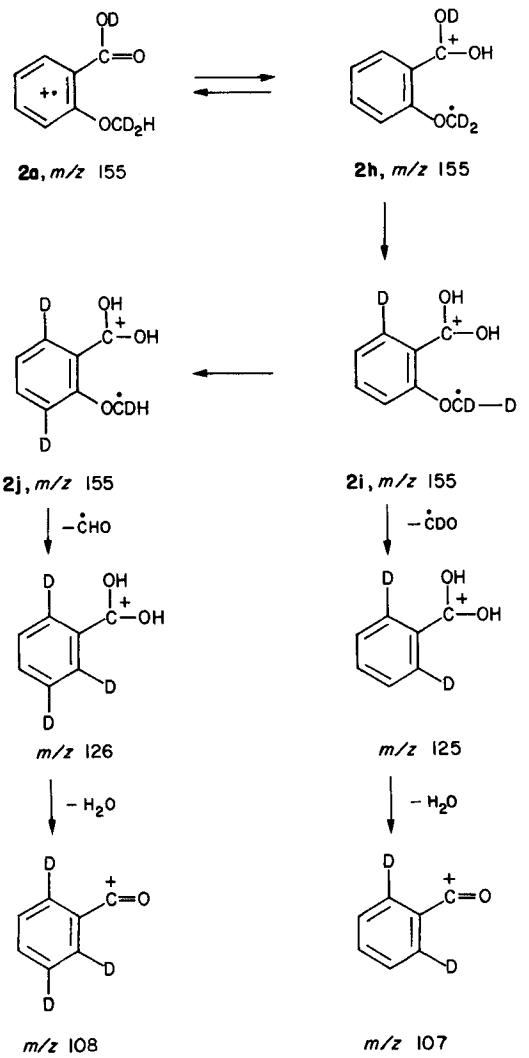


2e, *m/z* 155 **2f**, *m/z* 155



2g, *m/z* 155

Some type C isomers

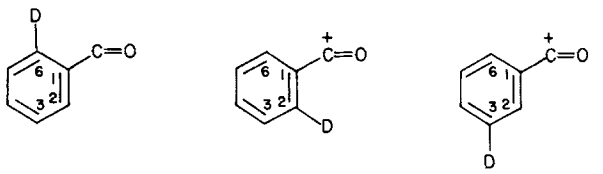


Scheme 4.

delocalized over the protonated carboxyl group to give a Type B molecular ion (**2b** and **2c**).[2]

If there is no random scrambling of ring hydrogens but only specific H/D exchange between the carboxyl and methoxyl groups together with rearrangements of the *ortho* hydrogens by Type 1 and 2 mechanisms, Type C isomers can be formed in which the charge is again considered to be delocalized over the carboxyl group and the unpaired electron on the methoxyl group. Type C isomers have a total of two different single (*ortho*) positions and two different double positions which are equivalent by rotation (**2d**). That is, there are four distinct positions which can be occupied by the three D atoms. With this in mind, one can write down systematically the structures of ten Type C isomers. Selected illustrative structures are given (**2d–2g**); some other Type C structures (**2h–2j**) and possible pathways to *m/z* 107 and 108 are shown in Scheme 4.

Type C structures will be attained at different rates and some may not be attained at all, for example **2i** is a possible precursor of *m/z* 107 and **2j** of *m/z* 108 both of which are observed in the 70 eV spectrum of **2**, but not in the 10 eV spectrum.



The abundant ion *m/z* 106 in the spectrum of **2** can be formed by several different pathways which lead to fragments of the same composition but with the deuterium attached to three different ring carbon atoms (ions *a*, *b*, and *c*).

It is also noteworthy that in some cases the deuterium atoms in CD_3 can each appear in a different fragment, OD or HOD, CDO, and attached to the ring.

In summary, there is a complex situation in the molecular ion: 14 isomers, three different rearrangements, and H/D exchange with its accompanying isotope effects, make further analysis involved. It is not attempted here.

EXPERIMENTAL

The methoxy-d_3-benzoic acids were prepared by methylation of the ethyl esters of the hydroxybenzoic acids with the same batch of CD_3I,[5] followed by alkaline hydrolysis of the ester, acidification and recrystallization. The isotopic composition of each was: d_3, 98.5; d_2, 1.5. Mass spectra were determined with a VG Micromass 7070F mass spectrometer: ionizing energy, 70 eV; filament current, 200 μA; accelerating voltage, 4 kV; source temperature, 200 °C, direct inlet probe; indicated source pressure, $8.0–8.5 \times 10^{-6}$ mbar.

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