Functional Group Interactions Apparent in the Electron Ionization Mass Spectra of Some Substituted *cis*-1,3-Cyclopentanedicarboxylic Acids and Their Derivatives

Pirjo Vainiotalo* and Pentti J. Mälkönen

University of Joensuu, Department of Chemistry, P.O. Box 111, SF-80101 Joensuu, Finland

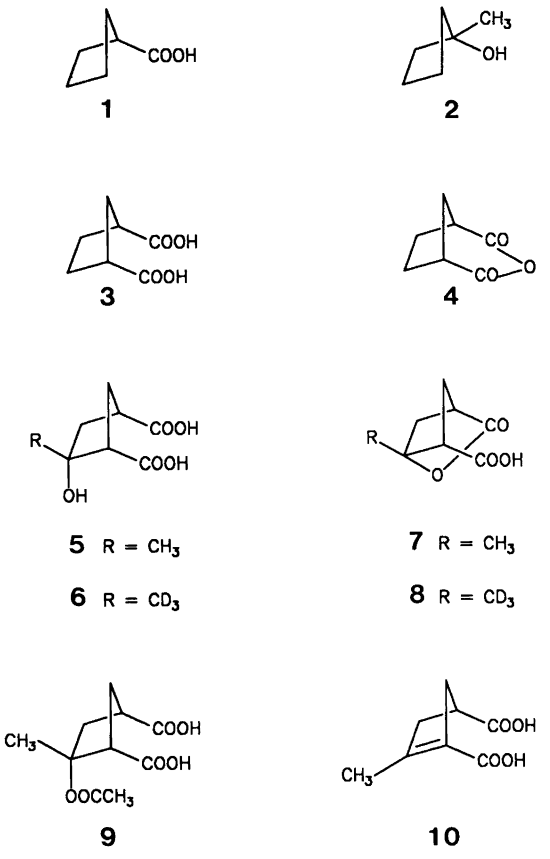
Vainiotalo, P. and Mälkönen, P. J., 1990. Functional Group Interactions Apparent in the Electron Ionization Mass Spectra of Some Substituted *cis*-1,3-Cyclopentanedicarboxylic Acids and Their Derivatives. – Acta Chem. Scand. 44: 500–503.

Electron ionization mass spectra have been recorded for some substituted *cis*-1,3-cyclopentanedicarboxylic acids and their derivatives. Very little direct interaction took place between the carboxy groups. Instead, interaction between one of the acid groups and a ring hydrogen atom facilitated the elimination of water, followed by the successive losses of CO and COOH. A strong effect was observed when a third substituent was introduced onto the cyclopentane ring. In particular a hydroxy or an acetoxy group at position 4 had a dominant effect in directing the decompositions of the molecular ions.

The effect of functional group interactions in the fragmentation of molecules with more than one functional group has long attracted attention in mass spectrometry.[1] Although many of the fragment ions formed from polyfunctional compounds can be related to a specific functional group, fragments frequently exist that can be rationalized only in terms of direct or indirect interaction between the functional groups.

Dicarboxylic acids are compounds, which typically show interactions between carboxy groups in the fragmentation of their molecular ions.[2–5] The main fragmentation route of 1,2-dicarboxylic acids starts with the elimination of carbon dioxide and/or water depending on the stereochemical arrangement of the carboxy groups.[3–5] When these groups are able to interact with each other a hydrogen atom may be transferred from one group to another and this is followed by expulsion of CO_2 or successive losses of H_2O and CO_2.[2–5] With cyclic diacids the loss of water has also been observed to occur as a consequence of interaction between a carboxy group and a ring hydrogen atom. The expulsion of CO follows this elimination.[4,5]

In this work we have examined several substituted *cis*-1,3-cyclopentanedicarboxylic acids and their derivatives, as depicted in Scheme 1. Under chemical ionization (CI) conditions most of them show functional group interactions that facilitate the elimination of water through intramolecular catalysis.[6] When isobutane or methane is used as the reagent gas, compound **3** decomposes through its anhydride (**4**) whereas compounds **5** and **9** seem first to form a lactone acid (**7**) structure.[6] Our main interest was to find out the kind of interactions and fragmentations that occur under electron ionization (EI) conditions. All fragmentation pathways were confirmed by exact mass measurement and metastable ion analysis. We would emphasize, however, that although the structures proposed for frag-



Scheme 1. The compounds studied.

* To whom correspondence should be addressed.

ment ions well describe the results, their existence has not been verified.

Ammonia CI mass spectra recorded[6] under conditions similar to those used in this work confirmed that the compounds are not dehydrated or decarboxylated thermally in the mass spectrometer.

Results and discussion

In order to distinguish the effects of functional group interactions in the mass spectra of the polyfunctional compounds **3–10**, we first studied the monofunctional compounds **1** and **2** as reference materials. The most important fragmentation of these compounds occurred through a rearrangement process. The base peak in the mass spectrum of cyclopentanecarboxylic acid (**1**) was at *m/z* 73, representing, at least formally, protonated acrylic acid. By analogy to processes presented by Kingston *et al.*[7] for some carbonyl compounds, the formation of this ion is best described in terms of a hydrogen transfer from the ring carbon at position 3 to the carbonyl oxygen, followed by rupture of the C(1)–C(2) and C(4)–C(5) bonds. Other primary fragment ions of compound **1** were $(M-OH)^+$, $(M-H_2O)^{+\cdot}$ and $(M-CO)^{+\cdot}$, but the abundance of the first two was extremely small.

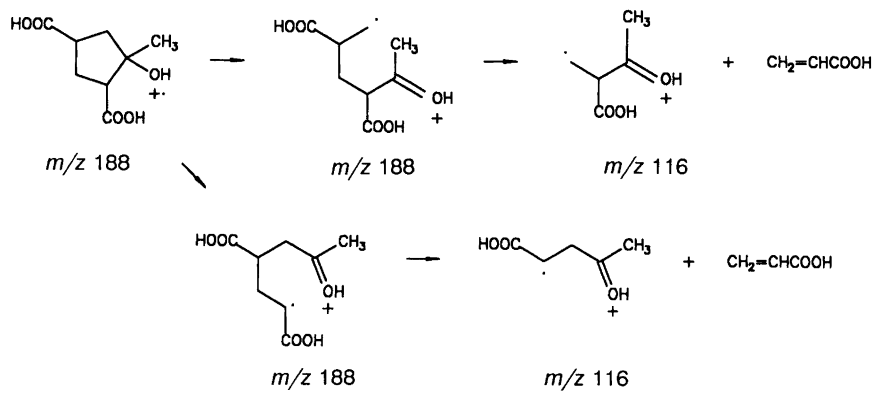
The $C_4H_7O^+$ ion at *m/z* 71, giving rise to the base peak in the spectrum of 1-methylcyclopentanol (**2**), was formed through a similar rearrangement reaction to that described earlier for cyclopentanol and cyclohexanol.[8]

Relative to the acid **1**, the fragmentation pattern changed drastically when a second acid group was introduced onto the cyclopentane ring, as can be seen from the mass spectrum of *cis*-1,3-cyclopentanedicarboxylic acid (**3**) in Table 1. The formation of protonated acrylic acid was no longer the most important reaction pathway, though it was still quite favourable. Instead, most of the fragmentation routes observed started with the elimination of water. Most likely, the *cis*-1,3-carboxy groups in the cyclopentane ring are both in equatorial position in the gas phase, as in the solid state,[9] but the energy barrier to the diaxial conformation is probably low. In the diaxial conformation the acid groups could easily interact with each other and one would expect the elimination of water from the molecular ion as a consequence. In this case the loss of water should be followed by elimination of carbon dioxide, as has been observed previously for some other diacids.[2–5] Although this reaction took place it was not very important. This also means that compound **3** did not decompose through the related anhydride structure (**4**) to any discernible degree, because compound **4** mainly decomposed through elimination of CO_2 from its molecular ion (Table 1). In this respect compound **3** behaved quite differently under EI conditions than under CI.[6]

The most prominent EI fragmentation pathway for compound **3** was the successive losses of H_2O, CO and COOH. This means that the second hydrogen atom needed for the lost water molecule did not originate from another acid

Table 1. Principal fragment ions (intensity ≥ 5 %) in the 70 eV mass spectra of the compounds studied. The data are uncorrected for isotopic contributions.

Compound	*m/z* (relative intensity)
1	114 (12) $M^{+\cdot}$, 86 (20), 73 (100), 69 (28), 68 (10), 67 (10), 55 (7), 42 (8), 41 (34), 39 (11), 27 (5)
2	100 (6) $M^{+\cdot}$, 85 (15), 82 (6), 72 (7), 71 (100), 67 (24), 58 (59), 57 (12), 55 (6), 43 (46), 41 (12), 39 (8), 27 (5)
3	158 (–) $M^{+\cdot}$, 112 (51), 97 (10), 95 (6), 86 (8), 73 (45), 68 (21), 67 (100), 66 (9), 65 (5), 55 (27), 45 (10), 43 (7), 41 (29), 40 (5), 39 (20), 29 (8), 27 (12)
4	140 (–) $M^{+\cdot}$, 96 (30), 68 (30), 67 (29), 55 (100), 53 (8), 41 (11), 40 (8), 39 (21), 27 (20)
5	188 (–) $M^{+\cdot}$, 155 (7), 152 (9), 142 (19), 126 (6), 125 (8), 124 (7), 116 (25), 115 (10), 113 (12), 112 (8), 110 (7), 102 (6), 100 (6), 99 (13), 98 (91), 97 (18), 84 (13), 83 (10), 82 (10), 81 (27), 79 (8), 73 (69), 71 (11), 69 (7), 59 (10), 56 (8), 55 (60), 53 (8), 45 (9), 43 (100), 41 (15), 39 (12), 27 (18), 15 (5)
6	191 (–) $M^{+\cdot}$, 173 (5), 157 (5), 155 (15), 145 (19), 129 (12), 128 (9), 127 (9), 119 (25), 118 (9), 114 (5), 113 (19), 112 (17), 110 (5), 111 (7), 105 (13), 103 (6), 102 (7), 101 (98), 100 (20), 99 (9), 97 (5), 88 (6), 87 (10), 85 (7), 84 (41), 83 (18), 82 (17), 81 (13), 74 (15), 73 (64), 70 (8), 69 (6), 62 (10), 61 (9), 57 (10), 56 (9), 55 (59), 46 (100), 45 (16), 44 (13), 43 (46), 41 (10), 39 (8), 29 (11), 27 (9)
7	170 (–) $M^{+\cdot}$, 152 (5), 126 (12), 113 (7), 111 (6), 110 (6), 99 (12), 98 (94), 97 (10), 82 (11), 81 (63), 80 (10), 79 (11), 56 (6), 55 (84), 53 (10), 45 (5), 44 (5), 43 (100), 41 (12), 39 (14), 27 (20)
8	173 (–) $M^{+\cdot}$, 155 (5), 129 (12), 113 (12), 102 (6), 101 (100), 100 (7), 99 (7), 84 (51), 83 (18), 82 (13), 81 (10), 73 (7), 62 (6), 56 (5), 55 (96), 54 (5), 46 (92), 45 (6), 44 (7), 43 (10), 41 (6), 39 (6), 27 (11)
9	230 (–) $M^{+\cdot}$, 152 (13), 142 (9), 126 (8), 125 (12), 124 (13), 113 (6), 111 (6), 99 (7), 98 (32), 97 (9), 83 (5), 82 (8), 81 (29), 80 (8), 79 (12), 73 (7), 61 (10), 55 (10), 45 (6), 44 (6), 43 (100), 41 (6), 27 (6)
10	170 (3) $M^{+\cdot}$, 153 (13), 152 (90), 125 (39), 124 (23), 108 (10), 107 (100), 97 (13), 96 (12), 95 (9), 81 (24), 80 (19), 79 (84), 78 (10), 77 (23), 67 (7), 65 (6), 55 (7), 53 (18), 52 (8), 51 (13), 50 (5), 45 (9), 43 (19), 41 (17), 39 (20), 27 (19)



Scheme 2. The formation of the *m/z* 116 ion from the molecular ion of compound **5**.

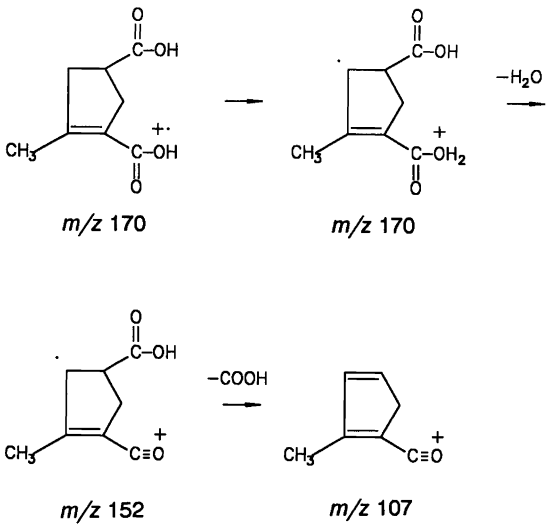
group but came from one of the ring carbon atoms. The spectrum of the carboxy-d_2 analogue of compound **3** verified this, but we were not able to determine the exact ratio of the D_2O and DHO losses due to the extremely small abundances of the ions. In any case this behaviour is closely analogous to that of *cis*-4-cyclohexene-1,2-dicarboxylic acid studied by Benoit and Holmes.[5] It also verifies the predominance of the diequatorial conformation of compound **3** in the gas phase. Although direct interaction between the functional groups was limited, the second substituent affected the energetics of the cyclopentane ring sufficiently to change the relative favourability of various fragmentation pathways.

A dramatic effect was observed when an additional substituent, a hydroxy group, was introduced onto position 4 of the cyclopentane ring *cis* relative to the acid groups, as can be seen from the mass spectrum of compound **5**. The hydroxy group played a dominant role in the decomposition of the molecular ion. Although the fragmentation route typical for compound **3**, involving successive losses of H_2O, CO and COOH and leading to the formation of ions *m/z* 170, 142 and 97, was clearly visible, it was no longer the most important route. Instead, there were two new fragmentation pathways initiated by the hydroxy group. The first, presented in Scheme 2, started as an α-cleavage reaction with respect to the hydroxy oxygen, with loss of acrylic acid and formation of the ion $C_5H_8O_3^{+\cdot}$ at *m/z* 116. This reaction sequence bears a close resemblance to the formation of the ion $C_4H_7O^+$ at *m/z* 71 with compound **2**, except that no hydrogen transfer was needed in the case of **5**, probably because the neutral fragment was stable acrylic acid. The *m/z* 116 ion then decomposed by elimination of water or a $C_2H_3O^{\cdot}$ radical, with formation of the *m/z* 98 or *m/z* 73 ion, respectively. The ion at *m/z* 98 formed one of the most intense peaks in the spectrum and was also formed in the second route initiated by the hydroxy group. This started as the elimination of H_2O (or D_2O in the case of the hydroxy-*d* carboxy-d_2 analogue) from the molecular ion and formation of the ion $C_8H_{10}O_4^{+\cdot}$ at *m/z* 170. This ion, possibly possessing the lactone acid structure (**7**), lost acrylic acid to form the *m/z* 98 ion by a process similar to the main fragmentation pathway of compound **7** and typical of bicyclo[2.2.1]heptane structures, see also Scheme 2.[10] Other fragmentations of the *m/z* 170 ion also resembled those of compound **7**. The formation of the lactone acid would be in analogy with the thermal[11] and chemical ionization results.[6] To test for this structure, the *m/z* 98 ions generated from compounds **5** and **7** were studied by the collision induced dissociation (CID) technique.[12] The CID spectra (Table 2) are seen to be closely, though not completely, similar; one must bear in mind, however, that the *m/z* 98 ion of compound **5** was formed through two routes which may have generated a mixture of structures. The spectra of the deuteriated compounds **6** and **8** allowed similar conclusions to be drawn.

Table 2. The CID spectra of the *m/z* 98 ions generated from compounds **5**, **7** and **9**. Intensities are normalized to a total fragment ion abundance of 100 %. The data are not corrected for metastable peaks.

m/z	**5**	**7**	**9**
43	22.2	17.9	24.8
53	8.2	5.5	11.1
55	43.3	43.5	37.8
69	8.2	9.2	11.1
70	18.1	23.9	12.1
81	–	–	3.1

When the hydroxy group in compound **5** is protected with an acetyl group (compound **9**), the stability of the molecule toward electron ionization decreases noticeably, as can be seen from Table 1. The spectrum of compound **9** was dominated by the $C_2H_3O^+$ ion at *m/z* 43, which probably was mostly formed directly from the molecular ion. The importance of the acetoxy group in directing the fragmentations of this compound was also revealed by the complete absence of the typical decomposition pathway observed for the other diacids studied, namely, the successive losses of H_2O, CO and COOH. Instead, the molecular



Scheme 3. The formation of the *m/z* 107 ion from the molecular ion of compound **10**.

ion first lost acetic acid to give rise to the ion $C_8H_{10}O_4^{+\cdot}$ at *m/z* 170. It is probable that a mixture of ions of different structures was formed, because the decomposition of the $C_8H_{10}O_4^{+\cdot}$ ion involved features typical of the decomposition of the γ-lactone structure (**7**) as well as of other structures. Other possible elimination products are β-lactone and/or unsaturated acids, but not compound **10** in any considerable amount because the abundance of the *m/z* 107 ion, which forms the base peak in the spectrum of compound **10**, would then have to be much larger. The *m/z* 98 ion formed from the *m/z* 170 ion, at least, did not have completely the same structure as that formed from compounds **5** and **7**, as can be seen from Table 2.

The addition of a double bond to the *cis*-1,3-cyclopentanedicarboxylic acid moiety, as in 2-methyl-1-cyclopentene-1,4-dicarboxylic acid (**10**), clearly affected the fragmentation behaviour (Table 1). Compared with the other diacids, compound **10** was more resistant towards electron ionization, even showing the molecular ion, in an unmistakable, though small amount. Also, the abundances of high mass fragment ions were noticeably greater than with the other acids. The most important fragmentation pathway was the successive losses of H_2O, COOH and CO. The fragmentation also took place in the order H_2O, CO and COOH, as in the case of compound **3**, but this sequence was much less favourable. A possible explanation for this preference is that conjugation between the double bond and the carboxy group lowered the ionization energy of the carboxy group, causing the ionization to occur mainly in this group. The proposed fragmentation of the resulting molecular ion is presented in Scheme 3. The ion $(M-H_2O-COOH)^+$ at *m/z* 107 gives rise to the base peak in the spectrum because of the stabilization caused by its conjugated double bond system. Irrespective of whether the hydrogen atom lost with water originates from the ring position 3 (as in Scheme 3) or 5, similar conjugation will be attained. The fragmentation routes starting with the elimination of water were so favourable that the rearrangement reaction leading to the formation of the *m/z* 73 ion, which was prominent for compound **3**, could no longer be observed. The molecular ion of compound **10** also lost COOH in one or two steps, analogously to cyclopentanecarboxylic acid (**1**).

Experimental

Measurements were made with a Jeol JMS D300 mass spectrometer equipped with a combined EI/CI ion source and connected to a Jeol JMA 2000H data system. Samples were introduced through a direct inlet probe at temperatures in the range 110–140 °C. Typical source conditions were: temperature 170 °C, electron energy 70 eV, accelerating voltage 3 kV and ionization current 300 μA. Accurate mass measurements were made at resolution 5000 using the data system. Fragmentation pathways were verified with metastable ion analysis and/or CID spectra using linked scans at constant B/E.

The preparation and stereochemical assignments of the compounds examined have been described elsewhere.[6]

References

1. Bosshardt, H. and Hesse, M. *Angew. Chem., Int. Ed. Engl. 13* (1974) 252.
2. Holmes, J. L. and St. Jean, T. *Org. Mass Spectrom. 3* (1970) 1505.
3. Benoit, F., Holmes, J. L. and Isaacs, N. S. *Org. Mass Spectrom. 2* (1969) 591.
4. Benoit, F. and Holmes, J. L. *Org. Mass Spectrom. 6* (1972) 541.
5. Benoit, F. and Holmes, J. L. *Org. Mass Spectrom. 6* (1972) 549.
6. Vainiotalo, P. and Mälkönen, P. J. *Org. Mass Spectrom. 22* (1987) 688.
7. Kingston, D. G. I., Hobrock, B. W., Bursey, M. M. and Bursey, J. T. *Chem. Rev. 75* (1975) 693.
8. Budzikiewicz, H., Djerassi, C. and Williams, D. H. *Mass Spectrometry of Organic Compounds*, Holden-Day, San Francisco 1967, p. 107.
9. Ahlgrén, M. and Mälkönen, P. J. *In preparation.*
10. Goto, T., Tatematsu, A., Hata, Y., Muneyuki, R., Tanida, H. and Tori, K. *Tetrahedron 22* (1966) 2213.
11. Mälkönen, P. J. *Suom. Kemistil. B 44* (1971) 12.
12. For leading reviews, see: (a) Levsen, K. and Schwarz, H. *Angew. Chem., Int. Ed. Engl. 15* (1976) 509; (b) Cooks, R. G., Ed., *Collision Spectroscopy*, Plenum Press, New York 1978; (c) Levsen, K. and Schwarz, H. *Mass Spectrom. Rev. 2* (1983) 77; (d) McLafferty, F. W., Ed., *Tandem Mass Spectrometry*, Wiley, New York 1983.

Received November 16, 1989.