The Behaviour of Stereoisomeric Ions in the Gas-Phase. The Case of some New Macrocyclic Ether-Tetraesters

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The electron impact mass spectrometric behaviour of some new diastereoisomeric macrocycles containing diglycolyl moiety as subcyclic unit is reported and discussed in detail with the aid of linked scans, exact mass measurements and collisionally activated decomposition mass analyzed ion kinetic energy spectra.

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Introduction.

Electron impact (EI) mass spectrometry usually fails in a clear characterization of stereoisomers.

Many papers on this subject demonstrated that stereoisomerism affects the EI induced fragmentation pattern only to a minor extent, mostly leading to different yields of the decomposition reaction, *i.e.* to minor differences in relative abundances of product ions [1].

In recent papers the mass spectrometric behaviour of stereoisomeric cyclohexanehexacarboxylic methyl esters [2] and 2,3,5,6-endobicyclo[2.2.2]-7-octenetetracarboxylic methyl esters [3] has been studied in detail with the aid of collisionally activated decomposition (CAD) experiments and we not only observed strong differences in relative abundances of product ions, but also different fragmentation pathways.

In the present paper we report another example of the power of mass spectrometry in the chemistry of stereoisomeric compounds, consisting in the study of the mass spectrometric behaviour of four new macrocyclic ether-tetraesters **1-4**, more exactly *trans*-2,5,8,15,18,21-hexaoxatricyclo[20,4,0,0^{9,14}]hexacosan-3,7,16,20-tetraone (**1-2**) and *cis*-2,5,8,15,18,21-hexaoxatricyclo[20,4,0,0^{9,14}]hexacosan-3,7,16,20-tetraone (**3,4**) [4], by means of linked scans [6], exact mass measurements and collisionally activated decomposition mass analysed ion kinetic energy spectra (CAD MIKES) [7].

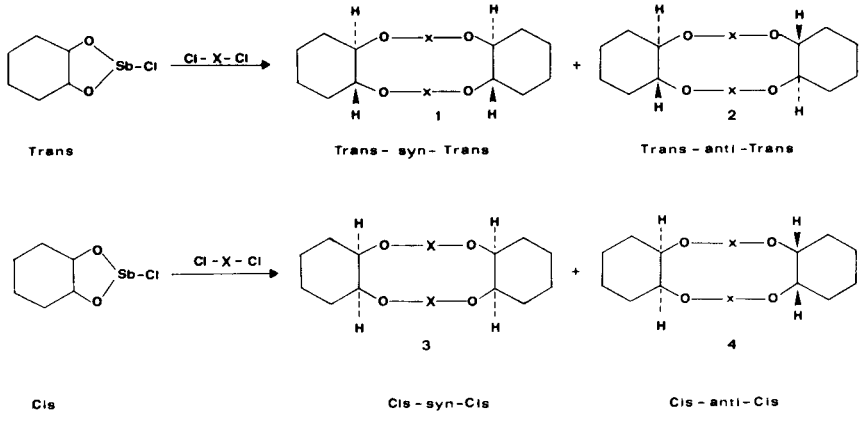
The title compounds are easily synthesized by reaction of 2-chloro-1,3,2-*trans*-cyclohexane stibolane or 2-chloro-1,3,2-*cis*-cyclohexane stibolane with diglycolyl chloride as reported in Scheme 1 [8].

The compounds **1-4** were separated by fractional crystallization and purified by column chromatography.

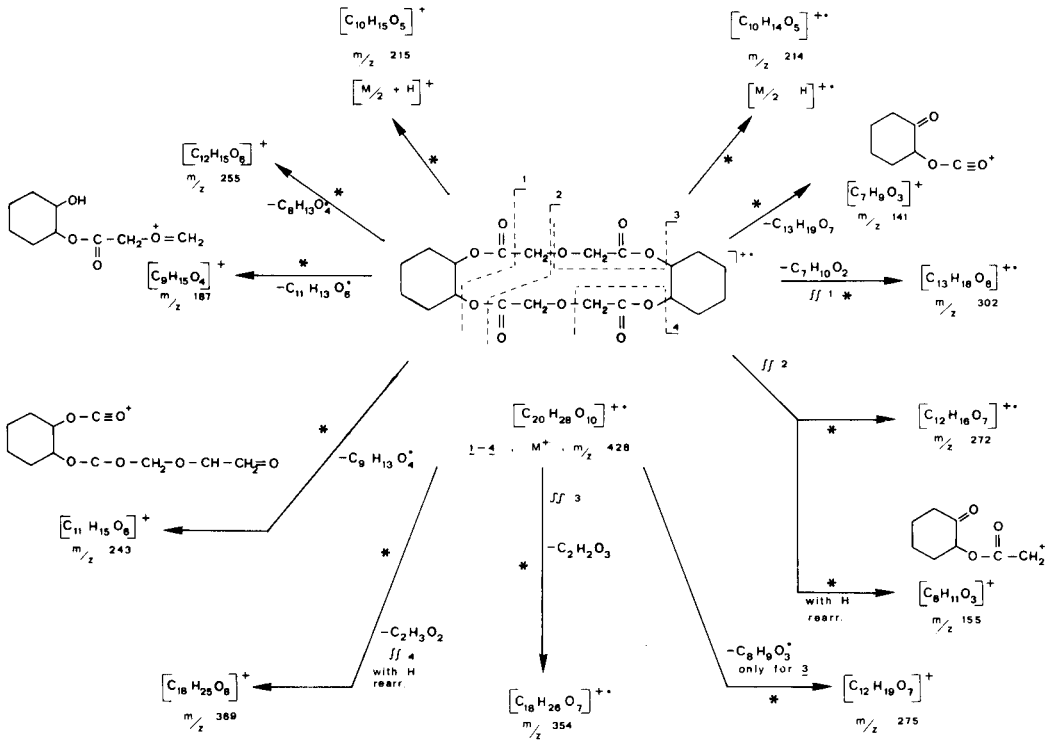
Results and Discussion.

The 70 eV EI mass spectra of compounds **1-4** are reported in Table I.

By means of exact mass measurements and linked scans (see Table II), the common primary decomposition pattern reported in Scheme 2 was obtained.



Scheme 1



Scheme 2

Table 1

EI Mass Spectrum of Compounds **1-4**

m/z	1	2	3	4
41	28	38	42	60
42	28	35	39	85
43	23	26	32	30
44	47	61	68	100
45	9	10	11	15
54	10	16	16	25
55	14	10	13	15
57	14	16	16	15
67	29	29	29	35
69	24	23	24	20
80	14	45	13	20
81	100	100	95	100
82	29	29	29	20
98	24	26	37	25
99	71	56	100	60
100	5	3	8	5
116	14	13	13	5
140	90	60	50	15
141	14	13	8	5
155	14	10	5	—
171	5	3	3	5
187	—	—	3	—
214	9	10	8	5
215	29	29	18	5
216	5	3	3	—
243	—	—	3	5
257	5	3	3	—
272	5	3	5	5
275	0.1	0.1	0.1	3
302	5	3	5	5
354	10	7	3	—
369	0.5	0.2	0.5	0.3
428	14	13	5	0.03
429	5	5	1	0.01
430	—	1	—	—

Molecular ions are always present, quite abundantly for **1** and **2** and rather poorly for **4** (0.03).

Protonated molecular ions are sometimes observed in mass spectrometry of macrocyclic polyether-ester compounds [9] and in the present case are almost or at least scarcely abundant.

For the title compounds the presence of many primary decomposition pathways is noteworthy (see Table II) while for catecholic macrocyclic [10] and for cyclohexane tetraesters [11], most of the total ion current was due to further decomposition routes. This behaviour must be ascribed to the presence of the ethereal oxygen between the two methylene groups.

Table 2

B/E = Constant Linked Scans of Moleculr Ions of Compounds **1-4**. Unimolecular Primary EI-Induced Decomposition

m/z	1	2	3	4
141	1	8	4	4
155	3	17	4	5
187	0.1	0.1	0.1	5
214	3	8	4	8
215	4	17	7	9
243	4	17	4	12
255	6	8	4	11
272	2	8	11	16
275	3	42	21	100
302	22	17	100	84
303	5	17	14	33
354	100	100	57	8
355	22	58	18	4
369	4	8	4	1

Table 3

CAD MIKES of Molecular Ions of Compounds **1-4**

m/z	**1**	**2**	**3**	**4**
81	57	17	50	7
100	25	10	44	14
116	11	4	12	6
140	53	39	52	10
155	98	78	96	24
171	—	—	—	—
205	19	18	39	31
214	30	21	28	11
215	33	28	39	16
257	14	10	15	14
272	7	6	20	14
275	10	13	32	100
302	25	33	100	47
330	7	9	10	9
348	11	10	15	11
354	100	100	83	9
369	11	11	9	4
400	3	2	3	3

Table 4

CAD MIKES of Ionic Species $(M/2 + H)^+$ Originating by EI of Compounds **1-4**

m/z	**1**	**2**	**3**	**4**
45	10	7	3	4
57	7	4	3	4
67	21	13	12	9
81	100	100	87	52
99	66	89	100	100
116	7	9	8	9
135	14	27	29	22
141	10	13	16	4

Table 5

CAD MIKES of Ionic Species $(M/2)^{+\cdot}$ Originating by EI of Compounds **1-4**

m/z	**1**	**2**	**3**	**4**
44	9	3	4	6
57	6	2	4	4
71	6	2	4	4
81	44	22	29	28
99	54	33	100	100
116	19	11	21	31
140	100	100	92	34
155	15	11	4	4
187	2	1	4	3
213	7	4	8	14

The formation of the $(M/2 + H)^+$ and to a minor extent, of the $(M/2)^{+\cdot}$ ionic species (m/z 215 and 214 respectively) proves to be favoured, paralleling the behaviour of catecholic as well as cyclohexane macrocyclic tetraesters [10,11].

Also in the present case, the formation of the $(M/2 + H)^+$ ion is difficult to depict because several positions of the macrocyclic ring could be involved in a symmetrical cleavage, giving rise to ions with identical mass and composition.

At any rate the different ratios $(M/2 + H)^+/(M/2)^{+\cdot}$ of compounds **1**, **2** and **3** with respect to compound **4** are noteworthy, thus proving that stereoisomerism clearly affects this decomposition process.

The main ring cleavage are reported directly in Scheme 2 and the formation mechanism of most of the product ions is quite obvious.

As already observed [11] also in this case, the H transfer from the cyclohexane ring to the acyclic species is present.

Being a "weak point" of the macrocyclic ring, the presence of the intermediate ethereal oxygen is the "driving force" of most of the fragmentation pathways (see Scheme 2).

Apart from the description of the fragmentation mechanisms, it should be noted that strong differences in relative abundances are present as well as peculiar fragmentation routes, which prove the capabilities of mass spectrometry in characterizing the stereoisomers.

These differences in the mass spectrometric behaviour of the title compounds are well enhanced by the B/E spectra (Table 2), *i.e.* considering the unimolecular decompositions which take place in a well-defined time window (*i.e.* with a well-defined reactions rate).

Following this point of view, it can be observed that in the first free field region, the most favoured decomposition reaction(s) are: i) for compounds **1** the losses of $C_7H_{10}O_2$ (m/z 302, cleavage 1 in Scheme 2) and $C_2H_2O_3$ (m/z 354, cleavage 3 in Scheme 2); ii) for compound 2 the same losses with and without H rearrangement (m/z 302 and 303; m/z 354 and 355); many other decomposition pathways are present, leading to ion at m/z 155, 215, 243 and 275; iii) for compound **3** the formation of ionic species at m/z 275, 302, 303, 354 and 355; iv) for compound **4** the formation of ionic species at m/z 243, 255, 272, 275, 302 and 303.

The closest similarity is between the B/E spectra of compounds **1** and **2**, but clear differences in relative abundances (see, for example, ions at m/z 155) lead to an unequivocal characterization of the two stereoisomers.

Greater differences are present with respect to compounds **3** and **4**.

The same behaviour is observed for the CAD MIKE spectra of molecular ions of compounds **1-4** (Table 3).

Again compounds **1** and **2** give rise to similar, but

always distinguishable, spectra.

The most abundant collisionally induced fragmentation product for compound **3** is the ionic species at m/z 302; while for compound **4**, it is represented by ions at m/z 275.

It is quite surprising that the maintenance of stereoisomerism, proved for the molecular ions, is retained also by the $(M/2 + H)^+$ and $(M/2)^{+\cdot}$ fragments.

In fact their CAD MIKE spectra (reported in Table 4 and 5 respectively) are still different, but in the present case the pairs **1-2** and **3-4** are practically superimposable, in agreement with the stereochemistry of the original products.

EXPERIMENTAL

All mass spectrometric measurements were performed on a VG ZAB 2F instrument operating in EI conditions (70 eV, 200 uA). Samples were directly introduced into the ion source at a temperature of 200°.

Exact mass measurements were performed with the peak matching technique at 30,000 resolving power (10% valley definition).

Metastable transitions were detected by B/E and B^2/E linked scans [6].

Collisionally activated decomposition experiments [7] were obtained by 8 keV ions colliding with nitrogen in the second free field region. The pressure in the collision cell was such as to reduce the main beam intensity to 30% of its usual value.

Compounds **1-4** were analytically pure samples synthetized and purified as previously described [8].

REFERENCES AND NOTES

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[4] At the present state of our research, we are in a position to attribute unequivocally the exact structure to the *trans* and *cis* isomers of the macrocycles, but we are not yet in a position to define which stereoisomer is *syn* and which is *anti*. Analogously as reported in the literature [5], we have arbitrarily called the compounds **1** *trans-syn-trans*, **2** *trans-anti-trans*, **3** *cis-syn-cis* and **4** *cis-anti-cis*.

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