Electron Impact Mass Spectrometry of Some Cyclic Tetraesters Containing a Tartaric Moiety

Gianni Podda*

Istituto di Chimica Farmaceutica e Tossicoligica Università di Cagliari, Via Ospedale 72, 09100 Cagliari, Italy

Pietro Traldi*

Istituto di Polarografia ed Elettrochimica Preparativa del CNR Corso Stati Uniti 4, 35100 Padova, Italy

Received December 27, 1984

The mass spectrometric behaviour of some cyclic tetraesters containing tartaric moiety is described and discussed in detail with the aid of linked scans and exact mass measurements. The peculiar fragmentation patterns are emphasized.

J. Heterocyclic Chem., **22**, 1129 (1985).

Introduction.

The great interest in crown ethers and polyether-esters as ion binders and catalytic reagents is represented by the several papers published during the past years [1,2].

Many of these compounds often exhibit biological and synthetic properties similar to those of some natural antibiotic like valinomycin [2] and nonactin [3-5].

Following our research in the field of macrocyclic chemistry, the stereoisomeric compounds **1-4** (see Scheme 1) were simply obtained by reaction of corresponding dioxastannolane with diacyl chlorides in benzene solution and purified by column chromatography as reported in experimental.

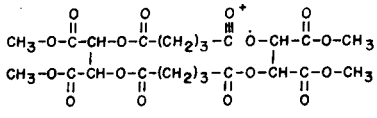
Persisting in our interest in mass spectrometry of ether and ether-tetraester compounds [6-9], we have undertaken the present study.

Results and Discussion.

The 70 eV electron impact mass spectra of compounds **1-4** are reported in Figures 1-4 respectively. They show quite abundant molecular ions, while the $[M + H]^+$ species common in EI mass spectrometry of crown ethers [7] containing aromatic moieties are completely absent in the present case. This behaviour can be interpreted considering the capability of trapping hydrogen atoms of crown ethers, which is strictly related to the presence of an aromatic system along the crown.

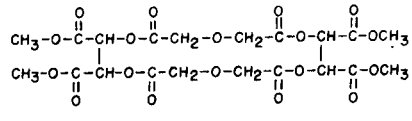
By means of linked scans and exact mass measurements, the common fragmentation pattern reported in Scheme 2 has been obtained. The more significative ionic species together with their m/z and relative abundance values are reported in Table 1.

The losses of methoxy and CH_3COO radicals (leading to ions **a** and **b**) is observed for all the examined compounds and can easily be explained by simple bond cleavages. More unusual is the primary loss of $\cdot OCHCOOCH_3$ which leads to quite abundant ionic species **c**. This EI induced decomposition process implicates the cleavage of two bonds and may suggest the presence of molecular ions in an open structure such as **1a** for compound **1** (and similar ones for compounds **2-4**).



1a

Starting from this ionic structure, the formation of ions **c** could simply originate through the cleavage of the CH-CH bond. It should be emphasized that for the strictly related compounds like **5**, in which the alkylic chain is interrupted by an ethereal oxygen [10]; decomposition pathways implicating the loss of CH_3-OCO-CHO are completely absent. Consequently, from the analytical point of view,

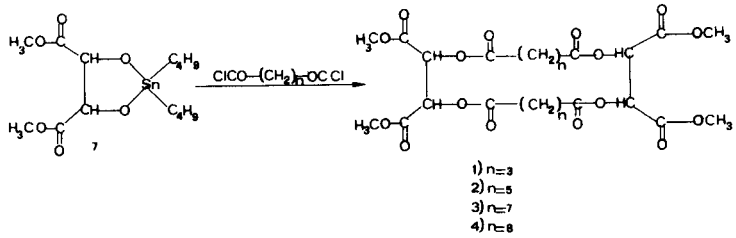


5

Table 1

The More Significative Ionic Species of EI Mass Spectra of Compounds **1-4**

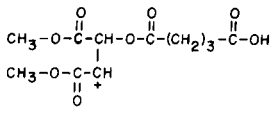
Ionic Species	1	2	3	4
M^+	548 (6)	604 (2)	660 (2)	688 (0,1)
a $[M\text{-}OCH_3]^+$	517 (6)	573 (6)	629 (8)	657 (8)
b $[M\text{-}COOCH_3]^+$	489 (44)	545 (26)	601 (14)	629 (8)
c $[M\text{-}OCHCOOHCH_3]^+$	460 (11)	516 (8)	572 (8)	600 (8)
d $[b\text{-}2COOCH_3]^+$	371 (16)	427 (17)	483 (31)	511 (22)
e $[M/2 + H]^+$	275 (46)	303 (30)	331 (47)	345 (22)
f $[e\text{-}H_2O]^+$	257 (7)	285 (16)	313 (2)	327 (2)
g $[e\text{-}C_2H_4O_2]^+$	215 (86)	243 (2)	271 (28)	285 (100)
h $[\dot{O}{=}C\text{-}(CH_2)_{n-1}\text{-}CH{=}C{=}O]$	97 (38)	125 (100)	153 (100)	167 (55)
i $[h - CO]^+$	69 (17)	97 (14)	125 (60)	139 (30)
l $[C_{15}H_{19}O_{11}]^+$	375 (100)	—	—	—



Scheme 1

this loss can be considered highly diagnostic of the presence of an alkyl chain in the cyclic moiety. Abundant $[M/2 + H]^+$ ionic species (**e**) are present for all the examined compounds. This decomposition process is usual in mass spectrometry of crown ethers as well as of macrocyclic tetraesters [6-10], and it must be emphasized that it usually occurs through many different symmetrical cleavages. In the present case B/E linked scans of the $[M/2 + H]^+$ ions point out the presence of peculiar ionic structures.

For example, in Figure 5 we report the B/E linked scan spectrum of the ions at m/z 275 originating from compound **1**. These ionic species show losses of H_2O (m/z 257), CO (247), $C_2H_4O_2$ (m/z 215) and $C_3H_5O_2$ (m/z 202). The first of these unimolecular decomposition processes suggests the presence of a hydroxyl group, the second of a terminal carbonyl while the last one is highly indicative of a $CH\text{-}CO\text{-}OCH_3$ moiety. Therfore for $[M/2 + H]^+$ ions we feel obliged to propose structure 6:



6

which fits well with the B/E data (Figure 5) and can be easily explained by symmetrical cleavages of the CH-O bonds. An analogous behaviour is observed also for compounds **2-4**. Ions *f* and **g** originate from ions **e** through losses of H_2O and C_2H_4O respectively. The formation of ionic species **h** has already been described for cyclic tetraesters compounds [10], and it can be explained by the low value of their ionization energy values (Stevenson-Audier rule).

Finally a peculiar behaviour of compound **1** must be pointed out, *i.e.* the formation of ions at m/z 375 (base peak of the spectra).

Thus the composition process is not so obvious at first sight, and for this reason we have undertaken further investigations. First of all, for this species exact mass measurement give 375,0929 (± 0,001), which corresponds well with the elemental composition $C_{15}H_{19}O_{11}$ (Calcd. 375.092723). Further, B^2/E linked scans indicate the ions **b** in Table 1, as the only precursors of the ionic species at

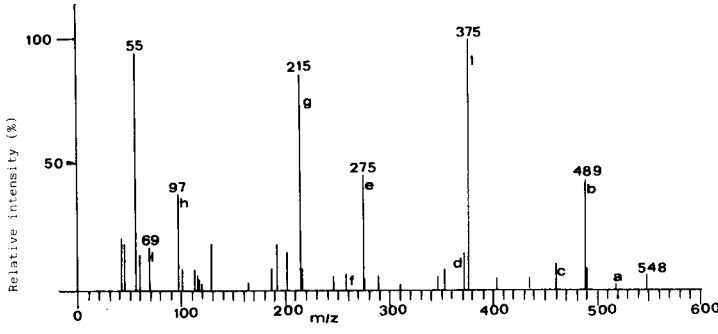


Figure 1 - 70 eV EI mass spectrum of compound 1

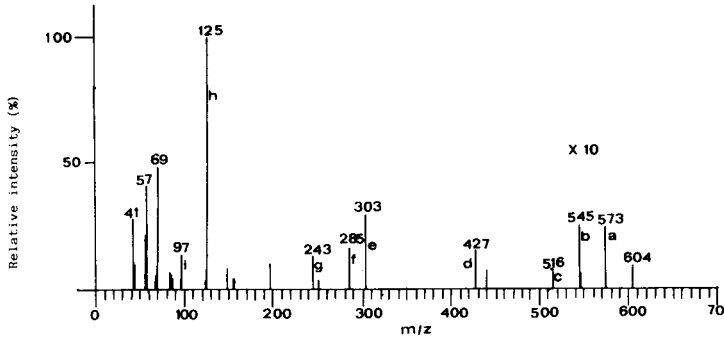


Figure 2 - 70 eV EI mass spectrum of compound 2

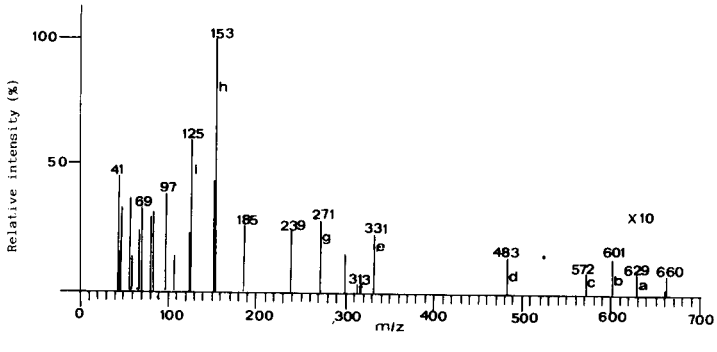


Figure 3 - 70 eV EI mass spectrum of compound 3

m/z 357, *i.e.* those originating from primary loss of $\cdot COOCH_3$ radicals. Therefore for the ions at m/z 375 we propose the structure reported in Scheme 1. Analogous

Scheme 2

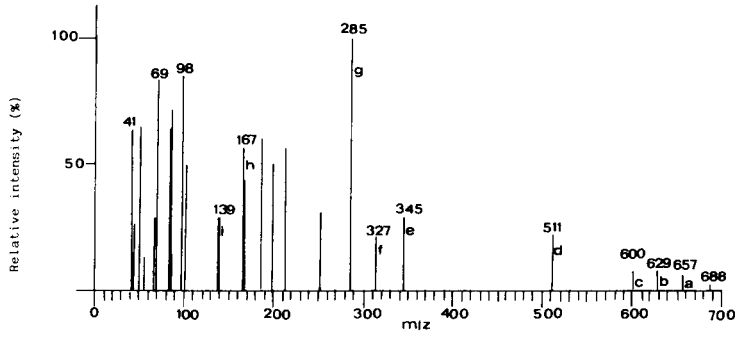


Figure 4 - 70 eV EI mass spectrum of compound 4

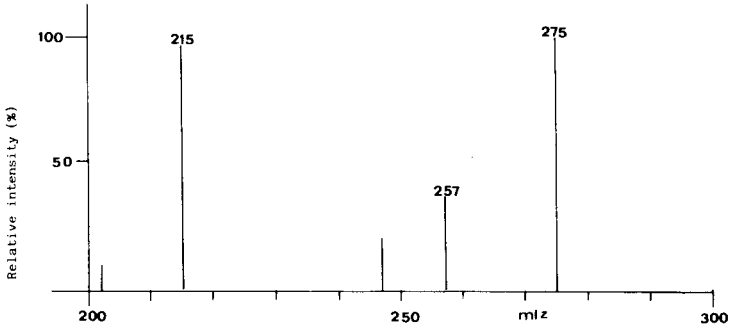


Figure 5 - B/E = cost linked scan of ionic species at m/z 275 originating from EI of compound 1

processes are forbidden for compounds **2-4**, probably due to entropic factors in the formation of a larger cyclic moiety. Further work is in progress on the separation of stereoisomeric compounds with the aim of investigating on their possibly different mass spectrometric behaviour.

EXPERIMENTAL

Microanalyses for CHN were carried out on a Carlo Erba model 1106 Elemental Analyzer. Melting points were determined using an electrothermal capillary melting point apparatus and are uncorrected. The ir spectra were recorded on a Perkin-Elmer 157 G spectrophotometer. The nmr spectra were determined on a Varian EM 360 L spectrometer; chemical shifts were measured in ppm (δ) using tetramethyl silane as an internal reference. All mass spectrometric measurements were performed on a VG-ZAB2F instrument operating in EI mode (10 eV, 200 uA). Samples were introduced by Direct Electron Impact (DEI) [11] technique, with a source temperature of 200°. Metastable transitions were detected by B/E and B^2/E linked scans [12]. Exact mass measurements were performed with the peak matching technique at a 30.000 resolving power (10% valley definition).

Starting Materials.

L(+)-dimethyl tartrate, dibutyltin oxide, glutaryl chloride, azeloyl chloride and sebacoyl chloride were used as received (EGA Chemie).

The pimeloyl chloride was prepared as described previously [13].

Compound **7** was prepared as in the literature [14].

2,2-Di-*n*-butyl-4,5-carbomethoxy-1,3,2-dioxastannolane (**7**).

A solution of L-dimethyl tartrate (28 mmoles) and dibutyltin oxide (28 mmoles) in 100 ml of dry benzene in a Dean-stark apparatus was refluxed overnight. A white solid was obtained which was filtered to give **7** in 86% yield, mp 180-185°; ir (potassium bromide): 1760 cm^{-1} (C=O); nmr (deuteriochloroform): δ 0.86-1.83 (m, 18H, 2 × C_4H_9-Sn), 3.58 (s, 6H, 2 × CH_3-O) and 4.63 (s, 2H, 2 × C*H*).

Anal. Calcd. for $C_{14}H_{26}O_6Sn$: C, 41.10; H, 6.40. Found: C, 41.11; H, 6.42.

General Synthesis.

The macrocyclic compounds **1-4** were prepared by the procedure described in early papers [15]. To a stirred hot solution of stannolane **7** (1 mmole) in 20 ml of benzene, a solution of diacyl chloride (1 mmole) in 5 ml of benzene was added dropwise. The resulting mixture was stirred under reflux for an additional night. The benzene solvent was then removed under vacuum and the crude product was treated with hexane to eliminate the dibutyltin dichloride. The residue was purified by column chromatography on silica gel using a mixture of benzene-ethyl acetate (5:1) as eluent. Using the general procedure, the following compounds were prepared and specific details are given for each compound.

2,3,11,12-Tetracarbomethoxy-1,4,10,13-tetraoxacyclooctadecane-5,9,14,18-tetraone (**1**).

The compound **7** (4.58 mmoles) and glutaryl chloride (4.58 mmoles) were used. The crude product was purified by column chromatography and the solid obtained was washed in diisopropyl ether to give **1** as a white solid, yield 35%, mp 112-115°; ir (potassium bromide): 1760 cm^{-1}

(C=O); nmr (deuteriochloroform): δ 5.62 (s, 4H, 4 × C*H*-O-CO), 3.72 (s, 12H, 4 × COOCH_3), 2.46 (t, 8H, 4 × CH_2-CO) and 2.14-1.86 (m, 4H, 2 × CH_2-CH_2-CO).

Anal. Calcd. for $C_{20}H_{28}O_{16}$: C, 48.18; H, 5.15. Found: C, 48.15; H, 5.17.

2,3,13,14-Tetracarbomethoxy-1,4,12,15-tetraoxacyclodocosane-5,11,15,22-tetraone (**2**).

The compound **7** (4.58 mmoles) and pimeloyl chloride (4.56 mmoles) were used. The crude product was purified by column chromatography and the obtained solid was washed in diisopropyl ether to give **2** as a white solid, yield 26%, mp 78-80°; ir (potassium bromide): 1740 cm^{-1} (C=O), nmr (deuteriochloroform): δ 5.64 (s, 4H, 4 × C*H*-O-CO), 3.70 (s, 12H, 4 × COOCH_3), 2.36 (t, 8H, 4 × CH_2-CO) and 1.78-1.40 (m, 12H, 6 × CH_2-CH_2-CO).

Anal. Calcd. for $C_{26}H_{36}O_{16}$: C, 51.65; H, 6.00. Found: C, 51.63; H, 6.02.

2,3,15,16-Tetracarbomethoxy-1,4,14,17-tetraoxacycloexacosane-5,13,18,26-tetraone (**3**).

The compound **7** (4.58 mmoles) and azeloyl chloride (4.58 mmoles) were used. The crude product was purified by column chromatography and the obtained solid was washed in diisopropyl ether to give **3** as a white solid, yield 25%, mp 72-74°; ir (potassium bromide): 1740 cm^{-1} (C=O); nmr (deuteriochloroform): δ 5.63 (s, 4H, 4 × C*H*-O-CO), 3.70 (2, 12H, 4 × COOCH_3), 2.36 (t, 8H, 4 × CH_2-CO) and 1.75-1.20 (m, 20H, 10 × CH_2-CH_2-CO).

Anal. Calcd. for $C_{30}H_{44}O_{16}$: C, 54.54; H, 6.71. Found: C, 54.53; H, 6.72.

2,3,16,17-Tetracarbomethoxy-1,4,15,18-tetraoxacyclooctacosane-5,14,19,28-tetraone (**4**).

The compound **7** (4.58 mmoles) and sebacoyl chloride (4.58 mmoles) were used. The crude product was purified by column chromatography to give **4** as a viscous oil, yield 24%; ir (film): 1740 cm^{-1}; nmr (deuteriochloroform): δ 5.62 (s, 4H, 4 × C*H*-O-CO), 3.70 (s, 12H, 4 × COOCH_3), 2.35 (t, 8H, 4 × CH_2-CO) and 1.73-1.06 (m, 24H, 12 × CH_2-CH_2-CO).

Anal. Calcd. for $C_{32}H_{48}O_{16}$: C, 55.80; H, 7.03. Found: C, 55.78; H, 7.01.

REFERENCES AND NOTES

[1] R. M. Izatt and J. J. Christensen, "Progress in Macrocyclic Chemistry", John Wiley and Sons, New York, 1970.

[2] J. S. Bradshaw, G. E. Mass, R. M. Izatt and J. J. Christensen, *Chem. Rev.*, **79**, 37 (1979).

[3] B. C. Pressman, *Ed. Proc. Fed. Am. Soc. Exp. Biol.*, **27**, 1283 (1968).

[4] A. Thore, D. L. Keisten, N. Shavit and A. San Pietro, *Biochemistry*, **7**, 3499 (1968).

[5] H. Lordy, *Fed. Proc., Fed. Am. Soc. Exp. Biol.*, **27**, 1278 (1968).

[6] S. Auricchio, O. Vajna de Pava, P. Traldi and A. Griffini, *Org. Mass Spectrom.*, **17**, 35 (1982).

[7] P. Traldi, U. Vettori, G. Podda, A. Maccioni and L. Corda, *Org. Mass Spectrom.*, **18**, 69 (1983).

[8] G. Podda, A. Maccioni, C. Anchisi, S. Daolio, B. Pelli and P. Traldi, *J. Heterocyclic Chem.*, **22**, 491 (1984).

[9] G. Podda, A. Maccioni, L. Corda, S. Daolio, P. Traldi and E. Vecchi, *Heterocycles*, **22**, 1071 (1984).

[10] B. Pelli, P. Traldi, G. Podda, C. Anchisi and L. Corda, *Org. Mass Spectrom.*, **2**, 164 (1985).

[11] P. Traldi, U. Vettori and F. Dragoni, *Org. Mass Spectrom.*, **7**, 587 (1982).

[12] A. P. Bruins, K. R. Jenning and S. Evans, *Int. J. Mass Spectrom., Ion. Phys.*, **26**, 395 (1978).

[13] E. E. Blaise and A. Koehler, *Bull. Soc. Chim. France.*, **5**, 681 (1909).

[14] R. C. Mehrotra and V. G. Gupta, *J. Organomet. Chem.*, **4**, 145 (1965); W. J. Considine, *ibid.*, **5**, 263 (1966); J. C. Pommier and J. Valade, *ibid.*, **12**, 433 (1968); T. Mukaiyama, I. Tomioka and M. Shimizu, *Chem. Letters*, 49 (1984).

[15] A. Maccioni, A. Plumitallo and G. Podda, *J. Heterocyclic Chem.*, **20**, 1397 (1983); C. Anchisi, L. Corda, A. M. Fadda, A. Maccioni and G. Podda, *ibid.*, **21**, 577 (1984); G. Podda, C. Anchisi, L. Corda, A. M. Fadda and A. Maccioni, *ibid.*, **21**, 1789 (1984).