Electron Impact Induced Fragmentation of Pyridyl Macrocyclic Polyethers (Crown Ethers)

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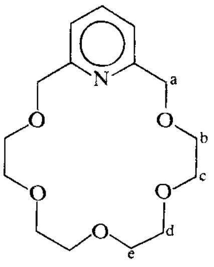
The mass spectra of pyridyl-18-crown-6 and pyridyl-15-crown-5 were determined. The spectra of five deuterium labeled analogues of pyridyl-18-crown-6, coupled with high resolution data, allowed formulation of fragmentation pathways, which are dominated by several series involving the loss of C_2H_4O units.

INTRODUCTION

The mass spectral characteristics of several types of macrocyclic polyethers (crown ethers) have been reported;[1-3] in general, they are rich in interesting, and in some cases, unique fragmentation pathways. Pyridyl-18-crown-6 (**1**) and pyridyl-15-crown-5 (**2**) are the subjects of the present mass spectral investigation.



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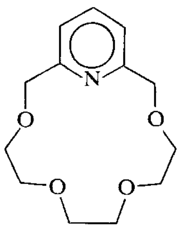

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RESULTS AND DISCUSSION

The electron impact mass spectra of **1** and **2** at 70 eV are shown in Figs. 1 and 2. Since these spectra are essentially the same $\leq m/z$ 224, the fragmentation pathways are probably very similar; therefore, only those of **1** will be described. The spectrum of **1** includes the molecular ion $[M]^{+\cdot}$ at m/z 297, the most abundant ion at m/z 122, and other principal fragmentation ions at m/z 268, 254, 238, 210, 181, 164, 150, 136, 107, 78, 65 and 45. The elemental compositions of these and other ions were determined by high resolution measurements and are compiled in Table 1.

The polyether carbons of **1** are designated a, b, c, d and e, and the 70 eV spectra of the corresponding deuterium labeled analogs[4] **1a**, **1b**, **1c**, **1d** and **1e** are given in Figs. 3–7. With the use of these spectra and the high resolution data of Table 1, fragmentation pathways for **1** are proposed as outlined below. These

Table 1. Elemental compositions of ions in the 70 eV spectrum of 1

Nominal mass	Composition	Nominal mass	Composition
297	$C_{15}H_{23}NO_5$	137	$C_8H_{11}NO$ (91%); $C_7H_7NO_2$ (9%)
296	$C_{15}H_{22}NO_5$	136	$C_7H_6NO_2$ (73%); $C_8H_{10}NO$ (27%)
269	$C_{14}H_{23}NO_4$	133	$C_6H_{13}O_3$
268	$C_{14}H_{22}NO_4$	122	C_7H_8NO
267	$C_{14}H_{21}NO_4$	121	C_7H_7NO (54%); $C_8H_{11}N$ (46%)
254	$C_{13}H_{20}NO_4$	120	C_7H_6NO (69%); $C_8H_{10}N$ (31%)
253	$C_{13}H_{19}NO_4$	107	C_7H_9N (99%); C_6H_5NO (1%)
238	$C_{13}H_{20}NO_3$ (93%); $C_{12}H_{16}NO_4$ (7%)	106	C_7H_8N
224	$C_{12}H_{18}NO_3$	93	C_6H_7N
210	$C_{11}H_{16}NO_3$	92	C_6H_6N
208	$C_{11}H_{14}NO_3$ (69%); $C_{12}H_{18}NO_2$ (31%)	89	$C_4H_9O_2$
194	$C_{11}H_{16}NO_2$	79	C_6H_7
181	$C_{10}H_{15}NO_2$	78	C_6H_6
180	$C_9H_{10}NO_3$ (83%); $C_{10}H_{14}NO_2$ (17%)	77	C_6H_5
166	$C_9H_{12}NO_2$	65	C_5H_5
164	$C_9H_{10}NO_2$	45	C_2H_5O
150	$C_8H_8NO_2$ (73%); $C_9H_{12}NO$ (27%)		

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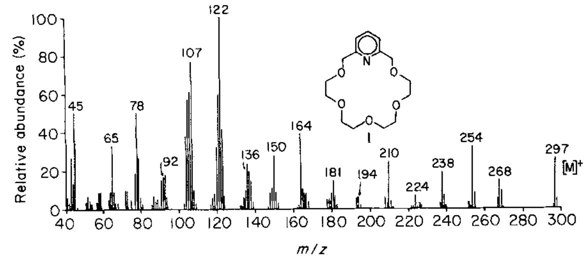


Figure 1. Mass spectrum of pyridyl-18-crown-6 (**1**).

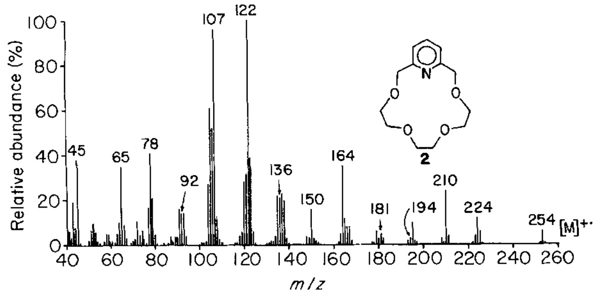


Figure 2. Mass spectrum of pyridyl-15-crown-5 (**2**).

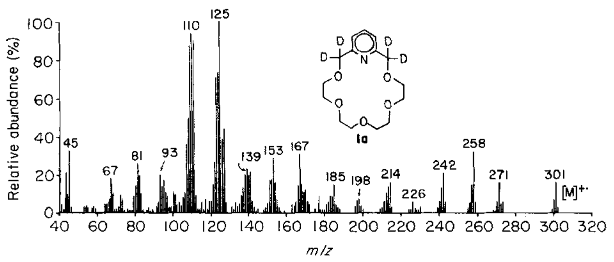


Figure 3. Mass spectrum of **1a**.

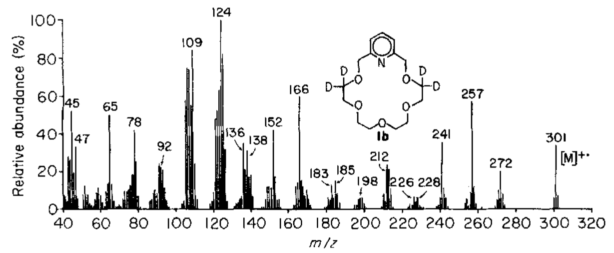


Figure 4. Mass spectrum of **1b**.

pathways were formulated without the benefit of metastable ion data, which were absent in the spectrum of **1** under the conditions used. However, each fragmentation mechanism illustrated with structural formulae satisfies at least one of the following criteria: (1) it is consistent with the deuterium labeling data; (2) it is directly analogous to another mechanism of this study supported by such data; or (3) it has a literature precedent. These criteria precluded the proposal of mechanisms for the formation of several prominent ions. As can be seen in Fig. 1, several of these ions are within groups whose members differ little in relative intensity. Furthermore, in most cases the data of Table 1 indicate that within such a group each ion differs from the next by only a hydrogen atom. Thus, under such circumstances, the deuterium labeling data most often did not allow the formulation of detailed mechanisms. Therefore, for several prominent and related ions, only suggested structures are given without mechanistic genesis.

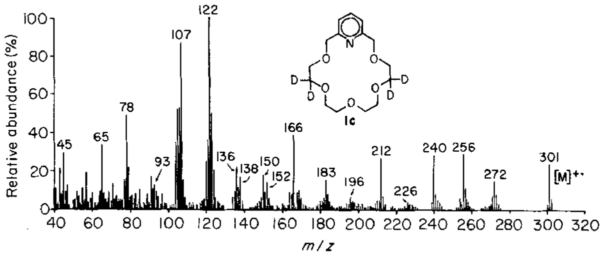


Figure 5. Mass spectrum of **1c**.

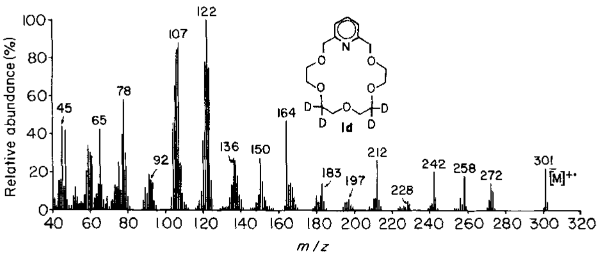


Figure 6. Mass spectrum of **1d**.

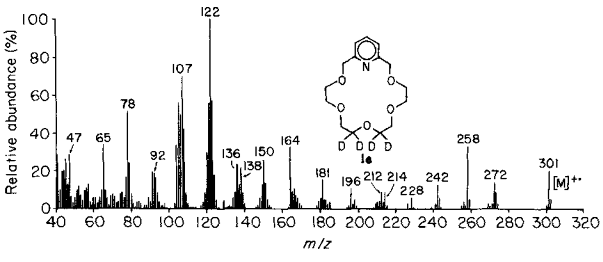
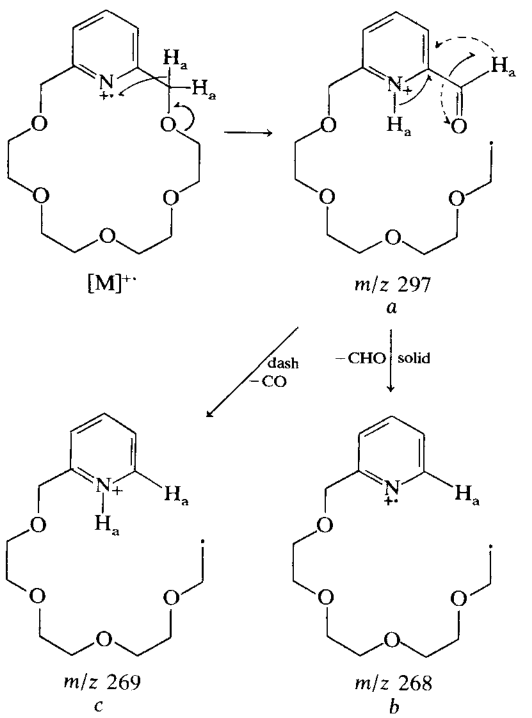


Figure 7. Mass spectrum of **1e**.

Formation of ions with *m/z* 269 and 268 involves the formal loss of CO and CHO, respectively, from $[M]^{+\cdot}$. Deuterium labeling indicates that the H is lost from the *a* position, since the spectrum of **1a** contains a peak at *m/z* 271, whereas the corresponding peaks in the spectra of **1b**–**1e** are at *m/z* 272. A mechanism for the formation of the mass 269 and 268 ions, *c* and *b*, respectively, from $[M]^{+\cdot}$ through ion *a* is outlined in Scheme 1. Furthermore, *b* and *c* could serve as precursors of two homologous series of ions by the loss of C_2H_4O units as also indicated in Scheme 1. Homologous series of ions separated by C_2H_4O units have been reported in the mass spectra of structurally related crown ethers.[2,3]

Deuterium labeling results suggest that the ions of mass 254 and 238 are formed in related mechanisms as outlined in Scheme 2. The corresponding peaks in the spectrum of **1b** are at *m/z* 257 and 241, at *m/z* 256 and 240 in that of **1c**, and at *m/z* 258 and



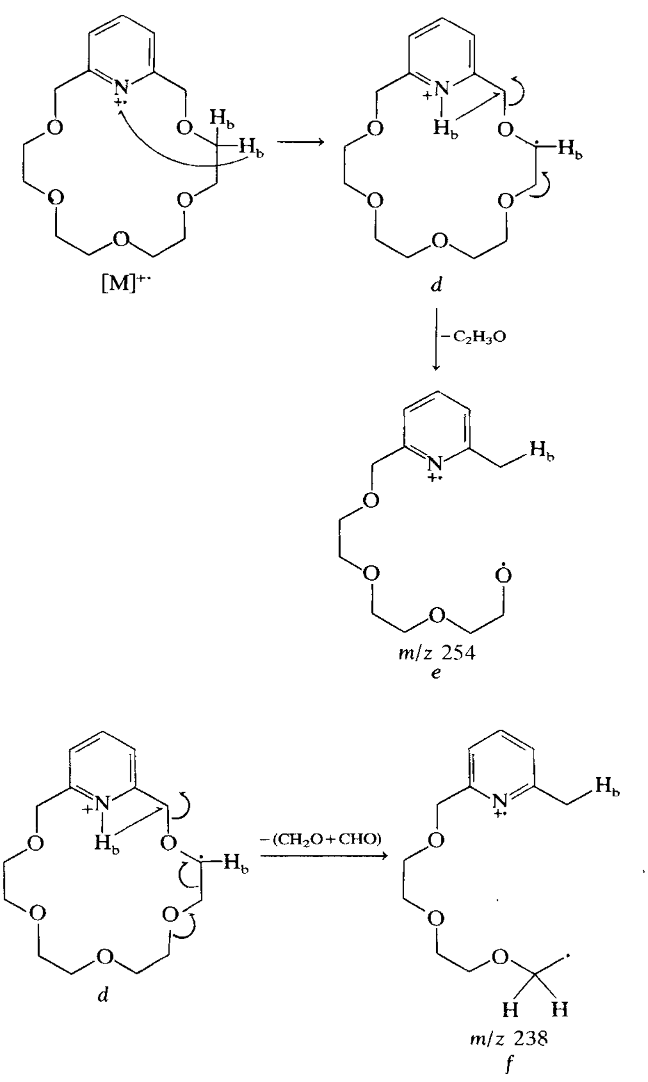
Homologous series from *b*: *m*/*z* 224 ($C_{13}H_{20}NO_4$); *m*/*z* 180 ($C_{10}H_{14}NO_2$); *m*/*z* 136 ($C_8H_{10}NO$); *m*/*z* 92 (C_6H_6N).
Homologous series from *c*: *m*/*z* 181 ($C_{10}H_{15}NO_2$); *m*/*z* 137 ($C_8H_{11}NO$); *m*/*z* 93 (C_6H_7N).

Scheme 1

242 in those of **1a**, **1d** and **1e**. High resolution data indicate the presence of a minor second ion ($C_{12}H_{16}NO_4$, 7%) of nominal *m*/*z* 238 in addition to ion *f* ($C_{13}H_{20}NO_3$, 93%); it corresponds to ion *bb* in Scheme 7. Ions *e* and *f* could function as precursors of two homologous series of ions by the loss of C_2H_4O units as summarized in Scheme 2.

Ion *b*′ of Scheme 3 is a resonance contributor to the ion of *m*/*z* 268 of Scheme 1, and it can serve as the precursor of ion *g*, *m*/*z* 122, whose structure is suggested by the deuterium labeling results. (An isomer of *g* could be formed as in Scheme 2, but its most likely structure (not shown) is less consistent with the deuterium labeling results.) Ions *h* and *i*, *m*/*z* 166 and 210, respectively, along with ion g, constitute another homologous series separated by C_2H_4O units. Deuterium labeling data for the prominent *m*/*z* 210 peak are not clear-cut but do suggest that there are at least two ions of *m*/*z* 210; ion *i* and an isomeric *m*/*z* 210 ion of Scheme 2 are likely possibilities.

Ion *e*′ of Scheme 4 is a resonance contributor to the ion of *m*/*z* 254 of Scheme 2, and it can serve as the precursor of ion *j*, *m*/*z* 136, in a process directly analogous to that of Scheme 3. (Ion *l* is isomeric with the most likely structure (not shown) for the *m*/*z* 224 ion referred to in Scheme 1.) Ions *k* and *l*, *m*/*z* 180 and 224, respectively, along with *j*, constitute a series separated by C_2H_4O units. High resolution data of Table 1 indicate that there are at least two ions of nominal *m*/*z* 180, with compositions $C_9H_{10}NO_3$ (83%) and $C_{10}H_{14}NO_2$ (17%). The latter corresponds to ion *k* and/or the *m*/*z* 180 ion of Scheme 1, and the former



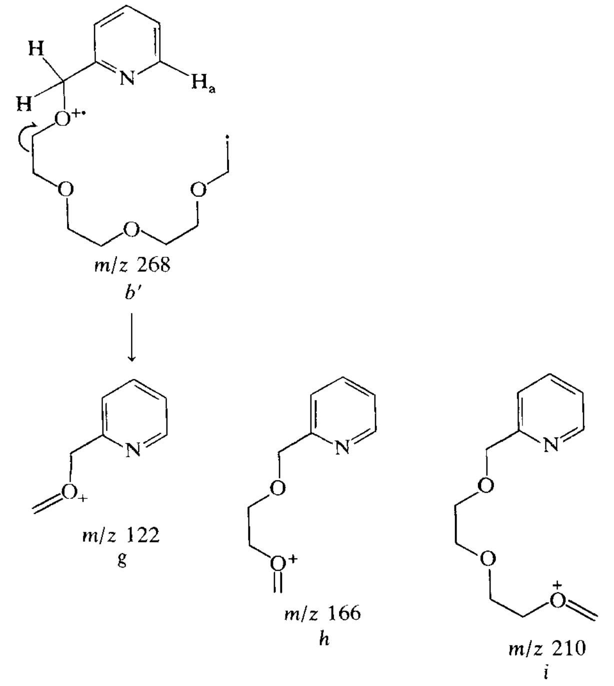
Homologous series from *e*: *m*/*z* 210 ($C_{11}H_{16}NO_3$); *m*/*z* 166 ($C_9H_{12}NO_2$); *m*/*z* 122 (C_7H_8NO).
Homologous series from *f*: *m*/*z* 194 ($C_{11}H_{16}NO_2$); *m*/*z* 150 ($C_9H_{12}NO$); *m*/*z* 106 (C_7H_8N).

Scheme 2

to ion *aa* of Scheme 7. High resolution data also indicate that there are at least two ions of nominal *m*/*z* 136, with compositions $C_7H_6NO_2$ (73%) and $C_8H_{10}NO$ (27%). The latter corresponds to ion *j* and/or the *m*/*z* 136 ion of Scheme 1, and the former to ion *y* of Scheme 7.

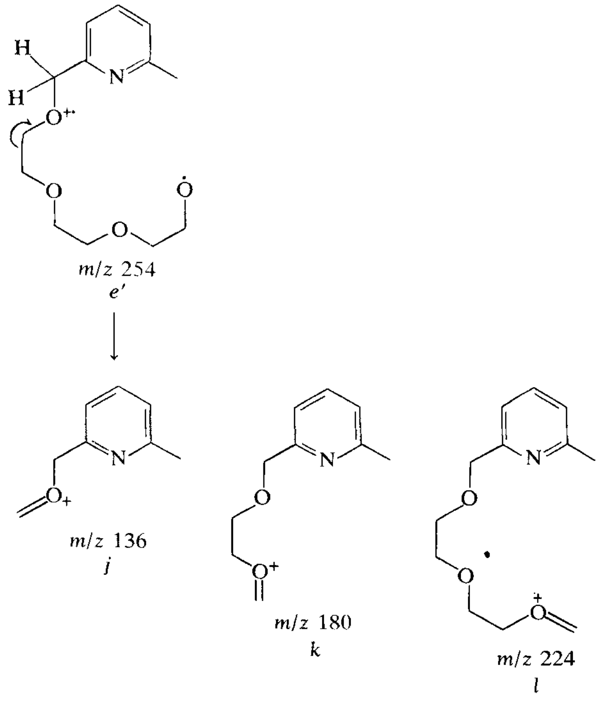
Scheme 5 illustrates the formation of ion *m*, *m*/*z* 296, which can serve as the precursor of another series of ions formed by the loss of C_2H_4O units. The structure of the major ion in the series, *n*, *m*/*z* 164, is consistent with the deuterium labeling data.

Scheme 6 outlines a sequence starting from ion *o*, a proposed structure for the *m*/*z* 106 ion, that leads through ion *p* to ions *q*, *r*, *s*, *t* and *u*. Analogous pathways for dialkylpyridines have been proposed.[5] Scheme 7 summarizes possible structures for additional ions which are consistent with the high resolution data, but whose formation could not be mechanistically described due to inconclusive deuterium labeling data. Ion *m* of Scheme 5 is a potential precursor of

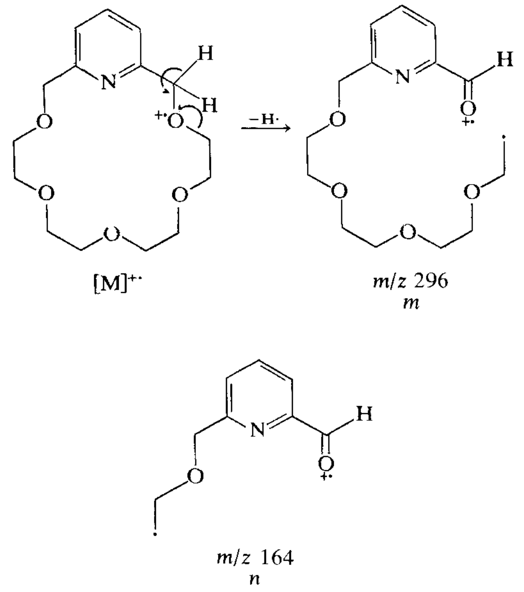


Scheme 3

ions y, z, aa and bb. High resolution data indicate that there are at least two ions of nominal m/z 107, with compositions C_7H_9N (99%) and C_6H_5NO (1%); the former corresponds to ion w and the latter to ion x. The data of Table 1 also indicate that there are two ions of nominal m/z 150 with compositions $C_8H_8NO_2$ (73%) and $C_9H_{12}NO$ (27%). The latter corresponds to the m/z 150 ion of Scheme 2 and the former to ion z; the deuterium labeling data are consistent with contributions from both proposed structures.

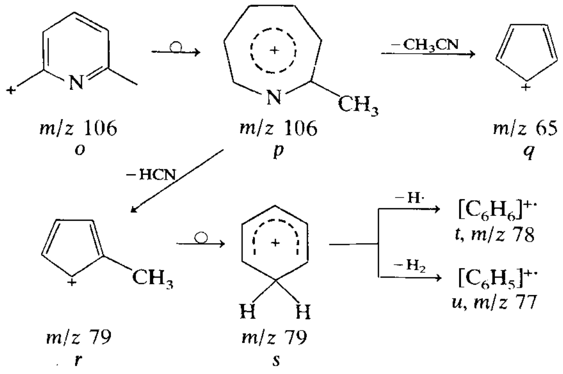


Scheme 4

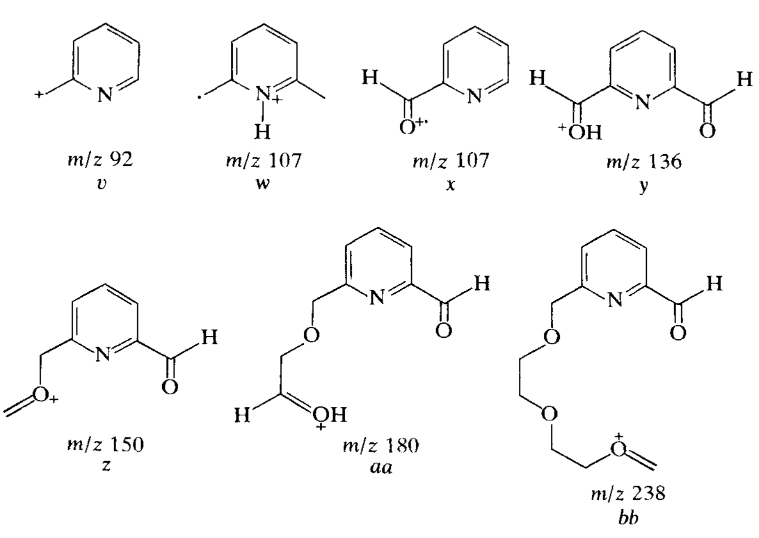


Homologous series from m: m/z 208 ($C_{11}H_{14}NO_3$); m/z 164, ion n; m/z 120 (C_7H_6NO).

Scheme 5

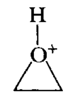


Scheme 6

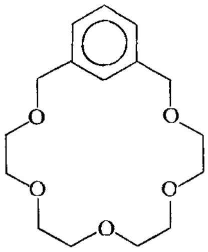


Scheme 7

The significant peak at *m/z* 45 is postulated to have structure *cc*. It represents the smallest member of a homologous series of protonated cyclic ether species which differ from one another by C_2H_4O units. Other members of the series are protonated dioxane, $[C_4H_9O_2]^+$, *m/z* 89; protonated 9-crown-3, $[C_6H_{13}O_3]^+$, *m/z* 133; and protonated 12-crown-4, $[C_8H_{17}O_4]^+$, *m/z* 177. Only minor peaks corresponding to these compositions were found at *m/z* 89 and 133, and no peak at *m/z* 177 was detected. Deuterium labeling results indicate that carbons *b*, *c*, *d* and *e* contribute to the structure of ion *cc*. In a study of the electron impact induced fragmentations of the closely related benzo-18-crown-5 (**3**), Gray *et al.*[2] observed the complete series of peaks at *m/z* 45, 89, 133 and 177.



m/z 45
cc



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In summary, the mass spectral characteristics of **1** are dominated by several fragmentation pathways involving the loss of C_2H_4O units. These and other pathways are apparently dependent on initial participation of the pyridyl nitrogen. Indeed, the nitrogen seems to be responsible for the significantly different mass spectral behavior of **1** compared with that of **3**.

EXPERIMENTAL

General

Low resolution spectra were recorded on a Varian MAT CH-5 mass spectrometer. The ionizing voltage was 70 eV, the filament current 300 μA, and the source temperature 150 °C. Samples were introduced by direct insertion with probe temperature 12–85 °C. High resolution spectra were recorded with a Varian MAT 711 (Department of Chemistry, Stanford University) and a DuPont 21–110B mass spectrometer (Laramie Energy Technology Center, Laramie, Wyoming). For analytical and preparative gas-liquid chromatography (GLC), a 6 ft × 1/4 in aluminum column packed with 1% SE-30 on 60–80 mesh AW-DMCS Chromosorb W was used with helium as carrier gas.

Pyridyl-18-crown-6 (1). This material was prepared[4] as described by Cram *et al.*[6]

Labeled crown ethers 1a, 1b, 1c, 1d and 1e. The syntheses of these materials are described elsewhere.[4]

Pyridyl-15-crown-5 (2). Under nitrogen, to a stirred slurry of 0.34 g (14 mmol) of NaH in 50 cm³ of THF (purified by distillation from $LiAlH_4$ under nitrogen) was added a solution of 0.696 g (5.00 mmol) of 2,6-bis(hydroxymethyl)pyridine[4,7] in 50 cm³ of THF. After gas evolution ceased, a solution of 2.48 g (5.40 mmol) of 3,6-dioxaoctane-1,8-diol di-*p*-toluenesulfonate[8] in 50 cm³ of THF was added, and the mixture was refluxed under nitrogen for 10 h, cooled to 25 °C, filtered, and concentrated on a rotary evaporator. The resulting oil was column chromatographed on neutral alumina with 1% $C_2H_5OH—CH_2Cl_2$ as eluent to give 0.43 g (43%) of crude **2** which was purified by bulb-to-bulb distillation (Kugelrohr) at 90 °C (0.5 mm) followed by preparative GLC (180 °C). Anal. calc. for $C_{13}H_{19}NO_4$: C, 61.66; H, 7.56%. Found: C, 61.50; H, 7.78%. ^1H NMR (100 MHz; $CDCl_3$; TMS) δ 3.45 (s, 4H, CH_2CH_2 nonadjacent to pyridine ring), 3.63 (A_2B_2, 8H, $ArCH_2OCH_2CH_2$), 4.61, (s, 4H, $ArCH_2$), 7.16 (d, $J = 8$ Hz, 2H, 3-ArH), 7.59 (t, $J = 8$ Hz, 1H, 4-ArH).

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