Mass Spectral Fragmentation Patterns of Heterocycles. IV [1].
Tetracyclic Phenothiazines. IX. Electron Impact Promoted
Mass Spectral Fragmentation of Pyrrolo[3,2,1-*kl*]phenothiazine

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The mass spectral fragmentation patterns of pyrrolo[3,2,1-*kl*]phenothiazine (1) and its 1,10-dideuterioderivative [2] are reported. The site of deuterium substitution in 2 was established by examination of its ^{13}C nuclear magnetic resonance spectrum. The heteroaromatic stability of 1 to electron impact is exemplified by the occurrence of the molecular ion as the base peak and the formation of a reasonably intense M^{2+} ion. An intense M-1 ion is also observed. The more abundant fragment ions appear to result from sulfur ionization. Fragment ions arising from ionization of the nitrogen constitute only a small fraction of the total ion current. Proposed fragmentation pathways of 1 are supported by the detection of appropriate metastable ions, exact mass measurements, and electron impact spectrum of 2.

As a part of our research on polycyclic phenothiazines as potential antipsychotic compounds [2], the mass spectral fragmentation behavior of pyrrolo[3,2,1-*kl*]phenothiazine (1) was investigated. The molecular ion corresponding to 1 was detected as one of the major ions in the electron impact induced mass spectra of some pyrido[3,2,1-*kl*]-phenothiazines in an earlier study [1]. It was of interest to determine the contribution of the further fragmentation of 1 to the overall fragmentation patterns observed for the pyrido[3,2,1-*kl*]phenothiazines.
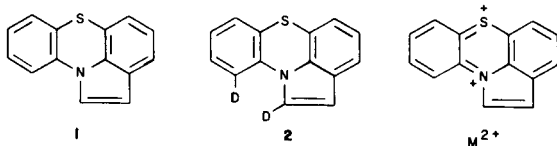
As with most polycyclic compounds containing heteroatoms, the ionization of 1 produces spectra containing an intense doubly charged ion [1,3], depicted as M^{2+} (m/e 111.5 relative intensity 19.2%) and even a triply-charged species (m/e 74.3) can be seen. The aromatic character of 1 is apparent from the observation that the molecular ion M^+ (m/e 223) is the base peak.

Primary fragmentations of the molecular ion of 1 are outlined in Scheme 1. Mass values of metastable ions are indicated with the arrows together with the calculated values in parentheses. Mass/charge values for each of the fragment ions of 1 and the corresponding deuterated compound 2 are also given. Exact mass data for key ions are listed in Table 1. It is clear that most of the major skeletal fragments of 1 result from ionization of the sulfur atom. The M-1 ion, depicted as I, could be stabilized due to interaction of the sulfur lone pair electrons with the arylcation center, a situation visualized as resulting from the proximity effect [4,5]. The hydrogen atom lost from $M^{+\cdot}$ could also have arisen from the 7-position, but studies on 2 ex-

clude either the 1- or 10-positions because of the absence of m/e 223 and the presence of m/e 224 in the spectrum of the latter compound.

Scheme I
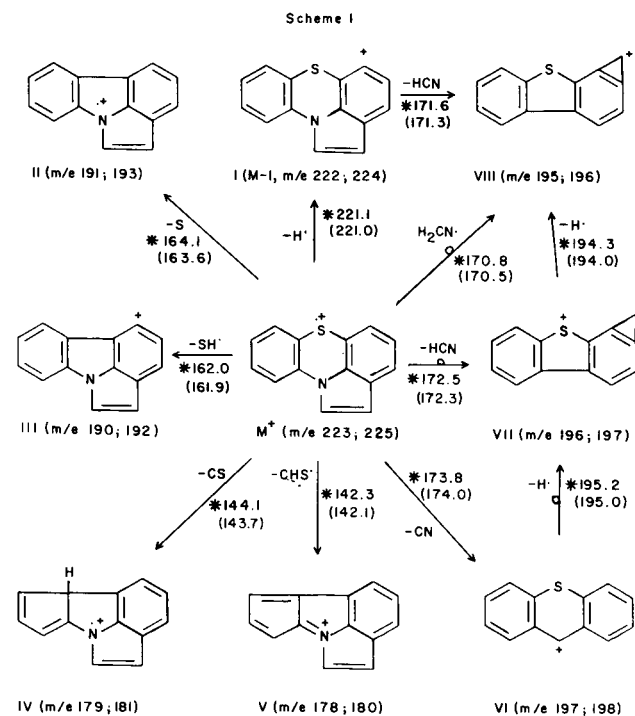
As in the electron impact induced fragmentations of simple phenothiazine [6], direct losses of elemental sulfur (S), sulfhydryl (·SH) and ·CSH radicals and elemental carbon monosulfide (CS) to form ions II, III, IV and V, predominate over direct losses of hydrogen cyanide (HCN) and cyanide (·CN) and dihydrogen cyanide ($H_2CN\cdot$) radicals to form VI, VII and VIII in the skeletal fragmentation of 1. The total relative abundance of ions II, III, IV and V of 25.6% as compared with 6.9% for VI, VII and VIII underscores this point. In fact, although the corresponding

Table 1

Exact Mass Measurements

Ion	Empirical Formula	Calcd.	Observed
M+·	$C_{14}H_9NS$	223.0456	223.0459
M-1 (I)	$C_{14}H_8NS$	222.0377	222.0377
M-2 (X)	$C_{14}H_7NS$	221.0299	221.0302
VIII	$C_{13}H_7S$	195.0268	195.0250
II	$C_{14}H_9N$	191.0735	191.0732
III	$C_{14}H_8N$	190.0657	190.0649
IV	$C_{13}H_9N$	179.0735	179.0720
V	$C_{13}H_8N$	178.0657	178.0644
IX	$C_{13}H_7N$	177.0579	177.0559
XI	$C_{13}H_8$	164.0626	164.0555
XII	$C_{13}H_7$	163.0546	163.0559
XIII	$C_{12}H_8$	152.0626	152.0600
XIV	$C_{12}H_7$	151.0547	151.0538

Table 2

^{13}C Chemical Shift Assignments
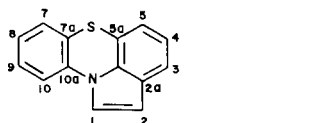
Position	Type	Chemical Shift (ppm) (a) Compound 1	Compound 2
10a	q	134.22	134.20
2b	q	131.83	131.85
2a	q	127.83	127.85
9	CH	127.14	127.02
7	CH	127.10	127.02
8	CH	124.61	124.58
4	CH	123.14	123.13
7a	q	121.37	121.37
1	CH	120.68	(120.92) (b)
3	CH	117.58	117.57
5a	q	116.97	116.99
5	CH	116.00	115.98
10	CH	114.22	(113.9) (c)
2	CH	105.16	104.99

(a) In deuteriochloroform with tetramethylsilane as an internal standard.
(b) Triplet in broad band proton decoupled spectrum $J_{13}C_{2}H$ = 28.2 Hz. (c) Triplet in broad band proton decoupled spectrum $J_{13}C_{2}H$ = 24.1 Hz.
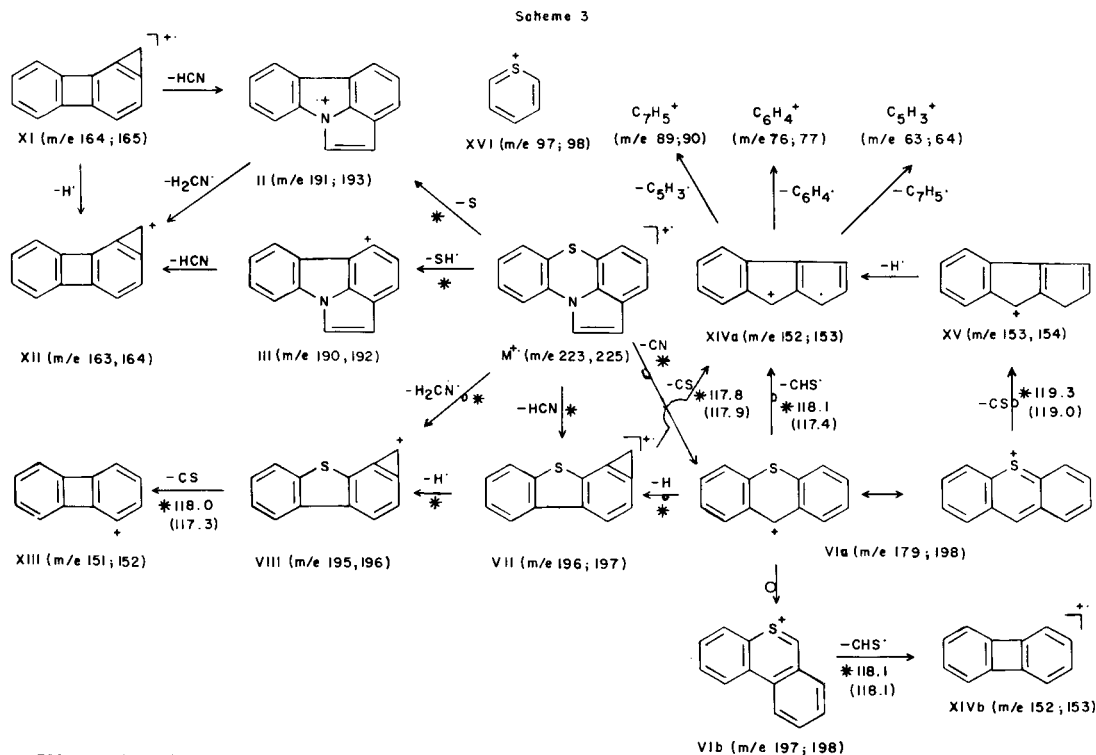
metastable ions apparently associated with the expulsions of ·CN, HCN and H_2CN· (or H· + HCN) from M+· were indeed observed, the only ion of sufficient abundance for exact mass measurements was VII formed by loss of H_2CN· radical. Although the source of the hydrogen atom lost with the expulsion of ·SH radical to give III, or the carbon atom and/or cabon and hydrogen atoms lost with the expulsion of CS and/or ·CSH radical to give IV and V respectively, are not known, it is evident from the spectrum of **2** that they are not derived from the 10-position. Thus, ions III, IV and V are each shifted two mass units in **2** compared with **1**. On the other hand, ion VIII formed by the

Scheme 2
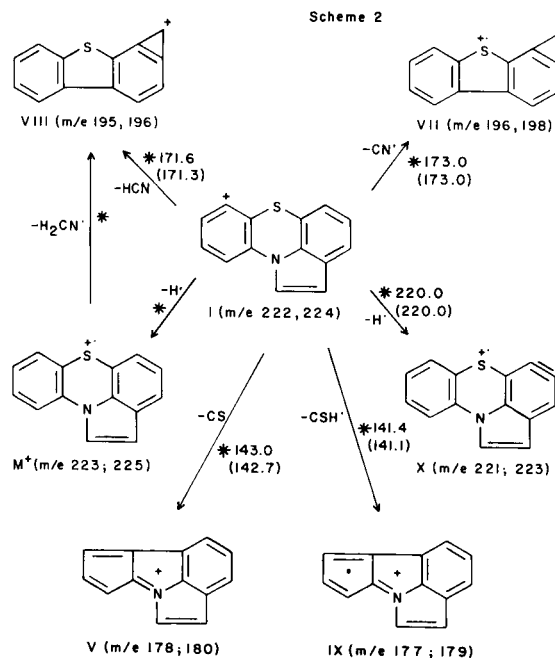
loss of H_2CN· radical (or H· + HCN) undergoes a shift of one mass unit to m/e 196 in **2**, indicating that DHCN radical (or DCN + H·) is expelled. It is most logical to assume that the C-1 carbon is lost and that C-2 is retained.

Fragmentation pathways for the M-1 ion (I) parallel those for M+·; except that evidence (in the form of metastable ions) for the loss of S or ·SH radical is lacking (Scheme 2). Thus, I appears to expell HCN and ·CN radical to form VIII and VII, respectively, and to lose CS and CSH· radical to form V and IX, respectively. Loss of a hydrogen atom to form a M-2 ion, shown as a benzyne radical cation X, also occurs.

Because of the stability of the molecular ion the relative abundances of secondary fragment ions formed from it (Scheme 3) are very low. Despite the relative abundance (12%) of the apparently very stable pyrrolocarbazole radical cation II only one fragment ion XI (m/e 164) derived from it (by the expulsion of HCN) could be detected. It is possible that loss of H_2CN· radical by II to give the related hydrocarbon ion XII (m/e 163) could also occur. The even electron ion III could also form XII by loss of HCN. It is conceivable that expulsion of S from VIII could occur to also give XII. Loss of CS from VIII to give XIII (m/e 151) is supported by the occurrence of the appropriate metastable ion. On the other hand, hydrocarbon ions XIVa (XIVb) and XV appear to be derived from VIa (VIb) and VII according to metastable ion studies. Lower mass hydrocarbon ions C_7H_5, C_6H_4 and C_5H_3 could arise from XIV (Shown in Scheme 3). Ions XI, XII, XIII and XV are also likely sources of these ions. The heteroaromatic thio-

Scheme 3

XI (m/e 164 ; 165)   —HCN→   II (m/e 191 ; 193)   XVI (m/e 97 ; 98)

C$_7$H$_5^+$ (m/e 89;90)   C$_6$H$_4^+$ (m/e 76,77)   C$_5$H$_3^+$ (m/e 63;64)

−H· ↓   −H$_2$CN·   −S   −C$_5$H$_3$·   −C$_6$H$_4$·   −C$_7$H$_5$·

XII (m/e 163,164)   —HCN→   III (m/e 190,192)   −SH· *   M$^+$· (m/e 223,225)   XIVa (m/e 152 ; 153)   −H·   XV (m/e 153, 154)

−CN

−H$_2$CN· *   −HCN *   −CS   *117.8 (117.9)   −CHS· *118.1 (117.4)   −CS *119.3 (119.0)

XIII (m/e 151 ; 152)   −CS *118.0 (117.3)   VIII (m/e 195,196)   −H· *   VII (m/e 196 ; 197)   −H *   VIa (m/e 179 ; 198)

VIb (m/e 197 ; 198)   −CHS· *118.1 (118.1)   XIVb (m/e 152 ; 153)

pyrilium ion XVI (m/e 97), possibly formed from VI, VII, or VIII or (less likely) direct from M$^+$·, is suggested to be a stable species [8] even in the ground state, based on molecular orbital calculations [8].

Proposed mechanisms for the expulsion of HCN (or H$_2$CN·) from the molecular ion (M$^+$·), and from the pyrrolocarbazole ion II, are outlined in Scheme 4. In each case, rearrangement to indolo species, XVI from M$^+$· and XVII from II, respectively, are thought to be involved. Although ions m/e 195, 196, 163 and 164 could exist as noncyclic structures, analogous to those proposed [9] for the expulsion of HCN and H$_2$CN· from indole (to give m/e 90 and 89, respectively), we consider the cyclic aromatic structures VII, VIII, XI and XII to be better representations of these ions.

The sites of deuterium substitution in the dideuterioderivative, 1,10-d$_2$-pyrrolo[3,2,1-kl]phenothiazine (2) prepared by treatment of 1 with excess n-butyl-lithium followed by quenching with deuterium oxide [10], were established by examination of the ^{13}C nuclear magnetic resonance spectra of 1 and 2. Comparative ^{13}C chemical shift data for 1 and 2 are listed in Table 2. The values for 1 agree favorably with data reported earlier by Gampe, et al. [11], except that the assignments for C$_5$ and C$_{10}$ are interchanged based on specific proton-carbon decoupling experiments [12]. The C$_1$ and C$_{10}$ carbons were observed as weak triplets in the proton decoupled spectrum of 2 with $J_{13}C^2H$ coupling constants of 28.2 and 24.1 Hz, respectively. The anticipated upfield isotope shifts [13] were observed for C-2 (10.17 ppm) and for C-9 (−0.12 ppm), confirming the assignment of deuterium substitution of C-1 and C-10.

Scheme 4

M$^+$· (m/e 223 ; 225)   ⇌   ⇌

⇌   XVI (m/e 223 ; 225)   −H$_2$CN·   VIII (m/e 195 ; 196)

* −S

XVII (m/e 191 ; 193)   −HCN *   XI (m/e 164,165)   −H·   XII (m/e 163 ; 164)

⇌   ⇌   II (m/e 191 ; 193)

EXPERIMENTAL

The mass spectra were recorded on a Varian MAT 311A double focusing mass spectrometer at 70 eV. The samples were introduced by direct

inlet probe and were heated at a rate of about 450° in 200 seconds. The metastable ion spectra were obtained by focusing on the parent ion and scanning the electrostatic sector and magnetic fields at a rate such that the ratio E/B remained constant at a constant accelerating voltage. The high resolution mass spectra were recorded at a resolution of 7000 and processed with a Varian SS-200 data system. The temperature of the sample was raised manually to attain the optimum spectrum. In all schemes, calculated metastable values are given in parentheses. Purity of the sample were checked by tlc. The ^{1}H and ^{13}C nuclear magnetic resonance spectra were recorded on a Brucker WM-250 Fourier transform nuclear magnetic resonance spectrometer equipped with a Brucker ASPECT-2000 computer and Diablo Model 44b disk accessory. The observation frequency for ^{1}H spectra was 250 MHz and that for ^{13}C spectra was 62.9 MHz. The samples were measured in deuteriochloroform solution and tetramethylsilane was used as the internal standard. The temperature stability was ±1°.

Pyrrolo[3,2,1-*kl*]phenothiazine (**1**).

This compound is reported in the literature [14]. We also have prepared it by an alternative method [15]. It had mp 116-117° lit [13] mp 117-118°; ^{1}H nmr [12]: δ (ppm) 7.31, d, $(J_{1,2} = 3.4$ Hz), H-1; 7.04, dd, $(J_{3,4} = 8.0$ Hz, $J_{3,5} = 0.9$ Hz), H-3; 6.78-6.97, m, (5H), H-4, H-7, H-8, H-9 and H-10; 6.56, dd, $(J_{5,4} = 7.4$ Hz, $J_{5,3} = 0.9$ Hz), H-5; 6.39, d, $(J_{2,1} = 3.4$ Hz), H-2; ms; m/e (%): 225 (M + 2, 5.6), 224 (M + 1, 17.2), 223 (M⁺, 100), 222 (28.6), 221 (0.7), 197 (0.7), 196 (2.1), 195 (4.1), 192 (2), 191 (12), 190 (4.8), 189 (1.2), 179 (3.4), 178 (5.4), 177 (2.0), 166 (0.3), 165 (0.7), 164 (2.0), 163 (2.1), 154 (0.2), 153 (1.1), 152 (4.6), 151 (3.6), 150 (2.0), 112 (3.4), 111.5 (M²⁺, 19.2), 111 (2.6), 110.5 (4.9), 98.5 (3), 98 (2.1), 97.5 (4.8), 97 (3.2), 89.5 (2), 89 (5.1), 88.5 (0.5), 84.5 (1.1), 81.5 (1.3), 77 (1.2), 76.5 (0.6), 76 (5.2), 75.5 (1.4), 75 (3.6), 74.3 (M³⁺, 0.7), 69 (2.7), 65 (0.4), 63 (4.5).

1,10-Dideuteriopyrrolo[3,2,1-*kl*]phenothiazine (**2**).

This compound was prepared by metallation of pyrrolo[3,2,1-*kl*]phenothiazine (**1**) with excess *n*-butyl-lithium followed by subsequent quenching with deuterium oxide [10]. It had mp 115-117° lit [14] mp 116-118° for nondeuterated parent compound **1**; nmr [12]: δ (ppm) 7.04, dd, $(J_{3,4} = 7.9$ Hz; $J_{3,5} = 0.8$ Hz), H-3; 6.77-6.96 (4H), H-4, H-7, H-8 and H-9; 6.54, dd, $(J_{5,4} = 7.3$ Hz, $J_{5,3} = 0.8$ Hz), H-5; 6.39, s, H-2 (doublet at 7.31 and 6.97 ppm in **1** were virtually absent in **2**; from integration measurements deuterium incorporation at C-1 and C-10 was greater than 95%); ms; m/e (%): 227 (M + 2, 5.5), 226 (M + 1, 18), 225 (M⁺, 100), 224 (28.8), 223 (7.7), 225 (M⁺, 100), 224 (28.8), 223 (7.7), 222 (0.8), 221 (0.4), 206 (0.5), 198 (1.3), 197 (3.6) 196 (2.5), 195 (0.7), 194 (2.2), 193 (14.9), 192 (5.2), 191 (2.2), 190 (0.8), 189 (0.4), 182 (0.6), 181 (4.2), 180 (6.1), 179 (2.5), 178 (1.3), 177 (0.4) 173 (0.2), 172 (0.4), 171 (0.4), 170 (0.5), 169 (0.3), 168 (0.3), 167

(0.7), 166 (1.6), 165 (3), 164 (1.3), 163 (0.4), 162 (0.2), 156 (0.3), 155 (0.8), 154 (3.9), 153 (5.6), 152 (3.8), 151 (1.8), 150 (0.5), 112.5 (M²⁺, 19.1), 112 (C_6H_8S, 3.4), 115 (3.8), 111 (2.6), 110 (0.2), 109 (0.5), 103 (4.7), 99.5 (2.2), 98.5 (3.7), 98 (4.7), 97.5 (2.1), 96.5 (2.7), 96 (0.7), 95.5 (0.6), 91 (1.4), 90.5 (2.1), 90 (5.3), 89.5 (1.3), 89 (1.2), 79 (1.9), 78 (1.3), 77.5 (0.6), 77 (6.6), 76.5 (2.8), 76 (4.3), 75.5 (1), 75 (M³⁺, 6.8), 74 (1.7), 71 (2.1), 69 (3.9), 67 (1.4), 66 (0.6), 65 (0.9), 64 (3.8), 63.5 (1.1), 63 (3.7).

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