JOURNAL OF MASS SPECTROMETRY, VOL. 32, 728–738 (1997)

Comparative Study of the Cyclization of Dithiocarbamate Derivatives of Polyhalopyridines Induced by Electron Impact and Carried Out in Solution

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Identical products of the intramolecular cyclization of pyridine derivatives were shown to be formed in solution and in the gas phase under electron impact conditions. The analogies and contradictions of this reaction proceeding in two different phases were studied. © 1997 by John Wiley & Sons, Ltd.

J. Mass Spectrom. **32**, 728–738 (1997)
No. of Figures: 9 No. of Tables: 2 No. of Refs: 6

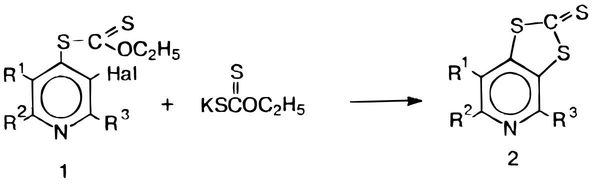
KEYWORDS: polyhalopyridines; dithiocarbamates; electron impact ionization; collision-induced dissociation; cyclization; monomolecular transformation

INTRODUCTION

Polychloropyridines containing *N*,*N*-dialkyldithiocarbamate and alkylxanthate groups in positions 2 or 4 or the pyridine ring may undergo intramolecular substitution reactions leading to 1,3-dithiolo[4,5-*c*]pyridines and bis-1,3-dithiolo[4,5-*b*;4′,5′-*e*] pyridines.[1]

The ability of mass spectrometry to mimic some intramolecular reactions catalyzed by acids or bases in solution has been demonstrated.[2–6] This led us to study the reactivity of the pyridine derivatives mentioned above in a mass spectrometer *vs.* the liquid phase.

The reaction of pyridine derivatives **1** with potassium carbethoxydithiolate results in the corresponding cyclization products **2** [Eqn (1)]. Carbonyl-containing heterocycles **3** may be obtained via similar reactions involving thioamides **4** as parent compounds.



(1)

These reactions take place via various intra- and intermolecular mechanisms, while several factors influence their rate and yields. The nature of the leaving group (Cl *vs.* F) and the presence of electron-withdrawing groups in the *para* position to the leaving group are the most important among these factors. The higher the electronegativity of the halogen and the stronger the electron-withdrawing effect of the substituent in the *para* position are, the easier the reaction proceeds.

EXPERIMENTAL

Compounds **1**–**8** were prepared at the Institute of Chemical Physics, Chernogolovka, as described[1] and were pure according to thin-layer chromatography and NMR spectroscopy. Mass spectrometric measurements (low- and high-resolution electron impact (EI) spectra and collision-induced decomposition (CID) spectra) were performed with a VG 70-250SEQ mass spectrometer. The source temperature was 250 °C, ionization energy 70 eV, emission current 250 mA (micro) and accelerating voltage 7 kV. Samples were introduced through the direct probe while their temperature was maintained as low as possible to prevent thermolysis. (The low-resolution EI spectra were also recorded with a Varian MAT-44S instrument. The effect of the source temperature in the range (120–250 °C was negligible, while an increase in the direct probe temperature led to changes in the spectra). Argon was used as the collision gas at a pressure sufficient to reduce the main beam signal by 20%. The CID spectra were recorded at collision energies of 50 and 100 eV.

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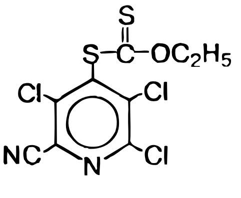
Contract grant sponsor: International Science Foundation.
Contract grant number: NBL000.

CCC 1076–5174/97/070728–11 $17.50

Received 4 February 1997
Accepted 27 March 1997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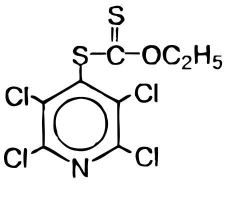
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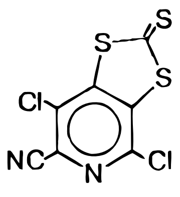
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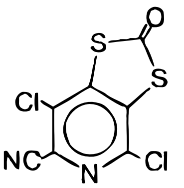
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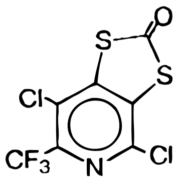
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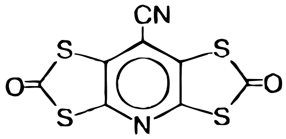
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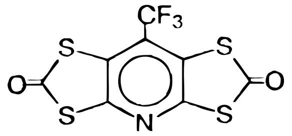
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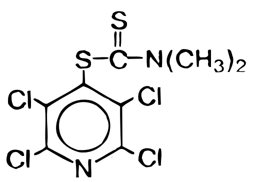
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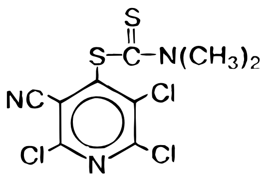
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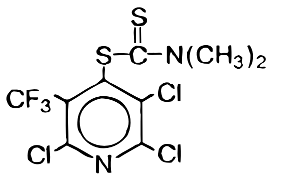
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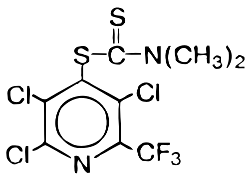
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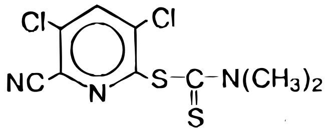
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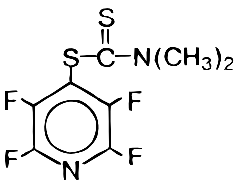
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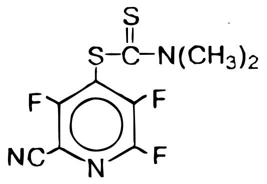
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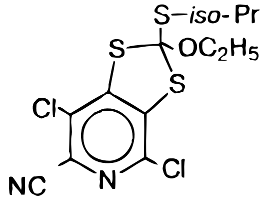
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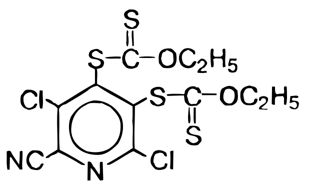
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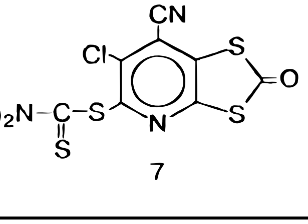
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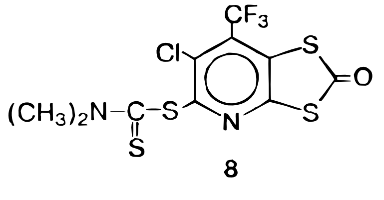
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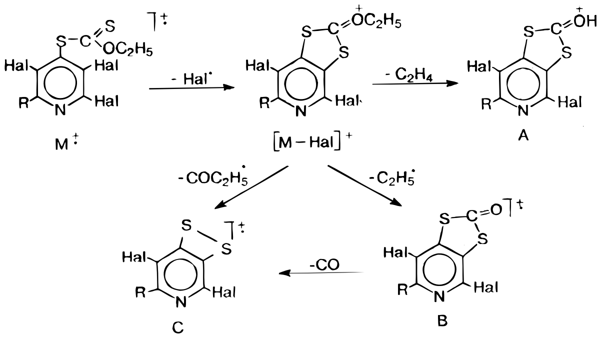
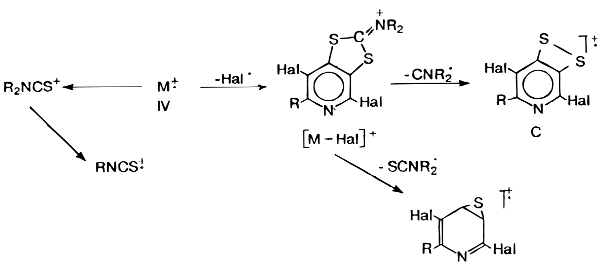
RESULTS AND DISCUSSION

The general fragmentation schemes for the first stages of decomposition of $M^{+\cdot}$ of **1** and **4** are shown in Schemes 1 and 2, respectively. The relative abundances (as a percentage of the total ion current) of the mentioned ions are presented in Tables 1 and 2. $M^{+\cdot}$ of these compounds are unstable and not observed in the spectra.

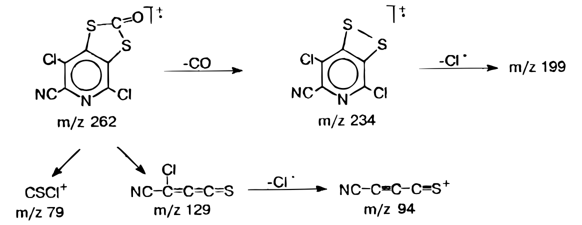
Since ions B of the proposed structure are identical with $M^{+\cdot}$ of the independently obtained compounds **3**, and ions C are the primary fragment ions appearing during decomposition of the molecular ions of **3**, it was of interest to obtain the CID spectra of the correspond-



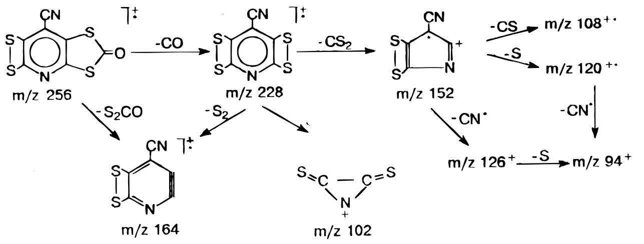
Scheme 1



Scheme 2



Scheme 3



Scheme 4

ing pairs of ions.

Figure 1(a)–(c) represent the CID spectra of *m*/*z* 262 for $M^{+\cdot}$ of **3a**; $[M - Cl, -C_2H_5]^{+\cdot}$ of **1a** and $[M - C_2H_5, -SCN(CH_3)_2]^{+\cdot}$ of intermediate **5** isolated after the cyclization reaction in solution. The spectra are remarkably similar to each other, confirming the identical structure of the ions at *m*/*z* 262. The fragmentation scheme shown in Scheme 3 may be proposed.

Similar CID experiments confirmed the identical structure of *m*/*z* 234 ions in the case of the $[M - CO]^{+\cdot}$ fragment of **3a** [Fig. 2(a)], the $[M - CS]^{+\cdot}$ fragment of **2** [Fig. 2(b)], the $[M - CSOC_2H_5, -CSOC_2H_5]^{+\cdot}$ fragment of **6** [Fig. 2(c)] and the $[M - Cl, -C_2H_5, -CO]^{+\cdot}$ fragment of **1a** [Fig. 2(d)], although one can note a decreased abundance of the ion at *m*/*z* 117. The composition C_3NSCl of the latter was obtained by HRMS. The structure of ion at *m*/*z* 278 ($M^{+\cdot}$ of **2**) is identical with that of $[M - CS(OC_2H_5)_2]^{+\cdot}$ of **6** [see Fig. 3(a) and (b)].

Compound **7** also undergoes electron impact-induced cyclization as the CID spectra of its fragment at *m*/*z* 256 ($[M - Cl, -CN(CH_3)_2]^{+\cdot}$) [Fig. 4(a)] appeared to be completely identical with that of the $[M - CO]^{+\cdot}$ ion of **3c** [Fig. 4(b)]. In this case, the fragmentation scheme shown in Scheme 4 may be proposed.

Figure 5(a) and (b) demonstrate the structural identity of *m*/*z* 271 ions, being the $[M - Cl, -CN(CH_3)_2, -CO]^{+\cdot}$ fragment of **8** and $[M - 2CO]^{+\cdot}$ ion of **3d**.

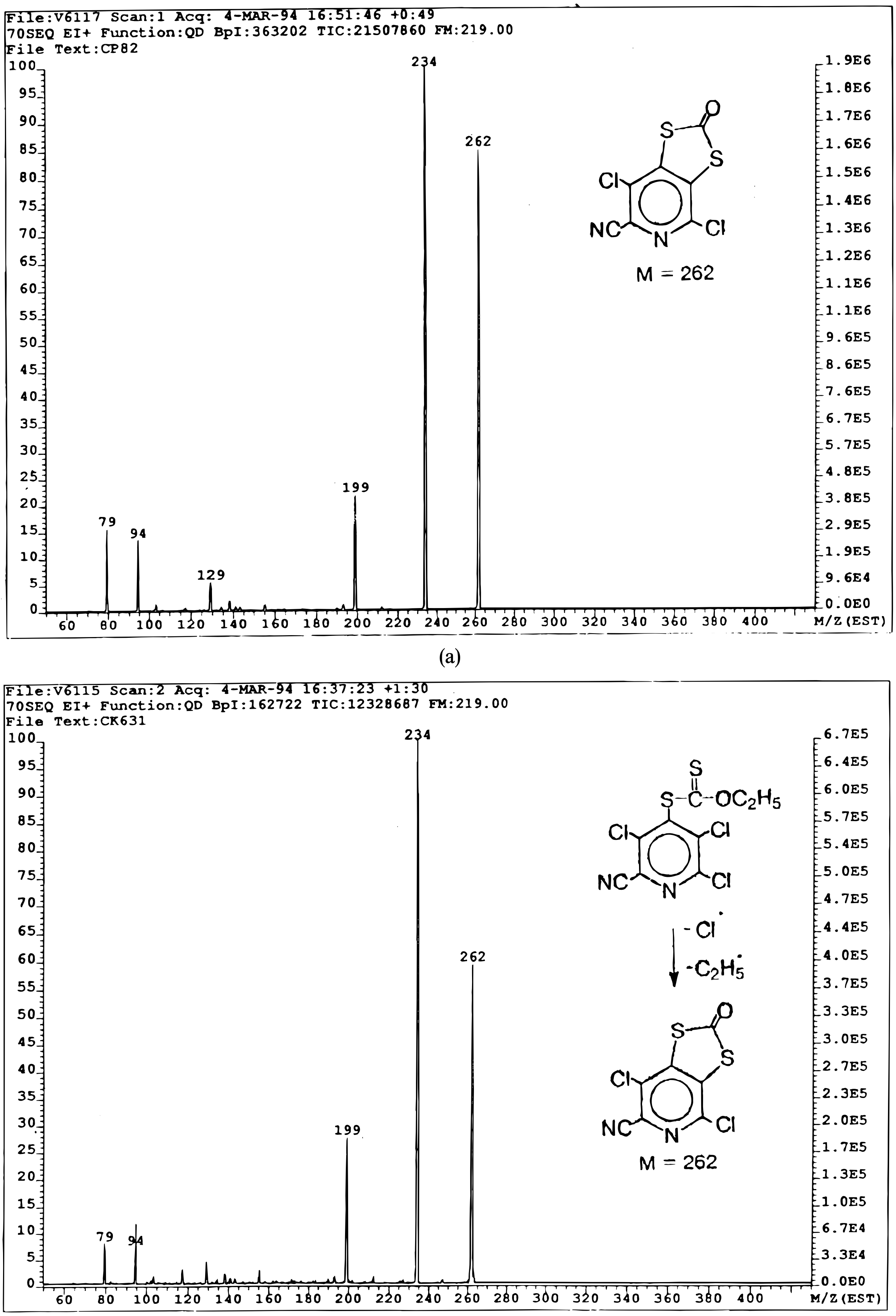
The data in Table 2 throw light on the nature of the halogen in this intramolecular substitution reaction. While the abundance of the $[M - Cl]^+$ ion is 28.4% (total ion current) for tetrachloro derivative **4a**, the corresponding $[M - F]^+$ ion is absent in the mass spectrum of the analogous tetrafluoro derivative **4f**. This proves that mass spectrometric cyclization with the loss of fluorine atom is not possible. In this case, the results

Table 1. Relative abundances (as a percentage of total ion current) of fragments in the mass spectra of compounds 1

Compound	$[M - Cl]^+$	A $[M - Cl, -C_2H_4]^+$	B $[M - Cl, -C_2H_5]^{+\cdot}$	C
1a	0.18	1.80	0.70	0.10
1b	7.79	4.40	1.09	0.10

Table 2. Relative abundances of fragments (as a percentage of total ion current) in the mass spectra of compounds 4

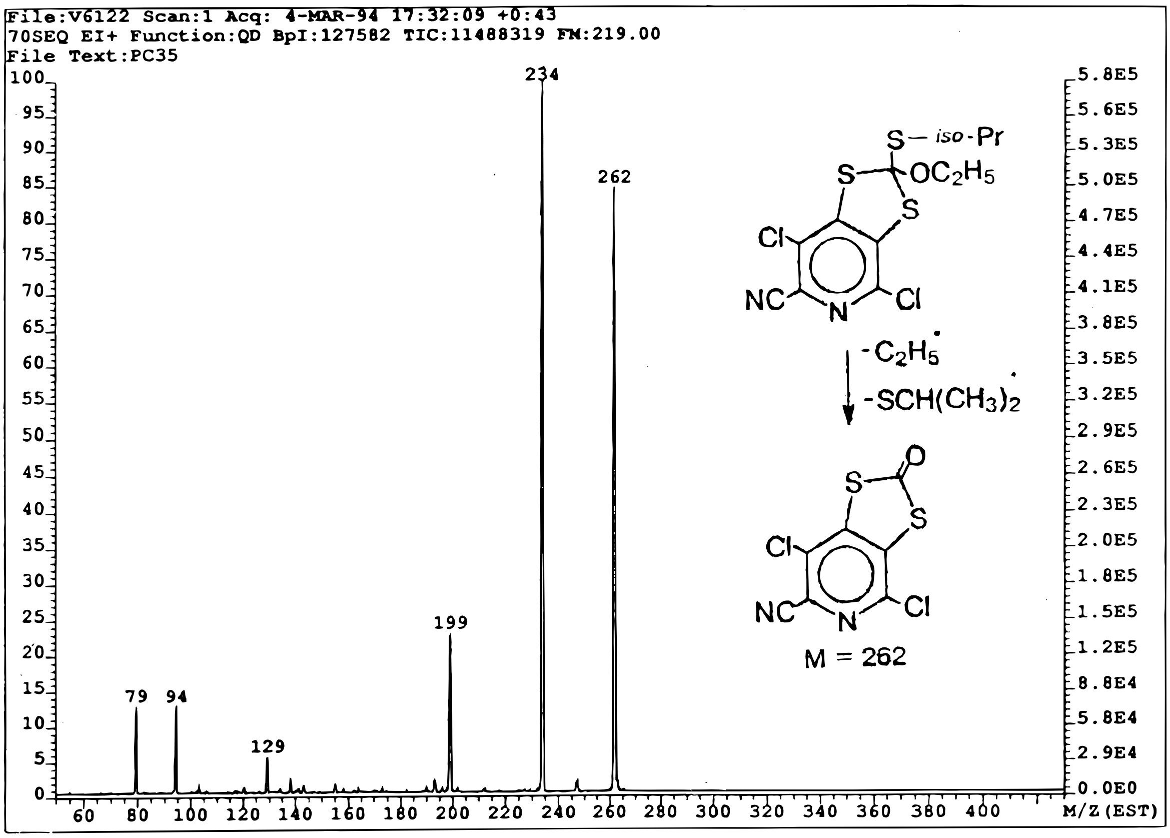
Compound	$RNCS^{+\cdot}$	R_2NCS^+	$[M - Hal]^+$	$[M - Hal, -CNR_2]^{+\cdot}$	$[M - Hal, -SCNR_2]^{+\cdot}$
4a	5.65	14.7	28.4	2.85	2.85
4b	6.05	18.3	21.2	0.76	1.66
4c	5.45	12.1	12.0	3.20	0.90
4d	6.82	16.9	19.2	1.61	0.37
4e	6.47	31.1	11.7	0.28	0.28
4f	8.20	29.3	–	–	–
4g	6.40	39.8	6.5	–	0.49



(a)

(b)

Figure 1. CID spectra of (a) *m*/*z* 262 for $M^{+\cdot}$ of **3a**, (b) $[M - Cl, -C_2H_5]^{+\cdot}$ (*m*/*z* 262) of **1a** and (c) $[M - C_2H_5, -SCH(CH_3)_2]^{+\cdot}$ (*m*/*z* 262) of **5**.



(c)

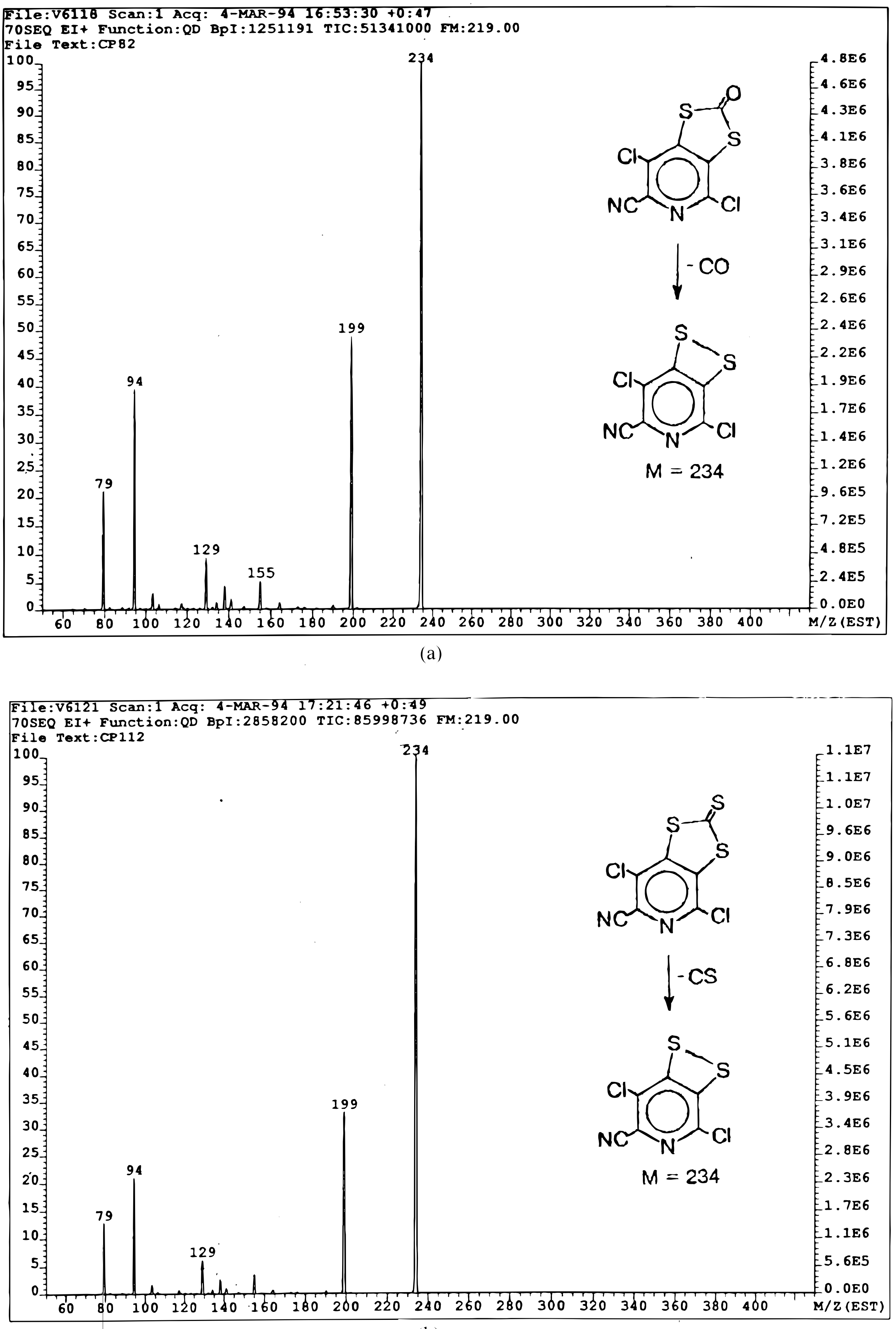
Figure 1. —(*Continued*)

for the gas and liquid phases appear to be different, as both tetrahalogenated compounds (**4a** and **4f**) do not produce cyclic structures in solution. The rationalization of this difference might involve the radical *vs.* anion losses in these cases. On the other hand, the introduction of an electron-withdrawing cyano group in positions 2 or 4 of the pyridine ring, favoring cyclization in solution, has the same effect in conditions of mass spectrometry. For example, the abundance of the $[M - F]^+$ ion for **4g** is 6.5%, indicating that the substitution readily takes place under EI conditions. This compound is also highly active in solution, requiring lower temperatures to carry on cyclization, while increasing its temperature to the level necessary for other compounds **4** leads to polymerization products.

Therefore, the cyclization of pyridine derivatives **1** and **4** leads to the same products in solution (reaction with potassium carbethoxydithiolates; may be followed by hydrolysis) and in the gas phase (EI ionization). The presence of electron-withdrawing groups in the *para* position to the leaving group favors the reaction, while chlorine is a better leaving group compared with fluorine under EI conditions (radical loss).

Acknowledgement

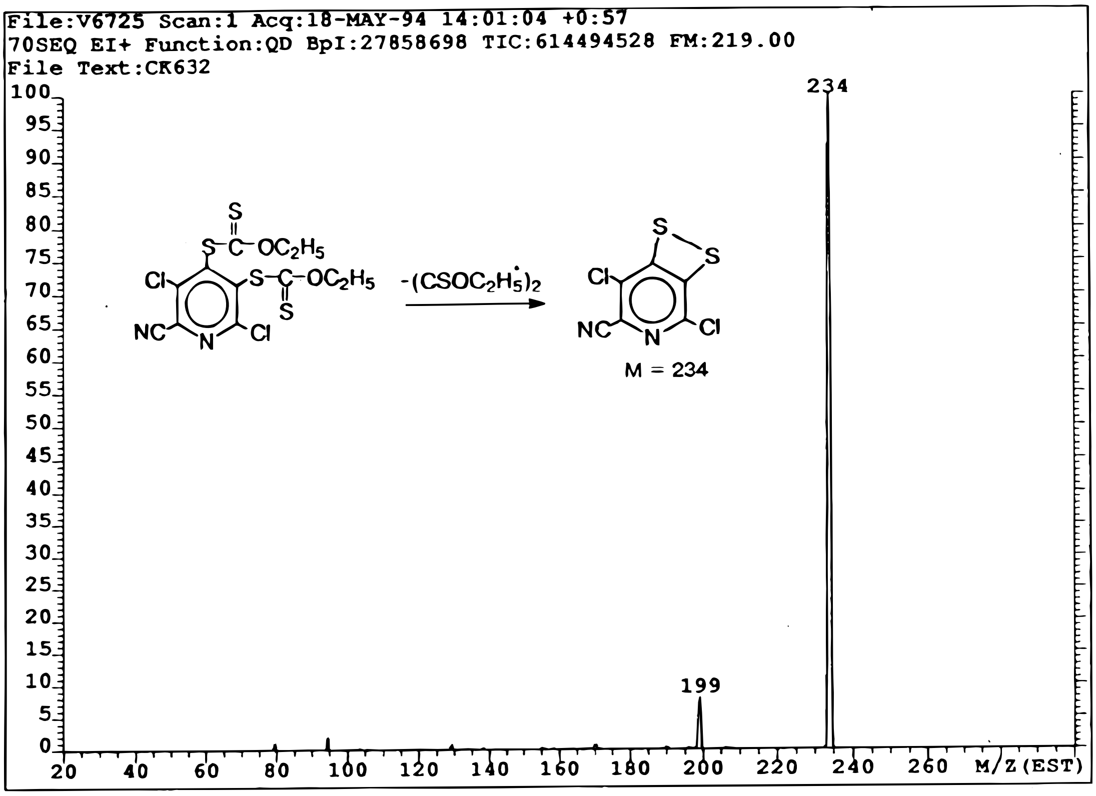
This research was made possible in part by Grant NBL000 from the International Science Foundation.



(a)

(b)

Figure 2. CID spectra of (a) $[M - CO]^{+\cdot}$ (*m/z* 234) of **3a**, (b) $[M - CS]^{+\cdot}$ (*m/z* 234) of **2**, (c) $[M - CSOC_2H_5, -CSOC_2H_5]^{+\cdot}$ (*m/z* 234) of **6** and (d) $[M - Cl, -C_2H_5, -CO]^{+\cdot}$ (*m/z* 234) of **1a**.



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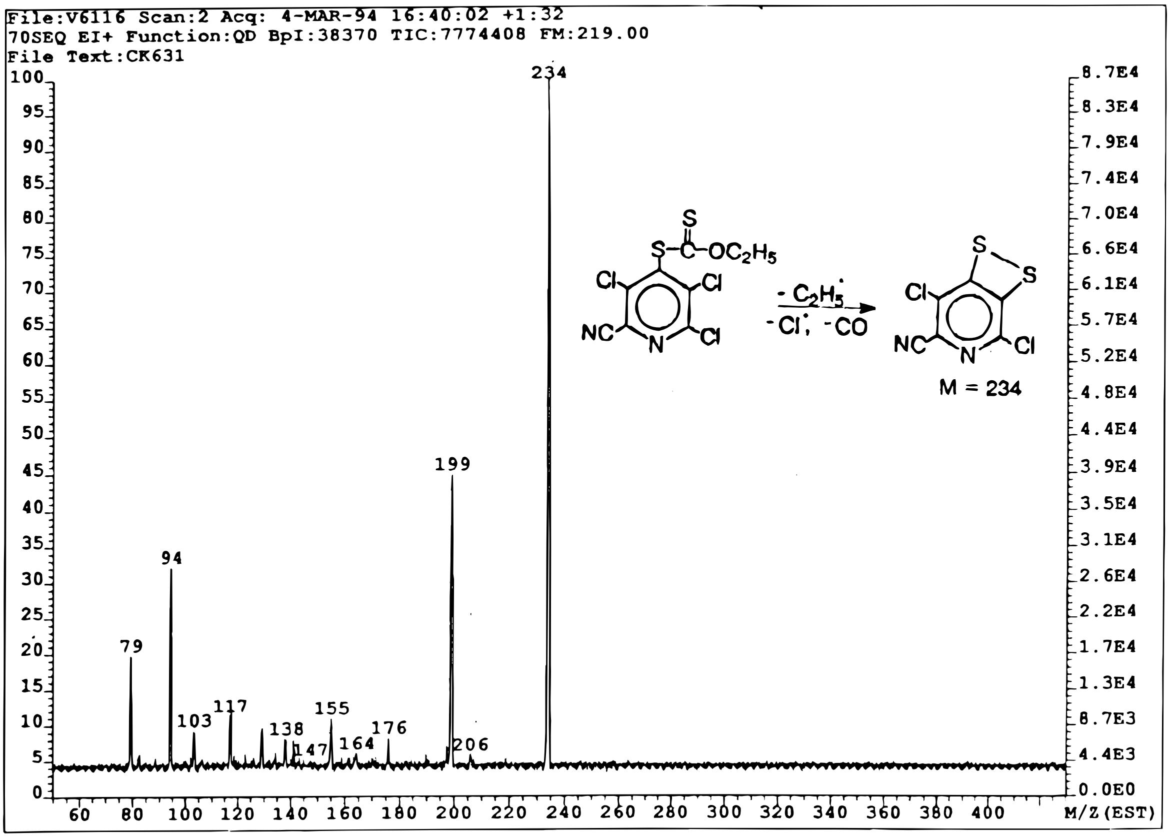
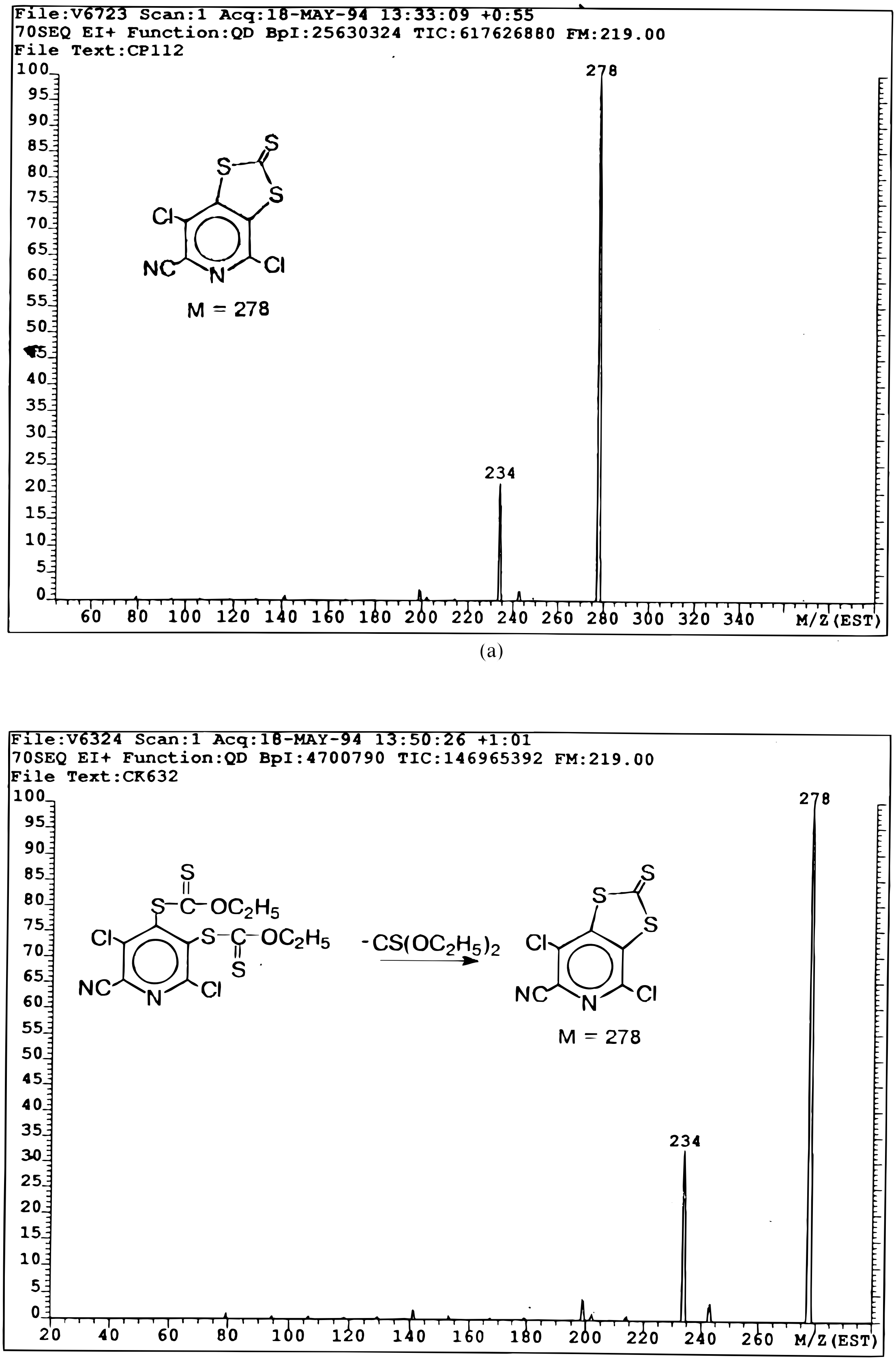


(d)

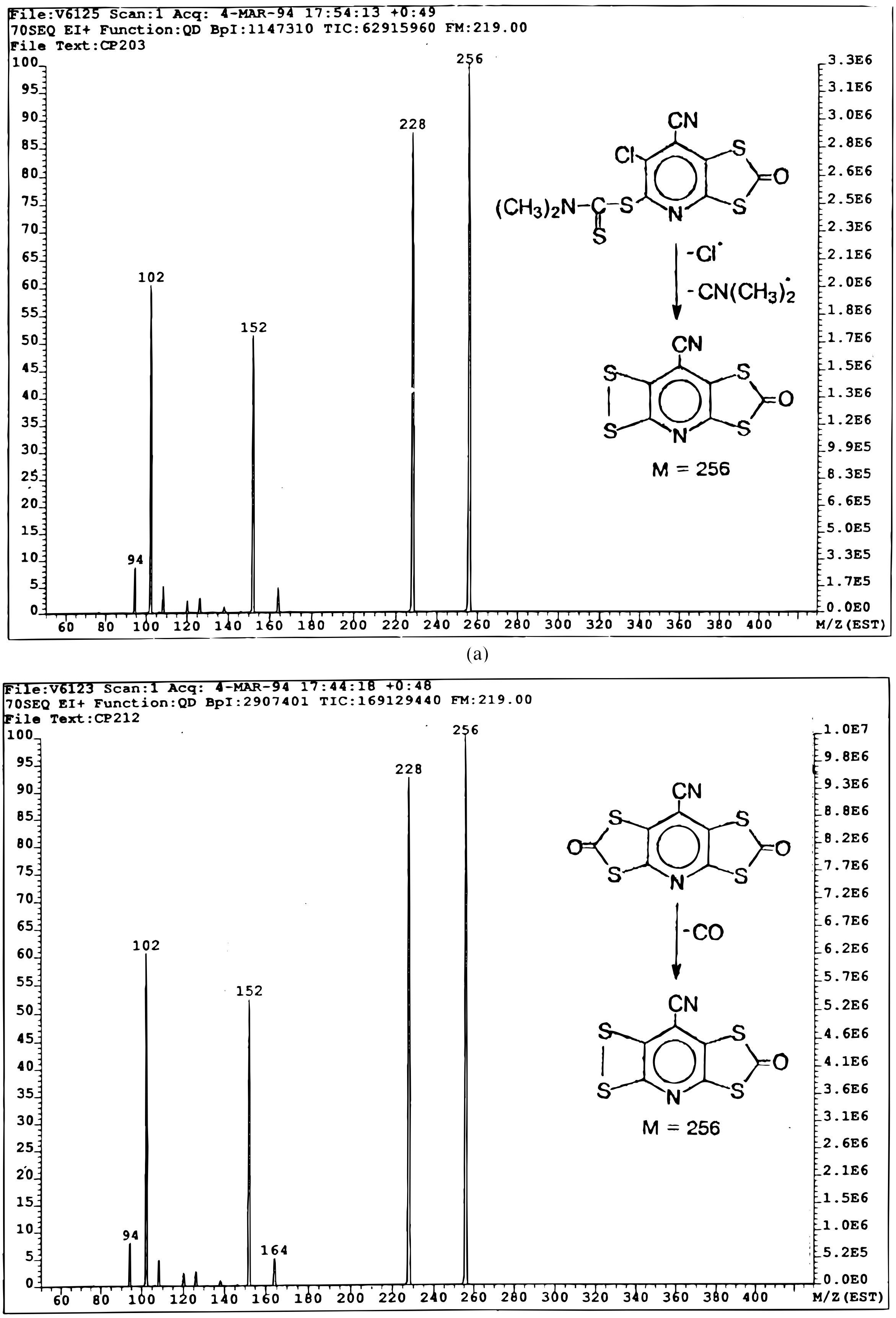
Figure 2.—(*Continued*)



(a)

(b)

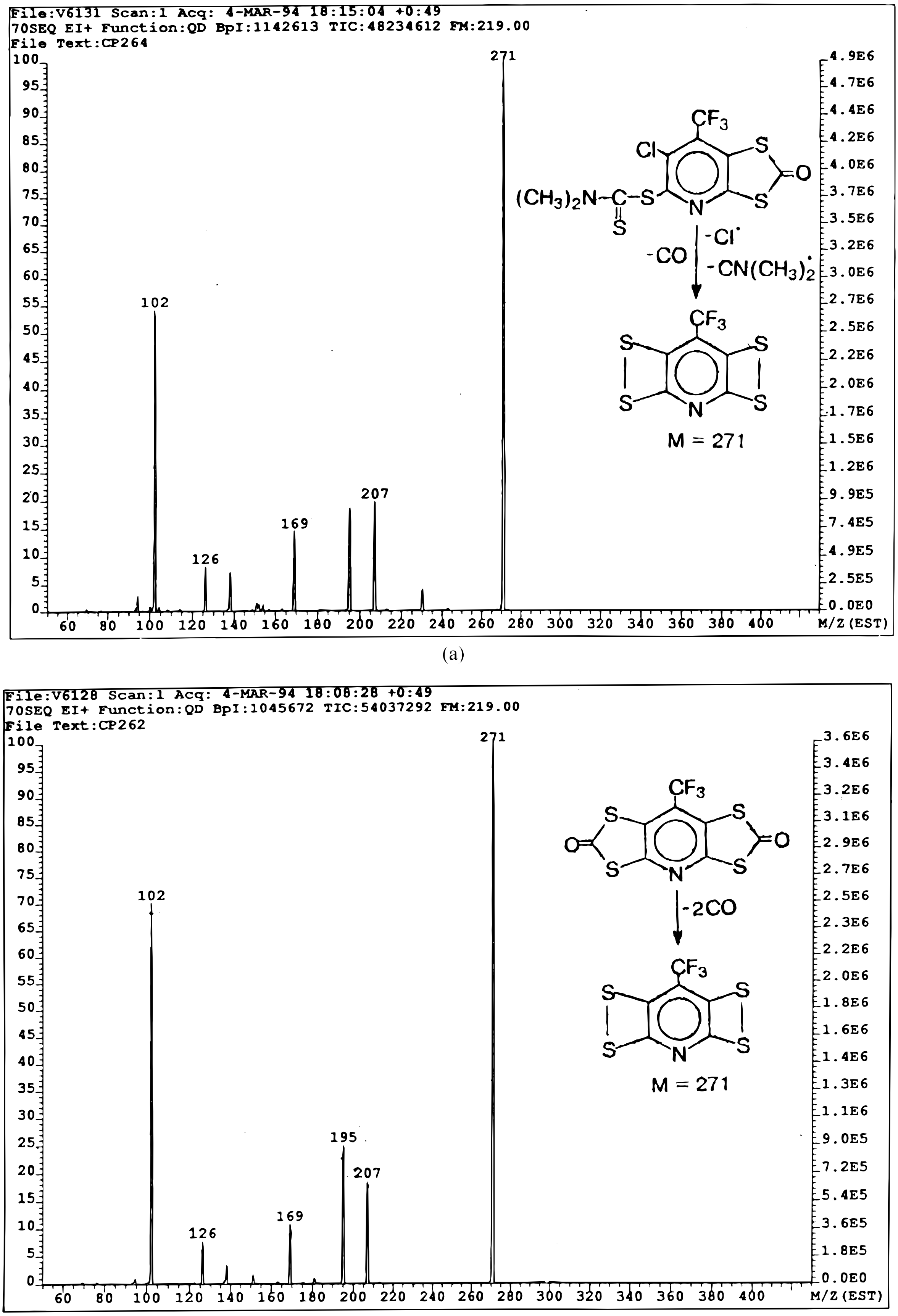
Figure 3. CID spectra of (a) *m/z* 278 ($M^{+\cdot}$ of **2**) and (b) $[M - CS(OC_2H_5)_2]^{+\cdot}$ (*m/z* 278) of **6**.



(a)

(b)

Figure 4. CID spectra of (a) $[M - Cl, -CN(CH_3)_2]^{+\cdot}$ (*m*/*z* 256) of **7** and (b) $[M - CO]^{+\cdot}$ (*m*/*z* 256) of **3c**.



(a)

(b)

Figure 5. CID spectra of (a) $[M - Cl, -CN(CH_3)_2, -CO]^{+\cdot}$ (*m*/*z* 271) of **8** and (b) $[M - 2CO]^{+\cdot}$ (*m*/*z* 271) of **3d**.

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