# A Study of the Mass Spectrometrical Fragmentation Patterns

of 1,3,6-Triazacycl[3.3.3]azines*

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The mass spectrometrical fragmentation patterns of seven members of the 1,3,6-triazacycl[3.3.3]azine system, *8a — g*, are discussed. Exact mass tables for the 2-methyl-substituted compounds *8c*, *8e*, and *8f* provide the basis for the molecular composition assignments in the spectra of these compounds and of *8a*, *8b*, *8d*, and *8g*. In accord with the assumption that the system is aromatic, an abundance of doubly charged ions, the structures of which are discussed, was found the spectra.

In the preceding paper [1] we have described the syntheses of seven members of the new heterocyclic, aromatic 1,3,6-triazacycl[3.3.3]azine system *8*,** and in this communication we wish to discuss the mass spectrometrical fragmentation patterns of *8a — g* (and also of 4-cyano-2,8-dimethyl-1,3,6-triazacycl[3.3.3]azine, *8h*).
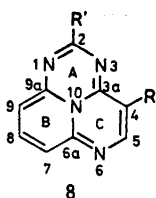
	R	R′
8a	H	H
8b	CN	H
8c	CN	CH$_3$
8d	COOEt	H
8e	COOEt	CH$_3$
8f	H	CH$_3$
8g	COOMe	H

All seven compounds displayed, as could be anticipated from their aromatic structures, large molecular ion peaks. The spectra, with assignments, are reproduced in Figs. 1a — 7a. Determinations of exact masses confirmed the assigned molecular formulas (*cf.* also Table 1 in Ref. 1). The assignments of

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* Presented in part at the "Second International Congress on Heterocyclic Chemistry" in Montpellier, July 7 — 12, 1969.
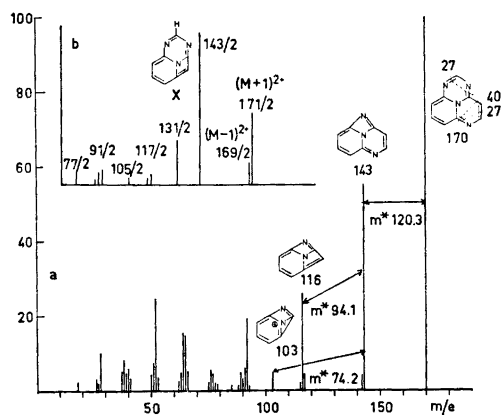** The compounds bear the same numbers in this communication as in Ref. 1.

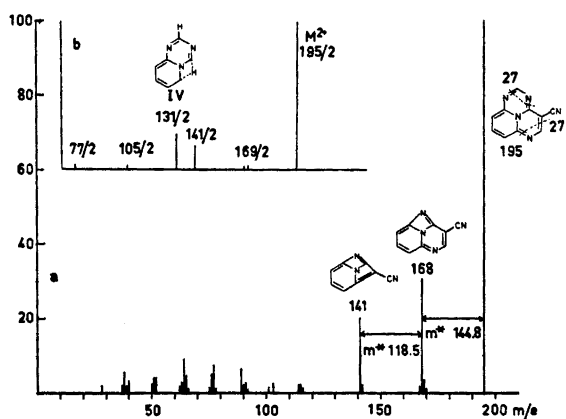*Fig. 1.* Ion spectra of *8a*, (a) singly charged; (b) doubly charged.

Fig. 2. Ion spectra of *8b*, (a) singly charged; (b) doubly charged.
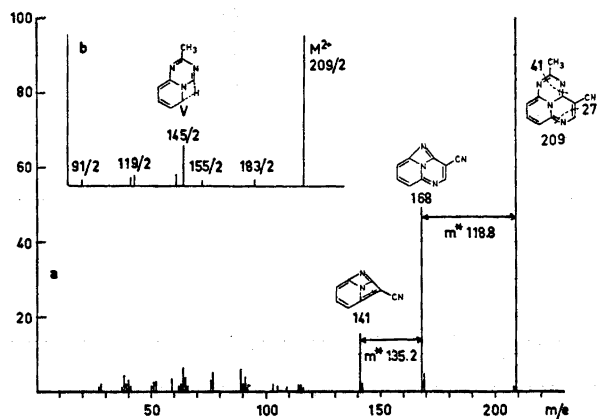

Fig. 3. Ion spectra of *8c*, (a) singly charged; (b) doubly charged.
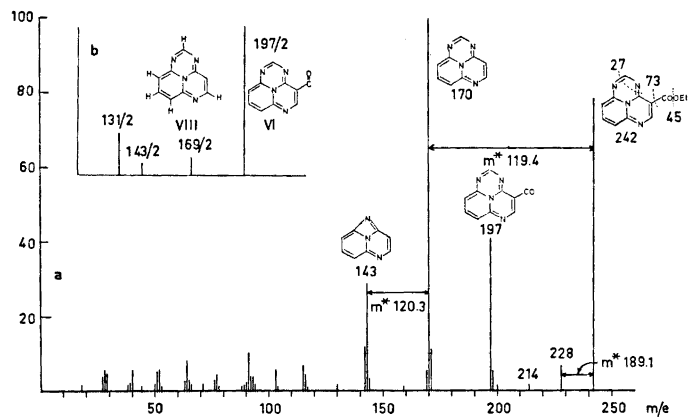
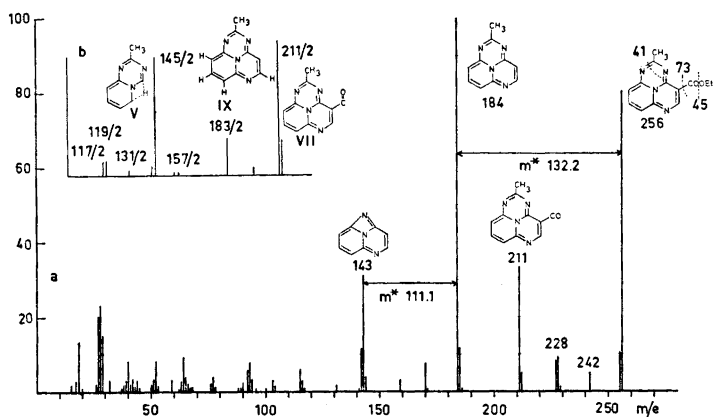*Fig. 4.* Ion spectra of *8d,* (a) singly charged; (b) doubly charged.

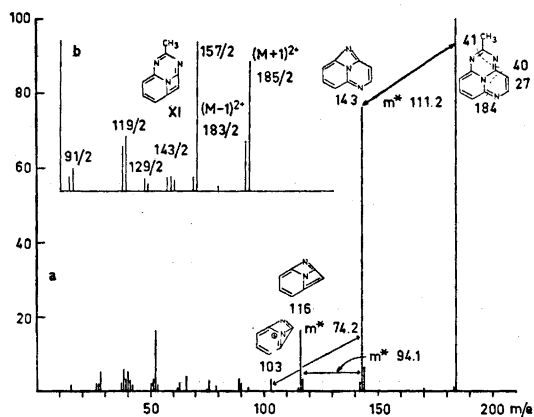*Fig. 5.* Ion spectra of *8e,* (a) singly charged; (b) doubly charged.

Fig. 6. Ion spectra of *8f,* (a) singly charged; (b) doubly charged.

molecular compositions of individual fragments proposed in Charts 1, 2, and 3 are based upon exact masses of "all fragments" in compounds *8c*, *8e*, and *8f* (*cf.* mass tables). The compositions of the fragments in the spectra of the norcompounds *8a*, *8b*, *8d*, and *8g* are derived by analogy with the corresponding ions in the respective methyl homolog. A number of fragmentation paths are supported by the presence of metastable ions indicated in the spectra and in the charts.
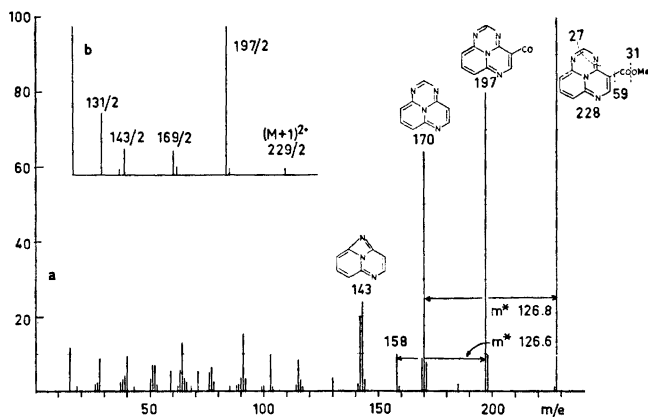

Fig. 7. Ion spectra of *8g*, (a) singly charged; (b) doubly charged.

A major common fragmentation path in N-heteroaromatic systems is the loss of HCN and, where a *C*-methyl group is adjacent to a ring nitrogen atom, of CH_3CN.* This type of fragmentation is observed in all seven compounds. In the spectra of *8c* and *8f*, 41 and in the spectra of *8a* and *8b*, 27 mass units are eliminated from the molecular ions, which are the base peaks in these spectra. In the 4-carbethoxy and 4-carbomethoxy derivatives this type of fragmentation is preceded by the loss of $COOC_2H_5 + H$ and $COOCH_3 + H$, respectively, from the molecular ions to form base peaks at $m/e = 170$ or 184 from which the elements of HCN or CH_3CN are then eliminated. In all compounds these fragmentations are followed by a second loss of HCN to form the third most intense (above $m/e \sim 100$) peak at $m/e = 116$ in the spectra of *8a* and *8f*, and at $m/e = 141$ in *8b* and *8c*. The fact that CH_3CN is the first fragment lost, where this is possible ($R' = CH_3$), leads to the proposal that the first elimination of HCN in the norcompounds ($R' = H$) involves C-2 and N-1 or C-2 and N-3, both possibilities giving rise to the same ion I (*cf.* Charts 1, 2, and 3). The second mole of HCN lost would therefore be derived from C-5 and N-6. In the cyano-substituted derivatives the fragments at $m/e = 141$ could conceivably have the hetaryne structure II,[3] resulting from an elimination of the cyano group and the adjacent H-5. This structure has the same molecular composition as III.

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* This has been observed in a large number of systems, *cf.* Refs. 2 – 5 in Ref. 2.
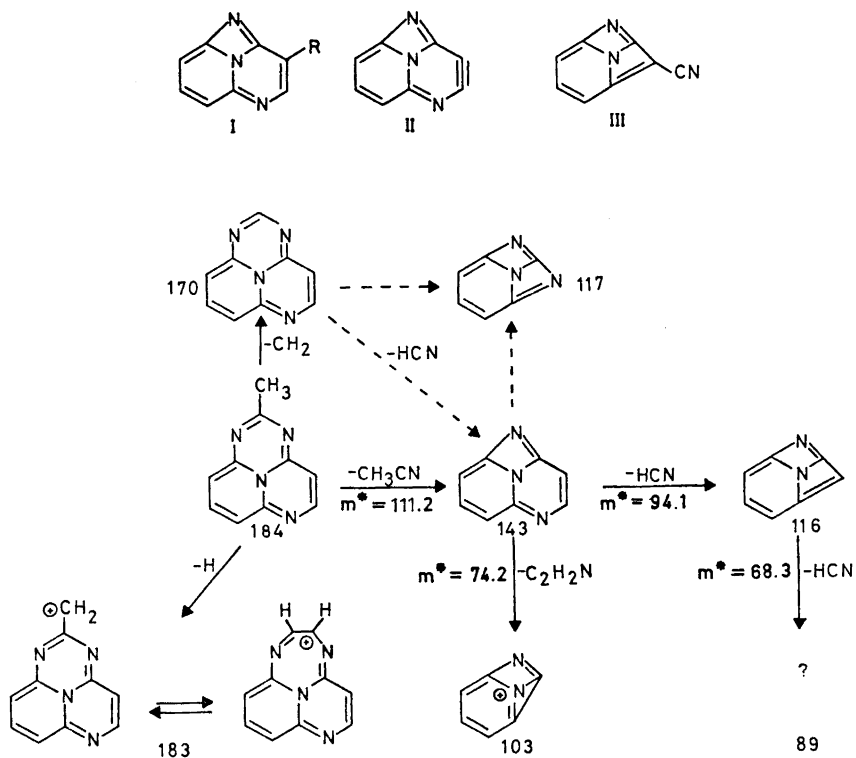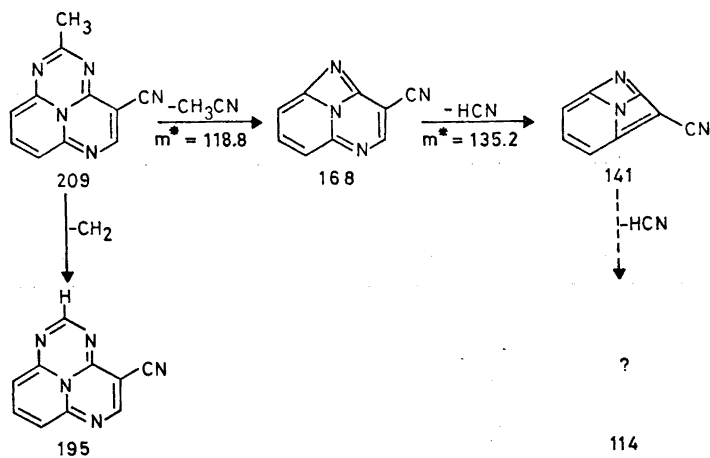
Chart 1. Fragments in the mass spectrum of 8f.

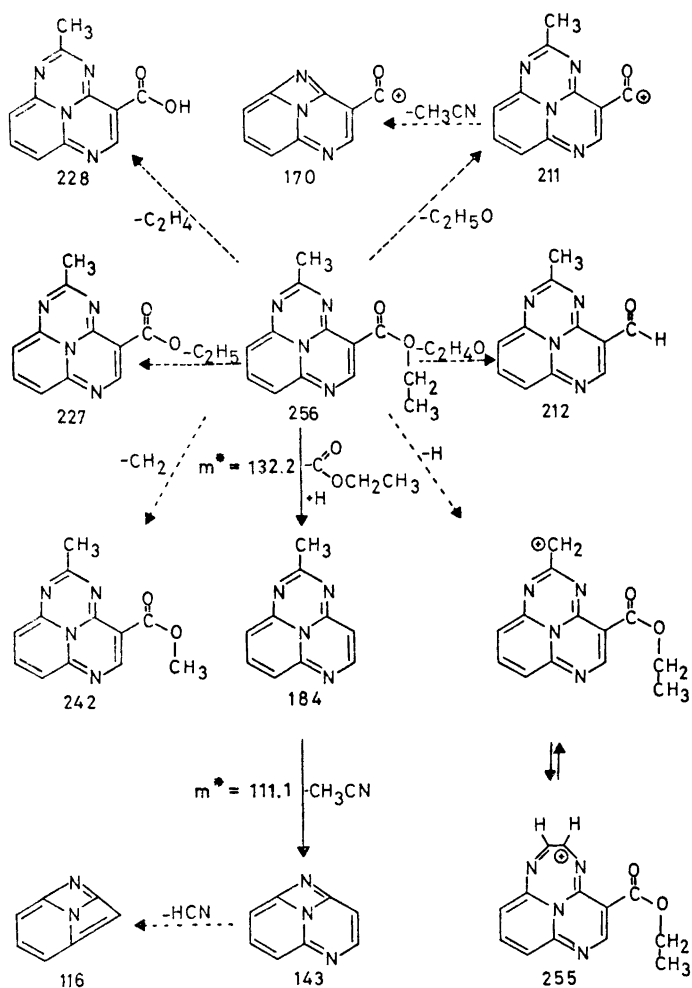Chart 2. Fragments in the mass spectrum of 8c.

Chart 3. Fragments in the mass spectrum of *8e*.

The methyl-substituted compounds *8c*, *8e*, and *8f* give rise to an M − 1 peak which could be stabilized in the following fashion.[4] The carbethoxy, but
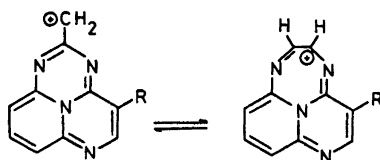
Table 1. Accurate mass measurements in 2-methyl-1,3,6-triazacycl[3.3.3]azine *(8f)*.

m/e found	Formula	m/e calc.	$\Delta m/e$
184.0748	$C_{10}H_8N_4$	184.0749	0.0001
183.0706	$C_{10}H_7N_4$	183.0671	35
170.0591	$C_9H_6N_4$	170.0592	1
143.0483	$C_8H_5N_3$	143.0483	0
117.0355	$C_6H_3N_3$	117.0327	28
116.0361	$C_7H_4N_2$	116.0374	13
115.0291	$C_7H_3N_2$	115.0296	5
103.0282	$C_6H_3N_2$	103.0296	5
93.0421	$C_5H_5N_2$	93.0453	32
90.0224	$C_5H_2N_2$	90.0218	6
89.0274	C_6H_3N	89.0265	9
89.0146	C_5HN_2	89.0140	6
79.0313	$C_4H_3N_2$	79.0296	17
78.0352	C_5H_4N	78.0344	8
78.0221	$C_4H_2N_2$	78.0218	3
77.0254	C_5H_3N	77.0265	11
76.0183	C_5H_2N	76.0187	4

Table 2. Accurate mass measurements in 4-cyano-2-methyl-1,3,6-triazacycl[3.3.3]azine *(8c)*.

m/e found	Formula	m/e calc.	$\Delta m/e$
209.0705	$C_{11}H_7N_5$	209.0701	0.0004
195.0570	$C_{10}H_5N_5$	195.0545	25
169.0430	$C_9H_5N_4$	169.0514	84
	$C_8{}^{13}CH_5N_4$	169.0470	40
168.0422	$C_9H_4N_4$	168.0436	14
167.0359	$C_9H_3N_4$	167.0357	2
142.0368	$C_8H_4N_3$	142.0405	37
	$C_7{}^{13}CH_4N_3$	142.0347	19
141.0313	$C_8H_3N_3$	141.0327	14
114.0229	$C_7H_2N_2$	114.0218	11
103.0280	$C_6H_3N_2$	103.0296	16
92.0373	$C_5H_4N_2$	92.0374	1
91.0293	$C_5H_3N_2$	91.0296	3
90.0233	$C_5H_2N_2$	90.0218	15
89.0258	C_6H_3N	89.0265	7
77.0238	C_5H_3N	77.0265	37
77.0127	C_4HN_2	77.0140	13
76.0175	C_5H_2N	76.0187	12

not the carbomethoxy, derivatives exhibit M − 14 and M − 28 peaks, which are absent in the spectra of all the other compounds. A likely explanation for these peaks is the ejection of CH_2 and of C_2H_4, respectively, from the ethyl ester group in *8d* and *8e*. These processes are supported by exact mass measurements for the fragments in *8e*. That the M − 14 peak at $m/e = 242$ is not the

Table 3. Accurate mass measurements in 4-carbethoxy-2-methyl-1,3,6-triazacycl[3.3.3]-azine (*8e*).

m/e found	Formula	m/e calc.	Δm/e
256.0974	$C_{13}H_{12}N_4O_2$	256.0960	0.0014
255.0896	$C_{13}H_{11}N_4O_2$	255.0882	14
242.0808	$C_{12}H_{10}N_4O_2$	242.0804	4
232.0949	$C_{11}H_{12}N_4O_2$	232.0960	11
228.0608	$C_{11}H_8N_4O_2$	228.0647	39
227.0525	$C_{11}H_7N_4O_2$	227.0569	44
214.0597	$C_{11}H_8N_3O_2$	214.0616	19
212.0663	$C_{11}H_8N_4O$	212.0698	35
211.0638	$C_{11}H_7N_4O$	211.0620	18
201.0763	$C_{10}H_9N_4O$	201.0776	13
199.0632	$C_{10}H_7N_4O$	199.0619	13
197.0852	$C_{11}H_9N_4$	199.0827	25
187.0593	$C_9H_7N_4O$	187.0620	27
186.0779	$C_{11}H_{10}N_2O$	186.0793	14
186.0492	$C_{10}H_6N_3O_2$	186.0429	63
	$C_9H_6N_4O$	186.0542	50
185.0792	$C_{10}H_9N_4$	185.0827	35
185.0441	$C_9H_5N_4O$	185.0463	22
184.1041	$C_{12}H_{12}N_2$	184.1000	41
184.0756	$C_{10}H_8N_4$	184.0749	7
184.0354	$C_{11}H_6NO_2$	184.0399	45
	$C_9H_4N_4O$	184.0385	31
183.0665	$C_{10}H_7N_4$	183.0671	6
177.0524	$C_8H_7N_3O_2$	177.0538	14
171.0366	$C_8H_3N_4O$	171.0307	59
170.0347	$C_9H_4N_3O$	170.0354	7
167.0311	$C_9H_3N_4$	167.0358	47
160.0699	$C_9H_8N_2O$	160.0636	63
160.0471	$C_8H_6N_3O$	160.0511	40
160.0261	$C_8H_4N_2O_2$	160.0273	12
159.0686	$C_8H_7N_4$	159.0671	15
158.0579	$C_8H_6N_4$	158.0592	13
158.0334	$C_8H_4N_3O$	158.0354	20
157.0633	$C_9H_7N_3$	157.0640	7
152.0784	$C_7H_{10}N_3O$	152.0824	40
151.0725	$C_7H_9N_3O$	151.0745	20
150.0267	$C_6H_4N_3O_2$	150.0303	36
149.0248	$C_6H_3N_3O_2$	149.0225	23
144.0501	$C_8H_6N_3$	144.0562	61
143.0448	$C_8H_5N_3$	143.0483	35
142.0375	$C_8H_4N_3$	142.0405	30
141.0278	$C_8H_3N_3$	141.0327	49
134.0716	$C_7H_8N_3$	134.0718	2
133.0548	$C_6H_5N_4$	133.0514	34
	C_8H_7NO	133.0528	20
132.0512	$C_7H_6N_3$	132.0562	50
132.0266	$C_7H_4N_2O$	132.0324	58
131.0425	$C_7H_5N_3$	131.0483	58
	$C_6H_3N_4$	131.0358	67
130.0380	$C_7H_4N_3$	130.0405	25
128.0445	$C_4H_6N_3O_2$	128.0460	15
120.0555	$C_8H_6N_3$	120.0562	7
116.0380	$C_7H_4N_2$	116.0374	6

Table 3. Continued.

115.0312	$C_7H_3N_2$	115.0296	16
109.0639	$C_5H_7N_3$	109.0640	1
108.0309	$C_5H_4N_2O$	108.0324	15
106.0322	C_6H_4NO	106.0293	29
105.0409	$C_6H_5N_2$	105.0453	31
104.0365	$C_6H_4N_2$	104.0374	9
103.0301	$C_6H_3N_2$	103.0296	5
94.0505	$C_5H_6N_2$	94.0531	26
94.0267	$C_3H_2N_4$	94.0279	12
92.0348	$C_5H_4N_2$	92.0374	26
91.0269	$C_5H_3N_2$	91.0296	27
90.0203	$C_5H_2N_2$	90.0218	15
89.0212	C_6H_3N	89.0265	53
88.0122	C_6H_2N	88.0187	65
83.0796	C_5H_9N	83.0735	61
82.0513	$C_4H_6N_2$	82.0531	18
81.0395	$C_4H_5N_2$	81.0453	58
79.0291	$C_4H_3N_2$	79.0296	5
78.0262	$C_4H_2N_2$	78.0218	44
77.0230	C_5H_3N	77.0265	35
76.0174	C_5H_2N	76.0187	13

result of a loss of CH_2 from the methyl group at C-2 is supported by analogous metastable peaks in the spectra of *8e* and *8g*.
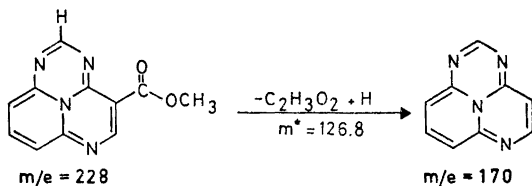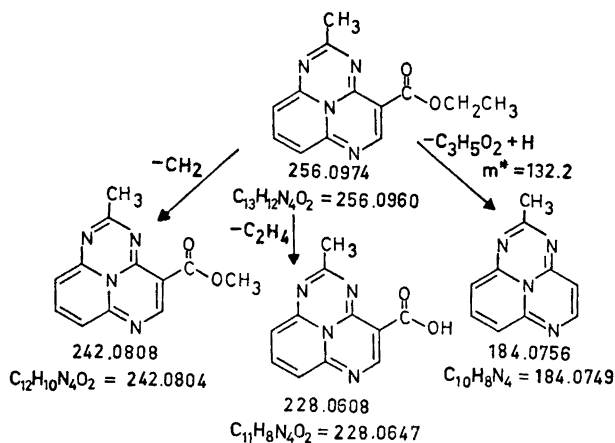
Some additional fragmentations and fragment structures are proposed in Charts 1, 2, and 3. All ions with $m/e > 103$ seem to be derived from fragmentations of rings A and C. For ions with $m/e = 77 - 100$, no intensity pattern characteristic for all the compounds can be recognized, and no well-supported structures can be proposed. It seems reasonable to assume, however, that these fragments contain an intact B ring (the original pyridine system). It has been observed [5] that γ-picoline does not eject CH_3CN to any considerable extent, and therefore we prepared the 8-methyl homolog of $8c$ from 2,6-diamino-4-methylpyridine. We expected that in the spectrum of 4-cyano-2,8-dimethyl-1,3,6-triazacycl[3.3.3]azine (Fig. 8), the ions corresponding to those in the $m/e = 77 - 100$ region in the spectrum of $8c$ would be displaced by 14 mass units. Fig. 8 shows that this is probably the case. Attempts to use the low resolution spectra of the 7-bromo, 9-bromo or 7,9-dibromo derivatives of $8c$ [6] for the same purpose were not successful since the first fragmentations in the spectra of these compounds result from the ejection of one or two atoms of bromine.*
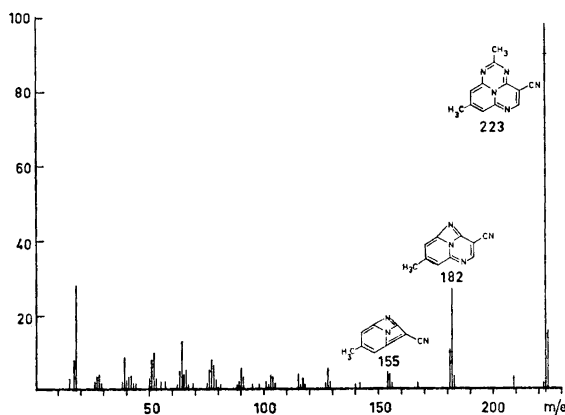

Fig. 8. Singly charged ion spectrum of *8h*.

The resonance energies obtained from the HMO calculations [1] indicated that the triazacyclazine system is aromatic, and this assumption is supported by the presence of abundant, doubly charged ions, the stability of which is increased when conjugated olefinic bonds and heteroatoms are present, particularly when they form 6 π electron (or 10 π electron, *etc.*) heteroaromatic systems.** In the doubly charged ion spectra of the 4-cyano cyclazine, *8b*, and of its methyl homolog, *8c*, the base peaks are represented by M^{2+}, with intensities of 3 and 6 %, respectively, of the intensities of the corresponding singly charged molecular ions, which are also base peaks. The ions appearing at $m/e = 131/2$ in the spectrum of *8b*, and at $145/2$ in the spectrum of *8c*, probably

have structures IV and V, respectively (*cf.* Figs. 2b and 3b and Table 4). In the doubly charged ion spectra of the carbethoxy compounds *8d* and *8e*, the base peaks at $m/e = 197/2$ and $211/2$, respectively, probably possess structures VI and VII (*cf.* Figs. 4b and 5b and Table 5). The ions at $m/e = 131/2$

Table 4. Accurate mass measurements in 4-cyano-2-methyl-1,3,6-triazacycl[3.3.3]azine (*8c*).

m/e^{2+} found	Formula	m/e calc.	$m/e \times 0.5$	$\Delta m/e$
104.5341	$C_{11}H_7N_5$	209.0701	104.5351	0.0010
79.5285	$C_7H_5N_5$	159.0545	79.5273	12
72.5303	$C_8H_7N_3$	145.0640	72.5320	17

Table 5. Accurate mass measurements in 4-carbethoxy-2-methyl-1,3,6-triazacycl[3.3.3]-azine (*8e*).

m/e^{2+} found	Formula	m/e calc.	$m/e \times 0.5$	$\Delta m/e$
128.0445	$C_{13}H_{12}N_4O_2$	256.0960	128.0480	0.0035
105.0301	$C_{11}H_7N_4O$	211.0620	105.0310	9
92.0348	$C_{10}H_8N_4$	184.0749	92.0375	27
91.5285	$C_{10}H_7N_4$	183.0671	91.5336	49
72.5281	$C_8H_7N_3$	145.0640	72.5320	39

and at 145/2 (in *8e* only) may be represented, as in compounds *8b* and *8c*, by structures IV and V, respectively, and for the ions at $m/e = 169/2$ and 183/2, respectively, structures VIII and IX are proposed. The presence of a fairly low-intensity M^{2+} ion in *8e* is proven by an exact mass measurement. For the carbomethoxy compound, *8g*, the doubly charged ion spectrum (*cf.* Fig. 7b) is practically identical to that of *8d*. An $(M+1)^{2+}$ peak at $m/e = 229/2$, not found in the spectrum of *8d*, is observed for *8g*. The doubly charged ion spectra of the parent cyclazine *8a*, and of its methyl homolog, *8f* (*cf.* Figs. 1b and 6b and Table 6), display base peaks at $m/e = 143/2$ and

Table 6. Accurate mass measurements in 2-methyl-1,3,6-triazacycl[3.3.3]azine (*8f*).

m/e^{2+} found	Formula	m/e calc.	$m/e \times 0.5$	$\Delta m/e$
92.5405	$C_{10}H_9N_4$	185.0827	92.5414	0.0009
	$C_9{}^{13}CH_9N_4$	185.0783	92.5392	13
92.0368	$C_{10}H_8N_4$	184.0749	92.0375	7
91.5367	$C_{10}H_7N_4$	183.0671	91.5336	31
78.5325	$C_9H_7N_3$	157.0640	78.5325	5
72.5341	$C_8H_7N_3$	145.0640	72.5320	21
71.5255	$C_8H_5N_3$	143.0483	71.5242	13

157/2, respectively, corresponding to $(M-27)^{2+}$ and having structures X and XI. No fragment formed by the loss of HCN from the molecular ion is present in the singly charged ion spectrum of *8f*. Both *8a* and *8f* form large $(M+1)^{2+}$ and $(M-1)^{2+}$ ions, and for *8f*, exact mass measurements ascertain an M^{2+} ion at $m/e = 184/2$ of unknown, but low, intensity. It is unlikely that the ion at $m/e = 185/2$ is derived from the ^{13}C isotope peak of the molecular ion, but an exact mass measurement does not distinguish it from $(M+1)^{2+}$ (*cf*. Table 6).

EXPERIMENTAL

General. Mass spectra were recorded with an LKB 900 mass spectrometer and exact mass determinations were made with a GEC-AEI 902 mass spectrometer. The mass tables were obtained with an Atlas MAT SM1 instrument. Nuclear magnetic resonance spectra were recorded with a Varian Model A-60 spectrometer. Ultraviolet and visible spectra were measured in ethanol with a Cary 15 spectrophotometer. Infrared spectra were determined in KBr with a Beckman IR 9 spectrophotometer.

2,6-Diamino-4-methylpyridine. Using a procedure of Bernstein *et al.*,[8] somewhat modified, this compound was synthesized in the following way. To a solution of 20 g (0.22 mol) of γ-picoline in 40 g of N,N-dimethylaniline, 36 g (0.92 mol) of sodium amide (50 % suspension in toluene) was added. The mixture, which turned black upon heating, was allowed to stand at 150° for 17 h, then at 190° for 4 h, and finally cooled to room temperature. The N,N-dimethylaniline was decanted off, the residual solid carefully decomposed with ice, and the resulting solution was extracted with three 300 ml portions of isopropyl alcohol. The isopropyl alcohol solution was evaporated to dryness *in vacuo*, and the tarry residue was triturated with chloroform. The dark solid obtained was recrystallized three times from chloroform, yielding 2 g (7 %) of a white solid with m.p. (after sublimation at 65°/1 torr) 103−104° (lit.[8] 109−111°); NMR (DMSO-d_6): $\delta = 1.98$ (singlet, 3H, CH$_3$), 5.52 (singlet, 2H, H-3 and H-5), and 5.08 (4H, NH$_2$).

Condensation of 2,6-diamino-4-methylpyridine with ethoxymethylenemalononitrile. To a solution of 220 mg (1.79 mmol) of 2,6-diamino-4-methylpyridine in 22 ml of benzene, 246 mg (2.28 mmol) of ethoxymethylenemalononitrile was added and the mixture was refluxed for 24 h. Upon cooling, a brown solid precipitated and was collected, dried and recrystallized from ethyl acetate−petroleum ether, yielding 230 mg (64 %) of a light-brown crystalline solid, m.p. 204−205°; UV: λ_{max} at 235, 272, 285, and 355 nm; NMR (DMSO-d_6): $\delta = 2.13$ (singlet, 3H, CH$_3$), 6.08 (singlet, 1H), 6.23 (singlet, 1H), 8.58 (singlet, 1H, CH=C(CN)$_2$), 6.05 (broad singlet, 2H, NH$_2$), and 11.25 (broad singlet, 1H, NH); MS: $M^+ = 199$.

4-Cyano-2,8-dimethyl-1,3,6-triazacycl[3.3.3]azine. A mixture of 50 mg (0.25 mmol) of the above condensation product, 0.3 ml of acetic anhydride, and 2 ml of glacial acetic acid was refluxed for 30 min, cooled and evaporated to dryness *in vacuo*. Column chromatography on 5 g of silica gel with chloroform as the eluting agent gave 40 mg (71 %) of a violet crystalline solid. Further purification was accomplished by sublimation (200°/1 torr), m.p. 292−293°; IR: 2220 cm^{-1}; UV: λ_{max} at 212, 240, 263, 330 ($\varepsilon = 13\ 380$), 349, 366, 384, 500, 540, 577 ($\varepsilon = 468$), and 623 nm; NMR (trifluoroacetic acid): $\delta = 2.33$ (singlet, 3H, CH$_3$ at C-8), 2.48 (singlet, 3H, CH$_3$ at C-2), 6.72 (fine structure, 1H, H-7 or H-9), 7.07 (fine structure, 1H, H-7 or H-9), and 8.18 (singlet, 1H, H-5); MS: $M^+ = 223.0848$ (calc. for C$_{12}$H$_9$N$_5 = 223.0858$).

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