TABLE III

ULTRAVIOLET ABSORPTION SPECTRA OF BENZO[c]QUINOLIZINIUM SALTS[a]

Compd III	Substituent	Anion	Maximum, mμ (log ε)
a	...	Cl	229 (4.27), 255 (4.42), 280 (3.98), 295[b] (3.62), 332[b] (3.68), 349 (4.03), 365 (4.16)
b	8-NO_2	Cl	255 (4.54), 288 (4.10), 310[b] (3.94), 342[b] (3.66), 357 (4.01), 374 (4.06)
c	4-CH_3, 8-NO_2	Cl	255 (4.57), 291 (4.02), 305[b] (3.92), 320 (3.79), 346 (3.72), 361 (4.06), 379 (4.12)
d	4-CH_3	Cl	231 (4.02), 256 (4.40), 285 (3.83), 305[b] (3.46), 333[b] (3.62), 354 (4.02), 371 (4.16)
e	9-Cl	Cl	234 (4.26), 260 (4.45), 300[b] (3.64), 340[b] (3.72), 357 (4.08), 374 (4.19)
f	4-CH_3, 9-Cl	Cl	234 (4.17), 258 (4.46), 303[b] (3.59), 313 (3.65), 345[b] (3.65), 361 (4.09), 379 (4.22)
g	5-CH_3	Cl	230 (4.13), 258 (4.36), 284 (3.88), 304[b] (3.46), 340[b] (3.46), 358 (3.88), 374 (3.98)
h	5-C_6H_5	Cl	236 (4.27), 258 (4.47), 310[b] (3.70), 361 (3.92), 375 (4.00)
i	5-$COOC_2H_5$	ClO_4	233 (4.32), 262 (4.62), 310[b] (3.82), 335 (3.82), 350 (4.12), 367 (4.23)

[a] Determined in 95% ethanol. [b] Infraction.

erlenmeyer flask (oil bath) for 1 hr at 170°. During this heating the product was slowly precipitated as a tan crystalline solid. The reaction mixture which was almost completely solid was cooled and then treated with boiling ethyl acetate. Filtration gave 2.5 g (50%) of pure benzo[c]quinolizinium chloride IIIa (X = Cl), mp 247–249°. Recrystallization from 95% ethanol–ethyl acetate produced no change in melting point. Evaporation of the ethyl acetate filtrate gave *trans*-2′-chloro-2-stilbazole (Ia) which recrystallized from ligroin (bp 60–90°) to yield 2.0 g (40%).

When the purified *cis* isomer IIa (X = Cl) was cyclized by heating at 170° for 1 hr, a 55% yield of the quinolizinium salt IIIa (X = Cl), based on *cis* isomer initially used, was obtained.

Method B. Benzo[c]quinolizinium Perchlorate (IIIa, X = ClO_4).—*trans*-2′-Chloro-2-stilbazole (2.0 g) and iodine (0.2 g) were heated at 240° for 6 hr. The semisolid mass was cooled, triturated several times with boiling ethyl acetate; and, the insoluble residue was dissolved in water and filtered. The aqueous solution was decolorized with charcoal and 25% perchloric acid was added. On filtration there was obtained 1.7 g of crude product which, after three recrystallizations from ethanol, was reduced to 1.2 g (55%) of tan needles, mp 187–189°.

The **bromide IIIa** (X = Br) was obtained from the aqueous solution by addition of 10% bromine in 50% aqueous hydrobromic acid to precipitate the perbromide IIIa (X = Br_3). Boiling this for 30 min in 50% aqueous acetone and evaporating to dryness gave the bromide IIIa (X = Br). Recrystallization from ethyl alcohol–ethyl acetate gave 1.2 g of tan irregular crystals, mp 241–243°.

Method C. 5-Carboethoxybenzo[c]quinolizinium Perchlorate (IIIi, X = ClO_4).—Ethyl 2-pyridylacetate (4.1 g), *o*-chlorobenzaldehyde (3.5 g), and acetic anhydride (5 ml) were refluxed for 15 hr. The acetic anhydride was evaporated and the residue was poured into water (150 ml). The aqueous layer was decanted from the black oily solid and treated with aqueous 25% perchloric acid (1 ml) precipitating very impure material which was filtered off and discarded. The filtrate was treated with excess 25% perchloric acid and the precipitate was collected. Crystallization from acetonitrile–ethyl acetate gave 1.4 g (20%) of tan needles, mp 212–215°.

2-Amino-Δ²-thiazolines from Aminoethyl Thiosulfates. The Mass Spectra of 2-Amino-Δ²-thiazolines and Related Compounds

DANIEL L. KLAYMAN AND GEORGE W. A. MILNE

Walter Reed Army Institute of Research, Division of Medicinal Chemistry, Washington, D. C. 20012, and The National Institutes of Health, National Heart Institute, Laboratory of Metabolism, Bethesda, Maryland 20014

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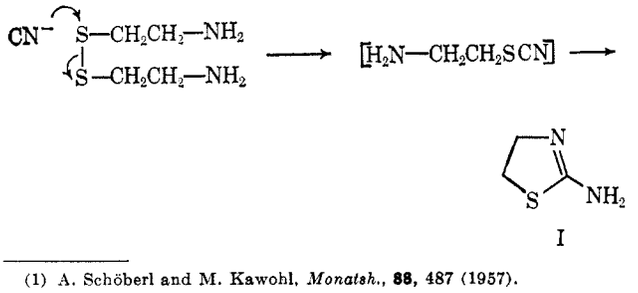
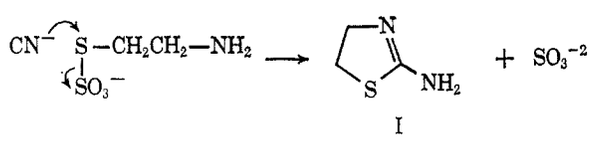
The attack of cyanide ion on primary and secondary aminoethyl thiosulfates yields 2-amino-Δ²-thiazolines. 2-Aminoethyl 2-aminoethanethiolsulfonate and 2-aminoethyl 2-aminoethanethiolsulfinate on treatment with cyanide also yield 2-amino-Δ²-thiazoline (I). The mass spectra of I, three isomeric methyl-2-amino-Δ²-thiazolines, 2-imino-3-amidinothiazolidine, and 2-amino-5,6-dihydro-4H-1,3-thiazine, made from thiosulfates by the above method, as well as 2-methylamino-Δ²-thiazoline and 2-amino-Δ²-selenazoline, have been analyzed and found to support the assigned structures. A previously undescribed variation of the McLafferty rearrangement is reported.

Among the various methods for the preparation of 2-amino-Δ²-thiazoline (I) is the reaction of cyanide ion with cystamine [bis(2-aminoethyl) disulfide].[1] The presumed intermediate, 2-aminoethylthiocyanate, cyclizes rapidly and has not been isolated. Footner and Smiles[2] reported that the action of cyanide ion on alkyl thiosulfates (Bunte salts) gives alkylthiocyanates and sulfite. When this reaction was applied to sodium 2-aminoethyl thiosulfate, a good yield of I was obtained. The cyanide displacement of sulfite from thiosulfate was tried on several other representative primary and secondary aminoethanethiosulfates to give the corresponding 2-amino-Δ²-thiazolines or 2-iminothiazolidines, when N-substituted aminoethanethiosulfates were the starting materials. This reaction was used to prepare 2-imino-3-methylthiazolidine



I

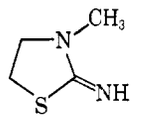


I

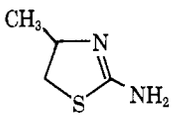
(1) A. Schöberl and M. Kawohl, *Monatsh.*, **88**, 487 (1957).

(2) H. B. Footner and S. Smiles, *J. Chem. Soc.*, **127**, 2887 (1925).

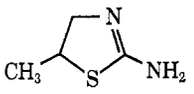
(II), 2-amino-4-methyl-Δ^2-thiazoline (III), and 2-amino-5-methyl-Δ^2-thiazoline (IV). Only 2-amino-Δ^2-



II



III

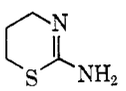


IV

thiazoline was isolated as a stable crystalline free base while the other derivatives were either oils or polymerized to varying extents and were isolated as salts. That these compounds exist in cyclic form was demonstrated by infrared spectroscopy. None of the compounds showed peaks near 4.67 μ (-SCN)[3] and each had a doublet very close to 6.01 and 6.10 μ (C=N, thiazolines).[4]

The synthesis of 2-amino-5-methyl-Δ^2-thiazoline (IV) by Hirsch[5] from impure 1-amino-2-bromopropane hydrobromide and potassium thiocyanate did not yield a pure product but one which was characterized only as a picrate. Repetition of this experiment with pure 1-amino-2-bromopropane hydrobromide revealed that the reaction proceeds at a slow rate even at reflux temperature. The hydrochloride of IV was prepared by our method from 2-aminopropane-1-thiosulfuric acid.

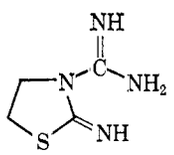
Schöberl, *et al.*,[6] were able to obtain 2-amino-5,6-dihydro-4H-1,3-thiazine (2-aminopentathiazoline, V) only as a picrate in the cyanide cleavage reaction with homocystamine [bis(3-aminopropyl) disulfide]. From 3-aminopropyl bromide hydrobromide and potassium thiocyanate they obtained 3-aminopropyl thiocyanate hydrobromide which was subsequently cyclized with cyanide ion to give V. Sodium 3-aminopropylthiosulfate, when treated with cyanide, gave a poor yield of V which was accompanied by a brownish polymer.



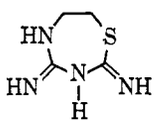
V

Polymer formation, indicative of intermolecular condensation, was less extensive when more dilute solutions of the reactants were used.

The reaction of sodium 2-guanidinoethyl thiosulfate with cyanide ion gave a product VI for which two structures (VIa and VIb) can be drawn depending upon



VIa

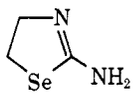


VIb

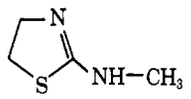
whether the cyclization takes place at the primary or secondary amine function of the guanidino group. Despite the evidence mentioned above that even a six-membered ring, V, forms with difficulty, the formation of a seven-membered ring structure was considered to have some likelihood. The infrared spectrum of the product (as its dihydrochloride) showed essentially no absorption at 6.01 μ, weak absorption at 6.09 μ, and a new peak at 5.90 μ (s). The Sakaguchi test[7] for substituted guanidines was positive and the compound absorbs in the ultraviolet region at 218 mμ (2-amino-Δ^2-thiazoline hydrochloride has a peak at 202 mμ). While this information suggests that structure VIa is the correct one, attempts to synthesize this compound by the guanidination of I using 2-methyl-2-thiopseudourea sulfate[8] or 1-guanyl-3,5-dimethylpyrazole nitrate[7] as a melt or heated in a 95% ethanol solution failed. That structure VIa is indeed correct was established by mass spectrometry (*vide infra*).

The reaction of cyanide ion with sodium 2-aminoethyl selenosulfate yielding 2-amino-Δ^2-selenazoline (VII) has been reported previously.[9]

The final compound in the series, 2-methylamino-Δ^2-thiazoline (VIII), cannot be prepared from an aminoalkyl thiosulfate but was made according to the method of Gabriel[10] from methyl isothiocyanate and bromoethylamine.

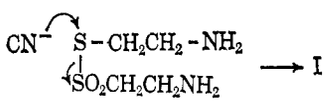


VII

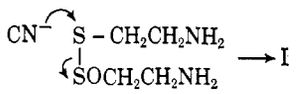


VIII

Efforts to synthesize I by the action of cyanide on 2-aminoethyl 2-aminoethanethiolsulfonate (IX) and on 2-aminoethyl 2-aminoethanethiolsulfinate (X) were successful but cyanide ion treatment of the mono- and disodium salts of 2-aminoethylphosphorothioic acid[11] did not give the desired product.



IX



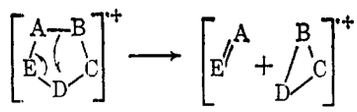
X

Mass Spectrometry.—Upon electron bombardment, a molecular ion derived from a thiazoline system fragments by a number of distinct routes depending upon the position and nature of any substituents in the ring. Consequently, the mass spectra of the thiazoline derivatives discussed in this paper are found in each case to permit unequivocal assignment of structure. The daughter ions resulting from the collapse of the thiazoline molecular ion will generally contain one or more "hetero" atoms which, by virtue of their unshared pairs of electrons, will stabilize the daughter ion. Thus the mass spectra of the thiazolines generally are found to be composed of a number of relatively abundant fragments.

While the fragmentation of a six-membered ring is known to be quite probable when the ring contains

(3) E. Lieber, C. N. R. Rao, and J. Ramachandran, *Spectrochim. Acta*, **13**, 296 (1959).
(4) W. Otting and F. Drawert, *Chem. Ber.*, **88**, 1469 (1955).
(5) P. Hirsch, *ibid.*, **23**, 964 (1890).
(6) A. Schöberl, M. Kawohl, and G. Hansen, *Ann.*, **614**, 83 (1958).
(7) R. A. B. Bannard, A. A. Casselman, W. F. Cockburn, and G. M. Brown, *Can. J. Chem.*, **36**, 1541 (1958).
(8) S. R. Safir, S. Kushner, L. M. Brancone, and Y. SubbaRow, *J. Org. Chem.*, **13**, 924 (1948).
(9) D. L. Klayman, *ibid.*, **30**, 2454 (1965).
(10) S. Gabriel, *Ber.*, **22**, 1139 (1889).
(11) S. Åkerfeldt, *Acta Chem. Scand.*, **13**, 1479 (1959).

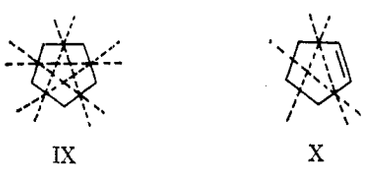
a double bond and one or more hetero atoms and is widely considered to occur in a concerted fashion which is formally the reverse of the Diels–Alder cycloaddition reaction,[12] it is less well recognized that the corresponding five-membered rings cleave in a somewhat similar fashion to give a system containing two of the ring atoms and one containing the other three as follows.[13]



Either fragment may emerge charged from the cleavage; this is presumably governed by the nature of the atoms involved and, most commonly, one observes peaks corresponding to both AE^+ and BCD^+.

It should also be noted that such cleavage is normally found to be secondary to so-called "simple" cleavages such as loss of a substituent.

There are, *a priori*, five directions in which the above fragmentation can occur (IX). These are not all possible if there is a double bond in the ring such as in X, in which two of the five fragmentations are inhibited by the double bond. Thus the 2-amino-Δ²-thiazoline system (I) would be expected to give a considerably

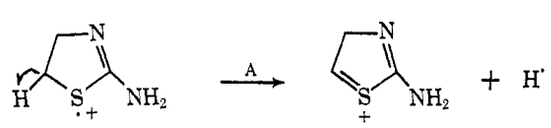


IX X

simpler spectrum than compounds such as II containing the isomeric 2-iminothiazolidine system (XI), and this is found to be the case.

I XI

The mass spectrum[14] of 2-amino-Δ²-thiazoline, shown in Figure 1,[15] has as its base peak the molecular ion at *m/e* 102. The peak at *m/e* 104, due to the ^{34}S satellite, has approximately the expected intensity of 4.44% of the parent peak. The molecular ion loses a hydrogen atom very readily, presumably by process A below,



$C_3H_6N_2S^+$ $C_3H_5N_2S^+$

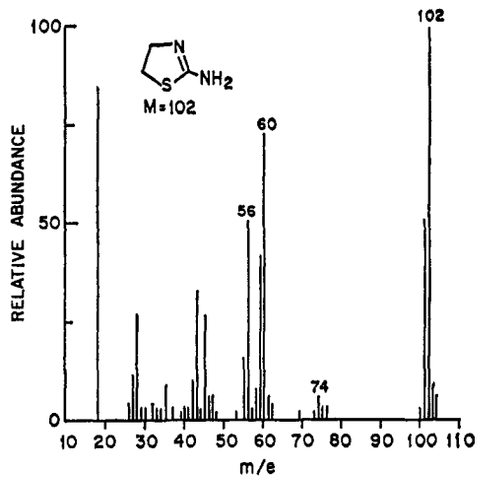
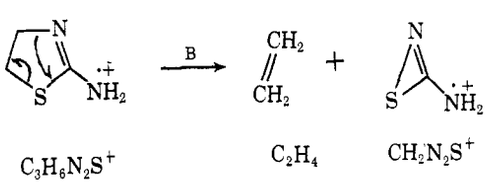


Figure 1.—Mass spectrum of 2 amino-Δ²-thiazoline (I).

giving an ion at *m/e* 101. The ^{34}S satellite of this ion will be at *m/e* 103, superimposed upon the ^{13}C satellite of the molecular ion. That the hydrogen atom is not lost from the primary amino group is confirmed by the observation that exchange of the primary amino hydrogen atoms for deuterium gives a compound whose molecular ion (*m/e* 104) fragments by loss of H· rather than D·.

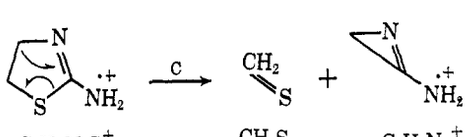
The ion at *m/e* 74 may be considered to be formed by pathway B, this being one of the three possible ring



$C_3H_6N_2S^+$ C_2H_4 $CH_2N_2S^+$

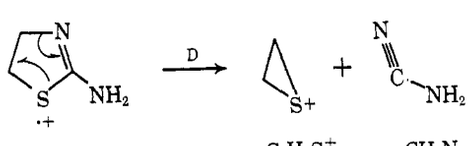
fragmentation reactions. The accurate mass to charge ratio of this ion is 73.9917, which compares favorably with the value of 73.9939 calculated for $CH_2N_2S^+$.

A second route for ring fragmentation is pathway C below, by which a neutral $CH_2{=}S$ fragment is lost and an ion at *m/e* 56 is observed. The absence of sulfur in this species is confirmed by accurate mass measurement (*vide infra*).



$C_3H_6N_2S^+$ CH_2S $C_2H_4N_2^+$

The final possible ring cleavage is that shown in pathway D below which leads to the relatively abun-



$C_3H_6N_2S^+$ $C_2H_4S^+$ CH_2N_2

dant ion at *m/e* 60 which is accompanied by satellites at *m/e* 61 and 62 with relative intensities 5 and 3% of the *m/e* 60 ion, respectively.

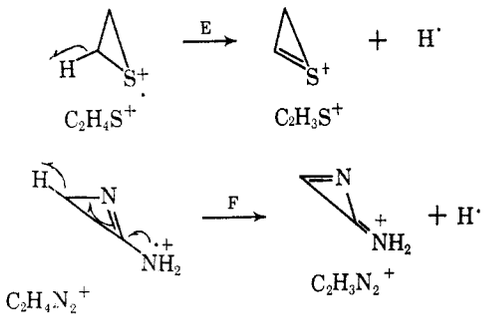
The remaining important peaks in the spectrum, at *m/e* 59 and 55, may reasonably be assumed to be

(12) K. Biemann, *Angew. Chem.*, **74**, 102 (1962); *Angew. Chem. Intern. Ed. Engl.*, **1**, 98 (1962); H. Budzikiewicz, J. I. Brauman, and C. Djerassi, *Tetrahedron*, **21**, 1855 (1965).

(13) G. W. A. Milne and L. A. Cohen, *ibid.*, in press; A. Senning, *Chem. Commun.*, **1**, 551 (1965); A. M. Duffield, H. Budzikiewicz, and C. Djerassi, *J. Am. Chem. Soc.*, **87**, 2920 (1965).

(14) All mass spectra were measured on an Associated Electrical Industries (U. K.) MS-9 double-focussing spectrometer at 70 ev. In all cases, the free base, its hydrochloride, or its hydrobromide salt was introduced directly into the electron beam. Accurate measurement of mass to charge ratio was carried out by comparison with a perfluorotributylamine standard, or, at *m/e* <69, with argon.

(15) Peaks arising from HCl or HBr in the mass spectra of the amine salts are not recorded in the figures or the tables.



formed by loss of a hydrogen atom from the ions at *m/e* 60 and 56, respectively, by mechanisms E and F.

Support for this general scheme of fragmentation is to be found in the appearance of metastable ions at essentially the calculated position for each of the cleavages. The metastable peaks are recorded in Table I.

TABLE I
METASTABLE IONS IN THE MASS SPECTRUM OF 2-AMINO-Δ^2-THIAZOLINE

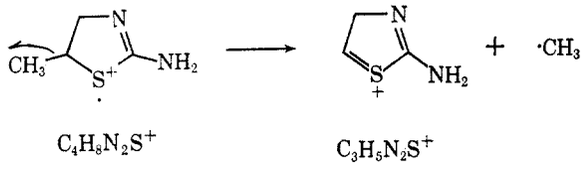
Fragmentation	Metastable ion, calcd	Metastable ion, found
A	100.0	100.0
B	53.6	53.2
C	30.7	31.0
D	35.4	35.5
E	58.0	58.1
F	54.0	54.1

This mass spectrum therefore supports the earlier conclusion[16] that 2-amino-Δ^2-thiazoline prefers to exist as such and not in the tautomeric iminothiazolidine form.

The mass spectra of 2-amino-5-methyl-Δ^2-thiazoline (IV), 2-amino-4-methyl-Δ^2-thiazoline (III), and 2-methylamino-Δ^2-thiazoline (VIII) reveal that these compounds fragment by the major pathways A–F, which have been established as important in the spectrum of the parent 2-amino-Δ^2-thiazoline.

The breakdown of IV by pathways B, C, and F leads to ions which do not contain C_5. These ions will therefore be at the same mass to charge ratio as the corresponding ions derived from 2-amino-Δ^2-thiazoline, *i.e.*, 74, 56, and 55. The ions formed by fragmentations A, D, and E will, however, contain the additional methyl group and will appear at *m/e* 115, 74, and 73.

A primary process in the fragmentation of IV is the loss of the methyl group to give an ion in which the charge is stabilized by resonance with sulfur. The resulting ion at *m/e* 101 does appear, as does the appropriate metastable ion at *m/e* 88.0 (calcd 88.0), but the ion is not an abundant one. These frag-



mentations account for the mass spectrum of IV which is given in Table II.

(16) Y. N. Sheinker, E. M. Peresleni, A. I. Kol'tsov, N. M. Bazhenov, and M. V. Vol'kenshtein, *Dokl. Akad. Nauk SSSR*, **148**, 878 (1963).

TABLE II
MASS SPECTRUM OF 2-AMINO-5-METHYL-Δ^2-THIAZOLINE

Ion, *m/e*[a]	Abundance[b]	Fragmentation	Metastable ion, Calcd	Metastable ion, Found
116	92	Molecular ion	...	...
115	13	A	114.0	114.1
101	25	$-[\cdot CH_3]$	88.0	88.0
74	51	B, D	47.2	47.1
73	10	E	72.0	72.0
56	100	C	27.0	27.0
55	14	F	54.0	54.0

[a] Ions containing ^{13}C, ^{33}S, and/or ^{34}S are not given in the tables. [b] Expressed as a percentage of the base peak (100%).

An interesting corollary to the foregoing analysis is that there should be two ions observable at a nominal mass to charge ratio of 74. These arise from fragmentations B and D and will thus have formulas $CH_2N_2S^+$ and $C_3H_6S^+$, respectively. The high-resolution spectrum of IV reveals this to be true, and accurate mass to charge measurement of the components of the doublet at *m/e* 74 shows them to be at *m/e* 73.9924 ($CH_2N_2S^+$ requires *m/e* 73.9939) and *m/e* 74.0165 ($C_3H_6S^+$ requires *m/e* 74.0190), respectively. Accurate measurements were made of the mass to charge ratio of a number of ions in the spectrum of IV with results given in Table III.

TABLE III
HIGH RESOLUTION MASS SPECTRUM OF 2-AMINO-5-METHYL-Δ^2-THIAZOLINE

Fragmentation	Ion	*m/e*, calcd	*m/e*, found
Molecular ion	$C_4H_8N_2S^+$	116.0408	116.041
$-[\cdot CH_3]$	$C_3H_5N_2S^+$	101.0173	101.017
D	$C_3H_6S^+$	74.0190	74.0165
B	$CH_2N_2S^+$	73.9939	73.9924
C	$C_2H_4N_2^+$	56.0374	56.0392

The mass spectrum of 2-amino-4-methyl-Δ^2-thiazoline is found to be perfectly in accord with the above generalizations. In this case, loss of the methyl group is an important process and the resulting ion actually constitutes the base peak of the spectrum. The spectrum is given in Table IV.

TABLE IV
MASS SPECTRUM OF 2-AMINO-4-METHYL-Δ^2-THIAZOLINE

Ion, *m/e*[a]	Abundance[b]	Fragmentation	Metastable ion, Calcd	Metastable ion, Found
116	45	Molecular ion	...	...
115	5	A	114.0	...
101	100	$-[\cdot CH_3]$	88.0	88.0
74	25	B, D	47.2	47.1
73	10	E	72.0	72.1
70	23	C	42.2	...
69	15	F	68.1	68.0

[a] See Table II, footnote *a*. [b] See Table II, footnote *b*.

Similarly, the mass spectrum of the last thiazoline, 2-methylamino-Δ^2-thiazoline (VIII) may be simply interpreted in terms of the fragmentations A–F as in Table V.

It is not without interest that in the fragmentation of 2-methylamino-Δ^2-thiazoline, loss of the methyl group is not an important process, as is evidenced by absence of the resulting ion at *m/e* 101.

TABLE V
MASS SPECTRUM OF 2-METHYLAMINO-Δ^2-THIAZOLINE

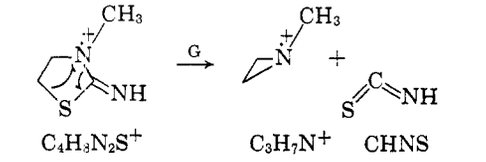
Ion, m/e[a]	Abundance[b]	Fragmentation	Metastable ion Calcd	Metastable ion Found
116	100	Molecular ion	...	...
115	19	A	114.0	114.1
88	5	B	66.8	66.4
70	23	C	42.2	43.0
60	23	D	31.0	30.9
59	16	E	58.0	58.1
69	5	F	68.0	...

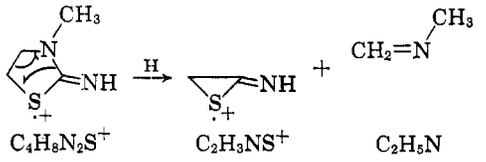
[a] See Table II, footnote *a*. [b] See Table II, footnote *b*.

The fragmentation of 2-amino-Δ^2-selenazoline is quite analogous to that of 2-amino-Δ^2-thiazoline. The six ions centered around m/e 148 are the molecular ions, appearing in approximately the relative abundances of the six isotopes of selenium.[17] The only other selenium containing ions are those centered about m/e 106 which are clearly the ions formed by fragmentation *via* pathway D, and those centered around m/e 120 resulting from fragmentation of type B. The third possible ring scission, type C, does occur, giving rise to the selenium-free ion at m/e 56. The three fragmentations resulting in the loss of a hydrogen atom, *i.e.*, types A, E, and F, all take place and although the ions resulting from the first two are somewhat obscured by selenium satellite ions, the ion at m/e 55, formed by a type F fragmentation of that at m/e 56, is clearly observed as is the metastable ion attending its formation at m/e 54.2 (calcd 54.1).

There being no double bond in the ring of 2-imino-3-methylthiazolidine (II) whose mass spectrum is shown in Figure 2, the ring in this compound may be cleaved in all five possible senses. Three of these correspond to fragmentations B, C, and D discussed previously with reference to the Δ^2-thiazoline system and give the ions at m/e 88, 70, and 60, together with the expected metastable ions at m/e 66.6, 42.2, and 31.0, respectively. The ion at m/e 60 loses a hydrogen atom by pathway E to give one at m/e 59.

In addition to such types of cleavage, two new routes leading to ring scission must be considered. These may be termed fragmentations G and H as follows.





Ions at m/e 57 ($C_3H_7N^+$) and 73 ($C_2H_3NS^+$) are observed although they are of somewhat limited abundance. The neutral species resulting from fragmentation G is the sulfur analog of isocyanic acid which is known[13,18] to emerge uncharged from a variety of fragmentations.

(17) J. R. White and A. E. Cameron, *Phys. Rev.*, **74**, 991 (1948).
(18) G. I. Glover, R. B. Smith, and H. Rapoport, *J. Am. Chem. Soc.*, **87**, 2003 (1965).

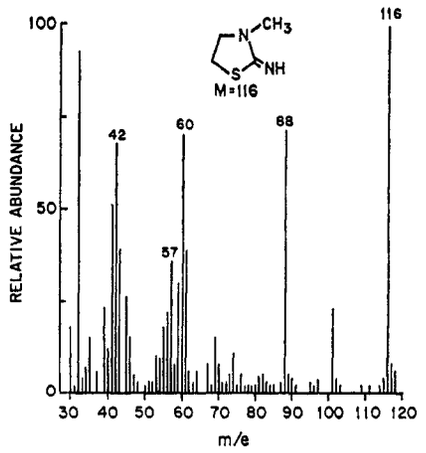


Figure 2.—Mass spectrum of 2-imino-3-methylthiazolidine (II).

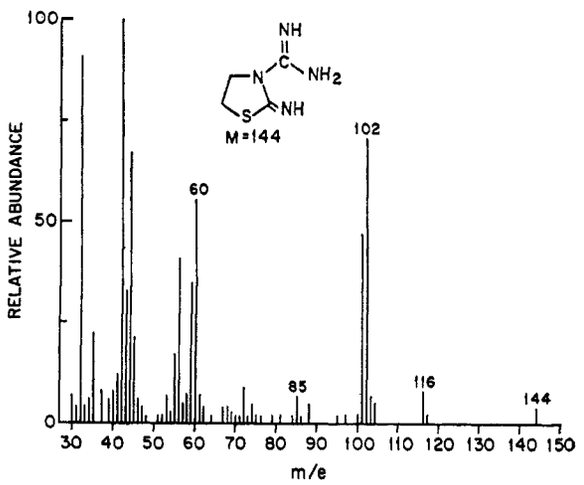
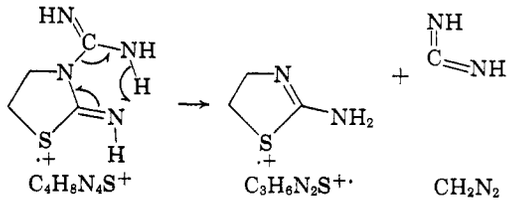


Figure 3.—Mass spectrum of 2-imino-3-amidinothiazolidine (VI).

The mass spectrum of 2-imino-3-amidinothiazolidine (VI), shown in Figure 3, may be satisfactorily analyzed in terms of the foregoing discussion. The amidino side chain may be lost *in toto* by a simple cleavage giving an ion at m/e 101, but the absence of the expected metastable peak at m/e 70.9 for such a cleavage leads to consideration of a different route for the formation of the ion at m/e 101.

Loss of the elements CH_2N_2 by the cyclic pathway shown below should be especially facile involving as it does, a transition state formally similar to that proposed by McLafferty[19] for the elimination of an olefin



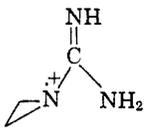
from alkyl esters and ketones. That this does indeed occur is confirmed not only by the appearance of an abundant ion at m/e 102 but also by the observation of the corresponding metastable ion at m/e 72.3 (calcd 72.4) and the appearance of the complementary fragment at m/e 42. This ion, $[HN{=}C{=}NH]^+$, will be highly stabilized by resonance and this accounts for its high abundance.

(19) F. W. McLafferty, *Anal. Chem.*, **31**, 82 (1959).

The ion at *m/e* 101 is formed by loss of a hydrogen atom from the ion at *m/e* 102, by a cleavage of the type A. The metastable ion accompanying this fragmentation is observed at *m/e* 100.2 (calcd 100.0). That the ion at *m/e* 101 is indeed $C_3H_5N_2S^+$ is confirmed by its mass to charge ratio of 101.015 ($C_3H_5N_2S^+$ requires *m/e* 101.0173).

Fragmentation of the molecular ion by pathway B will result in the release of C_2H_4 and the concomitant formation of the ion at *m/e* 116.

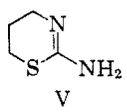
The accurate mass to charge ratio of the ion at *m/e* 85 is 85.0656 which permits assignment of the formula $C_3H_7N_3^+$ (*m/e* 85.0640) to this ion which may therefore be considered to be XII, the product of type G cleavage of the molecular ions.



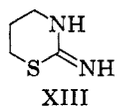
XII, $C_3H_7N_3^+$

An important process in the fragmentation of 2-Imino-3-amidinothiazolidine is ring scission of the type D to give the abundant ion at *m/e* 60. This ion is subject to fragmentation of the type E whereby it loses a hydrogen atom and is converted to the ion at *m/e* 59. The metastable ion accompanying this fragmentation is observed at *m/e* 58.2 (calcd 58.0). In view of this mass spectral evidence, structure VIb is no longer tenable and this compound must therefore have the structure VIa.

Although isomeric with the methyl substituted thiazolines and thiazolidines, 2-amino-5,6-dihydro-4H-1,3-thiazine (V) has a mass spectrum which is quite dissimilar to those given by compounds II, III, IV, or VIII and, furthermore, effectively precludes in the gas phase ion the tautomeric structure XIII.

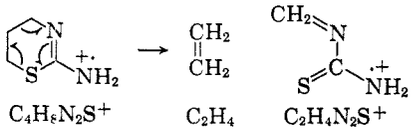


V



XIII

Probably the most important primary process in the fragmentation of this compound is the collapse of the ring in the reverse Diels–Alder sense[12] to give an ion at *m/e* 88 which is about half as abundant as the molecular ion which, at *m/e* 116, is the base peak of the



$C_4H_8N_2S^+$ C_2H_4 $C_2H_4N_2S^+$

spectrum. The metastable ion corresponding to this fragmentation appears in the calculated position at *m/e* 66.8.

Experimental Section[20]

2-Amino-Δ^2-thiazoline (I).—To a solution of 7.86 g (0.05 mole) of 2-aminoethanethiosulfuric acid[21a,b] and 2.0 g (0.05 mole) of sodium hydroxide in 100 ml of water was added 2.70 g (0.055 mole) of sodium cyanide. The solution was stirred for 4 hr at room temperature and then exhaustively extracted with chloroform (ten 40-ml portions) to give 4.64 g (90.8%) of the product. Recrystallization of I from ether gave colorless crystals (needles), mp 80–82° (lit. mp 78°,[22] 78–79°,[23] 80–82°,[24] 84–85°[10,25]), hydrochloride (from ethanol) mp 203–204° (lit.[23] mp 196–198°).

2-Imino-3-methylthiazolidine Hydrochloride (II HCl).—To a solution of 8.56 g (0.05 mole) of methylaminoethanethiosulfuric acid which may be prepared by either of two methods[21a,26] and 2.0 g (0.05 mole) of sodium hydroxide in 100 ml of water was added 2.70 g (0.055 mole) of sodium cyanide. After the solution had been stirred at room temperature for 4 hr, it was extracted with chloroform (five 30-ml portions). The combined extracts were dried over magnesium sulfate, treated with anhydrous hydrogen chloride, and evaporated to dryness under reduced pressure. The residue was dissolved in hot acetonitrile and the solution was cooled, causing the separation of the crystalline product. The 2-imino-3-methylthiazolidine hydrochloride, 6.03 g (79.0%), was recrystallized from acetonitrile to give a product which melted at 162.5–163°.

Anal. Calcd for $C_4H_9ClN_2S$: C, 31.47; H, 5.94; N, 18.36; S, 21.01. Found: C, 31.66; H, 6.04; N, 18.35; S, 21.26.

2-Amino-4-methyl-Δ^2-thiazoline Hydrochloride (III HCl).—This compound was made from 8.56 g (0.05 mole) of 2-aminopropane-1-thiosulfuric acid[21a] using the procedure immediately above. There was obtained 6.28 g (82.3%) of a product which melted at 123–124° after recrystallization from acetonitrile.

Anal. Calcd for $C_4H_9ClN_2S$: C, 31.47; H, 5.94; N, 18.36; S, 21.01. Found: C, 31.22; H, 6.35; N, 18.07; S, 21.15.

2-Amino-5-methyl-Δ^2-thiazoline Hydrochloride (IV HCl).—Starting with 0.856 g (5 mmoles) of 1-aminopropane-2-thiosulfuric acid[27] and utilizing the above procedure, there was obtained 0.43 g (56.4%) of the desired product, mp 131–132°.

Anal. Calcd for $C_4H_9ClN_2S$: C, 31.47; H, 5.94; N, 18.36; S, 21.01. Found: C, 31.51; H, 6.22; N, 18.27; S, 20.96.

2-Amino-5,6-dihydro-4H-1,3-thiazine Hydrochloride (V HCl).—To 8.56 g (0.05 mole) of 3-aminopropane-1-thiosulfuric acid,[28] 2.00 g (0.05 mole) of sodium hydroxide, and 250 ml of water was added 2.70 g (0.055 mole) of sodium cyanide and 250 ml of ether. The mixture was rapidly stirred at room temperature for 24 hr, the aqueous phase was extracted with ether (three 150-ml portions), and the ether solutions were combined and dried over magnesium sulfate. Hydrogen chloride was passed into the ether solution, the solvent was removed, and the resulting oil was treated twice with isopropyl alcohol and taken to dryness each time to give 1.60 g (20.9%) of 2-amino-5,6-dihydro-4H-1,3-thiazine hydrochloride which was recrystallized from isopropyl alcohol in needles, mp 156–157° (lit.[6] mp 144°). Contrary to the report of Schöberl, *et al.*,[6] V HCl is not hygroscopic.

Anal. Calcd for $C_4H_9ClN_2S$: C, 31.47; H, 5.94; N, 18.36; S, 21.01. Found: C, 31.74; H, 5.85; N, 18.44; S, 21.32.

2-Imino-3-amidinothiazolidine Dihydrochloride (VI 2HCl).—Starting with 9.96 g (0.05 mole) of 2-guanidinoethanethiosulfuric acid[29] and using the procedure immediately above, there was obtained 0.75 g (6.67%) of VI 2HCl, recrystallized from methanol as needles, mp 198–199°.

Anal. Calcd for $C_4H_{10}Cl_2N_4S$: C, 22.11; H, 4.64; Cl, 32.66; N, 25.80; S, 14.77. Found: C, 21.95; H, 5.56; Cl, 32.52; N, 25.61; S, 14.66.

Preparation of I from 2-Aminoethyl 2-Aminoethanethiolsulfonate Dihydrochloride (IX 2HCl).—A solution of 12.86 g (0.05 mole) of 2-aminoethyl 2-aminoethanethiolsulfonate dihydrochloride,[30] 4.0 g (0.10 mole) of sodium hydroxide, and 2.7 g

(20) Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected. Microanalyses were performed by Mr. Joseph Alicino, Metuchen, N. J. Infrared spectra were determined on a Beckman IR-5 spectrophotometer.

(21) (a) D. L. Klayman, W. F. Gilmore, and T. R. Sweeney, *Chem. Ind.* (London), 1632 (1965); (b) H. Bretschneider, *Monatsh.*, **81**, 372 (1950).

(22) A. Schöberl and G. Hansen, *Chem. Ber.*, **91**, 1056 (1958).

(23) K. K. Kuz'mina, N. G. Ostroumova, Y. V. Markova, and M. N. Shchukina, *Zh. Obshch. Khim.*, **32**, 3215 (1962).

(24) G. W. Raiziss and L. W. Clemence, *J. Am. Chem. Soc.*, **63**, 3124 (1941).

(25) E. J. Masters and M. T. Bogert, *ibid.*, **64**, 2709 (1942).

(26) D. L. Klayman and W. F. Gilmore, *J. Med. Chem.*, **7**, 823 (1964).

(27) D. L. Klayman, J. W. Lown, and T. R. Sweeney, *J. Org. Chem.*, **30**, 2275 (1965).

(28) A. Kaluszyner, P. Czerniak, and E. D. Bergmann, *Radiation Res.*, **14**, 23 (1961).

(29) A. Kaluszyner, *Bull. Res. Council Israel*, **9A**, 34 (1960).

(30) L. Field, T. C. Owen, R. R. Crenshaw, and A. W. Bryan, *J. Am. Chem. Soc.*, **83**, 4414 (1961).

(0.055 mole) of sodium cyanide in 100 ml of water was stirred for 4 hr at room temperature. Chloroform (ten 40-ml portions) was used to extract the product from the reaction mixture. Upon evaporation of the combined, dried chloroform extracts there was obtained 3.80 g (74.4%) of I, mp 80–82°.

2-Aminoethyl 2-Aminethanethiolsulfinate Dihydrochloride (X 2HCl)[31].—To an ice-cooled, stirred solution of 5.63 g (0.025 mole) of cystamine dihydrochloride in 200 ml of methanol was added dropwise 5.57 g of *m*-chloroperbenzoic acid (85+% assay) in 15 ml of isopropyl alcohol. The thiolsulfinate started to precipitate from solution as the addition approached completion. Stirring was continued for 1.5 hr. The precipitated product and two additional crops were collected and extracted with several portions of boiling ether to remove the *m*-chlorobenzoic acid contaminant. (The mother liquors were found to contain cystamine dihydrochloride, the corresponding thiolsulfonate and taurine.) The product, 4.48 g, darkened and softened at *ca.* 130° and melted at 150–152° dec. Recrystallization from water–ethanol afforded 3.35 g (55.5%) of X 2HCl as white crystals which darkened at *ca.* 135°, softened at *ca.* 140°, and melted at 154–155° dec. The thiolsulfinate oxidizes hydriodic acid to iodine.

Anal. Calcd for $C_4H_{14}Cl_2N_2OS_2$: C, 19.92; H, 5.85; N, 11.62; S, 26.58. Found: C, 20.11; H, 6.25; N, 11.69; S, 26.75.

Preparation of I from X 2HCl.—A solution of 2.47 g (0.01 mole) of X 2HCl, 0.80 g (0.02 mole) of sodium hydroxide, and 0.54 g (0.011 mole) of sodium cyanide in 20 ml of water was stirred for 4 hr at room temperature. Chloroform (five 30-ml portions) extracted 0.94 g (92.2%) of I, mp 80–82°, from solution.

(31) Procedure based upon that reported by A. Schöberl and H. Gräfje, *Ann.*, **617**, 71 (1958).

Acknowledgment.—We wish to thank Mr. Peter Merkel and Dr. Peter Coad (Walter Reed Army Institute of Research) for assistance in synthesizing some of the compounds used in this study.

The Alkylation of β-Keto Sulfoxides. A General Route to Ketones

P. G. GASSMAN AND G. D. RICHMOND[1]

The Department of Chemistry, The Ohio State University, Columbus, Ohio 43210

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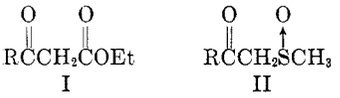
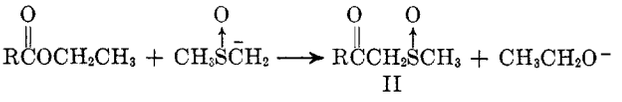
Procedures have been developed for the mono- and dialkylation of β-keto sulfoxides. Reductive cleavage of these alkylated β-keto sulfoxides with aluminum amalgam provides an attractive synthetic route to a wide variety of ketones.

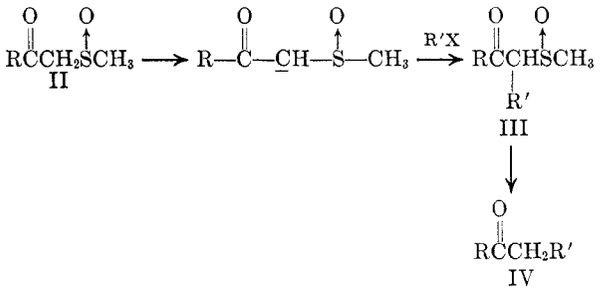
The classical acetoacetic ester synthesis is one of the most often quoted methods for the synthesis of ketones. A portion of most undergraduate texts is devoted to discussing this synthetic sequence. In practice, the acetoacetic ester type of synthesis is generally limited to the synthesis of methyl ketones. We wish to report a variation of this type of alkylation–cleavage procedure which permits the synthesis of a broad spectrum of ketones. Our method is based on the alkylation of β-keto sulfoxides followed by reductive cleavage of the carbon–sulfur bond with aluminum amalgam. The advantage of our method arises from the ease of preparation of β-keto sulfoxides compared with β-keto esters. Whereas β-keto esters (I), where R is other than methyl,



are not readily available, β-keto sulfoxides (II) can be prepared easily and in high yield with wide variation in the nature of the R group. Both Russell[2] and Corey[3]



have shown that esters react with dimethyl sulfoxide anion to produce β-keto sulfoxides in very high yield. In addition, it had been reported[3] that compounds such as II could be reductively cleaved to yield methyl ketones. Thus, the only completely unknown factors in the sequence shown below were whether II could be readily alkylated and whether substituted β-keto sulfoxides such as III could be cleaved reductively.



Addition of II (R = phenyl) to a solution of sodium ethoxide in ethanol gave little reaction. When sodium hydride or lithium hydride was used as base in tetrahydrofuran (THF) an immediate evolution of hydrogen gas occurred and the alkali metal salt of the β-keto sulfoxide precipitated. Numerous attempts to alkylate this salt were unsuccessful and only starting material was obtained when the reaction was worked up. The failure of these alkylation attempts was attributed to the insolubility of the salts of II. When dimethylformamide (DMF) was used as solvent and sodium hydride was the added base, II reacted vigorously to yield the *soluble* salt. Addition of methyl iodide to the DMF solution gave a high yield of crude monoalkylated β-keto sulfoxide, IIIa, where R is phenyl and R′ is methyl. These alkylated β-keto sulfoxides were very difficult to purify. As a result the yield of purified alkylation product when DMF was used as solvent was 30%. Carrying out the same alkylation using dimethyl sulfoxide (DMSO) as solvent gave a 70% yield of monoalkylation product. This increase in yield was due primarily to a different work-up of

(1) National Institutes of Health Predoctoral Fellow, 1965–present.

(2) G. A. Russell and H.-D. Becker, *J. Am. Chem. Soc.*, **85**, 3406 (1963); H.-D. Becker, G. J. Mikol, and G. A. Russell, *ibid.*, **85**, 3410 (1963).

(3) E. J. Corey and M. Chaykovsky, *ibid.*, **87**, 1345 (1965).