1-(2-Imidazolin-2-yl)-2-imidazolines. I. The Structure of Jaffé's Base and the Chemistry of Related Compounds

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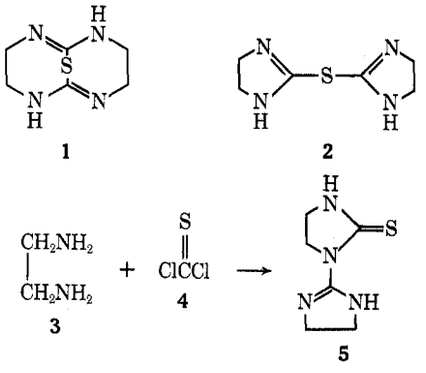
Received November 15, 1972

The synthesis of four potential starting materials for the preparation of 2-amino-1-(2-imidazolin-2-yl)-2-imidazolines is described. Treatment of 2-(methylthio)-2-imidazoline (**6**) with 2-(methylthio)-2-imidazoline hydriodide (**7**) gave 1-(2-imidazolin-2-yl)-2-(methylthio)-2-imidazoline hydriodide (**9**) and 1-(2-imidazolin-2-yl)-2-(methylthio)-2-imidazoline hydriodide methanethiol (**8**). Two minor products, 1-(2-imidazolin-2-yl)-2-[2-(methylthio)-2-imidazolin-1-yl]-2-imidazoline hydriodide (**10**) and 2,3,8,9-tetrahydro-5-(methylthio)-7*H*-imidazo[2,3-*b*][1,3,5]triazepine hydriodide (**11**), were also obtained. Reaction of 2-(methylthio)-2-imidazoline hydriodide (**7**) with triethylamine afforded triethyl[1-(2-imidazolin-2-yl)-2-imidazolin-2-yl]ammonium iodide hydriodide methanethiol (**12**) and 1-(2-imidazolin-2-yl)-2-(methylthio)-2-imidazoline dihydriodide methanethiol (**13**). The determination of the structures of the aforementioned compounds and their relationship to Jaffé's base, 1-(2-imidazolin-2-yl)-2-imidazolidinethione (**5**), is described. A novel hydrolysis, the transformation of 1-(2-imidazolin-2-yl)-2-(methylthio)-2-imidazoline dihydriodide methanethiol (**13**) to *S,S*-dimethyl dithiocarbonate (**17**) and 2-[(2-aminoethyl)amino]-2-imidazoline dihydroiodide (**18**), was observed. Evidence which suggests that previously described conversion of **6** to 1-(2-imidazolin-2-yl)-2-imidazolidinone (**14**)[4] proceeds *via* alkoxylimidazolinylimidazoline **21** is presented.

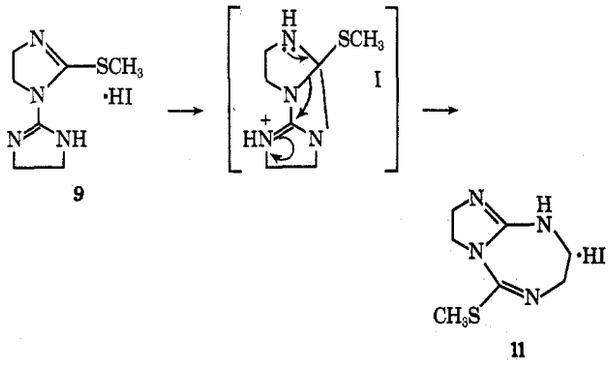
Structures **1**[1] and **2**[2] initially assigned to Jaffé's base, the product of the interaction of ethylenediamine (**3**) and thiophosgene (**4**),[1] were subsequently shown to be incorrect; the correct structure **5** was established



by the results of uv measurements[3] and confirmed by chemical interconversion.[4] During the course of an investigation concerned with the synthesis of 2-amino-1-(2-imidazolin-2-yl)-2-imidazolines as potential cardiovascular drugs, we obtained evidence compatible with structure **5** and studied some aspects of the chemistry of this class of compounds.

The starting material, 1-(2-imidazolin-2-yl)-2-(methylthio)-2-imidazoline hydriodide (**9**), required for the synthesis of 2-aminoimidazolinylimidazolines, was prepared by the reaction of 2-(methylthio)-2-imidazoline (**6**)[5] with 1 equiv of its hydriodide **7**.[6] Treatment of **6** with **7** gave **9** by precipitation from the reaction mixture and the corresponding methanethiol complex by concentration of the filtrate. Triimidazoline **10** and imidazotriazepine **11** were isolated by fractional crystallization of the residual reaction product.

The minor products were assigned triimidazoline and triazepine structures **10** and **11**, respectively, on the basis of plausible modes of formation, the former by reaction of either **8** or **9** with **6** and the latter by the internal rearrangement of **9** (and/or **8**) depicted below. The spectral properties (ir, uv, and nmr) of **10** and **11** were in accord with these structural postulations.

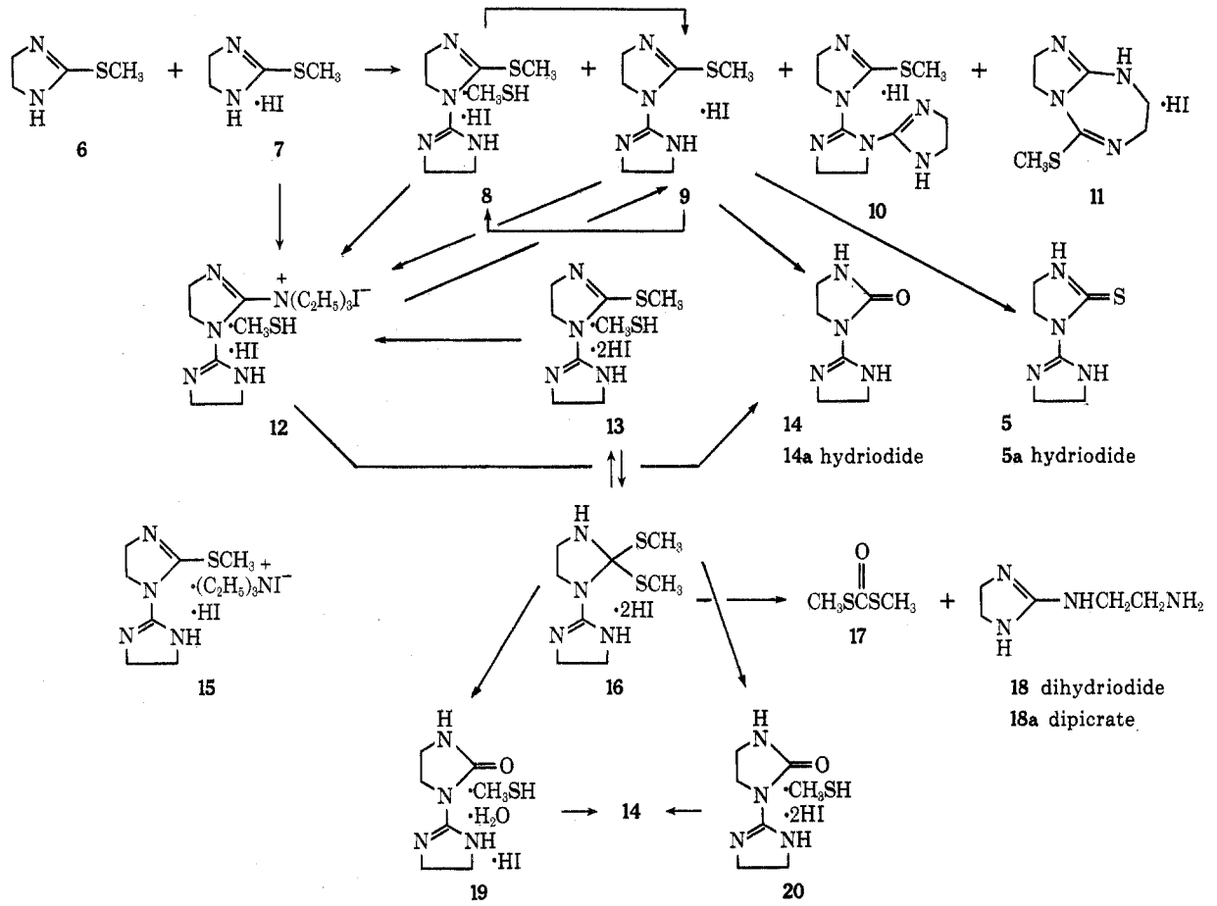


Two additional precursors of 2-aminoimidazolinylimidazolines became available when we found that reaction of imidazoline **7** with triethylamine afforded quaternary salt **12** by precipitation from the reaction mixture and methanethiol complex dihydriodide **13** by addition of 50% hydriodic acid to the filtrate.

Ammonolysis of **8** or **9** with triethylammonium iodide[7] and **13** with triethylamine gave quaternary iodide **12**. Hence, the imidazolinylimidazolines **8**, **9**, **12**, and **13** belong to the same chemical series and, as such, show ir absorption bands in the 1620–1660- and 1565–1600-cm^{-1} regions, characteristic of the imine and iminium functions,[8] respectively, and nmr signals in the 3.4–3.9-ppm region, assignable to the protons of the imidazoline rings.[9] As expected, the uv spectra of **8**, **9**, **12**, and **13** are transparent above 220 nm.

Structure **12** was assigned to the ammonolysis product solely on the basis of its solid-state (Nujol mull) ir spectrum, which exhibited an absorption band at 2550 cm^{-1}, a value within the accepted range for the sulfur–hydrogen stretching frequency of a thiol group.[10] That **12** exists in solution as the triethylammonium

(1) M. Jaffé and B. Kuhn, *Chem. Ber.*, **27**,1663(1894).
(2) T. B. Johnson and C. O. Edens, *J. Amer. Chem. Soc.*, **63**, 1058 (1941); T. B. Johnson and C. O. Edens, *ibid.*, **64**, 2706 (1942).
(3) H. Z. Lecher and K. Gubernator, *J. Amer. Chem. Soc.*, **75**, 1087 (1953); B. H. Chase and J. Walker, *J. Chem. Soc.*, 4443 (1955).
(4) G. I. Poos, J. Kleis, and C. K. Cain, *J. Org. Chem.*, **24**, 645 (1959).
(5) W. Wilson, *J. Chem. Soc.*, 1389 (1955).
(6) S. R. Aspinall and E. J. Bianco, *J. Amer. Chem. Soc.*, **73**, 602 (1951).
(7) S. B. Hendricks, *Z. Kristallogr.*, **67**, 42 (1928).
(8) L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," 2nd ed, Wiley, New York, N. Y., Chapter 15.
(9) The Sadtler Standard Spectra, Sadtler Research Laboratories, Inc., Philadelphia, Pa., 1967, Nmr Spectra No. 3599.
(10) Reference 8, Chapter 22.



iodide complex **15** of **9** was indicated by nmr spectroscopy. Excluding the signals due to the ethyl groups, the spectra of **9** and **12** in deuteriodimethyl sulfoxide were strikingly similar, each displaying three-proton singlets at δ 2.5 ppm assignable to the methylthio groups,[11] in addition to those associated with the imidazoline moieties. Rapid deposition of **9** from a warm solution of **12** and dichloromethane provided supportive chemical evidence for this conclusion.

A comparison of the nmr spectra of **8** and **9** indicated that **8** was the methanethiol complex of **9**. Whereas the spectrum of **9** showed a three-proton singlet at δ 2.54 ppm, assignable to the methylthiol group,[11] that of **8** displayed two three-proton singlets in the same region (δ 2.40 and 2.60 ppm), one assignable to methanethiol and the other to the methylthio group. This indication was substantiated by the thermal demethylthiolation of **8** to **9** and by the methylthiolation of **9** to **8**.

Acid hydrolysis of imidazolinylimidazolines **9** and **12** afforded imidazolinylimidazolidinone **14** in fair yield. Numerous attempts to convert Jaffé's base **5** to **14** by exchange with mercuric oxide[4] and thereby interrelate this work with that previously described by others[1-4] failed to give **14**. Attempts to achieve the desired interrelation by methylation of **5** to **9** with methyl iodide also failed, hydriodide **5a** being the only identifiable product. The goal was finally achieved by the thermal demethylation of **9** to **5**. Thus, the structures of the reported imidazolinylimidazolines are established.

A novel hydrolysis of 2-methylthioimidazolinylimidazoline **13**, which established the presence of di(methylthiol)imidazolidine **16** in aqueous solution, was observed during the course of our initial attempts to correlate the gross structure of **13** with that of the cyclic urea **14**. Treatment of **13** with boiling hydriodic acid gave *S,S*-dimethyl dithiocarbonate (**17**) and 2-[(2-aminoethyl)amino]-2-imidazoline dihydriodide (**18**) in comparable yields. The hydrolysis products, carbonate **17**[12] and imidazoline dipicrate **18a**,[13] were identical with authentic samples prepared by previously described procedures. Hydrolysis under milder conditions afforded a low yield of the expected cyclic urea **20**. Neutralization of **20** furnished **14**.

Even though **13** is recrystallizable from methanol, prolonged dissolution in this solvent results in extensive decomposition to imidazolinone **19**. Neutralization of **19** gave **14**.

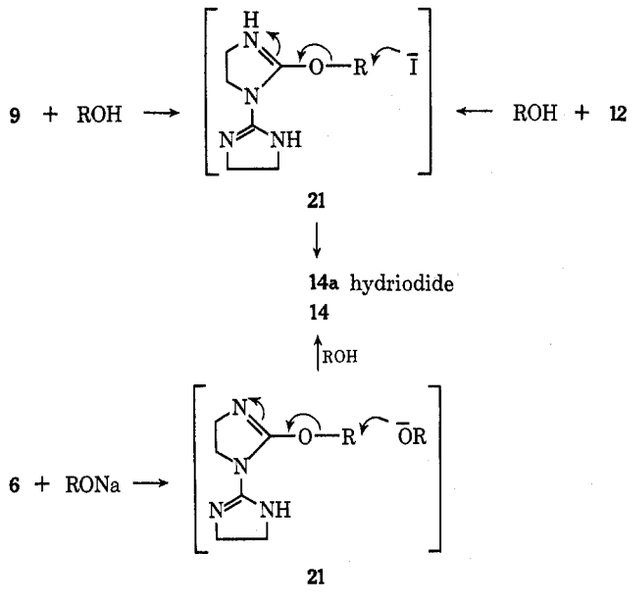
Methylthioimidazolinylimidazoline **9** and quaternary salt **12** reacted slowly with predried boiling methanol and 2-propanol under a blanket of nitrogen to give imidazolinylimidazolidinone **14a** in 25–30% yield in addition to unchanged **9** and **12** and were refractive in boiling 1-butanol, a weaker nucleophile than the primary and secondary alcohols. Hence, the conversion of **9** and **12** to **14a** was not a simple hydrolysis promoted by trace amounts of water but, more likely, involved alcoholysis of **9** and **12** to alkoxyimidazolinylimidazoline **21** followed by dealkylation of **21** by iodide to **14a**.

These observations coupled with the formation of **9** from **6** and **7** suggest that alkoxylimidazolinylimidazo-

(11) L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," 2nd ed, Pergamon Press, Elmsford, N. Y., 1969, p 164.

(12) H. Pelster and E. Muehlbauer, German Patent 1,131,205 (1964); *Chem. Abstr.*, **62**, P6398*b* (1965).

(13) A. F. McKay, M. N. Buchanan, and G. A. Grant, *J. Amer. Chem. Soc.*, **71**, 766 (1949).



line **21** is an intermediate in the reported conversion[4] of **6** to **14** by ethanolic sodium ethoxide, the ethoxide acting as a base for the transformation of **6** to **21** and a nucleophile for the transformation of **21** to **14**.

Methylthioimidazolinylimidazolines **8**, **9**, **12**, and **13** react with a variety of amines to give 2-aminoimidazolinylimidazolines. These compounds show interesting biological activities, which will be the subject of forthcoming publications.[14,15]

Experimental Section[16]

Reaction of 2-(Methylthio)-2-imidazoline (6) with 2-(Methylthio)-2-imidazoline Hydriodide (7).—A solution of imidazoline **6** (116 g, 1.00 mol), imidazoline hydriodide **7** (244 g, 1.00 mol), and acetonitrile (distilled from calcium hydride) (700 ml) was heated under reflux for 1.5 hr while a *moderate* stream of nitrogen was passed through the reaction mixture. The solution was allowed to stand at room temperature for 48 hr. The precipitate was collected, yield 25 g (8.0%) of 1-(2-imidazolin-2-yl)-2-(methylthio)-2-imidazoline hydriodide (**9**), mp 176–178° (resolidified) and 230–250°.

An analytical sample, prepared by repeated recrystallization from 2-propanol, had mp 173–175° (resolidified) and 230–250° dec; uv max 218 nm (ε 14,600); ir 1620 (C=N$^+$), 1565 cm^{-1} (C=N); nmr δ 2.54 (s, 3, CH_3S), 3.71, 3.91 (s, 8, CH_2CH_2), and 8.70 (D_2O-exchangeable broad m, 2, NH_2).

Anal. Calcd for $C_7H_{13}IN_4S$: C, 26.93; H, 4.20; I, 40.65; N, 17.95. Found: C, 27.22; H, 4.16; I, 40.79; N, 17.84.

The filtrate was concentrated to a volume of 400 ml and the precipitate was collected. Fractional recrystallization from acetonitrile and 2-propanol gave 103 g (29%) of 1-(2-imidazolin-2-yl)-2-(methylthio)-2-imidazoline hydriodide methanethiol (**8**) mp 101–102°, which was recrystallized from acetonitrile: mp 103–104° dec; uv max 219 nm (ε 47,700); ir 1660 (C=N$^+$), 1585 cm^{-1} (C=N); nmr δ 2.40 (s, 3, CH_3S), 2.60 (s, 3, CH_3S), 3.33 (s, 1, SH), 3.44 (s, 4, CH_2CH_2), 3.67 (s, 4, CH_2CH_2), and 8.1 (D_2O-exchangeable broad m, NH, NH_2^+).

Anal. Calcd for $C_8H_{17}IN_4S_2$: C, 26.67; H, 4.76; I, 35.22; N, 15.55; S, 17.80. Found: C, 26.82; H, 4.82; I, 35.16; N, 15.61; S, 17.79.

Also obtained was 7.05 g (1.9%) of 1-(2-imidazolin-2-yl)-2-[2-(methylthio)-2-imidazolin-1-yl]-2-imidazoline hydriodide (**10**): mp 191–192° dec; uv max 217 nm (ε 40,800); ir 1712 (C=N$^+$), 1680, 1585 cm^{-1} (C=N); nmr δ 2.33 (s, 3, CH_3S), 3.8 (m, 12, CH_2CH_2) and 9.3 (D_2O-exchangeable broad s, 2, NH_2).

Anal. Calcd for $C_{10}H_{17}IN_6S$: C, 31.59; H, 4.51; I, 33.37; N, 22.10; S, 8.73. Found: C, 31.61; H, 4.51; I, 33.20; N, 22.14; S, 8.82.

Also obtained was 1.9 g (0.5%) of 2,3,8,9-tetrahydro-5-(methylthio)-7*H*-imidazo[2,3-*b*][1,3,5]triazepine hydriodide (**11**): mp 183–184°; uv max 219 nm (ε 26,500); ir 1685 (C=N$^+$), 1550 cm^{-1} (C=N); nmr δ 2.35 (s, 3, CH_3S) 3.1–4.4 (m, 9, CH_2CH_2, NH), and 8.8 (D_2O-exchangeable broad m, 1, $^+$NH).

Anal. Calcd for $C_7H_{13}IN_4S$: C, 26.93; H, 4.20; I, 40.65; N, 17.95. Found: C, 27.15; H, 4.22; I, 40.61; N, 17.92.

The base of **11** had mp 167–169°; uv max end absorption; ir 1670, 1610 cm^{-1} (C=N); nmr ($CDCl_3$) δ 2.25 (s, 3, CH_3S), 3.0–4.0 (m, 8, CH_2CH_2), and 6.25 (s, 1, NH).

Anal. Calcd for $C_7H_{12}N_4S$: C, 45.63; H, 6.56; N, 30.41; S, 17.40. Found: C, 46.03; H, 6.70; N, 30.27; S, 17.04.

Conversion of 1-(2-Imidazolin-2-yl)-2-(methylthio)-2-imidazoline Hydriodide (9) to 1-(2-Imidazolin-2-yl)-2-(methylthio)-2-imidazoline Hydriodide Methanethiol (8).—A solution of imidazoline **9** (3.0 g, 9.6 mmol), methylmercaptan (25 g, 0.52 mol), and acetonitrile (175 ml) was allowed to stand at 0° for 5 min and then evaporated. Trituration of the residue with acetone gave 2.28 g (76%) of unchanged imidazoline **9**, mp 181–182° (resolidified) and 230–250°, alone and admixed with an authentic sample of **9**, and 0.10 g (12%) of methanethiol complex **8**, mp 100–102°, alone and admixed with an authentic sample of **8**.

The ir spectra of **9** and **8**, so obtained, were identical with those of the authentic samples.

Demethylthiolation of 1-(2-Imidazolin-2-yl)-2-(methylthio)-2-imidazoline Hydriodide Methanethiol (8).—A solution of methanethiol complex **8** and acetonitrile (100 ml) was heated under reflux for 66 hr while a vigorous stream of nitrogen was passed through the reaction mixture and then allowed to cool to room temperature. The precipitate was collected, washed with acetone, and dried, yield 1.05 g (66%) of imidazoline **9**, mp 183–185° (resolidified) and 230–250° dec, alone or admixed with a reference sample.

The ir spectra of the two samples were identical.

Triethyl[1-(2-imidazolin-2-yl)-2-imidazolin-2-yl]ammonium Iodide Hydriodide Methanethiol (12) and 1-(2-Imidazolin-2-yl)-2-(methylthio)-2-imidazoline Dihydriodide Methanethiol (13).—A solution of 2-(methylthio)-2-imidazoline hydriodide (**7**) (244 g, 1.00 mol), triethylamine (101 g, 1.00 mol), and 2-propanol (freshly distilled from calcium hydride) (1 l.) was heated under reflux for 2 hr while a vigorous stream of N_2 was passed through the solution. The reaction mixture was allowed to cool to room temperature and the precipitate was collected. Recrystallization from 2-propanol gave 79.7 g (30%) of quaternary salt **12**: mp 169–172° (resolidified) and 245–255° dec; uv max end absorption; ir 3300, 3150 (NH$^+$), 2550 (SH), 1630 (C=N$^+$), 1600 cm^{-1} (C=N); nmr δ 1.15 (t, 9, J = 6 Hz, CH_3), 2.51 (s, 3, CH_3S), 3.13 (q, 6, J = 6 Hz, CH_2), 3.70 and 3.86 (s, 8, CH_2CH_2), and 8.6 (D_2O-exchangeable broad m, 3 H, NH$^+$, SH).

Anal. Calcd for $C_{13}H_{29}I_2N_5S$: C, 28.85; H, 5.40; I, 46.89; N, 12.94; S, 5.92. Found: C, 28.98; H, 5.42; I, 46.75; N, 12.79; S, 5.94.

Hydriodic acid (50%) (140 ml) was added to the above filtrate and, after 30 min, the solid was collected and recrystallized from 2-propanol–water (4:1); yield 59.6 g (12%) of methanethiol dihydriodide **13**: mp 162–164°; uv max 218 nm (ε 36,800); ir 1668 (C=N$^+$), 1600, 1545 cm^{-1} (C=N); nmr (D_2O) δ 2.84, 2.89 (s, 6, CH_3S), and 3.9 (m, 8, CH_2CH_2).

Anal. Calcd for $C_8H_{18}I_2N_4S_2$: C, 19.68; H, 3.72; I, 52.00; N, 11.48; S, 13.13. Found: C, 19.97; H, 3.80; I, 52.13; N, 11.26; S, 13.22.

Preparation of 1-(2-Imidazolin-2-yl)-2-(methylthio)-2-imidazoline Dihydriodide Methanethiol (13) from 2-(Methylthio)-2-imidazoline (6) and 2-(Methylthio)-2-imidazoline Hydriodide (7).—A solution of imidazoline **6** (58.0 g, 0.500 mol), hydriodide **7** (122 g, 0.500 mol), and acetonitrile (1.5 l.) was heated under reflux for 2 hr and then allowed to cool to room temperature. Hydriodic acid (50%, 65 ml) was added and the precipitate was

(14) R. R. Wittekind, T. Capiris, J. Fahey, and J. Shavel, Jr., to be submitted for publication in *J. Med. Chem.*

(15) R. R. Wittekind, H. Kaplan, T. Capiris, J. Fahey, and J. Shavel, Jr., to be submitted for publication in *J. Pharm. Sci.*

(16) Melting points were determined in open capillary tubes on a Thomas-Hoover Unimelt, previously calibrated against known standards. The uv spectra were determined in 95% ethanol with a Beckman DK-1 spectrophotometer. The ir spectra were determined in Nujol mulls, unless otherwise indicated, on a Baird 455 spectrophotometer. The nmr spectra were measured in deuteriodimethyl sulfoxide, unless otherwise indicated, on a Varian A-60 spectrometer with tetramethylsilane as the internal standard. The mass spectra of all new compounds were determined on a Consolidated Electronics Corp. Model 21-103C or an Associated Electronic Industries MS 902 spectrograph and showed the expected molecular ion.

collected. Recrystallization from methanol gave 75.0 g (30%) of dihydriodide **13**, mp 160–161°, alone and admixed with a sample described in the preceding section.

Conversion of 1-(2-Imidazolin-2-yl)-2-(methylthio)-2-imidazoline Hydriodide (9) to Triethyl[1-(2-imidazolin-2-yl)-2-imidazolin-2-yl]ammonium Iodide Hydriodide Methanethiol (12).—A solution of imidazoline **9** (1.06 g, 3.39 mmol), triethylammonium iodide (0.777 g, 3.39 mmol), and 2-propanol (40 ml) was heated under reflux for 1 hr while a stream of N_2 was passed through the reaction mixture. The solution was allowed to cool to room temperature and the solid was collected; yield 1.29 g (77%) of quaternary salt **12**, mp 169–172° (resolidified) and 240–250° dec, alone or admixed with the initial sample.

The ir spectra of the two samples were identical.

Conversion of 1-(2-Imidazolin-2-yl)-2-(methylthio)-2-imidazoline Hydriodide Methanethiol (8) to Triethyl[1-(2-imidazolin-2-yl)-2-imidazolin-2-yl]ammonium Iodide Hydriodide Methanethiol (12).—A solution of imidazoline **8** (5.4 g, 0.015 mol), triethylammonium iodide (3.4 g, 0.015 mol), and 2-propanol (20 ml) was heated under reflux for 23 hr and allowed to cool to room temperature. The solid was collected. Recrystallization from 2-propanol gave 3.0 g (37%) of quaternary salt **12**, mp 169–171° (resolidified) and 245–250° dec, alone or admixed with an authentic sample of **12**.

The ir spectra of the two samples were superimposable.

Conversion of 1-(2-Imidazolin-2-yl)-2-(methylthio)-2-imidazoline Dihydriodide Methanethiol (13) to Triethyl[1-(2-imidazolin-2-yl)-2-imidazolin-2-yl]ammonium Iodide Hydriodide Methanethiol (12).—A solution of imidazoline **13** (4.88 g, 0.0100 mol), triethylamine (1.05 g, 0.0102 mol), and 2-propanol (110 ml) was boiled under reflux for 35 min, during which time a steady stream of nitrogen was bubbled through the solution. The reaction mixture was allowed to cool to room temperature and the precipitate was collected. Recrystallization from 2-propanol gave 2.72 g (50%) of quaternary salt **12**, mp 169–172° (resolidified) and 241–250° dec, alone or admixed with an authentic sample from the initial experiments.

The ir spectra of the samples were identical.

Conversion of Triethyl[1-(2-imidazolin-2-yl)-2-imidazolin-2-yl]-ammonium Iodide Hydriodide Methanethiol (12) to 1-(2-imidazolin-2-yl)-2-(methylthio)-2-imidazoline Hydriodide (9).—A mixture of quaternary salt **12** (8.43 g, 0.0155 mol) and dichloromethane (300 ml) was heated for 45 min and allowed to cool to room temperature. Unchanged quaternary salt **12** (2.92 g, 0.00538 mol) was collected. The filtrate was allowed to stand for several hours. The solid was collected; yield 3.00 g (11%) of **9**, mp 176–178° (resolidified) and 230–250°, alone and admixed with a sample prepared by the method described in the preceding experiment.

Hydrolysis of 1-(2-Imidazolin-2-yl)-2-(methylthio)-2-imidazoline Hydriodide (9).—A solution of imidazoline **9** (5.40 g, 0.0173 mol), water (100 ml), and 50% hydriodic acid (0.75 ml) was heated under reflux for 1 hr and then evaporated under reduced pressure. Trituration of the residue with 2-propanol followed by recrystallization from 2-propanol gave 3.57 g (73%) of 1-(2-imidazolin-2-yl)-2-imidazolidinone hydriodide (**14a**): mp 256–258° dec; uv max end absorption; ir 1740 (C=O), 1650 cm^{-1} (C=N^+); nmr δ 3.5 (m, 9, CH_2CH_2, NH) and 8.2 (D_2O-exchangeable broad m, 2, NH^+).

Anal. Calcd for $C_6H_{11}IN_4O$: C, 25.55; H, 3.93; I, 44.99; N, 19.86; O, 5.67. Found: C, 25.64; H, 4.15; I, 44.72; N, 19.65; O, 5.91.

Hydrolysis of Triethyl[1-(2-imidazolin-2-yl)-2-imidazolin-2-yl]ammonium Iodide Hydriodide Methanethiol (12).—A solution of quaternary salt **12** (42.8 g, 0.0870 mol), water (150 ml), and 50% hydriodic acid (1.5 ml) was heated under reflux for 7 days and then the solution was evaporated to dryness under reduced pressure. Recrystallization of the residue from 2-propanol gave 5.01 g (21%) of imidazolidinone hydriodide **14a**, mp 256–258° dec, alone or admixed with the sample obtained from the preceding experiment.

The ir spectra of the two samples were also identical.

The free base of **14a** was obtained by the usual procedure (neutralization with 1 *N* NaOH solution and extraction with Et_2O) and had mp 198–199° dec (lit.[4] mp 200–204°); uv max end absorption; ir 3380, 3200 (NH), 1720 (C=O), 1610 cm^{-1} (C=N); nmr δ 3.5 (m, 8, CH_2CH_2) and 7.3 (D_2O-exchangeable v br m, 2, NH).

Anal. Calcd for $C_6H_{10}N_4O$: C, 46.74; H, 6.54; N, 36.34. Found: C, 47.01; H, 6.74; N, 36.38.

Demethylation of 1-(2-Imidazolin-2-yl)-2-(methylthio)-2-imidazoline Hydriodide (9).—A solution of methylthioimidazoline hydriodide **9** (12.5 g, 0.0400 mol) and acetonitrile (300 ml) was heated under reflux under an atmosphere of nitrogen for 1 week and then cooled in an ice bath. The solid was collected. Recrystallization from 95% ethanol–water (5:1) gave 3.35 g (28%) of 1-(2-imidazolin-2-yl)-2-imidazolidinethione hydriodide (**5a**): mp 282–284° dec (lit.[4] mp 296–299° dec); uv max 223 nm (ϵ 26,700), 265 (12,600); ir 1630 (C=N^+), 1590 (C=N), 1120 cm^{-1} (C=S); nmr δ 4.0 (m, 9, CH_2CH_2, NH) and 9.7 (D_2O-exchangeable v br m, 2 H, NH^+).

Anal. Calcd for $C_6H_{11}IN_4S$: C, 24.17; H, 3.72; I, 42.56; N, 18.79; S, 10.75. Found: C, 24.32; H, 3.77; I, 42.75; N, 18.83; S, 10.59.

Methanolysis of 1-(2-Imidazolin-2-yl)-2-(methylthio)-2-imidazoline Dihydriodide Methanethiol (13).—Imidazoline **13** (60.0 g, 0.123 mol) was dissolved in the minimum volume of boiling methanol and the solution was allowed to stand at room temperature for 3 days. The precipitate was collected. Recrystallization from ethanol gave 20.1 g (47%) of 1-(2-imidazolin-2-yl)-2-imidazolidinone hydriodide methanethiol hydrate (**19**): mp 160–161° dec; uv max 216 nm (ϵ 18,700); ir 1670 (C=O), 1640 cm^{-1} (C=N^+); nmr δ 2.23 (s, 3, CH_3S), 3.25 (m, 6 H, CH_2CH_2, H_2O), 3.62 (s, 4, CH_2CH_2), and 7.9 (D_2O-exchangeable broad m, 4, NH).

Anal. Calcd for $C_7H_{17}IN_4O_2S$: C, 25.54; H, 4.29; I, 38.54; N, 17.02; O, 4.88; S, 9.74. Found: C, 25.75; H, 4.63; I, 38.15; N, 17.67; O, 5.14; S, 10.48.

Neutralization of 1-(2-Imidazolin-2-yl)-2-imidazolidinone Hydriodide Methanethiol Hydrate (19).—Dissolution of hydriodide **19** in 1 *N* NaOH solution followed by extraction and recrystallization from benzene gave imidazolidinone **14**, mp 200–203° dec (lit.[4] mp 200–205°) alone or admixed with the sample derived from **9**.

The ir spectra of the samples were identical.

Hydrolysis of 1-(2-Imidazolin-2-yl)-2-(methylthio)-2-imidazoline Dihydriodide Methanethiol (13).—A solution of imidazoline **13** (218 g, 0.486 mol), water (1.2 l.), and 50% HI solution (25 ml) was heated under reflux for 1 hr and then evaporated to dryness under reduced pressure. Recrystallization of the residue from 2-propanol–water (9:1) gave 14.9 g (6.7%) of 1-(2-imidazolin-2-yl)-2-imidazolidinone dihydriodide methanethiol (**20**): mp 258–259° dec; uv max 218 nm (ϵ 37,800); ir 1690 (C=O), 1550 cm^{-1} (C=N^+); nmr δ 2.44 (m, 4, CH_3SH), 2.8–4.2 (m, 8, CH_2CH_2), and 8.5 (D_2O-exchangeable v br m, 4, NH^+).

Anal. Calcd for $C_7H_{16}I_2N_4OS$: C, 18.35; H, 3.52; N, 12.23; O, 3.49. Found: C, 18.60; H, 3.60; N, 12.02; O, 3.70.

Neutralization of **20** with 5% NaOH solution followed by extraction with CH_2Cl_2 gave 37% of the base **14**, mp 199–200° dec alone or admixed with an authentic sample, prepared as previously described.

The ir spectra of the samples were identical.

A solution of imidazolidine **13** (244 g, 0.500 mol), water (1.2 l.), and 50% hydriodic acid (10 ml) was boiled under reflux for 1 hr and allowed to cool to room temperature. The layers were separated and the aqueous phase was extracted (CH_2Cl_2). The organic extracts were dried (Na_2SO_4) and evaporated. Distillation of the residual oil gave 20 g (33%) of *S,S*-dimethyl dithiocarbonate (**17**): bp 61–62° (17 mm); uv max 215 nm (ϵ 2500), 248 (4450); ir (CH_2Cl_2) 1640 cm^{-1} (C=O); nmr (CCl_4) δ 2.37 (s, 6,[17] CH_3S).

Anal. Calcd for $C_3H_6OS_2$: C, 29.49; H, 4.95; O, 13.10; S, 52.48. Found: C, 29.58; H, 4.94; O, 13.43; S, 52.21.

The filtrate was evaporated. 2-Propanol was added to the residue and the solid was collected. Recrystallization from 2-propanol–water (15:1) gave 60.7 g (31%) of 2-[(2-aminoethyl)-amino]-2-imidazoline dihydriodide (**18**): mp 210–212°; uv max 218 nm (ϵ 31,500); ir 1655 cm^{-1} (C=N^+); nmr δ 2.6–3.5 (m, 4, CH_2CH_2), 3.66 (s, 4, CH_2CH_2), and 8.1 (D_2O-exchangeable broad m, 4, NH).

Anal. Calcd for $C_5H_{14}I_2N_4$: C, 15.64; H, 3.67; N, 14.59; I, 66.10. Found: C, 15.93; H, 3.69; N, 14.71; I, 66.29.

2-[(2-Aminoethyl)amino]-2-imidazoline dipicrate, mp 198–200° (lit.[18] mp 199–200°), was prepared by basification (NaOH)

(17) Relative to benzene as the internal standard.

of an aqueous solution of the corresponding dihydriodide, evaporation, dissolution of the residue in ethanol, and treatment with picric acid and showed an ir spectrum identical with that of an authentic sample.[13]

Alcoholysis of 1-(2-Imidazolin-2-yl)-2-(methylthio)-2-imidazoline Hydriodide (9) and Triethyl[1-(2-imidazolin-2-yl)-2-imidazolin-2-yl]ammonium Iodide Hydriodide Methanethiol (12). A. With Methanol and 2-Propanol.—A solution of 9 or 12 (0.020 mol) and the alcohol (distilled from calcium hydride, 25 ml) was heated under reflux for 5 days while a stream of nitrogen was bubbled through the reaction mixture and then allowed to cool to room temperature. The precipitate was collected; yield 0.005–0.0067 mol (25–30%) of imidazolidinone hydriodide **14a**, mp 255–257° dec alone or admixed with an authentic sample.

The ir spectra of the samples were identical.

B. With *tert*-Butyl Alcohol.—A solution of 9 or 12 (0.020 mol) and *tert*-butyl alcohol (distilled from calcium hydride, 175 ml) was treated as above to give 0.0180–0.0185 mol (90–93%) of unchanged 9 or 12 by mixture melting point determination and ir spectroscopy.

Registry No.—**5a**, 38631-03-7; **6**, 20112-79-2; **7**, 5464-11-9; **8**, 38621-46-4; **9**, 36858-50-1; **10**, 38631-06-0; **11**, 38631-07-1; **11** HI, 38631-08-2; **12**, 36813-47-5; **13**, 38621-48-6; **14a**, 38631-09-3; **14a** HI, 38677-78-0; **17**, 868-84-8; **18**, 38631-10-6; **19**, 38744-27-3; **20**, 38621-49-7.

Acknowledgment.—We wish to thank Mrs. U. Zeek and Dr. R. C. Greenough and their associates for microanalysis and spectral determinations.

5-Imino-2-oxo-1,2,3-oxathiazolidines[1]

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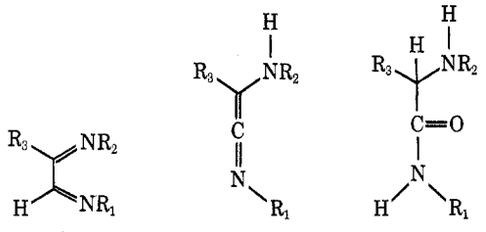
Received November 13, 1972

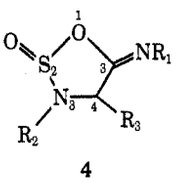
A series of aryl and aliphatic substituted 2-aminoamides have been prepared and treated with thionyl chloride and base to give 5-imino-2-oxo-1,2,3-oxathiazolidines in good yield. This structure was assigned on the basis of analytical, chemical, and spectral data as well as by comparisons with other 2-oxo-1,2,3-oxathiazolidines obtained previously. Asymmetry at sulfur is noted.

As part of our continuing study on the reactions of isonitriles with imines,[3] it became necessary to develop a general synthesis for unsymmetrically N-substituted 1,4-diaza-1,3-butadienes (**1**). Since a direct synthesis of **1** from 1,2-dicarbonyl compounds was precluded by imine interchange reactions,[4] we sought alternative approaches to **1**. Dehydration of readily available 2-aminoamides (**3**) to 2-aminoketenes (**2**) which might



1 **2** **3**

in turn be isomerizable to **1** constituted one attractive path.[5] Initial attempts at dehydration with PCl_5 and subsequent base treatment[7] or with P_2O_5[8] failed to give recognizable products. Reaction of **3** with thionyl chloride and subsequent treatment of the product with pyridine yielded compounds to which we have assigned the 5-imino-2-oxo-1,2,3-oxathiazolidine structure (**4**). In this paper, we wish to discuss the synthesis and structural assignment of this novel *functionally substituted* example of a relatively unexplored heterocyclic system.[9-13]



4

4	R_1	R_2	R_3
a	*o*-$C_6H_4CH_3$	*t*-Bu	H
b	*o*-$C_6H_4CH_3$	C_6H_5	H
c	*t*-Bu	C_6H_5	H
d	*i*-Pr	*t*-Bu	H
e	$CH_2C_6H_4$	*t*-Bu	H
f-1	C_6H_5	*t*-Bu	C_6H_5
f-2	C_6H_5	*t*-Bu	C_6H_5

Results and Discussion

A series of 2-aminoacetamides was prepared from the reactions of the appropriate 2-chloroacetamides and excess primary amines in benzene. These 2-aminoacetamides were in turn treated with excess thionyl chloride and subsequently (after removal of unreacted thionyl chloride) with excess pyridine. Equivalent results were obtained when base (triethylamine) was present during the thionyl chloride reaction.

The product in each reaction (Table I) was neutral and gave a mass spectral parent ion which corresponded to the original molecule plus SO minus 2 H. This empirical formula was confirmed by elemental analysis. The ir spectra indicated that the amide C=O band had

(1) Support of this work by the National Science Foundation (Grant GP-17642) is gratefully acknowledged.

(2) National Science Foundation Undergraduate Research Fellow, summer 1971.

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(4) *Cf.* S. Dayagi and Y. Degani in "The Chemistry of the Carbon–Nitrogen Double Bond," S. Patai, Ed., Interscience, New York, N. Y., 1970, p 81.

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