

2-Amino-2-thiazoline. V. (1,2) Phenylthioureido and Phenylureido Derivatives of 2-Thiazoline

Daniel L. Klayman, James J. Maul, and George W. A. Milne (3)

Walter Reed Army Institute of Research, Division of Medicinal Chemistry and
The National Institutes of Health, National Heart Institute, Laboratory of Metabolism

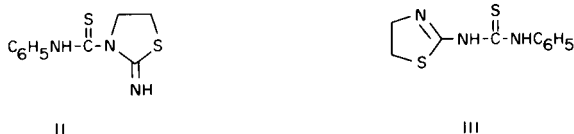
The reaction of 2-amino-2-thiazoline (I) with phenylisothiocyanate has been reported to give 2-imino-3-phenylthiocarbonylthiazolidine (II) at low temperatures and 1-phenyl-3-(2-thiazolin-2-yl)-2-thiourea (III) at *ca.* 100°. When performed by us, however, this reaction gave only a single mono-adduct regardless of the temperature. Nmr and chemical evidence indicates that structure III is the correct one. Treatment of I with phenylisocyanate also gave a mono-adduct which was established to be 1-phenyl-3-(2-thiazolin-2-yl)urea (V). Compound I does not form a simple di-adduct with excess phenylisothiocyanate but does so with phenylisocyanate to give 2-phenylcarbamoylimino-3-phenylcarbamoylthiazolidine (VI). The reaction of III with phenylisocyanate gives 2-phenylthiocarbonylimino-3-phenylcarbamoylthiazolidine (VII), however, the corresponding reaction of V with phenylisothiocyanate does not give the anticipated product but a mixture of compounds which includes VI and VII.

2-Amino-2-thiazoline (I), which can exist in two tauto-



meric forms, has exocyclic and ring amino groups of unlike basicities and with different steric requirements. In reactions such as alkylation (4) and sulfonylation (5), the 3-substituted derivative is obtained. However, reaction with nitrous acid (6) or an acyl halide (7) takes place at the 2-amino group. Recently, it was shown that cyanate ion reacts with the exocyclic amino group of I to give the 2-ureido derivative (8).

The reaction of phenylisothiocyanate with one equivalent of I hydrobromide, which had been treated with one equivalent of ethanolic potassium hydroxide, when performed "under strong cooling" was reported by Fromm and Kapeller-Adler (9) to give 2-imino-3-phenylthiocarbonylthiazolidine (II), m.p. 60°, resolidification 80°, m.p. 129°. They also reported that these reactants, when



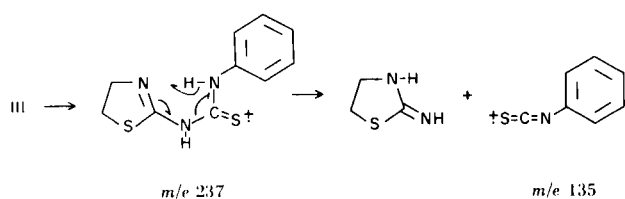
heated under reflux, gave 1-phenyl-3-(2-thiazolin-2-yl)-2-thiourea (III), m.p. 130°. This reaction was repeated by us under conditions as nearly as possible identical to those described by Fromm and Kapeller-Adler (*i.e.*, at 0-4° and at reflux temperature) giving only one mono-adduct, C₁₀H₁₁N₃S₂, m.p. 148-149°. This compound could be made more conveniently by the reaction of I (free base) and phenylisothiocyanate in ethanol or acetonitrile.

The nmr spectrum of the mono-adduct was examined in light of the recent study of 2-amino-2-thiazoline derivatives by Peresleni, *et al.* (10). These workers found signals in the nmr spectra of I and the 3-methyl, 3-ethyl and 3-benzyl derivatives at δ 5.48, 5.76, 5.73, and 6.38, respectively, which were attributed to the protons of the 2-amino group or the proton of the 2-imino group. The nmr spectrum of our mono-adduct showed moderately broad peaks for the two thiourea protons at δ 9.22 and 10.32 while a model compound, 1-phenyl-3-thiazoly-2-thiourea (11), has N-H bands at δ 10.60 and 12.30. The absence of an N-H band in the range found for imino protons in the spectra of the above-mentioned thiazolines, *i.e.* δ 5.0-6.5, suggests that the mono-adduct has structure III. Since none of the model compounds contained electron-withdrawing groups on the ring nitrogen atom and since the effect of the 3-phenylthiocarbonyl group on the chemical shift of the N-H proton of II was unknown, it was felt that the nmr evidence was not conclusive and that additional data in support of structure III was

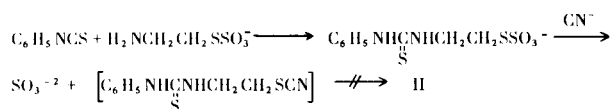
necessary.

The *S*-methyl derivative of III gave on alkaline hydrolysis a reaction typical (12) of thiopseudoureas derived from 1,3-disubstituted thioureas. It was stable to base at room temperature but generated methyl mercaptan readily on heating to *ca.* 90°. If structure II (a trisubstituted thiourea) were correct, its *S*-methyl derivative would not have been expected to generate methyl mercaptan under these conditions.

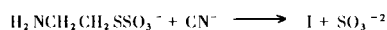
The mass spectrum (13) of III shows a fairly stable molecular ion at *m/e* 237, (C₁₀H₁₁N₃S₂⁺) (14) which collapses readily to give as the base peak at *m/e* 135, a "phenylisothiocyanate ion," (C₇H₅NS⁺), by a McLafferty rearrangement (15). A metastable ion at *m/e* 76.8 (calcd. 76.89) is observed for this fragmentation.



Earlier, we reported (16) the synthesis of II by the reaction of sodium 2-aminoethylthiosulfate with phenylisothiocyanate. The resultant phenylthioureido derivative was treated *in situ* with sodium cyanide to give in poor yield a compound believed to be II. Since this material



was identical to that obtained in the reaction of I with phenylisothiocyanate, the product of this latter reaction was mistakenly assigned structure II. Further investigation of the reaction of cyanide with sodium 2-phenylthioureidoethylthiosulfate revealed that the small amount of mono-adduct which was isolated from the reaction mixture was due to the condensation of phenylisothiocyanate with I, the latter having been formed by the attack of cyanide on some unreacted sodium 2-aminoethylthiosulfate. In our later work, when the unreacted phenylisothiocyanate was removed from the reaction mixture before the addition of



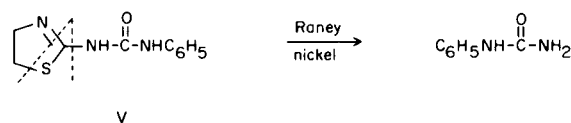
cyanide, no mono-adduct was formed. Success of the cyanide displacement on the divalent sulfur atom of the thiosulfate was apparent from the immediate precipitation of sodium sulfite from the aqueous-ethanolic solution. The desired cyclization, however, fails to occur, there being obtained only a yellow polymeric material.

While no mono-adduct was ever isolated having the anticipated properties of II, the possibility that II is an intermediate in the formation of III cannot be precluded. The reaction of I with excess phenylisothiocyanate is discussed in a companion paper in this series (17).

When I was treated with one equivalent of phenylisocyanate, a crystalline mono-adduct was obtained for which two structures were considered, 2-imino-3-phenylcarbamoylthiazolidine (IV) and 1-phenyl-3-(2-thiazolin-2-yl)-urea (V).

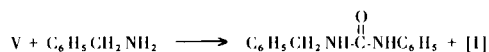
The nmr spectrum of the adduct, like that of III, did not show a peak in the region of δ 5.0-6.5 corresponding to a proton of the basic 2-imino group. There were two medium broad peaks at δ 8.62 and 9.30, due to the two protons of the urea nitrogen atoms. Thus, structure V was considered to be the correct one. However, inasmuch as the effect of the 3-phenylcarbamoyl group on the chemical shift of the 2-imino protons of IV was unknown, further evidence in support of structure V was sought.

Behringer and Zilliken (18) have reported that Raney nickel treatment of 2-amino-2-thiazoline-4-carboxylic acid in aqueous solution yielded α -alanine. When compound V was treated with Raney nickel, phenylurea was obtained, thereby confirming the structure of the phenylcarbamoyl



adduct. The reaction of phenylisocyanate with 2-amino-2-thiazoline-2-¹⁵N(I-¹⁵N) (8) gave the isotopically labeled mono-adduct. Treatment of the compound with Raney nickel gave phenylurea-3-¹⁵N, whose isotopic labeling was demonstrated by mass spectrometry. The molecular ion, (C₇H₈¹⁴N¹⁵NO)⁺, was found at *m/e* 137.061.

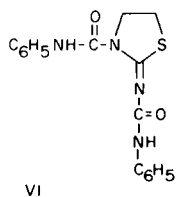
The phenylcarbamoyl group of V could be removed by refluxing a benzene solution of the compound with a two molar excess of benzylamine to give 1-benzyl-3-phenylurea in good yield. Compound V was undetectable by tlc after three hours. By comparison, when III was refluxed



in benzene with benzylamine under identical conditions to form 1-benzyl-3-phenyl-2-thiourea, five hours were required before all of the III disappeared.

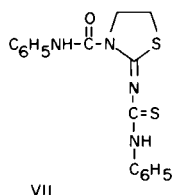
The reaction of I with two equivalents of phenylisocyanate or that of V with one equivalent of phenylisocyanate yielded the di-adduct, 2-phenylcarbamoyl-imino-3-phenylcarbamoylthiazolidine (VI). The 3-phenyl-

carbamoyl moiety of VI was found to be considerably more labile toward nucleophiles than the phenylcarbamoyl moiety attached to the 2-imino group. Compound VI



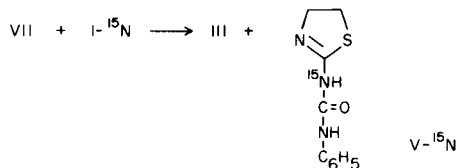
reacted readily with one equivalent of I to form two equivalents of V. When heated with isopropyl alcohol, VI gave V and the corresponding phenylurethan. Although the removal of the phenylcarbamoyl moiety from the 2-amino group of V with benzylamine took three hours to go to completion, the reaction of benzylamine with VI removed the 3-phenylcarbamoyl group in about 20 minutes.

When III was heated in chloroform solution with one equivalent of phenylisocyanate, a "cross product" was obtained to which the structure, 2-phenylthiocarbonylimino-3-phenylthiocarbonylimino-3-phenylthiazolidine (VIII) was assigned. As was found with VI, the 3-phenylcarbamoyl group was readily removable as exemplified in the reaction of VII with one equivalent of I in which III and V were isolated in essentially equimolar quantities.

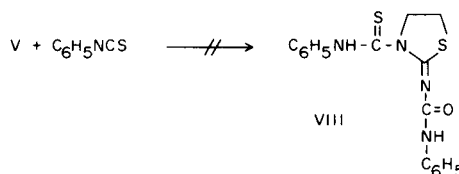


Inasmuch as the product of the reaction of I with phenylisothiocyanate had previously been incorrectly assigned structure II (16), it followed that the structure of the "cross product" was also depicted incorrectly in that the phenylcarbamoyl and phenylthiocarbonyl groups were shown in interchanged positions. The reaction of VII with one equivalent of I was utilized to confirm the structure of the "cross product". The two reactants were heated in chloroform solution until tlc revealed that no starting materials were present. Evaporation of the solvent gave a mixture of III and V, each component of which, without separation, was detected by high resolution mass spectrometry. Peaks of moderate intensity corresponding to the molecular ions of III and V appeared at m/e 237 and m/e 221, respectively. When this reaction was repeated using $I-^{15}\text{N}$ these ions were at m/e 237 and m/e

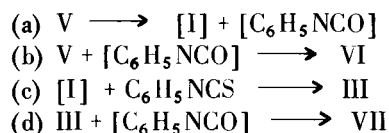
222. This indicated that the phenylcarbamoyl group was, indeed, located at the 3-position of VII.



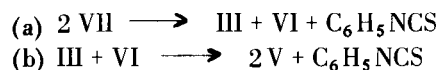
An attempt was made to synthesize the other "cross product," *i.e.*, 2-phenylcarbamoylimino-3-phenylthiocarbonylimino-3-phenylthiazolidine (VIII). When V was heated with excess phenylisothiocyanate in either acetonitrile, chloroform, benzene or methanol, only the starting materials were recovered. When V was heated 1 hour with ten



equivalents of phenylisothiocyanate neat, there was obtained from the reaction mixture III, VI, VII and a small amount of 2-phenylimino-3-phenyl-4-thioxothiazolo-[3,2-*a*]tetrahydro-*s*-triazine (IX) (17). No VIII was detected. A possible route by which VI and the original "cross product," VII, were formed is shown below.



It was interesting to find that when VII was refluxed for several hours in dry benzene, its yellow color slowly disappeared and the compound was transformed into V and phenylisothiocyanate. Compounds III and VI were detected as intermediates. This decomposition may be depicted as occurring in two steps, as shown. The second step was tested by heating equimolar quantities of III and VI in benzene. Again, the yellow color of the solution,



due to the III, was dispelled and the final products were V and phenylisothiocyanate.

Attempts to convert V to III using phosphorus pentasulfide in refluxing benzene, xylene or pyridine

solution failed. When III was treated for 0.5 hour with mercuric acetate in boiling acetonitrile or ethanol solution, there was obtained a compound, $C_{12}H_{13}N_3O_2S$ (X), which is assumed to be an *N*-acetyl derivative of V. By refluxing compound X for several hours in ethanol it was possible to remove the acetyl group to give V.

EXPERIMENTAL

Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected. Microanalyses were performed by Mr. Joseph F. Alicino, Metuchen, N. J. Infrared spectra were determined as potassium bromide pellets, unless specified otherwise, on a Beckman IR-5 spectrometer. Nmr spectra were run on 15-20% solutions of the compound in dimethylsulfoxide- d_6 on a Varian A-60 spectrometer using tetramethylsilane as the internal standard. Tlc was performed on Brinkmann analytical glass plates precoated with Silica Gel F-254 containing a fluorescent indicator and were developed with 1% methanol-chloroform unless specified otherwise.

1-Phenyl-3-(2-thiazolin-2-yl)-2-thiourea (III).

2-Amino-2-thiazoline (10.2 g., 0.1 mole) and 13.5 g. (0.1 mole) of phenylisothiocyanate in 50 ml. of ethanol were heated on a steam bath for ca. 0.5 hour. A yellow color developed almost immediately and separation of the product began in about 10 minutes. The reaction mixture was cooled and the crystals which separated were collected, 20.3 g. (86%), m.p. 146-148°. Recrystallization from acetonitrile gave pale yellow crystals, m.p. 148-149°; infrared (chloroform), 6.19 (weak, C=N, 6.35 μ (N-C=S); nmr: δ 3.23 and 3.47 (multiplets, CH_2-CH_2), δ 6.90-7.70 (multiplet, aromatic H) and δ 9.22 and 10.32 (singlets, N-H).

Anal. Calcd. for $C_{10}H_{11}N_3S_2$: C, 50.60; H, 4.67; N, 17.70; S, 27.02. Found: C, 50.55; H, 4.71; N, 17.81; S, 27.11.

1-Phenyl-2-methyl-3-(2-thiazolin-2-yl)-2-thiopseudourea Hydroiodide.

To 7.1 g. (0.03 mole) of III and 25 ml. of ethanol was added 5.1 g. (0.036 mole) of methyl iodide and the mixture was heated under reflux for 1.5 hours. The yellow solution was cooled causing separation of pale yellow crystals, 11.4 g. (95%), m.p. 162-163°. An analytical sample was obtained by recrystallization from ethanol, m.p. 163-164°.

Anal. Calcd. for $C_{11}H_{14}IN_3S_2$: C, 34.83; H, 3.72; N, 11.08; S, 16.91. Found: C, 34.84; H, 3.98; N, 11.04; S, 16.78.

Reaction of III with Benzylamine.

A mixture of 237 mg. (1 mmole) of III and 321 mg. (3 mmoles) of benzylamine in 7 ml. of dry acetonitrile was heated under reflux protected by a calcium chloride drying tube. The disappearance of III, monitored by tlc, was complete in 5 hours and was accompanied by the formation of I and 1-benzyl-3-phenyl-2-thiourea. A third decomposition product was observed (R_f 0.18, developed four times) which could not be identified.

1-Phenyl-3-(2-thiazolin-2-yl)urea (V).

A solution of 5.11 g. (0.05 mole) of I in 250 ml. of dry benzene and 5.96 g. (0.05 mole) of phenylisocyanate was heated at reflux for 0.5 hour while protected by a calcium chloride drying tube. The crystals which separated from the cooled solution were collected to give 8.78 g. (79%) of V, m.p. 147-148.5°. An analytical sample was prepared by recrystallization from ethanol which melted at 149.5-150° (lit. (19) m.p. 157-159°); infrared: 5.90 (C=O), 6.15 μ (C=N); nmr: δ 3.23 and 3.53

(multiplets, CH_2-CH_2), δ 6.83-7.77 (multiplet, aromatic H), δ 8.67 and 9.35 (singlets, N-H).

Anal. Calcd. for $C_{10}H_{11}N_3OS$: C, 54.28; H, 5.01; N, 18.99; S, 14.49. Found: C, 54.31; H, 5.27; N, 18.98; S, 14.62.

Treatment of V with Raney Nickel.

Activated Raney nickel (6.5 teaspoonsful) was added to a solution of 1.0 g. (4.5 mmoles) of V in 260 ml. of methanol and the mixture was heated on a steam bath for 0.5 hour. The reaction mixture was filtered, and the filtrate was evaporated to dryness. The residual solid was recrystallized from water to yield 0.23 g. (38%) of phenylurea, m.p. 137-140.5° (lit. (20) m.p. 144-145°). The infrared spectrum of this product was identical to that of an authentic sample of phenylurea.

Reaction of V with Benzylamine.

A mixture of V and 3 equivalents of benzylamine in dry acetonitrile was treated as described above for III. The disappearance of V, monitored by tlc (developed with methanol), was complete after 3 hours and was accompanied by the formation of I and 1-benzyl-3-phenylurea.

2-Phenylcarbamoylimino-3-phenylcarbamoylthiazolidine (VI).

A solution of 1.02 g. (0.01 mole) of I in 90 ml. of dry benzene and 2.50 g. (0.021 mole) of phenylisocyanate was heated at reflux for 0.5 hour while protected with a calcium chloride drying tube. The crystals which separated from the cooled solution were collected to give 3.30 g. (97%) of VI, m.p. (21) 172.5-175.5°. The compound melted at 177.5-179.5° after recrystallization from benzene; infrared: 5.85 (C=O), 6.08 (C=O), 6.25 μ (C=N).

Anal. Calcd. for $C_{17}H_{16}N_4O_2S$: C, 59.98; H, 4.74; N, 16.46; S, 9.42. Found: C, 60.27; H, 4.96; N, 16.56; S, 9.44.

Reaction of VI with I.

A solution of 69 ml. (0.2 mmole) of VI and 20 mg. (0.2 mmole) of I in 5 ml. of acetonitrile was heated at reflux for 10 minutes. By tlc it was determined that V was the exclusive product. The solvent was evaporated from the reaction mixture to yield 80 mg. (91%) of white solid, m.p. 149-151°, whose infrared spectrum was identical to that of V prepared by the method described earlier.

Compound VI was treated with 3 equivalents of benzylamine in dry acetonitrile as described above for III. The reaction was complete in 20 minutes and gave a mixture of V and 1-benzyl-3-phenylurea.

Reaction of VI with 2-Propanol.

A mixture of 1.0 g. (2.9 mmoles) of VI and 35 ml. of 2-propanol was heated at reflux for 3.5 hours until tlc indicated the disappearance of VI. A total of 0.46 g. (72%) of V was obtained as well as 0.31 g. (59%) of isopropylphenylcarbamate (from hexane), m.p. 84.5-86.5° (lit. (22) m.p. 90°). The infrared spectrum of this compound was identical to that of an authentic sample.

Preparation of 2-Phenylthiocarbamoylimino-3-phenylcarbamoylthiazolidine (VII).

A solution of 4.1 g. (17 mmoles) of III and 2.07 g. (17 mmoles) of phenylisocyanate in 400 ml. of chloroform was stirred at room temperature for 0.75 hour. The solution was concentrated at reduced pressure, with a minimum of heat, to 200 ml.; 200 ml. of dry benzene was added, and the yellow crystals which separated from the cooled solution were collected to give 4.13 g. (67%) of 2-phenylthiocarbamoyl-3-phenylcarbamoylthiazolidine (VII),

m.p. 143.5-144.5°; infrared: 5.95 (C=O), 6.25 (C=N), 6.40 μ (N-C=S).

Anal. Calcd. for $C_{17}H_{16}N_4OS_2$: C, 57.28; H, 4.53; N, 15.72; S, 17.99. Found: C, 57.12; H, 4.88; N, 15.78; S, 18.07.

Reaction of VII with I.

A solution of 71 mg. (0.02 mmole) of VII and 20 mg. (0.02 mmole) of I in 45 ml. of dry acetonitrile was heated at reflux for 35 minutes. The solvent was evaporated *in vacuo* to yield a yellow oil which was chromatographed on 20 g. of alumina (Fisher A540). Elution with 2% ethanol-ether gave 32 mg. (67%) of III, m.p. 144.5-145.5°, and with 5% ethanol-ether gave 19 mg. (43%) of V, m.p. 148.5-149.5°.

Using the identical procedure 10 mg. (0.0029 mmole) of VII was heated with 3 mg. (0.0029 mmole) of $1-^{15}N$ in 5 ml. of acetonitrile and the residue after evaporation of the solvent was analysed by mass spectrometry. Molecular ions were obtained for III and V. ^{15}N at *m/e* 237.038 ($C_{10}H_{11}N_3S_2^+$) and *m/e* 222.058 ($C_{10}H_{11}O^{14}N_2^{15}NS^+$), respectively.

Decomposition of VII in Refluxing Benzene.

A solution of 50 mg. (0.14 mmole) of VII and 35 ml. of dry benzene was heated under reflux. The reaction products were monitored by tlc which indicated that decomposition of VII began within *ca.* 10 minutes. After 3 hours VII had completely decomposed to III, V, VI and phenylisothiocyanate; after 6 hours only V and phenylisothiocyanate were present.

Reaction of III with VI in Benzene.

A solution of 16.6 mg. (0.07 mmole) of III and 23.8 mg. (0.07 mmole) of VI in 35 ml. of dry benzene was heated under reflux. By tlc it was determined that the reactants were completely converted to V and phenylisothiocyanate in 3 hours.

Reaction of VII with Benzylamine.

Compound VII was treated with 3 equivalents of benzylamine in dry acetonitrile as described above for III. Within 15 minutes all the VII had been consumed with formation of III and 1-benzyl-3-phenylurea. It was also observed that the excess benzylamine was reacting at a slower rate with the by-product, III, to yield 1-benzyl-3-phenyl-2-thiourea and I. A fifth decomposition product was observed, (R_f 0.088, developed four times), which has not been identified.

Reaction of V with Phenylisothiocyanate.

A mixture of 1.1 g. (5 mmoles) of V and 6.75 g. (50 mmoles) of phenylisothiocyanate was heated on a steam bath for 1 hour to give a yellow solution. By tlc it was determined that the products listed below were present. The solution was dissolved in 30 ml. of methanol-free chloroform and chromatographed on 100 g. of Woelm Activity I neutral alumina.

Eluant	Product
hexane	phenylisothiocyanate
25% ether-benzene	47 mg. IX
ether	318 mg. VII
1% acetonitrile-ether	339 mg. VI
50% acetonitrile-ether	227 mg. III
ethanol	200 mg. V

Reaction of III with Mercuric Acetate.

To a heated solution of 1.18 g. (5 mmoles) of III in 25 ml. of

acetonitrile was added 1.75 g. (5.5 mmoles) of mercuric acetate and the mixture was heated and stirred for 0.5 hour. The mercuric sulfide which formed was filtered from the hot mixture and the filtrate was evaporated to dryness under reduced pressure to give a syrup which crystallized on cooling. The product was recrystallized from benzene to give 0.82 g. (60%) of X, m.p. 160-161°; infrared: 5.91 (C=O), 6.00 (C=O), 6.10 μ (C=N).

Anal. Calcd. for $C_{12}H_{13}N_3O_2S$: C, 54.73; H, 4.98; N, 15.96; S, 12.18. Found: C, 54.63; H, 4.96; N, 15.96; S, 11.85.

By heating X for 6 hours in ethanol and evaporating the solution to dryness, the compound was converted to V in 70% yield (from ethanol), m.p. 150-151°. Compound V could be obtained directly from III by heating the latter with mercuric acetate in ethanol for *ca.* 6 hours.

REFERENCES

- (1) Part IV: D. L. Klayman and P. T. McIntyre, *J. Org. Chem.*, **33**, 884 (1968).
- (2) Part of this work was presented at the First International Congress of Heterocyclic Chemistry, University of New Mexico, Albuquerque, N. M., June 12-15 (1967).
- (3) National Institutes of Health.
- (4) S. Gabriel, *Ber.*, **22**, 1139 (1889); K. K. Kuz'mina, N. G. Ostroumova, Yu. V. Markova, and M. N. Shchukina, *Zh. Obshch. Khim.*, **32**, 3215 (1962); Yu. V. Markova, K. K. Kuz'mina, E. M. Peresleni, and M. N. Shchukina, *Zh. Org. Khim.*, **1**, 1475 (1965).
- (5) J. H. Hunter and H. G. Kolloff, *J. Am. Chem. Soc.*, **65**, 156 (1943).
- (6) L. C. King and E. W. Stern, *J. Org. Chem.*, **30**, 3222 (1965).
- (7) K. K. Kuz'mina, N. G. Ostroumova, Yu. N. Markova, and M. N. Shchukina, *Zh. Obshch. Khim.*, **32**, 3390 (1962).
- (8) D. L. Klayman, A. Senning, and G. W. A. Milne, *Acta Chem. Scand.*, **21**, 217 (1967).
- (9) E. Fromm and R. Kapeller-Adler, *Ann. Chem.*, **467**, 240 (1928).
- (10) E. M. Peresleni, V. I. Sheichenko, and Yu. N. Sheinker, *Zhur. Fiz. Khim.*, **40**, 38 (1966).
- (11) T. Uno and S. Akihama, *Yakugaku Zasshi*, **80**, 1015 (1960); *Chem. Abstr.*, **54**, 22,577 (1960).
- (12) D. L. Klayman and R. J. Shine, *Anal. Chim. Acta.*, **41**, 408 (1968).
- (13) Mass spectra were measured on an Associated Electrical Industries (U. K.). MS-9 double focusing mass spectrometer. Unless otherwise specified, the ionizing voltage was 70 ev. Accurate measurement of mass to charge ratio was carried out by comparison with a perfluorotributylamine standard.
- (14) This masses of all ions to which formulas have been assigned have been accurately measured and agree with the calculated mass within 10 parts per million.
- (15) This is a type of McLafferty rearrangement [F. W. McLafferty, *Anal. Chem.*, **31**, 82 (1959)] which is similar to one reported to occur with 3-amidino-2-iminothiazolidine [D. L. Klayman and G. W. A. Milne, *J. Org. Chem.*, **31**, 2349 (1966)].
- (16) D. L. Klayman, J. J. Maul, and G. W. A. Milne, *Tetrahedron Letters*, 281 (1967).
- (17) Part VI. D. L. Klayman and G. W. A. Milne, *Tetrahedron*, in press.
- (18) H. Behringer and P. Zilliken, *Ann. Chem.*, **574**, 140 (1951).
- (19) H. Najer, R. Giudicelli, J. Menin, and C. Morel, *Bull. Soc. Chim. France*, 323 (1963).

(20) H. C. White and F. W. Bergstrom, *J. Org. Chem.*, 7, 497 (1942).

(21) The melting point was determined in a sealed capillary tube using a Scientific Glass Co., Inc., melting point block. The Fisher-Johns apparatus gave inconsistent results, VI generally

melting at 167-170°.

(22) F. Gumpert, *J. Prakt. Chem.*, 32, 279 (1885).

Received April 5, 1968

Washington, D. C. 20012
Bethesda, Maryland 20014