References and Notes

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2-Amino-2-thiazoline. VIII.[1] A Nonregioselective Reaction of 2-Amino-2-thiazoline with Benzoyl Isothiocyanate to Give a Thermally Unstable Thiourea and a Thiazolotriazine

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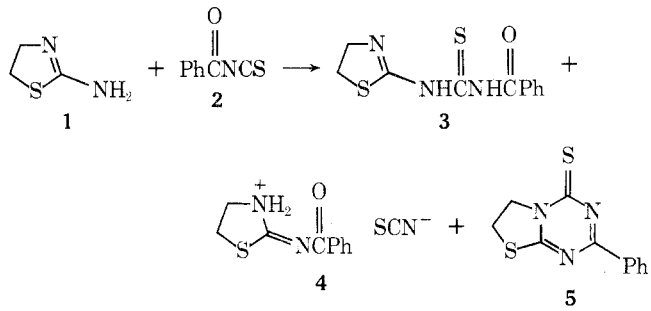
Received February 14, 1975

The reactions of 2-amino-2-thiazoline (**1**) with electrophiles giving products resulting from attack on either or both nitrogen atoms have been recently summarized.[2] Although the interaction of **1** with a given electrophile usually gives rise to a product resulting from a regioselective attack, behavior within a family of electrophiles cannot be predicted with certainty. The isothiocyanate family has provided a particularly perplexing series of examples in this regard. Yamamoto and Yoda,[3] for example, have reported that alkyl isothiocyanates react with **1** to give thiocarbamoyl derivatives resulting from nonregioselective attack on both nitrogen atoms. Phenyl isothiocyanate, on the other hand, exhibits regioselective attack on the exocyclic nitrogen atom of **1**,[4] whereas carbethoxy isothiocyanate undergoes the opposite mode of reaction and interacts with the ring nitrogen of **1**.[1] These examples demonstrate that reactions of **1** with isothiocyanates are characterized by lack of predictability as to regioselectivity.

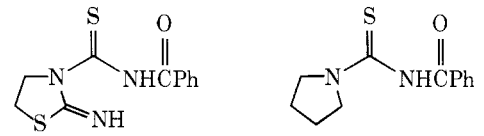
We report here the investigation of the reaction of **1** with another acyl isothiocyanate, namely, benzoyl isothiocyanate (**2**). If **2** were to behave as does carbethoxy isothiocyanate, regioselective attack of **2** on the ring nitrogen atom of **1** would produce a single derivative.

Results and Discussion

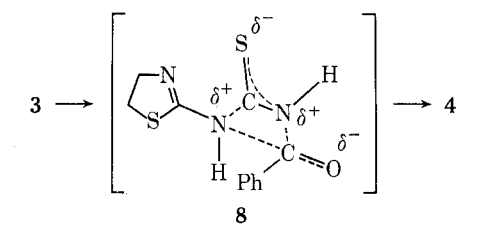
The reaction of 2-amino-2-thiazoline (**1**) with benzoyl isothiocyanate (**2**) was found to give three products: 1-benzoyl-3-(2-thiazolin-2-yl)-2-thiourea (**3**), 2-benzamido-2-thiazoline thiocyanic acid salt (**4**), and 6,7-dihydro-2-phenyl-4*H*-thiazolo[3,2-*a*]triazine-4-thione (**5**). The structural assignments of the products follow from their elemental analyses, chemical behavior, and spectral properties.



The ir spectrum of **3** shows diagnostic absorptions at 3280 and 1639 cm^{-1} in KBr and at 3440 and 1645 cm^{-1} in $CHCl_3$ solution, observations consistent with values reported for conjugated amides.[5] The alternate structure **6**, which would have resulted from attack of **2** on the ring nitrogen atom of **1**, may be ruled out on the following bases: the NMR spectrum of **3** shows NH signals at δ 10.12 and 11.35 (the imino NH of **6** would be expected to appear at much higher field[6]); the chemical behavior of **3** is also consistent with that of a disubstituted thiourea in that **3** gives a positive ammoniacal silver nitrate test, which **6** would not be expected to exhibit;[7] furthermore, the *S*-methyl derivative of **3**, generated in situ from **3** and iodomethane, proved to be stable to alkali at room temperature, but liberated methyl mercaptan after being heated at 100° for 30 sec. This latter test is diagnostic of 1,3-disubstituted thioureas.[7] A model compound, 1-(*N*-benzoylthiocarbamoyl)pyrrolidine (**7**), prepared from **2** and pyrrolidine, which would have been expected to behave similarly to **6**, gave negative results in both the ammoniacal silver nitrate and *S*-methyl tests mentioned above.

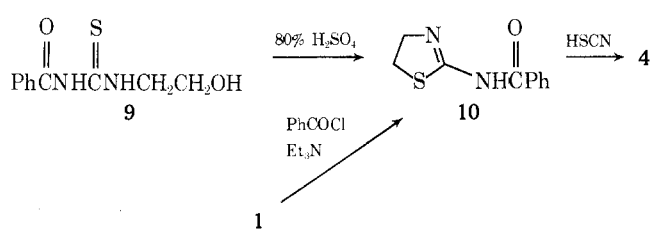


Compound **3** undergoes facile thermal conversion to **4** on being heated at the boiling point of common solvents for a short time. The phenomenon, first noted on attempted recrystallization of **3** from CH_3CN, probably proceeds through the transition state **8**. The alternate process, i.e., thermal retroreaction of **3** to give **1** and **2**, followed by benzoylation of **1** to give **4**, is untenable, since no **5** is produced. Qualitatively, the rate of thermolysis of **3** in boiling solvents to give **4** was shown to proceed as follows: very slowly in methylene chloride, slowly in chloroform or methanol, moderately rapidly in 1,2-dichloroethane, and very rapidly in dioxane. Also **3** undergoes rearrangement to **4** near its melting point as evidenced by the strong $FeCl_3$ test exhibited by the cooled melt of **3** as well as by its ir spectrum.



The structure of **4** was elucidated by its unequivocal synthesis as outlined in Scheme I. 1-Benzoyl-3-(2-hydroxyethyl)-2-thiourea (**9**) was prepared and cyclized to **10** as previously described.[8] The free base **10** was also prepared

Scheme I

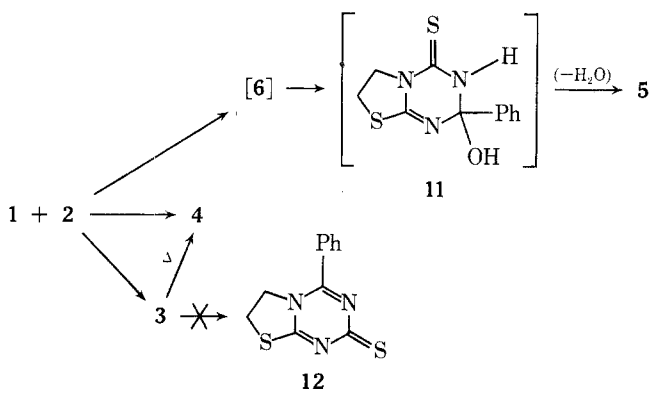


by treatment of 1 with benzoyl chloride and triethylamine. The thiocyanic acid salt of 10 was found to be identical with the sample produced in the reaction of 1 and 2. Crucial to the structure assignment of 4 as a thiocyanic acid salt is the strong peak in the ir spectrum of 4 at 2040 cm^{-1} and the intense $FeCl_3$ test.

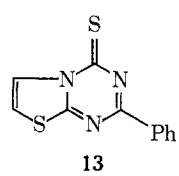
Reactions of 2 and amines giving benzoylated products are well documented.[9-12] These authors do not report having considered, however, that the amide products could have been formed via thermally unstable thiourea intermediates. As might be expected, none of these workers report the isolation of thiocyanic acid salts of their benzamide products; however, Durant[10] obtained 1-benzoyl-2-alkylthiosemicarbazide products from the reaction of 2 and substituted hydrazines, apparently resulting from reaction of intermediate benzhydrazides with concomitantly produced thiocyanic acid.

The structure of the cyclized product 5 follows from its elemental analysis, indicating loss of water from the elements of 1 and 2. Initial attack of 2 on the ring nitrogen atom of 1 would give the imino compound 6, following which cyclization to the carbinolamine intermediate 11 with subsequent loss of water would lead to 5 (Scheme II).

Scheme II



That the thiocarbonyl group of 5 is located at the 4 position rather than at the 2 position as indicated in the alternate structure 12 is shown by the chemical behavior of 3. If the product had structure 12, then of necessity 3 would have been an intermediate in its formation. Maintaining pure 3 under the reaction conditions, including in the presence of excess 2, produced no 12. Heating the reaction mixture caused only the conversion of 3 to 4, indicating by exclusion that 5 is the proper structure of the compound. Further evidence is provided by comparison of the uv spectrum of 5 [λ_{max} 286 nm (ϵ 42,000) and 360 (3190)] with that of the corresponding product from 2-aminothiazole, namely 13 [λ_{max} 301 nm (ϵ 41,000) and 376 (6500)], reported by Barnikow and Bödeker.[12] The bathochromic shift of ~15 nm of the maxima in the spectrum of 13 relative to that of 5 would be expected considering the additional conjugation provided by the 6,7 double bond of 13. Thus, evidence indicates that 5 is structured similarly to 13.



13

The reaction of 1 and 2 is therefore very similar to that reported[12] earlier for the reaction of 2-aminothiazole and 2, which produces the thiourea corresponding to 3, the thiazolotriazine 13, and, in slight contrast, the free base form of 2-benzamidothiazole. The latter is probably due to the reduced basicity of the ring nitrogen of the thiazole relative to that of the thiazoline ring.

The formation of the thermally unstable 3 leading to the amide product 4 could indicate that other less stable thioureas are intermediates in reactions of 2 leading to amide products. The lack of regioselectivity in the reaction of 1 with 2 further indicates that predictions of sites of reaction of 1 with electrophiles cannot be made as yet with any degree of certainty.

Experimental Section[13]

Reaction of 2-Amino-2-thiazoline (1) with Benzoyl Isothiocyanate (2). To a magnetically stirred solution of 4.08 g (0.04 mol) of 1 in 40 ml of CH_3CN was added 6.53 g (0.04 mol) of 2, causing a slightly exothermic reaction. Crystals precipitated from the solution very shortly; however, stirring was continued for an additional 10 hr at room temperature. The crystals, 2.97 g (28%), were collected and proved to be 1-benzoyl-3-(2-thiazolin-2-yl)-2-thiourea (3): mp 137–138° (from CH_2Cl_2); ir 3280 (NH), 3080 (CH), 1639 (C=O), 1613, 1593, 1571, and 1499 cm^{-1}; ir ($CHCl_3$) 3440 (NH), 3020 (CH), 1645 (C=O), and 1602 cm^{-1}; NMR (DMSO-d_6) δ 3.23 (t, J = 8 Hz, 2, CH_2S), 4.63 (t, J = 8 Hz, 2, CH_2N), 7.63 (m, 3, o- and p-ArH), 8.00 (m, 2, m-ArH), 10.0 (s, 1, NH), and 11.3 (s, 1, NH); uv (EtOH) λ_{max} 206 nm (ϵ 8410), 246 (sh, 9680), 294 (21,700); mass spectrum m/e (rel intensity) 265 (1), 247 (1), 205 (100), 177 (28), 129 (30), 105 (31), 77 (87), 59 (64), and 51 (44).

Anal. Calcd for $C_{11}H_{11}N_3OS_2$: C, 49.79; H, 4.18; N, 15.84; S, 24.17. Found: C, 49.69; H, 4.28; N, 15.48; S, 23.48.

The filtrate was reduced to about one-half volume under reduced pressure and cooled. The yellow material which separated was treated with a minimum of boiling $CHCl_3$ to give 1.44 g (14%) of an insoluble, essentially colorless solid, 2-benzamido-2-thiazoline thiocyanic acid salt (4), mp 150–153° (from CH_3CN). Further small quantities of 4 were obtained from work-up of the balance of the reaction product: ir 3120–2650 (broad, NH^+), 2040 ($SC{\equiv}N^-$), 1701 (C=O), 1590, and 1525 cm^{-1}; NMR (DMSO-d_6) δ 3.67 (m, 2, CH_2S), 4.20 (m, 2, CH_2N), 7.75 (m, 3, o- and p-ArH), 8.02 (m, 2, m-ArH), and 11.0 (s, 2, NH_2^+); uv (EtOH) λ_{max} 304 nm (ϵ 1920); mass spectrum m/e (rel intensity) 205 (42), 177 (13), 129 (14), 105 (100), 77 (61), 59 (40), and 51 (24).

Anal. Calcd for $C_{11}H_{11}N_3OS_2$: C, 49.79; H, 4.18; N, 15.84; S, 24.17. Found: C, 49.89; H, 4.26; N, 15.59; S, 23.51.

The CH_3CN mother liquor was evaporated to dryness under reduced pressure and the residue was dissolved in 30 ml of hot $CHCl_3$. The cooled solution yielded 0.97 g (10%) of 6,7-dihydro-2-phenyl-4H-thiazolo[3,2-a]triazine-4-thione (5) as fine yellow crystals: mp 242° (from $CHCl_3$); ir 1585, 1548, 1458, and 1425 cm^{-1}; NMR (CF_3COOH) δ 3.83 (t, J = 8 Hz, 2, CH_2S), 5.00 (t, J = 8 Hz, 2, CH_2N), 7.80 (m, 3, m- and p-ArH), 8.37 (m, 2, m-ArH); uv (EtOH) λ_{max} 207 nm (ϵ 9900), 227 (sh, 6840), 245 (sh, 9110), 286 (42,000), and 360 (3185); mass spectrum m/e (rel intensity) 249 (10), 248 (14), 247 (78), 214 (16), 188 (18), 128 (20), 104 (25), 103 (27), 85 (100), 77 (27), 60 (21), and 59 (16).

Anal. Calcd for $C_{11}H_9N_3S_2$: C, 53.42; H, 3.67; N, 16.99; S, 25.93. Found: C, 53.51; H, 3.82; N, 17.01; S, 25.59.

Alternative Synthesis of 4. The compound 2-benzamido-2-thiazoline was prepared by cyclization of 1-benzoyl-3-(2-hydroxyethyl)-2-thiourea with 80% H_2SO_4 in the manner described by Douglass and Dains[8] and by the direct benzoylation of 1. To a magnetically stirred solution of 5.1 g (0.05 mol) of 1 and 5.1 g (0.05 mol) of triethylamine in 60 ml of $CHCl_3$ was added dropwise 7.0 g (0.05 mol) of benzoyl chloride. After 0.4 hr, the solution was evaporated to dryness and the residue was washed three times with H_2O. The H_2O-insoluble residue was recrystallized from CH_3CN to give 5.06 g (49%) of 2-benzamido-2-thiazoline, mp 167–169° (lit.[8] mp 168°).

2-Benzamido-2-thiazoline (0.206 g, 1.0 mmol) was dissolved in 1.2 ml of 1 N HCl. To the solution was added 0.81 g (1.0 mmol) of sodium thiocyanate in 1 ml of H_2O. The two solutions were combined and cooled, causing the slow separation of 4. The latter, after collection and recrystallization from CH_3CN, melted at 149–150°, ir identical with that of 4 described earlier.

Thermolysis of 3. A. In Acetonitrile. A sample of 500 mg (1.89 mmol) of 3 was heated in 50 ml of boiling CH_3CN for approximately 30 min, i.e., until no remaining 3 was detectable by TLC (silica gel–benzene). The solution, which gave a strong $FeCl_3$ test for thio-

cyanate ion, was evaporated to dryness, yielding 485 mg (97%) of **4**, mp 149–152°.

B. In Other Solvents. The thermal stability of **3** was examined at the boiling point of common organic solvents as follows. A sample of 5 mg of **3** was heated in 1 ml of boiling solvent. At intervals of 1, 2, 5, 15, and 30 min, after adjusting the volume of the solution for evaporation, 2 drops of the solution were removed and tested for the presence of thiocyanate ion with 1 drop of 5% $FeCl_3$ solution. The results are summarized as follows: in methylene chloride (bp 42°), no conversion was noted after 30 min; in chloroform (bp 61°) and in methanol (bp 65°) only trace conversion of **3** to **4** was noted after 30 min; in CH_3CN (bp 81°) and in ethylene chloride (bp 83°) maximum intensity was noted after 5 min (no **3** detectable by TLC); and in dioxane (bp 102°) maximum intensity was noted after 1 min (no **3** detectable by TLC).

C. At Its Melting Point. A 5-ml beaker containing 100 mg of **3** was slowly increased in temperature on a hot stage. Samples (~1 mg) were removed at 60, 80, 100, and 120° and were tested for the presence of thiocyanate ion with 5% $FeCl_3$ solution, all giving negative results. At 135–140°, the sample melted and was completely converted to **4** as indicated by ir, TLC, and a positive $FeCl_3$ test.

1-(*N*-Benzoylthiocarbamoyl)pyrrolidine (7). To 1.00 g (6.13 mmol) of **2** in 5 ml of CH_3CN was added dropwise with cooling and stirring 0.88 g (12.4 mmol) of pyrrolidine. The mixture was stirred in an ice bath for 0.5 hr, filtered, and washed with CH_3CN. The colorless solid was collected and recrystallized from CH_3CN to give 0.48 g (34%) of 1-(*N*-benzoylthiocarbamoyl)pyrrolidine as colorless needles: mp 133–134°; ir 3100 (NH), 2960 (CH), 1642 (C=O), 1603, and 1530 cm^{-1}; NMR (DMSO-d_6) δ 1.93 (m, 4, 2 CCH_2), 3.67 (m, 5, 2 CH_2N + NH), 7.63 (m, 3, *o*- and *p*-ArH), and 8.00 (m, 2, *m*-ArH).

Anal. Calcd for $C_{12}H_{14}N_2OS$: C, 61.51; H, 6.02; N, 11.96; S, 13.68. Found: C, 61.55; H, 6.02; N, 12.06; S, 13.55).

As anticipated,[7] the compound failed to react with ammoniacal silver nitrate solution to give a black precipitate of silver sulfide and its *S*-methyl derivative did not release methyl mercaptan on attempted hot alkaline hydrolysis.

Registry No.—**1**, 1779-81-3; **2**, 532-55-8; **3**, 55103-06-5; **4**, 55103-07-6; **5**, 55103-08-7; **7**, 55103-09-8; **9**, 29146-60-9; **10**, 6558-36-7.

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(6) See the discussion in ref 4, pp 517–518. Also see chemical shift values quoted in ref 3 for compounds similar to **6**.
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(13) Infrared spectra were taken on a Beckman IR-5 spectrophotometer in KBr pellets unless otherwise indicated, and NMR spectra were determined on a Varian Associates T-60A spectrometer. Mass spectra were obtained at 70 eV and 290° on an LKB spectrometer. Uv spectra were taken on a Beckman DB-G recording spectrophotometer. Melting points were determined on a Fisher-Johns apparatus and are uncorrected.

Reduction of the 1,3-Dithiolium Cation with Hexacarbonylvanadate(1−)

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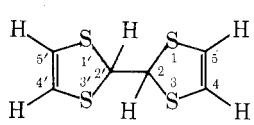
Contributions from the National Bureau of Standards (not subject to copyright) Inorganic Chemistry Section, National Bureau of Standards, Washington, D.C. 20234

Received April 4, 1975

While the reduction of 1,2-dithiolium cations has been extensively studied,[1-4] less information is available concerning the isomeric 1,3-dithiolium salts. An electrochemical reduction of the 2-thioethoxy-4,5-dithiomethoxy-1,3-dithiolium cation to the orthothiooxalate has been reported.[5] We wish to report a reductive coupling of the unsubstituted 1,3-dithiolium cation using sodium (bisdiglyme) hexacarbonylvanadate(1−) as the reducing agent. This is, to our knowledge, the first example of the use of $V(CO)_6^-$ as a reducing agent for organic compounds.

When solutions of 1,3-dithiolium hexafluorophosphate[6] and $Na(diglyme)_2V(CO)_6$ in acetone–tetrahydrofuran were mixed and the resulting solution diluted with water, white, crystalline 2,2′-bi(1,3-dithiolyl) (**1**) separated; the very air-sensitive $V(CO)_6$ was not isolated in this procedure.[7] The mass spectrum of **1** was characterized by strong M^+ and $M^+/2$ peaks. The 220-MHz ^1H NMR spectrum of **1** in acetone-d_6 consisted of two singlets at δ 4.73 and 6.20 in a 1:2 ratio. At 60 MHz, with a resolution better than 0.4 Hz, these signals showed unresolved fine structure.[8] Examination of the ^{13}C satellites in the ^1H NMR spectrum of **1** revealed $^3J_{H(4)H(5)} = 5.4 \pm 1$ Hz and $^3J_{H(2)H(2')} = 10.5 \pm 1$ Hz. The former value is similar to $^3J_{H(3)H(4)}$ in aromatic derivatives such as pyrrole and furan.[9] The latter coupling constant is larger than might be expected for vicinal protons but might be modified by the presence of the electronegative sulfur atoms or by a preference by **1** for a specific conformation. The ^{13}C NMR spectrum of **1** in carbon tetrachloride consisted of two doublets at 115.6 (J_{CH} = 184 Hz) and 60.3 ppm (J_{CH} = 160 Hz) [relative to internal $(CH_3)_4Si$] in a 2:1 intensity ratio.

The formation of **1** presumably proceeds through a one-electron reduction by $V(CO)_6^-$ of the 1,3-dithiolium cation to form the free radical **2**. Subsequent dimerization of **2** would then lead to **1**.



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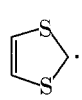

2

Experimental Section

A solution of 0.33 g (1.44 mmol) of $C_3H_3S_2^+PF_6^-$ in 10 ml of 1:1 acetone–tetrahydrofuran was added with stirring to 0.75 g (1.44 mmol) of $Na(C_6H_{14}O_3)_2V(CO)_6$[10,11] in 15 ml of the same solvent. The solution turned dark and a small amount of gas was evolved. The mixture was evaporated to ca. 5 ml on a rotary evaporator. Slow addition of water caused the product to separate as white flakes which were further purified by sublimation (90°, 10^{-3}mm). The yield was 0.09 g (59%), mp 150–151°. Anal. Calcd for $C_6H_6S_4$: C, 34.95; H, 2.91; S, 62.14. Found: C, 35.18; H, 3.04; S, 61.95. Ir (KBr) 3030 (w), 2950 (w), 1580 (w), 1525 (m), 1500 (w), 1245 (m), 1165 (s), 1075 (w), 855 (w), 780 (s), 730 (m), 695 (m), 435 (w), and 315 cm^{-1} (m); uv (C_2H_5OH) λ_{max} (log ϵ) 290 (3.23) and 309 nm (3.22); mass spectrum (70 eV) *m/e* (assignment, rel abundance) 208 ($^{12}C_6{}^1H_6{}^{32}S_3{}^{34}S$, 4.9), 206 ($M^+$, 27), 103 ($M^+/2$, 100), 45 ($HCS^+$, 25).

A mixture of 0.05 g of 2,2′-bi(1,3-dithiolyl), 0.1 g of active manganese dioxide, and 3 ml of acetonitrile was gently refluxed for 3 hr to give a yellow solution. Preparative thin layer chromatography (1:1 benzene–hexane, silica gel) afforded 0.013 g (26%) of tetrathiafulvalene, identified by its R_f and ultraviolet spectrum.

Acknowledgments. We are grateful to Dr. J. N. Lyerla and Mr. R. Bradley for obtaining the ^{13}C and ^1H satellite spectra and to Dr. A. Fatiadi for a sample of active manganese dioxide. One of us (A.R.S.) is grateful for a NRC Postdoctoral Research Associateship.

Registry No.—**1**, 51187-35-0; hexacarbonylvanadate(1−), 20644-87-5; 1,3-dithiolium cation, 288-75-5; 1,3-dithiolium hexafluorophosphate, 55298-73-2.