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2-Amino-2-thiazoline. VII.[1] Unequivocal Structure Assignment of the Products of the Reaction of 2-Amino-2-thiazoline and Its Analogs with Carbethoxy Isothiocyanate

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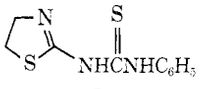
The reaction of 2-amino-2-thiazoline (**1**) with carbethoxy isothiocyanate (**3**) was found to give 2,3,6,7-tetrahydro-4*H*-thiazolo[3,2-*a*]-*s*-triazin-2-one-4-thione (**5**), the structure of which was confirmed by an X-ray crystallographic study. The reaction of **3** with 2-amino-5,6-dihydro-4*H*-1,3-thiazine (**15**), with 2-amino-4,4-dimethyl-2-thiazoline (**17**), and with 2-amino-2-selenazoline (**20**) also gave the analogous heterobicycles, 2,3,7,8-tetrahydro-4*H*,6*H*-thiazino[3,2-*a*]-*s*-triazin-2-one-4-thione (**16**), 2,3,6,7-tetrahydro-6,6-dimethyl-4*H*-thiazolo[3,2-*a*]-*s*-triazin-2-one-4-thione (**19**), and 2,3,6,7-tetrahydro-4*H*-selenazolo[3,2-*a*]-*s*-triazin-2-one-4-thione (**21**), respectively. The product **19** showed magnetic nonequivalence of the two methyl groups. Treatment of **5** with diazomethane gave two products, the result of both S- and N-methylation.

The differing nucleophilic character of the exocyclic and endocyclic nitrogen atoms of 2-amino-2-thiazoline (**1**) has been the subject of many studies. Reactions at the exocyclic nitrogen atom have been noted with nitrous acid,[2] acyl chlorides,[3] and cyanate ion,[4] whereas reactions with the endocyclic nitrogen have been reported in alkylations[2,5] and sulfonylations.[6] The condensation of **1** and isothiocyanates has been surrounded by some controversy. Fromm and Kapeller-Adler[7] reported that the reaction of **1** with phenyl isothiocyanate gave the product resulting from attack on the ring nitrogen when conducted at low temperature, but the exocyclic thiourea product at higher temperature. Klayman and coworkers,[8] who were able to isolate only a single monoadduct regardless of conditions, demonstrated by chemical and physicochemical means that the exocyclic nitrogen atom of **1** reacted with phenyl isothiocyanate, giving 1-(2-thiazolinyl)-3-phenyl-2-thiourea (**2**). Their work was confirmed by an X-ray crystallographic study.[9]



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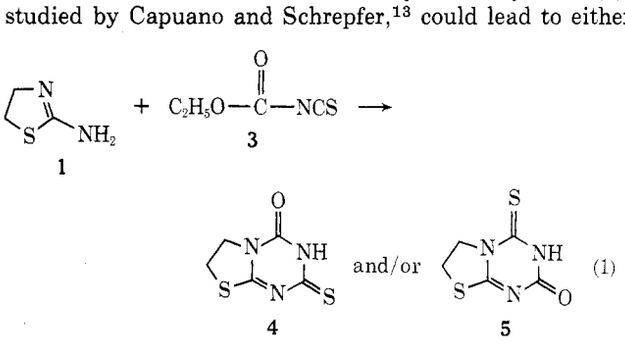
Carbethoxy isothiocyanate (**3**) is a useful reagent for the preparation of heterocyclic compounds through its reaction with amidines,[10] thiopseudoureas,[10] pseudoureas,[10] guanidines,[10] 2-aminopyridines,[11] 3-aminopyridazines,[12] 3-aminopyrazole,[13] 2-aminooxazoline,[13] 3-amino-1,2,4-triazoles,[13-15] 2-aminothiazoles,[16-18] enamines,[19] 2-amino-2-cyanoacetamide,[20] and 2-aminoacetonitrile.[21]

The reaction of **1** with carbethoxy isothiocyanate (**3**), studied by Capuano and Schrepfer,[13] could lead to either



1 **3** **4** **5**

(1)

or both of two possible products, **4** and **5** (eq 1). In fact, a single isomer is produced in the reaction, one to which Capuano and Schrepfer[13] assigned structure **4**; however, these workers presented no evidence for their structure assignment. The later work of Nagano, *et al.*,[16-18] indicated that 2-aminothiazole reacts with **3** to give, among other products, a heterobicycle resulting from attack of **3** on the endocyclic aromatic nitrogen atom. Extending the analogy to the case of **1**, the endocyclic attack could be favored, and structure **4**, proposed by the previous workers,[13] would thus be incorrect.

The present investigation was consequently undertaken to differentiate unequivocally between structures **4** and **5**,

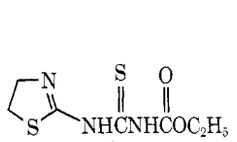
and to probe the steric and electronic requirements of the reaction of 1 with 3. Furthermore, the investigation included the study of the products of a previously reported methylation reaction, the structural assignments of which were suspect.

Results and Discussion

2-Amino-2-thiazoline (1). Two general procedures were employed to prepare the heterobicycles for study. The more convenient procedure (method A), based on that reported by Goerdeler and Neuffer[10] for the reaction of 3 with various acyclic ureas and their analogs, was to neutralize a hydrohalide salt of the starting material with aqueous sodium hydroxide, while a benzene solution of 3 was simultaneously added. In the second (method B), 3, generated *in situ,* was utilized in the reaction with the free base form of the starting thiazoline or related material.

The reaction of 2-amino-2-thiazoline (1) with 3 led to similar yields of the bicyclic product 4/5 by method A and method B. That the product was the same compound as that isolated by Capuano and Schrepfer[13] was shown by its elemental analysis and by the proximity of its melting point (281–283°) to that found by these earlier workers (275°).

The initial reaction of 1 with 3 could lead to two possible intermediates, 6 or 7. Steric considerations and the



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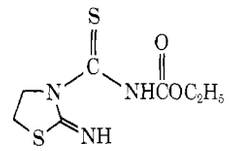
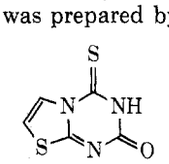


7

previously discussed indications that the isothiocyanate group preferentially attacks the exocyclic nitrogen atom of 1[8,9] would tend to favor the intermediate 6; however, in view of the duodirectional attack which 1 may undergo, 7 also could be the intermediate in the cyclization.

The ir spectrum of 4/5 was compared with those reported for 8 and 9, prepared by Nagano, *et al.*,[17a] which possess the same ring structure but with an additional C–C double bond in the five-membered ring. Compound 8 was formed directly on treatment of 2-aminothiazole with 3, and 9 was prepared by thermolysis of 1-(2-thiazolyl)-3-



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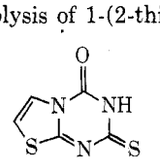

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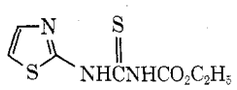
carbethoxy-2-thiourea (10, eq 2), which was also present in the reaction mixture. The structures of 8 and 9 were



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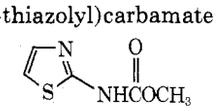
$$\xrightarrow{180\text{–}190^\circ} 9 \qquad (2)$$

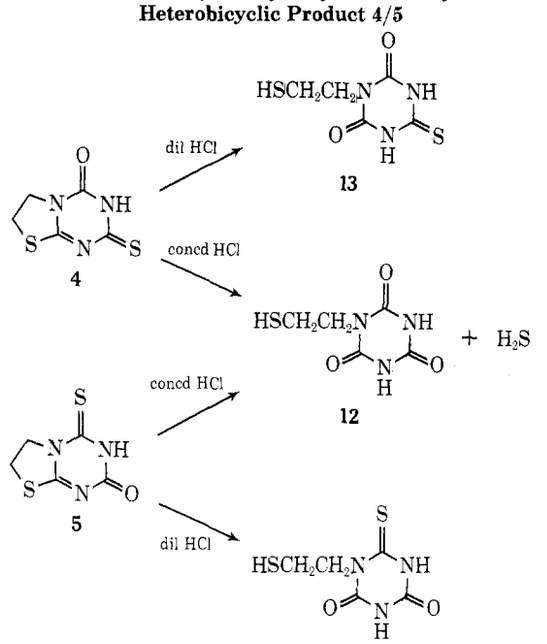
confirmed by conversion of 8 to the independently synthesized methyl *N*-(2-thiazolyl)carbamate (11) on treatment



11

with refluxing methanol, a process which would have given a thioncarbamate if the structure were 9; however, 4/5 was inert to these conditions. The spectrum of the model compound 8 shows an intense band at 1680 cm^{-1}, and that of 9 contains absorptions at 1755 and 1740 cm^{-1}.

Scheme I
Possible Acid-Catalyzed Hydrolytic Pathways for the Heterobicyclic Product 4/5



4 13 12 5 14

The ir spectrum of 4/5 shows, however, a strong carbonyl band at 1672 cm^{-1}. On this basis, compound 4/5 appears to be structured similarly to 8, which, in turn, is related to 5.

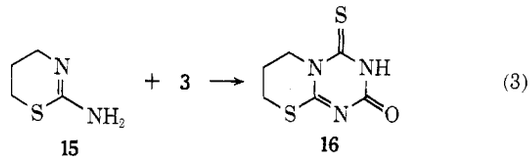
Klayman and Milne[1] have reported that the dihydrothiazolo ring of the 2,3,6,7-tetrahydro-4*H*-thiazolo[3,2-*a*]triazine system is labile to acid and opens to give a mercaptoethyltriazine compound. In concentrated acid, accompanying hydrolysis of the thiocarbonyl group of 4 or 5 would give 1-(2-mercaptoethyl)-1,2,3,4,5,6-hexahydro-*s*-triazine-2,4,6-trione (12, Scheme I). This experiment was conducted, and 12 was indeed obtained from the heterobicycle in high yield. The nmr spectrum of 12 showed the ring NH protons appearing at δ 11.55 in addition to complex upfield signals due to the mercaptoethyl side chain. An appropriate model for the magnetic environment of the NH protons of 12 could be provided by that of cyanuric acid, the nmr signal of which has been shown to appear at δ 11.1.[1]

Treatment of 4/5 with dilute acid opened the thiazoline ring but left the thiocarbonyl group intact (Scheme I). The ir spectrum of the product was similar to that of 12 except for the 1100–1300-cm^{-1} region, in which new bands, perhaps attributable to C=S stretching, appeared. Support for the correct *s*-triazine structure, 13 or 14, for this product could be provided by nmr spectrometry if exchange between the ring NH protons were slow on the nmr time scale. The spectrum of the hydrolyzed product showed, in addition to the upfield aliphatic region, a single broad absorption centered at δ 12.47. Thus the structure of the product could not be assigned, nor the structure of 4/5 inferred, by this technique, since the equivalent ring protons of 13 and exchange-averaged ring hydrogens of dissymmetric 14 would each appear as a single band.

Unequivocal evidence was provided by X-ray crystallography[22] that the structure of 4/5 is 2,3,6,7-tetrahydro-4*H*-thiazolo[3,2-*a*]-*s*-triazin-2-one-4-thione (5). The original structural assignment of Capuano and Schrepfer[13] is consequently shown to be incorrect. By extension of this finding, then, the structure of the product of the dilute acid-catalyzed hydrolysis of 5 is the unsymmetrical compound 1-(2-mercaptoethyl)-1,2,3,4,5,6-hexahydro-*s*-tria-

zine-4,6-dione-2-thione (14), the exchange between the ring protons of which must be too rapid to detect on the nmr time scale. The good agreement of the carbonyl stretching frequency of 5 with that of the analogous compound 8 indicates that such comparisons might be fruitful in diagnostic studies of structures of products of carbethoxy isothiocyanate (3) and bifunctional compounds in which the direction of attack may not be deduced *a priori*.

Other Analogs of 2-Amino-2-thiazoline. Treatment of 2-amino-5,6-dihydro-4*H*-1,3-thiazine (15) with carbethoxy isothiocyanate (3) gave the cyclized product 2,3,7,8-tetrahydro-4*H*,6*H*-thiazino[3,2-*a*]-*s*-triazin-2-one-4-thione (16) in 55 and 45% yields by methods A and B, respectively (eq 3). The relative positions of the carbonyl and thio-

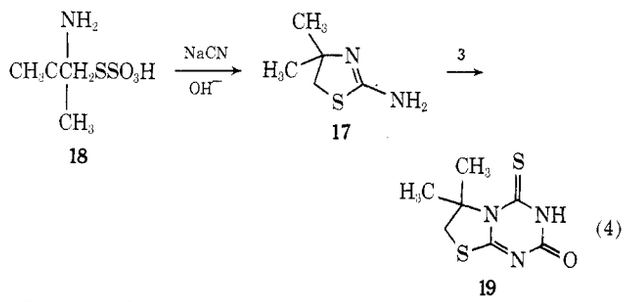


(3)

15 16

carbonyl groups of 16 and subsequently discussed analogs are assigned by analogy to 5 and by the similarity of their ir carbonyl stretching frequencies to that of 5. Whereas molecular models show the 2-amino-2-thiazoline ring to be essentially flat with only a slight pucker, the more flexible six-membered ring may assume a pseudo-chair or pseudo-boat conformation and their intermediate variations. In all of these conformations, the lone pair of electrons on the imino nitrogen atom, which must interact with the carbonyl carbon of the intermediate analogous to 7 to affect cyclization, is forced out of the quasi-plane of the SC=N moiety. This aspect of the ring system requires a more hindered arrangement of the atoms of the side chain than in the five-membered ring case; consequently, the cyclization step might be expected to be less favorable than in the case of 1; however, no significant difference in yield of 16 compared to that of 5 was obtained.

The steric effect of substitution in the 4 position of the thiazoline ring was investigated by beginning with 2-amino-4,4-dimethyl-2-thiazoline (17), prepared from 2-amino-2-methylpropanethiosulfuric acid (18) by treatment with alkaline sodium cyanide. Reaction of 17 with 3 gave the cyclized product 2,3,6,7-tetrahydro-6,6-dimethyl-4*H*-thiazolo[3,2-*a*]-*s*-triazin-2-one-4-thione (19) in 67% yield (method A) (eq 4), similar to the yield obtained from 1. The product 19 could not be obtained by the free base method (method B).



(4)

18 17 19

Compound 19 exhibits some interesting physical properties. For example, 19, obtained as tiny yellow needles, is the only colored compound of the series. The uv spectrum of 19 shows a 17-nm bathochromic shift of the 282-nm shoulder noted in the spectrum of 5, with formation of a new maximum at 299 nm. The electron-releasing effect of the large hydrocarbon portion at position 6 of 19 could raise the energy of its ground electronic state, causing a lower energy transition relative to that of 5. This considerable steric bulk could alternatively disrupt the energy levels of 19 relative to those of 5 by requiring hybridization changes. Separation of steric and electronic effects in these cases is tenuous at best. The most interesting physical property of 19, however, is the magnetic nonequivalence of the methyl groups in the 6 position. The two groups appear separated by 0.21 ppm at δ 1.67 and 1.88. A Fisher–Hirschfelder–Taylor molecular model of 19 (see Figure 1) shows that one methyl is held relatively rigidly in the diamagnetically anisotropic region of the thiocarbonyl group in position 4, whereas the other methyl group is below the plane formed by the two rings. Inversion of the dihydrothiazolo ring is sterically inhibited, and thus the magnetic environments of the two methyl groups are not averaged. This observed phenomenon provides a classic example of the diamagnetic anisotropy effect of the thiocarbonyl group, as has been noted in thioureas.[23]

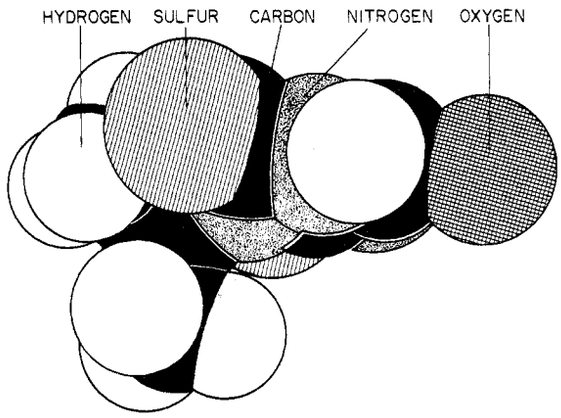
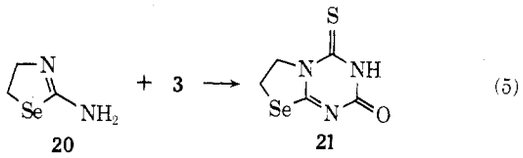


Figure 1. Fisher–Hirschfelder–Taylor model of 2,3,6,7-tetrahydro-6,6-dimethyl-4*H*-thiazolo[3,2-*a*]-*s*-triazin-2-one-4-thione (19).

Since the 8-oxygen analog of 5 had previously been prepared,[13] though by analogy with 5 the structure assignment was incorrect, it was decided to study the electronic effect of placing the next higher member of group 6a, selenium, into the starting material. Thus, 2-amino-2-selenazoline (20) was treated with 3 to give the product, 2,3,6,7-tetrahydro-4*H*-selenazolo[3,2-*a*]-*s*-triazin-2-one-4-thione (21), in 83 and 37% yields by methods A and B, respectively (eq 5), which indicated that the presence of the less electronegative selenium atom did not alter the reaction appreciably.



(5)

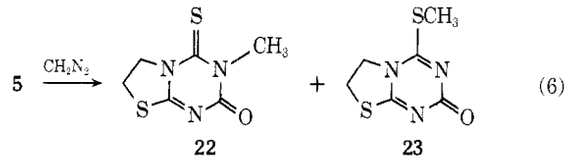
20 21

In conclusion, carbethoxy isothiocyanate (3) shows great promise in the preparation of heterocyclic compounds, the formation of which probably proceeds by a two-step dielectrophilic addition mechanism. The direction of attack of 3 on dinucleophiles may not be predicted with certainty, however, and structural assignments should be made circumspectly. The initial position of reaction may be influenced by steric and/or electronic factors; thus, further studies would be useful in developing diagnostic criteria for these reactions.

It appears that the physiological properties of carbethoxy isothiocyanate (3) have not been investigated. On exposure to the vapor of 3, three workers in this laboratory experienced its toxic effects, which included respiratory distress, headaches, and heart palpitations, the severity of which increased on repeated exposure. The reagent, therefore, should be handled with great caution in well-ventilated areas.

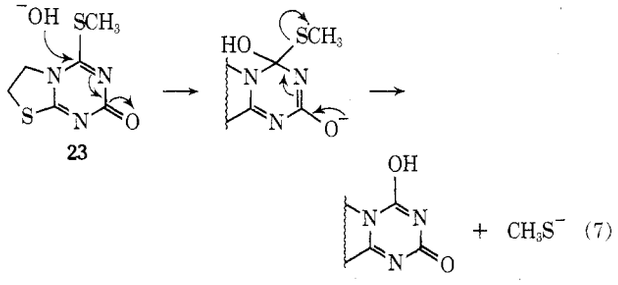
Reaction of 5 with Diazomethane. Capuano and

Schrepfer[13] treated **5** (believed by them to have structure **4**) with an excess of ethereal diazomethane and reported the isolation of solely the *N*-methyl product corresponding to **22**, mp 213°. When we repeated this reaction under the identical conditions, however, we obtained both the *N*-methyl (**22**, mp 149–150°) and the *S*-methyl (**23**, mp 218.5–219°) products (eq 6), which were separable by fractional crystallization. Thus, it appears that Capuano and Schrepfer not only failed to isolate the second product in the reaction, but also mistakenly assumed that N-methylation rather than S-methylation had occurred to give the 213° melting material.



22 23 (6)

The structures of **22** and **23** were assigned on the following bases. Compound **23** gives a strong nitroprusside test for thiol,[24] indicating displacement of methanethiolate ion from **23** (eq 7) under the strongly alkaline conditions of the test. No nitroprusside test was obtained from **22**, nor does the starting material **5** give such indication; consequently, production of thiol in strong base from **23** does not arise by opening of the dihydrothiazolo ring by hydroxide ion. Spectroscopic evidence also confirms the assignments. The carbonyl absorption in the ir spectrum of **23** appears at 1661 cm^{-1}, whereas that of **22** appears at 1701 cm^{-1}. It would be expected that the juxtaposition of the two carbon–nitrogen double bonds and the carbonyl of **23** would cause it to appear at lower frequency. The nmr spectrum of **23** shows a methyl absorption at δ 2.57, as opposed to a similar signal at δ 3.57 for **22**. The deshielding effects of the adjacent carbonyl and thiocarbonyl of **22** would cause the observed lower field signal in its spectrum. In addition, *N*-methyl signals generally appear at lower field than do *S*-methyl absorptions, though there is some overlap in the ranges.[25] The uv spectrum of **23** (λ_{max} 231 nm) is very different from that of **22** (λ_{max} 260 and 210 nm), which in turn is similar to that of the starting material **5** (λ_{max} 262 and 206 nm), as would be expected considering the analogous electronic structures of **5** and **22**. Finally, the base peak in the mass spectrum[26] of **23** appears at *m/e* 154, corresponding to a loss of 47 mass units (·SCH_3) from the molecular ion (*m/e* 201). No such peak appears in the spectrum of **22**. Thus, these data indicate that the compound isolated by Capuano and Schrepfer[13] was in fact **23**, and that the *N*-methyl isomer **22** was also produced in the reaction.



Experimental Section

Infrared spectra were determined on a Beckman IR-5 spectrophotometer in KBr pellets unless otherwise indicated. Nuclear magnetic resonance spectra were taken on a Varian Associates A-60 spectometer using TMS as the internal standard. Mass spectra were run on a Hewlett-Packard 5930 A mass spectometer, and ultraviolet spectra were taken on a Beckman DB-G recording spectrophotometer. Melting points were determined on a Kofler hot stage and are corrected. Microanalyses were performed by the analytical staff of the Stanford Research Institute, Menlo Park, Calif. 94025, and by Dr. Harry Agahigian of the Baron Consulting Company, Milford, Conn. 06477.

Reaction of Carbethoxy Isothiocyanate (3) with Amino Heterocycles. Method A. A procedure similar to that reported by Goerdeler and Neuffer[10] was employed. To a mixture of 10 mmol of the hydrohalide salt of the starting 2-amino heterocycle in 10 ml of water and 40 ml of benzene was added, simultaneously with vigorous stirring, 10 ml of a benzene solution of 1.8 g (14 mmol) of carbethoxy isothiocyanate (**3**)[10,27] and 10 ml of 1 *N* NaOH over 15 min. An additional 10 ml of 1 *N* NaOH was then added, and stirring was continued for 1 hr. The aqueous layer was separated; the benzene solution was extracted with 10 ml of 1 *N* NaOH, and the combined aqueous extracts were made acidic with 6 *N* H_2SO_4. The precipitated product was collected, washed with water, and recrystallized from aqueous DMF.

Method B. Ethyl chloroformate (4.34 g, 40 mmol) and 4.1 g (42 mmol) of potassium thiocyanate in 100 ml of acetone were heated on a steam bath for 15 min, and the precipitated KCl was removed by filtration through Celite. To the filtrate was added a solution of 10 mmol of the free base form of the starting heterocycle in 200 ml of CH_2Cl_2, and the resulting mixture was heated for 0.5 hr. The precipitated product was collected, and the filtrate was concentrated to give a second crop. The combined batches were washed with water to remove unreacted KSCN and recrystallized from aqueous DMF.

2,3,6,7-Tetrahydro-4*H*-thiazolo[3,2-*a*]-*s*-triazin-2-one-4-thione (5). Compound **5** was prepared from 2-amino-2-thiazoline (**1**) in 65 (method A) and 70% yields (method B) and was obtained as colorless plates: mp 281–283° (lit.[13,28] mp 275°); ir (KBr) 3040 (NH), 2900 (CH), 1672 (C=O), and 1540 cm^{-1} (NH); nmr (DMSO-d_6) δ 3.57 and 4.63 (m, A_2B_2, 4, SCH_2CH_2N), and 12.78 (broad s, 1, NH); uv (C_2H_5OH) 282 nm (sh, ϵ 10,400), 262 (max, 14,900), 245 (sh, 12,000), and 206 (max, 11,500); mass spectrum (70 eV) *m/e* (rel intensity) 187 (100), 128 (76), 86 (22), 82 (16), 60 (63), 59 (26), and 58 (13).

Anal. Calcd for $C_5H_5N_3OS_2$: C, 32.07; H, 2.69; N, 22.44; S, 34.25. Found: C, 32.19; H, 2.94; N, 22.47; S, 34.45.

A suspension of 1.87 g (10.0 mmol) of **5** in 100 ml of CH_3OH was heated under reflux for 18 hr. The undissolved solid was collected and dried to give 1.74 g (93% recovery) of **5**, mp 278–280°; ir (KBr) identical with that of **5**.

2,3,7,8-Tetrahydro-4*H*,6*H*-thiazino[3,2-*a*]-*s*-triazin-2-one-4-thione (16). Compound **16** was prepared from 2-amino-5,6-dihydro-4*H*-1,3-thiazine (**15**) hydrochloride[29] in 55 (method A) and 45% yield (method B) as colorless needles: mp 247–249°; ir (KBr) 3040 (NH), 2890 (CH), 1661 (C=O), and 1520 cm^{-1} (NH); nmr (DMSO-d_6) δ 2.29 (m, 2, CCH_2C), 3.30 (t, J = 6 Hz, 2, CH_2CH_2S), 4.38 (t, J = 5.5 Hz, 2, CH_2CH_2N), and 12.72 (broad s, 1, NH); uv (C_2H_5OH) 290 nm (sh, ϵ 8670), 270 (max, 19,900), 239 (sh, 12,100), and 206 (max, 15,200); mass spectrum (70 eV) *m/e* (rel intensity) 201 (48), 142 (100), 127 (13), 114 (81), 86 (57), 74 (11), and 59 (19).

Anal. Calcd for $C_6H_7N_3OS_2$: C, 35.81; H, 3.51; N, 20.88; S, 31.86. Found: C, 35.70; H, 3.60; N, 20.89; S, 31.66.

4,4-Dimethyl-2-amino-2-thiazoline (17). Using the procedure developed by Klayman and Milne,[28] a solution of 25.0 g (0.135 mol) of 2-amino-2-methylpropanethiosulfuric acid (**18**),[30] 5.6 g (0.14 mol) of NaOH, and 8.33 g (0.17 mol) of NaCN in 200 ml of water was stirred at room temperature for 16 hr. The solvent was removed under reduced pressure, and the residue was triturated with four 50-ml portions of $CHCl_3$. Evaporation of the dried $CHCl_3$ extracts gave a yellowish oil which crystallized on cooling. Trituration and recrystallization of the material from hexane gave 14.6 g (83%) of **17** as large prisms: mp 74–74.5°; ir (KBr) 3460 (NH_2), 2950 (CH), 1660 (C=N), 1590 (NH_2), and 1445 cm^{-1} (CH); nmr ($CDCl_3$) δ 1.32 (s, 6, 2 CH_3), 3.16 (s, 2, CH_2S), and 5.68 (s, 2, NH_2).

Anal. Calcd for $C_5H_{10}N_2S$: C, 46.12; H, 7.74; N, 21.51; S, 24.62. Found: C, 46.31; H, 7.81; N, 21.54; S, 24.80.

2,3,6,7-Tetrahydro-6,6-dimethyl-4*H*-thiazolo[3,2-*a*]-*s*-triazin-2-one-4-thione (19). Compound **19** was prepared by method A from 4,4-dimethyl-2-amino-2-thiazoline (**17**) in 67% yield as tiny yellow needles: mp 192–193°; ir (KBr) 3100 (NH), 2920 (CH), 1695 (C=O), and 1545 cm^{-1} (NH); nmr (DMSO-d_6) δ 1.67 (s, 3, CH_3), 1.88 (s, 3, CH_3), 3.48 (s, 2, CH_2S), and 12.67 (broad s, 1, NH); uv (C_2H_5OH) 299 nm (max, ϵ 10,100), 262 (max, 13,300), and 205 (max, 13,000); mass spectrum (70 eV) *m/e* (rel intensity) 215 (98), 200 (25), 156 (31), 141 (100), 88 (19), 86 (29), 73 (19), and 55 (23).

Anal. Calcd for $C_7H_9N_3OS_2$: C, 39.05; H, 4.21; N, 19.52; S, 29.79. Found: C, 38.82; H, 4.27; N, 19.58; S, 29.70.

2,3,6,7-Tetrahydro-4*H*-selenazolo[3,2-*a*]-*s*-triazin-2-one-4-thione (21). Compound **21** was prepared from 2-amino-2-selenazoline (**20**) hydrobromide[31] in 83 (method A) and 37% yield (method B) as colorless needles: mp 255–258° dec; ir (KBr) 3060 (NH), 2910 (CH), 1675 (C=O), and 1535 cm^{-1} (NH); nmr (DMSO-d_6) δ 3.56 and 4.71 (m, A_2B_2, 4, SCH_2CH_2N) and 12.33 (broad s, 1, NH); uv (C_2H_5OH) 277 nm (max, ϵ 19,500), 251 (sh, 11,700), and 206 (max, 14,400); mass spectrum (70 eV) *m/e* (rel intensity) 237 (17), 236 (11), 235 (63), 234 (12), 233 (34), 232 (15), 231 (17), 178 (12), 176 (44), 175 (12), 174 (25), 173 (15), 172 (14), 110 (23), 109 (12), 108 (100), 107 (28), 106 (57), 105 (30), and 104 (29).

Anal. Calcd for $C_5H_5N_3OSSe$: C, 25.65; H, 2.15; N, 17.95, S, 13.69; Se, 33.72. Found: C, 25.97; H, 2.34; N, 18.26; S, 13.84; Se, 33.4.

Acid-Catalyzed Hydrolysis of 5. A stirred suspension of 2.00 g (10.7 mmol) of **5** in 100 ml of 18% HCl was heated under reflux under an argon atmosphere for 6.5 hr, during which time considerable H_2S evolution was detected with lead(II) acetate paper. Cooling gave, on filtration, 1.53 g of analytically pure 1-(2-mercaptoethyl)-1,2,3,4,5,6-hexanhydro-*s*-triazine-2,4,6-trione (**12**). Evaporation of the filtrate and addition of 5 ml of H_2O gave an additional 0.37 g for a total yield of 94% of **12**: mp 256–258°; ir (KBr) 3100 (NH), 2760 (CH), 2551 (SH), 1727 and 1684 (C=O), and 1460 cm^{-1} (NH); nmr (DMSO-d_6) δ 2.64 (m, 3, CH_2S + SH), 3.90 (m, 2, CH_2N), and 11.55 (s, 2, 2 NH).

Anal. Calcd for $C_5H_7N_3O_3S$: C, 31.74; H, 3.73; N, 22.21; S, 16.95; SH, 17.48. Found: C, 31.68; H, 3.85; N, 22.07; S, 16.64; SH, 17.4.

Dilute Acid Hydrolysis of 5. A stirred suspension of 0.50 g (2.67 mmol) of **5** in 78 ml of 0.46 *N* HCl was heated under reflux for 20 min under an argon atmosphere, whereupon traces of H_2S evolution could be detected with lead(II) acetate paper. The reaction flask was immediately immersed in an ice bath, causing 0.485 g (89%) of 1-(2-mercaptoethyl)-1,2,3,4,5,6-hexahydro-*s*-triazine-4,6-dione-2-thione (**14**) to crystallize as fine needles: mp 172–174°; ir (KBr) 3110 (NH), 2750 (CH), 2551 (SH), 1748 and 1715 (C=O), 1485 (NH), 1255, 1215, 1165, and 1153 cm^{-1} (NH, C=O, and C=S combination bands); nmr (DMSO-d_6) δ 2.81 (m, 3, CH_2S + SH), 4.46 (m, 2, CH_2N), and 12.47 (broad s, 2, 2 NH).

Anal. Calcd for $C_5H_7N_3O_2S_2$: C, 29.25; H, 3.44; N, 20.47; S, 31.34; SH, 16.11. Found: C, 29.42; H, 3.42; N, 20.39; S, 31.06; SH, 16.6.

Treatment of 5 with Diazomethane. The experiment was conducted by repeating the conditions of Capuano and Schrepfer[13] as follows. To approximately 250 ml of an ethereal solution of diazomethane generated from 7.5 g of Diazald (Aldrich) was added 1.5 g (8.0 mmol) of **5** moistened with 1 ml of CH_3OH. The mixture was stirred for 26 hr in a loosely corked flask, and the solid phase (1.10 g, 69%), mp 150–211°, was collected. Concentrating the filtrate gave an additional 0.20 g, bringing the total yield of methylated product to 81%. An nmr spectrum of the crude mixture (DMSO-d_6) indicated the presence of both NCH_3 and SCH_3 isomers (approximate ratio NCH_3:SCH_3 = 3:2). Three recrystallizations of the mixture from CH_3CN gave colorless needles of 6,7-dihydro-4-methylthio-2*H*-thiazolo[3,2-*a*]-*s*-triazin-2-one (**23**), which gave a strong nitroprusside test: mp 218.5–219° (lit.[32] mp 213°); ir (KBr) 2990 (CH), 1661 (C=O), 1580 (C=N), and 1460 cm^{-1} (CH); nmr (DMSO-d_6) δ 2.57 (s, 3, SCH_3), 3.57 and 4.39 (m, A_2B_2, 4, SCH_2CH_2N); uv (C_2H_5OH) 236 nm (sh, ϵ 21,000) and 231 (max, 21,100); mass spectrum (70 eV) *m/e* (rel intensity) 201 (29), 154 (100), 128 (87), 94 (36), 86 (86), 69 (12), 60 (85), 59 (31), 58 (16), 47 (13), 46 (18), 45 (34), and 44 (11).

Anal. Calcd for $C_6H_7N_3OS_2$: C, 35.81; H, 3.51; N, 20.88; S, 31.86. Found: C, 35.81; H, 3.85; N, 20.96; S, 32.07.

The colorless solid isolated by evaporation of the first CH_3CN filtrate was recrystallized three times from CH_3OH to give very fine, colorless needles of 2,3,6,7-tetrahydro-3-methyl-4*H*-thiazolo-[3,2-*a*]-*s*-triazin-2-one-4-thione (**22**), which gave a negative nitroprusside test: mp 149–150°; ir (KBr) 2980 (CH), 1701 (C=O), 1580 (C=N), and 1455 cm^{-1} (CH); nmr (DMSO-d_6) δ 3.57 (s, 3, NCH_3), 3.62 and 4.68 (m, A_2B_2, 4, SCH_2CH_2N); uv (C_2H_5OH) 271 nm (sh, ϵ 14,600), 260 (max, 19,800), and 210 (max, 14,000); mass spectrum (70 eV) *m/e* (rel intensity) 201 (55), 129 (17), 128 (48), 86 (21), 74 (13), 73 (19), 72 (15), 60 (100), 59 (21), 58 (11), 45 (23), 28 (17), and 27 (12).

Anal. Calcd for $C_6H_7N_3OS_2$: C, 35.81; H, 3.51; N, 20.88; S, 31.86. Found: C, 35.92; H, 3.79; N, 20.89; S, 31.87.

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Registry No.—**1**, 1779-81-3; **3**, 16182-04-0; **5**, 51270-92-9; **12**, 51270-93-0; **14**, 51270-94-1; **15** hydrochloride, 2799-74-8; **16**, 51270-95-2; **17**, 51270-96-3; **18**, 4039-24-1; **19**, 51270-97-4; **20** hydrobromide, 2697-62-3; **21**, 51270-98-5.

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