

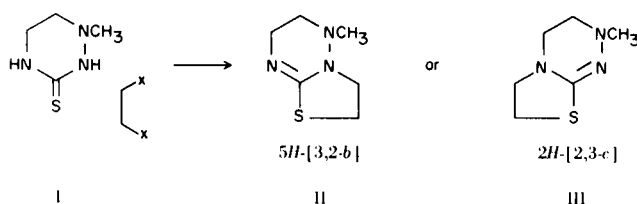
5*H*-Thiazolo[3,2-*b*]- and 2*H*-Thiazolo[2,3-*c*]-*as*-triazines

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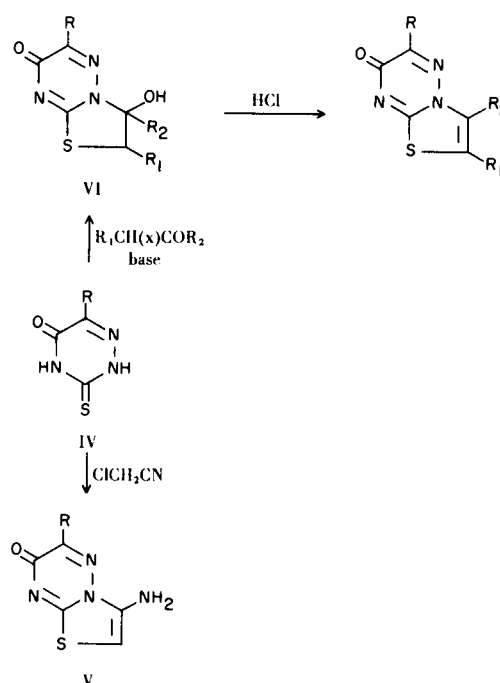
Derivatives of the 5*H*-thiazolo[3,2-*b*]- and 2*H*-thiazolo[2,3-*c*]-*as*-triazine systems were synthesized *via* condensation of tetrahydro-1-methyl-*as*-triazine-3(2*H*)-thione with ethylene dibromide and ethyl bromoacetate, respectively. An hypothesis is given for the formation of the [3,2-*b*] system in one of these reactions and the [2,3-*c*] system in the other. Structure proof was accomplished by an unequivocal synthesis of one of the [2,3-*c*] derivatives.

We are interested in the reactions of tetrahydro-1-methyl-*as*-triazine-3(2*H*)-thione (I) with various 1,2-disubstituted ethanes in which the substituents are fairly good leaving groups because hypothetically these condensations can give either a 5*H*-thiazolo[3,2-*b*]-*as*-triazine (II) or a 2*H*-thiazolo[2,3-*c*]-*as*-triazine (III) and neither of these systems has been reported.

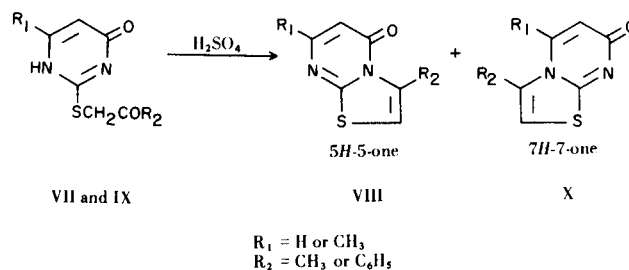


Results reported for similar condensations that yielded related condensed systems illustrate the variability in the direction of cyclization which can occur in these reactions. For example, Doleschall *et al.* reported (1) that the condensation of triazinonethione IV with chloroacetonitrile and with various α -haloketones yielded 7*H*-thiazolo[3,2-*b*]-triazin-7-ones (V and VI).

Andrew and Bradsher reported (2) that sulfuric acid cyclodehydration of *S*-acetyl- or phenacyl-5-methyl-2-thiouracil (VII) gave rise to 5*H*-thiazolo[3,2-*a*]pyrimidin-5-ones (VIII) in high yield (93 and 94%) and that under the same conditions cyclodehydration of *S*-acetyl- (or phenacyl)-2-thiouracil (IX) gave an 86% yield of the 7*H*-7-one isomer (X) in the case of the phenacyl sulfide

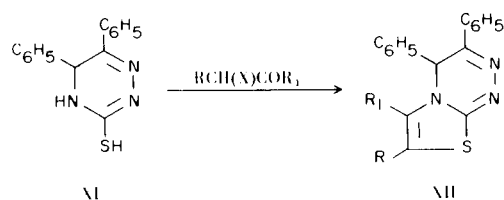


whereas the acetonil sulfide gave a mixture of 5*H*-5-one (19% yield) and 7*H*-7-one isomers (70% yield). Andrew

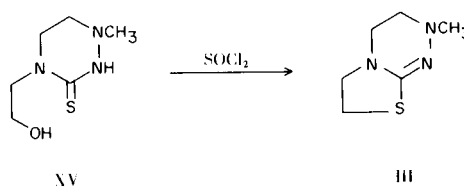
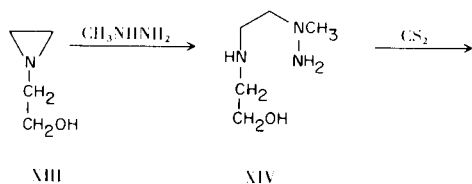


and Bradsher explained that the change in direction of cyclization caused by the introduction of a methyl group at position 6 of the pyrimidinone is probably due to steric repulsions between that methyl and the alkyl or aryl moiety of the ketosulfide chain that would occur if cyclization took place at N₁.

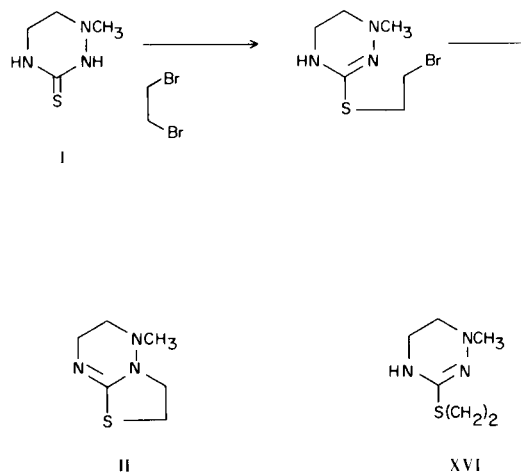
In contrast to the preceding results it has been reported (3) that mercaptodiphenyl-*as*-triazine XI reacted with α -haloketones in refluxing acetic acid or ethanol to give 4*H*-thiazolo[2,3-*c*]-*as*-triazines (XII).



For our study we chose as a point of departure one of the simplest examples, the condensation of tetrahydro-1-methyl-*as*-triazine-3(2*H*)-thione (I) with ethylene dibromide. However, prior to carrying out this condensation, the 2*H*-[2,3-*c*] system was synthesized by an unequivocal method in order to have one of the structural isomers on hand to compare with our condensation product or products. The unequivocal synthesis of 2-methyl-3,4,6,7-tetrahydro-2*H*-thiazolo[2,3-*c*]-*as*-triazine (III) was accomplished in the following manner: *N*-(β -hydroxyethyl)-aziridine (XIII) was added dropwise to stirred, refluxing methylhydrazine (10 mole excess) to which a catalytic amount of ammonium chloride had been added to give a 75% yield of 2-[(2-(1-methylhydrazino)ethyl)amino]ethanol (XIV). Hydrazinoethylaminoethanol (XIV) in refluxing 50% aqueous ethanol was treated with carbon disulfide to give a 45% yield of 1,4,5,6-tetrahydro-4-(2-hydroxyethyl)-1-methyl-*as*-triazine-3(2*H*)-thione (XV). Hydroxyethyltriazinethione (XV) in dimethylformamide was treated with thionyl chloride followed by basification to give a 79% yield of 2-methyl-3,4,6,7-tetrahydro-2*H*-thiazolo[2,3-*c*]-*as*-triazine (III).



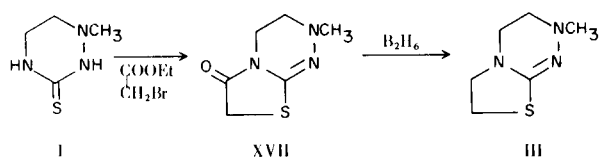
A priori we would expect that the condensation of triazinethione I with ethylene dibromide would also give thiazolotriazine isomer III because the preferred position of the double bond in tetrahydro-*as*-triazines is between N₂-C₃ rather than between C₃-N₄ (4). However, when one considers that this condensation most likely is a two-step process and that the initial displacement involves the thione sulfur to yield 3-(β -bromoethylthio)-1-methyl-1,4,5,6-tetrahydro-*as*-triazine followed by intramolecular displacement of bromide by either N₂ or N₄ one reaches the conclusion that the determining factor will be the comparable nucleophilicities of N₂ and N₄ in the 1,4,5,6-tetrahydro-*as*-triazine system. This being the case, because N₂ is a better nucleophile than N₄ for halide displacement at a quaternary carbon, the condensation should proceed in the following manner to give 5-methyl-3,4,6,7-tetrahydro-5*H*-thiazolo[3,2-*b*]-*as*-triazine (III).



When triazinethione I was allowed to react with ethylene dibromide in refluxing ethanol there was obtained two compounds separated by alumina chromatography and identified as thiazolotriazine (II) (20%) and 3,3'-(ethylenedithio)bis(1,4,5,6-tetrahydro-1-methyl-*as*-triazine) (XVI) (45%). Isolation of the ethylenedithio-bis-triazine compound indicates as suspected that the reaction is a two-step process and that the initial displacement is on sulfur followed by reaction at N₂ to give thiazolotriazine II. When the reaction was carried out in the presence of

sodium carbonate the yield of II was increased to 42% and no XVI was isolated. In neither experiment was the presence of II detected.

Tetrahydro-1-methyl-*as*-triazine-3(2*H*)-thione (I) was allowed to condense with ethyl bromoacetate in order to determine whether or not the direction of cyclization would be the same as with I and ethylene dibromide. The results of this experiment indicated that the cyclization occurred in the opposite direction to give 3,4-dihydro-2-methyl-2*H*-thiazolo[2,3-*c*]-*as*-triazin-6(7*H*)-one (XVII) (67%). The proof of structure of thiazolotriazinone XVII was accomplished by diborane reduction of XVII to the known thiazolotriazine (III) (83%).



The results of these two experiments indicate that when ring closure proceeds *via* S_N2 attack on a tetrahedral alkyl carbon, the direction of the ring closure depends upon the relative nucleophilicities of N_2 and N_4 in the triazine system. When ring closure proceeds *via* the comparatively stable tetrahedral carbon intermediate that is formed when N attacks trigonal carbonyl carbon, the direction depends upon the relative energies of intermediates XVIII and XIX. Intermediate XVIII is less energetic



than intermediate XIX because of overlap of the lone pair on N_1 with the π -system of the $C=N$. This conjugation is not possible in XIX.

The structurally isomeric thiazolotriazines II and III were subjected to infrared, ultraviolet, proton magnetic resonance, and mass spectral analysis in order to determine whether or not these methods could be used to differentiate structural isomers of this type. There is no ultraviolet absorbance between 220-400 $m\mu$, and no meaningful information was gleaned from the mass spectral fragmentations. The infrared spectra differed in the fingerprint region and the most intense peak in both spectra was the $C=N$ stretch. It was equally intense in both spectra and occurred at 1610 cm^{-1} so it could not be used to differentiate between the $C=N$ of II and the $C=N-N$ of III. The

pmr spectra of thiazolotriazine II and III are shown as Figure 1. The four pairs of methylene protons in each isomer have been designated based on comparisons of chemical shifts and couplings of methylene protons in related thiazolotriazines we have synthesized that contain similar but easily differentiated methylene protons. There is a significant difference in the position of the NCH_3 resonance of II and III. Whether or not the NCH_3 chemical shift is predictive of whether the compound is the 2*H*-[2,3-*c*] or the 5*H*-[3,2-*b*] isomer will require pmr analysis of additional isomeric pairs.

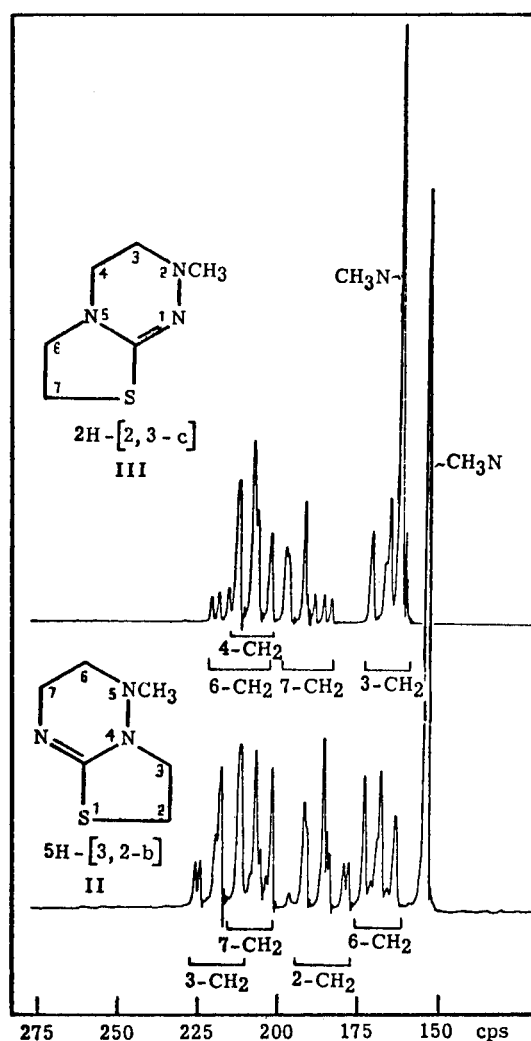


Figure 1. Pmr spectra of 10% solutions of 3,4,6,7-tetrahydro-2-methyl-2*H*-thiazolo[2,3-*c*]-*as*-triazine and 2,3,6,7-tetrahydro-5-methyl-5*H*-thiazolo[3,2-*b*]-*as*-triazine in deuteriochloroform with internal TMS at 0 cps.

Thiazolotriazines II and III were further characterized as their hydrobromides and methiodides. It is noteworthy that the pmr spectra of the methiodides of II and III show that the methyl group in each of the two methiodides that was introduced *via* the quaternization resonate at greatly different frequencies. Additional pmr spectra of other isomeric pairs may show that this, too, is significant for structure assignment.

This study will be continued in order to determine the results of reactions of tetrahydro-1-methyl-*as*-triazine-3(2*H*)-thione (I) with other 1,2-disubstituted ethanes.

EXPERIMENTAL

The melting points were obtained in an open capillary tube with the Thomas-Hoover Uni-Melt and are uncorrected. The elemental analyses were done by Midwest Microlabs., Inc., Indianapolis, Indiana. The pmr spectra were obtained at 60 Mc, with a Varian A-60 spectrometer. Infrared spectra were obtained with a Perkin-Elmer 337 grating spectrophotometer.

Tetrahydro-1-methyl-*as*-triazine-3(2*H*)-thione (I).

To a stirred, warm (55-60°) solution of 268 g. (3.0 moles) of 1-(β -aminoethyl)-1-methylhydrazine in 1,000 ml. of 50% ethanol was added, dropwise, over a period of 2 hours, 252 g. (3.3 moles) of carbon disulfide. A precipitate formed shortly after the addition of the carbon disulfide was completed. The mixture was stirred and heated at the reflux temperature for 2 hours, 25 ml. of concentrated hydrochloric acid was added dropwise, over a 20 minute period, and the stirring and heating was continued for an additional 1.5 hours. The solution was allowed to stand overnight at room temperature and then was suction filtered to give 290 g. (73%) of white crystals, m.p. 188-191° dec. Analytical recrystallization twice from methanol gave white crystals, m.p. 193° dec.; λ max (nujol) 3.15 (s), 8.18 (s), and 8.35 μ (s).

Anal. Calcd. for C₄H₉N₃S: C, 36.62; H, 6.91; S, 24.44. Found: C, 36.90; H, 7.28; S, 24.33.

2,3,6,7-Tetrahydro-5-methyl-5*H*-thiazolo[3,2-*b*]-*as*-triazine (II).

To a stirred mixture of 26 g. (0.2 mole) of thione I and 22 g. (0.21 mole) of sodium carbonate in 750 ml. of refluxing methanol was added 38 g. (0.2 mole) of 1,2-dibromoethane in 250 ml. of methanol during a 10 minute period. The mixture was allowed to stir and reflux for 88 hours. The reaction mixture was concentrated *in vacuo* to give a solid and oily residue which was taken up in chloroform and water. The phases were separated and the chloroform phase was washed with dilute sodium carbonate solution; the combined chloroform extracts were washed with water, brine and then dried over magnesium sulfate and concentrated *in vacuo* to give 28.5 g. of red-brown liquid, λ max (film) 3.1 (m, broad), 6.2 μ (v.s.); glc. (145-250° at 15°/min, 5 ft, 4% SE52/-chromasorb W/AW) showed one major (90%) component at about 3.8 minutes. Column chromatography of 1 g. of this oil on a 1.5 x 13 cm column of 25 g. of alumina [Baker 0537] failed to give a fraction whose infrared spectrum showed no 2.9-3.1 μ absorption. Distillation of the remaining red-brown liquid gave 13 g. (42%) of green-yellow liquid, b.p. 142-144° (1.7-2.5 mm), which was redistilled to give 13 g. of light green-yellow liquid, b.p. 140° (1.1 mm) -144° (3 mm); analytical sample boiled at 142° (1.2 mm); λ max (carbon tetrachloride) 3.2 (v.w.) and 6.2 μ (v.s.); nmr see Fig. 1.

Anal. Calcd. for C₆H₁₁N₃S: C, 45.83; H, 7.05; N, 26.72. Found: C, 45.53; H, 7.42; N, 26.35.

The hydrobromide of thiazolotriazine II (3.5 g.) prepared in ether and recrystallized from isopropyl alcohol-ether gave 4.7 g. (89%) of white crystals, m.p. 203-205°. Analytical recrystallization from methanol-ether gave white crystals, m.p. 204-205°; λ max (nujol) 3.15 (w), 3.22 (w), gradual increase in transmittance to 4 μ , and 6.15 μ (v.s.); nmr (deuterium oxide): δ 2.77 (NCH₃), 3.17-4.3 (complex multiplet) ppm.

Anal. Calcd. for C₆H₁₁N₃S·HBr: C, 30.26; H, 5.08; Br, 33.56; N, 17.64. Found: C, 30.54; H, 5.37; Br, 33.75; N, 17.23.

The methiodide of thiazolotriazine II (3.0 g.) prepared in ether gave 5.5 g. of tan and white crystals, m.p. 130-140°, which were recrystallized from isopropyl alcohol-ether to give 4.5 g. (76%) of faint tan crystals, m.p. 153-154.5°. Analytical recrystallization from isopropyl alcohol gave white, flaky crystals, m.p. 153-154.5°; λ max (nujol) 6.15 μ (s); nmr (deuterium oxide): δ 2.74 (NCH₃), 3.30 (NCH₃), [3.38, 3.47, 3.53, 3.6, 3.7 (3-4 protons)], [4.08, 4.22 and 4.35 (about 2 protons)], and 4.6 (about one-half proton).

Anal. Calcd. for C₇H₁₄IN₃S: C, 28.10; H, 4.71; I, 42.41; N, 14.04. Found: C, 28.07; H, 4.96; I, 42.77; N, 13.94.

3,4,6,7-Tetrahydro-2-methyl-2*H*-thiazolo[2,3-*c*]-*as*-triazine (III).

A solution of 44 g. (0.25 mole) of thione XV in 125 ml. of dimethylformamide was added dropwise to 290 g. (2.45 moles) of thionyl chloride at 25 \pm 2°. During the initial addition of thione XV to thionyl chloride, the temperature had been allowed to rise to 35° but the reaction seemed to darken more rapidly at 35° than at the lower temperature. The reaction solution was allowed to stir for an additional 30 minutes and then was poured into 1.5 l. of ether. The mixture was stirred vigorously and the ether was decanted from the red, heavy oil. Cautious addition of some isopropyl alcohol showed that a considerable amount of thionyl chloride was present in the red oil. It would be advisable to remove the excess thionyl chloride *in vacuo* at room temperature. The red oil was poured cautiously into a mixture of ice and excess solid sodium carbonate and the solution was extracted with four portions of chloroform. The combined extracts were dried over magnesium sulfate and concentrated *in vacuo* at 55° to give 59 g. of a dark oil which was azeotroped with tetrachloroethylene at 60° to give 43 g. of a dark oil. Distillation of this oil gave a fore-run of 8 g. of colorless liquid, b.p. 149° (0.3 mm) 153° (1 mm); analytical sample boiled at 152° (0.4 mm) and solidified to give white crystals that melted at 50.5-51.5°; infrared spectrum showed absence of OH and NH and λ max (film) 6.2 μ (s) (C=N); nmr, see Fig. 1.

Anal. Calcd. for C₆H₁₁N₃S: C, 45.83; H, 7.05; N, 26.72. Found: C, 46.29; H, 7.37; N, 26.41.

The hydrobromide of thiazolotriazine III (5.0 g.) prepared in ether and recrystallized from methanol-ether gave 7 g. (92%) of white crystals, m.p. 139-144°. Two additional recrystallizations gave white crystals, m.p. 141-142°; λ max (nujol) 4.0 (s, center of a broad multiplicity of absorptions), and 6.33 μ (v.s.); nmr (deuterium oxide): δ , 2.87 (NCH₃), and 3.27-4.23 (complex multiplets) ppm.

Anal. Calcd. for C₆H₁₁N₃S·HBr: C, 30.25; H, 5.07; Br, 33.55; N, 17.64. Found: C, 30.61; H, 5.38; Br, 33.44; N, 17.61.

The methiodide of thiazolotriazine III (3.0 g.) prepared in ether gave 5.9 g. (100%) of white crystals, m.p. 229-230.5°. Recrystallization from methanol gave white needles, m.p. 230.5-232°; λ max (nujol) 6.25 μ (v.s.); nmr (deuterium oxide): δ , 3.37 (NCH₃ and part of 3.42 (m)), 3.85 (NCH₃ and part of 3.9 (m)), and 4.55 (trace) ppm.

Anal. Calcd. for $C_7H_{14}IN_3S$: C, 28.10; H, 4.71; I, 42.42; N, 14.04. Found: C, 27.87; H, 4.88; I, 42.77; N, 14.02.

2-[(2-(1-Methylhydrazino)ethyl)amino]ethanol (XIV).

1-(2-Hydroxyethyl)aziridine (XIII), 412 g. (4.74 moles), was added dropwise over a 2.5 hour period to stirred, refluxing methylhydrazine, 1800 g. (39 moles), which contained 2 g. of ammonium chloride. The solution was allowed to stir and reflux overnight. The excess methylhydrazine was recovered by distillation and the remaining liquid was distilled to give 528 g. (84%) of a colorless liquid, b.p. 152° (17 mm); λ max (carbon tetrachloride) 3.04-3.17 (s, broad), 6.33 (m), and 9.4μ (v.s.); nmr (deuteriochloroform): δ , 2.45 (NCH₃), 2.6-2.8 (m), and 3.5-3.7 (m) ppm.

Anal. Calcd. for $C_5H_{15}N_3O$: C, 45.08; H, 11.35; N, 31.55. Found: C, 44.89; H, 11.69; N, 30.96.

1,4,5,6-Tetrahydro-4-(2-hydroxyethyl)-1-methyl-*as*-triazine-3(2*H*)-thione (XV).

A solution of 133 g. (1 mole) of 2-[(2-(1-methylhydrazino)ethyl)amino] ethanol (XIV) in 600 ml. of 50% aqueous ethanol was warmed to a gentle reflux, then 83.5 g. (1.1 moles) carbon disulfide was added during a one-hour period, near the end of which time a precipitate was formed in the yellow-green solution. The mixture was allowed to reflux for an additional 2 hours and then 12 ml. of concentrated hydrochloric acid was added dropwise and the solution allowed to reflux another 2 hours. A yellow solid, 2 g., was filtered and discarded; the filtrate was refrigerated over the weekend and subsequent filtration gave 34 g. (19%) of white crystals, m.p. $107-109.5^\circ$. Concentration of the filtrate afforded an additional 61 g. of light yellow solid, m.p. $97-101^\circ$, which was recrystallized from isopropyl alcohol to give 45 g. (26%) of white crystals, m.p. $108.5-110^\circ$.

Analytical recrystallization from isopropyl alcohol gave white crystals, m.p. $109-110.5^\circ$; infrared spectrum showed the absence of 6.2μ (C=N) and λ max (nujol) 3.1μ (v.s.); nmr (deuteriochloroform): δ , 2.68 (NCH₃), 3.2 (m), 3.5 (m), and 4.1 ppm.

Anal. Calcd. for $C_6H_{13}N_3OS$: C, 41.12; H, 7.47; N, 23.97; S, 18.29. Found: C, 41.35; H, 7.97; N, 23.75; S, 18.23.

3,3'-(Ethylenedithio)bis(1,4,5,6-tetrahydro-1-methyl-*as*-triazine) (XVI).

1,2-Dibromoethane, 28.5 g. (0.15 mole), in 100 ml. of methanol was added dropwise during a 4-5 hour period to a stirred suspension of 20.5 g. (0.15 mole) of thione I in 150 ml. of gently refluxing methanol. The resultant solution was allowed to reflux very gently for 2 days and then was added dropwise in 45 minutes to a stirred, gently refluxing solution of 16 g. (0.4 mole) of sodium hydroxide in 150 ml. of 30% aqueous methanol. The mixture was stirred for an additional hour and then was concentrated *in vacuo* to give a tan oil and solid mixture which was taken up in 100 ml. of water and extracted with chloroform (4 x 100 ml.). The combined chloroform extracts were washed with brine (2 x 75 ml.), dried over magnesium sulfate and concentrated *in vacuo* to give 18 g. of light orange oil, λ max (film) 3.1 (m.s., broad) and 6.3μ (v.s.). This oil was chromatographed on a 5 x 32 cm column of 550 g. of alumina [Baker 0537]. Elution with chloroform gave 5.0 g. (20.3%) of thiazolotriazine II, identified by its infrared spectrum. Continued elution with chloroform and 0.5-5% methanol in chloroform gave 10 g. (45%) of 3,3'-(ethylenedithio)bis(1,4,5,6-tetrahydro-1-methyl-*as*-triazine) (XVI) as an oil that solidified when triturated with ether and melted at $115-125^\circ$.

Analytical recrystallization from ethyl acetate gave off-white crystals, m.p. $131-132.5^\circ$, λ max (nujol) 2.98 (v.s.; broad trailing) and 6.25μ (v.s.); nmr (deuteriochloroform): δ , 2.72 (NCH₃), 3.77 (t, J = 5 cps), 3.17 (SCH₂CH₂S), 3.43-3.63 (m), and 5.1 (NH).

Anal. Calcd. for $C_{10}H_{20}N_6S_2$: C, 41.64; H, 6.99; N, 29.14. Found: C, 42.02; H, 7.18; N, 28.74.

3,4-Dihydro-2-methyl-2*H*-thiazolo[2,3-*c*]-*as*-triazin-6(7*H*)-one (XVII).

A mixture of 41 g. (0.031 mole) of thione I and 52.3 g. (0.31 mole) of ethyl bromoacetate in 100 ml. of ethanol was allowed to reflux overnight. The reaction solution was allowed to stand for 4 days at room temperature. The crystals were filtered and recrystallized from methanol-ether to give 53 g. (67%) of tan crystals, m.p. $162-167^\circ$. The analytical sample was prepared by several recrystallizations from methanol to give light cream-color crystals, m.p. $162-165^\circ$ (possible decomposition); λ max (nujol) 3.95 (s, broad), 5.8 (v.s.), 5.95 (w, sh.), 6.2 (w, sh.), and 6.3μ (v.s.).

Anal. Calcd. for $C_6H_9N_3OS \cdot HBr$: C, 28.58; H, 3.99; Br, 31.69; N, 16.66; S, 12.71. Found: C, 29.00; H, 4.31; Br, 32.15; N, 16.83; S, 13.05.

The free base, obtained by sodium bicarbonate neutralization of an aqueous solution of the hydrobromide of XVII, was recrystallized from methanol (with charcoal) to give off-white crystals, m.p. $109-111^\circ$; λ max (nujol) 5.9 , 6.2 , and 6.25μ ; nmr (deuteriochloroform): δ , 2.8 (NCH₃), 2.9 (t, J \approx 6 cps), 3.8 (t, J \approx 6 cps), and 3.82 (SCH₂CO) ppm.

Diborane Reduction of Thiazolotriazinone XVII to Thiazolotriazine III.

A diborane-tetrahydrofuran solution, 200 ml. (0.2 mole), was placed in a three-neck 1 l. round bottom flask equipped with a stirrer, thermometer, addition funnel, condenser with a drying tube atop, and a gas inlet tube; the system was placed under nitrogen and the solution was cooled to -8° . To this vigorously stirred solution was added 2.65 g. (0.015 mole) of thiazolotriazinone XVII in 100 ml. of tetrahydrofuran during a 15-minute period. The temperature then was allowed to rise to 5° , in 15 minutes, and then the solution was warmed to reflux for 2.5-3 hours. The reaction was cooled to 20° and 110 ml. of 50% aqueous tetrahydrofuran was added dropwise; there was gas exothermic reaction. After dropwise addition of 100 ml. of 18% hydrochloric acid, the reaction solution was concentrated *in vacuo* at 40° . To this residual liquid was added 60 ml. of 10 *N* sodium hydroxide to make the solution basic, about pH 10, while the mixture was kept at about 20° . The basic solution was extracted with chloroform (4 x 100 ml.) and the combined extracts were washed with 50 ml. of brine and then dried over magnesium sulfate. The chloroform solution was concentrated *in vacuo* to give 2 g. (82%) of a faintly green-yellow oil whose infrared spectrum was nearly identical to that of thiazolotriazine III.

Preparation of the methiodide of this oil gave a white solid which was recrystallized several times to give white crystals, m.p. $228-230^\circ$ (undepressed, m.p. $229-231^\circ$, on mixture with thiazolotriazine III methiodide), whose infrared spectrum was identical to that of thiazolotriazine III methiodide.

REFERENCES

- (1) G. Doleschall, G. Hornyak, M. Hornyak-Hamori, K. Lempert, and A. Wolfner, *Acta Chim. Acad. Sci. Hung.*, **53**, 385 (1967).
- (2) H. F. Andrew and C. K. Bradsher, *J. Heterocyclic Chem.*, **4**, 577 (1967).
- (3) U.S.S.R. Patent 175,968 (1965); *Chem. Abstr.*, **64**, 6671a (1966).
- (4) D. L. Trepanier, J. E. Richman, and A. D. Rudzik, *J. Med. Chem.*, **10**, 228 (1967).

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