Mesoionic Purinone Analogs. V. Synthesis of Mesoionic Thiazolo[3,2-*a*]-*s*-triazine-5,7-diones, Mesoionic 1,3,4-Thiadiazolo[3,2-*a*]-*s*-triazine-5,7-diones, and Their Monothione Derivatives[1]

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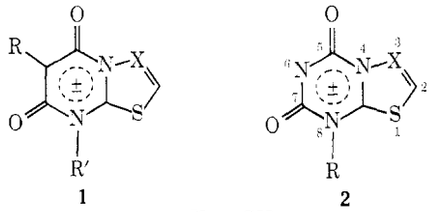
Mesoionic 8-alkylthiazolo- and -1,3,4-thiadiazolo[3,2-a]-*s*-triazine-5,7-diones have been prepared by the reactions of 2-alkylaminothiazoles (**3**) or 2-alkylamino-1,3,4-thiadiazoles with phenoxycarbonyl isocyanate. Mesoionic 8-alkylthiazolo[3,2-*a*]-*s*-triazin-5-one-7-thiones and -7-one-5-thiones are obtained from the reaction of **3** with phenoxycarbonyl isothiocyanate and ethoxycarbonyl isothiocyanate, respectively. These mesoionic xanthine analogs react readily with amines and are easily hydrolyzed in water.

We have previously described[2] the formulation and quantum chemical study of a large class of unknown mesoionic heterocycles which are isoconjugate with the purinones: xanthine, hypoxanthine, and purin-2-one. The synthesis and properties of the mesoionic xanthine analogs **1**, which may be viewed as ring-fused derivatives of known mesoionic 1,3-disubstituted pyrimidine-4,6-diones, have been recently reported.[3] We now report the synthesis of the mesoionic xanthine analogs **2** and their monothione derivatives.[4]



1 **2**

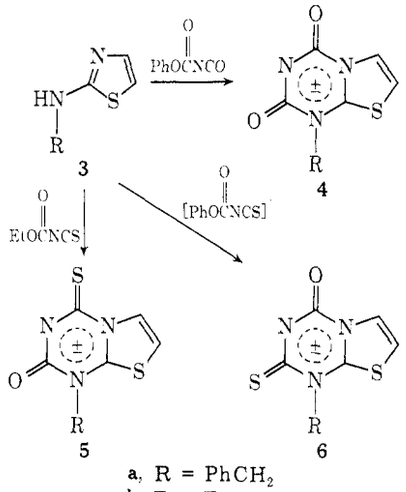
a, X = CH
b, X = N

4-Thiouracils have been prepared by the reaction of enamines with ethoxycarbonyl or phenoxycarbonyl isothiocyanate.[5] Uracils have been synthesized by the reaction of enamines with ethoxycarbonyl isocyanate.[6]

2-Alkylaminothiazoles **3a** and **3b** are acylated by ethoxycarbonyl isocyanate, but cyclization to give **4** was not observed. Phenoxycarbonyl isocyanate, however, reacts with **3a** and **3b** to produce mesoionic 8-substituted thiazolo[3,2,-*a*]-*s*-triazine-5,7-diones[7] (**4a** and **4b**), Scheme I. Structure assignment is based upon spectral evidence, including substantial downfield shift of both thiazole ring proton signals and alkyl group methylene proton signals, pseudocarbonyl group absorption at 1730 and 1669 cm^{-1}, and observed parent molecular ions.

Mesoionic thiazolotriazinediones **4** exhibit only low solubility in water and many organic solvents (EtOH, DMF, DMSO, etc). An aqueous solution of **4b** (buffered, pH 7.4) showed spectrophotometric evidence of decomposition after 24 hr at room temperature.

SCHEME I



a, R = $PhCH_2$
b, R = Et

They decompose rapidly when heated in aqueous or alcoholic solution. Compound **4a** reacts readily with ethylamine in ethanol with apparent nucleophilic attack of the 5-position pseudocarbonyl group resulting in ring-opened product **7**. The acylaminothiazole structure **7**, rather than the ring-acyl iminothiazoline structure **8**, is indicated by the ultraviolet absorption spectrum of the product.[8] Confirmation of this structure was obtained by the synthesis of **7** from **3a** as shown in Scheme II. Structure **9** was assigned to the phenylcarbamate ester, produced by the reaction of **3a** with phenylchloroformate, owing to its manner of preparation, and lack of an imino stretching band in its infrared spectrum.[8,9] Treatment of **9** with the sodium salt of ethylurea gives a product, **7**, identical with that obtained by the reaction of **4a** with ethylamine.

Reaction of **3a** and **3b** with phenoxycarbonyl isothiocyanate gives **6a** and **6b** while the analogous reaction employing ethoxycarbonyl isothiocyanate[10] produces the isomeric products **5a** and **5b** (Scheme I). Al-

(1) Taken from the Ph.D. dissertation to be submitted by B. Bhooshan in partial fulfillment of the requirements for the Ph.D. degree.

(2) R. A. Coburn, *J. Heterocycl. Chem.*, **8**, 881 (1971); R. A. Coburn, R. A. Carapellotti, and R. A. Glennon, *ibid.*, **10**, 479 (1973).

(3) R. A. Coburn and R. A. Glennon, *J. Heterocycl. Chem.*, **10**, 487 (1973).

(4) A report describing the preparation and properties of the corresponding monocyclic mesoionic 1,3-disubstituted *s*-triazine-4,6-diones is in preparation.

(5) J. Goerdeler and H. W. Pohland, *Chem. Ber.*, **95**, 526 (1963); J. Goerdeler and J. Gnad, *ibid.*, **98**, 1531 (1965).

(6) R. W. Lamon, *J. Heterocycl. Chem.*, **5**, 837 (1968).

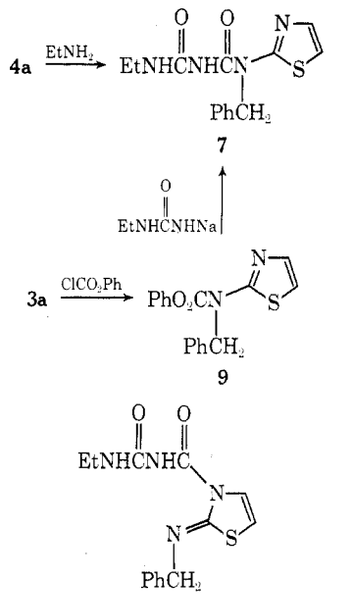
(7) Anhydro 8-substituted 5-hydroxythiazolo[3,2-*a*]-*s*-triazinium-7-one hydroxides.

(8) I. Y. Postovskii and I. B. Ludina, *J. Gen. Chem. USSR*, **29**, 604 (1959); S. G. Bogomolov, Y. N. Sheinker, and I. Y. Postovskii, *Dokl. Akad. Nauk SSSR*, **93**, 277 (1953). Ultraviolet absorption of typical models is as follows: 3-acetyl-2-methylimino-4-methylthiazoline-4, uv max (EtOH) 229 nm (log ϵ 2.98), 263 (1.95), and 307 (3.14); 2-(*N*-acetylmethylamino)thiazole, uv max (EtOH) 240 nm (log ϵ 2.45) and 275 (3.8).

(9) W. S. Paul, *Bull. Soc. Chim. Belg.*, **75**, 29 (1966).

(10) The reaction of 2-ethylaminothiazole and ethoxycarbonyl isothiocyanate has been recently reported to give low yields of 1-ethoxycarbonyl-3-ethyl-3-(2-thiazolyl)thiourea and *N*-ethoxycarbonyl-2-ethylaminothiazole. The order of reagent addition, reaction period, and product isolation procedure differ in this work from that previously described. M. Nagano, T. Matsui, J. Tobitsuka, and K. Oyamada, *Chem. Pharm. Bull.*, **21**, 74 (1973).

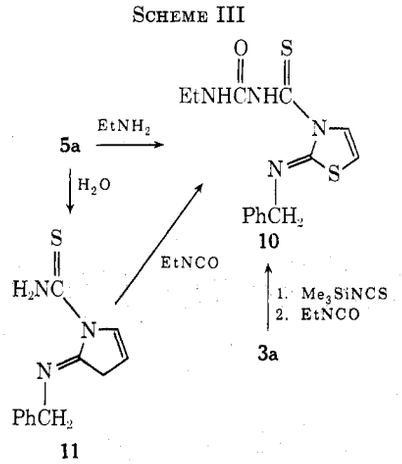
SCHEME II



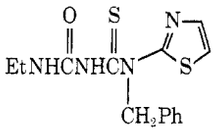
though **5a** and **6a** are easily distinguished, the physical and spectral properties of **5b** and **6b** are quite similar. In the latter case, reaction of the ethyl derivatives **5b** and **6b** with benzylamine gives different products, thus establishing their isomeric relationship.

The structure assignment of the isomeric monothiones **5a** and **6a** was based upon spectral evidence and by the products obtained in their reactions with ethylamine. Structure **10** was assigned to the product of the reaction of **5a** with ethylamine owing to its longest wavelength absorption at 305 nm and the low-field chemical shift of the benzyl methylene protons (δ 5.88). Heating **5a** with water gives thiourea **11**, whose spectral properties are also consistent with the imino structure. The ring-opened product **10** can be obtained from **11** by reaction with ethyl isocyanate or from **3a** by reaction with trimethylsilyl isothiocyanate followed by ethyl isocyanate, Scheme III.

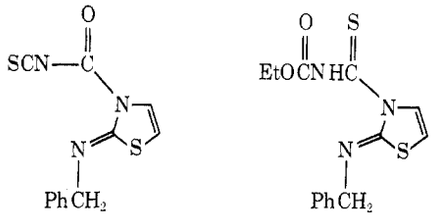
SCHEME III



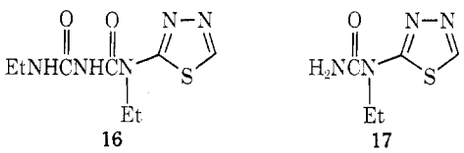
The thiobiuret obtained from **6a** by reaction with ethylamine was shown to be 1-benzyl-1-(2-thiazolyl)-5-ethyl-2-thiobiuret (**12**) based upon its uv and pmr spectra by comparison to those of **10**. It appears probable that the better leaving group leads to initial



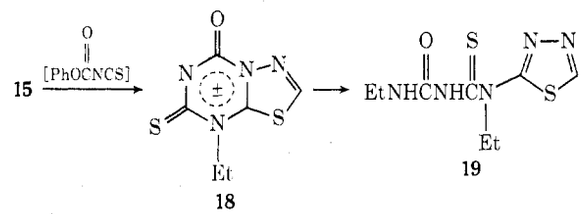
thiazole ring nitrogen acylation in reactions of phenoxycarbonyl isothiocyanate with **3a** and **3b** followed by cyclization of the resulting iminothiocyanate **13**, whereas ethoxycarbonyl isothiocyanate gives initially the thioacyl ester **14**, which then cyclizes to give **6a**.



Reaction of 2-ethylamino-1,3,4-thiadiazole (**15**) with phenoxycarbonyl isocyanate produces mesoionic 8-ethyl-1,3,4-thiadiazolo[3,2-*a*]-*s*-triazine-5,7-dione (**2b**, R = Et). This compound reacts very readily with ethylamine to produce 1-ethyl-1-(1,3,4-thiadiazol-2-yl)-5-ethylbiuret (**16**) and with water to give 1-ethyl-1-(1,3,4-thiadiazol-2-yl)urea (**17**).



Although **15** reacts with phenoxycarbonyl isothiocyanate to give **18**, no cyclized product could be obtained with ethoxycarbonyl isothiocyanate. Structure **18** was assigned based upon analogy to the results obtained in the reactions of **3a** and **3b** with phenoxycarbonyl isothiocyanate and by the structure of thiobiuret **19** obtained by the reaction of **18** with ethyl-



amine. Thiobiuret **19** can be identified as an aminothiadiazole derivative *via* its uv spectrum. The position of the thiocarbonyl group in **19** is indicated by the observation that with mesoionic analogs **5a** and **6a** nucleophilic attack occurs at the pseudocarbonyl group.

Experimental Section

Pmr spectra were obtained on a Varian T-60 spectrometer and chemical shifts are reported relative to TMS as an internal standard. Ultraviolet spectra were recorded on a Beckman Model DB spectrophotometer. Infrared spectra were obtained on a Perkin-Elmer Model 237 spectrophotometer. Microanalyses were performed by Galbraith Laboratories, Knoxville, Tenn. All melting points were determined with a Mel-Temp melting point apparatus and are uncorrected. Mass spectra were obtained with a Hitachi Perkin-Elmer RMC-6 single-focusing mass spectrometer, using a solid sample direct inlet.

anhydro-**5-Hydroxy-8-benzylthiazolo[3,2-*a*]-*s*-triazinium-7-one Hydroxide (4a).**—A solution of **3a** (1.9 g, 10 mmol) in anhydrous ethyl acetate (25 ml) was added dropwise with stirring to a solution of phenoxycarbonyl isocyanate[11] (1.77 g, 11 mmol) in ethyl acetate (30 ml). After 6 hr, the crude product which had precipitated was collected. Recrystallization from glacial acetic acid gave 0.82 g (31.6%) of **4a** as white crystals: mp 205–207° dec; ir (KBr) 1720 and 1669 cm^{-1} (C=O); nmr (CF_3CO_2H) δ 5.53 (s, 2 H), 7.56 (s, 5 H), 7.68 (d, 1 H), and 8.30 (d, 1 H); uv max (H_2O) 215 nm (ϵ 21,169) and 272 (5616); mass spectrum (70 eV) *m/e* (rel intensity) 259 (12), 190 (24), 189 (27), 91 (100), 65 (17), 44 (31).

Anal. Calcd for $C_{12}H_9N_3O_2S$: C, 55.60; H, 3.50; N, 16.21; S, 12.34. Found: C, 55.35; H, 3.35; N, 16.13; S, 12.10.

anhydro-**5-Hydroxy-8-ethylthiazolo[3,2-*a*]-*s*-triazinium-7-one Hydroxide (4b).**—A procedure identical with that described for the preparation of **4a** was employed with **3b** (1.28 g, 10 mmol). Recrystallization of the product from glacial acetic acid gave 1.0 g (50.7%) of **4b** as white crystals: mp 232–234° dec; ir (KBr) 1730 and 1669 cm^{-1} (C=O); nmr (CF_3CO_2H) δ 1.58 (t, 3 H), 4.40 (q, 2 H), 7.77 (d, 1 H), and 8.30 (d, 1 H); uv max (H_2O) 214 nm (ϵ 22,232) and 283 (6594); mass spectrum (70 eV) *m/e* (rel intensity) 197 (23), 182 (15), 169 (12), 128 (20), 127 (100), 126 (52), 113 (27), 100 (26), 99 (15), 86 (11), 76 (97).

Anal. Calcd for $C_7H_7N_3O_2S$: C, 42.65; H, 3.58; N, 21.31; S, 16.23. Found: C, 42.63; H, 3.54; N, 21.20; S, 16.07.

anhydro-**7-Hydroxy-8-benzylthiazolo[3,2-*a*]-*s*-triazinium-5-thione Hydroxide (5a).**—A solution of **3a** (1.9 g, 10 mmol) in anhydrous ethyl acetate (20 ml) was added to ethoxycarbonyl isothiocyanate (1.44 g, 11 mmol) in ethyl acetate over a period of 10 min. The reaction mixture was refluxed for 6 hr and cooled. The resulting precipitate was collected and washed with absolute ethanol. Recrystallization from trifluoroacetic acid–ether gave 0.85 g (31%) of **5a** as white crystals: mp 209–210° dec; ir (KBr) 1730 cm^{-1} (C=O); uv max (H_2O) 229 nm (ϵ 11,330), 275 (9200), and 320 (12,570); nmr (CF_3CO_2H) δ 5.96 (s, 2 H), 7.53 (s, 5 H), 7.70 (d, 1 H), and 7.26 (d, 1 H); mass spectrum (70 eV) *m/e* (rel intensity) 275 (3), 190 (12), 189 (30), 126 (8), 91 (100), 65 (17).

Anal. Calcd for $C_{12}H_9N_3OS_2$: C, 52.37; H, 3.30; N, 15.27; S, 23.26. Found: C, 52.20; H, 3.26; N, 15.35; S, 23.15.

anhydro-**7-Hydroxy-8-ethylthiazolo[3,2-*a*]-*s*-triazinium-5-thione Hydroxide (5b).**—A procedure identical with that described for the preparation of **5a** was employed with **3b** (1.28 g, 10 mmol). The product was recrystallized from trifluoroacetic acid–ether to give 1.0 g (46.9%) of **5b** as pale yellow crystals: mp 205–206° dec; ir (KBr) 1690 cm^{-1} (C=O); nmr (CF_3CO_2H) δ 1.56 (t, 3 H), 4.70 (q, 2 H), 7.77 (d, 1 H), and 8.26 (d, 1 H); uv max (EtOH) 225 nm (ϵ 8400), 274 (9100), and 320 (12,860); mass spectrum (70 ev) *m/e* (rel intensity) 213 (21), 180 (11), 155 (36), 128 (28), 127 (100), 126 (37), 113 (43), 100 (38), 86 (78).

Anal. Calcd for $C_7H_7N_3OS_2$: C, 39.42; H, 3.31; N, 19.70; S, 30.07. Found: C, 39.57; H, 3.44; N, 19.58; S, 29.80.

Treatment of **5b** with benzylamine (1 equiv) in tetrahydrofuran gave, after solvent evaporation and recrystallization of the residue from ethanol, a derivative, mp 60–62°.

anhydro-**5-Hydroxy-8-benzylthiazolo[3,2-*a*]-*s*-triazinium-7-thione Hydroxide (6a).**—Phenyl chloroformate (1.56 g, 10 mmol) was added to a suspension of potassium thiocyanate (1.0 g, 10 mmol) in anhydrous ethyl acetate (30 ml). After stirring for 15 min, a solution of **3a** (1.9 g, 10 mmol) in ethyl acetate (30 ml) was added. After 4 hr, the product was collected by filtration. Recrystallization from trifluoroacetic acid–ether gave 2.0 g (72.7%) of **6a** as white crystals: mp 208–209° dec; ir (KBr) 1669 cm^{-1} (C=O); nmr (CF_3CO_2H) δ 5.53 (s, 2 H), 7.58 (s, 5 H), 7.66 (d, 1 H), and 8.36 (d, 1 H); uv max (H_2O) 217 nm (ϵ 36,860), 256 (8500), and 302 (4250); mass spectrum (70 eV) *m/e* (rel intensity) 275 (6), 190 (20), 189 (53), 126 (11), 91 (100), 65 (18), 44 (17).

Anal. Calcd for $C_{12}H_9N_3OS_2$: C, 52.37; H, 3.30; N, 15.27; S, 23.26. Found: C, 52.31; H, 3.31; N, 15.09; S, 23.03.

anhydro-**5-Hydroxy-8-ethylthiazolo[3,2-*a*]-*s*-triazinium-7-thione Hydroxide (6b).**—A procedure identical with that described for the preparation of **6a** was employed with **3b** (1.28 g, 10 mmol). Recrystallization of the product from trifluoroacetic acid–ether gave 1.5 g (70.4%) of **6b** as white crystals: mp 201–203° dec; ir (KBr) 1675 cm^{-1} (C=O); nmr (CF_3CO_2H) δ 1.60 (t, 3 H), 4.40 (q, 2 H), 7.74 (d, 1 H), and 8.71 (d, 1 H); uv max (H_2O) 216 nm (ϵ 16,930), 239 sh (11,290), 276 (10,180), and 298 (10,550); mass spectrum (70 eV) *m/e* (rel intensity) 213 (20), 180 (11), 155 (33), 127 (100), 100 (16), 86 (17), 69 (26), 59 (25), 58 (52), 45 (32).

Anal. Calcd for $C_7H_7N_3OS_2$: C, 39.42; H, 3.31; N, 19.70; S, 30.07. Found: C, 39.38; H, 3.22; N, 19.68; S, 29.93.

Treatment of **6b** with benzylamine in tetrahydrofuran gave, after solvent evaporation and recrystallization of the residue from ethanol, a derivative, mp 142–143°, easily distinguished from the corresponding product obtained from **5b**.

1-Benzyl-1-(2-thiazolyl)-5-ethylbiuret (7). Method A.—To a suspension of **4a** (0.15 g) in ethanol (5 ml) was added ethylamine (0.5 ml, 70% aqueous solution). After stirring for 15 min, a clear solution was obtained. Addition of petroleum ether (bp 30–60°) gave 0.17 g (96%) of **7** as white needles: mp 134.5–135.5°; nmr ($CDCl_3$) δ 1.21 (t, 3 H), 3.41 (m, 2 H), 5.11 (s, 2 H), 6.95 (d, 1 H), 7.38 (s, 5 H), 7.48 (d, 1 H), 8.3 (broad s, 1 H); uv max (EtOH) 218 nm (ϵ 8840) and 267 (12,800).

Anal. Calcd for $C_{14}H_{16}N_4O_2S$: C, 55.26; H, 5.30; N, 18.41; S, 10.51. Found: C, 55.16; H, 5.32; N, 18.36; S, 10.69.

Method B.—To a suspension of sodium hydride (50 mg, 57% oil dispersion) in benzene (10 ml) was added ethylurea (88 mg). The mixture was stirred for 1 hr and a soluton of *N*-benzyl-*N*-(2-thiazolyl)phenylcarbamate (**9**, 310 mg) in benzene (5 ml) was added. The mixture was stirred for 2 hr, washed with water until the washing was neutral, and evaporated to dryness to give a solid (250 mg). Recrystallization from benzene–petroleum ether gave 0.2 g (66%) of **7** as white needles, mp 135–136°, identical (ir spectra and mixture melting point) with that prepared in method A.

Phenyl *N*-Benzyl-*N*-(2-thiazolyl)carbamate (9).—To a solution of **3a** (0.95 g, 5 mmol) in ethyl acetate (20 ml) was added triethylamine (1.0 ml, 7 mmol) and phenyl chloroformate (0.8 g, 5.1 mmol). The reaction mixture was refluxed for 30 min, washed twice with water, and evaporated to dryness. The residue was taken up in benzene and placed on a column (20 g) of silica gel (Woelm). Elution with benzene and recrystallization from benzene–petroleum ether yielded 0.62 g (40%) of **9** as white crystals: mp 91–92°; ir (KBr) 1725 cm^{-1} (C=O); uv max (EtOH) 218 nm (ϵ 14,300) and 262 (11,530); nmr ($CDCl_3$) δ 5.61 (s, 2 H), 7.03 (d, 1 H), 7.11–7.48 (m, 10 H), and 7.53 (d, 1 H).

Anal. Calcd for $C_{17}H_{14}N_2O_2S$: C, 65.80; H, 4.55; N, 9.03; S, 10.31. Found: C, 66.05; H, 4.53; N, 8.87; S, 10.11.

2-Benzylimino-*N*-ethylaminocarbonylthiazol-4-ine-3-thiocarboxamide (10). Method A.—Ethylamine (0.7 ml of 70% aqueous solution) was added to a suspension of **5a** (0.275 g, 1 mmol) in chloroform (10 ml). After 15 min a clear solution was obtained. Solvent was evaporated under reduced pressure and the residual oil (0.33 g) was crystallized from ethanol to give 0.25 g (78%) of **10** as white crystals: mp 114–115°; nmr ($CDCl_3$) δ 1.26 (t, 3 H), 3.5 (q, 2 H), 5.88 (s, 2 H), 7.06 (d, 1 H), 7.36 (s, 5 H), 7.58 (d, 1 H), 9.88 (broad s, 1 H), 14.15 (broad s, 1 H); uv max (EtOH) 216 nm (ϵ 8440) and 305 (18,390).

Anal. Calcd for $C_{14}H_{16}N_4OS_2$: C, 52.50; H, 5.04; N, 17.49; S, 19.98. Found: C, 52.79; H, 5.15; N, 17.39; S, 19.88.

Method B.—Trimethylsilyl isothiocyanate (0.72 g, 5.5 mmol) was added to a solution of **3a** (0.95 g, 5 mmol) in anhydrous tetrahydrofuran. After stirring for 1 hr, methanol (5 ml) was added. The solvent was removed under reduced pressure and the remaining oil (1.25 g) was dissolved in chloroform (10 ml). Ethyl isocyanate (0.47 g, 6 mmol) was added and the mixture was stirred for 4 hr. Chloroform was removed under reduced pressure and the residue was placed on a column (50 g) of silica gel (Woelm). Elution with benzene–ethyl acetate (9:1) and recrystallization from ethanol yielded 0.35 g (20%) of **10** as white crystals, mp 114–115°, identical (ir spectra and mixture melting point) with that prepared by method A.

Method C.—Sodium hydride (50 mg of 57% oil dispersion) was added to a solution of **11** (0.25 g, 1 mmol) in anhydrous tetrahydrofuran (15 ml). After stirring for 1 hr, ethyl isocyanate (0.1 g, 1.4 mmol) was added and the mixture was refluxed for 2 hr. The solvent was removed under reduced pressure and the residue was dissolved in ethyl acetate. The solution was washed with water until the washing was neutral and evaporated to dryness to give an oil. Crystallization from ethanol gave 0.12 g (37.5%) of **10** as white crystals, mp 114–115°, mmp 114–115°.

2-Benzyliminothiazol-4-ine-3-thiocarboxamide (11).—Water (10 ml) was added to a suspension of **5a** (0.9 g, 3.3 mmol) in tetra-

(11) A. J. Speziale, L. R. Smith, and J. E. Fedder, *J. Org. Chem.*, **30**, 4306 (1965).

hydrofuran (60 ml). After refluxing for 30 min, a clear solution was obtained. The solvent was evaporated under reduced pressure and the residue was recrystallized from 2-propanol to give 0.65 g (79.5%) of **11** as yellowish white crystals: mp 162–163°; nmr ($CDCl_3$) δ 5.90 (s, 2 H), 6.96 (d, 1 H), 7.36 (m, 8 H); uv max (EtOH) 217 nm (ε 10,600) and 293 (19,300); ir (KBr) 3330, 3150 (NH_2), and 1610 cm^{-1} (C=N).

Anal. Calcd for $C_{11}H_{11}N_3S_2$: C, 53.01; H, 4.45; N, 16.86; S, 25.68. Found: C, 53.22; H, 4.50; N, 16.77; S, 25.78.

1-Benzyl-1-(2-thiazolyl)-5-ethyl-2-thiobiuret (12).—To a suspension of **6a** (0.275 g, 1 mmol) in chloroform (10 ml) was added ethylamine (0.7 ml of 70% aqueous solution). After stirring for 30 min, the solvent was removed under reduced pressure. The residual oil was crystallized from ethanol to give 0.26 g (81.3%) of **12** as white crystals: mp 74–75°; nmr ($CDCl_3$) δ 1.43 (t, 3 H), 3.90 (q, 2 H), 5.35 (s, 2 H), 7.15 (d, 1 H), 7.53 (s, 5 H), 7.66 (d, 1 H), 10.45 (broad s, 1 H); uv max (EtOH) 220 nm (ε 13,670) and 269 (22,300).

Anal. Calcd for $C_{14}H_{16}N_4OS_2$: C, 52.50; H, 5.04; N, 17.49; S, 19.98. Found: C, 52.36; H, 5.10; N, 17.43; S, 20.20.

***anhydro*-5-Hyroxy-8-ethyl-1,3,4-thiadiazolo[3,2-*a*]-*s*-triazinium-7-one Hydroxide (2b, R = Et).**—To a solution of phenoxycarbonyl isocyanate (3.54 g, 22 mmol) in anhydrous ethyl acetate (50 ml) under nitrogen atmosphere was added a solution of **15** (2.58 g, 20 mmol) over a period of 15 min. The reaction mixture was stirred at room temperature for 2 hr and then refluxed for 4 hr. The crude product, which precipitated on cooling, was filtered and recrystallized from glacial acetic acid to give 3.22 g (81.3%) of **2b** (R = Et) as white crystals: mp 145–146°; ir (KBr) 1667 and 1734 cm^{-1} (C=O); nmr (CF_3CO_2H) δ 1.61 (t, 3 H), 4.45 (q, 2 H), and 9.80 (s, 1 H); mass spectrum (70 eV) *m/e* (rel intensity) 198 (17), 174 (11), 173 (11), 172 (12), 156 (12), 128 (28), 127 (12), 124 (12), 97 (26), 76 (29), 70 (100), 69 (46), 60 (32), 59 (33), 56 (20); uv max (H_2O) 221 nm (ε 9073) and 267 (28,900).

Anal. Calcd for $C_6H_6N_4SO_2$: C, 33.65; H, 2.82; N, 26.16; S, 29.89. Found: C, 33.51; H, 2.91; N, 26.21; S, 29.62.

1-Ethyl-1-(1,3,4-thiadiazol-2-yl)-5-ethylbiuret (16).—To a suspension of **2b** (R = Et) (0.2 g, 1 mmol) in chloroform was added ethylamine (0.7 ml of 70% aqueous solution). The reaction mixture became clear after 10 min. The solvent was removed under reduced pressure and the residue was recrystallized from benzene–petroleum ether to give 0.20 g (82%) of **20** as white crystals: mp 160–161°; nmr ($CDCl_3$) δ 1.25 (t, 3 H), 1.43 (t, 3 H), 3.40 (q, 2 H), 4.50 (q, 2 H), 8.40 (broad s, 1 H), 8.86 (s, 1 H), 10.08 (broad s, 1 H); uv max (EtOH) 218 nm (ε 5560) and 254 (11,650).

Anal. Calcd for $C_6H_{13}N_5O_2S$: C, 39.51; H, 5.39; N, 28.78; S, 13.15. Found: C, 39.44; H, 5.43; N, 28.66; S, 13.22.

1-Ethyl-1-(1,3,4-thiadiazol-2-yl)urea (17).—Water (10 ml) was added to a suspension of **2b** (R = Et) (0.54 g, 2.87 mmol) in tetrahydrofuran (50 ml). The mixture was refluxed for 10 min and solvent was removed under reduced pressure. The residue was recrystallized from tetrahydrofuran to give 0.16 g (34%) of **17** as white crystals: mp 173–174°; nmr (DMSO-d_6) δ 1.16 (t, 3 H), 4.15 (q, 2 H), and 9.13 (s, 1 H); uv max (EtOH) 222 nm (ε 4200) and 254 (9200).

Anal. Calcd for $C_5H_8N_4OS$: C, 34.87; H, 4.68; N, 32.54; S, 18.62. Found: C, 35.05; H, 4.72; N, 32.45; S, 18.72.

***anhydro*-5-Hydroxy-8-ethyl-1,3,4-thiadiazolo[3,2-*a*]-*s*-triazinium-7-thione Hydroxide (18).**—Phenyl chloroformate (1.56 g, 10 mmol) was added to a suspension of potassium thiocyanate (1.0 g, 10 mmol) in anhydrous ethyl acetate. After stirring for 15 min, a solution of **15** (1.29 g, 10 mmol) in ethyl acetate (25 ml) was added over a period of 15 min. The reaction mixture was stirred at room temperature for 3 hr and then refluxed for 4 hr. The crude product, which precipitated on cooling, was collected by filtration and recrystallized from trifluoroacetic acid–ether to give 1.65 g (77.1%) of **18** as yellow crystals: mp 153–154°; ir (KBr) 1706 cm^{-1} (C=O); nmr (CF_3CO_2H) δ 1.60 (t, 3 H), 4.43 (q, 2 H), 9.70 (s, 1 H); uv max (H_2O) 217 nm (ε 10,380) and 277 (28,100); mass spectrum (70 eV) *m/e* (rel intensity) 214 (2), 189 (16), 128 (23), 86 (23), 78 (12), 76 (100), 69 (13), 60 (25), 59 (37), 44 (26).

Anal. Calcd for $C_6H_6N_4OS_2$: C, 33.65; H, 2.82; N, 26.16; S, 29.73. Found: C, 33.51; H, 2.91; N, 26.21; S, 29.62.

1-Ethyl-1-(1,3,4-thiadiazol-2-yl)-5-ethyl-2-thiobiuret (19).—Ethylamine (0.7 ml of 70% aqueous solution) was added to a suspension of **18** (0.21 g, 1 mmol) in chloroform (10 ml). After stirring for 15 min at room temperature, the solvent was removed under reduced pressure and the residue was recrystallized from benzene–petroleum ether to give 0.16 g (62%) of **18** as white crystals: mp 139–140°; nmr ($CDCl_3$) δ 1.37 (q, 6 H), 3.68 (q, 2 H), 4.17 (q, 2 H), 8.91 (s, 1 H), 10.05 (broad s, 1 H), 10.83 (broad s, 1 H); uv max (EtOH) 216 nm (ε 9350) and 264 (19,500).

Anal. Calcd for $C_8H_{13}N_5OS_2$: C, 37.07; H, 5.05; N, 27.02; S, 24.68. Found: C, 37.34; H, 5.15; N, 26.98; S, 24.79.

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Registry No.—**2b** (R = Et), 39386-54-4; **3a**, 41593-98-0; **3b**, 13472-75-8; **4a**, 39386-60-2; **4b**, 39386-57-7; **5a**, 39386-58-8; **5b**, 39386-55-5; **5b** derivative, 41594-00-7; **6a**, 39386-59-9; **6b**, 39386-56-6; **6b** derivative, 41594-01-8; **7**, 41594-02-9; **9**, 41594-03-0; **10**, 41594-04-1; **11**, 41594-05-2; **12**, 41594-06-3; **15**, 13275-68-8; **16**, 41593-95-7; **17**, 41593-96-8; **18**, 39386-53-3; **19**, 41593-97-9; phenoxycarbonyl isocyanate, 5843-43-6; ethoxycarbonyl isothiocyanate, 16182-04-0; benzylamine, 100-46-9; phenyl chloroformate, 1885-14-9; ethylamine, 75-04-7; ethylurea, 625-52-5; triethylamine, 121-44-8; trimethylsilyl isothiocyanate 2290-65-5; sodium hydride, 7646-69-7.