Synthesis and Chemical Reactivity of some 1,2,4-Thiadiazolo[2,3-*a*]-pyrimidines and Related Compounds (1)

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A novel synthetic approach for 1,2,4-thiadiazolo[2,3-*a*]pyrimidines, 1,2,4-thiadiazolo[2,3-*c*]-pyrimidines and 1,2,4-thiadiazolo[2,3-*b*]indazoles is described. Several transformations of these heterocyclic systems are presented. 1,2,4-Thiadiazolo[2,3-*a*]pyrimidines undergo a very facile ring cleavage to give 3-amino-5-carbethoxyamino-1,2,4-thiadiazole and similar ring opening was observed also with the isomeric [2,3-*c*] system. On the other hand, 1,2,4-thiadiazolo[2,3-*a*]-pyridines undergo under similar conditions cleavage of the thiadiazole part of the bicycle.

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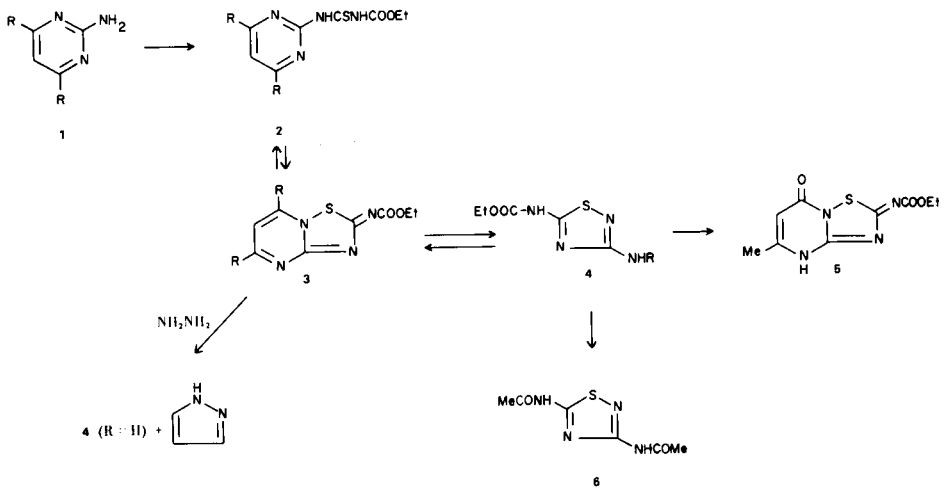
Recently, we have described a new synthetic approach for the preparation of 1,2,4-thiadiazolo[2,3-*a*]pyridines and some aza analogs (2). An X-ray structure determination of 2-ethoxycarbonylimino-2*H*-1,2,4-thiadiazolo[2,3-*a*]pyridine monohydrate revealed a very short S-O distance between the endocyclic sulfur atom and the side chain carbonyl oxygen atom (3), similar to the distance in compounds with a no-bond resonance structure.

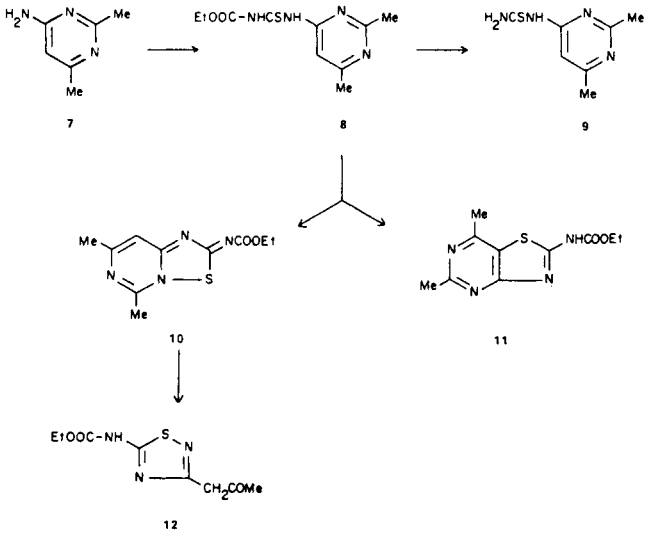
It seemed worth-while to extend the investigations on some other systems, in particular to 1,2,4-thiadiazolo-[2,3-*a*]pyrimidines. So far, only a few representatives of this bicyclic system have been described. They were obtained by oxidative cyclization of the corresponding pyrimidinylthioureas (4,5) or by Dimroth rearrangement of the isomeric 1,2,4-thiadiazolo[4,3-*a*]pyrimidine system (4). As in our previous studies on related systems, we have used the readily available carbethoxythiourea derivatives as the starting material. 2-Aminopyrimidine and its 4,6-dimethyl analog reacted with ethoxycarbonyl isothiocyanate to afford the corresponding carbethoxythiourea derivative (**2**, R = H or Me). By oxidative cyclization with bromine they were transformed into the corresponding 1,2,4-thiadiazolo[2,3-*a*]pyrimidines (**3**, R = H or Me). The bicyclic system thus obtained is stable, except in the presence of alkali or under the conditions of catalytic reduction. In the presence of hydrogen and palladized or platinized carbon it is transformed back into the carbethoxythiourea derivative (**2**). On the other hand, in the presence of hot dilute aqueous sodium hydroxide or sodium carbonate the pyrimidine ring of the bicycle is opened and 3-amino-5-carbethoxyamino-1,2,4-thiadiazole (**4**, R = H) is obtained. This compound is of interest as a potential precursor for the synthesis of fused bicyclic systems.

In fact, when **4** (R = H) was treated with 1,1,3,3-tetraethoxypropane and in the presence of polyphosphoric aicd, it was transformed into 1,2,4-thiadiazolo[2,3-*a*]-pyrimidine (**3**, R = H), obtained before by oxidative cyclization. From a similar experiment with acetylacetone the corresponding dimethyl analog (**3**, R = Me) was obtained. In an attempt to prepare the corresponding 7-one, compound **4** (R = H) was condensed with diethyl ethoxymethylenemalonate in the presence of polyphosphoric acid, but only the corresponding substituted amino compound (**4**, R = -CH=C(COOEt)$_2$) could be isolated. The desired bicycle (**5**) could be then obtained by condensing compound **4** (R = H) with ethyl acetoacetate. The structure of this compound as a 7-one and not as a 5-one



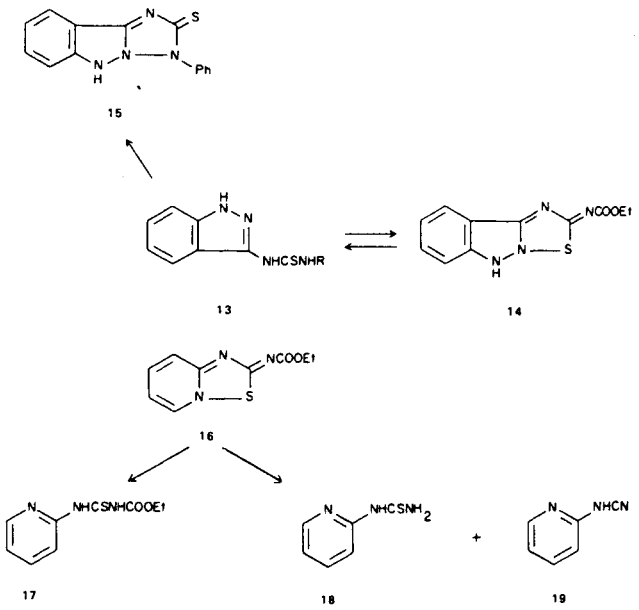
follows from the nmr evidence. The signal for the 5-methyl group in **5** appears as a singlet and this is consistent with the proposed 7-one structure. In the case of a 5-one structure the 7-methyl group would appear in nmr spectrum as a doublet, in accordance with our previous observations on some related bicyclic systems (6).

Our further interest was in the isomeric 1,2,4-thiadiazolo[2,3-*c*]pyrimidine system which should be formed in an analogous manner from 6-aminopyrimidines as starting material. According to one report, the cyclization step did not involve the ring nitrogen, but occurred at C_5 of the pyrimidine ring (7). Derivatives of this thiazolo[4,5-*d*]-pyrimidine ring system have been prepared also from the corresponding 6-aminopyrimidines by direct thiocyanation (8). We attempted to repeat the reaction in which 6-benzoylthioureido-2,4-dimethylpyrimidine is used as the starting material. The reaction was, however, not described in detail and although after several different attempts, the compound could not be obtained as described. Therefore, we have chosen another approach. 6-Amino-2,4-dimethylpyrimidine was treated with a solution of carbethoxyisothiocyanate in acetonitrile to give the corresponding carbethoxythiourea derivative (**8**). This compound, when treated with bromine in acetic acid yielded a product which by means of nmr spectroscopic examination was found to be a mixture of the 1,2,4-thiadiazolo[2,3-*c*]-pyrimidine (**10**) and thiazolo[4,5-*d*]pyrimidine (**11**) derivatives. It was possible to isolate the pure [2,3-*c*] isomer (**10**) and from the residue also a 1,2,4-thiadiazole derivative (**12**). The latter compound results from compound **10**



by cleavage of the pyrimidine ring. This evidence showed that the main cyclization reaction involves an attack on the pyrimidine ring nitrogen and not the C_5 position as postulated previously (7). The carbethoxy derivative (**8**) when treated with aqueous sodium hydroxide at room temperature afforded the corresponding thiourea (**9**).

It was of further interest to investigate the possibility of fusion of the thiadiazole ring to a five-membered heterocycle and therefore the corresponding carbethoxythioureidoindazole (**13**, R = COOEt) was used as the starting material. The oxidative cyclization occurred readily either with bromine or lead tetraacetate to give compound **14**. If, however, the phenylthioureido compound (**13**, R = Ph) was treated in the same way with bromine, a fused triazolo ring was formed (**15**). That the thiocarbonyl sulfur atom was not incorporated in the ring, but remained an exocyclic one, could be established by a positive iodine-azide reaction (9).



As shown above, the 1,2,4-thiadiazolo[2,3-*a*]pyrimidine ring is particularly suitable for the preparation of 1,2,4-thiadiazole derivatives by nucleophilic attack on the six-membered ring, followed by ring opening. It was therefore of interest to investigate the behaviour of related systems. Hydrogenolysis of 1,2,4-thiadiazolo[2,3-*a*]pyridine (**16**) afforded the corresponding carbethoxythioureidopyridine (**17**) and similar behaviour was encountered also in the pyrimidine (**3** → **2**, R = H) or indazole series (**14** → **13**, R = COOEt). In contrast to 1,2,4-thiadiazolo[2,3-*a*]-pyrimidines, 2-carbethoxyimino-1,2,4-thiadiazolo[2,3-*a*]-pyridine (**16**) was not attacked at the six-membered ring and instead the thiadiazole part was degraded. Thus, in the presence of a base, compound **16** was transformed into a mixture of *N*-(pyridyl-2′)thiourea (**18**) and 2-cyanaminopyridine (**19**).

EXPERIMENTAL (10)

N-Ethoxycarbonyl-*N*′-/2-(4,6-dimethyl)pyrimidinyl)thiourea (**2**, R = Me).

A solution of 2-amino-4,6-dimethylpyrimidine (**1**, R = Me)

(0.615 g.) in chloroform (30 ml.) was treated with carbethoxyisothiocyanate (0.66 g.) and the reaction mixture was heated under reflux for 30 minutes. The product which separated was filtered and crystallized from methanol, m.p. 179-181° (yield 0.6 g.); mass spectrum: M^+ = 254 (100%); nmr (DMSO-d_6, 70°): τ = 3.04 (s, H_5), -0.91 and -3.06 (broad s, NH), 5.82 (q, CH_2CH_3), 8.74 (t, CH_2CH_3), J_{Et} = 7.5 Hz.

Anal. Calcd. for $C_{10}H_{14}N_4O_2S$: C, 47.24; H, 5.55; N, 22.04; Found: C, 47.36; H, 5.59; N, 22.38.

In a similar manner was prepared:

N-Carbethoxy-*N'*-(pyrimidinyl-2)thiourea (**2**, R = H).

This compound was obtained from 2-aminopyrimidine (**1**, R = H) in 76% yield, m.p. 195-197° (from methanol); mass spectrum: M^+ = 226 (100%); nmr (DMSO-d_6, 102°): τ = 2.75 (t, H_5), 1.25 (d, H_4,H_6), 5.76 (q, CH_2), 8.70 (t, Me), -2.19 (broad, NH), J_{Et} = 7.5 Hz.

Anal. Calcd. for $C_8H_{10}N_4O_2S$: C, 42.48; H, 4.46; N, 24.77. Found: C, 42.42; H, 4.51; N, 24.80.

2-Ethoxycarbonylimino-5,7-dimethyl-2*H*-1,2,4-thiadiazolo[2,3-*a*]-pyrimidine (**3**, R = Me).

a) A mixture of 3-amino-5-carbethoxyamino-1,2,4-thiadiazole (**4**, R = H) (0.188 g.), acetylacetone (0.15 g.) and polyphosphoric acid (6 g.) was heated at 70° for 6 hours. The cold reaction mixture was treated with iced water (20 ml.) and neutralized with sodium bicarbonate. The separated product was filtered off and crystallized from methanol, m.p. 206-207° dec. (yield 0.07 g.); mass spectrum: M^+ = 252 (77%); nmr (DMSO-d_6, 122°): τ = 7.62 (s, 5- and 7-Me), 8.74 (t, CH_2CH_3), 5.95 (q, CH_2CH_3), 3.09 (broadened s, H_6), J_{Et} = 7.6.

Anal. Calcd. for $C_{10}H_{12}N_4O_2S$: C, 47.62; H, 4.80; N, 22.22. Found: C, 47.69; H, 4.92; N, 22.00.

b) The corresponding thiourea derivative (**2**, R = Me) (0.5 g.) was dissolved in acetic acid (10 ml.), the solution was cooled to 0-5° and under stirring a solution of bromine (0.32 g.) in glacial acetic acid (2 ml.) was added. The reaction mixture was stirred at room temperature for 1 hour, the suspension was poured into cold water and neutralized with sodium bicarbonate until *p*H 5. The product was filtered and crystallized from methanol, m.p. 197-200° of the hydrobromide salt (yield 0.21 g.); mass spectrum: m/e = 252 (77%) (M^+ - HBr); nmr (DMSO-d_6, 80°): τ = 2.86 (s, H_6), 7.59 (s, 5- and 7-Me), 8.72 (t, CH_2Me), 5.76 (q, CH_2CH_3), J_{Et} = 7.5 Hz.

Anal. Calcd. for $C_{10}H_{13}BrN_4O_2S$: N, 16.81. Found: N, 16.40.

2-Ethoxycarbonyl-2*H*-1,2,4-thiadiazolo[2,3-*a*]pyrimidine (**3**, R = H).

a) The compound was prepared according to the procedure as described above for the methyl analog under b), from compound **2** (R = H) in 63% yield, m.p. 237-240°; mass spectrum: M^+ = 224 (78%); nmr (DMSO-d_6, 132°): τ = 1.05 (dd, H_5), 2.75 (dd, H_6), 0.81 (dd, H_7), 5.71 (q, CH_2), 8.70 (t, Me), J_{Et} = 7.5 Hz.

Anal. Calcd. for $C_8H_8N_4O_2S$: C, 42.86; H, 3.60; N, 24.99. Found: C, 42.94; H, 3.89; N, 24.75.

b) A mixture of 3-amino-5-carbethoxyamino-1,2,4-thiadiazole (**4**, R = H) (0.12 g.), 1,1,3,3-tetraethoxypropane (0.2 g.) and polyphosphoric acid (5 g.) was heated at 55° for 5 hours. The reaction mixture was diluted with iced water, neutralized with sodium bicarbonate to *p*H 7 and extracted with chloroform. Upon evaporation of the solvent the residue was found to be identical in all respects with the product obtained as described under a) (yield 53 mg.).

2-Ethoxycarbonyl-5-methyl-1,2,4-thiadiazolo[2,3-*a*]pyrimidin-7-one (**5**).

A mixture of the corresponding thiadiazole (**4**, R = H) (0.376 g.), ethyl acetoacetate (0.28 g.) and polyphosphoric acid (10 g.) was heated on an oil bath at 80° for 4 hours. The cold solution was treated with iced water and neutralized with sodium bicarbonate to *p*H 6-7. The separated product was crystallized from methanol, m.p. 250-251° (yield 0.13 g.); mass spectrum: M^+ = 254 (72%); nmr (DMSO-d_6): τ = 4.05 (s, H_6), 7.72 (s, 5-Me), 5.61 (broad, NH), 8.73 (CH_2, t), 5.75 (q, Me), J_{Et} = 7.5 Hz.

Anal. Calcd. for $C_9H_{10}N_4O_3S$: C, 42.52; H, 3.97; N, 22.04. Found: C, 42.51; H, 4.28; N, 21.83.

3-Amino-5-carbethoxyamino-1,2,4-thiadiazole (**4**, R = H).

A mixture of compound **3** (R = H) (0.5 g.) and dilute sodium hydroxide (10 ml. of 1*N*) were heated under reflux for 2 hours. Upon neutralization with 1*N* hydrochloric acid the product separated and was filtered and crystallized from methanol, m.p. over 250° (lit. (11) gives m.p. over 300°) (yield 70 mg.); mass spectrum: M^+ = 188 (100%). The same compound was obtained if a solution of sodium carbonate was used in the reaction.

Anal. Calcd. for $C_5H_8N_4O_2S$: C, 31.92; H, 4.29; N, 29.78. Found: C, 32.04; H, 4.59; N, 29.95.

3,5-Diacetylamino-1,2,4-thiadiazole (**6**).

A mixture of the amino compound (**4**, R = H) (0.188 g.) and acetic anhydride (5 ml.) was heated for 2 hours. Upon cooling, the product separated and was crystallized from methanol, m.p. 300-302° dec. (yield 25 mg.); mass spectrum: M^+ = 200 (25%); nmr (DMSO-d_6): τ = 7.76 and 7.9 (s, Me), 6.34 (broad, NH), -0.65 (s, NH).

Anal. Calcd. for $C_6H_8N_4O_2S$: C, 36.00; H, 4.03; N, 27.99. Found: C, 36.30; H, 4.18; N, 27.92.

Reaction Between 3-Amino-5-carbethoxyamino-1,2,4-thiadiazole and Diethyl Ethoxymethylenemalonate.

A mixture of compound **4** (R = H) (0.188 g.), diethyl ethoxymethylenemalonate (3 ml.) and polyphosphoric acid (5 g.) was heated at 110° for 3 hours. The cold reaction mixture was treated with iced water (10 ml.) and neutralized with sodium bicarbonate to *p*H 6. The separated product was filtered and crystallized from methanol, m.p. 177-178°, to give compound **4** (R = -CH=C(COOEt)$_2$) in 46 mg. yield; mass spectrum: M^+ = 358 (63%); nmr (DMSO-d_6): τ = 1.26 (d, CH), 0.9 (d, NH=C), -2.86 (broad, N*H*-COOEt), 8.73 (t, Me), 8.75 (t, Me), 8.77 (t, Me), 5.66, 5.76 and 5.86 (q, CH_2), J_{Et} = 7.5, J_{NHCH} = 12 Hz.

Anal. Calcd. for $C_{13}H_{18}N_4O_6S$: C, 43.57; H, 5.06; N, 15.64. Found: C, 43.40; H, 5.11; N, 15.89.

Hydrazinolysis of 2-Carbethoxyimino-1,2,4-thiadiazolo[2,3-*a*]-pyrimidine.

The reaction was monitored in a nmr probe. The bicycle **3** (R = H) (30 mg.), hydrazine hydrate (0.2 ml. of 90%) and DMSO-d_6 (0.5 ml.) were heated at 75° and after 30 minutes the transformation was completed. A nmr analysis of the sample indicated that besides compound **4** (R = H) also pyrazole was formed. The nmr spectrum of pyrazole was found identical with that reported in the literature (12). The reaction mixture was then neutralized with 1*N* hydrochloric acid and the obtained 3-amino-5-carbethoxyamino-1,2,4-thiadiazole was found to be identical with an authentic specimen.

N-Carbethoxy-*N'*-(2,4-dimethylpyrimidinyl-6)thiourea (**8**).

A solution of the amine **7** (6.15 g.) in acetonitrile (120 ml.) was treated under stirring at room temperature with a solution of carbethoxy isothiocyanate (6.55 g.) in acetonitrile (20 ml.). The reaction mixture was stirred for 10 hours and left to stand in a closed and from moisture protected vessel for 2 days. The separated crystals were filtered off, suspended in water and filtered,

m.p. 168-172° (yield 3.6 g.); mass spectrum: M^+ = 254 (75%); nmr (DMSO-d_6): τ = 1.70 (s, H_5), 7.48 (s, 2-Me), 7.55 (s, 4-Me), 5.75 (q, CH_2Me), 8.70 (t, CH_2CH_3), -2.0 (broad, NH), J_{Et} = 7.0 Hz.

Anal. Calcd. for $C_{10}H_{14}N_4O_2S$: C, 47.24; H, 5.55; N, 22.04. Found: C, 47.44; H, 5.70; N, 22.16.

2,4-Dimethylpyrimidinyl-6-thiourea (**9**).

The above compound **8** (0.5 g.) was dissolved in aqueous sodium hydroxide (10 ml. of 1*N*) and allowed to stand at room temperature for 10 hours. The reaction mixture was acidified with hydrochloric acid (1:1) and the separated product was filtered off and crystallized from water, m.p. 234-235° (lit. (7) gives m.p. 223-224°); mass spectrum: M^+ = 182 (63%); nmr (DMSO-d_6): τ = 3.23 (s, H_5), 7.55 (s, 2-Me), 7.72 (s, 4-Me), -0.4 and 0.9 (broad, NH).

Anal. Calcd. for $C_7H_{10}N_4S$: C, 46.15; H, 5.52; N, 30.76. Found: C, 46.08; H, 5.63; N, 30.90.

Oxidative Cyclization of *N*-Carbethoxy-*N'*-(2,4-dimethylpyrimidinyl-6)thiourea.

A solution of the corresponding carbethoxythiourea **8** (1.27 g.) in glacial acetic acid (25 ml.) was cooled to about 10° and under stirring a solution of bromine (0.8 g.) in glacial acetic acid (10 ml.) was added dropwise. After addition was complete, stirring was continued for 1 hour, the reaction mixture was then poured on ice and under stirring a concentrated aqueous solution of ammonia was added until *p*H 5. The separated product was filtered off and divided into two parts. The first part was crystallized from 1-propanol to give compound **10**, m.p. 192-194°; mass spectrum: M^+ = 252 (83%); nmr (DMSO-d_6): τ = 2.55 (q, H_8), 7.25 (s, 5-Me), 7.53 (d, 7-Me), 5.75 (q, CH_2Me), 8.73 (t, CH_2CH_3), (t, CH_2CH_3), J_{Et} = 7.2, $J_{8H,7Me}$ = 0.4 Hz.

Anal. Calcd. for $C_{10}H_{12}N_4O_2S$: C, 47.62; H, 4.80; N, 22.22. Found: C, 47.60; H, 4.57; N, 22.34.

The second part of the crude product was treated with boiling *n*-heptane twice. The product which separated from *n*-heptane upon cooling was found on hand of nmr examination to be a mixture of the above bicyclic compound **10** and the isomeric thiazolo[4,5-*d*]pyrimidine (**11**). So far, it was not possible to separate both compounds.

The in *n*-heptane insoluble residue was crystallized from 1-propanol to give the 1,2,4-thiadiazole derivative **12**, m.p. 158-160°; mass spectrum: M^+ = 229 (60%); nmr (deuteriochloroform): τ = 7.82 (s, CH_3CO), 6.0 (s, CH_2CO), 5.60 (q, CH_2Me), 8.62 (t, CH_2CH_3), J_{Et} = 7.2 Hz.

Anal. Calcd. for $C_8H_{11}N_3O_3S$: C, 41.92; H, 4.84; N, 18.34. Found: C, 42.03; H, 5.06; N, 18.62.

2-Carbethoxyimino-1,2,4-thiadiazolo[2,3-*b*]indazole (**14**).

a) A solution of *N*-ethoxycarbonyl-*N'*-(indazolyl-3')thiourea (**13**) (**13**, R = COOEt) (0.528 g.) in acetic acid (3 ml.) was cooled to 0° and under stirring a solution of bromine (0.16 g.) in glacial acetic acid (2 ml.) was added portionwise. The suspension was left to stand at room temperature for 30 minutes, the product was filtered off and crystallized from methanol, m.p. over 315° (yield 0.11 g.); mass spectrum: M^+ = 262 (70%); nmr (DMSO-d_6, 98°): τ = 2.52 (m, $H_{6,7,8,9}$), 5.62 (q, CH_2), 8.64 (t, Me), J_{Et} = 7.5 Hz.

Anal. Calcd. for $C_{11}H_{10}N_4O_2S$: C, 50.38; H, 3.84; N, 21.37. Found: C, 50.35; H, 3.97; N, 21.40.

b) A solution of compound **13** (R = COOEt) (0.264 g.) in acetic acid (20 ml.) was treated with lead tetraacetate (0.48 g.), the reaction mixture was stirred for a while and poured into iced water (100 ml.). The obtained product was found to be identical in all respects with the compound as described under a).

N-Phenyl-*N'*-(indazolyl-3')thiourea (**13**, R = Ph).

A mixture of 3-aminoindazole (1 g.), ethanol (5 ml.) and phenyl isothiocyanate (1 g.) was heated under reflux for 1 hour. The product was filtered off and crystallized from ethanol, m.p. 197-200° (yield 1.4 g.); mass spectrum: M^+ = 268 (71%); nmr (DMSO-d_6): τ = 2.55 (m, $H_{4,5,6}$), 1.65 (m, H_7).

Anal. Calcd. for $C_{14}H_{12}N_4S$: C, 62.88; H, 4.51; N, 20.89. Found: C, 62.83; H, 4.61; N, 20.50.

3-Phenyl-2-thioxo-5*H*-1,2,4-triazolo[2,3-*b*]indazole (**15**).

The above phenylthiourea derivative (**13**, R = Ph) (0.7 g.) was dissolved in acetic acid (3 ml.) and upon cooling to about 0° a solution of bromine (0.42 g.) in glacial acetic acid (2 ml.) was added. The suspension was left at room temperature for 30 minutes, iced water (50 ml.) was added and the mixture was neutralized with ammonia to *p*H 7. The product was filtered off and crystallized from ethanol, m.p. 268-273° (yield 58%); mass spectrum: M^+ = 266 (35%); nmr (DMSO-d_6): τ = 2.73 (m, $H_{6,7,8,9}$).

Anal. Calcd. for $C_{14}H_{10}N_4S$: C, 63.15; H, 3.79; N, 21.04. Found; C, 63.08; H, 3.94; N, 20.79.

Hydrogenolysis of 2-Carbethoxyimino-1,2,4-thiadiazolo[2,3-*a*]-pyridine.

To a solution of the bicyclic compound **16** (0.5 g.) in methanol (100 ml.) was added the catalyst (0.5 g. of 10% palladized carbon or 10% platinized carbon) and the mixture was hydrogenated in a Parr hydrogenator at 3 atmospheres for 12 hours (in the case of platinum catalyst 2 days). Upon filtration the solution was evaporated to dryness and the residue was identified as *N*-ethoxy-*N'*-(pyridyl-2')thiourea (**17**) (yield 0.41 g.).

In a similar manner the pyrimidine analog **3** (R = H) or the tricyclic compound **14** were transformed into the corresponding carbethoxythiourea derivatives **2** (R = H) and **13** (R = COOEt), respectively.

Reaction of 2-Carbethoxyimino-1,2,4-thiadiazolo[2,3-*a*]pyridine with Sodium Carbonate.

The bicyclic compound **16** (0.223 g.) was treated with aqueous sodium carbonate (10 ml. of saturated solution) and the mixture was heated under reflux for 5 hours. The reaction mixture was cooled to about 0° and the separated crystals were filtered off and identified as *N*-(pyridyl-2')thiourea **18** (yield 75 mg.). The filtrate was extracted with chloroform and upon evaporation of the solvent the residue was identified as 2-cyanaminopyridine (**19**).

REFERENCES AND NOTES

(1) Heterocycles. CLXI.

(2) B. Koren, B. Stanovnik, and M. Tišler, *Org. Prep. Proced. Int.*, 7, 55 (1975).

(3) I. Leban, *Acta Cryst. B*, 32, 1601 (1976).

(4) K. T. Potts and J. Kane, *J. Org. Chem.*, 39, 3783 (1974).

(5) G. Barnikow and J. Bödeker, *J. Prakt. Chem.*, 313, 1148 (1971).

(6) A. Pollak, B. Stanovnik, and M. Tišler, *J. Org. Chem.*, 36, 2457 (1971).

(7) G. Barnikow and J. Bödeker, *Z. Chem.*, 5, 62 (1965).

(8) A. Maggiolo and G. H. Hitchings, *J. Am. Chem. Soc.*, 73, 4226 (1951).

(9) F. Feigl, "Spot Tests", Vol. 2, Elsevier Publishing Co., Amsterdam, 1954, p. 164.

(10) Melting points were taken on a Kofler micro hot stage. All nmr spectra were obtained on a JEOL JNM C60-HL spectrometer and mass spectra were recorded on a Hitachi-Perkin-Elmer RMU-6L instrument.

(11) M. Nagano, M. Oshige, T. Matsui, J. Tobitsuka, and K. Oyamada, *Chem. Pharm. Bull.*, **21**, 2396 (1973).

(12) "Varian High Resolution NMR Spectra Catalog", Vol. 2, spectrum No. 379.

(13) B. Koren, F. Kovač, A. Petrič, B. Stanovnik, and M. Tišler, *Tetrahedron*, **32**, 493 (1976).