Synthesis of Pyrido[2,3-*d*]pyrimidin-4-one Derivatives

A. Monge* and V. Martinez-Merino

Facultad de Farmacia, Departamento de Química Orgánica y Farmacéutica, Universidad de Navarra, Pamplona, Spain

E. Fernández-Alvarez*

Instituto de Química Orgánica General del CSIC, C/Juan de la Cierva, 3, 28006-Madrid, Spain

Received September 11, 1985

This paper describes one-pot synthesis of 5*H*-[1,3]thiazolo[3,2-*a*]pyrido[3,2-*e*]pyrimidin-5-one **4**, 5*H*-dipyrido[1,2-*a*:3′,2′-*e*]pyrimidin-5-one **10** and 5*H*-pyrido[3,2-*e*]pyrimido[1,2-*a*]pyrimidin-5-one **15** and some of their derivatives, starting with 2-chloro-3-pyridine carboxilic acid **1**. Compounds **4** and **10** reacted with phosphorus pentasulfide to give the respective 5-thione analogues, **5** from **4** and **11** from **10**.

Boiling the 5-thione derivatives with hydrazine hydrate, the respective 5-hydrazono derivatives **6** from **5** and **12** from **11** were obtained. The 5-acetyl hydrazono, **7**, and the 5-isopropylidenehydrazono, **8**, derivatives were also prepared from **6**, and the 5-propionylhydrazono derivatives, **13**, from **12**.

Compound **4** reacted with hydrazine to give an adduct with two molecules of hydrazine and the probable structure **16**. Treating this adduct with acetone a monohydrazone **17** was obtained. Boiling a suspension of this adduct in DMF, it gave 6,10-dihydro-6*H*-pyrido[3′,2′:5,6]pyrimido[2,1-*c*][1,2,4]triazin-5-one **20**.

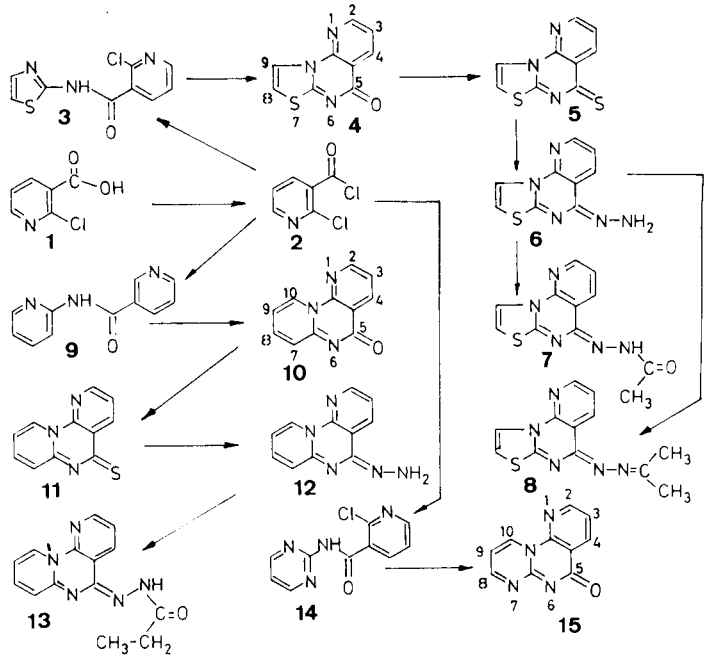
J. Heterocyclic Chem., **23**, 509 (1986).

The pyrido[2,3-*d*]pyrimidine-4-one derivatives are compounds with pharmacological interest. Osselaere and coworkers [1] have reported a high diuretic activity in some of these compounds, particulary with 2-(3-pyridyl)-3*H*-pyrido[2,3-*d*]pyrimidin-4-one, and most recently Parish and coworkers [2] have described high potassium-sparing diuretic activity with 1,2-dihydro-2-(3-pyridyl)-3*H*-pyrido-[2,3-*d*]pyrimidin-4-one; likewise, some patents [3] report other pharmacological activities for these type of compounds. However, pyrido[2,3-*d*]pyrimidin-4-one derivatives, fused with other rings through the positions 1 and 2 are very limited in the bibliography. Recently, Merchan and coworkers [3] have reported the synthesis of some 5*H*-[1,3]thiazolo[3,2-*a*]pyrido[3,2-*e*]pyrimidin-5-one derivatives by thermal cyclization of 2-chloro-3-pyridinecarboxamides of several 2-amino-1,3-thiazole derivatives. Likewise, we have described [5] the synthesis of some pyrido[2,3-*d*]pyrimidin-4-one derivatives, fused with different rings through the positions 1 and 2, and some of these compounds showed interesting diuretic or potassium-sparing diuretic activities [5]. More recently, we have found also antihypertensive activity.

The compounds were obtained [5] by three different methods: A. Thermal cyclization of 2-chloro-3-pyridinecarboxamides. B. Thermal cyclization of 2-arylthio-3-pyridinecarboxamides. C. Direct reaction of 2-aryl(alkyl)thio-3-pyridinecarbonyl chloride with the suitable amine.

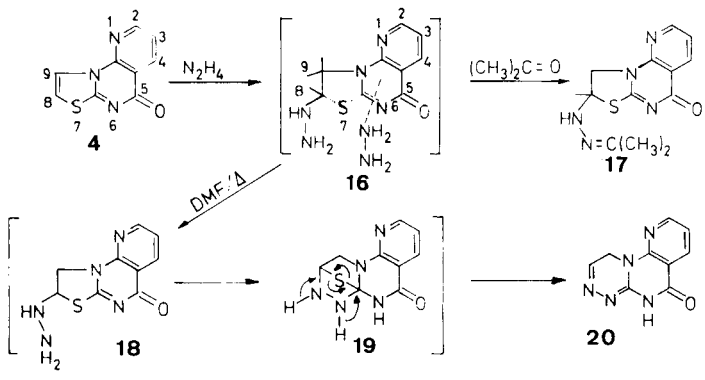
The paper reports the one-pot synthesis of compounds **4**, **10** and **15** and some of their hydrazono derivatives, from 2-chloro-3-pyridinecarboxylic acid, **1** (Scheme 1), as well as an unexpected synthesis of compounds **17** and **20** (Scheme 2).

Compounds **4**, **10** and **15** were obtained in a similar way. The crude acyl chloride **2**, obtained from **1** and thionyl chloride, was dissolved in chloroform/pyridine and the ice-bath cooled solution treated with the respective amine (2-aminothiazole, 2-aminopyridine, 2-aminopyrimidine). The crude amides **3**, **9** and **14**, respectively, were thermically cyclized to the monohydrochlorides of the compounds **4**, **10** and **15** with acceptable yields (50-80%).



SCHEME 1

Obtaining the amides was the most critical step, particularly for **14**. For this compound we examined fruitlessly different conditions suitable for **3** [4,5] and **9** [5], but only the use of chloroform/pyridine about 0°, as reported with other amides of 2-aminopyrimidine [6], was found satisfac-



SCHEME 2

tory. The free bases **4** and **10** were stable, but the free base **15** was unstable. Similar behaviour has been described with 3,4-dihydro-2*H*-pyrimido[1,2-*a*]pyrimidin-2-one [6].

When compounds **4**.HCl and **10** were treated with phosphorus pentasulfide in pyridine, **5** (85%) and **11** (90%) were obtained. Boiling these compounds with hydrazine hydrate gave the hydrazono derivatives **6** (78%) and **12** (90%), from which the derivatives **7**, **8** and **13** were obtained and satisfactorily characterized by elemental analysis and the ir and ^{1}H-nmr spectra.

When compound **4**.HCl was boiled with hydrazine hydrate in ethanol an unexpected compound was obtained (Scheme 2) with a molecular formula $C_9H_{13}N_7O_5$ from the elemental analysis that corresponds to $C_9H_5N_3OS$ (for **4**) + $2N_2H_4$. The ir spectra showed bands at about 3340, 3280 and 3170 for NH, a band at about 1670 for C=O and a band at about 1600 assigned to the C=N group. The ^{1}H-nmr spectra (trifluoroacetic acid) showed the expected signals for H-2, H-3 and H-4, a signal about δ = 5.50-5.75 (m), assigned to H-8 and two signals at about δ = 4.50-4.75 (dd, 1H) and 4.95-5.30 (1H) assigned to two non-equivalent protons at C-9. So that, one mole of hydrazine has been added to the double bond C(8)-C(9) on C-8. The position of the second mole of hydrazine is doubtful: it could be added to the double bond N(6)-C(6a) or it could be hydrazine of crystallization. At present we cannot give a solution. However one is to be expected from a crystallographic analysis. For these reasons in Scheme 2 we have formulated this compound in an indetermined form, **16**.

When **16** was boiled with acetone, **17** was obtained. The ir spectra of this compound showed bands at about 3220 (NH), 1645 (C=O) and 1600, 1585 (C=N); the ^{1}H-nmr (DMSO-d_6) spectra showed the expected signals for H-2, H-3, H-4, signals at δ = 1.35 (s) and 1.70 (s) for two non-equivalent methyl groups and signals at about δ = 5.60-5.75 (m, H-8) and δ = 4.50-4.65 (m, 2H-9). The ^{1}H-nmr spectra in trifluoroacetic acid was also recorded and it was very similar, but not identical, for values of δ >2.00, to the spectra of **16** in the same solvent. If the second molecule of hydrazine in **16** was hydrazine of crystallization, it would be expected to have practically identical spectra at δ >2.00 for **16** and **17** in the same solvent. According to this fact only it seems that in **16** the second molecule of hydrazine has been added to the double bond N(6)-C(6a) on C(6a) and it is not hydrazine of crystallization.

When compound **16** was warmed in boiling *N*,*N*-dimethylformamide **20** (91%) was obtained. This reaction has been hypothetically explained through the intermediates **18** and **19**. The ir spectra of **20** showed bands at about 3140 (NH), 1650 (C=O) and 1615, 1590 (C=N). The ^{1}H-nmr (DMSO-d_6) showed the expected signals for H-2, H-3, H-4 and H-9, a signal at δ = 4.65-4.85 (d) for two protons at C(10) and a signal at δ = 11.20 (s) for NH. The spectra in trifluoroacetic acid was similar.

Further studies on the diuretic and antihypertensive activities of the compounds reported in this paper are in course.

EXPERIMENTAL

Melting points were determined in a Kofler apparatus and they are uncorrected. Elemental analyses were obtained from vacuum-dried samples (over phosphorus pentoxide at 3-4 mm Hg, 2-3 hours, at about 60-70°). The ir spectra were recorded on a Perkin-Elmer 681 apparatus, using potassium bromide tablets for solid products and placing the products between crystals of sodium chloride for liquid products; the frequences were expressed in cm^{-1}. The ^{1}H-nmr spectra were obtained on a Perkin-Elmer R-32 (90 MHz) instrument, with TMS as the internal reference, at a concentration of about 0.1 g/ml and solvent as indicated; the chemical shifts are reported in ppm from TMS and are given in δ units.

Thin-layer chromatography (tlc) was carried out on silicagel (DSF-5, Cammaga 0.3 mm. thickness) with benzene: dioxane: acetic acid (90:25:40) as solvent and the plates were scanned under ultraviolet light, λ = 254 and 366 nm.

5*H*-[1,3]Thiazolo[3,2-*a*]pyrido[3,2-*e*]pyrimidin-5-one (**4**).

A suspension of **1** (20.0 g, 12.7 mmoles) in thionyl chloride (30 ml) was refluxed for 1.5 hours. The mixture was protected from humidity with a calcium chloride tube. The excess of thionyl chloride was removed in vacuum and the last portion of the reagent eliminated by repeated eva-

poration in vacuum with little portions of dried toluene. The residual crude material **2** was dissolved in chloroform (40 ml) and the solution cooled in an ice-bath. To the stirred solution were successively added in small portions, fresh dried pyridine (15 ml) and 2-aminothiazole (12.7 g, 12.7 mmoles). The mixture was warmed for 1 hour at 70°. Solvent was removed in vacuum and the residual portion of pryidine eliminated by repeated evaporation in vacuum with small portions of toluene. The residue of the crude amide **3** was suspended in *N,N*-dimethylformamide (25 ml) and concentrated hydrochloric acid (4.5 ml). The mixture was warmed for 1 hour at 120°, cooled and the solid material collected by filtration and washed with ethanol to give 24.3 g (80%) of the mono hydrochloride of **4**, mp 281-283° (DMSO/ethanol or DMSO/acetone); ir: 2100-2800 (=NH^+−), 1700 (C=O).

The free base **4** was obtained by treating **4**.HCl with sodium hydroxide mp 281-283° (ethanol); reported mp 281-283° [5], 283-285° [4].

5*H*-[1,3]Thiazolo[3,2-*a*]pyrido[3,2-*e*]pyrimidine-5-thione (**5**).

A mixture of **4**.HCl (10.0 g, 4.2 mmoles), phosphorus pentasulfide (10 g) and pryidine (20 ml) was refluxed for 1 hour under stirring. The cooled reaction mixture was treated with 2*N* ammonium hydroxide (200 ml) and extracted with chloroform (3 × 300 ml). The recollected organic extracts were washed with diluted ammonium hydroxide (200 ml) and water, dried (sodium sulfate) and filtered. Solvent was removed in vacuum and the residual material recrystallized to give 7.80 g (85%) of **5**, mp >250° (chloroform/methanol); ir: 1585 (C=N), 1380 (C=S).

Anal. Calcd. for $C_9H_5N_3S_2$: C, 49.31; H, 2.28; N, 19.17. Found: C, 49.38; H, 2.31; N, 19.20.

5-Hydrazono-5*H*-[1,3]thiazolo[3,2-*a*]pyrido[3,2-*e*]pyrimidine (**6**).

A mixture of **5** (5.0 g, 2.3 mmoles), ethanol (20 ml) and 60% hydrazine hydrate (20 ml) was warmed at about 60° for 0.5 hours. On cooling, **6** crystallized (3.4 g). Solvent of the filtrate was removed in vacuum and the residual oil treated with 2-propanol. A new portion of crystals was collected (0.5 g), total yield, 3.9 g (78%), mp 178-180° (toluene/methanol); ir: 3380 (NH), 1600 (C=N); nmr (DMSO-d_6): 6.00 (broad, NH_2, 2H), 6.82 (d, H-8, 1H), 7.35 (dd, H-3, 1H), 7.73 (d, H-9, 1H), 8.15 (dd, H-4, 1H), 8.38 (dd, H-2, 1H); nmr (trifluoroacetic acid): 7.26 (d, H-8, 1H), 7.62 (c, H-3, 1H), 8.32 (d, H-9, 1H), 8.62 (dd, H-4, 1H), 8.78 (dd, H-2, 1H).

Anal. Calcd. for $C_9H_7N_5S$: C, 49.77; H, 3.22; N, 32.26. Found: C, 49.75; H, 3.25; N, 32.29.

5-Acetylhydrazono-5*H*-[1,3]thiazolo[3,2-*a*]pyrido[3,2-*e*]pyrimidine (**7**).

Method A.

To a stirred solution of **6** (0.30 g, 1.4 mmoles) in chloroform (5 ml), acetyl chloride (1 ml) dissolved in chloroform (5 ml) was dropwise added. The mixture was stirred for 15 minutes at room temperature, methanol (10 ml) was added and the mixture stirred for 15 minutes more. Solvent was removed in vacuum and the residual material recrystallized from methanol/toluene to give 0.15 g (36%) of the monohydrochloride of **7**, mp 245-247°; ir: 2500-3350 (NH, NH^+), 1680 (C=O), 1595, 1605 (C=N); nmr (DMSO-d_6): 2.10 (s, CH_3, 3H), 5.50 (bs, NH^+, 1H), 7.88 (d, H-8, 1H), 7.98 (dd, H-3, 1H), 8.60 (d, H-9, 1H), 9.00 (dd, H-4, 1H), 9.37 (dd, H-2, 1H), 11.00 (s, NH-CO, 1H).

Anal. Calcd. for $C_{11}H_{10}ClN_5OS$: C, 44.67; H, 3.38; N, 23.69. Found: C, 44.96; H, 3.35; N, 23.49.

Method B.

To a stirred suspension of **6** (0.5 g, 2.3 mmoles) in toluene (10 ml) and triethylamine (0.23 g, 2.3 mmoles), a solution of acetyl chloride (0.18 g, 2.3 mmoels) in toluene (10 ml) was dropwise added. The mixture was stirred for 1 hour at room temperature. Water (25 ml) was added to the reaction mixture. The organic layer was separated and the solvent removed in vacuum. The resulting residue was recrystallized to give 0.50 g (83%) of **7**, mp 245-247° (from ethanol); ir: 3280 (NH), 1680 (C=O), 1605 (C=N).

Anal. Calcd. for $C_{10}H_9N_5OS$: C, 48.58; H, 3.64; N, 28.34. Found: C, 48.62; H, 3.70; N, 28.45.

5-Isopropylidenehydrazono-5*H*-[1,3]thiazolo[3,2-*a*]pyrido[3,2-*e*]pyrimidine (**8**).

A mixture of **6** (0.20 g, 0.92 mmole) and acetone (5 ml) was boiled for 20 minutes. Solvent was removed in vacuum and the residual material recrystallized to give 0.20 g of **8**, mp 169-171° (from acetone); ir: 1590, 1605, 1625 (C=N); nmr (trifluoroacetic acid): 2.80 (s, 2 CH_3, 6H), 7.68 (d, H-8, 1H), 7.95 (dd, H-3, 1H), 8.80 (d, H-9, 1H), 8.96 (dd, H-4, 1H), 9.12 (dd, H-2, 1H).

Anal. Calcd. for $C_{12}H_{11}N_5S$: C, 56.03; H, 4.28; N, 27.24. Found: C, 55.88; H, 4.10; N, 26.83.

5*H*-Dipyrido[1,2-*a*:3′,2′-*e*]pyrimidin-5-one (**10**).

The acyl chloride **2** was prepared from **1** (25.0 g, 15.9 mmoles) and thionyl chloride (35 ml) as above reported in the preparation of **4**. The crude acyl chloride **2** was dissolved in chloroform (50 ml) and dried pyridine (17 ml). The reaction mixture was cooled in an ice-bath and, under stirring, 2-aminopyridine (15.0 g, 15.9 mmoles) was added in small portions, the mixture was stirred for 1.5 hours. Solvent was removed in vacuum and the residual oil of crude **9** dissolved in DMF (25 ml). The solution was warmed at about 100° for 1 hour and cooled. The solid was collected by filtration to give 30.0 g (80%) of the monohydrochloride of **10**, mp 242-244° (from DMSO/acetone, reported [5], mp 242-244°); ir: 2300-2900 (NH^+), 1710 (C=O), 1650, 1610 (C=N); nmr (DMSO-d_6): 7.60-7.95 (m, 1H), 8.00-8.15 (m, 2H), 8.45-8.70 (m, 1H), 8.75-8.90 (m, 1H), 9.15-9.25 (m, 1H), 9.85-9.95 (m, 1H).

Anal. Calcd. for $C_{11}H_8ClN_3O$: C, 56.54; H, 3.45; N, 17.98; Cl, 15.57. Found: C, 56.48; H, 3.51; N, 18.00; Cl; 15.12.

The free base **10** was obtained by treating **10**.HCl with sodium hydroxide, mp 222-224° (from DMSO/methanol, reported [5] [7], mp 223°).

5*H*-Dipyrido[1,2-*a*:3′,2′-*e*]pyrimidine-5-thione (**11**).

This compound was obtained from **10** (10.0 g, 4.3 mmoles) in a similar way to the one above reported for **5**, 8.2 g (90%), mp 219-221° (from ethanol); ir: 1630, 1600 (C=N), 1370 (C=S); nmr (deuteriochloroform/-DMSO-d_6): 7.05-7.25 (m, H-9), 7.40-7.95 (m, H-3 H-7 H-8, 3H), 8.70-8.85 (dd, H-4, 1H), 9.05-9.20 (dd, H-2, 1H), 9.40-9.55 (dd, H-10, 1H).

Anal. Calcd. for $C_{11}H_7N_3S$: C, 61.97; H, 3.28; N, 19.72. Found: C, 61.95; H, 3.30; N, 19.69.

5-Hydrazono-5*H*-dipyrido[1,2-*a*:3′,2′-*e*]pyrimidine (**12**).

This compound was prepared in a similar way to the one above reported for **6**. Starting from 5.0 g (2.35 mmoles) of **11** we obtained 4.45 g (90%) of **12**, mp 149-151° (from toluene/methanol); ir: 3340 (NH), 1645, 1600 (C=N).

Anal. Calcd. for $C_{11}H_9N_5$: C, 62.56; H, 4.26; N, 33.17. Found: C, 62.52; H, 4.30; N, 33.15.

The dihydrochloride was prepared from methanol/hydrochloric acid, mp 228-230°; ir: 2400-3200 (NH^+), 1640, 1620 (C=N); nmr (deuterium oxide): 7.30 (m, H-9, $J_{9,10}$ = 10 Hz, 1H), 7.45 (dd, H-7, $J_{7,8}$ = 9 Hz, $J_{7,9}$ = 1.5 Hz, 1H), 7.75 (dd, H-3, $J_{3,4}$ = 9 Hz, 1H), 8.05 (m, H-8, $J_{8,9}$ = 7 Hz, 1H), 8.38 (dd, H-4, 1H), 8.85 (dd, H-2, $J_{2,3}$ = 5 Hz, $J_{2,4}$ = 1.5 Hz, 1H), 9.26 (dd, H-10, 1H).

Anal. Calcd. for $C_{11}H_{11}Cl_2N_5$: C, 46.47: H, 3.87; N, 24.64. Found: C, 46.74; H, 4.03; N, 24.50.

5-Propionylhydrazono-5*H*-dipyrido[1,2-*a*:3′,2′-*e*]pyrimidine (**13**).

This compound was prepared in a similar way as above described for **7**. Starting from **12** (1.0 g, 4.74 mmoles), triethylamine (0.48 g, 4.74 mmoles), toluene (15 ml) and propionyl chloride (0.44 g, 4.74 mmoles) in toluene (15 ml), to give 1.05 g (83%) of **13**, mp 190-192° (from ethanol); ir: 3320 (NH), 1670 (C=O), 1650, 1610 (C=N).

Anal. Calcd. for $C_{14}H_{13}N_5O$: C, 62.92; H, 4.87; N, 26.22. Found: C, 62.70; H, 4.92: N, 26.15.

5*H*-Pyrido[3,2-*e*]pyrimido[1,2-*a*]pyrimidine-5-one (**15**).

A solution of crude **2** in chloroform (25 ml), obtained from **1** (5.0 g, 3.7 mmoles) as above described in the preparation of **4** was dropped on a stir-

red suspension of 2-aminopyrimidine (3.0 g, 3.17 mmoles) in chloroform (25 ml) and pyridine (3 ml), cooled in an ice-bath. The reaction mixture was stirred for 1.5 hours and filtered. Solvent was removed in vacuum and the residual oil of crude **14** dissolved in DMF (5 ml). The solution was warmed for 15 minutes at 100° and cooled. The crystals of the monohydrochloride of **15** were collected and washed with acetone to give 3.7 g (50%) of **15**.HCl, mp >250° (from TFA/methanol); ir: 2225-2900 (NH^+), 1740 , 1715 (C=O); nmr (trifluoroacetic acid): 7.65-7.80 (m, H-9, 1H), 7.90-8.10 (dd, H-3, 1H), 9.10-9.25 (dd, H-4, 1H), 9.35-9.60 (m, H-2, H-8, H-10, 3H).

Anal. Calcd. for $C_{10}H_7ClN_4O$: C, 51.17; H, 2.98; N, 23.88. Found: C, 51.39; H, 3.07; N, 23.62.

6*a*,8-Dihydrazino-6,6*a*,8,9-tetrahydro-5*H*-[1,3]thiazolo[3,2-*a*]pyrido[3,2-*e*]-pyrimidin-5-one (**16**).

A mixture of **4**.HCl (15.0 g, 62.6 mmoles), ethanol (50 ml) and 60% hydrazine hydrate (50 ml) was boiled for 45 minutes. After dilution with ethanol (100 ml), the warmed suspension was filtered and the solid washed with hot ethanol to give 15.0 g (90%) of **16**, mp >250°; ir: 3340, 3280, 3170 (NH), 1640 (C=O), 1600 (C=N); nrm (trifluoroacetic acid): 4.50-4.75 (dd, H-9, $J_{9,8}$ = 7 Hz (*trans*), $J_{9,9}$ = 11 Hz, 1H), 4.95-5.30 (dd, H-9, $J_{9,8}$ = 1.5 Hz (*cis*), 5.50-5.75 (m, H-8, 1H), 7.40-7.70 (dd, H-3, $J_{3,4}$ = 7.5 Hz, 1H), 8.50-8.70 (dd, H-4, 1H), 8.23-8.90 (dd, H-2, $J_{2,3}$ = 4.5 Hz).

Anal. Calcd. for $C_9H_{13}N_7OS$: C, 40.44; H, 4.90; N, 36.68; S, 12.00. Found: C, 40.49; H, 5.10; N, 36.56; S, 12.21.

8,9-Dihydro-8-(N^2-isopropylidenehydrazino)-5*H*-[1,3]thiazolo]3,2-*a*]pyido[3,2-*e*]pyrimidin-5-one (**17**).

A suspension of **16** (0.50 g, 1.87 mmoles) in acetone (5 ml) was boiled for 15 minutes, and the cold suspension filtered to give 0.46 g (90%) of **17**, mp 200-202°; ir: 3220 (NH), 1645 (C=O), 1600, 1585 (C=N); nmr (DMSO-d_6): 1.35 (s, CH_3, 3H), 1.70 (s, CH_3, 3H), 4.50-4.65 (m, H-9, 2H), 5.60-5.75 (m, H-8, 1H), 6.03 (s, NH, 1H), 7.30-7.50 (dd, H-3, $J_{3,4}$ = 7.5 Hz, 1H), 8.20-8.40 (dd, H-4, 1H), 8.60-8.75 (dd, H-2, $J_{2,3}$ = 4.5 Hz, $J_{2,4}$ = 2 Hz, 1H); nmr (trifluoroacetic acid): 1.50 (s, CH_3, 3H), 1.75 (s, CH_3, 3H), 4.75-4.90 (dd, H-9, 2H), 5.90-6.05 (dd, H-8, 1H), 7.50-7.70 (dd, H-3, 1H), 8.40-8.60 (dd, H-4, 1H), 8.75-8.90 (dd, H-2, 1H).

Anal. Calcd. for $C_{12}H_{13}N_5OS$: C, 52.34; H, 4.76; N, 25.43; S, 11.64. Found: C, 52.31; H, 4.45; N, 25.56; S, 11.59.

6,10-Dihydro-5*H*-pyrido[3′,2′:5,6]pyrimido[2,1-*c*][1,2,4]triazin-5-one (**20**).

A suspension of **16** (15.0 g, 56.2 mmoles) in DMF (35 ml) was boiled for 0.5 hours. The cold suspension was diluted with ethanol (100 ml) and the solid material collected by filtration and washed with ethanol to give 10.3 g (91%) of **20**, mp >250° (from DMF/acetone); ir: 3140 (NH), 1650 (C=O), 1615, 1590 (C=N); nmr (DMSO-d_6): 4.65-4.85 (d, H-10, 2H), 7.20-7.55 (m, H-9, H-3, 2H), 8.20-8.40 (dd, H-4, 1H), 8.55-8.65 (dd, H-2, 1H), 11.20 (s, 1H, NH); nmr (trifluoroacetic acid): 5.20 (d, H-10, 2H), 7.45-7.75 (m, H-9, H-3, 2H), 8.45-8.75 (dd, H-4, 1H), 8.75-8.95 (dd, H-2, 1H).

Anal. Calcd. for $C_9H_7N_5O$: C, 53.72; H, 3.51; N, 34.81. Found: C, 53.50; H, 3.54; N, 35.17.

REFERENCES AND NOTES

[1] J. P. Osselaere and C. L. Lapiere, *Eur. J. Med. Chem.*, **9**, 305 (1974); J. P. Osselaere, *Pharm. Belg.*, **29**, 145 (1974); *Chem. Abstr.*, **81**, 63579p (1974); J. P. Osselaere, *Eur. J. Med. Chem.*, **9**, 310 (1974); J. P. Osselaere, *Arzneim.-Forsch.*, **25**, 1712 (1975); J. P. Osselaere, *J. Pharm. Belg.*, **31**, 51 (1976).

[2] H. A. Parish, R. D. Gilliom, N. P. Purcell, R. K. Browne, R. F. Spirr and H. D. White, *J. Med. Chem.*, **25**, 98 (1982).

[3] K. Noda, A. Nakagawa, K. Yamagata and H. Ide (Japan Kokai), Japan Patent 76,146,496 (1976); *Chem. Abstr.*, **87**, 53374w (1977); Pfizer Inc., British Patent 1,465,353 (1977); *Chem. Abstr.*, **87**, 85036k (1977); K. Noda, A. Nakagawa, T. Motomura, S. Miyata and S. Tosu, German Patent 2,523,730 (1976); *Chem. Abstr.*, **85**, 33068m (1976); Laboratories SMB, French Patent 2,206,101 (1974); *Chem. Abstr.*, **82**, 47720g (1975).

]4] F. L. Merchan, J. Garin, E. Melendez and T. Tejero., *Synthesis*, 154 (1983).

[5] A. Monge, V. Martinez, E. Cenarruzabeitia, B. Lasheras and E. Fernandez-Alvarez, *Eur. J. Med. Chem.*, **20**, 61 (1985).

[6] C. V. Greco and J. F. Warchol., *J. Org. Chem.*, **36**, 605 (1971).

[7] S. Carboni and M. Pardi, *Ann. Chim.* (Rome), **49**, 1220 (1959).