Amino Acids in the Synthesis of Heterocyclic Systems. The Synthesis of 4-Oxo-4*H*-pyrido[1,2-*a*]pyridines and 4-Oxo-4*H*-pyrido[1,2-*a*]pyrimidines

Janez Smodiš, Branko Stanovnik* and Miha Tišler

Department of Chemistry, University of Ljubljana,
61000 Ljubljana, Slovenia

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The pyridine and quinoline derivatives **2, 3,** and **6** with an activated methylene group at α-position in respect to the ring nitrogen atom were converted with **1, 8,** or **9** into fused pyrido[1,2-*a*]pyridine derivatives **4, 5, 7,** and **10**. In an analogous manner were the aminopyridines **16** and **17** transformed with thiazolone **9** into pyrido[1,2-*a*]pyrimidine derivatives **20, 21, 25,** and **26**.

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The chemistry of pyridoazines with a bridgehead nitrogen atom, such as quinolizines and azaquinolizines has been extensively reviewed in recent years [1-7].

In connection with our studies of heteroaryl substituted α-amino acids and their derivatives [8-10] and heterocyclic systems, in which an amino acid structural element is incorporated in the heterocyclic system [11,12] we have reported, recently, the transformation of nitrogen containing heterocyclic compounds, in which an active methyl group is attached at the α-position with respect to the ring nitrogen atom. They have been converted into the corresponding enamines, followed by treatment with 2-phenyl-5(4*H*)-oxazolone and cyclization into fused pyridinones [13,14].

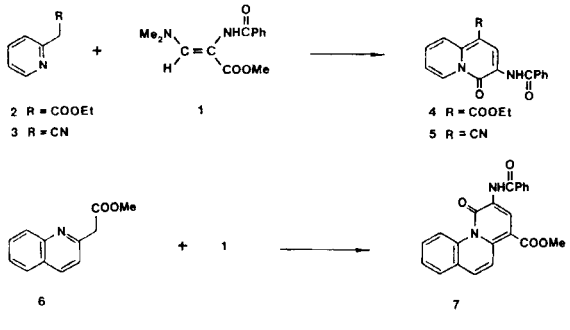
An analogous reaction sequence has been used for the synthesis of fused pyrimidinones from α-amino heterocycles [15-16].

2-Methyl substituted nitrogen containing six-membered heterocycles generally do not react with methyl 2-benzoylamino-3-dimethylaminopropenoate to give the corresponding pyrido[1,2-*a*]pyridine derivatives. Therefore, the corresponding enamines have been prepared with either DMFDMA or *t*-butoxy-bis(dimethylamino)methane. They have been transformed further with 2-phenyl-5(4*H*)-oxazolone into bicyclic systems [14].

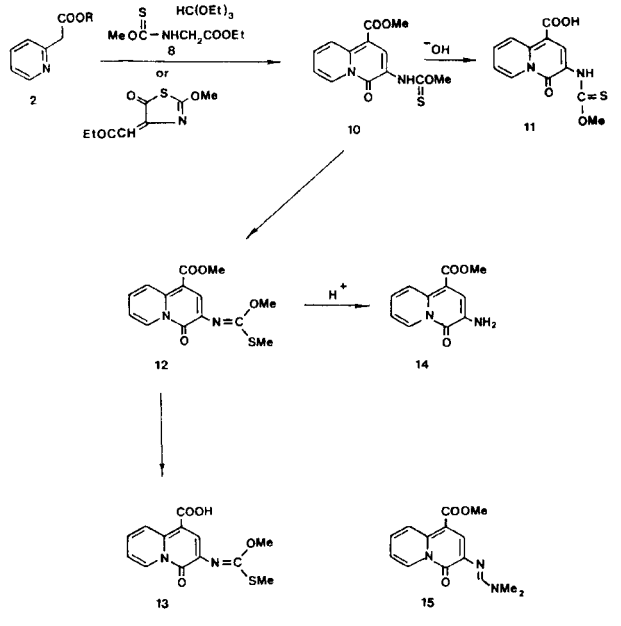
When the methylene group at the α-position with respect to the ring nitrogen atom is activated with an ester group, it reacts smoothly with methyl 2-benzoylamino-3-dimethylaminopropenoate to give the corresponding pyrido[1,2-*a*]pyridine derivatives. In this connection, methyl 2-pyridinylacetate (**2**) or 2-cyanomethylpyridine (**3**) were transformed with methyl 2-benzoylamino-3-dimethylaminopropenoate (**1**) into 3-benzoylamino-1-methoxycarbonyl-4*H*-pyrido[1,2-*a*]pyridin-4-one (**4**) and 3-benzoylamino-1-cyano-4*H*-pyrido[1,2-*a*]pyridin-4-one (**5**). Methyl 2-quinolinylacetate (**6**) gave the corresponding pyrido[1,2-*a*]quinoline derivative **7** in low yield (Scheme 1).

By heating methyl 2-pyridinylacetate (**2**) with a mixture of triethyl orthoformate and *N*-methoxythiocarbonylglycine (**8**) in acetic anhydride the corresponding 1-methoxycarbonyl-3-methoxythiocarbonylamino-4*H*-quinolizin-4-one **10** was formed. The hydrolysis of **10** with sodium hydroxide in ethanol gave the corresponding carboxylic acid derivative **11**. The methylation of the compound **10** with methyl iodide took place at the sulfur atom of the thiocarbonyl group at position 3 to give *O,S*-dimethyl (1-methoxycarbonyl-4-oxo-4*H*-quinolizinyl-1)isocyanato *O,S*-dimethyl acetal **12**. This is stable in basic media, so that selective

Scheme 1



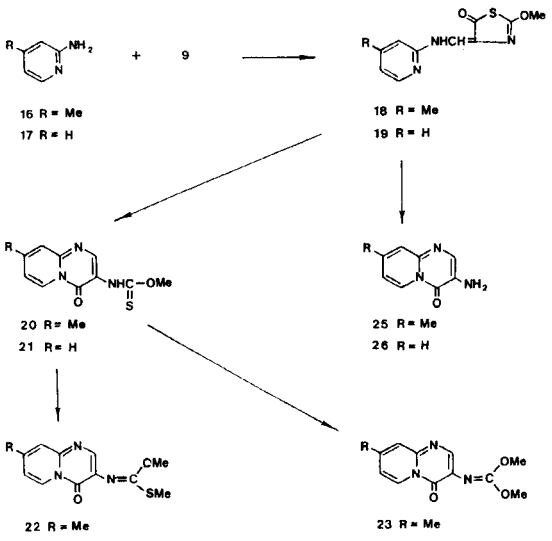
Scheme 2



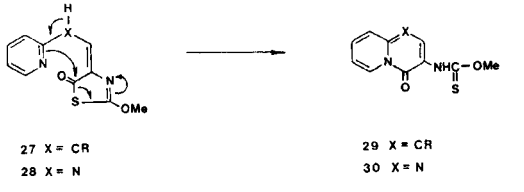
hydrolysis of the ester group gave the carboxylic acid **13**. On the other hand, the selective hydrolysis of *O,S*-dimethyl acetal group in acidic media afforded 3-amino-1-methoxycarbonyl-4*H*-quinolizin-4-one **14**. The amino group of **14** reacts with DMFDMA to give the corresponding *N,N*-dimethylformamidine derivative **15** (Scheme 2).

2-Methoxy-4-ethoxymethylene-5(4*H*)-thiazolone (**9**) reacts with a heterocyclic amine, such as pyridine derivatives **16** and **17** to give 4-heteroarylaminomethylene-2-methoxy-5(4*H*)-thiazolones **18a** and **19**. They are transformed in the presence of a base or a nucleophile into the corresponding pyrido[1,2-*a*]pyrimidines **20** and **21**. Compound **20** reacts with methyl iodide to form the corresponding *O,S*-dimethyl acetal **22**. This is transformed by prolonged heating into the corresponding *O,O*-dimethyl acetal **23**. The hydrolysis of *O,S*-dimethyl acetal **22** in ethanolic solution of hydrogen chloride gives the amino compound **24** in the form of the hydrogen chloride salt, which gives, after neutralization, the free 3-aminopyrido[1,2-*a*]-pyrimidine **23** (Scheme 3).

Scheme 3



Scheme 4



The formation of pyrido[1,2-*a*]pyridine derivative **10** and pyrido[1,2-*a*]pyrimidine derivatives **20, 21, 25,** and **26** can be explained by cyclization of the corresponding thiazolone intermediates **27** and **28** into derivatives of bicyclic systems **29** and **30**. They are further converted into the final products, dependent on the reaction conditions (Scheme 4).

EXPERIMENTAL

Melting points were taken on a Kofler micro hot stage. The ^{1}H nmr spectra were recorded on a Varian E-360 and JEOL JNM FT90QFT Spectrometers and microanalyses for C, H, and N on a Perkin-Elmer Analyser 2400.

The following compounds were prepared according to the procedures described in the literature: methyl 2-benzoylamino-3-dimethylaminopropenoate (**1**) [10] and 4-ethoxymethylene-2-methoxy-5(4*H*)-thiazolone (**9**) from methoxythiocarbonylglycine (**8**) and triethyl orthoformate in acetic anhydride [17].

3-Benzoylamino-1-methoxycarbonyl-4*H*-quinolizin-4-one (**4**).

A mixture of equimolar amounts of methyl 2-pyridinylacetate and methyl 2-benzoylamino-3-dimethylaminopropenoate (**1**) in acetic acid (2 ml of acetic acid/mmole of substrate was heated under reflux for 4 hours. The crystalline material, formed after cooling, was collected by filtration to give **4** in 55% yield, mp 189-190° (from ethanol); ^{1}H nmr (deuteriochloroform): δ 4.0 (s, 5H, COOMe), 7.22 (ddd, 1H, H_7), 7.4-7.75 (m, 4H, H_8, Ph), 7.95-8.2 (m, 2H, Ph), 9.1-9.45 (m, H_6, H_9, NHCO), 9.82 (s, 1H, H_2), $J_{H_6,H_7} = J_{H_7,H_8} = 6.5$ Hz, $J_{H_7,H_9} = 1.0$ Hz.

Anal. Calcd. for $C_{18}H_{14}N_2O_4$: C, 67.08; H, 4.38; N, 8.69. Found: C, 66.98; H, 4.35; N, 8.73.

In the same manner the following compounds were prepared:

3-Benzoylamino-2-cyano-4*H*-quinolizin-4-one (**5**).

This compound was prepared from 2-pyridylacetonitrile and **1** in 99% yield, mp 227-229° (from acetic acid); ^{1}H nmr (deuteriochloroform): δ 7.22 (ddd, 1H, H_7), 7.4-7.74 (m, 4H, H_8, Ph), 7.9-8.15 (m, 3H, Ph, NHCO), 9.0-9.25 (m, 2H, H_6, H_9), $J_{H_6,H_7} = J_{H_7,H_8} = 6.5$ Hz, $J_{H_7,H_9} = 1.0$ Hz.

Anal. Calcd. for $C_{17}H_{11}N_3O_2$: C, 70.58; H, 3.83; N, 14.52. Found: C, 70.40; H, 3.78; N, 14.46.

3-Benzoylamino-1-methoxycarbonyl-4*H*-benzo[*f*]quinolizine (**7**).

This compound was prepared from methyl 2-quinolinacetate and **1**. The crude product was separated into two fractions by chromatothrone using diisopropyl ether as the eluent. The first fraction is **7** in 22% yield, mp 120° (from ethanol); ^{1}H nmr (deuteriochloroform): δ 4.0 (s, 3H, COOMe), 7.4-7.8 (m, 8H, Ph, H_7, H_8, H_9), 7.9-8.2 (m, 2H, Ph), 8.9 (d, 1H, H_{10}), 9.52 (s, 1H, H_3), 9.45 (m, 1H, H_6), 9.75 (br s, 1H, NHCO), $J_{H_{10},H_{11}} = 10.0$ Hz.

Anal. Calcd. for $C_{22}H_{16}N_2O_4$: C, 70.96; H, 4.33; N, 7.52. Found: C, 70.64; H, 4.45; N, 7.51.

1-Methoxycarbonyl-3-methoxythiocarbonylamino-4-quinolizin-4-one (**10**).

A mixture of equimolar amounts of methyl 2-pyridinylacetate (**2**), triethyl orthoformate and *N*-methoxythiocarbonylglycine (**8**) in acetic anhydride (2 ml/mmole) was heated in an oil bath at 100° for 6 hours. The precipitate was, after cooling, collected by filtration to give **10** in 38% yield, mp 192-194° (from ethanol); ^{1}H nmr (deuteriochloroform): δ 3.95 (s, 3H, COOMe), 4.15 (s, 3H, CSOMe), 7.17 (ddd, 1H, H_7), 7.76 (ddd, 1H, H_8), 9.1-9.4 (m, 3H, H_6, H_9, H_2), 9.55 (br s, 1H, NHCS), $J_{H_6,H_7} = 7.0$ Hz, $J_{H_7,H_9} = 1.0$ Hz, $J_{H_8,H_9} = 6.0$ Hz.

Anal. Calcd. for $C_{13}H_{12}N_2O_4S$: C, 53.42; H, 4.14; N, 9.58. Found: C, 53.42; H, 4.11; N, 9.85.

1-Carboxy-3-methoxythiocarbonylamino-4*H*-quinolizin-4-one (**11**).

A mixture of **10** (100 mg) in methanol (4 ml) and sodium hydroxide (5*N*, 1 ml) was stirred at room temperature for 24 hours. The solvent was evaporated *in vacuo*, water (5 ml) was added to the residue and neutralized with hydrochloric acid (10%). The precipitate was collected by filtration to give **11**, in 63% yield, mp 235-239° (from ethanol); ^{1}H nmr (DMSO-d_6): δ 4.05 (s, 3H, OMe), 7.50 (ddd, 1H, H_7), 7.95 (ddd, 1H, H_8), 8.72 (br s, 1H, H_2), 9.3 (dd, 2H, H_6, H_9), 10.58 (br s, 1H, NHCS), 12.9-13.9 (br s, 1H, COOH), $J_{H_6,H_7} = J_{H_7,H_8} = 6.5$ Hz, $J_{H_7,H_9} = J_{H_6,H_8} = 1.0$ Hz, $J_{H_8,H_9} = 8.0$ Hz.

Anal. Calcd. for $C_{12}H_{10}N_2O_4S$: C, 51.79; H, 3.62; N, 10.07. Found: C, 51.28; H, 3.65; N, 9.90.

1-Methoxycarbonyl-3-(1-methylthio-1-methoxymethylene)amino-4*H*-quinolizin-4-one (**12**).

A mixture of **10** (150 mg), sodium methoxide, prepared from sodium (25 mg) and methanol (5 ml) and methyl iodide (0.1 ml) was left at room temperature for one hour. The solvent was evaporated *in vacuo*, the residue was suspended in water (5 ml) and extracted with chloroform (3 times, 5 ml each time). The crude product was purified by chromatothrone with a mixture of chloroform and methanol, 25:1, as eluent, to give **12**, yield 65%, mp 118-120° (from a mixture of toluene and *n*-hexane); ^{1}H nmr (deuteriochloroform): δ 2.38 (s, 3H, SMe), 3.92 (s, 3H, COOMe), 4.1 (s, 3H, OMe), 7.15 (ddd, 1H, H_7), 7.58 (ddd, 1H, H_8), 8.13 (s, 1H, H_2), 9.18-9.45 (m, 2H, H_6, H_9), $J_{H_6,H_7} = J_{H_7,H_8} = 6.5$ Hz, $J_{H_7,H_9} = 1.0$ Hz, $J_{H_8,H_9} = 8.0$ Hz.

Anal. Calcd. for $C_{14}H_{14}N_2O_4S$: C, 54.89; H, 4.61; N, 9.14. Found: C, 55.03; H, 4.66; N, 9.08.

1-Carboxy-3-(1-methylthio-1-methoxymethylene)amino-4-quinolizin-4-one (**13**).

To a suspension of **12** (85 mg) in methanol (2 ml), aqueous solution of sodium hydroxide (1*N*, 2 ml) was added and the mixture was heated under reflux for 45 minutes. The solvent was evaporated *in vacuo*, water (5 ml) was added to the residue, and the solution was adjusted with hydrochloric acid (10%) to *p*H = 3. The precipitate was collected by filtration to give **13** in 61% yield, mp 225-229° (from ethanol); ^{1}H nmr (DMSO-d_6): δ 2.37 (s, 3H, SMe), 4.03 (s, 3H, OMe), 7.4 (dd, 1H, H_7), 7.82 (ddd, 1H, H_8), 7.97 (s, 1H, H_2), 9.25 (m, 2H, H_6, H_9), 11.9-13.2 (br s, 1H, COOH, $J_{H_6,H_7} = J_{H_7,H_8} = 6.5$ Hz, $J_{H_6,H_8} = J_{H_7,H_9} = 1.0$ Hz, $J_{H_8,H_9} = 8.0$ Hz.

Anal. Calcd. for $C_{13}H_{12}N_2O_4S$: C, 53.42; H, 4.14; N, 9.58. Found: C, 53.04; H, 4.20; N, 9.66.

3-Amino-1-methoxycarbonyl-4*H*-quinolizin-4-one Hydrochloride (**14**).

To a solution of **12** (150 mg) in ethanol (5 ml) hydrochloric acid (37%, 0.5 ml) was added and the mixture was stirred for 2 hours at room temperature. The precipitate was collected by filtration to give **14** in 86% yield, mp 210° dec (from DMF); ^{1}H nmr (DMSO-d_6): δ 3.9 (s, 3H, COOMe), 5.5-6.2 (b s, 3H, NH_3^+), 7.52 (ddd, 1H, H_7), 7.75-8.15 (br s, 1H, H_8), 8.3-8.7 (br s, 1H, H_2), 8.95-9.3 (m, 2H, H_6, H_9), $J_{H_6,H_7} = J_{H_7,H_8} = 6.5$ Hz, $J_{H_7,H_9} = 1.0$ Hz.

Anal. Calcd. for $C_{11}H_{11}ClN_2O_3$: C, 51.87; H, 4.35; N, 11.00. Found: C, 51.73; H, 4.47; N, 11.00.

1-Methoxycarbonyl-3-(*N,N*-dimethylaminomethylene)amino-4*H*-quinolizin-4-one (**15**).

To a solution of **14** (30 mg) in toluene (5 ml) DMFDMA (0.1 ml) was added and the mixture was heated under reflux for 5 hours. The solvent was evaporated *in vacuo* and the solid residue recrystallized from a mixture of toluene and *n*-hexane to give **15** in 60% yield, mp 157-158°; ^{1}H nmr (deuteriochloroform): δ 3.1 (s, 6H, NMe_2), 3.93 (s, 3H, COOMe), 7.07 (ddd, 1H, H_7), 7.42 (d, 1H, H_8), 8.22 (s, 1H, CH=), 9.05-9.38 (m, 2H, H_6, H_9), $J_{H_6,H_7} = J_{H_6,H_7} = 7.0$ Hz, $J_{H_7,H_9} = 1.5$ Hz, $J_{H_8,H_9} = 8.0$ Hz.

Anal. Calcd. for $C_{14}H_{15}N_3O_3$: C, 61.53; H, 5.53; N, 15.38. Found: C, 61.28; H, 5.62; N, 15.67.

4-(4-Methyl-2-pyridinylamino)methylene-5(4*H*)-thiazolone (**18**).

A mixture of equivalent amounts of **9**, 2-amino-4-methylpyridine (**16**) and triethylamine in ethanol (5 ml/mmole) was left at room temperature for 24 hours. The precipitate was collected by filtration to give **18** in 37% yield, mp 184-186° (from ethanol); ^{1}H nmr (DMSO-d_6): δ 2.3 (s, 3H, 4'-Me), 4.15 (s, 3H, OMe), 6.98 (d, 1H, 5'-H), 7.2 (s, 1H, 3'-H), 8.25 (d, 1H, 6'-H), 8.35 (br s, 1H, NHC*H*), 10.55 (br s, 1H, N*H*CH), $J_{5'-H,6'-H} = 5.0$ Hz.

Anal. Calcd. for $C_{11}H_{11}N_3O_2S$: C, 53.00; H, 4.45; N, 16.86. Found: C, 53.02; H, 4.46; N, 17.17.

In the same manner the following compound was prepared:

2-Methoxy-4-(2-pyridinylamino)methylene-5(4*H*)-thiazolone (**19**).

This compound was prepared from **9** and 2-aminopyridine (**17**) in 40% yield, mp 168-169°, (from toluene); ^{1}H nmr (deuteriochloroform): δ 4.1 (s, 3H, OMe), 6.80-7.15 (m, 2H, 3'-H, 5'-H), 7.7 (ddd, 1H, 4'-H), 8.0-8.17 (br s, 2H, NHCH), 8.37 (dd, 1H, 6'-H), $J_{3'H,4'-H} = J_{4'-H,5'-H} = 7.7$ Hz, $J_{4'-H,6'-H} = 2.0$ Hz, $J_{5'-H,6'-H} = 5.0$ Hz.

Anal. Calcd. for $C_{10}H_9N_3O_2S$: C, 51.05; H, 3.86; N, 17.86. Found: C, 51.01; H, 3.91; N, 18.17.

8-Methyl-3-methoxythiocarbonylamino-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**20**).

A suspension of **18** (230 mg) in sodium methoxide, prepared from sodium (40 mg) in methanol (4 ml) was stirred at room temperature for 24 hours. Methanol was evaporated *in vacuo*, water (5 ml) was added to the solid residue and the solution was adjusted with hydrochloric acid (10%) to *p*H = 5. The precipitate was collected by filtration to give **20**, yield 60%, mp 200-204° (from a mixture of chloroform and ethanol, 1:1); ^{1}H nmr (deuteriochloroform): δ 2.5 (s, 3H, 8-Me), 4.18 (s, 3H, OMe), 7.02 (dd, 1H, H_7), 7.5 (d, 1H, H_9), 8.65 (br s, 1H, NHCS), 8.8 (s, 1H, H_2), 8.95 (d, 1H, H_6), $J_{H_6,H_7} = 7.5$ Hz, $J_{H_7,H_9} = 1.5$ Hz, ms: m/e 249 (66%) (M^+).

Anal. Calcd. for $C_{11}H_{11}N_3O_2S$: C, 53.00; H, 4.45; N, 16.86. Found: C, 52.89; H, 4.39; N, 17.03.

3-Methoxythiocarbonylamino-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**21**).

A mixture of *N*-methoxythiocarbonylglycine (**19**) (0.15 g, 0.001 mole) and triethylorthoformate (0.18 g) in acetic anhydride (2 ml) was heated at 100° for 1 hour. The volatile components were evaporated *in vacuo* and the oily residue was dissolved in ethanol (7 ml). A mixture of 2-aminopyridine (**17**, 94 mg, 0.001 mole) and triethylamine (112 mg, 0.0011 mole) was added and the mixture was left at room temperature for one week. The precipitate was collected by filtration to give **21**, yield 23%, mp 207-210° (from ethanol); ^{1}H nmr (deuteriochloroform): δ 4.03 (s, 3H, OMe), 7.5

(ddd, 1H, H_7), 7.82 (dd, 1H, H_9), 8.1 (s, 1H, H_2), 9.12 (dd, 1H, H_6), 10.65 (br s, 1H, NHCS), $J_{H_6,H_7} = J_{H_7,H_8} = 7.0$ Hz, $J_{H_6,H_8} = J_{H_7,H_9} = 1.5$ Hz, $J_{H_8,H_9} = 8$ Hz.

Anal. Calcd. for $C_{10}H_9N_3O_2S$: C, 51.05; H, 3.86; N, 17.86. Found: C, 50.72; H, 3.95; N, 18.22.

3-Dimethoxymethyleneamino-8-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**23**) and 8-Methyl-3-(1-methylthio-1-methoxymethylene)amino-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**22**).

A mixture of **21** (180 mg) and sodium methoxide, prepared from sodium (40 mg) in methanol (5 ml) and methyl iodide (0.1 ml) was stirred at room temperature for 3 hours. The volatile components were evaporated *in vacuo*, water (5 ml) was added to the residue and neutralized with hydrochloric acid (10%). The product was extracted with chloroform (3 times, 10 ml each time) and dried with sodium sulphate. The product was purified by chromatothrone, using chloroform as eluent to give, after evaporation of the solvent, **22**, yield 60 mg (23%), mp 158-160° (from a mixture of toluene and *n*-hexane); ^{1}H nmr (deuteriochloroform): δ 2.37 (s, 3H, SMe), 2.24 (s, 3H, OMe), 6.95 (dd, 1H, H_7), 7.42 (d, 1H, H_9), 8.05 (s, 1H, H_2), 9.0 (d, 1H, H_6), $J_{H_6,H_7} = 7.5$ Hz, $J_{H_7,H_9} = 1.5$ Hz.

Anal. Calcd. for $C_{12}H_{13}N_3O_2S$: C, 54.74; H, 4.98; N, 15.96. Found: C, 54.90; H, 5.00; N, 16.32.

The second fraction gave **23**, yield 8 mg (3%), mp 169-171° (from a mixture of toluene and *n*-hexane); ^{1}H nmr (deuteriochloroform): δ 2.42 (s, 3H, 8-Me), 3.90 (s, 6H, 2 x OMe), 6.90 (dd, 1H, H_7), 7.38 (d, 1H, H_9), 8.15 (s, 1H, H_2), 9.0 (d, 1H, H_6), $J_{H_6,H_7} = 7.5$ Hz, $J_{H_7,H_9} = 1.5$ Hz.

Anal. Calcd. for $C_{12}H_{13}N_3O_3$: C, 58.29; H, 5.30; N, 16.99. Found: C, 58.20; H, 5.31; N, 17.30.

3-Amino-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**26**).

A mixture of **19** and sodium methoxide, prepared from sodium (35 mg) and methanol (5 ml), was left at room temperature for 24 hours. Methyl iodide (0.1 ml) was then added and the mixture was stirred for another 3 hours. The volatile components were evaporated, ethanol (5 ml) and hydrochloric acid (37%, 0.5 ml) were added to the residue. The precipitate was collected by filtration, suspended in water, the solution was neutralized with sodium hydroxide (1 *N*) and extracted with chloroform (3 times, 10 ml each time) to give, after evaporation of chloroform, **26** in 61% yield, mp 178-179° (from toluene); ^{1}H nmr (deuteriochloroform): δ 3.9-4.3 (br s, 2H, NH_2), 7.02 (ddd, 1H, H_7), 7.2-7.7 (m, 2H, H_8, H_9), 8.05 (s, 1H, H_2), 9.03 (ddd, 1H, H_6), $J_{H_6,H_7} = J_{H_7,H_8} = 8.0$ Hz, $J_{H_7,H_9} = 1.5$ Hz, $J_{H_8,H_9} = 7.5$ Hz.

Anal. Calcd. for $C_8H_7N_3O$: C, 59.62; H, 4.38; N, 26.07. Found: C, 59.66; H, 4.52; N, 25.81.

In the same manner the following compound was prepared:

3-Amino-8-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**25**).

This compound was prepared from **18** in 34% yield, mp 215-225° (from toluene); ^{1}H nmr (deuteriochloroform): δ 2.4 (s, 3H, 8-Me), 3.7-4.2 (br s, 2H, NH_2), 6.88 (dd, 2H, H_7), 7.35 (d, 1H, H_9), 8.05 (s, 1H, H_2), 8.88 (d, 1H, H_6), $J_{H_6,H_7} = 7.5$ Hz, $J_{H_7,H_9} = 1.8$ Hz.

Anal. Calcd. for $C_9H_9N_3O$: C, 61.70; H, 5.18; N, 23.99. Found: C, 61.72; H, 5.19; N, 23.62.

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REFERENCES AND NOTES

[1] W. L. Mosby, Heterocyclic Systems with Bridgehead Nitrogen Atoms, Part **2**, A. Weissberger, ed, John Wiley and Sons, New York, 1961, pp 1001-1239.

[2] C. K. Bradsher, In Comprehensive Heterocyclic Chemistry, Vol **2**, A. R. Katritzky, C. W. Ress, eds, Pergamon Press, New York, 1984, p 525.

[3] G. Jones, *Adv. Heterocyclic Chem.*, **31**, 2 (1982).

[4] D. Leaver in Rodd's Chemistry of Carbon Compounds, Vol **IVH** Suppl, M. F. Ansell, ed, Elsevier, Amsterdam, 1987, p 33.

[5] I. Hermeczs and Z. Meszaros, *Adv. Heterocyclic Chem.*, **33**, 241 (1983).

[6] M. Tišler and B. Stanovnik, In Condensed Pyridazines Including Cinnolines and Phthalazines, R. N. Castle, ed, John Wiley and Sons, New York, 1973, p 761.

[7] G. W. H. Cheeseman and R. F. Cookson, Condensed Pyrazines, John Wiley and Sons, New York, 1979, p 463.

[8] B. Stanovnik, J. Svete and M. Tišler, *J. Heterocyclic Chem.*, **24**, 1809 (1987).

[9] J. Svete, B. Stanovnik, M. Tišler, L. Golič and I. Leban, *J. Heterocyclic Chem.*, **26**, 145 (1989).

[10] B. Stanovnik, J. Svete, M. Tišler, L. Žorž, A. Hvala and I. Simonič, *Heterocycles*, **27**, 903 (1988).

[11] B. Stanovnik, J. Svete and M. Tišler, *J. Heterocyclic Chem.*, **26**, 1273 (1989).

[12] B. Ornik, Z. Čadež, B. Stanovnik and M. Tišler, *J. Heterocyclic Chem.*, **27**, 1021 (1990).

[13a] J. W. Cornforth, In The Chemistry of Penicillin, H. T. Clarke, J. R. Johnson and R. Robinson, eds, Princeton University Press, Princeton, 1949, pp 757, 829; [b] O. Tsuge and M. Noguchi, *Heterocycles*, **16**, 2149 (1981).

[14] A. Čopar, B. Stanovnik and M. Tišler, *Bull. Soc. Chim. Belg.*, **100**, 533 (1991).

[15] B. Stanovnik, H. van de Bovenkamp, J. Svete, A. Hvala, I. Simonič and M. Tišler, *J. Heterocyclic Chem.*, **27**, 359 (1990).

[16] B. Stanovnik, The Chemistry of 2-Acylamino-3-dimethylaminopropenoates. Methyl 2-Benzoylamino-3-dimethylaminopropenoate in the Synthesis of Heterocyclic Systems. Progress in Heterocyclic Chemistry, Vol **5**, H. Suschitzky and E. F. V. Scriven, eds, Pergamon Press, 1993, pp 34-53.

[17] P. Aubert, E. B. Knott and L. A. Williams, *J. Chem. Soc.*, 2185 (1951).