UTILISATION OF 6-AMINO-2,3-DIMETHYLQUINOXALINE FOR THE SYNTHESIS OF TRICYCLIC PYRIDOQUINOXALINES *via* GOULD–JACOBS REACTION

Jozef SALOŇ[a1], Viktor MILATA[a2,*], Nadežda PRÓNAYOVÁ[b1] and Ján LEŠKO[b2]

[a] *Department of Organic Chemistry, Faculty of Chemical Technology, Slovak University of Technology, 812 37 Bratislava, Slovak Republic; e-mail: [1] j.salon@angelfire.com, [2] vmilata@cvt.stuba.sk*

[b] *Central Laboratory of Chemical Technique, Faculty of Chemical Technology, Slovak University of Technology, 812 37 Bratislava, Slovak Republic; e-mail: [1] pronayova@cvt.stuba.sk, [2] lesko@chtf.stuba.sk*

Received July 31, 2001
Accepted November 5, 2001

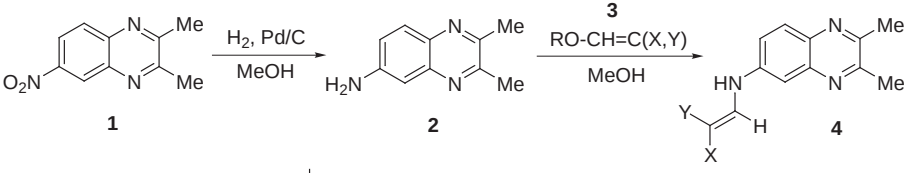
Treatment of 2,3-dimethylquinoxalin-6-amine with (alkoxymethylidene)malonic derivatives gave the corresponding (quinoxalylamino)ethenes, which on heating cyclized to angularly annelated pyrido[3,2-*f*]quinoxalin-10-ones.

Keywords: Fused heterocycles; Quinoxalines; Enaminones; Pyridoquinoxalines; Regioselective Gould–Jacobs reaction; Cyclization.

Quinoxalines and many of their fused derivatives have been prepared in an effort to produce biologically active materials[1]. Fused quinoxalines such as imidazoquinoxalines are strong cancerogens in food[2]. In continuation of our studies of the synthesis of fused quinoxalines, we report on the synthesis and spectral properties of some new fused tricyclic quinoxaline derivatives.

In a previous paper we described the preparation and spectral properties of 3-(quinoxalin-6-ylamino)- or 3-[(2,3-diphenylquinoxalin-6-yl)amino]-prop-2-enoic derivatives and their subsequent cyclization under the conditions of the Gould–Jacobs reaction[3,4]. The starting material for the synthesis of 6-substituted 2,3-dimethylquinoxaline derivatives **4** was 2,3-dimethylquinoxalin-6-amine (**2**), obtained by catalytic hydrogenation of 2,3-dimethyl-6-nitroquinoxaline (**1**). The amine was not isolated due to a general low stability of heterocyclic amines[5], but immediately in solution subjected to nucleophilic substitution with an (alkoxymethylidene)malonic derivative under mild conditions (stirring at ambient temperature or short boiling

of methanolic solutions), affording good yields of (quinoxalin-6-ylamino)-ethenes **4** (Scheme 1).



3,4	R	X	Y
a	Me	COOMe	COOMe
b	Et	COOEt	COOEt
c	Et	CN	CN
d	Et	COMe	COMe
e	Me	COMe	COOMe
f	Et	COMe	COOEt
g	Et	CN	COMe
h	Me	CN	COOMe
i	Et	CN	COOEt
j	Et	CO-O-CMe_2-O-CO	

SCHEME 1

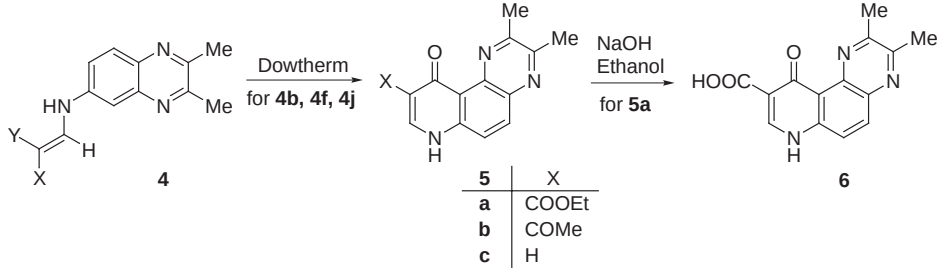
The compounds **4a**–**4d**, **4j** have identical the X and Y substituents, whereas compounds **4e**–**4i** (with different X and Y) are mixtures of *E* and *Z* isomers. The aim of our study was to establish the structure of **4** on the basis of their ^{1}H and ^{13}C NMR spectra. It was shown for cyanoacetate derivatives[6,7], that in DMSO prevailed the *E* isomer, while in $CDCl_3$ or acetone the *Z* isomer. The acetoacetate derivatives preferred the *E* isomers in all these solvents[8,9]: therefore a comparison of the structures of compounds **4** must be carried out very carefully, considering the used solvents.

The proton signals of the NH groups in the aminopropenoic acids **4a**, **4b**, **4d**–**4j** are doublets with coupling constants in the range 13–14 Hz resulting from the interaction with H-9. The doublets and their chemical shift range (10.01–12.89 ppm) give evidence of the formation of hydrogen bond with the carbonyl group of the acetyl or alkoxycarbonyl substituent and antiperiplanar conformation of the –HN–CH= moiety. In the case of **4c**, this configuration is not confirmed because of fast chemical exchange of the NH proton due to the absence of a stabilizing hydrogen bond. DMSO having basic properties causes a 0.1 ppm upfield shift of the methyl groups in the pyrazine ring.

The assignment of signals of **4e**–**4i** was complicated by the *E*–*Z* isomerism on the C9–C10 double bond. The *E* : *Z* ratio in **4e** and **4f** in $CDCl_3$ was 7 : 1, indicating that the configuration with the acetyl group hydrogen-bonded

to the amino group is preferred to a hydrogen bond with the alkoxycarbonyl group[8,9]. The cyanoacetic acid derivatives **4h** and **4i** gave also predominantly *E* isomers in the ratio 3 : 1 and 2 : 1, respectively. This is a caused by a mixture of $CDCl_3$ and DMSO used because of low solubility of these derivatives. In neat $CDCl_3$, the *Z* isomer predominates[6] due to steric factors. The proton-coupled ^{13}C NMR spectra of **4g**–**4i** allow distinguishing between COMe, COOMe, COOEt and CN signals in *cis* or *trans* position relative to H-9 (ref.[10]). The *E* : *Z* ratio in the 3-oxobutanenitrile derivative **4g** was 1 : 10, although it was prepared from the *E* isomer of EtOCH=C(CN)COMe. An explanation for different amounts of the *E* and *Z* isomers might be that the H-bond with the acetyl group could play a major role causing the isomerization during the reflux[6].

Substitution products **4b**, **4f**, and **4j** cyclize upon heating in an inert medium of Dowtherm at 250 °C to give regioselectively angularly annelated pyrido[3,2-*f*]quinoxalin-10-ones (Scheme 2). Formation of the linearly annelated isomer was not observed. Cyclization required a dilution of 1 : 15 (1 g/15 ml) and relatively short reaction times (10 min) at minimum temperature of 240 °C. Below the temperature, only isomerisation of the start-



5	X
a	COOEt
b	COMe
c	H

SCHEME 2

ing enamine **4f** was observed to produce the less thermodynamically stable *Z* isomer. The reaction progress was monitored by TLC after dissolving of small amount of the hot reaction mixture in acetone and subsequent development in chloroform to detect the remaining starting material. Angular annelation of the pyridine and pyrazine rings was confirmed by the coupling constants (about 9 Hz) resulting from the *ortho* interaction of the benzene ring protons. The same *ortho* interaction in the pyridine ring shows $^3J_{8,9}$ = 5.5 Hz. Hydrolysis of the resulting pyrido[3,2-*f*]quinoxaline derivative **5a** was successful only under alkaline conditions, in contrast to analogous methylimidazo or methyltriazolo analogs[11]. IR spectra of compounds **4**–**6** revealed stretching vibrations of the cyano group at 2 205–2 222 cm^{-1}, as well

as CH and NH bonds at 2 951–3 038 and 3 204–3 291 cm^{-1}, respectively. Vibrations of carbonyl groups were in the 1 624–1 726 cm^{-1} region, but that of the pyridone carbonyl group ranged from 1 580 to 1 617 cm^{-1}, both being often overlapped by C=C, HN–C=C vibrations[7]. The out-of-plane vibrations of aromatic protons γ(CH) appeared at 800 cm^{-1}.

The mass spectra of compounds **4**–**6** with the exception of **4e**, **4f**, **4j** and tricyclic derivatives **5a**, **5b**, **6** showed intense peaks of molecular ions. Origination of more intense species could be explained by bond fissions, mainly in the aminoethylene chain. Tricyclic condensed derivatives **5a** and **6** starting fragmentation on the substituents and the unsubstituted parent skeletons are therefore the most intensive peaks (*m/z* 225 daltons) in the spectra. Formation of some fragment ions was confirmed by the presence of the metastable transitions.

EXPERIMENTAL

Melting points were measured on a Kofler micro hot-stage, and their values were not corrected. IR spectra (0.5 mg of substance per 300 mg KBr) were recorded with an FTIR PU 9802 (Philips) spectrophotometer. NMR spectra were taken on spectrometer Varian VXR-300 (300 MHz for ^1H, 75 MHz for ^{13}C) with hexamethyldisiloxane as an internal standard. Deuteriochloroform was used as the solvent except for compounds: **4c** (in DMSO-d_6), **4g**–**4i** (in $CDCl_3$ + DMSO-d_6) and **6** (in a 10% NaOD solution in D_2O). Chemical shifts are given in ppm (δ-scale), coupling constants (*J*) in Hz. The electron impact mass spectra were taken with an MS 902S (AEI-Kratos) instrument at 70 eV energy and 100 μA current trap.

The alkoxymethylidene derivatives **3a**–**3c** are commercially available, while compounds **3d**–**3j** were synthetized by condensation of methyl or ethyl orthoformate with the corresponding methylidene compound[3,11]. 2,3-Dimethyl-6-nitroquinoxaline (**1**) was prepared according to ref.[12].

[(2,3-Dimethylquinoxalin-6-yl)amino]ethene Derivatives (**4a**–**4j**). General Procedure

2,3-Dimethyl-6-nitroquinoxaline (**1**) (1.0 g, 4.9 mmol) was dissolved in 30 ml of methanol, mixed with 100 mg of 3% Pd/C catalyst, and hydrogenated with magnetic stirring under 120 kPa until the hydrogen consumption stopped (about 330 ml). The catalyst was filtered off and the filtrate was treated immediately with 7 mmol of the derivative of 3-(alkoxymethylidene)prop-2-enoic acid or with 5-(ethoxymethylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione. Products **4g**, **4j** precipitated from the cooled solutions, while compounds **4a**–**4f**, **4h**, and **4i** precipitated after refluxing (30 min) and concentration of the solution. The precipitates were then recrystallized from the appropriate solvent.

2-[(2,3-Dimethylquinoxalin-6-ylamino)methylene]malonic acid dimethyl ester (**4a**). Yield: 61%. M.p. 169–170 °C (ethanol). IR: 2 951, 1 693, 1 655, 1 620, 802. ^1H NMR: 2.72 s, 3 H (CH_3); 2.73 s, 3 H (CH_3); 3.81 s, 3 H (OCH_3); 3.90 s, 3 H (OCH_3); 7.45 dd, 1 H, *J*(7,5) = 2.5, *J*(7,8) = 9.0 (H-7); 7.71 d, 1 H (H-5); 7.98 d, 1 H (H-8); 8.70 d, 1 H, *J*(9,NH) = 13.4 (H-9); 11.21 d, 1 H (NH). ^{13}C NMR: 23.0 (CH_3); 23.3 (CH_3); 51.6 (OCH_3); 51.8 (OCH_3); 94.5 (C-10); 112.8 (C-H); 120.5 (C-H); 130.2 (C-H); 138.7 (C-8a); 139.3 (C-6); 141.8 (C-4a); 151.5 (C-H); 152.8

(C-3); 154.8 (C-2); 165.4 (C=O); 169.2 (C=O). EI MS (*m/z*, rel.%): 315 (100) [M^+], 283 (94), 255 (44), 224 (81), 197 (25), 157 (25), 115 (25).

2-[(2,3-Dimethylquinoxalin-6-ylamino)methylene]malonic acid diethyl ester (**4b**). Yield: 65%. M.p. 116–117 °C (heptane). IR: 3 262, 2 980, 1 717, 1 659, 1 603, 830. ^{1}H NMR: 1.36 t, 3 H (OCH_2CH_3); 1.41 t, 3 H (OCH_2CH_3); 2.72 s, 3 H (CH_3); 2.73 s, 3 H (CH_3); 4.28 q, 2 H (OCH_2CH_3); 4.35 q, 2 H (OCH_2CH_3); 7.44 dd, 1 H, *J*(7,5) = 2.3, *J*(7,8) = 9.0 (H-7); 7.69 d, 1 H (H-5); 7.97 d, 1 H (H-8); 8.66 d, 1 H, *J*(9,NH) = 13.3 (H-9); 11.20 d, 1 H (NH). ^{13}C NMR: 14.3 (OCH_2CH_3); 14.5 (OCH_2CH_3); 23.0 (CH_3); 23.3 (CH_3); 60.3 (OCH_2CH_3); 60.7 (OCH_2CH_3); 95.3 (C-10); 112.5 (C-H); 120.5 (C-H); 130.1 (C-H); 138.6 (C-8a); 139.4 (C-6); 141.8 (C-4a); 151.0 (C-H); 152.6 (C-3); 154.7 (C-2); 165.1 (C=O); 168.9 (C=O). EI MS (*m/z*, rel.%): 343 (100) [M^+], 299 (86), 242 (33), 225 (48), 198 (33), 173 (24), 156 (19), 115 (29).

2-[(2,3-Dimethylquinoxalin-6-ylamino)methylene]malononitrile (**4c**). Yield: 57%. M.p. 200–201 °C (xylene). IR: 3 223, 2 222, 1 655, 831. ^{1}H NMR: 2.63 s, 3 H (CH_3); 2.64 s, 3 H (CH_3); 7.81 dd, 1 H, *J*(7,5) = 2.4, *J*(7,8) = 9.0 (H-7); 7.91 d, 1 H (H-8); 7.95 d, 1 H (H-5); 8.71 s, 1 H (H-9); 11.35 s, 1 H (NH). ^{13}C NMR: 22.6 (CH_3); 22.8 (CH_3); 53.3 (C-10); 114.0 (CN); 114.4 (C-H); 116.2 (CN); 120.4 (C-H); 129.2 (C-H); 138.0 (C-8a); 139.1 (C-6); 141.6 (C-4a); 153.1 (C-3); 154.8 (C-2); 155.9 (C-H). EI MS (*m/z*, rel.%): 249 (100) [M^+], 222 (22), 167 (65), 140 (22).

3-[(2,3-Dimethylquinoxalin-6-ylamino)methylene]pentane-2,4-dione (**4d**). Yield: 53%. M.p. 211–212 °C (ethanol). IR: 2 990, 1 624, 1 597, 820. ^{1}H NMR: 2.42 s, 3 H (CH_3); 2.56 s, 3 H (CH_3); 2.74 s, 3 H (CH_3); 2.75 s, 3 H (CH_3); 7.47 dd, 1 H, *J*(7,5) = 2.5, *J*(7,8) = 8.9 (H-7); 7.77 d, 1 H (H-5); 8.01 d, 1 H (H-8); 8.37 d, 1 H, *J*(9,NH) = 12.5 (H-9); 12.89 d, 1 H (NH). ^{13}C NMR: 23.1 (CH_3); 23.2 (CH_3); 27.3 (CH_3); 32.1 (CH_3); 113.1 (C-H); 114.2 (C-10); 121.0 (C-H); 130.4 (C-H); 139.0 (C-8a); 139.2 (C-6); 141.6 (C-4a); 150.9 (C-H); 153.2 (C-3); 154.9 (C-2); 194.9 (C=O); 201.6 (C=O). EI MS (*m/z*, rel.%): 283 (100) [M^+], 268 (35), 250 (50), 226 (50), 198 (35), 172 (88), 112 (35).

Methyl E/Z-2-[(2,3-dimethylquinoxalin-6-ylamino)methylene]-3-oxobutyrate (**4e**). Yield: 62%. M.p. 183–184 °C (ethanol). IR: 2 955, 1 698, 1 638, 1 593, 824. ^{1}H NMR (*E*-**4e**): 2.58 s, 3 H (CH_3); 2.71 s, 3 H (CH_3); 2.72 s, 3 H (CH_3); 3.81 s, 3 H (OCH_3); 7.45 dd, 1 H, *J*(7,5) = 2.6, *J*(7,8) = 8.9 (H-7); 7.71 d, 1 H (H-5); 7.96 d, 1 H (H-8); 8.61 d, 1 H, *J*(9,NH) = 12.9 (H-9). ^{13}C NMR (*E*-**4e**): 23.0 (CH_3); 23.2 (CH_3); 31.1 (CH_3); 51.3 (OCH_3); 103.5 (C-10); 113.4 (C-H); 120.6 (C-H); 130.2 (C-H); 138.9 (C-8a); 139.1 (C-6); 141.6 (C-4a); 151.2 (C-H); 153.0 (C-3); 154.8 (C-2); 166.8 (C=O); 200.6 (C=O). EI MS (*m/z*, rel.%): 299 (77) [M^+], 267 (18), 239 (100), 224 (100), 172 (27), 157 (23), 128 (23), 115 (27).

Ethyl E/Z-2-[(2,3-dimethylquinoxalin-6-ylamino)methylene]-3-oxobutyrate (**4f**). Yield: 83%. M.p. 134–135 °C (ethanol). IR: 2 978, 1 698, 1 638, 1 591, 824. ^{1}H NMR (*E*-**4f**): 1.38 t, 3 H (OCH_2CH_3); 2.59 s, 3 H (CH_3); 2.73 s, 3 H (CH_3); 2.74 s, 3 H (CH_3); 4.29 q, 2 H (OCH_2CH_3); 7.46 dd, 1 H, *J*(7,5) = 2.5, *J*(7,8) = 8.9 (H-7); 7.71 d, 1 H (H-5); 7.99 d, 1 H (H-8); 8.64 d, 1 H, *J*(9,NH) = 12.9 (H-9). ^{13}C NMR (*E*-**4f**): 14.6 (OCH_2CH_3); 23.1 (CH_3); 23.2 (CH_3); 31.1 (CH_3); 60.2 (OCH_2CH_3); 103.9 (C-10); 113.5 (C-H); 120.8 (C-H); 130.2 (C-H); 138.9 (C-8a); 139.3 (C-6); 141.7 (C-4a); 151.3 (C-H); 153.0 (C-3); 154.9 (C-2); 166.6 (C=O); 200.8 (C=O). EI MS (*m/z*, rel.%): 313 (76) [M^+], 267 (29), 239 (100), 224 (76), 198 (24), 172 (24), 157 (24), 142 (24), 115 (29).

E/Z-2-[(2,3-Dimethylquinoxalin-6-ylamino)methylene]-3-oxobutyronitrile (**4g**). Yield: 51%. M.p. 210–212 °C (xylene). IR: 2 205, 1 651, 1 605, 812. ^{1}H NMR (*Z*-**4g**): 2.46 s, 3 H (CH_3); 2.74 s, 3 H (CH_3); 2.74 s, 3 H (CH_3); 7.46 dd, 1 H, *J*(7,5) = 2.6, *J*(7,8) = 9.0 (H-7); 7.71 d, 1 H (H-5); 7.98 d, 1 H, *J*(9,NH) = 13.0 (H-9); 8.01 d, 1 H (H-8); 12.47 d, 1 H (NH). ^{13}C NMR (*Z*-**4g**): 23.1 (CH_3); 23.2 (CH_3); 28.7 (CH_3); 86.1 (C-10); 114.3 (C-H); 119.3 (CN); 120.0 (C-H); 130.5

(C-H); 138.1 (C-8a); 139.2 (C-6); 141.5 (C-4a); 151.2 (C-H); 153.7 (C-3); 155.2 (C-2); 197.6 (C=O). EI MS (*m/z*, rel.%): 266 (100) [M^+], 251 (41), 223 (82), 182 (29), 158 (29).

Methyl E/Z-2-cyano-3-(2,3-dimethylquinoxalin-6-ylamino)acrylate (**4h**). Yield: 58%. M.p. 219–221 °C (xylene). IR: 3 291, 2 955, 2 215, 1 715, 1 607, 830. ^{1}H NMR (*E*-**4h**): 2.74 s, 3 H (CH_3); 2.75 s, 3 H (CH_3); 3.86 s, 3 H (CH_3); 7.63 dd, 1 H, *J*(7,5) = 2.5, *J*(7,8) = 9.0 (H-7); 7.73 d, 1 H (H-5); 8.00 d, 1 H (H-8); 8.54 m, 1 H (H-9). ^{1}H NMR (*Z*-**4h**): 2.74 s, 3 H (CH_3); 2.75 s, 3 H (CH_3); 3.89 s, 3 H (CH_3); 7.51 dd, 1 H, *J*(7,5) = 2.5, *J*(7,8) = 9.0 (H-7); 7.70 d, 1 H (H-5); 8.01 d, 1 H (H-8); 8.21 m, 1 H (H-9). ^{13}C NMR (*E*-**4h**): 22.8 (CH_3); 23.0 (CH_3); 52.5 (OCH_3); 77.5 (C-10); 113.6 (C-H); 115.7 (CN); 120.5 (C-H); 129.9 (C-H); 138.5 (C-8a); 139.8 (C-6); 141.4 (C-4a); 151.9 (C-H); 153.3 (C-3); 155.2 (C-2); 165.6 (C=O). ^{13}C NMR (*Z*-**4h**): 22.8 (CH_3); 23.0 (CH_3); 52.4 (CH_3); 76.6 (C-10); 113.5 (C-H); 117.7 (CN); 120.5 (C-H); 130.2 (C-H); 138.6 (C-8a); 139.8 (C-6); 141.4 (C-4a); 152.1 (C-H); 153.5 (C-3); 155.3 (C-2); 167.6 (C=O). EI MS (*m/z*, rel.%): 282 (100) [M^+], 250 (44), 223 (28), 184 (22), 140 (22).

Ethyl E/Z-2-cyano-3-(2,3-dimethylquinoxalin-6-ylamino)acrylate (**4i**). Yield: 69%. M.p. 177–178 °C (xylene). IR: 3 289, 2 986, 2 215, 1 682, 1 607, 833. ^{1}H NMR (*E*-**4i**): 1.36 t, 3 H ($OCH_2C\mathbf{H}_3$); 2.73 s, 3 H (CH_3); 2.74 s, 3 H (CH_3); 4.31 q, 2 H ($OC\mathbf{H}_2CH_3$); 7.59 dd, 1 H, *J*(7,5) = 2.4, *J*(7,8) = 9.0 (H-7); 7.71 d, 1 H (H-5); 7.99 d, 1 H (H-8); 8.52 m, 1 H (H-9); 10.01 d, 1 H, *J*(NH,9) = 14.5 (NH). ^{1}H NMR (*Z*-**4i**): 1.39 t, 3 H ($OCH_2C\mathbf{H}_3$); 2.73 s, 3 H (CH_3); 2.74 s, 3 H (CH_3); 4.33 q, 2 H ($OC\mathbf{H}_2CH_3$); 7.46 dd, 1 H, *J*(7,5) = 2.4, *J*(7,8) = 9.0 (H-7); 7.66 d, 1 H (H-5); 8.00 d, 1 H (H-8); 8.14 m, 1 H (H-9); 10.97 d, 1 H, *J*(NH,9) = 13.2 (NH). ^{13}C NMR (*E*-**4i**): 14.4 (OCH_2CH_3); 22.9 (CH_3); 23.1 (CH_3); 61.5 (OCH_2CH_3); 78.0 (C-10); 113.5 (C-H); 116.0 (CN); 120.3 (C-H); 130.0 (C-H); 138.5 (C-8a); 139.6 (C-6); 141.5 (C-4a); 151.6 (C-H); 153.3 (C-3); 155.1 (C-2); 164.9 (C=O). ^{13}C NMR (*Z*-**4i**): 14.3 (OCH_2CH_3); 22.8 (CH_3); 23.0 (CH_3); 61.6 (OCH_2CH_3); 77.0 (C-10); 113.1 (C-H); 117.7 (CN); 120.1 (C-H); 130.3 (C-H); 138.7 (C-8a); 139.6 (C-6); 141.5 (C-4a); 151.9 (C-H); 153.4 (C-3); 155.3 (C-2); 167.3 (C=O). EI MS (*m/z*, rel.%): 296 (100) [M^+], 250 (56), 222 (68), 181 (24), 140 (24).

5-[(2,3-Dimethylquinoxalin-6-ylamino)methylene]-2,2-dimethyl-1,3-dioxane-4,6-dione (**4j**). Yield: 79%. M.p. 225–226 °C (xylene). IR: 3 204, 2 988, 1 726, 1 682, 1 599, 843. ^{1}H NMR: 1.78 s, 6 H (CH_3, CH_3); 2.74 s, 3 H (CH_3); 2.74 s, 3 H (CH_3); 7.59 dd, 1 H, *J*(7,5) = 2.1, *J*(7,8) = 8.9 (H-7); 7.89 d, 1 H (H-5); 8.03 d, 1 H (H-8); 8.79 d, 1 H, *J*(9,NH) = 14.2 (H-9); 11.43 d, 1 H (NH). ^{13}C NMR: 23.1 (CH_3); 23.3 (CH_3); 27.1 (CH_3, CH_3); 88.4 (C-10); 105.3 (C-13); 115.3 (C-H); 119.8 (C-H); 130.6 (C-H); 137.7 (C-8a); 139.4 (C-6); 141.5 (C-4a); 152.4 (C-H); 153.8 (C-3); 155.3 (C-2); 163.1 (C=O); 165.4 (C=O). EI MS (*m/z*, rel.%): 327 (29) [M^+], 269 (38), 224 (100), 197 (67), 156 (19), 115 (43).

2,3-Dimethyl-7*H*-pyrido[3,2-*f*]quinoxalin-10-ones (**5**). General Procedure

A mixture of **4b**, **4f** or **4j** (1 g) and 15 ml of Dowtherm was heated at 250 °C for 10 min. The reaction was monitored by TLC (Silufol 254 UV, $CHCl_3$). After cooling, heptane (100 ml) was added; the formed precipitate was collected by suction, washed several times with heptane and crystallized from the appropriate solvent.

9-Ethoxycarbonyl-2,3-dimethyl-7H-pyrido[3,2-f]quinoxalin-10-one (**5a**). Yield: 63%. M.p. 159–160 °C (toluene–cyclohexane). IR: 2 986, 1 694, 1 617, 1 503, 847. ^{1}H NMR: 1.49 t, 3 H ($OCH_2C\mathbf{H}_3$); 2.82 s, 6 H (CH_3, CH_3); 4.52 q, 2 H ($OC\mathbf{H}_2CH_3$); 8.12 d, 1 H and 8.16 d, 1 H, *J*(5,6) = 9.0 (H-5, H-6); 9.31 s, 1 H (H-8); 15.50 s, 1 H (NH). ^{13}C NMR: 14.5 (OCH_2CH_3); 22.4 (CH_3); 22.9 (CH_3); 62.2 (OCH_2CH_3); 111.0 (C-9); 111.8 (C-10a); 131.3 (C-H); 132.5 (C-H);

139.2 (C-10b); 139.8 (C-4a); 149.7 (C-3); 151.6 (C-6a); 153.9 (C-2); 154.3 (C-H); 167.3 (C=O); 166.7 (C-10). EI MS (*m/z*, rel.%): 297 (65) [M^+], 252 (57), 225 (100), 181 (17), 114 (17).

9-Acetyl-2,3-dimethyl-7H-pyrido[3,2-f]quinoxalin-10-one (**5b**). Yield: 47%. M.p. 219–221 °C (toluene–cyclohexane). IR: 1 667, 1 617, 1 499, 853. ^{1}H NMR: 2.80 s, 9 H (CH_3, CH_3, CH_3); 8.03 s, 2 H (H-5, H-6); 9.15 s, 1 H (H-8); 15.19 s, 1 H (NH). ^{13}C NMR: 22.5 (CH_3); 22.9 (CH_3); 32.3 (CH_3); 111.6 (C-10a); 117.8 (C-9); 131.3 (C-H); 132.2 (C-H); 138.9 (C-10b); 139.6 (C-4a); 149.6 (C-3); 151.5 (C-6a); 153.4 (C-H); 153.9 (C-2); 166.7 (C-10); 197.2 (C=O). EI MS (*m/z*, rel.%): 267 (46) [M^+], 252 (100), 169 (17).

2,3-Dimethyl-7H-pyrido[3,2-f]quinoxalin-10-one (**5c**). Yield: 68%. M.p. 191 °C (cyclohexane). IR: 2 990, 1 580, 1 510, 830. ^{1}H NMR: 2.81 s, 3 H (CH_3); 2.82 s, 3 H (CH_3); 7.10 d, 1 H, J(8,9) = 5.5 (H-8); 8.07 d, 1 H and 8.18 d, 1 H, J(5,6) = 9.3 (H-5, H-6); 8.76 d, 1 H (H-9). ^{13}C NMR: 22.7 (CH_3); 22.8 (CH_3); 109.1 (C-H); 112.5 (C-10a); 129.8 (C-H); 132.0 (C-H); 139.1 (C-10b); 139.6 (C-4a); 149.8 (C-3); 152.0 (C-6a); 152.0 (C-H); 153.3 (C-2); 165.9 (C-10). EI MS (*m/z*, rel.%): 225 (100) [M^+], 197 (50), 173 (25), 143 (17), 115 (42).

2,3-Dimethyl-10-oxo-7,10-dihydropyrido[3,2-*f*]quinoxaline-9-carboxylic Acid (**6**)

A mixture of ester **5a** (500 mg, 1.7 mmol), 10 ml of hot ethanol, and 5 ml of 1 M NaOH was refluxed for 2 h and then neutralized with HCl. The solid precipitating upon cooling was collected by suction, washed with water, and dried. Acid **6** (310 mg, 67%), m.p. 305 °C (decomp.; xylene–ethanol), was obtained. IR: 3 235, 3 038, 1 684, 1 587, 1 487, 824. ^{1}H NMR: 2.06 s, 6 H (CH_3, CH_3); 6.56 d, 1 H and 6.69 d, 1 H, J(5,6) = 9.3 (H-5, H-6); 8.30 s, 1 H (H-8). ^{13}C NMR: 23.8 (CH_3); 24.2 (CH_3); 114.4 (C-10a); 118.7 (C-9); 131.0 (C-H); 131.6 (C-H); 138.5 (C-10b); 139.8 (C-4a); 150.7 (C-3); 154.0 (C-H); 154.1 (C-6a); 154.6 (C-2); 168.9 (C-10); 175.0 (C=O). EI MS (*m/z*, rel.%): 269 (15) [M^+], 225 (100), 197 (22), 143 (13), 115 (17).

REFERENCES

1. Katritzky A. R., Boulton A. J. in: *Advances in Heterocyclic Chemistry*, Vol. 22, p. 368. Academic Press, New York 1978.
2. Wakabayashi K., Nagao M., Esumi H., Sugimura T.: *Cancer Res.* **1992**, *52 (Suppl)*, 2092.
3. Saloň J., Milata V., Prónayová N., Leško J.: *Monatsh. Chem.* **2000**, *131*, 293.
4. Milata V., Ilavský D., Chudík M., Zalibera Ľ., Leško J., Seman M., Belicová A.: *Monatsh. Chem.* **1995**, *126*, 1349.
5. Al-Shaar A. H., Gilmour D. J., Lythgoe D. J., McClenaghan I., Ramsden Ch. A.: *J. Chem. Soc., Chem. Commun.* **1989**, 551.
6. Michalik M.: *Z. Chem.* **1985**, *25*, 287.
7. Michalik M., Shoknecht A., Kristen H.: *Z. Chem.* **1983**, *23*, 57.
8. Michalik M.: *J. Prakt. Chem.* **1985**, *327*, 908.
9. Couchuron B., Le Saint J., Courtot P.: *Bull. Soc. Chim. Fr.* **1983**, 66.
10. Goljer I., Milata V., Ilavský D.: *Magn. Reson. Chem.* **1989**, *27*, 138.
11. Ohmori J., Sakamoto S., Kugota H., Shimizu-Sasamata M., Okada M., Kawasaki S., Hidaka K., Togami J., Furuya T., Murase K.: *J. Med. Chem.* **1994**, *37*, 467.
12. Klicnar J., Vetesnik P., Cimpl Z.: *Sb. Ved. Pr., Vys. Sk. Chemickotechnol., Pardubice* **1968**, *18*, 5; *Chem. Abstr.* **1970**, *72*, 66890.