HETEROCYCLES, Vol. 57, No. 8, 2002, pp. 1413 - 1421, Received, 22nd April, 2002

SYNTHESIS AND NMR STRUCTURAL ASSIGNMENT OF 3-BENZOYL-PYRROLO[2,3-*b*]QUINOXALIN-2(4*H*)-ONES*

Katarzyna Ostrowska,*[a] Marek Żylewski,[b] and Krzysztof Walocha

[a]Department of Organic Chemistry, Jagiellonian University, R.Ingardena 3, PL-30060 Kraków, Poland

Fax: +48-12-63-40-515; E-mail: ostrowsk@chemia.uj.edu.pl

[b]NMR Laboratory, Department of Organic Chemistry, Collegium Medicum, Jagiellonian University, Medyczna 9, PL-30688 Kraków, Poland

E-mail: mfzylews@cyf-kr.edu.pl

Abstract - A series of 3-benzoylpyrrolo[2,3-*b*]quinoxalin-2(4*H*)-ones, potential bioactive compounds have been synthesized. Their preparation is based on the efficient, regiospecific condensation of *o*-phenylenediamine with pyrrolidine-2,3,5-trione (**1**) or its enaminone derivatives**,** respectively, affording two polymorphic forms of the latter in solid. The NMR spectral assignment of 3-benzoylpyrrolo[2,3-*b*]quinoxalin-2(4*H*)-ones confirms the presence of only one isomer with enaminone moiety in solution.

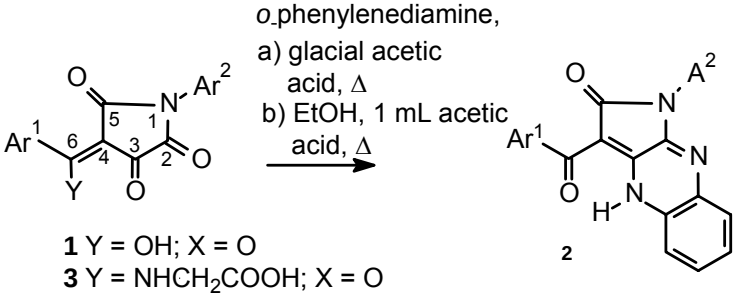
The quinoxaline-peptide antibiotic family including echinomycin,[1] levomycin and actinoleucin[2] or pyrroloquinoxaline[3, 4] system contains one or more quinoxaline rings, structural unit of several bioactive compounds, exhibiting properties of various types such as antiviral, antibacterial, antifungal, insecticidal and cytotoxic.[5] Synthesis of the pyrrolo[2,3-*b*]quinoxaline system has been extensively investigated due to a potential pharmacological activity. Its synthesis is readily accomplished by the annelation of *o*-phenylenediamine with 3-chloropyrrolidine-2-one,[6-13] 4-oxa-2,10-diazabenzo[*b*]azulene-1,3,9-trione[14] or pyrrole-2,3-dione[15-21] derivatives, and 3-aminoquinoxaline derivative with diethyl carbonate,[22] respectively.

1-Phenyl-4-phenylhydroxymethylidenepyrrolidine-2,3,5-trione (**1**),[23] used as a building block in our previous investigations on the synthesis of pyrrolo[3,4-*x*]diazacycloalkadiene[24,25] system, possesses α-dicarbonyl moiety susceptible to the double nucleophilic attack, thus seems to be a convenient starting material in the synthesis of the new potential bioactive pyrrolo[2,3-*b*]quinoxaline derivatives. It is

*Dedicated to memory of late Prof. Dr. hab. Wanda Żankowska-Jasińska

important to point out that **1** is an analogue of tetramic acid occurring in several natural products, as well as belongs to the pyrrolidinetrione derivatives, polycarbonyl heterocycle which has got a wide range of pharmacological and industrial applications.[26] The use of pyrrolidine-2,3,5-trione (**1**) in our synthesis of expected pharmacologically active fused pyrrolo[2,3-*b*]quinoxaline system enables insertion of an additional carbonyl group, which may facilitate linkage with receptors.

We recently reported[27] that the polycarbonyl compound (**1)** underwent condensation with nitrogen bases at C-6 or C-3 as a result of the presence of predominant *exo*-enol or *endo*-enol form of **1** depending on the solvent used. The NMR spectral data showed that methanol-d_4 favors a 90% *exo*-enol form of **1** whereas in toluene-d_8 this equilibrium is shifted to a 74% *exo*-enol form. We have never observed condensation at succinamide carbonyl carbon atom C-2 and this is in accordance with the lower reactivity of the latter.



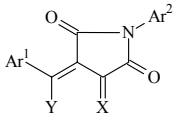
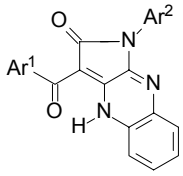
1 Y = OH; X = O
3 Y = $NHCH_2COOH$; X = O
4 Y = $NH(CH_2)_2COOH$; X = O
5 Y = $NH(CH_2)_3COOH$; X = O
6 Y = NHC_6H_5; X = O
7 Y = NHC_6H_5; X = S

Scheme 1.

Preliminary studies on the synthesis of the pyrrolo[2,3-*b*]quinoxaline system from pyrrolidinetrione (**1a**) in boiling ethanol with *o*-phenylenediamine in the presence of acetic acid (1 mL) afforded the corresponding heterocyclic derivative (**2a**) in yellow polymorphic form in 95 % yields, whereas the reaction of **1a** in glacial acetic acid gave two polymorphs of **2a**: yellow and orange (Scheme 1, Table 1). Unexpectedly, the same results were obtained in the reaction of enaminones (**3**,**4**,**5**,[27] **6**,[29] **7**[30]) with *o*-phenylenediamine. Regardless of solvent: glacial acetic acid or dry toluene, condensation always takes place at C-2 and C-3 with simultaneous hydrolysis at C-6, giving in every case both polymorphs of **2a** (Table 1). Precipitating at first from the hot reaction mixture an orange form was separated by filtering. Heating the latter in Dowtherm at 160 °C or recrystallization in glacial acetic acid led to the formation of a yellow form in 100% yield. It seems, that at first the orange polymorph is formed as the kinetically stable product that undergoes irreversible phase change to yellow one.

Furthermore, all the attempts of preparing the Schiff bases at C-10 benzoyl carbon atom of pyrrolo[2,3-*b*]quinoxaline derivative by condensation of **2a** with amino acids or aniline failed, indicating the stability of this thermodynamic product.

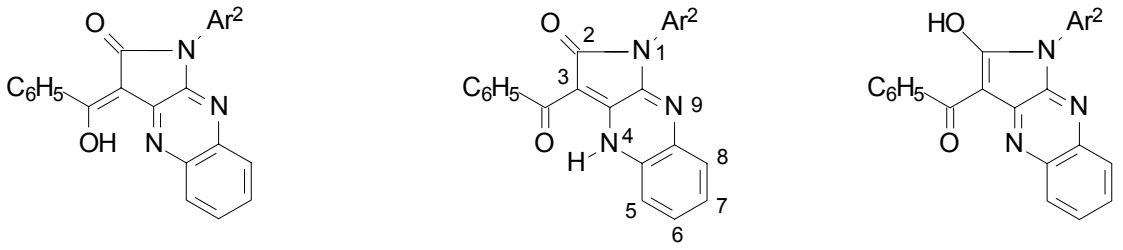
Table 1. Pyrrolo[2,3-*b*]quinoxalin-2-one derivatives (**2**).

Substrate 		Solvent		Product (**2**) Yield (%)	
				Yellow polymorph	Orange polymorph
1a[23]	Y = OH; X = O; Ar^1=Ar^2= C_6H_5	C_2H_5OH	**2a**	95	-
1a	Y = OH; X = O; Ar^1=Ar^2= C_6H_5	CH_3COOH	**2a**	32.5	42.6
1b	Y = OH; X = O; Ar^1= C_6H_5; Ar^2= 4-$C_2H_5OC_6H_4$	CH_3COOH	**2b**	74.4	-
1c[23]	Y = OH; X = O; Ar^1= C_6H_5; Ar^2= 2-$C_{10}H_7$	CH_3COOH	**2c**	33.7	38.6
1d[23]	Y = OH; X = O; Ar^1= 4-ClC_6H_4; Ar^2= C_6H_5	CH_3COOH	**2d**	82	-
1e[23]	Y = OH; X = O; Ar^1= C_6H_5; Ar^2= 4-ClC_6H_4	CH_3COOH	**2e**	95	-
3[27]	Y = $NHCH_2COOH$, X = O; Ar^1=Ar^2= C_6H_5	CH_3COOH	**2a**	21.1	13.4
4[27]	Y = $NHCH_2CH_2COOH$, X = O; Ar^1=Ar^2= C_6H_5	CH_3COOH	**2a**	29.4	18.1
5[27]	Y = $NHCH_2CH_2CH_2COOH$, X = O; Ar^1=Ar^2= C_6H_5	CH_3COOH	**2a**	24.2	15.1
6[29]	Y = NHC_6H_5, X =O; Ar^1=Ar^2= C_6H_5	CH_3COOH	**2a**	27.5	16.3
6	Y = NHC_6H_5, X = O; Ar^1=Ar^2= C_6H_5	Toluene	**2a**	21	12
7[30]	Y = NHC_6H_5, X = S; Ar^1=Ar^2= C_6H_5	CH_3COOH	**2a**	20.3	12.1

Due to a fine-crystalline form of both precipitates it was impossible to obtain X-Ray analysis. Moreover, the very low solubility of these products eliminated 2D NMR structural assignment. Thus, we tried to find other compounds which could help us to examine the reaction of *o*-phenylenediamine with other pyrrolidine-2,3,5-trione derivatives (Scheme 1, Table 1) and complete structural elucidation. However, only in the case of 1-(β-naphthyl) derivative two polymorphic forms were isolated. Pleasingly, 1-*p*-

ethoxyphenylpyrrolidine-2,3,5-trione (**1b**) gave the corresponding pyrrolo[2,3-*b*]quinoxalin-2-one derivative (**2b**)**.**

Elemental analyses, IR spectra taken in KBr, UV spectra taken in $CHCl_3$ (λ_{max}= 418, 395, 243 nm), MS and ^1H NMR spectra taken in DMSO-d_6 or $CDCl_3$ for yellow and orange polymorphs gave identical sets of data, indicating that in both cases condensation takes place at C-2 and C-3 carbonyl carbon atoms. Furthermore, ^1H NMR spectra taken in $CDCl_3$ reveal the signals for only one the same tautomeric form for **2** in solution.



A (A-1) **B** **C**

Scheme 2

Compound (**2**) can exist in three tautomeric forms (**A**, **B**, **C**). For form (**A)** geometrical isomers: *trans-s-cis* **A-1** and *cis-s-cis* **A-2** isomers (Scheme 2) can be taken into account.. The structural assignmet for **2b** has been confirmed by IR, 1D and 2D NMR experiment involving ^1H-^1H COSY 90-45, TOCSY, NOESY, ^1H-^{13}C COSY, GHMQC and GHSQC. The ^1H-^1H COSY 90-45, TOCSY correlations have shown the positions of H-6 and H-4" at 7.55, and H-7, H-3",5" at 7.47. All protons directly bonded to carbon atoms, except H-6, have been assigned by the GHSQC. The overall structure has been assembled by analysis of the long range ^1H-^{13}C connectivities (Table 2) gleaned from GHMQC experiment.

The NOESY experiment taken at 29 °C has revealed correlation between the most downfield shifted proton at 13.76 and H-5, that eliminates the presence of tautomer (**C**) and *cis-s-cis* of **A-2**. The imino-*endo-enol* (**C**) form for **2e** was previously described in the literature by Junjappa.[20] The reaction of **1e** with *o*-phenylenediamine in glacial acetic acid (Scheme 1) in our case gave derivative (**2e**) with melting point higher by 80 °C than quoted 246-247 °C,[21] that may suggest that product described in the literature is noncyclized Schiff bases of **1e**.

The NOESY spectrum of **2b** also has shown correlations between H-5/H-6; H-2"/H-3"; H-2'/ H-3'; H-OCH_2/H-CH_3. The IR spectrum of **2b** showed absorption bands at 3289 cm^{-1}, in the region characteristic for N-H bond vibration and the most downfield shifted C=O signal in ^{13}C NMR spectra has appeared at 189.09 ppm, which for enol should be placed at the higher field, as it is observed for polycarbonyl compound (**1**).

We assume that these results prove the enaminone (**B**) form, with possible rotation around the C-3, C-benzoyl bond, for pyrrolo[2,3-*b*]quinoxaline (**2b**) in solution. It is interesting that in this case imino-*endo*-*exo*-*enol* and enamino tautomeric equilibrium does not exist but the only thermodynamically stable enaminone tautomeric form is present. Thus this tautomer may be treated rather in terms of an isomer. Predominance of enaminones over enols for 2-substituted quinoxalines was previously explained,[27] however, as being stabilized by possible internal hydrogen bonding and benzo annelation.

Table 2. NMR spectral data on **2b** [300.08 MHz, DMSO-d_6, TMS, δ (ppm), *J*= Hz]

Atom	^{1}H	^{13}C	^{1}H ^{1}H COSY 90-45 [333.1 °K]	TOCSY [333.1 °K]	GHSQC [313.1 °K]	GHMQC [333.1 °K]
2	-	165.90				
3	-	94.26				
3a	-	148.61				
4	13.76 s	-				
4a	-	135.61				
5	8.24 1H, d, *J*=6.75	118.70	6	7, 8	5	H-5, C-7; H-5, C-4a
6	7.55 1H, m	127.15	7			
7	7.47 1H, m	125.54			7	H-7, C-4a; H-7, C-8; H-7, C-8a
8	7.74 1H, d, *J*= 7.04	127.50	7	6	8	H-8, C-7
8a	-	139.21				
9a	-	148.61				
10	-	189.09				
1’	-	125.85				
2’, 6’	7.42, 2H, d, *J*=8.80	128.99	3’, 5’	3’, 5’	2’, 6’	H-2’, C-4’
3’, 5’	7.06, 2H, d, *J*=8.80	114.43	2’, 6’	2’, 6’	3’, 5’	H-3’, C-4’; H-3’, C-1’
4’	-	157.75				
OCH_2	4.08 2H, q, *J*=7.04	63.29	CH_3	CH_3	OCH_2	
CH_3	1.35 3H, t, *J*=7.04	14.61	OCH_2	OCH_2	CH_3	
1”	-	138.85				
2”, 6”	7.86 2H, d, *J*=7.33	128.73	3”, 5”	3”, 4”	2”, 6”	H-2”,C-4”; H-2”, C-3”
3”, 5”	7.47 2H, m	127.4 0	2”, 6”		3”, 5”	
4”	7.55, 1H, m	131.38			4”	H-4’’, C-3”

This approach constitutes an efficient synthesis towards the potentially bioactive pyrrolo[2,3-*b*]-quinoxalin-2-ones using easily accessible and versatile starting materials. Additionally, NMR structural assignment confirms the shift of tautomer equilibrium towards more stable enaminone form in solution for 3-benzoyl-1-(4-ehtoxyphenyl)-1,4-dihydropyrrolo[2,3-*b*]quinoxalin-2(4*H*)-one (**2b)**.

EXPERIMENTAL

Mps were determined on a Boetius PHMK 05 melting point apparatus and are uncorrected. The ^{1}H NMR and ^{13}C NMR spectra were taken in *DMSO-d_6* and *$CDCl_3$* with a Bruker AMX 500 NMR spectrometer or

Mercury-300 Varian using *TMS* as internal standard. The IR spectra were measured in Nujol and hexachlorobutadiene (*HCBN*) with a Bruker IFS 48 spectrometer. The EI MS spectra were obtained on an LKB 9000 S spectrometer and Finnigan TSQ 700 triple quadruple mass spectrometr. Elemental analyses were carried out with an Eurovector analyser. We were not able to obtain ^{13}C NMR for **2d** because of its extremely low solubility.

General procedure for acylation with oxalyl chloride

To a stirred solution of 0.025 mol of anilide derivative in 150 mL of dry benzene 3.17 g (0.025 mol) of oxalyl chloride was added dropwise at rt. Gaseous HCl was removed through a reflux condenser. After the reaction was completed the mixture was heated up to the boiling point to remove the remainder of hydrogen chloride. From the cooled mixture the precipitate was filtered off and recrystallized from acetic acid.

1-p-Ethoxyphenyl-4-phenylhydroxymethylenepyrrolidine-2,3,5-trione (**1b**): mp 186 ºC: $\tilde{\nu}_{max}/cm^{-1}$ (HCB, nujol): 3446 (OH); 3066 (C-H, Ar); 2976 (C-H; CH_2CH_3); 1776, 1735, 1657 (C=O); 1603 (C=C, Ar); MS: *m/z* (%) = 337 (53) M^+; 309 (54) M^+-CO; 163 (100) $C_2H_5OC_6H_4NCO$; 105 (45) C_6H_5CO; ^{1}H-NMR (500.13 MHz, $CDCl_3$); δ 14.08 (1H, s, OH), 8.24 (2H, d, *J*=7.51 Hz), 7.69 (1H, t, *J*=7.26 Hz), 7.56 (2H, m, ArH), 7.36 (2H, m, ArH), 6.99 (2H, d, *J*=7.80 Hz), 4.07 (2H, q, *J*=6.90 Hz OCH_2), 1.43 (3H, t, *J*=6.90 Hz CH_3); ^{13}C-NMR (125.75 MHz, $CDCl_3$); δ 14.71 (CH_3), 63.80 (OCH_2), 98.05 (C-4), 115.08 (C-3'), 127.18, 128.51, 130.10, 135.15 (C-Ar), 159.21 (C-4'), 160.49 (C-5), 159.21 (C-2), 174.85 (C-3), 180.99 (C-6); *Anal*. Calcd for $C_{19}H_{15}NO_5$: C, 67.63; H, 4.48; N, 4.17. Found: C, 67.84; H; 4.60, N, 4.33.

General procedure for the reaction with o-phenylenediamine

To a solution of pyrrolidine-2,3,5-trione or enaminone (0.01 mol), respectively, in 100 mL of glacial acetic acid, 1.29 g (0.012 mol) of *o*-phenylenediamine was added. The solution was refluxed for 3 h. The mixture of both polymorphs of **2** was separated by partial filtration from the hot reaction mixture. Orange form, precipitating at first from the boiling reaction mixture was separated by filtering.

3-Benzoyl-1-phenyl-1,4-dihydropyrrolo[2,3-b]quinoxalin-2(4H)-one (**2a**): Yellow, mp 321 °C, orange, mp 324-325 °C; IR (HCB, nujol): $\tilde{\nu}_{max}/cm^{-1}$ 3238 (NH); 3062 (C-H, Ar); 1703 (C=O); 1642 (C=N); 1615 (C=C, Ar); MS: *m/z* (%) = 365 (100) M^+, 288 (18) M^+-C_6H_5, 105 (32) C_6H_5CO; ^{1}H-NMR (500.13 MHz, *DMSO-d*$_6$); δ 13.86 (1H, s, H-4), 8.28 (1H, d, $J_{7,8}$=8.02 Hz, H-5), 7.88 (2H, d, $J_{2',3'}$=7.69 Hz, H-2",6"), 7.76 (1H, d, $J_{7,8}$=8.05 Hz, H-8), 7.56-7.57 (6H, m, H-6, H-4", H-2',6', H-3',5'), 7.45-7.51 (4H, m, H-4', H-3", 5", H-7) ; ^{1}H-NMR (500.13 MHz, *CDCl*$_3$); δ 12.42, (1H, s, H-4), 8.10 (2H, d, *J*=6.95 Hz, H-2",6"), 7.91 (1H, d, *J*=8.76 Hz, H-5), 7.65 (2H, d, *J*=7.27 H-2',6'), 7.59-7.40 (9H, m, H-6, H-7, H-8, H-

Ar); ^{13}C-NMR (125.75 MHz, *DMSO-d_6*); δ 165.70 (C-2), 94.34 (C-3), 148.43 (C-3a), 135.60 (C-4a), 118.75 (C-5), 127.39 (C-6), 125.99 (C-7), 127.60 (C-8), 139.30 (C-8a), 148.43 (C-9a), 189.23 (C-10), 138.88, 133.17, 131.49, 128.79, 127.72 (C-Ar); *Anal*. Calcd for $C_{23}H_{15}N_3O_2$: C, 75.60; H, 4.14; N, 11.49. Found: C, 75.50; H, 4.21; N, 11.56.

3-Benzoyl-1-(4-ethoxyphenyl)-1,4-dihydropyrrolo[2,3-b]quinoxalin-2(4H)-one (**2b**): Yellow, mp 260 °C; IR (HCB, nujol): $\tilde{\nu}_{max}$/cm^{-1} 3289 (NH); 3062 (C-H, Ar); 1708 (C=O); 1650 (C=N); 1615 (C=C); 1600 (C=C, Ar); MS: *m/z* (%), 409 (100) M^+, 380 (18) M^+-C_2H_5, 105 (58) C_6H_5CO; ^{1}H-NMR (500.13 MHz, *$CDCl_3$*); δ 12.42 (1H, s, H-4), 8.07 (2H, d, *J*= 7.30 Hz, H-2",6"), 7.90 (1H, s, *J*=7.30 Hz, H-5), 7.57-7.45 (8H, m, H-Ar), 7.04 (2H, d, *J*=8.83 Hz); ^{13}C-NMR (125.75 MHz, *DMSO-d_6*); δ Table 2; *Anal*. Calcd for $C_{25}H_{19}N_3O_3$: C, 73.33; H, 4.68; N, 10.26. Found: C, 73.84; H, 4.83; N, 10.39.

3-Benzoyl-1-(2-naphthyl)-1,4-dihydropyrrolo[2,3-b]quinoxalin-2(4H)-one (**2c**): Yellow, mp 308 °C, orange, mp 310 °C; IR (HCB, nujol): $\tilde{\nu}_{max}$/cm^{-1} 3254 (NH); 3056 (C-H, Ar); 1713 (C=O); 1647 (C=N); 1620 (C=C); 1586 (C=C, Ar); MS: *m/z* (%) = 415 (100) M^+, 338 (12.6) M^+-C_6H_5, 105 (28) C_6H_5CO; ^{1}H-NMR (500.13 MHz, *DMSO-d_6*); δ 13.84 (1H, s, H-4), 8.27 (1H, d, *J*=8.12 Hz, H-5), 8.10 (1H, s, H-2'), 8.07 (1H, d, *J*= 8.72 Hz, H-8'), 7.90-8.02 (2H, m, H-4',5'), 7.90 (2H, d, *J*=7.33 Hz, H-2",6"), 7.75 (1H, d, *J*=7.98 Hz, H-8), 7.70 (1H, dd, J^3=8.69 Hz, J^4=2.00 Hz, H-7'), 7.54-7.61 (4H, m, H-Ar), 7.46-7.50 (3H, m, H-Ar); ^{1}H-NMR (500.13 MHz, *$CDCl_3$*); δ 12.45 (1H, s, H-4), 8.14 (1H, d, J^4= 1.87 Hz, H-2'), 8.10 (2H, d, *J*= 7.10 Hz, H-2",6"), 7.99 (1H,s, *J*=8.87 Hz, H-5), 7.92- 7.89 (3H, m, H-Ar), 7. 76 (1H, dd, J^3=8.70 Hz, J^4=2.07 Hz, H-8), 7.61- 7.46 (8H, H-Ar); ^{13}C-NMR (125.75 MHz, *DMSO-d_6*); δ 165.76 (C-2), 94.33 (C-3), 148.48 (C-3a), 135.57 (C-4a), 118.74 (C-5), 127.35 (C-6), 125.92 (C-7), 127.54 (C-8), 139.33 (C-8a), 148.48 (C-9a), 189.16 (C-10), 138.87, 132.77, 131.89, 131.40, 130.69, 128.72, 128.24, 127.86, 127.69, 127.61, 126.52, 126.11, 125.76 (C-Ar); *Anal*. Calcd for $C_{27}H_{17}N_3O_2$: C, 78.05; H, 4.13; N, 10.11. Found: C, 78.13; H, 4.045; N, 10.07.

3-(4-Chlorobenzoyl)-1-phenyl-1,4-dihydropyrrolo[2,3-b]quinoxalin-2-(4H)-one (**2d**): Yellow, mp 279 °C; IR (HCB, nujol): $\tilde{\nu}_{max}$/cm^{-1} 3237 (NH); 3061 (C-H, Ar); 1706 (C=O); 1645 (C=N); 1613 (C=C); 1591 (C=C, Ar); MS: *m/z* (%) = 399 (100) M^+, 139 (30) *p*-^{35}Cl-C_6H_4, 141 (9.7) *p*-^{37}Cl-C_6H_4; ^{1}H-NMR (300.08 MHz, *DMSO-d_6*); δ 13.84 (1H, s, H-4), 8.24 (1H, d, *J*=8.25 Hz, H-5), 7.87 (2H, d, *J*=8.52 Hz, H-2",6"), 7.75 (1H, d, *J*=6.60 Hz, H-8), 7.55-7.39 (9H, m, H-Ar); *Anal*. Calcd for $C_{23}H_{14}N_3O_2Cl$: C, 69.09; H, 3.53; N, 10.50. Found: C, 68.95; H, 3.74; N, 10.25.

3-Benzoyl-1-(4-chlorophenyl)-1,4-dihydropyrrolo[2,3-b]quinoxalin-2(4H)-one (**2e**): Yellow, mp 327 °C;

IR (HCB, nujol): $\tilde{\nu}_{max}/cm^{-1}$ 3250 (NH); 3053 (C-H, Ar); 1715 (C=O); 1650 (C=N); 1610 (C=C); MS: *m/z* (%) = 399 (100) M^+, 105 (28) C_6H_5CO; ^{1}H-NMR (500.13 MHz, *DMSO-d_6*); δ 13.8 (1H, s, H-4), 8.25 (1H, d, *J*=7.58 Hz, H-5), 7.87 (2H, d, *J*=7.24 Hz, H-2",6"), 7.75 (1H, d, *J*=8.07 Hz, H-8), 7.62 (4H, s, H-Ar^2), 7.56 (2H, t, *J*=6.80 Hz, H-Ar^1), 7.46-7.50 (3H, m, H-Ar^1); ^{13}C-NMR (125.77 MHz, *DMSO-d_6*); δ 165.42 (C-2), 94.29 (C-3), 148.11 (C-3a), 135.48 (C-4a), 118.77 (C-5), 127.44 (C-6), 125.96 (C-7), 127.55 (C-8), 139.38 (C-8a), 148.11 (C-9a), 189.11 (C-10), 127.49, 127.74, 127-73, 128.73 129.20, 131.44, 131.82, 132.07, 138.82 (C-Ar); *Anal*. Calcd for $C_{23}H_{14}N_3O_2Cl$: C, 69.09; H, 3.53; N, 10.50. Found: C, 69.0; H, 3.50; N, 10.41.

ACKNOWLEDGMENTS

We thank Dr. Anna Kolasa for useful discussions.

REFERENCES

1. A. Dell, D. H. Williams, H. R. Morris, G. A. Smith, J. Feeney, and G. C. K . Roberts, *J. Am. Chem. Soc.*,1975, **97,** 2497.
2. K. Sato, O. Shiratori, and K. Katagiri, *J. Antibiot.*, 1967, **A20**, 270.
3. G. Campiani, E. Morelli, S. Gemma, V. Nacci, S. Butini, M. Hamon, E. Novellino, G. Greco, A. Cagnotto, M. Goegan, L. Cervo, F. D. Valle, C. Fracasso, S.Caccia, and T. Mennini, *J. Med. Chem.,* 1999, **42**, 4362.
4. I. R. Ager, A. C. Barnes, G. W. Danswan, P. W. Hairsine, D. P. Kay, P. D. Kennwell, S. S Matharu, P. Miller, P. Robson, D. A. Rowlands, W. R. Tully, and R. Westwood, *J. Med. Chem.*,1988, **31**, 1098.
5. A. E. A. Porter, in "Comprehensive Heterocyclic Chemistry", ed. by A. R. Katritzky, C. W. Rees, A. J. Boulton, and A. Mckillop, Pergamon Press, Oxford, 1984, Vol. 3 , p. 195.
6. R. H. Wiley and S. C. Slaymaker, *J. Amer. Chem. Soc.,* 1958, **80**, 1385.
7. Patent, BASF, DE 1196205, 1965 (*Chem. Abstr*.,1965, **63**, 14884d).
8. P. Dimroth and F. Reichender, *Angew. Chem*., 1969, **81,** 742.
9. H. Nishi, K. Kitahara, and S. Tokita, *Nippon Kagaku Kaishi*, 1977, 146.
10. J. Toman, J. Klicnar, and V. Machacek, *Collect. Czech. Chem. Commun.*, 1977, **42**, 529.
11. M. Augustin and P. Jeschke, *J. Prakt. Chem*., 1987, **329**, 293.
12. M. Augustin and P. Jeschke, *J. Prakt. Chem*., 1987, **329**, 599.
13. L. Hanaineh-Abdelnour, S. Bayyuk, and R. Theodorie, *Tetrahedron*, 1999, **55,** 11859.
14. K. Kostka and E. Budzisz, *Pol. J. Chem*., 1991, **65,** 889.
15. H. Rupe and B. Pieper, *Helv. Chim. Acta*, 1929, **12,** 642.

16. W. R. Vaughan and R. C. Tripp, *J. Amer. Chem. Soc.*, 1960, **82**, 4370.
17. J. R. Merchant, R. J. Shah, and R. M. Bhandarker, *Recl. Trav. Chim. Pays-Bas*, 1962, **81**,131.
18. J. R. Merchant, M. A. Hakim, K. S. Pillay, and J. R. Patell, *J. Med. Chem.*, 1971, **14**, 1239.
19. J. R. Merchant, M. A. Hakim, and K. S. Pillay, *J. Indian Chem. Soc.*, 1972, **49**, 403.
20. G. Kollenz, *Justus Liebigs Ann. Chem.*, **1972**, 13.
21. M. L. Purkayastha, H. Chandrasekharam, and H. Junjappa, *Indian J. Chem.*, 1991, **30B**, 646.
22. D. D. Chapman, *J. Org. Chem.*, 1972, **37**, 2498.
23. W. Żankowska.-Jasińska, B. Zaleska, and K. Walocha, *Zesz. Nauk. Uniw. Jagiellonskiego.*, 1973,**18**,137.
24. W. Żankowska-Jasińska and K. Ostrowska, *J. Prakt. Chem.*, 1989, **331**, 700.
25. W. Żankowska-Jasińska and K. Ostrowska, *J. Prakt. Chem.*, 1991, **333**, 619.
26. B. Zaleska and S. Lis, *Synthesis*, 2001, 811.
27. K. Ostrowska, M. Ciechanowicz –Rutkowska, T. Pilati, and G. Żuchowski, *Monatsh. Chem.*, 1999, **130**, 555.
28. R. A. More O'Ferral and B. A. Murray, *J. Chem. Soc., Perkin Trans. 2*, 1994, **12**, 2461.
29. W. Żankowska-Jasińska, B. Zaleska, and K. Walocha, *Zesz. Nauk. Uniw. Jagiellonskiego*, 1976, **21**, 133.
30. K. Ostrowska, W. Żankowska-Jasińska, M. Ciechanowicz-Rutkowska, and T. Pilati, *J. Chem. Res.(S)*, 1996, 236.