Chemistry of Natural Compounds, Vol. 42, No. 5, 2006

DEOXYPEGAN-1-ONE DERIVATIVES. SYNTHESIS AND BOROHYDRIDE REDUCTION OF 3-[(*E*)-ARYLMETHYLIDENE]-3,9-DIHYDROPYRROLO[2,1-*b*]QUINAZOLIN-1(2H)-ONES

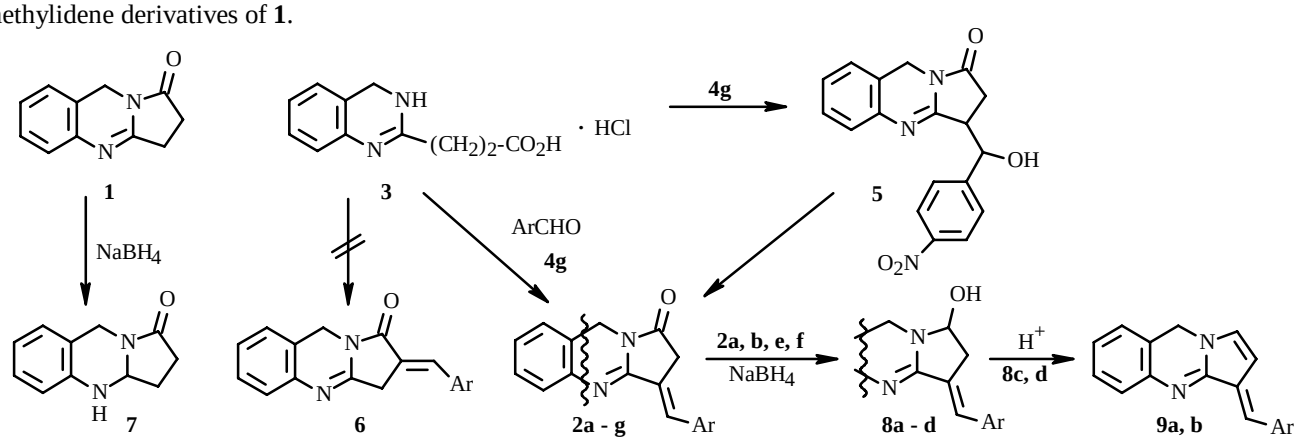
L. M. Potikha, N. V. Shkol′naya, and V. A. Kovtunenko

UDC 547.856.1+547.75

*3-[(*E*)-Arylmethylidene]-3,9-dihydropyrrolo[2,1-b]quinazolin-1(2H)-ones were prepared by reaction of quinazolyl-2-propionic acid hydrochloride with aromatic aldehydes in acetic anhydride in the presence of Et_3N. 3-[(*E*)-Arylmethylidene]-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-1-ols were formed by reduction of the 3-arylidene derivatives with sodium borohydride in methanol, readily lost water when heated with acids, and were converted into 3-[(*E*)-arylmethylidene]-3,9-dihydropyrrolo[2,1-b]quinazolines.*

Key words: reduction, 3,9-dihydropyrrolo[2,1-*b*]quinazolin-1(2H)-one, quinazolyl-2-propionic acid, 3-[(*E*)-arylmethylidene]-3,9-dihydropyrrolo[2,1-*b*]quinazolin-1(2H)-one, 3-[(*E*)-arylmethylidene]-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-1-ol, 3-[(*E*)-arylmethylidene]-3,9-dihydropyrrolo[2,1-*b*]quinazoline.

Several biologically active natural and synthetic compounds with distinct cholinotropic activity are based on the pyrrolo[2,1-*b*]quinazoline heterocyclic system. Many of them are used as medicinal agents [1-7], which makes it promising to search for new synthetic pathways to pyrrolo[2,1-*b*]quinazolines. The properties of 1,2,3,9-tetrahydro- and 9-oxo-dihydro derivatives of this heterosystem such as peganine, deoxypeganine, vasicinone, and deoxyvasicinone, the major alkaloids of *Peganum harmala* and *P. nigellastrum*, have been thoroughly studied in a series of reports [8-15]. However, the properties of deoxypegan-1-one (**1**) are practically unknown because of its scarcity. We found previously [16] that protonation, alkylation, and acylation of 3,9-dihydropyrrolo[2,1-*b*]quinazolin-1(2H)-one (**1**) occurs at $N_{(4)}$. The resulting pyrrolo[2,1-*b*]quinazolin-4-ium salts are hydrolytically unstable and readily cleave to form derivatives of quinazolyl-2-propionic acid or 1-(2-aminobenzyl)succinimide. Herein we report the results of the condensation with aldehydes and the properties of the prepared methylidene derivatives of **1**.



2a - g, 4a - g Ar: C_6H_5 (**a**), 4-ClC_6H_4 (**b**), 4-HO-C_6H_4 (**c**), 4-$(CH_3)_2N$-C_6H_4 (**d**), 4-CH_3-O-C_6H_4 (**e**), 3,4-$(OCH_3)_2$-C_6H_3 (**f**), 4-O_2N-C_6H_4 (**g**)
8a - d, Ar: 4-ClC_6H_4 (**a**), C_6H_5 (**b**), 4-CH_3O-C_6H_4 (**c**), 3,4-$(OCH_3)_2$-C_6H_3 (**d**)
9a, b Ar: 4-CH_3O-C_6H_4 (**a**), 3,4-$(OCH_3)_2$-C_6H_3 (**b**)

Taras Shevchenko Kiev University, Kiev, 01033, Ukraine, e-mail: potikha_l@mail.ru. Translated from Khimiya Prirodnykh Soedinenii, No. 5, pp. 463-467, September-October, 2006. Original article submitted June 9, 2006.

 0009-3130/06/4205-0576

TABLE 1. Spectral and Physical Chemical Properties of 3,9-Dihydropyrrolo[2,1-*b*]quinazolin-1(2H)-ones **2a-g**, **8a-d**, and **9a**,**b**

Compound empirical formula	mp, °C	Yield, % method	IR spectrum (KBr, ν, cm^{-1})	PMR spectrum (DMSO-d_6*, δ, ppm, J/Hz)				
				=CHAr 1H, s	ArH	$C_{(9)}H_2$, 2H, s	$C_{(2)}H_2$, 2H, s	other signals
2a $C_{18}H_{14}N_2O$	181-184 (EtOH)	58 (B), 70 (C)	1725 (C=O), 1610 (C=N), 1590, 1480, 1410, 1260, 760	7.61	7.57 (2H, d, J = 8.0, 2′-H, 6′-H), 7.43 (2H, t, J = 8.0, 3′-H, 5′-H), 7.36 (1H, t, J = 8.0, 4′-H), 7.23-7.16 (2H, m, 5-H, 7-H), 7.10 (2H, m, 6-H, 8-H)	4.85	3.61	-
2b** $C_{18}H_{13}ClN_2O$	235-237 (*i*-PrOH)	60 (B), 75 (C)	1725 (C=O), 1615 (C=N), 1590, 1480, 1405, 760	7.58	7.59 (2H, d, J = 8.4, 2′-H, 6′-H), 7.57 (1H, t, J = 8.4, 4′-H), 7.43 (2H, d, J = 8.4, 3′-H, 5′-H), 7.22-7.09 (4H, m, 5-H-8-H)	4.84	3.61	-
2c $C_{20}H_{19}N_3O$	207-210 (*i*-PrOH)	45 (B), 50 (C)	1735 (C=O), 1610 (C=N), 1580, 1370, 1180, 765	7.51	7.40 (2H, d, J = 8.8, 2′-H, 6′-H), 7.19-7.05 (4H, m, 5-H-8-H), 6.73 (2H, d, J = 8.8, 3′-H, 5′-H)	4.81	3.51	3.03 (6H, s, $N(CH_3)_2$)
2d $C_{19}H_{16}N_2O_2$	203-205 (EtOH)	60 (B), 68 (C)	1725 (C=O), 1615 (C=N), 1585, 1400, 1250 (C-O)	7.59	7.50 (2H, d, J = 8, 2′-H, 6′-H), 7.23-7.15 (2H, m, 5-H, 7-H), 7.08 (2H, m, 6-H, 8-H), 6.95 (2H, d, J = 8, 3′-H, 5′-H)	4.80	3.54	3.83 3H, s, OCH_3)
2e $C_{20}H_{18}N_2O_3$	187-190 (EtOH)	67 (B), 73 (C)	1720 (C=O), 1615 (C=N), 1580, 1250, 1230 (C-O)	7.52	7.20 (1H), m, 7-H), 7.15-7.06 (5H, m, 5-H, 6-H, 8-H, 2′-H, 6′-H), 6.97 (1H, d, J = 8.2, 5′-H	4.83	3.62	3.83 (3H, s, 4′-OCH_3), 3.85 (3H, s, 3′-OCH_3)
2g $C_{18}H_{13}N_3O_3$	227-229 (*i*-PrOH)	30 (A), 65 (C)	1780 (C=O), 1640 (C=N), 1510, 1340 ($^{s,as}NO_2$)	7.52	8.28 (2H, d, J = 8.8, 3′-H, 5′-H), 7.91 (2H, d, J = 8.8, 2′-H, 6′-H), 7.30 (1H, m, 7-H), 7.27-720 (3H, m, 5-H, 6-H, 8-H)	4.92	3.82	-
8a** $C_{18}H_{15}ClN_2O$	200-203 (*i*-PrOH)	60	3123 (OH), 1610 (C=N), 1590, 1480, 1410, 1260, 760	7.39	7.51 (2H, d, J = 8.0), 3′-H, 5′-H), 7.40 (2H, d, J = 8.0, 2′-H, 6′-H), 7.31 (1H, t, J = 8.0, 4′-H), 7.08 (1H, t, J = 8.0, 7-H), 6.97-6.89 (3H, m, 5-H, 6-H, 8-H)	4.81, d 4.52, d ^2J = 16.0	3.31, dd ^2J = 18.0 ^3J = 4.4; 2.80, dm ^2J = 18.0	6.12 (1H, d, ^3J = 7.2, OH); 5.10 (1H, m, 1-H)
8b $C_{18}H_{16}N_2O$	206-208 (*i*-PrOH)	70	3070 (OH), 1595 (C=N), 1480, 1375, 1060, 745	7.43	7.52 (2H, d, J = 8.0, 3′-H, 5′-H), 7.41 (2H, d, J = 8.0, 2′-H, 6′-H), 7.09 (1H, t, J = 8.0, 7-H), 6.97-6.90 (3H, m, 5-H, 6-H, 8-H)	4.80, d 4.52, d ^2J = 16.0	3.24, dd ^2J = 17.6 ^3J = 6.4; 2.76, dm ^2J = 17.6	6.12 (1H, d, ^3J = 8.5, OH); 5.11 (1H, m, 1-H)
8c $C_{19}H_{18}N_2O_2$	218-220 (p) (EtOH)	63	3100 (OH), 1610 (C=N), 1590, 1445, 1180, 760	7.36	7.45 (2H, d, J = 8.0, 3′-H, 5′-H), 7.06 (1H, t, J = 8.0, 7-H), 6.98-6.92 (3H, m, 5-H, 6-H, 8-H), 6.90 (2H, d, J = 8.0, 2′-H, 6′-H)	4.78, d 4.49, d ^2J = 16.0	3.25, dd ^2J = 17.6 ^3J = 5.5; 2.75, dm ^2J = 17.6	6.07 (1H, d, ^3J = 7.2, OH); 5.09 (1H, m, 1-H); 3.82 (3H, s,OCH_3)
8d $C_{20}H_{20}N_2O_3$	209-211 (EtOH)	70	3125 (OH), 1595 (C=N), 1435, 1250, 1325, 765	7.45	7.14-7.05 (3H, m, 2′-H, 5′-H, 6′-H), 7.01-6.86 (4H, m, 5-H-8-H)	4.81, d 4.54, d ^2J = 16.0	3.31, dd ^2J = 18.0 ^3J = 6.0; 2.80, dm ^2J = 18.0	6.09 (1H, d, ^3J = 7.6, OH); 5.08 (1H, m, 1-H); 3.86 (3H, s, 4′-OCH_3), 3.84 (3H, s, 3′-OCH_3)
9a $C_{20}H_{18}N_2O_3$	>300 (*i*-PrOH)	53	1640 (C=O), 1590 (C=N), 1380, 1290, 785	8.10	7.87 (3H, m, 5-H, 2′-H, 6′-H), 7.43 (1H, m, 7-H), 7.36 (1H, t, J = 8.0, 6-H), 7.27 (1H, d, J = 7.2, 8-H), 7.20 (2H, d, J = 7.6, 3′-H, 5′-H)	5.28	6.90 1H, d, ^3J = 4.0	6.88 (1H, d, ^3J = 4.0, 1-H), 4.06 (3H, s, OCH_3)
9b $C_{19}H_{16}N_2O_2$	>310 (*i*-PrOH)	40	1650 (C=O), 1600 (C=N), 1360, 1000, 780	8.10	7.61 (1H, d, J = 8.0, 5-H), 7.44 (2H, m, 7-H, 2′-H), 7.36 (1H, t, J = 7.6, 6-H), 7.26 (1H, d, J = 7.5, 8-H), 7.20 (2H, d, J = 8.5, 5′-H, 6′-H)	5.28	6.85 1H, d, ^3J = 4.0	6.91 (1H, d, ^3J = 4.0, 1-H), 4.08 (3H, s, 4′-OCH_3), 4.09 (3H, s, 3′-OCH_3)

*Spectra of **9a**, **b** were recorded in CF_3CO_2D.**Elemental analyses for Cl: found (calc.) 11.45 (11.48) for **2b**; 11.39 (11.41), **8a**.

One of the characteristic reactions of carbonyl compounds and imines with an activated methylene is the condensation with aldehydes. For pyrrolo[2,1-*b*]quinazolines, this reaction has been studied using 1,2,3,9-tetrahydro- and 9-oxo-2,3-dihydro derivatives of deoxypeganine [11, 12] and deoxyvasicinone [13-15] as examples. A series of 3-arylidene derivatives with a high level of biological activity were prepared [11-13, 17].

We hoped that it would be possible to prepare the corresponding 3-(arylmethylidene)-3,9-dihydropyrrolo [2,1-*b*]quinazolin-1(2H)-ones (**2a-g**). For this, we tested various conditions such as heating **1** or **1**·HCl with aldehydes in acetic anhydride (Method A), in mixtures with acetic anhydride and Et_3N (Method B) in propan-2-ol with added morpholine, and in mixtures of propan-2-ol, acetic anhydride, and Et_3N (Method C). However, complicated product mixtures were formed in most instances under these conditions. Obviously this was due to the hydrolytic instability of **1** and its protonated salt and to the tendency of 9-hydro derivatives of pyrrolo[2,1-*b*]quinazoline to oxidize [18, 19]. For these reasons attempts to condense aldehydes with 4-alkyl-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-4-ium salts were also unsuccessful [16].

An unexpectedly successful solution to this problem turned out to be the use under these conditions of quinazolyl-2-propionic acid hydrochloride (**3**). We found in the literature other examples of similar transformations. Thus, cyclic condensation products, 3-(arylmethylidene)-9-thioxypyrrolo[2,1-*b*]quinazolin-1(2H,9H)-ones were prepared by reacting 2-(2-carboxyethyl)-4(3H)-quinazolinethione with aromatic aldehydes [20]. 3-(1H-Benzimidazol-2-yl)propionic acid behaves similarly on heating with aldehydes in acetic anhydride [21]. The formation of the condensation products of (quinazolin-2-yl)- and (benzimidazo-2-yl)-propionic acids probably increases the nucleophilicity of the N-3 atom and, as a result, accelerates the cyclization and increases the hydrolytic stability of the final products.

We found indirect evidence of this in the dependence of the condensation product yields on the reaction conditions and the nature of the substituents in the benzene ring of the starting aldehyde (**4a-g**). Thus, the highest yields of **2** were obtained using aldehydes with donor substituents (**4e** and **4f**) in the presence of base (Table 1, Methods B and C). The exception was *p*-dimethylaminobenzaldehyde (**4d**), the carbonyl activity of which is low in basic medium. The reaction of **3**·HCl with *p*-nitrobenzaldehyde (Method C) produced the aldol condensation product 3-[hydroxy(4-nitrophenyl)methyl]-3,9-dihydropyrrolo[2,1-*b*]quinazolin-1(2H)-one (**5**).

Spectral data indicated that hydroxymethyl derivative **5** had formed. The PMR spectrum (DMSO-d_6) exhibited signals for ArCH(OH) protons at 6.02 ppm (d, ^3J = 4.4 Hz, OH) and 5.42 ppm (m, CH), for pyrrole protons $C_{(2)}H_2$–$C_{(3)}HR$ as an ABX-spin system at 3.37 ppm (m, H_X-3), and two doublets of doublets for methylenes at 2.43 ppm (^3J = 4.4 Hz, ^2J = 17.6 Hz) and 2.23 ppm (^3J = 9.6 Hz, ^2J = 17.6 Hz). The IR spectra contained ν_{OH} stretching vibrations at 3400 cm^{-1}. Compound **5** readily lost water on boiling in acetic anhydride to produce the correspoinding arylidene derivative **2g**. This same condensation product was produced but in lower yield (30%) by reacting **3**·HCl with *p*-nitrobenzaldehyde without base (Method A).

Because the $C_{(2)}H_2$ methylene in **1** or the α-methylene in **3** could be reactive toward electrophiles, we also considered the possibility that 2-arylidenepyrroloquinazolin-1-ones (**6**) could be formed. The PMR spectra of the condensation products in DMSO-d_6 did not enable the structures to be assigned unambiguously. However, their IR spectra (Table 1) indicated that structure **2** was present. The $\nu_{C=O}$ carbonyl vibrational frequency of the arylidene derivatives was greater by 5-10 cm^{-1} compared with that of **1** as a result of the increased electronegativity of C-2 bound to it. The decrease of $\nu_{C=N}$ by 10 cm^{-1} indicated that the conjugation had been lengthened so that the structure **2** was most probable. A different scenario could be proposed for the structure of **6**. A NOE experiment enabled the configuration of the prepared arylidene derivatives to be determined. Saturation at the resonance frequency of the ArHC=C–$C_{(2)}H_2$– methylene (**2e**, 3.54 ppm) increased the intensity of the doublet for aromatic protons H-2′ and H-6′ (7.50 ppm) by 4%, which indicated that the *E*-isomer had formed.

Analysis of the structures of the borohydride reduction products provided the final confirmation of the structures of the condensation products as 3-arylidene derivatives **2**. We hoped that reduction products with a $N_{(4)}$=$C_{(3a)}$ double bond would form under these conditions because the reaction of peganine and vasicinone derivatives with $NaBH_4$ occurred in this direction [22, 23]. 3,3a,4,9-Tetrahydropyrrolo[2,1-*b*]quinazolin-1(2H)-one (**7**) was prepared previously [24] from **1** although by electrochemical reduction. Hydrogenation of the $N_{(4)}$=$C_{(3a)}$ double bond occurred also without cleavage of the pyrrole ring during reaction of **1** with Na in amyl alcohol [25]. However, the carbonyl was also reduced to a methylene.

We found that the reaction of **1** with $NaBH_4$ in alcohol formed a complicated mixture of hydrolysis products. Carrying out the reaction in acetic acid produced a mixture containing hydrolysis products and **7** (<30% of the mixture according to PMR spectra in $CDCl_3$ and PMR spectra in $CDCl_3$ reported previously [24]). Repeated recrystallization from alcohol produced **7** in 90% purity. Its IR spectrum had a strong carbonyl vibration at 1680 cm^{-1}. This confirmed that the 3a,4-dihydro derivative of structure **7** had formed.

Arylidene derivatives **2** were hydrolytically more stable. The reaction occurred at room temperature in CH_3OH with an excess of $NaBH_4$ and produced the tetrahydro derivatives in good yields (60-70%). However, we could not prepare the corresponding tetrahydro derivatives under certain conditions. Thus, reaction of $NaBH_4$ with 3-(*p*-hydroxyarylidene) derivative **2c** produced a complicated mixture containing less than 30% tetrahydropyrroloquinazoline (according to PMR spectra of the mixture). For 3-(*p*-dimethylaminoarylidene) derivative **2d**, the reaction occurred very slowly and produced mainly hydrolysis products. An analogous result, but under more forcing conditions, occurred in an attempt to reduce 3-(*p*-nitroarylidene) derivative **2g**. Obviously the reason for the lack of success in this instance was the lower hydrolytic stability of **2g** under the influence of the electron-accepting nitro group.

PMR spectra (DMSO-d_6) of the reduction products exhibited in the range 6.08-6.14 ppm a signal for a proton exchanging with D_2O. The splitting of the signals for the methine proton (5.08-5.11 ppm, m) and the two methylene groups of the pyrrole at 3.30 ppm (1H, dd) and 2.75-2.80 ppm (1H, dm) with ^2J = 17.6-18.0 Hz was consistent with spin—spin coupling among them. A COSY HH experiment confirmed this. IR spectra contained vibration bands at 3070 cm^{-1} for OH or NH. However, chacteristic bands for carbonyls were not found (for **1**, a strong $\nu_{C=O}$ band at 1720 cm^{-1}). The ^{13}C NMR spectrum (CCl_4) of the reduction product with Ar = Ph (**8b**) also lacked a signal for a carbonyl in the characteristic range (δ > 160 ppm). The methine C resonated at weaker field (83.49 ppm) than would have been expected for C-3a if 3a,4-dihydro derivatives had formed.

It is well known [26, 27] that *N*-substituted succinimides are readily reduced by $NaBH_4$ to 5-hydroxy-2-pyrrolidinone derivatives. Obviously, for derivatives of **2**, the reaction proceeds along this same pathway and forms 3-[(*E*)-arylmethylidene]-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-1-ols (**8a-d**). This result is probably due to the increased electron density of $C_{(3a)}$ in arylidene derivatives **2**, on one hand, and the greater steric hindrance to attack of the bulky tetrahydroborate anion at the $C_{(3a)}$=$N_{(4)}$ group than at the $C_{(1)}$=O group.

The correctness of this conclusion about the structure of the reduction products was confirmed by the behavior of **8** in the presence of strong acids. Thus, dehydration occurred in trifluoroacetic acid (CF_3CO_2D) according to PMR spectra. This was indicated by the lack of a signal for methine proton H-1 and methylene $C_{(2)}H_2$ (Table 1) and by the change in multiplicity of the methylene signals of $C_{(9)}H_2$, which were observed as 2H singlets at 5.28-5.33 ppm and two 1H doublets for H-1 and H-2 at 6.80-6.90 ppm with SSCC 4.0 Hz.

Loss of water was also the principal fragmentation pathway in mass spectra of **8** (CF_3CO_2H ionization). This transformation was carried out preparatively by boiling **8c** and **8d** in HCl (conc.). This produced **9c** and **9d**. The dehydration rate decreased as the substituent donor effect in the benzene ring of the arylidene fragment decreased. For **9b**, only partial dehydration occurred on prolonged boiling in HCl (conc.). The principal reaction pathway (and only one for **8a**) was formation of hydrolysis products.

Compounds **8** were inert towards other electrophiles (alkyl- and acylhalides) regardless of the conditions, like the corresponding 1-oxo derivatives **2**.

EXPERIMENTAL

Melting points were determined on a Boetius heating stage and are uncorrected. IR spectra of compounds in KBr disks were recorded on a Pye Unicam SP3-300 instrument. NMR spectra of compounds in DMSO-d_6 and CF_3CO_2D solutions were obtained on a Mercury 400 (Varian; 400 MHz for ^1H; 100 MHz, ^{13}C) instrument with TMS internal standard. Mass spectra were obtained using HPLC in an Agilent/100-Series instrument (CI, CH_3CN, 0.05% formic acid). Chemical shifts are given on the δ scale. The course of reactions and the purity of products were monitored using TLC on Silufol UV-254 plates.

3-[(*E*)-Arylmethylidene]-3,9-dihydropyrrolo[2,1-*b*]quinazolin-1(2H)-ones (2a-f). Method A. A mixture of **3** (1 g, 0.005 mol) and aldehyde (0.005 mol) in acetic anhydride (5 mL) was boiled until the solid completely dissolved and was left to cool slowly. The precipitate that formed after several hours was filtered off and washed with alcohol.

Method B. A mixture of **3** (1 g, 0.005 mol) and aldehyde (0.0065 mol) was boiled in a mixture (5 mL, 1:1) of Et_3N and acetic anhydride until the solid completely dissolved and left to cool slowly. The precipitate that formed after several hours was filtered off and washed with alcohol.

Method C. A mixture of **3** (1 g, 0.005 mol) and aldehyde (0.0065 mol) was boiled in a mixture (10 mL, 1:1:2) of Et_3N, acetic anhydride, and propan-2-ol until the solid completely dissolved and left to cool slowly. The precipitate that formed after several hours was filtered off and washed with alcohol.

3-[Hydroxy(4-nitrophenyl)methyl]-3,9-dihydropyrrolo[2,1-*b*]quinazolin-1(2H)-one (5) was prepared by method C and was used for **2a-f**. Yield 0.9 g (53%), mp 213-215°C (*i*-PrOH).

IR spectrum (KBr, ν, cm^{-1}): 3400 (N–H), 1700 (C=O), 1630 (C=N), 1505, 1335 ($^{s,as}NO_2$), 1180, 1030, 1105, 850, 785. PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 8.23 (1H, d, ^3J = 8.8, H-3′, H-5′), 7.73 (1H, d, ^3J = 8.8, H-2′, H-6′), 7.21 (1H, d, ^3J = 8, H-7), 7.12 (3H, m, H-5, H-6, H-8), 6.0 [1H, d, ^3J = 3.0, CH(OH)-3], 5.42 [1H, d, ^3J = 3.0, CH(OH)-3], 4.76 (2H, m, $C_{(9)}H_2$), 3.37 (2H, m, $C_{(3)}H_2$), 2.43 (1H, dd, ^3J = 4.4, ^2J = 17.6, $C_{(2)}H_A$), 2.23 (1H, dd, ^3J = 9.6, ^2J = 17.6, $C_{(2)}H_B$). $C_{18}H_{15}N_3O_4$.

3-[(*E*)-(4-Nitrophenyl(methylidene)]-3,9-dihydropyrrolo[2,1-*b*]quinazolin-1(2H)-one (2g). Compound **5** (0.8 g, 0.005 mol) in acetic anhydride (5 mL) was boiled until the solid completely dissolved and left to cool slowly. The precipitate that formed after several hours was filtered off and washed with alcohol.

3-[(*E*)-Arylmethylidene]-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolin-1-ols (8a-d). A suspension of **2** (0.005 mol) in aqueous CH_3OH (5 mL) was treated in portions with a two-fold excess of $NaBH_4$ (0.37 g, 0.01 mol), heated for 5 h, cooled, and concentrated in vacuo. The dry solid was treated with water (20 mL), filtered off, and washed with water.

8a: Mass spectrum (CI, *m*/*z*, I_{rel}, %): 310.8 (100) $[M + H]^+$, 294.4 (15), 293.2 (48) $[M - H_2O]^+$, 201.2 (6), 169.2 (10), 156 (5).

8b: ^{13}C NMR spectrum (400 MHz, CCl_4, δ, ppm): 156.66 (C-3a), 136.39, 131.81, 129.66, 129.03, 128.62, 128.27, 127.23, 126.60, 124.25, 123.99 (C-3, C-4a—C-8a, C-1′—C-6′, =CHAr), 83.49 (C-1), 43.72 (C-9), 36.64 (C-2). Mass spectrum (CI, *m*/*z*, I_{rel}, %): 276 (100) $[M + H]^+$, 273 (90), 258.8 (26) $[M - H_2O]^+$, 169.2 (23), 157.2 (10).

8d: Mass spectrum (CI, *m*/*z*, I_{rel}, %): 337 (100) $[M + H]^+$, 234 (12), 318.8 (15) $[M - H_2O]^+$, 157.2 (30), 101.2 (10).

3-[(*E*)-Arylmethylidene]-3,9-dihydropyrrolo[2,1-*b*]quinazolines (9c, 9d). A mixture of **8c** or **8d** (0.005 mol) in HCl (5 mL, conc.) was heated for 2 h. The resulting red solution was cooled. The precipitate that formed was filtered off and crystallized from ethanol.

REFERENCES

1. D. Batsuren, M. V. Telezhenetskaya, and S. Yu. Yunusov, *Khim. Prir. Soedin.*, 736 (1980).
2. V. N. Plugar′, N. D. Abdullaev, Ya. V. Rashkes, M. R. Yagudaev, and N. Tulyaganov, *Khim. Prir. Soedin.*, 758 (1983).
3. J. Moormann and H. Mucke, Pat. WO 2003053445 A1 20030703, Germany, Appl. WO 2002-EP14274 20021214.
4. J. Moormann, H. Mucke, and K. Opitz, Pat. WO 2002102388 A2 20021227, Germany, Appl. WO 2002-EP6630 20020615.
5. K. Opitz, J. Moormann, T. Hille, and F. Becher, Pat. WO 2002087553 A2 20021107, Germany, Appl. WO 2002-EP4278 20020418.
6. B. Asmussen, T. Hille, H.-R. Hoffman, and K. Opitz, Pat. WO 2000048599 A1 20000824, Germany, Appl. WO 2000-EP972 20000208.
7. B. Ojo, L. A. Findsen, N. Igarashi, B. Kong, and K. Bejoy, *Drug Design and Discovery*, **14**, No. 1, 1 (1996).
8. Kh. Sh. Shakhidoyatov, A. Irisbaev, L. M. Yun, E. Oripov, and Ch. Sh. Kadyrov, *Khim. Prir. Soedin.*, 1564 (1976).
9. Kh. Shakhidoyatov, F. Kiyamitdinova, and Ch. Sh. Kadyrov, *Khim. Prir. Soedin.*, 765 (1975).
10. Kh. Sh. Shakhidoyatov, A. Irisbaeva, E. Oripov, and Ch. Sh. Kadyrov, *Khim. Prir. Soedin.*, 557 (1976).
11. R. Andreskewitz, H. Dollinger, C. Heine, P. A. J. Pouzet, F. Birke, and T. Bouyssou, Pat. WO 2004072074 A1 20040826, Germany, Appl. WO 2004-EP1043 20040205.
12. M. N. A. Rao, S. Krishnan, M. P. Jain, and K. K. Anand, *Indian J. Pharm. Sci.*, **44**, No. 6, 151 (1982).
13. V. N. Gupta, M. P. Jain, C. K. Atal, and M. Bhardawaj, *Indian J. Chem., Sect. B*, **21**, No. 1, 74 (1982).
14. Kh. Sh. Shakhidoyatov, E. Oripov, A. Irisbaev, and Ch. Sh. Kadyrov, *Khim. Prir. Soedin.*, 825 (1976).
15. P. Molina, A. Tarraga, and A. Gonzalez-Tejero, *Synthesis*, **11**, 1523 (2000).

16. L. M. Potikha, N. V. Shkol′naya, and V. A. Kovtunenko, *Khim. Prir. Soedin.*, 459 (2006).
17. X. Wu G. Qin, K. K. Cheung, and K. F. Cheng, *Tetrahedron*, **53**, 13323 (1997).
18. M. V. Telezhenetskaya and A. L. D′yakovov, *Khim. Prir. Soedin.*, 541 (1991).
19. A. L. D′yakonov and M. V. Telezhenetskaya *Khim. Prir. Soedin.*, 528 (1991).
20. M. S. Amine, A. M. F. Eissa, A. F. Shaaban, A. El-Sawy, and R. El-Sayed, *Ind. J. Heterocycl. Chem.*, **7**, No. 4, 289 (1998).
21. W. Kuzmierkiewicz, H. Fofs, E. Hac, and H. Strzalkowska-Grad, *Pharmazie*, **40**, No. 7, 462 (1985).
22. V. P. Bruskov and M. V. Telezhenetskaya, *Khim. Prir. Soedin.*, 220 (1990).
23. B. Kh. Zharekeev, M. V. Telezhenetskaya, Kh. N. Khashimov, and S. Yu. Yunusov, *Khim. Prir. Soedin.*, 679 (1974).
24. A. Chibani, R. Hazard, and A. Tallec, *Bull. Soc. Chim. Fr.*, **128**, 814 (1991).
25. E. Spath and N. Platzer, *Chem. Ber.*, **69**, 387 (1936).
26. A. Guzman, M. Romero, and J. M. Muchowski, *Can. J. Chem.*, **68**, No. 5, 791 (1990).
27. J. A. M. Hamersma, P. M. M. Nossin, and W. N. Speckamp, *Tetrahedron*, **41**, No. 10, 1999 (1985).