An Efficient Synthesis of Pyrrolo[1,2-*a*]quinazolin-5(1*H*)-one Derivatives with the Aid of Low-Valent Titanium Reagent

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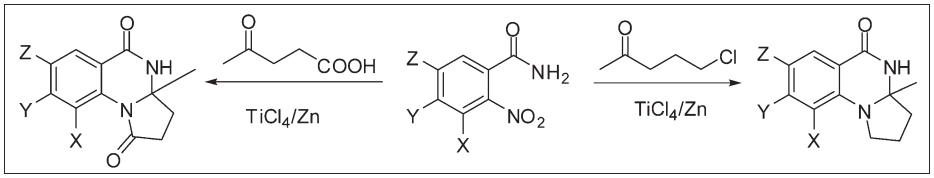

A short and facile synthesis of 2,3,3a,4-tetrahydropyrrolo[1,2-*a*]quinazolin-5(1*H*)-ones and 2,3,3a,4-tetrahydropyrrolo[1,2-*a*]quinazoline-1,5-diones in good yields via the novel reductive cyclization of 2-nitrobenzamides with haloketones or 4-oxopentanoic acid promoted by low-valent titanium reagent is described.

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INTRODUCTION

Quinazolinone is an important class of nitrogen-containing heterocycles [1], its structure widely exists in the natural products. Many with quinazolinone structure of compounds have important and wide range of medicinal value such as antibacterial, analgesics, inhibitor, and anticancer activity [2,3]. Quinazolindione derivatives are also a useful antiinflammatory agent [4]. For example, 6,7-dimethoxy-1*H*-quinazolin-2,4-dione is an important intermediate of prazosin [5], bunazosin [6], and doxazosin [7]. Prazosin, bunazosin, as well as doxazosin are effective adrenergic blockers, antihypertension drugs.

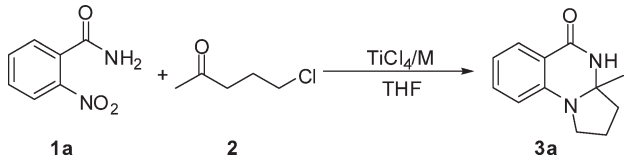
A number of synthetic strategies have been developed for the preparation of substituted quinazolinones. Stephen and Wedge [8] used 2-amino-*N*-argiobenzenesulfonamide as raw materials in the synthesis of 2-arylquinazolinone derivatives under the action of potassium hydroxide. Takeuchi [9] synthesized a series of 4(3*H*)-quinazoline ketones via intramolecular aza-Wittig reaction. Ferraccioli [10] and Schlapbach [11] successfully synthesized 2(1*H*)-quinazolinone derivatives via palladium-catalyzed. The synthesis of quinazolindiones commonly used *o*-aminobenzoic acid and urea [12,13], *o*-aminobenzamide with phosgene [14], *o*-aminobenzoic acid with potassium cyanate or chlorine sulfonyl isocyanate [15] as the raw material to synthesis. Mizuno and Iahino [16] have reported the simple solvent-free synthesis of 1*H*-quinazoline-2,4-dione using supercritical carbon dioxide and catalytic amount of base. Tatsuya *et al*. [17] have developed a method for the solid-phase synthesis of quinazoline-2,4-diones with various substituents on the aromaticring. Aeberli and Houlihan [18] have synthesized 3a-methyl- and 3a-phenyl-l,2,3,3a,4,5-hexahydropyrrolo[1,2-*a*]quinazoline-l,5-dionse by reaction of anthranilamides with 4-oxopentanoic acid and 4-oxo-4-phenylbutanoic acid. Recently, Iminov *et al*. [19,20] have reported the synthesis of pyrroloquinazoline carboxylic acids and 7a,8,9,10-tetrahydrocyclopenta[2,3]pyrrolo[1,2-*a*]quina- zoline-6,12(7*H*,11*H*)-diones from the reaction of 2-aminobenzamides with 2-oxoglutaric acid and 2-oxocyclopentaneheptaneacetic acids esters, respectively. However, many of these methods still suffer from drawbacks such as drastic conditions, unsatisfactory yields, long-reaction time, high temperature, complex manipulation, and inaccessible starting materials.

We have previously reported the synthesis of quinazolines [21], quinazoline-2,4-diones [22], imidazo[1,2-*c*]quinazolines [23], 2-thioxoquinazolinones, imidazo[1,2-*c*]quinazolin-5-amines, and benzimidazo[1,2-*c*]quinazolin-5-amines [24] by the reaction of nitro-compounds with orthoformates, triphosgene, aldehydes, ketones, and isothiocyanates, respectively, induced by low-valent titanium reagent. As our earlier works goes, herein, we wish to describe a new route to synthesizing 2,3,3a,4-tetrahydropyrrolo[1,2-*a*]quinazolin-5(1*H*)-ones and 2,3,3a,4-tetrahydropyrrolo[1,2-*a*]quinazoline-1,5-diones via the novel reductive cyclization of 2-nitrobenzamides with haloketones or 4-oxopentanoic acid mediated by low-valent titanium reagent.

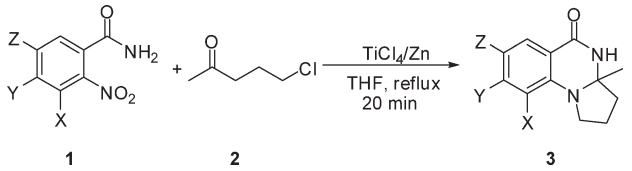
RESULTS AND DISCUSSION

On the basis of our previous experience, we selected *o*-nitrobenzamide **1a** and the 5-chloropentan-2-one **2** as

Scheme 1



Scheme 2



model substrates to optimize the experimental conditions for the proposed reductive cyclization reaction (Scheme 1).

As shown in Table 1, we briefly examined the effect of different temperatures and ratios. The results obtained from these experiments indicated that the reaction temperatures had a significant influence on the success of this reaction. To our delight, when refluxed the reaction proceeded smoothly in high yield (entry **4**) and the reaction time is only 20 min. To further evaluate the influence of ratio **1a** and $TiCl_4$/Zn, this reaction was carried out with different ratios. From the results, it is obvious that the best ratio is 1:4. Moreover, different metals ($TiCl_4$/M) were further investigated, As shown in Table 1, we concluded that Zn was the best metal for this reaction. The IR spectra of **3a** showed intense peaks at 3170 cm^{-1} for cyclic secondary amine (NH), 1661 cm^{-1} for carbonyl (C=O) stretching. ^{1}H-NMR spectra of **3a** showed a multiplet at δ 6–8 for the aromatic (4H) protons.

To demonstrate the efficiency and the applicability at the present method, we then performed the reaction of a variety of *o*-nitrobenzamides **1** via low-valent titanium system in anhydrous THF (Scheme 2). The results are summarized in Table 2.

A second part of the research was designed to determine the scope of the cyclization process with respect to changing the 5-chloropentan-2-one to 4-oxopentanoic acid. To our delight, the reaction was processed well. Treatment of *o*-nitrobenzamides **1** and 4-oxopentanoic acid **4** with $TiCl_4$/Zn in anhydrous THF under the same reaction conditions, the reductive cyclization products 3a-methyl-2,3,3a,4-tetrahydro-pyrrolo[1,2-*a*]quinazoline-1,5-diones **5** were obtained in good yields (Scheme 3). The results are summarized in Table 3.

As shown in Tables 2 and 3, the method proved to be suitable for substrates in which the *o*-nitrobenzamides functionality was substituted by either weak electron-withdrawing groups (such as halides) or electron-donating groups (such as methyl and methoxyl). Both the 5-chloropentan-2-one and the 4-oxopentanoic acid carried out very well under this reaction. A variety of substrates can participate in the process well to give the corresponding products **3** and **5** with good yields under the same reaction conditions. So we concluded that no obvious effects from the electronic or nature of the aromatic ring substrates were observed in the above reactions.

A proposed mechanistic pathway to products **3** from *o*-nitrobenzamides and haloketones is illustrated in Scheme 4, although the details are still unclear. In the initial step, *o*-nitrobenzamides **1** are reduced by Ti(0) to intermediate **A**. The amine compounds **A** then reacted with haloketones **2** to give the intermediate **B**. Intermediate **C** was formed by attack of the amino group onto the central carbon atom of the imine. Finally, products **3** were obtained by eliminating of a hydrogen chloride molecule.

All the products were characterized by ^{1}H-NMR, IR, and HRMS spectra. The structure of **3a** was further confirmed by X-ray diffraction analysis. The molecular structure of the product **3a** is shown in Figure 1 and its crystallographic data is shown in Table 4.

This new and simple process constitutes a synthetically attractive and versatile approach for the rapid

Table 1

Optimization for the reductive cyclization reaction.

Entry	Temperature (°C)	Ratio[a]	M	Time/min	Isolated yield (%)
1	r.t.	1:4	Zn	20	59
2	40	1:4	Zn	20	65
3	60	1:4	Zn	20	80
4	reflux	1:4	Zn	20	85
5	reflux	1:2	Zn	45	54
6	reflux	1:3	Zn	20	68
7	reflux	1:4	Fe	20	54
8	reflux	1:4	Mg	20	32
9	reflux	1:4	Sm	20	77
10	reflux	1:4	Al	20	73

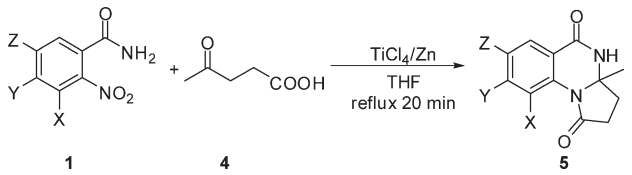
[a] Ratio of **1a** and low-valent titanium systems.

Table 2

Synthesis of compounds **3** from *o*-nitrobenzamides **1** and haloketone **2**.

Entry	X	Y	Z	Isolated yield (%)
3a	H	H	H	92
3b	H	H	Cl	91
3c	H	Cl	Cl	92
3d	H	H	CH_3	95
3e	H	H	CH_3O	74
3f	H	CH_3O	CH_3O	89
3g	CH_3	H	H	89

Scheme 3



construction of quinazolinone derivatives. A variety of substrates can participate in the process with moderate to good yields. The short reaction times (20 min) and simple reaction conditions render this method particularly attractive for the efficient preparation of biologically and medicinally interesting molecules.

EXPERIMENTAL

THF was distilled from sodium-benzophenone immediately prior to use. All reactions were conducted under N_2 atmosphere. Melting points were uncorrected. IR spectra were recorded on Varian F-1000 spectrometer in KBr with absorptions in cm^{-1}. ^{1}H-NMR spectra were determined on Varian-300 MHz spectrometer in DMSO-d_6 or $CDCl_3$ solution. J values are in Hz. Chemical shifts are expressed in ppm downfield from internal standard TMS. HRMS data were obtained using microma TOF-MS instrument or GCT-TOF instrument. X-ray crystallographic analysis was performed with a Rigaku Mercury CCD/AFC diffractometer.

General procedure for the synthesis of 3 and 5 is represented as follows. TiCl4 (0.45 mL, 4 mmol) was added dropwise using a syringe to a stirred suspension of zinc powder (0.52 g, 8 mmol) in freshly distilled anhydrous THF (10 mL) at r.t. under a dry N_2 atmosphere. After completion of the addition, the mixture was refluxed for 2 h. The suspension of the low-valent titanium reagent formed was cooled to r.t. and a solution of *o*-nitrobenzamide **1** (1 mmol) and 5-chloropentan-2-one **2** (1 mmol) or 4-oxopentanoic acid **4** (1 mmol) in THF (5 mL) was added dropwise. The reaction mixture was then refluxed for 20 min under N_2. After this period, the TLC analysis of the mixture showed the reaction to be completed. The reaction mixture was quenched with 5% HCl (15 mL) and extracted with $CHCl_3$ (3 × 20 mL). The combined extracts were washed with water (3 × 20 mL) and dried over anhydrous Na_2SO_4. After evaporation of the solvent under reduced pressure, the crude product was purified by recrystallization from 95% ethanol.

Table 3

Synthesis of compound **5** from o-nitrobenzamides **1** and 4-oxopentanoic acid **4**.

Compound.	X	Y	Z	Yield/ (%)
5a	H	H	H	74
5b	H	H	CH_3	83
5c	H	H	Cl	70
5d	H	H	CH_3O	80
5e	H	CH_3O	CH_3O	78
5f	H	Cl	H	73

Table 4

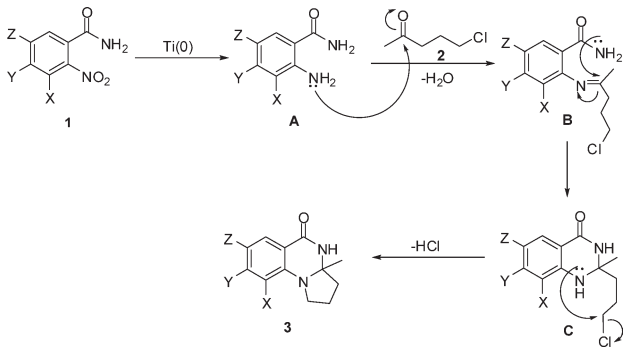
Crystallographic data of compound **3a**.

Empirical formula	$C_{12}H_{14}N_2O$
Formula weight	202.25
Temperature	293(2) K
Wavelength	0.71070 Å
Crystal system	Monoclinic
Space group	$P2_1/c$
Unit cell dimensions	$a = 6.809(3)$ Å αα = 90°
	$b = 22.125(8)$ Å
	ββ = 115.244(8)°
	$c = 24.034(5)$ Å γγ = 90°
Volume	1061.7(8) Å^3
Z	4
Density (calculated) Mg/m^3	1.265
Absorption coefficient mm^{-1}	0.082
F(000)	432
Crystal size	0.60 ×× 0.30 ×× 0.20 mm
Theta range for data collection	3.03 to 25.34°
Limiting indices	$-8 \le h \le 7$, $-25 \le k \le 26$, $-8 \le l \le 9$
Reflections collected	8803
Independent reflections	1930 [R(int) = 0.0788]
Data / restraints / parameters	1930 / 0 / 139
Goodness-of-fit on F^2	1.100
Final R indices [$I>2\sigma(I)$]	$R_1 = 0.0851$, $wR_2 = 0.1956$
R indices (all data)	$R_1 = 0.1593$, $wR_2 = 0.2276$
Largest diff. peak and hole	0.352 and −0.427 e.Å^{-3}

3a-Methyl-2,3,3a,4-tetrahydropyrrolo[1,2-a]quinaz- lin-5(1H)-one (3a). Mp: 164–165°C (ref. [25] 160–162°C). IR (potassium bromide): 3170, 3042, 2972, 2893, 2850, 1661, 1652, 1505, 1384, 1366, 1308, 1187, 1145, 800, 749, 627 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 1.40 (s, 3H, CH_3), 2.14–2.22 (m, 4H, 2 × CH_2), 3.44–3.56 (m, 2H, CH_2), 6.59 (d, J = 6.0 Hz, 1H, ArH), 6.77–6.81 (m, 1H, ArH), 7.01 (s, 1H, NH), 7.35–7.39 (m, 1H, ArH), 7.91–7.94 (m, 1H, ArH). HRMS [Found: m/z 202.1108 (M^+), Calcd. for $C_{12}H_{14}N_2O$: M 202.1106].

7-Chloro-3a-methyl-2,3,3a,4-tetrahydropyrrolo[1,2-a]quinazolin-5(1H)-one (3b). Mp: 178–180°C; IR (potassium bromide): 3163, 3035, 2962, 2877, 1661, 1607, 1501, 1435, 1375, 1283, 1258, 1186, 1151, 1126, 1070, 1012, 929, 897, 843, 786, 752, 730 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 1.24 (s, 3H, CH_3), 2.01–2.02 (m, 4H, 2 × CH_2), 3.42–3.64 (m, 2H, CH_2), 6.64 (d, J = 8.7 Hz, 1H, ArH), 7.33–7.37 (m, 1H, ArH), 7.56–7.58 (m, 1H, ArH), 8.45 (s, 1H, NH). HRMS [Found: m/z 236.0714 (M+), Calcd for $C_{12}H_{13}N_2O^{35}Cl$: M 236.0716].

Scheme 4. Proposed reaction mechanism.



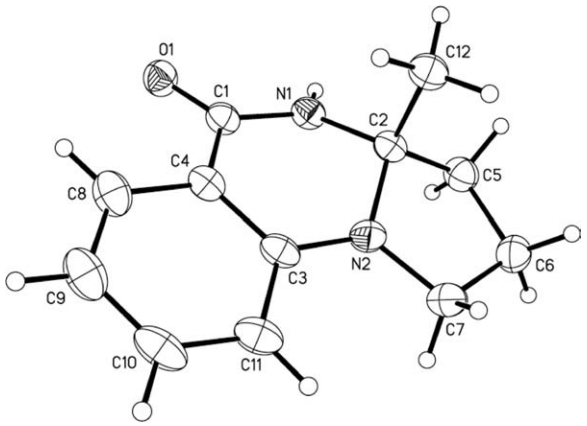


Figure 1. Molecular structure of 3a.

8-Choro-3a-methyl-2,3,3a,4-tetrahydropyrrolo[1,2-a]quinazolin-5(1H)-one (3c). Mp: 179–181°C; IR (potassium bromide): 3168, 3040, 2960, 2869, 1668, 1603, 1555, 1497, 1455, 1364, 1303, 1188, 1149, 1121, 991, 910, 876, 788 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 1.39 (s, 3H, CH_3), 2.16–2.19 (m, 4H, 2 × CH_2), 3.42–3.49 (m, 2H, CH_2), 6.54 (d, J = 1.8 Hz, 1H, ArH), 6.73 (dd, J_1 = 1.5 Hz, J_2 = 8.1 Hz, 1H, ArH), 6.99 (s, 1H, NH), 7.81 (d, J = 8.4 Hz, 1H, ArH). HRMS [Found: *m/z* 236.0715 (M^+), Calcd for $C_{12}H_{13}N_2O^{35}Cl$: M 236.0716].

3a,7-Dimethyl-2,3,3a,4-tetrahydropyrrolo[1,2-a]qui-nazolin-5(1H)-one (3d).. Mp: 155–157°C; IR (potassium bromide): 3166, 3031, 2979, 2849, 1652, 1619, 1514, 1488, 1430, 1371, 1287, 1186, 900, 801 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 1.38 (s, 3H, CH_3), 2.04–2.15 (m, 4H, 2 × CH_2), 2.28 (s, 3H, CH_3), 3.37–3.57 (m, 2H, CH_2), 6.16 (s, 1H, NH), 6.55 (d, J = 8.1 Hz, 1H, ArH), 7.18–7.21 (m, 1H, ArH), 7.74 (s, 1H, ArH). HRMS [Found: *m/z* 216.1264 (M^+), Calcd for $C_{13}H_{16}N_2O$: M 216.1263].

7-Methoxy-3a-methyl-2,3,3a,4-tetrahydropyrrolo [1,2-a] quinazolin-5(1H)-one (3e). Mp: 137–139°C; IR (potassium bromide): 3289, 3167, 3040, 2836, 1659, 1617, 1506, 1436, 1370, 1303, 1272, 1234, 1185, 1135, 1070, 1038, 893, 822, 787 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 1.39 (s, 3H, CH_3), 2.02–2.15 (m, 4H, 2 × CH_2), 3.31–3.44 (m, 1H, CH), 3.54–3.59 (m, 1H, CH), 3.81 (s, 3H, CH_3O), 6.47 (s, 1H, NH), 6.67 (d, J = 9.0 Hz, 1H, ArH), 7.00–7.04 (m, 1H, ArH), 7.46 (d, J = 3.0 Hz, 1H, ArH). HRMS [Found: *m/z* 232.1213 (M^+), Calcd for $C_{13}H_{16}N_2O_2$: M 232.1212].

7,8-Dimethoxy-3a-methyl-2,3,3a,4-tetrahydropyrrolo[1,2-a] quinazolin-5(1H)-one (3f). Mp: 197–199°C; IR (potassium bromide): 3170, 3031, 2970, 2843, 1652, 1615, 1510, 1455, 1394, 1317, 1299, 1244, 1219, 1121, 1082, 1044, 873, 808, 778 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 1.39 (s, 3H, CH_3), 2.02–2.13 (m, 4H, 2 × CH_2), 3.41 (t, J = 7.2 Hz, 1H, CH), 3.58 (s, 1H, CH), 3.87 (s, 3H, CH_3O), 3.89 (s, 3H, CH_3O), 6.18 (s, 1H, ArH), 6.35 (s, 1H, NH), 7.39 (1H, s, ArH). HRMS [Found: *m/z* 262.1317 (M^+), Calcd for $C_{14}H_{18}N_2O_3$: M 262.1317].

3a,9-Dimethyl-2,3,3a,4-tetrahydropyrrolo[1,2-a] quinazolin-5(1H)-one (3g). Mp: 159–161°C; IR (potassium bromide): 3166, 3040, 2971, 2872, 1659, 1595, 1481, 1430, 1392, 1299, 1205, 1162, 1082, 758 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 1.43 (s, 3H, CH_3), 2.00–2.13 (m, 2H, CH_2), 2.29 (s, 3H, CH_3), 3.00–3.04 (m, 1H, CH), 3.42–3.46 (m, 1H, CH), 3.55–3.74 (m, 2H, CH_2), 6.42 (s, 1H, NH), 7.04 (t, J = 7.5 Hz, 1H, ArH), 7.31 (d, J = 7.2 Hz, 1H, ArH), 7.89 (d, J = 7.8 Hz, 1H, ArH). HRMS [Found: *m/z* 216.1263 (M^+), Calcd for $C_{13}H_{16}N_2O$: M 216.1263].

3a-Methyl-2,3,3a,4-tetrahydropyrrolo[1,2-a]quina- zoline-1,5-dione (5a). Mp: 176–178°C (ref. [18] 179–180°C); IR (potassium bromide): 3177, 3056, 2925, 1718, 1683, 1603, 1490, 1465, 1387, 1352, 1278, 1246, 1211, 1153, 1004, 791, 758 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 1.58 (s, 3H, CH_3), 2.38–2.39 (m, 2H, CH_2), 2.68–2.71 (m, 2H, CH_2), 7.31 (d, J = 7.5 Hz, 1H, ArH), 7.60 (t, J = 7.5 Hz, 1H, ArH), 7.80 (s, 1H, NH), 8.07 (d, J = 8.1 Hz, 1H, ArH), 8.16 (d, J = 8.1 Hz, 1H, ArH). HRMS [Found: *m/z* 216.0901 (M^+), Calcd for $C_{14}H_{18}N_2O_3$: M 216.0899].

3a,7-Dimethyl-2,3,3a,4-tetrahydropyrrolo[1,2-a] quinazoline-1,5-dione (5b). Mp: 176–178°C; IR (potassium bromide): 3178, 3064, 2924, 2863, 1707, 1672, 1502, 1433, 1375, 1280, 1207, 1102, 1051, 912, 828, 784 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 1.55 (s, 3H, CH_3), 2.39 (s, 3H, CH_3), 2.66–2.72 (m, 2H, CH_2), 3.41–3.65 (m, 2H, CH_2), 7.39 (dd, J_1 = 1.5 Hz, J_2 = 8.1 Hz, 1H, ArH), 7.81 (s, 1H, NH), 7.86 (d, J = 0.9 Hz, 1H, ArH), 8.03 (d, J = 8.1 Hz, 1H, ArH). HRMS [Found: *m/z* 230.1054 (M^+), Calcd for $C_{13}H_{14}N_2O_2$: M, 230.1055].

7-Chloro-3a-methyl-2,3,3a,4-tetrahydropyrrolo[1,2-a] quinazoline-1,5-dione (5c). Mp: 223–225°C (Lit. [25] 222–223°C); IR (potassium bromide): 3181, 3077, 2865, 1723, 1679, 1486, 1439, 1368, 1266, 1204, 1163, 1109, 944, 841, 781, 700 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 1.57 (s, 3H, CH_3), 2.38–2.41 (m, 1H, CH), 2.68–2.71 (m, 1H, CH), 3.41–3.47 (m, 1H, CH), 3.54–3.65 (m, 1H, CH), 7.54 (dd, J_1 = 2.4 Hz, J_2 = 8.7 Hz, 1H, ArH), 7.85 (s, 1H, NH), 8.03 (d, J = 2.4 Hz, 1H, ArH), 8.14 (d, J= 8.7 Hz, 1H, ArH). HRMS [Found: *m/z* 250.0509 (M^+), Calcd for $C_{12}H_{11}N_2O_2^{35}Cl$: M 250.0509].

7-Methoxy-3a-methyl-2,3,3a,4-tetrahydropyrrolo[1,2-a]quinazoline-1,5-dione (5d). Mp: 186–188°C; IR (potassium bromide): 3156, 3067, 2920, 1675, 1499, 1373, 1252, 1090, 1033, 890, 787, 662 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ: 1.389 (s, 3H, CH_3), 2.18–2.24 (m, 2H, CH_2), 2.49–2.50 (m, 1H, CH), 2.62–2.74 (m, 1H, CH), 3.79 (s, 3H, CH_3O), 7.19 (dd, J_1 = 3.0 Hz, J_2 = 9 Hz, 1H, ArH), 7.37(d, J = 3.0Hz, 1H, ArH), 7.95 (d, J = 3.0 Hz, 1H, ArH), 8.95 (s, 1H, NH). HRMS (ESI): *m/z* $[M+Na]^+$, Calcd for $C_{13}H_{15}N_2O_3Na$: M 269.0902, found: 269.0920

7,8-Diethoxy-3a-methyl-2,3,3a,4-tetrahydropyrrolo[1,2-a]quinazoline-1,5-dione (5e). Mp: 174–176°C; IR (potassium bromide): 3176, 2930, 1657, 1484, 1380, 1327, 1273, 1090, 874, 786 cm^{-1}; ^{1}H-NMR($CDCl_3$) δ: 1.55 (s, 3H, CH_3), 2.35 (t, J = 7.8Hz, 2H, CH_2), 2.67 (t, J = 7.8Hz, 2H, CH_2), 3.93 (s, 3H, CH_3), 3.965 (s, 3H, CH_3), 7.47 (s, 1H, ArH), 7.69 (s, 1H, ArH), 7.77 (s, 1H, NH). HRMS (ESI): *m/z* $[M+H]^+$, Calcd for $C_{14}H_{16}N_2O_4$: M 277.1188, found: 277.1184.

8-Chloro-3a-methyl-2,3,3a,4-tetrahydropyrrolo[1,2-a]quinazoline-1,5-dione (5f). Mp: 222–224°C; IR (potassium bromide): 3181, 2924, 1662, 1511, 1466, 1304, 1039, 914, 756, 673 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 1.56 (s, 3H, CH_3), 2.38 (t, J = 7.5, 2H, CH_2), 2.707 (t, J = 7.8 Hz, 2H, CH_2), 7.25 (m, 1H, ArH), 7.80 (s, 1H, NH), 7.98 (d, J = 8.4 Hz, 1H, ArH), 8.23 (d, J = 1.8 Hz, 1H, ArH). HRMS (ESI): *m/z* $[M+Na]^+$, Calcd for $C_{12}H_{11}^{35}ClN_2O_2Na$: M 273.0407, found: 273.0426.

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REFERENCES AND NOTES

[1] Connolly, D. J.; Cusack, D.; O'sullivan, T. P.; Guiry, P. J. Tetrahedron 2005, 61, 10153.

[2] Hassanein, H. H.; Abdel, N. G. Bull Fac Pharm 1995, 33, 29.

[3] Bekhit, A. A.; Habib, N. S. Et-Din, A.; Bekhit, A. Boll Chim Farm 2001, 140, 297.

[4] Malllard, J.; Vincent, M.; Bernard, M. Chim Ther 1968, 3, 100.

[5] Merck. Merck Index; Merck: Whithouse Station, NJ, 1996, Vol. 12, p 7897.

[6] Merck. Merck Index; Merck: Whithouse Station, NJ, 1996, Vol. 12, p 1512.

[7] Merck. Merck Index; Merck: Whithouse Station, NJ, 1996, Vol. 12, p 3489.

[8] Stephen, H.; Wedge G. J Chem Soc 1956, 4420.

[9] Takeuchi, H.; Hagiwara S.; Eguchi, S. Tetrahedron 1989, 45, 6375.

[10] Ferraccioli, R.; Carenzi, D. Synthesis 2003, 1383.

[11] Schlapbach, A; Heng, R.; Di Padova, F. Bioorg Med Chem Lett 2004, 14, 357.

[12] Pastor, G; Blanchard, C.; Montginoul, C.; Torreilles, E.; Giral, L.; Texier, A. Bull Soc Chim Fr 1975, 1331.

[13] Khalifa, M.; Osman, A. N.; Ibrahim, M. G.; Ossman, A. R. E.; Ismail, M. A. Pharmaizie 1982, 37, 115.

[14] Michman, M.; Patai, S.; Wiesel, Y. Org Prep Proced Int 1978, 10, 13.

[15] Vorbrueggen, H.; Krolikiewicz, K. Tetrahedron 1994, 50, 6549.

[16] Mizuno, T.; Iahino, Y. Tetrahedron 2002, 58, 3155.

[17] Tatsuya, O.; Eiji, N.; Takashi, T.; Shingo, M. Tetrahedron 2003, 59, 5603.

[18] Aeberli, P.; Houlihan, W. J. J Org Chem 1968, 33, 2402.

[19] Iminov, R. T.; Tverdokhlebov, A. V.; Tolmachev, A. A.; Volovenko, Y. M.; Shishkina, S. V.; Shishkin, O. V. Tetrahedron 2009, 65, 8582.

[20] Iminov, R. T.; Tverdokhlebov, A. V.; Tolmachev, A. A.; Volovenko, Y. M.; Kostyuk, A. N.; Chernega, A. N.; Rusanov, E. B. Heterocycles 2008, 75, 1673.

[21] Shi, D. Q.; Rong, L. C.; Wang, J. X.; Zhuang, Q. Y.; Wang, X. S.; Hu, H. W. Tetrahedron Lett 2003, 44, 3199.

[22] Shi, D. Q.; Dou, G. L.; Li, Z. Y.; Ni, S. N.; Li, X. Y.; Wang, X. S.; Wu, H.; Ji, S. J. Tetrahedron 2007, 63, 9764.

[23] Shi, D. Q.; Wang, J. X.; Shi, C. L.; Rong, L. C.; Zhuang, Q. Y.; Hu, H. W. Synlett 2004, 1098.

[24] Dou, G. L.; Wang, M. M.; Shi, D. Q. J Comb Chem 2009, 11, 151.

[25] Houlihan, W. J.; Mountain Lakes, N. J.; Sandoz, Inc., Hanover, N. J. US Patent 1964, 447,566; Chem Abstr 1969, 71, 70630v.