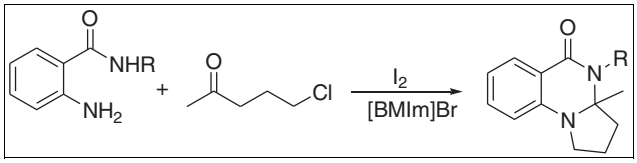
A Green Synthesis of Pyrrolo[1,2-*a*]quinazolin-5(1*H*)-one Derivatives in Ionic Liquids Catalyzed by Iodine

Jie-Xing Zhou,[a] Lian Lu,[b] Tuan-Jie Li,[b] Chang-Sheng Yao,[b] and Xiang-Shan Wang[b]*

[a]Department of Chemical Engineering, Huaihai Institute of Technology, Lianyungang, 222005, People's Republic China
[b]School of Chemistry and Chemical Engineering, Jiangsu Key Laboratory of Green Synthetic Chemistry for Functional Materials, Jiangsu Normal University, Xuzhou Jiangsu, 221116, People's Republic China
*E-mail: xswang1974@yahoo.com

Received February 12, 2012
DOI 10.1002/jhet.1768
Published online 3 February 2014 in Wiley Online Library (wileyonlinelibrary.com).



A series of 2,3,3*a*,4-tetrahydro-3*a*-methylpyrrolo[1,2-*a*]quinazolin-5(1*H*)-one derivatives were synthesized by a reaction of 2-aminobenzamide and 5-chloropentan-2-one at 80 °C catalyzed by iodine in ionic liquid of [BMIm]Br. Compared with the other methods, this novel method has the advantages of milder reaction conditions, high yields, environmental benignity, and metal-free catalyst.

J. Heterocyclic Chem., **51**, 1472 (2014).

INTRODUCTION

Pyrroloquinazoline and its derivatives are important heterocycles found in a variety of biologically molecules with a wide range of biological activities that confer applications as antitumor [1], modulators of chemokine [2], and anti-inflammatory activity [3]. In addition, some of them are used as thrombin receptor antagonists [4]. Therefore, much attention has been submitted to the synthesis of these interesting heterocyclic compounds both in organic synthetic and pharmaceutical chemistry. It was reported that they could be achieved by the reaction of isatoic anhydride, amine and 2-formylbenzoic acid [5], reduction of 2-nitrobenzamide with γ-ketonic acid or halogenated ketone in the presence of $SnCl_2$ [6], coupling cyclization of 2-aminobenzamide with 3-butynoic acid catalyzed by Platinum salt [7], or condensation cyclization of 2-aminobenzamide with γ-ketone acid ester [8].

Although a number of useful synthetic procedures to prepare these compounds have been developed [5–8], still several limitations remain, as well. For example, most of the procedures involve several steps, low yields, metal catalysts or in organic solvents. Thus, simple, efficient, and green method to synthesize pyrroloquinazoline would be attractive.

Ionic liquids have attracted increasing interest in the context of green chemistry in the past few years. They were initially introduced as alternative green reaction media because of their unique chemical and physical properties of non-volatility, non-flammability, thermal stability, and controlled miscibility [9]. The possibility of recycling them and the low vapor frame also ensure their utility in environmentally friendly technologies for a large number of organic transformations [10].

As a continuation of our research devoted to the development of new methods for the preparation of heterocycles in ionic liquid and with iodine-catalyzed reaction [11], we would like to report the synthesis of 2,3,3*a*,4-tetrahydro-3*a*-methylpyrrolo [1,2-*a*]quinazolin-5(1*H*)-one derivatives in ionic liquids. This method involves the reaction of 2-aminobenzamides with 5-chloropentan-2-one catalyzed by iodine.

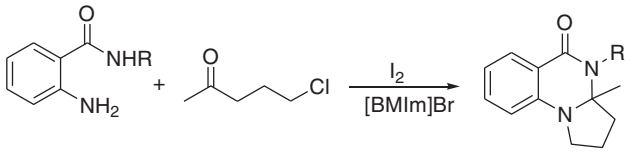
RESULTS AND DISCUSSION

Treatment of 2-aminobenzamides **1a-l** and 5-chloropentan-2-one **2** in ionic liquid of [BMIm]Br in the presence of 5 mol % iodine at 80 °C resulted in the corresponding 2,3,3*a*,4-tetrahydro-3*a*-methylpyrrolo[1,2-*a*]quinazolin-5(1*H*)-one derivatives **3a–l** in high yields (Scheme 1).

Using the conversion of 2-aminobenzamide **1a** and 5-chloropentan-2-one **2** as a model, several parameters, such as Lewis acids, catalyst amount, reaction temperature and solvents, were explored as shown in Table 1. **3a** was obtained successfully in the presence of various quantities of the catalyst, reaching a maximum of 90% yield using 5 mol% iodine as a catalyst (Table 1, entry 4). Different imidazolium ionic liquids and Lewis acids were also tested, and iodine-[BMIm]Br system appeared to be the best medium for this transformation (entry 4 vs 8–16).

After reaction completion as monitored by TLC, products were isolated by simple filtration after the addition of a small amount of water to the cooled reaction mixture. Water in the filtrate was removed by distillation under reduced pressure, and the [BMIm]Br in the residue could be reused after being evaporated at 80 °C for 4 h in *vacuum*. Successive reuse of the recycled ionic liquid in

Scheme 1. The reaction of 2-aminobenzamide and 5-chloropentan-2-one.



1a-l **2** **3a-l**

Table 1

Synthetic results of **3a** under different reaction conditions[a].

Entry	Temp/°C	Ionic liquid[b]	Cat. (mol %)	Yield (%)[c]
1	80	[BMIm]Br	I_2(0)	0
2	RT.	[BMIm]Br	I_2(5)	Trace
3	50	[BMIm]Br	I_2(5)	72
4	80	[BMIm]Br	I_2(5)	90
5	100	[BMIm]Br	I_2(5)	90
6	80	[BMIm]Br	I_2(10)	86
7	80	[BMIm]Br	I_2(20)	87
8	80	[EMIm]Br	I_2(5)	85
9	80	[PMIm]Br	I_2(5)	86
10	80	[EMIm] [BF_4]	I_2(5)	88
11	80	[PMIm] [BF_4]	I_2(5)	87
12	80	[BMIm] [BF_4]	I_2(5)	89
13	80	[BMIm]Br	CuI(5)	Trace
14	80	[BMIm]Br	$ZnCl_2$(5)	Trace
15	80	[BMIm]Br	$Yb(OTf)_3$ (5)	78
16	80	[BMIm]Br	$Sc(OTf)_3$ (5)	82

[a]Reaction condition: 2 mL solvent, 2-aminobenzamide (0.272 g, 2 mmol), and **2** (0.240 g, 2.0 mmol).
[b]BMIm = 1-butyl-3-methylimidazolium; EMIm = 1-ethyl-3-methylimidazolium; PMIm = 1-propyl-3-methylimidazolium.
[c]Isolated yields.

the model reaction gave high yields of **3a** (88%) even after the fourth cycle.

First of all, these optimized conditions were applied for the conversion of various kinds of 2-aminobenzamides **1a-l** into the corresponding pyrrolo[1,2-*a*]quinazolin-5(1*H*)-one analogs (Table 2, entries 1–12). All the structures of the products were characterized by ^{1}H NMR, IR, and HRMS, their data were in good agreement to the corresponding structures.

EXPERIMENTAL

Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded on a Tensor 27 spectrometer (Bruker Corporation: Karlsruhe, DE) in KBr pellet. ^{1}H NMR spectra was obtained from a solution in DMSO-d_6 or $CDCl_3$ with Me_4Si as internal standard using a Bruker-400 spectrometer (Bruker Corporation: Karlsruhe, DE). HRMS analyses were carried out using a Bruker-micro-TOF-Q-MS analyzer (Bruker Corporation: Karlsruhe, DE). The 2-aminobenzamides were prepared from isatoic anhydride and amines according to reference [12].

Table 2

The reaction time and yields of the products **3a**–**l**.

Entry	R	Time/h	Product	Yields /%
1	H	6	**3a**	90
2	4-MeC_6H_4	8	**3b**	92
3	4-$MeOC_6H_4$	8	**3c**	89
4	4-FC_6H_4	8	**3d**	86
5	Piperonylethyl	7	**3e**	92
6	C_6H_5	7	**3f**	90
7	$C_6H_5CH_2$	6	**3g**	86
8	4-$MeOC_6H_4CH_2$	6	**3h**	86
9	4-*i*-PrC_6H_4	8	**3i**	90
10	3-Cl-4-FC_6H_3	8	**3j**	86
11	Furan-2-ylmethyl	6	**3k**	90
12	$C_6H_5CH_2CH_2$	6	**3l**	88

[a]Reaction condition: 2-aminobenzamides (2.0 mmol), **2** (0.240 g, 2.0 mmol), iodine (0.025 g, 0.1 mmol), [BMIm]Br 2.0 mL, 80 °C.

General procedure for the synthesis of pyrrolo[1,2-a] quinazolin-5(1H)-one derivatives 3. A dry 50 mL flask was charged with 2-aminobenzamides **1** (2.0 mmol), 5-chloropentan-2-one **2** (0.240 g, 2.0 mmol), iodine (0.025 g, 0.1 mmol), and ionic liquid of [BMIm]Br (2 mL). The reaction mixture was stirred at 80 °C for 6–8 h, and then a small amount of water (5 mL) was added to the mixture, and the generated yellow solid was filtered off. The water in the filtrate was removed by distillation under reduced pressure, and the ionic liquid in the residue could be reusable by being evaporated at 80 °C for 4 h at *vacuum*. The crude yellow products were washed with water and purified by recrystallization from 95% EtOH, then dried at 80 °C for 2 h under *vacuum* to give **3**.

3a-Methyl-2,3,3a,4-tetrahydropyrrolo[1,2-a]quinazolin-5(1H)-one 3a: mp 167–168 °C (Lit. [6] 166–167 °C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.40 (s, 3H, CH_3), 2.02–2.19 (m, 4H, $2CH_2$), 3.43–3.57 (m, 2H, CH_2), 6.47 (s, 1H, NH), 6.58 (d, J = 8.0 Hz, 1H, ArH), 6.77–6.81 (m, 1H, ArH), 7.35–7.39 (m, 1H, ArH), 7.92 (d, J = 8.0 Hz, 1H, ArH). IR (KBr): 3166, 3040, 2971, 2877, 1658, 1606, 1504, 1488, 1476, 1455, 1436, 1389, 1365, 1341, 1313, 1210, 1189, 1164, 1146, 1123, 1035, 1007, 801, 757 cm^{-1}. HRMS (ESI, *m/z*): calcd for $C_{12}H_{14}N_2NaO$ $[M+Na]^+$ 225.1004, found 225.1004.

3a-Methyl-4-(p-tolyl)-2,3,3a,4-tetrahydropyrrolo[1,2-a]quinazolin-5(1H)-one 3b: mp 177–178 °C (Lit. [6] 172–174 °C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.55 (s, 3H, CH_3), 1.63–1.68 (m, 1H, CH), 1.96–2.01 (m, 1H, CH), 2.09–2.26 (m, 2H, CH_2), 2.38 (s, 3H, CH_3), 3.47–3.59 (m, 2H, CH_2), 6.58 (d, J = 8.0 Hz, 1H, ArH), 6.79–6.83 (m, 1H, ArH), 7.15 (d, J = 7.6 Hz, 2H, ArH), 7.22 (d, J = 8.4 Hz, 2H, ArH), 7.37–7.41 (m, 1H, ArH), 7.97 ~ 7.98 (m, 1H, ArH). IR (KBr): 3083, 2931, 1655, 1602, 1508, 1484, 1468, 1456, 1386, 1346, 1326, 1290, 1264, 1235, 1221, 1211, 1194, 1154, 1140, 1093, 1078, 1035, 1015, 831, 808, 761, 724, 715, 700 cm^{-1}. HRMS (ESI, *m/z*): calcd for $C_{19}H_{20}N_2NaO$ $[M+Na]^+$ 315.1473. Found 315.1488.

4-(4-Methoxyphenyl)-3a-methyl-2,3,3a,4-tetrahydropyrrolo[1,2-a] quinazolin-5(1H)-one 3c: mp 171–172 °C (Lit. [6] 164–166 °C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.53 (s, 3H, CH_3), 1.64–1.68 (m, 1H, CH), 1.94 ~ 1.99 (m, 1H, CH), 2.08–2.27 (m, 2H, CH_2), 3.47–3.59 (m, 2H, CH_2), 3.83 (s, 3H, CH_3O), 6.58 (d, J = 8.0 Hz, 1H,

ArH), 6.79–6.83 (m, 1H, ArH), 6.94 (d, J = 8.8 Hz, 2H, ArH), 7.19 (d, J = 7.6 Hz, 2H, ArH), 7.37–7.41 (m, 1H, ArH), 7.96–7.98 (m, 1H, ArH). IR (KBr): 3075, 3043, 2955, 2934, 2909, 2859, 2837, 1645, 1604, 1511, 1499, 1486, 1470, 1443, 1389, 1355, 1337, 1310, 1297, 1246, 1228, 1195, 1182, 1173, 1149, 1135, 1120, 1106, 1034, 999, 910, 849, 810, 755, 697 cm^{-1}. HRMS (ESI, *m/z*): calcd for $C_{19}H_{20}N_2NaO_2$ $[M + Na]^+$ 331.1422, found 331.1431.

4-(4-Fluorophenyl)-3a-methyl-2,3,3a,4-tetrahydropyrrolo[1,2-a] quinazolin-5(1H)-one 3d: mp 151–153 °C (Lit. [6] 152–154 °C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.54 (s, 3H, CH_3), 1.64–1.68 (m, 1H, CH), 1.96–2.03 (m, 1H, CH), 2.11–2.24 (m, 2H, CH_2), 3.48–3.60 (m, 2H, CH_2), 6.59 (d, J = 8.4 Hz, 1H, ArH), 6.81–6.84 (m, 1H, ArH), 7.09–7.13 (m, 2H, ArH), 7.23–7.25 (m, 2H, ArH), 7.38–7.42 (m, 1H, ArH), 7.97 (d, J = 7.6 Hz, 1H, ArH). IR (KBr): 3063, 3047, 2976, 2933, 2870, 1649, 1603, 1508, 1495, 1471, 1386, 1357, 1335, 1310, 1212, 1194, 1180, 1156, 1132, 1116, 1094, 1045, 1016, 995, 940, 875, 851, 825, 752, 697 cm^{-1}. HRMS (ESI, *m/z*): calcd for $C_{18}H_{18}N_2OF$ $[M + H]^+$ 297.1403, found 297.1413.

4-(2-Piperonylethyl)-3a-methyl-2,3,3a,4-tetrahydropyrrolo[1,2-a] quinazolin-5(1H)-one 3e: mp 115–116 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.27 (s, 3H, CH_3), 2.02–2.23 (m, 4H, $2CH_2$), 2.76–2.80 (m, 1H, CH), 3.02–3.11 (m, 2H, CH_2), 3.44–3.49 (m, 2H, CH_2), 3.93–3.98 (m, 1H, CH), 5.93 (s, 2H, CH_2), 6.50 (d, J = 8.4 Hz, 1H, ArH), 6.70–6.74 (m, 2H, ArH), 6.76–6.81 (m, 2H, ArH), 7.33–7.37 (m, 1H, ArH), 7.94 (d, J = 8.0 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 15.5, 15.8, 30.5, 32.5, 39.9, 41.4, 74.4, 95.6, 103.0, 104.1, 107.0, 110.1, 112.0, 116.5, 123.5, 128.1, 128.4, 138.9, 140.8, 142.4, 158.9. IR (KBr): 2963, 2940, 2923, 2902, 2847, 1635, 1607, 1499, 1480, 1446, 1402, 1382, 1356, 1328, 1313, 1255, 1185, 1167, 1143, 1117, 1101, 1044, 1005, 944, 925, 853, 819, 753, 702 cm^{-1}. HRMS (ESI, *m/z*): calcd for $C_{21}H_{23}N_2O_3$ $[M + H]^+$ 351.1709, found 351.1729.

3a-Methyl-4-phenyl-2,3,3a,4-tetrahydropyrrolo[1,2-a]quinazolin-5(1H)-one 3f: mp 122–124 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.57 (s, 3H, CH_3), 1.64–1.69 (m, 1H, CH), 1.95–2.02 (m, 1H, CH), 2.10–2.25 (m, 2H, CH_2), 3.47–3.59 (m, 2H, CH_2), 6.59 (d, J = 8.0 Hz, 1H, ArH), 6.81–6.84 (m, 1H, ArH), 7.28 (d, J = 7.6 Hz, 2H, ArH), 7.35–7.44 (m, 4H, ArH), 7.98 (d, J = 7.6 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 21.1, 22.3, 38.6, 45.7, 80.2, 112.8, 115.9, 117.6, 127.8, 128.6, 129.2, 129.5, 133.9, 139.1, 144.7, 164.0. IR (KBr): 3061, 3039, 2989, 2969, 2907, 2833, 1649, 1607, 1494, 1480, 1469, 1385, 1353, 1336, 1311, 1225, 1196, 1180, 1160, 1148, 1120, 1074, 1047, 1030, 998, 946, 849, 751, 699 cm^{-1}. HRMS (ESI, *m/z*): calcd for $C_{18}H_{19}N_2O$ $[M + H]^+$ 279.1497, found 279.1515.

4-Benzyl-3a-methyl-2,3,3a,4-tetrahydropyrrolo[1,2-a]quinazolin-5(1H)-one 3g: mp 145–146 °C (Lit. [6] 140–142 °C); ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.29 (s, 3H, CH_3), 1.94–1.99 (m, 1H, CH), 2.02–2.10 (m, 2H, CH_2), 2.17–2.85 (m, 1H, CH), 3.38–3.49 (m, 2H, CH_2), 4.23 (d, J = 15.6 Hz, 1H, CH), 5.23 (d, J = 15.6 Hz, 1H, CH), 6.52 (d, J = 8.0 Hz, 1H, ArH), 6.79–6.82 (m, 1H, ArH), 7.20–7.23 (m, 1H, ArH), 7.27–7.35 (m, 4H, ArH), 7.37–7.39 (m, 1H, ArH), 7.99 (d, J = 7.6 Hz, 1H, ArH). IR (KBr): 3069, 2969, 2924, 2852, 1634, 1606, 1499, 1483, 1470, 1454, 1432, 1396, 1372, 1352, 1321, 1310, 1292, 1274, 1187, 1165, 1155, 1142, 1121, 1076, 1064, 1038, 1028, 1005, 974, 950, 786, 755, 710, 769, 630 cm^{-1}. HRMS (ESI, *m/z*): calcd for $C_{19}H_{20}N_2NaO$ $[M + Na]^+$ 315.1473, found 315.1500.

4-(4-Methoxybenzyl)-3a-methyl-2,3,3a,4-tetrahydropyrrolo[1,2-a] quinazolin-5(1 H)-one 3h: mp 155–156 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.26 (s, 3H, CH_3), 1.94–2.02 (m, 1H, CH), 2.04–2.11 (m, 2H, CH_2), 2.23–2.31 (m, 1H, CH), 3.38–3.48 (m, 2H, CH_2), 3.77 (s, 3H, CH_3O), 4.23 (d, J = 15.2 Hz, 1H, CH), 5.10 (d, J = 15.2 Hz, 1H, CH), 6.51 (d, J = 8.0 Hz, 1H, ArH), 6.78–6.84 (m, 3H, ArH), 7.25–7.27 (m, 2H, ArH), 7.34–7.38 (m, 1H, ArH), 7.98 (d, J = 7.6 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 20.7, 20.8, 37.5, 44.9, 45.9, 55.3, 79.8, 112.2, 113.8, 115.3, 117.2, 128.7, 129.2, 131.3, 133.7, 144.4, 158.6, 164.3. IR (KBr): 2974, 2929, 2909, 2850, 1635, 1606, 1585, 1511, 1484, 1472, 1431, 1395, 1372, 1353, 1321, 1309, 1288, 1248, 1185, 1166, 1144, 1122, 1109, 1029, 1004, 980, 843, 833, 819, 758 cm^{-1}. HRMS (ESI, *m/z*): calcd for $C_{20}H_{22}N_2NaO_2$ $[M + Na]^+$ 345.1618, found 345.1618.

4-(4-Isopropylphenyl)-3a-methyl-2,3,3a,4-tetrahydropyrrolo [1,2-a]quinazolin-5(1H)-one 3i: mp 146–148 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.26 (d, J = 6.8 Hz, 6H, $2CH_3$), 1.55 (s, 3H, CH_3), 1.64–1.69 (m, 1H, CH), 1.96–2.03 (m, 1H, CH), 2.09–2.13 (m, 1H, CH), 2.18–2.26 (m, 1H, CH), 2.89–2.96 (m, 1H, CH), 3.46–3.59 (m, 2H, CH_2), 6.58 (d, J = 8.0 Hz, 1H, ArH), 6.79–6.83 (m, 1H, ArH), 7.18 (d, J = 7.6 Hz, 2H, ArH), 7.25–7.27 (m, 2H, ArH), 7.37–7.41 (m, 1H, ArH), 7.80 (d, J = 8.0 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 21.1, 22.2, 23.9, 33.8, 38.6, 45.8, 80.2, 112.7, 116.0, 117.5, 127.2, 129.2, 129.5, 133.8, 136.5, 144.6, 148.3, 163.9. IR (KBr): 3056, 3030, 2959, 2924, 2867, 1648, 1605, 1498, 1471, 1390, 1363, 1344, 1311, 1252, 1227, 1212, 1196, 1178, 1148, 1130, 1116, 1102, 1069, 1055, 1042, 1026, 993, 944, 868, 820, 751, 699 cm^{-1}. HRMS (ESI, *m/z*): calcd for $C_{21}H_{25}N_2O$ $[M + H]^+$ 321.1967, found 321.1981.

4-(3-Chloro-4-fluorophenyl)-3a-methyl-2,3,3a,4-tetrahydropyrrolo[1,2-a]quinazolin-5(1H)-one 3j: mp 144–146 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.54 (s, 3H, CH_3), 1.68–1.73 (m, 1H, CH), 1.95–2.07 (m, 1H, CH), 2.14–2.23 (m, 2H, CH_2), 3.49–3.59 (m, 2H, CH_2), 6.59 (d, J = 8.0 Hz, 1H, ArH), 6.81–6.85 (m, 1H, ArH), 7.18–7.22 (m, 2H, ArH), 7.35–7.43 (m, 2H, ArH), 7.96 (d, J = 7.6 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 21.1, 22.1, 38.6, 45.7, 80.2, 112.9, 115.3, 117.0, 121.3, 121.5, 129.5, 131.9, 134.3, 135.6, 144.6, 156.3, 158.7, 164.0. IR (KBr): 3061, 2971, 2869, 1649, 1608, 1500, 1471, 1397, 1377, 1359, 1311, 1287, 1259, 1213, 1183, 1149, 1137, 1126, 1060, 1029, 954, 919, 822, 751, 709, 695 cm^{-1}. HRMS (ESI, *m/z*): calcd for $C_{18}H_{17}ClFN_2O$ $[M + H]^+$ 331.1013, found 331.1026.

4-(Furan-2-ylmethyl)-3a-methyl-2,3,3a,4-tetrahydropyrrolo [1,2-a]quinazolin-5(1H)-one 3k: mp 130–131 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.19 (s, 3H, CH_3), 2.03–2.11 (m, 1H, CH), 2.17–2.21 (m, 2H, CH_2), 2.46–2.54 (m, 1H, CH), 3.40–3.51 (m, 2H, CH_2), 4.54 (d, J = 15.6 Hz, 1H, CH), 4.80 (d, J = 15.6 Hz, 1H, CH), 6.31–6.33 (m, 2H, ArH), 6.49 (d, J = 8.4 Hz, 1H, ArH), 6.75–6.79 (m, 1H, ArH), 7.33–7.36 (m, 2H, ArH), 7.95 (d, J = 7.6 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 20.6, 20.8, 37.6, 39.4, 45.0, 79.4, 108.5, 110.6, 112.3, 115.2, 117.2, 129.2, 133.7, 141.5, 144.3, 151.8, 163.9. IR (KBr): 3103, 3070, 2963, 2888, 2856, 1644, 1608, 1497, 1482, 1457, 1420, 1396, 1350, 1321, 1299, 1249, 1232, 1186, 1160, 1142, 1121, 1075, 1063, 1041, 1020, 1005, 964, 938, 877, 818, 809, 786, 773, 747, 695 cm^{-1}. HRMS (ESI, *m/z*): calcd for $C_{17}H_{18}N_2NaO_2$ $[M + Na]^+$ 305.1266, found 305.1267.

3a-Methyl-4-phenethyl-2,3,3a,4-tetrahydropyrrolo[1,2-a] quinazolin-5(1H)-one 3l: mp 91–93 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.27 (s, 3H, CH_3), 1.98–2.21 (m, 4H, $2CH_2$), 2.85–2.91 (m, 1H, CH), 3.07–3.13 (m, 2H, CH_2), 3.41–3.49 (m, 2H, CH_2), 3.98 ~ 4.04 (m, 1H, CH), 6.50 (d, J = 8.4 Hz, 1H, ArH), 6.77–6.81 (m, 1H, ArH), 7.20–7.26 (m, 1H, ArH), 7.27–7.37 (m, 5H, ArH), 7.95 (d, J = 8.0 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 20.8, 21.2, 36.0, 37.7, 45.2, 46.5, 79.7,

112.2, 115.4, 117.2, 126.4, 128.5, 128.8, 129.0, 133.6, 139.6, 144.2, 164.2. IR (KBr): 3060, 3025, 2971, 2943, 2865, 1638, 1606, 1497, 1486, 1472, 1433, 1398, 1374, 1356, 1319, 1308, 1295, 1247, 1205, 1182, 1164, 1140, 1040, 1030, 1004, 954, 944, 848, 744, 698 cm^{-1}. HRMS (ESI, *m/z*): calcd for $C_{20}H_{23}N_2O$ $[M+H]^+$ 307.1810, found 307.1812.

CONCLUSION

In conclusion, we found a mild and green method for the synthesis of 2,3,3*a*,4-tetrahydro-3*a*-methylpyrrolo [1,2-*a*]quinazolin-5(1*H*)-one derivatives via a reaction of 2-aminobenzamide and 5-chloropentan-2-one catalyzed by iodine in ionic liquid. The features of this procedure are mild reaction conditions, high yields, operational simplicity and metal-free catalyst.

Acknowledgments. We are grateful to the National Natural Science foundation of China (20802061), the Priority Academic Program Development of Jiangsu Higher Education Institutions, Qing Lan Project (10QLD008) of Jiangsu Education Committee and College Industrialization Project (JHB2012-31) of Jiangsu Province for financial support.

REFERENCES AND NOTES

[1] (a) Barraja, P.; Spano, V.; Diana, P.; Carbone, A.; Cirrincione, G. Tetrahedron Lett. 2009, 50, 5389; (b) Baek, D. -J. Yakhak Hoechi 2006, 50, 278; (c) Sarno, S.; Ruzzene, M.; Frascella, P.; Pagano, M. A.; Meggio, F.; Zambon, A.; Mazzorana, M.; Di Maira, G.; Lucchini, V.; Pinna, L. A. Mol. Cell Biochem 2005, 274, 69.

[2] Anderskewitz, R.; Dollinger, H.; Heine, C.; Pouzet, P. A. J; Birke, F.; Bouyssou, T. Pyrrolidinohydrochinazolines PCT Int Appl WO 2004072074 A1, Chem Abstr 2004, 141, 225.

[3] Rioja, I.; Terencio, M. C.; Ubeda, A.; Molina, P.; Tarraga, A.; Gonzalez-Tejero, A.; Alcaraz, M. J. Eur J Pharm 2002, 434, 177.

[4] (a) Dixit, A.; Kashaw, S. K.; Gaur, S.; Saxena, A. K. Bioorg. Med. Chem. 2004, 12, 3591; (b) Maryanoff, B. E.; Zhang, H.-C.; McComsey, D. F. Aminomethyl-pyrroloquinazoline compounds as thrombin receptor antagonists PCT Int Appl WO 2002068425 A1 Chem Abstr 2002, 137, 216956; (c) Ahn, H.-S.; Foster, C.; Boykow, G.; Stamford, A.; Manna, M.; Graziano, M. Biochem Pharm 2000, 60, 1425.

[5] Kumar, K. S.; Kumar, P. M.; Kumar, K. A.; Sreenivasulu, M.; Jafar, A. A.; Rambabu, D.; Krishna, G. R.; Reddy, C. M.; Kapavarapu, R.; Shivakumar, K.; Priya, K. K.; Parsa, K. V. L.; Pal, M. Chem Commun 2011, 47, 5010.

[6] (a) Wang, M. M.; Dou, G. L.; Shi, D. Q. J Comb Chem. 2010, 12, 582. (b) Zhao, X.; Shi, D.-Q. J Heterocycl Chem 2011, 48, 634.

[7] (a) Patil, N. T.; Kavthe, R. D.; Raut, V. S.; Shinde, V. S.; Sridhar, B. J Org Chem 2010, 75, 1277; (b) Feng, E. G.; Zhou, Y.; Zhang, D. Y.; Zhang, L.; Sun, H. F.; Jiang, H. L.; Liu, H. J Org Chem 2010, 75, 3274.

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

[9] (a) Welton, T. Chem Rev 1999, 99, 2071; (b) Dupont, J.; de Souza, R. F.; Suarez, P. A. Z. Chem Rev 2002, 102, 3667.

[10] Martins, M. A. P.; Frizzo, C. P.; Moreira, D. N.; Zanatta, N.; Bonacorso, H. G. Chem Rev 2008, 108, 2015.

[11] (a) Wang, X. S.; Sheng, J.; Lu, L.; Yang, K.; Li, Y. L. J Comb Chem 2011, 196, 1011; (b) Wang, X. S.; Yang, K.; Zhou, J.; Tu, S. J. J Comb Chem 2010, 12, 417.

[12] Heyman, D. A. J Heterocycl Chem 1978, 15, 573.