Lian Lu,[a] Ke Yang,[a] Mei-Mei Zhang,[b] and Xiang-Shan Wang[a]*

[a]School of Chemistry and Chemical Engineering, Jiangsu Key Laboratory of Green Synthetic Chemistry for Functional Materials, Jiangsu Normal University, Xuzhou Jiangsu 221116, China
[b]The Key Laboratory of Biotechnology on Medical Plant of Jiangsu Province, Jiangsu Normal University, Xuzhou Jiangsu 221116, China
*E-mail: xswang1974@yahoo.com

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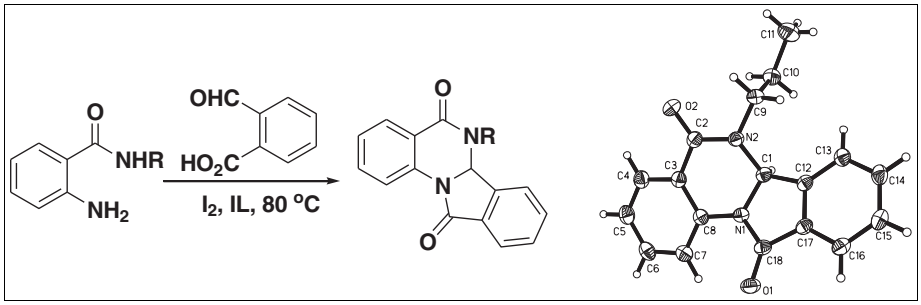

A mild, green, and facile method for the synthesis of 6,6*a*-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione derivatives is described in high yields using ionic liquids as green media. The method involves the reaction of 2-aminobenzamides with 2-formylbenzoic acid catalyzed by iodine and provides a new alkaloid library with potential activity for biomedical screening.

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INTRODUCTION

Indoloquinazolines are important core structures found in a variety of biologically molecules with a wide range of biological activities, such as antimicrobial [1], cytotoxic [2], insecticidal [3], and antibiotic activity [4]. Although a number of useful synthetic procedures have been developed to prepare these analogs, in the literatures [5], still several limitations remain as well, for example, most of the procedures involve several steps, low yields and inorganic solvents. Moreover, the starting materials are not often readily available. Therefore, a simple, efficient, and green method to synthesize indoloquinazoline 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 nonvolatility, nonflammability, thermal stability, and controlled miscibility [6]. The possibility of recycling them also ensures their utility in organic synthesis as green solvents for a large number of organic transformations [7].

As a continuation of our research devoted to the development of new methods for the preparation of heterocycles in ionic liquids and with iodine-catalyzed reaction [8], we would like to report the synthesis of 6,6*a*-dihydroisoindolo [2,1-*a*]quinazoline- 5,11-dione derivatives in ionic liquids. The method involves the reaction of 2-aminobenzamide with 2-formylbenzoic acid catalyzed by iodine.

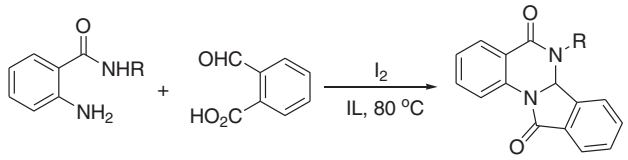
RESULTS AND DISCUSSION

Treatment of 2-aminobenzamides **1a–l** and 2-formylbenzoic acid **2** in ionic liquids of [BMIm]Br in the presence of 5 mol% iodine at 80°C resulted in the corresponding 6,6*a*-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione derivatives **3a–l** in high yields (Scheme 1).

Using the conversion of 2-aminobenzamide **1a** and 2-formylbenzoic acid **2** as a model, several parameters were explored as shown in Table 1. **3a** was not detected by TLC in the absence of iodine at 80°C (Table 1, entry 1) and was obtained successfully in the presence of various quantities of the catalyst, reaching a maximum of 93 % yield with 5 mol% iodine (Table 1, entries 4, 6, and 7). The yield of **3a** was also dependent on temperature (entries 2–5), proceeding smoothly at 80°C. Different imidazolium ionic liquids and Lewis acids were also tested, and iodine-[BMIm]Br appeared to be the best system 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 of [BMIm]Br in the model reaction gave high yields of **3a** (92 %) even after the fourth cycle.

Scheme 1. Reaction of **1a–l** and 2-formylbenzoic acid in ionic liquids.



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

First of all, these optimized conditions were applied for the conversion of various kinds of 2-aminobenzamides **1a–l** into the corresponding isoindolo[2,1-*a*]quinazoline analogs **3a–l** (Table 2, entries 1–12). The structure of product **3g** is confirmed by X-ray diffraction analysis; its crystal structure is shown in Figure 1.

Consistent with previous suggestions in the literatures [**5g**, **8b**], we suggest that iodine catalyzes the reaction as a mild Lewis acid. The proposed mechanism was shown in Scheme 2. The Schiff base **I** is formed by the condensation of **1** with **2**, and then, the intramolecular acylamino group attacks the iodine-activated Schiff base **II** to form the quinazoline **III**; finally, the intermediate **III** gives **3** by an intramolecular dehydration.

CONCLUSION

In summary, a mild, facile, and environmentally benign method is developed for the synthesis of isoindolo[2,1-*a*] quinazoline-5,11-dione derivatives in high yields catalyzed by iodine in ionic liquids. The advantages of this procedure include mild reaction conditions, high yields, one-pot, operational simplicity, and environmentally benign.

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 and ^{13}C NMR spectra were 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.).

General procedure for the synthesis of 6,6*a*-dihydroisoindolo [2,1-*a*] quinazoline-5,11-dione derivatives 3. A dry 50 mL flask was charged with 2-aminobenzamides **1a–l** (2.0 mmol), 2-formylbenzoic acid **2** (0.300 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 2–5 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, and then dried at 80°C for 2 h under vacuum to give **3a–l**.

6,6a-Dihydroisoindolo[2,1-a]quinazoline-5,11-dione (3a). m.p. 280–281°C (Lit. [5n]: 255–258°C). ^{1}H NMR (DMSO-d_6, 400 MHz): δ_H 6.53 (s, 1H, CH), 7.36 (t, J = 7.6 Hz, 1H, ArH), 7.66–7.82 (m, 3H, ArH), 7.89 (d, J = 7.6 Hz, 2H, ArH), 7.98 (d, J = 7.6 Hz, 1H, ArH), 8.08 (d, J = 8.0 Hz, 1H, ArH), 9.44 (s, 1H, NH). IR (KBr): 3148, 3059, 2931, 2880, 1730, 1677, 1606, 1495, 1475, 1393, 1361, 1306, 1217, 1186, 1125, 794, 756, 738, 693, 574 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{15}H_{10}N_2NaO_2$ $[M + Na]^+$ 273.0640, found 273.0639.

6-(4-Methylbenzyl)-6,6a-dihydroisoindolo[2,1-a]quinazoline-5,11-dione (3b). m.p. 203–204°C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ_H 2.20 (s, 3H, CH_3), 4.92 (d, J = 16.8 Hz, 1H, CH), 5.07 (d, J = 17.2 Hz, 1H, CH), 6.70 (s, 1H, CH), 6.97

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)	78
4	80	[BMIm]Br	I_2(5)	93
5	100	[BMIm]Br	I_2(5)	93
6	80	[BMIm]Br	I_2(10)	92
7	80	[BMIm]Br	I_2(20)	92
8	80	[EMIm]Br	I_2(5)	85
9	80	[PMIm]Br	I_2(5)	90
10	80	[EMIm][BF_4]	I_2(5)	86
11	80	[PMIm][BF_4]	I_2(5)	89
12	80	[BMIm][BF_4]	I_2(5)	92
13	80	[BMIm]Br	CuI(5)	trace
14	80	[BMIm]Br	TsOH(5)	73
15	80	[BMIm]Br	Yb($OTf)_3$(5)	65
16	80	[BMIm]Br	Sc($OTf)_3$(5)	78

[a]Reaction condition: 2 mL solvent, 2-aminobenzamide **1a** (0.272 g, 2.0 mmol), and **2** (0.300 g, 2.0 mmol). [b]BMIm, 1-butyl-3-methylimidazolium; EMIm, 1-ethyl-3-methylimidazolium; PMIm, 1-propyl-3-methylimidazolium. [c]Isolated yields.

Table 2

Synthetic results of **3a–l** in ionic liquids.[a]

Entry	R	Time (h)	Products	Yields (%)[b]
1	H	2	**3a**	93
2	4-Me$C_6H_4CH_2$	2.5	**3b**	92
3	$C_6H_5CH_2$	2	**3c**	95
4	4-Me$OC_6H_4CH_2$	3	**3d**	93
5	4-Me$OC_6H_4(CH_2)_2$	3	**3e**	94
6	Et	3.5	**3f**	90
7	*n*-Pr	4	**3g**	93
8	*n*-Bu	3	**3h**	92
9	Cyclopentyl	5	**3i**	86
10	(Furan-2-yl) methyl	4	**3j**	88
11	Naphthalen-2-yl	5	**3k**	85
12	Piperonylethyl	4	**3l**	90

[a]Reaction condition: 2 mL [BMIm]Br, **1a–l** (2.0 mmol), **2** (0.300 g, 2.0 mmol), and iodine (0.025 g, 0.1 mmol), 80°C. [b]Isolated yields.

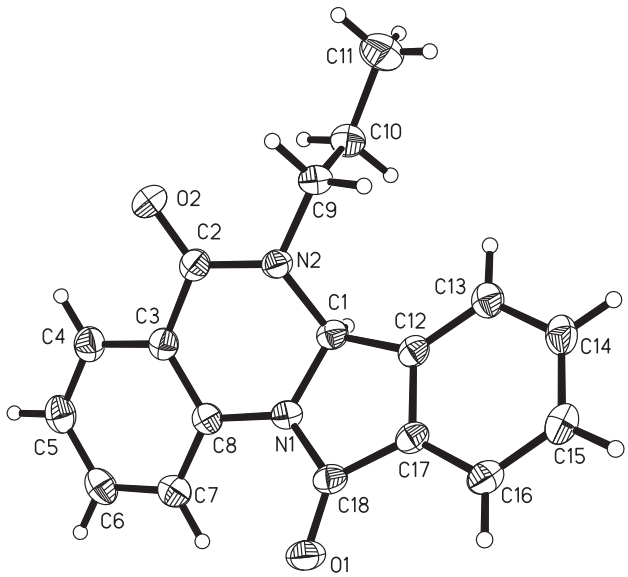


Figure 1. The crystal structure of product **3g**.

(d, J = 8.0 Hz, 2H, ArH), 7.03 (d, J = 8.0 Hz, 2H, ArH), 7.42 (t, J = 7.6 Hz, 1H, ArH), 7.62–7.66 (m, 2H, ArH), 7.71–7.78 (m, 2H, ArH), 7.86 ~ 7.87 (m, 1H, ArH), 8.06 (d, J = 8.0 Hz, 2H, ArH). ^{13}C NMR (100 MHz, DMSO-d_6): δ_C 46.1, 55.3, 70.7, 114.5, 120.2, 120.3, 125.0, 125.3, 125.5, 127.6, 128.1, 129.5, 130.6, 132.5, 132.8, 133.6, 136.9, 137.9, 158.8, 164.1,164.9. IR (KBr): 3059, 3018, 2925, 2870, 1729, 1660, 1603, 1516, 1487, 1470, 1414, 1353, 1291, 1215, 1160, 1110, 990, 880, 757, 745, 684 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{23}H_{18}N_2NaO_2$ $[M + Na]^+$ 377.1266, found 377.1289.

6-Benzyl-6,6a-dihydroisoindolo[2,1-a]quinazoline-5,11-dione (3c). m.p. 158–159°C(Lit. [5m]: 148–150°C). ^{1}H NMR (DMSO-d_6, 400 MHz): δ_H 5.03 (d, J = 16.8 Hz, 1H, CH), 5.09 (d, J = 16.8 Hz, 1H, CH), 6.72 (s, 1H, CH), 7.07 (d, J = 7.6 Hz, 2H, ArH), 7.12–7.15 (m, 1H, ArH), 7.19–7.23 (m, 2H, ArH), 7.43 (t, J = 7.6 Hz, 1H, ArH), 7.60–7.65 (m, 2H, ArH), 7.72–7.78 (m, 2H, ArH), 7.85–7.87 (m, 1H, ArH), 8.06 (d, J = 8.0 Hz, 2H, ArH). IR (KBr): 3054, 2927, 1723, 1661, 1602, 1487, 1469, 1413, 1355, 1313, 1288, 1215, 1157, 1110, 1094, 989, 763, 735, 686 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{22}H_{16}N_2O_2Na$ $[M + Na]^+$ 363.1109, found 363.1090.

6-(4-Methoxybenzyl)-6,6a-dihydroisoindolo[2,1-a]quinazoline-5,11-dione (3d). m.p. 133–134°C. (Lit. [5m]: 137–139°C). ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 3.79 (s, 3H, CH_3O), 4.55 (d, J = 16.4 Hz, 1H, CH), 5.46 (d, J = 16.4 Hz, 1H, CH), 6.34 (s, 1H, CH), 6.88 (d, J = 8.4 Hz, 2H, ArH), 7.13 (d, J = 8.8 Hz, 2H, ArH), 7.37 (t, J = 7.6 Hz, 1H, ArH), 7.48 (d, J = 7.2 Hz, 1H, ArH), 7.56–7.69 (m, 3H, ArH), 7.98–7.99 (m, 1H, ArH), 8.13 (d, J = 8.0 Hz, 1H, ArH), 8.22 (dd, J = 7.6 Hz, J' = 1.2 Hz, 1H, ArH). IR (KBr): 3053, 2961, 2932, 2837, 1727, 1638, 1604, 1512, 1487, 1469, 1413, 1355, 1289, 1246, 1215, 1177, 1158, 1108, 1032, 989, 760, 742, 684 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{23}H_{18}N_2O_3Na$ $[M + Na]^+$ 393.1215, found 393.1151.

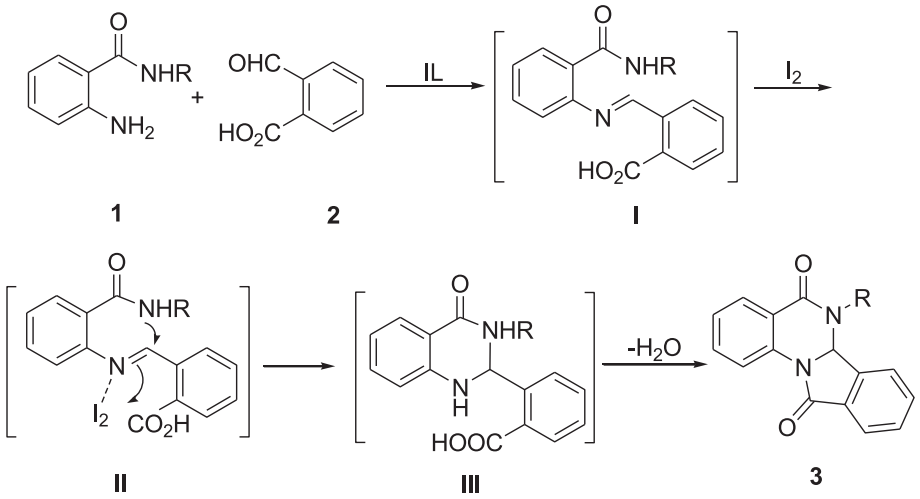
6-(4-Methoxyphenethyl)-6,6a-dihydroisoindolo[2,1-a]quinazoline-5,11-dione (3e). m.p. 140–141°C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ_H 2.34–2.44 (m, 1H, CH), 2.68–2.74 (m, 1H, CH), 3.71 (s, 3H, CH_3O), 3.87–3.99 (m, 2H, CH_2), 6.55 (s, 1H, CH), 6.76 (d, J = 8.0 Hz, 2H, ArH), 6.96 (d, J = 8.4 Hz, 2H, ArH), 7.40 (t, J = 7.6 Hz, 1H, ArH), 7.70–7.77 (m, 2H, ArH), 7.85–7.92 (m, 2H, ArH), 7.99–8.04 (m, 3H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 33.5, 45.0, 55.3, 70.7, 114.0, 120.1, 120.6, 125.25, 125.34, 125.41, 129.0, 129.7, 130.2, 130.6, 132.6, 133.0, 133.6, 136.7, 137.9, 158.2, 163.7, 164.7. IR (KBr): 3054, 2953, 2836, 1723, 1660, 1604, 1511, 1487, 1467, 1411, 1353, 1303, 1283, 1251, 1237, 1162, 1111, 1036, 821, 753, 742, 686 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{24}H_{20}N_2NaO_3$ $[M + Na]^+$ 407.1372, found 407.1350.

***6-Ethyl-6,6a-dihydroisoindolo[2,1-a]*quinazoline-5,11-dione (3f).** m.p. 159–160°C(Lit. [5m]: 157–160°C). ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.22 (t, J = 7.2 Hz, 3H, CH_3), 3.69–3.78 (m, 1H, CH), 3.99–4.08 (m, 1H, CH), 6.25 (s, 1H, CH), 7.31–7.35 (m, 1H, ArH), 7.61–7.79 (m, 4H, ArH), 8.03–8.05 (m, 1H, ArH), 8.10 (d, J = 8.0 Hz, 1H, ArH), 8.15 (dd, J = 8.0 Hz, J' = 1.6 Hz, 1H, ArH). IR (KBr): 2985, 2958, 2832, 1712, 1668, 1603, 1490, 1468, 1417, 1361, 1304, 1282, 1218, 1188, 1156, 1112, 1062, 984, 756, 737, 687 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{17}H_{15}N_2O_2$ $[M + H]^+$ 279.1134, found 279.1135.

6,6a-Dihydro-6-n-propylisoindolo[2,1-a]quinazoline-5,11-dione (3g). m.p. 135–136°C(Lit. [5m]: 127–130°C). ^{1}H NMR (DMSO-d_6, 400 MHz): δ_H 0.76 (t, J = 7.2 Hz, 3H, CH_3), 1.21–1.30 (m, 1H, CH), 1.39–1.44 (m, 1H, CH), 3.70 (t, J = 7.2 Hz, 2H, CH_2), 6.58 (s, 1H, CH), 7.38 (t, J = 7.2 Hz, 1H, ArH), 7.69–7.78 (m, 2H, ArH), 7.83–7.86 (m, 1H, ArH), 7.95–8.01 (m, 4H, ArH). IR (KBr): 2960, 2931, 2872, 1729, 1654, 1604, 1489, 1469, 1416, 1361, 1313, 1272, 1217, 1183, 1159, 1113, 1073, 958, 793, 755, 738, 687 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{18}H_{17}N_2O_2$ $[M + H]^+$ 293.1290, found 293.1292.

Crystal data for **3g**: $C_{18}H_{16}N_2O_2$; M = 292.33, red sheet crystals, 0.52 × 0.35 × 0.30 mm, orthorhombic, space group *Pna*2(1), a = 13.404(3), b = 22.292(5), c = 4.8853(10) Å, $\alpha = \beta = \gamma = 90°$, V = 1459.7(5)^3, Z = 4, D_c = 1.330 g.cm^{-3}. $F(000)$ = 616, μ(Mo$K\alpha$) = 0.088 mm^{-1}. Intensity data were collected on Rigaku Mercury diffractometer with graphite monochromated Mo$K\alpha$ radiation (λ = 0.71073 Å) using *phi and omega* scan mode with $3.04° < \theta < 25.67°$. 2611 unique reflections were measured, and 2211 reflections with $I > 2\sigma$ (I) were used in the refinement. Structure was solved by direct methods and expanded using Fourier techniques. The final cycle of full-matrix least squares technique to R = 0.0414 and wR = 0.0511.

Scheme 2. The possible mechanism for the formation of products **3**.



6-n-Butyl-6,6a-dihydroisoindolo[2,1-a]quinazoline-5,11-dione (3h). m.p. 141–142°C. ^{1}H NMR (DMSO-d_6, 400 MHz): δ_H 0.82 (t, J = 7.2 Hz, 3H, CH_3), 1.18–1.22 (m, 3H, CH + CH_2), 1.39–1.41 (m, 1H, CH), 3.71–3.77 (m, 2H, CH_2), 6.58 (s, 1H, CH), 7.36–7.40 (m, 1H, ArH), 7.69–7.78 (m, 2H, ArH), 7.84–7.88 (m, 1H, ArH), 7.95–8.01 (m, 4H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): 13.9, 20.1, 30.3, 42.9, 70.5, 120.1, 120.5, 125.1, 125.2, 125.3, 129.0, 130.7, 132.7, 132.9, 133.4, 136.6, 138.2, 163.7, 164.9. IR (KBr): 2949, 2930, 2862, 1727, 1655, 1604, 1489, 1469, 1415, 1358, 1309, 1284, 1216, 1157, 1113, 1084, 956, 756, 737, 688 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{19}H_{19}N_2O_2$ $[M+H]^+$ 307.1447, found 307.1448.

6-Cyclopentyl-6,6a-dihydroisoindolo[2,1-a]quinazoline-5,11-dione (3i). m.p. 158–160°C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.46–1.62 (m, 3H, CH_2 + CH), 1.95–2.17 (m, 3H, CH + CH_2), 2.24–2.36 (m, 2H, CH_2), 4.13–4.17 (m, 1H, CH), 6.16 (s, 1H, CH), 7.30 (t, J = 7.6 Hz, 1H, ArH), 7.58–7.62 (m, 1H, ArH), 7.66–7.73 (m, 3H, ArH), 8.04 (d, J = 6.8 Hz, 1H, ArH), 8.11 (d, J = 7.6 Hz, 1H, ArH), 8.14 (d, J = 8.0 Hz, 1H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 25.3, 29.3, 58.2, 72.2, 119.3, 121.4, 125.0, 125.2, 125.9, 128.8, 130.7, 132.5, 133.36, 133.43, 136.7, 138.2, 164.1, 164.5. IR (KBr): 2956, 2908, 2864, 1698, 1635, 1602, 1488, 1466, 1425, 1392, 1338, 1310, 1220, 1172, 1109, 758, 735, 689 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{20}H_{18}N_2O_2Na$ $[M+Na]^+$ 341.1266, found 341.1292.

6-((Furan-2-yl)methyl)-6,6a-dihydroisoindolo[2,1-a]quinazoline-5,11-dione (3j). m.p. 175–176°C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 4.45 (d, J = 16.4 Hz, 1H, CH), 5.44 (d, J = 16.4 Hz, 1H, CH), 6.37 (s, 1H, CH), 6.39–6.41 (m, 2H, ArH), 7.31–7.34 (m, 1H, ArH), 7.42–7.43 (m, 1H, ArH), 7.62–7.72 (m, 3H, ArH), 7.79–8.05 (m, 2H, ArH), 8.09 (dd, J = 8.0 Hz, J' = 0.4 Hz, 1H, ArH), 8.15 (dd, J = 8.0 Hz, J' = 1.2 Hz, 1H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 39.6, 71.0, 108.8, 110.9, 120.2, 120.4, 125.1, 125.3, 126.1, 129.2, 130.7, 132.8, 133.7, 136.8, 138.1, 142.1, 150.4, 164.0, 165.1. IR (KBr): 3125, 3053, 2955, 1719, 1668, 1602, 1489, 1468, 1411, 1359, 1333, 1298, 1278, 1215, 1185, 1158, 1065, 1028, 1011, 756, 743, 682 cm^{-1}. HRMS (ESI, *m/z*): calcd for $C_{20}H_{14}N_2O_3Na$ $[M+Na]^+$ 353.0902, found 353.0900.

6,6a-Dihydro-6-(naphthalen-2-yl)isoindolo[2,1-a]quinazoline-5,11-dione (3k). m.p. 227–228°C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 6.10 (d, J = 8.0 Hz, 1H, ArH), 6.65 (s, 1H, CH), 7.13 (t, J = 7.2 Hz, 1H, ArH), 7.35–7.98 (m, 11H, ArH), 8.22–8.24 (m, 2H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 72.3, 113.2, 114.6, 120.0, 120.4, 124.5, 125.2, 125.9, 126.8, 127.1, 127.8, 128.0, 128.2, 129.5, 130.3, 132.1, 132.2, 133.2, 133.5, 134.0, 136.5, 137.1, 137.7, 161.0, 165.4. IR (KBr): 3048, 1721, 1673, 1601, 1487, 1465, 1403, 1348, 1306, 1288, 1216, 1162, 1117, 807, 764, 750, 733, 707 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{25}H_{16}N_2NaO_2$ $[M+Na]^+$ 399.1109, found 399.1140.

6-Piperonylethyl-6,6a-dihydroisoindolo[2,1-a]quinazoline-5,11-dione (3l). m.p. 137–138°C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ_H 2.38–2.51 (m, 1H, CH), 2.63–2.68 (m, 1H, CH), 3.82–4.01 (m, 2H, CH_2), 5.94 (s, 2H, CH_2), 6.42 (dd, J = 8.0 Hz, J' = 1.2 Hz, 1H, ArH), 6.52 (s, 1H, CH), 6.53–6.54 (m, 1H, ArH), 6.67 (d, J = 8.0 Hz, 1H, ArH), 7.39 (t, J = 7.6 Hz, 1H, ArH), 7.69–7.75 (m, 2H, ArH), 7.82–7.90 (m, 2H, ArH), 7.98–8.02 (m, 3H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 34.2, 44.9, 70.7, 100.9, 108.4, 109.1, 120.2, 120.5, 121.7, 125.2, 125.36, 125.40, 129.0, 130.6, 131.9, 132.6, 133.0, 133.6, 136.7, 137.9, 146.2, 147.6, 163.8, 164.7. IR (KBr, ν, cm^{-1}): 3057, 2955, 2907, 2853, 1723, 1655, 1602, 1487, 1467, 1414, 1352, 1309, 1287, 1255, 1215, 1185, 1162, 1108, 1037, 921, 800, 753, 742, 685. HRMS (ESI, *m/z*): calcd for $C_{24}H_{19}N_2O_4$ $[M+H]^+$ 399.1345, found 399.1338.

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REFERENCES AND NOTES

[1] (a) Rohini, R.; Shanker, K.; Reddy, P. M. r.; Sekhar, V. C.; Ravinder, V. Arch Pharm 2009, 342, 533; (b) Grandolini, G.; Ambrogi, V.; Perioli, L.; Giannangeli, M.; Jovicevic, L.; Rossi, V. Farmaco 1997, 52, 679.

[2] Sharma, V. M.; Prasanna, P.; Adi Seshu, K. V.; Renuka, B.; Laxman Rao, C. V.; Sunil Kumar, G.; Narasimhulu, C. P.; Aravind Babu,

P.; Puranik, R. C.; Subramanyam, D.; Venkateswarlu, A.; Rajagopal, S.; Kumar, K. B. S.; Rao, C. S.; Mamidi, N. V. S. R.; Deevi, D. S.; Ajaykumar, R.; Rajagopalan, R. Bioorg Med Chem Lett 2002, 12, 2303.

[3] Miyazawa, M.; Fujioka, J.; Ishikawa, Y. J. Sci Food Agr 2002, 82, 1574.

[4] Staskun, B.; Wolfe, J. F. Afr J Chem 1992, 45, 5.

[5] (a) Frere, S.; Thiery, V.; Bailly, C.; Besson, T. Tetrahedron 2003, 59, 773; (b) Arumugam, N.; Srinivasan, P. C. Heterocycles 2003, 60, 1191; (c) Lichitsky, B. V.; Kozhinov, D. V.; Vorontsova, L. G.; Starikova, Z. A.; Dudinov, A. A.; Krayushkin, M. M. Russ Chem Bull 2002, 51, 1869; (d) Battistuzzi, G.; Cacchi, S.; Fabrizi, G.; Marinelli, F.; Parisi, L. M. Org Lett 2002, 4, 1355; (e) Dave, C. G.; Shah, R. D. Heterocycles 1998, 48, 529; (f) Becker, J. Y.; Shakkour, E.; Sarma, J. A. R. P. J Chem Soc Chem Commun 1990, 1016; (g) Wang, M.; Dou, G.; Shi, D. J Comb Chem 2010, 12, 582; (h) Yamato, M.; Takeuchi, Y. Chem Pharm Bull 1982, 30, 1036; (i) Feng, E.; Zhou, Y.; Zhang, D. Y.; Zhang, L.; Sun, H. F.; Jiang, H. L.; Liu, H. J Org Chem 2010, 75, 3274; (j) Iminov, R. T.; Tverdokhlebov, A. V.; Tolmachev, A. A.; Volovenko, Y. M.; Shishkina, S. V.; Shishkin, O. V. Tetrahedron 2009, 65, 8582; (k) Zhao, X.; Shi, D. Q. J Heterocycl Chem 2011, 43, 634; (l) Iminov, R. T.; Tverdokhlebov, A. V.; Tolmachev, A. A.; Volovenko, Y. M.; Kostyuk, A. N.; Chernega, A. N.; Rusanov, E. B. Herterocycles 2008, 75, 1673; (m) Kumar, K. S. Chem Commun 2011, 47, 5010; (n) Bunce, R. A. J Heterocycl Chem 2011, 48, 991.

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

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

[8] (a) Wang X. S.; Wu J. R.; Zhou J.; Tu S. J. J Comb Chem 2009, 11, 1011; (b) Wang, X. S.; Yang, K.; Zhou, J.; Tu, S. J. J Comb Chem 2010, 12, 417.