Organic & Biomolecular Chemistry

Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: S. Guo, J. Zhai, F. Wang and X. Fan, *Org. Biomol. Chem.*, 2017, DOI: 10.1039/C7OB00256D.

ROYAL SOCIETY OF CHEMISTRY

rsc.li/obc

View Article Online
DOI: 10.1039/C7OB00256D

Journal Name

ARTICLE

One-pot three-component selective synthesis of isoindolo[2,1-*a*]quinazoline derivatives via palladium-catalyzed cascade cyclo-condensation/cyclocarbonylation sequence

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

Shenghai Guo,* Jianhui Zhai, Fang Wang, and Xuesen Fan*

A practical and highly efficient procedure for the selective preparation of 6,6a-dihydroisoindolo[2,1-*a*]quinazoline-5,11-diones through palladium-catalyzed one-pot three-component cascade reaction of 2-aminobenzamides with 2-bromobenzaldehydes and carbon monoxide under atmospheric pressure has been developed. This cascade reaction, in which four new C-C/C-N bonds and two new rings are simultaneously constructed, is triggered by a cyclocondensation of 2-aminobenzamides with 2-bromobenzaldehydes, followed by a Pd-catalyzed cyclocarbonylation of the *in situ* formed 2,3-dihydroquinazolin-4(1*H*)-ones with CO (1 atm). Compared with the existing methods, the present protocol has the advantages of readily available starting materials, broad substrate scope, structural diversity of products, and free of high-pressure equipment.

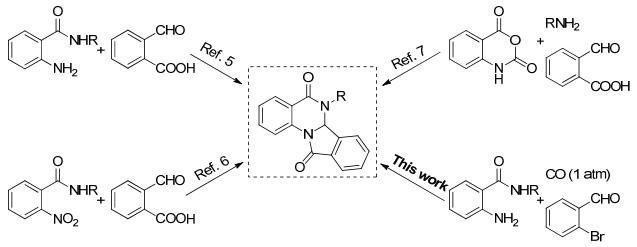
Introduction

Isoindoloquinazoline derivatives, as an important class of quinazoline-containing heterocyclic compounds, are attracting increasing interest as they are frequently encountered in natural products and synthetic compounds with a wide range of bioactivities.[1] Among them, isoindolo[2,1-*a*]quinazoline derivatives have been utilized as not only potent inhibitors of TNF-α[2] and cancer cell proliferation,[3] but also efficient stabilizer of organic materials against degradation caused by heat, light and/or oxidation.[4] In general, isoindolo[2,1-*a*]quinazoline derivatives could be obtained through annulation of 2-formylbenzoic acid derivatives with the corresponding nucleophiles. For instance, Wang and other groups reported an efficient synthesis of isoindolo[2,1-*a*]quinazoline derivatives through cascade reaction of 2-formylbenzoic acid with 2-aminobenzamides or 2-aminobenzohydrazides in different solvents (Scheme 1).[5] Foroumadi and Bunce independently disclosed a synthesis of isoindolo[2,1-*a*]quinazoline-5,11-diones via one-pot reduction/cyclization cascade reaction of 2-nitrobenzamides with 2-formylbenzoic acid in the presence of reductants (such as: $SnCl_2$ or Fe) (Scheme 1).[6] Pal and other groups demonstrated that 6,6a-dihydroisoindolo[2,1-*a*]quinazoline-5,11-diones could be efficiently synthesized by a three-component domino reaction of 2-formylbenzoic acid with isatoic anhydride and amines under different reaction conditions (Scheme 1).[2,7] While the above-mentioned synthetic routes are generally effective and reliable, all of them require the use of 2-formylbenzoic acid derivatives, which are unfortunately difficult-to-obtain from commercial sources and very expensive, especially for the substituted ones. Therefore, the development of novel and general synthetic approaches toward isoindolo[2,1-*a*]quinazoline derivatives from commercially available and inexpensive starting materials remains in high demand for both organic and medicinal chemists.

Meanwhile, palladium-catalyzed carbonylative multicomponent reaction turns out to be one of the most powerful tools for the construction of various carbonyl-containing acyclic and cyclic organic compounds with a substantial increase in molecular complexity.[8] Among these reactions, palladium-catalyzed three-component carbonylative cyclizations of aromatic halides with carbon monoxide and organic nucleophiles have been proven to be highly effective in the synthesis of various quinazoline derivatives.[9] However, to the best of our knowledge, an efficient synthesis of isoindolo[2,1-*a*]quinazoline derivatives by employing palladium-catalyzed three-component cyclocarbonylation has not been reported yet until now. In a continuation of our efforts to explore novel synthetic apporaches toward valuable quinazoline-containing heterocyclic compounds,[10] we disclose herein a practical synthesis of 6,6a-dihydroisoindolo[2,1-*a*]quinazoline-5,11-diones from inexpensive commercial reagents 2-aminobenzamides, 2-bromobenzaldehydes, and carbon monoxide (1 atm) (Scheme 1). Now, we would like to report our results in this regard.

Collaborative Innovation Center of Henan Province for Green Manufacturing of Fine Chemicals, Henan Key Laboratory of Organic Functional Molecule and Drug Innovation, School of Chemistry and Chemical Engineering, Henan Normal University, Xinxiang, Henan 453007, China. E-mail: shguo@htu.cn; xuesen.fan@htu.cn.

Electronic Supplementary Information (ESI) available: ^{1}H and ^{13}C NMR spectra of compounds **3a-3u, 4,** and **5**. See DOI: 10.1039/x0xx00000x



Scheme 1. Synthetic routes toward isoindolo[2,1-*a*]quinazoline derivatives.

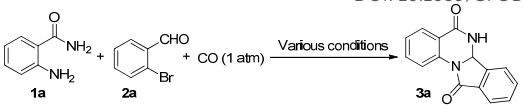
Results and discussion

Initially, 2-aminobenzamide (**1a**) and 2-bromobenzaldehyde (**2a**) were chosen as model substrates to optimize the reaction conditions with regard to ligands, Pd catalysts, bases, and solvents (Table 1). To our delight, treatment of **1a** (0.4 mmol) and **2a** (0.4 mmol) with CO (1 atm) in the presence of $Pd(OAc)_2$ (5 mol %), *n*-butyl di(1-adamantyl)phosphine ($BuPAd_2$) (15 mol %), and DABCO (3.0 equiv.) in DMSO (2 mL) at 120 °C for 10 h could afford the expected 6,6a-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione (**3a**) in 46% isolated yield (entry 1). Next, with $Pd(OAc)_2$ as catalyst, other ligands including 2-dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl (X-Phos), tris(2-furanyl)phosphine (TFP), tricyclohexylphosphine (TCHP), triphenylphosphine (PPh_3), and tri-(*tert*-butyl) phosphonium tetrafluoroborate ($[(t\text{-}Bu)_3PH]BF_4$) were screened (entries 2-6). Among them, $[(t\text{-}Bu)_3PH]BF_4$ gave the best result (63%). Then, the effect of different Pd catalysts such as $Pd(PPh_3)_2Cl_2$, $Pd_2(dba)_3$, and $PdCl_2$ on this reaction was also investigated (entries 7-9). Of these catalysts, $PdCl_2$ exhibited the highest catalytic activity. In addition, five other bases including DBU, Et_3N, morpholine, piperidine, and K_2CO_3 were also tried, however, all of them were less effective than DABCO (entries 10-14 vs 9). In following studies, we found that when DMF, NMP, and EtOH were used to replace DMSO as the reaction medium, lower yields of **3a** were observed (entries 15-17). Decreasing or increasing the reaction temperature from 120 °C resulted in decreased yields of **3a** (entries 18-19). Moreover, it was also observed that reducing the loadings of Pd catalyst and ligand gave **3a** in a lower yield of 32% (entry 20). Finally, $PdCl_2$, $[(t\text{-}Bu)_3PH]BF_4$, and DABCO were proved to be essential for the formation of **3a** (entries 21-23).

With the optimized reaction conditions (Table 1, entry 9) in hand, the scope and limitation of this novel cascade reaction leading to isoindolo[2,1-*a*]quinazolines (**3**) were then explored and the results are shown in Table 2. First, the reactions of several 2-bromobenzaldehyde derivatives (**2**) with 2-aminobenzamide (**1a**) and carbon monoxide (1 atm) were investigated. We found that substituted 2-bromobenzaldehydes (**2**) bearing either electron-donating groups (-Me and -OMe) or electron-withdrawing groups (-F, -Cl, and $-CF_3$) on the phenyl ring at different positions were all compatible with the reaction conditions to afford the corresponding isoindolo[2,1-*a*]quinazoline derivatives **3b**-**3f** in 60%-85% isolated yields and no obvious electronic effect was observed. In addition, we also studied the cascade reactions of

Table 1. Optimization of reaction conditions for the synthesis of **3a**[a]

View Article Online
DOI: 10.1039/C7OB00256D



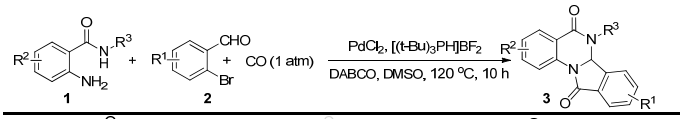
1a 2a 3a

Entry	Catalyst	Ligand	Base	Solvent	Yield(%)[b]
1	$Pd(OAc)_2$	$BuPAd_2$	DABCO	DMSO	46
2	$Pd(OAc)_2$	X-Phos	DABCO	DMSO	32
3	$Pd(OAc)_2$	TFP	DABCO	DMSO	48
4	$Pd(OAc)_2$	TCHP	DABCO	DMSO	44
5	$Pd(OAc)_2$	PPh_3	DABCO	DMSO	39
6	$Pd(OAc)_2$	$[(t\text{-}Bu)_3PH]BF_4$	DABCO	DMSO	63
7	$Pd(PPh_3)_2Cl_2$	$[(t\text{-}Bu)_3PH]BF_4$	DABCO	DMSO	48
8	$Pd_2(dba)_3$	$[(t\text{-}Bu)_3PH]BF_4$	DABCO	DMSO	56
9	$PdCl_2$	$[(t\text{-}Bu)_3PH]BF_4$	DABCO	DMSO	82
10	$PdCl_2$	$[(t\text{-}Bu)_3PH]BF_4$	DBU	DMSO	nd
11	$PdCl_2$	$[(t\text{-}Bu)_3PH]BF_4$	Et_3N	DMSO	18
12	$PdCl_2$	$[(t\text{-}Bu)_3PH]BF_4$	morpholine	DMSO	nd
13	$PdCl_2$	$[(t\text{-}Bu)_3PH]BF_4$	piperidine	DMSO	32
14	$PdCl_2$	$[(t\text{-}Bu)_3PH]BF_4$	K_2CO_3	DMSO	nd
15	$PdCl_2$	$[(t\text{-}Bu)_3PH]BF_4$	DABCO	DMF	60
16	$PdCl_2$	$[(t\text{-}Bu)_3PH]BF_4$	DABCO	NMP	68
17[c]	$PdCl_2$	$[(t\text{-}Bu)_3PH]BF_4$	DABCO	EtOH	nd
18[d]	$PdCl_2$	$[(t\text{-}Bu)_3PH]BF_4$	DABCO	DMSO	54
19[e]	$PdCl_2$	$[(t\text{-}Bu)_3PH]BF_4$	DABCO	DMSO	62
20[f]	$PdCl_2$	$[(t\text{-}Bu)_3PH]BF_4$	DABCO	DMSO	32
21	-	$[(t\text{-}Bu)_3PH]BF_4$	DABCO	DMSO	nd
22	$PdCl_2$	-	DABCO	DMSO	nd
23	$PdCl_2$	$[(t\text{-}Bu)_3PH]BF_4$	-	DMSO	nd

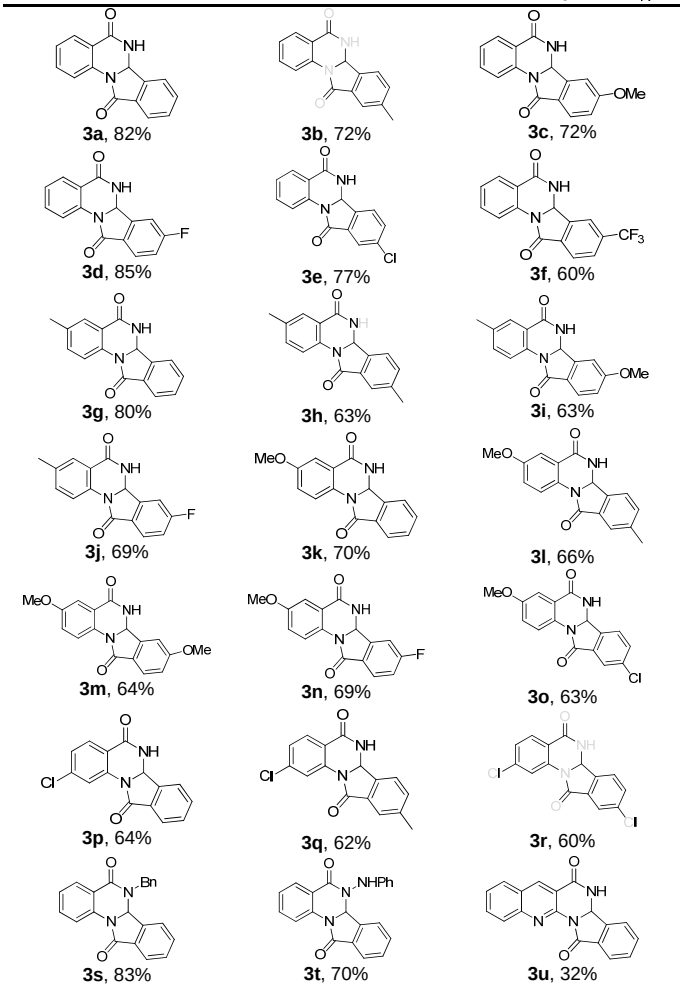
[a] The reactions were run with: **1a** (0.4 mmol), **2a** (0.4 mmol), CO (1 atm), catalyst (0.02 mmol), ligand (0.06 mmol), base (1.2 mmol), solvent (2 mL), 120 °C, 10 h. [b] Isolated yield; nd = not detected. [c] The reaction was run at 80 °C. [d] The reaction was run at 100 °C. [e] The reaction was run at 130 °C. [f] With the use of catalyst (0.008 mmol) and ligand (0.024 mmol).

three other aldehydes (**2**), including 2-bromonicotinaldehyde, 2-bromothiophene-3-carbaldehyde, and 2-chlorobenzaldehyde, with 2-aminobenzamide (**1a**) under atmospheric CO pressure. Unfortunately, all of them could not afford the desired isoindolo[2,1-*a*]quinazolines (**3**). Next, the substrate scope of 2-aminobenzamide derivatives (**1**) were examined. The results indicated that 2-aminobenzamides (**1**) having a methyl, methoxyl, or chloro group on the phenyl moiety could take part in this reaction smoothly to deliver the desired products **3g**-**3r** in modest to good yields. Meanwhile, substrates (**1**) with electron-donating substituents (R^2) generally gave the desired

Table 2. Scope for the synthesis of isoindolo[2,1-*a*]quinazoline derivatives (**3**) [a,b]



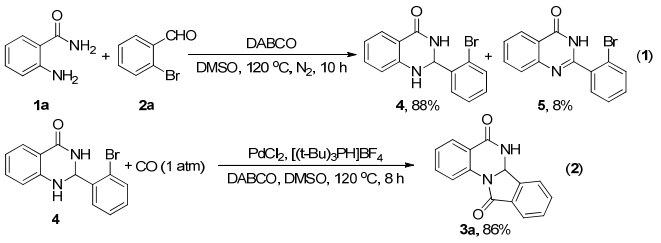
1 2 3



[a] Reaction conditions: **1** (0.4 mmol), **2** (0.4 mmol), CO (1 atm), $PdCl_2$ (0.02 mmol), $[(t\text{-}Bu)_3PH]BF_4$ (0.06 mmol), DABCO (1.2 mmol), DMSO (2 mL), 120 °C, 10 h. [b] Isolated yields are shown.

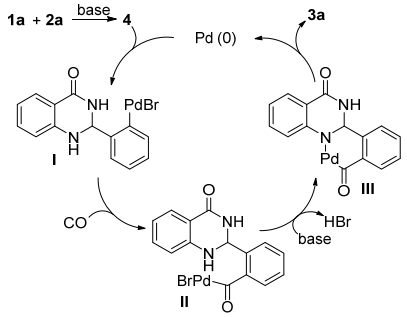
products in yields higher than those with electron-withdrawing substituents (**3g** and **3k** vs **3p**). To further extend the scope of amide substrates (**1**), we also studied the reactions of *N*-Bn and *N*-NHPh substituted 2-aminobenzamides with 2-bromobenzaldehyde (**2a**) and CO (1 atm) under the optimized reaction conditions. It turned out that the reactions underwent smoothly to yield the corresponding isoindolo[2,1-*a*]quinazoline derivatives **3s** and **3t** in 83% and 70% yields, respectively. Finally, the palladium-catalyzed three-component reaction of 2-aminoquinoline-3-carboxamide with **2a** and CO (1 atm) was also tried under the optimized reaction conditions. To our delight, the desired product **3u** could be obtained in 32% isolated yield.

To gain some insights into the mechanism for the formation of products **3**, the following control experiments were carried out, and the results are demonstrated in Scheme 2. First, treatment of a mixture of **1a** and **2a** with the use of DABCO as base under nitrogen atmosphere afforded compound **4** (88%) along with **5** (8%) (Scheme 2, eq 1). Second, the palladium-catalyzed cyclocarbonylation of **4** with CO (1 atm) by using $[(t\text{-}Bu)_3PH]BF_4$ as ligand and DABCO as base provided **3a** in 86% isolated yield (Scheme 2, eq 2).



Scheme 2. Control experiments.

On the basis of the above results and previous reports,[8i,11] a possible mechanism for the formation of **3a** is demonstrated in Scheme 3. Initially, the oxidative addition of Pd (0) to compound **4**, which is formed *in situ* via the cyclocondensation of 2-aminobenzamide (**1a**) with 2-bromobenzaldehyde (**2a**) under basic conditions, gives rise to a palladium complex **(I)**. Next, the insertion of CO into the C-Pd bond of complex (**I**) affords an acylpalladium complex (**II**), which then eliminates hydrogen bromide regioselectively to yield intermediate **III** under the promotion of base. Finally, reductive elimination of **III** delivers **3a** and regenerates the Pd(0) species. In addition, it is also possible that the intramolecular nucleophilic attack of NH on the carbonyl group of acylpalladium complex (**II**) gives the product (**3a**) and the active Pd(0) species.



Scheme 3. Possible mechanism for the formation of **3a.**

Conclusions

In conclusion, we have successfully developed a facile and efficient protocol for the selective synthesis of isoindolo[2,1-*a*]quinazoline derivatives via palladium-catalyzed three-component carbonylative cyclization of 2-aminobenzamides with 2-bromobenzaldehydes under atmospheric pressure of carbon monoxide. Compared with the existing procedures, the present synthetic route exhibits good functional group tolerance, commercially available starting materials, high regioselectivity, and operational simplicity. Further development of novel palladium-catalyzed three-component carbonylative cyclization reactions for the construction of

other quinazoline-fused heterocyclic compounds is currently underway in our laboratory.

Experimental Section

General

Unless noted, all commercial reagents and solvents were used without further purification. Melting points were recorded with a micro melting point apparatus and uncorrected. The ^{1}H NMR spectra were recorded at 400 or 600 MHz. The ^{13}C NMR spectra were recorded at 150 MHz. High-resolution mass spectra (HRMS) were collected in ESI mode by using a MicrOTOF mass spectrometer. All reactions were monitored by thin-layer chromatography (TLC) using silica gel plates (silica gel 60 F254 0.25 mm) and components were visualized by observation under UV light (254 and 365 nm)

General procedure for the preparation of isoindolo[2,1-*a*]quinazoline derivatives (3).

To a schlenk tube (15 mL) containing a solution of 2-aminobenzamide **1** (0.4 mmol) in DMSO (2 mL) were added 2-bromobenzaldehyde **2** (0.4 mmol), $PdCl_2$ (0.02 mmol), $[(t\text{-}Bu)_3PH]BF_4$ (0.06 mmol), DABCO (1.2 mmol) under CO (1 atm) atmosphere. Then, the mixture was stirred at 120 ^{o}C for 10 h. After being cooled to room temperature, the reaction was quenched with NH_4Cl and extracted with ethyl acetate. The combined organic layer was washed with H_2O and brine, and then dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel to afford the corresponding 6,6a-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione **3**.

6,6a-Dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione (3a)[2]. Petroleum ether/ethyl acetate (1:1) as eluent; white solid (82 mg, 82%), mp 256-258 ^{o}C. ^{1}H NMR (DMSO, 400 MHz) δ 6.52 (s, 1H), 7.35 (t, *J* = 8.0 Hz, 1H), 7.66-7.73 (m, 2H), 7.80 (t, *J* = 7.2 Hz, 1H), 7.88-7.90 (m, 2H), 7.97-7.98 (m, 1H), 8.08 (d, *J* = 8.0 Hz, 1H), 9.41(s, 1H); ^{13}C NMR (DMSO, 150 MHz) δ 67.5, 120.0, 120.5, 124.3, 124.6, 125.3, 128.7, 130.7, 131.6, 133.7, 134.0, 137.6, 141.2, 164.1, 165.0. MS (ESI) *m/z* 251 $[M + H]^+$.

9-Methyl-6,6a-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione (3b). Petroleum ether/ethyl acetate (1:1) as eluent; white solid (76 mg, 72%), mp 255-257 ^{o}C. ^{1}H NMR (DMSO, 400 MHz) δ 2.45 (s, 3H), 6.47 (s, 1H), 7.34 (t, *J* = 7.6 Hz, 1H), 7.59 (d, *J* = 7.6 Hz, 1H), 7.67-7.71 (m, 2H), 7.75 (d, *J* = 7.6 Hz, 1H), 7.96 (d, *J* = 7.6 Hz, 1H), 8.06 (d, *J* = 8.0 Hz, 1H), 9.38 (s, 1H); ^{13}C NMR (DMSO, 150 MHz) δ 21.4, 67.4, 120.0, 120.5, 124.3, 124.4, 125.2, 128.7, 131.8, 134.0, 134.5, 137.7, 138.6, 140.6, 164.1, 165.1. HRMS (ESI) calcd for $C_{16}H_{13}N_2O_2$ $[M + H]^+$ 265.0972, found 265.0976.

8-Methoxy-6,6a-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione (3c). Petroleum ether/ethyl acetate (1:1) as eluent; white solid (81 mg, 72%), mp 258-260 ^{o}C. ^{1}H NMR (DMSO, 400 MHz) δ 3.89 (s, 3H), 6.46 (s, 1H), 7.19 (dd, *J* = 2.0, 8.4 Hz, 1H), 7.32 (t, *J* = 8.0 Hz, 1H), 7.47 (d, *J* = 1.6 Hz, 1H), 7.66-7.70 (m, 1H), 7.79 (d, *J* = 8.4 Hz, 1H), 7.95 (d, *J* = 6.4 Hz, 1H), 8.04 (d, *J* = 7.6 Hz, 1H), 9.30 (s, 1H); ^{13}C NMR (DMSO, 150 MHz) δ 56.4, 67.1, 109.6, 117.1, 119.9, 120.3, 123.7, 124.9, 125.9, 128.6, 134.0, 137.8, 143.7, 163.9, 164.1, 164.8. HRMS (ESI) calcd for $C_{16}H_{13}N_2O_3$ $[M + H]^+$ 281.0921, found 281.0918.

8-Fluoro-6,6a-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione (3d). Petroleum ether/ethyl acetate (1:1) as eluent; white solid (91 mg, 85%), mp 235-237 ^{o}C. ^{1}H NMR (DMSO, 400 MHz) δ 6.59 (s, 1H), 7.44 (t, *J* = 7.6 Hz, 1H), 7.78 (t, *J* = 6.8 Hz, 1H), 7.94-7.99 (m, 3H), 8.02-8.05 (m, 1H), 8.13 (d, *J* = 8.0 Hz, 1H), 9.52 (s, 1H); ^{13}C NMR (DMSO, 150 MHz) δ 67.1, 112.3 (d, *J* = 25.2 Hz, 1C), 118.3 (d, *J* = 24.2 Hz, 1C), 119.9, 120.3, 125.3, 127.0 (d, *J* = 9.9 Hz, 1C), 128.1, 128.7, 134.1, 137.5, 143.8 (d, *J* = 9.8 Hz, 1C), 163.9, 164.0, 165.4 (d, *J* = 249.3 Hz, 1C). HRMS (ESI) calcd for $C_{15}H_9FN_2NaO_2$ $[M + Na]^+$ 291.0540, found 291.0541.

9-Chloro-6,6a-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione (3e). Petroleum ether/ethyl acetate (1:1) as eluent; white solid (88 mg, 77%), mp 242-244 ^{o}C. ^{1}H NMR (DMSO, 400 MHz) δ 6.52 (s, 1H), 7.35 (t, *J* = 7.2 Hz, 1H), 7.51-7.55 (m, 1H), 7.69-7.72 (m, 2H), 7.93-7.98 (m, 2H), 8.06 (d, *J* = 8.0 Hz, 1H), 9.38 (s, 1H); ^{13}C NMR (DMSO, 150 MHz) δ 67.3, 120.0, 120.5, 124.1, 125.5, 126.5, 128.7, 133.6, 133.8, 134.1, 135.6, 137.3, 139.8, 163.6, 164.0. HRMS (ESI) calcd for $C_{15}H_{10}ClN_2O_2$ $[M + H]^+$ 285.0425, found 285.0429.

8-(Trifluoromethyl)-6,6a-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione (3f). Petroleum ether/ethyl acetate (2:1) as eluent; white solid (76 mg, 60%), mp 245-247 ^{o}C. ^{1}H NMR (DMSO, 400 MHz) δ 6.60 (s, 1H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.71-7.75 (m, 1H), 7.99 (dd, *J* = 0.8, 7.6 Hz, 1H), 8.04-8.11 (m, 3H), 8.31 (s, 1H), 9.45 (s, 1H); ^{13}C NMR (DMSO, 150 MHz) δ 67.5, 120.1, 120.5, 122.2 (q, *J* = 3.3 Hz, 1C), 124.2 (q, *J* = 271.4 Hz, 1C), 125.1, 125.5, 127.9 (q, *J* = 4.4 Hz, 1C), 128.7, 133.2 (q, *J* = 31.7 Hz, 1C), 134.1, 135.5, 137.2, 141.8, 163.6, 163.8. HRMS (ESI) calcd for $C_{16}H_9F_3N_2NaO_2$ $[M + Na]^+$ 341.0508, found 341.0512.

3-Methyl-6,6a-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione (3g). Petroleum ether/ethyl acetate (1:1) as eluent; white solid (84 mg, 80%), mp 243-245 ^{o}C. ^{1}H NMR (DMSO, 400 MHz) δ 2.38 (s, 3H), 6.48 (s, 1H), 7.52 (dd, *J* = 2.0, 8.4 Hz, 1H), 7.67 (t, *J* = 8.0 Hz, 1H), 7.77-7.81 (m, 2H), 7.87-7.89 (m, 2H), 7.96 (d, *J* = 8.0 Hz, 1H), 9.39 (s, 1H); ^{13}C NMR (DMSO, 150 MHz) δ 21.0, 67.5, 120.0, 120.3, 124.2, 124.6, 128.7, 130.6, 131.8, 133.6, 134.5, 134.6, 135.2, 141.2, 164.2, 164.8. HRMS (ESI) calcd for $C_{16}H_{12}N_2NaO_2$ $[M + Na]^+$ 287.0791, found 287.0794.

3,9-Dimethyl-6,6a-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione (3h). Petroleum ether/ethyl acetate (1:1) as eluent; white solid (70 mg, 63%), mp 265-267 ^{o}C. ^{1}H NMR (DMSO, 400 MHz) δ 2.37 (s, 3H), 2.45 (s, 3H), 6.42 (s, 1H), 7.49-7.52 (m, 1H), 7.58 (d, *J* = 7.6 Hz, 1H), 7.68 (s, 1H), 7.73-7.76 (m, 2H), 7.94 (d, *J* = 8.4 Hz, 1H), 9.33 (s, 1H); ^{13}C NMR (DMSO, 150 MHz) δ 21.0, 21.4, 67.4, 120.0, 120.3, 124.29, 124.31, 128.7, 131.9, 134.3, 134.50, 134.54, 135.3, 138.6, 140.5, 164.2, 164.9. HRMS (ESI) calcd for $C_{17}H_{15}N_2O_2$ $[M + H]^+$ 279.1128, found 279.1142.

8-Methoxy-3-methyl-6,6a-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione (3i). Petroleum ether/ethyl acetate (1:1) as eluent; white solid (74 mg, 63%), mp 257-259 ^{o}C. ^{1}H NMR (DMSO, 400 MHz) δ 2.36 (s, 3H), 3.89 (s, 3H), 6.40 (s, 1H), 7.18 (dd, *J* = 2.0, 8.4 Hz, 1H), 7.45-7.50 (m, 2H), 7.75-7.79 (m,

2H), 7.92 (d, *J* = 8.4 Hz, 1H), 9.26 (s, 1H); ^{13}C NMR (DMSO, 150 MHz) δ 21.0, 56.3, 67.1, 109.6, 117.0, 119.8, 120.1, 123.8, 125.8, 128.7, 134.2, 134.5, 135.5, 143.7, 163.8, 164.2, 164.7. HRMS (ESI) calcd for $C_{17}H_{14}N_2NaO_3$ [M + Na]$^+$ 317.0897, found 317.0899.

8-Fluoro-3-methyl-6,6a-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione (3j). Petroleum ether/ethyl acetate (2:1) as eluent; white solid (78 mg, 69%), mp 251-253 °C. ^{1}H NMR (DMSO, 400 MHz) δ 2.38 (s, 3H), 6.48 (s, 1H), 7.50-7.55 (m, 2H), 7.70 (dd, *J* = 2.0, 8.0 Hz, 1H), 7.78 (d, *J* = 1.2 Hz, 1H), 7.93 (t, *J* = 2.8 Hz, 1H), 7.95 (t, *J* = 2.8 Hz, 1H), 9.34 (s, 1H); ^{13}C NMR (DMSO, 150 MHz) δ 21.0, 67.1 (d, *J* = 2.1 Hz, 1C), 112.3 (d, *J* = 25.1 Hz, 1C), 118.3 (d, *J* = 23.0 Hz, 1C), 119.9, 120.1, 126.9 (d, *J* = 9.9 Hz, 1C), 128.2, 128.7, 134.6, 134.7, 135.1, 143.8 (d, *J* = 11.0 Hz, 1C), 163.8, 164.1, 165.3 (d, *J* = 249.3 Hz, 1C). HRMS (ESI) calcd for $C_{16}H_{12}FN_2O_2$ [M + H]$^+$ 283.0877, found 283.0865.

3-Methoxy-6,6a-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione (3k). Petroleum ether/ethyl acetate (1:1) as eluent; white solid (78 mg, 70%), mp 236-238 °C. ^{1}H NMR (DMSO, 600 MHz) δ 3.83 (s, 3H), 6.47 (s, 1H), 7.30 (dd, *J* = 2.0, 6.0 Hz, 1H), 7.46 (d, *J* = 2.0 Hz, 1H), 7.67 (t, *J* = 5.2 Hz, 1H), 7.77 (t, *J* = 5.2 Hz, 1H), 7.86-7.88 (m, 2H), 7.98 (d, *J* = 6.0 Hz, 1H), 9.44 (s, 1H); ^{13}C NMR (DMSO, 150 MHz) δ 56.0, 67.5, 112.0, 120.6, 121.6, 121.7, 124.2, 124.6, 130.6, 131.0, 131.8, 133.5, 141.1, 156.7, 163.9, 164.8. HRMS (ESI) calcd for $C_{16}H_{13}N_2O_3$ [M + H]$^+$ 281.0921, found 281.0932.

3-Methoxy-9-methyl-6,6a-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione (3l). Petroleum ether/ethyl acetate (1:1) as eluent; white solid (78 mg, 66%), mp 264-266 °C. ^{1}H NMR (DMSO, 600 MHz) δ 2.45 (s, 3H), 3.83 (s, 3H), 6.42 (s, 1H), 7.29 (dd, *J* = 2.4, 8.4 Hz, 1H), 7.45 (d, *J* = 2.4 Hz, 1H), 7.58 (d, *J* = 7.8 Hz, 1H), 7.67 (s, 1H), 7.74 (d, *J* = 7.8 Hz, 1H), 7.97 (d, *J* = 9.0 Hz, 1H), 9.40 (s, 1H); ^{13}C NMR (DMSO, 150 MHz) δ 21.4, 56.0, 67.4, 112.0, 120.5, 121.6, 121.7, 124.2, 124.3, 131.1, 132.0, 134.2, 138.5, 140.5, 156.6, 163.9, 164.9. HRMS (ESI) calcd for $C_{17}H_{15}N_2O_3$ [M + H]$^+$ 295.1077, found 295.1082.

3,8-Dimethoxy-6,6a-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione (3m). Petroleum ether/ethyl acetate (1:1) as eluent; white solid (79 mg, 64%), mp 267-269 °C. ^{1}H NMR (DMSO, 400 MHz) δ 3.82 (s, 3H), 3.88 (s, 3H), 6.40 (s, 1H), 7.18 (d, *J* = 8.4 Hz, 1H), 7.27 (dd, *J* = 2.8, 8.8 Hz, 1H), 7.43-7.44 (m, 2H), 7.77 (d, *J* = 8.4 Hz, 1H), 7.94 (d, *J* = 8.8 Hz, 1H), 9.34 (s, 1H); ^{13}C NMR (DMSO, 150 MHz) δ 56.0, 56.4, 67.2, 109.8, 111.9, 117.0, 120.6, 121.4, 121.5, 123.8, 125.7, 131.2, 143.6, 156.5, 163.7, 163.9, 164.7. HRMS (ESI) calcd for $C_{17}H_{14}N_2NaO_4$ [M + Na]$^+$ 333.0846, found 333.0842.

8-Fluoro-3-methoxy-6,6a-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione (3n). Petroleum ether/ethyl acetate (1:1) as eluent; white solid (83 mg, 69%), mp 237-239 °C. ^{1}H NMR (DMSO, 400 MHz) δ 3.83 (s, 3H), 6.46 (s, 1H), 7.31 (dd, *J* = 3.2, 8.8 Hz, 1H), 7.46 (d, *J* = 3.2 Hz, 1H), 7.63-7.70 (m, 2H), 7.88-7.91 (m, 1H), 7.97 (d, *J* = 8.8 Hz, 1H), 9.49 (s, 1H); ^{13}C NMR (DMSO, 150 MHz) δ 56.0, 67.2, 110.5 (d, *J* = 23.0 Hz, 1C), 112.1, 120.6, 120.8 (d, *J* = 23.0 Hz, 1C), 121.6, 121.7, 126.8 (d, *J* = 8.7 Hz, 1C), 130.8, 134.3 (d, *J* = 8.7 Hz, 1C), 137.1, 156.8, 163.62 (d, *J* = 3.3 Hz, 1C), 163.65 (d, *J* = 246.0 Hz, 1C), 163.8. HRMS (ESI) calcd for $C_{16}H_{11}FN_2NaO_3$ [M + Na]$^+$ 321.0646, found 321.0645.

9-Chloro-3-methoxy-6,6a-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dion (3o). Petroleum ether/ethyl acetate (1:1) as eluent; white solid (79 mg, 63%), mp 249-251 °C. ^{1}H NMR (DMSO, 400 MHz) δ 3.83 (s, 3H), 6.47 (s, 1H), 7.31 (dd, *J* = 3.2, 8.8 Hz, 1H), 7.45 (d, *J* = 3.2 Hz, 1H), 7.86-7.89 (m, 3H), 7.97 (d, *J* = 8.8 Hz, 1H), 9.50 (s, 1H); ^{13}C NMR (DMSO, 150 MHz) δ 56.1, 67.3, 112.1, 120.6, 121.65, 121.69, 123.9, 126.5, 130.7, 133.4, 134.0, 135.5, 139.7, 156.9, 163.4, 163.8. HRMS (ESI) calcd for $C_{16}H_{11}ClN_2NaO_3$ [M + Na]$^+$ 337.0350, found 337.0361.

2-Chloro-6,6a-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione (3p). Petroleum ether/ethyl acetate (1:1) as eluent; white solid (73 mg, 64%), mp 253-255 °C. ^{1}H NMR (DMSO, 600 MHz) δ 6.54 (s, 1H), 7.42 (dd, *J* = 1.8, 8.4 Hz, 1H), 7.69 (t, *J* = 7.8 Hz, 1H), 7.81 (t, *J* = 7.8 Hz, 1H), 7.90 (t, *J* = 6.6 Hz, 2H), 7.97 (d, *J* = 8.4 Hz, 1H), 8.11 (d, *J* = 1.8 Hz, 1H), 9.51 (s, 1H); ^{13}C NMR (DMSO, 150 MHz) δ 67.7, 119.3, 119.4, 124.5, 124.7, 125.3, 130.6, 130.8, 131.2, 134.0, 138.3, 138.5, 141.2, 163.4, 165.0. HRMS (ESI) calcd for $C_{15}H_{10}ClN_2O_2$ [M + H]$^+$ 285.0425, found 285.0432.

2-Chloro-9-methyl-6,6a-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione (3q). Petroleum ether/ethyl acetate (1:1) as eluent; white solid (74 mg, 62%), mp 262-264 °C. ^{1}H NMR (DMSO, 400 MHz) δ 2.46 (s, 3H), 6.49 (s, 1H), 7.41 (dd, *J* = 2.0, 8.4 Hz, 1H), 7.62 (d, *J* = 7.6 Hz, 1H), 7.72 (s, 1H), 7.76 (d, *J* = 7.6 Hz, 1H), 7.96 (d, *J* = 8.4 Hz, 1H), 8.10 (d, *J* = 2.0 Hz, 1H), 9.46 (s, 1H); ^{13}C NMR (DMSO, 150 MHz) δ 21.4, 67.5, 119.3, 119.4, 124.4, 124.5, 125.2, 130.6, 131.4, 134.8, 138.3, 138.57, 138.60, 140.8, 163.4, 165.1. HRMS (ESI) calcd for $C_{16}H_{11}ClN_2NaO_2$ [M + Na]$^+$ 321.0401, found 321.0399.

2,9-Dichloro-6,6a-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione (3r). Petroleum ether/ethyl acetate (1:1) as eluent; white solid (76 mg, 60%), mp 235-237 °C. ^{1}H NMR (DMSO, 600 MHz) δ 6.54 (s, 1H), 7.44 (dd, *J* = 1.8, 8.4 Hz, 1H), 7.91 (m, 2H), 7.94 (s, 1H), 7.97 (d, *J* = 7.8 Hz, 1H), 8.09 (d, *J* = 1.8 Hz, 1H), 9.53 (s, 1H); ^{13}C NMR (DMSO, 150 MHz) δ 67.5, 119.3, 119.5, 124.2, 125.6, 126.6, 130.6, 133.4, 133.9, 135.7, 138.2, 138.4, 139.7, 163.2, 163.7. HRMS (ESI) calcd for $C_{15}H_8Cl_2N_2NaO_2$ [M + Na]$^+$ 340.9855, found 340.9851.

6-Benzyl-6,6a-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione (3s)[2]. Petroleum ether/ethyl acetate (2:1) as eluent; white solid (113 mg, 83%), mp 153-155 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.63 (d, *J* = 16.8 Hz, 1H), 5.51 (d, *J* = 16.8 Hz, 1H), 6.36 (s, 1H), 7.20-7.26 (m, 3H), 7.32-7.43 (m, 4H), 7.53-7.61 (m, 2H), 7.64-7.69 (m, 1H), 7.96-7.98 (m, 1H), 8.12-8.14 (m, 1H), 8.23 (dd, *J* = 1.2, 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 46.7, 70.7, 120.3, 125.0, 125.4, 125.5, 126.3, 127.3, 129.1, 129.5, 130.6, 132.6, 132.7, 133.8, 136.2, 137.0, 137.8, 164.1, 164.9 (one ^{13}C signal was not observed). MS (ESI) *m/z* 341 [M + H]$^+$.

6-(Phenylamino)-6,6a-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione (3t)[5b]. Petroleum ether/ethyl acetate (2:1) as eluent; white solid (95 mg, 70%), mp 181-183 °C. ^{1}H NMR (DMSO, 600 MHz) δ 6.50 (d, *J* = 7.8 Hz, 2H), 6.64 (t, *J* = 7.2 Hz, 1H), 6.65 (s, 1H), 6.97 (t, *J* = 7.8 Hz, 2H), 7.41 (t, *J* = 7.8 Hz, 1H), 7.57 (t, *J* = 7.8 Hz, 1H), 7.61 (t, *J* = 7.2 Hz, 1H), 7.78 (t, *J* = 7.8 Hz, 1H), 7.81 (d, *J* = 7.8 Hz, 1H), 7.91 (d, *J* = 7.8 Hz, 1H), 8.00 (d, *J* = 7.2 Hz, 1H), 8.15 (d, *J* = 7.8 Hz, 1H), 8.37 (s, 1H); ^{13}C NMR (DMSO, 150 MHz) δ 72.7, 113.1, 119.7, 120.0, 120.6, 124.2, 125.7, 127.1,

129.0, 129.1, 130.8, 132.0, 133.6, 134.5, 137.5, 139.7, 148.8, 165.2, 165.6. MS (ESI) *m/z* 342 $[M + H]^+$.

4b,5-dihydroisoindolo[1',2':2,3]pyrimido[4,5-*b*]quinoline-6,14-dione (3u). DCM/MeOH (20:1) as eluent; light yellow solid (38 mg, 32%), mp > 300 °C. ^{1}H NMR (DMSO, 600 MHz) δ 6.70 (s, 1H), 7.65 (t, *J* = 7.8 Hz, 1H), 7.72 (t, *J* = 7.2 Hz, 1H), 7.85 (t, *J* = 7.8 Hz, 1H), 7.91 (t, *J* = 7.8 Hz, 1H), 7.93-7.95 (m, 2H), 8.03 (d, *J* = 8.4 Hz, 1H), 8.20 (d, *J* = 7.8 Hz, 1H), 9.02 (s, 1H), 9.69 (s, 1H); ^{13}C NMR (DMSO, 150 MHz) δ 67.2, 116.6, 124.7, 124.9, 126.2, 127.0, 128.3, 130.1, 130.9, 131.5, 133.0, 134.0, 139.6, 141.0, 148.0, 148.6, 163.4, 164.0. HRMS (ESI) calcd for $C_{18}H_{12}N_3O_2$ $[M + H]^+$ 302.0924, found 302.0911.

2-(2-Bromophenyl)-2,3-dihydroquinazolin-4(1*H*)-one (4)[12]. Petroleum ether/ethyl acetate (2:1) as eluent; white solid (107 mg, 88%), mp 173-175 °C. ^{1}H NMR (DMSO, 600 MHz) δ 6.09 (s, 1H), 6.72 (t, *J* = 7.2 Hz, 1H), 6.76 (d, *J* = 7.8 Hz, 1H), 6.99 (s, 1H), 7.25-7.28 (m, 1H), 7.32-7.34 (m, 1H), 7.45 (t, *J* = 7.2 Hz, 1H), 7.65-7.69 (m, 3H), 8.19 (s, 1H); ^{13}C NMR (DMSO, 150 MHz) δ 66.9, 115.1, 115.2, 118.0, 122.7, 127.9, 128.6, 129.6, 131.2, 133.3, 133.9, 139.6, 148.2, 164.1. MS (ESI) *m/z* 304 $[M + H]^+$.

2-(2-Bromophenyl)quinazolin-4(3*H*)-one (5)[13]. Petroleum ether/ethyl acetate (2:1) as eluent; white solid (9.5 mg, 8%), mp 160-162 °C. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.40 (t, *J* = 7.8 Hz, 1H), 7.49 (t, *J* = 7.8 Hz, 1H), 7.52-7.55 (m, 1H), 7.71-7.74 (m, 2H), 7.82 (m, 2H), 8.27 (d, *J* = 7.8 Hz, 1H), 10.49 (brs, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 120.9, 121.1, 126.5, 127.4, 127.97, 128.0, 131.3, 132.0, 133.7, 134.9, 135.0, 148.9, 152.1, 162.2. MS (ESI) *m/z* 302 $[M + H]^+$.

Acknowledgements

We thank the National Natural Science Foundation of China (Grants 21202040 and 21572047), Project Funded by China Postdoctoral Science Foundation (2014M552007 and 2015T80771), and the Program for Innovative Research Team in Science and Technology in University of Henan Province (15IRTSTHN003) for financial support.

Notes and references

1 (a) J. Plowman, K. D. Paull, G. Atassi, S. D. Harrison, D. J. Dykes, H. J. Kabbe, V. L. Narayanan and O. C. Yoder, *Invest. New Drugs,* 1988, **6**, 147-153; (b) W. R. Waud, S. D. Harrison, K. S. Gilbert, W. R. Laster and D. P. Griswold, *Cancer Chemother. Pharmacol.,* 1991, **27**, 456-463; (c) Y. Luo, Y.-F. Ren, T.-C. Chou, A. Y. Chen, C. Yu, L. F. Liu and C. C. Cheng, *Pharm. Res.,* 1993, **10**, 918-923; (d) K. Dzierzbicka, P. Trzonkowski, P. Sewerynek and A. Myśliwski, *J. Med. Chem.,* 2003, **46**, 978-986; (e) K. Dzierzbicka, W. Januchta and A. Skladanowski, *Curr. Med. Chem.,* 2012, **19**, 4475-4487; (f) E. H. El-Tamany, S. Z. Sowellim, A. A. Hamed and A. S. Radwan, *Res. Chem. Intermed.,* 2015, **41**, 2675-2685.

2 K. Siva Kumar, P. Mahesh Kumar, K. Anil Kumar, M. Sreenivasulu, A. A. Jafar, D. Rambabu, G. Rama Krishna, C. Malla Reddy, R. Kapavarapu, K. Shivakumar, K. Krishna Priya, K. V. L. Parsa and M. Pal, *Chem. Commun.,* 2011, **47**, 5010-5012.

3 N. T. Patil, P. G. V. V. Lakshmi, B. Sridhar, S. Patra, M. Pal Bhadra and C. R. Patra, *Eur. J. Org. Chem.,* 2012, 1790-1799.

4 W. Hölzl and B. Rotzinger, Isoindolo[2,1-*a*]quinazoline derivatives for stabilization of organic materials, Patent WO2013/139799 A1, 2013.

5 (a) L. Lu, K. Yang, M.-M. Zhang and X.-S. Wang, *J. Heterocycl. Chem.,* 2014, **51**, 630-634; (b) R.-Z. Jin, W.-T. Zhang, Y.-J. Zhou and X.-S. Wang, *Tetrahedron Lett.,* 2016, **57**, 2515-2519; (c) K. V. Sashidhara, L. R. Singh, G. R. Palnati, S. R. Avula and R. Kant, *Synlett,* 2016, **27**, 2384-2390; (d) R. V. Devi, A. M. Garande and P. M. Bhate, *Synlett,* 2016, **27**, 2807-2810.

6 (a) M. Mahdavi, R. Najafi, M. Saeedi, E. Alipour, A. Shafiee and A. Foroumadi, *Helv. Chim. Acta,* 2013, **96**, 419-423; (b) R. A. Bunce and B. Nammalwar, *J. Heterocycl. Chem.,* 2011, **48**, 991-997.

7 (a) G. Rajeshwar Reddy, T. Ram Reddy, R. Gangadhara Chary, S. C. Joseph, S. Mukherjee and M. Pal, *Tetrahedron Lett.,* 2013, **54**, 6744-6746; (b) K. V. Sashidhara, G. R. Palnati, R. P. Dodda, S. R. Avula and P. Swami, *Synlett.,* 2013, **24**, 105-113; (c) F. Esmaeili-Marandi, M. Saeedi, I. Yavari, M. Mahdavi and A. Shafiee, *Helv. Chim. Acta,* 2016, **99**, 37-40.

8 For selected examples, see: (a) A. Brennführer, H. Neumann and M. Beller, *Angew. Chem., Int. Ed.,* 2009, **48**, 4114-4133; (b) X.-F. Wu, H. Neumann and M. Beller, *Chem. Soc. Rev.,* 2011, **40**, 4986-5009; (c) X.-F. Wu, H. Neumann and M. Beller, *Chem. Rev.,* 2013, **113**, 1-35 and references cited therein; (d) L. He, H. Li, H. Neumann, M. Beller and X.-F. Wu, *Angew. Chem., Int. Ed.,* 2014, **53**, 1420-1424; (e) Y. Xu, J. Zhao, H. Chen, W. Wu and H. Jiang, *Chem. Commun.,* 2014, **50**, 2488-2490; (f) H. Li, W. Li, A. Spannenberg, W. Baumann, H. Neumann, M. Beller and X.-F. Wu, *Chem. Eur. J.,* 2014, **20**, 8541-8544; (g) S. Perrone, M. Capua, A. Salomone and L. Troisi, *J. Org. Chem.,* 2015, **80**, 8189-8197; (h) Y. He, X. Zhang and X. Fan, *Chem. Commun.,* 2015, **51**, 16263-16266; (i) C. Shen, N. Y. T. Man, S. Stewart and X.-F. Wu, *Org. Biomol. Chem.,* 2015, **13**, 4422-4425; (j) G. M. Torres, J. S. Quesnel, D. Bijou and B. A. Arndtsen, *J. Am. Chem. Soc.,* 2016, **138**, 7315-7324; (k) C. Shen, A. Spannenberg and X.-F. Wu, *Angew. Chem., Int. Ed.,* 2016, **55**, 5067-5070; (l) X.-F. Wu, *Chem. Eur. J.*, 2015, **21**, 12252-12265; (m) J.-B. Peng, X. Qi and X.-F. Wu, *ChemSusChem*, 2016, **9**, 2279-2283; (n) X.-F. Wu, *RSC Adv.*, 2016, **6**, 83831-83837; (o) J.-B. Peng, X. Qi and X.-F. Wu, *Synlett*, 2017, **28**, 175-194.

9 (a) J. Chen, K. Natte, H. Neumann and X.-F. Wu, *RSC Adv.,* 2014, **4**, 56502-56505; (b) L. Akerbladh and L. R. Odell, *J. Org. Chem.,* 2016, **81**, 2966-2973; (c) X.-F. Wu, L. He, H. Neumann and M. Beller, *Chem. Eur. J.,* 2013, **19**, 12635-12638; (d) F. Zeng and H. Alper, *Org. Lett.,* 2010, **12**, 3642-3644; (e) F. Zeng and H. Alper, *Org. Lett.,* 2010, **12**, 1188-1191; (f) J. Chen, K. Natte, A. Spannenberg, H. Neumann, P. Langer, M. Beller and X.-F. Wu, *Angew. Chem., Int. Ed.,* 2014, **53**, 7579-7583; (g) C. Larksarp and H. Alper, *J. Org. Chem.,* 2000, **65**, 2773-2777; (h) J. E. R. Sadig, R. Foster, F. Wakenhut and M. C. Willis, *J. Org. Chem.,* 2012, **77**, 9473-9486; (i) H. Li, L. He, H. Neumann, M. Beller and X.-F. Wu, *Green Chem.,* 2014, **16**, 1336-1343.

10 (a) S. Guo, J. Wang, X. Fan, X. Zhang and D. Guo, *J. Org. Chem.,* 2013, **78**, 3262-3270; (b) X. Fan, B. Li, S. Guo, Y. Wang and X. Zhang, *Chem. Asian J.,* 2014, **9**, 739-743; (c) S. Guo, J. Wang, Y. Li and X. Fan, *Tetrahedron,* 2014, **70**, 2383-2388; (d) S. Guo, Y. Li, L. Tao, W. Zhang and X. Fan, *RSC Adv.,* 2014, **4**, 59289-59296; (e) S. Guo, L. Tao, W. Zhang, X. Zhang and X. Fan, *J. Org. Chem.,* 2015, **80**, 10955-10964; (f) S. Guo, J. Zhai and X. Fan, *Org. Biomol. Chem.,* 2017, doi: 10.1039/c6ob02699k.

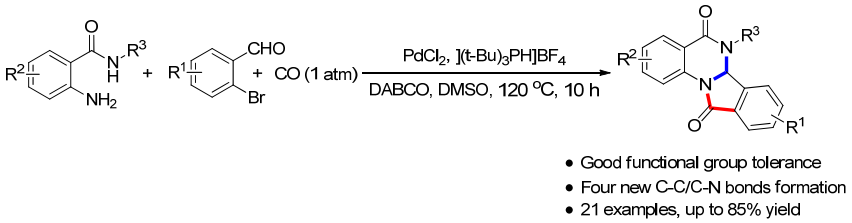
11 (a) M. Mori, K. Chiba and Y. Ban, *J. Org. Chem.,* 1978, **43**, 1684-1687; (b) S. Guo, L. Tao, F. Wang and X. Fan, *Chem. Asian J.,* 2016, **11**, 3090-3096; (c) J. Zhang, X. Zhang and X. Fan, *J. Org. Chem.,* 2016, **81**, 3206-3213.

View Article Online
DOI: 10.1039/C7OB00256D

12 S. K. Ghosh and R. Nagarajan, *RSC Adv.,* 2016, **6**, 27378-27387.
13 J. K. Laha, K. V. Patel, K. S. S. Tummalapalli and N. Dayal, *Chem. Commun.,* 2016, **52**, 10245-10248.

View Article Online
DOI: 10.1039/C7OB00256D

Graphical Abstract



An efficient route to 6,6a-dihydroisoindolo[2,1-*a*]quinazoline-5,11-diones via Pd-catalyzed carbonylative cyclization of 2-aminobenzamides with 2-bromobenzaldehydes under atmospheric CO pressure is reported.