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Graphical Abstract

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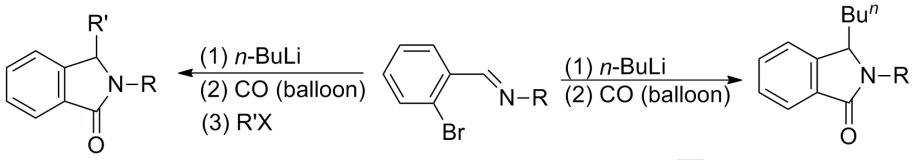
Hai-Jun Li, Yu-Qing Zhang and Liang-Fu Tang
Department of Chemistry, State Key Laboratory of Elemento-Organic Chemistry, Nankai University, Tianjin 300071, People's Republic of China



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ABSTRACT

A simple and efficient one-pot synthesis of 2,3-disubstituted isoindolinones via the reaction of *o*-lithiated aromatic imines with carbon monoxide under one atmospheric pressure has been developed. Preliminary *in vitro* tests for fungicidal activity of these isoindolinone derivatives have been carried out, indicating that most of them exhibit good fungicidal activities.

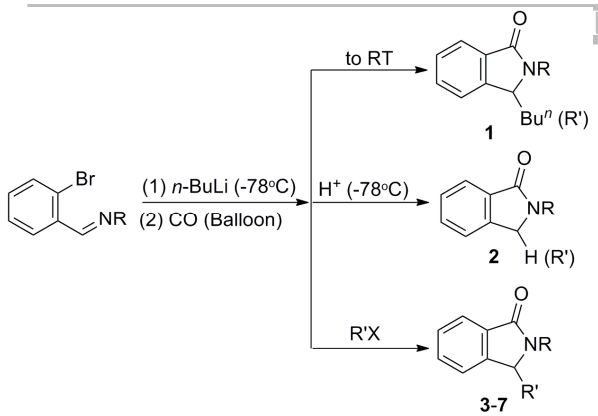
1. Introduction

Isoindolinones have received extensive attention in recent years because the isoindolinone skeleton presents in numerous natural products and synthetic pharmaceuticals with a wide range of biological activities.[1] In view of crucial applications of isoindolinone derivatives, their synthetic methodologies have been widely investigated.[2] A variety of methods for the synthesis of isoindolinones have been developed in literatures, which generally fall into two categories[3] or are divided into eight retrosynthetic cuts.[4] In the first strategy, phthalimides[5] or phthalimidines[6] are directly used as starting materials to prepared isoindolinones especially 3-substituted derivatives. The second approach is the construction of the lactam ring through various cyclization reactions of functionalized aromatic compounds. Despite many traditional annulative methods, such as the amination reaction of *o*-halomethyl or *o*-acylbenzoate derivatives,[1] have been successfully applied to generate isoindolinones and enriched the structural diversity as well as the structure-activity relationship of isoindolinones, the development of convenient and practical synthetic methods for these compounds continues to remain an active area of research. Some new approaches, such as the transition metal-catalyzed carbonylation[7] and C–H functionalization,[8] Diels–Alder[9] and inverse-electron demand Diels–Alder[10], aza-Wittig[11] and radical cyclization[12] reactions as well as organocatalytic reactions[13] have been developed for the construction of the basic isoindolinone skeleton. The *o*-lithiation/cyclization procedures have also been reported to produce substituted isoindolinones,[4,14] in most of which *o*-lithiated benzamides were used as the nucleophiles. In spite of all these achievements, the starting materials were not readily available in many of above-mentioned methods, which were usually obtained by multistep reactions. Consequently, the development of new synthetic routes for isoindolinone derivatives from simple and readily available starting materials is highly desirable. Herein, we report a simple and efficient one pot synthesis of isoindolinones via the reaction of *o*-lithiated aromatic imines with carbon monoxide under one atmospheric pressure.

2. Results and discussion

2.1. Reaction of o-lithiated aromatic imines with carbon monoxide

* Corresponding author. Tel.: +86-022-2350-2458; fax: +86-022-2350-2458; e-mail: lftang@nankai.edu.cn



Scheme 1. Synthesis and reaction of *o*-lithiated aromatic imines with carbon monoxide.

The metal-mediated synthesis of isoindolinones from arylimines has been reported.[15] Additionally, the reaction of organolithium reagent with carbon monoxide is an important and direct synthetic method for carbonyl compounds.[16] The construction of the isoindolinone skeleton through the imine addition–cyclization sequence has been mentioned,[14d] but the synthetic methodology for isoindolinones through *o*-lithiated aromatic imines was not reported.[14e,14f] We found that *in situ* treatment of *o*-lithiated aromatic imines prepared by the lithium-halide exchange reactions with CO under one atmospheric pressure at –78 °C and slow warming to room temperature (Scheme 1) rendered 3-*n*-butyl substituted isoindolinones (**1**) in moderate yields (Table 1, Entries 1–5). It should be pointed out that significant amount of **2e** was isolated in the synthetic process of **1e** (Entry 5). If aqueous acid was added to the reaction mixture before elevating the temperature, compounds **2** were obtained (Entries 6–10). In addition, when active alkyl halides, such as CH_3I, $ArCH_2Br$ and $BrCH_2CO_2C_2H_5$, were used as the electrophiles, compounds **3**–**6** were obtained in moderate to good yields (Entries 11–26). The steric hindrance of substituents of imines has little effect on the reaction. The good yields were obtained even for the bulky *tert*-butyl and 2,6-dimethylphenyl groups. The low solubility and slow dissociation rate of paraformaldehyde are possibly responsible for the low yield of **7** (Entry 27). Compounds **1b** (41%) and **2b** (14%) were also isolated in this reaction.

Compounds **1**–**7** have been characterized by ^1H and ^{13}C NMR spectra, while the new compounds have been also characterized by IR and HRMS. Additionally, the structures of **1b** and **4c** have been confirmed by X-ray single-crystal diffraction, which are shown in Supporting information.

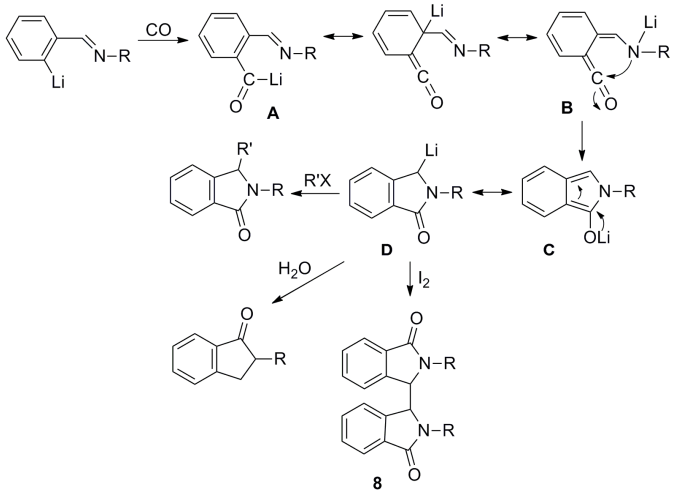
*2.2. Possible formation pathway of **1**–**7***

The formation of **1** is very interesting since no extra electrophiles were introduced and all organic components emerged in products. The plausible pathway for the formation of isoindolinone derivatives is depicted in Scheme 2. Initially, reaction of aryl lithium with CO gave the corresponding acyl lithium (**A**),[17] which resonated to nitrogen anion (**B**) through conjugated double bonds. A polarity reversal took place in this process, namely the nucleophilic carbon (acyl anion) changing to the electrophilic carbon (ketene). Subsequently, the nitrogen anion attacked the ketene carbonyl to form the key enolate (**C**), which has a carbanion resonance form (**D**). The alkylation reaction of the enolate intermediate with *n*-butyl bromide formed in the lithium-halide exchange reaction yielded compound **1**. The nucleophility of the enolate intermediate to *n*-butyl bromide is

Table 1
Synthesis of substituted isoindolinones

Entry	1–7	R	R′	Isolated yield (%)
1	**1a**	Et	Bu^n	66
2	**1b**	Pr^i	Bu^n	57
3	**1c**	Bu^t	Bu^n	78
4	**1d**	*cyclo*-C_6H_{11}	Bu^n	59
5	**1e**	2,6-$Me_2C_6H_3$	Bu^n	31
6	**2a**	Et	H	88
7	**2b**	Pr^i	H	57
8	**2c**	Bu^t	H	63
9	**2d**	*cyclo*-C_6H_{11}	H	70
10	**2e**	2,6-$Me_2C_6H_3$	H	57
11	**3a**	Et	Me	66
12	**3b**	Pr^i	Me	74
13	**3c**	Bu^t	Me	85
14	**3d**	*cyclo*-C_6H_{11}	Me	63
15	**3e**	2,6-$Me_2C_6H_3$	Me	70
16	**4a**	Et	$C_6H_5CH_2$	64
17	**4b**	Pr^i	$C_6H_5CH_2$	55
18	**4c**	Bu^t	$C_6H_5CH_2$	64
19	**4d**	*cyclo*-C_6H_{11}	$C_6H_5CH_2$	64
20	**4e**	2,6-$Me_2C_6H_3$	$C_6H_5CH_2$	74
21	**5a**	Et	4-$MeC_6H_4CH_2$	79
22	**5b**	Pr^i	4-$MeC_6H_4CH_2$	70
23	**5c**	Bu^t	4-$MeC_6H_4CH_2$	69
24	**5d**	*cyclo*-C_6H_{11}	4-$MeC_6H_4CH_2$	70
25	**5e**	2,6-$Me_2C_6H_3$	4-$MeC_6H_4CH_2$	59
26	**6**	Pr^i	$C_2H_5O_2CCH_2$	56
27	**7**	Pr^i	$HOCH_2$	27

weak, as supported by the isolation of **2e** in the synthetic process of **1e**. If more reactive alkyl halides compared to *n*-butyl bromide were used as alkylation reagents, the *n*-butyl group would be replaced, which was proved by the successful synthesis of compounds **3**–**6**. Compounds **2** were easily obtained by the protonation of the enolate intermediate. Also as corroboration of the mechanistic deduction, the treatment of the enolate intermediate with I_2 also led to the oxidative coupling product **8** in good yield.



Scheme 2. Possible pathway for the formation of isoindolinones.

2.3. Fungicidal activity

Preliminary *in vitro* tests for fungicidal activity of all compounds have been carried out by the fungi growth inhibition method.[18] The data are summarized in Table 2, which indicate that most of compounds exhibit good fungicidal activities. All of 2-cyclohexyl isoindolinone derivatives (**1d–5d**) have high activities to *Cercospora rachidicola*. The steric factor of 2-substituents of isoindolinones has little effect on the fungicidal

Table 2

Antifungal activity of **1**–**27** (Percent inhibition)[a]

Comp.	*Cercospora beticola*	*Cercospora rachidicola*	*Alternaria solani*	*Botrytis cinerea*	*Gibberella zeae*	*Macrophoma kuwatsukai*	*Sclerotinia sclerotiorum*	*Valsa mali*	*Thanatephorus cucumeris (Frank) Domk*
1a	0.0	0.0	11.1	6.5	17.7	21.0	17.9	23.4	0.0
1b	21.7	30.8	0.0	0.0	67.7	17.7	0.0	34.0	45.8
1c	4.4	15.4	33.3	9.7	17.7	11.3	16.1	23.4	37.5
1d	26.1	69.2	22.2	25.8	55.9	32.3	76.8	55.3	41.7
1e	17.4	7.7	11.1	0.0	11.8	24.2	21.4	12.8	29.2
2a	4.4	7.7	16.7	6.5	35.3	25.8	10.7	70.2	16.7
2b	17.4	23.1	11.1	16.1	17.7	25.8	32.1	19.2	20.8
2c	8.7	23.1	16.7	16.1	23.5	33.9	0.0	34.0	0.0
2d	17.4	61.5	27.8	29.0	5.9	25.8	19.6	23.4	25.0
2e	4.4	38.5	61.1	6.5	14.7	82.3	16.1	21.3	12.5
3a	4.4	15.4	16.7	9.7	11.8	14.5	3.6	2.1	12.5
3b	13.1	30.8	11.1	16.1	8.8	25.8	26.8	46.8	20.8
3c	13.0	15.4	16.7	48.4	2.9	25.8	44.6	40.4	37.5
3d	13.0	46.2	38.9	6.5	8.8	33.9	8.9	19.2	54.2
3e	30.4	53.9	55.6	100.0	11.8	27.4	23.2	27.7	12.5
4a	45.8	65.4	38.2	38.2	76.5	24.2	29.0	80.9	64.7
4b	47.9	38.5	44.1	79.4	72.1	24.2	68.4	68.1	23.5
4c	41.7	53.9	44.1	67.7	85.3	24.2	65.8	63.8	23.5
4d	45.8	53.9	64.7	61.8	73.5	28.8	52.6	53.2	29.4
4e	35.4	46.2	64.7	76.5	73.5	30.3	63.2	58.5	23.5
5a	45.8	46.2	44.1	58.8	73.5	16.7	57.9	83.0	29.4
5b	54.2	38.5	47.1	73.5	23.5	36.4	60.5	80.9	23.5
5c	33.3	38.5	52.9	52.9	50.0	36.4	56.6	66.0	23.5
5d	33.3	53.9	55.9	70.6	64.7	57.6	59.2	61.7	5.9
5e	33.3	61.5	47.1	73.5	91.2	34.9	63.2	66.0	17.7
6	25.0	15.4	17.7	47.1	55.9	15.2	26.3	34.0	5.9
7	33.3	15.4	17.7	11.8	29.4	24.2	39.5	25.5	0.0
Positive control[b]	80.8	55.6	46.9	71.4	75.0	91.2	100.0	88.1	84.1

[a] Concentration: 50 μg/mL in DMF.
[b] Positive control: azoxystrobin

activity. For example, compounds **2e–5e** display good activities to *Alternaria solani*. Moreover, the inhibition percentage of **3e** *in vitro* for *Botrytis cinerea* and **5e** for *Gibberella zeae* is approximate to 100% and 91.2%, respectively, and significantly higher than that of other compounds. In addition, it seems that the 3-benzyl isoindolinones are more active than other derivatives, supported by the higher inhibition percentage of **4** and **5** against the tested fungi than that of **1–3**, demonstrating that the aryl groups may strongly affect the fungicidal activity possibly through the π-π stacking interactions with the enzymes, similar to those findings reported in the antibacterial activity of isoindolinones.[1e]

In summary, a simple and efficient one pot synthesis of isoindolinones from the readily available starting materials has been developed. Preliminary *in vitro* tests for fungicidal activity of these isoindolinone derivatives indicate that most of them exhibit good fungicidal activities.

3. Experimental

3.1. General

All reactions were carried out under an argon atmosphere. Solvents were dried by standard methods and freshly distilled prior to use. NMR (^{1}H and ^{13}C) were recorded on a Bruker 400 spectrometer using $CDCl_3$ as the solvent, and the chemical shifts were reported in ppm with respect to the reference (internal $SiMe_4$ for ^{1}H and ^{13}C NMR spectra). IR spectroscopic data were obtained from a Tensor 27 spectrometer as KBr pellets. HR mass spectra were obtained on a Varian QFT-ESI spectrometer. Melting points were measured with an X-4 digital micro melting-point apparatus and were uncorrected. The imines were prepared by the condensation reaction of *o*-bromobenzaldehyde with the corresponding amine according to the published methods.[19]

*3.2. Typical procedure for the synthesis of **1***

A hexane solution of *n*-BuLi (1.6 M, 1.25 mL, 2 mmol) was added to the solution of imine (2 mmol) in THF (35 mL) at −78 °C under an argon atmosphere. After the resulting mixture was stirred for 30 min, CO was bubbled into the solution. The CO atmosphere was kept with a balloon at the exit. The reaction mixture was continuously stirred at low temperature for 1 h, allowed to reach room temperature slowly and stirred overnight. The solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica with ethyl acetate/petroleum ether (V/V = 1:5) as the eluent to give the product.

*3.2.1. 2-Ethyl-3-n-butylisoindolin-1-one (**1a**).* Yellow oil; ^{1}H NMR δ 0.80 (t, J = 7.3 Hz, 3H), 0.86−1.08 (m, 2H), 1.21−1.27 (m, 5H), 1.88−2.05 (m, 2H), 3.19 (qd, J = 7.1 Hz, J = 14.2 Hz, 1H), 4.04 (qd, J = 7.4 Hz, J = 14.6 Hz, 1H), 4.63 (dd, J = 3.5 Hz, J = 5.2 Hz,1H), 7.41−7.45 (m, 2H), 7.52 (dt, J = 1.1 Hz, J = 7.4 Hz, 1H), 7.83 (d, J = 7.5 Hz, 1H); ^{13}C NMR δ 13.7, 13.9, 22.6, 24.4, 30.2, 34.6, 58.7, 122.0, 123.4, 127.9, 131.2, 132.9, 145.2, 168.3; IR ($\nu_{C=O}$) 1682 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{20}NO$ $[M+H]^+$: 218.1545, found: 218.1541.

*3.2.2. 2-Isopropyl-3-n-butylisoindolin-1-one (**1b**).* Yellow solid; mp: 47−49 °C; ^{1}H NMR δ 0.82 (t, J = 7.3 Hz, 3H), 1.02−1.31 (m, 4H), 1.42 (d, J = 6.9 Hz, 3H), 1.47 (d, J = 7.0 Hz, 3H), 1.92−2.10 (m, 2H), 4.32 (sept., J = 6.9 Hz, 1H), 4.69 (dd, J = 3.3 Hz, J = 5.2 Hz, 1H), 7.38 (dd, J = 0.7 Hz, J = 7.5 Hz, 1H), 7.43 (t, J = 7.3 Hz, 1H), 7.52 (dt, J = 1.2 Hz, J = 7.4 Hz, 1H), 7.81 (d, J = 7.5 Hz, 1H); ^{13}C NMR δ 13.9, 20.3, 21.2, 22.7, 24.2, 32.0, 44.9, 59.5,

121.8, 123.3, 127.9, 131.1, 133.2, 145.4, 168.7; IR ($\nu_{C=O}$) 1678 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{22}NO$ $[M+H]^+$: 232.1701, found: 232.1701.

*3.2.3. 2-tert-Butyl-3-n-butylisoindolin-1-one (**1c**).* Yellow oil; ^1H NMR δ 0.79 (t, J = 7.2 Hz, 3H), 1.09−1.26 (m, 4H), 1.60 (s, 9H), 1.94−2.06 (m, 2H), 4.80 (dd, J = 2.7 Hz, J = 5.6 Hz, 1H), 7.33 (d, J = 8.0 Hz, 1H), 7.40 (t, J = 7.2 Hz, 1H), 7.48 (dt, J = 1.2 Hz, J = 7.4 Hz, 1H), 7.76 (d, J = 7.5 Hz, 1H); ^{13}C NMR δ 13.9, 22.6, 24.3, 28.6, 34.9, 55.1, 60.2, 121.4, 123.0, 127.7, 131.0, 133.8, 145.9, 169.4; IR ($\nu_{C=O}$) 1683 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{24}NO$ $[M+H]^+$: 246.1858, found: 246.1857.

*3.2.4. 2-Cyclohexyl-3-n-butylisoindolin-1-one (**1d**).* Yellow oil; ^1H NMR δ 0.80 (t, J = 7.3 Hz, 3H), 1.08−1.28 (m, 4H), 1.35−1.47 (m, 2H), 1.71−2.17 (m, 10H), 3.91 (tt, J = 3.7 Hz, J = 12.1 Hz, 1H), 4.68−4.70 (m, 1H), 7.37 (d, J = 7.5 Hz, 1H), 7.42 (t, J = 7.4 Hz, 1H), 7.51 (dt, J = 1.0 Hz, J = 7.4 Hz, 1H), 7.81 (d, J = 7.5 Hz, 1H); ^{13}C NMR δ 13.9, 22.7, 24.1, 25.6, 26.1, 26.3, 30.7, 31.4, 32.1, 53.3, 59.6, 121.7, 123.3, 127.8, 131.1, 133.2, 145.5, 168.7; IR ($\nu_{C=O}$) 1684 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{25}NNaO$ $[M+Na]^+$: 294.1834, found: 294.1830.

*3.2.5. 2-(2,6-Dimethylphenyl)-3-n-butylisoindolin-1-one (**1e**).* Yellow oil; ^1H NMR δ 0.84 (t, J = 7.2 Hz, 3H), 1.22−1.34 (m, 3H), 1.41−1.53 (m, 1H), 1.65−1.74 (m, 1H), 1.78−1.86 (m, 1H), 2.17 (s, 3H), 2.31 (s, 3H), 4.85 (dd, J = 5.5 Hz, J = 7.3 Hz, 1H), 7.14−7.25 (m, 3H), 7.52−7.64 (m, 3H), 7.99 (d, J = 7.5 Hz, 1H); ^{13}C NMR δ 13.9, 18.4, 18.9, 22.8, 28.2, 32.9, 62.4, 122.9, 124.3, 128.2, (2C), 128.7, 128.9, 131.6, 131.8, 134.9, 136.1, 138.1, 146.6, 167.4; IR ($\nu_{C=O}$) 1694 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{23}NNaO$ $[M+Na]^+$: 316.1677, found: 316.1667.

*3.3. Typical procedure for the synthesis of **2***

A hexane solution of *n*-BuLi (1.6 M, 1.25 mL, 2 mmol) was added to the solution of imine (2 mmol) in THF (35 mL) at −78 °C under an argon atmosphere. After the resulting mixture was stirred for 30 min, CO was bubbled into the solution. The CO atmosphere was kept with a balloon at the exit. The reaction mixture was stirred at low temperature for 1 h, hydrochloric acid (1.0 M, 2 mL, 2 mmol) was slowly added dropwise. Then, the reaction mixture was allowed to reach room temperature slowly. The solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica with ethyl acetate/petroleum ether (*V*/*V* = 1:5) as the eluent to give the product.

*3.3.1. 2-Ethylisoindolin-1-one (**2a**).*[5b] Yellow oil; ^1H NMR δ 1.24 (t, J = 7.3 Hz, 3H), 3.64 (q, J = 7.3 Hz, 2H), 4.35 (s, 2H), 7.39–7.43 (m, 2H), 7.47–7.51 (m, 1H), 7.80 (d, J = 8.2 Hz, 1H); ^{13}C NMR δ 13.6, 37.0, 49.3, 122.7, 123.5, 127.9, 131.1, 133.0, 141.1, 168.2.

*3.3.2. 2-Isopropylisoindolin-1-one (**2b**).*[5b] White solid; mp: 82−84 °C; ^1H NMR δ 1.31 (d, J = 6.8 Hz, 6H), 4.36 (s, 2H), 4.70 (sept., J = 6.8 Hz, 1H), 7.42–7.51 (m, 2H), 7.50–7.59 (m, 1H), 7.86 (d, J = 8.2 Hz, 1H); ^{13}C NMR δ 20.9, 42.6, 45.0, 122.7, 123.6, 128.0, 131.0, 133.4, 141.2, 167.8; HRMS (ESI) calcd for $C_{11}H_{14}NO$ $[M+H]^+$: 176.1075, found: 176.1072.

*3.3.3. 2-tert-Butylisoindolin-1-one (**2c**).*[20] White solid; mp: 52−54 °C; ^1H NMR δ 1.59 (s, 9H), 4.48 (s, 2H), 7.44 (dd, J = 7.4 Hz, J = 12.7 Hz, 2H), 7.52 (dt, J = 3.7 Hz, J = 7.4 Hz, 1H), 7.81 (d, J = 7.5 Hz, 1H); ^{13}C NMR δ 28.1, 48.5, 54.4, 122.3, 123.2, 127.9, 130.9, 134.5, 140.7, 168.9; HRMS (ESI) calcd for $C_{12}H_{16}NO$ $[M+H]^+$: 190.1232, found: 190.1229.

*3.3.4. 2-Cyclohexylisoindolin-1-one (**2d**).*[21] White solid; mp: 97−99 °C; ^1H NMR δ 1.15–1.26 (m, 1H), 1.45–1.52 (m, 4H), 1.70–1.77 (m, 1H), 1.85–1.91 (m, 4H), 4.23–4.32 (m, 1H), 4.37 (s, 2H), 7.45–7.48 (m, 2H), 7.51–7.55 (m, 1H), 7.86–7.88 (m, 1H); ^{13}C NMR δ 25.5, 25.6, 31.5, 46.0, 50.5, 122.7, 123.6, 127.9, 131.0, 133.4, 141.3, 167.9.

*3.3.5. 2-(2,6-Dimethylphenyl)isoindolin-1-one (**2e**).*[22] White solid; mp: 113−115 °C; ^1H NMR δ 2.22 (s, 6H), 4.63 (s, 2H), 7.18–7.19 (m, 2H), 7.23–7.25 (m, 1H), 7.56 (t, J = 7.6 Hz, 2H), 7.64 (dt, J = 1.2 Hz, J = 7.5 Hz, 1H), 8.00 (d, J = 7.4 Hz, 1H); ^{13}C NMR δ 18.0, 51.2, 122.9, 124.4, 128.3, 128.5, 128.6, 131.7, 132.4, 135.5, 136.8, 141.7, 167.8.

*3.4. Typical procedure for the synthesis of **3–6***

A hexane solution of *n*-BuLi (1.6 M, 1.25 mL, 2 mmol) was added to the solution of imine (2 mmol) in THF (35 mL) at −78 °C under an argon atmosphere. After the resulting mixture was stirred for 30 min, CO was bubbled into the solution. The CO atmosphere was kept with a balloon at the exit. The reaction mixture was stirred at low temperature for 1 h, R′X (2 mmol) was added dropwise. The resulting mixture was continuously stirred at low temperature for 1 h, allowed to reach room temperature slowly and stirred overnight. The solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica with ethyl acetate/petroleum ether (*V*/*V* = 1:5) as the eluent to give the product.

*3.4.1. 2-Ethyl-3-methylisoindolin-1-one (**3a**).*[23] Pale yellow oil; ^1H NMR δ 1.25 (t, J = 7.2 Hz, 3H), 1.48 (d, J = 6.7 Hz, 3H), 3.32 (dq, J = 7.1 Hz, J = 14.2 Hz, 1H), 3.98 (dq, J = 7.4 Hz, J = 14.6 Hz, 1H), 4.58 (q, J = 6.7 Hz, 1H), 7.44 (dd, J = 7.3 Hz, J = 13.2 Hz, 2H), 7.54 (td, J = 1.0 Hz, J = 7.4 Hz, 1H), 7.83 (d, J = 7.5 Hz, 1H); ^{13}C NMR δ 13.8, 18.2, 34.6, 55.2, 121.9, 123.5, 128.1, 131.3, 132.1, 146.9, 167.8.

*3.4.2. 2-Isopropyl-3-methylisoindolin-1-one (**3b**).*[23b] Pale yellow oil; ^1H NMR δ 1.41 (d, J = 6.9 Hz, 3H), 1.44 (d, J = 7.0 Hz, 3H), 1.54 (d, J = 6.7 Hz, 3H), 4.35–4.44 (m, 1H), 4.63 (q, J = 6.6 Hz, 1H), 7.38 (d, J = 7.5 Hz, 1H), 7.43 (t, J = 7.4 Hz, 1H), 7.52 (t, J = 7.4 Hz, 1H), 7.81 (d, J = 7.5 Hz, 1H); ^{13}C NMR δ 20.4, 20.6, 21.8, 44.4, 55.4, 121.7, 123.3, 128.0, 131.2, 132.3, 147.1, 168.0.

*3.4.3. 2-tert-Butyl-3-methylisoindolin-1-one (**3c**).*[24] Pale yellow oil; ^1H NMR δ 1.56 (d, J = 6.4 Hz, 3H), 1.61 (s, 9H), 4.76 (q, J = 6.4 Hz, 1H), 7.33 (d, J = 7.5 Hz, 1H), 7.40 (t, J = 7.4 Hz, 1H), 7.49 (td, J = 1.1 Hz, J = 7.5 Hz, 1H), 7.76 (d, J = 7.5 Hz, 1H); ^{13}C NMR δ 23.9, 28.8, 55.0, 56.4, 121.4, 123.2, 127.8, 131.1, 132.9, 147.5, 168.7.

*3.4.4. 2-Cyclohexyl-3-methylisoindolin-1-one (**3d**).* Pale yellow oil; ^1H NMR δ 1.19–1.30 (m, 1H), 1.39–1.48 (m, 1H), 1.55 (d, J = 6.7 Hz, 3H), 1.72–1.96 (m, 8H), 3.92–4.01 (m, 1H); 4.64 (q, J = 6.5 Hz, 1H), 7.39 (d, J = 7.5 Hz, 1H), 7.44 (t, J = 7.3 Hz, 1H), 7.53 (t, J = 7.2 Hz, 1H), 7.83 (d, J = 7.4 Hz, 1H); ^{13}C NMR δ 20.8, 25.6, 26.1, 26.2, 30.9, 31.9, 52.9, 55.6, 121.7, 123.4, 127.9, 131.2, 132.3, 147.2, 168.0; IR ($\nu_{C=O}$) 1683 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{19}NNaO$ $[M+Na]^+$: 252.1364, found: 252.1358.

*3.4.5. 2-(2,6-Dimethylphenyl)-3-methylisoindolin-1-one (**3e**).* Red solid; mp: 141–143 °C; ^1H NMR δ 1.43 (d, J = 6.8 Hz, 3H), 2.19 (s, 3H), 2.28 (m, 3H), 4.94 (q, J = 6.8 Hz, 1H), 7.16–7.26 (m, 3H), 7.54 (dd, J = 7.7 Hz, J = 16.1 Hz, 2H), 7.65 (dt, J = 0.9 Hz, J = 7.5 Hz, 1H), 7.99 (d, J = 7.5 Hz, 1H); ^{13}C NMR δ 18.1, 18.3, 18.8, 58.1, 122.1, 124.3, 128.3, 128.4, 128.7, 128.8, 131.6, 131.8, 134.3, 136.4, 138.1, 147.4, 167.3; IR ($\nu_{C=O}$) 1695 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{17}NNaO$ $[M+Na]^+$: 274.1208, found: 274.1204.

*3.4.6. 3-Benzyl-2-ethylisoindolin-1-one (**4a**).* Yellow oil; ^1H NMR δ 1.29 (t, J = 7.2 Hz, 3H), 2.83 (dd, J = 8.2 Hz, J = 13.8 Hz,

1H), 3.32 (qd, *J* = 7.1 Hz, *J* = 14.1 Hz, 1H), 3.43 (dd, *J* = 4.7 Hz, *J* = 13.8 Hz, 1H), 4.14 (qd, *J* = 7.3 Hz, *J* = 14.6 Hz, 1H), 4.83 (dd, *J* = 4.7 Hz, *J* = 8.1 Hz, 1H), 6.91 (dd, *J* = 2.5 Hz, *J* = 5.6 Hz, 1H), 7.09–7.13 (m, 2H), 7.26–7.31 (m, 3H), 7.38–7.44 (m, 2H), 7.78–7.81 (m, 1H); ^{13}C NMR δ 13.7, 35.0, 38.4, 59.7, 122.9, 123.5, 127.0, 128.1, 128.5, 129.5, 130.8, 132.5, 136.0, 144.8, 168.1; IR ($\nu_{C=O}$) 1685 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{17}NNaO$ [M+Na]$^+$: 274.1208, found: 274.1200.

*3.4.7. 3-Benzyl-2-isopropylisoindolin-1-one (**4b**)*. Pale yellow solid; mp: 84–86 °C; ^{1}H NMR δ 1.51 (d, *J* = 6.8 Hz, 3H), 1.60 (d, *J* = 7.0 Hz, 3H), 2.62 (dd, *J* = 9.8 Hz, *J* = 13.5 Hz, 1H), 3.65 (dd, *J* = 4.4 Hz, *J* = 13.5 Hz, 1H), 4.23–4.35 (m, 1H), 4.81 (dd, *J* = 4.4 Hz, *J* = 9.8 Hz, 1H), 6.56 (d, *J* = 7.6 Hz, 1H), 7.18 (d, *J* = 6.5 Hz, 2H), 7.28–7.42 (m, 5H), 7.80 (d, *J* = 7.5 Hz, 1H); ^{13}C NMR δ 20.5, 21.5, 40.4, 45.6, 61.0, 123.1, 123.2, 127.1, 128.1, 128.6, 129.6, 130.6, 132.9, 136.7, 145.0, 168.4; IR ($\nu_{C=O}$) 1685 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{20}NO$ [M+H]$^+$: 266.1545, found: 266.1543.

*3.4.8. 3-Benzyl-2-tert-butylisoindolin-1-one (**4c**)*. White solid; mp: 90–92 °C; ^{1}H NMR δ 1.74 (s, 9H), 2.44–2.50 (m, 1H), 3.82 (d, *J* = 13.4 Hz, 1H), 4.95 (d, *J* = 9.8 Hz, 1H), 6.48 (d, *J* = 7.5 Hz, 1H), 7.08 (d, *J* = 6.1 Hz, 2H), 7.25–7.39 (m, 5H), 7.75 (d, *J* = 7.5 Hz, 1H); ^{13}C NMR δ 28.8, 42.9, 55.3, 61.4, 122.6, 123.1, 127.1, 127.9, 128.5, 129.6, 130.2, 133.3, 136.7, 145.2, 169.0; IR ($\nu_{C=O}$) 1683 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{21}NNaO$ [M+Na]$^+$: 302.1521, found: 302.1518.

*3.4.9. 3-Benzyl-2-cyclohexylisoindolin-1-one (**4d**)*. Pale yellow solid; mp: 96–98 °C; ^{1}H NMR δ 1.26–1.45 (m, 3H), 1.72–2.01 (m, 6H), 2.17–2.25 (m, 1H), 2.63 (dd, *J* = 9.6 Hz, *J* = 13.5 Hz, 1H), 3.65 (dd, *J* = 4.5 Hz, *J* = 13.5 Hz, 1H), 3.79–3.88 (m, 1H), 4.82 (dd, *J* = 4.5 Hz, *J* = 9.6 Hz, 1H), 6.58 (d, J = 7.6 Hz, 1H), 7.19 (d, J = 6.5 Hz, 2H), 7.28–7.41 (m, 5H), 7.80 (d, *J* = 7.5 Hz, 1H); ^{13}C NMR δ 25.6, 26.2, 26.3, 30.8, 31.4, 40.6, 54.1, 61.1, 123.0, 123.3, 127.1, 128.0, 128.6, 129.6, 130.5, 132.9, 136.8, 145.1, 168.4; IR ($\nu_{C=O}$) 1683 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{23}NNaO$ [M+Na]$^+$: 328.1677, found: 328.1673.

*3.4.10. 3-Benzyl-2-(2,6-dimethylphenyl)isoindolin-1-one (**4e**)*. Pale yellow solid; mp: 104–106 °C; ^{1}H NMR δ 2.26 (s, 3H), 2.35 (s, 3H), 2.67 (dd, *J* = 11.0 Hz, *J* = 13.1 Hz, 1H), 3.26 (dd, *J* = 4.2 Hz, *J* = 13.1 Hz, 1H), 5.10 (dd, *J* = 4.2 Hz, *J* = 10.9 Hz, 1H), 6.68 (d, *J* = 7.6 Hz, 1H), 7.16 (d, *J* = 6.7 Hz, 2H), 7.20–7.36 (m, 6H), 7.41 (t, *J* = 7.5 Hz, 1H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.99 (d, *J* = 7.5 Hz, 1H); ^{13}C NMR δ 18.6, 19.0, 39.0, 63.4, 123.4, 124.2, 127.1, 128.4, 128.5, 128.7, 128.9, 129.0, 129.5, 131.3, 131.6, 134.2, 136.3, 136.9, 138.1, 145.7, 167.1; IR ($\nu_{C=O}$) 1699 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{21}NNaO$ [M+Na]$^+$: 350.1521, found: 350.1514.

*3.4.11. 2-Ethyl-3-(p-methylbenzyl)isoindolin-1-one (**5a**)*. Pale yellow oil; ^{1}H NMR δ 1.28 (t, *J* = 7.2 Hz, 3H), 2.33 (s, 3H), 2.78 (dd, *J* = 8.1 Hz, *J* = 13.8 Hz, 1H), 3.27–3.40 (m, 2H), 4.12 (qd, *J* = 7.4 Hz, *J* = 14.6 Hz, 1H), 4.79 (dd, *J* = 4.6 Hz, *J* = 8.1 Hz, 1H), 6.94 (dd, *J* = 3.9 Hz, *J* = 4.7 Hz, 1H), 6.97 (d, *J* = 7.9 Hz, 2H), 7.08 (d, *J* = 7.8 Hz, 2H), 7.39–7.41 (m, 2H), 7.79 (dd, *J* = 2.9 Hz, *J* = 5.7 Hz, 1H); ^{13}C NMR δ 13.7, 21.1, 35.0, 38.0, 59.8, 123.0, 123.4, 128.1, 129.2, 129.3, 130.8, 132.5, 132.9, 136.5, 145.0, 168.0; IR ($\nu_{C=O}$) 1689 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{19}NNaO$ [M+Na]$^+$: 288.1364, found: 288.1357.

*3.4.12. 2-Isopropyl-3-(p-methylbenzyl)isoindolin-1-one (**5b**)*. Pale yellow oil; ^{1}H NMR δ 1.68 (d, *J* = 6.8 Hz, 3H), 1.76 (d, *J* = 7.0 Hz, 3H), 2.56 (s, 3H), 2.75 (dd, *J* = 9.8 Hz, *J* = 13.5 Hz, 1H), 3.77 (dd, *J* = 4.3 Hz, *J* = 13.5 Hz, 1H), 4.40–4.52 (m, 1H), 4.95 (dd, *J* = 4.3 Hz, *J* = 9.8 Hz, 1H), 6.78 (d, *J* = 7.6 Hz, 1H), 7.23 (d, *J* = 7.9 Hz, 2H), 7.32 (d, *J* = 7.8 Hz, 2H), 7.46–7.51 (m, 1H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.97 (d, *J* = 7.5 Hz, 1H); ^{13}C NMR δ 20.5, 21.1, 21.4, 40.0, 45.6, 61.1, 123.1, 123.2, 128.0, 129.3, 129.4, 130.5, 132.9, 133.5, 136.7, 145.2, 168.4; IR ($\nu_{C=O}$) 1683 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{21}NNaO$ [M+Na]$^+$: 302.1521, found: 302.1519.

*3.4.13. 2-tert-Butyl-3-(p-methylbenzyl)isoindolin-1-one (**5c**)*. Pale yellow solid; mp: 86–88 °C; ^{1}H NMR δ 1.71 (s, 9H), 2.34 (s, 3H), 2.41 (dd, *J* = 9.9 Hz, *J* = 13.5 Hz, 1H), 3.74 (dd, *J* = 3.0 Hz, *J* = 13.5 Hz, 1H), 4.90 (dd, *J* = 3.2 Hz, *J* = 9.8 Hz, 1H), 6.51 (d, *J* = 7.5 Hz, 1H), 6.94 (d, *J* = 7.9 Hz, 2H), 7.09 (d, *J* = 7.8 Hz, 2H), 7.25 (dt, *J* = 1.0 Hz, *J* = 7.5 Hz, 1H), 7.35 (t, *J* = 7.3 Hz, 1H), 7.73 (d, *J* = 7.5 Hz, 1H); ^{13}C NMR δ 21.1, 28.8, 42.4, 55.2, 61.5, 122.7, 123.1, 127.8, 129.2, 129.4, 130.2, 132.3, 133.5, 136.6, 145.4, 169.0; IR ($\nu_{C=O}$) 1668 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{23}NNaO$ [M+Na]$^+$: 316.1677, found: 316.1670.

*3.4.14. 2-Cyclohexyl-3-(p-methylbenzyl)isoindolin-1-one (**5d**)*. Pale yellow solid; mp: 94–96 °C; ^{1}H NMR δ 1.23–1.41 (m, 3H), 1.69–1.98 (m, 6H), 2.14–2.23 (m, 1H), 2.36 (s, 3H), 2.55 (dd, *J* = 9.7 Hz, *J* = 13.5 Hz, 1H), 3.59 (dd, *J* = 4.3 Hz, *J* = 13.6 Hz, 1H), 3.78–3.86 (m, 1H), 4.76 (dd, *J* = 4.4 Hz, *J* = 9.6 Hz, 1H), 6.58 (d, *J* = 7.6 Hz, 1H), 7.04 (d, *J* = 7.9 Hz, 2H), 7.12 (d, *J* = 7.8 Hz, 2H), 7.26–7.30 (m, 1H), 7.37 (t, *J* = 7.4 Hz, 1H), 7.77 (d, *J* = 7.5 Hz, 1H); ^{13}C NMR δ 21.1, 25.6, 26.2, 26.3, 30.8, 31.4, 40.1, 54.1, 61.1, 123.1, 123.2, 128.0, 129.3, 129.4, 130.5, 132.9, 133.6, 136.6, 145.2, 168.4; IR ($\nu_{C=O}$) 1669 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{25}NNaO$ [M+Na]$^+$: 342.1834, found: 342.1831.

*3.4.15. 2-(2,6-Dimethylphenyl)-3-(p-methylbenzyl)isoindolin-1-one (**5e**)*. Pale yellow solid; mp: 115–117 °C; ^{1}H NMR δ 2.23 (s, 3H), 2.32 (s, 3H), 2.36 (s, 3H), 2.58 (dd, *J* = 11.2 Hz, *J* = 13.0 Hz, 1H), 3.19 (dd, *J* = 4.0 Hz, *J* = 13.1 Hz, 1H), 5.04 (dd, *J* = 4.1 Hz, *J* = 11.0 Hz, 1H), 6.67 (d, *J* = 7.5 Hz, 1H), 7.01 (d, *J* = 7.9 Hz, 2H), 7.13 (d, *J* = 7.8 Hz, 2H), 7.17–7.26 (m, 3H), 7.38 (dt, *J* = 1.0 Hz, J = 7.5 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 1H), 7.96 (d, *J* = 7.5 Hz, 1H); ^{13}C NMR δ 18.5, 19.0, 21.1, 38.5, 63.4, 123.5, 124.2, 128.3, 128.4, 128.9, 129.0, 129.4, 129.4, 131.2, 131.7, 133.8, 134.2, 136.3, 136.6, 138.1, 145.8, 167.1; IR ($\nu_{C=O}$) 1701 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{23}NNaO$ [M+Na]$^+$: 364.1677, found: 364.1665.

*3.4.16. 2-Isopropyl-3-ethylcarboxylmethylisoindolin-1-one (**6**)*. Yellow oil; ^{1}H NMR δ 1.23 (t, *J* = 7.1 Hz, 3H), 1.43 (d, *J* = 6.9 Hz, 3H), 1.48 (d, *J* = 7.0 Hz, 3H), 2.60 (dd, *J* = 8.3 Hz, *J* = 16.0 Hz, 1H), 3.07 (dd, *J* = 4.1 Hz, *J* = 16.0 Hz, 1H), 4.11–4.28 (m, 3H), 4.98 (dd, *J* = 4.1 Hz, *J* = 8.2 Hz, 1H), 7.39–7.52 (m, 3H), 7.80 (d, *J* = 7.4 Hz, 1H); ^{13}C NMR δ 14.1, 20.4, 21.1, 39.0, 45.3, 56.4, 61.0, 122.2, 123.4, 128.4, 131.4, 132.7, 145.1, 168.3, 170.3; IR ($\nu_{C=O}$) 1689 and 1732 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{21}NO_3$ [M+H]$^+$: 262.1443, found: 262.1444.

*3.5. Synthesis of **7***

A hexane solution of *n*-BuLi (1.6 M, 1.25 mL, 2 mmol) was added to the solution of (*N*-isopropyl)-*o*-bromobenzylideneamine (0.45 g, 2 mmol) in THF (35 mL) at −78 °C under an argon atmosphere. After the resulting mixture was stirred for 30 min, CO was bubbled into the solution. The CO atmosphere was kept with a balloon at the exit. The reaction mixture was stirred at low temperature for 1 h, paraformaldehyde (0.12 g, 4 mmol) was added. The resulting mixture was continuously stirred at low temperature for 1 h, allowed to reach room temperature slowly and stirred overnight. The reaction mixture was quenched with 1 M HCl (2 mL, 2 mmol). The solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica with ethyl acetate/petroleum ether (*V*/*V* = 1:4) as the eluent to give the product as colorless oils. Yield 0.11 g (27%); ^{1}H NMR δ 1.37 (d, *J* = 6.8 Hz, 3H), 1.41 (d, *J* =

7.0 Hz, 3H), 3.72 (s, br, 1H), 3.84 (dd, 1H, J = 5.4 Hz, J = 11.2 Hz, 1H), 4.09 (dd, 1H, J = 4.0 Hz, J = 11.1 Hz, 1H), 4.34 (sept., J = 6.9 Hz, 1H), 4.63 (t, J = 4.5 Hz, 1H), 7.37 (t, J = 7.4 Hz, 1H), 7.46 (t, J = 7.4 Hz, 1H), 7.53 (d, J = 7.5 Hz, 1H), 7.70 (d, J = 7.5 Hz, 1H); ^{13}C NMR δ 20.2, 21.3, 45.2, 61.5, 63.6, 122.8, 123.2, 128.3, 131.3, 132.9, 143.8, 169.1; IR (ν_{OH}) 3369 and ($\nu_{C=O}$) 1666 cm^{-1}; HRMS (ESI) calcd for $C_{12}H_{17}NO_2$ $[M+H]^+$: 206.1181, found: 206.1180.

3.6. Synthesis of ***8***

A hexane solution of *n*-BuLi (1.6 M, 1.25 mL, 2 mmol) was added to the solution of (*N*-*tert*-butyl)-*o*-bromobenzylideneamine (0.48 g, 2 mmol) in THF (35 mL) at −78 °C under an argon atmosphere. The resulting mixture was stirred for 30 min, CO was bubbled into the solution. The CO atmosphere was kept with a balloon at the exit. After the reaction mixture was stirred at low temperature for 1 h, I_2 (0.51 g, 2 mmol) was added, and the low temperature bath was removed immediately. The reaction mixture was continuously stirred overnight at the ambient temperature. The solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica with ethyl acetate/petroleum ether (*V*/*V* = 1:4) as the eluent to give known 3,3′-bis(2-*tert*-butylisoindol-1-one) (**8**).[20a] Yield 56%. The NMR spectra showed the presence of two stereoisomers (*syn* and *anti* in *ca*. 1:1 ratio), led by the steric repulsion between bulky *tert*-butyl groups as well as *tert*-butyl groups and benzene ring.[20a] These two isomers were isolated by their different solubility in ethyl acetate/hexane (*V*/*V* = 1:5). The *syn* isomer was soluble while the *anti* isomer was insoluble. Data of *syn*-**8**: mp: 215–217 °C; ^{1}H NMR δ 1.83 (s, 18H), 5.37 (s, 2H), 7.11 (t, J = 7.5 Hz, 2H), 7.20 (t, J = 7.0 Hz, 2H), 7.36 (d, J = 7.6 Hz, 4H); ^{13}C NMR δ 29.4, 56.1, 62.6, 122.4, 122.7, 128.2, 130.9, 134.0, 140.0, 170.6; IR ($\nu_{C=O}$) 1680 cm^{-1}. Data of *anti*-**8**: mp: 225–227 °C; ^{1}H NMR δ 1.11 (s, 9H), 1.78 (s, 9H), 5.23 (s, 1H), 5.56 (s, 1H), 6.07 (s, 1H), 7.27–7.90 (m, 8H); ^{13}C NMR δ 28.6, 29.1, 55.1, 57.2, 63.6, 66.0, 122.0, 122.6, 123.4, 123.6, 128.8, 129.3, 131.8, 132.3, 133.2, 134.2, 141.2, 144.2, 169.8, 171.5; IR ($\nu_{C=O}$) 1682 cm^{-1}. HRMS (ESI) calcd for $C_{24}H_{29}N_2O_2$ $[M+H]^+$: 377.2229, found: 377.2227.

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Supplementary Material

CCDC 1407659 and 1407660 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. Crystal structure determinations of **1b** and **4c** and their molecular structures along with their data are provided.

Supporting Information

A simple and efficient synthesis of isoindolinone derivatives based on reaction of ortho-lithiated aromatic imines with CO

Hai-Jun Li, Yu-Qing Zhang and Liang-Fu Tang∗

Department of Chemistry, State Key Laboratory of Elemento-Organic Chemistry, Nankai University, Tianjin 300071, People's Republic of China

Crystal structure determinations

Crystals of **1b** and **4c** suitable for X-ray analyses were obtained by slow diffusion of hexane into their CH_2Cl_2 solutions at –18 ^oC. All intensity data were collected on a Rigaku Saturn CCD detector for **1b** as well as SuperNova Eos detector for **4c** using graphite monochromated Mo-Kα radiation (λ = 0.71073 Å). Semi-empirical absorption corrections were applied using the Crystalclear program.[1] The structures were solved by direct methods and difference Fourier map using SHELXS of the SHELXTL package and refined with SHELXL[2] by full-matrix least-squares on F^2. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were added geometrically and refined with riding model position parameters. A summary of the fundamental crystal data for **1b** and **4c** is listed in Table S1.

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∗ Corresponding author. Tel.: +86-022-2350-2458; fax: +86-022-2350-2458; e-mail: lftang@nankai.edu.cn

Table S1

Crystal data and refinement parameters for complexes **1b** and **4c**

Complex	**1b**	**4c**
Formula	$C_{15}H_{21}NO$	$C_{19}H_{21}NO$
Formula weight	231.33	279.37
Crystal size (mm)	0.20×0.18×0.12	0.18×0.12×0.08
Crystal system	Monoclinic	Monoclinic
Space group	$P2_1/n$	$P2_1/n$
a (Å)	9.5272(19)	9.2123(7)
b (Å)	9.804(2)	8.7120(7)
c (Å)	14.277(3)	19.1984(15)
α □(°)	90	90
β□ (°)	99.26(3)	94.503(7)
γ□(°)	90	90
T (K)	113(2)	133(1)
V (Å) ^{3}	1316.2(5)	1536.1(2)
Z	4	4
D_c (g.cm^{-3})	1.167	1.208
F(000)	504	600
μ□□(mm^{-1})	0.072	0.074
θ Range (°)	2.53–27.87	3.16–25.01
No. of measured reflections	13213	5190
No. of unique reflections (R_{int})	3136 (0.0469)	2693 (0.0279)
No. of observed reflections with ($I>2\sigma(I)$)	2201	2216
No. of parameters	158	194
GOF	1.019	1.082
Residuals *R*, *R*w	0.0442, 0.0996	0.0394, 0.0942

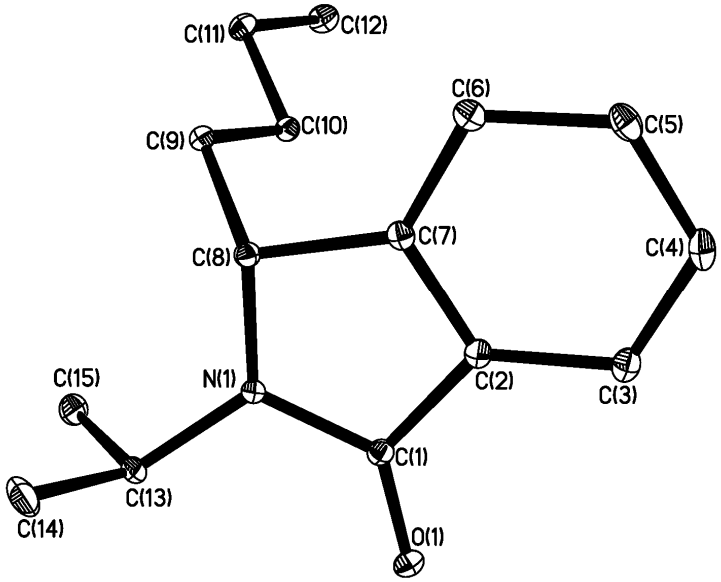

Fig.1. The molecular structure of **1b**. The thermal ellipsoids are drawn at the 30% probability level. Selected bond distances (Å) and angles (^{o}): C(1)–O(1) 1.235(1), C(1)–N(1) 1.370(2), C(8)–N(1) 1.478(2), C(8)–C(9) 1.538(2) Å; C(1)–N(1)–C(8) 112.8(1), C(8)–N(1)–C(13) 124.6(1), O(1)–C(1)–N(1) 125.9(1), O(1)–C(1)–C(2) 127.3(1), N(1)–C(1)–C(2) 106.8(1), N(1)–C(13)–C(15) 113.9(1), C(14)–C(13)–C(15) 112.0(1)^{o}.

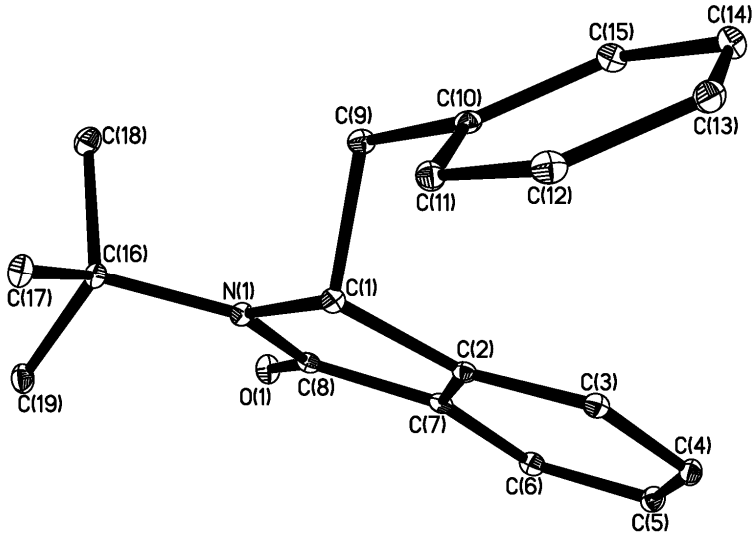

Fig.2. The molecular structure of **4c**. The thermal ellipsoids are drawn at the 30% probability level. Selected bond distances (Å) and angles (^{o}): C(8)–O(1) 1.225(2), C(8)–N(1) 1.364(2), C(1)–N(1) 1.475(2), C(1)–C(9) 1.543(2) Å; C(1)–N(1)–C(8) 112.0(1), C(1)–N(1)–C(16) 124.7(1), C(1)–C(9)–C(10) 111.5(1), O(1)–C(8)–N(1) 126.7(1), N(1)–C(8)–C(7) 106.9(1), N(1)–C(1)–C(9) 113.3(1), N(1)–C(1)–C(2) 102.3(1), N(1)–C(16)–C(17) 110.2(1), C(17)–C(16)–C(19) 106.8(1)^{o}.

The End