Organic & Biomolecular Chemistry

Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: Y. Zhu, Q. Yuan, Z. Chen and F. Zhang, *Org. Biomol. Chem.*, 2017, DOI: 10.1039/C6OB02409B.

ROYAL SOCIETY OF CHEMISTRY

rsc.li/obc

View Article Online
DOI: 10.1039/C6OB02409B

Journal Name

ARTICLE

Palladium-Catalyzed Carbonylative Synthesis of Isocoumarins and Phthalides by using Phenyl Formate as a Carbon Monoxide Source

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

DOI: 10.1039/x0xx00000x

www.rsc.org/

Qing Yuan, Zhen-Bang Chen , Fang-Ling Zhang and Yong-Ming Zhu *

A simple and efficient palladium-catalyzed intramolecular carbonylative synthesis of isocoumarins and phthalides from the easily available starting materials by employing phenyl formate as a CO surrogate has been achieved. The approach constructs target compounds in good to excellent yields with the advantages of lower toxicity, milder conditions, easily operation and wide functional group tolerance.

Introduction

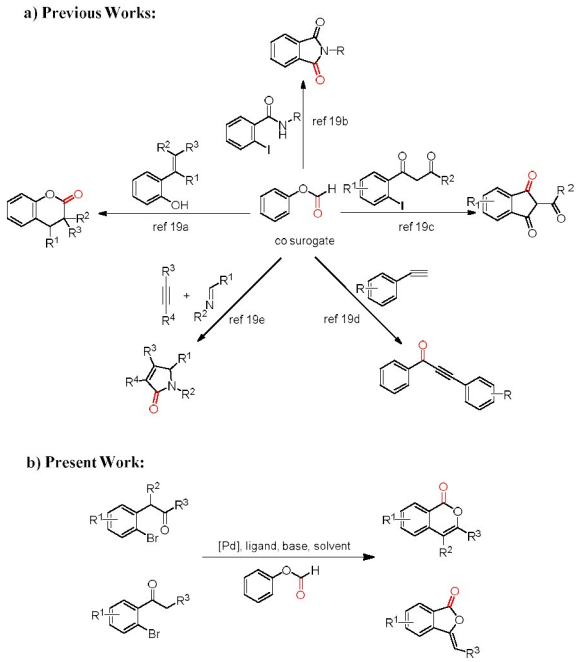
Isocoumarins and phthalides are an important class of lactonic natural products widely existing in microbes and higher plants,[1] which have a lot of biological activities, including antimicrobial,[2] anticancer,[3] antiallergic,[4] antifungal,[5] and anti-HIV.[6] They are also important intermediates to further build other bioactive compounds.[7] Therefore, many medicinal chemists have been focused on the synthesis of lactones. So far, various methods to synthesize those compounds have been reported. These methods include (a) cyclization of 2 –alkenyl or 2-allyl benzoic acid derivatives;[8] (b) condensation of benzoic acid derivatives with alkenes or alkynes;[9] (c) palladium-catalyzed carbonylative cyclization via trapping of acylpalladium derivatives with internal enolates;[10] (d) the reaction of phthalic acid with chloride or ester under microwave;[11] (e) NHC catalytic oxidative cyclization of 2 - alkynyl benzaldehyde;[12] (g) the reflux cyclization of δ-carbonyl amides derivatives;[13] (h) CO insertion reactions;[14] (i) copper catalyzed 2 - halogenated benzoic acid and its derivatives with 1, 3 – diketone to synthesize isocoumarins.[15]

However, the disadvantages of these reactions are obvious; including high toxicity, multistep reactions, difficult operation, harsh reaction conditions, etc. Thus, we are making an effort to investigate more simple and efficient approach for constructing this class of valuable lactones.

In recent years, transition-metal-catalyzed carbonylative transformations of aryl halides by employing CO gas as carbonyl source has been developed [16] and further studied, which provides an important strategy for the synthesis of carbonyl compounds including isocoumarins and phthalides. However, CO is a toxic and flammable gas usually used under the conditions of high pressure. Further, the substrate scope is limited to a small range, all above drawbacks severely restrict its common applications. Thus, considerable efforts have been put to find versatile CO surrogates in carbonylation processes to circumvent the use of high toxic CO.[17] Phenyl formate, a kind of environmentally friendly reagent, has emerged as a vital CO building block for various compounds. Two groups have independently reported the use of phenyl formate as a CO surrogate to etherify aryl halides.[18] Besides a wide range of organic compounds including lactones,[19a] phthalimides,[19b] indanones, [19c] alkynones[19d]and γ-lactams[19e] have been achieved by employing phenyl formate as a CO source (Scheme1). During the last few years, our group has been involved in constructing bioactive compounds by using CO surrogate. [19c][20] As part of our ongoing interest in phenyl formate as a CO surrogate , herein, we report an efficient one-pot synthesis of isocoumarins and phthalides via palladium-catalyzed intramolecular carbonylative annulation using phenyl formate as a “CO-Free” Source.

College of Pharmaceutical Sciences, Soochow University, Suzhou, 215123, China. E-mail: zhuyongming@suda.edu.cn.
† Electronic Supplementary Information (ESI) available: See
DOI: 10.1039/x0xx00000x

View Article Online
DOI: 10.1039/C6OB02409B
ARTICLE Journal Name

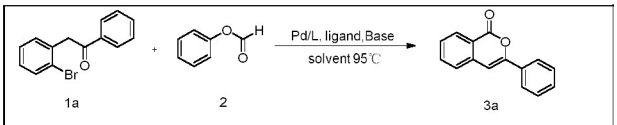


Scheme1 Synthesis of various compounds using phenyl formate as a "CO-Free" Source

Results and Discussion

At the beginning of our study, we used **1a** to react with phenyl formate **2** in the presence of $PdCl_2(MeCN)_2$ and XantPhos with K_3PO_4 as the base and Dimethyl Sulphoxide (DMSO) as a solvent under nitrogen at 95°C. As we expected, desired isocoumarin **3a** was obtained in 78% yield (table 1, entry 1). However, minor amounts of **1a** remained. Then, we changed base to optimize the reaction conditions. In contrast with K_3PO_4, K_2CO_3, K_2HPO_4, Sodium tert-butoxide gave decreased yield (table 1, entries 1-4), only trace of the desired compound was isolated (table 1, entry 4).When add an organic base *DBU,* the desired product was isolated in 64% yield (table 1, entry 5). To our delight, the yield was raised to 85% when organic base Et_3N was introduced (table 1, entry 6). Next, a series of monoand and bidentate ligands were screened, none of them were found to compete with DPPF (table1, entries 6-11). Other commercially available catalysts were tested, $PdCl_2(MeCN)_2$ was superior to $Pd(OAC)_2$(table 1, entries 11 and 15). Afterwards, solvents switching showed that DMSO appeared to be the best solvent (table 1, entries 11-14). It suggested that polar solvents conduced to the carbonylative cyclization process. When using ethyl formate and methyl formate as CO source, only few of the desired **3a** was observed (table 1, entries16 and 17). Phenyl formate is much higher active CO donor than ethyl formate and methyl formate in this system. Further, reaction time, reaction temperature and solvent quantity were optimized as well. Finally, the optimal reaction condition were phenyl formate (2 equiv), $PdCl_2(MeCN)_2$ (5 mol %), DPPF (10 mol %) as the catalyst system, with Et_3N (2 equiv) as the base and DMSO (1.5 mL) as the solvent under nitrogen atmosphere at 95 °C.

Table1. Optimization of the reaction conditions for isocoumarins synthesis[a,b]



1a 2 3a

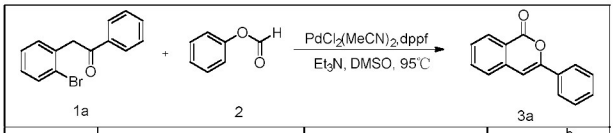
entry	2	Catalyst	Ligand	Base	solvent	yield[b]
1	2	$PdCl_2(MeCN)_2$	XantPhos	K_3PO_4	DMSO	78%
2	2	$PdCl_2(MeCN)_2$	XantPhos	K_2CO_3	DMSO	70%
3	2	$PdCl_2(MeCN)_2$	XantPhos	K_2HPO_4	DMSO	60%
4	2	$PdCl_2(MeCN)_2$	XantPhos	NaOtBu	DMSO	5%
5	2	$PdCl_2(MeCN)_2$	XantPhos	DBU	DMSO	64%
6	2	$PdCl_2(MeCN)_2$	XantPhos	Et_3N	DMSO	85%
7	2	$PdCl_2(MeCN)_2$	Dpephos	Et_3N	DMSO	55%
8	2	$PdCl_2(MeCN)_2$	PCy_3	Et_3N	DMSO	36%
9	2	$PdCl_2(MeCN)_2$	$P(t\text{-}Bu)_3\text{-}HBF_4$	Et_3N	DMSO	79%
10	2	$PdCl_2(MeCN)_2$	DPPE	Et_3N	DMSO	58%
11	2	$PdCl_2(MeCN)_2$	DPPF	Et_3N	DMSO	91%
12	2	$PdCl_2(MeCN)_2$	DPPF	Et_3N	DMF	82%
13	2	$PdCl_2(MeCN)_2$	DPPF	Et_3N	toluene	75%
14	2	$PdCl_2(MeCN)_2$	DPPF	Et_3N	THF	45%
15	2	$Pd(OAC)_2$	DPPF	Et_3N	DMSO	43%
16[c]	2	$PdCl_2(MeCN)_2$	DPPF	Et_3N	DMSO	0%
17[q]	2	$PdCl_2(MeCN)_2$	DPPF	Et_3N	DMSO	0%

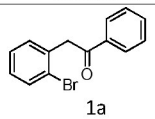
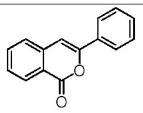
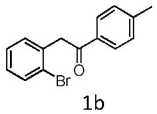
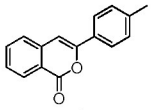
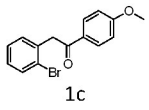
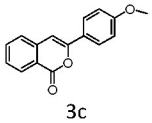
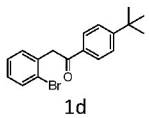
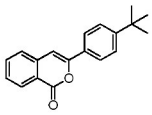
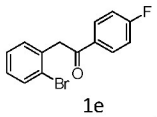
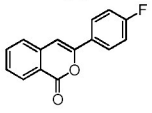
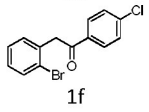
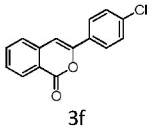
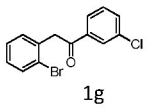
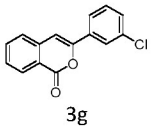
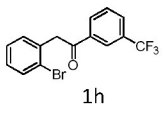
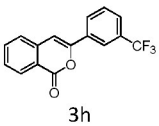
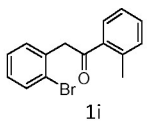
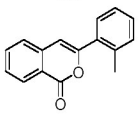
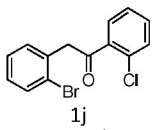
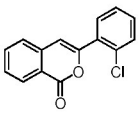
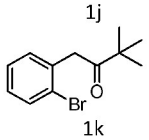
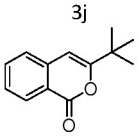
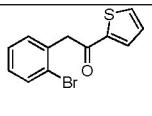
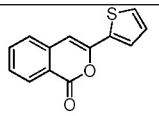
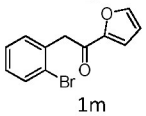
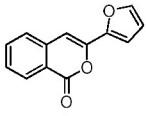
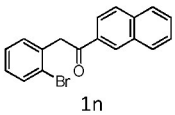
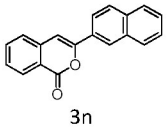
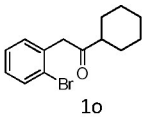
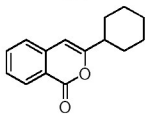
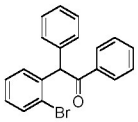
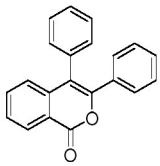
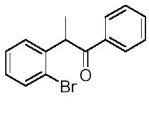
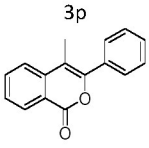
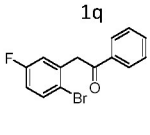
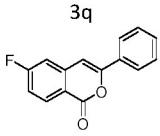
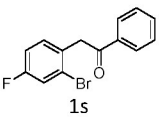
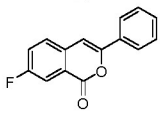
[a]General conditions: the reactions were run on a 0.5 mmol scale in solvent (1.5mL), 2(1 mmol), catalyst (0.025mmol), ligand (0.05 mmol), base (1mmol) under nitrogen in a sealed tube at 95 °C for 24 h. XantPhos=4,5-Bis(diphenylphosphino)-9,9-dimethylxanthene,DPEPhos=bis[(2-diphenylphosphino)phenyl]ether, PCy_3=tricyclohexylphosphine,$P(t\text{-}Bu)_3\text{-}HBF_4$=Tri-tert-butylphosphinetetrafluoroborae, DPPE=1,2-Bis(diphenylphosphino)ethane, DPPF= 1,1′-bis(diphenylphosphino)ferrocene, [b] Isolated yield by silica gel chromatography. [c]Using ethyl formate as a CO surrogate. [q] Using methyl formate as a CO surrogate.

With the optimized reaction conditions in hand, next, we investigate the scope and generality of this reaction. As shown in table 2, a wide range of functional groups in R^3, including aryl (Table 2, entries 1–10), heteroaryl (Table 2, entries12 and 13) alkyl (Table 2, entries 11 and 15), naphthalene (table 2, entry 14) ,were well tolerated in this system. Various substituents on the aryl ring, which include electron-withdrawing and electron-donating groups could be converted into the corresponding compounds **3** in moderate to good yields. Electron-rich phenyl halides (table 2, **3b**, **3c**, **3d**, **3i**) afforded higher yields than the electron-poor phenyl halides (table 2, **3e-3h**, **3j**). Additionally, other substrates in R^2 and R^1, such as **1p**, **1q** , **1r** and **1s** also provided desired products **3p**, **3q** , **3r** and **3s** in moderate yields under general conditions (table 2, entries16–19).

View Article Online
DOI: 10.1039/C6OB02409B

Table 2. Synthesis of isocoumarins from substrates (**1a–1s**) via palladium-catalyzed intramolecular carbonylative annulations[a,b]



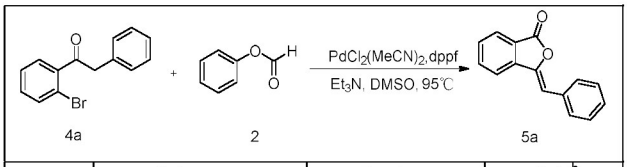
Entry	substrate	Product	yield[b]
1	 1a	 3a	91%
2	 1b	 3b	90%
3	 1c	 3c	89%
4	 1d	 3d	86%
5	 1e	 3e	85%
6	 1f	 3f	78%
7	 1g	 3g	75%
8	 1h	 3h	77%
9	 1i	 3i	81%
10	 1j	 3j	51%
11	 1k	 3k	81%
12	 1l	 3l	82%
13	 1m	 3m	74%
14	 1n	 3n	86%
15	 1o	 3o	65%
16	 1p	 3p	89%
17	 1q	 3q	55%
18	 1r	 3r	58%
19	 1s	 3s	69%

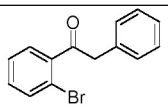
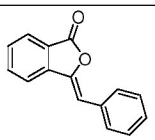
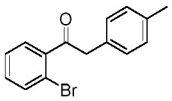
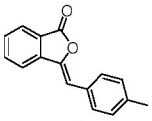
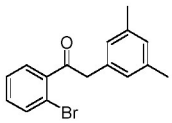
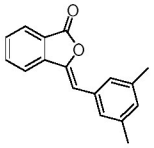
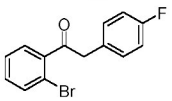
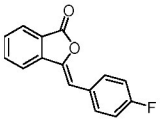
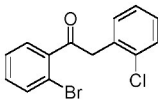
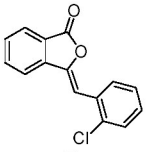
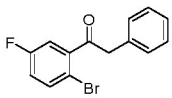
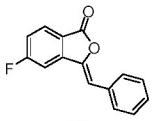
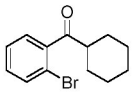
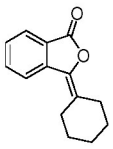
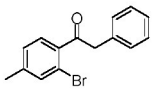
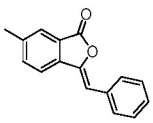
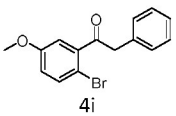
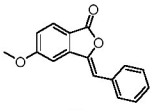
[a] General conditions: all reactions were run on a 0.5 mmol scale in solvent(1.5mL),2(1mmol),$PdCl_2(MeCN)_2$(0.025mmol),DPPF(0.05mmol), Et_3N(1mmol) under nitrogen in a sealed tube at 95 °C for 24 h. [b] Isolated yield by silica gel chromatography.

To further demonstrate the applicable scope of this method, a variety of substrates **4a-4i** were investigated, and the results are summarized in table 3. Gratifyingly, this approach successfully generates phthalides. Various electron-donating and electron-withdrawing substituents on the aryl ring and bromobenzene ring could be transformed into the corresponding phthalides in good to excellent yields. Electron-rich substituents afforded higher yields than the electron-poor ones (Table 3, entries 2–9). Substrates with cyclohexyl group generated products **5g** in moderate yields (Table 3, entries 7).

Table3. Synthesis of Phthalides from Substrates (**4a–4i**)

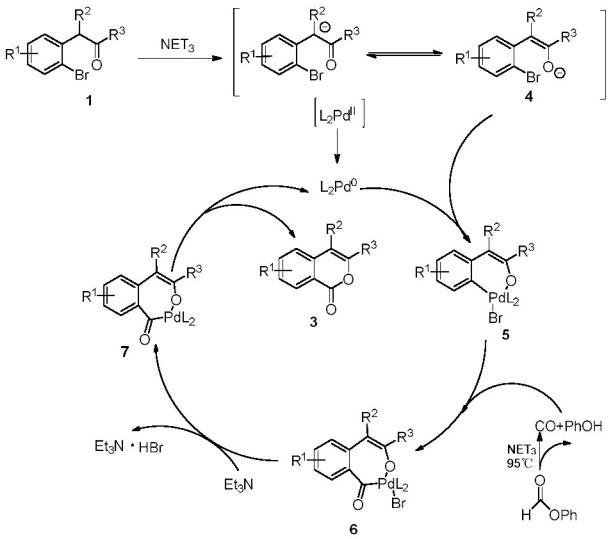
View Article Online
DOI: 10.1039/C6OB02409B



Entry	Substrate	Product	yield[b]
1	 4a	 5a	82%
2	 4b	 5b	80%
3	 4c	 5c	82%
4	 4d	 5d	75%
5	 4e	 5e	78%
6	 4f	 5f	66%
7	 4g	 5g	42%
8	 4h	 5h	85%
9	 4i	 5i	81%

[a] General conditions: all reactions were run on a 0.5 mmol scale in solvent (1.5mL), 2(1 mmol), $PdCl_2(MeCN)_2$ (0.025mmol), DPPF (0.05 mmol), Et_3N(1mmol) under nitrogen in a sealed tube at 95 °C for 24 h. [b] Isolated yield by silica gel chromatography.

Based on the experimental results, a plausible mechanism for this reaction is depicted in Scheme 2. Firstly, substrate **1** is enolic activated into **4**, while the phenyl formate decomposes into one molecule of CO and phenol in the presence of base. Then, the in situ generated Pd^0 species undergo an oxidative addition to **4** to give palladium complex **5**, followed by CO insertion to form acyl palladium species **6**. At last, the product **3** is achieved via an intramolecular attack of the nucleophile on acyl palladium species **6** and eductive elimination under the presence of base (Et3N).



Scheme2 Plausible reaction mechanism

Conclusions

In summary, an efficient one-pot palladium-catalyzed carbonylative synthesis of isocoumarins and phthalides from the stable and available substrates by employing phenyl formate as a CO surrogate has been developed, which demonstrates the utility of phenyl formate in intermolecular C-O bond construction. Compared to the conventional methods known for synthesizing lactones, [8-15] the new procedure presented here is more convenient and environmentally friendly. Moreover, a wide range of substrates have been transformed into their corresponding lactones in good to excellent yields under mild conditions with high efficiency and good functional-group compatibility. This protocol may aid the further development of the reactions incorporating phenyl formate and be very attractive in synthetic bioactive compounds and medicinal chemistry.

Experimental

General Information.

Reactants and reagents were purchased from commercial suppliers and used without further purification. All anhydrous solvents used

View Article Online
DOI: 10.1039/C6OB02409B

in the reactions were dried and freshly distilled. TLC was performed on silica HSGF254 plates. Melting points were determined with a digital melting-point apparatus. NMR spectra were run in a solution of CDCl3 or DMSO-d6 with tetramethylsilane (TMS) as internal standard and were reported in parts per million (ppm). ^{1}H and ^{13}C NMR spectra were obtained at400/101 MHz (^{1}H/^{13}C). High-resolution mass spectra (HRMS) analyses were carried out on a chemical ionization (CI) apparatus using time-of-flight (TOF) mass spectrometry.

General procedure for the Synthesis of lactones. Substrate **1** or **4** (0.5 mmol), $PdCl_2(MeCN)_2$ (0.05 equiv, 6 mg, 0.025mmol), DPPF(0.1 equiv, 28 mg, 0.05mmol), HCO_2Ph (2 equiv, 112μL, 1 mmol), Et_3N (2 equiv, 101mg, 1 mmol) and anhydrous DMSO(1.5mL) were add added into a 15 mL sealed tube, The tube was purged with nitrogen gas and stirred at 95°C for 24 h. After completion of the reaction (confirmed by TLC analysis), the reaction mixture was diluted with water (20mL) and extracted with EtOAc (3×10mL). The combined organic layers were dried over Na_2SO_4 and evaporated. The residue was purified on a silica gel column using petroleum ether/EtOAC as the eluent to give the pure target product.

3-Phenyl-1H-isochromen-1-one (3a). White solid, mp: 86-87℃, 101 mg, yield 91%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, *J* = 8.2 Hz, 1H), 7.92 – 7.81 (m, 2H), 7.75 – 7.64 (m, 1H), 7.53 – 7.37 (m, 5H), 6.93 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ161.9, 153.1, 137.0, 134.4, 131.4, 129.5,129.1, 128.3, 127.7, 125.5 ,124.8,120.0, 101.4, 76.9,76.6,76.3. LRMS (ESI): m/z calcd for $C_{15}H_{10}O_2$ $[M + H]^+$,223.1; found: 223.0.

3-p-Tolyl-1H-isochromen-1-one (3b). White solid, mp: 108-110℃, 106 mg, yield 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, *J* = 8.2 Hz, 1H), 7.76 (d, *J* = 8.2 Hz, 2H), 7.69 (t, *J* = 7.6 Hz, 1H), 7.49 – 7.44 (m, 2H), 7.25 (d, *J* = 8.0 Hz, 2H), 6.89 (s, 1H), 2.39 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.0, 153.4, 139.8, 137.2, 134.4, 129.1, 129.1, 128.7, 127.4, 125.4, 124.7, 119.9, 100.6, 76.9, 76.6, 76.3, 20.9. LRMS (ESI): m/z calcd for $C_{16}H_{12}O_2$ $[M + H]^+$, 237.1; found: 237.0.

3-(4-Methoxyphenyl)-1H-isochromen-1-one (3c). White solid, mp: 114-116℃, 112 mg, Yield 89%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, *J* = 8.1 Hz, 1H), 7.79 (d, *J* = 8.9 Hz, 2H), 7.67 (t, *J* = 7.2 Hz, 1H), 7.46 – 7.40 (m, 2H), 6.94 (d, *J* = 8.9 Hz, 2H), 6.80 (s, 1H), 3.84 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.1, 160.6, 153.2, 137.4, 134.4 129.2, 127.2, 126.4, 125.2, 124.1, 119.7, 113.8, 99.8, 76.9, 76.6, 76.2, 54.9.LRMS (ESI): m/z calcd for $C_{16}H_{12}O_3$ $[M + H]^+$,253.1;found: 253.1.

3-(4-(tert-butyl)phenyl)-1H-isochromen-1-one (3d). Yellow solid, mp: 64-66 ℃, 120mg, Yield 86%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, *J* = 7.8 Hz, 1H), 7.83 (d, *J* = 7.3 Hz, 2H), 7.71 (d, *J* = 6.4 Hz, 1H), 7.48 (s, 4H), 6.93 (s, 1H), 1.36 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.0, 153.4, 153.0, 137.3, 134.4, 129.2, 128.7, 127.5, 125.4(d, *J* = 4.9 Hz), 124.6, 120.0, 100.7, 76.8, 76.5, 76.2, 34.4, 30.7. HRMS (CI): m/z calcd for $C_{19}H_{18}O_2$ $[M + H]^+$, 279.1385; found: 279.1376.

3-(4-Fluorophenyl)-1H-isochromen-1-one (3e). Yellow solid, mp: 130-132℃, 102mg, Yield 85%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, *J* = 8.0 Hz, 1H), 7.88 – 7.83 (m, 2H), 7.71 (t, *J* = 7.6 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.14 (t, *J* = 8.6 Hz, 2H), 6.88 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.5, 162.0, 161.7, 152.3, 136.9, 134.5, 129.2, 127.8, 126.8 (d, *J* = 8.5 Hz), 125.5, 119.9, 115.6, 115.4, 101.1 (d, *J* = 1.6 Hz), 76.9, 76.6, 76.3.LRMS (ESI): m/z calcd for $C_{15}H_9F0_2$ $[M + H]^+$, 241.1; found: 241.0.

3-(4-chlorophenyl)-1H-isochromen-1-on (3f). White solid, mp: 144-146℃, 100mg, Yield 78%.^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 7.8 Hz, 1H), 7.78 (d, *J* = 8.6 Hz, 2H), 7.70 (t, *J* = 7.5 Hz, 1H), 7.48 (t, *J* = 8.7 Hz, 2H), 7.40 (d, *J* = 8.6 Hz, 2H), 6.90 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.9, 153.1, 137.0, 134.4, 131.4, 129.5, 129.1, 128.3, 127.7, 125.5, 124.8, 120.0, 101.4, 76.9, 76.6, 76.3. LRMS (ESI): m/z calcd for $C_{15}H_9ClO_2$ $[M + H]^+$, 257.0; found: 257.0.

3-(3-chlorophenyl)-1H-isochromen-1-one (3g). White solid, mp: 161-163℃, 96mg, Yield75% ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, *J* = 7.9 Hz, 1H), 7.88 (s, 1H), 7.75 (dd, *J* = 14.9, 6.0 Hz, 2H), 7.53 (t, *J* = 8.7 Hz, 2H), 7.40 (d, *J* = 5.0 Hz, 2H), 6.97 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.7, 136.6, 134.6, 129.6, 129.5, 129.3, 128.1, 125.7, 124.9, 122.8, 102.2, 76.9, 76.5, 76.2. LRMS (ESI): m/z calcd for $C_{15}H_9ClO_2$ $[M + H]^+$, 257.0; found: 257.0.

3-(3-(trifluoromethyl)phenyl)-1H-isochromen-1-one(3h).White solid, mp: 100-102℃, 112mg, Yield 77%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, *J* = 7.9 Hz, 1H), 8.13 (s, 1H), 8.08 (d, *J* = 7.9 Hz, 1H), 7.76 (t, *J* = 7.6 Hz, 1H), 7.69 (d, *J* = 7.9 Hz, 1H), 7.63 – 7.53 (m, 3H), 7.04 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.4, 151.6, 136.5, 134.6, 132.4, 129.4, 129.0, 128.3, 127.9, 126.0(d, *J* = 3.7 Hz), 125.8, 121.6 (d, *J* = 3.9 Hz), 120.3, 102.5, 76.9, 76.5, 76.2. LRMS (ESI): m/z calcd for $C_{16}H_9F_3O_2$ $[M + H]^+$, 291.1; found: 290.8.

3-(o-tolyl)-1H-isochromen-1-one (3i). White solid, mp: 92-94℃, 96mg, Yield 81%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, *J* = 8.2 Hz, 1H), 7.75 – 7.66 (m, 3H), 7.54 – 7.47 (m, 2H), 7.35 (t, *J* = 7.7 Hz, 1H), 7.24 (s, 1H), 6.95 (s, 1H), 2.43 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.0, 153.4, 138.2, 137.2, 134.4, 131.4, 130.3, 129.2, 128.3, 127.6, 125.5 (d, *J* = 2.6 Hz), 121.9, 120.1, 101.3, 76.9, 76.5, 76.2, 21.0. HRMS (CI): m/z calcd for$C_{16}H_{12}O_2$ $[M + H]^+$, 237.0916; found: 237.0899.

3-(2-chlorophenyl)-1H-isochromen-1-one (3j). White solid, mp: 113-115℃, 65mg, Yield 51%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, *J* = 7.9 Hz, 1H), 7.77 – 7.70 (m, 2H), 7.57 – 7.47 (m, 3H), 7.36 (dd, *J* = 5.6, 3.8 Hz, 2H), 6.99 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.9, 151.0, 136.5, 134.5 131.9, 131.1, 130.45 – 129.95 (m), 129.1, 128.2, 126.54 125.8, 120.2, 107.2, 76.9, 76.6, 76.3. LRMS (ESI): m/z calcd for $C_{15}H_9ClO_2$[M + H]$^+$, 257.0; found: 256.9.

3-(tert-butyl)-1H-isochromen-1-one (3k). Colorless oil, 82mg, Yield 81%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (dd, *J* = 8.0, 0.5 Hz, 1H), 7.58 – 7.52 (m, 1H), 7.32 (t, *J* = 7.6 Hz, 1H), 7.27 (d, *J* = 7.9 Hz, 1H), 6.20 (s, 1H), 1.21 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.6, 162.5, 137.2, 134.2, 128.8, 127.1, 125.1, 119.5, 99.3, 77.0, 76.7, 76.4, 35.1, 27.4.LRMS (ESI): m/z calcd for $C_{13}H_{14}O_2$ $[M + H]^+$, 203.1; found: 203.2.

3-(thiophen-2-yl)-1H-isochromen-1-one (3l). Yellow solid, mp: 110-112℃, 94mg, Yield 82%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 7.9 Hz, 1H), 7.68 (td, *J* = 7.8, 1.1 Hz, 1H), 7.59 (dd, *J* = 3.7, 0.9 Hz, 1H), 7.45 (dd, *J* = 12.3, 7.6 Hz, 2H), 7.39 (dd, *J* = 5.0, 0.9 Hz, 1H), 7.10 (dd, *J* = 4.9, 3.8 Hz, 1H), 6.77 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.2, 149.0, 137.0, 135.2, 134.5, 129.3, 127.7, 127.5, 126.9, 125.7, 125.3, 119. 8, 100.4, 76.9, 76.6, 76.3.LRMS (ESI): m/z calcd for $C_{13}H_8O_2S$ $[M + H]^+$, 229.0; found: 229.1.

3-(furan-2-yl)-1H-isochromen-1-one (3m). White solid, mp: 114-116℃, 79mg, Yield 74%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.2 Hz, 1H), 7.68 (t, *J* = 7.5 Hz, 1H), 7.50 – 7.42 (m, 3H), 6.92 (d, *J* = 3.3 Hz, 1H), 6.84 (s, 1H), 6.53 – 6.50 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.2, 146.4, 145.6, 143.6, 136.9, 134.5, 129.4, 127.5, 125.5, 120.0, 111.7, 109.7, 99.6, 76.9, 76.6, 76.2.LRMS (ESI): m/z calcd for $C_{13}H_8O_3$ $[M + H]^+$, 213.1; found: 213.1.

3-(naphthalen-2-yl)-1H-isochromen-1-one (3n). White solid, mp: 157-159℃, 117mg, Yield 86%.^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (s,

View Article Online
DOI: 10.1039/C6OB02409B

1H), 8.35 (d, *J* = 7.9 Hz, 1H),7.91 (m, 4H), 7.75 (t, *J* = 7.4 Hz, 1H), 7.55 (d, *J* = 6.6 Hz, 4H), 7.11 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.9, 153.1, 137.1, 134.5, 133.4, 132.7, 129.3, 128.5, 128.4, 128.1, 127.7, 127.2, 126.8, 126.4, 125.6, 124.8, 121.5, 120.1, 101.8, 76.9, 76.6, 76.23. LRMS (ESI): m/z calcd for $[M + H]^+$, 273.1; found: 272.9.

3-cyclohexyl-1H-isochromen-1-one (3o). White solid mp: 92-94℃, 74mg, Yield 65%.^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.0 Hz, 1H), 7.67 (t, *J* = 7.6 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 1H), 7.37 (d, *J* = 7.9 Hz, 1H), 6.23 (s, 1H), 2.49 – 2.36 (m, 1H), 2.04 (d, *J* = 12.7 Hz, 2H), 1.86 (d, *J* = 12.7 Hz, 2H), 1.74 (d, *J* = 12.3 Hz, 1H), 1.48-1.26 (m,6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.7, 161.9, 137.3, 134.2, 129.0, 127.0, 124.8, 119.8, 100.4, 76.9, 76.5, 76.2, 41.4, 30.1, 25.5, 25.4. LRMS (ESI): m/z calcd for $C_{15}H_{16}O_2$ $[M + H]^+$, 229.1; found: 229.3.

3,4-diphenyl-1H-isochromen-1-one (3p). White solid mp: 168-170℃, 133mg,Yield 89%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, *J* = 7.8 Hz, 1H), 7.63 (t, *J* = 7.6 Hz, 1H), 7.51 (t, *J* = 7.5 Hz, 1H), 7.41 (d, *J* = 5.1 Hz, 3H), 7.33 (d, *J* = 7.5 Hz, 2H), 7.25 – 7.15 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.8, 150.5, 138.4, 134.2, 133.8, 132.4, 130.8, 129.1, 128.7, 128.6, 128.5, 127.6 (d, *J* = 3.3 Hz), 127.4, 124.9, 120.0, 116.4, 76.9, 76.6, 76.3. LRMS (ESI): m/z calcd for $C_{21}H_{14}O_2$ $[M + H]^+$, 299.1; found: 299.1.

4-methyl-3-phenyl-1H-isochromen-1-one (3q). White solid, mp: 113-115℃, 65mg, Yield 55%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 – 8.36 (m, 1H), 7.83 – 7.78 (m, 1H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.61 – 7.52 (m, 3H), 7.46 (q, *J* = 6.0 Hz, 3H), 2.32 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.0, 150.7, 138.3, 134.3, 132.8, 129.3, 129.0 128.9, 127.8, 127.5, 122.9, 120.3, 76.9, 76.6, 76.2, 13.1. HRMS (CI): m/z calcd for $C_{16}H_{12}O_2$ $[M + H]^+$, 237.0916; found: 237.0900.

6-fluoro-3-phenyl-1H-isochromen-1-one (3r). White solid, mp: 154-156℃, 70mg, Yield 58%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.5 Hz, 1H), 7.88 (d, *J* = 6.5 Hz, 2H), 7.55 – 7.42 (m, 5H), 6.96 (d, *J* = 2.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.6, 161.0 (d, *J* = 3.6 Hz), 160.1, 152.7 (d, *J* = 2.9 Hz), 133.6 (d, *J* = 2.6 Hz), 131.2, 129.6, 128.4, 127.8, 127.7, 124.7, 123.0, 122.8, 121.7, 121.6, 114.8, 114.6, 100.5 (d, *J* = 1.2 Hz), 76.9, 76.6), 76.2. LRMS (ESI): m/z calcd for $C_{15}H_9FO_2$ $[M + H]^+$, 241.1 ; found: 240.9.

7-fluoro-3-phenyl-1H-isochromen-1-one(3s). White solid, mp: 153-155℃, 83mg, Yield 69%. 1H NMR (400 MHz, CDCl3) δ 7.96 (d, J = 8.1 Hz, 1H), 7.86 (d, J = 7.0 Hz, 2H), 7.58 – 7.38 (m, 5H), 6.95 (s, 1H). ^{13}C NMR (101 MHz, CDCl3) δ 160.1, 152.6, 133.54, 131.2, 129.6, 128.4, 127.8, 124.7, 122.9, 114.6, 100.5, 76.9, 76.6, 76.3. HRMS (CI): m/z calcd for $C_{15}H_9FO_2$ $[M +H]^+$, 241.0665; found: 241.0663.

(Z)-3-benzylideneisobenzofuran-1(3H)-one (5a). White solid, mp: 83-85℃, 91mg, Yield 82%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.7 Hz, 1H), 7.84 (d, *J* = 7.8 Hz, 2H), 7.79 – 7.69 (m, 2H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.31 (t, *J* = 7.4 Hz, 1H), 6.42 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.7, 144.1, 140.1, 134.1, 132.6, 129.7, 129.3, 129.1, 128.3, 128.0, 125.1, 122.9, 119.4, 114.9, 106.7, 76.9, 76.6, 76.3. LRMS (ESI): m/z calcd for $C_{15}H_{10}O_2$ $[M + H]^+$, 223.1;found: 223,1.

(Z)-3-(4-methylbenzylidene)isobenzofuran-1(3H)-one(5b).White solid, mp: 146-148℃, 95mg, Yield 80%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.7 Hz, 1H), 7.78 – 7.69 (m, 4H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 2H), 6.41 (s, 1H), 2.39 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.7, 143.5, 140.3, 138.2, 133.9, 129.8, 129.6, 129.07 (s), 125.1, 122.9, 119.2, 106.7, 76.9, 76.5, 76.2, 21.0. LRMS (ESI): m/z calcd for $C_{16}H_{12}O_2$ $[M + H]^+$,237.1; found: 236.9.

(Z)-3-(3,5-dimethylbenzylidene)isobenzofuran-1(3H)-one(5c). White solid, mp: 143-145℃, 102mg, Yield 82%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.7 Hz, 1H), 7.79 – 7.68 (m, 2H), 7.54 (t, *J* = 7.3 Hz, 1H), 7.48 (s, 2H), 6.97 (s, 1H), 6.37 (s, 1H), 2.37 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.8, 143.8, 140.3, 137.8, 133.9, 132.4, 129.9, 129.1, 127.5, 125.1, 122.9, 119.2, 107.0, 76.9, 76.6, 76.2, 20.9. LRMS (ESI): m/z calcd for $C_{17}H_{14}O_2$ $[M + H]^+$, 251.1; found: 251.1.

(Z)-3-(4-fluorobenzylidene) isobenzofuran-1(3H)-one (5d). White solid, mp: 138-140℃, 90mg, Yield 75%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.7 Hz, 1H), 7.84 (dd, *J* = 8.7, 5.5 Hz, 2H), 7.75 (dt, *J* = 14.7, 7.4 Hz, 2H), 7.56 (t, *J* = 7.3 Hz, 1H), 7.11 (t, *J* = 8.7 Hz, 2H), 6.39 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 163.3, 160.8, 143.7, 140.0, 134.1, 134.1, 131.4 (d, *J* = 8.2 Hz), 129.4, 125.2 122.9, 119.3, 115.5, 115.3, 105.4, 76.9, 76.5, 76.2.LRMS (ESI): m/z calcd for $C_{15}H_9FO_2$ $[M + H]^+$,241.1; found: 240.9.

(Z)-3-(2-chlorobenzylidene)isobenzofuran-1(3H)-one (5e). White solid, mp: 153-155℃, 100mg, Yield 78%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, *J* = 8.0 Hz, 1H), 7.96 (d, *J* = 7.7 Hz, 1H), 7.87 (d, *J* = 7.8 Hz, 1H), 7.76 (t, *J* = 7.6 Hz, 1H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.43 (d, *J* = 8.0 Hz, 1H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.23 (d, *J* = 7.7 Hz, 1H), 6.91 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 145.3, 140.0, 134.2, 133.3, 131.3, 130.5, 129.8, 129.1, 128.8, 126.7, 125.2, 123.0, 119.8, 101.8, 76.9, 76.5, 76.2. LRMS (ESI): m/z calcd for $C_{15}H_9ClO_2$ $[M + H]^+$, 257.0; found: 256.7

(Z)-3-benzylidene-5-fluoroisobenzofuran-1(3H)-one (5f). White solid, mp: 156-158℃, 79mg, Yield 66%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.7 Hz, 1H), 7.84 (dd, *J* = 8.7, 5.5 Hz, 2H), 7.75 (dt, *J* = 14.7, 7.4 Hz, 2H), 7.56 (t, *J* = 7.3 Hz, 1H), 7.11 (t, *J* = 8.7 Hz, 2H), 6.39 (s, 1H).^{13}C NMR (101 MHz, $CDCl_3$) δ 167.7, 165.4, 165.2, 143.1 (d, *J* = 4.2 Hz), 142.8, 142.7, 132.2, 129.8, 128.4, 127.7, 127.6, 119.1, 117.9, 117.6, 107.8, 106.3, 106.0, 76.9, 76.6, 76.2.LRMS (ESI): m/z calcd for $C_{15}H_9ClO_2$ $[M + H]^+$, 241.1; found: 240.9.

3-cyclohexylideneisobenzofuran-1(3H)-one (5g). White solid, mp: 71-74℃, 45mg, Yield 42%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.7 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.66 (t, *J* = 7.7 Hz, 1H), 7.46 (t, *J* = 7.4 Hz, 1H), 2.73 – 2.69 (m, 2H), 2.65 – 2.61 (m, 2H), 1.68 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.7, 138.5, 138.2,133.6, 127.9, 127.8, 125.5, 125.1, 122.4, 76.9, 76.5, 76.2, 29.0, 28.1, 27.2, 26.8, 25.6.LRMS (ESI): m/z calcd for $C_{14}H_{14}O_2$ $[M + H]^+$,215.1; found: 215.0.

(Z)-3-benzylidene-6-methylisobenzofuran-1(3H)-one (5h) .White solid, mp: 136-138 ℃ ,100mg, Yield 85%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.2 Hz, 2H), 7.70 (s, 1H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.52 (d, *J* = 7.9 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 2H), 7.30 (t, *J* = 7.4 Hz, 1H), 2.48 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.9, 144.2, 140.0, 137.8, 135.4, 132.8, 129.5, 129.2, 128.3, 127.7, 124.9, 119.2, 76.9, 76.6, 76.3, 21.1. HRMS(CI): m/z calcd for $C_{16}H_{12}O_2$ $[M +H]^+$, 237.0916; found: 237.0903.

(Z)-3-benzylidene-5-methoxyisobenzofuran-1(3H)-one (5i) .White solid, mp: 141-143 ℃ , 102mg, Yield 81%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 12.8, 8.0 Hz, 3H), 7.40 (t, *J* = 7.5 Hz, 2H), 7.31 (t, *J* = 7.4 Hz, 1H), 7.13 (d, *J* = 1.6 Hz, 1H), 7.05 (dd, *J* = 8.5, 2.0 Hz, 1H), 6.36 (s, 1H), 3.95 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.3, 164.6, 144.0, 142.7, 132.7, 129.6, 128.3, 127.9, 126.6, 117.8, 115.6, 106.3, 102.2, 76.9, 76.6, 76.3, 55.5. HRMS (CI): m/z calcd for $C_{16}H_{12}O_3$ $[M +H]^+$, 253.0865; found: 253.0858.

Acknowledgements

View Article Online
DOI: 10.1039/C6OB02409B

We gratefully acknowledge financial support by the PAPD (A Project Funded by the Priority Academic Program Development of Jiangsu Higher Education Institutions) and NSFC (National Nature Science Foundation of China, No. 21172162).

Notes and references

1 (a) J. J. Beck and S. C. Chou, *J. Nat. Prod.*, 2007, 70, 891–900; (b) T. H. Chou, I. S. Chen and T. L. Hwang, *J. Nat. Prod.*, 2008, 71, 1692–1695; (c) J. Kornsakulkarn, C. Thongpanchang and S. Lapanun, *J. Nat. Prod.*, 2009, 72, 1341–1343; (d) V. Rukachaisirikul, A. Rodglin and Y. Sukpondma, *J. Nat. Prod.*, 2012, 75, 853–858.

2 K. Nozawa, M. Yamada and Y. Tsuda, *Chem. Pharm. Bull.*, 1981, 29, 2491–2495.

3 (a) T. Kawano, N. Agata, S. Kharbanda, D. Avigan, D. Kufe, *Cancer Chemother. Pharmacol*, 2007, 59, 329–335；(b) M. E. Riveiro, A. Moglioni, R.Vazquez, N.Gomez, G. Facorro, L. Piehl, Celis. De, E. R., C. Shayo and C. Davio, *Bioorg, Med. Chem.*, 2008, 16, 2665–2675.

4 M. Yoshikawa, E. Harada, Y. Naitoh, K. Inoue, H. Matsuda, H. Shimoda, J. Yamahara and N. Murakami, *Chem. Pharm. Bull.*, 1994, 42, 2225–2230.

5 (a) K. M. Meepagala, G. Sturtz and D. E. Wedge, J. Agric. *Food Chem.*, 2002, 50, 6989–6992; (b) D. Engelmeier, F. Hadacek, O. Hofer, G. Lutz-Kutschera, M. Nagl, G. Wurz and H. J. Greger, *Nat. Prod.* 2004, 67, 19–25.

6 L. M. Bedoya, E. DelOlmo and R. Sancho, Bioorg. *Med. Chem. Lett.*, 2006, 16, 4075–4079.

7 (a) E. Del Olmo, M. García Armas, M. I. Ybarra, J. L. López, P. Oporto, A. Giménez, E. Deharoe and San Felicianoa, A. Bioorg. Med.,Chem. Lett., 2003, 13, 2769–2772; (b) A. E. Kümmerle, M. M. Vieira, M. Schmitt, A. L. P. Miranda, C. A. M. Fraga, J. J. Bourguignon and E. J. Barreiro, Bioorg. *Med. Chem. Lett.*, 2009, 19, 4963–4966; (c) A. R. Ramesha and A. K. Roy, *Synth. Commun.*, 2001, 31, 2419–2422.

8 (a)T. Yao and R. C. Larock, *J. Org. Chem.*, 2003, 68, 5936–5942; (b)R. Rossi, A. Carpita and F. Bellina, *Tetrahedron*, 2003, 59, 2067–2081; (c) M. Uchiyama, H. Ozawa and K. Takuma, *Org. Lett.*, 2006, 8, 5517–5520; (d) M. Hellal, J. J. Bourguignon and Bihel, *Tetrahedron Lett.*, 2008, 49, 62–65; (e) S. A. Shahzad, C. Venin and T. Wirth, Eur. *J. Org. Chem.*, 2010, 18, 3465–3472.

9 (a) V. Subramanian, V. R. Batchu and D. Barange, *J. Org. Chem.*, 2005, 70, 4778–4783; (b) K. Cherry, J. Parrain and P. J. Thibonnet, *J. Org. Chem.*, 2005, 70, 6669–6675; (c) K. Ueura, T. Satoh and M. J. Miura, *Org. Chem.*, 2007, 72, 5362–5367.

10 (a) E. Negishi, C. Copéret and T. Sugiham, *Tetrahedron*, 1994, 50, 425–436; (b) R. F. Mark and C. W. Michael, *Chem. Commun.*, 2009, 6744–6746.

11 (a) K. M. Khan, S. Ahmed and Z. A. Khan, *Lett. Org. Chem.*, 2005, 2, 532–534; (b) S. S. Tajudeen and F. N. Khan, *Synth. Commun.*, 2007, 37, 3649–3656; (c) K. M. Khan, S. Ahmed and Z. A. Khan, *Nat. Prod. Res.*, 2008, 22, 1120–1127.

12 J. H. Park, S. V. Bhilare and S. W. Youn, *Org. Lett.*, 2011, 13, 2228–2231.

13 A. Kurume, Y. Kamata and M. Yamashita, *Chem. Pharm., Bull.*, 2008, 56, 1264–1269.

14 (a) P. G.Ciattini, G. Mastropietro and E.Morera, *Tetrahedron Lett.*, 1993, 34, 3763–3766; (b) E. Negishi, C. Copéret, T. Sugihara, *Tetrahedron,* 1994, 50, 425–436; (c) E. Negishi, H. Makabe and I.Shimoyama, *Tetrahedron*, 1998, 54, 1095–1106; (d) A. C. Tadd, M. R. Fielding and M. C. Willis, *Chem. Commun.*, 2009, 6744–6746.

15 (a) X. S. Fan, Y. He and L. Y. Cui, Eur. *J. Org. Chem.*, 2012, 4, 673–677; (b) S.-J. Cai, F. Wang and C. J. Xi, *J. Org. Chem.*, 2012, 77, 2331–2336; (c) V. Kavala,; C.-C.Wang, D. K. Barange, *J. Org. Chem.*, 2012, 77, 5022–5029.

16 (a) A. Brennführer, H. Neumann and M. Beller, *Angew. Chem.*, 2009, 121, 4176–4196; (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. (d) Q. Liu, H. Zhang and A. Lei, *Angew. Chem.*, 2011, 123, 10978–10989; (e) C. F. Barnard, *J. Organometallics*, 2008, 27, 5402–5422.

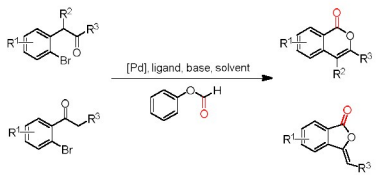
17 (a) T. Morimoto and K. Kakiuchi, *Angew. Chem.*, 2004, 43, 5580–5588; (b) L. R. Odell, F. Russo and M. Larhed, *Synlett*, 2012, 23, 685–689. (c) L.Wu, Q. Liu, R. Jackstell and M. Beller, *Angew. Chem. Int. Ed.*, 2014, 53, 6310–6320.

18 (a)T. Ueda, H. Konishi and K. Manabe, *Org. Lett.*, 2013, 15, 5370–5373; (b) T. Ueda, H. Konishi and K. Manabe, *Tetrahedron Lett.*, 2012, 53, 5171–5175; (c) T. Ueda, H. Konishi and K. Manabe, *Org.Lett.*, 2012, 14, 3100,–3103; (d) T. Fujihara, T. Hosoki, Y. Katafuchi, T. Iwai, J. Terao and Y. Tsuji, *Chem. Commun.*, 2012, 48, 8012–8014.

19 (a) H. Wang, B. Dong, Y. Wang, J. Li and Y. Shi, *Org. Lett.*, 2014, 16, 186–189. (b) Sujit. P. Chavan, Bhalchandra. M. Bhanage, *Eur. J. Org. Chem*. 2015, 2405–2410 (c) Y. Zhang, J. L. Chen, Z. B. Chen, Y. M. Zhu and S. J. Ji, *J. Org. Chem.*, 2015, 80, 10643-10650. (d) Li, H.; Neumann, H.; Beller, M.; Wu, X.-F. *Angew. Chem.*, Int. Ed. 2014, 53, 3183–3186. (e) Hoshimoto, Y.; Ohata, T.; Sasaoka, Y.; Ohashi, M.; S. Ogoshi, *J. Am. Chem. Soc.* 2014, 136, 15877–15880.

20 (a) X. D. Fei, Z. Y Ge, T. Tang, Y. M. Zhu and S. J. Ji, *J. Org. Chem.*, 2012, 77, 10321–10328; (b) T. Tang, X. D. Fei, Z. Y. Ge, Z. Chen, Y. M. Zhu and S. J. Ji, *J. Org. Chem.*, 2013, 78, 3170–3175. (c) Y. Zhang, X. Jiang, J. M. Wang, J. L. Chen and Y. M. Zhu, *RSC Adv.*, 2015, 5, 17060–17063.

Graphics



View Article Online
DOI: 10.1039/C6OB02409B