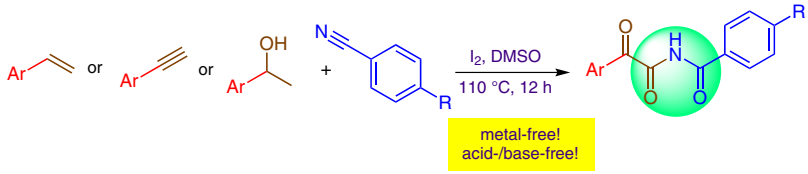
Synthesis H. P. Kalmode et al. Paper

The Oxidative Cross-Coupling of Benzonitriles with Multiform Substrates: A Domino Strategy Inspired Easy Access to α-Ketoimides

Hanuman P. Kalmode[a]
Kamlesh S. Vadagaonkar[a]
Atul C. Chaskar*[a,b]

[a] Department of Dyestuff Technology, Institute of Chemical Technology, Mumbai 400019, India
[b] National Centre for Nanosciences and Nanotechnology, University of Mumbai, Mumbai 400098, India
achaskar25@gmail.com

This work is dedicated to our mentor Prof. P. M. Bhate on the occasion of his 61st birthday.



Received: 18.10.2014
Accepted after revision: 06.12.2014
Published online: 14.01.2015
DOI: 10.1055/s-0034-1379955; Art ID: ss-2014-n0634-op

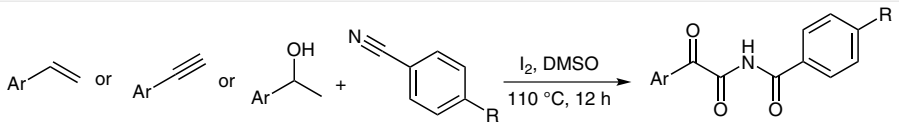
Abstract An iodine-promoted highly efficient convergent synthesis of α-ketoimides from multiform substrates and benzonitriles through oxidative imidation reaction is described. This domino oxidative imidation process involves cleavage of C–H bond and construction of C–O and C–N bonds. This method could be a powerful compliment to the existing methods owing to its use of abundantly available starting materials and reagents.

Key words iodine, metal-free synthesis, Kornblum oxidation, α-ketoimides, multiform substrates

Amides, imides, α-ketoamides, and α-ketoimides are crucial structural units in numerous natural products, drugs, and proteins.[1] All these molecules are very important due to their ability to easily undergo functional group manipulation during synthesis of various biologically active heterocyclic ring systems.[2] Imides are present in biologically active molecules and have been targets of interest for the synthesis of pharmaceuticals.[1] α-Ketoamides are potent inhibitors of the hepatitis C virus NS3 serine protease, cathepsin K, calpain inhibitor such as SNJ-1945 and p38 MAP kinase, etc.[3] Hence, numerous methodologies have been developed for synthesizing this group of building blocks.

Conventionally, amides are prepared by coupling a carboxylic acid or its derivatives with amines[4] while acyl halides are used for the preparation of imides.[5] The literature reported methods for the synthesis of α-ketoamides are amidation of α-keto acids,[6] α-ketoaryl halides,[7] cyano ketones,[8] oxidation or photochemical reaction of amides,[9] double carboxylative amidation of aryl halides,[10] oxidation of acyl cyanophosphoranes followed by the amidation of α,β-diketone nitrile,[11] and reaction of isocyanides with aromatic acyl chlorides.[12] Li[13] and Liu et al.[14] synthesized amides from aldehydes using copper and *n*-Bu_4NI, respectively, together with TBHP. In recent years, I_2 in combination with DMSO has proved to be an environment-friendly, metal-free effective system for the series of organic reactions particularly in C–H functionalization. This approach has emerged as an attractive tool in organic synthesis due to its diverse applications.

α-Ketoamides are synthesized via copper-catalyzed oxidative coupling of aryl acetylenes, aryl acetaldehydes, α-carbonyl aldehydes, and aryl methyl ketones with anilines.[15] However, the use of toxic metal oxidants restrict the utility of these methods, especially in the case of the synthesis of drug intermediates owing to possible contamination of these with trace amount of heavy metals. Iodine or iodine-peroxide has emerged as an effective reagent for sp^3 C–H bond oxidative amidation of methyl ketones.[16] Wu et al. extensively demonstrated the promising applications of



Scheme 1 The oxidative imidation of ethylenearenes, ethynearenes, and 1-arylethanols with benzonitriles

multi-pathway coupled domino (MPCD) strategies[17] while Zhang and co-workers had employed anodic oxidation of aryl methyl ketones.[18] The oxidative amidation of 2-oxoaldehyde was achieved using dimethyl sulfoxide[19] whereas polysubstituted oxazoles were obtained through domino oxidative cyclization by using I_2/TBHP.[20a] Wang et al. reported the synthesis of 2,5-disubstituted oxazoles by using 2-amino-1-phenylethanone and aromatic aldehydes,[20b] 2-phenylquinazolines from 2-amino benzophenones and benzylic amines,[20c] quinazolines from α-amino acids and 2-aminobenzoketones,[20d] ketones from benzylic methylenes, and nitriles from primary amines by using I_2/TBHP.[20e] Chiral α-ketoimides have been derived from Oppolzer's sultam by the diastereoselective addition of Grignard reagents, as reported by Jurczak and co-workers.[21]

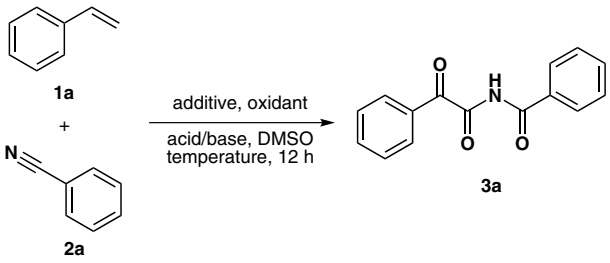
Moreover, to the best of our knowledge, no reports have been demonstrated by using multiform substrates and benzonitriles to construct α-ketoimide skeleton. In the context of the advantages of domino reaction and limitations of aforementioned methods, herein we present the I_2-promoted sequential cleavage of C–H bond and formation of C–O, C–N bonds of multiform substrates with benzonitriles, which is highly desirable. We have centered our attention on oxidative imidation of ethylenearenes **1**, ethynearenes **4**, and 1-arylethanols **5** (Scheme 1).

To initiate our study, the reaction of styrene (**1a**) with benzonitrile (**2a**) in the presence of different additives, oxidants, and acids or bases in DMSO was chosen as a model reaction. The reaction of styrene (**1a**) (1.0 mmol) and benzonitrile (**2a**) (3.0 mmol) with 0.5 equivalent of I_2 at 100 °C for 12 hours could only afford the expected product in 12% yield (Table 1, entry 1).

Varying concentrations of I_2 were scanned to improve the yield and 1.5 equivalents of I_2 was found to be the optimal amount for the oxidative coupling reaction (Table 1, entries 2–4). Increase in the concentration of benzonitrile (**2a**) from 3 to 5 equivalents with 1.5 equivalents of I_2 provided **3a** in 52% yield (entry 5). Further increase in the concentration of benzonitrile from 5 to 15 equivalents afforded the desired product **3a** from 66–77% yield (entries 6, 7). Next, the reactions at varying temperatures (entries 8, 9) were carried out to increase the yield, and 110 °C was found to be the optimum temperature for the oxidative imidation reaction. The reaction could not occur in the absence of I_2 (entry 10), which suggests that the I_2 played a crucial role in the reaction.

Generally in situ hydration of the nitrile group is performed in the presence of acid or base. To optimize the oxidative imidation reaction a variety of acids and bases were used. It was found that acids or bases could not promote the reaction effectively (Table 1, entries 11–18). The range of different oxidizing agents (TBHP, DTBP, IBX, DMP, DIB, and HTIB) for the oxidative imidation reaction was also investigated. A 47% yield was observed in the case of TBHP whereas other oxidants gave relatively lower yields (entries 19–24). Then, to further investigate the scope of additive, different additives such as NIS, KI, CuI, and TBAI were used for this reaction. Low to moderate yields (23–56%) were obtained (entries 25–28) by using above mentioned additives. Thus, the optimized conditions for the oxidative coupling

Table 1 Optimization Studies for the Oxidative Imidation of Styrene with Benzonitrile[a]



Entry	Additive (equiv)	Oxidant (equiv)	Acid	Base	Temp (°C)	Yield (%)[b]
1[a]	I_2 (0.5)	–	–	–	100	12
2[a]	I_2 (1.0)	–	–	–	100	28
3[a]	I_2 (1.5)	–	–	–	100	41
4[a]	I_2 (2.0)	–	–	–	100	37
5[c]	I_2 (1.5)	–	–	–	100	52
6[d]	I_2 (1.5)	–	–	–	100	66
7[e]	I_2 (1.5)	–	–	–	100	77
8[e]	I_2 (1.5)	–	–	–	110	86
9[e]	I_2 (1.5)	–	–	–	120	84
10[e]	–	–	–	–	110	0
11[e]	I_2 (1.5)	–	PTSA	–	110	54
12[e]	I_2 (1.5)	–	AcOH	–	110	49
13[e]	I_2 (1.5)	–	TFA	–	110	43
14[e]	I_2 (1.5)	–	H_2SO_4	–	110	38
15[e]	I_2 (1.5)	–	–	DIPEA	110	16
16[e]	I_2 (1.5)	–	–	DBU	110	14
17[e]	I_2 (1.5)	–	–	Et_3N	110	trace
18[e]	I_2 (1.5)	–	–	$NaHCO_3$	110	0
19[e]	I_2 (1.5)	TBHP	–	–	110	47
20[e]	I_2 (1.5)	DTBP	–	–	110	33
21[e]	I_2 (1.5)	IBX	–	–	110	44
22[e]	I_2 (1.5)	DMP	–	–	110	40
23[e]	I_2 (1.5)	DIB	–	–	110	37
24[e]	I_2 (1.5)	HTIB	–	–	110	34
25[e]	NIS (1.5)	–	–	–	110	29
26[e]	KI (1.5)	–	–	–	110	26
27[e]	CuI (1.5)	–	–	–	110	23
28[e]	TBAI (1.5)	–	–	–	110	56

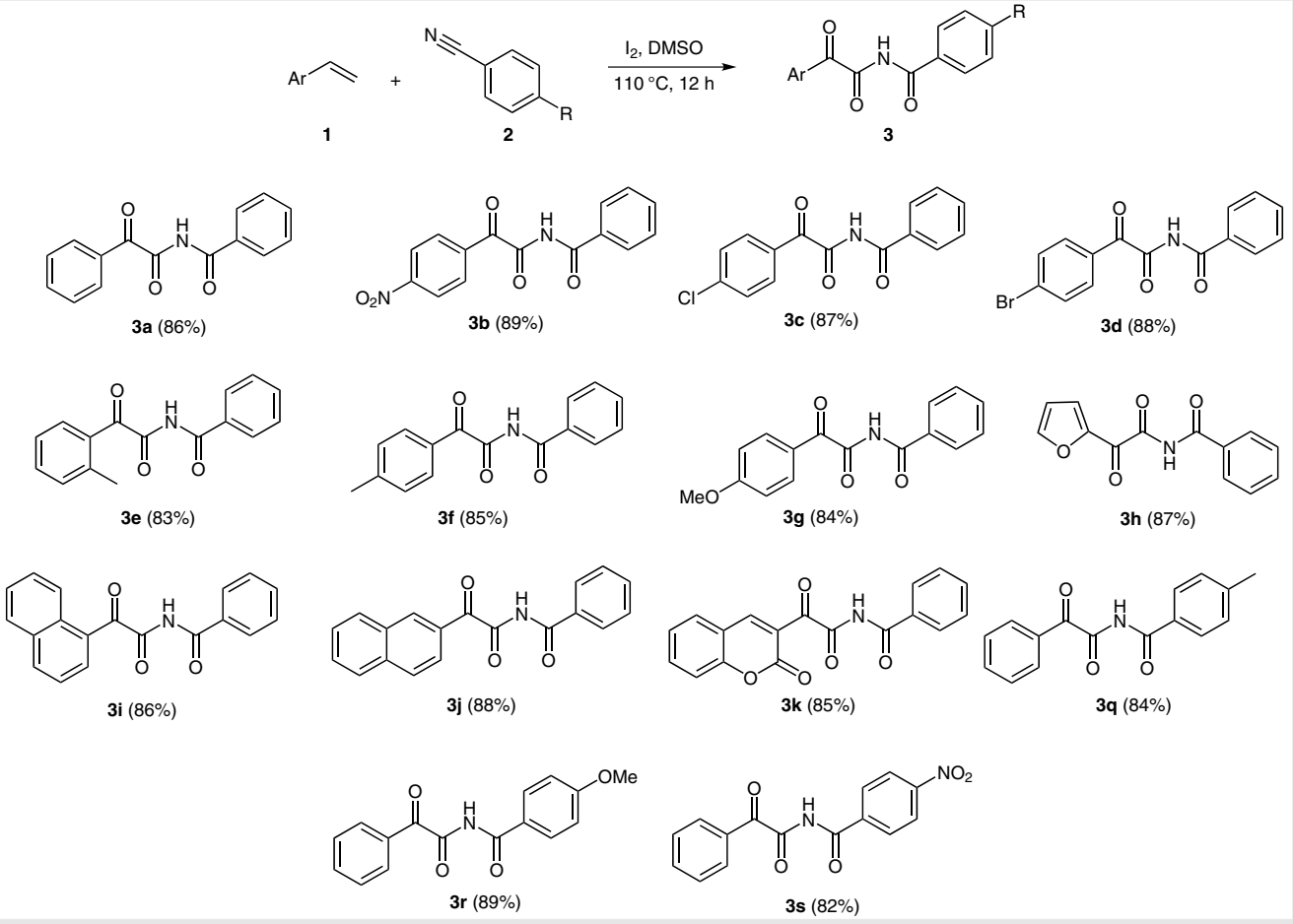
[a] Reaction conditions: **1a** (1.0 mmol), **2a** (3.0 mmol), additive (0.5–2.0 mmol), oxidant (1.0 mmol), and acid or base (1.0 mmol) in DMSO (2.0 mL) were heated in a sealed tube for 12 h. TBHP: *tert*-butyl hydroperoxide; DTBP: di-*tert*-butyl peroxide; IBX: *o*-iodoxybenzoic acid; DMP: 1,1,1-triacetoxy-1,1-dihydro-1,2-benziodoxol-3(1*H*)-one; DIB: (diacetoxyiodo)benzene; HTIB: [hydro(tosyloxy)iodo]benzene.
[b] Isolated yields.
[c] Amount of **2a**: 5.0 mmol.
[d] Amount of **2a**: 10.0 mmol.
[e] Amount of **2a**: 15.0 mmol.

reaction involved the use of 1.5 equivalents of I_2 and 15 equivalents of benzonitrile with styrene in DMSO (2 mL) at 110 °C. Very similar results were obtained when styrene (**1a**) was replaced by phenylacetylene (**4a**) and 1-phenylethanol (**5a**).

In order to study the scope of this protocol, various ethylenearenes **1** were reacted with benzonitriles **2** (Scheme 2). Various functional groups were found to be compatible under the optimized reaction conditions. Ethylenearenes with methyl, methoxy, nitro, and halogen substituents on the phenyl ring underwent oxidative cross coupling reaction with benzonitrile (**2a**) smoothly to form the corresponding α-ketoimides **3b**–**g** in 83–89% yields. 1-Ethylenenaphthalene and 2-ethylenenaphthalene afforded the corresponding α-ketoimides **3i** and **3j** in 86 and 88% yield, respectively. Notably, heteroaryl ethylenes such as 2-vinylfuran and 3-vinyl-2*H*-chromen-2-one reacted well with selectivity to afford the corresponding α-ketoimides **3h** and **3k** in 87 and 85% yield, respectively.

To extend the scope of this reaction, benzonitriles with neutral (4-Me), electron-deficient (4-NO_2), and electron-rich (4-OMe) groups on the phenyl ring were reacted with styrene (**1a**) to furnish the corresponding products **3q**–**s** in 82–89% yields (Scheme 2). These results indicate that there is a small influence on reaction efficiency due to steric and electronic nature of the ethylenearenes **1** and benzonitriles **2**.

Delighted with these encouraging results, our attention was next turned to the oxidative imidation of ethynylarenes **4** with benzonitriles **2**. With the optimal conditions in hand, the scope of the imidation was investigated. The reaction of phenylacetylene (**4a**) with benzonitrile (**2a**) using I_2 in DMSO gave the corresponding α-ketoimide **3a** in 88% yield. Various substituents on the phenyl ring such as 4-F, 3-Cl, 2,4-Cl_2, 2-Br, and 4-Br were compatible with reaction conditions and the desired products **3l**–**o**, and **3d** were obtained in good to excellent yields (84–90%) (Scheme 3). Further, 2-ethynylnaphthalene and 3-ethynyl-2*H*-chromen-2-one also gave the desired products **3j** and **3k** in 87 and 88%

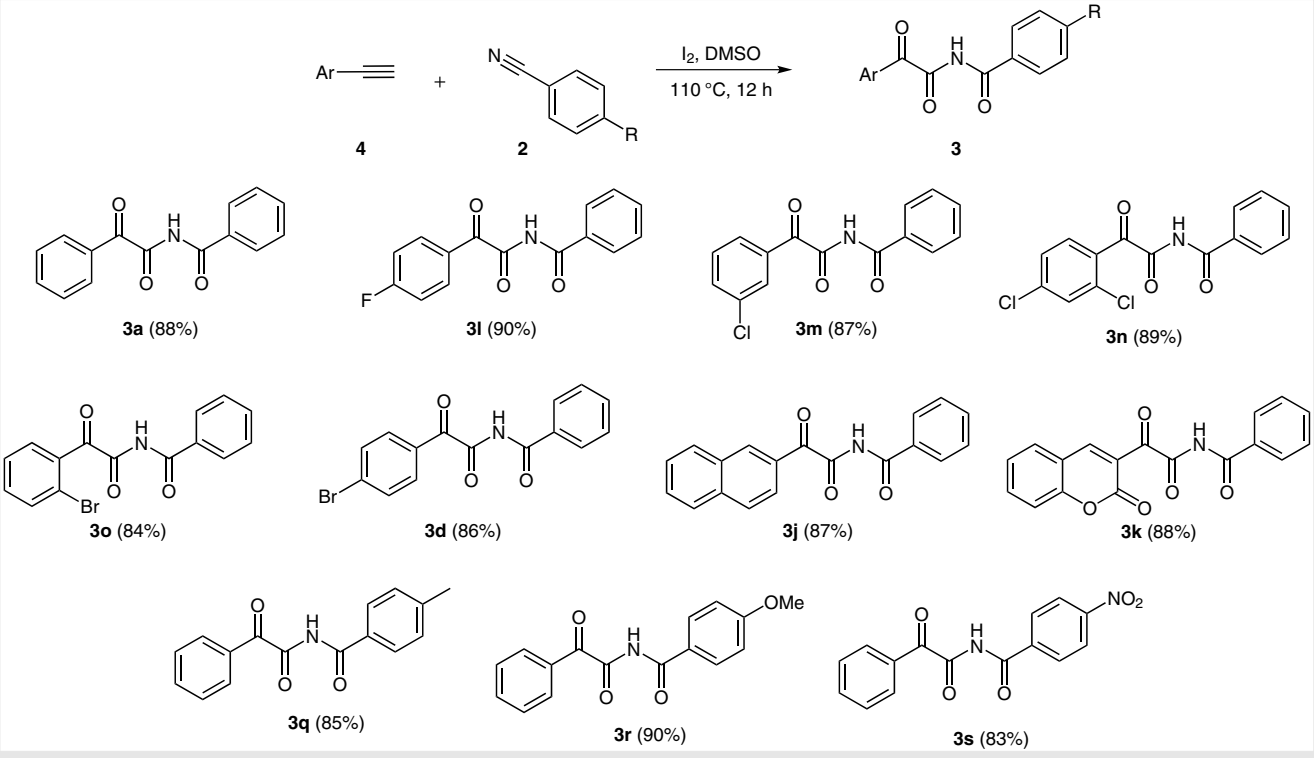


Scheme 2 I_2-promoted synthesis of α-ketoimides from ethylenearenes and benzonitriles. *Reaction conditions*: **1** (1.0 mmol), **2** (15.0 mmol), and I_2 (1.5 mmol) were heated in a sealed tube at 110 °C for 12.0 h in DMSO (2.0 mL).

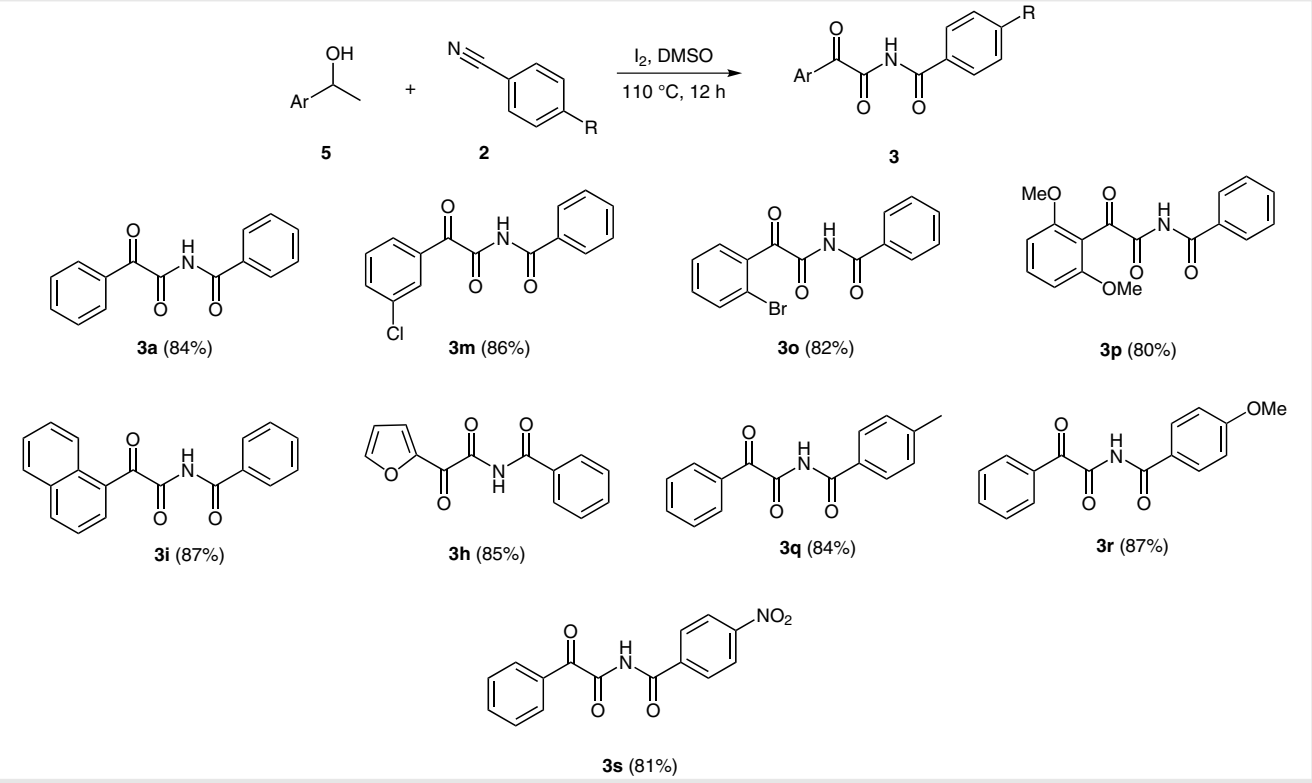
yield, respectively (Scheme 3). Then, the range of various substituted benzonitriles were screened. It was found that the 4-Me-, 4-NO_2-, and 4-OMe-substituted benzonitriles reacted smoothly to form the corresponding oxidative coupling products **3q**–**s** in good yields (83–90%) (Scheme 3).

With all these results of ethylenearenes **1** and ethynylarenes **4** in hand, we focused on the outcome of the reaction between various 1-arylethanols (**5**) and benzonitriles (**2**). 1-Phenylethanol (**5a**) was first treated with benzonitrile (**2a**) to give the *N*-(2-oxo-2-phenylacetyl)benzamide (**3a**) in 84% yield. Next, the effect of various functional groups onto the oxidative imidation reaction was studied (Scheme 4). We found that methoxy and halogen groups were compatible with the reaction conditions and gave the corresponding imides **3m**, **3o**, and **3p** in good yields (80–86%). The reaction of 1-(naphthalen-1-yl)ethanol with benzonitrile (**2a**) gave the corresponding product **3i** in 87% yield. 1-(Furan-2-yl)ethanol reacted smoothly to give *N*-[2-(furan-2-yl)-2-oxoacetyl]benzamide (**3h**) in 85% yield (Scheme 4). Benzonitriles bearing 4-Me, 4-NO_2 and 4-OMe substituents on the phenyl ring reacted smoothly to offer the corresponding products **3q**–**s** in 81–87% yields (Scheme 4).

A series of control experiments (Scheme 5) were performed in order to confirm our proposed mechanism. When styrene (**1a**) or phenylacetylene (**4a**) or 1-phenylethanol (**5a**) was treated with I_2 in DMSO, the successive formation of acetophenone (**A**), phenacyl iodide (**B**), and phenyl glyoxal (**C**) was observed (Scheme 5a). Phenacyl iodide (**B**) reacted with benzonitrile (**2a**) under optimum conditions forming α-ketoimide **3a** exclusively in 78% yield (Scheme 5, b). In the presence of I_2, phenylglyoxal (**C**) was reacted with **2a** to afford the oxidative coupling product **3a** in 89% yield (Scheme 5, c2). These results effectively confirmed that the phenacyl iodide (**B**) and phenylglyoxal (**C**) were the key intermediates in this transformation. However, this reaction cannot be performed smoothly in the absence of I_2 (Scheme 5, c1 and d). This result clearly highlights the significant role of I_2 in oxidative imidation reaction. When the substrate **1a** or **4a** or **5a** was reacted with benzonitrile (**2a**) in the presence of I_2 in DMF under standard conditions, formation of α-ketoimide **3a** was not observed (Scheme 5, e), thus proving the dual role played by DMSO as a solvent and an oxidant in this transformation. α-Ketoimide **3a** was formed in 81% yield when the substrate **1a** or **4a** or **5a** was reacted with benzamide (**6a**) under optimum conditions (Scheme 5, f). Furthermore, it was found that when benzonitrile (**2a**; 1.0 equiv) was treated with 1.5 equivalents of I_2 in DMSO, the benzamide (**6a**) was formed in 96% yield (Scheme 5, g). These results showed that benzonitrile (**2a**) is converted in situ into benzamide (**6a**) and



Scheme 3 I_2-promoted synthesis of α-ketoimides from ethynylarenes and benzonitriles. *Reaction conditions*: **4** (1.0 mmol), **2** (15.0 mmol), and I_2 (1.5 mmol) were heated in a sealed tube at 110 °C for 12.0 h in DMSO (2.0 mL).



Scheme 4 I_2-promoted synthesis of α-ketoimides from 1-arylethanols and benzonitriles. *Reaction conditions*: **5** (1.0 mmol), **2** (15.0 mmol), and I_2 (1.5 mmol) were heated in sealed tube at 110 °C for 12.0 h in DMSO (2.0 mL).

then reacts with phenylglyoxal (**B**), generated in situ from the diverse substrate **1a** or **4a** or **5a**, to afford the target product **3a**.

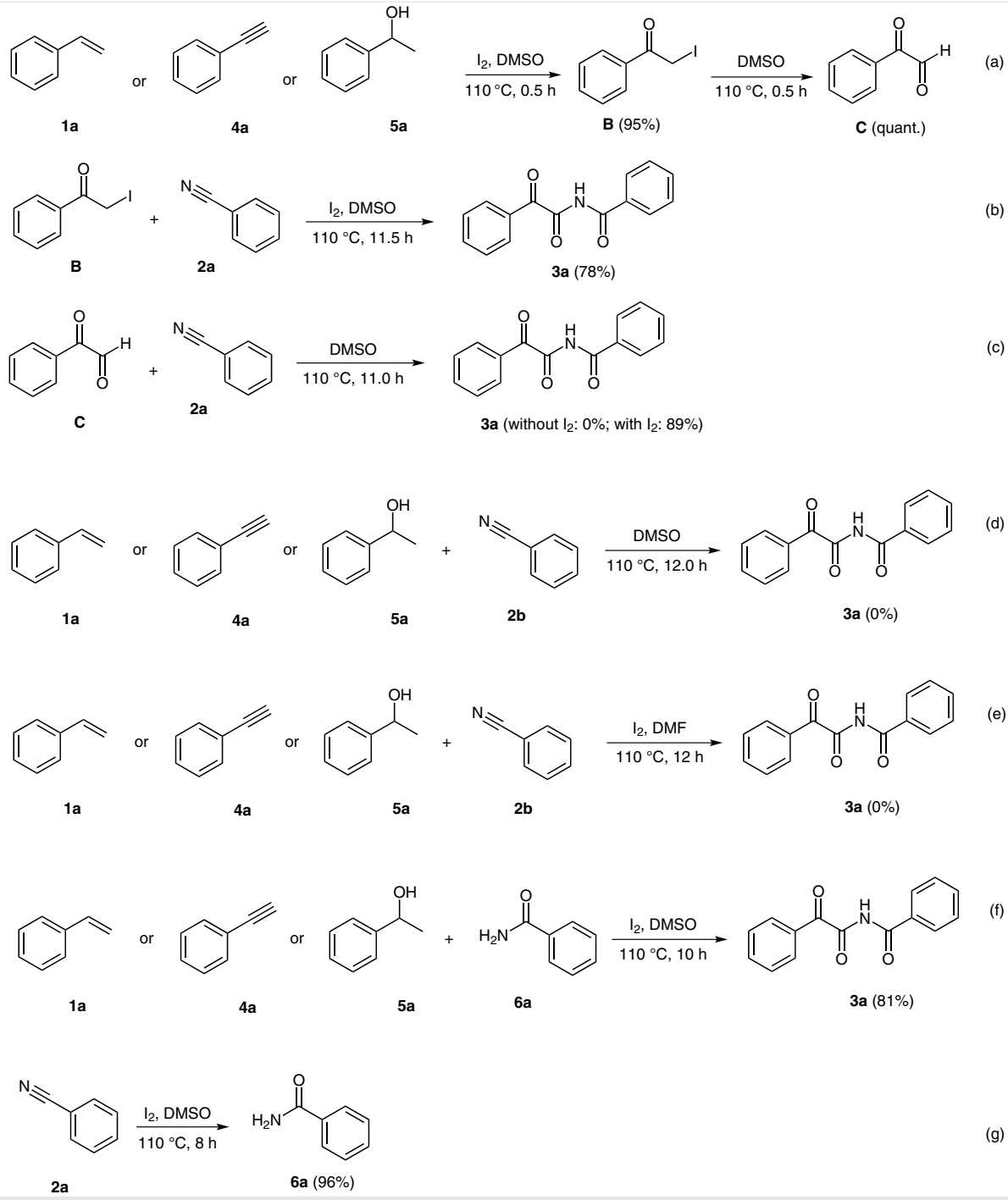
Based on our control experiments, a possible mechanism (Scheme 6) is proposed for the I_2 promoted oxidative imidation reaction of styrene (**1a**), or phenylacetylene (**4a**), or 1-phenylethanol (**5a**) with benzonitrile (**2a**) in DMSO at 110 °C. 1-Phenylethanol (**5a**) under optimal conditions forms acetophenone (**A**), which eventually gets converted into α-iodoacetophenone (**B**). This was confirmed by using TLC, GC-MS, and ^{1}H NMR analysis. A key intermediate α-iodoacetophenone (**B**) was also obtained from the substrate **1a** or **4a**. The α-iodoacetophenone (**B**) is further transformed to phenylglyoxal (**C**) through Kornblum oxidation, which on reaction with benzamide (**6a**) generated in situ from benzonitrile (**2a**), furnishes the α-ketoimide **3a** exclusively.

In conclusion, an iodine-promoted domino strategy for the synthesis of α-ketoimides from multiform substrates has been developed. The striking features of this protocol are the utilization of a simple and cheap additive, readily available starting materials and environmentally benign conditions. We strongly believe that this various functional group compatible and metal-free tandem synthetic approach would be useful for the synthesis of complex molecules in the field of medicine and materials.

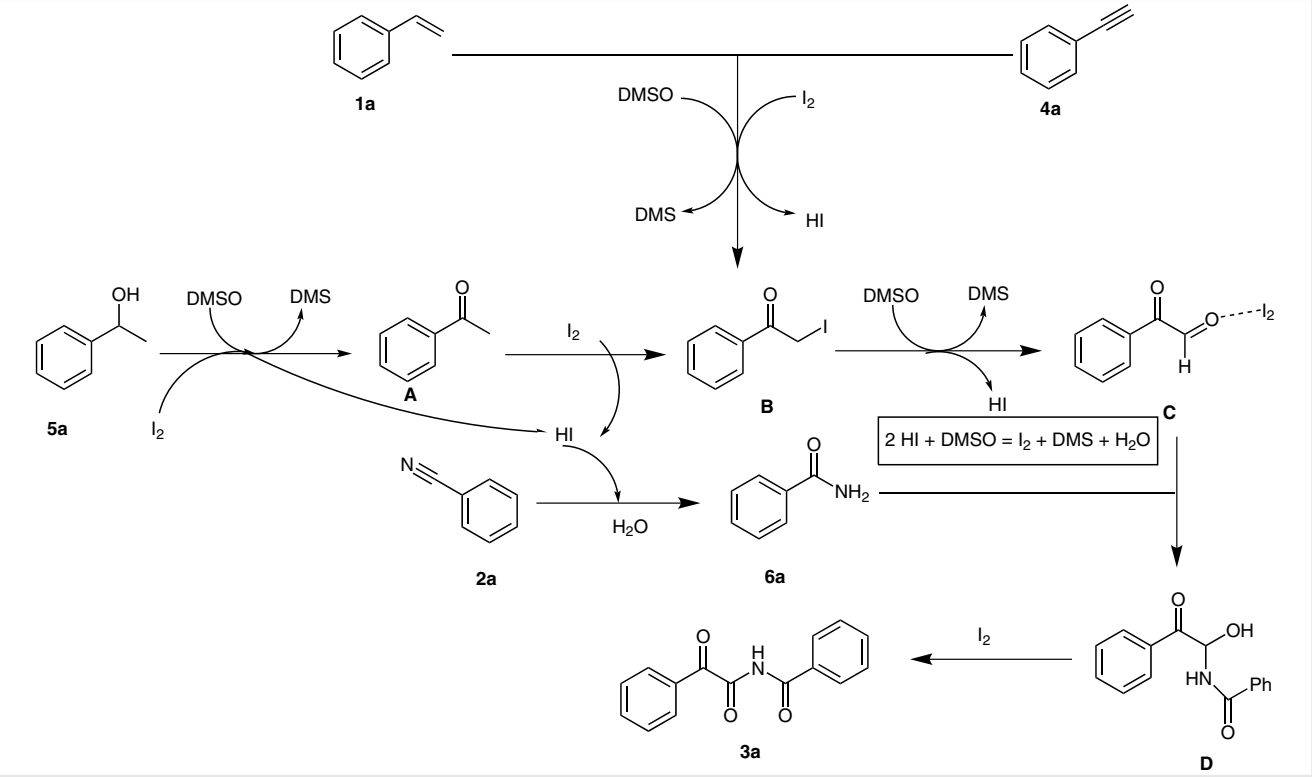
Chemical reagents were obtained from commercial suppliers and used without further purification. All reactions were performed in sealed tube and monitored by TLC performed on aluminum plates (0.25 mm, E. Merck) precoated with silica gel Merck 60 F-254. Developed TLC plates were visualized under a short-wavelength UV lamp. Reactions were conducted under atmospheric conditions in anhydrous solvents such as DMSO and DMF. Yields refer to spectroscopically (^{1}H, ^{13}C NMR) homogeneous material obtained after column chromatography. Column chromatography was performed on silica gel (100–200 mesh size) supplied by S. D. Fine Chemicals Limited, India. IR spectra were recorded on a JASCO FT/IR-4100 LE with attenuated total reflection (ATR) method. NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 solution on Agilent/Bruker 300, 400, and 500 MHz spectrometers. Chemical shifts (δ) for ^{1}H NMR spectra are reported relative to TMS (δ = 0.0 ppm) as an internal standard. Standard abbreviations were used to denote peak multiplicities. Coupling constant *J* is given in Hz. High-resolution mass spectra were obtained by using positive electrospray ionization (ESI) by time-of-flight (TOF) method.

α-Ketoimides 3; General Procedure

A sealed tube equipped with a magnetic stirring bar was charged with ethylenearene **1** or ethynylarene **4**, or 1-arylethanol **5** (1.0 mmol), benzonitrile **2** (15.0 mmol), I_2 (1.5 mmol), and DMSO (2.0 mL). The reaction vessel was heated at 110 °C for 12 h. After disappearance of the reactant as monitored by TLC, the reaction mass was quenched with 10% aq $Na_2S_2O_3$ (10 mL) and extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with brine (20 mL), dried



Scheme 5 Control experiments



Scheme 6 Plausible reaction mechanism

(Na_2SO_4), and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with *n*-hexane–EtOAc (75:25) as eluent to afford the corresponding α-ketoimide **3**.

***N*-(2-Oxo-2-phenylacetyl)benzamide (3a)**

Yield: 1.31 g (88%); light yellow solid; mp 138–140 °C.

IR (ATR): 3445, 3288, 1723, 1684, 1596, 1346, 1210, 761, 714 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 9.86 (br s, 1 H), 8.13 (d, *J* = 7.2 Hz, 2 H), 7.92 (d, *J* = 7.6 Hz, 2 H), 7.62–7.69 (q, *J* = 7.6 Hz, 2 H), 7.50–7.55 (m, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 186.75, 165.44 (2 C=O), 134.85, 134.13, 132.53, 131.19, 130.30, 129.28, 129.08, 128.26.

HRMS (ESI): *m*/*z* calcd for $[(C_{15}H_{11}NO_3)H]$ $[M + H]^+$: 254.0817; found: 254.0822.

***N*-[2-(4-Nitrophenyl)-2-oxoacetyl]benzamide (3b)**

Yield: 1.08 g (89%); yellow solid; mp 80–82 °C.

IR (ATR): 3256, 1718, 1693, 1675, 1530, 1342, 1205, 765, 718 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 12.10 (br s, 1 H), 8.40 (d, *J* = 8.7 Hz, 2 H), 8.20 (d, *J* = 8.7 Hz, 2 H), 7.86 (t, *J* = 6.9, 1.5 Hz, 2 H), 7.43–7.55 (m, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 185.21, 170.09, 168.21, 150.56, 136.04, 133.51, 131.42, 130.08, 128.40, 127.16, 123.15.

HRMS (ESI): *m*/*z* calcd for $[(C_{15}H_{10}N_2O_5)H]$ $[M + H]^+$: 299.0668; found: 299.0673.

***N*-[2-(4-Chlorophenyl)-2-oxoacetyl]benzamide (3c)**

Yield: 1.07 g (87%); yellow solid; mp 72–74 °C.

IR (ATR): 3447, 1695, 1590, 1421, 1214, 1091, 693 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 10.03 (br s, 1 H), 8.07 (d, *J* = 8.1 Hz, 2 H), 7.92 (d, *J* = 7.5 Hz, 2 H), 7.46–7.66 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 185.39, 169.31, 165.41, 141.47, 134.12, 131.50, 131.01, 130.90, 129.39, 129.17, 128.19.

HRMS (ESI): *m*/*z* calcd for $[(C_{15}H_{10}ClNO_3)H]$ $[M + H]^+$: 288.0427; found: 288.0422.

***N*-[2-(4-Bromophenyl)-2-oxoacetyl]benzamide (3d)**

Yield: 958 mg (88%); yellow solid; mp 74–76 °C.

IR (ATR): 3444, 1695, 1585, 1219, 1071, 978, 695 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 9.67 (br s, 1 H), 8.03 (d, *J* = 7.0 Hz, 2 H), 7.89 (d, *J* = 7.5 Hz, 2 H), 7.65–7.69 (distorted dd, *J* = 8.0, 5.5 Hz, 3 H), 7.53 (t, *J* = 5.5 Hz, 2 H).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 186.55, 170.64, 167.39, 134.03, 132.34, 131.66, 131.44, 131.25, 130.70, 130.21, 128.78.

HRMS (ESI): *m*/*z* calcd for $[(C_{15}H_{10}BrNO_3)H]$ $[M + H]^+$: 331.9922; found: 331.9926.

***N*-[2-Oxo-2-(*o*-tolyl)acetyl]benzamide (3e)**

Yield: 1.13 g (83%); white solid; mp 152–154 °C.

IR (ATR): 3445, 3290, 1712, 1692, 1675, 1602, 1341, 1242, 1218, 742 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.74 (br s, 1 H), 7.81 (d, *J* = 6.0 Hz, 4 H), 7.54 (distorted t, *J* = 7.0, 6.0 Hz, 1 H), 7.46 (distorted t, *J* = 7.0, 6.0 Hz, 4 H), 2.42 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 186.82, 168.89, 165.91, 141.61, 134.66, 134.60, 134.01, 132.76, 130.79, 129.05, 128.18, 127.69, 123.21, 21.41.

HRMS (ESI): *m*/*z* calcd for [($C_{16}H_{13}NO_3$)H] [M + H]$^+$: 268.0973; found: 268.0976.

N-[2-Oxo-2-(*p*-tolyl)acetyl]benzamide (3f)

Yield: 1.16 g (85%); white solid; mp 156–158 °C.

IR (ATR): 3450, 3292, 1720, 1685, 1675, 1612, 1352, 1254, 1226, 749 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.70 (br s, 1 H), 8.09 (d, *J* = 8.0 Hz, 2 H), 7.90 (d, *J* = 7.5 Hz, 2 H), 7.64 (t, *J* = 7.5, 7.0 Hz, 1 H), 7.52 (t, *J* = 8.0, 7.5 Hz, 2 H), 7.33 (d, *J* = 8.0 Hz, 2 H), 2.45 (s, 3 H).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 187.25, 171.07, 167.09, 145.00, 133.90, 130.44, 129.97, 129.68, 128.97, 128.75, 21.29.

HRMS (ESI): *m*/*z* calcd for [($C_{16}H_{13}NO_3$)H] [M + H]$^+$: 268.0973; found: 268.0969.

N-[2-(4-Methoxyphenyl)-2-oxoacetyl]benzamide (3g)

Yield: 1.06 g (84%); off-white solid; mp 158–160 °C.

IR (ATR): 3448, 3295, 1718, 1691, 1675, 1604, 1269, 1152, 738 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.13 (br s, 1 H), 8.23 (d, *J* = 4.4 Hz, 2 H), 8.07 (d, *J* = 5.6 Hz, 1 H), 7.93 (s, 2 H), 7.64 (s, 1 H), 7.52 (s, 1 H), 6.99 (distorted t, *J* = 7.6, 6.4 Hz, 2 H), 3.90 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 184.58, 165.11, 164.04, 133.79, 133.22, 132.35, 129.10, 128.07, 125.34, 114.36, 113.77, 55.66.

HRMS (ESI): *m*/*z* calcd for [($C_{16}H_{13}NO_4$)H] [M + H]$^+$: 284.0923; found: 284.0919.

N-[2-(Furan-2-yl)-2-oxoacetyl]benzamide (3h)

Yield: 1.35 g (87%); off-white solid; mp 154–156 °C.

IR (ATR): 3241, 1723, 1652, 1465, 1411, 1351, 1273, 773 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.01 (s, 1 H), 8.55 (t, *J* = 3.6, 3.2 Hz, 1 H), 8.24 (d, *J* = 3.2 Hz, 1 H), 8.20 (s, 1 H), 7.82 (s, 1 H), 7.67 (s, 1 H), 7.54 (distorted t, *J* = 3.2, 2.0 Hz, 2 H), 7.48 (d, *J* = 3.2 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.30, 164.39, 160.90, 157.59, 148.51, 137.24, 131.16, 128.71, 124.77, 113.27, 110.94.

HRMS (ESI): *m*/*z* calcd for [($C_{13}H_9NO_4$)Na] [M + Na]$^+$: 266.0429; found: 266. 0430.

N-[2-(Naphthalen-1-yl)-2-oxoacetyl]benzamide (3i)

Yield: 920 mg (87%); light yellow solid; mp 74–76 °C.

IR (ATR): 3442, 3281, 1715, 1681, 1645, 1397, 1318, 1219, 768, 695 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.79 (s, 1 H), 9.12 (d, *J* = 8.4 Hz, 1 H), 8.12 (d, *J* = 8.0 Hz, 2 H), 7.93 (distorted t, *J* = 7.2 Hz, 3 H), 7.72 (t, *J* = 7.6 Hz, 1 H), 7.48–7.65 (m, 5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 188.69, 172.43, 165.23, 135.54, 134.11, 133.96, 133.60, 131.29, 131.08, 129.18, 129.14, 128.72, 128.10, 127.98, 126.99, 125.86, 124.31.

HRMS (ESI): *m*/*z* calcd for [($C_{19}H_{13}NO_3$)H] [M + H]$^+$: 304.0973; found: 304.0967.

N-[2-(Naphthalen-2-yl)-2-oxoacetyl]benzamide (3j)

Yield: 1.04 g (88%); light yellow solid; mp 184–186 °C.

IR (ATR): 3448, 1715, 1684, 1627, 1465, 1251, 710 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.84 (s, 1 H), 8.82 (s, 1 H), 8.15 (d, *J* = 8.4 Hz, 1 H), 7.89–8.00 (m, 5 H), 7.51–7.65 (m, 5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 186.50, 165.29 (2 C=O), 136.57, 134.13, 134.07, 132.63, 131.54, 130.35, 129.86, 129.73, 129.35, 129.19, 128.24, 128.10, 127.30, 124.54.

HRMS (ESI): *m*/*z* calcd for [($C_{19}H_{13}NO_3$)H] [M + H]$^+$: 304.0973; found: 304.0969.

N-[2-Oxo-2-(2-oxo-2*H*-chromen-3-yl)acetyl]benzamide (3k)

Yield: 994 mg (88%); yellow solid; mp 216–218 °C.

IR (ATR): 3262, 1725, 1708, 1671, 1602, 1563, 1252, 956, 760 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.39 (s, 1 H), 9.07 (s, 1 H), 8.03–8.10 (dd, *J* = 8.0, 7.6 Hz, 3 H), 7.84 (t, *J* = 7.6 Hz, 1 H), 7.72 (t, *J* = 7.6, 7.2 Hz, 1 H), 7.49–7.59 (m, 4 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 182.73, 170.16, 167.93, 158.83, 154.80, 148.65, 135.56, 134.00, 131.46, 130.10, 128.84, 128.64, 125.44, 119.93, 118.11, 116.54.

HRMS (ESI): *m*/*z* calcd for [($C_{18}H_{11}NO_5$)Na] [M + Na]$^+$: 344.0534; found: 344.0537.

N-[2-(4-Fluorophenyl)-2-oxoacetyl]benzamide (3l)

Yield: 1.22 g (90%); off-white solid; mp 158–160 °C.

IR (ATR): 3438, 1694, 1589, 1423, 1214, 1085, 698 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 12.48 (s, 1 H), 7.98–8.05 (m, 4 H), 7.70 (t, *J* = 7.2 Hz, 1 H), 7.55 (t, *J* = 7.8, 7.5 Hz, 2 H), 7.44 (t, *J* = 8.7 Hz, 2 H).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 186.16, 170.84, 167.34, 165.55 (d, J_F = 252.3 Hz), 134.00, 132.00 (d, J_F = 9.75 Hz), 130.36, 129.20 (d, J_F = 2.8 Hz), 128.83, 128.80, 116.45 (d, J_F = 22.3 Hz).

HRMS (ESI): *m*/*z* calcd for [($C_{15}H_{10}FNO_3$)H] [M + H]$^+$: 272.0723; found: 272.0729.

N-[2-(3-Chlorophenyl)-2-oxoacetyl]benzamide (3m)

Yield: 1.10 g (87%); light white solid; mp 74–76 °C.

IR (ATR): 3445, 3275, 1713, 1694, 1678, 1513, 1238, 768 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.59 (br s, 1 H), 8.11 (s, 1 H), 8.02 (d, *J* = 8.0 Hz, 1 H), 7.89 (d, *J* = 7.5 Hz, 2 H), 7.63–7.68 (distorted dd, *J* = 8.5 Hz, 2 H), 7.54 (distorted t, *J* = 7.0, 6.5 Hz, 2 H), 7.48 (distorted t, *J* = 7.5 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 185.08, 170.85, 169.35, 134.62, 133.38, 132.80, 132.45, 130.16, 129.75, 128.75, 128.18, 127.44, 125.50.

HRMS (ESI): *m*/*z* calcd for [($C_{15}H_{10}ClNO_3$)H] [M + H]$^+$: 288.0427 found 288.0423.

N-[2-(2,4-Dichlorophenyl)-2-oxoacetyl]benzamide (3n)

Yield: 1.01 g (89%); yellow solid; mp 78–80 °C.

IR (ATR): 3451, 3279, 1717, 1687, 1673, 1509, 1244, 759 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 12.55 (s, 1 H), 8.07 (t, *J* = 9.0, 8.4 Hz, 2 H), 7.95 (d, *J* = 7.2 Hz, 1 H), 7.86 (s, 1 H), 7.66–7.75 (distorted q, *J* = 9.6, 8.7, 6.9 Hz, 2 H), 7.60 (distorted t, *J* = 6.9 Hz, 2 H).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 183.93, 170.40, 167.75, 139.68, 134.92, 134.16, 133.40, 130.82, 130.16, 129.35, 128.92, 128.80, 128.36.

HRMS (ESI): *m*/*z* calcd for [($C_{15}H_9Cl_2NO_3$)H] [M + H]$^+$: 322.0037; found: 322.0035.

N-[2-(2-Bromophenyl)-2-oxoacetyl]benzamide (3o)

Yield: 925 mg (84%); yellow solid; mp 70–72 °C.

IR (ATR): 3456, 3274, 1719, 1688, 1587, 1211, 747 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.13 (s, 1 H), 7.91–8.02 (distorted ddd, *J* = 7.6, 6.8 Hz, 2 H), 7.68 (d, *J* = 7.2 Hz, 1 H), 7.58–7.64 (distorted q, *J* = 7.2 Hz, 1 H), 7.43–7.52 (m, 5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 186.50, 168.73, 165.71, 137.10 134.56, 134.32, 134.05, 132.82, 130.87, 129.10, 128.25, 127.62, 123.12.

HRMS (ESI): *m*/*z* calcd for [($C_{15}H_{10}BrNO_3$)H] [M + H]$^+$: 331.9922; found: 331.9929.

N-[2-(2,6-Dimethoxyphenyl)-2-oxoacetyl]benzamide (3p)

Yield: 826 mg (80%); light yellow solid; mp 124–126 °C.

IR (ATR): 3448, 3287, 1708, 1677, 1655, 1602, 1252, 1160, 742 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.05 (s, 1 H), 7.96 (d, *J* = 6.8 Hz, 2 H), 7.59 (t, *J* = 8.4, 6.8 Hz, 2 H), 7.46 (d, *J* = 6.8 Hz, 2 H), 7.17 (d, *J* = 7.2 Hz, 1 H), 6.93 (d, *J* = 8.4 Hz, 1 H), 3.84 (s, 3 H), 3.74 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 185.14, 170.92, 165.96, 154.92, 154.33, 133.84, 130.58, 129.04, 128.21, 124.11, 122.65, 114.40, 112.22, 56.75, 55.89.

HRMS (ESI): *m*/*z* calcd for [($C_{17}H_{15}NO_5$)H] [M + H]$^+$: 314.1028; found: 314.1031.

4-Methyl-N-(2-oxo-2-phenylacetyl)benzamide (3q)

Yield: 1.33 g (85%); white solid; mp 148–150 °C.

IR (ATR): 3352, 3288, 1719, 1681, 1674, 1518, 1256, 1228, 751 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.76 (br s, 1 H), 8.12 (d, *J* = 7.5 Hz, 2 H), 7.80–7.81 (distorted dd, *J* = 8.0, 1.5 Hz, 2 H), 7.66 (distorted tt, *J* = 7.5, 1.5 Hz, 1 H), 7.53 (distorted tt, *J* = 7.5, 1.5 Hz, 2 H), 7.30 (d, *J* = 7.5 Hz, 2 H), 2.43 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 186.85, 165.27 (2 C=O), 145.27, 134.79, 132.55, 130.24, 129.97, 129.06, 128.30, 21.85.

HRMS (ESI): *m*/*z* calcd for [($C_{16}H_{13}NO_3$)H] [M + H]$^+$: 268.0973; found: 268.0970.

4-Methoxy-N-(2-oxo-2-phenylacetyl)benzamide (3r)

Yield: 1.50 g (90%); white solid; mp 162–164 °C.

IR (ATR): 3260, 1721, 1685, 1675, 1585, 1254, 1226, 749 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.83 (br s, 1 H), 8.09 (d, *J* = 7.5 Hz, 2 H), 7.89 (d, *J* = 9.0 Hz, 2 H), 7.65 (t, *J* = 7.5 Hz, 1 H), 7.52 (t, *J* = 8.0 Hz, 2 H), 6.97 (d, *J* = 9.0 Hz, 2 H), 3.87 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 186.99, 164.80, 164.42, 134.70, 132.63, 130.58, 130.11, 129.06, 123.05, 114.55, 55.76.

HRMS (ESI): *m*/*z* calcd for [($C_{16}H_{13}NO_4$)H] [M + H]$^+$: 284.0923; found: 284.0925.

4-Nitro-N-(2-oxo-2-phenylacetyl)benzamide (3s)

Yield: 1.45 g (83%); light yellow solid; mp 188–190 °C.

IR (ATR): 3336, 3250, 1736, 1680, 1515, 1356, 1208, 1168, 768, 720 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.54 (br s, 1 H), 8.38 (d, *J* = 9.0 Hz, 2 H), 8.28 (d, *J* = 8.5 Hz, 2 H), 7.89 (d, *J* = 7.0 Hz, 2 H), 7.68 (t, *J* = 7.5 Hz, 1 H), 7.55 (t, *J* = 8.0, 7.5 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 186.27, 170.20, 165.57, 151.62, 137.10, 136.20, 134.57, 131.14, 129.46, 128.22, 124.21.

HRMS (ESI): *m*/*z* calcd for [($C_{15}H_{10}N_2O_5$)H] [M+ H]$^+$: 299.0668; found: 299.0671.

Acknowledgment

Financial support from the Council of Scientific and Industrial Research, New Delhi [sanction no. 01(2427)/10/EMR-II dated 28/12/2010 and pool scheme no. 8644-A], India, to carry out this work is gratefully acknowledged. H.P.K. and K.S.V. thank Council of Scientific and Industrial Research and University Grants Commission-Special Assistance Programme, New Delhi, respectively, for the award of Senior Research Fellowships. The authors thank Prof. Prakash M. Bhate for his generous support.

Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0034-1379955.

References

(1) (a) Humphrey, J. M.; Chamberlin, A. R. *Chem. Rev.* **1997**, *97*, 2243. (b) Carey, J. S.; Laffan, D.; Thomson, C.; Williams, M. T. *Org. Biomol. Chem.* **2006**, *4*, 2337. (c) Allen, C. L.; Williams, J. M. J. *Chem. Soc. Rev.* **2011**, *40*, 3405. (d) Ozawa, F.; Soyama, H.; Yamamoto, T.; Yamamoto, A. *Tetrahedron Lett.* **1982**, *23*, 3383. (e) Couve-Bonnaire, S.; Carpentier, J.-F.; Castanet, Y.; Mortreux, A. *Tetrahedron Lett.* **1999**, *40*, 3717. (f) Mehdi, S. *Bioorg. Chem.* **1993**, *21*, 249. (g) Patel, D. V.; Gless, R. D. J.; Webb, H. H. K.; Anandan, S. K.; Aavula, B. R. Patent WO 2008073623, **2008**. (h) Tanaka, H.; Kuroda, A.; Marusawa, H.; Hatanaka, H.; Kino, T.; Goto, T.; Hashimoto, M.; Taga, T. *J. Am. Chem. Soc.* **1987**, *109*, 5031. (i) Hagihara, M.; Schreiber, S. L. *J. Am. Chem. Soc.* **1992**, *114*, 6570. (j) Qian, J.; Cuerrier, D.; Davies, P. L.; Li, Z.; Powers, J. C.; Campbell, R. L. *J. Med. Chem.* **2008**, *51*, 5264. (k) Ovat, A.; Li, Z. Z.; Hampton, C. Y.; Asress, S. A.; Fernández, F. M.; Glass, J. D.; Powers, J. C. *J. Med. Chem.* **2010**, *53*, 6326. (l) Li, Z.; Ortega-Vilain, A. C.; Patil, G. S.; Chu, D. L.; Foreman, J. E.; Eveleth, D. D.; Powers, J. C. *J. Med. Chem.* **1996**, *39*, 4089.

(2) (a) Wang, J.; Liu, C.; Yuan, J.; Lei, A. *Chem. Commun.* **2014**, *50*, 4736. (b) Hirai, K.; Shikakura, K.; Yano, T.; Ishikawa, C.; Ugai, S.; Yamada, O. Patent WO 199622285, **1996**. (c) Rao, K. V.; Rock, C. P. *J. Heterocycl. Chem.* **1996**, *33*, 447. (d) Yang, L.; Wang, D.-X.; Huang, Z.-T.; Wang, M.-X. *J. Am. Chem. Soc.* **2009**, *131*, 10390. (e) Reddy, Y. D.; Kumar, P. P.; Devi, B. R.; Dubey, P. K.; Kumari, Y. B. *Lett. Drug Des. Discovery* **2014**, *10*, 226. (f) Ram, S. R.; Devi, A. R.; Iyengar, D. S. *Chem. Lett.* **2002**, *31*, 718. (g) Eveleth, D. D.; Powers, J. C. *J. Med. Chem.* **1996**, *39*, 4089. (h) Chatterjee, S.; Dunn, D.; Tao, M.; Wells, G.; Gu, Z.; Bihovsky, R.; Ator, M. A.; Siman, R.; Mallamo, J. P. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 2371. (i) Dubowchik, G. M.; Ditta, J. L.; Herbst, J. J.; Bollini, S.; Vinitsky,

A. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 559. (j) Chen, Y.; Zhang, Y.; Zhang, H.; Liu, D.; Gu, M.; Li, J.; Wu, F.; Zhu, X.; Li, J.; Nan, F. *J. Med. Chem.* **2006**, *49*, 1613. (k) Sheha, M. M.; Mahfouz, N. M.; Hassan, H. Y.; Youssef, A. F. *Eur. J. Med. Chem.* **2000**, *35*, 887. (l) Crowley, C. A.; Delaet, N. G. J.; Ernst, J.; Grove, C. G.; Hepburn, B.; King, B.; Larson, C. J.; Miller, S.; Pryor, K.; Shuster, L. J. Patent WO 2007146712, **2007**. (m) Knust, H.; Nettekoven, M.; Pinard, E.; Roche, O. Patent WO 2009016087, **2009**. (n) Alvarez, S.; Alvarez, R.; Khanwalkar, H.; Germain, P.; Lemaire, G.; Rodríguez-Barrios, F.; Gronemeyer, H.; de Lera, A. R. *Bioorg. Med. Chem.* **2009**, *17*, 4345. (o) Natarajan, A.; Wang, K.; Ramamurthy, V.; Scheffer, J. R.; Patrick, B. *Org. Lett.* **2002**, *4*, 1443. (p) Liu, Q.; Rovis, T. *J. Am. Chem. Soc.* **2008**, *130*, 14066. (q) Sai, K. K. S.; Esteves, P. M.; da Penha, E. T.; Klumpp, D. A. *J. Org. Chem.* **2008**, *73*, 6506. (r) Tomita, D.; Yamatsugu, K.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2009**, *131*, 6946. (s) Coffinier, D.; El Kaim, L.; Grimaud, L. *Org. Lett.* **2009**, *11*, 1825. (t) Zhang, Z.; Zhang, Q.; Ni, Z.; Liu, Q. *Chem. Commun.* **2010**, *46*, 1269. (u) Jesuraj, J. L.; Sivaguru, J. *Chem. Commun.* **2010**, *46*, 4791.

(3) (a) Yang, Y.; Wang, G.; Cao, X.; Yan, X.; Chen, L. *J. Chem. Res.* **2011**, *35*, 657. (b) Sperry, J. *Synthesis* **2011**, 3569. (c) Bogen, S. L.; Arasappan, A.; Velazquez, F.; Blackman, M.; Huelgas, R.; Pan, W.; Siegel, E.; Nair, L. G.; Venkatraman, S.; Guo, Z.; Doll, R.; Shih, N.-Y.; Njoroge, F. G. *Bioorg. Med. Chem.* **2010**, *18*, 1854. (d) Xu, G. G.; Etzkorn, F. A. *Org. Lett.* **2010**, *12*, 696. (e) Montalban, A. G.; Boman, E.; Chang, C.-D.; Ceide, S. C.; Dahl, R.; Dalesandro, D.; Delaet, N. G. J.; Erb, E.; Gibbs, A.; Kahl, J.; Kessler, L.; Lundström, J.; Miller, S.; Nakanishi, H.; Roberts, E.; Saiah, E.; Sullivan, R.; Wang, Z.; Larson, C. J. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 5456. (f) Jones, I. L.; Schofield, D. J.; Strevens, R. R.; Horton, P. N.; Hursthouse, M. B.; Tomkinson, N. C. O. *Tetrahedron Lett.* **2007**, *48*, 521. (g) Cuerrier, D.; Moldoveanu, T.; Inoue, J.; Davies, P. L.; Campbell, R. L. *Biochemistry* **2006**, *45*, 7446. (h) Holenz, J.; Mercè, R.; Díaz, J. L.; Guitart, X.; Codony, X.; Dordal, A.; Romero, G.; Torrens, A.; Mas, J.; Andaluz, B.; Hernández, S.; Monroy, X.; Sánchez, E.; Hernández, E.; Pérez, R.; Cubí, R.; Sanfeliu, O.; Buschmann, H. *J. Med. Chem.* **2005**, *48*, 1781. (i) Barrett, D. G.; Catalano, J. G.; Deaton, D. N.; Long, S. T.; McFadyen, R. B.; Miller, A. B.; Miller, L. R.; Wells-Knecht, K. J.; Wright, L. L. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 2209. (j) Natarajan, A.; Wang, K.; Ramamurthy, V.; Scheffer, J. R.; Patrick, B. *Org. Lett.* **2002**, *4*, 1443. (k) Mueller-Westerhoff, U. T.; Zhou, M. *Tetrahedron Lett.* **1993**, *34*, 571. (l) Inoue, Y. *Chem. Rev.* **1992**, *92*, 741.

(4) (a) Valeur, E.; Bradley, M. *Chem. Soc. Rev.* **2009**, *38*, 606. (b) Al-Zoubi, R. M.; Marion, O.; Hall, D. G. *Angew. Chem. Int. Ed.* **2008**, *47*, 2876. (c) Srinivas, K. V. N. S.; Das, B. *J. Org. Chem.* **2003**, *68*, 1165. (d) Dunetz, J. R.; Xiang, Y.; Baldwin, A.; Ringling, J. *Org. Lett.* **2011**, *13*, 5048. (e) Allen, C. L.; Chhatwal, A. R.; Williams, J. M. J. *Chem. Commun.* **2012**, *48*, 666. (f) Li, J.; Subramaniam, K.; Smith, D.; Qiao, J. X.; Li, J. J.; Qian-Cutrone, J.; Kadow, J. F.; Vite, G. D.; Chen, B.-C. *Org. Lett.* **2012**, *14*, 214.

(5) Simas, A. B. C.; de Sales, D. L.; Pais, K. C. *Tetrahedron Lett.* **2009**, *50*, 6977.

(6) (a) Ocain, T. D.; Rich, D. H. *J. Med. Chem.* **1992**, *35*, 451. (b) Nakamura, M.; Inoue, J.; Yamada, T. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 2807. (c) Papanikos, A.; Rademann, J.; Meldal, M. *J. Am. Chem. Soc.* **2001**, *123*, 2176. (d) Hua, R.; Takeda, H.; Abe, Y.; Tanaka, M. *J. Org. Chem.* **2004**, *69*, 974.

(7) (a) Dubowchik, G. M.; Vrudhula, V. M.; Dasgupta, B.; Ditta, J.; Chen, T.; Sheriff, S.; Sipman, K.; Witmer, M.; Tredup, J.; Vyas, D. M.; Verdoorn, T. A.; Bollini, S.; Vinitsky, A. *Org. Lett.* **2001**, *3*, 3987. (b) Chiou, A.; Markidis, T.; Constantinou-Kokotou, V.; Verger, R.; Kokotos, G. *Org. Lett.* **2000**, *2*, 347. (c) Singh, R. P.; Shreeve, J. M. *J. Org. Chem.* **2003**, *68*, 6063.

(8) Yang, Z.; Zhang, Z.; Meanwell, N. A.; Kadow, J. F.; Wang, T. *Org. Lett.* **2002**, *4*, 1103.

(9) (a) Buu-Hoï, N. P.; Saint-Ruf, G.; Bourgeade, J. C. *J. Heterocycl. Chem.* **1968**, *5*, 545. (b) Chen, Y.-H.; Zhang, Y.-H.; Zhang, H.-J.; Liu, D.-Z.; Gu, M.; Li, J.-Y.; Wu, F.; Zhu, X.-Z.; Li, J.; Nan, F.-J. *J. Med. Chem.* **2006**, *49*, 1613. (c) Zaleska, B.; Lis, S. *Synth. Commun.* **2001**, *31*, 189. (d) Yoshifuji, S.; Arakawa, Y. *Chem. Pharm. Bull.* **1989**, *37*, 3380. (e) Wasserman, H. H.; Ives, J. L. *J. Org. Chem.* **1985**, *50*, 3573. (f) Ke-Qing, L.; Gang, J.; Hu, C.; Jian-Hua, X. *Tetrahedron Lett.* **1998**, *39*, 2381. (g) Ling, K.-Q.; Ye, J.-H.; Chen, X.-Y.; Ma, D.-J.; Xu, J.-H. *Tetrahedron* **1999**, *55*, 9185.

(10) (a) Liu, J.; Zhang, R.; Wang, S.; Sun, W.; Xia, C. *Org. Lett.* **2009**, *11*, 1321. (b) Ozawa, F.; Soyama, H.; Yanagihara, H.; Aoyama, I.; Takino, H.; Izawa, K.; Yamamoto, T.; Yamamoto, A. *J. Am. Chem. Soc.* **1985**, *107*, 3235. (c) Hermange, P.; Lindhardt, A. T.; Taaning, R. H.; Bjerglund, K.; Lupp, D.; Skrydstrup, T. *J. Am. Chem. Soc.* **2011**, *133*, 6061. (d) Friis, S. D.; Taaning, R. H.; Lindhardt, A. T.; Skrydstrup, T. *J. Am. Chem. Soc.* **2011**, *133*, 18114. (e) Uozumi, Y.; Arii, T.; Watanabe, T. *J. Org. Chem.* **2001**, *66*, 5272. (f) Iizuka, M.; Kondo, Y. *Chem. Commun.* **2006**, 1739. (g) Murphy, E. R.; Martinelli, J. R.; Zaborenko, N.; Buchwald, S. L.; Jensen, K. F. *Angew. Chem. Int. Ed.* **2007**, *46*, 1734.

(11) (a) Wasserman, H. H.; Petersen, A. K.; Xia, M. *Tetrahedron* **2003**, *59*, 6771. (b) Wasserman, H. H.; Ho, W.-B. *J. Org. Chem.* **1994**, *59*, 4364.

(12) (a) Semple, J. E.; Owens, T. D.; Nguyen, K.; Levy, O. E. *Org. Lett.* **2000**, *2*, 2769. (b) Bouma, M.; Masson, G.; Zhu, J. *J. Org. Chem.* **2010**, *75*, 2748. (c) Grassot, J.-M. Masson G.. Zhu J. *Angew. Chem. Int. Ed.* **2008**, *47*, 947.

(13) Yoo, W.-J.; Li, C.-J. *J. Am. Chem. Soc.* **2006**, *128*, 13064.

(14) Liu, Z.; Zhang, J.; Chen, S.; Shi, E.; Xu, Y.; Wan, X. *Angew. Chem. Int. Ed.* **2012**, *51*, 3231.

(15) (a) Zhang, C.; Jiao, N. *J. Am. Chem. Soc.* **2010**, *132*, 28. (b) Zhang, C.; Xu, Z.; Zhang, L.; Jiao, N. *Angew. Chem. Int. Ed.* **2011**, *50*, 11088. (c) Zhang, C.; Zong, X.; Zhang, L.; Jiao, N. *Org. Lett.* **2012**, *14*, 3280. (d) Du, F.-T.; Ji, J.-X. *Chem. Sci.* **2012**, *3*, 460.

(16) (a) Lamani, M.; Prabhu, K. R. *Chem. Eur. J.* **2012**, *18*, 14638. (b) Wei, W.; Shao, Y.; Hu, H.; Zhang, F.; Zhang, C.; Xu, Y.; Wan, X. *J. Org. Chem.* **2012**, *77*, 7157. (c) Zhang, X.; Wang, L. *Green Chem.* **2012**, *14*, 2141.

(17) (a) Wu, X.; Gao, Q.; Liu, S.; Wu, A. *Org. Lett.* **2014**, *16*, 2888. (b) Xue, W.-J.; Zhang, W.; Zheng, K.-L.; Dai, Y.; Guo, Y.-Q.; Li, H.-Z.; Gao, F.-F.; Wu, A. *Asian J. Org. Chem.* **2013**, *2*, 638. (c) Zhu, Y.; Jia, F.; Liu, M.; Wu, A. *Org. Lett.* **2012**, *14*, 4414. (d) Xue, W.-J.; Li, Q.; Zhu, Y.-P.; Wang, J.-G.; Wu, A. *Chem. Commun.* **2012**, *48*, 3485. (e) Gao, M.; Yang, Y.; Wu, Y.; Deng, C.; Cao, L.; Meng, X.; Wu, A. *Org. Lett.* **2010**, *12*, 1856.

(18) Zhang, Z.; Su, J.; Zha, Z.; Wang, Z. *Chem. Commun.* **2013**, *49*, 8982.

(19) Mupparapu, N.; Khan, S.; Battula, S.; Kushwaha, M.; Gupta, A. P.; Ahmed, Q. N.; Vishwakarma, R. A. *Org. Lett.* **2014**, *16*, 1152.

(20) (a) Jiang, H.; Huang, H.; Cao, H.; Qi, C. *Org. Lett.* **2010**, *12*, 5561. (b) Wan, C.; Gao, L.; Wang, Q.; Zhang, J.; Wang, Z. *Org. Lett.* **2010**, *12*, 3902. (c) Zhang, J.; Zhu, D.; Yu, C.; Wan, C.; Wang, Z. *Org. Lett.* **2010**, *12*, 2841. (d) Yan, Y.; Wang, Z. *Chem. Commun.* **2011**, *47*, 9513. (e) Zhang, J.; Wang, Z.; Wang, Y.; Wan, C.; Zheng, X.; Wang, Z. *Green Chem.* **2009**, *11*, 1973.

(21) Raszplewicz, K.; Sikorska, L.; Kiegiel, K.; Balakier, T.; Jurczak, J. *Polish J. Chem.* **2005**, *79*, 1901.