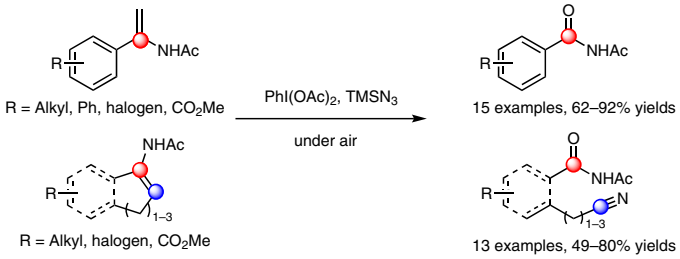
Synthesis G. Liu et al. Paper

Oxidative Cleavage of Enamides with Hypervalent Iodine(III)/ $TMSN_3$ under an Air Atmosphere

Ge Liu
Yan Li*
Jie Sheng
Xi-Sheng Wang*

Hefei National Laboratory for Physical Sciences at the Microscale and Department of Chemistry, University of Science and Technology of China, 96 Jinzhai Road, Hefei, Anhui 230026, P. R. of China
liyan08@ustc.edu.cn
xswang77@ustc.edu.cn



Received: 29.03.2017
Accepted after revision: 05.05.2017
Published online: 20.06.2017
DOI: 10.1055/s-0036-1589041; Art ID: ss-2017-h0205-op

Abstract An oxidative cleavage of C–C double bonds of enamides promoted by hypervalent iodine(III)/$TMSN_3$ under an air atmosphere is developed. This reaction provides a new approach to construct various cyanobenzamides, which offers further synthetic potential for the preparation of industrial and pharmaceutical nitrogen- and oxygen-containing molecules, and exhibits good functional group tolerance, broad substrate scope and mild conditions.

Key words oxidative cleavage, enamides, hypervalent iodine(III), $TMSN_3$, air atmosphere

Oxidative cleavage of carbon–carbon double bonds of alkenes represents an essential transformation in organic synthesis for both academic research and industrial applications.[1] The most common and fundamental protocols for the direct cleavage of C–C double bonds are ozonolysis[2] and Lemieux–Johnson oxidation,[3] although the safety concerns and toxicity of the oxidants has limited their utility to some extent. A recent alternative protocol is transition-metal catalysis using oxometals as oxygen-transfer agents in combination with a co-oxidant,[4] but there are still concerns regarding toxicity and the use of expensive metals. In accordance with the green trends in organic chemistry, metal-free oxidation has emerged as an attractive approach to cleave alkene double bonds. For instance, Ochiai and co-workers have developed an ecofriendly method using organoiodine reagents as catalysts and *m*CPBA as the co-oxidant.[5] The Vinod group has introduced an iodonium ion, generated from the oxidation of 4-iodobenzoic acid by Oxone in situ,[6] to facilitate the cleavage of alkenes. Meanwhile, Jiao et al. have reported an *N*-hydroxyphthalimide (NHPI)-catalyzed oxidative cleavage of olefins with molecular oxygen as the oxidant.[7]

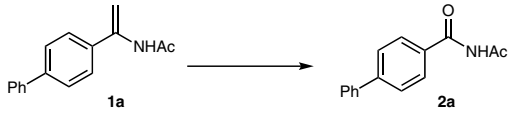
More remarkably, different from known methods to construct only oxygen-containing motifs, the Jiao group has recently developed a TEMPO-catalyzed oxygenation and nitrogenation through selective cleavage of simple alkenes with molecular oxygen as the terminal oxidant, which afforded various oxonitriles for the further synthesis of nitrogen- and oxygen-containing molecules.[8] However, this transformation was not efficient under an air atmosphere, and required a relatively high temperature. Moreover, only simple alkenes were compatible with this reaction, and electron-rich alkenes such as enamides have not been studied. Herein, we report a mild and easily handled method for the oxidative cleavage of enamides, in which $PhI(OAc)_2$ (PIDA) was used to promote the reaction with $TMSN_3$ under an air atmosphere.[9]

Our initial study started with *N*-[1-(biphenyl-4-yl)vinyl]acetamide (**1a**) as the model substrate in the presence of the Zhdankin reagent (BI-N_3) and a catalytic amount of CuCl (5 mol%) in toluene at 80 °C for 24 hours under an air atmosphere. To our delight, the desired product **2a** was obtained successfully in 23% yield (Table 1, entry 1). While copper salts were believed to promote the N–I(III) bond disconnection in previous reports,[10] our control experiment showed that CuCl was not involved in this reaction (entry 2). Next, a careful solvent screening revealed that MeCN afforded the oxidative diacylamine product in 57% yield, while diethyl ether and NMP gave none of the desired product (entries 3–7). Considering that BI-N_3 was prepared from the hypervalent iodine(III) reagent BI-OAc and $TMSN_3$, we tried to generate the analogue of BI-N_3 in situ with readily available I(III) reagents and $TMSN_3$ or NaN_3 (entries 9–13). Gratifyingly, the easiest to handle, $PhI(OAc)_2$, gave a higher yield of 76% with $TMSN_3$ (1.5 equiv) as the co-reagent at 40 °C. Given that some by-products could be detected under the reaction conditions, a reduction of the reaction time to 12 hours and decreasing the reaction temperature to 0 °C

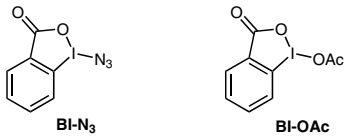
gave an enhanced 87% yield (entry 19). Finally, the addition of molecular sieves led to a slightly higher yield of 92% (entry 20). Of note is that only a 24% yield was obtained when using Jiao's method[8] to cleave the C–C double bond of enamide **1a** (entry 21).

With optimized reaction conditions in hand, a range of enamides was subjected to this oxidative cleavage reaction to investigate the scope. First, a variety of acyclic aryl enamides with different substituents were studied.

Table 1 Optimization of the Reaction Conditions[a]



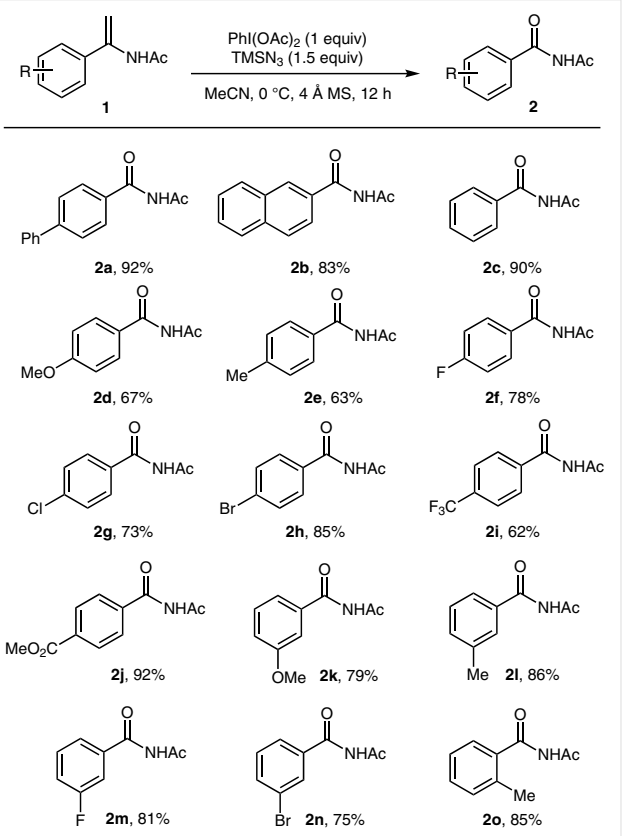
Entry	Reagent (equiv)	Solvent	Temp (°C)	Yield (%)[b]
1[c]	BI-N_3 (1.0)	toluene	80	23
2	BI-N_3 (1.0)	toluene	80	31
3	BI-N_3 (1.0)	toluene	60	39
4	BI-N_3 (1.0)	Et_2O	60	0
5	BI-N_3 (1.0)	$MeNO_2$	60	39
6	BI-N_3 (1.0)	NMP	60	0
7	BI-N_3 (1.0)	MeCN	60	57
8	BI-N_3 (1.0)	MeCN	40	62
9	BI-OAc (1), $TMSN_3$ (1.5)	MeCN	40	54
10	$PhI(OAc)_2$ (1), $TMSN_3$ (1.5)	MeCN	40	76[d]
11	$PhI(OCOCF_3)_2$ (1), $TMSN_3$ (1.5)	MeCN	40	41[d]
12	PhIO (1), $TMSN_3$ (1.5)	MeCN	40	63[d]
13	$PhI(OAc)_2$ (1), NaN_3 (1.5)	MeCN	40	43[d]
14	$PhI(OAc)_2$ (1), $TMSN_3$ (1.1)	MeCN	40	66[d]
15	$PhI(OAc)_2$ (1), $TMSN_3$ (2)	MeCN	40	70[d]
16	$PhI(OAc)_2$ (1.6), $TMSN_3$ (2)	MeCN	40	70[d]
17[e]	$PhI(OAc)_2$ (1), $TMSN_3$ (1.5)	MeCN	40	76[d]
18[e]	$PhI(OAc)_2$ (1), $TMSN_3$ (1.5)	MeCN	r.t.	75[d]
19[e]	$PhI(OAc)_2$ (1), $TMSN_3$ (1.5)	MeCN	0	87[d]
20[e,f]	$PhI(OAc)_2$ (1), $TMSN_3$ (1.5)	MeCN	0	92[d]
21[g]	TEMPO (15 mol%), $TMSN_3$ (1.5)	MeCN	80	24[d]



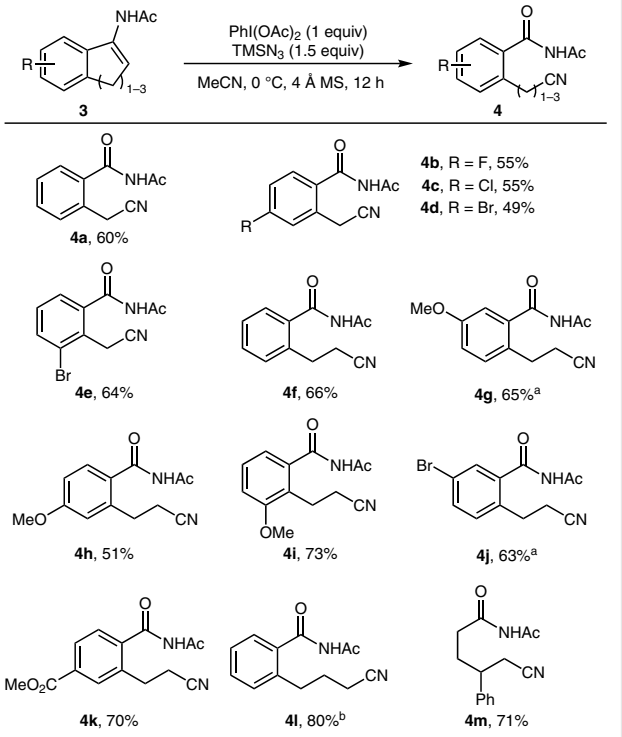
[a] Reaction conditions: **1a** (0.1 mmol, 1 equiv), solvent (2 mL), 24 h, under air.
[b] GC yield.
[c] CuCl (10 mol%) was used.
[d] Yield of isolated product.
[e] Reaction time = 12 h.
[f] 4 Å MS (200 mg) were added.
[g] Reaction run under O_2 (1 atm).

As shown in Scheme 1, investigation of the effects of substituents on the phenyl ring showed that both electron-donating groups (Me, OMe, and Ph) and electron-withdrawing groups (F, Cl, Br, CF_3, and CO_2Me) were well tolerated in this transformation, affording the corresponding products in moderate to high isolated yields after smooth cleavage of the C–C double bonds. Besides *para*-substituents on the phenyl rings, *ortho*- and *meta*-substituents were also compatible with this oxidative cleavage, which indicates that steric hindrance may not have a major effect on the transformation.

Inspired by the efficient oxidative cleavage of acyclic aryl enamides, we next surveyed cyclic enamides in this reaction to produce the corresponding bifunctional products. As shown in Scheme 2, to our delight, the C–C double bonds in cyclic enamides could also be successfully cleaved, affording the desired cyano diacylamine products, but with slightly lower isolated yields compared with the acyclic aryl enamides. The structures of the products further confirmed that the β-carbons in the enamides were converted into cyano groups.



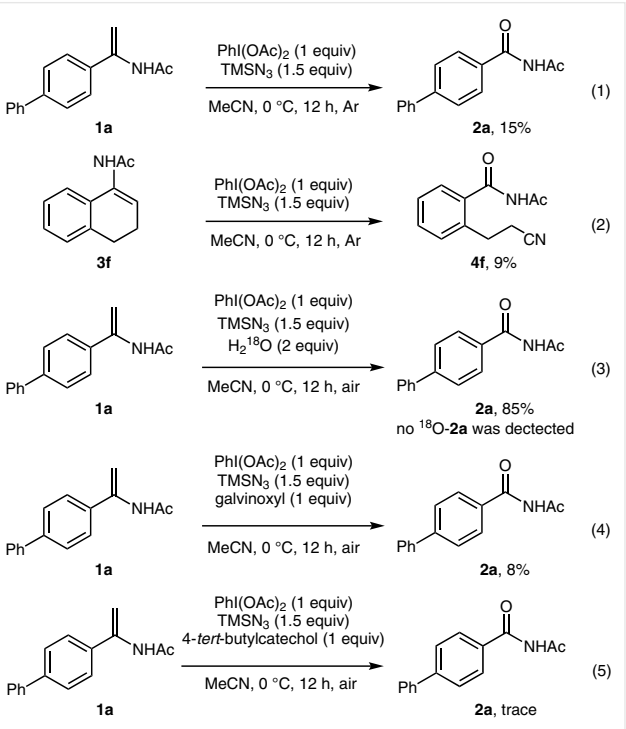
Scheme 1 Substrate scope of acyclic aryl enamides. *Reagents and conditions*: **1** (0.1 mmol, 1 equiv), $PhI(OAc)_2$ (1 equiv), $TMSN_3$ (1.5 equiv), MeCN (2 mL), 4 Å MS (200 mg), 0 °C, 12 h.



Scheme 2 Substrate scope of cyclic enamides. *Reagents and conditions*: **1** (0.1 mmol, 1 equiv), $PhI(OAc)_2$ (1 equiv), $TMSN_3$ (1.5 equiv), MeCN (2 mL), 4 Å MS (200 mg), 0 °C, 12 h. [a] Li_2CO_3 was added. [b] Reaction at −10 °C.

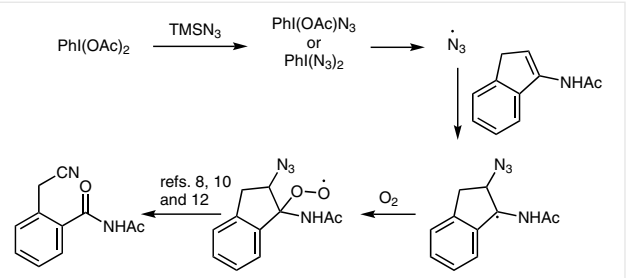
The electronic and steric effects of substituents on the phenyl rings were not obvious, as electron-withdrawing (CO_2Me), electron-donating (OMe) and *ortho*-substituted (Br, OMe) cyclic aryl enamides were all smoothly cleaved and bifunctionalized. Five- (**3a–e**), six- (**3f–k**) and seven- (**3l**) membered cyclic enamides gave the corresponding cyano diacylamines in good yields, which showed that ring strain had almost no effect on this protocol. Aliphatic cyclic enamide **3m** was also suitable for this transformation affording *N*-acetyl δ-cyanopentanamide **4m** in 71% yield.

To gain some insights into the mechanism of this transformation, a series of control experiments was carried out (Scheme 3). First, the reaction was performed under an argon atmosphere, which resulted in the yield of **2a** being significantly decreased to 15%, whilst the cyanobenzamide product **4f** was obtained in only 9% yield (eqs 1 and 2, Scheme 3), which indicated that $PhI(OAc)_2$ was not the sole oxidant and that molecular oxygen in air was involved in the reaction. Next, two equivalents of $H_2{}^{18}O$ were included in the standard conditions without the addition of molecular sieves. In this case, none of the ^{18}O-containing product was obtained, however, almost the same yield of **2a** was obtained [eq 3, Scheme 1 (see Table 1, entry 19)]. This result further demonstrated that the oxygen atom of the benzoyl group in **2a** originated from molecular oxygen and not the trace water in MeCN. Addition of radical scavengers inhibited the oxidation, which indicated that the process may involve a radical pathway (eqs 4 and 5, Scheme 1).



Scheme 3 Control experiments

Based on the results mentioned above and previous reports on the Zhdankin reagent,[11] a plausible mechanism via a radical path can be proposed. As shown in Scheme 4, the ligand exchange between $PhI(OAc)_2$ and $TMSN_3$ affords $PhI(N_3)_2$ or $PhI(OAc)N_3$ in situ, which undergoes thermal homolytic cleavage to generate an azide radical. The azide radical is then captured by the carbon–carbon double bond of the enamide to produce a benzyl radical, which is subsequently trapped by molecular oxygen to form a peroxy radical. Heterolysis of the O–O bond and release of N_2 cleaves the C–C bond to give the cyano diacylamine, as described in previous reports.[8,10,12]



Scheme 4 A plausible mechanism

In conclusion, we have developed a method for the oxidative cleavage of the C–C double bonds of enamides, which was promoted by hypervalent iodine(III) under mild reaction conditions with O_2 as the terminal oxidant. This protocol exhibits good functional group tolerance with both acyclic and cyclic enamides to afford useful diacylamine products. Further studies on the synthetic applications of this process for the total synthesis of complex molecules are ongoing in our lab.

Enamides **1** were prepared according to the reported procedure.[13] All commercially available compounds were used without further purification. TLC was performed on plates precoated with silica gel F254, purchased from Shandong Huanghai Chemical Co. Ltd., and visualized with a UV lamp (254 nm). Yields refer to those of chromatographically purified compounds. Column chromatography was performed on silica gel (200–300) purchased from Shandong Huanghai Chemical Co. Ltd. Melting points were obtained using a Beijing Tektronix X-4 digital microscopic melting point apparatus. NMR spectra were recorded on a Bruker-400 (400 MHz for ^{1}H; 100 MHz for ^{13}C) instrument and the spectra are internally referenced to $SiMe_4$ at δ 0.00 for ^{1}H, and the $CDCl_3$ signal at δ 77.16 for ^{13}C. High-resolution mass spectra were recorded on P-SIMS-Gly of BrukerDaltonics Inc. Waters Xevo G2 QTof using ESI-TOF (electrospray ionization–time of flight).

Diacylamines 2 and 4; General Procedure

Enamide **1** or **3** (0.1 mmol, 1.0 equiv), $PhI(OAc)_2$ (32.2 mg, 0.1 mmol, 1.0 equiv), $TMSN_3$ (19.6 μL, 0.15 mmol, 1.5 equiv), 4 Å MS (200 mg) and MeCN (2 mL) were combined in a 35 mL sealed tube. The reaction mixture was stirred at 0 °C for 12 h. After cooling to r.t., the reaction mixture was filtered through a plug of silica, washed with EtOAc, concentrated under vacuum and the residue purified by column chromatography on silica gel (gradient elution: PE and EtOAc) to give the corresponding product.

N-Acetyl-[1,1′-biphenyl]-4-carboxamide (2a)

White solid; yield: 22 mg (92%); mp 166–168 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.00 (s, 1 H), 7.96 (d, *J* = 8.3 Hz, 2 H), 7.72 (d, *J* = 8.2 Hz, 2 H), 7.63 (d, *J* = 7.4 Hz, 2 H), 7.48 (t, *J* = 7.4 Hz, 2 H), 7.42 (t, *J* = 7.2 Hz, 1 H), 2.64 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 174.0, 165.7, 146.2, 139.6, 131.3, 129.1, 128.54, 128.49, 127.7, 127.4, 25.8.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{13}NO_2Na$: 262.0844; found: 262.0844.

N-Acetyl-2-naphthamide (2b)

White solid; yield: 18 mg (83%); mp 147–152 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.16 (s, 1 H), 8.42 (s, 1 H), 8.07–7.80 (m, 4 H), 7.71–7.46 (m, 2 H), 2.67 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 174.0, 166.0, 135.6, 132.5, 129.9, 129.4, 129.13, 129.07, 128.8, 128.0, 127.3, 123.7, 25.8.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{13}H_{11}NO_2Na$: 236.0687; found: 236.0680.

N-Acetylbenzamide (2c)

White solid; yield: 15 mg (90%); mp 114.4–121.3 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.10 (s, 1 H), 7.92–7.83 (m, 2 H), 7.60 (t, *J* = 7.4 Hz, 1 H), 7.50 (t, *J* = 7.7 Hz, 2 H), 2.61 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 174.0, 166.0, 133.4, 132.8, 129.1, 127.9, 25.8.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_9H_9NO_2Na$: 186.0531; found: 186.0526.

N-Acetyl-4-methoxybenzamide (2d)

White solid; yield: 13 mg (67%); mp 110–116 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.83 (s, 1 H), 7.85 (d, *J* = 7.7 Hz, 2 H), 6.97 (d, *J* = 7.7 Hz, 2 H), 3.87 (s, 3 H), 2.60 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.9, 165.2, 163.8, 130.0, 124.8, 114.3, 55.7, 25.7.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{10}H_{11}NO_3Na$: 216.0637; found: 216.0630.

N-Acetyl-4-methylbenzamide (2e)

White solid; yield: 11 mg (63%); mp 146–149 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.03 (s, 1 H), 7.78 (d, *J* = 8.0 Hz, 2 H), 7.29 (d, *J* = 8.0 Hz, 2 H), 2.60 (s, 3 H), 2.42 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.6, 165.6, 144.3, 129.8, 127.8, 25.7, 21.7.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{10}H_{11}NO_2Na$: 200.0687; found: 200.0678.

N-Acetyl-4-fluorobenzamide (2f)

White solid; yield: 14 mg (78%); mp 106–109 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.24 (s, 1 H), 7.95 (t, *J* = 8.3 Hz, 2 H), 7.18 (t, *J* = 8.3 Hz, 2 H), 2.60 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 174.2, 165.9 (d, *J* = 255.5 Hz), 164.9, 130.6 (d, *J* = 9.3 Hz), 128.9 (d, *J* = 3.0 Hz), 116.3 (d, *J* = 22.1 Hz), 25.8.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_9H_8FNO_2Na$: 204.0437; found: 204.0433.

N-Acetyl-4-chlorobenzamide (2g)

White solid; yield: 14 mg (73%); mp 135–139 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.18 (s, 1 H), 7.85 (d, *J* = 8.5 Hz, 2 H), 7.48 (d, *J* = 8.5 Hz, 2 H), 2.61 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 174.0, 165.0, 139.9, 131.1, 129.4, 129.3, 25.7.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_9H_8ClNO_2Na$: 220.0141; found: 220.0136.

N-Acetyl-4-bromobenzamide (2h)

White solid; yield: 21 mg (85%); mp 147–159 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.18 (s, 1 H), 7.77 (d, *J* = 8.6 Hz, 2 H), 7.64 (d, *J* = 8.6 Hz, 2 H), 2.60 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 174.2, 165.2, 132.4, 131.6, 129.5, 128.5, 25.9.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_9H_8BrNO_2Na$: 263.9636; found: 263.9637.

N-Acetyl-4-(trifluoromethyl)benzamide (2i)

White solid; yield: 14 mg (62%); mp 139–144 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.08 (s, 1 H), 8.01 (d, *J* = 8.2 Hz, 2 H), 7.78 (d, *J* = 8.3 Hz, 2 H), 2.63 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.8, 164.8, 136.1, 134.9 (q, *J* = 33.3 Hz), 128.4, 126.2 (q, *J* = 4.0 Hz), 123.6 (q, *J* = 272.7 Hz), 25.8.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{10}H_8F_3NO_2Na$: 254.0405; found: 254.0408.

***N*-Acetyl-4-(methoxycarbonyl)benzamide (2j)**

White solid; yield: 20 mg (92%); mp 107–108 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.10 (s, 1 H), 8.15 (d, *J* = 8.1 Hz, 2 H), 7.95 (d, *J* = 8.1 Hz, 2 H), 3.95 (s, 3 H), 2.62 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.7, 166.0, 165.1, 136.5, 134.3, 130.2, 127.9, 52.7, 25.8.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{11}H_{11}NO_4Na$: 244.0586; found: 244.0582.

***N*-Acetyl-3-methoxybenzamide (2k)**

White solid; yield: 15 mg (79%); mp 85–88 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.02 (s, 1 H), 7.50–7.34 (m, 3 H), 7.12 (d, *J* = 7.7 Hz, 1 H), 3.86 (s, 3 H), 2.60 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 174.0, 165.8, 160.1, 134.1, 130.1, 119.9, 119.8, 112.7, 55.6, 25.9.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{10}H_{11}NO_3Na$: 216.0637; found: 216.0629.

***N*-Acetyl-3-methylbenzamide (2l)**

White solid; yield: 15 mg (86%); mp 76–79 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.00 (s, 1 H), 7.77–7.60 (m, 2 H), 7.47–7.33 (m, 2 H), 2.60 (s, 3 H), 2.42 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.8, 166.1, 139.1, 134.1, 132.7, 129.0, 128.5, 124.9, 25.7, 21.4.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{10}H_{11}NO_2Na$: 200.0687; found: 200.0681.

***N*-Acetyl-3-fluorobenzamide (2m)**

White solid; yield: 15 mg (81%); mp 79–83 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.10 (s, 1 H), 7.63 (t, *J* = 9.3 Hz, 2 H), 7.49 (dd, *J* = 13.5, 7.9 Hz, 1 H), 7.35–7.27 (m, 1 H), 2.61 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.9, 164.7, 163.0 (d, *J* = 250.7 Hz), 135.0 (d, *J* = 6.9 Hz), 130.8 (d, *J* = 7.8 Hz), 123.3 (d, *J* = 2.7 Hz), 120.5 (d, *J* = 21.1 Hz), 115.4 (d, *J* = 23.3 Hz), 25.8.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_9H_8FNO_2Na$: 204.0437; found: 204.0431.

***N*-Acetyl-3-bromobenzamide (2n)**

White solid; yield: 18 mg (75%); mp 136–140 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.08 (s, 1 H), 8.06 (s, 1 H), 7.80 (d, *J* = 7.7 Hz, 1 H), 7.73 (d, *J* = 8.0 Hz, 1 H), 7.38 (t, *J* = 7.9 Hz, 1 H), 2.61 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.8, 164.6, 136.3, 134.7, 131.2, 130.6, 126.3, 123.3, 25.8.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_9H_8BrNO_2Na$: 263.9636; found: 263.9637.

***N*-Acetyl-2-methylbenzamide (2o)**

White solid; yield: 15 mg (85%); mp 82–83 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.33 (s, 1 H), 7.48–7.35 (m, 2 H), 7.32–7.18 (m, 2 H), 2.58 (s, 3 H), 2.49 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.0, 168.0, 137.6, 134.0, 131.9, 131.7, 127.0, 126.2, 25.6, 20.2.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{10}H_{11}NO_2Na$: 200.0687; found: 200.0683.

***N*-Acetyl-2-(cyanomethyl)benzamide (4a)**

White solid; yield: 12 mg (60%); mp 135–138 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.92 (s, 1 H), 7.67–7.53 (m, 3 H), 7.47 (s, 1 H), 4.08 (s, 2 H), 2.57 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.3, 166.9, 132.9, 132.4, 130.9, 130.8, 128.7, 128.0, 117.7, 25.7, 22.3.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{11}H_{10}N_2O_2Na$: 225.0640; found: 225.0634.

***N*-Acetyl-2-(cyanomethyl)-4-fluorobenzamide (4b)**

Brown solid; yield: 12 mg (55%); mp 130–134 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.78 (s, 1 H), 7.72–7.63 (m, 1 H), 7.36 (d, *J* = 9.0 Hz, 1 H), 7.18–7.15 (m, 1 H), 4.10 (s, 2 H), 2.56 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.4, 166.0, 164.7 (d, *J* = 256.5 Hz), 134.4 (d, *J* = 8.6 Hz), 130.6 (d, *J* = 9.4 Hz), 128.5 (d, *J* = 3.0 Hz), 118.4 (d, *J* = 23.6 Hz), 117.1, 115.7 (d, *J* = 21.6 Hz), 25.7, 22.4.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{11}H_9FN_2O_2Na$: 243.0546; found: 243.0548.

***N*-Acetyl-4-chloro-2-(cyanomethyl)benzamide (4c)**

White solid; yield: 13 mg (55%); mp 137–139 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.72 (s, 1 H), 7.61 (s, 1 H), 7.57 (d, *J* = 8.0 Hz, 1 H), 7.46 (d, *J* = 8.0 Hz, 1 H), 4.07 (s, 2 H), 2.57 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.0, 165.9, 139.3, 133.0, 131.0, 130.6, 129.2, 129.0, 117.0, 25.7, 22.2.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{11}H_9ClN_2O_2Na$: 259.0250; found: 259.0247.

***N*-Acetyl-4-bromo-2-(cyanomethyl)benzamide (4d)**

Pale brown solid; yield: 14 mg (49%); mp 159–160 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.90 (s, 1 H), 7.76 (s, 1 H), 7.62 (d, *J* = 8.3 Hz, 1 H), 7.50 (d, *J* = 8.3 Hz, 1 H), 4.06 (s, 2 H), 2.56 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.1, 166.1, 133.9, 133.0, 132.0, 131.1, 129.2, 127.6, 117.1, 25.7, 22.1.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{11}H_9BrN_2O_2Na$: 302.9745; found: 302.9746.

***N*-Acetyl-3-bromo-2-(cyanomethyl)benzamide (4e)**

White solid; yield: 18 mg (64%); mp 197–198 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.65 (s, 1 H), 7.82 (d, *J* = 7.9 Hz, 1 H), 7.55 (d, *J* = 7.6 Hz, 1 H), 7.35 (t, *J* = 7.9 Hz, 1 H), 4.17 (s, 2 H), 2.59 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.7, 166.3, 136.9, 135.9, 130.2, 127.5, 126.8, 116.5, 25.7, 21.9.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{11}H_9BrN_2O_2Na$: 302.9745; found: 302.9743.

***N*-Acetyl-2-(2-cyanoethyl)benzamide (4f)**

White solid; yield: 14 mg (66%); mp 99–104 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.66 (s, 1 H), 7.52 (t, *J* = 7.5 Hz, 2 H), 7.43–7.35 (m, 2 H), 3.10 (t, *J* = 7.1 Hz, 2 H), 2.78 (t, *J* = 7.1 Hz, 2 H), 2.55 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.9, 167.5, 138.6, 133.5, 132.4, 131.8, 127.8, 127.6, 119.3, 29.8, 25.6, 19.6.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{12}H_{12}N_2O_2$: 239.0797; found: 239.0790.

***N*-Acetyl-2-(2-cyanoethyl)-5-methoxybenzamide (4g)**

Pale brown solid; yield: 16 mg (65%); mp 95–97 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.50 (s, 1 H), 7.52 (d, *J* = 8.6 Hz, 1 H), 6.91 (s, 1 H), 6.86 (d, *J* = 8.7 Hz, 1 H), 3.88 (s, 3 H), 3.12 (t, *J* = 7.1 Hz, 2 H), 2.80 (t, *J* = 7.0 Hz, 2 H), 2.55 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.2, 166.8, 162.6, 141.8, 129.9, 125.1, 119.4, 117.8, 112.8, 55.7, 30.3, 25.5, 19.5.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{13}H_{14}N_2O_3Na$: 269.0902; found: 269.0904.

***N*-Acetyl-2-(2-cyanoethyl)-4-methoxybenzamide (4h)**

White solid; yield: 13 mg (51%); mp 119.4–121 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.78 (s, 1 H), 7.53 (d, *J* = 8.6 Hz, 1 H), 6.89 (d, *J* = 2.5 Hz, 1 H), 6.84 (dd, *J* = 8.6, 2.5 Hz, 1 H), 3.86 (s, 3 H), 3.10 (t, *J* = 7.1 Hz, 2 H), 2.78 (t, *J* = 7.1 Hz, 2 H), 2.52 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.4, 166.9, 162.5, 141.7, 130.0, 125.0, 119.4, 117.7, 112.6, 55.6, 30.2, 25.5, 19.4.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{13}H_{14}N_2O_3$: 269.0902; found: 269.0899.

***N*-Acetyl-2-(2-cyanoethyl)-3-methoxybenzamide (4i)**

White solid; yield: 18 mg (73%); mp 140.6–141.5 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.53 (s, 1 H), 7.33 (t, *J* = 8.0 Hz, 1 H), 7.05 (t, *J* = 8.2 Hz, 2 H), 3.88 (s, 3 H), 3.11 (t, *J* = 7.5 Hz, 2 H), 2.68 (t, *J* = 7.5 Hz, 2 H), 2.55 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.7, 167.4, 158.3, 135.8, 128.8, 126.5, 119.9, 118.8, 113.7, 55.9, 25.6, 23.4, 17.5.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{13}H_{14}N_2O_3Na$: 269.0902; found: 269.0898.

***N*-Acetyl-5-bromo-2-(2-cyanoethyl)benzamide (4j)**

White solid; yield: 19 mg (63%); mp 132.6–136.5 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.80 (s, 1 H), 7.72–7.58 (m, 2 H), 7.39–7.17 (m, 1 H), 3.04 (t, *J* = 7.0 Hz, 2 H), 2.77 (t, *J* = 6.9 Hz, 2 H), 2.54 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.8, 166.2, 137.3, 135.3, 133.4, 130.7, 121.5, 119.1, 29.3, 25.6, 19.5.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{12}H_{11}BrN_2O_2Na$: 316.9902; found: 316.9898.

Methyl 4-(Acetylcarbamoyl)-3-(2-cyanoethyl)benzoate (4k)

White solid; yield: 19 mg (70%); mp 121.7–122.2 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.83 (s, 1 H), 8.02 (d, *J* = 8.5 Hz, 2 H), 7.59 (d, *J* = 7.9 Hz, 1 H), 3.94 (s, 3 H), 3.14 (t, *J* = 7.2 Hz, 2 H), 2.78 (t, *J* = 7.2 Hz, 2 H), 2.54 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.7, 167.0, 165.8, 138.5, 137.6, 133.4, 132.4, 129.0, 127.7, 119.0, 52.8, 29.6, 25.7, 19.4.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{14}N_2O_4Na$: 297.0851; found: 297.0846.

***N*-Acetyl-2-(3-cyanopropyl)benzamide (4l)**

White solid; yield: 18 mg (80%); mp 52.7–55.4 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.58 (s, 1 H), 7.47 (t, *J* = 7.3 Hz, 2 H), 7.32 (t, *J* = 7.0 Hz, 2 H), 2.92 (t, *J* = 7.1 Hz, 2 H), 2.55 (s, 3 H), 2.38 (t, *J* = 7.1 Hz, 2 H), 2.08–1.89 (m, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.9, 167.8, 140.1, 133.9, 132.0, 131.2, 127.3, 127.0, 119.6, 32.3, 27.4, 25.5, 16.9.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{13}H_{14}N_2O_2Na$: 253.0953; found: 253.0950.

***N*-Acetyl-5-cyano-4-phenylpentanamide (4m)**

Colorless liquid; yield: 17 mg (71%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.86 (s, 1 H), 7.35 (t, *J* = 7.3 Hz, 2 H), 7.29 (d, *J* = 7.0 Hz, 1 H), 7.21 (d, *J* = 7.4 Hz, 2 H), 3.03 (td, *J* = 11.7, 6.8 Hz, 1 H), 2.64 (d, *J* = 7.0 Hz, 2 H), 2.44 (t, *J* = 6.7 Hz, 2 H), 2.26 (s, 3 H), 2.24–2.14 (m, 1 H), 2.12–2.00 (m, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.3, 172.0, 140.5, 129.2, 128.0, 127.3, 118.4, 41.5, 34.8, 29.3, 25.3, 25.1.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{16}N_2O_2Na$: 267.1109; found: 267.1111.

Funding Information

We gratefully acknowledge the National Science Foundation of China (21602213, 21522208, 21372209) for financial support.

Supporting Information

Supporting information for this article is available online at https://doi.org /10.1055/s-0036-1589041.

References

(1) (a) Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483. (b) Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413. (c) Minatti, A.; Muniz, K. *Chem. Soc. Rev.* **2007**, *36*, 1142. (d) McDonald, R. I.; Liu, G.; Stahl, S. S. *Chem. Rev.* **2011**, *111*, 2981. (e) Sheldon, R. A.; Kochi, J. K. *Metal-Catalyzed Oxidations of Organic Compounds*; Academic Press: New York, **1981**.

(2) (a) Criegee, R. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 745. (b) Bailey, P. S. *Ozonation in Organic Chemistry*; Academic Press: New York, **1978**.

(3) Pappo, R.; Allen, D. Jr.; Lemieux, R. U.; Johnson, W. S. *J. Org. Chem.* **1956**, *21*, 478.

(4) (a) Kinneary, J. F.; Albert, J. S.; Burrows, C. J. *J. Am. Chem. Soc.* **1988**, *110*, 6124. (b) Barton, D. H. R.; Wang, T. L. *Tetrahedron Lett.* **1994**, *35*, 1519. (c) Baucherel, X.; Uziel, J.; Juge, S. *J. Org. Chem.* **2001**, *66*, 4504. (d) Travis, B. R.; Narayan, R. S.; Borhan, B. *J. Am. Chem. Soc.* **2002**, *124*, 3824. (e) Kogan, V.; Quintal, M. M.; Neumann, R. *Org. Lett.* **2005**, *7*, 5039. (f) de Boer, J. W.; Brinksma, J.; Browne, W. R.; Meetsma, A.; Alsters, P. L.; Hage, R.; Feringa, B. L. *J. Am. Chem. Soc.* **2005**, *127*, 7990. (g) Xing, D.;

Guan, B.; Cai, G.; Fang, Z.; Yang, L.; Shi, Z. *Org. Lett.* **2006**, *8*, 693. (h) Neisius, N. M.; Plietker, B. *J. Org. Chem.* **2008**, *73*, 3218. (i) Wang, A.; Jiang, H. *J. Org. Chem.* **2010**, *75*, 2321.

(5) Miyamoto, K.; Sei, Y.; Yamaguchi, K.; Ochiai, M. *J. Am. Chem. Soc.* **2009**, *131*, 1382.

(6) Thottumkara, P. P.; Vinod, T. K. *Org. Lett.* **2010**, *12*, 5640.

(7) Lin, R.; Chen, F.; Jiao, N. *Org. Lett.* **2012**, *14*, 4158.

(8) Wang, T.; Jiao, N. *J. Am. Chem. Soc.* **2013**, *135*, 11692.

(9) For a preliminary study on the oxidative cleavage of simple alkenes with the hypervalent iodine/$TMSN_3$ system, see: Ehrenfreund, J.; Zbiral, E. *Tetrahedron* **1970**, *26*, 2945.

(10) Zhou, W.; Zhang, L.; Jiao, N. *Angew. Chem. Int. Ed.* **2009**, *48*, 7094.

(11) (a) Stang, P. J.; Zhdankin, V. V. *Chem. Rev.* **1996**, *96*, 1123. (b) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2002**, *102*, 2523. (c) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2008**, *102*, 5299.

(12) (a) Kita, Y.; Tohma, H.; Takada, T.; Mitoh, S.; Fujita, S.; Gyoten, M. *Synlett* **1994**, 427. (b) Chen, D. J.; Chen, Z. C. *Tetrahedron Lett.* **2000**, *41*, 7361. (c) Pedersen, C. M.; Marinescu, L. G.; Bols, M. *Org. Biomol. Chem.* **2005**, *3*, 816. (d) Matcha, K.; Narayan, R.; Antonchick, A. P. *Angew. Chem. Int. Ed.* **2013**, *52*, 7985.

(13) (a) Zhou, H.; Xu, Y. H.; Chung, W. J.; Loh, T. P. *Angew. Chem. Int. Ed.* **2009**, *48*, 5355. (b) Guan, Z. H.; Zhang, Z. Y.; Ren, Z. H.; Wang, Y. Y.; Zhang, X. M. *J. Org. Chem.* **2011**, *76*, 339.