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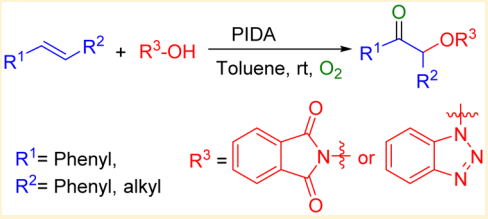
Phenyliodonium Diacetate Mediated Oxidative Functionalization of Styrenes with Molecular Oxygen: Synthesis of α-Oxygenated Ketones

Supravat Samanta, Ramachandra Reddy Donthiri, Chitrakar Ravi, and Subbarayappa Adimurthy*

Academy of Scientific & Innovative Research, CSIR-Central Salt & Marine Chemicals Research Institute, G.B. Marg, Bhavnagar 364 002. Gujarat, India

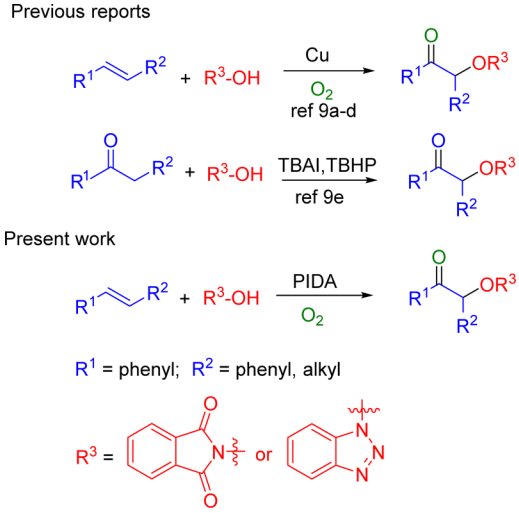
Supporting Information

ABSTRACT: Synthesis of α-oxygenated ketones from styrenes mediated by phenyliodonium diacetate in the presence of molecular oxygen and *N*-hydroxyphthalimide or *N*-hydroxybenzotriazole has been described. Addition of carbonyl oxygen at the α-position and formation of C−O bond at the β-position of styrenes was achieved under metal-free conditions. The present method is applicable for wide range of styrenes with a variety of functional groups.



Ideally, the use of molecular oxygen as a source for the oxidation and oxidative functionalization of C−H bonds under mild reaction conditions to construct various oxygenated molecules would be the most important approach and considered to be an essential area of research.[1] Molecular oxygen is a desirable source to incorporate in organic molecules as it is environmentally safe and abundantly available.[2] Considering the importance of oxygen incorporation in organic molecules, a number of transition-metal catalysts have been developed,[3] but limited reports exist for such activation of molecular oxygen under metal-free conditions.[4] Alkenes the simple and important molecules and have a wide range of applications in organic synthesis to obtain oxygenated molecules such as 1,2-diols,[5] α-hydroxy ketones,[6] and 1,2-dicarbonyl compounds.[7] Many transition-metal-catalyzed reactions were developed for the incorporation of oxygen in hydrocarbons by the activation of molecular oxygen.[8] Recently, the Punniyamurthy,[9a] Woerpel,[9b] Liang,[9c] and Lei[9d] groups independently reported a copper-catalyzed oxidation of alkenes with molecular oxygen and hydroxylamine derivatives (*N*-hydroxyphthalimide (NHPI),[10] *N*-hydroxybenzotriazole (HOBt), or *N*-hydroxy-*N*-phenylcarbamate) to synthesize α-oxygenated ketones. However, the reported approaches are all in the presence of transition-metal catalysts. Very recently, Prabhu's group described the α-oxygenation of aryl ketones under metal-free conditions.[9e] Notably, α-oxygenated ketones are extensively useful in both medicinal and biological sciences.[11] These ketones are useful for the synthesis of α-halo ketones, α-azido ketones, β-keto alkoxyamines, and vinyl phosphates.[9a,b] Considering the importance of these α-oxygenated ketones, the development of metal-free conditions is desirable to avoid the possible contamination of traces of metals in the final products. The significant importance of the iodine or derivatives as an alternative to transition-metal catalysts and our continuous efforts for the development of such reactions[12] inspired us to investigate the possibility of phenyliodonium diacetate (PIDA) mediated dioxygenation of alkenes with molecular oxygen and hydroxylamine derivatives (Scheme 1).

Scheme 1. Aerobic Dioxygenation of Alkenes



To the best of our knowledge, no such reports are available for the synthesis of α-oxygenated ketones from alkenes under metal-free conditions.

We initiated our studies with 4-methylstyrene **1a** as a model substrate for the synthesis of 2-(2-oxo-2-(*p*-tolyl)ethoxy)-isoindoline-1,3-dione **3a** using commercially available NHPI **2** and PIDA at room temperature under O_2 atmosphere, and the results are illustrated in Table 1. We obtained a 61% yield of **3a** when the reaction was performed using 0.25 mmol of **1a**, 0.25 mmol of **2**, and 0.5 mmol of PIDA in toluene at room temperature after 18 h (entry 1). No reaction was observed when the same reaction was performed with other oxidants like $KHSO_5$, $K_2S_2O_8$, NIS, *m*-CPBA, TBHP, DTBP, and I_2 (entries 2−8). Furthermore, when a reaction with 0.5 mmol

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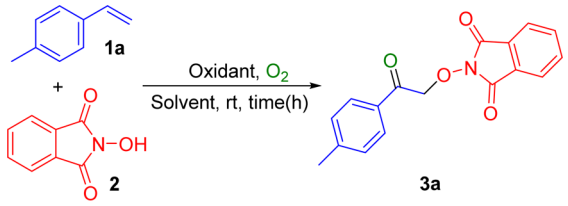
Table 1. Optimization of the Reaction Conditions for 3a[a]



entry	oxidant (equiv)	solvent	time (h)	yield of **3a** (%)
1	PIDA (2)	toluene	18	61
2	$KHSO_5$ (2)	toluene	18	0
3	$K_2S_2O_8$ (2)	toluene	18	0
4	NIS (2)	toluene	18	0
5	*m*-CPBA (2)	toluene	18	0
6	TBHP (2)	toluene	18	0
7	DTBP (2)	toluene	18	0
8	I_2 (2)	toluene	18	0
9[b]	**PIDA (2)**	**toluene**	**18**	**85**
10	PIDA (2)	toluene	24	85
11	PIDA (1.5)	toluene	18	70
12	PIDA (2)	toluene	12	76
13		toluene	18	0
14	PIDA (2)	DCE	36	60
15	PIDA (2)	CH_3CN	36	56
16	PIDA (2)	DMF	36	65
17	PIDA (2)	DMSO	36	27
18	PIDA (2)	dioxane	36	38
19	PIDA (2)	EtOH	36	25
20	PIDA (2)	H_2O	36	16
21	IBX (2)	toluene	24	65

[a]Reaction conditions unless otherwise stated: **1a** (0.25 mmol), **2** (0.25 mmol), 0.50 mmol of oxidant, solvent (2.0 mL), rt, O_2 atmosphere (O_2 balloon), isolated yields. [b]For entries 9–21. 0.4 mmol of **1a** and 0.25 mmol of **2** were used.

of PIDA, 0.4 mmol of **1a**, and 0.25 mmol of **2** was performed under the same conditions, **3a** was isolated in 85% yield (entry 9). No improvement of yield was observed by prolonged reaction to 24 h (entry 10). When the amount of PIDA or the reaction time was descreased, the yield of the product also decreased (entries 11 and 12), and in the absence of PIDA no product formation was observed (entry 13). When the reaction was performed in other solvents or with other hypervalent iodine reagents, the yield was not improved (entries 14–21).

On the basis of the results obtained from the screening of the reaction conditions, the optimized conditions were fixed as 0.4 mmol of **1a**, 0.25 mmol of **2**, and 0.5 mmol of PIDA in 2.0 mL of toluene at room temperature under O_2 atmosphere for 18 h.

Having optimized conditions in hand, we explored the substrate scope for the present transformation by employing various alkenes, and the results are compiled in Table 2. The styrene reacted smoothly with **2** under the optimized conditions and gave the product **3b** in 84% yield. Different substituents at the *para* position of styrene such as bromo, chloro, fluoro, methoxy, acetoxy, phenyl, and *tert*-butyl were well tolerated and afforded the corresponding α-oxygenated ketones (**3c–i**) in good yields. The reaction of either *meta*- or *ortho*-substituted styrenes and di- or trisubstituted styrenes also smoothly proceeded to yield the corresponding products (**3j–o**) with 63–78% yields. Vinylnaphthalene also led to the α-oxygenated ketone **3p** in 81% yield. In the case of *trans*-β methylstyrene and *trans*-stilbene, the products **3q** and **3r** were isolated in 63% and 61% yields, respectively. Cyclic alkenes like 1,2-dihydronaphthalene, 1*H*-indene, and cyclohexa-1,3-diene reacted smoothly to give the corresponding products (**3s–u**) in good yields. Notably, cinnamyl alcohol was also oxidized to give the product **3v** in 47% yield. However, the present protocol is not efficient to oxidize vinylpyridine and cyclohexene (**3w** and **3x**).

In order to see the effect of α-substituents on styrene, we performed a reaction with α-methylstyrene and obtained a number of unidentified products. In place of methyl, when α-bromostyrene derivatives were subjected to the same reaction conditions, we obtained the corresponding keto products **3a–c** in 64–73% yields. This indicates no effect of bromo substitution at the α-position of styrene (Scheme 2).

On the basis of literature reports of HOBt for oxidation reactions,[9b,e] we studied the reactivity of HOBt in place of NHPI under optimized conditions, and the oxidation of styrenes with HOBt gave the corresponding α-oxygenated ketones **6a–6d** in moderate yields (Table 3).

To gain insight into the reaction mechanism, a reaction was performed by the addition of 0.5 mmol of (2,2,6,6-tetramethyl-1-piperidin-1-yl)oxyl (TEMPO) under optimized conditions, and a TEMPO adduct **7** was isolated in 87% yield instead of keto product **3a** (Scheme 3, eq 1). It indicates that the reaction may proceed through a radical pathway. Further, the same reaction was performed under argon atmosphere, and only traces of the desired product **3a** were observed (Scheme 3, eq 2). This reaction indicates the molecular oxygen is the source of carbonyl oxygen. To know whether the reaction proceeds through the intermediate (2-hydroperoxy-2-(*p*-tolyl)-ethyl)isoindoline-1, 3-dione **8**, we subjected **8** to oxidation in the presence of PIDA and isolated the keto product **3a** in 92% yield (Scheme 3, eq 3).

On the basis of the above observations and the literature reports,[9a,c,d,13] a plausible reaction mechanism has been proposed (Scheme 4). Initially, the reaction of NHPI with PIDA generates a PINO$^\bullet$ radical. Reaction of PINO$^\bullet$ with olefin generates alkyl radical intermediate **A**. In the presence of oxygen, **A** converts to peroxy radical **B**, whose internal reaction with NHPI generates peroxide intermediate **8**. Finally oxidation of **8** in the presence of PIDA leads to the desired product **3a**.

CONCLUSION

In conclusion, we have developed an efficient method for the synthesis of α-oxygenated ketones directly from styrenes by employing commercially available NHPI through PIDA-mediated aerobic dioxygenation at room temperature. The present method is advantageous as it is applicable for a wide range of substrates with a variety of functional group tolerances under metal-free conditions.

EXPERIMENTAL SECTION

General Methods. All commercially available chemicals and reagents were used without any further purification unless otherwise indicated. ^{1}H and ^{13}C NMR spectra were recorded at 500, 200, and 125 and 50 MHz, respectively. The spectra were recorded in $CDCl_3$ as solvent. Multiplicity was indicated as follows: s (singlet), d (doublet), t (triplet), m (multiplet), dd (doublet of doublets), etc., and coupling constants (J) are given in hertz (Hz). Chemical shifts are reported in ppm relative to TMS as an internal standard. The peaks around δ values of ^{1}H NMR (7.26) and ^{13}C NMR (77.0) correspond to

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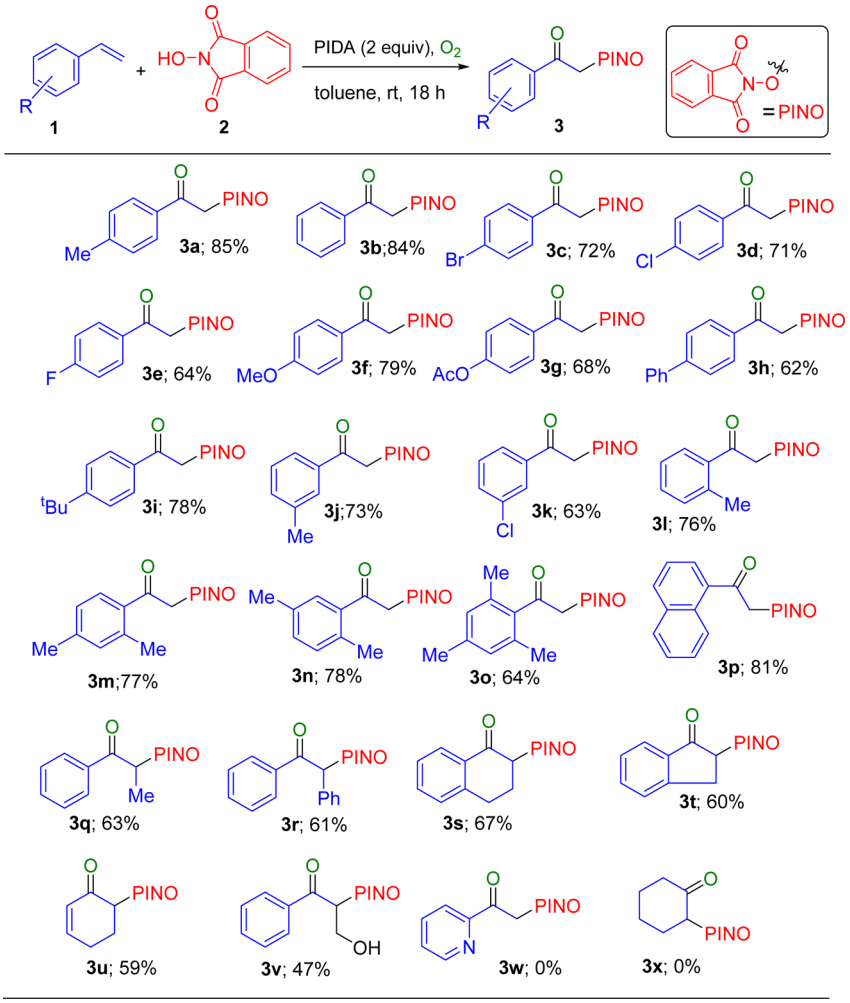
Table 2. Substrate Scope for α-Oxygenated Ketones from Olefins with NHPI[a]



[a]Reaction conditions otherwise stated: 0.40 mmol of **1a**, 0.25 mmol of **2**, and 0.50 mmol of PIDA in 2.0 mL of toluene, isolated yields.

Scheme 2. Oxidation of α-Bromostyrenes

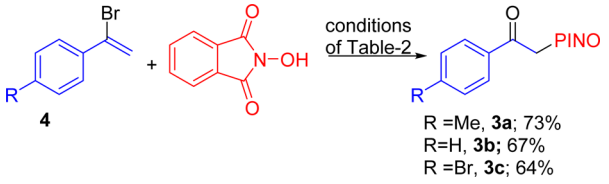
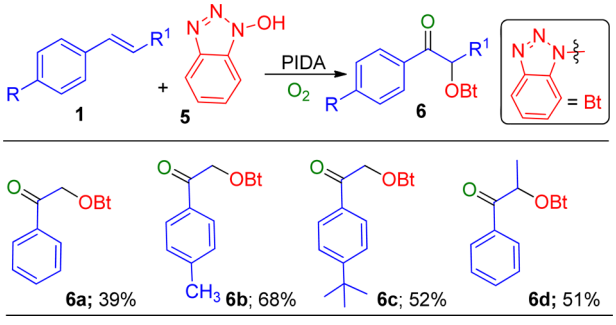
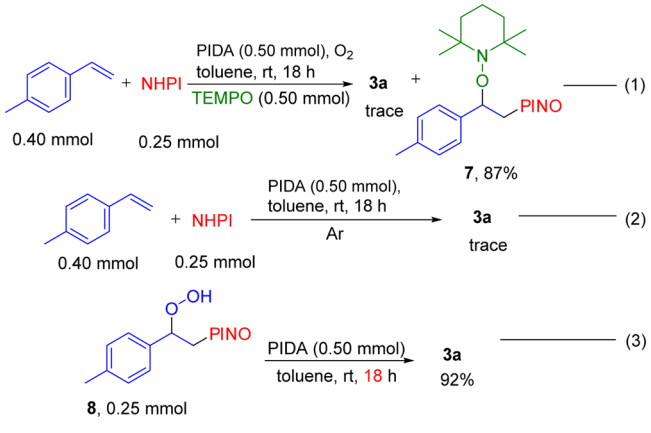


Table 3. Oxidation of Styrenes with HOBt[a]



[a]Conditions: 0.4 mmol of **1**, 0.25 mmol of **5** (HOBt), and 0.5 mmol of PIDA in 2.0 mL of toluene at rt, in O_2 atmosphere for 24 h, isolated yields.

Scheme 3. Mechanistic Experiments



deuterated solvent $CDCl_3$. All products were purified through column chromatography using silica gel (100–200 mesh size) using ethyl acetate/hexane as eluent.

Typical Experimental Procedure for the Synthesis of 2-(2-Oxo-2-*p*-tolylethoxy)isoindoline-1,3-dione (3a). In a reaction tube, 47.2 mg (0.40 mmol) of 4-methylstyrene (**1a**), 40.75 mg (0.25 mmol) of *N*-hydroxyphthalimide (**2**), and 161 mg (0.50 mmol) of PIDA were added in 2.0 mL of toluene. After the reaction mixture was stirred under oxygen atmosphere at room temperature for 18 h,

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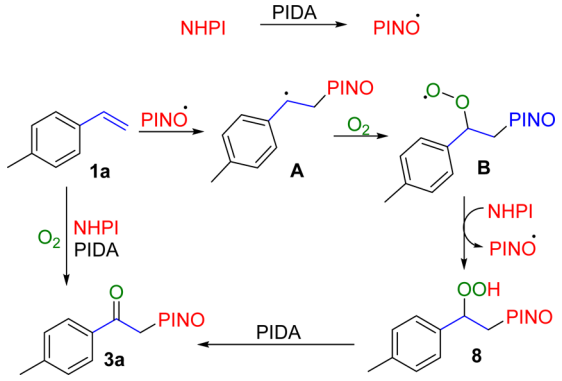
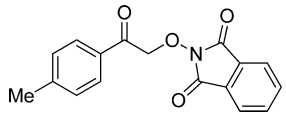
Scheme 4. Plausible Mechanism



10 mL of water was added. The mixture was extracted with DCM (3 × 10 mL) and dried over anhydrous Na_2SO_4. After removal of DCM under vacuum, the remaining crude mixture was purified by column chromatography (silica gel 100−200 mesh size) using hexane and ethyl acetate, and the product **3a** was isolated in 85% yield.

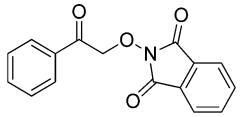
Typical Experimental Procedure for the Synthesis of 2-((1*H*-benzo[*d*][1,2,3]triazol-1-yl)oxy)-1-phenylethanone (6a). In a reaction tube, 41.6 mg (0.40 mmol) of styrene, 33.75 mg (0.25 mmol) of HOBt (**5**), and 161 mg (0.50 mmol) of PIDA were added in 2.0 mL of toluene. After the reaction mixture was stirred under oxygen atmosphere at room temperature for 24 h, 10 mL of water was added. The mixture was extracted with DCM (3 × 10 mL) and dried over anhydrous Na_2SO_4. After removal of DCM under vacuum, the remaining crude mixture was purified by column chromatography (silica gel 100−200 mesh size) using hexane and ethyl acetate, and the product **6a** was isolated in 39% yield.

Charecterization Data of All Compounds. *2-(2-Oxo-2-p-tolylethoxy)isoindoline-1,3-dione (**3a**):*[9a]



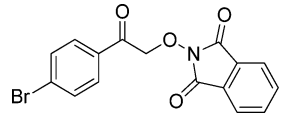
yield (63 mg, 85%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, J = 8.0 Hz, 2H), 7.84−7.83 (m, 2H), 7.76−7.74 (m, 2H), 7.29 (d, J = 8.0 Hz, 2H), 5.42 (s, 2H), 2.42 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 191.8, 163.0, 145.1, 134.6, 131.9, 129.5, 128.8, 128.4, 123.7, 78.4, 21.7.

*2-(2-Oxo-2-phenylethoxy)isoindoline-1,3-dione (**3b**):*[9a]



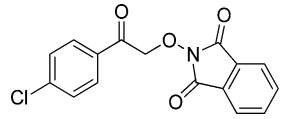
yield (59 mg, 84%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, J = 8.0 Hz, 2H), 7.84−7.82 (m, 2H), 7.75−7.73 (m, 2H), 7.62−7.59 (m, 1H), 7.50 (t, J = 8.0 Hz, 2H), 5.44 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) 192.5, 163.2, 134.9, 134.6,134.3, 129.1, 129.0, 128.5, 123.9, 78.7.

*2-(2-(4-Bromophenyl)-2-oxoethoxy)isoindoline-1,3-dione (**3c**):*[9a]



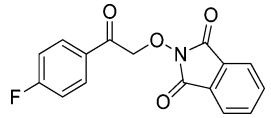
yield (65 mg, 72%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, J = 8.5 Hz, 2H), 7.85−7.84 (m, 2H), 7.77−7.76 (m, 2H), 7.66 (d, J = 8.5 Hz, 2H), 5.37 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) 191.5, 162.9, 134.7, 133.1, 132.2, 130.0, 129.4, 128.7, 123.8, 78.6.

*2-(2-(4-Chlorophenyl)-2-oxoethoxy)isoindoline-1,3-dione (**3d**):*[9a]



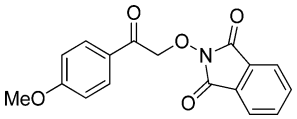
yield (56 mg, 71%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, J = 7.5 Hz, 2H), 7.84−7.83 (m, 2H), 7.765−7.76 (m, 2H), 7.49 (t, J = 7.0 Hz, 2H), 5.37 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) 191.3, 163.0, 140.6, 134.7, 132.7,129.9, 129.2, 128.7, 123.7, 78.6.

*2-(2-(4-Fluorophenyl)-2-oxoethoxy)isoindoline-1,3-dione (**3e**):*[9a]



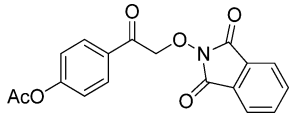
yield (48 mg, 64%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10−8.07 (m, 2H), 7.86−7.84 (m, 2H), 7.77−7.76 (m, 2H), 7.20 (t, J = 8.5 Hz, 2H), 5.38 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) 190.8, 167.2 (d, J_{1C-F} = 254.7 Hz), 163.0, 134.7, 131.3, 131.2, 128.7, 123.7, 116.1 (J_{2C-F} = 21.8 Hz) 78.6.

*2-(2-(4-Methoxyphenyl)-2-oxoethoxy)isoindoline-1,3-dione (**3f**):*[9a]



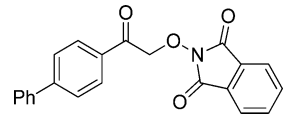
yield (61.5 mg, 79%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, J = 8.5 Hz, 2H), 7.82−7.81 (m, 2H), 7.74−7.72 (m, 2H), 6.95 (d, J = 8.5 Hz, 2H), 5.36 (s, 2H), 3.86 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 190.7, 164.2, 163.0, 134.6, 130.8, 128.8, 127.5, 123.6, 114.0, 78.4, 55.5.

*4-(2-((1,3-Dioxoisoindolin-2-yl)oxy)acetyl)phenyl acetate (**3g**):*[9a]



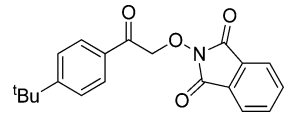
yield (57 mg, 68%); ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.08 (d, J = 8.4 Hz, 2H), 7.86−7.83 (m, 2H), 7.78−7.74 (m, 2H), 7.26 (d, J = 8.6 Hz, 2H), 5.41 (s, 2H), 2.33 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) 191.1, 168.6, 163.0, 155.0, 134.7, 131.9, 130.1, 128.7, 123.7, 122.0, 78.5, 21.1.

*2-(2-([1,1′-Biphenyl]-4-yl)-2-oxoethoxy)isoindoline-1,3-dione (**3h**):*[9a]



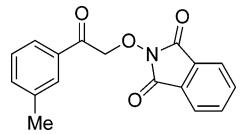
yield (55 mg, 62%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (d, J = 8.5 Hz, 2H), 7.86−7.84 (m, 2H), 7.76−7.74 (m, 2H), 7.72 (d, J = 8.5 Hz, 2H), 7.63 (d, J = 8.0 Hz, 2H), 7.47−7.45 (m, 2H), 7.42−7.39 (m, 1H), 5.47 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) 191.8, 163.0, 146.7, 139.5, 134.6, 133.0, 128.9, 128.8, 128.7, 128.4, 127.4, 127.2, 123.7, 78.5.

*2-(2-(4-tert-Butylphenyl)-2-oxoethoxy)isoindoline-1,3-dione (**3i**):*



white solid; mp 163 °C; Yield (65 mg, 78%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, J = 8.5 Hz, 2H), 7.84−7.82 (m, 2H), 7.75−7.73 (m, 2H), 7.50 (d, J = 8.5 Hz, 2H), 5.43 (s, 2H), 1.32 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) 191.8, 163.0, 157.9, 134.6, 131.8, 128.8, 128.3, 125.8, 123.7, 78.4, 35.2, 31.0; FT-IR (KBr) 3061, 2962, 1788, 1732, 1695, 1465, 1368, 1245, 1187, 1136, 1073, 979, 877, 699; HRMS $[M + H]^+$ calcd for $C_{20}H_{20}NO_4$ 338.1392, found 338.1409.

*2-(2-Oxo-2-m-tolylethoxy)isoindoline-1,3-dione (**3j**):*[9a]



yield (54 mg, 73%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84−7.82 (m, 2H), 7.79 (s, 1H), 7.76−7.74 (m, 3H), 7.42 (d, J = 8.0 Hz, 1H),

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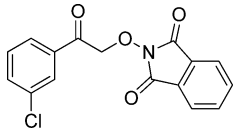
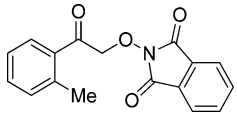
7.38 (t, J = 7.5 Hz, 1H), 5.43 (s, 2H), 2.40 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 192.3, 163.0, 138.7, 134.9, 134.6, 134.4, 128.8, 128.7, 125.4, 123.7, 78.4, 21.3.

*2-(2-(3-Chlorophenyl)-2-oxoethoxy)isoindoline-1,3-dione (**3k**):*[9a]



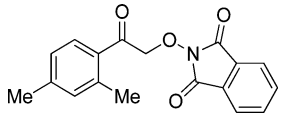
yield (50 mg, 63%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.92 (d, J = 7.5 Hz, 1H), 7.85−7.84 (m, 2H), 7.77−7.76 (m, 2H), 7.59 (d, J = 8.0 Hz, 1H), 7.47 (t, J = 8.0 Hz, 1H), 5.39 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) 191.2, 162.9, 135.9, 135.2, 134.7, 134.0, 130.1, 128.7, 128.6, 126.6, 123.7, 78.6.

*2-(2-Oxo-2-o-tolylethoxy)isoindoline-1,3-dione (**3l**):*[9a]



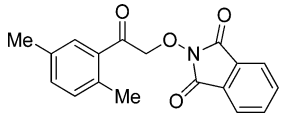
yield (56 mg, 76%); ^{1}H NMR (500 MHz, $CDCl_3$); δ 7.85 (dd, J_1 = 8.0 Hz, J_2 = 2.5 Hz, 2H), 7.76−7.75 (m, 3H), 7.4 (t, J = 7.5 Hz, 1H), 7.31 (t, J = 7.5 Hz, 2H), 5.33 (s, 2H), 2.56 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 195.3, 163.0, 139.7, 134.6, 134.3, 132.5, 132.3, 129.2, 128.8, 125.7, 123.7, 79.5, 21.3.

*2-(2-(2,4-Dimethylphenyl)-2-oxoethoxy)isoindoline-1,3-dione (**3m**):*[9a]



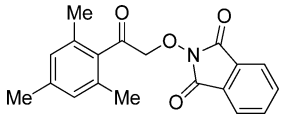
yield (59 mg, 77%); ^{1}H NMR (500 MHz, $CDCl_3$); δ 7.84−7.82 (m, 2H), 7.75−7.73 (m, 2H), 7.68 (d, J = 8.5 Hz, 1H), 7.09 (s, 2H), 5.31 (s, 2H), 2.54 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$):194.4, 163.0, 143.3, 140.1, 134.6, 133.2, 131.2, 129.5, 128.8, 126.3, 123.6, 79.3, 21.4.

*2-(2-(2,5-Dimethylphenyl)-2-oxoethoxy)isoindoline-1,3-dione (**3n**):*



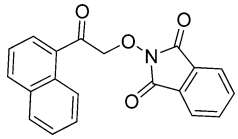
white solid; mp 162 °C Yield (60 mg, 78%); ^{1}H NMR (500 MHz, $CDCl_3$); δ 7.86−7.84 (m, 2H), 7.77−7.75 (m, 2H), 7.56 (s, 1H), 7.25 (d, J = 7.5 Hz, 1H), 7.18 (d, J = 8.0 Hz, 1H), 5.33 (s, 2H), 2.51 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 195.3, 163.0, 136.5, 135.3, 134.5, 134.2, 133.2, 132.1, 129.7, 128.8, 123.6, 79.4, 20.7. FT-IR (KBr) 2973, 2909, 1785, 1731, 1705, 1465, 1359, 1250, 1187, 1127, 1053, 980, 875, 705; HRMS $[M + H]^+$ calcd for $C_{18}H_{16}NO_4$ 310.1079, found 310.1091.

*2-(2-Mesityl-2-oxoethoxy)isoindoline-1,3-dione (**3o**):*[9a]



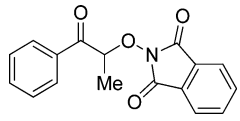
yield (51 mg, 64%); ^{1}H NMR (500 MHz, $CDCl_3$); δ 7.83−7.81 (m, 2H), 7.75−7.73 (m, 2H), 6.84 (s, 2H), 5.06 (s, 2H), 2.27 (s, 6H), 2.26 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 203.2, 163.0, 139.8, 135.3, 134.8, 134.1, 128.9, 128.7, 123.8, 80.9, 21.3, 19.2.

*2-(2-(Naphthalen-1-yl)-2-oxoethoxy)isoindoline-1,3-dione (**3p**):*[9a]



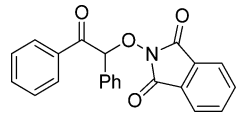
Yield (67 mg, 81%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.77 (d, J = 8.5 Hz, 1H), 8.05−8.02 (m, 2H), 7.88−7.85 (m, 2H), 7.82−7.80 (m, 1H), 7.77−7.75 (m, 2H), 7.62 (t, J = 7.0 Hz, 1H), 7.55−7.51 (m, 2H), 5.47 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$):195.3, 163.0, 134.8, 134.6, 134.1, 131.5, 130.3, 129.2, 128.7, 128.5, 128.4, 126.6, 125.6, 124.1, 123.6, 79.4.

*2-((1-oxo-1-phenylpropan-2-yl)oxy)isoindoline-1,3-dione (**3q**):*[9a]



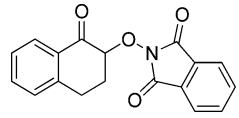
yield (46 mg, 63%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 (d, J = 7.5 Hz, 2H), 7.83−7.82 (m, 2H), 7.75−7.74 (m, 2H), 7.61−7.58 (m, 1H), 7.51 (t, J = 7.5 Hz, 2H), 5.77 (m, 1H), 1.69 (d, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 195.3, 163.6, 134.9, 134.6, 133.7, 129.2, 128.8, 128.6, 123.7, 83.6, 16.2.

*2-(2-Oxo-1,2-diphenylethoxy)isoindoline-1,3-dione (**3r**):*[9a]



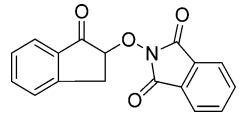
yield (54 mg, 61%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, J = 7.0 Hz, 2H), 7.76−7.74 (m, 2H), 7.70−7.68 (m, 2H), 7.62−7.60 (m, 2H), 7.53 (t, J = 7.5 Hz, 1H), 7.42 (t, J = 7.5 Hz, 2H), 7.35−7.34 (m, 3H), 6.76 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) 192.7, 163.1, 134.7, 134.4, 133.6, 132.5, 129.9, 129.3, 129.0, 128.8, 128.64, 128.6, 123.5, 88.2.

*2-((1-Oxo-1,2,3,4-tetrahydronaphthalen-2-yl)oxy)isoindoline-1,3-dione (**3s**):*[9a]



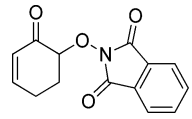
yield (51 mg, 67%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, J = 8.0 Hz, 1H), 7.83−7.82 (m, 2H), 7.77−7.73 (m, 2H), 7.53 (t, J = 7.5 Hz, 1H), 7.35 (t, J = 7.5 Hz, 1H), 7.28 (d, J = 8.5 Hz, 1H), 4.96−4.94 (m, 1H), 3.36−3.30 (m, 1H), 3.04−2.96 (m, 1H), 2.60−2.52 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) 192.5, 163.5, 143.4, 134.6, 134.3, 131.4, 129.0, 128.8, 128.1, 127.2, 123.8, 84.5, 28.4, 25.9.

*2-((1-Oxo-2,3-dihydro-1H-inden-2-yl)oxy)isoindoline-1,3-dione (**3t**):*[9a]



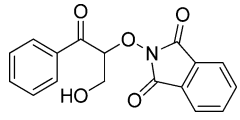
yield (44 mg, 60%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87−7.86 (m, 2H), 7.80−7.76 (m, 3H), 7.67−7.64 (m, 1H), 7.49 (d, J = 7.5 Hz, 1H), 7.43 (t, J = 7.5 Hz, 1H), 5.14−5.11 (m, 1H), 3.65−3.60 (m, 1H), 3.44−3.40 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) 199.4, 163.3, 150.8, 136.2, 134.6, 134.5, 128.8, 128.2, 126.6, 124.9, 123.7, 82.9, 32.5.

*2-((2-Oxocyclohex-3-en-1-yl)oxy)isoindoline-1,3-dione (**3u**):*[9a]



yield (38 mg, 60%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85−7.84 (m, 2H), 7.78−7.77 (m, 2H), 7.15−7.13 (m, 1H), 6.11 (d, J = 10.0 Hz, 1H), 5.03−5.02 (m, 1H), 2.79−2.75 (m, 1H), 2.45−2.44 (m, 1H), 2.36−2.34 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) 197.7, 164.0, 145.4, 134.7, 131.7, 128.7, 123.7, 80.8, 34.4, 27.8.

*2-((3-Hydroxy-1-oxo-1-phenylpropan-2-yl)oxy)isoindoline-1,3-dione (**3v**):*[9b]



yield (36 mg, 47%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (d, J = 8.0 Hz, 2H), 7.86−7.84 (m, 2H), 7.79−7.78 (m, 2H), 7.63 (m, 1H), 7.52 (t, J = 7.5 Hz, 2H), 5.54−5.52 (m, 1H), 4.19−4.15 (m, 1H), 4.05−4.01 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) 193.7, 164.3, 135.1, 135.0, 133.9, 129.0, 128.7, 128.6, 124.0, 88.4, 60.7.

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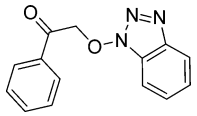
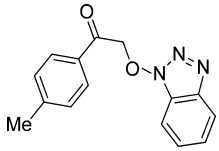
*2-((1H-Benzo[d][1,2,3]triazol-1-yl)oxy)-1-phenylethanone (**6a**):*[9b]



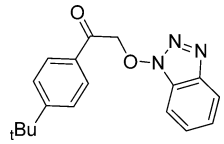
yield (25 mg, 39%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, J = 8.5 Hz, 1H), 7.94–7.90 (m, 3H), 7.65 (t, J = 7.5 Hz, 1H), 7.58–7.55 (m, 1H), 7.52 (t, J = 8.0 Hz, 2H), 7.41–7.38 (m, 1H), 5.94 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) 191.8, 143.4, 134.1, 133.3, 129.1, 128.0, 127.9, 124.5, 120.0, 109.0, 80.0.

*2-((1H-Benzo[d][1,2,3]triazol-1-yl)oxy)-1-p-tolylethanone (**6b**):*[9b]



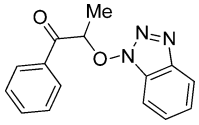
yield (45 mg, 68%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, J = 8.0 Hz, 1H), 7.94 (d, J = 8.0 Hz, 1H), 7.80 (d, J = 8.5 Hz, 2H), 7.57 (t, J = 7.5 Hz, 1H), 7.40 (t, J = 8.0 Hz, 1H), 7.29 (d, J = 8.0 Hz, 2H), 5.90 (s, 2H), 2.41(s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 191.3, 145.6, 143.4, 131.3, 129.7, 128.2, 127.9, 124.8, 119.8, 110.4, 79.9, 21.8.

*2-((1H-Benzo[d][1,2,3]triazol-1-yl)oxy)-1-(4-tert-butylphenyl)-ethanone (**6c**):*



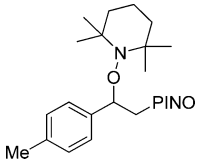
white solid; mp 89 °C Yield (40 mg, 52%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, J = 8.5 Hz, 1H), 7.94 (d, J = 8.0 Hz, 1H), 7.87–7.83 (m, 2H), 7.50 (d, J = 8.5 Hz, 2H), 7.40–7.37 (m, 2H), 5.91 (s, 2H), 1.33(s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$):191.2, 158.4, 143.4, 131.2, 128.1, 127.8, 126.0, 125.9, 124.7, 119.8, 110.3, 79.8, 35.2, 30.9; FT-IR (KBr) 3064, 2965, 1695, 1605, 1367, 1250, 1185, 1130, 981, 878, 698; HRMS $[M + H]^+$ calcd for $C_{18}H_{20}N_3O_2$: 310.1556 found: 310.1540.

*2-((1H-benzo[d][1,2,3]triazol-1-yl)oxy)-1-phenylpropan-1-one (**6d**):*[9b]



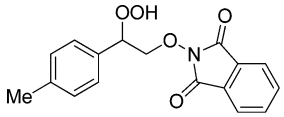
yield (34 mg, 51%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97–7.94 (m, 3H), 7.83 (d, J = 8.5 Hz, 1H), 7.61 (t, J = 7.5 Hz, 1H), 7.54 (d, J = 7.5 Hz, 1H), 7.49 (t, J = 7.5 Hz, 2H), 7.37 (t, J = 8.0 Hz, 1H), 6.38–6.34 (m, 1H), 1.79 (d, J = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 195.4, 143.6, 134.3, 134.2, 128.9, 128.6, 128.2, 128.0, 124.7, 119.8, 110.1, 85.3, 16.9.

*2-(2-((2,2,6,6-Tetramethylpiperidin-1-yl)oxy)-2-p-tolylethoxy)-isoindoline-1,3-dione (**7**):*[13d]



colorless liquid; yield (99 mg, 87%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78–7.76 (m, 2H), 7.71–7.69 (m, 2H), 7.35 (d, J = 8.0 Hz, 2H), 7.14 (d, J = 8.0 Hz, 2H), 5.11–5.09 (m, 1H), 4.74–4.71 (m, 1H), 4.51–4.49 (m, 1H), 2.30 (s, 3H), 1.47 (s, 3H), 1.37–1.32 (m, 6H), 1.18 (s, 3H), 1.04 (s, 3H), 0.74 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 163.0, 137.2, 136.9, 134.1, 128.7, 128.6, 127.7, 123.1, 82.8, 79.9, 59.9, 59.8, 40.2, 34.0, 33.9, 33.8, 21.0, 20.1, 17.0; FT-IR (neat) 2930, 1789, 1735, 1464, 1369, 1250, 1186, 1128, 1081, 1019, 877, 817, 702.

*2-(2-Hydroperoxy-2-p-tolylethoxy)isoindoline-1,3-dione (**8**):*[13d]



colorless liquid; yield (54 mg, 72%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.56 (br, s, 1H), 7.84–7.82 (m, 2H), 7.76–7.74 (m, 2H), 7.28 (d, J = 8.0 Hz, 2H), 7.16 (d, J = 8.0 Hz, 2H), 5.38 (t, J = 5.5 Hz, 1H), 4.49 (d, J = 5.5 Hz, 2H), 2.31(s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 163.7, 138.7, 134.7, 132.7, 129.3, 128.6, 127.1, 123.7, 85.2, 78.8, 21.1.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00266.

NMR spectra for all compounds and HRMS spectra for new compounds (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: adimurthy@csmcri.org.

Notes

The authors declare no competing financial interest.
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