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碘(III)介导的碳自由基参与的氧化偶联反应

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摘要 氧取代 *N*-羟基邻苯二甲酰亚胺衍生物广泛存在于天然产物和药物中, 其合成具有重要的意义. 大多数烯烃、酮、酯、醛和醇的 C=C/C—H 键的活化方法通常需要用到金属或过氧化物. 以廉价安全的醋酸碘苯作为脱氢剂, *N*-羟基邻苯二甲酰亚胺为自由基前体, 实现了烯烃的双氧化、羰基 α 位氢的氧化、醛氢氧化及伯醇的氧化酯化反应. 该方法主要通过自由基机理, 具有环境友好、产率高及底物适用范围广等优点. 反应体系简单实用, 可以很好地应用于氧取代 *N*-羟基邻苯二甲酰亚胺衍生物的合成.

关键词 氧化交叉偶联; PINO (phthalimide nitrogen-oxygen)自由基; 非金属; 碘(III)

Iodine(III)-Promoted Oxidative Cross-Coupling Reactions of C—H Bonds via a Free Radical Process

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Abstract The synthesis of oxygen-substituted *N*-hydroxy phthalimide derivatives is essential due to their ubiquity in natural products and pharmaceuticals. Metals or peroxides are often required for most C=C/C—H bond activation methods used for olefins, ketones, esters, aldehydes and alcohols. Using cheap and safe iodobenzene diacetate as a feasible dehydrogenation agent and *N*-hydroxy phthalimide as free radical precursor, the dioxidation of olefins, *α*-oxidation of carbonyl compounds, oxidation of aldehydes, and oxidative esterification of primary alcohols were successfully realized. This method occurs via a radical mechanism and has the characteristics of mild metal-free reaction conditions, good compatibility and wide substrate scope.

Keywords oxidative cross-coupling; phthalimide nitrogen-oxygen radical; metal-free; iodine(III)

1 Introduction

Oxygen-substituted *N*-hydroxy phthalimide (NHPI) derivatives exist in the building blocks of natural products and pharmaceuticals.[1] Meanwhile, hydrazinolysis of oxygen-substituted NHPI derivatives enables the synthesis of alkoxyamines, which are privileged core structural frameworks in organic compounds with biological activity.[2] Moreover, *N*-hydroxyimide esters have high reactivity, which can also be used as coupling intermediates in organic synthesis.[3] In the traditional condensation method, *N*,*N*′-dicyclohexyl carbodiimide is sensitive and the by-products are difficult to remove. Therefore, the development of a more effective and environmentally-friendly synthetic strategy for the preparation of NHPI esters has therefore attracted considerable research interest.[4]

Oxidative C—O bond formation has emerged as a promising approach during the targeted synthesis of *N*-hydroxyimide esters. Thus, olefins,[5] carbonyl compounds[6] and alcohols[7] are used as substrates for this reaction to synthesize various esters (Scheme 1). However, most of these reactions have disadvantages, such as the use of transition-metal catalysts or stoichiometric amounts of *tert*-butyl hydroperoxide (volatile, toxic and explosive),

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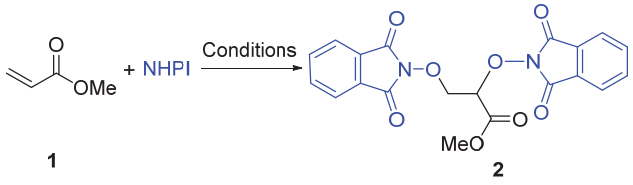
which restrict the application of these oxidative reactions. Considering its industrial and eco-friendly applications, iodine(III) promotes the functionalization of C=C/C—H bonds with NHPI and has become one of the most important and efficient strategies reported to date. Recently, Liu and co-workers[6l] developed a iodobenzene diacetate (PIDA) promoted cross dehydrogenative coupling (CDC) reaction between NHPI and aryl ketones.

Although the limited substrate scope (only aryl ketones are reactive) restricts the applications of such reactions, this method requires only moderate and catalyst-free conditions. Our previous work has also reported the C—O bond CDC reaction of NHPI with unactivated alkanes, nitriles, ethers and thioethers using PIDA.[8] Hypervalent iodine(III) reagents have the characteristics of low toxicity, easy operation, recyclability, low cost, mild oxidation[9] and the production of free radicals.[10] For the sake of expanding the application of iodine(III) reagents and further explore of the role of iodine(III), we disclose the PIDA-promoted functionalization of C=C/C—H bonds including the dioxidation of olefins, α-oxidation of the carbonyl compounds, oxidation of aldehydes and oxidative esterification of primary alcohols. This approach has many outstanding advantages, including simple and mild reaction conditions, high yields, environmentally-friendliness and wide substrate scope.

2 Results and discussion

The model reaction of NHPI with methyl acrylate was performed using ^{t}BuOOH, H_2O_2, $PhI(OCOCF_3)_2$ and PIDA (Table 1, Entries 1～4). Ester **2** was formed in 85% yield when PIDA was applied as the oxidant (Entry 4). The reaction time and the molar ratio of PIDA were varied on the basis of our previous work.[8] From Entry 4 to Entry 8, increasing the reaction time lead to an insufficient increase in the product yield and 2 h was determined to be the optimal reaction time. The influence of the molar ratio of the PIDA was then screened (Entries 9～13). Upon increasing the amount of PIDA from 0.1 to 1.2 equiv., the yield of product **2** reached 86%. Further increasing the amount of PIDA to 1.5 or 2 equiv. could not further improve the yield of product **2**.

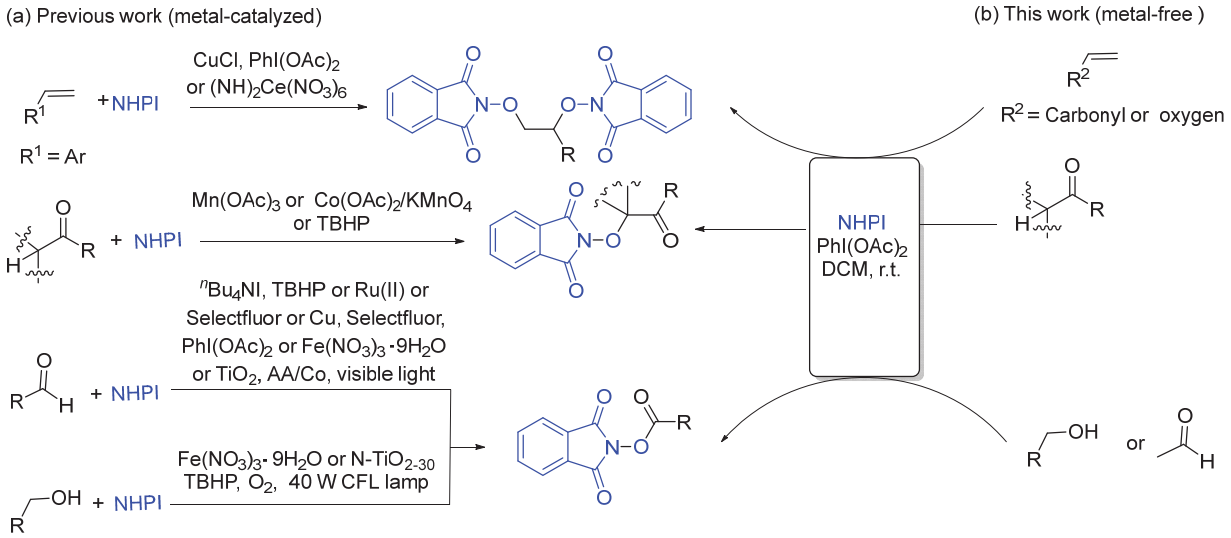
Table 1 Optimization of the reaction conditions[a]



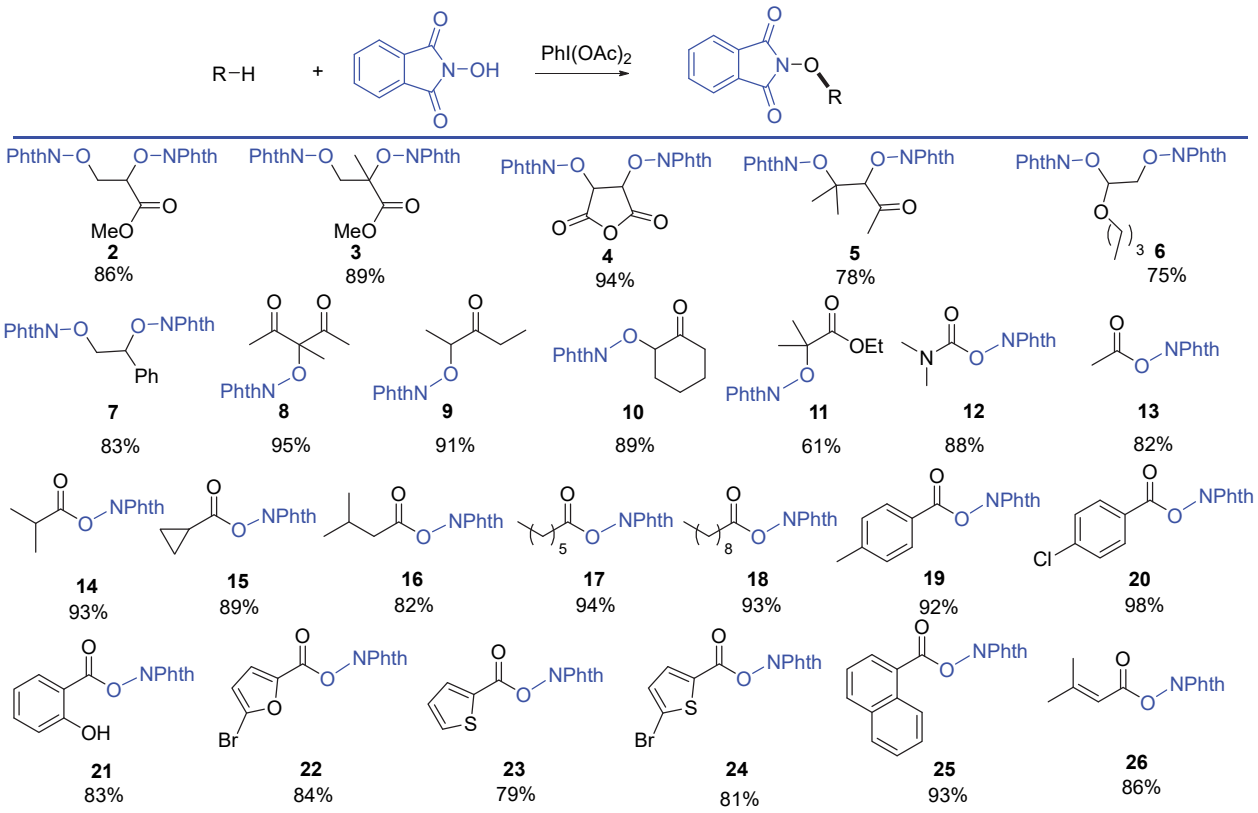
Entry	Oxidant (equiv.)	Time/h	Yield[b]/%
1	TBHP (2)	2	N.D.
2	H_2O_2 (2)	2	N.D.
3	$PhI(OCOCF_3)_2$ (2)	2	Trace
4	$PhI(OAc)_2$ (2)	2	85
5	$PhI(OAc)_2$ (2)	4	86
6	$PhI(OAc)_2$ (2)	6	83
7	$PhI(OAc)_2$ (2)	8	85
8	$PhI(OAc)_2$ (2)	12	82
9	$PhI(OAc)_2$ (0.1)	2	37
10	$PhI(OAc)_2$ (0.5)	2	53
11	$PhI(OAc)_2$ (1.0)	2	72
12	$PhI(OAc)_2$ (1.2)	2	86
13	$PhI(OAc)_2$ (1.5)	2	84

[a] General procedure: NHPI (1 mmol), methyl acrylate (2 mmol), and PIDA (0.1～2 mmol) were added to dichloromethane (DCM) (2 mL) and the resulting reaction mixture was stirred at room temperature. [b] Isolated yield.

To explore the substrate scope of the optimized reaction conditions, the oxidation of various substrates including olefins, ketones, esters, aldehydes and primary alcohols with NHPI were investigated (Scheme 2). Firstly, the scope of different substituted olefins was studied. Double bonds bearing ester carbonyl, ketone carbonyl, ether and benzene ring substituents were obtained in high yield and their reactions afforded the desired products (**2**～**7**) in



Scheme 1 Oxidative coupling using NHPI



Reagents and conditions: NHPI (1 mmol), substrate (2 mmol), and PIDA (1.2 mmol) were added to DCM (2 mL) and the resulting reaction mixture was stirred at room temperature for 2 h. Isolated yield.

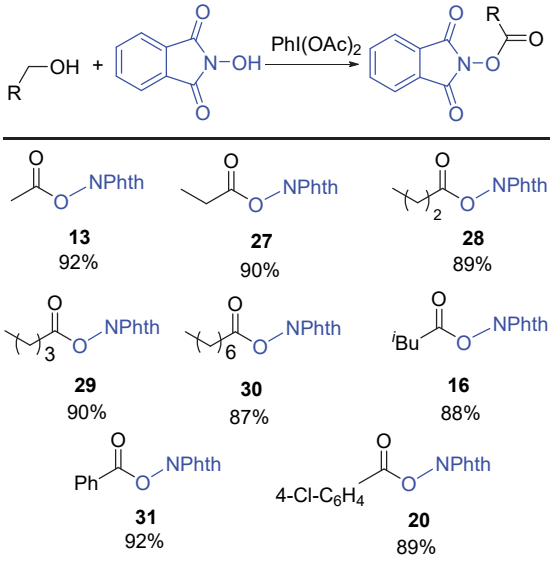
Scheme 2 Oxidation of different types of substrates with NHPI

75%～94% yield. In contrast to compounds **2**, **3**, **4** and **7**, the yields of compounds **5** (78%) and **6** (75%) were relatively low, which were attributed to the by-product obtained via the *α*-oxidation of the ketone carbonyl group or oxygen atom, which were detected by liquid chromatograph mass spectrometer (LC-MS).

Furthermore, unactivated ketones and esters without double bonds were also suitable in the reaction, and their corresponding products (**8**～**11**) were obtained in 61%～95% yields. Unexpectedly, the coupling product of aldehyde hydrogen in *N*,*N*-dimethylformamide (DMF) and NHPI was obtained in 88% yield.

Thus, a wide range of substrates, such as aliphatic aldehydes, aromatic aldehydes, furaldehyde, thiophenecarboxaldehyde and 1-naphth aldehyde were applied in the oxidation reaction. All of the aldehydes studied gave the desired oxidative product (**13**～**25**) in satisfactory yield. The introduction of halogen and hydroxyl-substituents in the aromatic aldehyde has little influence on the desired transformation. When 3-methylbut-2-enal, which containing a double bond and aldehyde hydrogen atom, was used as the substrate, the aldehyde hydrogen condensation product (**26**) was obtained in 86% yield.

Considering the oxidizing capability of iodine(III), the optimum conditions were developed for the functionalization of different alcohols. The further studies suggest that both aliphatic alcohols and aromatic alcohols can afford their corresponding oxidative esterification products in good yield (Scheme 3).



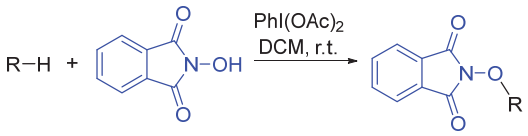
Reagents and conditions: NHPI (1 mmol), alcohol (2 mmol) and PIDA (1.2 mmol) were added to DCM (2 mL) and the resulting reaction mixture was stirred at room temperature for 2 h. Isolated yield.

Scheme 3 Oxidative reaction of different alcohols with NHPI

In order to demonstrate the practicality and reliability of the developed method, the oxidation of methyl methacry-

late, 3-methyl-2,4-pentanedione, 4-chlorobenzaldehyde and ethanol with NHPI was conducted on a gram-scale and the slightly decreased yields listed in Table 2. To investigate the mechanism of these reactions, three kinds of radical scavengers [2,2,6,6-tetramethylpiperidinooxy (TEMPO), 2,6-di-*tert*-butyl-4-methylphenol (BHT) and 2,2-diphenyl-1-picrylhydrazyl (DPPH)] were used to hinder the generation of free radicals in the reaction. Under the optimal reaction conditions, 2 equiv. of TEMPO, BHT or DPPH were added to the reaction of methyl methacrylate, 3-methyl-2,4-pentanedione, 4-chlorobenzaldehyde and ethanol, respectively. The results show that only the reaction system of TEMPO and BHT could obtain the target products (**8** and **20**) in low yield.

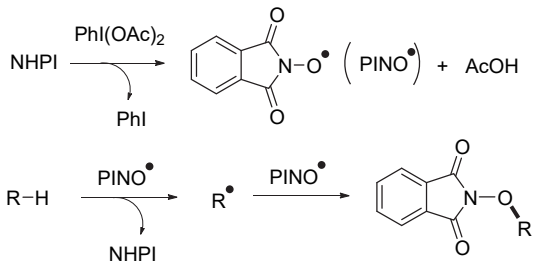
Table 2 Gram-scale reaction and radical trapping experiment



Substrate	Product	Yield[c]	Yield[d]/%		
			TEMPO	BHT	DPPH
Methyl methacrylate	**3**	82	Trace	Trace	Trace
3-Methyl-2,4-pentanedione	**8**	89	15	14	Trace
4-Chlorobenzaldehyde	**20**	90	17	18	Trace
C_2H_5OH	**13**	86	Trace	Trace	Trace

[a] General procedure: NHPI (1 mmol), methyl acrylate (2 mmol) and PIDA (0.1～2 mmol) were added to DCM (2 mL) and the resulting reaction mixture was stirred at room temperature. [b] Isolated yield. [c] Without radical trapping reagent. [d] In the presence of a radical trapping reagent.

The generation of a small amount of the target products indicates that the main reaction route proceeds via a radical pathway. A proposed reaction mechanism is presented in Scheme 4 based on the literature[11] and our inhibitory tests. Initially, NHPI reacts with $PhI(OAc)_2$ and produces the phthalimide nitrogen-oxygen (PINO) radical. The PINO radical then induces the substrate to form a C-centred radical via hydrogen abstraction. The C-centred radical is then coupled with the PINO radical to form the desired NHPI ester.



R = olefins, ketones, esters, aldehydes, and primary alcohols

Scheme 4 Proposed reaction mechanism

3 Conclusions

A metal-free oxidative coupling reaction of various C=C/C—H reagents with NHPI has been developed using a PIDA-mediated free radical reaction. The process gives high yields and exhibits excellent functional group tolerance. In addition, the reaction was carried out under mild reaction conditions at room temperature and simple hydrazinolysis can convert the products into their corresponding hydroxylamine derivatives. The method was compatible for the C=C/C—H functionalization of olefins, ketones, esters, aldehydes and alcohols, and provides a simple, safe and convenient way to prepare substituted NHPI derivatives.

4 Experimental section

4.1 General information.

NMR spectroscopy was recorded on a Bruker AV-400 instrument using $CDCl_3$ as solvent, and tetramethylsilane (TMS) as an internal reference. High-resolution mass spectrometry (HRMS) was obtained using an Agilent Technologies LC-TOF instrument. The solvents and reaction materials used in the experiment were purchased commercially.

4.2 General procedure for the synthesis of substituted NHPI derivatives

A solution of the substrate (2 mmol), PIDA (1.2 mmol), and NHPI (1 mmol) in DCM (2 mL) was stirred at room temperature for 2 h under an air atmosphere. After the reaction was completed, the mixture was concentrated under reduced pressure to give the crude product. The crude product was purified by flash silica gel column chromatography (PE/EtOAc, V∶V=20∶1→10∶1) to give the target product.

Methyl 2,3-bis((1,3-dioxoisoindolin-2-yl)oxy)propanoate (**2**): White solid, 86% yield. m.p. 175～177 ℃ (lit.[5d] 176～178 ℃); ^{1}H NMR (400 MHz, chloroform-*d*) δ: 7.87～7.84 (m, 4H), 7.83～7.76 (m, 4H), 5.26 (dd, J=5.8, 3.8 Hz, 1H), 4.84 (dd, J=12.0, 6 Hz, 1H) 4.76 (dd, J=12.0, 3.6 Hz, 1H), 3.89 (s, 3H); ^{13}C NMR (101 MHz, chloroform-*d*) δ: 166.5, 163.2, 163.0, 134.7, 128.8, 123.8, 123.7, 82.6, 76.6, 53.2. ^{1}H NMR and ^{13}C NMR data correspond to the reported values.[5d]

Methyl 2,3-bis((1,3-dioxoisoindolin-2-yl)oxy)-2-methylpropanoate (**3**): White solid, 89% yield. m.p. 164～165 ℃; ^{1}H NMR (400 MHz, chloroform-*d*) δ: 7.88～7.84 (m, 4H), 7.80～7.29 (m, 4H), 4.71 (q, J=10.0 Hz, 2H), 3.91 (s, 3H), 1.93 (s, 3H); ^{13}C NMR (101 MHz, chloroform-*d*) δ: 168.7, 164.2, 162.8, 134.8, 134.5, 128.9, 128.8, 123.8, 123.6, 86.4, 78.8, 53.3, 18.0; HRMS (ESI-TOF) calcd for $C_{15}H_{17}NO_3Na$ $(M+Na)^+$ 447.0799, found 447.0799.

2,2'-((2,5-Dioxotetrahydrofuran-3,4-diyl)bis(oxy))bis(isoindoline-1,3-dione) (**4**): White solid, 94% yield. m.p. 120～122 ℃; ^{1}H NMR (400 MHz, chloroform-*d*) δ: 7.95 (dd, J=5.5, 3.1 Hz, 4H), 7.86 (dd, J=5.5, 3.1 Hz, 4H), 7.46 (s, 2H); ^{13}C NMR (101 MHz, chloroform-*d*) δ: 162.5, 135.2, 128.7, 124.3, 100.2; HRMS (ESI-TOF) calcd for $C_{15}H_{18}NO_3$ $(M+H)^+$ 423.0459, found 423.0464.

2,2'-((2-Methyl-4-oxopentane-2,3-diyl)bis(oxy))bis-(isoindoline-1,3-dione) (**5**): Yellow solid, 78% yield. m.p. 154～155 ℃; ^{1}H NMR (400 MHz, chloroform-*d*) *δ*: 7.87～7.85 (m, 4H), 7.80～7.29 (m, 4H), 4.69 (s, 1H), 2.69 (s, 3H), 2.20 (s, 3H), 1.70 (s, 3H); ^{13}C NMR (101 MHz, chloroform-*d*) *δ*: 205.3, 165.1, 163.1, 134.7, 129.1, 128.7, 123.7, 95.6, 88.0, 31.0, 28.8, 23.2, 22.6; HRMS (ESI-TOF) calcd for $C_{15}H_{17}NO_3Na$ $(M+Na)^+$ 445.1006, found 445.1010.

2,2'-((1-Butoxyethane-1,2-diyl)bis(oxy))bis(isoindoline-1,3-dione) (**6**): White solid, 75% yield. m.p. 134～136 ℃; ^{1}H NMR (400 MHz, chloroform-*d*) *δ*: 7.88～7.81 (m, 4H), 7.78～7.76 (m, 4H), 5.59～5.37 (m, 1H), 4.67 (dd, *J*=12.1, 2.5 Hz, 1H), 4.40～4.35 (m, 2H), 3.80 (q, *J*=7.2 Hz, 1H), 1.54～1.49 (m, 2H), 1.33～1.27 (m, 2H), 0.85 (t, *J*=7.3 Hz, 3H); ^{13}C NMR (101 MHz, chloroform-*d*) *δ*: 164.2, 163.3, 134.7, 134.5, 129.0, 128.8, 123.7, 123.6, 107.0, 76.9, 70.9, 31.4, 19.0, 13.9; HRMS (ESI-TOF) calcd for $C_{15}H_{17}NO_3Na$ $(M+Na)^+$ 447.1163, found 447.1167.

2,2'-((1-Phenylethane-1,2-diyl)bis(oxy))bis(isoindoline-1,3-dione) (**7**): White solid, 83% yield. m.p. 180～181 ℃ (lit.[5d] 179～180 ℃); ^{1}H NMR (400 MHz, chloroform-*d*) *δ*: 7.82～7.77 (m, 4H), 7.74～7.68 (m, 4H), 7.58～7.56 (m, 2H), 7.37～7.36 (m, 3H), 5.87 (dd, *J*=7.2, 3.6 Hz, 1H), 4.94 (dd, *J*=11.6, 7.6 Hz, 1H), 4.57 (dd, *J*=11.6, 3.6 Hz, 1H); ^{13}C NMR (101 MHz, chloroform-*d*) *δ*: 163.5, 163.2, 134.5, 134.3, 134.1, 129.7, 129.0, 128.8, 128.7, 128.2, 123.6, 123.5, 85.8. ^{1}H NMR and ^{13}C NMR spectradata correspond to the reported values.[5d]

2-((3-Methyl-2,4-dioxopentan-3-yl)oxy)isoindoline-1,3-dione (**8**): White solid, 95% yield. m.p. 104～106 ℃ (lit.[6k] 105～107 ℃); ^{1}H NMR (400 MHz, chloroform-*d*) *δ*: 7.87～7.88 (m, 2H), 7.84～7.82 (m, 2H), 2.57(s, 6H), 1.52 (s, 3H); ^{13}C NMR (101 MHz, chloroform-*d*) *δ*: 203.0, 164.0, 135.0, 128.6, 124.0, 96.6, 26.2, 15.9. ^{1}H NMR and ^{13}C NMR data correspond to the reported values.[6k]

2-((3-Oxopentan-2-yl)oxy)isoindoline-1,3-dione (**9**): White solid, 91% yield. m.p. 157～158 ℃; ^{1}H NMR (400 MHz, chloroform-*d*) *δ*: 7.88～7.81 (m, 4H), 7.78～7.76 (m, 4H), 5.59～5.37 (m, 1H), 4.67 (dd, *J*=12.1, 2.5 Hz, 1H), 4.40～4.35 (m, 2H), 3.80 (q, *J*=7.2 Hz, 1H), 1.54～1.49 (m, 2H), 1.33～1.27 (m, 2H), 0.85 (t, *J*=7.3 Hz, 3H); ^{13}C NMR (101 MHz, chloroform-*d*) *δ*: 164.2, 163.3, 134.7, 134.5, 129.0, 128.8, 123.7, 123.6, 107.0, 76.9, 70.9, 31.4, 19.0, 13.9; HRMS (ESI-TOF) calcd for $C_{15}H_{17}NO_3Na$ $(M+Na)^+$ 270.0737, found 270.0736.

2-((2-Oxocyclohexyl)oxy)isoindoline-1,3-dione (**10**): Brown solid, 89% yield. m.p. 136～138 ℃ (lit.[13] 136～139 ℃); ^{11}H NMR (400 MHz, chloroform-*d*) *δ*: 7.83～7.86 (m, 2H), 7.76～7.79 (m, 2H), 4.87 (t, *J*=6.4 1H), 3.08～3.02 (m, 1H), 2.45～2.38 (m, 1H), 2.35～2.32 (m, 1H), 2.25～2.20 (m, 1H), 2.11～2.08 (m, 1H), 2.00～1.87 (m, 1H), 1.77～1.71 (m, 1H); ^{13}C NMR (101 MHz, chloroform-*d*) *δ*: 206.7, 163.4, 134.6, 128.8, 123.7, 87.6, 39.9, 32.5, 27.1, 21.4. ^{1}H NMR and ^{13}C NMR data correspond to the reported values.[13]

Ethyl 2-((1,3-dioxoisoindolin-2-yl)oxy)-2-methylpropanoate (**11**): White solid, 61% yield. m.p. 76～77 ℃ (lit.[6k] 74～76 ℃); ^{1}H NMR (400 MHz, chloroform-*d*) *δ*: 7.87～7.84 (m, 2H), 7.79～7.77 (m, 2H), 4.30 (q, *J*=7.2 Hz, 2H), 1.64 (s, 6H), 1.37 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (101 MHz, chloroform-*d*) *δ*: 170.8, 164.5, 134.6, 120.0, 123.6, 86.5, 62.0, 23.0, 14.0. ^{1}H NMR and ^{13}C NMR data correspond to the reported values.[6k]

1,3-Dioxoisoindolin-2-yl dimethylcarbamate (**12**): White solid, 88% yield. m.p. 156～157 ℃; ^{1}H NMR (400 MHz, chloroform-*d*) *δ*: 7.87 (dd, *J*=5.2, 2.8 Hz, 2H), 7.77 (dd, *J*=5.2, 2.8 Hz, 2H), 3.17 (s, 3H), 3.03 (s, 3H); ^{13}C NMR (101 MHz, chloroform-*d*) *δ*: 162.7, 152.4, 134.6, 129.0, 123.9, 37.8, 36.3; HRMS (ESI-TOF) calcd for $C_{15}H_{17}NO_3Na$ $(M+Na)^+$ 257.0533, found 257.0532.

1,3-Dioxoisoindolin-2-yl acetate (**13**): White solid, 82% yield. m.p. 162～166 ℃ (lit.[14] 160～165 ℃); ^{1}H NMR (400 MHz, chloroform-*d*) *δ*: 7.93～7.90 (m, 2H), 7.83～7.81 (m, 2H), 2.43 (s, 3H); ^{13}C NMR (101 MHz, chloroform-*d*) *δ*: 166.6, 161.9, 134.8, 128.9, 124.0, 17.7. ^{1}H NMR and ^{13}C NMR data correspond to the reported values.[14]

1,3-Dioxoisoindolin-2-yl isobutyrate (**14**). White solid, 93% yield. m.p. 66～67 ℃ (lit.[15] 66～67 ℃); ^{1}H NMR (400 MHz, chloroform-*d*) *δ*: 7.90 (dd, *J*=5.2, 2.8 Hz, 2H), 7.80 (dd, *J*=5.2, 2.8 Hz, 2H), 2.98 (q, *J*=7.2 Hz, 1H), 1.40 (d, *J*=7.2 Hz, 6H); ^{13}C NMR (101 MHz, chloroform-*d*) *δ*: 173.1, 162.0, 134.7, 129.0, 123.9, 31.8, 18.8. ^{1}H NMR and ^{13}C NMR data correspond to the reported values.[15]

1,3-Dioxoisoindolin-2-yl cyclopropanecarboxylate (**15**): White solid, 89% yield. m.p. 106～107 ℃; ^{1}H NMR (400 MHz, chloroform-*d*) *δ*: 7.92 (dd, *J*=5.6, 3.6 Hz, 2H), 7.81 (dd, *J*=5.6, 3.6 Hz, 2H), 2.02～1.98 (m, 1H), 1.31～1.29 (m, 2H), 1.23～1.20 (m, 2H); ^{13}C NMR (101 MHz, chloroform-*d*) *δ*: 171.2, 162.1, 134.7, 129.0, 124.0, 10.7, 10.3; HRMS (ESI-TOF) calcd for $C_{15}H_{17}NO_3Na$ $(M+Na)^+$ 254.0424, found 254.0425.

1,3-Dioxoisoindolin-2-yl 3-methylbutanoate (**16**): White solid, 82% yield. m.p. 67～68 ℃; ^{1}H NMR (400 MHz, chloroform-*d*) *δ*: 7.90～7.87 (m, 2H), 7.81～7.78 (m, 2H), 2.54 (d, *J*=7.2 Hz, 2H), 2.30～2.23 (m, 1H), 1.59 (s, 1H), 1.10 (d, *J*=6.8 Hz, 6H); ^{13}C NMR (101 MHz, chloroform-*d*) *δ*: 168.8, 162.0, 134.7, 129.0, 124.0, 39.9, 26.1, 22.2. ^{1}H NMR and ^{13}C NMR data correspond to the reported values.[15]

1,3-Dioxoisoindolin-2-yl heptanoate (**17**): Yellow solid, 94% yield. m.p. 208～209 ℃; ^{1}H NMR (400 MHz, chloroform-*d*) *δ*: 7.83～7.81 (m, 2H), 7.73～7.71 (m, 2H), 2.59 (t, *J*=7.2 Hz, 2H), 1.73～1.70 (m, 2H), 1.41～1.34 (m, 2H), 1.28～1.22 (m, 4H), 0.84 (q, *J*=6.4 Hz, 3H); ^{13}C NMR (101 MHz, chloroform-*d*) *δ*: 169.7, 162.0, 134.7, 129.0, 123.9, 31.3, 31.0, 28.5, 24.6, 22.4, 14.0. ^{1}H NMR and ^{13}C NMR data correspond to the reported values.[6g]

1,3-Dioxoisoindolin-2-yl decanoate (**18**): Yellow solid, 93% yield. m.p. 228～229 ℃; ^{1}H NMR (400 MHz, chloroform-*d*) *δ*: 7.90～7.88 (m, 2H), 7.80～7.78 (m, 2H), 2.66 (t, *J*=7.6 Hz, 2H), 1.78 (q, *J*=7.6 Hz, 2H), 1.46～1.41

(m, 2H), 1.36～1.26 (m, 9H), 0.88 (t, J=6.4 Hz, 3H); ^{13}C NMR (101 MHz, chloroform-*d*) δ: 169.7, 162.0, 134.7, 129.0, 124.0, 31.8, 31.0, 29.3, 29.2, 29.1, 28.8, 24.7, 22.7, 14.1. ^{1}H NMR and ^{13}C NMR data correspond to the reported values.[16]

1,3-Dioxoisoindolin-2-yl 4-methylbenzoate (**19**): White solid, 92% yield. m.p. 162～164 ℃ (lit.[17] 163～165 ℃); ^{1}H NMR (400 MHz, chloroform-*d*) δ: 8.11 (d, J=8.0 Hz, 2H), 7.96 (dd, J=5.6, 3.6 Hz, 2H), 7.84 (dd, J=5.6, 3.6 Hz, 2H), 7.36 (d, J=8.0 Hz, 2H), 2.49 (s, 3H); ^{13}C NMR (101 MHz, chloroform-*d*) δ: 162.8, 162.2, 146.1, 134.8, 130.7, 129.6, 129.1, 124.0, 122.4, 22.0. ^{1}H NMR and ^{13}C NMR data correspond to the reported values.[17]

1,3-Dioxoisoindolin-2-yl 4-chlorobenzoate (**20**): White solid, 98% yield. m.p. 178～181 ℃ (lit.[7a] 180～182 ℃); ^{1}H NMR (400 MHz, chloroform-*d*) δ: 8.17 (d, J=8.4 Hz, 2H), 7.96 (dd, J=5.6, 3.6 Hz, 2H), 7.86 (dd, J=5.6, 3.6 Hz, 2H), 7.55 (d, J=8.0 Hz, 2H); ^{13}C NMR (101 MHz, chloroform-*d*) δ: 162.1, 162.0, 141.7, 134.9, 132.0, 129.4, 129.0, 124.1, 123.7. ^{1}H NMR and ^{13}C NMR data correspond to the reported values.[7a]

1,3-Dioxoisoindolin-2-yl 2-hydroxybenzoate (**21**): Yellow solid, 83% yield. m.p. 157～159 ℃; ^{1}H NMR (400 MHz, chloroform-*d*) δ: 7.92 (dd, J=5.6, 3.6 Hz, 2H), 7.81 (dd, J=5.6, 3.6 Hz, 2H), 2.02～1.98 (m, 1H), 1.31～1.29 (m, 2H), 1.23～1.20 (m, 2H); ^{13}C NMR (101 MHz, chloroform-*d*) δ: 171.2, 162.1, 134.7, 129.0, 124.0, 10.7, 10.3; HRMS (ESI-TOF) calcd for $C_{15}H_{17}NO_3Na$ $(M+Na)^+$ 306.0373, found 306.0374.

1,3-Dioxoisoindolin-2-yl 5-bromofuran-2-carboxylate (**22**): Yellow solid, 84% yield. m.p. 133～134 ℃; ^{1}H NMR (400 MHz, chloroform-*d*) δ: 7.97～7.96 (m, 2H), 7.86～7.84 (m, 2H), 7.50 (d, J=3.6 Hz, 1H), 6.63 (d, J=3.6 Hz, 1H); ^{13}C NMR (101 MHz, chloroform-*d*) δ: 161.7, 153.5, 141.5, 134.9, 130.9, 128.8, 124.3, 124.2, 114.8; HRMS (ESI-TOF) calcd for $C_{15}H_{17}NO_3Na$ $(M+Na)^+$ 357.9322, found 357.9323.

1,3-Dioxoisoindolin-2-yl thiophene-2-carboxylate (**23**): Yellow solid, 79% yield. m.p. 144～147 ℃ (lit.[6g] 145～147 ℃); ^{1}H NMR (400 MHz, chloroform-*d*) δ: 8.11 (d, J=3.6 Hz, 1H), 7.97～7.95 (m, 2H), 7.86～7.82 (m, 3H), 7.26 (t, J=4.4 Hz, 1H); ^{13}C NMR (101 MHz, chloroform-*d*) δ: 162.0, 158.3, 136.7, 135.7, 134.8, 128.9, 128.4, 127.1, 124.1. ^{1}H NMR and ^{13}C NMR data correspond to the reported values.[6g]

1,3-Dioxoisoindolin-2-yl 5-bromothiophene-2-carboxylate (**24**): Yellow solid, 81% yield. m.p. 210～212 ℃; ^{1}H NMR (400 MHz, chloroform-*d*) δ: 7.97～7.94 (m, 2H), 7.856～7.84 (m, 3H), 7.23 (d, J=4.0 Hz, 1H); ^{13}C NMR (101 MHz, chloroform-*d*) δ: 161.8, 157.2, 137.0, 134.9, 134.9, 131.6, 128.9, 124.2, 124.1; HRMS (ESI-TOF) calcd for $C_{15}H_{17}NO_3Na$ $(M+Na)^+$ 373.9093, found 373.9094.

1,3-Dioxoisoindolin-2-yl 1-naphthoate (**25**): Brown solid, 93% yield. m.p. 184～187 ℃ (lit.[17] 185～187 ℃); ^{1}H NMR (400 MHz, chloroform-*d*) δ: 8.88 (dd, J=8.4, 1.2 Hz, 1H), 8.57 (dd, J=7.2, 1.2 Hz, 1H), 8.20 (d, J=8.0 Hz, 1H), 8.00～7.97 (m, 3H), 7.86 (dd, J=5.6, 3.2 Hz, 2H), 7.72～7.67 (m, 1H), 7.65～7.61 (m, 2H); ^{13}C NMR (101 MHz, chloroform-*d*) δ: 163.1, 162.3, 135.6, 134.8, 133.7, 132.0, 131.5, 129.1, 128.8, 128.7, 126.8, 125.3, 124.5, 124.1, 121.6. ^{1}H NMR and ^{13}C NMR data correspond to the reported values.[17]

1,3-Dioxoisoindolin-2-yl 3-methylbut-2-enoate (**26**): White solid, 86% yield. m.p. 117～119 ℃ (lit.[6g] 118～119 ℃); ^{1}H NMR (400 MHz, chloroform-*d*) δ: 7.91 (dd, J=5.6, 3.6 Hz, 2H), 7.80 (dd, J=5.6, 3.6 Hz, 2H), 6.01 (t, 1H), 2.25 (s, 3H), 2.07 (s, 3H); ^{13}C NMR (101 MHz, chloroform-*d*) δ: 165.6, 162.4, 161.8, 134.7, 129.0, 123.9, 110.0, 28.0, 21.1. ^{1}H NMR and ^{13}C NMR data correspond to the reported values.[6g]

1,3-Dioxoisoindolin-2-yl propionate (**27**): White solid, 90% yield. m.p. 84～87 ℃ (lit.[6g] 86～88 ℃); ^{1}H NMR (400 MHz, chloroform-*d*) δ: 7.91～7.88 (m, 2H), 7.81～7.78 (m, 2H), 2.65 (t, J=7.2 Hz, 2H), 1.87～1.78 (m, 2H), 1.08 (t, J=7.6 Hz, 2H); ^{13}C NMR (101 MHz, chloroform-*d*) δ: 170.4, 162.0, 134.8, 128.9, 124.0, 24.6, 8.7. ^{1}H NMR and ^{13}C NMR data correspond to the reported values.[6g]

1,3-Dioxoisoindolin-2-yl butyrate (**28**): White solid, 89% yield. m.p. 191～193 ℃; ^{1}H NMR (400 MHz, chloroform-*d*) δ: 7.90～7.87 (m, 2H), 7.80～7.78 (m, 2H), 5.26 (dd, J=5.8, 3.8 Hz, 1H), 4.84 (dd, J=12.0, 6 Hz, 1H) 4.76 (dd, J=12.0, 3.6 Hz, 1H), 3.89 (s, 3H); ^{13}C NMR (101 MHz, chloroform-*d*) δ: 169.5, 162.0, 134.8, 129.0, 124.0, 32.8, 18.3, 13.4. ^{1}H NMR and ^{13}C NMR data correspond to the reported values.[6g]

1,3-Dioxoisoindolin-2-yl pentanoate (**29**): White solid, 90% yield. m.p. 156～157 ℃; ^{1}H NMR (400 MHz, chloroform-*d*) δ: 7.89～7.87 (m, 2H), 7.80～7.77 (m, 2H), 2.67 (t, J=7.6 Hz, 2H),1.81～1.73 (m, 2H), 1.52～1.43 (m, 2H), 0.97 (t, J=7.6 Hz, 1H); ^{13}C NMR (101 MHz, chloroform-*d*) δ: 169.7, 162.0, 134.7, 129.0, 124.0, 30.7, 26.7, 22.0, 13.6. ^{1}H NMR and ^{13}C NMR data correspond to the reported values.[6g]

1,3-Dioxoisoindolin-2-yl octanoate (**30**): White solid, 87% yield. m.p. 208～209 ℃; ^{1}H NMR (400 MHz, chloroform-*d*) δ: 7.90～7.88 (m, 2H), 7.80～7.78 (m, 2H), 2.67 (t, J=7.2 Hz, 2H), 1.81～1.77 (m, 2H), 1.46～1.42 (m, 2H), 1.37～1.28 (m, 6H) 0.90 (t, J=7.2 Hz, 1H); ^{13}C NMR (101 MHz, chloroform-*d*) δ: 169.7., 162.0, 134.7, 129.0, 124.0, 31.6, 31.0,28.8, 24.7, 22.6, 14.1. ^{1}H NMR and ^{13}C NMR data correspond to the reported values.[6g]

1,3-Dioxoisoindolin-2-yl benzoate (**31**). White solid, 92% yield. m.p. 168～171 ℃ (lit.[6g] 168～170 ℃); ^{1}H NMR (400 MHz, chloroform-*d*) δ: 8.21～8.19 (m, 2H), 7.93 (dd, J=5.6, 3.2 Hz, 2H), 7.82 (dd, J=5.6, 3.2 Hz, 2H), 7.72～7.69 (m, 1H), 7.56～7.52 (m, 2H); ^{13}C NMR (101 MHz, chloroform-*d*) δ: 162.8, 162.1, 134.9, 134.8, 130.7, 129.0, 128.9, 125.3, 124.0. ^{1}H NMR and ^{13}C NMR data correspond to the reported values.[6g]

4.3 Reaction of radical trapping experiment.

The solution of substrate (2 mmol), PIDA (1.2 mmol), NHPI (1 mmol) and radical trapping (2 mmol) in DCM (2

mL) was stirred at room temperature for 2 h under air. After the reaction completed, the mixture was concentrated under reduced pressure and was purified by flash silica gel column chromatography (PE/EtOAc, V ∶ V = 20 ∶ 1→10 ∶ 1) to give the product.

Supporting Information The spectra of compounds **2**～**31**. The Supporting Information is available free of charge via the Internet at http://sioc-journal.cn.

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