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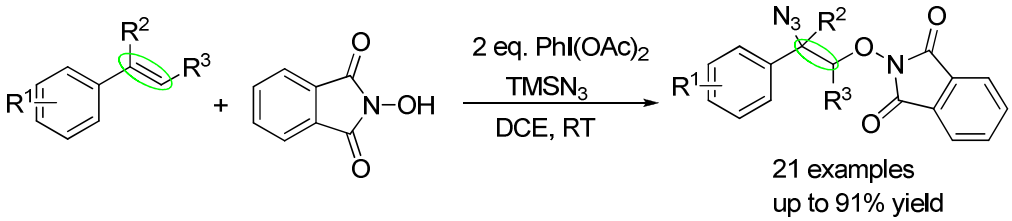
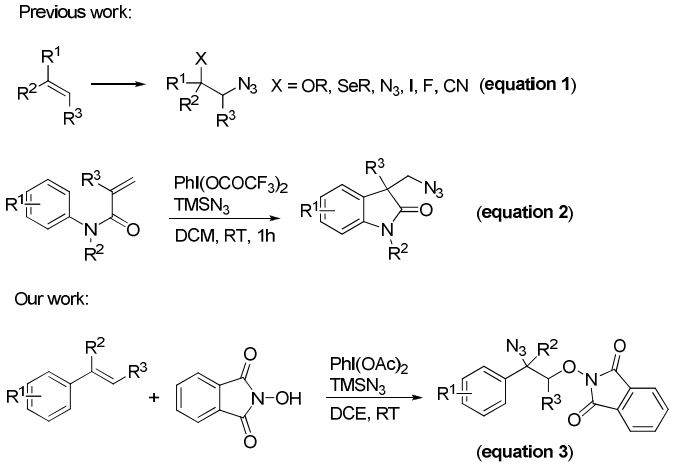


A novel and facile oxyazidation of alkenes under metal-free and mild conditions has been reported. A remarkable feature of the developed procedure is consecutive construction of C-O and C-N bonds in one step. The process allows quick and selective assembly of alkyl azide from readily available starting materials, where N-hydroxyphthalimide was used as an oxygen-radical precursor and $TMSN_3$ as the N_3 source. A range of aromatic alkenes bearing synthetically useful functional groups were tolerated.

INTRODUCTION

Nitrogen-containing compounds occupy a significant position in natural products, material science, and pharmaceuticals, which has inspired the search for more milder and efficient C-N bond-forming reactions.[1] As highly important nitrogen-containing compounds, organic azides gained great attention and have been recognized as efficient synthetic intermediates, which can be easily transformed into amines under reductive conditions.[2] The traditional methods for most organic azides syntheses are based on the transformation of alkyl halides *via* a S_N2 reaction. Recently, chemists found that using azidyl radicals in the functionalization

of alkenes can directly realize various straightforward transformations for the construction of substituted organic azides.[3] For example, in the past decade, several groups have reported some methods of azidyl radical addition to alkenes followed by formation of C-X (X= O, Se, N, I, F, CN) bonds using $TMSN_3$, NaN_3 or IN_3 as the N_3 source (Scheme 1, equation 1).[4] However, to the best of our knowledge, these procedures are not well developed, and up to now straightforward and efficient approaches for organic azide syntheses by the addition of the oxygen radical to alkenes followed C-N bonds formation have been rarely reported. In addition, direct azidation of alkene under metal-free oxidation conditions was also developed.[4a,5] For instance, in 2013, the Antonchick[5a] group has independently reported a novel azidation method for the construction of azide oxindoles from alkene compounds using $PhI(OCOCF_3)_2$ as oxidant (Scheme 1, equation 2). Herein, we report a metal-free functionalization of alkenes by the addition of oxygen radicals followed by trapping with an azidyl source at room temperature to give synthetically useful 2-azido-2-phenylethoxy-isoindolinone compounds, which could provide a broad range of possibilities for further derivatization (Scheme 1, equation 3).



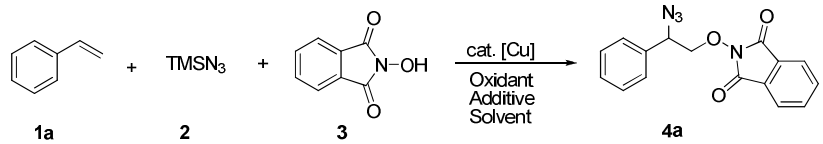
Scheme 1. Azidation of alkenes.

RESULTS/DISCUSSION

It was revealed that N-hydroxyphthalimide (NHPI) can generate the phthalimide N-oxyl (PINO) radical, which is an active catalytic species to realize C-H bond functionalization.[6] Recently, PINO was also utilized

as a stoichiometric reactant in organic synthesis to construct the C-O bond.[7] We envisaged that PINO can be also utilized as a stoichiometric reactant for radical addition, and the results are reported herein. Our investigation began with the reaction of styrene **1a**, $TMSN_3$, and N-hydroxyphthalimide using 20 mmol% CuCl as catalyst and $PhI(OAc)_2$ as oxidant, and the target product **4a** was obtained in 57% yield at ambient temperature (see Table 1, entry 1). In order to increase the yield, several copper catalysts were evaluated, including CuCl, CuBr, CuI, $Cu(OTf)_2$, $CuBr_2$, $Cu(OAc)_2$, and $CuCl_2{\cdot}2H_2O$, wherein $CuCl_2{\cdot}2H_2O$ displayed high catalytic activity (see Table S1, entry 18). When 4Å MS was added into the reaction system, the yield was increased. To our delight, in the absence of copper catalyst, **4a** was still formed (Table 1, entry 4), which meant that the copper catalyst did not play a decisive role in the reaction. When 2.0 equiv. $PhI(OAc)_2$ was used, the yield increased to 70% similar to previous results (entry 2 *vs* entry 5). $PhI(OCOCF_3)_2$ (2.0 equiv.) gave a lower yield (entry 6). When NaN_3 was used as the nitrogen source instead of $TMSN_3$, a very low yield was obtained (entry 7). Meanwhile, screening of solvents revealed that DCE was the best for the reaction under metal-free conditions (entries 8-12). Control experiment showed that only a little product was detected by GC in the reaction in the absence of oxidant ($PhI(OAc)_2$).

Table 1. Selected List of Screening for the Optimized Conditions.[a]

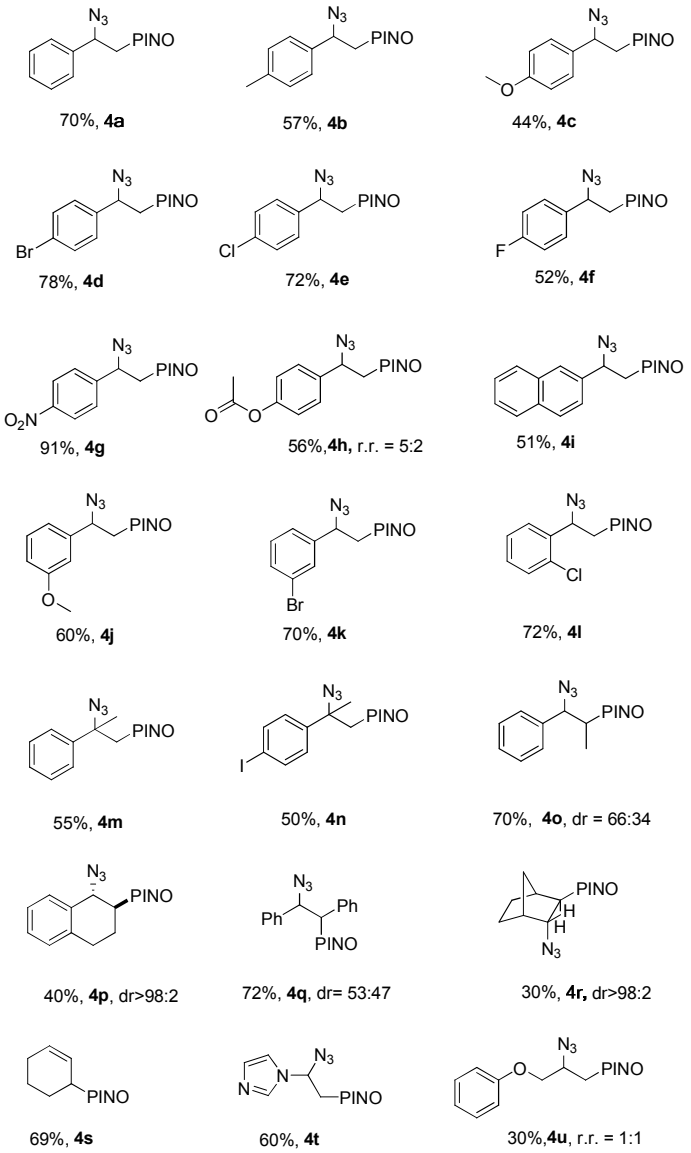


1a **2** **3** **4a**

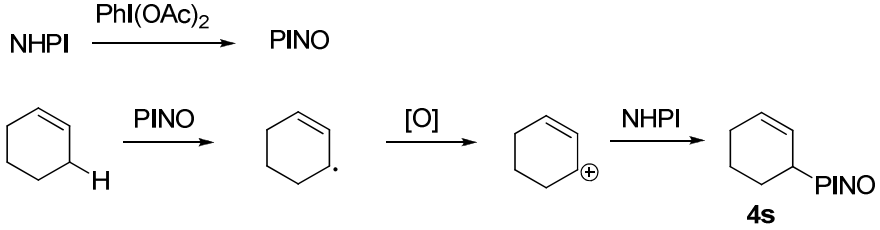
Entry	**1a : 2 : 3**	Catalyst (%)	Oxidant	Solvent	Yield[%][b]
1	1:2:1.2	20% CuCl	1.2 eq. $PhI(OAc)_2$	DCE	57%
2	***2:2:1***	***10% $CuCl_2{\cdot}2H_2O$***	***1.2 eq. $PhI(OAc)_2$***	***DCE+4Å MS***	***73%***
3	2:2:1	5% $CuCl_2{\cdot}2H_2O$	1.2 eq. $PhI(OAc)_2$	DCE+4Å MS	52%
4	2:2:1	—	1.2 eq. $PhI(OAc)_2$	DCE+4Å MS	47%
5	***2:3:1***	**—**	***2.0 eq. $PhI(OAc)_2$***	***DCE+4Å MS***	***70%***
6	2:3:1	—	2.0 eq. $PhI(OCOCF_3)_2$	DCE+4Å MS	64%
7[c]	2:3:1	—	2.0 eq. $PhI(OAc)_2$	DCE+4Å MS	20%
8	2:3:1	—	2.0 eq. $PhI(OAc)_2$	CH_3CN+4Å MS	40%
9	2:3:1	—	2.0 eq. $PhI(OAc)_2$	DCM+4Å MS	30%
10	2:3:1	—	2.0 eq. $PhI(OAc)_2$	THF+4Å MS	20%
11	2:3:1	—	2.0 eq. $PhI(OAc)_2$	toluene+4Å MS	45%
12	2:3:1	—	2.0 eq. $PhI(OAc)_2$	actone+4Å MS	56%
13	2:3:1	—	—	DCE+4Å MS	<5%

[a] Conditions: **3** (0.3 mmol), **1a** (equiv.), azide (equiv.) in solvent (2.0 mL), at room temperature, in air, 12h. [b] Yields of isolated product after chromatography on silica gel. [c] 2 equiv. NaN_3 was used instead of $TMSN_3$.

Using the optimized conditions (Table 1, entry 21), the scope of the transformation was investigated. As shown in scheme 2, a great variety of substituted styrenes were converted to the corresponding alkyl azides in good to moderate yields. Several useful functional groups were tolerated, including fluoro, chloro, bromo, iodo, nitro, ester, ether and alkyl substituents, at the different positions of styrenes. An electron-withdrawing substituent favored product formation, whereas an electron-donating group gave slightly lower yields. When 4-vinylphenyl acetate was employed, poor regioselectivity was observed (**4h**, regioisomeric ratio = 5:2). Naphthalenes bearing vinyl groups at position 2 afforded the desired products in 51% (**4i**) yield. α-Methyl styrene gave the corresponding product **4m** in moderate yield; (E)-*β*-methyl styrene was also compatible, and provided a mixture of diastereoisomers **4o** (dr = 66:34). Dihydronaphthalene can also participate in the reaction, but gave a low yield (**4p**). (*E*)-1,2-Diphenylethene gave a mixture of diastereoisomers **4q** (dr = 53:47). Several non-styrenes also reacted. For example, norbornylene can deliver the target product, and only the major isomer was separated in spite of a low yield (**4r**).When cyclohexene was employed as a substrate, cyclohexenyl-PINO (**4s**) was selectively obtained in good yield. A possible mechanism for the formation of cyclohexenyl-PINO product (**4s**) was proposed (Scheme 3). The imidazole analogue of styrene gave the expected **4t** in moderate yield, while allyl phenyl ether gave a mixture of products with no apparent regioselectivity (r.r. = 1:1, **4u**).



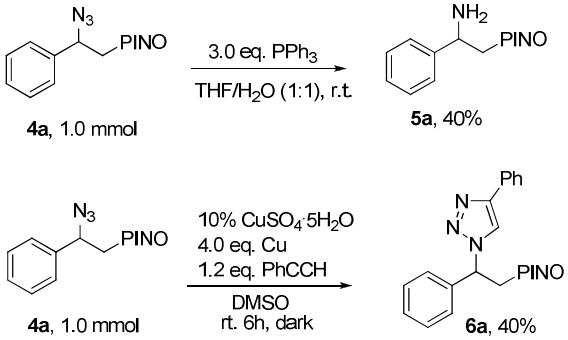
Scheme 2. Scope of metal-free oxyazidation of alkenes. Reaction conditions: **alkene** (0.6 mmol, 2.0 equiv.), **$TMSN_3$** (0.9 mmol, 3.0 equiv.), **3** (0.3 mmol), $PhI(OAc)_2$ (0.6 mmol, 2.0 equiv.), DCE (3.0 mL), 4Å M.S.,12 h, in air, at room temperature. r.r.= regioisomeric ratio (major : minor). PINO = phthalimide N-oxyl.



Scheme 3. The mechanism for the formation of **4s**.

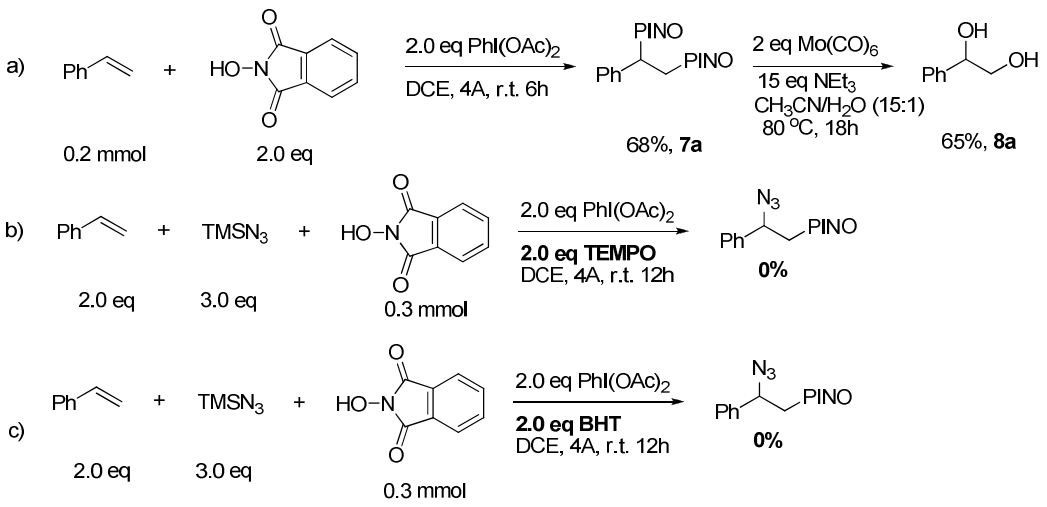
As mentioned above, azido compounds are very useful synthetic intermediates and building blocks in

organic synthesis. Hence, the azido products were further utilized in other transformations. In the presence of PPh_3 and water, 2-(2-azido-2-phenylethoxy)-isoindoline-1,3-dione (**4a**) was efficiently reduced to the corresponding amine product **5a** in 40% yield at room temperature.[4b] The product **4a** can also undergo the classical click reaction in the presence of $CuSO_4{\cdot}5H_2O$ (10 mmol%) and Cu powder (4.0 equiv.) at room temperature to afford the corresponding triazole **6a** in 40% yield (Scheme 4). [3j]



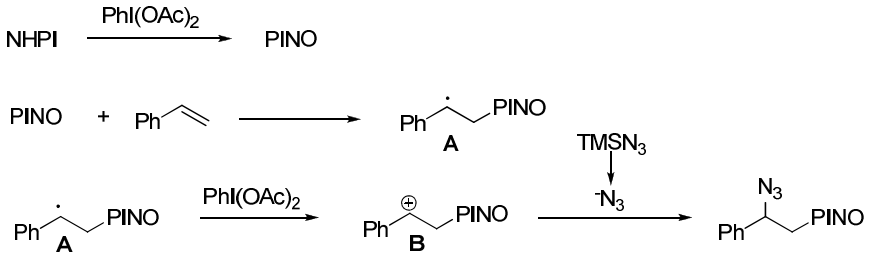
Scheme 4. Further synthetic transformations

In order to gain insight into the mechanism, some control experiments were carried out (Scheme 5). In the absence of $TMSN_3$ the dioxygenation product **7a** was obtained in 68% yield, which was consistent with a mechanism involving the PINO radical intermediate. The structure of the product **7a** was further confirmed by X-ray crystallography (see the Supporting Information).[8] The product **7a** can be transformed into 1-phenylethane-1,2-diol **8a** in moderate yield by cleavage of the N-O bond with $Mo(CO)_6$ (Scheme 5-a). To gain further understanding about the reaction mechanism, inhibition experiments were conducted. When 2.0 equiv. of TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy) or BHT (2,6-di-tert-butyl-4-methylphenol) was added into the reaction system, the desired transformation was found to be completely inhibited, providing further evidence that a radical addition mechanism was involved in this transformation (Scheme 5-b and c).



Scheme 5. Mechanistic experiments

According to the above experimental results and related published research studies[7c,9], a possible mechanism is outlined in Scheme 6. First, NHPI is oxidized to give the oxygen-centred radical PINO. PINO then quickly reacts with styrene to give radical **A**, which can be further oxidized to cation **B** in the presence of $PhI(OAc)_2$. Last, cation **B** was attacked by $^-N_3$ to give the azido product.



Scheme 6. Proposed Mechanism

In conclusion, we have developed an efficient metal-free oxyazidation of activated and unactivated alkenes for the synthesis of alkyl azides that holds great potential for the subsequent transformation of the azido unit. A radical addition process is involved in this transformation with the formation of C-O and C-N bonds. Further investigations on the scope and synthetic application of these reactions are ongoing in our group.

EXPERIMENTAL SECTION

General Remarks: Column chromatography was carried out on silica gel. Unless noted ^{1}H NMR spectra

were recorded on 400 MHz in $CDCl_3$ and *d*-DMSO, ^{13}C NMR spectra were recorded on 100 MHz in $CDCl_3$ and *d*-DMSO. IR spectra were recorded on an FT-IR spectrometer and only major peaks are reported in cm^{-1}. Melting points were determined on a microscopic apparatus and were uncorrected. All new products were further characterized by HRMS (high resolution mass spectra), high resolution mass spectrometry (HRMS) spectra was obtained on a micrOTOF-Q instrument equipped with an ESI source; copies of their ^1H NMR and ^{13}C NMR spectra are provided. Commercially available reagents **1**, **2**, **3** and solvents were used without further purification.

Typical procedure for the synthesis of products 4

To a solution of N-hydroxyphthalimide (**3**, 0.3 mmol, 48.9 mg) in DCE (3.0 mL) was added styrene (**1**, 0.6 mmol), $TMSN_3$ (**2**, 0.9 mmol), $PhI(OAc)_2$ (193.2 mg, 2.0 equiv.) and 4Å MS (40 mg). The reaction mixture was then stirred for 12 h at room temperature in air. After the reaction, the resulting mixture was quenched with water and extracted twice with EtOAc. The combined organic extracts were washed with brine, dried over Na_2SO_4 and concentrated. Purification of the crude product by flash column chromatography afforded the product **4 (**petroleum ether/ethyl acetate as eluent (6:1)).

Characterization data of compounds 4

2-(2-azido-2-phenylethoxy)isoindoline-1,3-dione (**4a**, 70%, 64.7mg), M.P.=66-68 ^oC, white solid, ^1H NMR (400 MHz, $CDCl_3$): 7.68-7.76 (m, 4 H), 7.51-7.52 (m, 2 H), 7.36-7.37 (m, 3 H), 5.50-5.53 (m, 1 H), 3.89-3.94 (*dd*, 1 H, *J* = 12.0 Hz, 8.0 Hz), 3.59-3.63 (*dd*, 1 H, *J* = 12.0 Hz, 4.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): 163.3, 135.8, 134.9, 134.4, 134.1, 129.0, 128.5, 127.8, 123.4, 87.5, 54.1; IR (cm^{-1}): 3064, 3035, 2935, 2105, 1789, 1736, 1668, 1459, 1370, 1187, 1126, 1077, 1019, 976, 877, 761, 701; HRMS (ESI) m/z: calcd for $C_{16}H_{12}N_4NaO_3$: M+Na = 331.0807; found: 331.0814.

2-(2-azido-2-p-tolylethoxy)isoindoline-1,3-dione (**4b**, 57%, 55.1mg), M.P.=64-65 ^oC, white solid, ^1H NMR (400 MHz, $CDCl_3$): 7.73-7.75 (m, 2 H), 7.67-7.69 (m, 2 H), 7.38-7.40 (m, 2 H), 7.16-7.18 (m, 2 H), 5.47-5.50 (*dd*, 1 H, *J* = 8.0 Hz, 4.0 Hz), 3.88-3.93 (*dd*, 1 H, *J* = 12.0 Hz, 8.0 Hz), 3.56-3.61 (*dd*, 1 H, *J* = 14.0 Hz, 6.0 Hz), 2.32 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.5, 139.7, 134.5, 132.0, 128.8, 127.9, 123.5, 87.4, 54.2, 21.3; IR (cm^{-1}): 2926, 2103, 1735, 1368, 975, 876, 814, 702; HRMS (ESI) m/z: calcd for $C_{17}H_{14}N_4NaO_3$: M+Na = 345.0964; found: 345.0958.

2-(2-azido-2-(4-methoxyphenyl)ethoxy)isoindoline-1,3-dione (**4c**, 44%, 44.6mg), oil, ^1H NMR (400 MHz, $CDCl_3$): 7.68-7.76 (m, 4 H), 7.42-7.44 (m, 2 H), 6.87-6.89 (m, 2 H), 5.46-5.49 (m, 1 H), 3.89-3.94 (*dd*, 1 H, *J* = 12.0 Hz, 8.0 Hz), 3.79 (s, 3 H), 3.57-3.62 (*dd*, 1 H, *J* = 16.0 Hz, 4.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): 163.4, 160.6, 134.4, 129.4, 128.6, 126.8, 123.4, 113.9, 87.0, 55.1, 53.9; IR (cm^{-1}): 2936, 2106, 1735, 1611, 1514, 1369, 1252, 1026, 975, 703; HRMS (ESI) m/z: calcd for $C_{17}H_{14}N_4NaO_4$: M+Na = 361.0913; found:

361.0907.

2-(2-azido-2-(4-bromophenyl)ethoxy)isoindoline-1,3-dione (**4d**, 78%, 90.3mg), M.P.=91-92°C, pale yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$): 7.69-7.77 (m, 4 H), 7.49-7.51 (m, 2 H), 7.41-7.43 (m, 2 H), 5.45-5.48 (m, 1 H), 3.85-3.90 (*dd*, 1 H, *J* = 14.0 Hz, 4.0 Hz), 3.58-3.62 (*dd*, 1 H, *J* = 12.0 Hz, 4.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): 163.3, 134.5, 132.1, 131.7, 129.5, 129.4, 128.5, 123.5, 86.8, 53.9; IR (cm^{-1}): 2930, 2105, 1735, 1369, 1285, 1073, 1013, 975, 790, 702; HRMS (ESI) m/z: calcd for $C_{16}H_{11}N_4NaBrO_3$: M+Na = 408.9912; found: 408.9907.

2-(2-azido-2-(4-chlorophenyl)ethoxy)isoindoline-1,3-dione (**4e**, 72%, 73.9mg), M.P.= 93-94 °C, pale yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$): 7.76-7.78 (m, 2 H), 7.70-7.72 (m, 2 H), 7.45-7.49 (m, 2 H), 7.34-7.37 (m, 2 H), 5.47-5.50 (m, 1 H), 3.85-3.91 (*dd*, 1 H, *J* = 16.0 Hz, 8.0 Hz), 3.58-3.62 (*dd*, 1 H, *J* = 12.0 Hz, 4.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): 163.3, 134.5, 129.2, 128.8, 128.6, 123.5, 86.8, 53.9; IR (cm^{-1}): 2931, 2105, 1736, 1671, 1368, 828, 702; HRMS (ESI) m/z: calcd for $C_{16}H_{11}N_4NaClO_3$: M+Na = 365.0417; found: 365.0412.

2-(2-azido-2-(4-fluorophenyl)ethoxy)isoindoline-1,3-dione (**4f**, 52%, 50.9mg), M.P.=69-70°C, pale yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$): 7.76-7.78 (m, 2 H), 7.70-7.72 (m, 2 H), 7.50-7.52 (m, 2 H), 7.04-7.10 (m, 2 H), 5.47-5.50 (*dd*, 1 H, *J* = 8.0 Hz, 4.0 Hz), 3.87-3.92 (*dd*, 1 H, *J* = 14.0 Hz, 6.0 Hz), 3.58-3.63 (*dd*, 1 H, *J* = 14.0 Hz, 6.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): 163.4, 134.5, 129.9, 129.8, 128.6, 123.5, 115.7, 115.5, 86.8, 54.0; IR (cm^{-1}): 2934, 2105, 1736, 1512, 836, 702; HRMS (ESI) m/z: calcd for $C_{16}H_{11}N_4NaFO_3$: M+Na = 349.0713; found: 349.0707.

2-(2-azido-2-(4-nitrophenyl)ethoxy)isoindoline-1,3-dione (**4g**, 91%, 96.4mg), M.P.=87-88°C, pale yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$): 8.24-8.26 (m, 2 H), 7.73-7.80 (m, 6 H), 5.56-5.59 (*dd*, 1 H, *J* = 4.0 Hz, 4.0 Hz), 3.88-3.93 (*dd*, 1 H, *J* = 14.0 Hz, 6.0 Hz), 3.67-3.72 (*dd*, 1 H, *J* = 14.0 Hz, 6.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): 163.3, 148.5, 142.2, 134.8, 128.7, 123.7, 86.6, 53.9; IR (cm^{-1}): 2931, 2107, 1736, 1522, 1348, 853, 702; HRMS (ESI) m/z: calcd for $C_{16}H_{11}N_5NaO_5$: M+Na = 376.0658; found: 376.0652.

4-(1-azido-2-(1,3-dioxoisoindolin-2-yloxy)ethyl)phenyl acetate (**4h**, 56%, r.r. = 5:2, 61.5mg), ^{1}H NMR (400 MHz, $CDCl_3$): 8.29-8.31 (m, 0.4 H), 8.21-8.23 (m, 0.4 H), 7.90-7.95 (m, 0.5 H), 7.82-7.86 (m, 0.5 H), 7.74-7.76 (m, 2 H), 7.68-7.70 (m, 2 H), 7.54-7.56 (m, 2 H), 7.11-7.14 (m, 2 H), 6.12-6.16 (m, 0.4 H), 5.52-5.55 (m, 1.0 H), 4.28-4.34 (m, 0.4 H), 3.86-3.90 (m, 1.0 H), 3.77-3.80 (m, 0.4 H), 3.58-3.62 (m, 1.0 H), 2.29 (s, 1.2 H), 2.28 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): 169.0, 168.9, 163.3, 159.1, 157.2, 151.5, 151.0, 135.8, 134.4, 134.1, 132.5, 127.9, 123.4, 122.1, 121.7, 86.8, 58.8, 54.1, 50.5, 20.9; IR (cm^{-1}): 2932, 2106,

1738, 1665, 1509, 1370, 1199, 976, 911, 702; HRMS (ESI) m/z: calcd for $C_{18}H_{14}N_4NaO_5$: M+Na = 389.0862; found: 389.0856.

2-(2-azido-2-(naphthalene-2-yl)ethoxy)isoindoline-1,3-dione (**4i**, 51%, 54.8mg), oil, ^{1}H NMR (400 MHz, $CDCl_3$): 7.93 (s, 1 H), 7.85-7.87 (m, 1 H), 7.78-7.83 (m, 2 H), 7.66-7.69 (m, 3 H), 7.59-7.61 (m, 2 H), 7.43-7.45 (m, 2 H), 5.68-5.71 (m, 1 H), 3.96-4.02 (*dd*, 1 H, *J* = 16.0 Hz, 8.0 Hz), 3.64-3.68 (*dd*, 1 H, *J* = 12.0 Hz, 4.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): 163.4, 134.3, 133.7, 132.7, 132.4, 128.5, 128.1, 127.8, 127.7, 126.7, 126.4, 124.5, 123.4, 87.6, 54.1; IR (cm^{-1}): 3058, 2930, 2103, 1734, 1368, 1186, 1126, 975, 751, 702; HRMS (ESI) m/z: calcd for $C_{20}H_{14}N_4NaO_3$: M+Na = 381.0964; found: 381.0958.

2-(2-azido-2-(3-methoxyphenyl)ethoxy)isoindoline-1,3-dione (**4j**, 60%, 60.8mg), oil, ^{1}H NMR (400 MHz, $CDCl_3$): 7.68-7.76 (m, 4 H), 7.24-7.28 (m, 1 H), 7.14-7.15 (m, 1 H), 7.04-7.06 (m, 1 H), 6.87-6.90 (m, 1 H), 5.51-5.54 (m, 1 H), 3.86-3.91 (*dd*, 1 H, *J* = 12.0 Hz, 8.0 Hz), 3.83 (s, 3 H), 3.57-3.61 (*dd*, 1 H, *J* = 12.0 Hz, 4.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): 163.3, 159.6, 136.5, 134.4, 129.5, 128.7, 123.4, 119.9, 115.6, 112.7, 87.4, 55.2, 54.3; IR (cm^{-1}): 2940, 2104, 1735, 1602, 1368, 1268, 876, 787, 702; HRMS (ESI) m/z: calcd for $C_{17}H_{14}N_4NaO_4$: M+Na = 361.0913; found: 361.0907.

2-(2-azido-2-(3-bromophenyl)ethoxy)isoindoline-1,3-dione (**4k**, 70%, 81.1mg), M.P.=65-66^{o}C, pale yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$): 7.77-7.79 (m, 2 H), 7.71-7.73 (m, 2 H), 7.67 (s, 1 H), 7.48-7.52 (m, 2 H), 7.25-7.29 (m, 1 H), 5.42-5.45 (*dd*, 1 H, *J* = 8.0 Hz, 4.0 Hz), 3.85-3.90 (*dd*, 1 H, *J* = 14.0 Hz, 6.0 Hz), 3.59-3.63 (*dd*, 1 H, *J* = 16.0 Hz, 4.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): 163.3, 137.4, 134.5, 130.1, 128.6, 126.3, 123.6, 122.5, 86.8, 54.1; IR (cm^{-1}): 3065, 2928, 2104, 1737, 1470, 1369, 1188, 1125, 976, 877, 787, 701; HRMS (ESI) m/z: calcd for $C_{16}H_{11}N_4NaBrO_3$: M+Na = 408.9912; found: 408.9907.

2-(2-azido-2-(2-chlorophenyl)ethoxy)isoindoline-1,3-dione (**4l**, 72%, 73.9mg), M.P.=60-61^{o}C, pale yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$): 7.97-7.99 (m, 1 H), 7.77-7.79 (m, 2 H), 7.70-7.73 (m, 2 H), 7.37-7.41 (m, 1 H), 7.29-7.33 (m, 2 H), 6.04-6.06 (m, 1 H), 3.80-3.85 (*dd*, 1 H, *J* = 14.0 Hz, 6.0 Hz), 3.66-3.70 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.2, 134.5, 132.9, 132.8, 130.3, 127.1, 123.5, 84.1, 53.4; IR (cm^{-1}): 2928, 2105, 1738, 1367, 975, 876, 759, 702; HRMS (ESI) m/z: calcd for $C_{16}H_{11}N_4NaClO_3$: M+Na = 365.0417; found: 365.0412.

2-(2-azido-2-phenylpropoxy)isoindoline-1,3-dione (**4m**, 55%, 53.1mg), oil, ^{1}H NMR (400 MHz, $CDCl_3$): 7.82-7.84 (m, 2 H), 7.74-7.77 (m, 2 H), 7.69-7.71 (m, 2 H), 7.37-7.42 (m, 3 H), 3.86-3.94 (m, 2 H), 1.82 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): 165.1, 139.3, 134.6, 128.6, 128.2, 126.5, 123.5, 89.6, 58.6, 21.7; IR (cm^{-1}): 3061, 2934, 2104, 1736, 1187, 1115, 972, 767, 702; HRMS (ESI) m/z: calcd for $C_{17}H_{14}N_4NaO_3$:

M+Na = 345.0964; found: 345.0958.

2-(2-azido-2-(4-iodophenyl)propoxy)isoindoline-1,3-dione (**4n**, 50%, 67.2mg), oil, ^{1}H NMR (400 MHz, $CDCl_3$): 7.82-7.85 (m, 2 H), 7.73-7.77 (m, 4 H), 7.42-7.44 (m, 2 H), 3.84 (*dd*, *J* = 12.0 Hz, 32.0 Hz, 2 H), 1.75 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): 165.0, 139.3, 137.3, 134.7, 128.9, 128.5, 123.6, 94.8, 89.2, 58.3, 21.7; IR (cm^{-1}): 2984, 2105, 1791, 1736, 1368, 1310, 1077, 927, 876, 705; HRMS (ESI) m/z: calcd for $C_{17}H_{13}N_4NaIO_3$: M+Na = 470.9930; found: 470.9925.

2-(1-azido-1-phenylpropan-2-yloxy)isoindoline-1,3-dione (**4o**, 70%, 67.6mg), dr=66:34, ^{1}H NMR (400 MHz, $CDCl_3$): 7.70-7.72 (m, 2 H), 7.66-7.69 (m, 2 H), 7.52-7.54 (m, 1.3 H), 7.46-7.48 (m, 0.8 H), 7.34-7.39 (m, 3 H), 5.28-5.31 (*dd*, 1 H, *J* = 8.0 Hz, 4.0 Hz), 4.01-4.08 (m, 1 H), 1.43 (*d*, 2 H, *J* = 4.0 Hz), 1.10 (*d*, 1 H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): 163.3, 134.3, 128.7, 128.4, 128.1, 123.3, 91.6, 90.6, 59.8, 59.5, 16.3, 15.9; IR (cm^{-1}): 2932, 2107, 1736, 1668, 1374, 983, 876, 701; HRMS (ESI) m/z: calcd for $C_{17}H_{14}N_4NaO_3$: M+Na = 345.0964; found: 345.0958.

2-(1-azido-1,2,3,4-tetrahydronaphthalen-2-yloxy)isoindoline-1,3-dione (**4p**, 40%, 40.1mg), dr>98:2 M.P.=104-105 ^{o}C, white solid, ^{1}H NMR (400 MHz, $CDCl_3$): 7.85-7.87 (m, 2 H), 7.75-7.80 (m, 3 H), 7.25-7.32 (m, 2 H), 7.16-7.18 (m, 1 H), 5.07-5.08 (d, *J* = 3.6 Hz, 1 H), 4.36-4.37 (m, 1 H), 2.91-2.96 (m, 2 H), 2.55-2.59 (m, 1 H), 2.10-2.16 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.9, 137.3, 134.6, 132.1, 129.5, 126.5, 123.6, 84.2, 58.5, 24.6, 22.9; IR (cm^{-1}): 2932, 2099, 1734, 1370, 1258, 974, 876, 775, 752, 702; HRMS (ESI) m/z: calcd for $C_{18}H_{14}N_4NaO_3$: M+Na = 357.0964; found: 357.0958.

2-(2-azido-1,2-diphenylethoxy)isoindoline-1,3-dione (**4q**, 72%, 82.9mg), M.P.=111-113^{o}C, white solid, dr=53:47, ^{1}H NMR (400 MHz, $CDCl_3$): 7.57-7.59 (m, 2 H), 7.53-7.55 (m, 2 H), 7.47-7.50 (m, 1 H), 7.19-7.39 (m, 5 H), 7.04-7.09 (m, 4 H), 5.57-5.60 (m, 1 H), 5.10-5.12 (m, 0.45 H), 4.99-5.01 (m, 0.51 H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.0, 134.1, 128.4, 127.7, 123.1, 123.0, 91.1, 89.5, 68.6, 67.6; IR (cm^{-1}): 2927, 2105, 1735, 979, 876, 760, 701; HRMS (ESI) m/z: calcd for $C_{22}H_{16}N_4NaO_3$: M+Na = 407.1120; found: 407.1115.

2-(3-azidobicyclo[2.2.1]heptan-2-yloxy)isoindoline-1,3-dione (**4r**, 30%, 26.8mg, major stereoisomer), M.P. = 75-76 ^{o}C, white solid, ^{1}H NMR (400 MHz, $CDCl_3$): 7.84-7.86 (m, 2 H), 7.75-7.77 (m, 2 H), 4.39-4.40 (t, ^{3}J = 2.0 Hz, 1 H), 3.73-3.75 (t, ^{3}J = 2.4 Hz, 1 H), 2.70 (m, 1 H), 2.33-2.35 (m, 1 H), 2.09-2.15 (m, 1 H), 1.71-1.76 (m, 1 H), 1.64-1.67 (m, 1 H), 1.38-1.56 (m, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.7, 134.6, 128.8, 123.6, 95.0, 68.5, 42.1, 40.1, 34.7, 26.3, 19.7; IR (cm^{-1}): 2962, 2096, 1736, 1372, 1019, 786, 703; HRMS (ESI) m/z: calcd for $C_{15}H_{14}N_4NaO_3$: M+Na = 321.0964; found: 321.0958.

2-(cyclohex-2-enyloxy)isoindoline-1,3-dione (**4s**, 69%, 50.3mg), m.p.= 62-63 ^{o}C, white solid, ^{1}H NMR (400 MHz, $CDCl_3$): 7.83-7.85 (m, 2 H), 7.74-7.77 (m, 2 H), 6.07-6.10 (m, 1 H), 5.92-5.95 (m, 1 H), 4.75-4.76 (m, 1 H), 2.12-2.20 (m, 1 H), 1.99-2.05 (m, 3 H), 1.79-1.87 (m, 1 H), 1.61-1.64 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): 164.2, 134.9, 134.3, 128.9, 123.8, 123.4, 80.8, 27.2, 25.1, 18.1; IR (cm^{-1}): 2938, 2099, 1734, 1650, 1540, 1518, 790, 702;

2-(2-azido-2-(1H-imidazol-1-yl)ethoxy)isoindoline-1,3-dione (**4t**, 60%, 53.6mg), M.P.=142-143^{o}C, white solid, ^{1}H NMR (400 MHz, *d*-DMSO): 8.63 (s, 1 H), 8.46-8.53 (m, 1 H), 8.08-8.16 (m, 3 H), 7.95-7.97 (m, 1 H), 7.62 (s, 1 H), 6.57-6.60 (m, 1 H), 4.66-4.71 (m, 1 H), 4.50-4.55 (m, 1 H); ^{13}C NMR (100 MHz, *d*-DMSO): 168.7, 167.4, 166.7, 137.6, 134.0, 131.8, 129.9, 128.4, 123.6, 118.0, 87.3, 50.9, 21.2; IR (cm^{-1}): 3442, 2113, 1675, 1650, 1026, 1003, 824, 764; HRMS (ESI) m/z: calcd for $C_{13}H_{11}N_6O_3$: M+H = 299.0893; found: 299.0887.

2-(2-azido-3-phenoxypropoxy)isoindoline-1,3-dione (**4u**, 30%, 30.4mg), r.r.=1:1, ^{1}H NMR (400 MHz, $CDCl_3$): 7.71-7.84 (m, 4 H), 7.23-7.28 (m, 3 H), 7.02 (m, 1 H), 6.85-6.88 (m, 0.6 H), 6.73-6.77 (m, 0.4 H), 6.20-6.21 (m, 0.9 H), 5.67-5.72 (m, 0.5 H), 5.51-5.53 (m, 0.6 H), 4.96-4.98 (m, 0.3 H), 4.70-4.72 (m, 0.3 H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.6, 156.5, 150.5, 146.9, 134.4, 134.2, 129.6, 129.4, 128.8, 123.4, 122.5, 117.4, 117.0, 116.2, 114.5, 105.3, 104.3, 103.7, 84.6, 74.8, 70.1, 50.5; IR (cm^{-1}): 2935, 2106, 1734, 1493, 1224, 968, 878, 757, 700; HRMS (ESI) m/z: calcd for $C_{17}H_{14}N_4O_4Na$: M+Na = 361.0913; found: 361.0907.

Synthetic transformation of product 4a to 5a and 6a.

The reaction of 2-(2-azido-2-phenylethoxy)isoindoline-1,3-dione **4a** (308 mg, 1.0 mmol) and PPh_3(786 mg, 3.0 mmol) were placed in a Schlenk tube under air, followed by the addition of THF (2.0 mL) and water (2.0 mL). The reaction was conducted at room temperature for 12h. After that, 5.0 mL water was added and the reaction was extracted by ethyl acetate twice (10 mL each time). The crude product was purified by flash column chromatography on silica gel (eluent: petroleum ether / ethyl acetate = 3: 1) to afford the product **5a** (112.8 mg, solid).

2-(2-amino-2-phenylethoxy)isoindoline-1,3-dione (**5a**, 40%, 112.8 mg), M.P.=113-114 ^{o}C, pale yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$): 7.79-7.80 (m, 2 H), 7.67-7.68 (m, 2 H), 7.28-7.40 (m, 5 H), 5.19 (s, 2 H, NH_2), 4.91-4.94 (*dd*, 1 H, *J* = 4.0 Hz, 4.0 Hz), 4.06-4.09 (*dd*, 1 H, *J* = 4.0 Hz, 4.0 Hz), 3.80-3.85 (*dd*, 1 H, *J* = 16.0 Hz, 4.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): 167.9, 138.3, 133.7, 131.7, 126.7, 123.0, 83.2, 41.6; IR (cm^{-1}): 3473, 3061, 3033, 2940, 1772, 1711, 1424, 1393, 1370, 1188, 1063, 1025, 923, 759, 716; HRMS (ESI) m/z: calcd for $C_{16}H_{15}N_2O_3$: M+H = 283.1083; found: 283.1097.

The reaction of 2-(2-azido-2-phenylethoxy)isoindoline-1,3-dione **4a** (308 mg, 1.0 mmol), ethynylbenzene (122.4 mg, 1.2 mmol), $CuSO_4 \cdot 5H_2O$ (25.0 mg, 0.1 mmol) and Cu powder (256 mg, 4.0 mmol) were placed in a flame-dried Schlenk tube under air, followed by the addition of DMSO (4.0 mL).The reaction was conducted at room temperature for 6 h in dark place. After that, 5.0 mL water was added and the reaction was extracted by ethyl acetate. The crude product was purified by flash column chromatography on silica gel (eluent: petroleum ether / ethyl acetate = 1: 1) to afford the product **6a** (164 mg, solid).

2-(2-phenyl-2-(4-phenyl-1H-1,2,3-triazol-1-yl)ethoxy)isoindoline-1,3-dione (**6a**, 40%, 164mg), M.P.= 193-194 ^oC, pale yellow solid , ^1H NMR (400 MHz, $CDCl_3$): 8.13 (s, 1 H), 7.83-7.84 (m, 2 H), 7.66-7.71 (m, 4 H), 7.47-7.49 (m, 2 H), 7.39-7.43 (m, 3 H), 7.36-7.37 (m, 3 H), 5.79-5.82 (m, 1 H), 5.02-5.07 (m, 1 H), 4.86-4.90 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.3, 147.7, 134.6, 134.1, 130.0, 128.8, 128.7, 128.5, 127.7, 125.7, 123.6, 121.1, 86.8, 53.6; IR (cm^{-1}): 2926, 1734, 1540, 1516, 763, 699; HRMS (ESI) m/z: calcd for $C_{24}H_{18}N_4O_3Na$: M+Na = 433.1277; found: 433.1271.

Typical procedure for the synthesis of product 7a

The reaction of N-Hydroxyphthalimide (**3**, 0.4 mmol, 65.2 mg) in DCE (3.0 mL) was added styrene (**1**, 0.2 mmol, 20.8 mg), $PhI(OAc)_2$ (128.8 mg, 0.4 mmol) and 4Å MS (40 mg). The reaction mixture was then stirred for 12 h at room temperature in air. The resulting mixture was quenched with water and extracted twice with EtOAc. The combined organic extracts were washed with brine, dried over Na_2SO_4 and concentrated. Purification of the crude product by flash column chromatography afforded the product **7a (**petroleum ether/ethyl acetate as eluent (3:1), 68%, 58.2 mg).

Compound **7a**, M.P.=180-181^oC, white solid, ^1H NMR (400 MHz, $CDCl_3$): 7.66-7.79 (m, 8 H), 7.55-7.58 (m, 2 H), 7.34-7.36 (m, 3 H), 5.85-5.87 (m, 1 H), 4.91-4.95 (m, 1 H), 4.54-4.58 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.3, 162.9, 134.4, 134.2, 128.6, 128.0, 123.4, 123.3, 85.6, 79.2; IR (cm^{-1}): 2924, 1788, 1733, 1653, 1540, 1462, 1394, 1375, 1187, 1131, 1076, 1021, 972, 878, 700; HRMS (ESI) m/z: calcd for $C_{24}H_{16}N_2O_6Na$: M+Na = 451.0906; found: 451.0901.

Typical procedure for the synthesis of compound 8a

A mixture of **7a** (58.2 mg, 0.136 mmol), $Mo(CO)_6$ (71.8 mg, 0.272 mmol), Et_3N (206 mg, 2.04mmol) in MeCN-H_2O (15:1, 3 mL) was stirred at 80^oC for 18h. Afterwards, the mixture was concentrated, and the residue purified by chromatography on silica (ethyl acetate/hexane= 1:1) to give **8a** (12.2 mg, 65%). ^{1} H NMR (400 M H_Z, $CDCl_3$): 7.24-7.28 (m, 5 H), 4.72-4.75 (dd, *J* = 8.0, 4.0 Hz, 1 H), 4.06 (s, 2 H), 3.55-3.67 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): 140.5, 128.4, 127.8, 126.0, 74.6, 67.9; the spectral data were

identical to the values of the previous reports: commercially available -CAS#16355-00-3.

Supporting Information Available: Representative experimental procedures, X-ray crystallographic data of **7a**, and ^{1}H NMR and ^{13}C NMR spectra of all compounds are available free of charge *via* the Internet at http://pubs.acs.org.

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8. CCDC 1026407 (**7a**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif.

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