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Mn-catalyzed diazidation and azidooxygenation of alkenes

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Dedicated to Professor Tien-Yau Luh on the occasion of his 76th birthday

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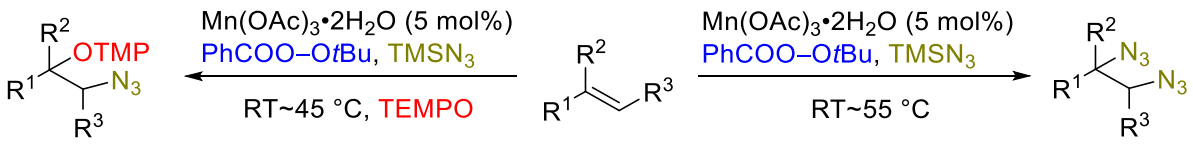
Abstract

A method of Mn-catalyzed alkene diazidation has been developed, using peroxide as the oxidant under mild conditions. Furthermore, azidooxygenation products were afforded by addition of TEMPO to alkenes. The reactions are general and not sensitive to oxygen and moisture, whereas, the experimental procedure is simple. The products are formed in high yields. The catalyst loading can be reduced to 1 mol %, providing good yield of the desired product. A radical addition and combination pathway could possibly be involved in these transformations.



Keywords: Mn catalysis, radical, diazidation, azidooxygenation, alkene difunctionalization

Introduction

Alkyl azides are a class of important scaffolds, which can be used as versatile reactants and are widely used in drug discovery, biological and material sciences.[1,2] The addition of two azide radicals or an azide radical and other one radical or a nucleophile with alkenes are one type of the most significant and efficient strategies for the synthesis of aliphatic azides.[3-8] Azide radicals are generally produced by the oxidation or homolytic cleavage of azido precursors under thermal,[9-15] photoredox[16-19] or electrochemical[17,20-23] conditions. For instance, Loh reported a copper-catalyzed vicinal diazidation of styrenes using an azidoiodine(III) reagent as the azide radical source;[24] Greaney reported a light-switchable diazidation or methoxy azidation of styrene-type double bonds;[25] Lin reported a manganese-catalyzed electrochemical diazidation of alkenes, exhibiting exceptional substrate generality and functional group compatibility.[26]

Manganese has been widely used as a catalyst or a stoichiometry oxidant in a number of redox reactions by the virtue of environmentally benign and sustainable nature, also by low cost and versatile reactivities.[27-29] Notably, manganese salts and complexes are excellent catalyst in a variety of azidation reactions of organic compounds, including radical mono- or diazidations of alkenes and other compounds, and inert aliphatic C–H azidations. Meanwhile, peroxides are highly useful oxidants for the radical azidation reactions.[9,30-35] In 2017, we reported a manganese-catalyzed oxidative carboazidation of acrylamides using *tert*-butyl peroxybenzoate (TBPB) as the oxidant (Figure 1, **a**).[36] Then, employing the same oxidant, Bao reported copper-catalyzed diazidation of olefins in acetonitrile or water under heating conditions (Figure 1, **b**).[37] In 2018, Xu reported an olefin diazidation protocol enabled by an iron(II) catalyst, which used oxygen and moisture sensitive iron catalyst, and a bidentate or tridentate ligand was necessary (Figure 1, **c**).[38] Herein we describe a manganese-catalyzed diazidation and radical oxyfunctionalization of alkenes under mild conditions, which is not sensitive to oxygen and moisture (Figure 1, **d**).

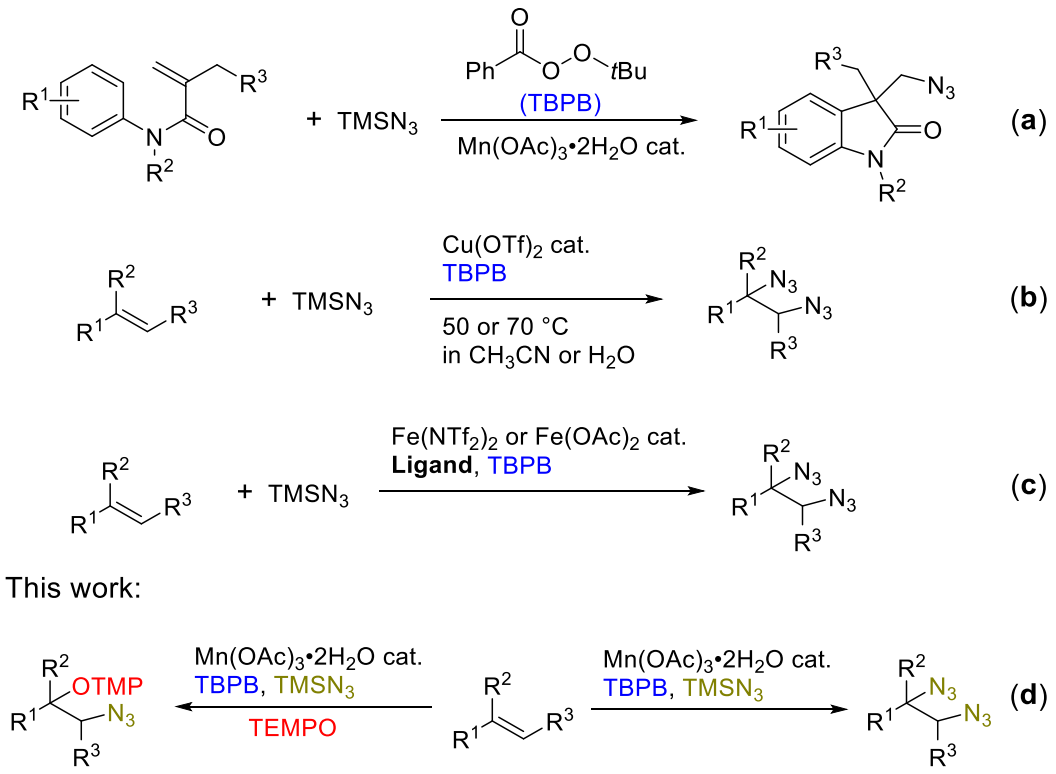


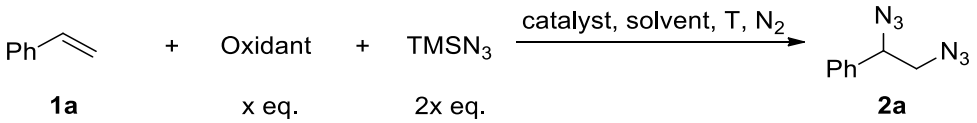
Figure 1. Azidation reactions of alkenes.

Results and Discussion

We commenced our study by using styrene (**1a**) as the model substrate, peroxide as the oxidant, azidotrimethylsilane ($TMSN_3$) as the azide source and metal salt as the catalyst. The reaction using TBPB (*tert*-butyl peroxybenzoate, oxidant, 1.5 eq.) and $Mn(OAc)_3{\cdot}2H_2O$ (catalyst, 10 mol %) in acetonitrile (ACN) at room temperature for 12 h afforded the desired diazidation product **2a** in 76% isolated yield (table 1, entry 1). DMF (*N*,*N*-dimethylformamide) was not a suitable solvent, however, reaction in THF (sensitive to alkoxy radical) could provide good yield of the product, and the reactions in a cheap solvent DCM afforded excellent yields (entries 4–6). Then we found that 1.25 equivalents of TBPB and 5 mol% Mn catalyst were enough for providing 88% yield of the desired product (entries 4–8). The reaction could afford satisfactory yield upon elevation the reaction temperature (entries 9 and 10), and 77% yield of the product could be obtained using only 1 mol % of the catalyst at 40 °C (entry 10). Reaction using other oxidants, such as BPO (benzoyl peroxide), DTBP (di-*tert*-butyl peroxide), DCP (dicumyl peroxide) et. al., resulted in little or no diazidation product (entries 11–13). Then we screened several metal catalysts, such as manganese, iron, copper and silver salts, and we found that manganese(II) acetate is also a viable catalyst for this method (entries 14–20). The reaction enabled by a manganese catalyst containing two crystal water molecules is not sensitive to water and oxygen (entry 21), but large amount of water inhibits it seriously (entry 22).

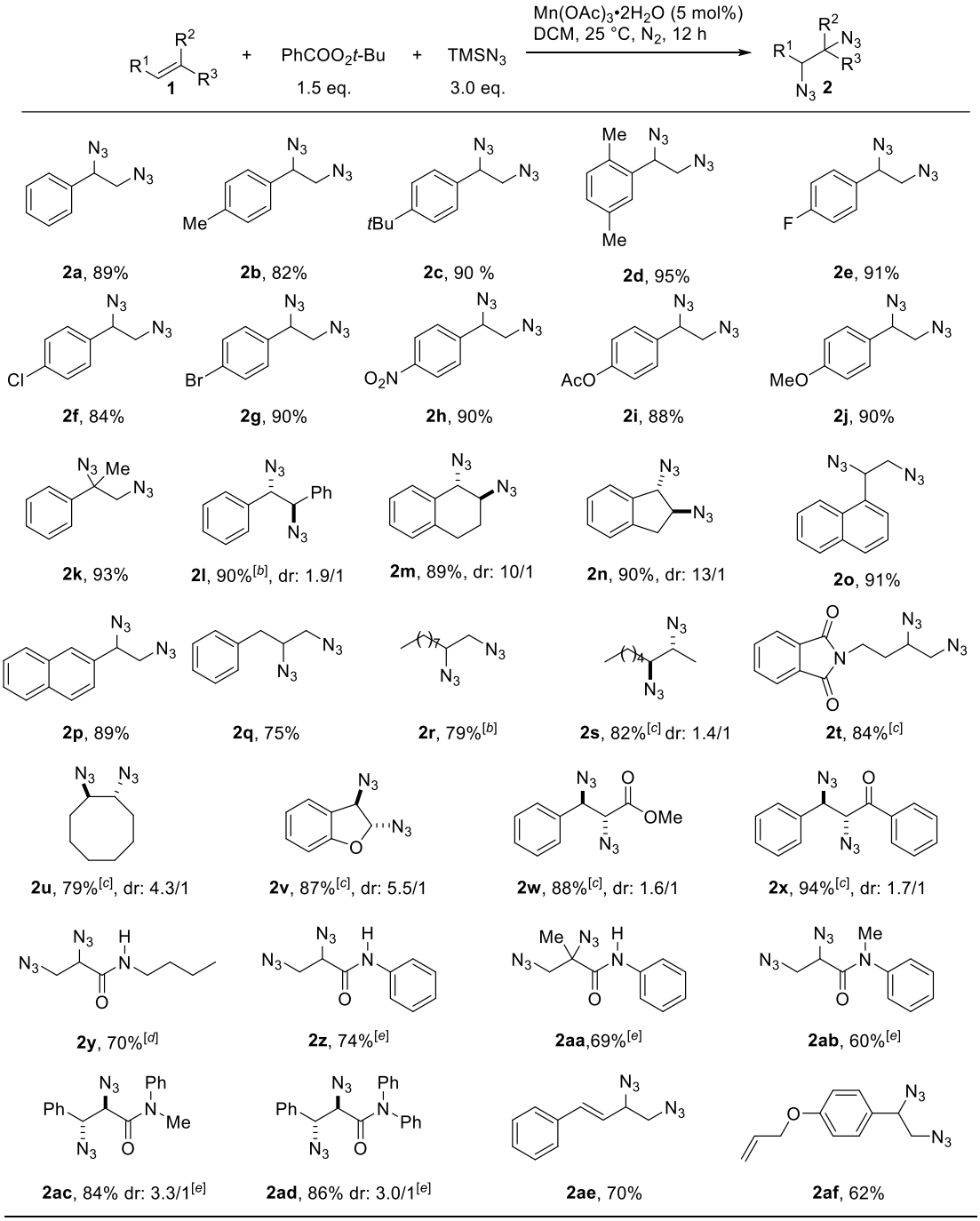
One of the optimized reaction conditions (Table 1, entry 5) was used for investigation the scope of this diazidation method. For substituents on the phenyl of styrene, the position and electronic nature had little effect on the efficiency of the reaction (**2a**–**2j**). Alkenes with α,α-disubstituted and vicinal disubstituted structure afforded the desired product in excellent yields (**2k**–**2n**), good dr could be obtained using cyclic substrates (**2m** and **2n**). Reactions using 1- or 2-vinylnaphthalene resulted in about 90% yield of the products (**2o** and **2p**). Except for styrene-type substrates, alkyl alkenes including inner, terminal and cyclic alkenes were also suitable substrates (**2q**–**2u**). In addition, heterocyclic compounds such as benzofuran took part in the reaction smoothly, affording dearomatized diazide product in high yield (**2v**). C–C double bonds in α,β-unsaturated ester and α,β-unsaturated ketone were also viable in this transformation (**2w** and **2x**). For some substrates that were not so active, elevation the temperature to 40 °C (DCE used as the solvent) made the reactions complete in 12 hours (**2r**–**2x**). The diastereoselectivity of this method depends on the structure of the substrates, the acyclic alkenes gave low dr value (**2s**, **2w** and **2x**), while cyclic alkenes provided higher dr (**2u** and **2v**). The transformation of α,β-unsaturated amides needed higher temperature, especially for *N*-alkyl amide such as **2y**, resulting in a little lower yields (**2y**–**2ad**). Notably, good yields of mono-diazidation products of 1,3-diene and allyl styrene could be obtained (**2ae** and **2af**).

Table 1. Reaction conditions optimization



Entry	Oxidant (x eq.)	cat. (mol %)	solvent	Yield[a]
1	TBPB (1.5)	$Mn(OAc)_3·2H_2O$ (10)	ACN	76%
2	TBPB (1.5)	$Mn(OAc)_3·2H_2O$ (10)	DMF	<5%
3	TBPB (1.5)	$Mn(OAc)_3·2H_2O$ (10)	THF	68%
4	TBPB (1.5)	$Mn(OAc)_3·2H_2O$ (10)	DCM	90%
5	TBPB (1.5)	$Mn(OAc)_3·2H_2O$ (5)	DCM	89%
6	TBPB (1.25)	$Mn(OAc)_3·2H_2O$ (5)	DCM	88%
7	TBPB (1.1)	$Mn(OAc)_3·2H_2O$ (5)	DCM	79%
8	TBPB (1.25)	$Mn(OAc)_3·2H_2O$ (3)	DCM	79%
9	TBPB (1.25)	$Mn(OAc)_3·2H_2O$ (3)	DCM	85%[b]
10	TBPB (1.25)	$Mn(OAc)_3·2H_2O$ (1)	DCM	77%[c]
11	BPO (1.25)	$Mn(OAc)_3·2H_2O$ (5)	DCM	8%
12	DTBP (1.25)	$Mn(OAc)_3·2H_2O$ (5)	DCM	n.d.
13	DCP (1.25)	$Mn(OAc)_3·2H_2O$ (5)	DCM	5%
14	TBPB (1.25)	$Mn(OAc)_2$ (5)	DCM	74%
15	TBPB (1.25)	$MnSO_4$ (5)	DCM	n.d.
16	TBPB (1.25)	$MnCl_2$ (5)	DCM	n.d.
17	TBPB (1.25)	$FeCl_3$ (5)	DCM	47%
18	TBPB (1.25)	$FeCl_2$ (5)	DCM	36%
19	TBPB (1.25)	CuCl (5)	DCM	n.d.
20	TBPB (1.25)	AgOAc (5)	DCM	n.d.
21	TBPB (1.5)	$Mn(OAc)_3·2H_2O$ (5)	DCM	79%[d]
22	TBPB (1.25)	$Mn(OAc)_3·2H_2O$ (5)	DCM	14%[e]

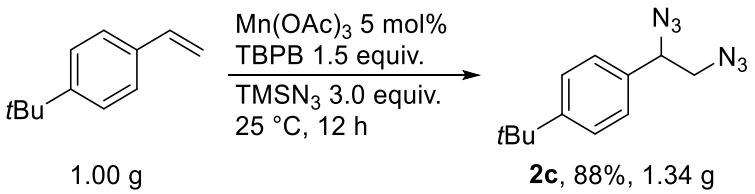
[a]Styrene 0.2 mmol scale, in solvent 2 mL under N_2 atmosphere; Isolated yield; $TMSN_3$: peroxide = 2 : 1; [b]At 40 °C; [c]1 mmol scale, at 40 °C; [d]0.6 mmol scale, in 10 mL Schlenk tube and 6 mL DCM, under sealed air (about 4 mL air); [e]Addition of 3 equivalents of H_2O.



[a]Isolated yield; dr: Diastereomeric ratio; [b]*trans*-Stilbene was used; [c]Using dichloroethane as solvent, at 40 °C; [d]Using dichloroethane as solvent, at 55 °C; [e]Using dichloroethane as sovent, at 45 °C.

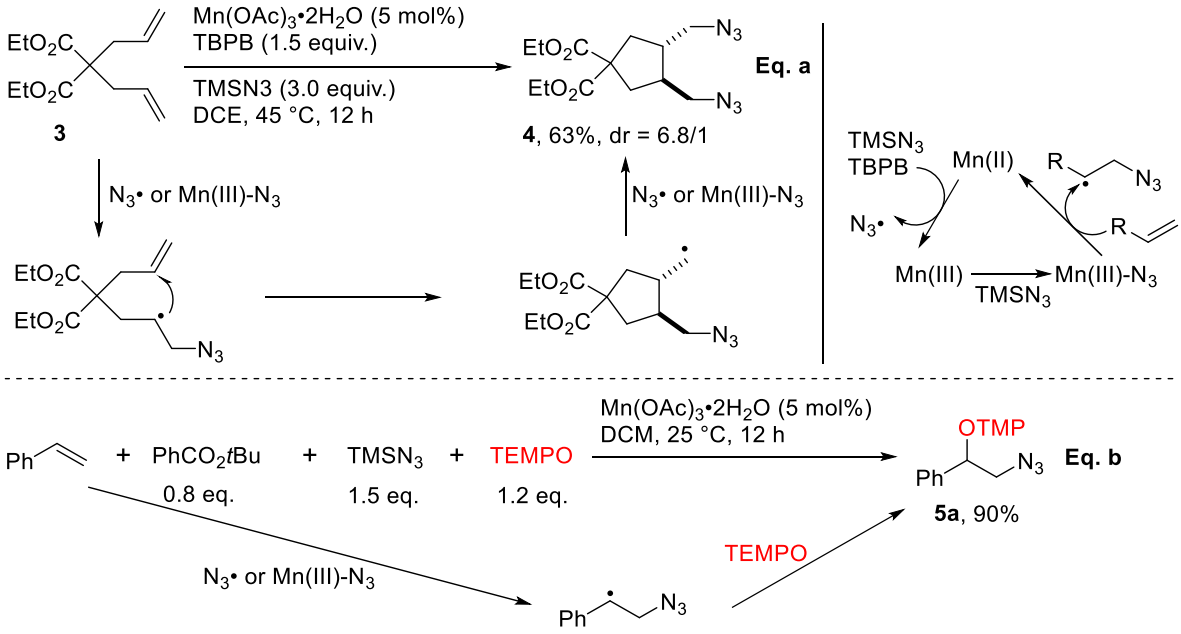
Scheme 1. Scope of manganese-catalyzed diazidation of alkenes.[a]

Gram-scale reaction of 4-*t*Bu styrene also afforded the desired product in high yield, resulting in 1.34 g of the diazidation product (Scheme 2).



Scheme 2. Gram-scale reaction of 4-*t*Bu styrene.

Then two reactions were used to investigate the mechanism (Scheme 3). Diene **3** could be converted into a cyclic diazido product (Scheme 3, Eq. a), while the addition of TEMPO (2,2,6,6-tetramethylpiperidin-1-oxyl) to the reaction, high yield of azidooxygenation product could be obtained (Scheme 3, Eq. b). A radical reaction process could possibly be involved in these two types of reactions as shown in Scheme 3, which is analogous to mechanism reported by Loh[24] and Kashyap[39].



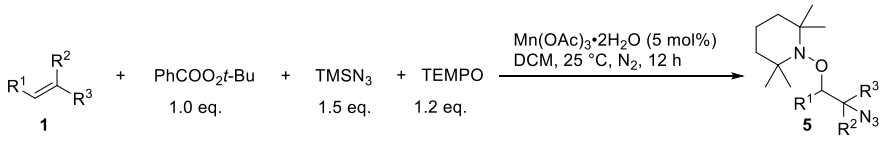
Scheme 3. Primary mechanism study.

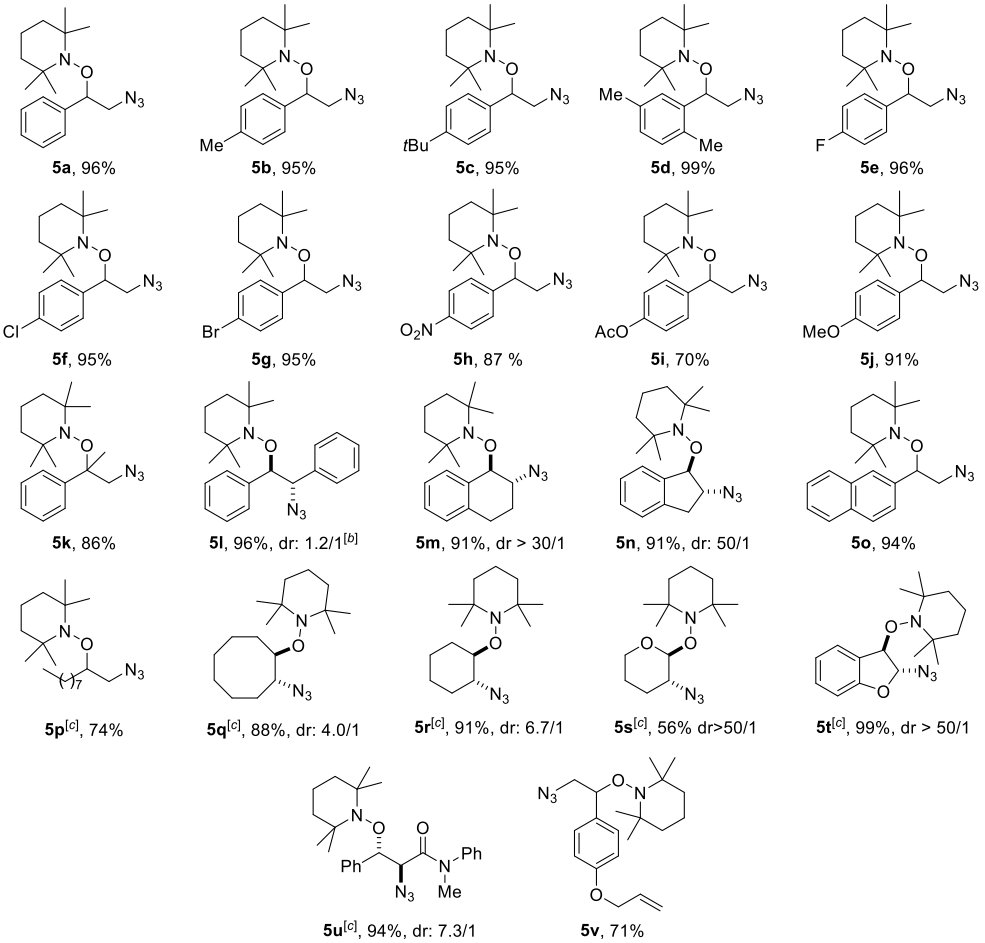
The result of Scheme 3 (Eq. b) indicated that simple addition of TEMPO could provide high yield of azidooxygenation product. After simple screening of the conditions, high yield of the desired product could be afforded (Table 2), and the conditions shown in entry 2 were used for the investigation of the scope of the scope of this mothed.

Table 2. Reaction conditions optimization for azidooxygenation of alkenes

Entry	TBPB/equiv.	$TMSN_3$/equiv.	TEMPO/equiv.	Yield[a]
1	0.8	1.5	1.2	90%
2	1.0	1.5	1.2	96%
3	1.2	1.5	1.2	95%
4	1.5	1.5	1.2	97%
5	1.2	1.2	1.2	89%

[a]Isolated yield.





[a]Isolated yield; dr: diastereomeric ratio; [b]*trans*-Stilbene was used; [c]In DCE, at 45 °C.

Scheme 4. Scope of manganese-catalyzed azidooxygenation of alkenes.[a]

With the optimized conditions of azidooxygenation in hand, we commenced to explore the scope of this method (Scheme 4). In general, terminal styrene-type alkenes bearing various substituents were good substrates for this transformation (**5a**–**5j, 5o**), so was the 1,1-disubstituted alkene (**5k**), mostly giving the product in excellent yields. Reactions of 1,2-disubstituted alkenes proceeded smoothly. While transformation of acyclic *trans*-stilbene afforded low dr value (**5l**), reactions of cyclic alkene such indene and 1,2-dihydronaphthalene exhibited excellent stereoselectivity (dr > 30, **5m** and **5n**). Facial reaction of alkyl alkenes still needed higher temperature (45 °C), and the dr was moderate (**5p**–**5r**). However, oxacyclic compounds, 3,4-dihydro-2*H*-pyran and benzofuran, were also suitable candidates, and afforded nearly pure *trans*-products (**5s** and **5t**). α,β-Unsaturated amide was also well tolerated (**5u**), giving good anti-selectivity. Product of mono-azidooxygenation of allyl styrene could be afforded in good yield (**5v**).

Conclusions

We have developed methods for the efficient diazidation and azidooxygenation of a variety of alkenes, which are not sensitive to oxygen and moisture. These methods are suitable for styrene-type alkenes, alkyl alkenes, heterocyclic compounds and α,β-unsaturated carboxylic acid derivatives. Gram scale diazidation reaction also afforded high yield of the product. Primary mechanism study indicated that a radical addition and combination pathway could possibly be involved in these transformations.

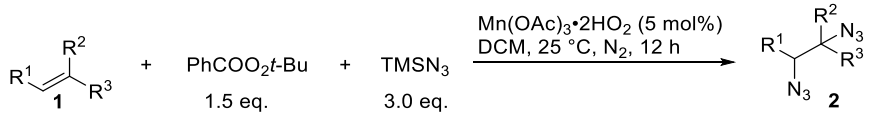
Experimental Section

General. All air- and moisture-sensitive manipulations were carried out with standard Schlenk techniques under nitrogen. ^{1}H and ^{13}C NMR spectra were recorded on a on a Bruker AV-500 spectrometer (500 MHz and 126 MHz, respectively). ^{1}H and ^{13}C NMR chemical shifts are reported vs tetramethylsilane signal or residual proton solvent signals. High resolution mass spectra (HRMS) was recorded on Agilent G6500 iFunnel Q-TOF LC/MS.

THF was distilled over sodium benzophenone ketyl under nitrogen. Acetonitrile (ACN) and 1,2-dichloroethane (DCE) were distilled over CaH_2 under nitrogen. *N*,*N*-dimethylformamide was used before vacuum distillation over CaH_2 under nitrogen.

All other chemicals and solvents were purchased from commercial company and used as received.

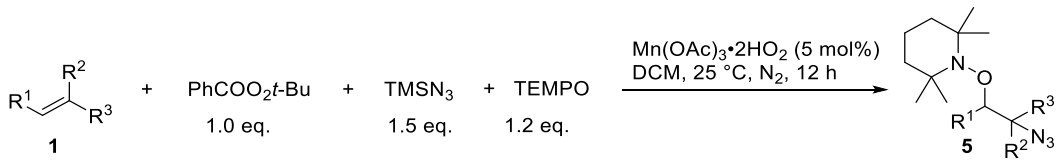
Procedure for diazidation of alkenes



10 mL Schlenk tube was charged with $Mn(OAc)_3$•$2H_2O$ 4.0 mg (5 mol %, solid alkenes also were added in this step), then the tube was evacuated and refilled with nitrogen for three times and 1 mL DCM, 0.3 mmol alkene, TBPB 86 µL (0.45 mmol, 1.5 equiv.), $TMSN_3$ 124 µL (95%, 0.90 mmol, 3.0 equiv.) and another 1 mL DCM was added in order, then the reaction mixture was stirred for 12 hours at 25 °C. The mixture was concentrated in

vacuo the residue was father purified by flash chromatography on silica gel with petroleum ether and ether (for some substrates petroleum ether and ethyl acetate was used) to afford the desired product.

Procedure for oxyazidation of alkenes



10 mL Schlenk tube was charged with $Mn(OAc)_3•2H_2O$ 4.0 mg (5 mol %, solid alkenes also was added in this step) and TEMPO 56 mg (0.36 mmol, 1.2 equiv.), this tube was evacuated and refilled with nitrogen for three times and 1 mL DCM, 0.3 mmol alkene, TBPB 57 µL (0.3 mmol, 1.0 equiv.), $TMSN_3$ 62 µL (95%, 0.45 mmol, 1.5 equiv.) and another 1 mL DCM was added in order, then the reaction mixture was stirred for 12 hours at 25 °C. The mixture was concentrated in *vacuo* the residue was further purified by flash chromatography on silica gel with petroleum ether and ether (for some substrates petroleum ether and ethyl acetate was used) to afford the desired product.

(1,2-Diazidoethyl)benzene (2a).[38] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.46 – 7.30 (m, 5H), 4.68 (dd, *J* 8.4, 4.8 Hz, 1H), 3.51 (dd, *J* 13.0, 8.5 Hz, 1H), 3.44 (dd, *J* 12.5, 4.5 Hz, 1H)

1-(1,2-Diazidoethyl)-4-methylbenzene (2b).[24] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.27 – 7.21 (m, 4H), 4.67 (dd, *J* 8.4, 4.9 Hz, 1H), 3.52 (dd, *J* 12.7, 8.4 Hz, 1H), 3.45 (dd, *J* 12.7, 4.9 Hz, 1H), 2.40 (s, 3H).

1-(*tert*-Butyl)-4-(1,2-diazidoethyl)benzene (2c).[24] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.50 – 7.43 (m, 2H), 7.29 (m, 2H), 4.68 (dd, *J* 8.6, 4.7 Hz, 1H), 3.53 (dd, *J* 12.8, 8.5 Hz, 1H), 3.46 (dd, *J* 12.7, 4.7 Hz, 1H), 1.36 (s, 9H).

2-(1,2-Diazidoethyl)-1,4-dimethylbenzene (2d).[24] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.21 (d, *J* 1.7 Hz, 1H), 7.17 – 7.08 (m, 2H), 4.93 (dd, *J* 8.9, 4.4 Hz, 1H), 3.53 (dd, *J* 12.8, 8.9 Hz, 1H), 3.42 (dd, *J* 12.8, 4.4 Hz, 1H), 2.39 (s, 3H), 2.37 (s, 3H).

1-(1,2-Diazidoethyl)-4-fluorobenzene (2e).[24] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.36 – 7.28 (m, 2H), 7.15 – 7.06 (m, 2H), 4.66 (dd, *J* 8.2, 5.0 Hz, 1H), 3.49 (dd, *J* 12.7, 8.1 Hz, 1H), 3.42 (dd, *J* 12.8, 5.0 Hz, 1H).

1-chloro-4-(1,2-diazidoethyl)benzene (2f).[24] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.42 – 7.36 (m, 2H), 7.31 – 7.24 (m, 2H), 4.65 (dd, *J* 8.1, 5.0 Hz, 1H), 3.49 (dd, *J* 12.8, 8.0 Hz, 1H), 3.43 (dd, *J* 12.7, 5.0 Hz, 1H).

1-Bromo-4-(1,2-diazidoethyl)benzene (2g).[24] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.61 – 7.54 (m, 2H), 7.27 – 7.21 (m, 2H), 4.67 (dd, *J* 8.0, 5.0 Hz, 1H), 3.51 (dd, *J* 12.8, 8.1 Hz, 1H), 3.45 (dd, *J* 12.8, 5.0 Hz, 1H).

1-(1,2-Diazidoethyl)-4-nitrobenzene (2h).[24] Light yellow oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.33 – 8.23 (m, 2H), 7.59 – 7.49 (m, 2H), 4.80 (dd, *J* 7.3, 5.4 Hz, 1H), 3.59 – 3.47 (m, 2H).

4-(1,2-Diazidoethyl)phenyl acetate (2i).[37] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.40 – 7.33 (m, 2H), 7.20 – 7.13 (m, 2H), 4.70 (dd, *J* 8.4, 4.7 Hz, 1H), 3.51 (dd, *J* 12.8, 8.4 Hz, 1H), 3.45 (dd, *J* 12.8, 4.7 Hz, 1H), 2.33 (s, 3H). ^{13}C NMR δ 169.1, 150.9, 133.8, 128.0, 122.2, 64.9, 55.9, 21.0. HRMS *m/z* (ESI) calcd. For $C_{10}H_{14}N_7O_2$ $(M+NH_4)^+$: 264.1203, found 264.1202.

1-(1,2-Diazidoethyl)-4-methoxybenzene (2j).[24] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.32 – 7.25 (m, 2H), 7.00 – 6.93 (m, 2H), 4.65 (dd, *J* 8.3, 5.0 Hz, 1H), 3.85 (s, 3H), 3.51 (dd, *J* 12.7, 8.3 Hz, 1H), 3.43 (dd, *J* 12.7, 5.0 Hz, 1H).

(1,2-Diazidopropan-2-yl)benzene (2k).[38] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.51 – 7.41 (m, 4H), 7.41 – 7.35 (m, 1H), 3.52 (d, *J* 12.5 Hz, 1H), 3.43 (d, *J* 12.6 Hz, 1H), 1.80 (s, 3H).

***anti*-1,2-Diazido-1,2-diphenylethane (*anti*-2l)**.[39] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.46 – 7.38 (m, 2H), 7.34 – 7.25 (m, 6H), 7.14 – 7.06 (m, 2H), 4.67 (s, 2H).

***syn*-1,2-Diazido-1,2-diphenylethane (*syn*-2l)**.[39] ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.46 – 7.38 (m, 2H), 7.34 – 7.25 (m, 6H), 7.14 – 7.06 (m, 2H), 4.72 (s, 2H).

***trans*-1,2-Diazido-1,2,3,4-tetrahydronaphthalene (*trans*-2m)**.[38] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.44 – 7.37 (m, 1H), 7.35 – 7.25 (m, 2H), 7.18 (m, 1H), 4.46 (d, *J* 6.6 Hz, 1H), 3.90 (m, 1H), 3.03 – 2.84 (m, 2H), 2.28 (m, 1H), 2.07 – 1.93 (m, 1H).

***trans*-1,2-Diazido-2,3-dihydro-1H-indene (*trans*-2n)**.[38] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.43 – 7.31 (m, 3H), 7.31 – 7.26 (m, 1H), 4.80 (d, *J* 5.6 Hz, 1H), 4.20 (dd, *J* 6.9, 5.6 Hz, 1H), 3.38 (dd, *J* 16.0, 7.3 Hz, 1H), 2.97 (dd, *J* 16.0, 6.6 Hz, 1H).

1-(1,2-Diazidoethyl)naphthalene (2o).[24] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.03 (d, *J* 8.4 Hz, 1H), 7.93 (d, *J* 8.1 Hz, 1H), 7.89 (d, *J* 8.2 Hz, 1H), 7.65 – 7.58 (m, 2H), 7.57 – 7.49 (m, 2H), 5.46 (dd, *J* 8.0, 4.9 Hz, 1H), 3.72 – 3.57 (m, 2H).

2-(1,2-Diazidoethyl)naphthalene (2p).[24] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.94 – 7.78 (m, 4H), 7.58 – 7.48 (m, 2H), 7.43 (dd, *J* 8.5, 1.8 Hz, 1H), 4.85 (dd, *J* 8.4, 4.9 Hz, 1H), 3.60 (dd, *J* 12.8, 8.4 Hz, 1H), 3.53 (dd, *J* 12.8, 4.9 Hz, 1H).

(2,3-Diazidopropyl)benzene (2q).[39] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.36 (m, 2H), 7.33 – 7.29 (m, 1H), 7.27 – 7.22 (m, 2H), 3.75 (m, 1H), 3.43 (dd, *J* 12.7, 4.0 Hz, 1H), 3.32 (dd, *J* 12.7, 6.9 Hz, 1H), 2.91 (d, *J* 7.0 Hz, 2H).

1,2-Diazidodecane (2r).[40] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 3.49 – 3.42 (m, 1H), 3.38 (dd, *J* 12.7, 4.0 Hz, 1H), 3.31 (dd, *J* 12.6, 7.4 Hz, 1H), 1.58 – 1.49 (m, 2H), 1.50 – 1.19 (m, 12H), 0.88 (t, *J* 7.0 Hz, 3H).

***anti*-2,3-Diazidooctane (*anti*-2s)**.[41] Colorless oil.^{1}H NMR (500 MHz, Chloroform-*d*) δ 3.57 – 3.46 (m, 1H), 3.35 – 3.26 (m, 1H), 1.63 – 1.43 (m, 4H), 1.43 – 1.25 (m, 8H), 0.90 (t, 3H).

***syn*-2,3-Diazidooctane (*syn*-2s)**.[41] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 3.57 – 3.46 (m, 1H), 3.21 – 3.13 (m, 1H), 1.63 – 1.43 (m, 4H), 1.43 – 1.25 (m, 8H), 0.90 (t, 3H).

2-(3,4-Diazidobutyl)isoindoline-1,3-dione (2t). White solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.85 (dp, *J* 5.3, 1.7 Hz, 2H), 7.77 – 7.69 (m, 2H), 3.89 – 3.76 (m, 2H), 3.57 – 3.50 (m, 1H), 3.47 (dd, *J* 12.6, 4.0 Hz, 1H), 3.41 (ddt, *J* 12.7, 7.4, 1.0 Hz, 1H), 1.95 – 1.86 (m, 1H), 1.86 – 1.76 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.2, 134.1, 131.8, 123.3, 59.7, 54.8, 34.6, 30.7. HRMS *m/z* (APCI) calcd. For $C_{12}H_{12}N_7O_2$ $(M+H)^+$: 286.1052, found 286.1059.

***trans*-1,2-Diazidocyclooctane (*trans*-2u)**.[40] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 3.57 – 3.48 (m, 2H), 2.00 – 1.35 (m, 12H).

***cis*-1,2-Diazidocyclooctane (*cis*-2u)**.[40] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 3.79 – 3.73 (m, 2H), 2.00 – 1.35 (m, 12H).

***trans*-Diazido-2,3-dihydrobenzofuran (*trans*-2v)**.[42] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.43 – 7.37 (m, 2H), 7.11 – 7.06 (m, 1H), 7.03 (d, *J* 8.1 Hz, 1H), 5.78 (d, *J* 1.3 Hz, 1H), 4.63 (s, 1H).

***cis*-Diazido-2,3-dihydrobenzofuran (*cis*-2v)**.[42] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.37 – 7.32 (m, 2H), 7.06 (t, *J* 7.8 Hz, 1H), 6.97 (d, *J* 8.1 Hz, 1H), 5.86 (d, *J* 6.3 Hz, 1H), 4.91 (d, *J* 6.3 Hz, 1H).

***anti*-Methyl-2,3-diazido-3-phenylpropanoate (*anti*-2w).**[41] Colorless oil. ^{1}H NMR (500 MHz, Chloroform10.3987/R-1977-01-0033-*d*) δ 7.49 – 7.36 (m, 5H), 5.08 (d, *J* 5.8 Hz, 1H), 4.05 (d, *J* 5.8 Hz, 1H), 3.77 (s, 3H).

***syn*-Methyl-2,3-diazido-3-phenylpropanoate (*syn*-2w)**.[41] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.50 – 7.37 (m, 5H), 4.93 (d, *J* 8.0 Hz, 1H), 4.13 (d, *J* 8.1 Hz, 1H), 3.85 (s, 3H).

***anti*-2,3-Diazido-1,3-diphenylpropan-1-one (*anti*-2x).** White solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.01 – 7.97 (m, 2H), 7.68 – 7.62 (m, 1H), 7.54 – 7.50 (m, 2H), 7.48 – 7.44 (m, 5H), 5.12 (d, *J* 9.8 Hz, 1H), 4.68 (d, *J* 9.4 Hz, 1H). HRMS *m/z* (DART Positive) calcd. For $C_{15}H_{13}N_6O$ $(M+H)^+$: 293.1145, found 293.1141.

***syn*-2,3-Diazido-1,3-diphenylpropan-1-one (*syn*-2x).** ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.43 – 7.37 (m, 2H), 7.11 – 7.06 (m, 1H), 7.03 (d, *J* 8.1 Hz, 1H), 5.78 (d, *J* 1.3 Hz, 1H), 4.63 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.8, 135.0, 134.9, 134.1, 129.2, 129.0, 128.8, 128.5, 127.6, 66.3, 66.0. HRMS *m/z* (DART Positive) calcd. For $C_{15}H_{13}N_6O$ $(M+H)^+$: 293.1145, found 293.1141.

2,3-Diazido-*N*-butylpropanamide (2y). Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 6.48 (s, 1H), 4.13 (dd, *J* 7.0, 3.4 Hz, 1H), 3.86 (dd, *J* 12.9, 3.4 Hz, 1H), 3.67 (dd, *J* 12.9, 7.0 Hz, 1H), 3.27 (m, *J* 7.0, 5.9, 1.1 Hz, 2H), 1.55 – 1.46 (m, 2H), 1.40 – 1.30 (m, 2H), 0.93 (t, *J* 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.1, 63.5, 53.0, 39.4, 31.3, 19.9, 13.6. HRMS *m/z* (ESI) calcd. For $C_7H_{14}N_7O$ $(M+H)^+$: 212.1254, found 212.1255.

2,3-Diazido-*N*-phenylpropanamide (2z). Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.23 (s, 1H), 7.57 – 7.51 (m, 2H), 7.39 – 7.31 (m, 2H), 7.20 – 7.14 (m, 1H), 4.28 (dd, *J* 7.0, 3.3 Hz, 1H), 3.95 (dd, *J* 12.9, 3.4 Hz, 1H), 3.77 (dd, *J* 12.9, 7.1 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.3, 136.4, 129.4, 125.2, 120.1, 63.6, 53.0. HRMS *m/z* (ESI) calcd. For $C_9H_{10}N_7O$ $(M+H)^+$: 232.0941, found 232.0943.

2,3-Diazido-2-methyl-*N*-phenylpropanamide (2aa).[21] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.36 (s, 1H), 7.58 – 7.52 (m, 2H), 7.38 – 7.31 (m, 2H), 7.16 (tt, *J* 7.3, 1.2 Hz, 1H), 3.81 (d, *J* 12.7 Hz, 1H), 3.63 (d, *J* 12.7 Hz, 1H), 1.66 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.5, 136.7, 129.0, 125.0, 120.0, 67.1, 57.5, 20.1. HRMS *m/z* (ESI) calcd. For $C_{10}H_{12}N_7O$ $(M+H)^+$: 246.1098, found 246.1099.

2,3-Diazido-N-methyl-*N*-phenylpropanamide (2ab). Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.50 – 7.43 (m, 2H), 7.40 (tt, 1H), 7.26 – 7.21 (m, 2H), 3.73 – 3.62 (m, 2H), 3.52 (dd, *J* 12.1, 6.8 Hz, 1H), 3.33 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.0, 142.0, 130.2, 128.7, 127.1, 57.3, 51.4, 37.8. HRMS *m/z* (ESI) calcd. For $C_{10}H_{12}N_7O$ $(M+H)^+$: 246.1098, found 246.1099.

***trans*-2,3-Diazido-*N*-methyl-*N*,3-diphenylpropanamide (*anti*-2ac).** White solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.48 (dd, *J* 8.0, 6.7 Hz, 2H), 7.44 – 7.39 (m, 1H), 7.37 – 7.28 (m, 5H), 7.19 (dd, *J* 6.7, 2.9 Hz, 2H), 5.03 (d, *J* 10.2 Hz, 1H), 3.66 (dd, *J* 10.2, 0.9 Hz, 1H), 3.40 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.2, 142.2, 135.4, 130.0, 129.1, 128.9, 128.5, 127.5, 127.4, 65.7, 60.9, 37.7. HRMS *m/z* (ESI) calcd. For $C_{16}H_{16}N_7O$ $(M+H)^+$: 322.1411, found 322.1406.

***cis*-2,3-Diazido-*N*-methyl-*N*,3-diphenylpropanamide (*syn*-2ac).** ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.43 – 7.26 (m, 6H), 7.19 – 7.14 (m, 2H), 6.54 (brs, 2H), 5.03 (d, *J* 10.0 Hz, 1H), 3.64 (d, *J* 10.0 Hz, 1H), 3.04 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.5, 141.7, 134.9, 129.8, 129.1, 128.7, 128.4, 127.8, 126.9, 66.6, 63.0, 37.1. HRMS *m/z* (ESI) calcd. For $C_{16}H_{16}N_7O$ $(M+H)^+$: 322.1411, found 322.1406.

***trans*-2,3-Diazido-*N*,*N*,3-triphenylpropanamide (*anti*-2ad)**. White Solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.48 (t, *J* 7.5 Hz, 2H), 7.44 – 7.31 (m, 10H), 7.28 – 7.20 (m, 4H), 5.10 (d, *J* 10.2 Hz, 1H), 3.79 (d, *J* 10.2 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.5, 141.7, 141.2, 135.2, 129.9, 129.2, 128.9, 128.9, 128.5, 128.4, 127.4, 126.6, 126.0, 66.0, 61.7. HRMS *m/z* (ESI) calcd. For $C_{21}H_{18}N_7O$ $(M+H)^+$:384.1567, found 384.1562.

(*E*)-(3,4-Diazidobut-1-en-1-yl)benzene (2ae).[43] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.45 – 7.39 (m, 2H), 7.40 – 7.32 (m, 2H), 7.35 – 7.27 (m, 1H), 6.74 (d, *J* 15.8 Hz, 1H), 6.13 (dd, *J* 15.8, 8.0 Hz, 1H), 4.32 – 4.21 (m, 1H), 3.46 – 3.35 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 135.5, 135.3, 128.7, 128.6, 126.8, 122.9, 63.9, 54.5. HRMS *m/z* (APCI) calcd. For $C_{10}H_{11}N_4$ $(M-N_2+H)^+$: 187.0978, found 187.0981.

1-(Allyloxy)-4-(1,2-diazidoethyl)benzene (2af). Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.31 – 7.24 (m, 2H), 7.01 – 6.94 (m, 2H), 6.08 (ddt, *J* 17.4, 10.6, 5.3 Hz, 1H), 5.45 (dq, *J* 17.2, 1.6 Hz, 1H), 5.33 (dq, *J* 10.4, 1.4 Hz, 1H), 4.64 (dd, *J* 8.3, 5.0 Hz, 1H), 4.58 (dt, *J* 5.2, 1.6 Hz, 2H), 3.51 (dd, *J* 12.7, 8.3 Hz, 1H), 3.43 (dd, *J* 12.7,

5.0 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.0, 132.9, 128.4, 128.2, 117.8, 115.1, 68.8, 65.0, 55.8. HRMS *m/z* (DART Positive) calcd. For $C_{11}H_{12}N_3O$ $(M\text{-}N_3)^+$: 202.0975, found 202.0974.

Diethyl-3,4-bis(azidomethyl)cyclopentane-1,1-dicarboxylate (4). Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 4.19 (qd, *J* 7.2, 0.8 Hz, 5H), 3.40 – 3.27 (m, 4H), 2.51 – 2.43 (m, 2H), 2.43 – 2.34 (m, 2H), 2.12 (dd, *J* 13.9, 7.1 Hz, 1H), 1.25 (t, *J* 7.1 Hz, 7H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.0 (d, *J* 13 Hz), 61.8 (d, *J* 12 Hz), 58.6, 51.4, 40.5, 37.1, 14.0.

1-(2-Azido-1-phenylethoxy)-2,2,6,6-tetramethylpiperidine (5a).[44] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.37 (d, *J* 4.1 Hz, 4H), 7.34 – 7.29 (m, 1H), 4.85 (dd, *J* 6.9, 4.6 Hz, 1H), 3.75 (dd, *J* 12.3, 4.6 Hz, 1H), 3.67 (dd, *J* 12.3, 6.9 Hz, 1H), 1.63 – 1.27 (m, 6H), 1.35 (s, 3H), 1.22 (s, 3H), 1.06 (s, 3H), 0.71 (s, 3H).

1-(2-Azido-1-(p-tolyl)ethoxy)-2,2,6,6-tetramethylpiperidine (5b).[44] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.24 (m, 2H), 7.16 (m, 2H), 4.80 (dd, *J* 7.0, 4.7 Hz, 1H), 3.74 (dd, *J* 12.3, 4.7 Hz, 1H), 3.63 (dd, *J* 12.3, 7.0 Hz, 1H), 2.36 (s, 3H), 1.62 – 1.26 (m, 6H), 1.33 (s, 3H), 1.20 (s, 3H), 1.04 (s, 3H), 0.72 (s, 3H).

1-(2-Azido-1-(4-(tert-butyl)phenyl)ethoxy)-2,2,6,6-tetramethylpiperidine (5c).[44] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.37 – 7.32 (m, 2H), 7.28 – 7.23 (m, 2H), 4.81 (dd, *J* 6.9, 4.6 Hz, 1H), 3.76 (dd, *J* 12.2, 4.7 Hz, 1H), 3.62 (dd, *J* 12.3, 7.0 Hz, 1H), 1.31 (s, 9H), 1.31 (s, 9H), 1.19 (s, 3H), 1.05 (s, 3H), 0.72 (s, 3H).

1-(2-Azido-1-(2,5-dimethylphenyl)ethoxy)-2,2,6,6-tetramethylpiperidine (5d).[18] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.29 – 7.23 (m, 1H), 7.07 – 6.98 (m, 2H), 5.09 (dd, *J* 6.3, 5.2 Hz, 1H), 3.77 – 3.67 (m, 2H), 2.37 (s, 3H), 2.34 (s, 3H), 1.65 – 1.28 (m, 6H), 1.38 (s, 3H), 1.23 (s, 3H), 1.05 (s, 3H), 0.75 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.9, 135.1, 131.8, 129.9, 128.1, 128.0, 81.7, 60.0, 59.8, 54.7, 40.4, 34.3, 33.3, 21.1, 20.3, 20.2, 19.1, 17.0. HRMS *m/z* (ESI) calcd. For $C_{19}H_{31}N_4O$ $(M+H)^+$: 331.2492, found 331.2487.

1-(2-Azido-1-(4-fluorophenyl)ethoxy)-2,2,6,6-tetramethylpiperidine (5e).[44] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.34 – 7.29 (m, 2H), 7.08 – 7.02 (m, 2H), 4.81 (dd, *J* 7.0, 4.7 Hz, 1H), 3.72 (dd, *J* 12.3, 4.7 Hz, 1H), 3.62 (dd, *J* 12.3, 7.1 Hz, 1H), 1.61 – 1.25 (m, 9H), 1.32 (s, 3H), 1.19 (s, 3H), 1.03 (s, 3H), 0.67 (s, 3H).

1-(2-Azido-1-(4-chlorophenyl)ethoxy)-2,2,6,6-tetramethylpiperidine (5f).[44] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.36 – 7.32 (m, 2H), 7.32 – 7.28 (m, 2H), 4.82 (dd, *J* 6.8, 4.5 Hz, 1H), 3.72 (dd, *J* 12.3, 4.5 Hz, 1H), 3.65 (dd, *J* 12.3, 6.8 Hz, 1H), 1.63 – 1.25 (m, 6H), 1.33 (s, 3H), 1.20 (s, 3H), 1.04 (s, 3H), 0.70 (s, 3H).

1-(2-Azido-1-(4-bromophenyl)ethoxy)-2,2,6,6-tetramethylpiperidine (5g).[44] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.52 – 7.46 (m, 2H), 7.26 – 7.21 (m, 2H), 4.80 (dd, *J* 6.8, 4.6 Hz, 1H), 3.71 (dd, *J* 12.4, 4.6 Hz, 1H), 3.65 (dd, *J* 12.3, 6.8 Hz, 1H), 1.65 – 1.24 (m, 6H), 1.32 (s, 3H), 1.19 (s, 3H), 1.04 (s, 3H), 0.70 (s, 3H).

1-(2-Azido-1-(4-nitrophenyl)ethoxy)-2,2,6,6-tetramethylpiperidine (5h).[45] Colorless solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.26 – 8.18 (m, 2H), 7.57 – 7.49 (m, 2H), 4.94 (dd, *J* 6.5, 4.3 Hz, 1H), 3.76 (dd, *J* 12.5, 6.5 Hz, 1H), 3.71 (dd, *J* 12.5, 4.3 Hz, 1H), 1.63 – 1.24 (m, 6H), 1.33 (s, 3H), 1.20 (s, 3H), 1.04 (s, 3H), 0.67 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.4, 128.2, 123.4, 84.4, 60.2, 60.1, 54.8, 40.3 (2×CH_2), 34.4, 34.0, 20.2 (2×CH_3), 16.9. HRMS *m/z* (ESI) calcd. For $C_{17}H_{26}N_5O_3$ $(M+H)^+$: 348.203, found 348.2024.

4-(2-Azido-1-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)ethyl)phenyl acetate (5i).[44] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.38 – 7.32 (m, 2H), 7.12 – 7.06 (m, 2H), 4.83 (dd, *J* 6.7, 4.6 Hz, 1H), 3.74 (dd, *J* 12.4, 4.7 Hz, 1H), 3.63 (dd, *J* 12.4, 6.7 Hz, 1H), 1.63 – 1.24 (m, 6H), 1.32 (s, 3H), 1.19 (s, 3H), 1.03 (s, 3H), 0.70 (s, 3H).

1-(2-Azido-1-(4-methoxyphenyl)ethoxy)-2,2,6,6-tetramethylpiperidine (5j).[44] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.30 – 7.22 (m, 2H), 6.92 – 6.85 (m, 2H), 4.77 (dd, *J* 7.1, 4.9 Hz, 1H), 3.85 – 3.77 (m, 6H), 3.74 (dd, *J* 12.2, 4.8 Hz, 1H), 3.59 (dd, *J* 12.2, 7.2 Hz, 1H), 1.60 – 1.24 (m, 6H), 1.31 (s, 3H), 1.18 (s, 3H), 1.03 (s, 3H), 0.69 (s, 3H).

1-((1-Azido-2-phenylpropan-2-yl)oxy)-2,2,6,6-tetramethylpiperidine (5k).[44] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.53 – 7.48 (m, 2H), 7.38 – 7.32 (m, 2H), 7.31 – 7.25 (m, 1H), 3.63 (d, *J* 11.8 Hz, 1H), 3.45 (d, *J*

11.8 Hz, 1H), 1.74 (d, *J* 0.7 Hz, 3H), 1.59 – 1.36 (m, 5H), 1.28 (m, 1H), 1.21 (s, 3H), 1.20 (s, 3H), 1.05 (s, 3H), 0.49 (s, 3H).

***anti*-1-(2-Azido-1,2-diphenylethoxy)-2,2,6,6-tetramethylpiperidine (*anti*-5l)**.[18] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.24 – 7.11 (m, 6H), 7.01 (m, 1.5 Hz, 4H), 5.13 (d, *J* 8.0 Hz, 1H), 5.01 (d, *J* 8.0 Hz, 1H), 1.77 – 0.91 (m, 15H), 0.62 (s, 3H).

***syn*-1-(2-Azido-1,2-diphenylethoxy)-2,2,6,6-tetramethylpiperidine (*syn*-5l)**.[18] ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.24 – 7.10 (m, 6H), 6.98 – 6.93 (m, 4H), 5.63 (d, *J* 3.6 Hz, 1H), 4.90 (d, *J* 3.5 Hz, 1H), 1.79 – 0.86 (m, 15H), 0.31 (s, 3H).

***trans*-1-((2-Azido-1,2,3,4-tetrahydronaphthalen-1-yl)oxy)-2,2,6,6-tetramethylpiperidine (*anti*-5m)**.[18] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.48 (dd, *J* 7.6, 1.4 Hz, 1H), 7.23 (td, *J* 7.4, 1.4 Hz, 1H), 7.15 (td, *J* 7.3, 1.2 Hz, 1H), 7.10 (d, *J* 7.6 Hz, 1H), 4.79 (d, *J* 3.0 Hz, 1H), 4.28 (q, *J* 3.1 Hz, 1H), 2.94 – 2.76 (m, 2H), 2.36 – 2.26 (m, 1H), 2.04 – 1.94 (m, 1H), 1.62 – 1.22 (m, 9H), 1.15 (s, 3H), 0.98 (s, 3H), 0.36 (s, 3H).

***trans*-1-((2-Azido-2,3-dihydro-1H-inden-1-yl)oxy)-2,2,6,6-tetramethylpiperidine (5n)**.[18] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.57 (d, *J* 7.5 Hz, 1H), 7.32 – 7.19 (m, 3H), 5.34 (d, *J* 4.0 Hz, 1H), 4.46 – 4.37 (m, 1H), 3.37 (dd, *J* 16.1, 7.2 Hz, 1H), 2.88 (dd, *J* 16.2, 5.2 Hz, 1H), 1.69 – 1.24 (m, 6H), 1.30 (s, 3H), 1.20 (s, 3H), 1.11 (s, 3H), 1.05 (s, 3H).

1-(2-Azido-1-(naphthalen-2-yl)ethoxy)-2,2,6,6-tetramethylpiperidine (5o).[44] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.97 – 7.80 (m, 4H), 7.57 – 7.45 (m, 3H), 5.04 (dd, *J* 6.9, 4.7 Hz, 1H), 3.86 (dd, *J* 12.4, 4.6 Hz, 1H), 3.79 (dd, *J* 12.4, 6.9 Hz, 1H), 1.72 – 1.19 (m, 12H), 1.10 (s, 3H), 0.72 (s, 3H).

1-((1-Azidodecan-2-yl)oxy)-2,2,6,6-tetramethylpiperidine (5p). Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 3.94 – 3.84 (m, 1H), 3.53 (dd, *J* 12.5, 4.4 Hz, 1H), 3.34 (dd, *J* 12.5, 5.4 Hz, 1H), 1.82 – 1.71 (m, 1H), 1.63 – 1.39 (m, 7H), 1.37 – 1.21 (m, 12H), 1.13 (d, *J* 7.2 Hz, 12H), 0.88 (t, *J* 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 80.9, 60.1, 59.8, 53.3, 40.3 (2×CH_2 at TEMPO-), 34.3, 34.1, 31.8, 31.3, 29.9, 29.5, 29.2, 25.7, 22.6, 20.4 (2×CH_3 at TEMPO-), 17.2, 14.1. HRMS *m/z* (ESI) calcd. For $C_{19}H_{39}N_4O$ $(M+H)^+$: 339.3118, found 339.3114.

***trans*-1-((2-Azidocyclooctyl)oxy)-2,2,6,6-tetramethylpiperidine (*trans*-5q)**.[43] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 4.13 – 4.09 (m, 1H), 3.52 (ddd, *J* 8.8, 6.3, 2.7 Hz, 1H), 2.80 – 2.70 (m, 1H), 1.95 – 1.86 (m, 1H), 1.85 – 1.77 (m, 1H), 1.77 – 1.11 (m, 21H), 1.08 (s, 3H), 1.01 (s, 3H). HRMS *m/z* (ESI) calcd. For $C_{17}H_{32}N_4O$ $(M+H)^+$: 309.2649, found 309.2645.

***cis*-1-((2-Azidocyclooctyl)oxy)-2,2,6,6-tetramethylpiperidine (*cis*-5q)**.[43] ^{1}H NMR (500 MHz, Chloroform-*d*) δ 4.09 – 4.02 (m, 2H), 2.17 – 2.09 (m, 1H), 1.85 – 1.77 (m, 2H), 1.77 – 1.05 (m, 27H). HRMS *m/z* (ESI) calcd. For $C_{17}H_{32}N_4O$ $(M+H)^+$: 309.2649, found 309.2645.

***trans*-1-((2-Azidocyclohexyl)oxy)-2,2,6,6-tetramethylpiperidine (*trans*-5r)**.[44] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 3.71 (ddd, *J* 10.4, 8.7, 3.9 Hz, 1H), 3.32 (ddd, *J* 10.4, 8.6, 4.5 Hz, 1H), 2.40 – 2.29 (m, 1H), 1.99 – 1.91 (m, 1H), 1.77 – 1.01 (m, 24H).

***cis*-1-((2-Azidocyclohexyl)oxy)-2,2,6,6-tetramethylpiperidine (*cis*-5r)**.[44] ^{1}H NMR (500 MHz, Chloroform-*d*) δ 4.12 – 4.07 (m, 1H), 3.76 (ddd, *J* 11.7, 4.0, 2.9 Hz, 1H), 2.06 (dq, *J* 12.0, 4.0 Hz, 1H), 1.89 – 1.83 (m, 1H), 1.77 – 0.96 (m, 24H).

***trans*-1-((3-Azidotetrahydro-2H-pyran-2-yl)oxy)-2,2,6,6-tetramethylpiperidine (5s)**.[44] White solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 5.34 (d, *J* 3.1 Hz, 1H), 3.92 – 3.83 (m, 1H), 3.72 – 3.65 (m, 1H), 3.63 – 3.57 (m, 1H), 1.98 – 1.86 (m, 2H), 1.83 – 1.73 (m, 1H), 1.61 – 1.28 (m, 7H), 1.23 (s, 3H), 1.13 (s, 9H).

***trans*-1-((2-Azido-2,3-dihydrobenzofuran-3-yl)oxy)-2,2,6,6-tetramethylpiperidine (5t)**.[44] Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.51 (dd, *J* 7.5, 1.3 Hz, 1H), 7.31 (td, *J* 7.8, 1.4 Hz, 1H), 7.02 – 6.97 (m, 1H), 6.95 (d, *J* 8.1 Hz, 1H), 6.15 (d, *J* 1.0 Hz, 1H), 5.14 (s, 1H), 1.63 – 1.29 (m, 7H), 1.23 (s, 3H), 1.10 (s, 3H), 1.08 (s, 3H), 0.95 (s, 3H).

***anit*-2-Azido-N-methyl-N,3-diphenyl-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propenamide (*anti*-5u)**. Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.53 – 7.47 (m, 2H), 7.46 – 7.41 (m, 1H), 7.41 – 7.36 (m, 2H), 7.30 – 7.25 (m, 3H), 7.20 – 7.16 (m, 2H), 5.22 (d, *J* 8.2 Hz, 1H), 4.25 (d, *J* 8.2 Hz, 1H), 3.39 (s, 3H), 1.56 – 1.08 (m, 15H), 0.98 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.3, 142.8, 137.1, 129.8, 129.7, 128.3, 128.1, 127.5, 127.4, 83.7, 60.7, 59.1, 58.8, 40.8, 40.1, 37.7, 33.9, 33.0, 20.5, 20.1, 16.9. HRMS *m/z* (ESI) calcd. For $C_{25}H_{34}N_5O_2$ $(M+H)^+$: 436.2707, found 436.2701.

1-(1-(4-(Allyloxy)phenyl)-2-azidoethoxy)-2,2,6,6-tetramethylpiperidine (5v). Colorless oil. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.30 – 7.23 (m, 2H), 6.94 – 6.86 (m, 2H), 6.12 – 6.02 (m, 1H), 5.42 (dq, *J* 17.2, 1.6 Hz, 1H), 5.29 (dq, *J* 10.5, 1.4 Hz, 1H), 4.78 (dd, *J* 7.1, 4.9 Hz, 1H), 4.54 (dt, *J* 5.3, 1.6 Hz, 2H), 3.74 (dd, *J* 12.3, 4.9 Hz, 1H), 3.59 (dd, *J* 12.2, 7.1 Hz, 1H), 1.68 – 1.24 (m, 10H), 1.19 (s, 3H), 1.03 (s, 3H), 0.69 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.3, 133.2, 132.9, 128.8, 117.6, 114.3, 84.3, 68.7, 60.0 (2×C), 55.2, 40.4 (2×CH_2), 34.3, 34.1, 20.3 (2×CH_3), 17.1. HRMS *m/z* (ESI) calcd. For $C_{20}H_{31}N_4O_2$ $(M+H)^+$: 359.2442, found 359.2435.

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Supplementary Material

Available as separate file downloadable from journal website.

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