

Copper Catalyzed Oxyazidation of Unactivated Alkenes: A Facile Synthesis of Isoxazolines Featuring an Azido Substituent

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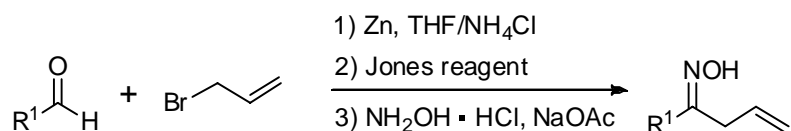
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I. General Information

Unless stated otherwise, all reactions were carried out under an argon atmosphere. All solvents were purified and dried according to standard methods prior to use. ^1H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded on a Varian instrument (300 MHz, 75 MHz and 282 MHz) spectrometer in CDCl_3 using tetramethylsilane (TMS) as internal standard unless otherwise noted. Data for ^1H NMR are recorded as follows: chemical shift (δ , ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, br = broad, q = quartet or unresolved, coupling constant(s) in Hz, integration). Data for ^{13}C NMR and ^{19}F NMR are reported in terms of chemical shift (δ , ppm). High resolution mass spectra (HRMS) were obtained by the ESI ionization sources.

Materials: $\text{Cu}(\text{OAc})_2$ was prepared from $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$ by refluxing in acetic anhydride and washed with dry Et_2O ¹. Azido iodine(III) reagents **4**² and **5**² were synthesized according to the literature procedures. All other reagents were commercially available and used as received.

II. General procedure for the synthesis of oxime 1a-1s



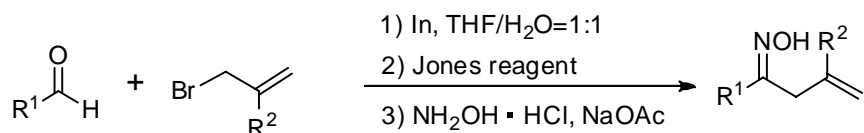
1) To a solution of the allylbromide (2.0 equiv) in anhydrous THF was slowly added the zinc dust (2.0 equiv) at 0 °C. Aldehyde (1.0 equiv) was dissolved in anhydrous THF and added to the solution. The resulting suspension was stirred overnight at this temperature. The reaction was quenched with NH_4Cl (aq.) carefully at 0 °C, filtered and extracted with ethyl acetate for 3 times. The combined organic layers were washed with brine, dried over Na_2SO_4 , filtered and concentrated in *vacuo*. The crude homoallylic alcohol product was directly used in the next step without further purification.³

2) A solution of the homoallylic alcohol in diethyl ether was stirred at 0 °C while

Jones reagent (2.0-4.0 equiv) was added dropwise. The resulting mixture was allowed to warm to room temperature and stirred for 1 hour. The diethyl ether layer was then separated from the aqueous layer, which was extracted with ethyl acetate for 3 times. The combined organic layers were washed with brine, dried over Na₂SO₄, filtered and concentrated in *vacuo*. The crude ketone product was directly used in the next step without further purification.⁴

3) To a solution of sodium acetate (7.0 equiv) in ethanol hydroxylamine hydrochloride (5.0 equiv, dissolved in H₂O) was added. The mixture was stirred at room temperature while the ketone (dissolved in ethanol) was added. The mixture was stirred overnight and then, extracted with ethyl acetate 3 times. The combined organic layers were washed with brine, dried over Na₂SO₄, filtered and concentrated in *vacuo*. The crude material was purified by flash chromatography on silica gel to afford the corresponding oxime **1**.⁵

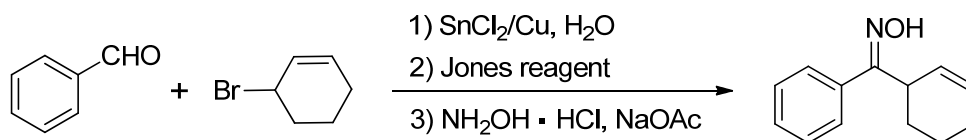
General procedure for the synthesis of oxime **1t**



1) A round bottomed flask charged with a solution of the 3-bromo-2-methylprop-1-ene or its analogues (1.1 equiv)⁵ and indium (1.1 equiv) in THF/H₂O (1:1) was kept at room temperature with stirring. The aldehyde was added to the solution and the resulting suspension was stirred overnight. Saturated ammonium chloride solution was slowly added at 0 °C. The resulting mixture was extracted with ethyl acetate for 3 times. The combined organic layers were washed with brine, dried over Na₂SO₄, filtered and concentrated in *vacuo*. The crude product was directly used in the next step without further purification.⁶

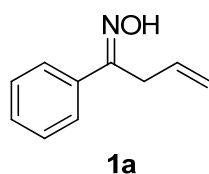
Steps 2) and 3) are same as above-mentioned.

General procedure for the synthesis of oxime 1u

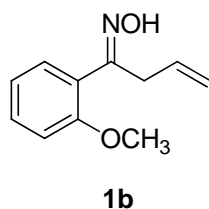


1) To a mixture of benzaldehyde (1.0 equiv) and 3-bromo-1-cyclohexene (1.8 equiv) in water, $\text{SnCl}_2 \cdot \text{H}_2\text{O}$ (2.0 equiv) and copper powder (1.0 equiv) were added. This mixture was vigorously stirred at room temperature for 24 h. Then the mixture was extracted with ethyl acetate (3×30 mL). The combined organic layers were dried over anhydrous Na_2SO_4 , filtered and evaporated. The crude material was purified by flash chromatography on silica gel to afford the product **1u**.

Steps 2) and 3) are same as above-mentioned.

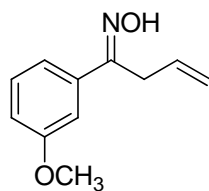


1-phenyl-but-3-en-1-one oxime: Colorless solid. ^1H NMR (300 MHz, CDCl_3) δ 8.88 (s, 1H), 7.67-7.62 (m, 2H), 7.39-7.35 (m, 3H), 6.02-5.88 (m, 1H), 5.21-5.09 (m, 2H), 3.60 (dt, $J = 6.3$ Hz, 1.8 Hz, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ 156.9, 135.6, 132.1, 129.4, 128.6, 126.4, 117.2, 31.2.



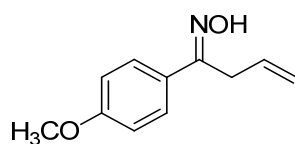
1-(2-methoxyphenyl)but-3-en-1-one oxime: White solid. ^1H NMR (300 MHz, CDCl_3) δ 9.96 (br, 1H), 7.35-7.23 (m, 2H), 6.96-6.88 (m, 2H), 5.88-5.75 (m, 1H), 5.10-4.97 (m, 2H), 3.81 (s, 3H), 3.54 (d, $J = 6.6$ Hz, 2H). ^{13}C NMR (75 MHz, CDCl_3)

δ 157.5, 157.3, 132.5, 130.3, 130.1, 125.4, 120.6, 116.9, 110.9, 55.3, 33.4. **HRMS**
(ESI): $C_{11}H_{13}NO_2+H$, Calcd: 192.1019, Found: 192.1023.



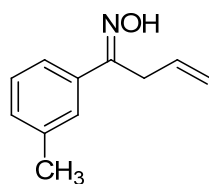
1c

1-(3-methoxyphenyl)but-3-en-1-one oxime: Yellow oil. **1H NMR** (300 MHz, $CDCl_3$) δ 9.94 (br, 1H), 7.31-7.25 (m, 1H), 7.22-7.19 (m, 2H), 6.93-6.89 (m, 1H), 6.00-5.86 (m, 1H), 5.21-5.07 (m, 2H), 3.80 (s, 3H), 3.58 (dt, $J = 6.3$ Hz, 1.5 Hz, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 159.7, 156.8, 137.0, 132.2, 129.6, 119.0, 117.2, 115.2, 111.8, 55.3, 31.4. **HRMS (ESI):** $C_{11}H_{13}NO_2+H$, Calcd: 192.1019, Found: 192.1023.



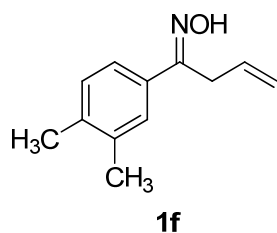
1d

1-(4-methoxyphenyl)but-3-en-1-one oxime: Yellow oil. **1H NMR** (300 MHz, $CDCl_3$) δ 7.60-7.55 (m, 2H), 6.93-6.88 (m, 2H), 6.01-5.88 (m, 1H), 5.20-5.08 (m, 2H), 3.82 (s, 3H), 3.58 (dt, $J = 6.3$ Hz, 1.8 Hz, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 171.3, 160.5, 156.2, 132.3, 127.7, 117.0, 113.9, 55.3, 31.1.

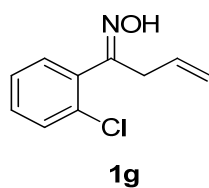


1e

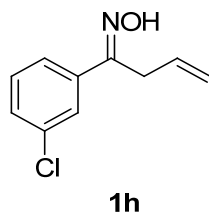
1-(m-tolyl)but-3-en-1-one oxime: Yellow oil. **1H NMR** (300 MHz, $CDCl_3$) δ 10.08 (br, 1H), 7.43 (s, 1H), 7.41(d, $J = 8.7$ Hz, 1H), 7.25-7.13 (m, 2H), 5.99-5.86 (m, 1H), 5.19-5.06 (m, 2H), 3.59-3.57 (m, 2H), 2.33 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 157.2, 138.3, 135.7, 132.3, 130.3, 128.6, 127.2, 123.8, 117.2, 31.5, 21.6.



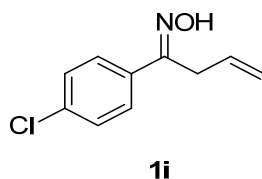
1-(3,4-dimethylphenyl)-but-3-en-1-one oxime: Yellow oil. ^1H NMR (300 MHz, CDCl_3) δ 9.34 (br, 1H), 7.40-7.34 (m, 2H), 7.13 (d, $J = 7.8$ Hz, 1H), 6.01-5.87 (m, 1H), 5.20-5.06 (m, 2H), 3.58 (dt, $J = 6.0$ Hz, 1.5 Hz, 2H), 2.26 (d, $J = 4.2$ Hz, 6H). ^{13}C NMR (75 MHz, CDCl_3) δ 156.9, 138.2, 136.8, 133.1, 132.3, 129.9, 127.5, 123.9, 117.1, 31.2, 20.0, 19.7. **HRMS (ESI):** $\text{C}_{12}\text{H}_{15}\text{NO}+\text{H}$, Calcd: 190.1226, Found: 190.1229.



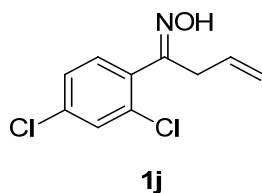
1-(2-chlorophenyl)but-3-en-1-one oxime: Yellow oil. ^1H NMR (300 MHz, CDCl_3) δ 8.85 (br, 1H), 7.42-7.39 (m, 1H), 7.34-7.26 (m, 3H), 5.83-5.70 (m, 1H), 5.12-5.00 (m, 2H), 3.55 (td, $J = 6.9$ Hz, 1.5 Hz, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ 157.8, 135.3, 132.7, 131.2, 130.7, 130.0, 129.8, 126.7, 118.0, 33.7. **HRMS (ESI):** $\text{C}_{10}\text{H}_9\text{ClNO}+\text{H}$, Calcd: 196.0524, Found: 196.0526.



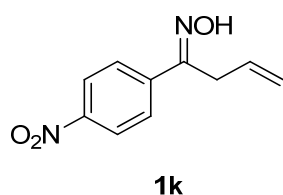
1-(3-chlorophenyl)but-3-en-1-one oxime: Yellow oil. ^1H NMR (300 MHz, CDCl_3) δ 9.12 (br, 1H), 7.62-7.61 (m, 1H), 7.53-7.50 (m, 1H), 7.37-7.28 (m, 2H), 5.98-5.85 (m, 1H), 5.20-5.11 (m, 2H), 3.56 (dt, $J = 6.0$ Hz, 1.5 Hz, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ 155.9, 137.4, 134.6, 131.6, 129.8, 129.4, 126.5, 124.5, 117.5, 31.0.



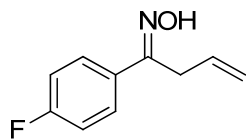
1-(4-chlorophenyl)but-3-en-1-one oxime: Colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 9.09 (s, 1H), 7.59-7.54 (m, 2H), 7.37-7.32 (m, 2H), 5.98-5.85 (m, 1H), 5.19-5.09 (m, 2H), 3.57 (dt, $J = 6.3$ Hz, 1.8 Hz, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ 156.2, 135.5, 133.9, 131.8, 128.8, 127.7, 117.5, 31.1.



1-(2,4-dichlorophenyl)but-3-en-1-one oxime: Colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 8.85 (br, 1H), 7.43 (d, $J = 1.8$ Hz, 1H), 7.28-7.19 (m, 2H), 5.80-5.66 (m, 1H), 5.11-5.02 (m, 2H), 3.52 (d, $J = 6.6$ Hz, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ 157.1, 135.4, 133.8, 133.6, 131.5, 130.9, 129.8, 127.1, 118.3, 33.6. **HRMS (ESI):** $\text{C}_{10}\text{H}_9\text{Cl}_2\text{NO} + \text{H}$, Calcd: 230.0134, Found: 230.0140.

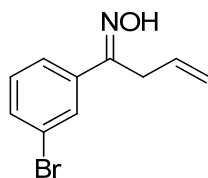


1-(4-nitrophenyl)but-3-en-1-one oxime: Yellow solid. ^1H NMR (300 MHz, CDCl_3) δ 9.42 (d, $J = 7.5$ Hz, 1H), 8.26-8.22 (m, 2H), 7.83-7.79 (m, 2H), 5.99-5.86 (m, 1H), 5.21-5.14 (m, 2H), 3.63 (td, $J = 6.3$ Hz, 1.8 Hz, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ 155.6, 148.2, 141.6, 131.2, 127.2, 123.8, 117.9, 30.8. **HRMS (ESI):** $\text{C}_{10}\text{H}_{10}\text{N}_2\text{O}_3 + \text{H}$, Calcd: 207.0764, Found: 207.0767.



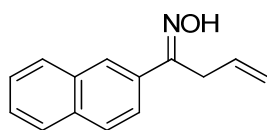
1l

1-(4-fluorophenyl)but-3-en-1-one oxime: Yellow oil. ^1H NMR (300 MHz, CDCl_3) δ 9.85 (br, 1H), 7.64-7.57 (m, 2H), 7.09-7.02 (m, 2H), 5.98-5.85 (m, 1H), 5.20-5.09 (m, 2H), 3.57 (dt, $J = 6.0$ Hz, 1.5 Hz, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ 163.5 (d, $J = 303.0$ Hz, CF), 156.1, 131.9, 131.7 (d, $J = 3.0$ Hz), 128.3 (d, $J = 8.3$ Hz), 117.4, 115.6 (d, $J = 21.0$ Hz), 31.3. ^{19}F NMR (282 MHz, CDCl_3) δ -111.6.



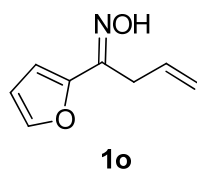
1m

1-(3-bromophenyl)but-3-en-1-one oxime: Colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 9.97 (s, 1H), 7.76 (t, $J = 1.8$ Hz, 1H), 7.55-7.46 (m, 2H), 7.21 (t, $J = 7.8$ Hz, 1H), 5.96-5.83 (m, 1H), 5.18-5.09 (m, 2H), 3.55 (dd, $J = 4.8$ Hz, 1.5 Hz, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ 156.1, 137.6, 132.4, 131.6, 130.1, 129.5, 125.1, 122.8, 117.6, 31.3. **HRMS (ESI):** $\text{C}_{10}\text{H}_{10}\text{BrNO} + \text{H}$, Calcd: 240.0019, Found: 240.0022.

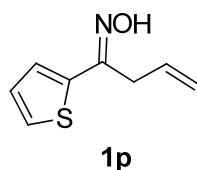


1n

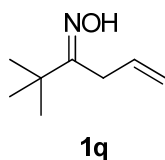
1-(naphthalen-2-yl)but-3-en-1-one oxime: White solid. ^1H NMR (300 MHz, CDCl_3) δ 8.94 (br, 1H), 8.04 (s, 1H), 7.89-7.82 (m, 4H), 7.53-7.47 (m, 2H), 6.08-5.95 (m, 1H), 5.27-5.11 (m, 2H), 3.72 (dt, $J = 6.0$ Hz, 1.8 Hz, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ 156.9, 133.7, 133.1, 132.9, 132.2, 128.5, 128.3, 127.7, 126.8, 126.4, 126.3, 123.6, 117.2, 30.8.



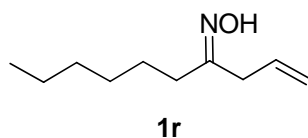
1-(furan-2-yl)but-3-en-1-one oxime: Yellow oil. ^1H NMR (300 MHz, CDCl_3) δ 7.80 (s, 1H), 7.47 (d, $J = 1.2$ Hz, 1H), 6.66 (d, $J = 3.3$ Hz, 1H), 6.45 (dd, $J = 3.6$ Hz, 1.8 Hz, 1H), 5.99-5.86 (m, 1H), 5.22-5.09 (m, 2H), 3.47 (dt, $J = 6.3$ Hz, 1.5 Hz, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ 149.4, 148.8, 143.8, 131.8, 117.3, 111.3, 110.6, 30.1.



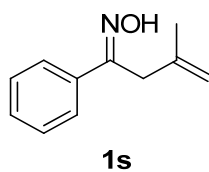
1-(thiophen-2-yl)but-3-en-1-one oxime: White solid. ^1H NMR (300 MHz, CDCl_3) δ 9.33 (s, 1H), 7.28-7.25 (m, 2H), 7.02 (t, $J = 4.5$ Hz, 1H), 6.02-5.89 (m, 1H), 5.25-5.11 (m, 2H), 3.61-3.59 (m, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ 152.7, 139.1, 131.8, 127.3, 127.0, 126.9, 117.5, 31.3.



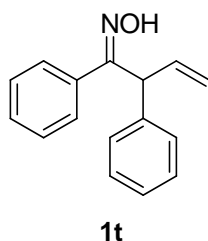
1-(tert-butyl)but-3-en-1-one oxime: Yellow oil. ^1H NMR (300 MHz, CDCl_3) δ 9.45 (br, 1H), 6.01-5.90 (m, 1H), 5.13-5.03 (m, 2H), 3.14 (d, $J = 6.0$ Hz, 2H), 1.14 (s, 9H). ^{13}C NMR (75 MHz, CDCl_3) δ 164.5, 133.1, 116.5, 37.8, 30.4, 27.8.



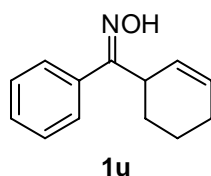
1-heptylbut-3-en-1-one oxime: Yellow oil. ^1H NMR (300 MHz, CDCl_3) δ 10.05 (br, 1H), 5.93-5.76 (m, 1H), 5.18-5.11 (m, 2H), 2.37-2.32 (m, 2H), 1.52-1.45 (m, 2H), 1.30-1.25 (m, 8H), 0.91-0.86 (m, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 160.7, 133.2, 117.8, 38.7, 31.5, 29.5, 27.5, 25.4, 22.5, 14.1.



1-phenyl-but-3-methyl-3-en-1-one oxime: Colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 9.17 (br, 1H), 7.66-7.60 (m, 2H), 7.38-7.35 (m, 3H), 4.84 (s, 1H), 4.75 (s, 1H), 3.55 (s, 2H), 1.82 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 156.9, 140.3, 135.8, 129.2, 128.5, 126.3, 112.2, 34.3, 23.1.

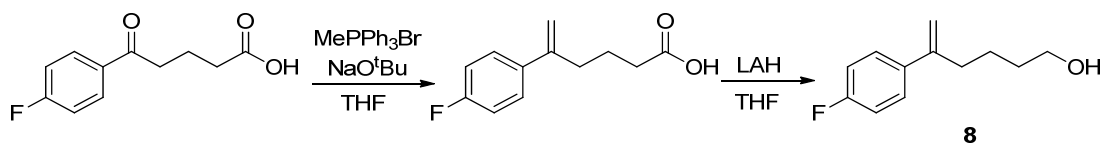


1,2-diphenyl-but-3-en-1-one oxime: White solid. This compound was obtained as a 1:3 mixture of *Z/E* isomers. ^1H NMR (300 MHz, CDCl_3): δ 9.66 (s, 1H, NOH), 8.51 (s, 1H, NOH), 7.40-7.14 (m, 20H), 6.30-6.19 (m, 1H), 6.19-6.07 (m, 1H), 5.52 (d, J = 8.4 Hz, 1H), 5.26-5.02 (m, 4H), 4.57 (d, J = 7.2 Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3): δ 159.5, 159.2, 139.3, 139.1, 137.4, 135.6, 135.3, 133.2, 129.0, 128.7, 128.6, 128.6, 128.6, 128.3, 128.0, 127.9, 127.8, 127.6, 127.1, 126.7, 118.9, 117.0, 55.8, 47.7.



cyclohex-2-en-1-yl(phenyl)methanone oxime: White solid. This compound was obtained as a 1:1.4 mixture of *Z/E* isomers. ^1H NMR (300 MHz, CDCl_3): δ 9.73 (s, 1H, NOH), 9.07 (s, 1H, NOH), 7.46-7.15 (m, 10H), 5.85-5.70 (m, 3H), 5.51 (d, J = 10.8 Hz, 1H), 4.30-4.15 (m, 1H), 3.89-3.34 (m, 1H), 2.05-1.49 (m, 12H). ^{13}C NMR (75 MHz, CDCl_3): δ 162.2, 161.2, 135.5, 133.4, 129.2, 128.8, 128.7, 128.2, 128.1, 127.8, 127.7, 127.6, 126.4, 126.4, 41.7, 35.2, 26.8, 26.0, 24.9, 24.7, 22.2, 20.6.

III. Procedure for the synthesis of enol 8

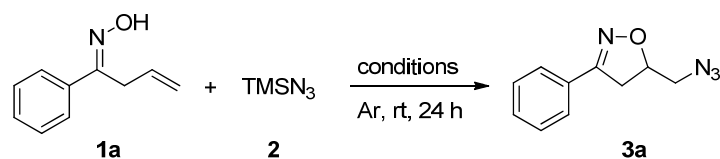


To a suspension of methyltriphenylphosphonium bromide (39 mmol, 13.93 g) in THF (70 mL) was added sodium *tert*-butoxide (78 mmol, 7.50 g) at 0 °C. The mixture was then stirred for 30 min. 4-(4-fluorobenzoyl)butyric acid (30 mmol, 6.31 g) was then added to the reaction mixture at 0 °C. The mixture was allowed to warm to room temperature and stirred for 16 hours. After evaporation of THF, dichloromethane and 1 N NaOH were added. The aqueous layer was washed with dichloromethane. 12 N HCl was then added until pH of the aqueous layer was ca. 2. The aqueous layer was then extracted with dichloromethane twice and dried over Na_2SO_4 . Concentration of the organic layer gave 5-(4-fluorophenyl)pent-5-enoic acid as a white solid (quant. yield). The product was used for next step without further purification.⁷

5-(4-fluorophenyl)pent-5-enoic acid (10 mmol, 2.08 g) was dissolved in THF (20 mL). Lithium aluminum hydride (21 mmol, 0.80 g) was added portionwise at 0 °C. The reaction mixture was stirred for 30 min. Then quenched with 2 N NaOH and filtered through a pad of celite. The organic layer was extracted with diethyl ether and dried over Na_2SO_4 , filtered and concentrated in *vacuo*. The crude product was purified by flash chromatography on silica gel to afford the 5-(4-fluorophenyl)hex-5-en-1-ol as pale yellow oil in 91% yield.⁷ **¹H NMR** (300 MHz, CDCl_3) δ 7.30-7.25 (m, 2H), 6.95-6.89 (m, 2H), 5.14 (s, 1H), 4.97 (s, 1H), 3.53 (t, J = 6.0 Hz, 2H), 2.44-2.40 (m, 2H), 1.61 (s, 1H), 1.53-1.38 (m, 4H). **¹³C NMR** (75 MHz, CDCl_3) δ 162.2 (d, J = 244.5 Hz, CF), 147.3, 137.2 (d, J = 3.0 Hz), 127.7 (d, J = 8.3 Hz), 115.1 (d, J = 21.0 Hz), 112.4, 62.7, 35.2, 32.2, 24.3. **¹⁹F NMR** (282 MHz, CDCl_3) δ -115.4. **HRMS (ESI):** $\text{C}_{12}\text{H}_{15}\text{FO}+\text{H}$, Calcd: 195.1180, Found: 195.1184.

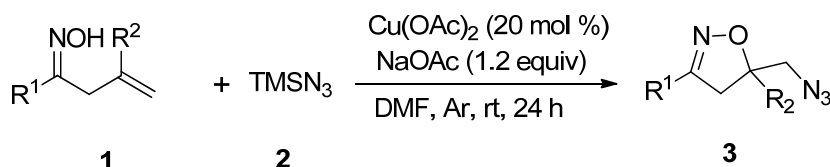
IV. General procedures of alkene oxyazidation

Table S1. Optimization of Reaction Conditions.^a



Entry	Catalyst	Additive	Solvent	Yield (%) ^b
1	Cu(OTf) ₂	-	DMF	10
2	Cu(OTf) ₂	NaOAc	DMF	83
3	Cu(OTf) ₂	K ₂ CO ₃	DMF	71
4	Cu(OTf) ₂	Cs ₂ CO ₃	DMF	76
5 ^c	Cu(OTf) ₂	-	DMF	10
6	Cu(OAc)₂	NaOAc	DMF	89
7	CuCl ₂ ·2H ₂ O	NaOAc	DMF	62
8	CuI	NaOAc	DMF	75
9	CuBr	NaOAc	DMF	80
10	CuCl	NaOAc	DMF	81
11 ^d	Cu(OAc) ₂	NaOAc	DMF	51
12 ^e	Cu(OAc) ₂	NaOAc	CH ₃ CN	70
13	Cu(OAc) ₂	NaOAc	THF	19
14	Cu(OAc) ₂	NaOAc	CHCl ₃	10
15	Cu(OAc) ₂	NaOAc	toluene	trace
16 ^f	Cu(OAc) ₂	NaOAc	DMF	79
17 ^g	Cu(OAc) ₂	NaOAc	DMF	70
18	-	NaOAc	DMF	trace
19	FeCl ₃	NaOAc	DMF	20
20	Yb(OTf) ₃	NaOAc	DMF	8
21	Al(OTf) ₃	NaOAc	DMF	10
22	Ni(OAc) ₂ ·4H ₂ O	NaOAc	DMF	trace
23	Zn(OTf) ₂	NaOAc	DMF	trace
24	Sc(OTf) ₃	NaOAc	DMF	trace
25	In(OTf) ₃	NaOAc	DMF	trace

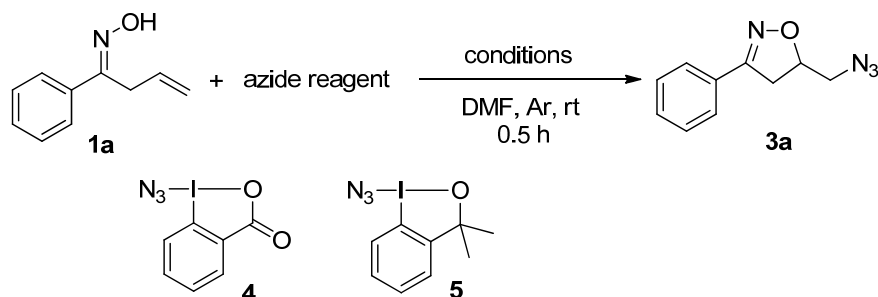
^a All reactions were carried out by using **1** (0.2 mmol), compound **2** (1.5 equiv), anhydrous basic additive (1.2 equiv), catalyst (20 mol %), and solvent (2 mL), under argon and stirred at room temperature for 24 h, except as noted. ^b Isolated yield. ^c Under oxygen atmosphere. ^d 0.2 equiv of NaOAc, 50 °C. ^e Dry solvents were used in all cases. ^f 22 mol % of 2,2'-bipyridine was used. ^g 22 mol % of 1,10-phenanthroline was used.



Method A: Under an argon atmosphere, a 10 mL flask was charged with TMSN₃ (**2**, 0.3 mmol, 40 μ L), oxime (**1**, 0.2 mmol), NaOAc (0.24 mmol, 20 mg), Cu(OAc)₂ (0.04 mmol, 7 mg) and DMF (2.0 mL). The mixture was stirred at room temperature for 24 hours. After the reaction was completed by TLC monitoring, the mixture was

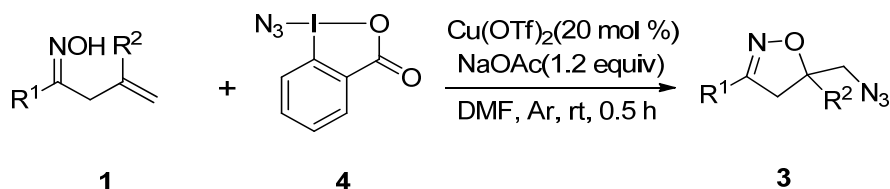
quenched with water, extracted with ethyl acetate, dried over sodium sulphate, concentrated in *vacuo* and purified by column chromatography (petroleum ether/AcOEt 15:1-8:1) to afford the product **3**.

Table S2. Oxyazidation with Azido Iodine(III) Reagents.^a



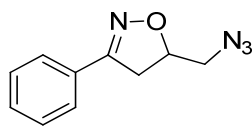
Entry	Catalyst	Additive	Azide reagent	Yield (%) ^b
1	Cu(OTf) ₂	-	4	60
2 ^c	Cu(OTf) ₂	-	4	62
3	Cu(OTf) ₂	-	5	49
4	Cu(OTf) ₂	NaOAc	4	91
5	Cu(OAc) ₂	NaOAc	4	90

^a All reactions were carried out by using **1** (0.2 mmol), compound **2** (1.5 equiv), anhydrous basic additive (1.2 equiv), catalyst (20 mol %), and solvent (2 mL), under argon and stirred at room temperature for 24 h, except as noted. ^b Isolated yield. ^c 24 h.



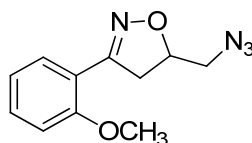
Method B: Under an argon atmosphere, a 10 mL flask was charged with ketoxime (**1**, 0.2 mmol), azido iodine(III) reagent (**4**, 0.3 mmol, 87 mg), NaOAc (0.24 mmol, 20 mg), Cu(OTf)₂ (0.04 mmol, 15 mg) and DMF (2.0 mL). The mixture was stirred for 30 min. After the reaction was completed by TLC monitoring, the mixture was quenched with water, extracted with ethyl acetate, dried over sodium sulphate, concentrated in *vacuo* and purified by column chromatography (petroleum ether/AcOEt 15:1-8:1) to afford the product **3**.

V. Characterization of products



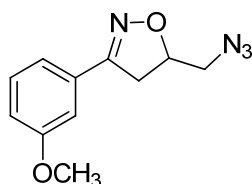
3a

3-phenyl-5-(1-azido)-4,5-dihydroisoxazole: 89% yield for method **A**, 91% yield for method **B**. Colorless solid. ^1H NMR (300 MHz, CDCl_3) δ 7.70-7.67 (m, 2H), 7.45-7.40 (m, 3H), 4.98-4.88 (m, 1H), 3.57-3.42 (m, 3H), 3.23 (dd, $J = 16.8$ Hz, 6.9 Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 156.5, 130.4, 129.1, 128.8, 126.8, 79.2, 53.5, 37.8. **HRMS (ESI):** $\text{C}_{10}\text{H}_{10}\text{N}_4\text{O}+\text{H}$, Calcd: 203.0927, Found: 203.0929.



3b

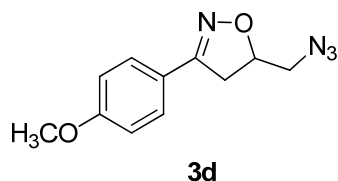
3-(2-methoxyphenyl)-5-(1-azido)-4,5-dihydroisoxazole: 73% yield for method **A**, 75% yield for method **B**. Yellow oil. ^1H NMR (300 MHz, CDCl_3) δ 7.73 (dd, $J = 7.8$ Hz, 1.5 Hz, 1H), 7.42-7.36 (m, 1H), 7.00-6.93 (m, 2H), 4.89-4.80 (m, 1H), 3.86 (s, 3H), 3.57 (dd, $J = 17.4$ Hz, 10.5 Hz, 1H), 3.50-3.38 (m, 2H), 3.31 (dd, $J = 17.4$ Hz, 6.9 Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 157.6, 156.2, 131.6, 129.4, 120.8, 118.2, 111.4, 79.1, 55.5, 53.6, 40.5. **HRMS (ESI):** $\text{C}_{11}\text{H}_{12}\text{N}_4\text{O}_2+\text{H}$, Calcd: 233.1033, Found: 233.1039.



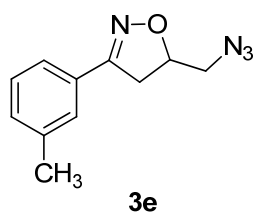
3c

3-(3-methoxyphenyl)-5-(1-azido)-4,5-dihydroisoxazole: 67% yield for method **A**, 64% yield for method **B**. Yellow oil. ^1H NMR (300 MHz, CDCl_3) δ 7.34-7.27 (m, 2H), 7.18 (d, $J = 7.5$ Hz, 1H), 6.99-6.95 (m, 1H), 4.96-4.87 (m, 1H), 3.83 (s, 3H),

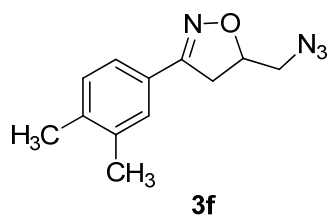
3.56-3.39 (m, 3H), 3.20 (dd, $J = 16.8$ Hz, 6.9 Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 159.7, 156.5, 130.3, 129.8, 119.4, 116.7, 111.3, 79.3, 55.4, 53.5, 37.8. **HRMS (ESI):** $\text{C}_{11}\text{H}_{12}\text{N}_4\text{O}_2 + \text{H}$, Calcd: 233.1033, Found: 233.1040.



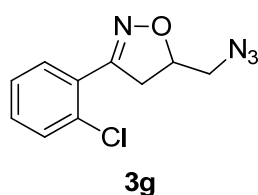
3-(4-methoxyphenyl)-5-(1-azido)-4,5-dihydroisoxazole: 80% yield for method **A**, 86% yield for method **B**. Yellow oil. ^1H NMR (300 MHz, CDCl_3) δ 7.61 (d, $J = 8.4$ Hz, 2H), 6.92 (d, $J = 8.7$ Hz, 2H), 4.92-4.84 (m, 1H), 3.84 (s, 3H), 3.54-3.38 (m, 3H), 3.18 (dd, $J = 16.5$ Hz, 6.9 Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 161.2, 156.1, 128.3, 121.6, 114.2, 78.9, 55.4, 53.5, 38.1. **HRMS (ESI):** $\text{C}_{11}\text{H}_{12}\text{N}_4\text{O}_2 + \text{H}$, Calcd: 233.1033, Found: 233.1037.



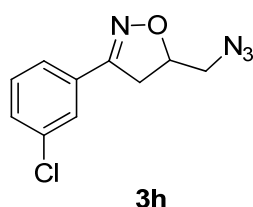
3-(3-methylphenyl)-5-(1-azido)-4,5-dihydroisoxazole: 75% yield for method **A**, 60% yield for method **B**. Yellow oil. ^1H NMR (300 MHz, CDCl_3) δ 7.51 (s, 1H), 7.44 (d, $J = 7.5$ Hz, 1H), 7.32-7.21 (m, 2H), 4.94-4.85 (m, 1H), 3.54-3.38 (m, 3H), 3.19 (dd, $J = 16.8$ Hz, 6.9 Hz, 1H), 2.37 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 156.6, 138.5, 131.2, 129.0, 128.7, 127.3, 124.0, 79.1, 53.5, 37.9, 21.4. **HRMS (ESI):** $\text{C}_{11}\text{H}_{12}\text{N}_4\text{O} + \text{Na}$, Calcd: 239.0903, Found: 239.0906.



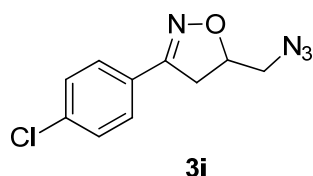
3-(3,4-dimethphenyl)-5-(1-azido)-4,5-dihydroisoxazole: 79% yield for method **A**, 65% yield for method **B**. White solid. $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 7.47 (s, 1H), 7.36 (dd, $J = 7.8$ Hz, 1.8 Hz, 1H), 7.15 (d, $J = 7.8$ Hz, 1H), 4.92-4.83 (m, 1H), 3.52-3.37 (m, 3H), 3.17 (dd, $J = 16.8$ Hz, 6.9 Hz, 1H), 2.28 (s, 6H). $^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ 156.6, 139.4, 137.1, 130.0, 127.8, 126.6, 124.4, 79.0, 53.5, 38.0, 19.8, 19.8. **HRMS (ESI):** $\text{C}_{12}\text{H}_{14}\text{N}_4\text{O}+\text{H}$, Calcd: 231.1240, Found: 231.1243.



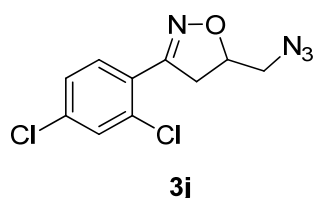
3-(2-chlorophenyl)-5-(1-azido)-4,5-dihydroisoxazole: 63% yield for method **A**, 50% yield for method **B**. Yellow oil. $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 7.65 (dd, $J = 7.2$ Hz, 1.8 Hz, 1H), 7.44 (dd, $J = 7.8$ Hz, 1.5 Hz, 1H), 7.40-7.29 (m, 2H), 5.00-4.91 (m, 1H), 3.67-3.53 (m, 2H), 3.48-3.34 (m, 2H). $^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ 156.5, 132.8, 131.1, 130.6, 130.6, 128.6, 127.1, 79.8, 53.4, 40.2. **HRMS (ESI):** $\text{C}_{10}\text{H}_9\text{ClN}_4\text{O}+\text{H}$, Calcd: 237.0538, Found: 237.0548.



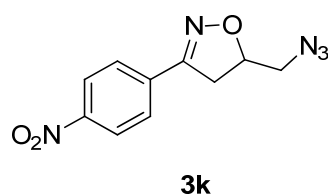
3-(3-chlorophenyl)-5-(1-azido)-4,5-dihydroisoxazole: 71% yield for method **A**, 63% yield for method **B**. Yellow oil. $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 7.66 (s, 1H), 7.57 (d, $J = 7.5$ Hz, 1H), 7.42-7.33 (m, 2H), 5.00-4.91 (m, 1H), 3.57 (dd, $J = 12.9$ Hz, 4.2 Hz, 1H), 3.48-3.38 (m, 2H), 3.20 (dd, $J = 16.8$ Hz, 7.2 Hz, 1H). $^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ 155.5, 134.8, 130.9, 130.3, 130.1, 126.7, 124.8, 79.6, 53.4, 37.5. **HRMS (ESI):** $\text{C}_{10}\text{H}_9\text{ClN}_4\text{O}+\text{H}$, Calcd: 237.0538, Found: 237.0540.



3-(4-chlorophenyl)-5-(1-azido)-4,5-dihydroisoxazole: 77% yield for method **A**, 71% yield for method **B**. Yellow oil. ^1H NMR (300 MHz, CDCl_3) δ 7.61 (d, J = 8.7 Hz, 2H), 7.39 (d, J = 8.4 Hz, 2H), 4.98-4.89 (m, 1H), 3.56 (dd, J = 13.2 Hz, 4.5 Hz, 1H), 3.48-3.38 (m, 2H), 3.20 (dd, J = 16.8 Hz, 6.9 Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 155.6, 136.3, 129.0, 128.0, 127.6, 79.5, 53.4, 37.6. **HRMS (ESI):** $\text{C}_{10}\text{H}_9\text{ClN}_4\text{O}+\text{Na}$, Calcd: 259.0357, Found: 259.0359.

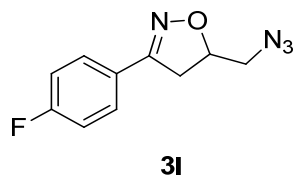


3-(2,4-dichlorophenyl)-5-(1-azido)-4,5-dihydroisoxazole: 57% yield for method **A**, 76% yield for method **B**. Yellow oil. ^1H NMR (300 MHz, CDCl_3) δ 7.62 (d, J = 8.4 Hz, 1H), 7.46 (d, J = 2.1 Hz, 1H), 7.32-7.27 (m, 1H), 5.00-4.91 (m, 1H), 3.65-3.54 (m, 2H), 3.47-3.32 (m, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ 155.6, 136.5, 133.5, 131.4, 130.4, 127.5, 127.1, 80.0, 53.3, 39.9. **HRMS (ESI):** $\text{C}_{10}\text{H}_8\text{Cl}_2\text{N}_4\text{O}+\text{Na}$, Calcd: 292.9967, Found: 292.9969.

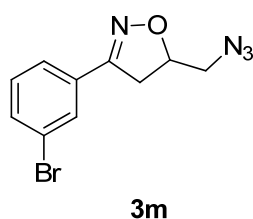


3-(4-nitrophenyl)-5-(1-azido)-4,5-dihydroisoxazole: 78% yield for method **A**, 75% yield for method **B**. Yellow solid. ^1H NMR (300 MHz, CDCl_3) δ 8.28 (d, J = 8.7 Hz, 2H), 7.85 (d, J = 9.0 Hz, 2H), 5.08-4.99 (m, 1H), 3.64 (dd, J = 13.2 Hz, 4.2 Hz, 1H), 3.54-3.45 (m, 2H), 3.28 (dd, J = 16.8 Hz, 7.2 Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ

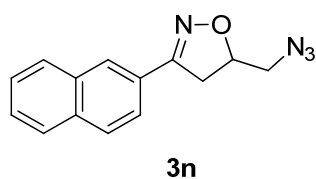
155.1, 148.6, 135.2, 127.5, 124.1, 80.2, 53.3, 37.1. **HRMS (ESI):** C₁₀H₉N₅O₃+Na, Calcd: 270.0598, Found: 270.0601.



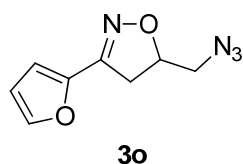
3-(4-fluorophenyl)-5-(1-azido)-4,5-dihydroisoxazole: 82% yield for method **A**, 71% yield for method **B**. Yellow oil. **¹H NMR** (300 MHz, CDCl₃) δ 7.70-7.65 (m, 2H), 7.14-7.08 (m, 2H), 4.98-4.89 (m, 1H), 3.55 (dd, *J* = 13.2 Hz, 4.5 Hz, 1H), 3.48-3.40 (m, 2H), 3.21 (dd, *J* = 16.5 Hz, 6.9 Hz, 1H). **¹³C NMR** (75 MHz, CDCl₃) δ 163.8 (d, *J* = 249.8 Hz, CF), 155.6, 128.7 (d, *J* = 8.3 Hz), 125.4 (d, *J* = 3.0 Hz), 115.9 (d, *J* = 21.8 Hz), 79.3, 53.4, 37.8. **¹⁹F NMR** (282 MHz, CDCl₃) δ -109.5. **HRMS (ESI):** C₁₀H₉FN₄O+Na, Calcd: 243.0653, Found: 243.0658.



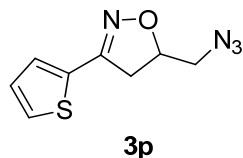
3-(3-bromophenyl)-5-(1-azido)-4,5-dihydroisoxazole: 70% yield for method **A**, 72% yield for method **B**. Creamy white solid. **¹H NMR** (300 MHz, CDCl₃) δ 7.81 (s, 1H), 7.62-7.53 (m, 2H), 7.31-7.26 (m, 1H), 4.99-4.90 (m, 1H), 3.56 (dd, *J* = 13.2 Hz, 4.2 Hz, 1H), 3.47-3.38 (m, 2H), 3.19 (dd, *J* = 16.8 Hz, 7.2 Hz, 1H). **¹³C NMR** (75 MHz, CDCl₃) δ 155.5, 133.2, 131.1, 130.3, 129.6, 125.3, 122.8, 79.6, 53.4, 37.4. **HRMS (ESI):** C₁₀H₉BrN₄O+Na, Calcd: 302.9852, Found: 302.9856.



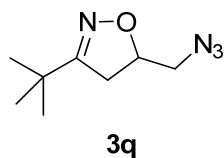
3-(naphthalen-2-yl)-5-(1-azido)-4,5-dihydroisoxazole: 75% yield for method **A**, 85% yield for method **B**. White solid. ^1H NMR (300 MHz, CDCl_3) δ 7.99-7.84 (m, 5H), 7.54- 7.52 (m, 2H), 5.02-4.93 (m, 1H), 3.62-3.46 (m, 3H), 3.35 (dd, J = 16.8 Hz, 6.9 Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 156.7, 134.1, 132.9, 128.6, 128.4, 127.9, 127.3, 127.1, 126.8, 126.7, 123.5, 79.4, 53.5, 37.8. **HRMS (ESI):** $\text{C}_{14}\text{H}_{12}\text{N}_4\text{O}+\text{Na}$, Calcd: 275.0903, Found: 275.0909.



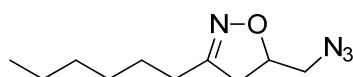
3-(furan-2-yl)-5-(1-azido)-4,5-dihydroisoxazole: 43% yield for method **A**, 46% yield for method **B**. Yellow oil. ^1H NMR (300 MHz, CDCl_3) δ 7.53 (d, J = 0.9 Hz, 1H), 6.75 (d, J = 3.3 Hz, 1H), 6.51 (dd, J = 3.3 Hz, 1.8 Hz, 1H), 4.93-4.84 (m, 1H), 3.55-3.37 (m, 3H), 3.19 (dd, J = 16.8 Hz, 6.9 Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 148.7, 144.6, 144.4, 112.2, 111.8, 78.9, 53.2, 37.7. **HRMS (ESI):** $\text{C}_8\text{H}_8\text{N}_4\text{O}_2+\text{Na}$, Calcd: 215.0539, Found: 215.0543.



3-(thiophen-2-yl)-5-(1-azido)-4,5-dihydroisoxazole: 73% yield for method **A**, 79% yield for method **B**. Yellow oil. ^1H NMR (300 MHz, CDCl_3) δ 7.41 (dd, J = 5.1 Hz, 1.2 Hz, 1H), 7.22 (dd, J = 3.6 Hz, 0.9 Hz, 1H), 7.07 (dd, J = 5.1 Hz, 3.6 Hz, 1H), 4.96-4.87 (m, 1H), 3.56-3.42 (m, 3H), 3.23 (dd, J = 16.8 Hz, 7.2 Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 152.3, 131.4, 128.8, 128.6, 127.4, 79.5, 53.3, 38.6. **HRMS (ESI):** $\text{C}_8\text{H}_8\text{N}_4\text{OS}+\text{Na}$, Calcd: 231.0311, Found: 231.0316.

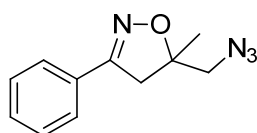


3-(tert-butyl)-5-(1-azido)-4,5-dihydroisoxazole: 74% yield for method **A**, 73% yield for method **B**. Yellow oil. $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 4.77-4.68 (m, 1H), 3.42 (dd, $J = 12.9$ Hz, 4.2 Hz, 1H), 3.31 (dd, $J = 12.9$ Hz, 5.1 Hz, 1H), 3.08 (dd, $J = 17.1$ Hz, 10.5 Hz, 1H), 2.83 (dd, $J = 17.1$ Hz, 6.6 Hz, 1H), 1.22 (s, 9H). $^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ 165.8, 78.1, 53.6, 37.2, 33.0, 28.2, 28.0. **HRMS (ESI):** $\text{C}_8\text{H}_{14}\text{N}_4\text{O}+\text{Na}$, Calcd: 205.1060, Found: 205.1057.



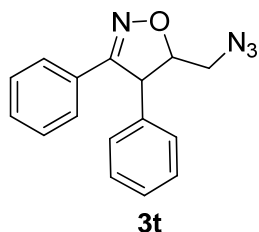
3r

3-hetyl-5-(1-azido)-4,5-dihydroisoxazole: 68% yield for method **A**, 60% yield for method **B**. Yellow oil. $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 4.77-4.68 (m, 1H), 3.44 (dd, $J = 12.9$ Hz, 4.2 Hz, 1H), 3.32 (dd, $J = 12.9$ Hz, 5.1 Hz, 1H), 3.04 (dd, $J = 17.1$ Hz, 10.5 Hz, 1H), 2.78 (dd, $J = 17.1$ Hz, 6.9 Hz, 1H), 2.36 (t, $J = 7.5$ Hz, 2H), 1.62-1.52 (m, 2H), 1.40-1.26 (m, 6H), 0.91-0.87 (m, 3H). $^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ 159.0, 77.8, 53.5, 39.9, 31.4, 28.8, 27.5, 26.3, 22.5, 14.0. **HRMS (ESI):** $\text{C}_{10}\text{H}_{18}\text{N}_4\text{O}+\text{H}$, Calcd: 211.1553, Found: 211.1557.



3s

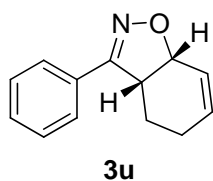
3-phenyl-5-methyl-5-(1-azido)-4,5-dihydroisoxazole: 42% yield for method **A** (80 °C), 66% yield for method **B**. Colorless oil. $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 7.75-7.60 (m, 2H), 7.50-7.35 (m, 3H), 3.51 (d, $J = 12.9$ Hz, 1H), 3.42-3.32 (m, 2H), 3.07 (d, $J = 16.8$ Hz, 1H), 1.52 (s, 3H). $^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ 156.5, 130.2, 129.5, 128.7, 126.6, 86.3, 57.6, 43.3, 23.9. **HRMS (ESI):** $\text{C}_{11}\text{H}_{12}\text{N}_4\text{O}+\text{H}$, Calcd: 217.1084, Found: 217.1092.



3,4-diphenyl-5-(1-azido)-4,5-dihydroisoxazole: White solid.

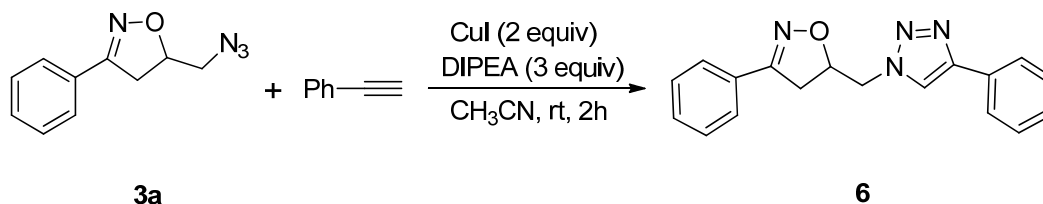
Method **A**: 62% yield. dr = 11:1. **¹H NMR** (300 MHz, CDCl₃) δ 7.63-7.57 (m, 2.2H), 7.37-7.16 (m, 9.1H), 4.91-4.83 (m, 0.1H), 4.75 (d, *J* = 9.6 Hz, 0.1H), 4.70-4.65 (m, 1.0H), 4.61 (d, *J* = 5.1 Hz, 1.0H), 3.60-3.55 (m, 1.0H), 3.54-3.49 (m, 1.0H), 3.33 (dd, *J* = 12.9 Hz, 7.2 Hz, 0.1H), 3.04 (dd, *J* = 12.9 Hz, 5.7 Hz, 0.1H). **¹³C NMR** (75 MHz, CDCl₃) δ 158.2, 138.3, 130.1, 129.4, 128.6, 128.3, 128.0, 127.5, 127.4, 88.1, 57.2, 52.9. **HRMS (ESI):** C₁₆H₁₄N₄O+H, Calcd: 279.1240, Found: 279.1253.

Method **B**: 80% yield. dr = 4:1. **¹H NMR** (300 MHz, CDCl₃) δ 7.63-7.57 (m, 2.5H), 7.37-7.16 (m, 10.4H), 4.91-4.83 (m, 0.3H), 4.75 (d, *J* = 9.6 Hz, 0.3H), 4.70-4.65 (m, 1.0H), 4.61 (d, *J* = 5.1 Hz, 1.0H), 3.60-3.55 (m, 1.0H), 3.54-3.49 (m, 1.0H), 3.33 (dd, *J* = 12.9 Hz, 7.2 Hz, 0.3H), 3.04 (dd, *J* = 12.9 Hz, 5.7 Hz, 0.3H). **¹³C NMR** (75 MHz, CDCl₃) δ 159.9, 158.3, 138.4, 132.8, 130.2, 130.1, 129.5, 129.3, 128.7, 128.7, 128.5, 128.4, 128.3, 128.0, 127.5, 127.4, 127.3, 88.2, 83.4, 57.2, 55.9, 52.9, 50.4.



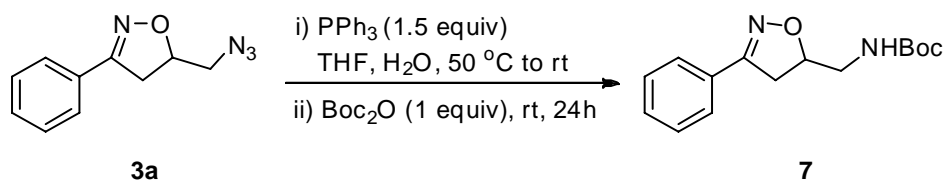
3-phenyl-3a,4,5,7a-tetrahydrobenzo[d]isoxazole: 44% yield for method **A**, 81% yield for method **B**. White solid. **¹H NMR** (300 MHz, CDCl₃) δ 7.74-7.70 (m, 2H), 7.44-7.40 (m, 3H), 6.22-6.17 (m, 1H), 6.07-6.02 (m, 1H), 4.86-4.82 (m, 1H), 3.56-3.47 (m, 1H), 2.17-1.93 (m, 3H), 1.58-1.46 (m, 1H). **¹³C NMR** (75 MHz, CDCl₃) δ 161.2, 133.2, 130.0, 129.2, 128.8, 126.9, 122.3, 77.0, 44.1, 23.1, 22.4. **HRMS (ESI):** C₁₃H₁₃NO+Na, Calcd: 222.0889, Found: 222.0897.

VI. Procedure for formation of 6



To a solution of phenylacetylene (0.1 mmol, 11 μ L) and azide **3a** (0.1 mmol, 20 mg) in 1 mL of anhydrous acetonitrile were added CuI (0.2 mmol, 38 mg) and N,N-diisopropylethylamine (0.3 mmol, 53 μ L) at room temperature, and the mixture was stirred for 2 hours until the disappearance of azide (monitored by TLC). The reaction was quenched with NH_4Cl (aq.), extracted with ethyl acetate, washed with brine, dried over anhydrous sodium sulfate, concentrated in *vacuo* and purified by column chromatography (petroleum ether/AcOEt 4:1) to afford the product **6** (0.091 mmol, 27.5 mg) as a white solid in 91% yield. **^1H NMR** (300 MHz, DMSO) δ 8.63 (s, 1H), 7.86 (d, $J = 7.2$ Hz, 2H), 7.75-7.60 (m, 2H), 7.55-7.40 (m, 5H), 7.40-7.30 (m, 1H), 5.30-5.10 (m, 1H), 4.80-4.60 (m, 2H), 3.66 (dd, $J = 17.1$ Hz, 11.1 Hz, 1H), 3.41-3.33 (m, 1H). **^{13}C NMR** (75 MHz, DMSO) δ 156.8, 146.2, 130.6, 130.2, 128.9, 128.8, 127.9, 126.6, 125.1, 122.3, 78.7, 52.4, 37.5. **HRMS (ESI):** $\text{C}_{18}\text{H}_{16}\text{N}_4\text{O}+\text{H}$, Calcd: 305.1397, Found: 305.1404.

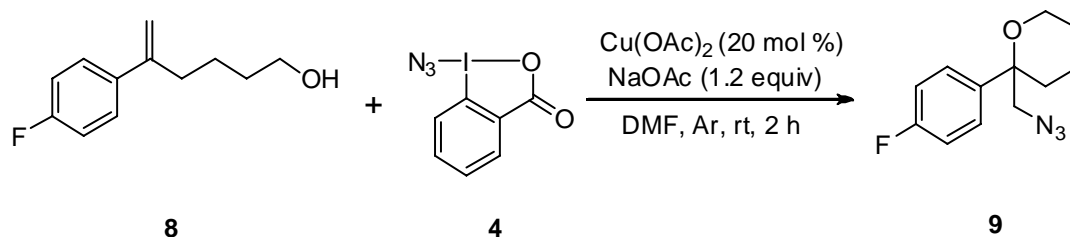
VII. Procedure for formation of 7



In a 10 mL oven and vacuum-dried round-bottom flask, **3a** (0.36 mmol, 73 mg) and triphenylphosphine (0.54 mmol, 142 mg) was taken. To this mixture dry THF (1 mL) was added and the resulting solution was heated at 50 $^\circ\text{C}$ for 4 hours. The reaction mixture was cooled to room temperature and 2 mL of water was added. The resulting solution was stirred at room temperature for 16 hours. To the

reaction mixture solution of di-tert-butylidicarbonate (0.36 mmol, 79 mg) in THF (1 mL) was added. Resulting mixture was stirred at room temperature for 24 hours. The reaction mixture was diluted with CH₂Cl₂ and washed with H₂O. Aqueous was extracted with CH₂Cl₂. The combined organic phase was dried over sodium sulphate and concentrated under reduced pressure. Purification by column chromatography on silica gel by using 80:20 petroleum ether/AcOEt as eluent afforded **7** as a white solid (98 mg, 99% yield). ¹H NMR (300 MHz, CDCl₃) δ 7.75-7.60 (m, 2H), 7.50-7.35 (m, 3H), 4.98 (br, 1H), 4.90-4.80 (m, 1H), 3.44-3.35 (m, 3H), 3.15 (dd, *J* = 16.8 Hz, 7.2 Hz, 1H), 1.40 (s, 9H). ¹³C NMR (75 MHz, CDCl₃) δ 157.0, 156.3, 130.2, 129.3, 128.7, 126.7, 80.1, 79.7, 43.6, 37.4, 28.3. HRMS (ESI): C₁₅H₂₀N₂O₃+Na, Calcd: 299.1366, Found: 299.1371.

VIII. Procedure for formation of **9**

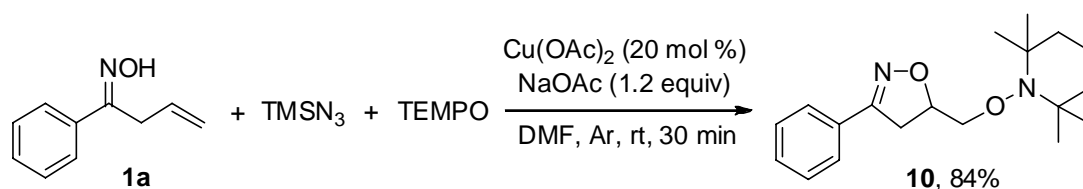


DMF (2 mL) was added to 5-(4-fluorophenyl)hex-5-en-1-ol (**8**, 0.2 mmol, 39 mg), azido iodine(III) reagent (**4**, 0.3 mmol, 87 mg), NaOAc (0.24 mmol, 20 mg) and Cu(OAc)₂ (0.04 mmol, 7 mg) under Argon. The mixture was stirred for 2 h at room temperature. After the reaction was completed by TLC monitoring, the mixture was quenched with water, extracted with ethyl acetate, dried over sodium sulphate, concentrated in *vacuo* and purified by column chromatography (petroleum ether/AcOEt 6:1-4:1) to afford the product **9** as colorless oil in 56% yield. ¹H NMR (300 MHz, CDCl₃) δ 7.38-7.32 (m, 2H), 7.13-7.06 (m, 2H), 3.63 (s, 2H), 3.60 (t, *J* = 6.3 Hz, 2H), 2.16-2.05 (m, 1H), 2.00-1.89 (m, 1H), 1.65-1.51 (m, 2H), 1.41-1.32 (m, 1H), 1.27-1.14 (m, 1H). ¹³C NMR (75 MHz, CDCl₃) δ 162.2 (d, *J* = 246.8 Hz, CF), 134.8 (d, *J* = 3.8 Hz), 127.9 (d, *J* = 7.5 Hz), 115.7 (d, *J* = 21.8 Hz), 68.9, 62.4, 59.8,

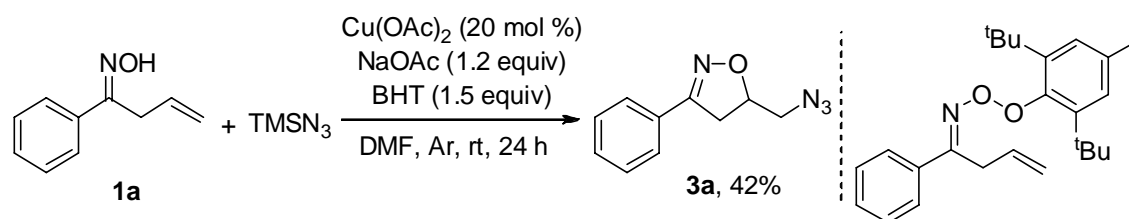
36.3, 32.4, 20.0. ^{19}F NMR (282 MHz, CDCl_3) δ -114.1. HRMS (ESI): $\text{C}_{12}\text{H}_{14}\text{FN}_3\text{O}+\text{H}$, Calcd: 236.1194, Found: 236.1192.

IX. the mechanistic study

PART A



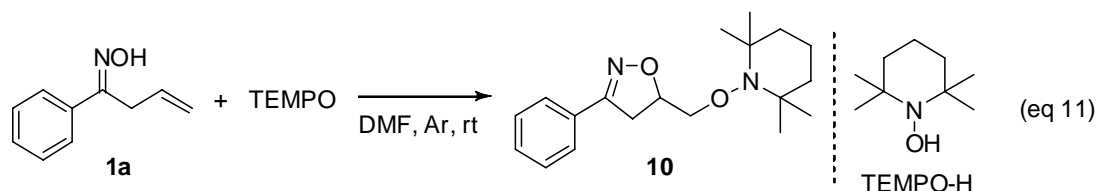
The reaction was carried out according to **General procedures of alkene oxyazidation**, except TEMPO (47 mg, 1.5 equiv) was used. The mixture was stirred at room temperature for 30 min, and then quenched with water, extracted with ethyl acetate, dried over sodium sulphate, concentrated in *vacuo* and purified by column chromatography (petroleum ether/ AcOEt 15:1) to afford the product **10** (white solid, 53 mg, 84%). ^1H NMR (300 MHz, CDCl_3) δ 7.70-7.67 (m, 2H), 7.41-7.39 (m, 3H), 4.92-4.83 (m, 1H), 4.02-3.93 (m, 2H), 3.38 (dd, J = 16.5 Hz, 11.1 Hz, 1H), 3.25 (dd, J = 16.2 Hz, 7.5 Hz, 1H), 1.49-1.42 (m, 5H), 1.32-1.25 (m, 1H), 1.19 (s, 6H), 1.07 (s, 6H). ^{13}C NMR (75 MHz, CDCl_3) δ 156.2, 129.9, 129.7, 128.7, 126.7, 79.2, 77.6, 60.1, 39.6, 37.1, 33.1, 33.0, 20.1, 17.0. HRMS (ESI): $\text{C}_{19}\text{H}_{28}\text{N}_2\text{O}_2+\text{H}$, Calcd: 317.2224, Found: 317.2229.



The reaction was carried out according to **General procedures of alkene oxyazidation**, except BHT (66 mg, 1.5 equiv) was used. The mixture was stirred at room temperature for 24 h, and then quenched with water, extracted with ethyl acetate, dried over sodium sulphate, concentrated in *vacuo* and purified by column chromatography (petroleum ether/ AcOEt 10:1) to afford the product **3a** (17 mg, 42%).

The BHT adduct was detected by ESI-HRMS measurement of the crude reaction mixture (**HRMS (ESI):** C₂₅H₃₃NO₂+Na, Calcd: 402.2404, Found: 402.2409).

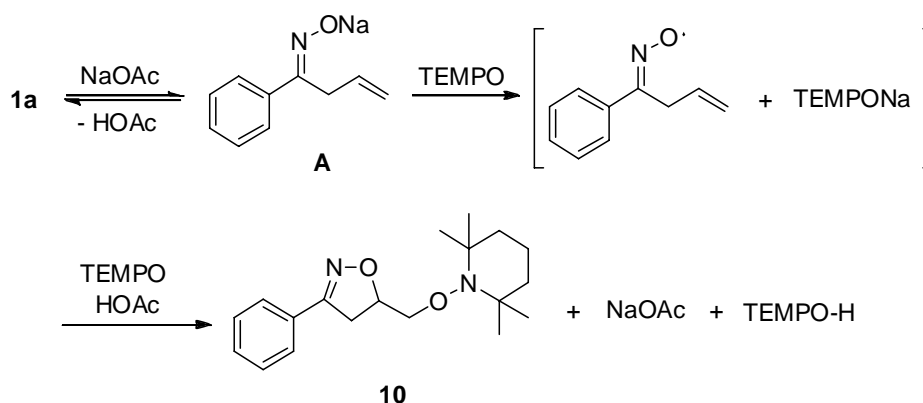
Table S3. Inorganic Base Catalyzed Alkene Radical Dioxygenation.



Entry	Base	Reaction time (h)	Yield (%)
1	none	24	trace
2	NaOAc (20 mol %)	0.5	40
3	Na ₂ CO ₃ (20 mol %)	0.5	39
4	Cu(OAc) ₂ (20 mol %)	0.5	18

Under an argon atmosphere, a 10 mL flask was charged with oxime **1a** (32 mg, 0.2 mmol), TEMPO (31 mg, 0.2 mmol), base (0.04 mmol), and DMF (2.0 mL). The mixture was stirred at room temperature for the above indicated time. After the reaction was completed by TLC monitoring, the mixture was quenched with water, extracted with ethyl acetate, dried over sodium sulphate, concentrated in *vacuo* and purified by column chromatography (petroleum ether/AcOEt 15:1-8:1) to afford the product **10**. TEMPO-H was detected by ESI-HRMS measurement of the crude reaction mixture (**HRMS (ESI):** C₉H₁₉NO₂+H, Calcd: 158.1539, Found: 158.1540).

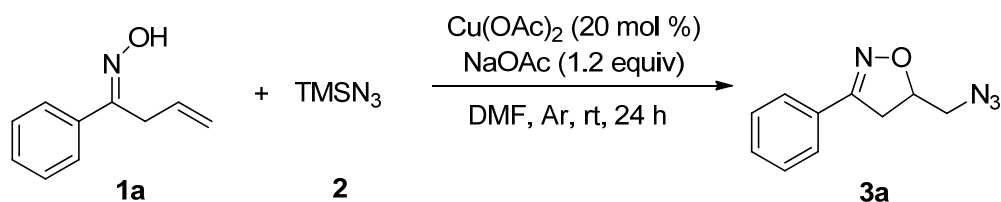
Scheme S1. Proposed Mechanism of NaOAc Catalyzed Alkene Radical Dioxygenation.

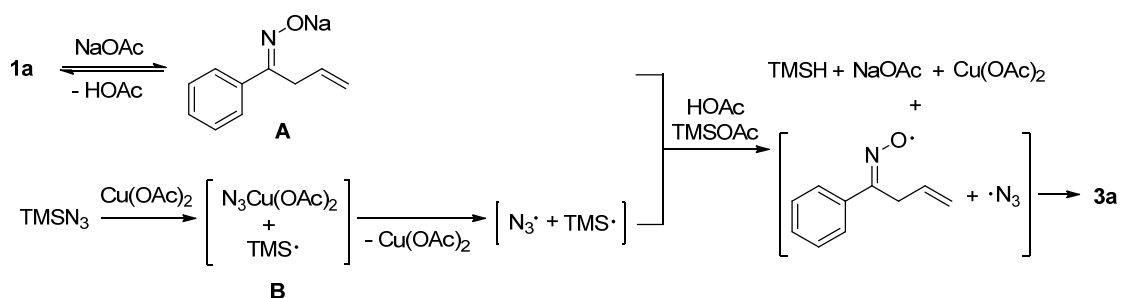


Since TEMPO is not able to initiate the oxime radical formation at room temperature (Table S3, entry 1), the reaction might be initiated from the oxime side, which was catalyzed by NaOAc. Based on experiment results in Table S3 and above considerations, a plausible mechanism of the radical alkene dioxygenation was proposed in Scheme S1. Intermediate **A** is generated by the reaction of oxime **1a** and NaOAc, which then converted to the oxime radical along with the formation of TEMPONa. The oxime radical was cyclized and subsequently trapped by TEMPO to give the dioxygenation product with the regeneration of NaOAc catalyst. The selectively cross coupling of the adduct radical and TEMPO radical is steered by the “persistent radical effect”.

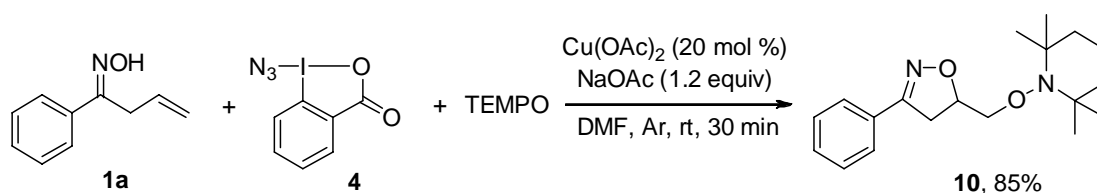
PART B

Scheme S2. Proposed Mechanism of Alkene Oxyazidation.

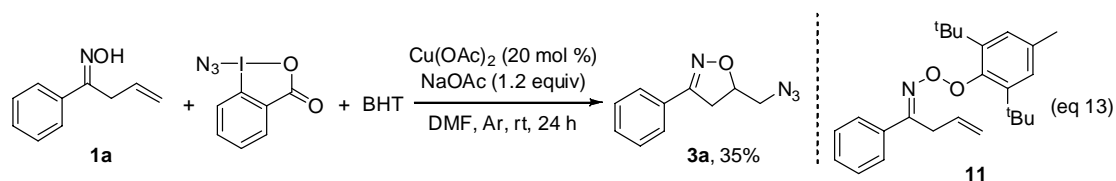




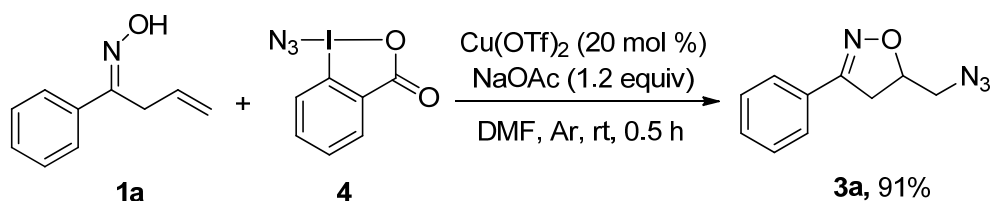
Although the mechanism of this transformation is not completely clear yet, based on the experimental results in Table S3, and considerations in **PART A**, a plausible mechanism is proposed in Scheme S2. Intermediate **A** is initially generated by the reaction of oxime **1a** and NaOAc. Meanwhile, intermediate **B** is formed through a copper catalyzed atom transfer process along with a TMS radical.⁸ **A** is converted to the corresponding oxime radical,⁹ which is intramolecular cyclized and then trapped by the N_3 radical. The selectively cross coupling of the adduct radical and N_3 radical is steered by the “persistent radical effect”,¹⁰ forming the oxyazidation product **3a**.¹¹ However, at this stage, another possibility of the reaction pathway cannot be rule out: $Cu(OAc)_2$ attract N_3 in $TMSN_3$ to form the intermediate **B**, which add to **C** and form the carbon radical through the atom transfer radical addition pathway,⁸ the carbon radical is selectively coupled with oxygen radical to give the ring closure product by the “persistent radical effect”.¹⁰



The reaction was carried out according to **General procedures of alkene oxyazidation**, except **4** (87 mg, 0.3 mmol) was used. The mixture was stirred at room temperature for 30 min, and then quenched with water, extracted with ethyl acetate, dried over sodium sulphate, concentrated in *vacuo* and purified by column chromatography (petroleum ether/AcOEt 15:1) to afford the product **10** (white solid, 54 mg, 85%).



The reaction was carried out according to eq 10, except **4** (87 mg, 0.3 mmol) was used. The mixture was stirred at room temperature for 24 h, and then quenched with water, extracted with ethyl acetate, dried over sodium sulphate, concentrated in *vacuo* and purified by column chromatography (petroleum ether/AcOEt 10:1) to afford the product **3a** (14 mg, 35%). The compound **11** was detected by ESI-HRMS measurement of the crude reaction mixture.



Based on above experimental results and considerations in **PART A** and **B**, this reaction is likely happened by the similar mechanism in Scheme S2.

X. Reference

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- (11) Although NaOAc is regenerated in the proposed mechanism and could be used in catalytic amount (0.2 equiv), it is not effectively catalyzed the transformation at room temperature, see: Table 1, entry 5.

XI. NMR Spectra of new compounds

