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Copper catalyzed oxidative difunctionalization of terminal unactivated alkenes

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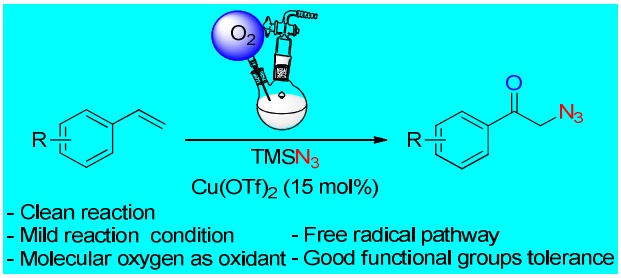


Abstract

The copper(II)-promoted free radical oxidative difunctionalization of terminal alkenes to access ketoazides by utilizing molecular oxygen has been reported. A series of styrene derivatives have been evaluated and found to be compatible to give the desired difunctionalized product in moderate to good yields. The role of molecular oxygen both as oxidant and oxygen atom source in this catalytic transformation has been unquestionably demonstrated by ^{18}O labelling studies and a radical mechanistic pathway involving the oxidative formation of azidyl

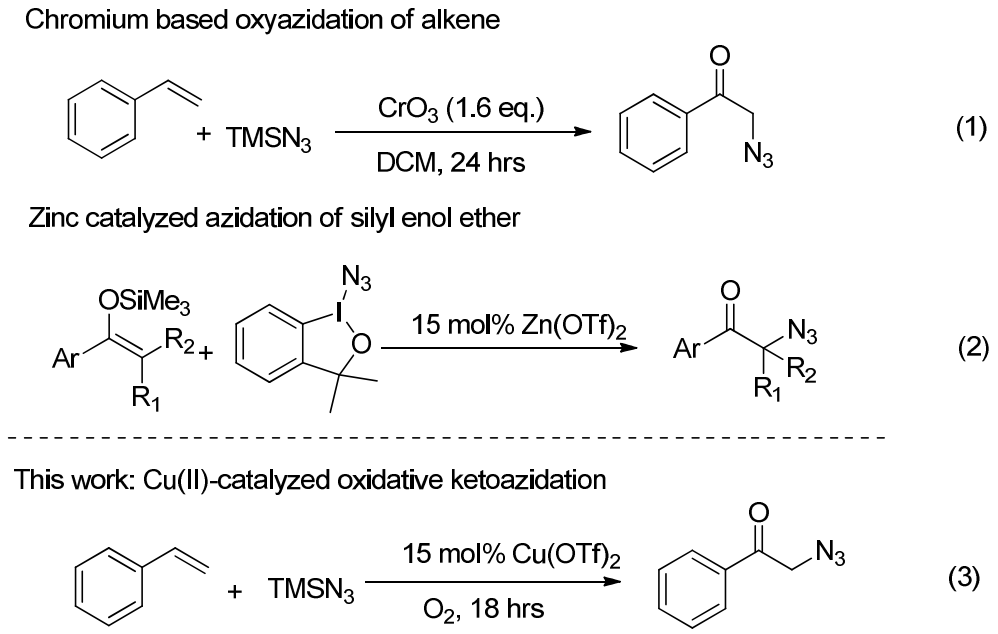
radicals is also designed. This environment-friendly catalytic oxidative protocol can transform aldehyde to nitrile.

Introduction

Organic azides are the key structural motifs that have received a considerable attention due to significant contribution in material science, natural products**,** and pharmaceuticals.[1] They are metabolically more active and well-known chemotherapeutic drugs that can be utilized as prodrugs of primary amines.[2] Azides are also distinctive moieties in various pharmacophores such as azidocillin, azidothymidine (AZT), or the COX-2 inhibitor and celecoxib derivative.[3] Nevertheless, azidation of alkene is a viable option for the synthesis of productive organic azides which are the irreplaceable origin of numerous *aza*-containing compounds such as amides, amines imines, aziridines, and triazoles.[4] Moreover, vicinal difunctionalization of olefinic double bond including diazidation,[5] azidocyanation,[6] carboazidation,[7] azidotrifluoromethylation,[8] hydroxy-azidation,[9] and ketoazidation,[10] have been efficaciously used to contribute valuable molecules. Thus, consequential efforts were made to develop new and highly effective approaches in this field.

In 1995, Vankar *et al.* reported α-azidoketone from alkene upon its treatment with $TMSN_3$ as an azide source.[11] This methodology, suffered from high uploading of metal salt (eqn 1, Scheme 1), impetus us to envision an environment friendly protocol from green chemistry point of view. In 2013, catalytic azidation of silyl enol ether using a benziodoxole-originated azide transfer reagent has been demonstrated by Waser and co-workers[12] (eqn 2, Scheme 1). Nevertheless, catalytic oxidative ketoazidation of unactivated alkenes using simple starting materials remains a standing challenge. As of late, the progression of ecologically agreeable oxidation protocols based on metal catalysts is highly fascinating. More specifically, the strategy involving metal

catalysts liable for activating molecular oxygen is of ultimate interest.[13] Therefore, as part of our ongoing interest in oxidative catalysis and vicinal difunctionalization of alkenes,[14] we reasoned that an environmentally benign oxidative catalytic protocol for the ketoazidation of alkene is of highly desired.



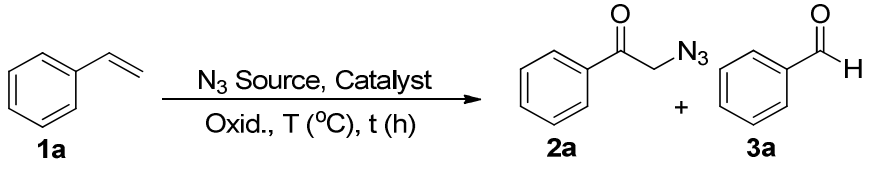
Scheme 1 Approaches to synthesize ketoazide.

Results and Discussion

The initial investigation was intended to set an optimized condition. Styrene was chosen as the model substrate for copper catalyzed oxidative difunctionalization with azide to inspect a variety of parameters and the results are summarized in Table 1. In the presence of 10 mol% $Cu(OTf)_2$, the reaction of styrene (**1a**, 0.5 mmol) and $TMSN_3$ (4 equiv) in 4 mL of MeCN was performed for 12 hours in the presence of molecular oxygen. To our delight, 47% yield of the desired ketoazide was obtained (Table 1, entry 1). All polar and non-polar solvents such as toluene, DCM, and DMSO except MeCN were found ineffective to proceed the reaction (Table

1, entries 2-4). Changing the catalysts from organometallic copper salts to inorganic copper salts led to inferior results except for $CuSO_4$ that responded well to give envisioned product **2a** and side product **3a** (Table 1, entries 5-9). As $Cu(OTf)_2$ proceeded the transformation selectively, while $CuSO_4$ salt gave a high yield. Therefore, we decided to optimize both of them (for more detail see the Supporting Information). The reaction under argon was not effective that the subtle condition resulting in oxidant is important (Table 1, entry 10). In aerobic reaction condition, along with the desired product, a noticeable yield of aldehyde was also observed (Table 1, entry 11). Molecular oxygen which is a green and cost-effective oxidant plays a vital role in selective conversion, makes this oxidative practice environment-friendly. However, attempt to utilize another azide source such as NaN_3 was not effective (Table 1, entry 12). The same salt of zinc metal was failed to precede the product (Table 1, entry 13). Moreover, the amount of solvent, catalyst, and azide source was optimized; as a result, 4.5 equivalent of $TMSN_3$, 15 mol% of $Cu(OTf)_2$ and 4 mL of MeCN were found to be the best amount for this transformation (entries 14-19). Next, we studied the effect of time and temperature, the best outcome was observed at room temperature for 18 hours, and while either lowering or raising of both time and temperature was found the lower yield (Table 1, entries 20-22). To further improve the yield of desired product different additives were also investigated (see Table S3 in the Supporting Information). Thus, the optimized reaction conditions were $TMSN_3$ (4.5 equivalent), and $Cu(OTf)_2$ (15 mol %), in CH_3CN at room temperature under a molecular oxygen atmosphere for 18 hours.

Table 1 Optimization of reaction conditions.[a]



Entry	Solvent	N_3 source (eq)	Catalyst (10 mol %)	Yield [b] (%), ratio (**2a**:**3a**)[c]
1	MeCN	$TMSN_3$	$Cu(OTf)_2$	47 (47 : 0)
2	Toluene	$TMSN_3$	$Cu(OTf)_2$	0
3	DCM	$TMSN_3$	$Cu(OTf)_2$	0
4	DMSO	$TMSN_3$	Cu(OTf)2	0
5	MeCN	$TMSN_3$	$Cu(CH_3CN)_4 \cdot PF_6$	22 (12 : 10)
6	MeCN	$TMSN_3$	$Cu(acac)_2$	26 (14 : 12)
7	**MeCN**	**$TMSN_3$**	**$CuSO_4$**	**86 (72 : 14)**
8	MeCN	$TMSN_3$	$CuBr_2$	15(15 : traces)
9	MeCN	$TMSN_3$	CuCN	0
10[d]	MeCN	$TMSN_3$	$Cu(OTf)_2$	traces
11[e]	MeCN	$TMSN_3$	$Cu(OTf)_2$	71 (46 : 25)
12	MeCN	NaN_3	$Cu(OTf)_2$	traces
13	MeCN	$TMSN_3$	$Zn(OTf)_2$	0
14[f]	MeCN	$TMSN_3$	$Cu(OTf)_2$	60 (60 : 0)
15[g]	MeCN	$TMSN_3$	$Cu(OTf)_2$	43 (43 : 0)
16[h]	MeCN	$TMSN_3$	$Cu(OTf)_2$	52 (52 : 0)
17[i]	MeCN	$TMSN_3$	$Cu(OTf)_2$	54 (54 : 0)
18[j]	MeCN	$TMSN_3$	$Cu(OTf)_2$	55 (55 : 0)
19[k]	MeCN	$TMSN_3$	$Cu(OTf)_2$	73(47 : 0)
20[l]	**MeCN**	**$TMSN_3$**	**$Cu(OTf)_2$**	**80 (80 : 0)**
21[m]	MeCN	$TMSN_3$	$Cu(OTf)_2$	15 (15 : 0)

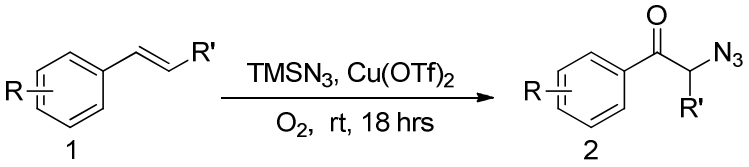
22[n]	MeCN	$TMSN_3$	$Cu(OTf)_2$	11 (11 : 0)

[a] Conditions: **1a** (0.5 mmol), N_3 source (4 equivalent), and Catalyst (10 mol %) in solvent (4 mL) utilizing air as oxidant at rt for 12 h. [b] Yield determined by ^{1}H-NMR using mesitylene as an internal standard. [c] ^{1}H-NMR yield ratio of ketoazidation and aldehyde product. [d] Rection under argon. [e] aerobic reaction. [f] 4.5 equivalent of $TMSN_3$. [g] Used 3 equivalent of $TMSN_3$. [h] Used 3 mL of MeCN. [i] Used 5 mL of MeCN . [j] 5 mol% of the catalyst. [k]15 mol% of the catalyst. [l] Reaction for 18 h. [m] at 50 °C for 18 h. [n] at 0 °C for 18.

Having the optimal reaction conditions in hand, we next evaluated the scope of this reaction and the results are summarized in Table 2. The reaction of $TMSN_3$ and variety of styrene derivatives gave the desired product **2**. The oxidative catalytic system was compatible with halide, ester, ether, and alkyl group at the *para*- position. The presence of electron poor substituents on styrene (**2b-f**) offered the desired product in good yields 56-79%. Electron-donating groups (**2g-i**) responded to this protocol to give moderate to good yields. The compounds having electron rich groups with no resonance effect, only inductive effect, for example, methyl and *t*-butyl *para*-substituted styrene (**2h-i**) usually improves the ketoazidation outcome while the methoxy group (**2g**) on the same position inhibits the transformation due to the robust resonance influence which showed that this oxidative catalytic transformation depends upon on the electronic properties. Meanwhile, styrenes having substituents *meta*- and *ortho*-position (**1j-n)** were also investigated under standard reaction conditions and found the desired products in moderate to good yields. The lower response of *ortho*-substituted styrene to this protocol showed a prominent role of the steric parameter. An even more significant desired product was observed for disubstituted styrenes (**2o-p)**. To extend further the generality of this oxidative catalytic methodology, we also investigated various vinylic substituted styrenes. Alkyl

and nitrile functional failed to deliver the desired product but phenyl substitution gave the corresponding product only 45% which indicate that this protocol is specific for terminal alkenes (**2q-s**). Furthermore, the scope of reaction with respect to fused ring system was also considered. To our delight, this oxidative catalytic protocol was capable to transform the vinyl naphthalene (**2t)** to the required product in good yield. On the other hand, no oxidative difunctionalization was observed in case of aliphatic as well as heterocyclic olefins (see Figure S1 in the Supporting Information).

Table 2 Scope of ketoazidation of alkenes.[a]



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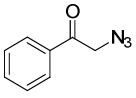
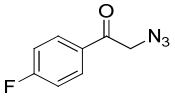
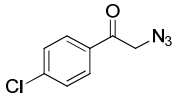
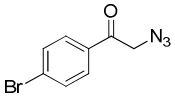
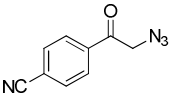
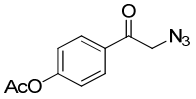
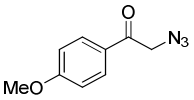
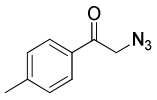
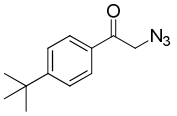
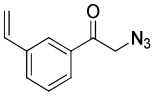
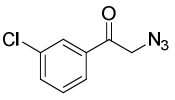
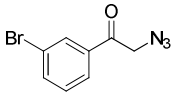
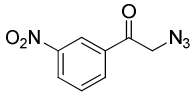
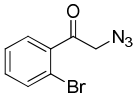
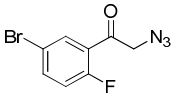
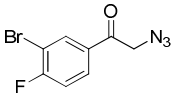
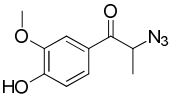
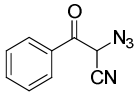
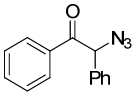
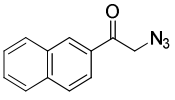
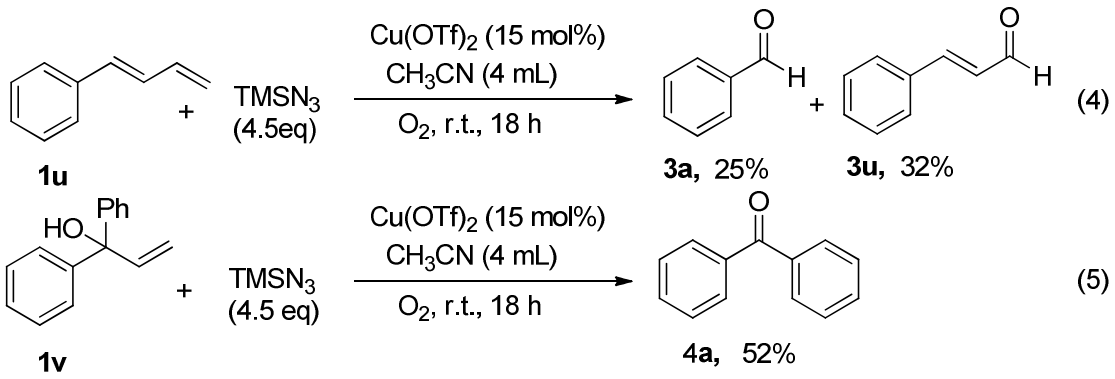
 **2a,** 80% (77%)	 **2b**, 79% (75%)	 **2c,** 62% (58%)	 **4d,** 66% (60%)	 **2e**, 56% (52%)	 **2f,** 60% (57%)
 **2g,** 30% (27%)	 **2h,** 76% (73%)	 **2i,** 70% (68%)	 **2j,** 77% (73%)	 **2k,** 60% (55%)	 **2l,** 58% (51%)
 **2m,** 52% (50%)	 **2n**, 41% (35%)	 **2o,** 58% (75%)	 **2p,** 75% (70%)	 **2q,** traces	 **2r**, 0%
 **2s,** 45% (40%)	 **2t,** 58% (53%)				

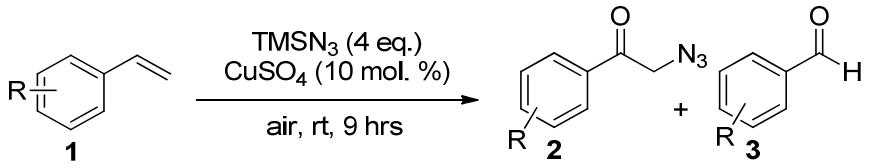
[a] Conditions: **1a** (0.5 mmol) $TMSN_3$ (4.5 equivalent) and catalyst (15 mol %) in solvent (4 mL) at rt for 18 h and yield determined by ^{1}H-NMR using mesitylene as an internal standard while isolated yield is in parenthesis.

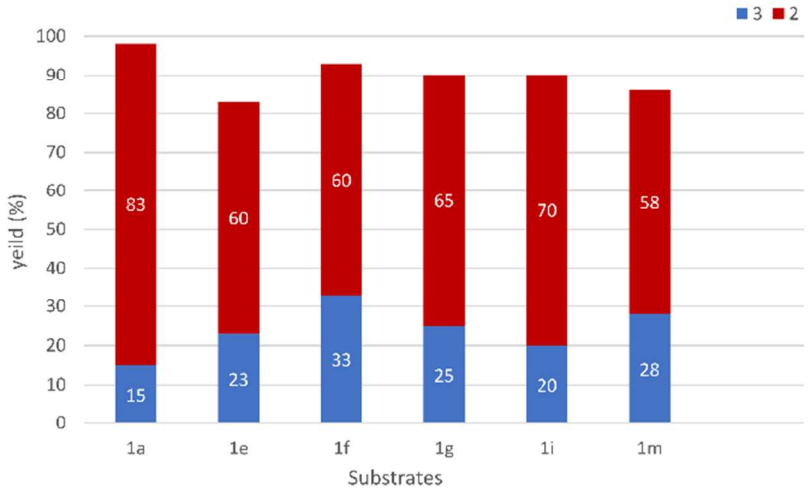
The substrate **1u** underwent oxidative cleavage to **3a** and **3u** (eqn 4, scheme 2), while *α,α*-diarylallylic alcohols substrate **1v** was degraded to benzophenone[15] in 52% yield (eqn 5, scheme 2).



Scheme 2 Oxidative cleavage of olefins.

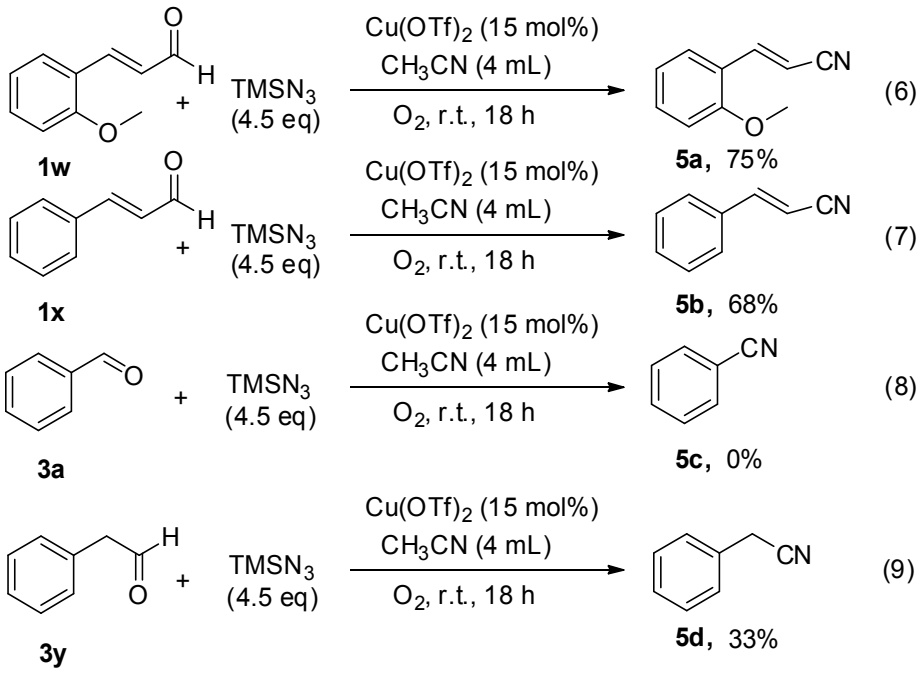
The optimized reaction condition for method B was $TMSN_3$ (4 equiv), and $CuSO_4$ (10 mol %), in 4 mL of CH_3CN at room temperature in an aerobic condition (see the supplementary data). The scope of this methodology is depicted in graph 1. Both electron donating and electron withdrawing derivatives of styrene responded well to give the respective ketoazides along with oxidative cleaved benzaldehyde products in noticeable yield. The overall yields of reactions were excellent.





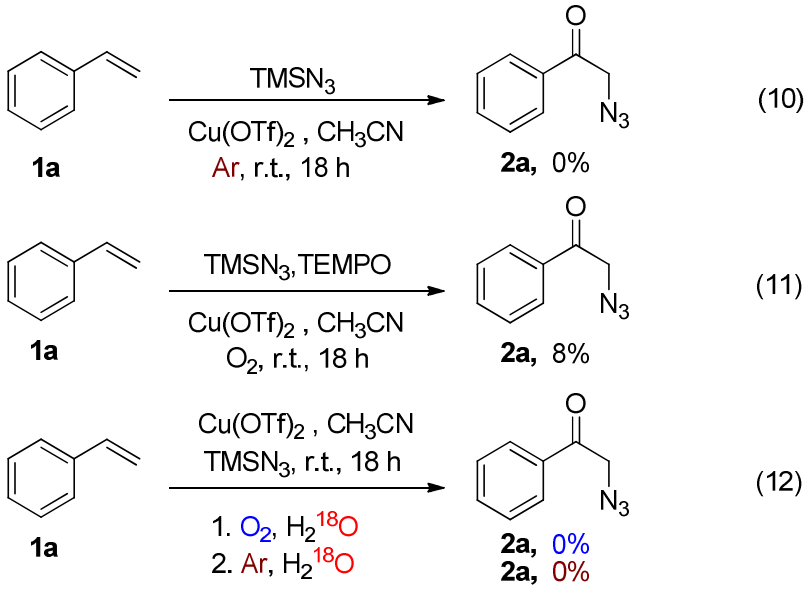
Graph 1 Scope of ketoazidation of alkenes utilizing method B.

As mentioned above, we envisioned an environment friendly protocol for difunctionalization of the alkene. Interestingly, this protocol function well to transform aldehyde to nitrile function (**5a-b)** in good yield (eqn 6-7 scheme 3).[16] To evaluate further, benzaldehyde found ineffective to this oxidative protocol (eqn 8, scheme 3) while phenyl acetaldehyde responded to system and gave the nitrile product in 33% (eqn 9, scheme 3).



Scheme 3 Approaches to synthesize nitrile from the aldehyde.

To certify this assumption and acquire straightforward proof, chemical trapping of radicals was performed by using well-known radical-trapping reagents TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy). Chemical trapping was carried out under standardized reaction conditions and the desired difunctionalized product was achieved in 8% yield (eqn 11, scheme 4). This observation was consistent with the hypothesis that the reaction likely involved free-radical intermediates and proceeded via a single-electron-transfer (SET) process triggered by copper-II oxidation. As reaction under argon, in the absence of oxidant, was incapable to transform alkenes to give the difunctionalized ketoazide that declares a prominent role of molecular oxygen both as oxidant and source of an oxygen atom (eqn 10, scheme 4). To further investigate the source of oxygen atom oxygen isotopic labelling using $H_2{}^{18}O$ reactions were performed, both in the presence and absence of molecular oxygen (eqn 12, scheme 4) and in either case no ketoazidation was observed through gas chromatography mass spectrometry (GC-MS) analysis.



Scheme 4 Control experiments.

On the basis of above experimental results, a plausible mechanistic pathway for the difunctionalization of alkene is outlined to interpret the observed reactivates in Figure 1. Oxidation of the azide anion by copper catalyst would proceed to the corresponding radical. Plausibly, the addition of the ultimate radical to the styrene would yield the less hindered benzylic radical **A**, which later trapped by molecular oxygen to produce peroxy radical **B** as an intermediate on exposure to molecular oxygen that might undergo to ketoazide by two pathways.[10d,17] In pathway I, the radical intermediate **C** is formed from the intermediate **B** by the abstraction of a nearby hydrogen**,** subsequently undergoes 1,2-hydride shift to produce intermediate **D** that ultimately yield ketoazide. To complete the catalytic cycle, hydroxy radical reoxidized the copper-I back to copper-II. Whereas, in case of pathway II, copper-I is oxidized into copper-II by peroxy radical intermediate **B** to form an intermediate **E** that subsequently, oxidizes $TMSN_3$ to generate azido radical and intermediate **F**, which finally, transformed to ketoazides.

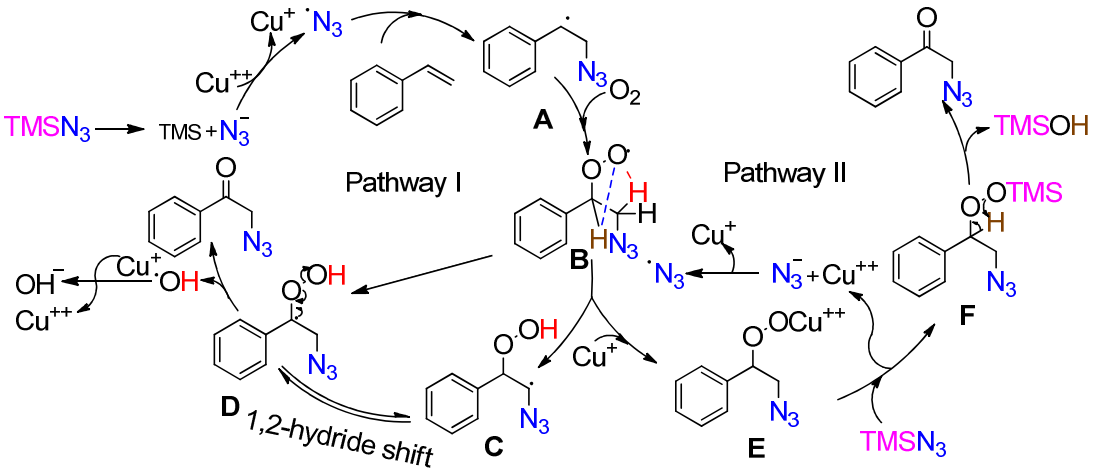


Figure 1 Plausible mechanism of the reaction.

Conclusion

In conclusion, we have reported a simple, mild and environment friendly, copper catalyzed oxidative protocol for the difunctionalization of alkene *via* a radical pathway. A wide variety of functional groups have been evaluated and found to be compatible to give the desired difunctionalized products in moderate to good yields. This catalytic oxidative protocol was capable to transform terminal aldehyde to nitrile. Research on the synthetic utility of this oxidative protocol and more mechanistic details are presently being pursued in our laboratories.

Experimental Section

General information: The ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ solution at 500 (125) MHz spectrometer at 20-25 ^{o}C. ^{1}H NMR spectra were reported in parts per million using TMS ($\delta = 0.00$ ppm) as an internal standard. ^{13}C NMR spectra were reported in parts per million using solvent $CDCl_3$ ($\delta = 77.2$ ppm) as an internal standard. High-resolution mass spectra (HRMS) electrospray ionization (ESI) was carried out on a UPLC-Q-ToF MS spectrometer. All reagents were purchased from commercial suppliers and used as received. All experiments were conducted in the atmosphere. Column chromatography and thin-layer chromatography (TLC) which was used to monitor the reactions were performed on silica gel. **1e, 1g**, **1j,** and **1m**, were prepared following the reported procedure.

General protocol for the preparation of alkene. [18]

Step 1: 36 g of PPh_3 and 100 mL of toluene (dried) were added into a 500 mL round bottom flask, which produced a clean solution. Then 11 mL of CH_3I was added into the above clean solution at 0°C drop wisely. Then a condenser was put on the round bottom flask and the solution was heated to reflux for 4 hr, which would produce white solid. The white solid was

filtered and dried under the vacuum, which was used directly without further purification (100% yield, white solid).

Step 2: Triphenylphosphine methyliodide salt (2.5 g, 6.2 mmol) prepared in step 1 was added into 30 mL dried Et_2O, which resulted in a cloudy solution and KO^{t}Bu (1.57 g, 14 mmol) was added into the round bottom flask at 0°C, the color of which changed from white into yellow immediately. The mixture remained stirring for 4 hr. Then 0.7 g (4.63 mmol) of 3-nitrobenzaldehyde was added into the round bottom flask and kept reacting for 10 hr at room temperature. After TLC analysis showed all the aldehyde was consumed completely, the reaction was terminated and filtrated, washed by Et_2O. Organic solvent was removed on the rota-vapor and the residue was purified by flash column chromatography (pure hexane) to get the desired olefin product, which was confirmed by ^{1}H-NMR (60% unoptimized yield).

Method A: General procedure for synthesis of 2

In schlenk line with a magnetic stirring bar and $Cu(OTf)_2$ (0.027 g, 0.15 mmol) were placed in a two neck round bottom flask at room temperature and air was exchanged with argon three times for 5-10 min. After that styrene (0.5 mmol) and $TMSN_3$ (0.296 mL, 4.5 mmol) were successively in the excess of argon. The reaction mixture was subjected to oxygen balloon and stirred for 18 h. Subsequently, a saturated aqueous solution of sodium thiosulfate ($Na_2S_2O_3$) was added, and the mixture was diluted with water and extracted with dichloromethane. The combined organic phases were dried over magnesium sulfate. and concentrated in vacuo. The residue was chromatographed on a silica gel column to get ketoazidation 2 and results are summerized in Table 2.

Method B: General procedure for synthesis of 2 and 3

The styrene (0.5 mmol) was dissolved in 4 mL of CH_3CN in the reaction tube. $TMSN_3$ (0.263 mL, 4.0 mmol) and $CuSO_4$ (0.008 g, 0.10 mmol) were added consecutively. The reaction mixture was stirred at room temperature for 9 hours. Subsequently, A saturated aqueous solution of sodium thiosulfate ($Na_2S_2O_3$) was added, and the mixture was diluted with water and extracted with dichloromethane. The combined organic phases were dried over magnesium sulfate. and concentrated in vacuo. The residue was chromatographed on a silica gel column to give ketoazidation **2** and **3 and** results are depicited in the **graph 1.**

^{1}H- and ^{13}C-NMR analytical data

4-cyanostyrene (1e)[19] Brown liquid, 257 mg, 43% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.61 (2H, d, *J* = 8.0 Hz, ArH), 7.48 (2H, d, *J* = 8.0 Hz, ArH), 6.73 (1H, dd, *J* = 17.5, 11 Hz, CH), 5.88 (1H, d, *J* = 17.5 Hz, CH), 5.45 (1H, d, *J* = 11 Hz, CH).

4-methoxysyrene (1g)[20] colorless liquid, 280 mg, 45% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.33 (2H, d, *J* = 8.5 Hz, ArH), 6.84 (2H, d, *J* = 8.5 Hz, ArH), 6.65 (1H, dd, *J* = 17.5, 10.5 Hz, CH), 5.60 (1H, d, *J* = 17.5 Hz, CH), 5.11 (1H, d, *J* = 11.0 Hz, CH), 3.78 (3H, s, CH_3).

3-vinyl styrene (1j)[21] colorless liquid, 362 mg, 60% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.43 (1H, s, ArH), 7.31-7.28 (3H, m, ArH), 6.72 (2H, dd, *J* = 17.5, 11.0 Hz, ArH), 5.77 (2H, d, *J* = 17.5 Hz, ArH), 5.26 (3H, d, *J* = 11.0 Hz, ArH).

3-nitro styrene (1m)[20] Brown liquid, 366 mg, 53% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.26 (1H, t, *J* = 2 Hz, ArH), 8.12-8.09 (1H, m, ArH), 7.71 (1H, d, *J* = 8.0, Hz, ArH), 7.50 (1H, t, *J* = 8 Hz, ArH), 6.77 (1H, dd, *J* = 17.5, 10.5 Hz, CH **)** 5.90 (1H, d, *J* = 18 Hz, CH), 5.45 (1H, d, *J* = 11 Hz, CH).

2-Azido-1-phenylethanone (2a)[22] Yellow oil, 60 mg, 77% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.91 (2H, d, *J* = 7.5 Hz, ArH), 7.63 (1H, t, *J* = 7.5 Hz, ArH), 7.50 (2H, t, *J* = 8 Hz, ArH), 4.57 (2H, s, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ 193.4, 134.6, 134.3 129.2, 128.1, 55.1.

2-Azido-1-(4-fluorophenyl)ethanone (2b)[23] White solid, 67.2 mg, 75% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.97-7.93 (2H, m, ArH), 7.18 (2H, t, *J* = 8.5 Hz, ArH), 4.55 (2H, s, CH_2).

2-Azido-1-(4-chlorophenyl)ethanone (2c)[23] White solid, 59.5 mg, 58% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.85 (2H, d, *J* = 8.5 Hz, ArH), 7.48 (2H, d, *J* = 9.0 Hz, ArH), 4.54 (2H, s, CH_2).

2-Azido-1-(4-bromophenyl)ethanone (2d)[24] Off white solid, 71.7 mg, 60% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.78 (2H, d, *J* = 8.5 Hz, ArH), 7.65 (2H, d, *J* = 8.5 Hz, ArH), 4.53 (2H, s, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ 192.5, 133.2, 132.5, 129.6, 129.5, 55.0.

2-Azido-1-(4-cyanophenyl)ethanone (2e)[25] Light yellow solid, 48.4 mg, 52% yield.^{1}H NMR (500 MHz, $CDCl_3$): δ 8.02 (2H, d, *J* = 8.5 Hz, ArH), 7.82 (2H, d, *J* = 8.5 Hz, ArH), 4.58 (2H, s, CH_2).

2-Azido-1-(4-acetoxyphenyl)ethanone (2f)[10d] White solid,62.4 mg, 57% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.94 (2H, d, *J* = 8.5 Hz, ArH), 7.24 (2H, d, *J* = 8.5 Hz, ArH), 4.54 (2H, s, CH_2), 2.33 (3H, s, CH_3).

2-Azido-1-(4-methoxyphenyl)ethanone (2g)[10d,23,26] White solid, 25.8 mg, 27% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.89 (2H, d, *J* = 8.5 Hz, ArH), 6.96 (2H, d, *J* = 8.5 Hz, ArH), 4.51 (2H, s, CH_2), 3.88 (3H, s, OCH_3).

2-Azido-1-(4-methylphenyl)ethanone (2h)[26] Off white solid, 63.9 mg, 73% yield.^{1}H NMR (500 MHz, $CDCl_3$): δ 7.80 (2H, d, *J* = 8.0 Hz, ArH), 7.29 (2H, d, *J* = 8.0 Hz, ArH), 4.53 (2H, s, CH_2), 2.43 (3H, s, CH_3).

2-Azido-1-(4-(*tert*-butyl)phenyl)ethanone (2i)[24] White solid, 73.8 mg, 68% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.84 (2H, d, *J* = 8.5 Hz, ArH); 7.50 (2H, d, *J* = 8.5 Hz, ArH), 4.53 (2H, s, CH_2), 1.34 (9H, s, CH_3).

2-Azido-1-(3-chlorophenyl)ethanone (2k).[27] Brown solid, 53.6 mg, 55% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.89 (1H, t, *J* = 1.5 Hz, ArH), 7.78 (1H, d, *J* = 8 Hz, ArH), 7.60 (1H, dd, *J* = 8.0, 1.0 Hz, ArH), 7.46 (1H, t, *J* =8 Hz, ArH), 4.54 (2H, s, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ 192.3, 136.1, 135.6, 134.2, 130.5, 128.3, 126.2, 55.1.

2-Azido-1-(3-bromophenyl)ethanone (2l).[28] Light yellow solid, 61.2 mg, 51% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.03 (1H, s, ArH), 7.78 (1H, d, *J* = 4 Hz, ArH), 7.74 (1H, s, ArH), 7.39 (1H, s, ArH), 4.55 (2H, s, CH_2).

2-Azido-1-(3-nitrophenyl)ethanone (2m).[29] Yellow crystals, 51.5 mg, 50% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.73 (1H, s, ArH), 8.49 (1H, d, *J* = 7.5 Hz, ArH), 8.29 (1H, d, *J* = 7.5 Hz, ArH), 7.78 (1H, t, *J* = 8 Hz, ArH), 4.69 (2H, s, CH_2). ^{13}C NMR (125 MHz, $CDCl_3$): δ 191.7, 148.6, 135.6, 133.7, 130.5, 128.4, 122.9, 55.2.

2-Azido-1-(2-bromophenyl)ethanone (2n).[29] Pale yellow solid, 41.8 mg, 35% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.64 (1H, d, *J* = 7.5 Hz, ArH). 7.46-7.40 (1H, m, ArH), 7.37 (1H, td, *J* = 7.5, 2 Hz, ArH), 4.48 (2H, s, CH_2).

2-Azido-1-(1,2-diphenyl)ethanone (2s).[30] White solid, 47.4 mg, 40% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.88 (2H, d, *J* = 7.5 Hz, ArH), 7.51 (1H, t, *J* = 7.5 Hz, ArH), 7.42-7.35 (7H, m, ArH), 5.72 (1H, s, CH).

2-Azido-1-(naphthalen-2-yl)ethanone (2u).[24] White solid, 56 mg, 53% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.39(1H, s, ArH), 7.97-7.87 (4H, m, ArH), 7.64 (2H, t, *J* = 8 Hz, ArH), 7.58 (1H, t, *J* = 8.0 Hz, ArH), 4.70 (2H, s, CH_2).

Benzaldehyde (3a).[31] Yellow oil, 10.6 mg, 20% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.01 (1H s, CHO), 7.87 (2H, dd, *J* = 7.5, 1.5 Hz, ArH), 7.64-7.60 (1H, m, ArH) 7.52 (2H, t, *J* = 8.0 Hz, ArH).

4-cyanobenzaldehyde (3e).[32] Off white solid, 11.8 mg, 18% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.10 (1H s, CHO), 8.00 (2H, d, *J* = 23.5 Hz, ArH), 7.86 (2H, d, *J* = 8.5 Hz, ArH).

4-*acetoxy*benzaldehyde (3f)[33] White solid, 22.2 mg, 27% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.99 (1H s, CHO), 7.92 (2H, d, *J* = 8.5 Hz, ArH), 7.28 (2H, d, *J* = 8.0 Hz, ArH), 2.33 (3H, s, CH_3).

4-*methoxy*benzaldehyde (3g).[31b] White solid, 14.9 mg, 22% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.89 (1H s, CHO), 7.85 (2H, d, *J* = 8.5 Hz, ArH), 7.01 (2H, d, *J* = 9.0 Hz, ArH), 3.90 (3H, s, CH_3).

4-*ter*. butylbenzaldehyde (3i).[34] White solid, 14.6 mg, 18% yield.^{1}H NMR (500 MHz, $CDCl_3$): δ 9.98 (1H s, CHO), 7.82 (2H, d, *J* = 8.5 Hz, ArH), 7.55 (2H, d, *J* = 8.0 Hz, ArH), 1.35 (9H, s, CH_3).

3-nitrobenzaldehyde (3m).[31c] Off white solid, 17.4 mg, 23% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.14 (1H s, CHO), 8.73 (1H, s, ArH), 8.50 (1H, dd, *J* = 8.0, 1.0 Hz, ArH), 8.25 (1H, d, *J* = 7.5 Hz, CH_9), 7.79 (1H, t, *J* = 8.0 Hz, ArH).

Benzophenone (4a).[31a] White solid, 45.5 mg, 50% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.8 (2H m, CH), 7.58 (4H, t, *J* = 7.5 Hz, ArH), 7.48 (4H, t, *J* = 7.5 Hz, ArH).

3-(2-Methoxyphenyl)-acrylonitrile (5a).[35] Brown liquid, 55.7 mg, 70% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.62 (1H, d, *J* = 16.5 Hz, CH), 7.41-7.36 (2H, m, ArH), 6.97 (2H, t, *J* = 7.5 Hz, ArH), 6.93 (2H, t, *d* = 8.0 Hz, ArH), 6.05 (1H, d, *J* = 16.5 Hz, ArH), 3.89 (3H, s, CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.4, 146.6, 132.5, 129.1, 122.7, 121.0, 119.2, 111.5, 97.10, 55.7.

phenylacrylonitrile (5b).[31a] Brown liquid, 41.9 mg, 65% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.45-7.25 (6H, m, ArH), 5.88 (1H, d, *J* = 17 Hz, CH).

phenylacetonitrile (5d).[36] Colourles liquid, 17.6 mg, 30% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38-7.35 (2H, m, ArH), 7.32 (3H, t, *J* = 5 Hz, ArH), 3.73 (2H, s, CH_2).

^{1}H- and ^{13}C-NMR Spectra for new compounds

2-Azido-1-(3-vinylphenyl)ethanone (2j): white solid, 68.3 mg, 73% yield, mp = 40-42 °C ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.90 (1H, s, ArH), 7.74 (1H, d, *J* = 8.0 Hz, ArH), 7.64 (1H, d, *J* = 8.0 Hz, ArH), 7.44 (1H, t, *J* = 8.0 Hz, ArH), 6.74 (1H, dd, *J* = 17.5, 11.0 Hz, ArH), 5.83 (1H, d, *J* = 17.5 Hz, ArH), 5.36 (1H, d, *J* = 10.5 Hz, ArH), 4.55 (2H, s, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ 193.3, 138.5, 135.7, 134.8, 131.6, 129.2, 127.1, 125.7, 115.9, 55.0. HRMS (m/z) calculated for $C_{10}H_9N_3ONa^+$: 210.0643, found: 210.0636.

2-Azido-1-(5-bromo-2-fluorophenyl)ethanone (2o): Yellow crystals, 70.7 mg, 55% yield, mp = 62-64.2 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.23(1H, d, *J* = 8.5 Hz, ArH), 7.80 (1H, td, *J* = 7.5, 0.5 Hz, ArH), 7.71-7.68 (1H, m, ArH), 7.43 (1H, dd, *J* = 7.5, 1 Hz, ArH), 4.32 (2H, s, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ 190.5 (1C, d, *J* = 5.37 Hz, CO), 161.3 (1C, d, *J* = 253.37 Hz, ArC), 138.6 (1C, d, *J* = 9.12 Hz, ArC), 133.6 (1H, d, *J* = 3.12 Hz, ArC), 124.2 (1C, d, *J* = 15.75 Hz, ArC), 118.8 (1H, d, *J* = 25.25 Hz, ArC), 118.1 (1C, d, *J* = 3.0 Hz, ArC), 58.8 (1C, d, *J* = 12.6 Hz, CH_2). HRMS (m/z) calculated for $C_8H_5BrFN_3ONa^+$: 279.9498, found: 279.9486.

2-Azido-1-(3-bromo-4-fluorophenyl)ethanone (2p): White solid. 89.9 mg, 70% yield mp = 71.2-73.8 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.14 (1H, dd, *J* = 6.5, 2 Hz, ArH), 7.89-7.86 (1H, m, ArH), 7.25 (1H, t, *J* = 8.5 Hz, ArH), 4.56 (2H, s, CH_2).^{13}C NMR (125 MHz, $CDCl_3$): δ 190.9 (1C, s, $CO_)$, 162.6 (1C, d, *J* = 255.62 Hz, ArC), 134.0 (1C, d, *J* = 1.5 Hz, ArC), 131.9 (1C, d, *J* = 3.62 Hz, ArC), 129.3 (1C, d, *J* = 8.62 Hz, ArC), 117.2 (1C, d, *J* = 22.87 Hz, ArC), 110.3 (1C, d, *J* = 21.62 Hz, ArC), 54.8 (1C, s, CH_2). HRMS (m/z) calculated for $C_8H_5BrFN_3ONa^+$: 279.9498, found: 279.9484.

Supporting Information.

Experimental procedures, and ^{1}H NMR and ^{13}C NMR Spectra for compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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