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tert-Butyl Nitrite Mediated Different Functionalizations of Internal Alkenes: Paths to Furoxans and Nitroalkenes

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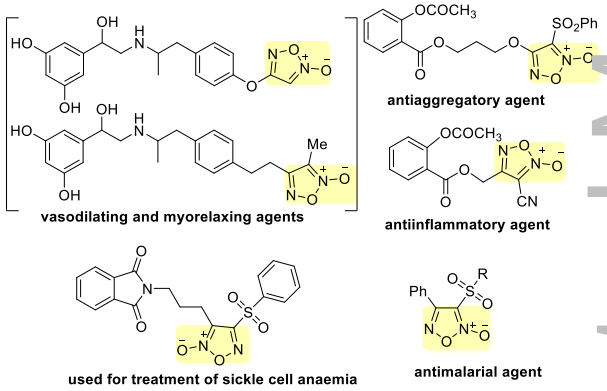
Abstract: *tert*-Butyl nitrite (TBN) reacts differently with various internal alkenes leading to interesting and useful products. Synthesis of 1,2,5-oxadiazole-*N*-oxides (furoxans) has been achieved from internal alkenes using *tert*-butyl nitrite (TBN), quinoline and $K_2S_2O_8$. Under an identical reaction condition α,β-unsaturated carboxylic acids and cyclic and acyclic internal alkenes both afforded nitroalkenes as the sole product via decarboxylative and direct nitration path respectively.

Keywords: *tert*-Butyl nitrite (TBN); furoxans; nitroalkenes; isoxazolines; internal alkenes

Furoxan (or 1,2,5-oxadiazole 2-oxide) is a heterocycle of the isoxazole family and is an important scaffold in medicinal chemistry.[1] Derivatives of furoxans or furoxan *N*-oxides are of significant importance in organic synthesis, since they are an integral part of several potential therapeutic agents such as furoxans-praziquantel,[2a] *N*-acyl derivatives of furoxans,[2b] furoxans-pthalimide,[2c] furoxanyl-*N*-acylhydraxones,[2d] furoxanylacyl-salicyclic acid,[2e] furoxan-farnesylthiosalicylic acid,[2f] furoxans amodiaquine,[2g] furoxans-phenylsulfonyl,[2h] 4-furoxanyl nitrone,[2i] furoxan-chalcones,[2j] furoxan-fenoterol,[2k] furoxan-oleanolic acid,[2l] furoxans-dibenzoyl,[2m] furoxan-ibuprofen,[2n] etc. Moreover, furoxan derivatives have drawn phenomenal biological and pharmaceutical interests, some of which are reported to have antioxidant,[3a] vasodilator,[3a] leishmanicidal,[3b] anticancer,[3c] antibacterial,[2i] antimalarial,[2l] antihistaminic,[3d] and anti HIV[3e] activities. Furoxan derivatives are known to release nitric oxide (NO) in the presence of thiol co-factors, thus activating the soluble guanylate cyclase.[1,4] Consequently, many research groups pursued studies on the development of furoxan-based drugs.[5] Selected furoxan derivatives possessing potential pharmaceutical applications are shown in Figure 1.[2i,3a,5c,6]

Figure 1. Some representative bioactive furoxans.



Existing strategies for furoxan synthesis involve dehydration of α-nitro oximes,[7a] dimerization of nitrile *N*-oxides,[7b] oxidation of α-dioximes,[7c] reaction of styrenes with $NOBF_4$.[7d] However, any *tert*-butyl nitrite mediated synthesis of furoxans from internal alkenes is still unexplored. In this regard, synthesis of furoxans from easily accessible and biologically demanding internal alkenes bearing an allylic stereogenic centre may generate potential applications as both stereogenic centre[8a] and furoxan moiety[8b,c] are important parts of many biologically active compounds, thus are expected to receive considerable interest from biological and pharmaceutical point of view.

Alkenes which are simple organic molecules have been widely applied in organic synthesis for the construction of a diverse array of complex molecules. One of the finest approaches to build such class of

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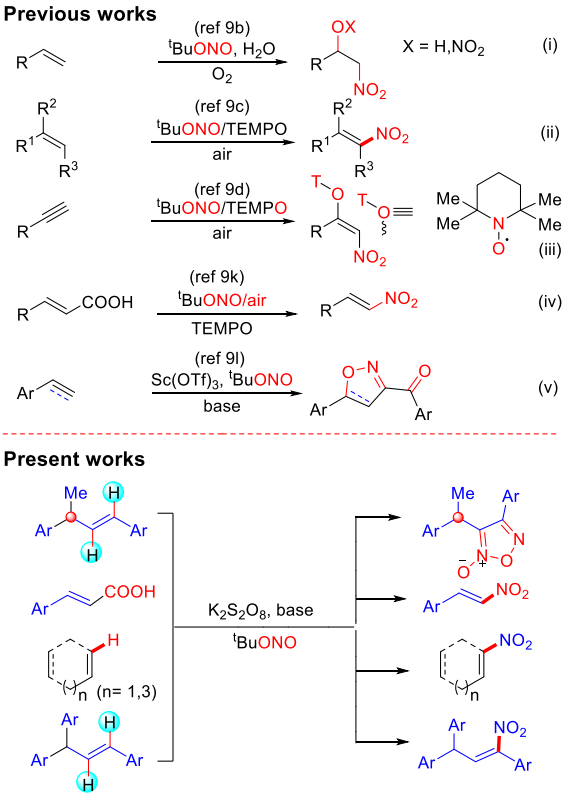
molecules in a single operation is via the direct 1,2-difunctionalization of alkenes. In this context, *tert*-butyl nitrite (TBN) has emerged as a versatile reagent in organic synthesis.[9a] Therefore, it has been employed for the oxidative nitration,[9b] [Scheme 1 (i)], stereoselective nitration[9c] [Scheme 1 (ii)], aerobic oxynitration[9d] [Scheme 1 (iii)] of terminal olefins [(Scheme 1)], metal free nitration of 2-oxindoles[9e] and phenols,[9f] metal free synthesis of isatins,[9g] synthesis of quinoxaline *N*-oxides,[9h] substituted pyrazole *N*-oxides,[9i] cyclization of *o*-alkynylanilines[9j] and TEMPO mediated decarboxylative nitration of α,β-unsaturated carboxylic acids [(Scheme 1 (iv)].[9k] Recently our group has reported a *tert*-butyl nitrite-mediated domino synthesis of isoxazolines and isoxazoles respectively from styrenes and phenylacetylenes [Scheme 1(v)].[9l] However, *tert*-butyl nitrite-mediated difunctionalization of any internal olefin is less explored so far. Thus, treatment of an internal alkene with TBN may lead to the formation of similar isoxazoline[9l] or a completely different reactivity may drive the formation of some other product? Therefore, we were curious to investigate the reaction of various internal alkenes with TBN.



cheme 1. *tert*-Butylnitrite mediated functionalization of olefins.

Our initial investigation started by reacting an internal alkene (**1**) with *tert*-butyl nitrite (**a**). Alkene (*E*)-1,3-diphenyl-1-butene (**1**) was chosen as the model substrate as this core unit contains an allylic carbon stereogenic centre which represents a privileged and biologically important molecular scaffold.[8a] Initially, alkene (**1**) was treated with *tert*-butyl nitrite (**a**) (2 equiv.) in the presence of well explored $FeCl_3$ (2.5 mol%) catalyst, and base 1,4-diazabicyclo[2.2.2]octane (DABCO) (1 equiv.) in 1,2-dichloroethane (DCE) (1.5 mL) at 85 °C for 5.0 h. A new product (**1a**) was isolated in 33% yield after column chromatographic separation (Table 1, entry 1). Spectroscopic (^{1}H and ^{13}C NMR) analysis of the product (**1a**) revealed the disappearance of both alkene protons at 6.40 ppm. However, appearance of a doublet at 1.23 ppm and a multiplet at 3.27 ppm suggests that the PhCH(CH_3)- part is intact thereby confirming di-functionalization across the double bond of (**1**). Further, HRMS analysis of the product indicates loss of two protons and addition of two NO groups. Finally, the exact structure of the product was confirmed by X-ray crystallographic analysis of one of its derivative (**8a**) as shown in Figure 2. Fascinated by the formation of this interesting furoxan skeleton, this reaction was further screened by varying various other Lewis acid catalysts. Among the catalysts screened such as $AlCl_3$ (37%), $Fe(OTf)_3$ (39%) and $Sc(OTf)_3$ (44%) (Table 1, entries 2-4), it was observed that $Sc(OTf)_3$ provided better yield (44%). However, the use of other bivalent metal catalysts such as $Cu(OTf)_2$ and $Zn(OTf)_2$ provided the desired product (**1a**) in lesser yields 19% and 17% respectively (Table 1, entries 5-6). Interestingly, the use of organic base quinoline (Table 1, entry 9) *in lieu* of DABCO, DBU, DMAP (Table 1, entries 4, 7, 8) provided the product (**1a**) in an improved yield (56%). Reaction carried out in the absence of $Sc(OTf)_3$ catalyst was detrimental to product formation (Table 1, entry 10), suggesting the involvement of $Sc(OTf)_3$ in facilitating the reaction. When the reaction was performed in the absence of base under otherwise identical condition the yield of (**1a**) decreased to 39% (Table 1, entry 11). These results suggest the active involvement of both catalyst and base in this reaction. In order to further improve the product yield, various oxidant/additive combinations were employed in lieu of a single oxidant. It was found that the use of additive Oxone® along with TBN improved the product yield upto 59% (Table 1, entry 12). By changing the additive from Oxone® to potassium persulphate ($K_2S_2O_8$) the product yield improved upto 62% (Table 1, entry 13). Surprisingly, when the reaction was carried out in the absence of $Sc(OTf)_3$ catalyst, but in the presence of TBN, $K_2S_2O_8$ and quinoline the yield of (**1a**) improved to 64% (Table 1, entry 14). This observation suggests that the reaction is neither mediated by a redox process nor by a Lewis acid catalyst. However, when the reaction was carried out in the absence of base the product formation (**1a**) dropped to 29% (Table 1, entry 15). In the presence of $K_2S_2O_8$ (1 equiv.) alone i.e in the absence of any catalyst and base the reaction gave 51% yield (Table 1, entry 16). When the reaction was carried out at 100 °C the yield remained unchanged (64 %) of (**1a**) (Table 1, entry 17) but a decrease in the reaction temperature to 70 °C provided reduced yield (52%) of

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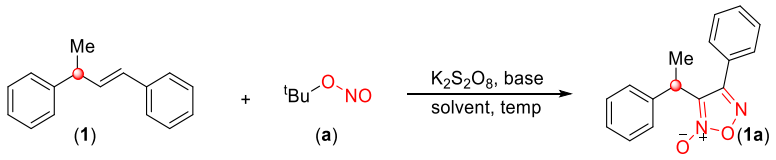
Table 1. Screening of reaction conditions.[a]



Entry	Catalyst (mol %)	Base (equiv.)	Solvent (1.5 mL)	Additive (equiv.)	Yield %[b]
1	$FeCl_3$ (2.5)	DABCO (1)	DCE		33
2	$AlCl_3$ (2.5)	DABCO (1)	DCE		37
3	$Fe(OTf)_3$ (2.5)	DABCO (1)	DCE		39
4	$Sc(OTf)_3$ (2.5)	DABCO (1)	DCE		44
5	$Cu(OTf)_2$ (2.5)	DABCO (1)	DCE		19
6	$Zn(OTf)_2$ (2.5)	DABCO (1)	DCE		17
7	$Sc(OTf)_3$ (2.5)	DBU (1)	DCE		44
8	$Sc(OTf)_3$ (2.5)	DMAP (1)	DCE		27
9	$Sc(OTf)_3$ (2.5)	Quinoline (1)	DCE		56
10		Quinoline (1)	DCE		23
11	$Sc(OTf)_3$ (2.5)		DCE		39
12	$Sc(OTf)_3$ (2.5)	Quinoline (1)	DCE	Oxone® (1)	59
13	$Sc(OTf)_3$ (2.5)	Quinoline (1)	DCE	$K_2S_2O_8$ (1)	62
14		Quinoline (1)	DCE	$K_2S_2O_8$ (1)	64
15	$Sc(OTf)_3$ (2.5)		DCE	$K_2S_2O_8$ (1)	29
16			DCE	$K_2S_2O_8$ (1)	51
17		Quinoline (1)	DCE	$K_2S_2O_8$ (1)	64[c]
18		Quinoline (1)	DCE	$K_2S_2O_8$ (1)	52[d]
19		**Quinoline (1)**	**CH_3CN**	**$K_2S_2O_8$ (1)**	**73**
20		Quinoline (1)	DMSO	$K_2S_2O_8$ (1)	21
21		Quinoline (1)	DMF	$K_2S_2O_8$ (1)	43
22		Quinoline (1)	AcOH	$K_2S_2O_8$ (1)	51
23		Quinoline(1)		$K_2S_2O_8$ (1)	27
24		Quinoline (2)	CH_3CN	$K_2S_2O_8$ (1)	76
25		Quinoline (1)	CH_3CN	$K_2S_2O_8$ (2)	60

[a]*Reaction conditions:* **1** (0.50 mmol), $K_2S_2O_8$ (0.50 mmol), base (0.50 mmol), *tert*-butylnitrite (1.0 mmol) at 85 °C. [b]Yield after 5.0 h. [c]Temperature 100 °C. [d]Temperature 70 °C.

the product (Table 1, entry 18). Subsequently screening of other solvents such as CH_3CN, DMSO, DMF, AcOH, solvent CH_3CN was found to give the best yield 73% (Table 1, entries 19-22) under otherwise identical condition. Since most of the reagents are liquid at room temperature the reaction was attempted under a neat condition, unfortunately the reaction was unclean giving multitude of products and reducing the isolated yield to 27% (Table 1, entry 23). A marginal improvement in the yield (76%) of the product was observed by increasing the quinoline amount to 2 equivalents (Table 1, entry 24). However, a twofold loading of $K_2S_2O_8$ was found to be counterproductive for the reaction giving only 60% yield (Table 1, entry 25). After a series of screening, it was found that this *bis*-functionalization is best achieved using alkene (**1**) (0.5 mmol), TBN (2 equiv.), quinoline (1 equiv.), $K_2S_2O_8$ (1 equiv.) at 85 °C for 5.0 h.

After establishing the optimized reaction condition for furoxan (**1a**) formation from internal alkene (**1**) as shown in (Table 1), we explored the reaction between various (*E*)-1,3-diphenyl-1-butenes (**1-9**) with TBN (**a**). This reaction proceeded well with a variety of alkenes bearing electron-donating as well as electron-withdrawing groups in their phenyl rings. Phenyl rings of these alkenes possessing moderately electron-donating groups such as 4-Me (**2**) 4-^{t}Bu (**3**), 4-Ph (**4**), gave their corresponding products (**2a**, 57%), (**3a**, 55%), (**4a**, 59%), in moderate yields (Scheme 2). Alkene substrates having moderately electron-withdrawing groups such as 4-Cl (**5**), 4-Br (6), 4-F (**7**) in the phenyl rings provided their corresponding products (**5a**, 71%), (**6a**, 73%), (**7a**, 75%) in good yields as shown in (Scheme 2). Alkenes possessing strongly electron-withdrawing group such as 3-NO_2 (**8**) also resulted in the formation of furoxan (**8a**) in good yield (79%). Internal alkene having tri-methyl (**9**) substitution in its phenyl ring reacted successfully and provided the corresponding furoxan (**9a**, 51%) in a relatively lesser yield (Scheme 2). The lower yield of product obtained for the substrate (**9**) is possibly due to the steric hindrances due to ortho substitutions.

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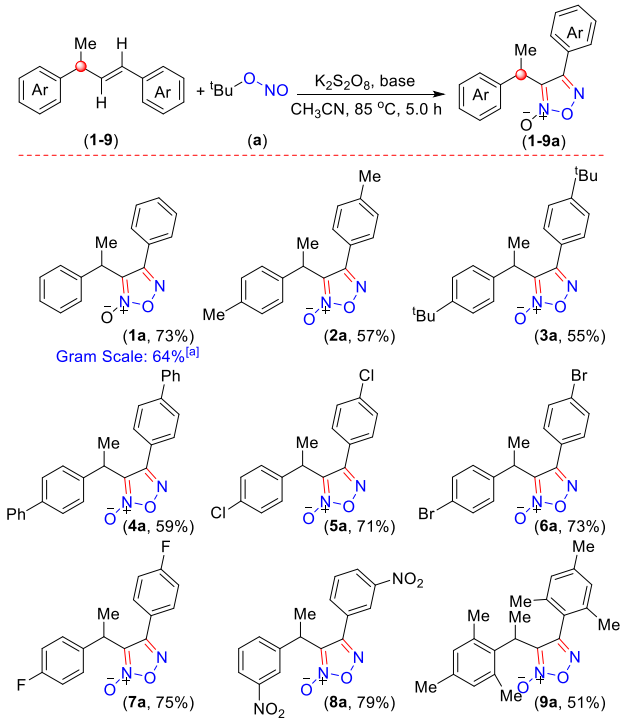


Scheme 2. Substrate scope for furoxan synthesis. *Reaction conditions:* (**1-9**) (0.50 mmol), $K_2S_2O_8$ (0.50 mmol), quinoline (0.50 mmol), *tert* butyl nitrite (1.0 mmol) in CH_3CN (1.5 mL) at 85 °C for 5 h. Isolated yields.[a] TBN and $K_2S_2O_8$ was added in 4 equal lots over a period of 4 h.

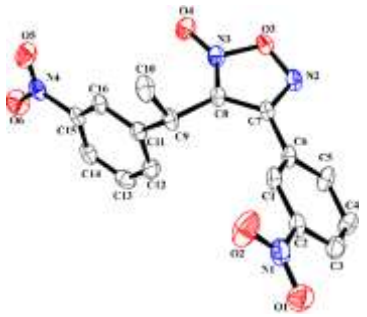
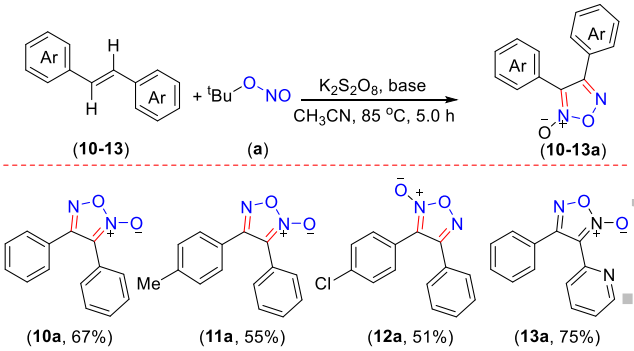


Figure 2. ORTEP molecular diagram of (**8a**).[10]

In addition to these unsymmetrical benzylic internal alkenes this method is equally amenable to 1,2-disubstituted symmetrical and unsymmetrical stilbenes. When *trans*-stilbene (**10**) was treated with TBN it provided corresponding furoxan (**10a**) in 67% yield (Scheme 3). In addition, unsymmetrical *trans*-stilbenes possessing moderately electron-donating 4-Me (**11**) and electron-withdrawing 4-Cl (**12**) substituents in one of the phenyl ring reacted successfully providing their expected products (**11a**) and (**12a**) in 55% and 51% yields respectively. A heterocyclic *trans*-stilbene (**13**) also reacted successfully and provided the corresponding furoxan (**13a**) in a good yield (75%). At present we are not sure about the position of *N*-oxide as towards which phenyl ring it is oriented but based on the mechanism proposed in (Scheme 4), the *N*-oxide is expected to be towards phenyl side in (**11a**), 4-Cl phenyl side in (**12a**) and towards pyridine ring in (**13a**) (Scheme 3)

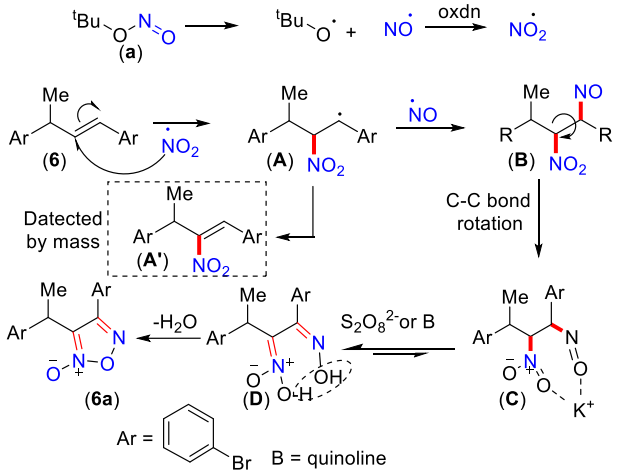
To demonstrate the applicability of the reaction in large scale, internal alkene (**1**) (5 mmol, 1.04 g) was reacted with TBN (10 mmol) and $K_2S_2O_8$ (5 mmol) the product was obtained in 51% yield. Interestingly, when TBN and $K_2S_2O_8$ were added in four equal lots over a period of 4 h the yield of the product (**1a**) improved up to 64% (Scheme 2).



Scheme 3. Substrate scope for furoxan synthesis from *trans*-stilbenes. *Reaction conditions:* **(10-13)** (0.50 mmol), $K_2S_2O_8$ (0.50 mmol), quinoline (0.50 mmol), *tert* butyl nitrite (1.0 mmol) in CH_3CN (1.5 mL) at 85 °C for 5 h. Isolated yields.

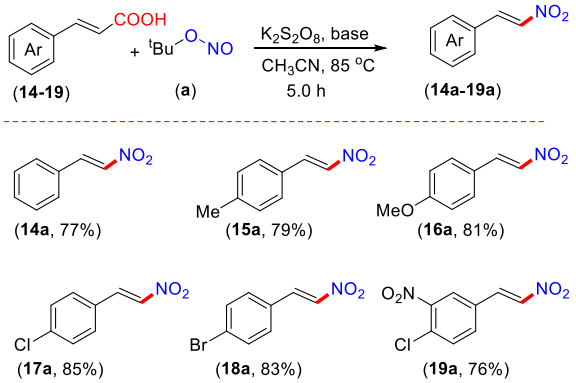
To check whether the reaction is proceeding via a radical path, (*E*)-4,4'-(but-2-ene-1,3-diyl)bis(bromobenzene) (**6**) was reacted with *tert*-butylnitrite (**a**) in the presence of an equimola quantity of radical scavenger (2,2,6,6-tetramethylpiperidin-1-yl)oxidanyl (TEMPO). Formation of (<2%) of the product (**6a**) (Scheme S1) [see supporting information (SI)] suggests a possible radical pathway for this transformation. On the basis of the literature reports, intermediates detected by HRMS analysis of the reaction mixtures a plausible mechanism has been proposed for the furoxan formation. Initially, the heterolytic cleavage of *tert*- butyl nitrite produces a NO radical and a *tert*-butoxy radical (Scheme 4). The NO radical under an aerobic reaction condition gets converted to a NO_2 radical.[11] Subsequently, the NO_2 radical attacks at the nonbenzylic carbon of the olefin (**6**) to generate a nitroalkane benzyl radical intermediate (**A**) (Scheme 4). The radical intermediate (**A**) then reacts with the NO• radical at its benzylic position to give a nitro nitroso intermediate (**B**). Alternatively, the intermediate (**A**) loses a proton giving product (**A´**), which has been detected by HRMS analysis of the reaction aliquots. This pattern of preferential attack of NO• at the benzylic position is consistent with our isoxazoline synthesis involving a terminal alkene and TBN.[9] The intermediate (**B**) then undergo a C–C bond rotation which is perhaps facilitated by the co-ordination of K^+ with two of the oxygen atoms from NO and NO_2 groups forming an intermediate (**C**). The nitroso intermediate (**C**) isomerizes to a *bis*-

oxime type intermediate (**D**) in the presence of base, from which furoxan (**6a**) is generated via the loss of a water molecule (Scheme 4). Formation of intermediates (**B**)/(**D**) have been detected by HRMS analysis of the reaction mixture [Fig. S1, S2 see supporting information (SI)].



Scheme 4. Plausible mechanism for 1,2,5-oxadiazole-N-oxide synthesis.

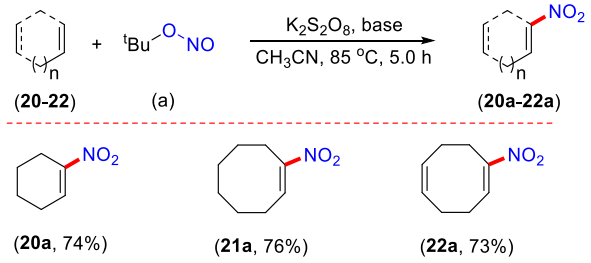
Further, to check whether this strategy of furoxan synthesis is applicable to other internal alkenes such as α,β-unsaturated acids or not? *trans*-cinnamic acid (**14**) was reacted with TBN (**a**) under an identical reaction condition. The reaction proceeded well and provided product (**14a**) in good yield (77%). Spectroscopic (IR, ^{1}H and ^{13}C NMR) analysis of the isolated product (**14a**) showed the absence of COOH group. The HRMS analysis of the new product revealed the loss of a COOH group and incorporation of a NO_2 group. Here, perhaps *tert*-butyl nitrite (**a**) is serving as a decarboxylative nitrating agent because their corresponding ester did not yield any trace of the nitroalkene (nor even furoxan). To explore the generality of this strategy, the reaction of electron-donating such as 4-Me (**15**), 4-OMe (**16**) and electron-withdrawing such as 4-Cl (**17**), 4-Br (**18**), and 3-NO_2-4-Cl (**19**) substituents present in the aryl ring of the cinnamic acids all afforded β-nitration products (**15a**, 79%), (**16a**, 81%), (**17a**, 85%), (**18a**, 83%) and (**19a**, 76%) (Scheme 5) in good yields. Prior to this report there are reports on decarboxylative nitration using HNO_3,[12a-c] ^{t}BuONO in combination with CuCl[12d] and TEMPO.[9k] Few other methods such as Henry reaction involving nitroalkanes,[12e] and direct nitration of alkenes using $AgNO_2$[12f] have also been reported for the synthesis of nitroalkenes. Although few decarboxylative nitration are reported, which have been achieved either using metal catalyst or the use of harsh reaction conditions such as high temperature, highly acidic conditions or stoichometric amounts of metal nitrates.[12] It may be mentioned here that the nitro-olefins are a distinguished class of synthetic intermediates, which have been used in the preparation of a wide variety of biorelevant compounds and pharmaceuticals.[13] Thus, the present metal free decarboxylative nitration is an economical, safer and greener approach for the synthesis of nitroalkenes. The proposed mechanism for the reaction is expected to be similar to the one proposed by Prabhu et.al using TBN and CuCl[12d] and Maiti using TEMPO and TBN[9k] as shown in (Scheme 8).



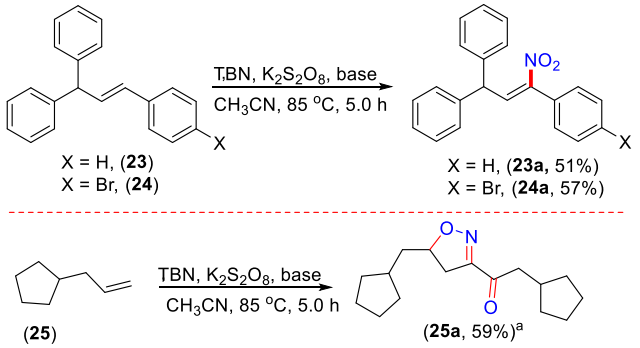
Scheme 5. Nitration of α,β-unsaturated carboxylic acids. *Reaction conditions:* (**14-19**) (0.50 mmol), $K_2S_2O_8$ (0.50 mmol), quinoline (0.50 mmol), *tert*-butyl nitrite (1.0 mmol) in CH_3CN (1.5 mL) at 85 ˚C for 5 h. Isolated yields.

Encouraged by the above differential reactivity of *tert*-butyl nitrite (TBN) with two classes of alkenes one leading to furoxans and the other decarboxylative nitration giving nitroalkenes, this strategy was then applied to alicyclic alkenes to see the type of product it would result. To our delight alicyclic alkenes such as cyclohexene (**20**), cycloctene (**21**) and cycloctadiene (**22**) yielded nitroalkenes under an identical reaction condition affording products (**20a**, 74%), (**21a**, 76%) and (**22a**, 73%) respectively in good yields as shown in (Scheme 6). Surprisingly, none of the substrates (**20-22**) gave any trace of their furoxan products. Here the reaction stops at the mono-nitration stage, however, for the furoxan synthesis generation of vicinal nitro-nitroso intermediate is essential (Scheme 4). All the substrates in Scheme 2 and (Scheme 3) form stable benzyl radical after initial mono nitration (Scheme 4), but in alicyclic alkenes formation of such stable benzylic radical is not possible as a result none of the substrates gave furoxan as their products. Nevertheless formation of similar nitro alkenes have been reported using TBN in the presence of TEMPO but only from terminal alkenes.[9c] Acyclic *trans*-alkenes such as prop-2-ene-1,1,3-triyltribenzene (**23**) and 3-(4-bromophenyl)prop-2-ene-1,1-diyl)dibenzene (**24**) provided their 3-nitroproducts (**23a**) and (**24a**) in 51% and 57% yields respectively rather than the expected 2-nitroproducts. The structure of the product (**23a**) is 3-nitro and not 2-nitro has been confirmed by

X-ray crystallographic analysis (Figure S3).[14] Similarly the structure of (**24a**) is ascertained by NOE experiments (SI). Interestingly, under the present reaction condition terminal alkene viz. allyl cyclopentane (**25**) afforded the isoxazoline product (**25a**, 59%) (Scheme 7). This result is not surprising since we have recently reported the formation of isoxazoline from terminal alkenes using TBN, quinoline in the presence of catalyst $Sc(OTf)_3$.[9l]

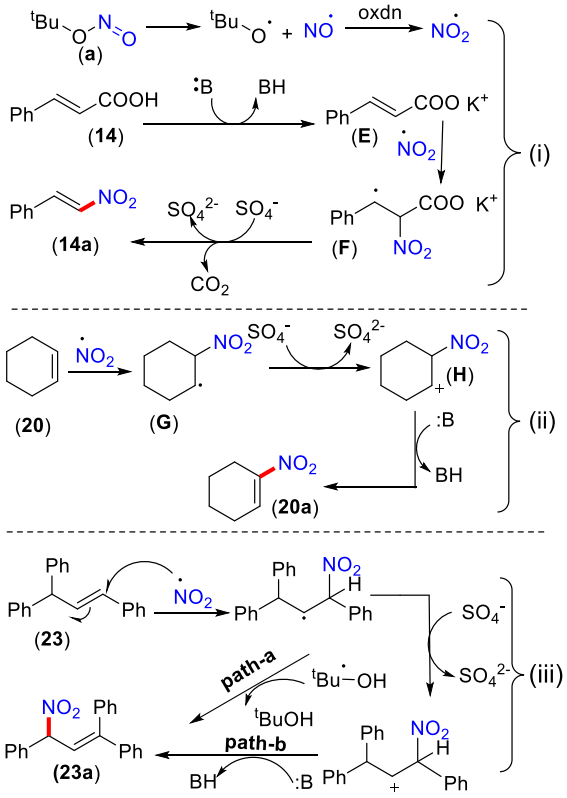


Scheme 6. Nitration of alicyclic alkenes.
Reaction conditions: (**20-22**) (0.50 mmol), $K_2S_2O_8$ (0.50 mmol), quinoline (0.50 mmol), *tert*-butyl nitrite (1.0 mmol) in CH_3CN (1.5 mL) at 85 °C for 5 h. Isolated yields.



Scheme 7. Nitration of acyclic alkenes.
Reaction conditions: (**23-25**) (0.50 mmol), $K_2S_2O_8$ (0.50 mmol), quinoline (0.50 mmol), *tert*-butyl nitrite (1.0 mmol) in CH_3CN (1.5 mL) at 85 °C for 5 h. Isolated yields.
[a]Using allylcyclopentane (1.0 mmol).

To account for the formation of nitroalkenes from α,β-unsaturated carboxylic acids and alicyclic alkenes, the following mechanism has been proposed. The carboxylic acid reacts with the base and form its potassium salt (**E**) [Scheme 8 (i)]. The NO_2 radical generated via heterolytic cleavage of TBN and subsequent oxidation reacts with (**E**) to form a radical intermediate (**F**), which upon oxidative decarboxylation gives (**14a**) [Scheme 8 (i)]. An analogous mechanism has been proposed for the formation of nitroalkenes from alicyclic alkenes. The NO_2 radical reacts with alicyclic alkene (**20**) to form a radical intermediate (**G**) [Scheme 8 (ii)], one electron oxidation of (**G**) gives rise to the carbocation intermediate (**H**). In the presence of base, the intermediate (**H**) loses a proton to give (**20a**) [Scheme 8 (ii)]. Mechanism for the formation of the unexpected 3-nitroprop-1-ene-1,1,3-triyl)tribenzene (**23a**) is shown in [Scheme 8 (iii)].



Scheme 8. Plausible mechanism for synthesis of nitroolefins.

In conclusion we have demonstrated the differential reactivity of various alkenes with *tert*-butyl nitrite (TBN). Internal benzylic alkenes such as (*E*)-1,3-diphenyl-1-butene gave furoxan as the exclusive product in the presence of $K_2S_2O_8$, base and TBN. While α,β-unsaturated esters are inert to TBN but α,β-unsaturated acids under an identical condition undergo a rapid decarboxylation giving nitroalkenes. On the other hand, acyclic internal alkenes yielded nitro alkenes as the sole product, whereas terminal aliphatic alkenes gave isooxazolines as their product. In the furoxan formation, TBN is serving as a NO_2 cum NO synthon and as a decarboxylative nitrating agent when the substrates are α,β-unsaturated acids.

Experimental Section

General Procedure for the Synthesis of 4-Phenyl-3-(1-phenylethyl)-1,2,5-oxadiazole 2-oxide (1a)
To an oven-dried 25 mL round bottom flask fitted with a reflux condenser were added (*E*)-but-1-ene-1,3-diyldibenzene (104 mg, 0.5 mmol), $K_2S_2O_8$ (135 mg, 0.5 mmol), quinoline (0.059 mL, 0.5 mmol), *tert*-butyl nitrite (0.119 mL, 1.0 mmol) and acetonitrile (1.5 mL) Then the reaction mixture was heated at 85 °C for 5.0 h. After the completion of the reaction excess solvent was evacuated under reduced pressure. The reaction mixture was admixed with ethyl acetate 20 mL and washed with water (2 x 10

mL). The separated organic layer was dried over anhydrous sodium sulphate (Na_2SO_4), and evaporated under reduced pressure. The crude product so obtained was purified by silica gel column chromatography using hexane as the eluent to give pure 4-phenyl-3-(1-phenylethyl)-1,2,5-oxadiazole 2-oxide (**1a**, 98 mg, 73% yield). The identity and purity of the product was confirmed by spectroscopic analysis.

General Procedure for the Synthesis of *E*-(2-Nitrovinyl)benzene (14a)

To an oven-dried 25 mL round bottom flask fitted with a reflux condenser were added *trans*-cinnamic acid (74 mg, 0.5 mmol), $K_2S_2O_8$ (135 mg, 0.5 mmol), quinoline (0.059 mL, 0.5 mmol), *tert*-butyl nitrite (0.119 mL, 1.0 mmol) and acetonitrile (1.5 mL). Then the reaction mixture was heated at 85 °C for 5.0 h. After the completion of the reaction excess solvent was evacuated under reduced pressure. The reaction mixture was admixed with ethyl acetate 20 mL washed with water (2 x 10 mL). The separated organic layer was dried over anhydrous sodium sulphate (Na_2SO_4), and evaporated under reduced pressure. The crude product so obtained was purified by silica gel column chromatography using hexane as the eluent to give pure *E*-(2-nitrovinyl)benzene (**14a**, 57 mg, 77% yield). The identity and purity of the product was confirmed by spectroscopic analysis.

General Procedure for the Synthesis of 1-Nitrocyclohex-1-ene (20a)

To an oven-dried 25 mL round bottom flask fitted with a reflux condenser were added cyclohexene (41 mg, 0.5 mmol), $K_2S_2O_8$ (135 mg, 0.5 mmol), quinoline (0.059 mL, 0.5 mmol), *tert*-butyl nitrite (0.119 mL, 1.0 mmol) and acetonitrile (1.5 mL) Then the reaction mixture was heated at 85 °C for 5.0 h. After completion of the reaction excess solvent was evacuated under reduced pressure. The reaction mixture was admixed with ethyl acetate 20 mL and water (2 x10 mL) and the separated organic layer was dried over anhydrous sodium sulphate (Na_2SO_4), and evaporated under reduced pressure. The crude product so obtained was purified by silica gel column chromatography using hexane as the eluent to give pure 1-nitrocyclohex-1-ene (**20a**, 47 mg, 74% yield). The identity and purity of the product was confirmed by spectroscopic analysis.

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[10] CCDC-1812965 (**8a**) contains the supplementary crystallographic data for this paper.These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. See also the Supporting Information.

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[14] CCDC-1854783 (**23a**) contains the supplementary crystallographic data for this paper.These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. See also the Supporting Information.

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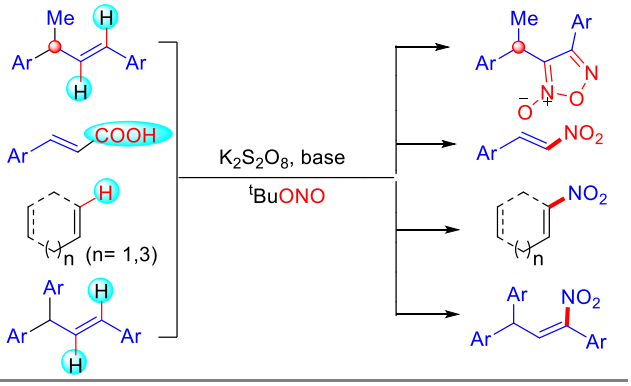

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