Organic & Biomolecular Chemistry

ROYAL SOCIETY OF CHEMISTRY

REVIEW

View Article Online
View Journal | View Issue

Cite this: *Org. Biomol. Chem.*, 2025, **23**, 7023

Denitrative radical-induced coupling reactions of nitroalkenes

Alessandro Palmieri and Marino Petrini *

Received 30th May 2025,
Accepted 7th July 2025

DOI: 10.1039/d5ob00904a

rsc.li/obc

The classical reactivity of nitroalkenes, involving regioselective 1,4-addition by nucleophilic reagents, can be modified in β-nitrostyrenes using free radical species, which selectively add to nitro-bearing unsaturated carbon. The resulting stabilized benzylic radical undergoes a denitrative process leading to the formation of substituted alkenes. Alkyl and aryl radicals can be employed in this process, which can also be extended to the use of sulfur- and phosphorus-centered radicals. These radical species can be generated using oxidative, reductive or photocatalyzed procedures, which also ensure notable diastereoselectivity in alkene formation. Although currently applied only to β-nitrostyrenes, this approach could potentially be extended to any nitroalkene bearing a radical-stabilizing group at the beta position.

1. Introduction

The powerful electron-withdrawing character of the nitro group makes nitroalkenes some of the strongest electrophilic compounds in organic synthesis.[1] The reduced electronic density of the double bond in these derivatives can be profitably exploited in conjugate addition reactions with a plethora of nucleophilic partners of various origins.[2] Alongside this reactivity, the low-energy LUMO of the unsaturated system makes nitroalkenes excellent dienophiles and dipolarophiles in cycloaddition processes.[3] Taking advantage of their heterodienic nature, nitroalkenes can also participate in [4 + 2] cycloadditions, leading to cyclic nitronates, which, in turn, are reactive 1,3-dipoles that can be used in further cyclization processes.[4] Apart from the latter application, the products obtained in these transformations usually retain the nitro group, which can be further converted into a primary amino group[5] or a carbonyl group by the known Nef reaction (Scheme 1).[6] Synthetic processes involving nitroalkenes may follow a different pathway, entailing a tandem elimination of

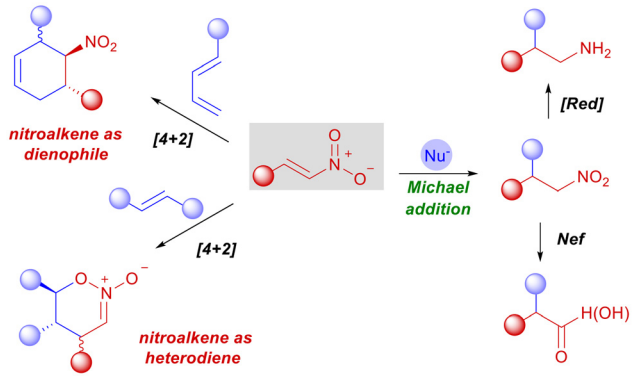
School of Science and Technology, Chemistry Division, University of Camerino, ChIP, Via Madonna delle Carceri, 62032 Camerino (MC), Italy.
E-mail: marino.petrini@unicam.it; Tel: (+39)-0737-402253

Alessandro Palmieri.

Alessandro Palmieri obtained his Laurea degree cum laude in Chemistry in 2002 from the University of Camerino (Italy), where, five years later, he received a PhD degree in Chemical Sciences. In 2008, he moved, as a visiting postdoctoral fellow, to the ITC laboratory at the University of Cambridge (Prof. Steven V. Ley). In 2014, he was appointed Associate Professor of Organic Chemistry at the University of Camerino. His research interests involve (i) the chemistry of aliphatic nitro compounds, (ii) the realization of new one-pot protocols for generating and derivatizing heterocyclic systems, (iii) the preparation of solid-supported reagents, (iv) the development of new sustainable processes and (v) flow chemistry protocols.

Marino Petrini.

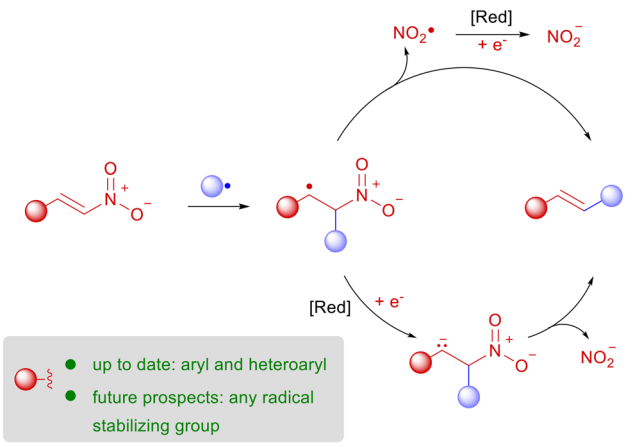
Marino Petrini obtained his Laurea degree in Chemistry in 1980 (University of Camerino, Italy). In 1983, he became a Research Associate at the University of Camerino, and during 1987–88, he was a visiting scientist at the University of Montreal (Prof. S. Hanessian). In 1992, he was appointed Associate Professor and later Full Professor of Organic Chemistry at the University of Camerino. His research interests mainly deal with the following topics: synthesis and reactivity of aliphatic and aromatic nitro compounds; functionalization of azole derivatives; synthesis and reactivity of imino derivatives.



Scheme 1 Classical reactivity of nitroalkenes in cycloadditions and conjugate additions.

the nitro group that restores the unsaturation, finally leading to a formal substitution reaction. This approach has been fruitfully exploited for the preparation of functionalized alkenyl derivatives, in which the nitro moiety has been, in turn, substituted with alkyl, aryl, and carbonyl groups as well as heteroatomic systems (Scheme 2). In most of these procedures, the regioselective addition of a radical to the nitroalkene affords a benzylic radical, which, by elimination of a nitro radical, gives the final unsaturated derivative.[7] The nitro radical may eventually be reduced under the reaction conditions, leading to a stable nitrite anion. Alternatively, reduction of the initially formed benzylic radical affords a stabilized carbanion, which, by elimination of a nitrite anion, leads to the target alkene.[8] It should be observed that all these methods generally lead to the formation of the more stable *E* diastereomer, unless peculiar stereoelectronic factors provide a different reaction outcome.

The described denitrative process on nitroalkenes has a close counterpart in the decarboxylative radical coupling reaction of cinnamic acids.[9] In a related way, the radical addition occurs at the alpha position of the carboxylate anion. The resulting radical intermediate can be oxidized to the parent carbocation, which, by loss of carbon dioxide, regenerates the double bond. Both of these strategies are really competing since take advantage by the easy availability of the corresponding substrates. In this context, it should be observed that the preparation of β-nitrostyrenes occurs under milder reaction conditions than that of cinnamic acids, which often entail high-temperature decarboxylative condensation procedures. The utilization of cinnamic acids and β-nitrostyrenes allows the corresponding coupling processes to be carried out exploiting recently devised electrochemical and photochemical procedures.[10] Homolytic cleavage of carbon–sulfur bonds has also been exploited in the radical-mediated desulfonylation of vinylic sulfones.[11] This approach has been mostly employed in the reaction of 1,2-bis(arylsulfonyl)ethenes with different carbon-centered radical sources, efficiently leading to various functionalized alkenylated products. However, the final elimination of a bulky arylsulfonyl group from the reactant notably lowers the atom economy of the corresponding process. This article highlights the most relevant and synthetically useful protocols for the preparation of linear alkenyl derivatives starting from β-nitrostyrenes, employing the general strategy depicted in Scheme 2. Particular emphasis has been given to the mechanistic aspects of the reported transformations, evidencing the nature and the selectivity of different radical species involved in these processes. A couple of excellent review articles on this topic, including other aspects of the denitrative cross-coupling of β-nitrostyrenes, are also available for the readers' benefit.[12] It should be observed that although currently limited to the utilization of β-nitrostyrenes, this synthetic approach could be formally extended to every nitroalkene bearing a radical stabilizing group at the beta position. The direct elimination of nitrite anions from the Michael adducts of nitroalkenes has been particularly exploited in several processes aimed at the synthesis of heterocyclic and carbocyclic derivatives. These procedures have been largely reviewed and will not be discussed in this article.[13]



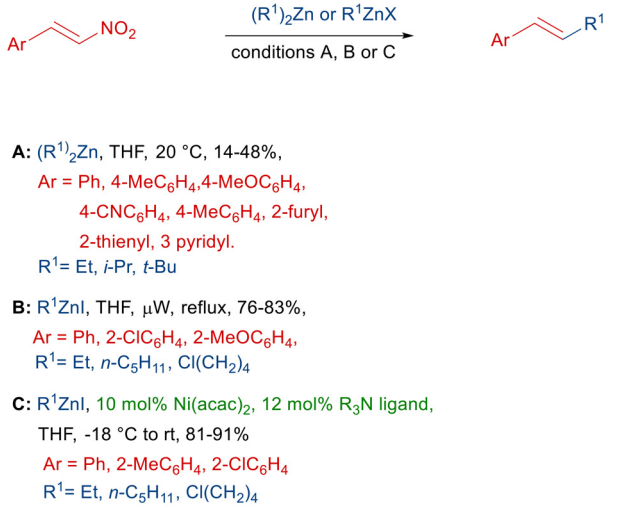
Scheme 2 Radical additions to nitroalkenes leading to functionalized alkenes.

2. Denitrative alkylation

The very first denitrative alkylation of nitroalkenes was disclosed by Russell and Yao more than thirty years ago, evaluating the photoinduced reaction of *t*-butylmercury chloride with β-nitrostyrene in the presence of potassium iodide.[14] The formation of the corresponding adduct (40% yield) was made possible by the *t*-butyl radical generated by decomposition of the anionic complex *t*-BuHgICl$^-$. This process is peculiar to the cited reagent couple and has not been further developed.

2.1 Reaction with organozinc reagents

The capability of dialkylzinc reagents in promoting the denitrative alkylation of nitroalkenes has been reported by Seebach,[15] and is probably associated with the hybrid radical/ionic character of these organometallic compounds (Scheme 3).[16] The original procedure (conditions A), using

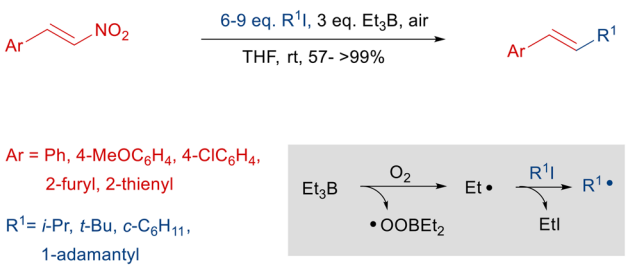


Scheme 3 Reaction of β-nitrostyrenes with organozinc reagents.

dialkylzinc, is not particularly effective, leading to the target alkenes in moderate yields. Better results are obtained by employing alkylzinc iodides under microwave activation (conditions B),[17] or by adding nickel(II) acetylacetonate in the presence of tertiary amines as ligands (conditions C).[18] The formation of alkenes has also been evidenced in the reaction of β-nitrostyrenes with trialkylgallium[19] and alkylmanganese reagents.[20] In the latter reaction, the process apparently does not involve an alkyl radical addition to the olefin, but rather a regioselective nucleophilic addition to the nitro group, followed by a 1,2 shift of the alkyl group at the alpha position. As a matter of fact, the alkene derivatives are always obtained together with notable amounts of β-alkylated nitro compounds arising from a regiocomplementary Michael addition to the β-nitrostyrene.

2.2 Reaction with boron and aluminum derivatives

The homolytic cleavage of carbon–boron bonds in trialkylboranes, mediated by atmospheric oxygen, has been suitably exploited for the synthesis of alkenes from β-nitrostyrenes under classical thermal conditions.[21] The ethyl radical transfer from triethylborane to alkyl iodides allows a more viable use of this strategy for the synthesis of alkenes (Scheme 4).[22] A large excess of alkyl iodides is required in order to suppress the competitive addition of the ethyl radical on the nitroalkene. Since β-nitrostyrenes can be conveniently obtained by a nitroaldol-elimination reaction, the nitroalkene and the subsequent denitrative alkylation with triethylborane and alkyl iodides can be combined in a one-pot process, directly leading to the alkenyl derivative.[23] Triethylaluminum is also effective in a similar process, which, however, requires the presence of a radical initiator such as benzoyl peroxide, as trialkylaluminums are more resistant to the homolytic cleavage by oxygen.[24]



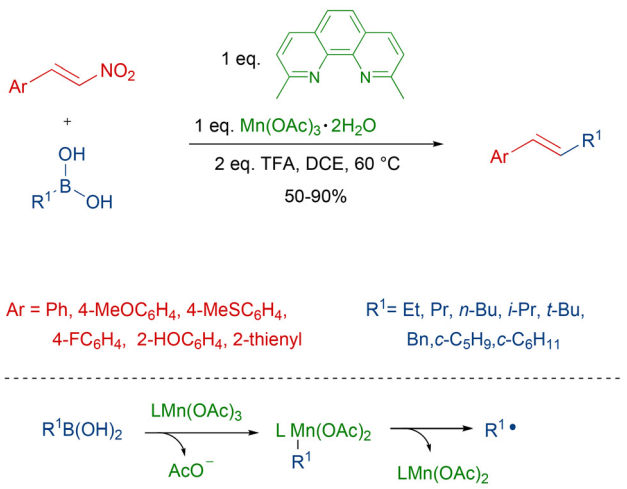
Scheme 4 Ethyl radical transfer in the generation of alkyl radicals.

Alkylboronic acids can generate alkyl radicals under oxidative conditions, providing a more atom-economical approach compared to trialkylboranes. Alkyl radical formation from boronic acids can be attained using manganese(III) acetate in the presence of a suitable phenanthroline ligand (Scheme 5).[25]

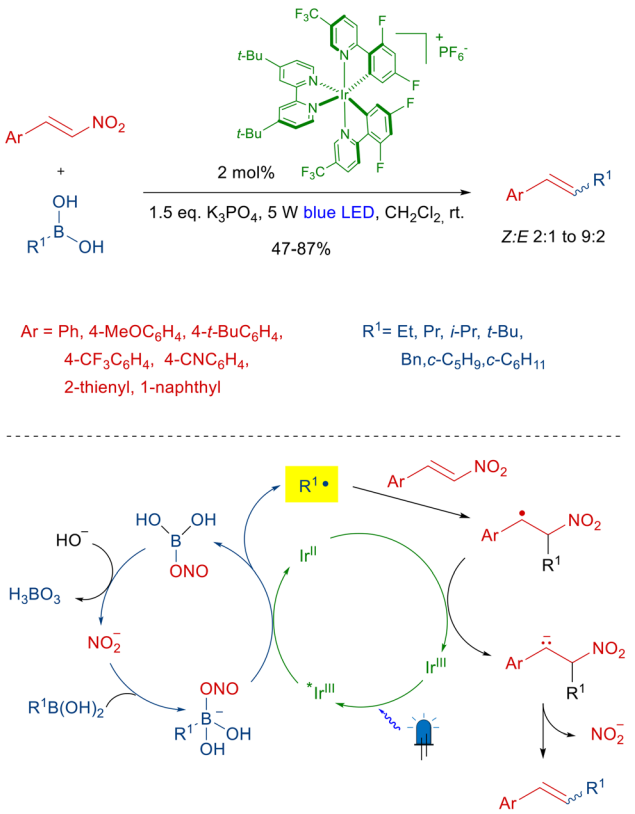
The alkyl transfer to the manganese complex is followed by reductive elimination, which generates a radical and a reduced manganese complex. The latter complex can be eventually re-oxidized under aerobic conditions. The transition metal usage can be minimized by exploiting a photocatalyzed process for the generation of the alkyl radical species from boronic acids (Scheme 6).[26] Upon irradiation with a blue LED in the presence of $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ as the catalyst, β-nitrostyrenes are converted into alkenes with a marked preference for the *Z* diastereomer. This transformation is the result of a couple of catalytic cycles in which the alkyl radical is generated by the reaction of the nitrated alkylboronic acid with the excited state of the catalyst formed upon visible light irradiation. In the final steps, the radical adduct with the nitroalkene is reduced by the Ir(II) species to the corresponding anion, which finally yields the alkene, releasing the nitrite anion.

2.3 Reaction with 4-alkyl-substituted Hantzsch esters

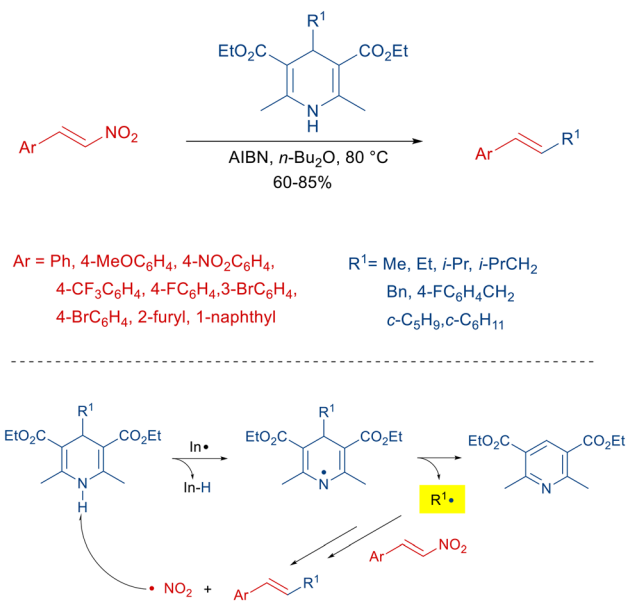
The homolytic cleavage of 4-alkyldihydropyrans (Hantzsch esters) is able to provide the needed alkyl radical for nitroalkene to alkene conversion (Scheme 7).[27] Hydrogen abstraction



Scheme 5 Generation of alkyl radicals by Mn(III)-induced decomposition of boronic acids.



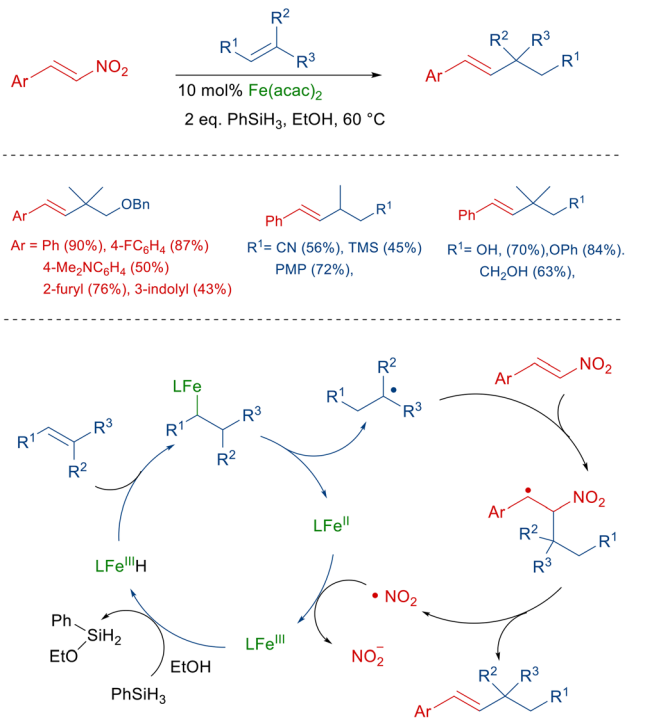
Scheme 6 Photocatalyzed reaction of boronic acids with β-nitrostyrenes.



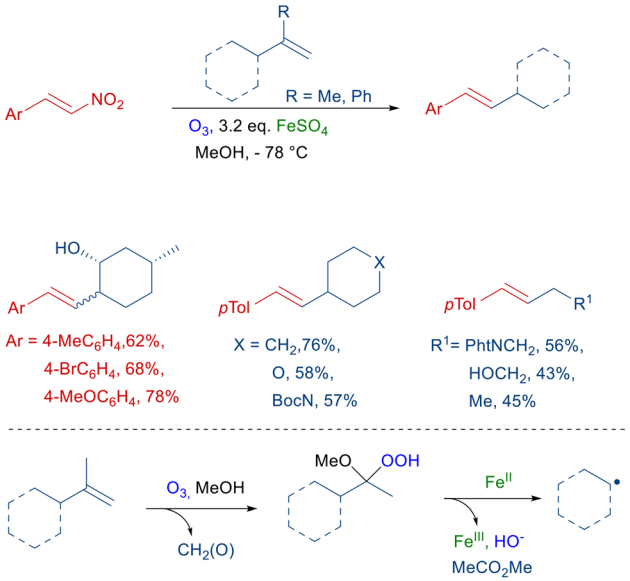
Scheme 7 Hantzsch esters as radical donors in the denitrative alkylation of β-nitrostyrenes.

from the Hantzsch ester by a radical initiator, generated by thermal decomposition of AIBN, leads to a stabilized dihydropyran radical, which, upon fragmentation, affords a substituted pyridine and the alkyl radical. The usual mechanism then yields the alkene and the nitro radical, which, upon reacting with the Hantzsch ester, ensures proper propagation of the chain reaction. In a related process, the reaction has been performed at room temperature using di-*tert*-butyl peroxide, which, upon irradiation with a xenon lamp, provided the initiator for the radical reaction.[28]

The generation of alkyl radicals can be easily achieved by hydrometallation/carbon–metal bond cleavage of alkenes under reductive conditions, as portrayed in Scheme 8.[29] Functionalized alkenes can be employed in the reaction with β-nitrostyrenes using $Fe(acac)_2$ as the catalyst in the presence of phenylsilane. The preliminarily oxidized form of the catalyst reacts with the silane, leading to an iron hydride species that promotes the hydrometallation of the alkene. The subsequent carbon–metal homolytic cleavage generates the alkyl radical that adds to the β-nitrostyrene following the usual pathway. The nitro radical ultimately released from the reaction finally oxidizes the iron(II) species formed after the carbon–metal cleavage, regenerating the active form of the catalyst. Later on, a similar procedure was devised using $Ni(acac)_2$ in the presence of triethoxysilane with satisfactory results.[30] Oxidative demolition of alkenes using ozone in the presence of iron(II) sulfate leads to the formation of alkyl radicals, which may add to β-nitrostyrenes following the usual general mechanism (Scheme 9).[31] A notable number of olefins can be used for this purpose, including terminal alkenes, which are prone to generate primary radicals. However, as expected, the latter unsaturated systems give rather modest results in this process. The



Scheme 8 Fe(II)-catalyzed reductive radical formation from alkenes in the presence of phenylsilane.

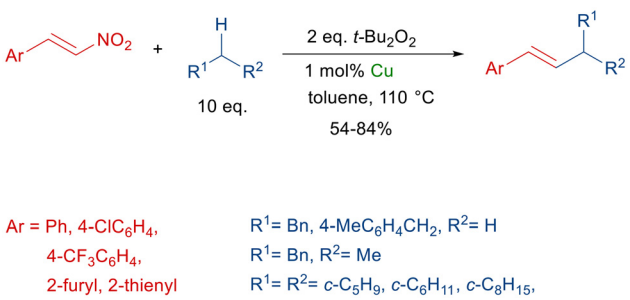


Scheme 9 Oxidative cleavage of alkenes with alkyl radical generation.

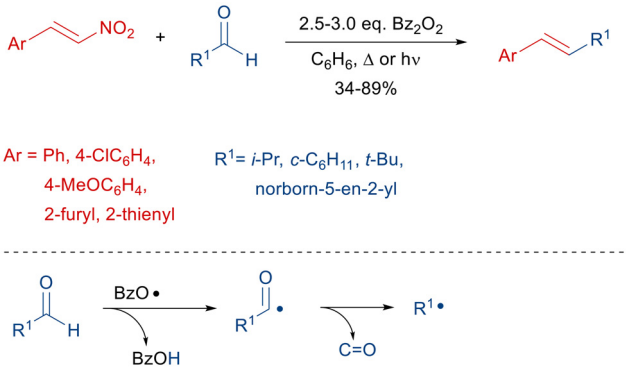
radical formation occurs by preliminary ozonization, leading to an intermediate hydroperoxide that is then reductively decomposed in the presence of the iron(II) salt.

2.4 Other alkyl radical sources

The easiest way to access alkyl radicals is the homolytic cleavage of carbon–hydrogen bonds in alkanes. This operation often requires the generation of somewhat stabilized secondary, tertiary or benzylic radicals in order to be successful. Copper-catalyzed decomposition of di-*t*-butyl peroxide may provide a steady concentration of the alkoxy radical, as in the example reported in Scheme 10.[32] Addition of different cycloalkanes (5- to 8-membered rings) to β-nitrostyrenes can also be performed using benzoyl peroxide without any added catalyst.[33] The reaction is carried out using the cycloalkane as solvent under reflux conditions. Abstraction of the formyl hydrogen atom by the benzoyloxy radical generates an acyl radical, which, upon decarbonylation, leads to the formation of an alkyl radical suitable for the reaction with β-nitrostyrenes (Scheme 11).[34] Only secondary or tertiary alkyl radicals are



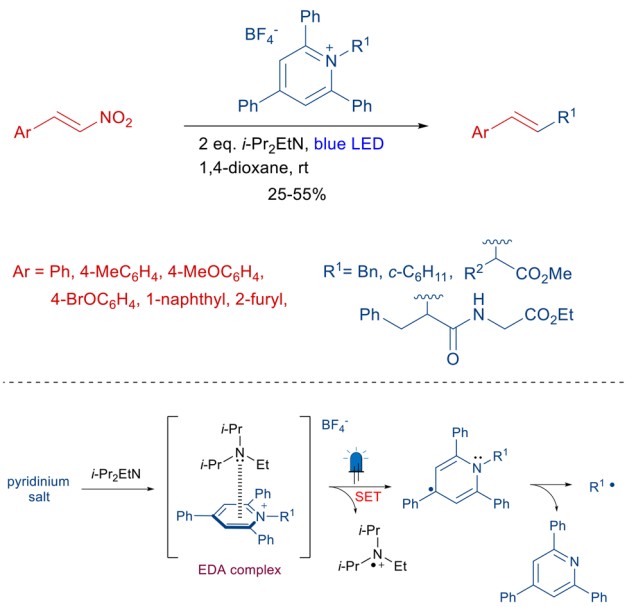
Scheme 10 Homolytic cleavage of C–H bonds in alkanes using *t*-butylperoxide.



Scheme 11 Decarbonylative generation of alkyl radicals from aldehydes.

accessible with this protocol, involving the use of benzoyl peroxide as the initial radical source, either by thermal or photochemical activation.

Homolytic cleavage of carbon–nitrogen bonds in *N*-alkylpyridinium salts can also be exploited for the generation of alkyl radicals (Scheme 12).[35] The whole transformation is based on the preliminary formation of an electron donor–acceptor (EDA) complex upon reaction of the pyridinium salt with diisopropylethyl amine. Upon irradiation with visible blue light, a SET reaction generates a nitrogen-centered radical cation and a dihydropyridyl radical, which fragments into an alkyl radical and the stable 2,4,6-triphenylpyridine. The radical cation is converted into an iminium ion in a later stage of the process by reaction with the nitro radical. Although the yields of the obtained alkenyl derivatives are generally rather moderate, the application of this method to the



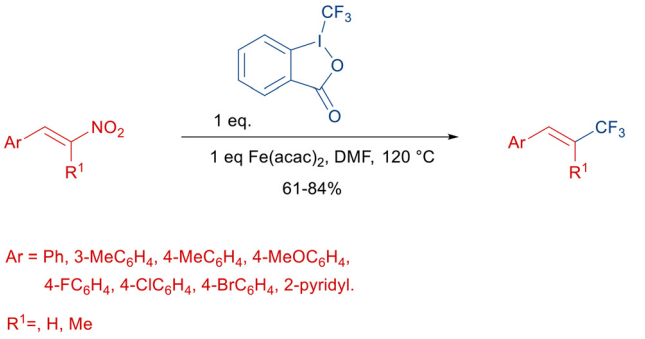
Scheme 12 Alkyl radicals obtained by decomposition of EDA complexes of *N*-alkylpyridinium salts.

introduction of highly functionalized alkyl groups is remarkable. A similar EDA complex can be formed upon interaction of diisopropylethylamine and *O*-pyridyloximes of cyclobutanone derivatives under related reaction conditions (Scheme 13).[36] The SET process enabled under blue LED irradiation generates a cyclic radical anion, which, upon oxygen–nitrogen cleavage, yields an iminyl radical.

Ring opening of the latter intermediate leads to a γ-cyanopropyl radical, which may react with β-nitrostyrenes leading to γ-unsaturated nitriles *via* the usual general mechanism. Heteroatoms as well as various substituents can be embedded in the cyclobutyl moiety, enabling the preparation of a wide array of functionalized nitrile derivatives. Alkylated 2,2′-biquinoline derivatives have also been employed as reagents for the formation of alkyl radicals under copper catalysis.[37] Reactions of alkyl radicals achieved under these reaction conditions afford the corresponding alkenes in very moderate yields (up to 47%), making this synthetic method hardly competitive over the existing ones.

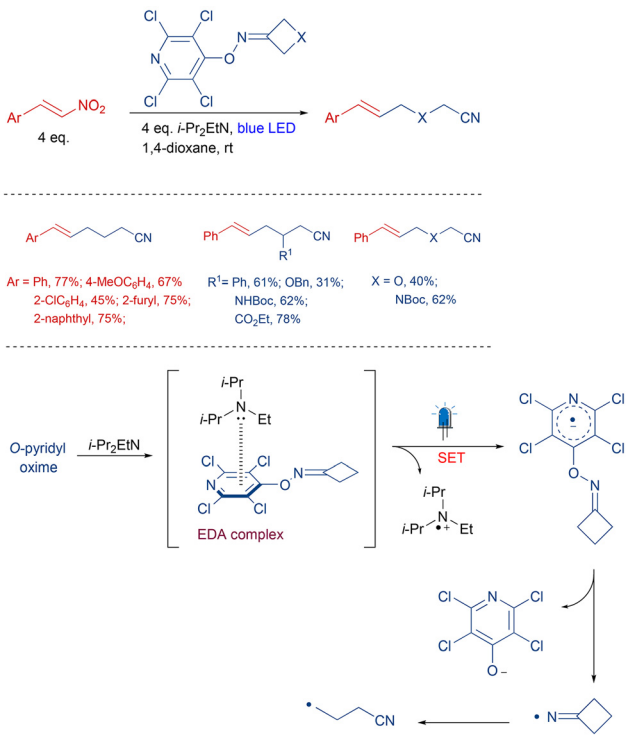
3. Denitrative trifluoromethylation

Various reagents embedding the trifluoromethyl group can be used to generate the corresponding radical amenable for reaction with nitroalkenes in denitrative reactions. 1-(Trifluoromethyl)-1λ^3,2-benziodoxol-3(1*H*)-one, also known as the Togni-II reagent, undergoes a thermal homolytic cleavage of the carbon–iodine bond, enabling the denitrative substitution in β-nitrostyrenes (Scheme 14).[38] In order to achieve an appropriate conversion, the nitroalkene must be activated by an iron(II) complex to facilitate the elimination of the nitro group.

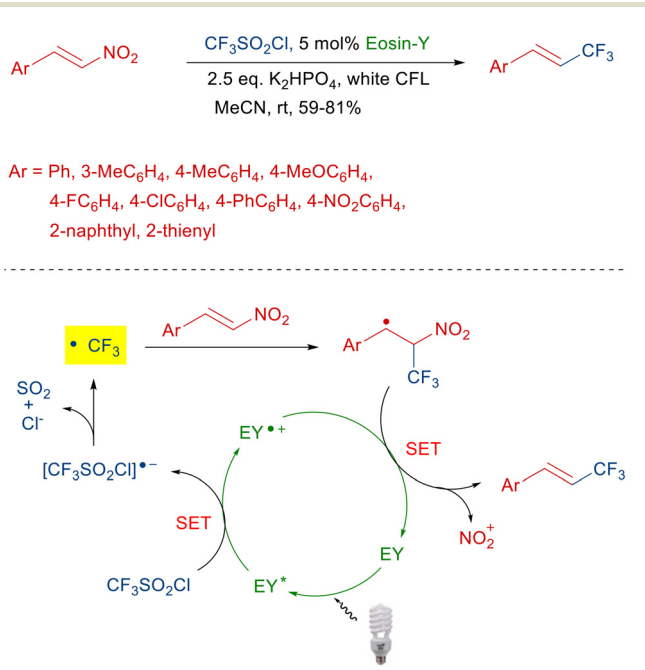


Scheme 14 Trifluoromethylation of β-nitrostyrenes using the Togni-II reagent.

An alternative photocatalyzed process for the same transformation employs trifluoromethanesulfonyl chloride and eosin-Y as a photoredox catalyst (Scheme 15).[39] The excited state of the catalyst is achieved by white CFL irradiation, and a subsequent SET process involving the trifluorosulfonyl chloride generates the corresponding fluorinated radical and the radical cation of the catalyst. The usual intermediate, obtained by radical addition to β-nitrostyrene, undergoes an oxidative SET reaction with the cationic form of the catalyst, leading to the alkene and a nitronium ion. As with many photoinduced protocols, this method occurs under milder reaction conditions and avoids transition metal usage. The introduction of



Scheme 13 Generation of γ-cyanopropyl radicals by photoinduced decomposition of a pyridyl radical anion.



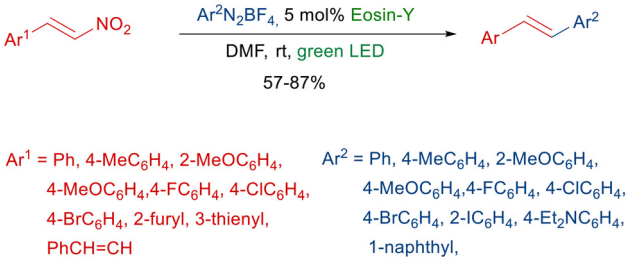
Scheme 15 Generation of trifluoromethyl radicals by photochemical decomposition of trifluoromethanesulfonyl chloride.

a trifluoromethyl group can be coupled with a further alkylative process by exploiting a three-component photoredox reaction involving β-nitrostyrenes, terminal alkenes and sodium trifluoromethanesulfinate (Scheme 16).[40] This reaction entails a chain elongation of the obtained alkenes, and a notable number of functionalized terminal alkenes can be used for this purpose.

9-Mesityl-10-methylacridinium perchlorate is employed as a catalyst, and the formation of the trifluoromethyl radical follows the usual activation by blue LED irradiation and the subsequent SET process. The selectivity in the radical cycle is based on the electrophilic nature of the trifluoromethyl radical, which reacts faster with the electron-rich terminal alkene rather than the electron-poor nitroalkene. The obtained adduct is nucleophilic in character and thus the reaction with the β-nitrostyrene is faster than the related process with the terminal alkene, which would result in polymerization.

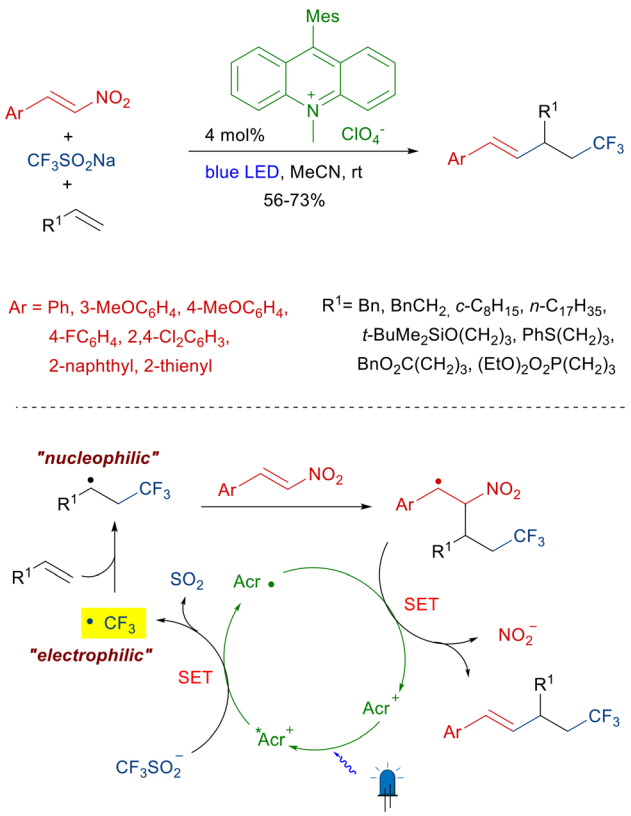
4. Denitrative arylation

Arylation and heteroarylation of β-nitrostyrenes afford stilbenes and related derivatives, belonging to an important class of naturally occurring compounds with relevant pharmacological profiles.[41] The generation of aryl radical species has been initially pursued by photoinduced decomposition of aryldiazonium salts (Scheme 17).[42] Apart from the different light source, the mechanistic course of this process follows that portrayed in Scheme 15 for trifluoromethylation reactions. Interestingly, this procedure can also be applied to 1-phenyl-4-nitrobutadiene, leading to the preparation of 1,4-diarylbutadienes.

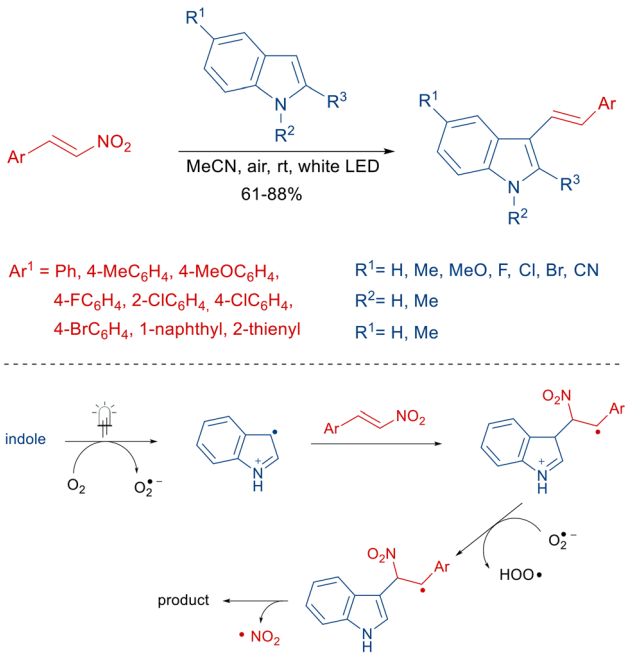


Scheme 17 Denitrative arylation of β-nitrostyrenes by photoinduced decomposition of aryldiazonium salts.

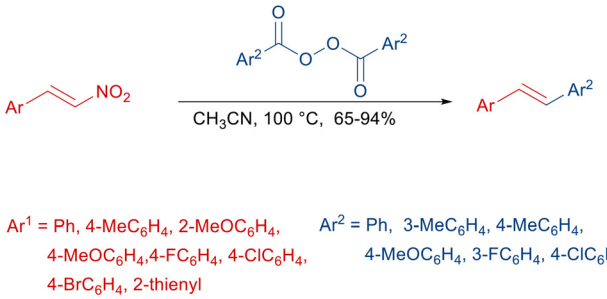
Recently, a related uncatalyzed protocol has been introduced for the photoinduced 3-indolation of β-nitrostyrenes under aerobic conditions (Scheme 18).[43] White LED irradiation of indoles in the presence of atmospheric oxygen forms a radical cation, which adds to β-nitrostyrenes in the usual manner. The aromaticity of the indole ring is restored upon deprotonation by the superoxide anion, and the resulting benzylic radical ultimately affords alkenylated indoles by loss of the nitro radical. The classical thermal decomposition of aroyl peroxides releases carbon dioxide and an aryl radical, which can participate in denitrative additions to β-nitrostyrenes (Scheme 19).[44] The process is quite efficient in terms of the chemical yields of the resulting stilbenes, but the



Scheme 16 Trifluoromethylative chain elongation in the denitrative radical coupling of β-nitrostyrenes.



Scheme 18 Coupling of β-nitrostyrenes with 3-indolyl radicals.



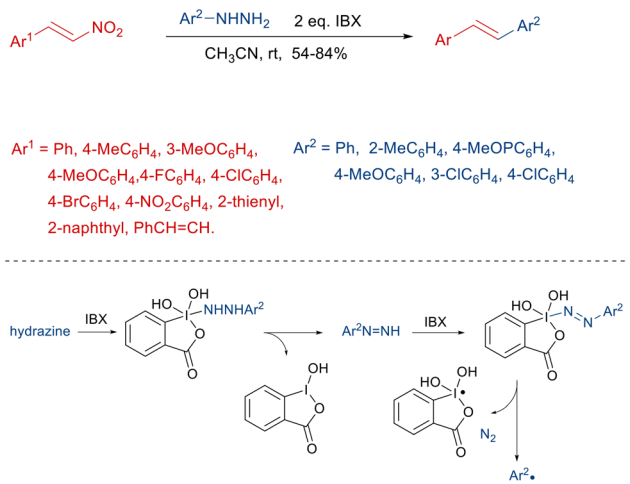
Scheme 19 Formation of aryl radicals by thermal decomposition of aroyl peroxides.

hazard in handling the peroxide reactants as well as their reduced availability strongly limits its practical application.

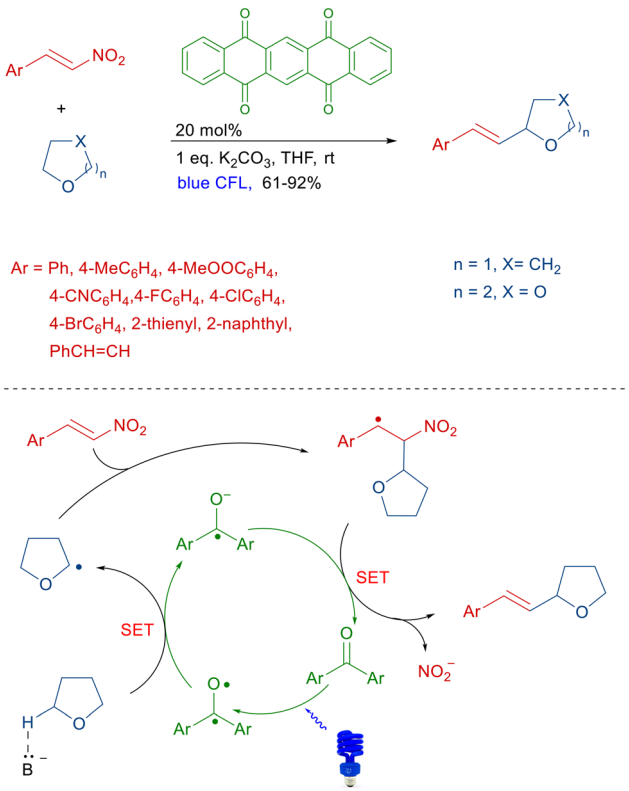
The mild oxidative homolytic cleavage of the carbon–nitrogen bond in arylhydrazines provides the basis for the denitrative synthesis of stilbenes from β-nitrostyrenes (Scheme 20).[45] The oxidant *O*-iodoxybenzoic acid (IBX) converts the arylhydrazine into an aryldiazine, which is further oxidized by a second molecule of IBX to the aryl radical and molecular nitrogen.

5. Denitrative alkoxyalkylation

Hydrogen abstraction at the α-position of ethers leads to the formation of α-alkoxy radicals, which can be fruitfully employed in denitrative additions to β-nitrostyrenes. Because of selectivity problems in the generation of the radical, efficient processes can be achieved only with cyclic or symmetric ethers (Scheme 21).[46] The photoredox process is catalyzed by 5,7,12,14-pentacenetetrone and occurs under blue CFL irradiation of the reaction mixture. The excited diradical state of the catalyst enables the formation of an α-alkoxy radical with the assistance of a base. After the usual addition



Scheme 20 Oxidative decomposition of arylhydrazines by IBX.



Scheme 21 Photoinduced denitrative alkoxyalkylation of β-nitrostyrenes by cyclic ethers.

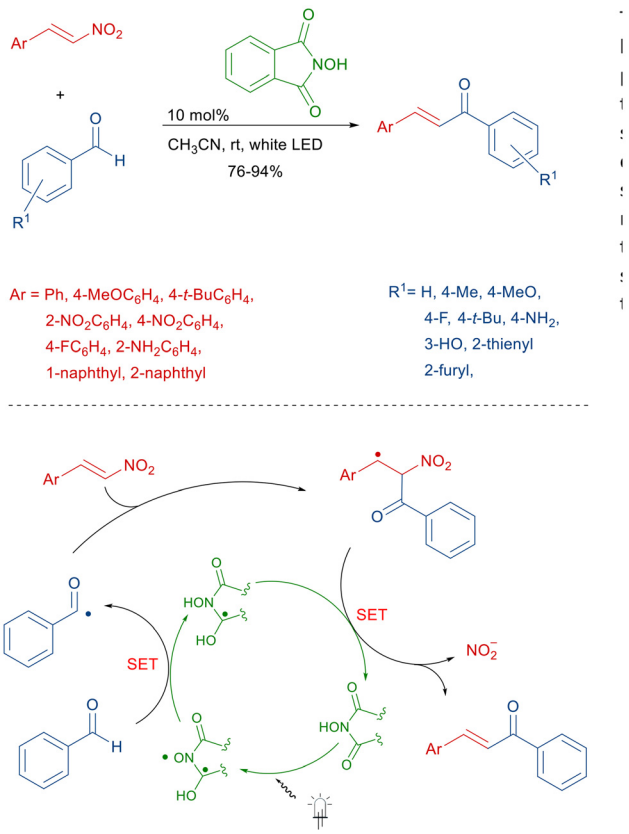
to the β-nitrostyrene, the formed benzyl radical is reduced by the radical anion of the catalyst with the formation of the final product and the nitrite anion.

α-Alkoxy radicals obtained by hydrogen abstraction from alkyl esters have also been employed in the reaction with β-nitrostyrenes.[47] This reaction is promoted by benzoyl peroxide but has a narrow field of application, being limited to ethyl esters of acetic, isobutyric and pivalic acids. Any other ester affords a mixture of products with poor regioselectivity.

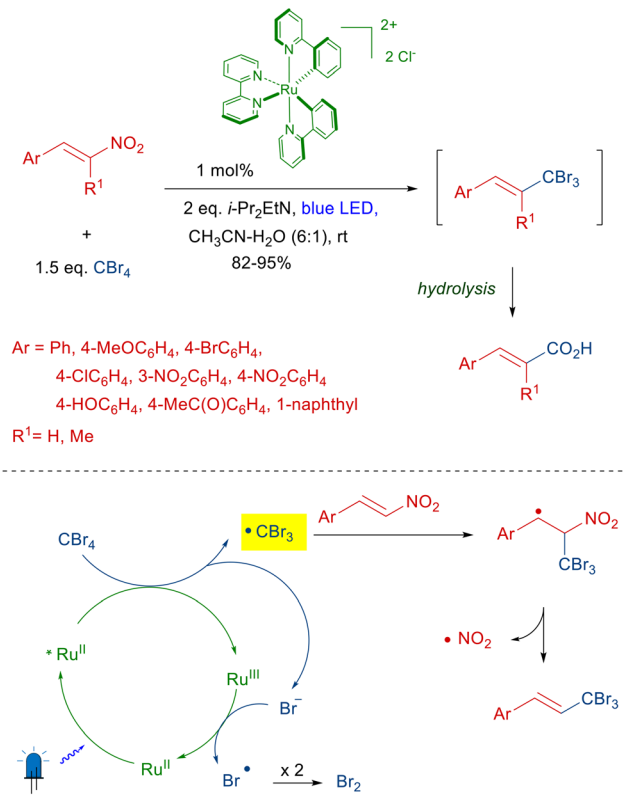
6. Denitrative acylation

In contrast to what is observed with alkanals (*cf.* Scheme 11), hydrogen abstraction from arylaldehydes, under photoredox conditions, leads to the formation of relatively stable acyl radicals, which can be employed in denitrative acylation of β-nitrostyrenes (Scheme 22).[48] Thus, upon white LED irradiation, *N*-hydroxyphthalimide generates a diradical, which promotes hydrogen abstraction in arylaldehydes. The nitro radical formed by the usual terminal fragmentation is finally reduced by the hydroxyalkyl radical, regenerating the catalytic system.

Functionalized cinnamic acids can be prepared by the reaction of β-nitrostyrenes with carbon tetrabromide under photoredox catalysis by $Ru(bpy)_3Cl_2$ (Scheme 23).[49] The excited state of the catalyst is obtained by blue LED irradiation and allows



Scheme 22 Denitrative acylation of β-nitrostyrenes with aldehydes under photochemical conditions.



Scheme 23 Synthesis of cinnamic acids by one-pot denitrative tribromomethylation-hydrolysis of β-nitrostyrenes.

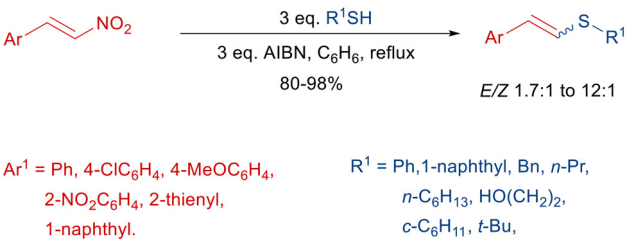
the carbon tetrabromide to be converted into a tribromomethyl radical and a bromide anion. The carbon-centered radical adds to the nitroalkene in the usual manner, leading to a β-tribromomethylstyrene, which is then hydrolyzed to the corresponding cinnamic acid. The oxidized ruthenium(III) catalyst is finally reduced by the bromide anion, yielding molecular bromine and regenerating the active catalytic species.

7. Denitrative thiolation and sulfonylation

Sulfur-centered radicals can be easily generated because of their inherent stability.[50] This enables the substitution of the nitro group in β-nitrostyrenes with sulfur-bearing reagents at various oxidation states.

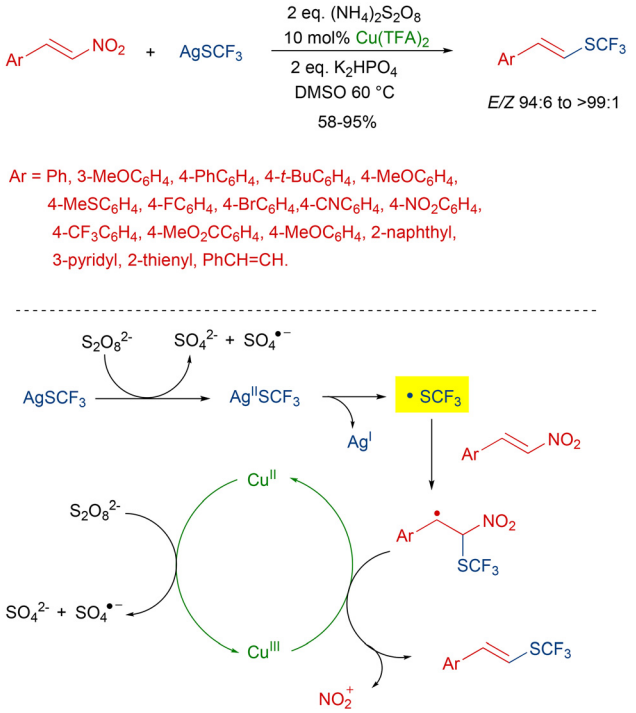
7.1 Denitrative thiolation

The classical conjugate addition of thiols to β-nitrostyrenes can be totally suppressed towards denitrative thiolation, provided that a radical initiator such as AIBN is introduced into the reaction mixture (Scheme 24).[51] The corresponding vinyl sulfides are obtained with different levels of diastereoselectivity according to their thermodynamic stability. This transformation is not a chain reaction and thus a notable amount of the radical initiator is required to maintain the concentration of the thiyl radical at a suitable level. It should be observed that under neat conditions at room temperature, the Michael addition is the predominant process.



Scheme 24 Synthesis of vinyl sulfides by denitrative thiolation of β-nitrostyrenes.

Different functional groups other than alkyl or aryl frameworks can be linked to the sulfur atom as in the trifluoromethylthiolation of nitroalkenes using silver(I) trifluoromethanethiolate (Scheme 25).[52] In this reaction, the trifluoromethylthiyl radical is generated by oxidation of the silver salt with ammonium persulfate. The copper(II)/copper(III) redox couple is used to ensure the oxidation of the nitrogen dioxide released at the late stage of the process and is fed by ammonium persulfate.



Scheme 25 Cu(II)-catalyzed trifluoromethylthiolation of β-nitrostyrenes.

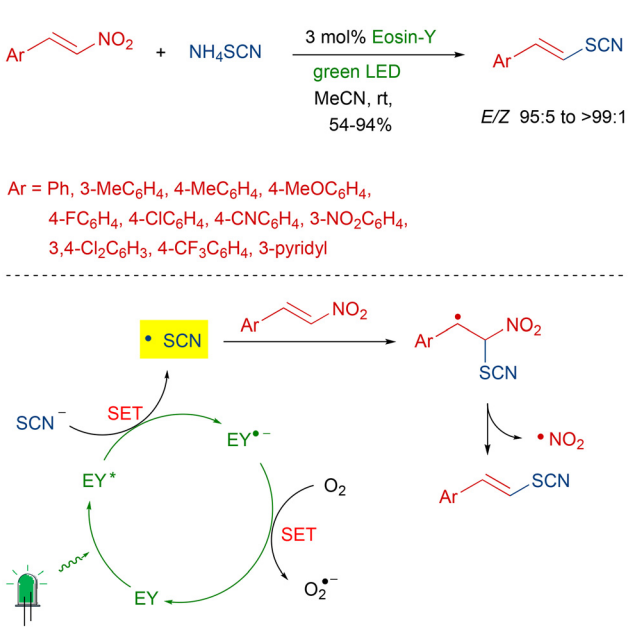
The thiocyanation of β-nitrostyrenes can be carried out under photoredox conditions using eosin-Y as a catalyst and ammonium thiocyanate as a reagent (Scheme 26).[53] The thiocyanate radical formation is ensured by the excited form of the catalyst through an oxidative SET process. The neutral eosin-Y is then restored by an oxidation of the corresponding radical anion, provided by atmospheric oxygen, whose presence has been proved to be mandatory to efficiently support the catalytic cycle. Elemental sulfur can be directly employed in the thiophosphonylation of β-nitrostyrenes exploiting a three-component coupling involving the utilization of dialkylphosphonates (Scheme 27).[54]

In a preliminary step, under basic conditions, the elemental sulfur converts the phosphonate into the *S*-thiophosphate, which is then oxidized by the excited form of the catalyst. The thiyl radical thus formed adds to the β-nitrostyrene and, by a subsequent fragmentation, yields the final product and nitrogen dioxide, which is reduced in the catalytic cycle to the nitrite anion.

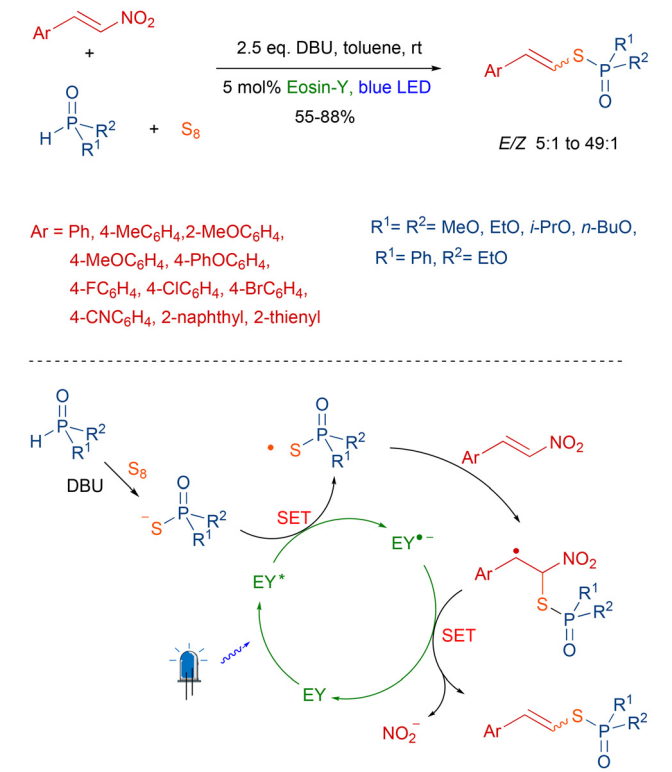
7.2 Denitrative arylsulfonylation

The denitrative arylsulfonylation of β-nitrosyrenes enables a rapid entry to functionalized vinyl sulfones, which are central motifs in drug discovery and organic synthesis.[55] Sulfonyl radicals can be generated from arylsulfinate salts by oxidation with potassium persulfate in the presence of silver(I) nitrate at room temperature and under an inert atmosphere (Scheme 28, route a).[56] The same protocol can be adapted for the arylsulfonylation of the same substrates using arylthiols as reactants under aerobic conditions, provided that a higher temperature is applied (Scheme 28, route b).[57] In the latter process, the initially formed vinyl sulfides are further oxidized by oxygen in a silver-catalyzed reaction.

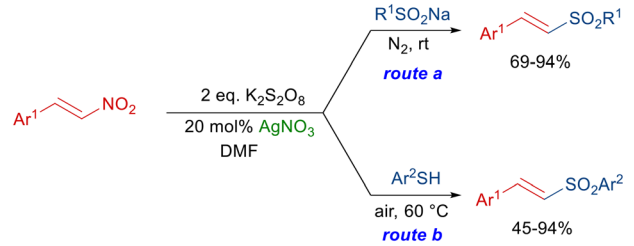
Similarly, the manganese(III)/manganese(II) redox couple can be used for the generation of sulfonyl radicals in the reac-



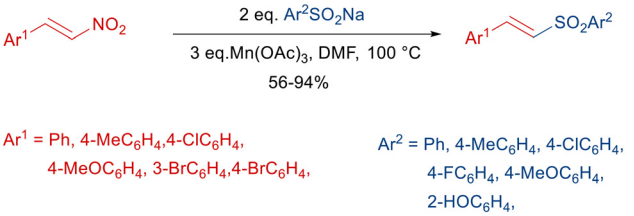
Scheme 26 Photoredox thiocyanation catalyzed by eosin-Y.



Scheme 27 Denitrative thiophosphonylation of β-nitrostyrenes.



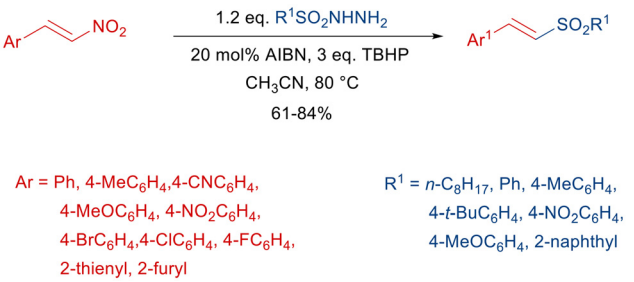
Scheme 28 Convergent synthesis of vinyl sulfones by oxidative coupling of sodium aryl(alkyl)sulfinates or arylthiols to β-nitrostyrenes.



Scheme 29 Mn(III)-promoted synthesis of vinyl sulfones.

tion with β-nitrostyrenes (Scheme 29).[58] A large excess of the oxidizing agent is required for an efficient reaction, which is limited to the introduction of arylsulfonyl groups.

Oxidative decomposition of alkyl- and arylsulfonylhydrazines can generate the corresponding sulfonyl radicals amenable to use in the reaction with β-nitrostyrenes (Scheme 30).[59] The formation of vinyl sulfones occurs in the presence of *tert*-butylperoxide (TBHP) with a catalytic amount of azobisisobutyronitrile (AIBN) as a radical initiator. The proposed mechanism shows some inconsistencies since the generation of the sulfonyl radical is exclusively attributed to the interaction between the hydrazine and the cyanoisopropyl radical formed by decomposition of AIBN. This is obviously hardly possible



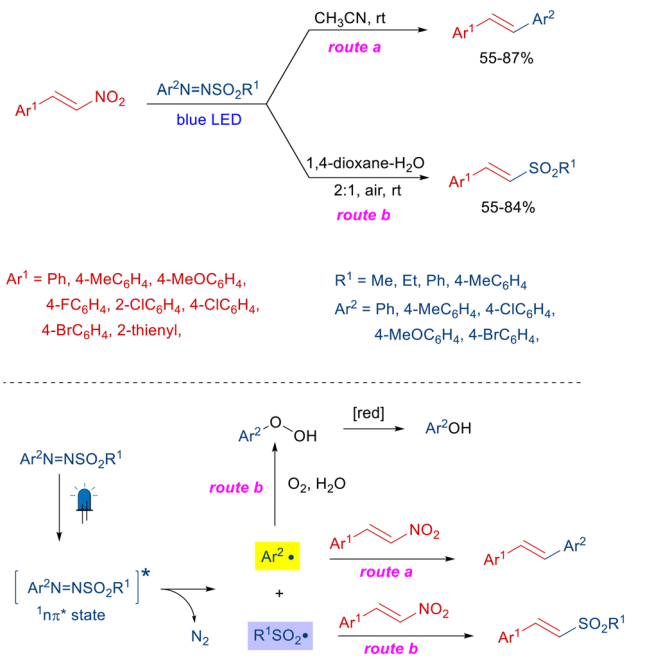
Scheme 30 Synthesis of vinyl sulfones from sulfonyl hydrazines.

considering that AIBN is used in just 20 mol%. Furthermore, the role played by TBHP in this process is not adequately outlined. In a related paper, a catalytic amount of iodine is used for the same purpose with TBHP as the excess oxidizing agent.[60] The photoinduced reaction of arylazosulfones with β-nitrostyrenes represents an interesting example of a chemodivergent process that can be directed toward the synthesis of stilbenes or vinyl sulfones depending on the reaction conditions (Scheme 31).[61]

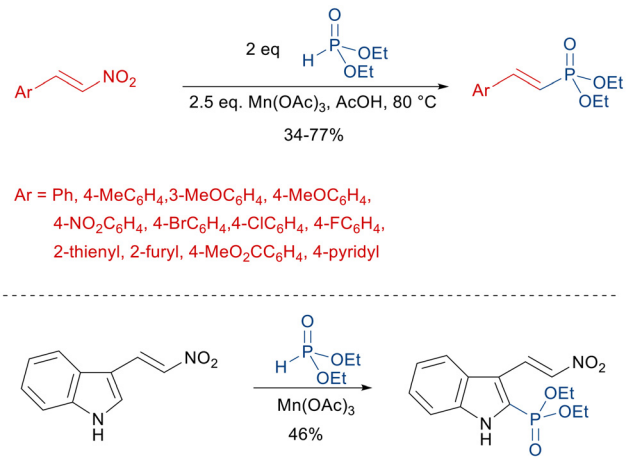
Upon irradiation with a blue LED, arylazosulfones are excited to the $^1n\pi^*$-state and after decomposition, an aryl and a sulfonyl radical are formed. Under anhydrous conditions, the reaction of the aryl radical is very fast, enabling the preferential formation of stilbene products (route a). However, under moist aerobic conditions, scavenging of the aryl radical is effective, leaving the sulfonyl radical free to react with the β-nitrostyrene, ultimately yielding the vinyl sulfone (route b).

8. Denitrative phosphonylation

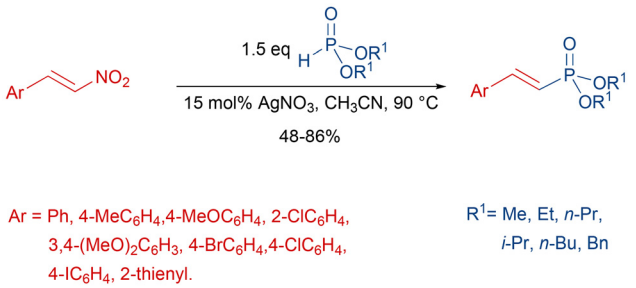
Some metal salts that have been proved effective in generating carbon- and sulfur-centered radicals can be used for the denitrative phosphonylation of β-nitrostyrenes using dialkyl phosphites, as in the case of manganese(III) acetate portrayed in Scheme 32.[62] An interesting behavior has been observed in the reaction of β-nitrovinylindole with diethylphosphonate, which affords the 2-phosphonylated β-nitrovinylindole arising from the vinylogous conjugate addition of the phosphonyl radical, albeit in moderate yield. In a related process, silver(I) nitrate is able to catalyze the same reaction with superior results over



Scheme 31 Chemodivergent synthesis of stilbenes and vinyl sulfones from arylazosulfones.



Scheme 32 Mn(III)-promoted reaction of diethylphosphonate with β-nitrostyrenes.



Scheme 33 Synthesis of vinyl phosphonates by Ag(I)-catalyzed coupling of dialkyl phosphonates with β-nitrostyrenes.

the use of manganese(III) acetate (Scheme 33).[63] The Ag(I)/Ag(0) redox couple is operative in the formation of the phosphonyl radical species.

9. Conclusion and outlook

Addition reactions on conjugated nitroalkenes can lead to regiocomplementary products depending on the electronic nature of the added reactants. Nucleophilic reagents mostly undergo 1,4-additions, driven by the enhanced electrophilic character of the β-carbon, ultimately leading to functionalized nitroalkanes. Conversely, radical-centered species preferentially add to the α-carbon of nitroalkenes, generating a second radical that can further evolve into denitrated alkenes through two distinct routes. In the first one, the carbon–nitrogen bond undergoes homolytic cleavage and releases a nitro radical, which can be further reduced or oxidized according to the reaction conditions. Alternatively, a reduction of the radical adduct affords a carbanion, which, upon β-elimination of a nitrite anion, leads to the target alkene. In both pathways, the formation of a stabilized radical adduct is mandatory for a successful process, and thus this transformation is particularly effective for β-nitrostyrenes, which, upon radical addition, afford benzylic radicals and the corresponding anions upon monoelectronic reduction. Synthetic protocols for these denitrative reactions enable the introduction of simple and functionalized alkyl, aryl, and acyl frameworks. Similarly, sulfur- and phosphorus-centered radicals can also be added to β-nitrostyrenes, leading to heterovinyl derivatives. Modern techniques for radical generation, including photocatalyzed processes, are employed for these denitrative reactions. Currently, the level of functionalization of the employed nitroalkenes is limited to β-nitrostyrenes, also including the presence of heteroaryl groups. The same limitation is evidenced in a related process carried out on cinnamic acids, which are strong competitors of β-nitrostyrenes in the preparation of alkenylbenzene derivatives by decarboxylative radical-induced coupling. Future efforts would be directed towards the utilization of β-disubstituted nitroalkenes, nitrocycloalkenes or nitroolefins bearing radical-stabilizing groups other than aryls at the beta position. These foreseeable advancements would notably increase the impact of this strategy in the target-oriented synthesis of unsaturated compounds of practical interest.

Author contributions

A. P. and M. P. wrote the manuscript. M. P. supervised the writing.

Conflicts of interest

There are no conflicts to declare.

Data availability

No primary research results, software or code have been included and no new data were generated or analysed as part of this article.

Acknowledgements

We gratefully acknowledge the financial support from the University of Camerino. The research network CINMPIS-Bari is also gratefully acknowledged.

References

1 (*a*) V. V. Perekalin, E. S. Lipina, V. M. Berestovitskaya and D. A. Efremov, *Nitroalkenes: Conjugated Nitro Compounds*, Wiley, Chichester, 1994; (*b*) N. Ono, *The Nitro Group in Organic Synthesis*, Wiley-VCH, New York, 2001.
2 (*a*) S. Paladhi, J. H. Park, B. Jana, H. Y. Bae and C. E. Song, *Adv. Synth. Catal.*, 2023, **365**, 2789–2817; (*b*) I. N. N. Namboothiri, M. Bhati, M. Ganesh,

B. Hosamani, T. V. Baiju, S. Manchery and K. Bera, *Catalytic Asymmetric Reactions of Conjugated Nitroalkenes*, CRC Press, Boca Raton, 2020; (*c*) D. A. Alonso, A. Baeza, R. Chinchilla, C. Gómez, G. Guillena, I. M. Pastor and D. J. Ramón, *Molecules*, 2017, **22**, 895.

3 M. Chaudhary, S. Shaik, M. Magan, S. Hudda, M. Gupta, G. Singh and P. Wadhwa, *Curr. Org. Synth.*, 2025, **22**, 2–22.

4 (*a*) R. Y. Baiazitov and S. E. Denmark, in *Methods and Applications of Cycloaddition Reactions in Organic Syntheses*, ed. N. Nishiwaki, Wiley, 2014, Ch. 16, pp. 471–550; (*b*) S. E. Denmark and J. J. Cottell, in *The Chemistry of Heterocyclic Compounds: Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry Toward Heterocycles and Natural Products*, ed. A. Padwa and W. H. Pearson, Wiley-Interscience, New York, 2002, pp. 83–167; (*c*) S. E. Denmark and A. Thorarensen, *Chem. Rev.*, 1996, **96**, 137–165.

5 R. Ballini, E. Marcantoni and M. Petrini, Nitroalkenes as Amination Tools, in *Amino Group Chemistry*, ed. A. Ricci, Wiley-VCH, Weinheim, 2008, Ch. 3, pp. 93–148.

6 (*a*) R. Ballini and M. Petrini, *Adv. Synth. Catal.*, 2015, **357**, 2371–2402; (*b*) R. Ballini and M. Petrini, *Tetrahedron*, 2004, **60**, 1017–1047.

7 Homolytic cleavage of the C–N bond in nitroalkane derivatives represents the basis for radical-induced denitrations; for a recent review, see: D. Valachová, M. Marčeková, O. Caletková, A. Kolarovič and P. Jakubec, *Eur. J. Org. Chem.*, 2023, **26**, e202201341.

8 R. Ballini and A. Palmieri, *Adv. Synth. Catal.*, 2019, **361**, 5070–5097.

9 For some recent examples, see: (*a*) X.-J. Shang, R. Chu, R. Luo, Y. Zhang and Z.-Q. Liu, *Synlett*, 2025, **36**, 1013–1016; (*b*) E. Zhou, H. Xu, K. Zheng, J. Jin, J. Qiao and C. Shen, *Catal. Commun.*, 2024, **187**, 106886; (*c*) F. Fei and X. Yang, *Tetrahedron*, 2023, **130**, 133169; (*d*) X.-Y. Lu, M.-Y. Ge, T.-H. Tao, X.-M. Sun, M.-T. Gao, S.-T. Bao, Q.-L. Liu, Z.-J. Xia and J. Xia, *Org. Chem. Front.*, 2022, **9**, 831–837.

10 (*a*) X. Wang, Y. Wu, S. Xu, H. Qu and C. Chen, *Eur. J. Org. Chem.*, 2025, **28**, e202401144; (*b*) S.-M. Yang, T.-J. He, D.-Z. Lin and J.-M. Huang, *J. Org. Chem.*, 2019, **84**, 1958–1962.

11 X.-Q. Chu, D. Ge, Y.-Y. Cui, Z.-L. Shen and C.-J. Li, *Chem. Rev.*, 2021, **121**, 12548–12680.

12 (*a*) S. T. Sivanandan, M. J. Jesline, D. K. Nair and T. Kumar, *Asian J. Org. Chem.*, 2023, **12**, e202200555; (*b*) M. Marčeková, B. Ferko, K. R. Detková and P. Jakubec, *Molecules*, 2020, **25**, 3390.

13 (*a*) D. Zou, W. Wang, Y. Hua and T. Jia, *Org. Biomol. Chem.*, 2023, **21**, 2254–2271; (*b*) C. Li, K. Yin, X. Zhou, F. Zhang and Z. Shen, *Tetrahedron Lett.*, 2023, **149**, 133717; (*c*) A. Z. Halimehjani, I. N. N. Namboothiri and S. E. Hooshmand, *RSC Adv.*, 2014, **4**, 48022–48084; (*d*) A. Z. Halimehjani, I. N. N. Namboothiri and S. E. Hooshmand, *RSC Adv.*, 2014, **4**, 51794–51829; (*e*) A. Z. Halimehjani, I. N. N. Namboothiri and S. E. Hooshmand, *RSC Adv.*, 2014, **4**, 31261–31299.

14 G. A. Russell and C.-F. Yao, *Heteroat. Chem.*, 1992, **3**, 209–218.

15 D. Seebach, H. Schäfer, B. Schmidt and M. Schreiber, *Angew. Chem., Int. Ed. Engl.*, 1992, **31**, 1587–1588.

16 T. Akindele, K.-I. Yamada and K. Tomioka, *Acc. Chem. Res.*, 2009, **42**, 345–355.

17 Y. Hu, J. Yu, S. Yang, J.-X. Wang and Y. Yin, *Synth. Commun.*, 1999, **29**, 1157–1164.

18 Y. Hu, J. Yu, S. Yang, J.-X. Wang and Y. Yin, *Synlett*, 1998, 1213–1214.

19 Y. Han, Y.-Z. Huang and C.-M. Zhou, *Tetrahedron Lett.*, 1996, **37**, 3347–3350.

20 I. N. N. Namboothiri and A. Hassner, *J. Organomet. Chem.*, 1996, **518**, 69–77.

21 C.-F. Yao, C.-M. Chu and J.-T. Liu, *J. Org. Chem.*, 1998, **63**, 719–722.

22 J.-T. Liu, Y.-J. Jang, Y.-K. Shih, S.-R. Hu, C.-M. Chu and C.-F. Yao, *J. Org. Chem.*, 2001, **66**, 6021–6028.

23 J.-T. Liu and C.-F. Yao, *Tetrahedron Lett.*, 2001, **42**, 6147–6150.

24 J.-Y. Liu, J.-T. Liu and C.-F. Yao, *Tetrahedron Lett.*, 2001, **42**, 3613–3615.

25 Z. Yu, J. Hu, Y. Yu, Y. Yuan and S. Guo, *Synlett*, 2023, **34**, 1597–1602.

26 M. Xu, C. Zhao, Y. Huang, S. Hu, D. Cheng and X. Xu, *Asian J. Org. Chem.*, 2024, **13**, e202300544.

27 G. Li, L. Wu, G. Lv, H. Liu, Q. Fu, X. Zhang and Z. Tang, *Chem. Commun.*, 2014, **50**, 6246–6248.

28 S. Zhang, Y. Li, J. Wang, X. Hao, K. Jin, R. Zhang and C. Duan, *Tetrahedron Lett.*, 2020, **61**, 151721.

29 J. Zheng, D. Wang and S. Cui, *Org. Lett.*, 2015, **17**, 4572–4575.

30 N. Zhang, Z.-J. Quan and X.-C. Wang, *Adv. Synth. Catal.*, 2016, **358**, 3179–3183.

31 M. Swain, G. Sadykhov, R. Wang and O. Kwon, *Angew. Chem., Int. Ed.*, 2020, **59**, 17565–17571.

32 S. Guo, Y. Yuan and J. Xiang, *New J. Chem.*, 2015, **39**, 3093–3097.

33 Y.-J. Jang, Y.-K. Shih, J.-Y. Liu, W.-Y. Kuo and C.-F. Yao, *Chem. – Eur. J.*, 2003, **9**, 2123–2128.

34 Y.-J. Jang, M.-C. Yan, Y.-F. Lin and C.-F. Yao, *J. Org. Chem.*, 2004, **69**, 3961–3963.

35 B. Ferko, M. Marčeková, K. R. Detková, J. Doháňošová, D. Berkeš and P. Jakubec, *Org. Lett.*, 2021, **23**, 8705–8710.

36 J. Gao, Z.-P. Ye, Y.-F. Liu, X.-C. He, J.-P. Guan, F. Liu, K. Chen, H.-Y. Xiang, X.-Q. Chen and H. Yang, *Org. Lett.*, 2022, **24**, 4640–4644.

37 S. Ratnam, S. Unone and D. Janssen-Müller, *Chem. – Eur. J.*, 2023, **29**, e202301685.

38 J. Ma, W. Yi, G. Lu and C. Cai, *Adv. Synth. Catal.*, 2015, **357**, 3447–3452.

39 S. P. Midya, J. Rana, T. Abraham, B. Aswin and E. Balaraman, *Chem. Commun.*, 2017, **53**, 6760–6763.

40 A. D. Kulthe, P. S. Mainkar and S. M. Akondi, *Chem. Commun.*, 2021, **57**, 5582–5585.

41 T. Teka, L. Zhang, X. Ge, Y. Li, L. Han and X. Yan, *Phytochemistry*, 2022, **197**, 113128.

42 N. Zhang, Z.-J. Quan, Z. Zhang, Y.-X. Da and X.-C. Wang, *Chem. Commun.*, 2016, **52**, 14234–14237.
43 R. Chawla, R. Kapoor and L. D. S. Yadav, *Synlett*, 2020, **31**, 1394–1399.
44 A. K. Yadav and K. N. Singh, *New J. Chem.*, 2017, **41**, 14914–14917.
45 G. Wagh, S. Autade, P. C. Patil and K. G. Akamanchi, *New J. Chem.*, 2018, **42**, 3301–3309.
46 M. Zhang, L. Yang, H. Yang, G. An and G. Li, *ChemCatChem*, 2019, **11**, 1606–1609.
47 M.-C. Yan, Y.-J. Jang, J. Wu, Y.-F. Lin and C.-F. Yao, *Tetrahedron Lett.*, 2004, **45**, 3685–3687.
48 S. Tripathi, R. Kapoor and L. D. S. Yadav, *Adv. Synth. Catal.*, 2018, **360**, 1407–1413.
49 S. Tripathi and L. D. S. Yadav, *New J. Chem.*, 2018, **42**, 3765–3769.
50 (*a*) C. Russo, F. Brunelli, G. C. Tron and M. Giustiniano, *Eur. J. Org. Chem.*, 2023, **26**, e202300743; (*b*) Z. Zhang, X. Wang, P. Sivaguru and Z. Wang, *Org. Chem. Front.*, 2022, **9**, 6063–6076; (*c*) W. Guo, K. Tao, W. Tan, M. Zhao, L. Zheng and X. Fan, *Org. Chem. Front.*, 2019, **6**, 2048–2066; (*d*) M. P. Bertrand and C. Ferreri, Sulfur-Centered Radicals, in *Radicals in Organic Synthesis*, ed. P. Renaud and M. P. Sibi, Wiley-VCH, 2001, Ch. 5.5, pp. 485–504.
51 C.-M. Chu, Z. Tu, P. Wu, C.-C. Wang, J.-T. Liu, C.-W. Kuo, Y.-H. Shin and C.-F. Yao, *Tetrahedron*, 2009, **65**, 3878–3885.
52 C. Zheng, S. Huang, Y. Liu, C. Jiang, W. Zhang, G. Fang and J. Hong, *Org. Lett.*, 2020, **22**, 4868–4872.
53 R. Kapoor, R. Chawl and L. D. S. Yadav, *Tetrahedron Lett.*, 2020, **61**, 152505.
54 X.-Y. Huang, Y. Zhu, Z.-C. Ding, H.-T. Tang, Y.-M. Pan, W.-G. Duan and F.-H. Cui, *Adv. Synth. Catal.*, 2024, **366**, 5015–5019.
55 (*a*) J. Tong, J. Shu, Y. Wang, Y. Qi and Y. Wang, *Life Sci.*, 2024, **352**, 122904; (*b*) R. Ahmadi and S. Emami, *Eur. J. Med. Chem.*, 2022, **234**, 114255; (*c*) Y. Fang, Z. Luo and X. Xu, *RSC Adv.*, 2016, **6**, 56661–59676.
56 T. Keshari, R. Kapoorr and L. D. S. Yadav, *Eur. J. Org. Chem.*, 2016, 2695–2699.
57 K. Zhou, X. Wang, C. Wang and Y. Chen, *Tetrahedron Lett.*, 2025, **155**, 155425.
58 G. Nie, X. Deng, X. Lei, Q. Hu and Y. Chen, *RSC Adv.*, 2016, **6**, 75277–75281.
59 S. Kumar, R. Singh and K. N. Singh, *Asian J. Org. Chem.*, 2018, **7**, 359–362.
60 B. Aegurla and R. K. Peddinti, *Asian J. Org. Chem.*, 2018, **7**, 946–954.
61 R. Chawla, S. Jaiswal, P. K. Dutta and L. D. S. Yadav, *Org. Biomol. Chem.*, 2021, **19**, 6487–6492.
62 J.-F. Xue, S.-F. Zhou, Y.-Y. Liu, X. Pan, J.-P. Zou and O. T. Asekun, *Org. Biomol. Chem.*, 2015, **13**, 4896–4902.
63 J.-W. Yuan, L.-R. Yang, P. Mao and L.-B. Qu, *RSC Adv.*, 2016, **6**, 87058–87065.