Organic & Biomolecular Chemistry

Accepted Manuscript

ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/obc

REVIEW www.rsc.org/xxxxxx | XXXXXXXX

Recent Advances in the Synthesis of Nitroolefin Compounds

Guobing Yan*, Arun Jyoti Borah and Lianggui Wang

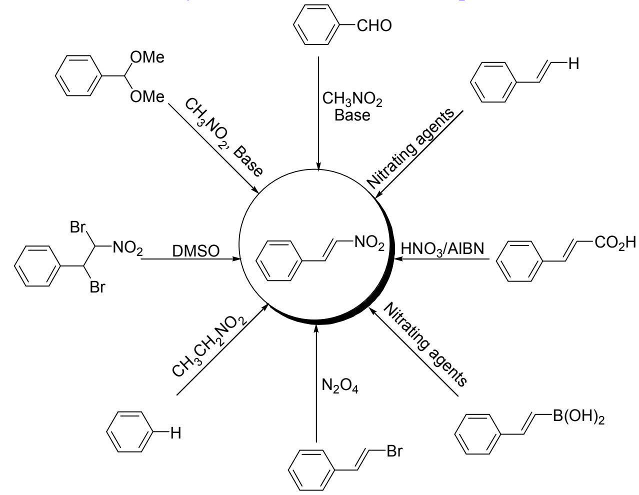
DOI: 10.1039/b000000x [DO NOT ALTER/DELETE THIS TEXT]

Development of methodology for the preparation of nitroolefins is of significant interest to organic chemists. Recently, numerous useful methods have been developed, mainly including direct nitration of olefinic C-H bonds, nitro-decarboxylation of aromatic α,β-unsaturated carboxylic acids, *ipso*-nitration of vinylboronic acids and multidehydrogenative cross-coupling reaction of (hetero)arenes with nitroethane. This review will focus on the recent achievements of nitroolefin synthesis and their mechanisms are also discussed.

1 Introduction

Nitroolefins are versatile intermediates in synthetic organic chemistry as well as in the chemical industry.[1] They are widely used in different constructions of carbon-carbon bond, such as Michael reaction,[2] Diels-Alder cycloaddition,[3] and Morita-Baylis-Hillman reaction.[4] In addition, the nitro group can be easily converted into other useful functional groups.[1,5] They found wide applications in materials, pharmaceuticals, agrochemicals and so on.[6] Hence, development of efficient methods for their preparation is a very important subject. The classical method namely the Henry reaction, relies upon base-mediated condensation of carbonyl compounds with nitroalkanes and followed by subsequent dehydration.[7] Alternatively, simple approach is based on the direct nitration of olefins C-H bonds with different nitrating agents, such as metal nitrates, nitric acid, nitric oxide and nitrogen dioxide.[8] However, these reactions suffer from some issues like use of harsh reaction conditions, imperfect functional group tolerance and formation of undesired *E/Z* mixtures. Although significant progress has been made in the area of direct nitration of olefins, however there is a great need for new methods that can overcome such problems (Scheme 1).

Recently, numerous useful methods have been developed for the synthesis of nitroolefins, such as direct nitration of olefinic C-H bonds, nitro-decarboxylation of aromatic α,β-unsaturated carboxylic acids, *ipso*-nitration of vinylboronic acids, and so on. In this review, we will focus on recent advances in the synthesis of nitroolefins as well as discussion of their mechanisms. Therefore, we sincerely hope that this review will serve as a handy reference for chemists interested in organic nitro chemistry and discovering novel nitration methods for the synthesis of nitroolefin compounds.



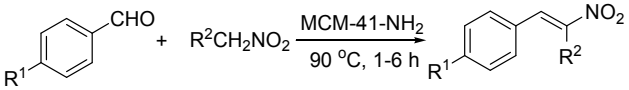
Scheme 1 Recent protocols for the synthesis of nitroolefins.

2 Condensation reactions of aldehydes and their derivatives with nitroalkanes

The most common two-step synthesis of nitroolefins is the Henry reaction, which is a classic aldol-type reaction between carbonyl compounds and nitroalkanes followed by an elimination reaction with removal of water when an acidic α-proton is available.[7] The typical step of carbon-carbon bond formation proceeds smoothly under mild basic conditions, while dehydration step requires harsh conditions, which strongly influence the overall yield. In spite of some drawbacks, this reaction is still widely used in industry as

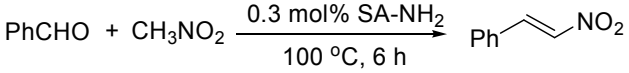
well as in academia. In recent years, homogeneous or heterogeneous catalytic systems have been developed to improve this reaction, even in combination with modern synthetic techniques such as microwave, ultrasound, ionic liquids, solid phase synthesis, and so on. Therefore, the latest useful approaches will be introduced in this section.

In 2001, Sartori and co-workers reported the use of propylamine supported on MCM-41 silica as a reusable catalyst in the nitro-aldol condensation between aldehydes and nitroalkanes to provide *E*-nitroolefins (Scheme 2).[9] The supported catalyst not only exhibits high efficiency, but also can be easily removed from the reaction mixture by filtration and successively performed for five catalytic cycles under the same reaction conditions. In this reaction, the supported primary aminopropyl moiety first reacts with the aldehyde to form an imine compound. The addition of nitromethane to the imine gives the unstable supported β-nitroamine compound, in which β-scission takes place to afford nitroolefin as the final product.



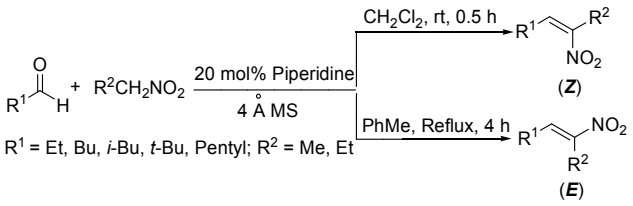
Scheme 2 MCM-41-NH_2-promoted nitro-aldol reaction of aldehydes and nitroalkanes.

In 2007, Iwasawa and co-workers developed a novel silica-alumina-supported organic amines (SA-NR_2) as catalyst, which enables coexistence of strong acid and base at the neighboring position of the solid surface without acid-base interaction. The SA-supported aminopropyl functional group (SA-NH_2) catalyst exhibits high catalytic activity for nitro-aldol reaction of benzaldehyde and nitromethane (Scheme 3).[10] After completion of the reaction, the SA-NH_2 catalyst can be easily separated from the reaction mixture and reused with retention of high catalytic activity and selectivity. After that, the same group reported the immobilization of organic primary amines in acidic montmorillonite interlayers (H-mont-NH_2), which was found to be active for a tandem deacetalization-nitro-aldol reaction of benzaldehyde dimethyl acetal with nitromethane, affording nitrostyrene.[11]



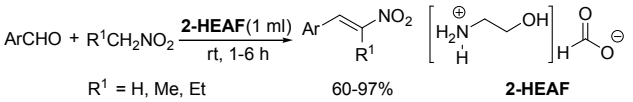
Scheme 3 SA-NH_2-catalyzed nitro-aldol reaction of aldehyde and nitromethane.

In 2008, Fioravanti and co-workers reported piperidine-catalyzed condensation reaction of aliphatic aldehydes with nitroalkanes in the presence of 4Å molecular sieves (Scheme 4).[12] The stereoselectivity of this reaction can be controlled simply by changing reaction conditions, such as solvent and temperature, to obtain pure *E*- and *Z*-nitroolefins in high to excellent yields. Except for piperidine, the role of molecular sieves is crucial for the stereochemical control, especially for the synthesis of the *Z*-nitroolefins.



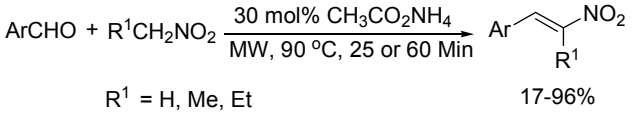
Scheme 4 Piperidine-catalyzed the condensation reaction of aliphatic aldehydes with nitroalkanes.

Alizadeh and co-workers reported the first utilization of ionic liquid, 2-hydroxyethylammonium formate (2-HEAF) as a recyclable promoter and medium for green and highly efficient synthesis of β-nitroolefins at room temperature (Scheme 5).[13] This ionic liquid bearing hydroxy group, ammonium acidic moiety and formate anion showed a special feature, which has ambiphilic dual activation role in the reaction. This reaction exhibits broader range of substrate scope and excellent functional group tolerance. In addition, the reaction is free from the use of hazardous organic solvent and toxic catalyst. Furthermore, the ionic liquid can be recovered and recycled for subsequent reactions.



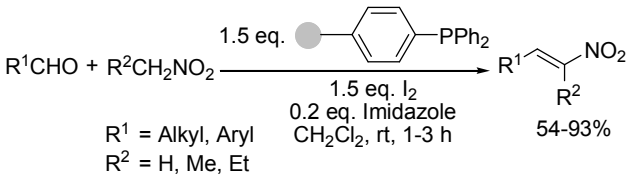
Scheme 5 2-HEAF-promoted condensation reaction of aldehydes with nitroalkanes.

Pujol and co-workers reported a novel one-pot synthesis of nitroolefins using ammonium acetate as a catalyst and microwave irradiation or ultrasound as the energy source (Scheme 6).[14] Compared to the traditional heating conditions, the time required for this reaction was much shorter and side products formation were not observed, such as the dimers of nitrostyrenes or dinitro compounds. In addition, the better yields of the reaction can be obtained under microwave conditions, particularly for heterocyclic aldehydes. Later on, Dharmaraj and co-workers reported the utility of nickel hydroxyapatite nanocomposite (Ni-HAp) as green catalyst in a solvent free microwave-assisted nitro-aldol reaction.[15]



Scheme 6 Microwave-promoted condensation reaction of aldehydes with nitroalkanes.

In 2013, Bez and co-workers developed the first solid phase synthesis of nitroolefins from aldehydes (Scheme 7).[16] The use of resin-bound triphenylphosphine can simplify the purification process, because triphenylphosphine oxide as byproduct can be easily removed from the reaction mixture by simple filtration. In addition, this protocol has several advantages over conventional dehydrating reagents used in solution chemistry, such as improved yield, mild reaction conditions, no inert atmosphere and two-step one-pot strategy. Both aliphatic and aromatic aldehydes are suitable under this transformation.

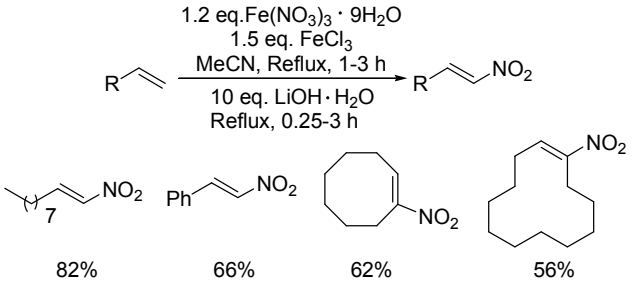


Scheme 7 Solid phase method for the synthesis of nitroolefins.

3 Nitration of olefins C-H bonds

The direct nitration of olefinic C-H bond is apparently more attractive. It is quite challenging to achieve this transformation, due to highly sensitive nature of the vinylic side chain. In the past several decades, much efforts have been made to develop the nitrating agents for the nitration of olefins, such as MNO_3(M=Na, K)-H_3PO_4,[17] $NaNO_2$-$HgCl_2$,[18] $AgNO_2$/PhSeBr/$HgC1_2$,[19] $AgNO_2/I_2$,[20] NO_2X-Et_3N,[21] HNO_3-H_2SO_4,[22] $RONO_2$,[23] $C(NO_2)_4$,[24] $CeNH_4(NO_3)_4$,[25] N_2O_4,[26] NO_2,[27] NO[28] and so on. In spite of much progress in this area, still there are some drawbacks like poor stereoselectivity, and imperfect functional group tolerance as well as general safety concerns. More recently, numerous new methods have been developed for the nitration of olefins. In this section, the most recent useful applications will be introduced.

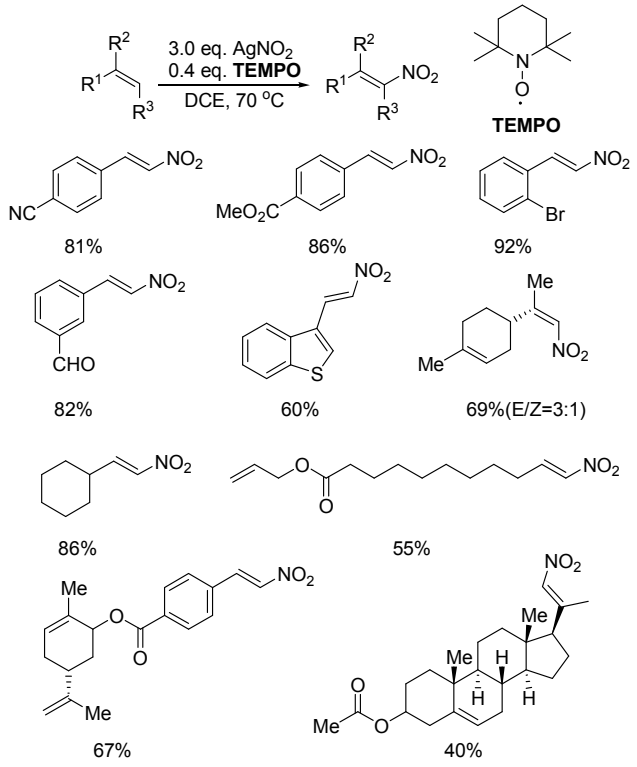
It is well-known that nitro radical can be *in situ* generated from the thermal decomposition of metal nitrates, which has been applied in the synthesis of nitro compounds.[29] In 2010, Taniguchi and co-workers developed an iron-mediated nitration reaction of alkenes to give halo-nitro compounds. This reaction undergoes the radical addition of nitrogen dioxide, which is *in situ* generated by thermal decomposition of iron(III) nitrate, and subsequent trapping of the resultant radical by a halogen atom in the presence of halogen salt. Application of this methodology for the synthesis of nitroolefins has been achieved through dehydrohalogenation with $LiOH{\cdot}H_2O$ (Scheme 8).[30] Aliphatic alkenes, cycloalkenes and styrene are all compatible with this transformation. The use of nontoxic, inexpensive, accessible iron reagents as the catalyst and the simple, safe experimental procedure increases the synthetic and commercial utility of this method.



Scheme 8 Iron-mediated direct nitration reaction of alkenes.

In 2013, Maiti and co-workers developed an efficient and highly regio- and stereoselective nitration of olefins using silver nitrite ($AgNO_2$) in combination with 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO).[31] This new approach represents an exceedingly practical and safe method for the synthesis of nitroolefins. Not only a wide range of functional groups can be tolerated, but also a wide array of aromatic, aliphatic, and heteroaromatic olefins can be carried out successfully for the direct nitration (Scheme 9). It was found that the electronic and steric effects of the substituents had little or no effect on the yields of the reaction. In addition, this protocol is applicable to the gram-scale synthesis of β-nitrostyrene with excellent yield under the optimized condition. More importantly, all these reactions can exclusively afford *E*-nitro products.

Interestingly, the site selectivity of olefin nitration is sensitive to the steric and electronic environment. For a substrate with multiple olefins, selective nitration took place at the terminal olefin in the presence of cyclic internal olefin or internal olefin. In addition, for a substrate with two terminal olefins embedded in different electronic environments, nitration occurred exclusively at the olefin existing in the close vicinity of a electron-rich group. This methodology can be also applied to the nitration of complex natural products. Nitration can be exclusively achieved at styrene by covalently attaching substituted aliphatic olefins in an electronically unbiased natural product skeleton. Disubstituted terminal olefin was selectively nitrated in the presence of cyclic internal olefin. Although stereogenic centers were involved in these cases, nitration took place with retention of stereochemistry. These results indicated that this new method can be applied in synthesis of large pharmacological molecules. On the basis of electronic and steric environment of the olefin, the site of nitration can be predicted in the multiple olefins. The order of reactivity of olefins can be concluded in Figure 1.



Scheme 9 Nitration of olefins with $AgNO_2$/TEMPO.

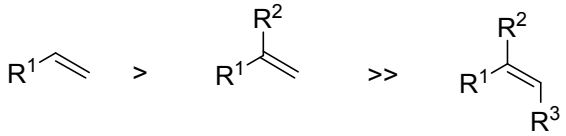


Figure 1 The order of reactivity of olefins.

A plausible mechanism for nitration of olefin was proposed by the author (Figure 2). Nitro radical can be *in situ* generated from $AgNO_2$ under the reaction conditions. The addition of nitro radical into the carbon-carbon double bond of olefin results in the formation of a carbon-centered radical **A** at the

more substituted (or benzylic) position that determines the regioselectivity of the reaction in terms of stability of the radical. Next, nitroolefin can be formed through two paths. In one hand, TEMPOH is generated upon abstraction of H-atom from intermediate **A**. And then TEMPOH can be oxidized to TEMPO by excess $AgNO_2$. Thus, $AgNO_2$ may play a dual role in the reaction, as source of nitro radical and stoichiometric oxidant. On the other hand, TEMPO may intercept the carbon-centered radical to form a TEMPO-alkane-NO_2 intermediate **B**, which can afford stereoselective nitroolefin *via anti*-elimination.

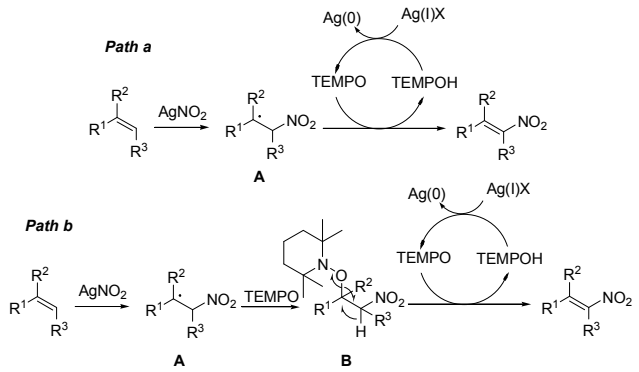
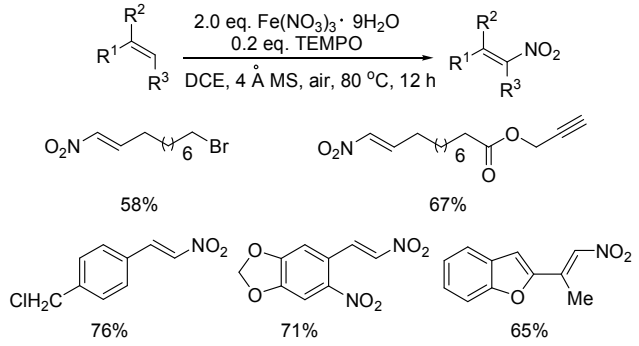


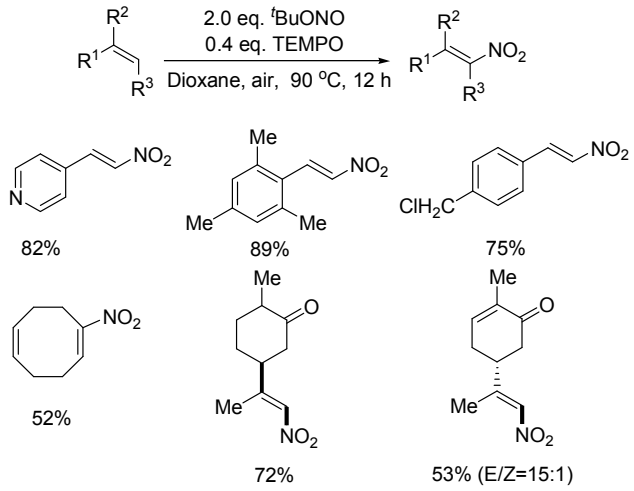
Figure 2 Possible mechanism.

In order to avoid using the expensive silver nitrite, the same group used cheap and easily available ferric nitrate as nitrating agent (Scheme 10).[32] A broader range of substrates such as aliphatic, aromatic, heteroaromatic olefins can undergo this reaction in excellent yields. This protocol exhibits an excellent *E*-selectivity in all the observed cases. Aditionally, this reaction can tolerate the chloromethyl group of 1-(chloromethyl)-4-(2-nitrovinyl)benzene, which failed to produce the desired nitro compound with $AgNO_2$, because it can be easily oxidized to the corresponding aldehyde under the previous condition.



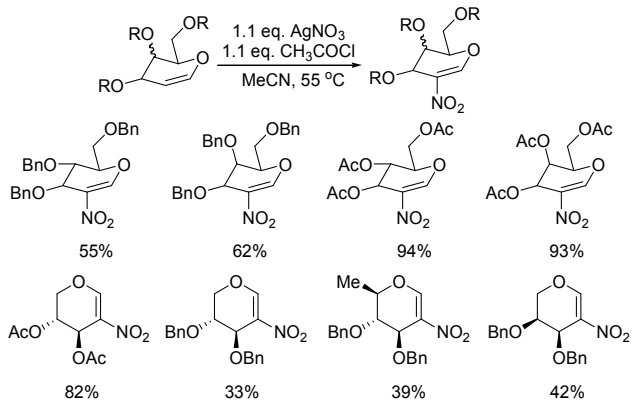
Scheme 10 Nitration of olefins with $Fe(NO_3)_3$/TEMPO.

From the point of view of organic synthesis, the development of efficient nitration of olefins under metal-free conditions is highly desirable, due to its close association with the pharmaceutical industry. The same group reported the metal-free stereoselective nitration of olefins using *tert*-butyl nitrite (^{t}BuONO) and TEMPO (Scheme 11).[33] Within the realm of nitrating agents, nitric oxide has been envisaged as a metal-free alternative for nitration of olefin, because it can generate a nitro radical in the presence of air. The thermal decomposition of *tert*-butyl nitrite can readily lead to the formation of nitric oxide under the heating conditions. A broader range of olefins with diverse functionalities has been nitrated in high yields. The procedure is operationally simple and relatively safe. In addition, site selective nitration in a complex molecule makes this method advantageous.



Scheme 11 Nitration of olefins with ^{t}BuONO/TEMPO.

In 2011, Vankar and co-worker developed a new reagent system for the synthesis of 2-nitroglycals from the corresponding glycals (Scheme 12).[34] This reagent system includes acetyl chloride, silver nitrate and acetonitrile which can introduce the nitro group. The interaction of acetyl chloride and silver nitrate in the reaction system can firstly produce a new source of acetyl nitrate, which behaves as an excellent source of nitronium ion **A**. Subsequently, the electrophilic addition of olefin with nitronium ion can take place to give carbocation intermediate **B**, followed by deprotonation to afford the nitroolefin product (Figure 3). Although Application of this methodology for the nitration of simple olefins has been achieved, but poor regio- and stereoselectivities has been observed in all the cases.



Scheme 12 Nitration of glycals with $AgNO_3$/AcCl.

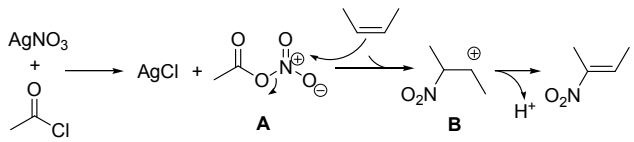
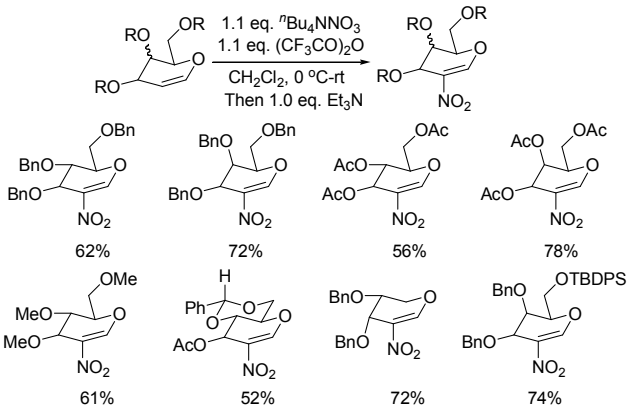


Figure 3 Possible mechanism.

In order to avoid the formation of nitroacetamide byproducts *via* acetonitrile attack at the carbocation, the same group developed another reagent system for the synthesis of 2-nitroglycals from various protected glycals (Scheme 13).[35] They used tetrabutylammonium nitrate (TBAN) replacing silver nitrate which is only soluble in acetonitrile. This new

system tetrabutylammonium nitrate (TBAN)- trifluoroacetic anhydride (TFAA)- triethylamine (TEA) gives exclusively 2-nitroglycal products with good yields. It is worth noting that some non-carbohydrate olefins can be successfully converted to the corresponding nitroolefins with high stereoselectivity and in good yields by using this new method. They proposed a plausible mechanism for this transformation (Figure 4). The nitronium trifluoroacetate species **B** can be *in situ* generated from tetrabutylammonium nitrate (TBAN)-trifluoroacetic anhydride (TFAA), which reacts with an olefin to form nitro trifluoroacetate **D** *via* a carbocation **C**. Subsequent elimination of the trifluoroacetate moieties under the base condition provides the nitroolefin as single product.



Scheme 13 Nitration of glycals with ^{n}Bu$_4$NNO$_3$/(CF$_3$CO)$_2$O.

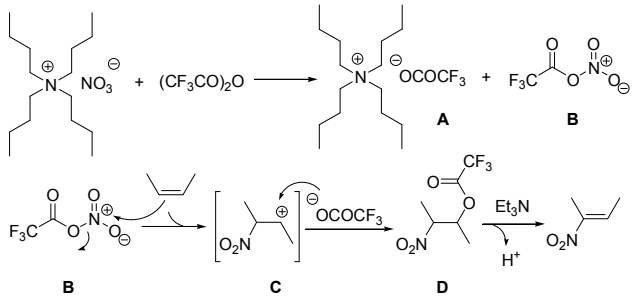
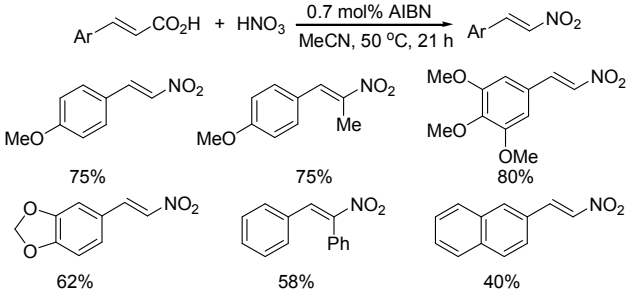


Figure 4 Possible mechanism.

4 Nitration of α,β-unsaturated carboxylic acids

Carboxylic acids are commercially available with a large structural variation. They are easy to store, simple to handle and convenient to prepare by means of a large number of well established methods. The ready availability of carboxylic acids make them extremely promising raw materials for chemical synthesis. Recently decarboxylative nitration of aromatic α,β-unsaturated carboxylic acids has been developed for the synthesis of nitroolefins.

In 2002, Roy and co-workers reported a facile nitrodecarboxylation of aromatic α,β-unsaturated carboxylic acids under the effect of nitric acid and catalytic AIBN (Scheme 14).[36] From the effect of various additives, they postulated that an acyloxy radical can be generated either by the decomposition of acylnitrate or by the reaction of a NO_3 radical with acid. Then the NO_2 radical can combine in a bimolecular fashion with the acyloxy radical to promote nitrodecarboxylation (Figure 5).



Scheme 14 AIBN-catalyzed nitrodecarboxylation of α,β-unsaturated carboxylic acids.

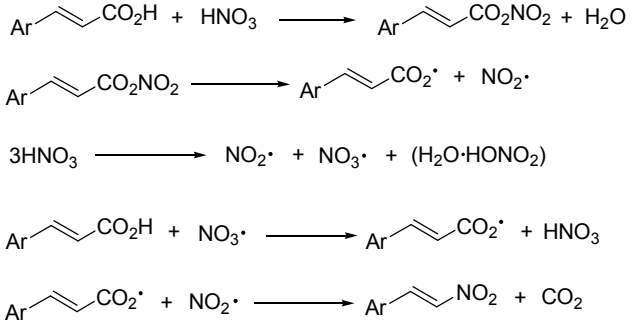
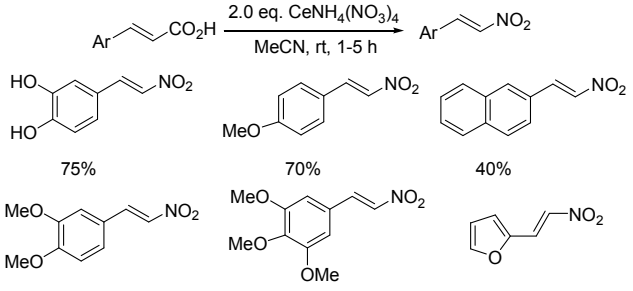


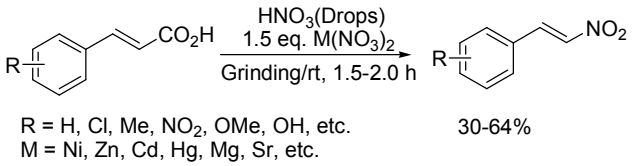
Figure 5 Possible mechanism.

In 2004, Fiorentino and co-workers had shown nitrodecarboxylation of cinnamic acids using cerium (IV) ammonium nitrate supported on silica (CAN/SiO_2) as a nitrating reagent.[37] However, the nitration of the aromatic ring was also observed in all the cases, which dramatically limits the application of this reaction. After that, Rao and co-workers developed a simple and efficient method for the nitrodecarboxylation of aryl α,β-unsaturated carboxylic acids using ceric ammonium nitrate as a nitrating reagent at room temperature (Scheme 15).[38] It is worth noting that the solvent of the reaction, acetonitrile, is crucial for the exclusive formation of the *ipso*-products, without the ring-substituted products.



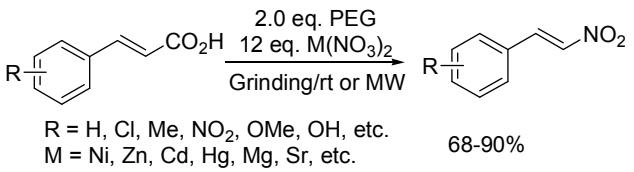
Scheme 15 Nitration of α,β-unsaturated carboxylic acids with $CeNH_4(NO_3)_4$.

In 2007, Rajanna and co-workers developed a solvent-free method for the decarboxylative nitration of α,β-unsaturated aliphatic and aromatic carboxylic acids (Scheme 16).[39] This reaction proceeds in the presence of a few drops of HNO_3 together with a variety of metal nitrates at room temperature. The method involves simple and safe work-up procedures. The reaction represents an alternative simple and practical protocol for the synthesis of β-nitrostyrenes and nitroalkenes.



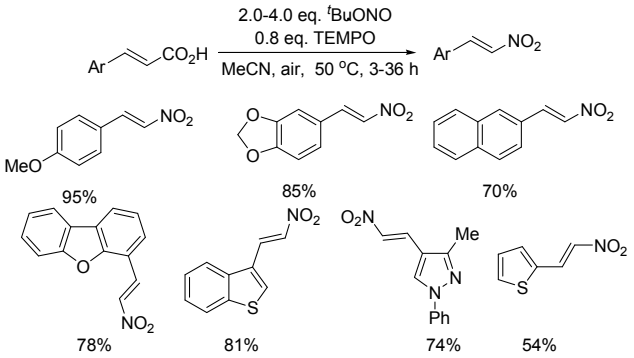
Scheme 16 Nitration of α,β-unsaturated carboxylic acids with HNO_3/MNO_3 under solvent-free conditions.

After that, Saiprakash and co-workers reported polyethylene glycol supported reaction for the synthesis of nitroolefins from α,β-unsaturated carboxylic acids under mineral acids free and solvent-free microwave irradiated and grinding conditions (Scheme 17).[40] The addition of PEG accelerated enormously the rate of the reaction and the yields were significantly increased. PEG-300 has been found to be much more efficient than other PEGs.



Scheme 17 PEG-supported nitration of α,β-unsaturated carboxylic acids with $M(NO_3)_2$ under solvent-free conditions.

In 2013, Maiti and co-workers developed a metal-free decarboxylative nitration protocol for the synthesis of nitroolefins from α,β-unsaturated carboxylic acids using *tert*-butyl nitrite and TEMPO (Scheme 18).[41] A broad range of substrate scope of α,β-unsaturated carboxylic acids bearing aromatic and heterocyclic moieties smoothly proceeded under the mild condition and produced exclusively *E*-nitro compounds. In addition, the practicality of the method has been achieved by a successful gram scale reaction.



Scheme 18 Nitration of α,β-unsaturated carboxylic acids with ^{t}BuONO/TEMPO.

They proposed a plausible mechanism for the reaction (Figure 6). The homolytic cleavage of *tert*-butyl nitrite generates nitric oxide radical under the heated conditions, which can form a nitro radical in the presence of air. In the presence of free radical, an acyloxy radical **A** can be generated from α,β-unsaturated carboxylic acids. The addition of a nitro radical into the carbon-carbon double bond of species **A** gives a benzylic radical **B**, which will further combine with TEMPO. There are two possible pathways in this step. The addition of TEMPO could lead to preferential formation of an energetically more favourable intermediate **C** over **D**. Subsequently, *anti*-elimination of intermediate **C** takes place and selectively produces *E*-nitroolefins. However, a mixture of *E* and *Z* isomers was observed without TEMPO.

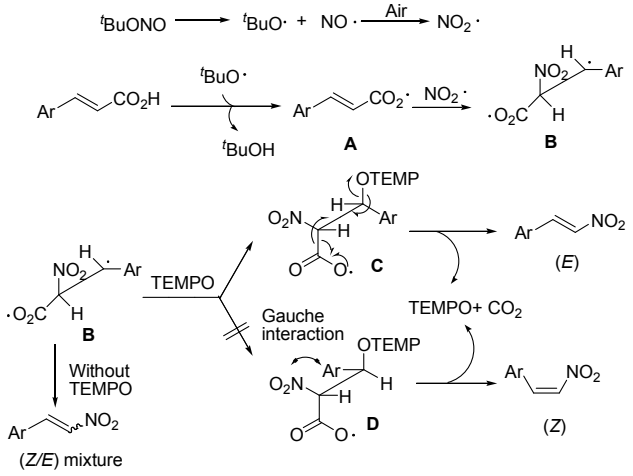
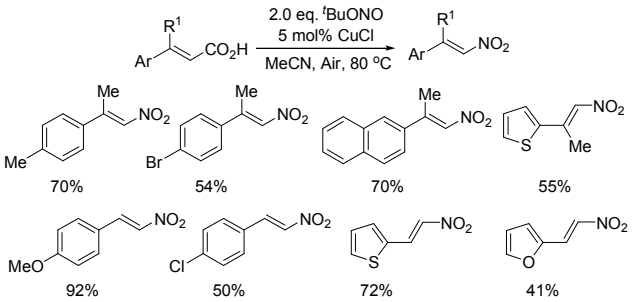


Figure 6 Possible mechanism.

Later on, Prabhu and co-workers reported the copper-catalyzed nitrodecarboxylation of substituted cinnamic acid derivatives with *tert*-butyl nitrite as nitrating source for the synthesis of nitroolefins (Scheme 19).[42] *β,β*-disubstituted nitroolefin derivatives can be easily synthesized by this new method, which are generally difficult to access through other conventional methods. Thiophene and furan derivatives are well tolerated under the reaction conditions. In addition, the reaction exhibits excellent stereoselectivity and gives exclusively *E*-nitroolefins.

In the proposed mechanistic path of the reaction (Figure 7), the α,β-unsaturated acid first reacts with Cu(I) catalyst to form the corresponding Cu(II) salt **A**, which further reacts with a nitro radical generated from the homolytic cleavage of *tert*-butyl nitrite in the presence of air to form a benzylic radical **B**. Subsequent decarboxylation of the benzylic radical **B** provides the corresponding nitroolefins.



Scheme 19 Copper-catalyzed nitration of α,β-unsaturated carboxylic acids with ^{t}BuONO.

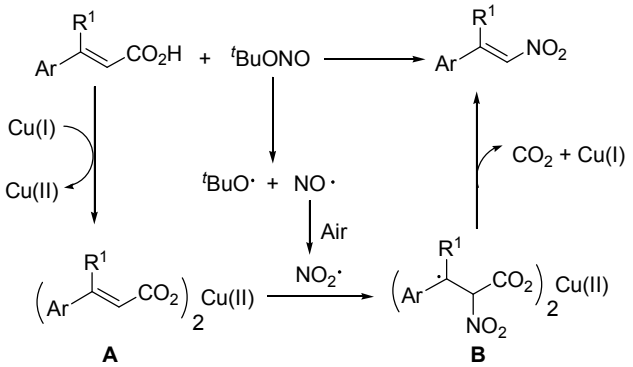
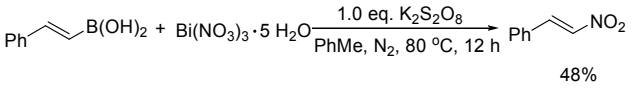


Figure 7 Possible mechanism.

5 Nitration of vinylboronic acids

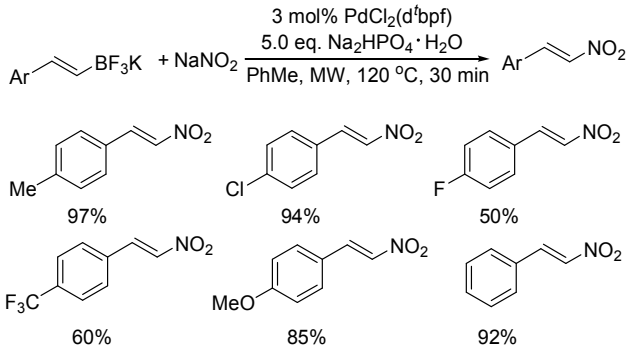
Organoboronic acids have been widely used in organic synthesis for functional group transformations due to their commercial availability and excellent stability to air and moisture.[43] In recent years, much attention from chemists have been devoted for the development of *ipso*-nitration protocols *via* nitrodemetallation route. There are many examples on the *ipso*-nitration of arylboronic acids in the literature.[44] However, similar reaction of vinylboronic acid is sparse in the literature.

In 2012, Maiti and co-workers reported the use of bismuth nitrate/perdisulfate as a new nitrating agent for *ipso*-nitration of arylboronic acids. This reaction is also suitable for the *ipso*-nitration of vinylboronic acids (Scheme 20).[45] A radical-based mechanism is proposed for *ipso*-nitration of arylboronic acids, whereas the reaction mechanism of vinylboronic acids is indistinct.



Scheme 20 *Ipso*-nitration of vinylboronic acids with bismuth nitrate/perdisulfate.

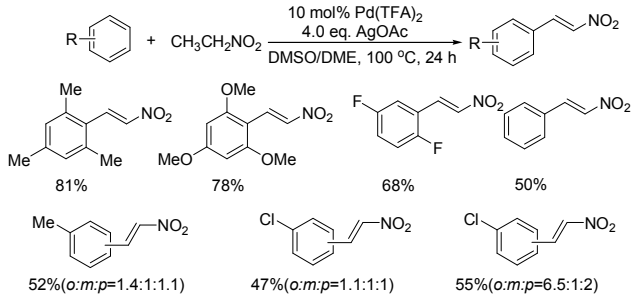
After that, AI-Masum and co-workers reported palladium-catalyzed cross-coupling reaction of potassium styryltrifluoroborates with sodium nitrite under microwave conditions for the synthesis of nitroolefins in high yields (Scheme 21).[46] Both electron-rich and electron-poor groups on the aromatic ring are tolerable under the reaction condition. This reaction would undergo transmetallation twice.



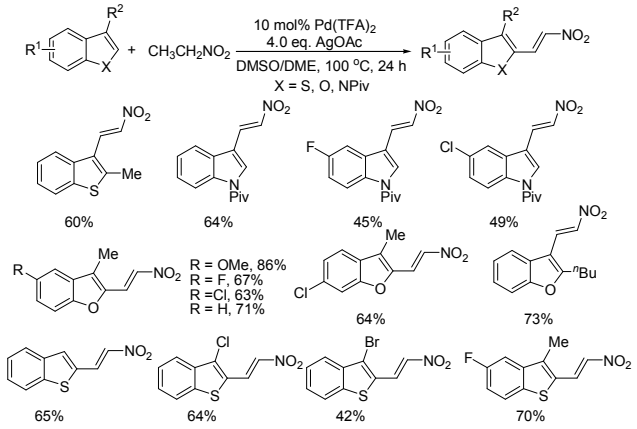
Scheme 21 Palladium-catalyzed nitration of potassium styryltrifluoroborates with sodium nitrite.

6 Cross-coupling reactions of arenes with nitroethane

In the past several decades, much progress has been made in the cross-dehydrogenative coupling through catalytic methods.[47] Recently, Su and co-workers reported the palladium-catalyzed multidehydrogenative cross-coupling reactions of arenes with nitroethane for the synthesis of β-aryl nitroethylenes (Scheme 22).[48] A broader range of substituted benzenes smoothly undergoes this transformation. The reactivity and regioselectivity are predominantly controlled by the electronic effect of the substituents rather than steric hindrance. Electron-rich arenes show higher efficiency than electron-poor substrates. In spite of being sterically encumbered, 1,3,5-trimethoxybenzene can provide the desired product in good yield. Additionally, the electron-rich heteroarenes such as indoles, benzothiophenes and benzofurans are also suitable for the cross-coupling with nitroethane (Scheme 23). A variety of functional groups can be tolerated in these cross-couplings, such as fluoro, chloro, bromo, methyl, and methoxyl. Although the mechanism of this reaction is not yet clear, their preliminary observations indicate that the direct β-arylation product of nitroethane might be the intermediate in this transformation which is followed by dehydrogenation to give β-aryl nitroethylenes.



Scheme 22 Palladium-catalyzed cross-coupling reactions of simple arenes with nitroethane.

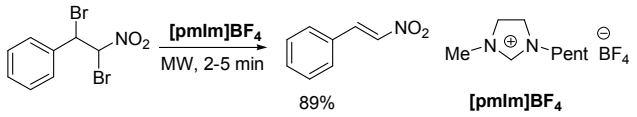


Scheme 23 Palladium-catalyzed cross-coupling reactions of Heteroarenes with nitroethane.

7 Other reactions

Organohalides are a class of organic compounds, which play a very important role in synthetic organic chemistry as well as in the chemical industry. For example, the addition of free radical reagents to halogenated olefins is an important transformation in organic synthesis. In 1960, Stevens reported the addition of dinitrogen tetroxide into β-bromostyrene for the synthesis of β-nitrostyrene *via* a radical pathway.[49] In addition, the dehydrohalogenation or dehalogenation of alkyl halides is the most common method for the construction of carbon-carbon double bond. In 2005, Ranu and co-workers developed a novel and efficient protocol for the stereoselective debromination of *vicinal*-dibromides to *E*-alkenes by using ionic liquid under microwave irradiation.[50] The method is applicable to a wide variety of substrates. Among these, β-nitrostyrene can be easily synthesized by this method (Scheme 24). In 2007, Li and co-workers reported dimethyl sulfoxide-mediated debromination of a variety of 1,2-dihalo compounds in absence of metal or an oxidant.[47] The β-nitrostyrene product can be obtained in moderate yield

by this method (Scheme 25). The advantages of the reaction are excellent stereoselectivity as well as the mild reaction condition, easy and simple handling.



Scheme 24 [pmIm]BF_4-promoted debromination of *vicinal*-dibromides.

Scheme 25 DMSO-mediated debromination of *vicinal*-dibromides.

8 Conclusions and perspectives

In summary, we have presented an overview on the synthesis of nitroolefins in recent years. Numerous new homogeneous or heterogeneous catalytic systems have been developed for improving the nitro-aldol condensation between aldehydes and nitroalkanes. Many novel nitrating reagents such as nitrate salts, nitrite salts and *tert*-butyl nitrite, etc. have been explored for the direct nitration of olefins C-H bond. In addition, the *ipso*-nitration protocols of aryl α,β-unsaturated carboxylic acids and vinylboronic acids serve as an important complementary route to nitroolefins. Furthermore, palladium-catalyzed cross-dehydrogenative coupling of arene *via* C-H bond activation with nitroethane provides an attractive alternative to the conventional methods. Mechanistic insights could help us to understand the nature of these reactions.

However, there are still some major drawbacks that need to be addressed in this field. Most of these methodologies have been efficiently applied for the nitration of substrates containing aromatic ring, whereas the corresponding reaction of heteroaromatic and aliphatic substrates suffer from some issues like poor activity or regioselectivity. So developing methods to extend the substrates scope is highly demanding in this area. In addition, the exploration of robust catalytic systems will continue to drive this field. As a consequence, new achievements are expected to appear in the near future.

Acknowledgements

We thank the Natural Science Foundation of Zhejiang Province (*No. LY12B02006, LY13B020005*) for financial support.

References

[a] *Department of Chemistry, Lishui University, No. 1, Xueyuan Road, Lishui City 323000, Zhejiang Province, P. R. China; Fax: (+86)-578-2271-250, Tel: (+86)-578-2271-250; E-mail: 0gbyan@tongji.edu.cn*

† Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/b000000x/

‡ Footnotes should appear here. These might include comments relevant to but not central to the matter under discussion, limited experimental and spectral data, and crystallographic data.

1 (a) N. Ono, *The Nitro Group in Organic Synthesis*; Wiley-VCH: Weinheim, **2001**; (b) H. Feuer, A. T. Nielsen, *Nitro Compounds*; VCH Publishers, Inc.: New York, **1990**; (c) A. G. M. Barrett, G. G. Graboski, *Chem. Rev.* 1986, **86**, 751; (d) R. Ballini, G. Bosica, D. Fiorini, A. Palmieri, M. Petrini, *Chem. Rev.* 2005, **105**, 933.

2 (a) O. M.Berner, L. Tedeschi, D. Enders, *Eur. J. Org. Chem.* 2002, 1877. (b)T. Ishii, S. Fujioka, Y. Sekiguchi, H. Kotsuki, *J. Am. Chem. Soc.* 2004, **126**, 9558. (c) H. B. Huang, E. N. Jacobsen, *J. Am. Chem. Soc.* 2006, **128**, 7170. (d) C. B. Tripathi, S. Kayal, S. Mukherjee, *Org. Lett.* 2012, **14**, 3296.

3 (a) J. March, *Advanced Organic Chemistry,* 3rd ed.; John Wiley & Sons: New York, **1985**. (b) R. C. Larock, *Comprehensive Organic Transformations;* VCH: New York, **1989**. (c) S. E. Denmark, A. Thorarensen, *Chem. Rev.* 1996, *96*, 137. (d) D. A. Evans, S. Mito, D. Seidel, *J. Am. Chem. Soc.* 2007, **129**, 11583. (e) T. Arai, A. Mishiro, N. Yokoyama, K. Suzuki, H. Sato, *J. Am. Chem. Soc.* 2010, **132**, 5338. (f) Y. K. Liu, M. Nappi, E. Arceo, S. Vera, P. Melchiorre, *J. Am. Chem. Soc.* 2011, **133**, 15212. (g) L. Albrecht, G. Dickmeiss, F. C. Acosta, C. Rodriguez-Escrich, R. L. Davis, K. A. Jorgensen, *J. Am. Chem. Soc.* 2012, **134**, 2543.

4 (a) D. Basavaiah, B. S. Reddy, S. S. Badsara, *Chem. Rev.* 2010, **110**, 5447. (b) D. K. Nair, S. M. Mobin, I. N. N. Namboothiri, *Org. Lett.* 2012, **14**, 4580. (c) K, Kaur, I. N. Namboothiri, Chimia 2012, **66**, 913.

5 (a) G. Rosini, R. Ballini, *Synthesis* 1988, 833. (b) R. Tamura, A. Kamimura, N. Ono, *Synthesis* 1991, 423.

6 (a) Y. Meah, V. Massey, *Proc. Natl. Acad. Sci. U.S.A.* 2000, **97**, 10733; (b) S. Kaap, I. Quentin, D.Tamiru, M. Shaheen, K. Eger, H. J. Steinfelder, *Biochem. Pharmacol.* 2003, **65**, 603; (c) H. Uehara, R. Imashiro, G. Hernandez-Torres, C. F. Barbas, *Proc.Natl. Acad. Sci. U.S.A.* 2010, **107**, 20672; (d) M. A. Reddy, N. Jain, D. Yada, C. Kishore, V. J. Reddy, P. S. Reddy, A. Addlagatta, S. V. Kalivendi, B. Sreedhar, *J. Med. Chem.* 2011, **54**, 6751; (k) L. Q. Lu, J. R. Chen, W. J. Xiao, *Acc. Chem. Res.* 2012, **45**, 1278.

7 (a) L. Kurti, B. Czako, *Strategic Applications of Named Reactions in Organic Synthesis;* Elsevier Academic Press: Amsterdam, 2005; (b) S. Fioravanti, L. Pellacani, P. A. Tardella, M. C. Vergari, *Org. Lett.* 2008, **10**, 1449; (c) N. Neelakandeswari, G. Sangami, P. Emayavaramban, R. Karvembu, N. Dharmaraj, H. Y. Kim, *Tetrahedron Lett.* 2012, **53**, 2980. (d) F. A. Luzzio, *Tetrahedron* 2001,**57**, 915.

8 For selected publications, see: (a) T. Mukaiyama, E. Hata, T. Yamada, *Chem. Lett.* 1995, 505; (b) H. Suzuki, T. Mori, *J. Org. Chem.* 1997, **62**, 6498; (c) R. S. Varma, K. P. Naicker, P. J. Liesen, *Tetrahedron Lett.* 1998, **39**, 3977; (d) P. J. Campos, B. Garcia, M. A. Rodriguez, *Tetrahedron Lett.* 2000, **41**, 979; (e) I. Jovel, S. Prateeptongkum, R. Jackstell, N. Vogl, C. Weckbecker, M. Beller, *Adv. Synth. Catal.* 2008, **350**, 2493; (f) P. K. Kancharla, Y. S. Reddy, S. Dharuman, Y. D. Vankar, *J. Org. Chem.* 2011, **76**, 5832.

9 G. Demicheli, R. Maggi, A. Mazzacani, P. Righi, G. Sartoria, F. Bigia, *Tetrahedron Lett.* 2001, **42**, 2401.

10 K. Motokura, M. Tada, Y. Iwasawa, *J. Am. Chem. Soc.* 2007, **129**, 9540.

11 K. Motokura, M. Tada, Y. Iwasawa, *J. Am. Chem. Soc.* 2009, **131**, 7944.

12 S. Fioravanti, L. Pellacani, P. A. Tardella, M. C. Vergari, *Org. Lett.* 2008, **10**, 1449.

13 A. Alizadeh, M. M. Khodaei, A. Eshghi, *J. Org. Chem.* 2010, **75**, 8295.

14 J. M. Rodríguez, M. D. Pujol, *Tetrahedron Lett*. 2011, **52**, 2629.

15 N. Neelakandeswari, G. Sangami, P. Emayavaramban, R. Karvembu, N. Dharmaraj, H. Y. Kim, *Tetrahedron Lett.* 2012, **53**, 2980.

16 L. Rokhum, G. Bez, *Tetrahedron Lett.* 2013, **54**, 5500.

17 A. D. Grebenyuk, R. A. Ismailova, R. B. Tokbolatov, T. Ovadova, *Zh. Org. Khim.* 1990, **26**, 680.

18 E. J. Corey, H. Estreicher, *J. Am. Chem. Soc.* 1978, **100**, 6294.

19 T. Hayama, S. Tomoda, Y. Takeuchi, Y. Normura, *Tetrahedron Lett.* 1982, **23**, 4733.

20 S.-S. Jew, H.-D. Kim, Y.-S. Cho, C.-H. Cook, *Chem. Lett.* 1986, 1747.

21 W. W. Sy, A. W. By, *Tetrahedron Lett.* 1985, **26**, 1193.

22 S. W. Tinsley, *J. Org. Chem.* 1961, **26**, 4723.

23 A. V. Stepanov, V. V. Veselovsky, *Russ. Chem. Rev.* 2003, **72**, 327.

24 C. P. Butts, J. L. Calvert, L. Eberson, M. P. Hartshorn, W. T. Robinson, *J. Chem. Soc., Perkin Trans. 2* 1994, **7**, 1485.

25 J.-L. Grenier, J.-P. Catteau, Ph. Cotelle, *Synth. Commun.* 1999, **29**, 1201.
26 O. Siri, L. Jaquinod, K. M. Smith, *Tetrahedron Lett.* 2000, **41**, 3583.
27 M. Tanaka, E. Muro, H. Ando, Q. Xu, M. Fujiwara, Y. Souma, Y. Yamaguchi, *J. Org. Chem.* 2000, **65**, 2972.
28 (a) E. Hata, T. Yamada, T. Mukaiyama, *Bull Chem. Soc. Jpn.* 1995, **68**, 3626; (b) T. Mukaiyama, E. Hata, T. Yamada, *Chem. Lett.* 1995, 505.
29 (a)T. Taniguchi, H. Ishibashi, *Org. Lett.* 2010, **12**, 124; (b) S. Manna, S. Maity, S. Rana, S. Agasti, D. Maiti, *Org. Lett.* 2012, **14**, 1736; (c) Y.-K. Liu, S.-J. Lou, D.-Q. Xu, Z.-Y. Xu, *Chem.-Eur. J.* 2010, **16**, 13590; (d) Y.-M. Li, X.-H. Wei, X.-A. Li, S.-D. Yang, *Chem. Commun.* 2013, **49**, 11701.
30 T. Taniguchi, T. Fujii, H. Ishibashi, *J. Org. Chem.* 2010, **75**, 8126.
31 S. Maity, S. Manna, S. Rana, T. Naveen, A. Mallick, D. Maiti, *J. Am. Chem. Soc.* 2013, **135**, 3355.
32 T. Naveen, S. Maity, U. Sharma, D. Maiti, *J. Org. Chem.* 2013, **78**, 5949.
33 S. Maity, T. Naveen, U. Sharma, D. Maiti, *Org. Lett.* 2013, **15**, 3384.
34 P. K. Kancharla, Y. S. Reddy, S. Dharuman, Y. D. Vankar, *J. Org. Chem.* 2011, **76**, 5832.
35 S. Dharuman, P. Gupta, P. K. Kancharla, Y. D. Vankar, *J. Org. Chem.* 2013, **78**, 8442.
36 J. P. Das, P. Sinha, S. Roy, *Org. Lett.* 2002, **4**, 3055.
37 A. Messere, A. Gentili, I. Garella, F. Temussi, B. D. Blasio, A. Fiorentino, *Synth. Commun.* 2004, **34**, 3317.
38 A. S. Rao, P. V. Srinivas, K. S. Babu, J. M. Rao, *Tetrahedron Lett.* 2005, **46**, 8141.
39 S. Ramgopal, K. Ramesh, A. Chakradhar, N. Maasi Reddy, K. C. Rajanna, *Tetrahedron Lett.* 2007, **48**, 4043.
40 K. C. Rajanna, K. Ramesh, S. Ramgopal, S. Shylaja, P. G. Reddy, P. K. Saiprakash, *Green Sustainable Chem.* 2011, **1**, 132.
41 S. Manna, S. Jana, T. Saboo, A. Maji, D. Maiti, *Chem. Commun.* 2013, **49**, 5286.
42 B.V. Rokade, K. R. Prabhu, *Org. Biomol. Chem.* 2013, **11**, 6713.
43 (a) D. G. Hall, *Boronic Acids: Preparation, Applications in Organic Synthesis and Medicine* (Ed.), Wiley-VCH, Weinheim, **2005**; (b) N. Miyaura, A. Suzuki, *Chem. Rev.* 1995, **95**, 2457.
44 G. Yan, M. Yang, *Org. Biomol. Chem.* 2013, **11**, 2554.
45 S. Manna, S. Maity, S. Rana, S. Agasti, D. Maiti, *Org. Lett.* 2012, **14**, 1376.
46 M. AI-Masum, N. Saleh, T. Islam, *Tetrahedron Lett.* 2013, **54**, 1141.
47 C.-J. Li, *Acc. Chem. Res.* 2009, **42**, 335.
48 M. Zhang, P. Hu, J. Zhou, G. Wu, S. Huang, W. Su, *Org. Lett.* 2013, **15**, 1718.
49 T. Stevens, *J. Org. Chem.* 1960, **25**, 1658.
50 B. C. Ranu, R. Jana, *J. Org. Chem.* 2005, **70**, 8621.
51 W. Li, J. Li, M. Lin, S. Wacharasindhu, K. Tabei, T. S. Mansour, *J. Org. Chem.* 2007, **72**, 6061.