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Highly double selective nitration of nitrostilbenes over zeolite†

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Cite this: *Chem. Commun.*, 2014, **50**, 10710

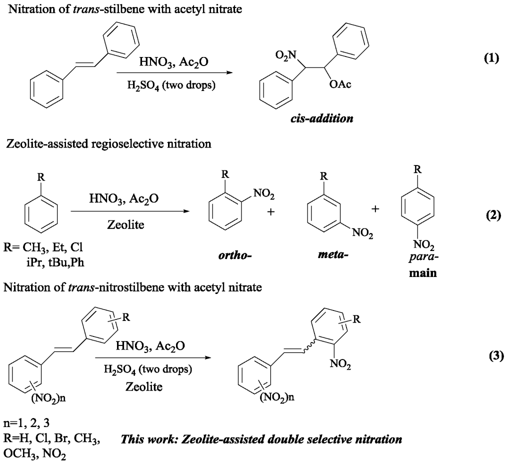
Received 20th June 2014,
Accepted 14th July 2014

DOI: 10.1039/c4cc04688a

www.rsc.org/chemcomm

A feasible zeolite-assisted *ortho* C–H nitration of nitrostilbenes has been developed for the first time, which can be used *in situ*. It uses acetyl nitrate as a mild, easily handled and commercially available nitrating reagent, leading to the synthesis of polynitrostilbenes with double selectivities and in good yields.

Nitrostilbenes, such as 2,2′,4,4,6,6′-hexanitrostilbene (HNS), are well-known, high-energy materials with excellent thermal stability and detonation properties.[1] Furthermore, nitrostilbene-based derivatives can be found in various natural products,[2] and are playing an increasingly prominent role in the area of non-linear optical (NLO) application.[3] In energetic materials chemistry, the presence of nitro groups tends to decrease the heat of formation but contributes markedly to the overall energetic performance.[4] There is a lot of interest and challenges in the syntheses and chemistry of energetic materials, containing C═C unsaturated double bonds together with more nitro groups attached in the molecule. However, traditional nitration conditions are limited in scope due to poor regioselectivity and poor chemoselectivity arising from overnitration and the lack of compatibility with easily oxidized functionalities, which result in complexity of the mixture of products formed. Acetyl nitrate in acetic anhydride solution as typical electrophilic reagent reacts rapidly with many alkenes to give mixtures of nitro-alkenes, β-nitro nitrates, and β-nitro acetates.[5] For example, nitration of styrenes and stilbenes with acetyl nitrate gave 40–70% yields of β-nitro acetates[6] [eqn (1), Scheme 1]. Recently, Maiti and co-workers reported the preparation of (*E*)-nitroolefins from nitration of olefins using $AgNO_2$/TEMPO,[7] *t*-BuONO/TEMPO,[8] and $Fe(NO_3)_3$/TEMPO.[9] These methods while offering significant improvements in direct nitration of olefins have problematic issues, which include metal reagent employed, absence of recovery and reuse of the catalyst.



Scheme 1 Nitration with acetyl nitrates.

The use of solid catalysts is potentially attractive because of the ease of recovery and reuse of the catalyst, in addition to possibilities that the solid might enhance the selectivity, particularly if it is a zeolite.[10] Our initial successes in regioselective nitration of simple aromatics or naphthalene over zeolite by Kyodai nitration make us prefer this direction.[11] Improved *para*-regioselection for single ring aromatics has also been achieved with zeolites as the catalyst,[12] particularly when nitric acid is used in combination with acid anhydride [eqn (2), Scheme 1]. Although this method is effective, a situation may arise where one needs to introduce a nitro group through nitration of substrates with –C═C– unsaturated double bonds as well as aromatic rings. Furthermore, nitration of nitrostilbenes exhibits a high degree of selectivity, including regioselective and chemoselectivity towards aryl rings and –C═C– double bond. Herein, we report a zeolite-assisted double selective nitration method by which nitrostilbenes can be converted to their *ortho*-nitrated derivatives in high yield using *in situ* acetyl nitrate as a mild,

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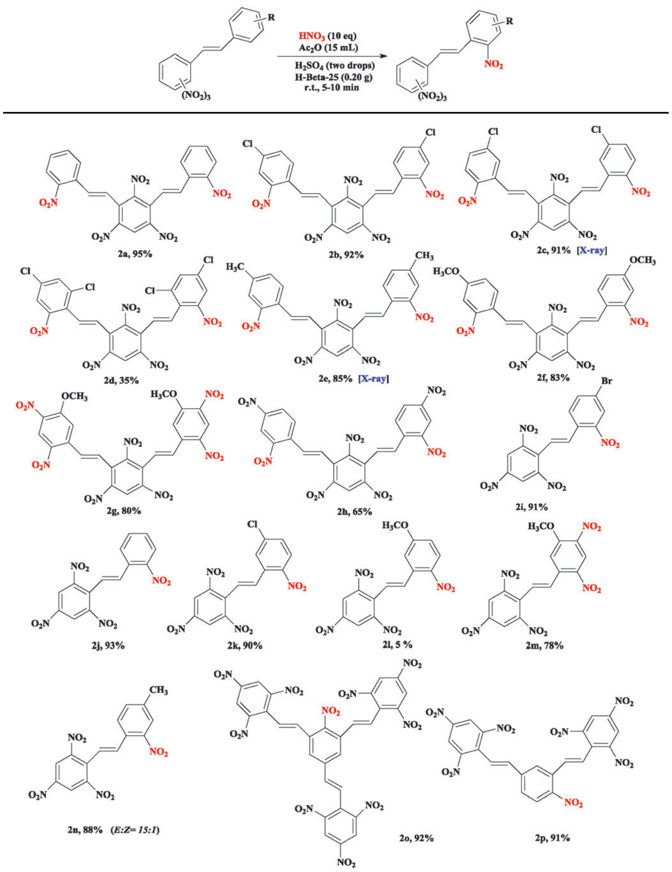
† Electronic supplementary information (ESI) available: Detailed experimental procedures, spectral data, electrostatic potential calculations and crystallographic data. CCDC 965295 and 999375. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c4cc04688a

easily handled and commercially available nitrating reagent [eqn (3), Scheme 1].

Our initial nitration of *trans*,*trans*-1,3-distyryl-2,4,6-trinitrobenzene using HNO_3/H_2SO_4, and a complex mixture of products was observed, which are mainly consisted of oxidation products (Table S1, entry 1, ESI†). However, when treated with HNO_3/Ac_2O, an isolated *ortho*-nitrated product **1** along with a wide product distributions were observed (Table S1, entries 2–4, ESI†). With the presence of zeolites ($SiO_2:Al_2O_3$ = 25) in HNO_3/Ac_2O, an exciting result was obtained. By further optimizing the amount of nitration reagent, catalyst species and loading amount, we discovered that 10 equiv. of HNO_3, 0.20 g of zeolite in excess acetic anhydride at room temperature in 5 min could provide 95% isolated yield of **1** (Table S1, entry 4, ESI†). Remarkably, running the nitration with NO_2/O_2 or NO_2/O_3 had no positive effect on the outcome of the reaction (Table S1, entries 12 and 13, ESI†). The $-C{=}C-$ double bonds in nitration products disappeared, which might be attributed to oxidation in the double bonds.

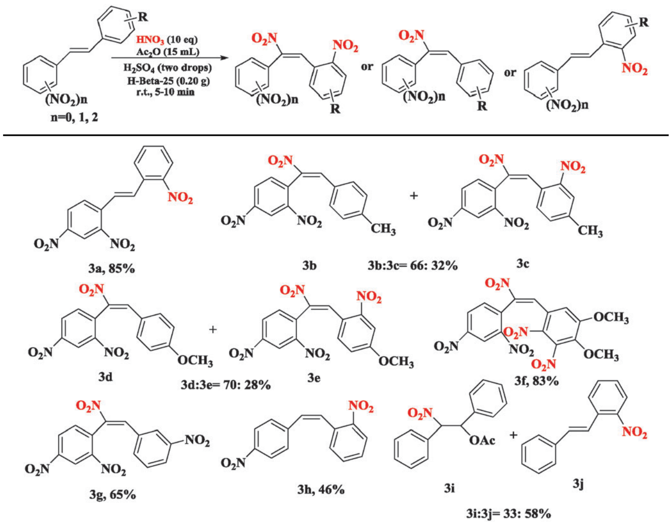
With the fully optimized reaction conditions, we explored the scope and limitations of the method. Generally, all the nitration products were obtained in a good isolated yield (Table 1). (*E*)-1,3,5-Trinitro-2-styrylbenzene gave excellent yields of the desired nitro product (**2j**, 93%) under the optimized conditions. High regioselectivity for the less hindered *ortho* C–H bond was observed for substrates bearing a *para* chloro (**2b**) and bromo (product **2i**) or *meta* chloro group (**2c** and **2k**). In contrast, when another chloro group was introduced in *ortho* position (**2d**), the major product isolated with the same regioselectivity but with low yields. However, if the sterically challenging *ortho*-substituted nitrostilbenes derivatives as substrates often provided complex mixtures under usual conditions.[13] *Para*-substituents with $-CH_3$ or $-OCH_3$ reacted smoothly to afford the expected nitro products (**2e** and **2f**). However, when (*E*)-2-(4-methylstyryl)-1,3,5-trinitrobenzene was selected as substrate, small amounts of *Z*-isomer was detected (**2n**). Notably, if the $-OCH_3$ group appeared in *meta*-position, di-nitration products were isolated in good yields (**2g** and **2m**). Strong electron-withdrawing substituent with 4-nitro also gave a nitro product (**2h**), albeit in lower yield. Unfortunately, 3-nitro nitrostilbenes (*e.g.* (*E*)-1,3,5-trinitro-2-(3-nitrostyryl) benzene) did not form the desired nitration product under the reaction conditions. Attempting the reaction on other types of nitrostilbenes, which were found to be problematic under traditional conditions, resulting in successful nitration in excellent yields (**2o** and **2p**). The regiochemical designation of the products (**2c** and **2e**) was unequivocally proven by single crystal X-ray diffraction.[14]

Table 1 Substrate scope of nitrostilbenes nitration



Next, we investigated the nitration of nitrostilbenes analogues by decreasing the number of nitro groups under identical conditions (Table 2). The presence of (*E*)-2,4-dinitro-1-styrylbenzene did not alter the expected outcome of the reaction (**3a**, 85%). However, the principal (*E*)-α,2,4-trinitrostilbenes, as well as *ortho*-nitrated products, were found, when the hydrogen atom in *para*-position was substituted by $-CH_3$ or $-OCH_3$ group (**3b–e**). With the presence of another methoxy group, two nitro groups were introduced in aryl ring and one nitro group in $-C{=}C-$ double bond (**3f**). If strong electron-withdrawing nitro group was introduced in *meta* position, **3g** was afforded in acceptable yields. Moreover, isomerization of the *trans*-geometry of the reactant 2,4-trinitrostilbenes to *cis*-geometry in the products occurred, which was similar to the report by Srinivasan's nitration with fuming nitric acid.[15] This isomerization may be due to the favorable π–π interaction between the two aryl rings during nitration. Further investigation on nitrating

Table 2 Nitration of other nitrostilbenes



trans-stilbene and *trans*–*para*-nitrostilbene under usual conditions revealed that this protocol was *ortho* C–H nitration enhanced (**3h–j**).

In order to check the possibility of reuse of the zeolite, it was recovered following extraction of the products and was regenerated by heating overnight in air at 450 °C. Nitration reactions were then conducted under identical conditions using the recovered zeolite. The results showed that under the standard conditions, there was only a slight decrease (to 93%) in the yield of **2a** even after using the same zeolite six times under identical conditions. To demonstrate the scalability of the selective nitration method, 3,3′-((1*E*,1′*E*)-(2,4,6-trinitro-1,3-phenylene)bis-(ethene-2,1-diyl))bis(chlorobenzene) was reacted on a 15 mmol scale. In this experiment, the desired nitrostilbene product (**2c**) was separated in excellent yield (90%).

Nitration by acetyl nitrate with high *ortho*–*para* ratios is caused by ''*ortho* effect'' on steric ground[16] or coordination mechanism.[17] Prins *et al.* applied liquid and solid-state MAS NMR to Ac_2O/HNO_3 liquid and in beta zeolite and identified acetyl nitrate and acetic acid, which were coordinated to the aluminium framework of the zeolite.[18] The Brønsted acid site in the zeolite wall is responsible for the generation of NO_2^+ ion from acetyl nitrate during electrophilic attack on substrates.[5,6,19] It is further supported by the results that when increasing the Si/Al ratio in beta zeolite, a decrease in *ortho*-selectivity is observed (Table S1, entries 6, 8 and 9, ESI†). Moreover, the higher selectivity for the zeolite may be ascribed to the 3D structure of zeolite in comparison to the 2D structure of K10 (Table S1, entries 6 and 11, ESI†).

Molecular electrostatic potential[20] (ESP) was employed in the explanation of chemoselectivity, which reveals the regions of the molecule to which an electrophile would initially be attracted. The structure of *trans*-stilbene was shown to be nearly planar, while the structures of nitrostilbenes were twisted upon increasing the number of nitro groups (Fig. S1, S2, S4, S6 and S8, ESI†). Moreover, the ESP surface minima of *trans*-stilbene was about −14.35 kcal mol^{-1} and the electrons were well dispersed over the molecule (Fig. 1(a) and Table S7, ESI†). However, the ESP surface minima of nitrostilbenes were concentrated on the nitro-group for its lone pair electrons (Fig. 1(b) and (c)). The ESP quantitative analysis of *trans* –C═C– double bond and aryl rings, *trans*-stilbene (−14.23 kcal mol^{-1}, −14.35 kcal mol^{-1}), *trans*-1-styryl-2,4-dinitrobenzene (−1.47 kcal mol^{-1}, −6.35 kcal mol^{-1}), and *trans*,*trans*-1,3-distyryl-2,4,6-trinitrobenzene (−1.35 kcal mol^{-1}, −7.26 kcal mol^{-1}) well explained the decreases in chemical activity of *trans* –C═C– double bonds (Tables S2, S4 and S6, ESI†). Furthermore, the ESP surface minima values of nitrostilbenes in aryl rings were higher than *trans*-stilbene's but lower than those of their corresponding *trans* –C═C– double bond's.

The average negative values around corresponding atoms are also presented in Fig. 1 (right), and the *meta* position of the aryl ring owned the minimum values for nitrostilbenes. However, it was found that the existing nitro group decreased the electrostatic interaction of *trans* –C═C– double bond with NO_2^+ sharply, which would favor substitution at the *ortho* position of the benzene ring. The high regioselectivity for nitration of nitrostilbenes by acetyl nitrate attributed to a linear coordination mechanism.[21] Initially, acetyl nitrate was activated by zeolite and gave NO_2^+ as a nucleus complex of the attacking electrophile with the –C═C– double bond, and migration to the nucleus could conceivably take place by means of the delocalized electron cloud with the extended π–π conjugation. Since entrance to the nucleus would occur nearest the *ortho* position, this site should then be most susceptible to substitution (Scheme 2).

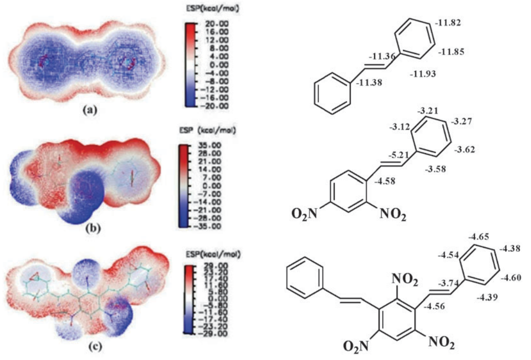
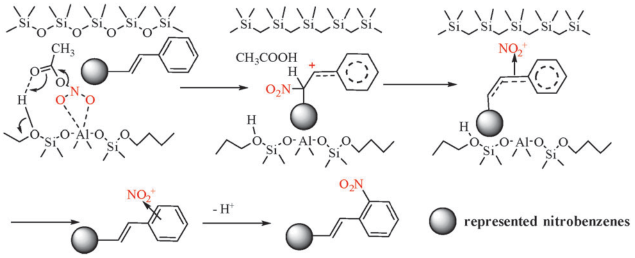


Fig. 1 Electrostatic potential distribution (left) and average negative values around corresponding atoms in kcal mol^{-1} (right).



Scheme 2 Possible mechanism for zeolite-assisted regioselective *ortho*-nitration of nitrostilbenes.

In conclusion, we have developed a novel heterogeneous method by which nitrostilbenes can be nitrated with double selectivities in high yield using acetyl nitrate as the nitrating agent. This method uses very mild conditions and generates little waste compared to alternative nitration protocols. Preliminary results, including experimental details and ESP analysis, suggest that the reaction proceeds through an electrophile and linear coordination mechanisms. Efforts in further expanding the scope of the reaction and elucidating the mechanism are ongoing and will be reported in due course.

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