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ortho-Alkenylation of anilines with aromatic terminal alkynes over nanosized zeolite beta

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A simple, efficient and environmentally benign catalytic system has been successfully developed for highly regioselective electrophilic alkenylation of anilines with aromatic terminal alkynes over nanosized zeolite beta, which exhibits highest catalytic activity among other conventional zeolites. The scope of the reaction was explored with various anilines and alkynes. However, the substrates (aniline or alkynes) with strong electron-withdrawing groups were failed to react under present catalytic conditions (except 4-nitroaniline). Moreover, the catalyst is recyclable and can be reused without significant loss in its catalytic activity.

Catalytic electrophilic aromatic substitution is one of the most useful approaches for the incorporation of carbon substituents onto aromatic rings.¹ In particular, the *ortho*-alkenylation of aromatic amines with carbon-carbon multiple bonds is of significant importance. However, it is not easily accessible process under normal Friedel-Crafts conditions² due to the coordination of the Lewis acid with the nitrogen atom of amino group, which leads to the deactivation of aromatic ring. Anilines substituted at the *ortho* position with an alkenyl groups (2-(1-phenylethenyl)anilines) are important precursors to a variety of heterocycles including indoles, quinolines and cinnolines, which are key structural units for a variety of biologically important compounds.³ They have also been used as synthetic intermediates in several total synthetic methods.⁴ Usually anilines with phenylacetylene gave the enamines in the presence of Lewis acids.⁵ To the best of our knowledge, there is only one report available in the literature on *ortho*-alkenylation of aromatic amines with phenylacetylene. However, main drawbacks associated with this method are lack of substrate scope (only limited to phenylacetylene) and the recyclability of catalyst was not studied.⁶ Thus, there is a much room to develop a simple, efficient and eco-friendly catalytic system for *ortho*-alkenylation of anilines with

aromatic terminal alkynes.

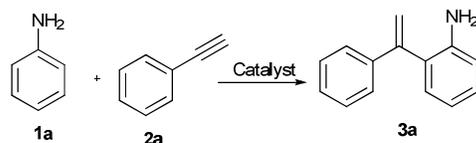
In recent years, there is a substantial interest to design heterogeneous catalytic systems towards eco-friendly, clean and shape selective reactions. Catalysts based on various zeolites have main importance both in the petroleum and fine chemical industries,⁷ due to their unique physical and chemical properties, such as uniform channel size, large internal surface area, unique molecular shape selectivity, strong acidity and good thermal/hydrothermal stability. The large pore zeolite like H β has received much attention because of the large available micropore volume, large-pore channel system and the existence of active sites in diverse concentrations that are needful in a number of acid-catalyzed reactions.⁸ However, zeolites often show inadequate activity and/or fast deactivation because of poor diffusion efficiency.⁹ The slow transport in the zeolite micropores leads to unwanted secondary side reactions or slow reaction rates. In order to get benefit fully from the unique sorption and shape-selectivity effects in the micropores, the diffusion path length in the micropores should be extremely small.¹⁰ Nanosized zeolite crystals with narrow particle size distributions and sizes less than 100 nm have received much interest due to their great potential applications in catalysis and adsorption. The reduction of particle size from the micrometer to the nanometer scale leads to significant changes in the material properties, such as high external surface areas, reduced diffusion path lengths and more exposed active sites.¹¹ In continuation of our efforts toward the development of novel and eco-friendly synthetic protocols using zeolites,¹² we wish to describe here a simple and efficient catalytic method for *ortho*-alkenylation of anilines with aromatic terminal alkynes over nanosized zeolite beta. Nanosized zeolite beta was prepared according to the procedure described in our earlier report, which was systematically characterized by various spectroscopic techniques, such as, X-ray diffraction (XRD), Scanning Electronic Microscopy (SEM), Fourier Transform Infrared Spectroscopy (FT-IR), NH₃-TPD and ²⁷Al NMR spectroscopy.¹³

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Initially, we investigated the suitable reaction conditions for *ortho*-alkenylation of anilines with aromatic terminal alkynes using aniline and phenylacetylene as a model system (Table 1). In order to choose the best catalyst, the reaction was carried out over various zeolites and MCM-41 at 120 °C in sealed vial for 3 h in toluene (Table 1). Among the catalysts examined, H β zeolite showed the higher catalytic activity and furnished the 2-(1-phenylethenyl)aniline (**3a**) in 61% yield (Table 1, entry 5). Under the same reaction conditions, H-mordenite and HY provided the **3a** in $\leq 30\%$ yield (Table 1, entries 2 and 3). HZSM-5, MCM-41 and NaY delivered $\leq 15\%$ yield of **3a** (Table 1, entries 1, 4 and 6). Then, we tested the reaction with nanosized zeolite beta under similar reaction conditions, which afforded the corresponding product in highest yield (90%) compared to other catalysts (Table 1, entry 7). The best performance of nanosized zeolite beta is probably attributable to the higher acidity of nanosized zeolite beta ($412 \mu\text{mol g}^{-1}$) than the H β zeolite ca. $269 \mu\text{mol g}^{-1}$.¹³

Table 1 Optimization of reaction conditions^a

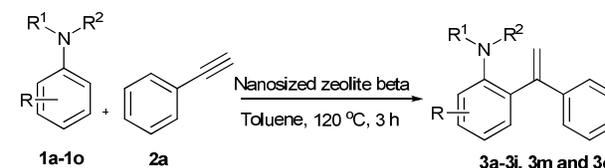
| Entry | Catalyst | Conversion 1a (%) ^b | Selectivity 3a (%) ^b | 3a Yield (%) ^c |
|-------|------------------------|--|---|-------------------------------------|
| 1 | HZSM-5 | 17 | 93 | 15 |
| 2 | H-Mordenite | 23 | 98 | 22 |
| 3 | HY | 35 | 93 | 30 |
| 4 | NaY | 5 | 96 | 3 |
| 5 | H β | 65 | 98 | 61 |
| 6 | MCM-41 | 14 | 91 | 11 |
| 7 | Nanosized zeolite beta | 96 | 97 | 90 |
| 8 | Absence of catalyst | 00 | - | - |
| 9 | Nanosized zeolite beta | 56 | 98 | 52 ^d |
| 10 | Nanosized zeolite beta | 23 | 98 | 20 ^e |
| 11 | Nanosized zeolite beta | 66 | 99 | 62 ^f |
| 12 | Nanosized zeolite beta | 50 | 97 | 46 ^g |
| 13 | Nanosized zeolite beta | 95 | 98 | 91 ^h |

^a Reaction conditions: **1a** (2 mmol), **2a** (2 mmol), catalyst (100 mg), toluene (1 mL), 120 °C, 3 h, sealed vial. ^b Conversion and selectivity based on GC. ^c Isolated yields. ^d Catalyst (50 mg). ^e Catalyst (25 mg). ^f 110 °C. ^g 100 °C. ^h 130 °C.

Once nano beta was found as the best catalyst for the *ortho*-alkenylation of aniline with phenylacetylene, the influence of temperature was studied. The reaction was remarkably accelerated by varying the reaction temperature from 100 to 120 °C and the yield was enhanced from 46 to 90% (Table 1, entries 7 and 11-13) probably due to the particles move faster and collide more frequently on the catalyst surface as increase in the reaction temperature. The present reaction was also conducted with different amounts of catalyst and it was found that 100 mg of catalyst leads to the best result (Table 1, entry 7). The desired product was not observed in the absence of catalyst, thus confirming the role of the catalyst in the reaction (Table 1, entry 8). After extensive screening, we have observed

that 100 mg of nanosized zeolite beta was optimum for 2 mmol of aniline and 2 mmol of phenylacetylene in order to get the maximum yield of the desired product in toluene (1 mL) at 120 °C (Table 1, entry 7).

Having the optimized conditions in hand, we investigated the versatility of this methodology by reacting the various anilines with phenylacetylene and the results are summarized in Table 2. Various electron-donating and electron-withdrawing groups were well tolerated with the

Table 2 *ortho*-Alkenylation of anilines with phenylacetylene over nanosized zeolite beta^a

| Entry | R | R ¹ | R ² | Conversion 1a-1o (%) ^b | Selectivity 3a-3o (%) ^b | Product; yield (%) ^c |
|-------|---------------------|----------------|----------------|---|---|---------------------------------------|
| 1 | H | H | H | 95 | 97 | 3a ; 90 |
| 2 | 4-MeO | H | H | 98 | 99 | 3b ; 96 |
| 3 | 4-Me | H | H | 97 | 98 | 3c ; 93 |
| 4 | 2-MeO | H | H | 90 | 98 | 3d ; 85 |
| 5 | 2-Me | H | H | 79 | 98 | 3e ; 75 |
| 6 | 2,4-Me,Me | H | H | 84 | 98 | 3f ; 78 |
| 7 | 4-Cl | H | H | 94 | 98 | 3g ; 89 |
| 8 | 2-Br | H | H | 76 | 98 | 3h ; 70 |
| 9 | 4-Br | H | H | 93 | 97 | 3i ; 86 |
| 10 | 4-NO ₂ | H | H | 36 | 97 | 3j ; 32 |
| 11 | 4-CONH ₂ | H | H | 00 | - | 3k ; - |
| 12 | 4-COOH | H | H | 00 | - | 3l ; - |
| 13 | H | Me | H | 69 | 98 | 3m ; 65 |
| 14 | H | Me | Me | 00 | - | 3n ; - |
| 15 | 3,4-anthryl | H | H | 91 | 97 | 3o ; 86 |

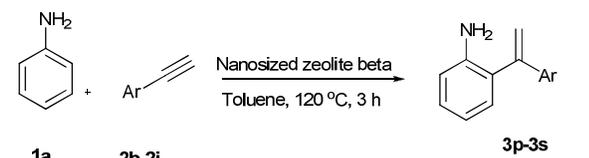
^a Reaction conditions: **1a-1o** (2 mmol), **2a** (2 mmol), nanosized zeolite beta (100 mg), toluene (1 mL), 120 °C, 3 h, sealed vial. ^b Conversion and selectivity based on GC. ^c Isolated yields.

present catalytic system and gave the desired products **3a-3j**, **3m** and **3o** in low to excellent yields (Table 2, entries 1-15). In all cases, the complete *ortho*-regioselectivity was observed. Aniline produced the corresponding *ortho*-alkenylated product with 90% yield in 3 h (Table 2, entry 1). Aniline substituted with activating groups reacted smoothly and furnished the respective *ortho*-alkenylated products in good to excellent yields under these reaction conditions (Table 2, entries 2-6). However, the *ortho*-substituted anilines show relatively lower yields with respect to the corresponding para isomer probably due to some steric hindrance (Table 2, entries 4, 5 and 8). Halo substituted anilines, such as 4-chloroaniline (**1g**), 2-bromoaniline (**1h**) and 4-bromoaniline (**1i**) could be transformed into the corresponding 2-(1-phenylethenyl)anilines **3g-3i** in 70-89% yield (Table 2, entries

7-9). In case of highly deactivating anilines, such as (4-nitroaniline (**1j**), 4-aminobenzamide (**1k**) and 4-aminobenzoic acid (**1l**), the corresponding products were obtained in low or zero yields (Table 2, entries, 10-12). The *N*-alkylated aniline **1m** afforded the respective product **3m** with 65% yield (Table 2, entry 13), whereas *N,N*-disubstituted aniline i.e., *N,N*-dimethylaniline (**3n**) failed to react under similar reaction conditions (Table 2, entry 14). Polycyclic aromatic amine **1o** was also reacted smoothly to provide the corresponding *ortho*-alkenylated product **3o** in 86% yield (Table 2, entry 15).

To extend the scope of this reaction further, we investigated the reaction of other aromatic terminal alkynes with aniline and the results are summarized in Table 3. Activating group present on aromatic ring of phenylacetylene i.e., 1-ethynyl-4-methylbenzene yielded the respective product in 88% yield (Table 3, entry 1). Halo substituted phenylacetylenes such as 1-ethynyl-4-fluorobenzene (**2c**), 1-ethynyl-3-chlorobenzene (**2d**), and 1-ethynyl-4-bromobenzene (**2e**) afforded the corresponding *ortho*-alkenylated products in 78-87% yield (Table 3, entries 2-4). Unfortunately, highly deactivating groups present on aromatic ring of phenylacetylene such as 1-ethynyl-4-nitrobenzene (**2f**), methyl 4-ethynylbenzoate (**2g**), 1-ethynyl-4-(trifluoromethyl)benzene (**2h**) and heteroaromatic alkyne i.e 2-ethynylpyridine (**2i**) were unsuccessful under similar reaction conditions (Table 3, entries 5-7).

Table 3 *ortho*-Alkenylation of aniline with arylacetylenes over nanosized zeolite beta^a



| Entry | Ar | Conversion 1a (%) ^b | Selectivity 3p-3w (%) ^b | Product; yield (%) ^c |
|-------|---|--|--|---------------------------------------|
| 1 | 4-C ₆ H ₄ Me | 94 | 98 | 3p ; 88 |
| 2 | 4-C ₆ H ₄ F | 92 | 99 | 3q ; 87 |
| 3 | 3-C ₆ H ₄ Cl | 89 | 98 | 3r ; 83 |
| 4 | 4-C ₆ H ₄ Br | 83 | 98 | 3s ; 78 |
| 5 | 4-C ₆ H ₄ NO ₂ | 00 | - | 3t ; - |
| 6 | 4-C ₆ H ₄ COOMe | 00 | - | 3u ; - |
| 7 | 4-C ₆ H ₄ CF ₃ | 00 | - | 3v ; - |
| 8 | C ₅ H ₄ N | 00 | - | 3w ; - |

^a Reaction conditions: **1a** (2 mmol), **2b-i** (2 mmol), nanosized zeolite beta (100 mg), toluene (1 mL), 120 °C, 3 h, sealed vial. ^b Conversion and selectivity based on GC. ^c Isolated yields.

The reusability of the catalyst is one of the most significant properties for the industrial applications and environmental considerations. The catalyst (nanosized zeolite beta) was easily separated from the reaction mixture by simple filtration. Further, recycling of catalyst was carried out by performing the reaction of aniline with phenylacetylene under standard reaction conditions and the reused catalyst showed consistent

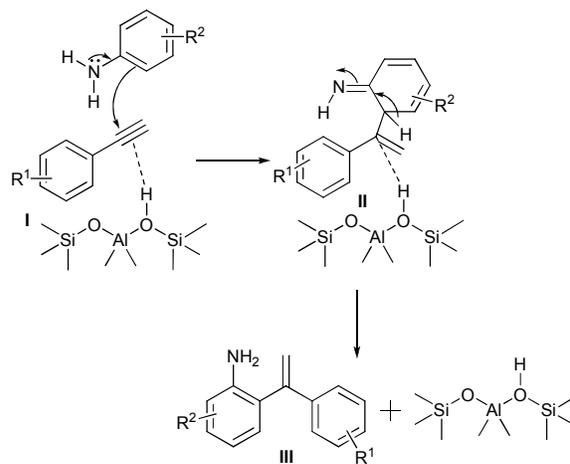
activity even after fifth reuse (Table 4). The XRD analysis of reused catalyst matched well with fresh catalyst, thus suggesting that crystallinity of the reused catalyst are comparable to the original material (*see the supporting information* Fig. S1). There was no leaching of aluminium or silicon from nanosized zeolite beta observed and confirmed by elemental analysis.

Table 4 *ortho*-Alkenylation of aniline with phenylacetylene-reusability of the catalyst^a

| Entry | Cycle | Conversion 1a (%) ^b | Selectivity 3a (%) ^b | 3a Yield (%) ^c |
|-------|--------|--|---|----------------------------------|
| 1 | First | 95 | 97 | 90 |
| 2 | Second | 92 | 98 | 88 |
| 3 | Third | 93 | 98 | 89 |
| 4 | Fourth | 90 | 97 | 85 |
| 6 | Fifth | 91 | 99 | 87 |

^a Reaction conditions: **1a** (2 mmol), **2a** (2 mmol), nanosized zeolite beta (100 mg), toluene (1 mL), 120 °C, 3 h, sealed vial. ^b Conversion and selectivity based on GC. ^c Isolated yields.

The plausible reaction mechanism for the *ortho*-alkenylation of anilines with phenylacetylene over nanosized zeolite beta is illustrated in Scheme 1. It is assumed that alkyne (**I**) adsorbs on the Bronsted acid sites of zeolite, which subsequently reacts with aniline to give the intermediate **II**. Finally, the resulting intermediate **II** restoring its aromaticity to produce the respective *ortho*-alkenylated product **III**.



Scheme 1 Plausible reaction mechanism for the *ortho*-alkenylation of anilines with aromatic terminal alkynes.

Conclusions

In summary, a simple and efficient protocol for the *ortho*-alkenylation of anilines with aromatic terminal alkynes over nanosized zeolite beta has been successfully developed. The scope and limitations of this process are demonstrated with various substituted anilines and aromatic alkynes. However, the substrates (anilines or alkynes) having strong electron-withdrawing groups were unsuccessful with this catalytic system (except 4-nitroaniline). This method demonstrates

several notable advantages including use of non-hazardous and reusable catalysts, higher yields of the desired products, high atom economy, simple work-up procedure and mild reaction conditions, which make it an attractive and useful alternative to the existing method.

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Notes and references

- (a) R. M. Roberts and A. A. Khalaf, *Friedel-Crafts Alkylation Chemistry*, Marcel Dekker, New York, 1984; (b) R. Taylor, *Electrophilic Aromatic Substitution*; Wiley, New York, 1990; (c) H. Heaney, *Comprehensive Organic Chemistry*, Pergamon, Oxford, 1991, Vol. 2, pp 733; (d) H. Wynberg, *Comprehensive Organic Chemistry*, Pergamon, Oxford, 1991, Vol. 2, pp 769; (e) O. Meth-Cohn and S. P. Stanforth, *Comprehensive Organic Chemistry*, Pergamon, Oxford, 1991, Vol. 2, pp 777; (f) H. Ishibashi and M. Ikeda, *M. Rev. Heteroatom Chem.*, 1996, **14**, 59.
- T. Sugawara, *J. Synth. Chem. Jpn.*, 1978, **36**, 480.
- (a) C. Hausch and G. Helmkamp, *J. Am. Chem. Soc.*, 1951, **73**, 3080; (b) C. Hausch, D. G. Crosby, M. Sadoski, A. Leo and D. Percival, *J. Am. Chem. Soc.*, 1951, **73**, 704; (c) L. Guo Qiang and N. H. Baine, *J. Org. Chem.*, 1988, **53**, 4218.
- (a) R. Smith and T. livinghouse, *J. Org. Chem.*, 1983, **48**, 1554; (b) P. D. Magnus and N. L. Sear, *Tetrahedron*, 1984, **40**, 2795; (c) J. B. Jiang, D. P. Hesson, B. A. Dusak, D. L. Dexter, G. J. Kang and E. Hamel, *J. Med. Chem.*, 1990, **33**, 1721.
- (a) R. Sarma and D. Prajapati, *Chem. Commun.*, 2011, **47**, 9525; (b) C. Simona; N. J. Clayden, B. Manfred and W. A. Joseph, *Chem. Commun.*, 2009, **7**, 797.
- A. Arienti, F. Bigi, R. Maggi, E. Marzi, P. Moggi, M. Rastelli, G. Sartori and F. Tarantola, *Tetrahedron*, 1997, **53**, 3795.
- (a) A. Dyer, *An introduction to zeolite molecular sieves*, Wiley, Chichester, 1988; (b) D. W. Breck, *Zeolite molecular sieves*, Wiley, New York, 1974; (c) C. S. Cundy and P. A. Cox, *Chem. Rev.*, 2003, **103**, 663; (d) W. E. Farneth and R. J. Gorte, *Chem. Rev.*, 1995, **95**, 615.
- (a) K. Smith, A. Musson and G. A. DeBoos, *Chem. Commun.*, 1996, 469; (b) G. Bellusi, G. Pazzuconi, C. Perego, G. Girotti and G. Terzoni, *J. Catal.*, 1995, **157**, 227; (c) A. M. Camiloti, S. L. Jahn, N. D. Velasco, L. F. Moura and D. Cardoso, *Appl. Catal.*, A. 1999, **182**, 107; (d) S. Mintova, V. Valtchev, T. Onfroy, C. Marichal, H. Knozinger and T. Bein, *Microporous Mesoporous Mater.*, 2006, **90**, 237; (e) K. P. de Jong, C. M. A. M. Mesters, D. G. R. Peferoen, P. T. M. van Brugge and C. de Groot, *Chem. Eng. Sci.*, 1996, **51**, 2053.
- G. Majano, S. Mintova, O. Ovsitser, B. Mihailova and T. Bein, *Microporous Mesoporous Mater.*, 2005, **80**, 227.
- (a) J. Kecht, B. Mihailova, K. Karaghisoff, S. Mintova and T. Bein, *Langmuir*, 2004, **20**, 5271; (b) M. Tsapatsis, M. Lovallo, T. Okubo, M. E. Davis and M. Sadakata, *Chem. Mater.*, 1995, **7**, 1734; (c) L. Tosheva, V. P. Valtchev, *Chem. Mater.*, 2005, **17**, 2494.
- (a) J. P. Gilson and E. G. Derouane, *J. Catal.*, 1984, **88**, 538; (b) J. H. Kim, T. Kunieda and M. Niwa, *J. Catal.*, 1998, **173**, 433.
- (a) N. Narender, K. S. K. Reddy, M. A. Kumar, C. N. Rohitha and S. J. Kulkarni, *Catal. Lett.*, 2010, **134**, 175; (b) K. V. V. K. Mohan, N. Narender and S. J. Kulkarni, *Microporous Mesoporous Mater.*, 2007, **106**, 229; (c) K. V. V. K. Mohan, N. Narender and S. J. Kulkarni, *Green Chem.*, 2006, **8**, 368; (d) N. Narender, K. V. V. K. Mohan, R. V. Reddy, P. Srinivasu, S. J. Kulkarni and K. V. Raghavan, *J. Mol. Catal. A: Chem.*, 2003, **192**, 73; (e) N. Narender, P. Srinivasu, S. J. Kulkarni and K. V. Raghavan, *J. Catal.*, 2001, **202**, 430; (f) N. Narender, P. Srinivasu, S. J. Kulkarni and K. V. Raghavan, *Green Chem.*, 2000, **2**, 104; (g) M. Naresh, M. M. Reddy, P. Swamy, M. A. Kumar, K. Srujana, C. Durgaiah and N. Narender, *Catal. Commun.*, 2015, **61**, 41.
- M. M. Reddy, M. A. Kumar, P. Swamy, M. Naresh, K. Srujana, L. Satyanarayana, A. Venugopal and N. Narender, *Green chem.*, 2013, **15**, 3474.