Solid acid catalysts for fluorotoluene nitration using nitric acid

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Fluorotoluenes have been nitrated regioselectively in the liquid phase under mild conditions using solid acid catalysts. Excellent yields were obtained with 70% nitric acid as nitrating agent. Nitration of 2-fluorotoluene at 90 °C showed 55% conversion with 90% selectivity for 2-fluoro-5-nitrotoluene whereas 3-fluorotoluene showed more than 79% conversion even at 60 °C with 67% selectivity for 3-fluoro-6-nitrotoluene and 30% selectivity for 3-fluoro-4-nitrotoluene. In the case of 4-fluorotoluene, side chain nitration was observed instead of ring nitration with 53% conversion and 59% selectivity for 4-fluoro-α-nitrotoluene. Among the different catalysts studied for fluorotoluene nitration, Fe/Mo/SiO_2, MoO_3/SiO_2 and H-beta showed higher conversion and selectivity in all three isomers due to higher acidity. A recycling study of catalyst H-beta for nitration of 3-fluorotoluene showed no significant loss in conversion as well as selectivity even after 5 recycles indicating the high stability of the catalyst. Compared to the conventional process, fluorotoluene nitration over solid acid catalysts is a highly regioselective, clean and environmentally friendly process with a simpler work up procedure.

Introduction

Nitration of aromatic substrates is one of the most important and widely studied chemical reactions[1] and has been an active area of industrial chemistry for over a century. The nitration process is used for the production of many commercially important large volume nitroaromatics, which are vital intermediates for dyes, pharmaceuticals, perfumes, and pesticides and hence desired by industry. Despite this, industry still largely relies upon the early technology involving a mixture of nitric acid and sulfuric acid. Mixed acid nitration systems, however, have many disadvantages like low selectivity, overnitration, oxidized product formation and generation of environmentally hazardous waste.[2] Therefore it is essential to have an alternative nitration method, which will overcome these problems. The use of solid acid catalysts is a very attractive alternative because of the ease of separation, recyclability of the catalysts and improved regioselectivity.

Fluoronitrotoluenes are important due to their application as intermediates in the synthesis of antibacterial antibiotics, herbicides, drug intermediates, certain heterocyclics and also as electrophiles.[3–9] Major drawbacks of conventional nitration using fuming nitric acid are low conversion and poor selectivity.[10–12] In recent years there has been a spate of activity aimed at the development of new nitration methods using solid acid catalysts; however very limited success has been achieved. Comparatively very little attention has been given to nitration of fluorotoluenes using solid acid catalysts. Selective nitration of 2-fluorotoluene to produce 2-fluoro-5-nitrotoluene (90%) using nitric acid and acetic anhydride over H-beta zeolite has been reported.[13] However, the explosion hazards of acetyl nitrate and removal of the by-product (acetic acid) are drawbacks for its practical utilization.[12–13] Nitration of 3-fluorotoluene has been achieved using a similar method but with less selectivity for 3-fluoro-6-nitrotoluene (59–61%).[12–13] Lower regioselectivity was observed in the case of 4-fluorotoluene nitration using ionic liquids.[14] In continuation of our earlier efforts on nitration of aromatics,[15–18] the present work deals with nitration of fluorotoluenes and the results are discussed in the following section.

Results and discussion

Catalyst characterization

The MoO_3/SiO_2 catalyst prepared by a sol–gel process using ethyl silicate-40 as silica source showed the mesoporous (pore diameter 78 Å) nature of the material with a surface area of 145 $m^2\ g^{-1}$. The phase purity of the catalysts was investigated by X-ray diffraction analysis. The XRD pattern of H-beta matched well with the literature, confirming its phase purity. The XRD patterns of MoO_3/SiO_2 and $Fe_2O_3/MoO_3/SiO_2$ calcined at 500 °C showed the presence of a MoO_3 crystalline phase without any crystalline silica reflections indicating a high dispersion of MoO_3 on the amorphous silica support. The XRD pattern of B_2O_3/ZrO_2 calcined at 650 °C showed a cubic structure indicating stabilization of zirconia into a cubic phase by addition of boron. The absence of boron oxide peaks in the XRD suggests a high dispersion of B_2O_3 on zirconia. The XRD pattern of $CeO_2/Fe_2O_3/MoO_3$ calcined at 500 °C showed the presence of a two-phase system containing a crystalline MoO_3

Green Context

The nitration of aromatic compounds is one of the classic examples of an organic process where the principles of green chemistry need to be better applied. Hazardous reagents, dangerous waste and the potential for making explosive by-products all add to the difficulties of current processes. Here the use of solid acid catalysts for the commercially important nitration of fluorotoluene is described. The reaction is safer, more efficient and gives less waste. ***JHC***

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phase as the major component and Fe_2O_3 as the minor component without any CeO_2 reflections suggesting the formation of a solid solution or high dispersion of CeO_2 on molybdenum oxide. Fig. 1 shows the results of temperature programmed desorption (TPD) results of the catalysts which show the acidity of the catalysts to be in the order Fe/Mo/SiO_2 > Mo/SiO_2 > H-Beta > B_2O_3/ZrO_2 > Ce/Fe/Mo. However in case of H-beta even though the number of weak acid sites is less, the TPD shows desorption of ammonia at higher temperature suggesting the presence of strong acid sites compared to MoO_3/SiO_2. TPD results also show the presence of a few strong acid sites in the case of $Fe_2O_3/MoO_3/SiO_2$ and a lesser number of weak acid sites as compared to MoO_3/SiO_2.

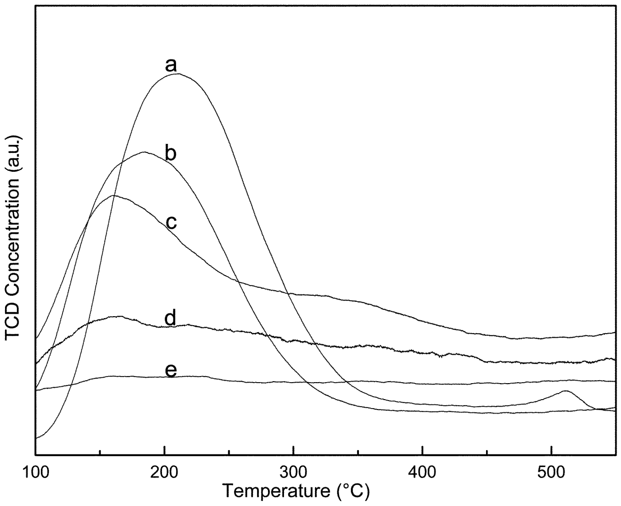


Fig. 1 Temperature programmed desorption of ammonia a) $Fe_2O_3/MoO_3/SiO_2$ b) MoO_3/SiO_2 c) H-Beta d) B_2O_3/ZrO_2 e) $CeO_2/Fe_2O_3/MoO_3$ (TCD = Thermal Conductivity Detector).

Nitration reactions

The liquid phase nitration of fluorotoluene was carried out using 70% (w/w) nitric acid in equimolar quantities in the presence and absence of catalysts. The recycling study was done by using H-beta catalyst.

Nitration of 2-fluorotoluene (2-FT). Nitration of 2-fluorotoluene (**I**, Scheme 1) on MoO_3/SiO_2 at 90 °C showed 55.24% conversion, which decreased to 11% when the reaction temperature was 60 °C. No reaction was observed with 30 wt% nitric acid at 60 °C. The results of liquid phase nitration of 2-fluorotoluenes using different catalysts are given in Table 1.

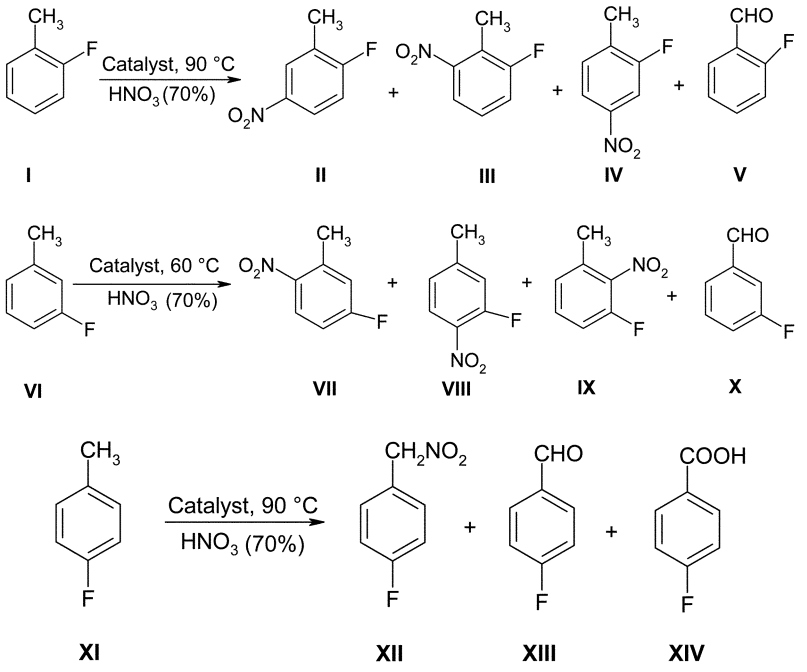
Table 1 Nitration of 2-fluorotoluene (**I**)[a]

Catalyst	2- FT conversion (wt%)	Product selectivities[b]			
		II	**III**	**IV**	**V**
Mo/SiO_2	55.25	88.9	2.7	3.2	5.2
Fe/Mo/SiO_2	54.9	84.7	4.1	8.4	2.8
B_2O_3/ZrO_2	35.6	95.6	1.7	1.2	1.5
Ce/Fe/Mo	36.1	90.8	3.7	3.9	1.7
H-Beta	31.8	89.4	3.8	4.7	2.1
Blank	14.7	88.7	4.0	4.3	3.0

[a] Reaction conditions: fluorotoluene/HNO_3 mole ratio = 1.0, HNO_3 (wt%) = 70, catalyst amount = 10% of fluorotoluene weight, temperature = 90 °C. [b] wt% by GC, reaction time = 20 h.

It is seen that maximum conversion of 55.24% with 88.9% selectivity for 2-fluoro-5-nitrotoluene (**II**) over MoO_3/SiO_2 was obtained due to the higher number of acid sites compared to other catalysts. The conversion of 2-fluorotoluene varied from 55.24% to 31.8% for various catalysts indicating the influence of the acidity on the reaction. However, the selectivity for **II** was in the range of 85–95%, which can be attributed to the *para* directing nature of fluorine, with almost no influence of the structure of the acid catalyst. The conversion was very low (15%) when the reaction was carried out in the absence of catalyst.

Nitration of 3-fluorotoluene (3-FT). Nitration of 3-fluorotoluene (**VI**) at 60 °C showed a maximum conversion of 79.2% with 67% selectivity for 3-fluoro-6-nitrotoluene (**VII**) and 29.5% selectivity for 3-fluoro-4-nitrotoluene (**VIII**) with H-beta catalyst. Increase in the reaction temperature from 60 to 90



Scheme 1

°C did not increase the conversion considerably, however the selectivity for nitro products decreased due to formation of oxidation products. The results of liquid phase nitration of 3-fluorotoluene at 60 °C over various solid acid catalysts are shown in Table 2. The conversion was in the range of 69.7–79.2% whereas the selectivity for nitro products was more or less the same (60–67%). The higher selectivity for **VII** and **VIII** can be attributed to the *ortho* and *para* directing nature of the fluorine and methyl groups. The highest selectivity for **VII** indicates the stronger influence of the *para* directing nature of fluorine as compared to methyl. Conversion increased from 61% to 79.5% when the reaction was carried out in the absence and presence of catalyst respectively.

Table 2 Nitration of 3-fluorotoluene (**VI**)[a]

Catalyst	3-FT conversion (wt%)	Product selectivities [b]			
		VII	**VIII**	**IX**	**X**
Mo/SiO_2	74.7	62.4	32.4	5.2	0.0
H-Beta	79.2	67.0	29.5	3.5	0.0
$Fe/Mo/SiO_2$	75.3	60.4	33.2	6.4	0.0
B_2O_3/ZrO_2	66.6	66.1	29.5	4.4	0.0
Ce/Fe/Mo	69.7	61.5	31.3	5.9	1.3
Blank	61.0	65.3	29.0	5.7	0.0

[a] Reaction conditions: fluorotoluene/HNO_3 mole ratio = 1.0, HNO_3 (wt%) = 70, catalyst amount = 10% of fluorotoluene weight, temperature = 60 °C. [b] wt% by GC, reaction time = 20 h.

Nitration of 4- fluorotoluene (4-FT). The liquid phase nitration results are given in Table 3. It is interesting to see that instead of ring nitration, side chain nitration is predominant. In the case of 4-fluorotoluene (**XI**), the *ortho* and *para* directing nature of methyl as well as fluorine strongly influences the nitration reaction. The formation of the side chain nitration product, 4-fluoro-α-nitrotoluene (**XII**), as a main product along with oxidation products such as 4-fluorobenzaldehyde **(XIII)** and 4-fluorobenzoic acid **(XIV)** with the formation of very small ring nitration products was observed. It is clearly seen that in 4-fluorotoluene both *para* positions (*para* to fluorine and methyl group) are occupied and not available for nitration. The positions available for nitration are *meta* either to fluorine or to methyl, which explains the absence of ring nitration products. Side chain nitration has also been observed in the liquid phase nitration of toluene[17] and *o*-xylene[18] with nitric acid using solid acid catalysts. Side chain nitration of polymethylbenzenes has been reported in which the polymethylbenzenes containing methyl groups in positions 1 & 4 often undergo side chain nitration along with ring nitration.[19] Even though in the absence of catalyst the conversion was found be 51%, the oxidation products were formed predominantly (51%) compared to nitration products (49%). This shows that in the absence of catalysts oxidation is favored whereas in the presence of catalyst nitration is favored.

Table 3 Nitration of 4-fluorotoluene (**XI**)[a]

Catalyst	4-FT conversion (wt%)	Product selectivities [b]			
		XII	**XIII**	**XIV**	Others
Mo/SiO_2	52.6	58.9	6.9	23.6	10.6
H-Beta	42.7	81.0	5.8	4.6	8.6
$Fe/Mo/SiO_2$	38.5	67.9	4.5	23.1	4.5
B_2O_3/ZrO	52.0	67.5	10.9	14.9	6.7
Ce/Fe/Mo	29.6	67.5	8.3	6.2	18.0
Blank	51.1	49.0	5.2	45.8	0.0

[a] Reaction conditions: fluorotoluene/HNO_3 mole ratio = 1.0, HNO_3 (wt%) = 70, catalyst amount = 10% of fluorotoluene weight, temperature = 90 °C. [b] wt% by GC, reaction time = 20 h.

A comparative study of all the three isomers showed, as expected, maximum conversion for 3-fluorotoluene whereas in the case of 4-fluorotoluene preferential side chain nitration was observed rather than ring nitration. This trend in the reactivity is correlated to the availability of the *ortho* and *para* positions with respect to fluorine. In 3-fluorotoluene both these positions are available which results in higher reactivity (70–80% conversion). In case of 2-fluorotoluene both *ortho* and *para* positions with respect to fluorine are *meta* to the methyl group and *vice versa* reducing its reactivity to a considerable extent (31 to 55% conversion). The catalyst structure and acid strength have less influence on conversion and product distribution.

During the recycling study the catalyst H-beta was recycled five times and the conversion of 3-fluorotoluene decreased from 79% to 75% without any appreciable change in product selectivity showing the stability of the catalyst in the reaction environment. The results of the recycling study are given in Table 4.

Table 4 Effect of catalyst recycling [a]

Cycle	Catalyst weight/ mg	Conv. of 3-FT (wt%)	Product selectivities [b]			
			VII	**VIII**	**IX**	**X**
Fresh	220	79.2	67.0	29.5	3.5	0.0
1st	209	79.1	66.8	28.9	4.3	0.0
2nd	197	78.5	68.0	29.2	2.8	0.0
3rd	185	77.1	66.7	30.1	3.0	0.2
4th	174	74.9	65.8	29.7	3.9	0.6

[a] Reaction conditions: catalyst: H-Beta, 3-fluorotoluene/HNO_3 mole ratio = 1.0, HNO_3, (wt%) = 70, catalyst amount = 10% of 3-fluorotoluene weight, temperature = 60 °C. [b] wt% by GC, reaction time = 20 h.

Experimental

Catalyst preparation and characterization

Commercially available H-beta zeolite (Si/Al = 30) was procured from United Catalyst India Ltd. MoO_3/SiO_2 (MoO_3: 20 wt%) was prepared by dissolving 35.28 g of ammonium molybdate in 150 ml hot distilled water and adding it dropwise to a solution of 120 g ethyl silicate-40 (CAS registry No. 18954-71-7) as a silica source in 50 ml isopropyl alcohol with constant stirring. The resulting greenish gel was air dried, ground and calcined at 500 °C in air in a muffle furnace for its use in nitration reactions.

$Fe_2O_3/MoO_3/SiO_2$ was prepared by the same procedure as above with addition of a solution of 5.65 g of ferric nitrate in isopropyl alcohol with constant stirring to the solution of ammonium molybdate. The resulting gel was air dried, ground and calcined. Borate zirconia catalyst was prepared by the procedure reported earlier.[18] The mixed metal catalyst $CeO_2/Fe_2O_3/MoO_3$ was prepared by the procedure mentioned elsewhere.[20]

The catalysts were characterized for their physical and chemical properties using X-ray diffraction analysis (XRD) (Rigaku, Miniflex, Cu-Kα radiation) and temperature programmed desorption (TPD) of ammonia (Micromeritics Autochem 2910). In a general procedure for NH_3-TPD, the catalyst was placed in a quartz tube (0.4–0.5 diameter fraction) and was activated in a helium atmosphere (70 ml min^{-1}) from 30 to 500 °C followed by cooling the sample to 80 °C and a dose of 10% ammonia in helium was passed for 30 min then heated to 100 °C for 10 min to remove physisorbed ammonia. After cooling down to 80 °C, the TPD program (10 °C min^{-1}, up to 750 °C) was started.

Reaction study

All liquid phase nitration reactions were carried out in a batch reactor, under atmospheric pressure. In a typical run: 20 mmol fluorotoluene (2.2 g), 20 mmol nitric acid (1.8 g, 70 wt%) and freshly activated catalyst (10 wt%, 0.22 g, based on fluorotoluene) were continuously stirred in a 50 ml two-necked round-bottomed flask maintained at the required temperature under atmospheric pressure. For the recycling study, after each cycle the catalyst was filtered, washed with acetone, dried at 100 °C and reused for the next cycle. The samples were periodically collected, neutralized with sodium hydrogen carbonate and analyzed by gas chromatography (Perkin Elmer autosystem XL, equipped with capillary column PE-1, 30 m, 0.25 mm ID, 1 μm film thickness and flame ionization detector). Products were also confirmed by GC/MS (SHIMADZU, DB-I column) and GC/IR (Perkin Elmer Spectrum 2001, column: DB-1, 25 m, 0.32 mm ID) and ^{1}H NMR (BRUKER, 500 MHz, using TMS as internal standard in $CDCl_3$).

The side chain nitrated product **XII** was isolated by column chromatographic separation using silica gel (60 mesh) column (3 × 35 cm) using ethyl acetate–petroleum ether (5 : 95) as eluent. A white crystalline product was obtained, yield: 1.02 g, 32%; ^{1}H NMR : δ 5.40 (s, 2 H); δ 7.11 (t, J = 8.34 Hz, 2 H); δ 7.44 (dd, J = 8.34 Hz, 2 H); *m/z*; 155 (M^+)

Conclusion

Fluorotoluenes are nitrated in the liquid phase in good yields with higher regioselectivity under mild conditions over H-beta zeolite and different solid acid catalysts using stoichiometric quantities of 70% nitric acid. The conversion is governed by the acid strength of the solid acid catalyst and the selectivity by the availability of the *para* position with respect to fluorine because of the stronger *para* directing nature of fluorine compared to methyl. Since the available ring positions in the case of 4-fluorotoluene are *meta* to both fluorine and methyl groups, side chain nitration of methyl group is observed instead of ring nitration. The results of nitration of fluorotoluenes using solid acid catalyst clearly demonstrate the influence of the relative positions of fluorine and methyl on the product distribution.

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