Zeolite-mediated regioselective nitration of phenol in solid state

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Abstract

Phenol (**I**) is nitrated regioselectively by fuming nitric acid inside the cages of faujasite zeolites. While nitration as hexane slurry in CsY and molecular sieve 5 Å leads to predominant formation of *para*-nitrophenol (**III**), a remarkable *ortho*-selectivity is observed in solid state nitration to yield exclusively *ortho*-nitrophenol (**II**). Loading level of the substrate inside the supercage alters significantly the relative yield of the various products. Other advantage of this zeolite-mediated nitration include significant reduction in polynitration and absence of mixed nitrating agents. © 2002 Elsevier Science B.V. All rights reserved.

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1. Introduction

Nitration of aromatic substrates is a widely studied reaction of great industrial significance as many nitro-aromatics are extensively utilised and act as chemical feedstocks for a wide range of useful materials such as dyes, pharmaceuticals, perfumes and plastics. A major problem [1] associated with the earlier technology is the use of corrosive liquid phase nitric acid–sulphuric acid mixture, responsible for the generation of large amounts of wastes, which are costly to treat. Overnitration, oxidation of by-products and poor selectivity are other associated problems. This necessitates the need for new, novel and simpler methods for nitration which can overcome the problems pointed out earlier. Other liquid phase applications involving in situ generated acyl nitrates are actively considered and their bulkiness is expected to lead to selectivity. Heterogeneous catalysts based on aluminosilicates, which are environmentally friendly, are other attractive alternates.

Claycop (copper(II) nitrate supported on K10-montmorillonite) has been used [2] in the nitration of toluene with high *para*-selectivity in the presence of acetic anhydride in carbon tetrachloride. Lanthanide(III) triflate (which operates by generating triflic acid, a very strong acid) is also employed [3] but the chlorinated solvents are required and the selectivity is poor.

Zeolites, with their well defined cages and channels, find extensive applications [4–6] in organic reactions, either as an active participant or as an inert support. Zeolite-based solid acid catalysts are potentially attractive due to the easy removability of substrate/product, catalyst recycling and possible regioselectivity due to their constraining environment. In the nitration of toluene, large pore mordenite [7] gives 60% selectivity using benzoyl nitrate in carbon tetrachloride. Smith et.al. have used H$^+$-form of zeolite β and acetyl nitrate for the highly regioselective *para*-nitration of toluene [8,9]. Quantitative yield of mononitration under mild conditions, very good

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selectivity, recovery and reuse of the catalysts are other advantages. Recently, novel nitration systems composing of nitric acid, trifluoroacetic anhydride and H-β are reported [10] for the nitration of deactivated aromatic compounds. The *para*-selective nitration of halogenobenzenes using a nitrogen dioxide–oxygen–zeolite H-β/HY system is also reported [11]. Zeolite-assisted nitration of neat toluene and chlorobenzene with a nitrogen dioxide/molecular oxygen system is reported [12] and a remarkable enhancement of *para*-selectivity is observed. The same group also reports, in the double Kyodai nitration of the same substrates over zeolites, a high preference for the 2,4-dinitro isomer at the second nitration stage [13].

In some of the earlier studies, a polar solvent such as acetonitrile is employed which tends to retain the substrate in the solvent phase rather than in the interior of the zeolite cages. Also, nitration of arenes with strongly activating groups (wherein polynitration is a serious handicap to selective nitration) in zeolite environment is not explored. With these goals in mind, nitration of phenol (**I**) inside the cages/channels of zeolite media using fuming nitric acid is carried out and the results are presented below.

2. Experimental

In a typical experiment, to a solution of **I** in hexane (5 ml) kept at 0–5 °C, activated zeolite (500 mg, preheated to 450 °C in a muffle furnace) is added and kept stirring as a hexane slurry. A known amount of fuming nitric acid is added and the solution is magnetically stirred for 30 min while maintaining the temperature at 0–5 °C. After bringing the reaction mixture to room temperature, the hexane portion is removed and overnight extraction of the zeolite using dichloromethane is carried out.

The combined hexane and dichloromethane portion, after removal of the solvent, is analysed by GC (Shimadzu 17A Model, SE-30, 10% capillary column, FID detector, high purity nitrogen as the carrier gas). The retention time of **I** is taken as the internal reference.

Reactions in the solid state are carried out as follows: to a solution of **I** in hexane (5 ml), activated zeolite is added and the mixture stirred for 6 h. The solvent is then removed by rotary evaporation. To this solid sample (kept at 0–5 °C), nitric acid is added for a period of 5 min, with continuous shaking. The reaction mixture is kept aside for 30 min at room temperature and then subjected to overnight extraction with dichloromethane. Products are identified by their GC retention times and also by the co-injection with authentic samples. In all the zeolites, except CaY, the recovered mass balance is about 90%.

3. Results and discussion

3.1. Nitration in hexane slurry

As a deviant from some of the previous studies of zeolite-induced nitration of deactivated/weakly activated aromatic substrates, in the present study, HPLC grade hexane (non-polar) is chosen as the solvent of choice. This ensures the presence of **I** predominantly inside the cages/channels of zeolite, which are more polar. To demonstrate this, nitration is carried out at two different loading levels. At a lower loading level which corresponds to 3.6 molecules per supercage in NaY, picric acid (**IV**) is the major product followed by the *para*-nitrophenol (**III**). With NaX zeolites, the selectivity is less pronounced compared to the solution reaction and the amount of the *ortho*-isomer **II** increases at the expense of **III** and **IV** (Scheme 1). However, when the reaction is carried out inside the narrow channels of molecular sieve 5 Å and also in CsY (with much larger cations which reduce the cage size and are expected to exert steric hindrance to nitration), the formation of the *para*-isomer **III** is more pronounced. With more acidic CaY zeolites, conversion is low (isolated yield is only 50%) indicating stronger binding of the reaction mixture with the zeolite, thus limiting their utility in the present study. There is no reaction when 1:1 dilute HNO_3 is added, as the cages are blocked by water molecules.

At a higher loading level of **I** (corresponding to 39 molecules per supercage), the influence of the zeolite environment is lost. As the results in Table 1 indicate, in both the faujasite NaY and NaX zeolites, an identical product distribution (in which **II** is the major product followed by a significant amount of **IV**) is obtained. Thus, with excess amount of **I**, most of them are forced to stay outside the zeolite cage and nitration occurs, predominantly in the solution
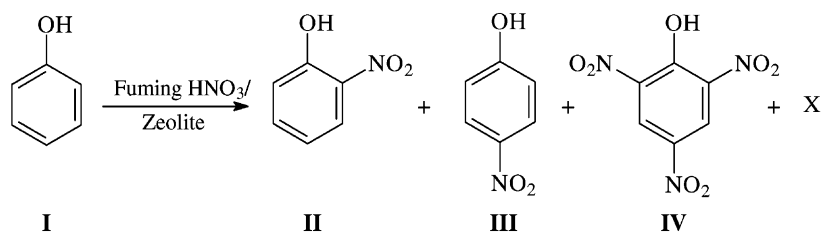
Scheme 1.

phase. This assumption is supported by the observation of a similar product distribution in the absence of zeolites under identical conditions. When a narrow channel molecular sieve (i.d. ~5 Å) is used, the amount of **III** has increased. It is relevant to note that zeolite-mediated *para*-selectivity within narrow pore zeolites as ZSM-5 is well known [14]. It is also likely that stronger binding with the more acidic CaA (Si:Al ratio 1) through the phenolic hydroxyl group, renders the *ortho*-position less accessible, leading to improved *para*-selectivity.

3.2. Solid state nitration

A remarkable regioselectivity in nitration is observed, when **I** is treated with fuming nitric acid in the presence of NaY zeolite in the solid state (Table 2). With a loading level corresponding to 8 molecules per supercage, **II** is the exclusive product. The significantly higher loading level coupled with the constrained environment of zeolite in solid state forbids free mobility of **I** inside the supercage and this results in exclusive formation of **II**. An increase in the

Table 1
Percentage conversion and product proportions in the nitration of I by fuming nitric acid[a]

Zeolite	Conversion (%)	Product proportions of[b]			
		II[b]	**III**[b]	**IV**[b]	X[c]
At lower loading level of PhOH[d]					
Nil	100	50	19	10	21
NaY	100	17	37	41	5
NaX	44	43	21	36	–
CaY[e]	57	8	2	–	90
CsY	76	16	76	8	–
Molecular sieve 5 Å	100	11	72	16	1
HNO₃ (1:1 diluted)	nil	–	–	–	–
At Higher Loading Level of PhOH[f]					
Nil	100	59	23	9	9
NaY	100	52	32	16	–
NaX	79	57	33	4	6
CaY	100	56	33	10	–
CsY	100	58	32	8	2
Molecular sieve 5 Å	100	48	43	8	1

[a] As a hexane slurry, at 0–5 °C for 30 min, with 500 mg of zeolite and 0.6 ml of fuming nitric acid; analysed by GC; error limit ±5%.
[b] Percentage conversions are normalised to 100; for structures of **II–IV** refer to Scheme 1.
[c] Unidentified products.
[d] With 70 mg of **I** (corresponds to a loading level of 3.6 molecules per supercage).
[e] Isolated yield is ~50% only.
[f] With 800 mg of **I** (corresponds to a loading level of 39 molecules per supercage).

Table 2

Percentage conversion and product proportions in nitration of (**I**) in the presence of NaY zeolite in solid state[a,b]

Amount of			Conversion (%)	Product proportions of[c]			
HNO_3 (ml)	**I** (ml)	NaY (mg)		**II**[c]	**III**[c]	**IV**[c]	X[d]
0.03	0.15	500	23	100	–	–	–
0.03	0.15	750	19	100	–	–	–
0.03	0.15	1000	12	100	–	–	–
0.03	0.08	500	13	100	–	–	–
0.06	0.15	500	40	69	17	11	3
0.09	0.15	500	59	52	16	27	5
0.12	0.15	500	58	25	9	54	12

[a] 0.15 ml (1.75 mmol) of **I** in 500 mg of NaY zeolite corresponds to a loading level of 8.2 molecules per supercage. After the addition of HNO_3 at 0–5 °C for a period of 5 min, the solid sample is kept at room temperature for 30 min.

[b] Analysed by GC; error limit ±5%.

[c] Percentage conversions are normalised to 100; for structures of **II**–**IV** refer to Scheme 1.

[d] Unidentified products.

amount of nitric acid, while increasing the percentage conversion, decreases the regioselectivity. The amount of the **II** decreases, with a concomitant increase in the amount of **IV**. An increase in the amount of zeolite, while retaining the regioselectivity, however, causes a decrease in the percentage conversion. This may be due to the reduction in mobility and diffusion of the reagents in the solid environment. Regioselectivity in the solid state is also observed in the *X*-type faujasites too. For example, solid state nitration of **I** in NaX zeolite yields only **II**, (with a slight decreased percentage conversion, 19% compared to 23% in NaY zeolite). The result is also independent of the reaction scale. For example, doubling the amount of zeolite and the reagents, has also resulted in the same **II** (20% conversion), without sacrificing the selectivity.

4. Conclusions

Thus, the observed results clearly indicate regioselective nitration of **I** in different zeolite environments. While solid state nitration enables exclusive formation of **II** in NaY, the same reaction in slurry in the presence of molecular sieve 5 Å and also with CsY (with a bulkier cation) leads to predominant formation of **III**. The relative yield of the various products also depends on the loading level of the substrate inside the supercage. Other advantages of the present study include significant reduction in polynitration, (for example 2,4-dinitrophenol which is a common by-product from ordinary nitration, is totally absent under the present conditions) the absence of mixed nitrating agents (no need for in situ generation of active nitrating species) and demonstration of the reaction inside the supercage (as evident from the absence of any significant variation in product distribution at a higher loading level, in which case the reaction is predominantly outside the cage). Thus, zeolites provide an ideal platform for mild, safer and regioselective nitration of an electron-rich substrate too, as in the case of substrate **I**. They are also reusable and are environmentally benign. Their ability to function as molecular sieves also provides an added advantage as they help in retaining the by-product, water in their cages.

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