Chapter 6

Nitration Of Phenol

Electrophilic aromatic substitution reactions are of considerable importance in the production of fine chemicals. However, the traditional processes suffer a number of disadvantages, such as low selectivity towards the desired product and the requirement for large quantities of mineral or Lewis acids as activators. In addition, these acids are responsible for corrosion problems within the plant and the generation of large volumes of spent reagents, which, given the current environmentally conscious climate, are increasingly unacceptable. Inorganic solid acids offer significant benefits for these processes by providing both effective catalysis and, in some cases, enhanced selectivity, and are easily removable from reaction mixtures. Herein, we report a green nitration process using transition metal loaded sulfated titania catalysts and try to correlate the activity with the acidity of these systems.

6.1 INTRODUCTION

Aromatic nitro compounds represent particularly versatile chemical feedstocks for a wide range of industrial products, such as pharmaceuticals, agrochemicals, dye stuffs and explosives. Nitration of organic compounds has long been a very active and rewarding area of research and is the subject of a large body of literature. Nitrophenols are important intermediates for the manufacture of drugs and pharmaceuticals[1]. Traditionally, nitration has been performed by a mixture of nitric and sulfuric acids (mixed acid method)[2].

However, the method is notoriously unselective for nitration of substituted aromatic compounds and the disposal of the spent acid reagents presents a serious environmental issue. The obvious disadvantage of the commercial manufacturing process currently used has led to a substantial effort to develop viable alternatives, using solid acid catalysts, other sources of NO_2^+, organic nitrating agents, other acids replacing H_2SO_4, etc. Compared to the conventional process, phenol nitration over solid acid catalyst is a clean and environment friendly process with a simpler workup procedure for quantitative isolation of the products. Solid acids effectively play the role of sulfuric acid in the reaction, assisting the formation of nitronium species. The general scheme of the reaction can be written as in figure 6.1.
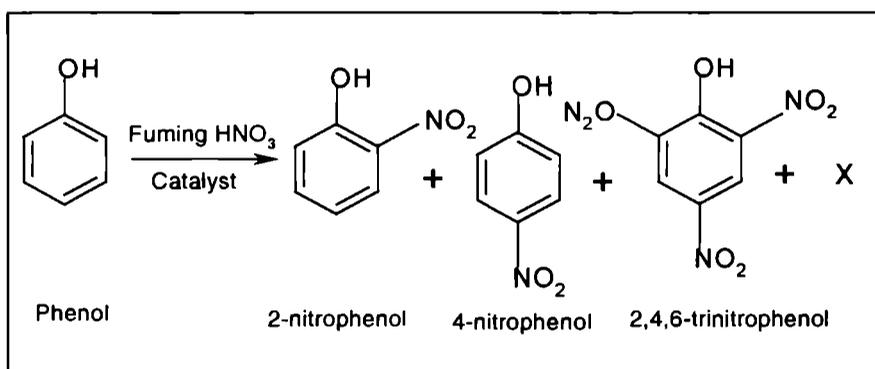

Figure 6.1 General scheme for nitration of phenol

Recently, novel nitration systems composing of nitric acid, trifluoroacetic anhydride and H-β are reported for the nitration of deactivated aromatic compounds[3]. The *para*-selective nitration of halogenobenzenes using a nitrogen dioxide-oxygen-zeolite H-β/HY systems is also reported[4]. Yadav *et al.*[5] proposed the selective synthesis of *para*-nitro derivative from chlorobenzene by using nitric acid over an electrically engineered sulfated zirconia carbon molecular sieve catalyst. Tomasz[6] has recently achieved a high yield and selectivity for the nitration of phenol to *p*-nitrophenol over metal oxide catalysts.

o-nitrophenol is an important starting material used in multiple step synthesis of valuable compounds[7]. Mixed metal oxides treated with sulfuric acid were found to be efficient for the nitration reaction[8]. The increase in the activity was attributed to the increase in the Brönsted acidity created by the high temperature treatment with sulfuric acid. The life of the catalyst depends on the support's capability of holding sulfuric acid to prevent its diffusion. Sato *et al.*[9] succeeded in maintaining high nitration activity of the supported sulfuric acid catalyst for more than two months by co-feeding trace amounts of sulfuric acid.

To our knowledge, very little study has been done on the regioselective nitration of phenol using nitric acid as a nitrating agent over solid acid catalyst. Phenol is selectively nitrated in solid phase to *o*-nitrophenol in high yield using concentrated nitric acid over solid acid catalysts. Regioselective nitration of phenol to *o*-nitrophenol as a special case has been studied under different reaction conditions.

6.2 PROCESS OPTIMIZATION

Nitration of phenol was carried out in the solid state. To a solution of phenol, activated catalyst was added and the mixture was mulled to get a homogeneous paste. This is kept at 0-5°C and nitric acid is added drop wise with continuous shaking. The reaction mixture is kept aside for 30 minutes at room temperature and then extracted with dichloromethane, after 2 h. Products are identified by G.C. analysis using BP-1 capillary column (12 m x 0.32 mm) and FID detector. Prior to injection in G.C. unreacted nitric acid in the reaction mixture was neutralized using sodium carbonate solution to a pH of 6-7. Reaction was done under varying conditions to optimize the reaction parameters.

I. Effect of Nitric acid Concentration

The catalytic activity of titania system was tested by varying the percentage of nitric acid. Concentrated, 1:1, 1:5 and 1:10 nitric acid in water were used for the reaction. As we expected, increase in the concentration of

nitric acid increases the conversion of phenol. The results are shown in figure 6.2. Selectivity towards *o*-nitrophenol increases when concentration of nitric acid increases.
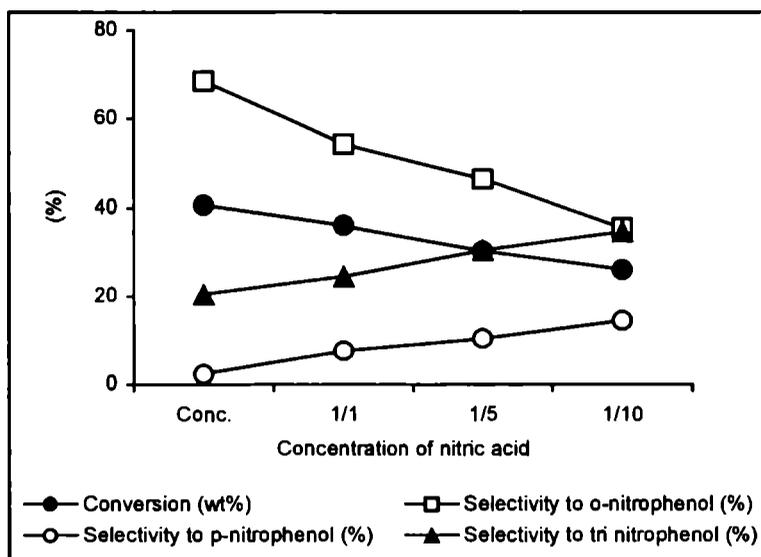

Figure 6.2 Influence of concentration of nitric acid on
conversion and product selectivity

Amount of catalyst: 0.1 g T, temperature: 0°C. Reaction time: 2 h, phenol: nitric acid: 1:1.

Previous reports suggest the absence of any significant alteration of the product selectivity with change in the concentration of nitrating agent[10]. However, a slight alteration of product selectivities was observed in this case when the nitric acid concentration was varied. The selectivity for *o*-nitrophenol decreased from 68.58 to 54.32% when the nitric acid concentration changes from concentrated to 1:1.

The approximate charge distribution of phenonium ion arising from the protonation of benzene as calculated by Olah and co-workers[11] is shown in figure 6.3. If used as a model for the arenium ion in the electrophilic aromatic substitution, the *para* substituent has a greater effect on the adjacent carbon than an *ortho*

substituent. In the absence of other effects, this would predict a product ratio higher than 33 for the *para* isomer and less than 67 for the *ortho* isomer.
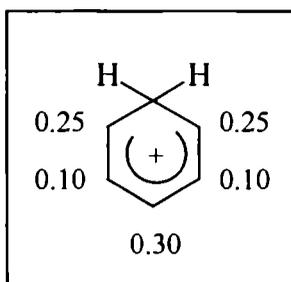

Figure 6.3 Approximate charge distribution in the phenonium ion

ii. Effect of Volume Ratio

Phenol to nitric acid ratio influences the percentage conversion and selectivity of the products. We varied the amount of nitric acid (concentrated) from 0.5 to 5 mL keeping the volume of phenol as 1 mL. The results are summarized in table 6.1. As the amount of nitric acid increases, conversion also increases. When 5 mL of nitric acid is used, the conversion is 60.62%, but the selectivity towards *ortho* isomer showed a constant decline, as the volume of nitric acid changes from 0.5 to 5 mL (from 78.94 to 23.77%). An increase in the amount of nitric acid, though increases the percentage conversion, decreases the regioselectivity.

Volume of phenol was changed in order to know its effect on the percentage conversion and selectivity. On increasing the volume of phenol from 0.5 to 5 mL, keeping the volume of nitric acid constant, the percentage conversion decreases. On the other hand the selectivity towards *o*-nitrophenol increases. For further studies we used an optimum volume ratio of phenol: nitric acid as 1:1 in which the selectivity towards *o*-nitrophenol is maximum with respect to percentage conversion.

Table 6.1 Influence of volume ratio on the catalytic activity and product selectivity

Phenol : HNO_3	Conversion of phenol (wt%)	Selectivity (%)		
		o-nitrophenol	p-nitrophenol	trinitrophenol
1:5	60.62	23.77	18.57	38.64
1:2	51.38	39.49	10.54	27.93
1:1	40.74	68.58	2.31	20.54
1:0.5	33.78	78.94	-	17.32
5:1	21.41	75.98	-	12.63
2:1	34.58	70.62	-	15.48
1:1	40.74	68.58	2.31	20.54
0.5:1	54.10	48.63	9.64	28.75

Amount of catalyst: 0.1 g T, Reaction temperature: 0°C, Reaction time: 2 h,
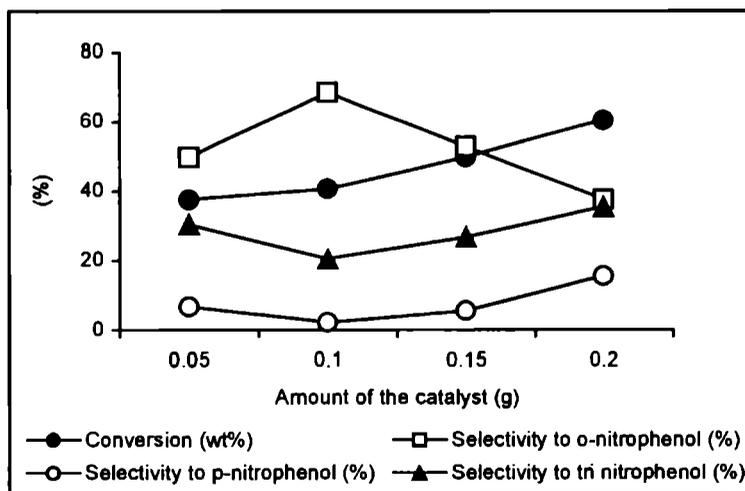
iii. Effect of Amount of the Catalyst.

Figure 6.4 Influence of amount of the catalyst on conversion
and product selectivity

Amount of the catalyst plays an important role in any catalytic reaction. An increase in the amount of the catalyst proved beneficial for the reaction as evident from figure 6.4. The conversion increases with increase in the amount of catalyst. But the selectivity towards o-nitrophenol initially increases and after an optimum amount of the catalyst, it declines. Thus an optimum amount of 0.1g is sufficient for the reaction to take place.
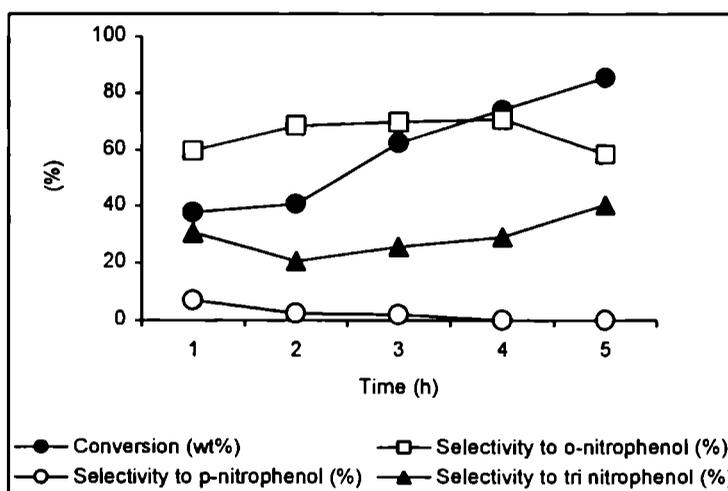
IV. Effect of Time on Stream-Deactivation study

Figure 6.5 Deactivation study on conversion of phenol and product selectivity

After the reaction, the products were extracted with dichloromethane at different time intervals. The results are furnished in figure 6.5. As the reaction time increases from 2 to 5 h there is an increase in the conversion. The selectivity to o-nitrophenol remains as such in the initial period. As time increases the o-nitrophenol selectivity decreases. Meanwhile 2,4,6-trinitrophenol selectivity increases and after 24 h, the major product is 2,4,6-trinitrophenol.

6.3 COMPARISON OF DIFFERENT SYSTEMS

Tables 6.2 and 6.3 present the results of nitration of phenol over the prepared systems under the optimized reaction conditions. From the results it is clear that the sulfated titania systems comprising transition metal oxides show good activity towards nitration of phenol. Pure titania shows the least activity.

Table 6.2 Influence of the type of metal loaded in the nitration of phenol

Systems	Conversion of phenol (wt%)	Selectivity (%)		
		o-nitrophenol	*p*-nitrophenol	2,4,6-trinitrophenol
T	40.74	68.58	2.31	20.54
ST	85.60	92.35	3.85	1.35
STCr(3)	87.79	90.78	2.38	1.16
STMn(3)	80.21	89.51	5.88	2.56
STFe(3)	70.77	84.06	6.08	1.54
STCo(3)	86.53	94.02	2.07	2.85
STNi(3)	85.00	92.65	1.69	3.28
STCu(3)	88.61	97.67	-	1.11
STZn(3)	83.82	91.75	1.39	4.48

Amount of catalyst: 0.1 g T, Reaction temperature: 0°C, Reaction time: 2 h,
Phenol: Concentrated nitric acid: 1:1.

Maximum conversion is observed for the system with 6 wt% metal content. The highest conversion is found to be 90% for STCu(6) and STCr(6). The conversion then reduces slightly for 9 wt% loading. Preferential formation of *ortho* isomer is observed in all cases. When the reaction was carried out without catalyst, the conversion was low (34%) with nearly equal amounts of

ortho- and *para-* isomers. This suggests the influence of solid acid catalysts on the conversion and selectivity.

Table 6.3 Influence of amount of metal loading in the nitration of phenol

Systems	Conversion of phenol (wt%)	Selectivity (%)		
		o-nitrophenol	p-nitrophenol	2,4,6-trinitrophenol
STCr(6)	90.00	97.51	-	1.37
STMn(6)	84.64	96.94	1.02	1.12
STFe(6)	80.82	80.47	4.57	3.27
STCo(6)	89.22	94.19	4.08	1.04
STNi(6)	88.76	94.31	3.18	2.08
STCu(6)	90.00	98.26	-	1.38
STZn(6)	87.80	84.17	5.24	2.07
STCr(9)	89.00	95.57	2.04	1.69
STMn(9)	82.46	86.74	6.49	1.89
STFe(9)	77.61	70.98	10.08	4.16
STCo(9)	88.56	90.98	5.43	1.54
STNi(9)	86.26	94.57	2.47	2.16
STCu(9)	89.00	95.36	-	3.50
STZn(9)	85.43	80.65	6.28	3.64

Amount of catalyst: 0.1 g T, Reaction temperature: 0°C, Reaction time: 2 h,
Phenol: Concentrated nitric acid: 1:1.

Esakkidurai *et al.*[12] reported regioselective nitration of phenol in solid state over modified zeolites. Sato *et al.*[13] examined various metal oxides and found that TiO_2 or ZrO_2 as an essential component for the vapour phase nitration of benzene using aqueous nitric acid. Dagade *et al.*[14] reported the nitration of phenol over different solid acids using 30% nitric acid. Sato *et al.*[8]

proved that Brönsted acid sites are the active sites for the vapour phase nitration. The same authors reported that metal oxides treated by sulfuric acid at 500°C such as $SO_4^{2-}/[TiO_2\text{-}MoO_3]$, $SO_4^{2-}/[TiO_2\text{-}WO_3]$ and SO_4^{2-}/TiO_2 show increase of nitration activity. The increase of the nitration activity is attributed to the increase in acidity of the catalysts by SO_4^{2-} treatment. Brei and coworkers[15] observed that the catalytic activity correlate with the acidic strength for the nitration of benzene over WO_3/ZrO_2 catalysts.

A closer scrutiny clearly establishes a crude association between the catalytic activity and the amount of Brönsted acid sites as obtained from the thermodesorption studies of 2,6-DMP. The reason for the low activity for the titania is the low acidity of the system. The active site for the nitration by nitric acid is the Brönsted acid sites. However, the high activity cannot be explained simply by the solid acidity (acid strength and acid amount) of the catalyst.
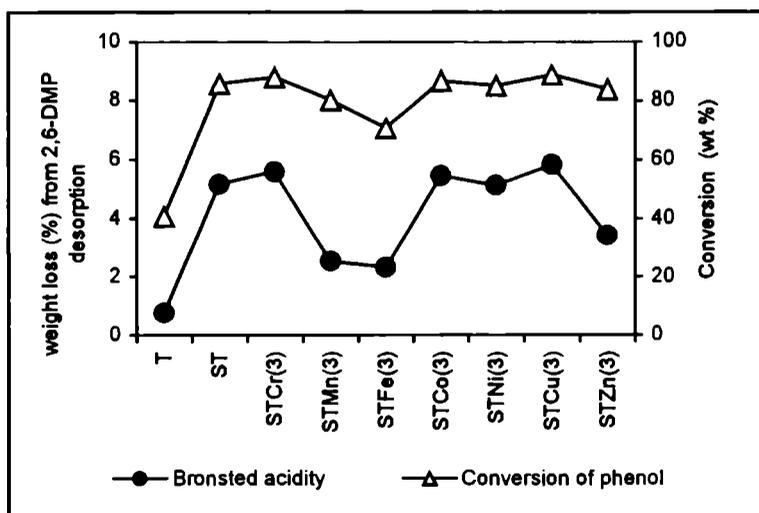

Figure 6.6 Correlation between conversion of phenol and Brönsted acidity

The product selectivity remained almost constant irrespective of the nature of the metal incorporated. With increase of the metal oxide content, the acidity of the catalyst increases up to 6 wt%, and then gradually decreases.

This difference in the nitration activity can be explained by the difference in the acidity strength. The correlation between the nitration activity and the Brönsted acidity is given in figures 6.6 and 6.7. The typical Brönsted acid catalyst namely 80% tungstioic acid on SiO_2, was examined by Sato *et al.*[13] as a reference catalyst, and it was found to have low activity due to low dispersion of heteropolyacids on SiO_2.
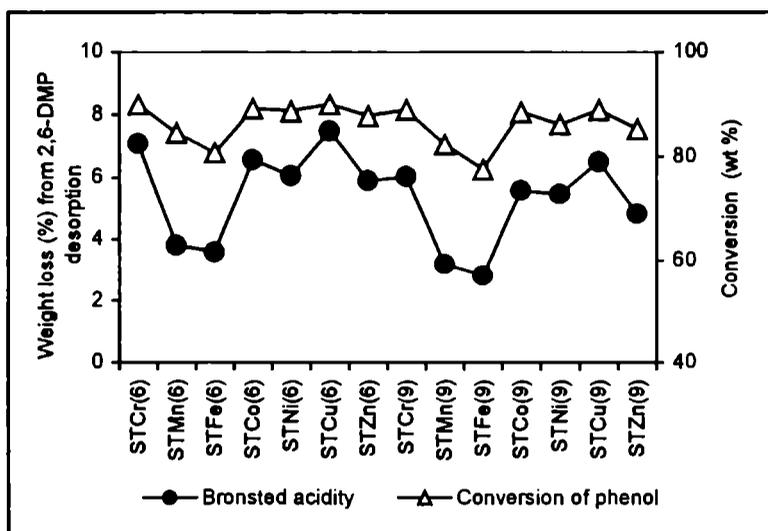

Figure 6.7 Correlation between conversion of phenol and Brönsted acidity

Among the various catalysts examined for the nitration of phenol, copper and chromium loaded catalysts are found to be most active. The life of various catalysts depends on the support's capability of holding sulfuric acid to prevent its effusion. Even on very good supports like silica gel, silica sand, etc., the sulfuric acid effuses slightly and gradually, and the activity of the sulfuric acid catalyst supported on these carriers is suddenly lost after a certain time on stream[9].

6.4 MECHANISM OF NITRATION REACTION

The nitration proceeds *via.* nitronium ion mechanism, in which the nitronium ion is generated by the interaction of nitric acid with the Brönsted acid sites and thus catalytic activity depends on Brönsted acidity. A close examination of the experimental results suggests a simple correlation between the Brönsted acidity of the systems and the catalytic activity towards nitration (figures 6.6 and 6.7). The Brönsted acid sites were found to have an influential hand on the reaction. Fairly strong acidity is necessary for formation of nitronium ion from nitric acid in the reaction conditions and the nitration activity is proportional to the acid amount.
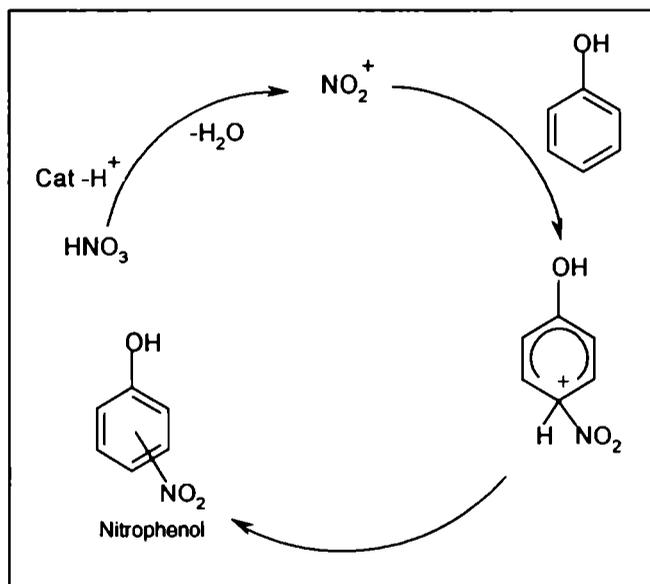

Figure 6.8 Plausible mechanism for the nitration of phenol using nitric acid

Brei *et al.*[15] explained that strong Brönsted sites are necessary for an effective formation of intermediate NO_2^+ ions from nitric acid. Attraction between cationic species and aromatic compounds are well known and originate from the fact that the 'edge' of the aromatic ring is positively charged, and the 'face' is negatively charged[16]. Because of the electronegative hydroxyl

group of phenol, the electron cloud of the aromatic ring is pulled towards this group. This will make the approach by the positively charged attacking species, the nitronium ion, more favorable. A plausible mechanism for the reaction is suggested in figure 6.8.

6.5 CONCLUSION

In conclusion, we have discovered a very efficient nitration process in the presence of sulfated titania catalysts under mild reaction conditions. Thus, it is much eco-safer protocol of nitration. The key points of the investigation can be summarized as:

≴ Regioselective nitration of phenol using HNO_3 over solid acid catalyst without any use of acetic anhydride/acylnitrate, metal nitrates or H_2SO_4 is a comparatively clean and environmental friendly process.

≴ Phenol is selectively nitrated to *o*-nitrophenol in high yields with nitric acid over sulfated titania catalysts.

≴ The catalytic activity is influenced significantly by the reaction parameters like concentration of nitric acid, amount of the catalyst, molar ratio and time on stream.

≴ A predominant formation of the *ortho* isomer was observed in all the cases suggesting involvement of the statistical factors in determining the relative product selectivity.

≴ The nitration proceeds *via* nitronium ion mechanism, and the increase of nitration activity can be attributed to the increase of Brönsted acidity by the sulfation of metal oxides.

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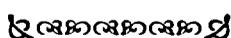
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