para-Selective nitration of halogenobenzenes using a nitrogen dioxide–oxygen–zeolite system

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The nitration of halogenobenzenes using zeolite Hβ or zeolite HY as a solid inorganic catalyst and a combination of liquid nitrogen dioxide and gaseous oxygen as the nitrating reagent leads to high yields and significant *para*-selectivities in a relatively clean process for aromatic nitration.

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 turn 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. Major efforts are therefore being made towards developing processes that can reduce the volumes of spent liquors produced. Inorganic solids can offer significant benefits for these processes by providing both effective catalysis and, in some cases, enhanced selectivity. Additionally they are easily removed from reaction mixtures and in some cases recycling is possible. For example, we have utilised zeolites to enhance the *para*-selectivity in chlorination,[1] bromination,[2] acylation[3] and methanesulfonylation[4] reactions of simple aromatic substrates.

Aromatic nitro compounds represent particularly versatile chemical feedstocks for a wide range of industrial products, such as pharmaceuticals, agrochemicals, dyestuffs and explosives. Traditionally, nitration has been performed by a mixture of nitric and sulfuric acids (mixed acid method).[5] 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. In order to address these problems several alternative methods for aromatic nitration have been developed recently. For example, lanthanide triflates have been used to catalyse nitration with nitric acid, which avoids the use of large volumes of sulfuric acid in the process.[6] However, this provides no enhancement of selectivity. Selectivity of the nitration process can be enhanced by solid catalysts such as clays, but primarily zeolites, which can improve selectivity using alkyl nitrates,[7] acyl nitrates,[8] or even nitric acid itself.[9,10] We have reported the use of zeolite Hβ in conjunction with a mixture of acetic anhydride and nitric acid, which currently offers the best combination of yield and *para*-selectivity for nitration of simple aromatic compounds.[11] None of these methods, however, are totally devoid of disadvantages.

Another approach towards clean nitration involves the use of dinitrogen tetroxide in combination with oxygen or ozone as an oxidant.[12] The method where ozone is employed most likely involves dinitrogen pentoxide, as this is known to be a highly active nitrating agent. The method utilising oxygen is less clear cut and requires the use of tris(pentane-2,4-dionato)iron(III) (Fe(acac)$_3$) as a catalyst in an organic solvent.[13] In principle, this could lead to a highly atom-efficient process [eqn. (1)], but it is not regioselective. Therefore, we decided to study the use of dinitrogen tetroxide as a nitrating agent in the presence of zeolites, in order to determine if they were able to catalyse the process and impart *para*-selectivity.

$$4\text{ArH} + 2\text{N}_2\text{O}_4 + \text{O}_2 \xrightarrow{\text{Catalyst}} 4\text{ArNO}_2 + 2\,\text{H}_2\text{O} \qquad (1)$$

Zeolites have been used before in the vapour phase nitration of aromatic compounds using nitrogen dioxide. However, this process did not involve oxygen, was complicated, required a high flow rate for the carrier gas (N_2, 880 ml min^{-1}) and showed poor *para*-selectivity.[14] We now report that certain zeolites can indeed catalyse the process of nitration, as shown in eqn. (1), whilst simultaneously providing enhanced *para*-selectivity.

Initially, an attempt was made to reproduce approximately the conditions of Suzuki for nitration of chlorobenzene. Liquid N_2O_4 (approx. 10 ml) was condensed into a trap at −78 °C and was then warmed to 0 °C. Fe(acac)$_3$ (0.355 g) and chlorobenzene (10 mmol) were then added, the system was flushed with oxygen and the mixture was stirred at 0 °C for 48 h. The product thus obtained contained nitrochlorobenzenes in proportions (2-:3-:4-nitrochlorobenzene proportions of $32:<1:67$) that approximated to those reported by Suzuki, but also showed significant quantities of a product based upon nitration of acetylacetone.

We then carried out similar reactions in which various zeolites were used as catalysts instead of Fe(acac)$_3$ in an attempt to determine which zeolite, if any, would be the most applicable to *para*-selective aromatic nitration. Zeolite β and zeolite Y have three dimensional channels and large pore sizes and were selected on this basis. Mordenite, which has linear large pores, and ZSM-5, which has a medium pore size, were chosen for comparison. Additionally, variation of the cation type was undertaken, with H^+, Na^+, K^+ and NH_4^+ being used in the case of zeolite β, and H^+ and Na^+ in the case of zeolite Y. Finally, zeolite ZSM-5 was tested with two specific Si/Al ratios. Thus, the effects of pore size, channel structure, acidity, cation size and Si/Al ratio could all be assessed. A reaction in the presence of chromatographic silica was also included for comparison. The results are shown in Table 1.

As shown in Table 1, reaction occurred in the presence of all of the zeolites, and all of the reactions gave higher yields than in the absence of any catalyst. The large, three-dimensional-pore zeolites gave higher yields, comparable with those achieved with Fe(acac)$_3$ as catalyst, but the medium pore zeolites and the linear large pore zeolite gave lower yields, as did the silica. All of the zeolites demonstrated higher *para*-selectivity than that obtained with Fe(acac)$_3$, except for NH_4β. This last result may reflect the fact that this was the only zeolite not calcined (heated in air to a high temperature), since this would have caused loss of ammonia and formation of Hβ.

Mordenite and ZSM-5 gave lower *para*-selectivities as well as lower yields, which probably reflects more restricted diffusion through the pores and competition from reaction at the external surface of the solid. The selectivity was also low for the reaction in the presence of silica. The ZSM-5 sample with the higher Si/Al ratio gave a higher *para*-selectivity than that with the lower ratio, possibly because of the process of dealumination, which would have opened up the pore structure of

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Table 1 The effect of zeolite type on the nitration of chlorobenzene[a]

Zeolite	Si/Al	*t*/h	Conversion (%)[b]	Yield (%)[b]	Proportions[b]		
					ortho	*meta*	*para*
None[c]	—	50	6	2	39	0	61
SiO_2[c]	—	50	40	28	29	< 1	70
Hβ	25	50	100	90	14	< 1	85
Naβ	24	50	100	96	15	0	85
Kβ	24	50	97	92	21	0	79
NH_4β	25	50	76	70	30	1	69
HY	30	50	100	91	16	2	82
NaY	28	50	100	91	16	1	83
HMord.	10.5	50	36	28	27	0	73
HZSM-5	50	72	44	42	28	2	70
HZSM-5	150	72	48	32	20	< 1	79

[a] All reactions were carried out with zeolite (1.0 g), chlorobenzene (10.0 mmol), 1,2-dichloroethane (30 ml) and nitrogen dioxide (*ca.* 10 ml) at 0 °C. [b] Calculated by quantitative GC. [c] For comparison.

the zeolite, causing it somewhat to resemble the larger pore systems. However, the yield with the higher Si/Al ratio sample was less, possibly because of the lower density of effective catalytic sites. Interestingly, the nature of the cation present appeared to have a negligible effect on the reactions, the H^+, Na^+ and K^+ forms of the zeolites giving very similar results for each reaction where comparison was possible. Evidently, the process does not rely upon strong acid catalysis and does not depend significantly on cation size. Perhaps the role of the active site is merely to bring together the reagents and substrates within the confines of the pores by simple co-adsorption. Alternatively, perhaps the active site facilitates cleavage of dinitrogen tetroxide to give monomeric nitrogen dioxide, which has been suggested as the active reagent in vapour phase reactions.[15]

Zeolites Hβ and Naβ produced the greatest selectivity for *para*-chloronitrobenzene (85%) and the highest yields (90 and 96%). Therefore, zeolite Hβ was tested with a range of other substrates. The results are shown in Table 2.

Table 2 The nitration of toluene, benzene and halogenobenzenes with nitrogen dioxide and zeolite Hβ in 1,2-dichloroethane[a]

Substrate	*t*/h	Conversion (%)[b]	Yield (%)[b]	Proportions[b]		
				ortho	*meta*	*para*
Toluene	24	100	85	53	2	45
Benzene	45	55	50	—	—	—
Fluorobenzene	48	100	95	7	0	93
Chlorobenzene	48	98	95	14	< 1	85
Bromobenzene	48	> 99	94	22	< 1	77
Iodobenzene	48	99	95	37	1	62

[a] All reactions were carried out with zeolite (1.0 g), substrate (10.0 mmol), 1,2-dichloroethane (30 ml) and nitrogen dioxide (*ca.* 10 ml) at 0 °C. [b] Calculated by quantitative GC.

After 24 h toluene had been completely consumed and produced a reasonable yield of mononitrotoluenes (85%). The *para*-selectivity was fairly low, though greater than for mixed acid nitrations. The reaction with benzene was slow, being only *ca.* 50% complete after 48 h. However, all the halogenobenzenes gave good yields and reasonable *para*-selectivities. This work therefore demonstrates that zeolites β and Y, with H^+, Na^+ or K^+ cations, can be efficient inorganic catalysts for the nitration of halogenobenzenes with dinitrogen tetroxide and oxygen and produce high *para*-selectivities and yields compared to classical nitration methods.

Furthermore, this method represents a low energy and potentially clean synthesis of halonitrobenzenes using an easily recycled solvent and catalyst system. However, at this preliminary point the reactions involve a large excess of dinitrogen tetroxide, long reaction times and the use of an undesirable chlorinated solvent. Therefore, our future efforts in this area will be concentrated on minimising these factors.

The reaction of chlorobenzene illustrates the general procedure for the nitration process. In an ice-water cooling bath was placed a 100 ml round-bottom flask containing a mixture of chlorobenzene (10 mmol), zeolite (1.0 g), and 1,2-dichloroethane (30 ml). The flask was flushed with oxygen gas for 20 min at 0 °C. Liquid nitrogen dioxide (*ca.* 10 ml, *ca.* 280 mmol) was added quickly all at once to the stirred mixture, and the flask was connected to an oxygen gas balloon. After 50 h at 0 °C, the mixture was filtered through a medium porosity sintered glass funnel, and the filtrate was diluted with water. 1,2-Dichloroethane was added and the organic phase was separated and dried over magnesium sulfate. The isomer distribution was determined by gas chromatography (PU 4400) (octadecane was added as an internal standard).

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