Superior methodology for the nitration of simple aromatic compounds

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Simple aromatic compounds such as benzene, alkylbenzenes and halogenobenzenes are nitrated in quantitative yield and with high *para*-selectivity in a solvent free process by use of a stoichiometric quantity of nitric acid and acetic anhydride at 0–20 °C in the presence of zeolite beta as catalyst; the zeolite can be recycled and the only by-product is acetic acid, which is easily separated from the nitration product by distillation; the process is inexpensive and highly convenient and represents the best currently available methodology for the clean syntheses of a range of simple nitroaromatic compounds.

The chemical industry is experiencing increased pressure to reduce its negative impact on the natural environment.[1] Central to the case is the need for processes offering good methodology without excessive cost. For many chemical processes there is a need for the development of cleaner synthetic methods than are currently available. Nitration of aromatic compounds is a pertinent example. Here we report a new synthetic method which provides quantitative conversion of a range of simple aromatic compounds into their corresponding mononitro compounds, consumes only a stoichiometric amount of nitric acid, requires neither heating nor the use of a solvent, and utilizes a re-usable zeolite catalyst to enhance the *para*-selectivity of the process.

Nitration of aromatic compounds is one of the most widely studied and notoriously unselective of reactions.[2] Nitro compounds find uses in many industrial applications and *para*-isomers are commonly the more commercially desirable products. However, traditional methods make use of aggressive mixtures of sulfuric and nitric acids that tend to produce mixtures of mono- and poly-nitroaromatics and oxidative byproducts. Disposal of the waste products and 'spent' acids is environmentally unfriendly and can be costly.

Use of solid acid catalysts such as Nafion™ and other polysulfonic acid resins reduces the corrosive nature of the reaction mixtures but does not substantially improve regioselection for the *para*-isomer.[3] We have previously reported a method for *para*-selective nitration of some aromatic compounds using benzoyl nitrate and a zeolite catalyst.[4] For example, toluene was nitrated over large port mordenite in tetrachloromethane to give mononitrotoluenes in almost quantitative yield with over 60% of the *para*-isomer, compared to *ca.* 40% using traditional methods. A modification using ZSM-11 pre-treated with tributylamine is reported to result in excellent *para*-selectivity (98%) but, unfortunately, only in low yield.[5] A system using propyl nitrate over ZSM-5 with toluene as its own solvent can produce mononitrotoluenes in 54% isolable yield with good *para*-selectivity ($o:m:p$ = 5:0:95) but requires very large amounts of a commercially unavailable catalyst (ZSM-5 with Si/Al = 1000) and a 16 h reflux.[6] Copper(II) nitrate supported on montmorillonite clay quantitatively nitrates toluene in the presence of acetic anhydride but affords high *para*-regioselection only under conditions of high dilution and over a 120 h reaction time.[7]

The above methods are not commercially viable in general for manufacturing scale operation. We have therefore attempted to develop a novel process which uses nitric acid as the reagent, avoids excessive quantities of solvent or unacceptable reaction conditions (time, temperature) and makes use of the shape selective properties of a zeolite catalyst to improve the *para*-selectivity.

We chose mononitration of toluene as the test reaction during development of the method. Following the success of our previous work with benzoyl nitrate as the reagent[4] we decided to try *in situ* generation of acetyl nitrate from nitric acid and acetic anhydride according to eqn. (1). This would provide a

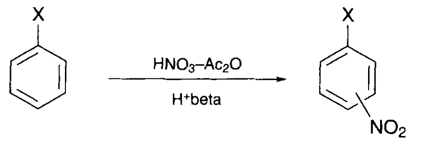
$$HNO_3 + (MeCO)_2O \rightarrow MeCO_2NO_2 + MeCO_2H \qquad (1)$$

cheaper reagent and avoid the need for its isolation or extraction. The amount of acetic anhydride was chosen so as to be the minimum that would allow quantitative conversion into acetyl nitrate and removal of any water present in the nitric acid used. As a consequence, the process would be solvent free and the only byproduct of the reaction would be acetic acid.

Many different zeolites were tested in the reaction under identical conditions and zeolite beta in its proton form was shown to be both the most active and the most highly selective of those tried. It was therefore selected for further study.

The order of addition of the materials had a significant effect on the *para*-selectivity of the process (see Table 1 for a selection of the orders tried). The best order involved pre-mixing the zeolite with nitric acid followed by addition of the anhydride and lastly the toluene. This is consistent with the formation of acetyl nitrate predominantly within the pores of the zeolite, where reaction subsequently takes place with the toluene.

The optimum conditions were applied to a range of aromatic substrates according to eqn. (2) The results are shown in



(2)

Table 2. As can be seen from the table, the reaction is very successful with a range of substrates of moderate activity. The yields in such cases are uniformly high and *para*-selectivities are amongst the highest on record for high yielding reactions.

Table 1 The effect of the order of addition of reagents on the nitration of toluene[a]

Order of introduction[b]	t/ min	Yield (%)	Product proportions (%)[c]		
			ortho	*meta*	*para*
A–B–C–D	30	>99	18	3	79
C–A–B–D	30	>99	24	3	73
B–C–A–D	30	>99	25	3	72
D–B–C–A	30	>99	35	4	62

[a] 35 mmol of toluene, 5 ml (53 mmol) of acetic anhydride, 35 mmol of nitric acid (90%), 1 g of zeolite H+beta. [b] A = nitric acid, B = H+beta, C = acetic anhydride, D = toluene. [c] Determined by GC.

Furthermore, the catalyst could be easily recovered and re-used by simple vacuum distillation of the reaction mixture. The second usage of the catalyst, with toluene as substrate, gave identical results to the first. By the fourth usage under the same conditions the yield was only slightly down, to 94%, and likewise the proportion of *para*-product, to 72%. A protocol involving replacement of 10–20% of used catalyst by a similar amount of new catalyst after each reaction would therefore provide very good results with minimal catalyst wastage.

The following procedure is representative. Nitric acid (2.45 g, 90%, 35 mmol) and dried H^+beta (1.0 g) were stirred together at 0 °C for 5 min. Addition of acetic anhydride (5 ml, 53 mmol) resulted in an exothermic reaction causing a temporary rise in temperature to *ca.* 10–15 °C. After a further 5 min the aromatic substrate (35 mmol) was added dropwise and the mixture was then allowed to warm to room temperature and stirred for a further 30 min. The products were obtained by direct vacuum distillation of the mixture, first at 30 mmHg to give the acetic acid byproduct and then at 0.2 mmHg, to give the nitro compound. The residual catalyst was then ready for re-use with no additional treatment necessary.

Table 2 The effect of X on the nitration of PhX according to eqn. (2)

X	*t*/min	Yield[a] (%)	Product proportions (%) *ortho*	*meta*	*para*
F	30	>99	6	0	94
Cl	30	>99	7	0	93
Br	5	>99	13	0	87
H	30	>99	—	—	—
Me	30	>99	18	3	79
Et	10	>99	15	3	82
^{i}Pr	30	>99	9	3	88
^{t}Bu	30	92	8	trace	92
Ph	30	70	trace	0	>99
NO_2[b]	120	13	1	92	7

[a] All yields are of isolated products following distillation. The identity of the products was established by GC, ^1H NMR, ^{13}C NMR and GC-MS, and proportions of isomers were determined by GC. [b] The reaction with nitrobenzene was carried out at 50 °C.

It is clear that the nitric acid–acetic anhydride–H^+beta system offers a highly efficient method for the nitration of a range of aromatic compounds of moderate activity. We believe that this is the best available methodology for such *para*-selective nitration reactions,[8] since it uses only stoichiometric quantities of nitric acid and acetic anhydride to give quantitative yields of isolated products with very high *para*-selectivity, the catalyst is re-usable, solvent is not needed and an aqueous work-up is not required.

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Footnote

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