A novel method for the nitration of deactivated aromatic compounds

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Novel nitration systems comprising nitric acid, trifluoroacetic anhydride and zeolite Hβ, with or without acetic anhydride, are described. The system having no acetic anhydride is more active and readily nitrates deactivated substrates such as nitrobenzene, benzonitrile, benzoic acid or 4-nitrotoluene to give predominantly the product substituted meta to the deactivating group.

The system incorporating acetic anhydride is more moderate in activity, and nitrates moderately deactivated systems such as halogenobenzenes quantitatively within two hours at ice–salt bath temperature, and provides very high selectivity for the para-nitratated product. This system also nitrates 2-nitrotoluene to give high selectivity for 2,4-dinitrotoluene production. Furthermore, the system can be used for direct double nitration of toluene and gives a 92% yield of 2,4-dinitrotoluene with a 2,4- : 2,6-dinitrotoluene ratio of 25 : 1. Even greater selectivity (96% yield and 70 : 1 selectivity) can be achieved in the latter reaction by conducting the reaction in one flask but in two stages, with trifluoroacetic anhydride added only in the second stage.

Introduction
The industrially important process of nitration is probably the most studied of all the electrophilic aromatic substitution reactions and yet industry still relies on early technology utilising large amounts of strong mineral acids, which has many disadvantages. Nitration reactions are notoriously unselective; they often lead to by-product formation from oxidation of the substrate; the acids are highly corrosive and used in excess; and work-up requires an aqueous washing step resulting in the production of acidic effluent which is environmentally unfriendly and costly to treat. However, with increasing pressure on industry to minimise the environmental impact of its processes, research has intensified on the replacement of the bulk acidic media by an acidic solid. As well as potentially catalysing a reaction, allowing it to proceed under milder, safer conditions, zeolites offer the possibility of influencing the regioselectivity of the reaction and minimising the environmental impact of the process.

Acidic solids have been used for selective nitration reactions, in particular the noninitiation of aromatic compounds. For example, claycop (copper(ii) nitrate supported on K10 montmorillonite clay) has been used to nitrate toluene with high para selectivity in the presence of acetic anhydride in tetra-chloromethane. More recently, the highly acidic zeolite Hβ has been found to catalyse the nitration of simple aromatic substrates, for example toluene, by a mixture of nitric acid and acetic anhydride at room temperature and provides improved selectivity towards the para position over traditional mixed-acid systems. This system offers excellent possibilities for nitration of substrates which are moderate in activity. However, it is not very successful with deactivated substrates.

We now report further research in this field, with the focus on the nitration of deactivated substrates and on the dinitration of toluene with regioselectivity towards 2,4-dinitrotoluene. Indeed, we have been able to develop an optimised nitration system for the nitration of such deactivated aromatic substrates and for highly selective dinitration of toluene to give 2,4-dinitrotoluene.

Normally, the nitration of deactivated compounds (and therefore the polynitration of toluene) is carried out using aggressive nitric acid–oleum mixtures. Nitroaromatics such as 1,3-dinitrobenzene and 2,4-dinitrotoluene are important intermediates for the production of industrially important chemicals and are used in the preparation of polymers, explosives, dyes, pharmaceuticals, agrochemicals and fragrances.

The dinitration of toluene with mixed acids produces 2,4- and 2,6-dinitrotoluenes in a ratio of 4 : 1, from which 2,4-dinitrotoluene is isolated for the manufacture of toluene disocyanate (TDI) and toluenediamine, both of which are used in the manufacture of polyurethanes. Zirconium and hafnium derivatives have been reported to be useful catalysts for the nitration of o-nitrotoluene, but ratios of 2,4- : 2,6-dinitrotoluene were modest (66 : 34). Nitrogen dioxide has been used to polynitrate aromatic compounds at low temperatures in the presence of ozone and a catalyst such as methanesulfonic acid. For example, nitrobenzene was nitrated to give a 99% yield of dinitrobenzene with regioselectivity o : m : p 8 : 91 : 1. A patent has reported the use of metal nitrates supported on clays for the nitration of aromatic compounds. One of the examples quoted was the dinitration of toluene using claycop, acetic anhydride, and nitric acid in the presence of carbon tetrachloride, producing dinitrotoluenes in a yield of 85% with a ratio of 2,4- : 2,6-dinitrotoluene of 9 : 1. The degree of nitration achieved depended on the amount of modified clay used and the reaction time. This method, however, requires a large excess of nitric acid, the use of carbon tetrachloride and long reaction times (6 hours in the case of the dinitration of toluene). Other examples quoted included the production of 1,3-dinitrobenzene from benzene in a 70% yield after 12 hours at room temperature.

The highest recorded selectivity for the direct nitration of toluene to 2,4-dinitrotoluene involves nitric acid over a zeolite β catalyst and gives a 2.4 : 2.6 ratio of 14. Full results are yet to be published.

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After our success in nitrating moderately active monosubstituted benzenes with benzoyl nitrate and acetyl nitrate, which are not reactive enough to take the nitration of toluene further than the first step, we decided to try trifluoroacetyl nitrate, which can be generated in situ from trifluoroacetic anhydride and nitric acid [eqn. (1)].

\[(CF_3CO_2)O + HNO_2 \rightarrow CF_3CO_2ONO_2 + CF_3CO_2H\]  

(1)

Although trifluoroacetyl nitrate is known to be more active than acetyl nitrate, it has not been widely used in nitration reactions. However, unreactive aromatic substrates, such as nitrobenzene and bromobenzene, have been successfully nitrated using fuming nitric acid and trifluoroacetic anhydride in equimolar proportions at 45–55°C. More nitrobenzene was formed in 65% yield from nitrobenzene, and bromobenzene was nitrated to give a mixture of nitrated products (o-nitro-, p-nitro- 24%, and the 2,4-dinitro-derivative 60%).

More reactive aromatic compounds such as anisole yielded predominantly diazonium salts when treated in a similar way. Toluene gave only traces of diazonium salts and no dinitration was reported.

Our hope was that the use of a zeolite might enhance the yields and selectivities available in nitration of deactivated substrates with trifluoroacetyl nitrate generated according to eqn. (1). We now report that this is indeed the case.

Results and discussion

Preliminary investigations

Our initial studies involved the nitration of p-nitrotoluene, which nitrates exclusively to give 2,4-dinitrotoluene. We found that the trifluoroacetyl nitrate mixture [eqn. (1)] was active enough to nitrate this substrate in high yield at room temperature without the need for a zeolite. In the case of the nitration of o-nitrotoluene, there were two main products, 2,4-dinitrotoluene and 2,6-dinitrotoluene. Again, we found that the trifluoroacetyl nitrate mixture alone was active enough to effect nitration. However, the presence of Hβ did improve the regioselectivity slightly towards the 2,4-isomer (2:4:2,6 ratio 2:1 compared to 2:1 without the zeolite), although it did not affect the overall reaction rate or the product yield very much.

There are two possible explanations for the lack of catalysis by the zeolite. 1) The pores of the zeolite are too small for the substrate to enter or for the dinitrated products to be formed within them. 2) The free solution reaction occurs so fast that the bulk of the reactants do not have time to diffuse into the pore system and so reaction occurs primarily in free solution or at the external surface of the zeolite.

If the latter explanation were correct, it should be possible to slow down the overall reaction by addition of a diluent such as dichloromethane or acetic anhydride, thereby giving the zeolite a better chance to exert an influence over the reaction. Indeed, addition of acetic anhydride led to a slower reaction and zeolite Hβ then exerted a greater influence over both the rate and selectivity.

The reaction was performed in the presence of a series of different zeolites under identical conditions and Hβ was found to be the best zeolite for regioselective nitration. Also, only a stoichiometric amount of nitric acid and the minimum amount of trifluoroacetic anhydride to achieve quantitative conversion to trifluoroacetyl nitrate were needed for complete reaction. This system was therefore chosen for more detailed study.

Nitration of o-nitrotoluene

Of the two main products from the nitration of o-nitrotoluene the 2,4-isomer is the more commercially desirable. Classically, using mixed acids, the ratio of 2,4-:2,6-isomers is about 2:1.

<table>
<thead>
<tr>
<th>Amount of AcO(_2)O/ml</th>
<th>Yield of dinitrotoluenes (%)</th>
<th>Proportions of isomers 2,4-:2,6:2,4-:2,6-ratio(^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>99</td>
<td>74:26:29</td>
</tr>
<tr>
<td>1.0</td>
<td>97</td>
<td>78:22:35</td>
</tr>
<tr>
<td>2.5</td>
<td>98</td>
<td>84:16:52</td>
</tr>
<tr>
<td>3.5</td>
<td>99</td>
<td>94:5.5:17</td>
</tr>
<tr>
<td>4.0</td>
<td>98</td>
<td>94:5.4:17</td>
</tr>
</tbody>
</table>

Reactions carried out using Hβ (1.0 g) o-nitrotoluene (17.5 mmol), nitric acid (17.5 mmol of 90%), TFAA (3.5 ml 24 mmol) and acetic anhydride (see table) at –10°C for 2 hours. By quantitative GC. \(^c\) Proportions of isomers (%) in the product mixture, determined by GC (to 2 significant figures). \(^d\) Ratio calculated directly from GC data.

As indicated above, the trifluoroacetyl nitrate mixture in the presence of zeolite quantitatively nitrated o-nitrotoluene with a slight improvement in the regioselectivity towards the 2,4- isomer (Table 1). On addition of acetic anhydride to the mixture (eqn. (2)), prior to addition of the substrate, the selectivity was improved further without detrimental effect on the overall reactivity. No further improvement in selectivity was observed after the volume of acetic anhydride added was about equal to that of the minimum amount of trifluoroacetic anhydride (Table 1).

The effect of the amount of zeolite was next investigated for a 17.5 mmol scale reaction using the optimal amount of acetic anhydride discovered above. As was expected, the amount of zeolite present directly affects reactivity and selectivity, with the highest ratio of 2,4-:2,6- being around 17:1 (Table 2). The selectivity steadily improved with increasing amount of zeolite until ca. 1 g was used, with larger amounts having only marginal additional effects.

In order to check whether the standard period of 2 hours used for the reactions thus far was actually required, a reaction using the same conditions as those described in Table 2, with 1 g of zeolite, was stopped after 1 hour. The yield of dinitrotoluenes was only 90%, and the proportion of 2,4-:2,6- was almost unchanged (16:6). Therefore, it appeared sensible to continue to use 2 hours for the reaction period.

<table>
<thead>
<tr>
<th>Amount of Hβ/g</th>
<th>Yield of dinitrotoluenes (%)</th>
<th>Proportions of isomers 2,4-:2,6:2,4-:2,6-ratio(^d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>16</td>
<td>66:34:2.0</td>
</tr>
<tr>
<td>0.25</td>
<td>93</td>
<td>84:16:5.1</td>
</tr>
<tr>
<td>0.5</td>
<td>94</td>
<td>88:12:7.3</td>
</tr>
<tr>
<td>0.75</td>
<td>93</td>
<td>93:6.5:14</td>
</tr>
<tr>
<td>1.0</td>
<td>99</td>
<td>94:5.5:17</td>
</tr>
<tr>
<td>1.5</td>
<td>99</td>
<td>94:5.4:17</td>
</tr>
<tr>
<td>2.0</td>
<td>99</td>
<td>94:5.5:17</td>
</tr>
<tr>
<td>3.0</td>
<td>99</td>
<td>94:5.4:17</td>
</tr>
</tbody>
</table>

Reactions were carried out using Hβ (see table), o-nitrotoluene (17.5 mmol), nitric acid (17.5 mmol of 90%), TFAA (3.5 ml 24 mmol) and acetic anhydride (3.5 ml 37 mmol) at –10°C for 2 hours. By quantitative GC. \(^d\) Proportions of isomers (%) in the product mixture, determined by GC (to 2 significant figures). \(^d\) Ratio calculated directly from GC data.
The effect of temperature on the reaction was also investigated and the results are reported in Table 3. At 20 °C, a decrease in yield was observed but with no effect on selectivity. This can be explained by loss from the system of trifluoroacetic anhydride, which has a boiling point of 39.5 °C. Therefore, lower temperatures are preferable. However, if the temperature is too low, then a marked decrease in reactivity is observed and so the optimal temperature was found to be around −10 °C (cooling in an ice−salt bath).

p-Nitrotoluene could also be nitrated with the optimised system used for o-nitrotoluene, but this reaction is much slower and so for quantitative yields it is quicker to use trifluoroacetic anhydride, nitric acid and zeolite Hβ (i.e. without addition of acetic anhydride). It was of interest to know if a common system could be developed, which could then be applied to the direct dinitration of toluene without the need to carry out a single step nitration of toluene [eqn. (3)] under conditions similar to those developed for the selective nitration of o-nitrotoluene, but using two equivalents of nitric acid. We also used a slightly smaller quantity of acetic anhydride, so as not to inhibit too much the further nitration of the less reactive p-nitrotoluene. The results are shown in Table 4.

As the results in Table 4 show, the reaction was very selective, producing dinitrotoluenes in almost quantitative yield and with high selectivity using 1 g zeolite, and still providing good selectivity even when only 0.5 g of zeolite was used. Nevertheless, the ratio of 2,4-:2,6-isomers was less than would be predicted if the first step were to give o- and p-nitrotoluenes in the published ratio for nitric acid−acetic anhydride−Hβ (ca. 4 : 1), and the p-nitrotoluene were to give only 2,4-dinitrotoluene while the o-nitrotoluene were to react as described in Tables 1−3, giving a 17 : 1 ratio of 2,4-:2,6-isomers. In this case the ratio expected for the overall process would be in the region of 98:2 to 99:1. It seemed likely that the problem was a less selective first step in the presence of trifluoroacetic anhydride. Therefore, a two-step sequence, in which trifluoroacetic anhydride was introduced only during the second step, was investigated.

**Dinitration of toluene in a single step**

The dinitration of toluene using mixed acids gives a mixture of isomers from the further nitration of the o-, m- and p-nitrotoluenes formed as intermediates. The predominant products are 2,4- and 2,6-dinitrotoluenes, formed in a ratio of 4 : 1. This ratio has been improved to 9 : 1 using claysop, nitric acid and acetic anhydride,7 and to 14 : 1 using nitric acid and zeolite Hβ,8 but yields are also lower in such systems. We attempted to carry out a single step nitration of toluene [eqn. (3)] under

\[
\text{CH}_3 \quad 2\text{HNO}_3, \text{Ac}_2\text{O}, \text{TFAA} \quad \text{Hβ, 2 h} \quad \text{CH}_3 \quad \text{NO}_2 \quad \text{NO}_2 \quad \text{CH}_3 \quad \text{O}_2\text{N} + \text{others}
\]

\((3)\)

\[
\text{CH}_3 \quad \text{NO}_2 \quad \text{NO}_2 \quad \text{CH}_3 \quad \text{HNO}_3, \text{Ac}_2\text{O} \quad \text{Hβ, 30 min} \quad \text{CH}_3 \quad \text{NO}_2 \quad \text{NO}_2
\]

\((4)\)

Indeed, when the reaction was carried out in this way, a 98% yield of dinitrotoluenes, with a 38 : 1 ratio of 2,4-:2,6-isomers was obtained.

To try to improve this selectivity even further we investigated the effect of addition of extra zeolite for the second step, and these results are shown in Table 5. Zeolite HY and zeolite Hβ, which are both large pore zeolites, were tried, but Hβ still proved to be the optimal zeolite, giving the highest selectivity towards the 2,4-isomer.

Using a two-step reaction, we have now improved the regioselectivity of the dinitration of toluene to give a ratio of 2,4-:2,6- of 70:1, with quantitative yields after 2 hours at around −10 °C.

Pure 2,4-dinitrotoluene could be isolated in 90% yield from this system simply by filtering the zeolite, concentrating the mother liquor, and recrystallization from acetone.

---

**Table 3** Effect of reaction temperature

<table>
<thead>
<tr>
<th>Temp/°C</th>
<th>Yield of dinitrotoluenes (%) a</th>
<th>2,4-</th>
<th>2,6-</th>
<th>2,4-:2,6-ratio a</th>
</tr>
</thead>
<tbody>
<tr>
<td>−78</td>
<td>2</td>
<td>92</td>
<td>8.4</td>
<td>11</td>
</tr>
<tr>
<td>−41</td>
<td>71</td>
<td>93</td>
<td>6.7</td>
<td>13</td>
</tr>
<tr>
<td>10</td>
<td>98</td>
<td>94</td>
<td>5.5</td>
<td>17</td>
</tr>
<tr>
<td>0</td>
<td>95</td>
<td>94</td>
<td>5.6</td>
<td>17</td>
</tr>
<tr>
<td>20</td>
<td>90</td>
<td>94</td>
<td>5.5</td>
<td>17</td>
</tr>
</tbody>
</table>

* Reactions were carried out using Hβ (1.0 g), o-nitrotoluene (17.5 mmol), nitric acid (17.5 mmol of 90%), trifluoroacetic anhydride (24 mmol) and acetic anhydride (3.5 ml, 37 mmol) at the temperature stated in the table for 2 hours. a By quantitative GC. Proportions of isomers (%) in the product mixture, determined by GC (to 2 significant figures). b Ratio calculated directly from GC data.

**Table 4** Dinitration of toluene according to eqn. (3) a

<table>
<thead>
<tr>
<th>Amount of zeolite (g)</th>
<th>Yield of dinitrotoluenes (%) a</th>
<th>2,4-</th>
<th>2,6-</th>
<th>2,4-:2,6-ratio a</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>98</td>
<td>89</td>
<td>6.4</td>
<td>14</td>
</tr>
<tr>
<td>1.0</td>
<td>98</td>
<td>92</td>
<td>3.8</td>
<td>24</td>
</tr>
</tbody>
</table>

* Reactions were carried out using Hβ (see table), nitric acid (35 mmol of 90%), acetic anhydride (24 mmol), trifluoroacetic anhydride (24 mmol) and toluene (17.5 mmol) at −10 °C for 2 hours. a By quantitative GC. Absolute yields of isomers (%) in the product mixture, determined by GC (to 2 significant figures); other isomers derived primarily from m-nitrotoluene make up the rest. b Ratio calculated directly from GC data.

**Table 5** Effect of addition of extra zeolite during the second step a

<table>
<thead>
<tr>
<th>Zeolite</th>
<th>Yield of dinitrotoluenes (%) a</th>
<th>2,4-</th>
<th>2,6-</th>
<th>2,4-:2,6-ratio a</th>
</tr>
</thead>
<tbody>
<tr>
<td>HY</td>
<td>98</td>
<td>95</td>
<td>2.5</td>
<td>38</td>
</tr>
<tr>
<td>Hβ</td>
<td>99</td>
<td>96</td>
<td>1.4</td>
<td>70</td>
</tr>
</tbody>
</table>

* Reactions were carried out using Hβ (1.0 g), nitric acid (17.5 mmol of 90%), acetic anhydride (24 mmol) and toluene (17.5 mmol) at room temperature for 30 minutes for the first step; then extra nitric acid (17.5 mmol, 90%), trifluoroacetic anhydride (24 mmol) and extra zeolite (1.0 g) at −10 °C for the second step. a By quantitative GC. Proportions of isomers by GC (to 2 significant figures), other isomers derived predominantly from m-nitrotoluene make up the rest. b Ratio calculated directly from GC data.
Nitration of other deactivated aromatic compounds

In view of the success in achieving selective conversion of o-nitrotoluene into 2,4-dinitrotoluene, and of the direct conversion of toluene into 2,4-dinitrotoluene, it was of interest to investigate the nitration of other deactivated substrates using the reagent system developed. Three reagent systems were considered: (i) nitric acid–acetylene–Hβ, as used in reactions of toluene and other moderately active substrates; (ii) nitric acid–trifluoroacetic anhydride–Hβ, as used in the further nitration of p-nitrotoluene; and (iii) nitric acid–trifluoroacetic anhydride–acetic acid–Hβ, as used in the selective nitration of o-nitrotoluene.

The nitric acid–acetylene–Hβ system has already been shown to be capable of nitrating moderately deactivated substrates such as halogenobenzenes, albeit more slowly and in somewhat lower yields than for toluene. However, when it was used under the standard conditions for the nitration of o-nitrotoluene, a substrate bearing both an activating and a deactivating substituent, it gave only 20% conversion, and with slightly lower selectivity for the 2,4-dinitrotoluene isomer than when trifluoroacetic anhydride was used. Furthermore, under the same conditions it gave only a small amount of different products when applied to nitrobenzene, a substrate bearing only a single, strongly deactivated substituent. In view of these results, no further attention was paid to this reagent system.

A series of deactivated monosubstituted benzenes was subjected to the system nitric acid–trifluoroacetic anhydride–Hβ [eqn. (5)]. These substrates included several meta-directing deactivating groups, as well as several ortho-directing halogenobenzenes. The results are shown in Table 6.

As the results in Table 6 show, the halogenobenzenes were all quantitatively nitrated under the reaction conditions. The selectivities for the para-isomer were good, but somewhat less than for the previously reported reaction involving acetylene anhydride, which is not surprising given the greater activity of the present reagent system. Reasonable yields of mononitrated products were also obtained from the meta-directing substrates under the standard conditions, and individual optimization of the reaction conditions would probably allow quantitative conversion in such cases. There was some increase in the amount of both the ortho- and para-isomers, in comparison to mixed acid nitration, for two of the substrates, but meta-nitro products were still vastly predominant.

Finally, attention was turned to the system nitric acid–trifluoroacetic anhydride–acetic acid–Hβ [eqn. (6)]. The same substrates were used, and the results of subjecting all six substrates to a standard set of conditions are given in Table 7. With the halogenobenzenes, the reactivity was largely unaffected by the addition of acetic anhydride, reactions being essentially quantitative under the standard conditions. However, improvement in the para-selectivity was observed compared with the reaction using only trifluoroacetic anhydride. From the mixed-acid nitration of chlorobenzene, the p:o ratio is 2, which is also observed in nitration using nitrogen dioxide, oxygen and Fe(acac),. This ratio has been improved using acetyl nitrate and zeolite Hβ to p:o = 13, and now the nitric acid–trifluoroacetic anhydride–acetic acid–Hβ system has been found to give the same high regioselectivity (Table 7) but in higher yield, more quickly and at a reduced temperature.

In the case of the meta-directing substrates, the reaction rates were slower in the presence of acetic anhydride and the yields were lower under the standard conditions. There was, in most cases, an increase in the proportion of the para-isomer, to a remarkable 19% in the case of benzonitrile, presumably as a result of shape-selectivity imposed on the transition state. In the case of benzoic acid, there was also an increase in the proportion of the ortho-isomer, possibly resulting from rearrangement of benzyol nitrate formed in situ. However, in all cases the meta-isomer was still vastly predominant, so there seems little reason to carry out reactions of deactivated, monosubstituted meta-directing substrates with this reagent system.

The remarkably high proportion of para-product from benzonitrile, and the excellent selectivity for 2,4-dinitrotoluene on nitration of 2-nitrotoluene with this system, however, encouraged us to try the reaction with 2-methylbenzonitrile. The reaction proved to be successful [eqn. (7)], giving almost quantitative conversion into mononitro products and a 2,4:2,6-cyanonitrotoluene ratio of 6.5, compared with only 1.8 in the case of mixed acids.

### Table 6 Nitration of PhX according to eqn. (5)*

<table>
<thead>
<tr>
<th>X</th>
<th>Yield (%)</th>
<th>2°</th>
<th>3°</th>
<th>4°</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO₂</td>
<td>72</td>
<td>5</td>
<td>88</td>
<td>7</td>
</tr>
<tr>
<td>COOH</td>
<td>86*</td>
<td>2</td>
<td>97</td>
<td>1</td>
</tr>
<tr>
<td>CN</td>
<td>54</td>
<td>13</td>
<td>74</td>
<td>13</td>
</tr>
</tbody>
</table>

* Reactions carried out using Hβ (1 g), substrate (17.5 mmol), nitric acid (17.5 ml, 17.5 mmol), and TFAA (3.5 ml, 17.5 mmol) at −10 °C for 2 hours. Total yield of mononitrated products by quantitative GC. Proportions of isomers (%) in the product mixture, determined by GC. By quantitative HPLC.

### Table 7 Nitration of PhX according to eqn. (6)*

<table>
<thead>
<tr>
<th>X</th>
<th>Yield (%)</th>
<th>2°</th>
<th>3°</th>
<th>4°</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO₂</td>
<td>25</td>
<td>2</td>
<td>91</td>
<td>7</td>
</tr>
<tr>
<td>COOH</td>
<td>74*</td>
<td>11</td>
<td>79</td>
<td>10</td>
</tr>
<tr>
<td>CN</td>
<td>17</td>
<td>10</td>
<td>71</td>
<td>19</td>
</tr>
</tbody>
</table>

* Reactions carried out using Hβ (1 g), substrate (17.5 mmol), nitric acid (17.5 ml, 17.5 mmol), TFAA (3.5 ml, 17.5 mmol) and acetic anhydride (3.5 ml) at −10 °C for 2 hours. By quantitative GC. Proportions of isomers (%) in the product mixture, determined by GC. By quantitative HPLC.
Conclusions

The use of nitrating systems containing nitric acid, trifluoroacetic anhydride and zeolite Hβ allows nitration of deactivated aromatic substrates. For monosubstituted benzenes carrying a meta-directing group (NO₂, CO₂H, CN), this system provides high yields of the mono-nitroderivatives. The normal preference for meta-substituted product is seen, though in some cases there may be a small increase in the amount of ortho- and/or para-products compared with mixed acid systems. The nitric acid–trifluoroacetic anhydride–Hβ system is also useful for nitration of 4-nitrotoluene to 2,4-dinitrotoluene.

For deactivated substrates of somewhat higher reactivity, such as halogenobenzenes, 2-nitrotoluene and 2-methylbenzonitrile, it is better to use a system that has been moderated by addition of acetic anhydride, in a volume approximately equal to that of the trifluoroacetic anhydride. The lower activity of the system allows greater control over the selectivity. Halogenobenzenes give almost quantitative mononitration with very high selectivity for the para-nitro products. 2-Nitrotoluene gives very high selectivity for 2,4-dinitrotoluene, while 2-methylbenzonitrile gives around 87% of 2-cyano-4-nitrotoluene. In both the latter two cases the selectivity for nitration at the 4-position (relative to the methyl) is much greater than for mixed acid systems.

By adaptation of the latter process it has proved possible to double nitrate toluene selectively without isolation of any intermediate. If the reaction is carried out in a single step, the yield of 2,4-dinitrotoluene is 92% and the ratio of 2,4-4,6-dinitrotoluenes is 25:1. The yield can be improved to 96% and the selectivity to 70:1 by carrying out the nitration in two stages, with the trifluoroacetic anhydride added only for the second stage. However, the reaction is still conducted all in one flask and without isolation of any intermediate. This is easily the most selective double nitration of toluene ever recorded.

It is recognised that trifluoroacetic anhydride’s volatility, toxicity and cost may render it unattractive for larger scale commercial processes, but in our previous work with acetic anhydride alone we showed that acetic acid could be recovered quantitatively, and recovery should be equally easy with the more volatile trifluoroacetic acid. In the earlier work we also showed that the zeolite could be reused several times, while acetic anhydride is consumed. The methods demonstrated here could therefore prove attractive, particularly for smaller scale syntheses.

Experimental

Nitration procedure: nitration using nitric acid, trifluoroacetic anhydride, acetic anhydride and zeolite Hβ

A cooled mixture (ice–salt bath, bath temp. = −10 °C) of acetic anhydride (3.5 ml, 37 mmol) and trifluoroacetic anhydride (3.5 ml, 17.5 mmol) was added to a stirring mixture of zeolite Hβ (1.0 g, Si:Al ratio = 12.5) and nitric acid (1.23 g, 90%, 17.5 mmol) with cooling in an ice–salt bath (temp. = −10 °C) and the mixture was stirred for 5 min at constant temperature. The substrate (17.5 mmol) was then added and the mixture was stirred for 2 h at around −10 °C. The zeolite was removed by suction filtration and washed with copious amounts of acetone. The mother liquors were combined.

The yields and compositions of the product mixtures were analysed by quantitative GC or HPLC using an internal standard (hexadecane or heptadecane in the case of GC and 4-hydroxybenzaldehyde in the case of HPLC), and identities were proved by comparison with authentic samples. The results are given in Table 6.

Nitration procedure: two-step nitration of toluene

Acetic anhydride (2.48 g, 24 mmol) was added to a stirring mixture of nitric acid (1.23 g, 90%, 17.5 mmol) and Hβ (0.5 g, Si:Al = 12.5) at 0 °C and the mixture was stirred for 5 min at constant temperature. Toluene (1.61 g, 17.5 mmol) was then added and the mixture was stirred for 2 h at around −10 °C. The zeolite was removed by suction filtration and washed with copious amounts of acetone. The mother liquors were combined.

The yields and composition of product mixtures were analysed by quantitative GC using hexadecane as the internal standard. The results are shown in Table 4.

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References


