

# Regioselective Nitration of Deactivated Mono-Substituted Benzenes Using Acyl Nitrates Over Reusable Acidic Zeolite Catalysts

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**Abstract** Nitration of benzonitrile was investigated using a nitric acid/acid anhydride/zeolite catalyst system under different reaction conditions. Trifluoroacetic and chloroacetic anhydrides were found to be the most active among the anhydrides tried. Also, zeolites H $\beta$  and Fe<sup>3+</sup> $\beta$  (Si/Al = 12.5) were found to be the most active catalysts. For example, nitration of benzonitrile with trifluoroacetyl nitrate under reflux conditions in dichloromethane gave 3- and 4-nitrobenzonitriles in quantitative yield, of which the *para*-isomer represented 24–28%. The yield of *para*-isomer was improved to 33% when passivated H $\beta$  was used under similar reaction conditions. This is easily the most *para*-selective nitration of benzonitrile ever recorded. Also, no *ortho*-isomer was formed under the conditions tried. The zeolite can be easily recovered, regenerated by heating and reused up to six times to give results similar to those obtained with a fresh sample of the catalyst. The nitration system was applied successfully to a range of deactivated mono-substituted benzenes to give *para*-isomers in significantly higher proportions than in the corresponding traditional nitration reactions.

**Keywords** Nitration · Deactivated mono-substituted benzenes · Acyl nitrate · Acidic zeolite catalysis · H $\beta$  · Regioselectivity

## 1 Introduction

Nitration of aromatic compounds is one of the most important and widely studied chemical reactions [1–5] because nitroaromatic compounds are intermediates for the production of industrially important chemicals such as polyurethanes, explosives, agrochemicals, pharmaceuticals, fragrances and dyes [6, 7].

The traditional method for nitration, involving use of a mixture of nitric and sulfuric acids, though still in widespread commercial use, suffers from many disadvantages, including the generation of large quantities of corrosive waste and in many cases the production of mixtures of isomers in which the most desirable one is not in high yield. This has stimulated much research aimed at development of alternative procedures that generate less waste and provide product mixtures in which the most desirable isomer (often the *para*-isomer) is much more abundant.

In the case of nitration of monosubstituted benzenes containing an *ortho/para*-directing substituent such as an alkyl or halogeno group much progress has been made [8–17]. For example, we have shown that nitration of toluene using a stoichiometric mixture of nitric acid and acetic anhydride over a reusable zeolite H $\beta$  catalyst allows production of the *para*-isomer in 80% yield, with the isomeric nitrotoluenes and easily recoverable acetic acid as the only by-products [8, 9].

By contrast, nitration of highly deactivated substrates such as monosubstituted benzenes having substituents such as nitro, cyano, acyl or sulfonyl groups, has received much less attention. In such cases the reactions are usually quite selective for the *meta*-isomer, but utilize relatively forcing conditions and a large quantity of sulfuric acid. Under such conditions, *para*-isomers are usually produced in very low yields [1]. For example, nitration of benzonitrile gives

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nitrobenzonnitriles in which the *ortho/meta/para* ratio is 17/81/2 [1].

Alternative systems developed recently for nitration of deactivated aromatics include nitric acid in the presence of P<sub>2</sub>O<sub>5</sub> supported on silica gel [18], nitrogen dioxide at low temperatures in the presence of ozone [19], N<sub>2</sub>O<sub>5</sub> in the presence of Fe(acac)<sub>3</sub> as a catalyst [20], urea nitrate and nitrourea [21], nitroguanidine and ethylene glycol dinitrate in concentrated acid [22], vanadium(V) oxytrinitrate in dichloromethane at room temperature [23], and nitric acid in the presence of MCM-41-supported metal bis[(perfluoroalkyl)sulfonyl]imides in dichloroethane [24]. However, such reagents still give mainly the *meta*-products and moreover, *ortho*-isomers are often formed in relatively high proportions. None of these methods show significant improvement in the proportion of the *para*-isomers.

It is well recognised that zeolites and other solid catalysts can play an important role in the development of greener organic syntheses through their abilities to act as recyclable heterogeneous catalysts, support reagents, entrain by-products, avoid aqueous work-ups and enhance product selectivities [25–32]. For example, we have shown that zeolites or other solids can have advantages in alkylation [33], acylation [34, 35], methanesulfonylation [36], bromination [37] and chlorination [38], as well as nitration [8–13] of aromatic compounds.

Indeed, we have previously shown that nitration of deactivated substrates using a system comprising nitric acid, trifluoroacetic anhydride (sometimes with added acetic anhydride) and zeolite H $\beta$  at low temperature (–10 °C) gives the corresponding nitro products with higher proportions of the *para*-isomers, in one case up to as high as 19% [39], but with a low overall yield. Also, under some of the conditions tried there was almost no *ortho*-isomer. We were interested to see if a process could be devised that would give even higher yields of *para*-isomers for such highly deactivated substrates. Therefore, we decided to undertake a detailed study of nitration of benzonitrile and other deactivated aromatics over zeolites by use of acid anhydrides and nitric acid, which are assumed to produce acyl nitrates in situ (Scheme 1).

Such nitrating agents would not react readily with the substrates in the absence of a catalyst, so that the influence of the catalyst would be critical. We now report our findings.



**Scheme 1** Generation acyl nitrates from reaction of nitric acid with acid anhydrides

## 2 Experimental

### 2.1 Materials

Chemicals and solvents were purchased from Aldrich Chemical Company and used without further purification. Nitric acid (100%) was purchased from BDH Laboratory Supplies. Commercial zeolites were purchased from Aldrich Chemical Company or Zeolyst International. All zeolite catalysts were freshly calcined at 550 °C for a minimum of 6 h prior to use.

### 2.2 Analysis and Characterisation of the Products

Product mixtures from the nitration reactions of deactivated mono-substituted benzenes were subjected to gas chromatography using a Shimadzu Gas Chromatograph fitted with a ZEBRON ZB-5 (5% phenyl polysiloxane) 30 m length column. The GC conditions used for analysis were: 70 °C for 1 min, ramped to 250 °C at 20 °C/min and held for 3 min. The injection temperature was 250 °C and the detection temperature 250 °C. Tetradecane was used as a GC standard.

Methyl benzoate and ethyl benzoate were prepared according to the literature procedure [40], by reaction of benzoic acid with the appropriate alcohol in the presence of sulfuric acid as a catalyst, and their structures were confirmed by NMR spectroscopy.

GC was the method of choice, unless otherwise indicated, to quantify the product mixtures and to determine the yield (%) and the total mass balance.

### 2.3 Typical Experimental Procedure for Zeolite Cation-Exchange

The standard procedure for cation-exchange involved calcination of supplied H $\beta$  (5 g) at 550 °C to remove the template, then stirring in a refluxing aqueous solution of the corresponding metal chloride (1 M, 50 mL) for 1 h, filtration, washing with water (50 mL), repetition of the whole exchange process then washing with water until halide-free before calcination at 550 °C.

### 2.4 Procedure for the Surface Passivation of Zeolite

Passivation of external surface of zeolite  $\beta$  was performed at room temperature by treatment of calcined zeolite  $\beta$  with an excess of pure trimethylchlorosilane in dichloromethane (DCM). The mixture was stirred for 5 min and solvent and excess reagent was removed by a dry nitrogen stream. The zeolite was dried in an air oven at 120 °C for 6 h then crushed to a powder. No attempt was made to measure the internal and external acidity of the zeolite after the silanisation process.

### 2.5 Typical Experimental Procedure for the Nitration of Deactivated Aromatic Compounds Using Nitric acid, Trifluoroacetic Anhydride and Zeolite H $\beta$ Catalyst

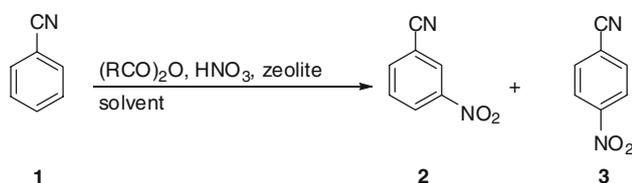
Quantities are recorded in the footnotes to the appropriate tables or text. All reactions were carried out in a 250 mL two-necked round bottomed flask equipped with a water condenser, fitted with a calcium chloride tube, and a magnetic stirrer. In a typical experiment, a mixture of zeolite H $\beta$  (Si/Al = 12.5; 0.10–2.0 g), nitric acid (100%; 0.80 mL, 19 mmol), trifluoroacetic anhydride (3.50 mL, 25 mmol) and the deactivated aromatic compound (9.5 mmol) in DCM (20 mL) was heated under reflux for the appropriate reaction time. At the end of the reaction period, the bulk sample was filtered and the catalyst was washed with analytical grade acetone (3  $\times$  20 mL). Tetradecane (0.0600 g) was added as a GC standard and the solution was made up to 100 mL with acetone. The mixture was analysed by gas chromatography and the yields of all identified components were calculated.

The yields of 3-nitrobenzonitrile (3-NBN), 4-nitrobenzonitrile (4-NBN) and other products are recorded in tables. Results from variation of the procedure and use of different substrates are also recorded in tables. Details of the conditions are recorded in footnotes to the tables.

### 3 Results and Discussion

Initially, we attempted nitration of benzonitrile (**1**; 9.5 mmol) with HNO<sub>3</sub> (19 mmol) and chloroacetic anhydride (19 mmol), over zeolite H $\beta$  (HBEA, Si/Al = 12.5; 2 g) in dichloromethane (DCM, 20 mL) at room temperature for 2 h. The reaction produced only 3-nitrobenzonitrile (**2**) and 4-nitrobenzonitrile (**3**), with no *ortho*-nitrated product (Scheme 2).

The combined yield of nitrobenzonitriles **2** and **3** was 21% and the **2/3** ratio was 17/4, with *ca.* 79% of **1** remaining. The absence of *ortho*-isomer was interesting. Since the cyano group is linear and provides little steric hindrance to *ortho*-nitration, and since traditional nitration produces significantly more *ortho*-nitrated product than



**Scheme 2** Nitration of benzonitrile using a HNO<sub>3</sub>/(RCO)<sub>2</sub>O/zeolite system

*para*-, a higher *ortho/para* ratio was expected. The low yield of nitrobenzonitriles (NBNs) prompted us to investigate the reaction further in an attempt to find conditions under which the yield could be improved.

The progress of the reaction was tested by conducting identical reactions over different reaction times from 5 min to 24 h. After 5 min the yield of **2** was 4% and there was just a trace of **3**, but by 30 min the yield of **2** was 17% and that of **3** was 4%. The product yields remained constant thereafter. Clearly, the reaction is quite rapid under these conditions, with 21% conversion within 30 min, but the reaction stops for some reason at this point.

A similar series of reactions was conducted in refluxing DCM. The results obtained are recorded in Table 1.

As the results in Table 1 indicate, for reaction times up to 4 h the selectivity of the reaction remained more or less constant (**2/3** *ca.* 4:1), but thereafter the rate of reaction was very low and virtually all of the additional product was **2**. It seemed likely that this very slow reaction producing almost exclusively **2** was the intrinsic reaction between **1** and a nitrating agent (chloroacetyl nitrate or nitric acid) without intervention of the zeolite, implying that the activity of the zeolite was lost after a certain reaction time. It is unlikely that the zeolite was destroyed more quickly and at lower conversion at room temperature than at *ca.* 40 °C (refluxing DCM), but the loss of activity could be consistent with equilibrium formation of an inactive complex between the zeolite and the chloroacetic acid produced in the reaction (Scheme 3).

At the higher temperature the equilibrium position would lie further to the side of the uncomplexed zeolite, allowing both a more rapid reaction and a higher conversion before the rate of the catalysed reaction was reduced virtually to zero.

**Table 1** Nitration of benzonitrile (**1**) in DCM using (ClCH<sub>2</sub>CO)<sub>2</sub>O/HNO<sub>3</sub>/H $\beta$  for various reaction times under reflux conditions

Reaction time (h)	Yields (%) <sup>a</sup>		
	<b>1</b>	<b>2</b>	<b>3</b>
0.1	80	16	4
0.5	58	35	7
2	32	54	15
4	25	56	18
8	22	60	17
24	20	63	17

A mixture of H $\beta$  (Si/Al = 12.5; 2.00 g), nitric acid (0.80 mL, 19 mmol), chloroacetic anhydride (3.30 g, 19 mmol) and **1** (1.03 g, 9.5 mmol) in DCM (20 mL) was refluxed for the appropriate reaction time

<sup>a</sup> Yields calculated by quantitative GC using tetradecane as standard

**Scheme 3** Possible deactivation of zeolite by complexation

In order to gain further insight into this possibility, the reaction was carried out with different quantities of zeolite. The results obtained are recorded in Table 2.

The results (Table 2) showed that for amounts of catalyst between 0.5 and 2.0 g the yield of nitrobenzonitriles (NBNs) obtained after 4 h increased with the amount of catalyst, though not in a linear way. The result with 3 g of zeolite probably reflects difficulty in stirring the mixture efficiently. Qualitatively the results with 0.5–2.0 g of zeolite were consistent with the possible existence of an equilibrium of the type depicted in Scheme 3, but without an independent measure of the quantity of at least one of the species involved it was not possible to draw any quantitative conclusions. Therefore, attention was next turned to attempting to find alternative ways to improve the yield and proportion of the *para*-isomer.

Several different acidic zeolites (2 g for 9.5 mmol of **1**) were screened for efficacy in a 4 h reaction. In order to illustrate the effect of zeolite on yield, the reaction was also attempted without zeolite. The results obtained are recorded in Table 3.

In the absence of any catalyst, no reaction occurred. Also, when the reaction was carried out over zeolite H-ZSM-5 (a medium pore zeolite), no NBNs were formed, presumably because the pores are not large enough to accommodate the reacting species and the number of acidic sites on the surface is low. The results were very similar when ferrierite and mordenite were used as catalysts. Ferrierite and mordenite, although they have relatively large entry ports to the channels, contain one-dimensional channel systems, which restricts diffusion within the channels and inhibits interaction between species. By contrast, all samples of large pore zeolites with three-

**Table 3** Nitration of benzonitrile (**1**) over various zeolite catalysts according to Scheme 2 under reflux conditions

Catalyst (Si/Al ratio)	Yields (%) <sup>a</sup>		
	<b>1</b>	<b>2</b>	<b>3</b>
No catalyst	100	–	–
H $\beta$ (12.5)	25	56	18
H $\beta$ (150)	42	46	11
H $\beta$ (300)	27	62	12
HY (12.5)	80	14	4
HY (28)	70	27	2
Ferrierite	100	–	–
H-Mordenite (20)	98	–	–
HZSM-5 (30)	100	–	–

A mixture of zeolite (2.00 g), nitric acid (0.80 mL, 19 mmol), chloroacetic anhydride (3.30 g, 19 mmol) and **1** (1.03 g, 9.5 mmol) in DCM (20 mL) was refluxed for 4 h

<sup>a</sup> Yields calculated by quantitative GC using tetradecane as standard

dimensional channels (zeolites  $\beta$  and Y) showed significant conversions of benzonitrile into nitrobenzonitriles.

The Si/Al ratio of the zeolites used influenced the selectivity of the reactions, with the samples having lower Si/Al ratios giving higher proportions of 4-substituted product than those with higher Si/Al ratios. Thus, when zeolite HY (Si/Al = 12.5) was used as a catalyst the **3:2** ratio was 4:14. However, over zeolite HY (Si/Al = 28) the reaction was much less *para*-selective, giving a ratio of 2:27. Similarly, with zeolite H $\beta$  the **3:2** ratio varied from 18:56 over H $\beta$  (Si/Al = 12.5) to 12:62 over H $\beta$  (Si/Al = 300). None of the zeolites tried gave a better conversion than the one originally studied and further studies therefore concentrated on the use of zeolite H $\beta$  (Si/Al = 12.5).

In order to test the effect of solvent in the reaction, reactions were carried out in several different refluxing solvents. The results are recorded in Table 4.

**Table 2** Nitration of benzonitrile (**1**) over various quantities of zeolite H $\beta$ 

H $\beta$ (Si/Al = 12.5; g)	Yields (%) <sup>a</sup>		
	<b>1</b>	<b>2</b>	<b>3</b>
–	100	–	–
0.5	46	44	11
1	37	48	14
2	25	56	18
3	55	35	11

A mixture of H $\beta$  (Si/Al = 12.5), nitric acid (0.80 mL, 19 mmol), chloroacetic anhydride (3.30 g, 19 mmol) and **1** (1.03 g, 9.5 mmol) in DCM (20 mL) was refluxed for 4 h

<sup>a</sup> Yields calculated by quantitative GC using tetradecane as standard

**Table 4** Nitration of benzonitrile (**1**) according to Scheme 2 over zeolite H $\beta$  (Si/Al = 12.5) in different refluxing solvents

Solvent	Reflux temperature (°C)	Yields (%) <sup>a</sup>		
		<b>1</b>	<b>2</b>	<b>3</b>
Dichloromethane	40	25	56	18
Chloroform	61	37	48	14
1,2-Dichloroethane	83	70	24	8
Acetone	56	100	–	–

A mixture of H $\beta$  (Si/Al = 12.5, 2.00 g), nitric acid (0.80 mL, 19 mmol), chloroacetic anhydride (3.30 g, 19 mmol) and **1** (1.03 g, 9.5 mmol) in solvent (20 mL) was refluxed for 4 h

<sup>a</sup> Yields calculated by quantitative GC using tetradecane as standard

No NBNs were formed when acetone was used as solvent. However, for chlorinated hydrocarbon solvents the reaction proceeded and the *para/ortho* ratio was similar for all such solvents. Reflux temperature seemed to be the major factor influencing the yield of the NBNs. The yields of **2** and **3** were highest when the reaction was carried out in the lowest boiling solvent (DCM) and lowest in high-boiling dichloroethane (DCE). It seemed likely that the chloroacetyl nitrate intermediate was breaking down or escaping from the reaction mixture at elevated temperatures. In order to test this possibility, mixtures containing solvent (chloroform or DCE), zeolite, nitric acid and chloroacetic anhydride, in the same proportions as used for the reactions represented in Table 4, but without benzonitrile, were heated at reflux for 4 h, after which benzonitrile was added and the mixtures were then refluxed for a further 4 h. For the case of DCE, no NBNs were formed and 100% of the benzonitrile remained. In the case of chloroform, just 17% of 3-NBN and 6% of 4-NBN were formed and 76% of benzonitrile remained. This clearly supports the view that the active reagent is lost from the mixtures during heating. It seemed that the best solvent was DCM and had already been used in the earlier studies.

The effect of quantity of chloroacetic anhydride is shown in Table 5. There was a trend to higher overall product yields with increasing anhydride amount, but the amount of *para*-isomer remained constant. Perhaps, if an equilibrium such as that shown in Scheme 3 is operating, after a certain conversion level the activity of the zeolite is effectively eliminated so that any further reaction proceeds in a manner more like traditional nitration.

Despite all the different parameters varied, the maximum yield of *para*-nitrobenzonitrile achieved using chloroacetic anhydride was 18%. Therefore, attention was focused on the effect of other anhydrides. Various anhydrides with different reactivity (acetic, propionic, chloroacetic, dichloroacetic and trifluoroacetic anhydrides) were reacted with nitric acid to produce the corresponding acyl

nitrates in situ (Scheme 1) and then used for nitration of benzonitrile according to Scheme 2. The results are recorded in Table 6.

Clearly, acetyl and propionyl nitrates were not reactive enough for such a deactivated substrate. The results with dichloroacetic anhydride were unusual—the *para/meta* ratio was relatively high (0.37), but there was also a significant quantity of the *ortho*-isomer.

On the other hand, both chloroacetyl and trifluoroacetyl nitrates produced only **2** and **3**, with trifluoroacetyl nitrate giving a higher yield than chloroacetyl nitrate but with a slightly lower *para/meta* ratio (0.28; cf. 0.32 for chloroacetyl nitrate).

Trifluoroacetic anhydride is intrinsically more reactive than chloroacetic anhydride, so a higher reaction rate might be expected. However, this alone does not explain why a higher yield was obtained, since deactivation of the zeolite rather than lack of intrinsic reactivity appeared to be the limiting factor with chloroacetyl nitrate. Perhaps the greater volatility of trifluoroacetic acid, resulting in a significant proportion of it being in the vapour phase under the reaction conditions, and a lower tendency for it to complex the zeolite, allow a greater amount of free zeolite (Scheme 3) to remain to catalyse the reaction. If so, it might also be possible to use a smaller quantity of zeolite and still obtain a high yield of product. Therefore, a series of reactions was conducted over various quantities of H $\beta$ . In order to avoid any possibility that hydrolysis of some of the anhydride would lead to a lower proportion of trifluoroacetyl nitrate, the quantity of anhydride was raised to 25 mmol (for 19 mmol of HNO<sub>3</sub>). The results are shown in Table 7.

The results clearly indicated that nitration of benzonitrile under these conditions could be catalysed with as little as 0.10 g of H $\beta$ . The reaction was nearly complete (96%) and the yield of 4-nitrobenzonitrile was 24%, with a

**Table 5** Nitration of benzonitrile (**1**) with various quantities of chloroacetic anhydride

Chloroacetic anhydride (mmol)	Yields (%) <sup>a</sup>		
	<b>1</b>	<b>2</b>	<b>3</b>
19	25	56	18
20	19	60	18
25	–	81	18
30	–	80	18

A mixture of H $\beta$  (Si/Al = 12.5, 2.00 g), nitric acid (0.80 mL, 19 mmol), chloroacetic anhydride and **1** (1.03 g, 9.5 mmol) in DCM (20 mL) was refluxed for 4 h

<sup>a</sup> Yields calculated by quantitative GC using tetradecane as standard

**Table 6** Nitration of benzonitrile (**1**) according to Scheme 2 over zeolite H $\beta$  (Si/Al = 12.5) using various acid anhydrides

Acid anhydride	Yields (%) <sup>a</sup>			
	<b>1</b>	<b>2</b>	<b>3</b>	Other
Acetic	100	–	–	
Propionic	72	–	–	
Chloroacetic	25	56	18	
Dichloroacetic	34	41	15	10 <sup>b</sup>
Trifluoroacetic	4	75	21	

A mixture of H $\beta$  (Si/Al = 12.5, 2.00 g), nitric acid (0.80 mL, 19 mmol), acid anhydride (19 mmol) and **1** (1.03 g, 9.5 mmol) in DCM (20 mL) was refluxed for 4 h

<sup>a</sup> Yields calculated by quantitative GC using tetradecane as standard

<sup>b</sup> 2-Nitrobenzonitrile was produced in 10% yield

**Table 7** Nitration of benzonitrile (**1**) using TFAA over various quantities of zeolite H $\beta$ 

H $\beta$ (Si/Al = 12.5; g)	Yields (%) <sup>a</sup>		
	<b>1</b>	<b>2</b>	<b>3</b>
–	100	–	–
0.10	4	72	24
0.25	–	77	23
0.50	–	77	23
2.0	–	76	24
4.0	–	77	23

A mixture of H $\beta$  (Si/Al = 12.5), nitric acid (0.80 mL, 19 mmol), TFAA (3.50 mL, 25 mmol) and **1** (1.03 g, 9.5 mmol) in DCM (20 mL) was refluxed for 4 h

<sup>a</sup> Yields calculated by quantitative GC using tetradecane as standard

*para/meta* ratio of 0.33. There was no advantage in using the zeolite in more than 0.25 g quantity for the particular conditions chosen, since neither the yield nor the selectivity of the reaction was influenced by the amount of the zeolite beyond that.

We further investigated the effect of reaction time in the presence of only 0.1 g of the catalyst. Nitrobenzonitriles were obtained in 59% yield (46% of **2** and 13% of **3**) after 30 min and in 95% yield (72% of **2** and 23% of **3**) after 2 h. Thereafter the remaining **1** was converted very slowly, eventually giving a mixture of **2** (75%) and **3** (24%) after 6 h.

Samples of zeolite H $\beta$  were recovered from the above reactions, regenerated by calcination at 550 °C and reused in similar nitration reactions. The yields of **2** and **3** obtained showed that the zeolite could be reused at least five times with no reduction in either the yields or selectivity.

The maximum yield of 4-nitrobenzonitrile (**3**) obtained thus far was in the region of 24% and it seemed likely that this was the maximum that could be achieved using H $\beta$  as the catalyst. Therefore, a range of cation-exchanged  $\beta$  zeolites was prepared for testing as catalysts. For these tests the conditions used were reflux for 4 h with zeolite (2.0 g), HNO<sub>3</sub> (19 mmol) and TFAA (25 mmol). The results are reported in Table 8.

The results recorded in Table 8 showed some interesting features. For example, the yield of nitrobenzonitriles was only 7%, with no 4-NBN formed, when K<sup>+</sup> $\beta$  was used as catalyst (Entry 2). K<sup>+</sup> is a large univalent cation and may block entry to the pores of the zeolite, spoiling its potential as a catalyst. Also, K<sup>+</sup> $\beta$  is not very acidic. The small amount of nitrobenzonitrile produced may have arisen by reaction at the small number of sites on the external surface, thereby reducing the tendency to produce *para*-isomer.

For the divalent cation-exchanged zeolites the yield of NBNs was high in the case of Zn<sup>2+</sup> $\beta$  and Cd<sup>2+</sup> $\beta$  (Entries 3 and 4) but only moderate with Hg<sup>2+</sup> $\beta$  (Entry 5). The higher

**Table 8** Nitration of benzonitrile (**1**) according to Scheme 2 over various cation-exchanged zeolites  $\beta$ 

Entry	Zeolite	Yields (%) <sup>a</sup>		
		<b>1</b>	<b>2</b>	<b>3</b>
1	H <sup>+</sup> $\beta$	–	76	24
2	K <sup>+</sup> $\beta$	90	7	–
3	Zn <sup>2+</sup> $\beta$	2	80	17
4	Cd <sup>2+</sup> $\beta$	–	78	22
5	Hg <sup>2+</sup> $\beta$	54	34	11
6	Al <sup>3+</sup> $\beta$	2	77	22
7	Fe <sup>3+</sup> $\beta$	–	77 (73)	24 (28)
8	In <sup>3+</sup> $\beta$	–	85	15
9	La <sup>3+</sup> $\beta$	–	87	14
10	Ce <sup>3+</sup> $\beta$	–	85	15

A mixture of zeolite (2.00 g), nitric acid (0.80 mL, 19 mmol), TFAA (3.50 mL, 25 mmol) and **1** (1.03 g, 9.5 mmol) in DCM (20 mL) was refluxed for 4 h

Figures in parentheses are for similar reactions, but with 4 g of zeolite Fe<sup>3+</sup> $\beta$

<sup>a</sup> Yields calculated by quantitative GC using tetradecane as an internal standard

yields with the smaller divalent cations could reflect easier entry to the pore network. The lower yield with Hg<sup>2+</sup> $\beta$  would be consistent with the larger cation causing greater constriction to access to the pore network. There was also a slight increase in *para*-selectivity going from Zn<sup>2+</sup> $\beta$  to Hg<sup>2+</sup> $\beta$  as the cations get larger, but at the expense of overall yield.

All trivalent cations (Entries 6–10) produced quantitative yields of nitrobenzonitriles of which the 4-nitrobenzonitrile yield was in the range of 14–24%. Fe<sup>3+</sup> $\beta$  and Al<sup>3+</sup> $\beta$  gave the best *para*-selectivities among this group of zeolites. Furthermore, 4-NBN (**3**) was obtained in 28% yield when 4.0 g of Fe<sup>3+</sup> $\beta$  zeolite was used compared with 24% when 2 g was used, while use of only 0.1 g of Fe<sup>3+</sup> $\beta$  resulted in 22% of **3**, 58% of **2** and 21% unreacted **1**. Therefore, Fe<sup>3+</sup> $\beta$  behaved in a manner broadly similar to that of H $\beta$ .

Unfortunately, none of the ion-exchanged zeolites resulted in a significantly higher proportion of **3** than with H $\beta$ , so attention was turned to the possibility that surface-passivated zeolite would offer further improvement by eliminating reaction catalysed at the external surface of the zeolite and by introducing further constraints on access to the pores.

Samples of H $\beta$  and Fe<sup>3+</sup> $\beta$  zeolites (each with Si/Al = 12.5) were treated with chlorotrimethylsilane in DCM and then dried at 120 °C. A series of nitration experiments was then conducted with various quantities of these passivated  $\beta$  zeolites over a 2 h period at reflux. The results are recorded in Table 9.

**Table 9** Nitration of benzonitrile (**1**) according to Scheme 2 over various quantities of passivated zeolite

Passivated zeolite (g)	Yields (%) <sup>a</sup>		
	<b>1</b>	<b>2</b>	<b>3</b>
H $\beta$ (0.10)	40	45	15
H $\beta$ (0.25)	4	65	30
H $\beta$ (0.50)	5	64	31
H $\beta$ (1.00)	–	67	33
H $\beta$ (2.00)	–	67	33
Fe <sup>3+</sup> $\beta$ (0.10)	22	60	20
Fe <sup>3+</sup> $\beta$ (0.25)	6	70	24
Fe <sup>3+</sup> $\beta$ (0.50)	4	71	24
Fe <sup>3+</sup> $\beta$ (1.00)	2	73	26
Fe <sup>3+</sup> $\beta$ (2.00)	–	73	28

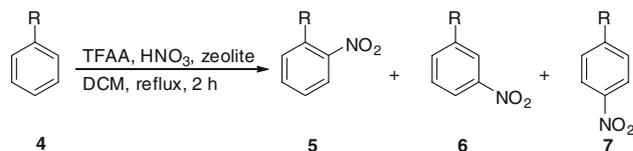
A mixture of passivated zeolite, nitric acid (19 mmol, 0.8 mL), trifluoroacetic anhydride (25 mmol, 3.5 mL) and **1** (9.5 mmol) in DCM (20 mL) was refluxed for 2 h

<sup>a</sup> Yields calculated by quantitative GC using tetradecane as an internal standard

With either of the catalysts the reaction was more or less complete within the 2 h reflux period provided at least 0.25 g of the passivated catalyst was used. In the case of passivated Fe<sup>3+</sup> $\beta$  there was only a small increase in the proportion of **3**, but with passivated H $\beta$  the proportion rose to over 30%. With 1 g of passivated H $\beta$  under these conditions the reaction was complete, giving 67% of **2** and 33% of **3**, which is easily the highest proportion of **3** ever achieved in nitration of benzonitrile.

At this point it was appropriate to investigate the scope of the new process with other deactivated mono-substituted benzenes. Therefore, a series of substrates was subjected to nitration in three different ways—using a traditional mixed acid procedure to provide a baseline for “normal” nitration, using the TFAA/nitric acid/zeolite H $\beta$  approach (Scheme 4) and using the latter approach with passivated zeolite H $\beta$ . The results are shown in Table 10 (mixed acid and zeolite H $\beta$  approaches) and 11 (using passivated H $\beta$ ).

Tables 10 and 11 show that nitration of deactivated aromatics **4** was general and gave quantitative yields of nitro products in most cases. The results also revealed that both types of zeolite H $\beta$ , but especially the passivated one, enhanced the *para*-selectivity in all such nitration reactions. Nitration of benzonitrile, butyl phenyl ketone, *tert*-butyl phenyl ketone and benzoic acid gave the highest proportions of *para*-isomers, several being over 30%. Furthermore, in all cases except one (*tert*-butyl phenyl ketone) the *ortho*-products were obtained in lower proportions than by traditional nitration, in several cases the amount being so low as to be unmeasurable. The proportion of the *meta*-isomer was in most cases not very different than that produced in the traditional nitration reaction, the increase in the amount of

**Scheme 4** Nitration of deactivated aromatics **4** using a HNO<sub>3</sub>/TFAA/zeolite system**Table 10** Nitration of deactivated aromatics **4** using nitric acid and TFAA over zeolite H $\beta$  according to Scheme 4 and comparison with use of ‘mixed acids’

Entry	R	Yield (%) <sup>a</sup>		
		<b>5</b>	<b>6</b>	<b>7</b>
1	CN	– (17)	76 (80)	24 (2)
2	NO <sub>2</sub>	– (6)	92 (91)	7 (2)
3	CHO	10 (22)	76 (72)	14 (1)
4	COMe	– (–) <sup>b</sup>	67 (75) <sup>b</sup>	15 (–) <sup>b</sup>
5	COBu	10 (18) <sup>c</sup>	52 (27) <sup>c</sup>	30 (–) <sup>c</sup>
6	COBu <sup>f</sup>	38 (33)	26 (41)	36 (26)
7	CO <sub>2</sub> H	– (27)	75 (72)	21 (1)
8	CO <sub>2</sub> Me	4 (20)	85 (69)	10 (3)
9	CO <sub>2</sub> Et	8 (20)	77 (78)	12 (3)
10	CO <sub>2</sub> Bu	10 (20)	75 (74)	13 (2)

A mixture of H $\beta$  (Si/Al = 12.5, 0.25 g), nitric acid (0.80 mL, 19 mmol), TFAA (3.50 mL, 25 mmol) and **4** (9.5 mmol) in DCM (20 mL) was refluxed for 4 h

Figures in parentheses are for similar reactions using mixed acids. To a stirred mixture of HNO<sub>3</sub> (9.5 mmol) and H<sub>2</sub>SO<sub>4</sub> (19 mmol) the appropriate substrate (9.5 mmol) was added and the mixture stirred for 10 min at 0 °C

<sup>a</sup> Yields normally calculated by quantitative GC using tetradecane as standard

<sup>b</sup> Yields calculated by <sup>1</sup>H NMR spectroscopy

<sup>c</sup> Reaction was carried out using only nitric acid rather than mixed acid; starting material (*ca.* 55%) remained. A similar reaction with mixed acid was aggressive and none of the expected products was detected by GC

*para*-isomer having been more or less matched by a decrease in the amount of the *ortho*-isomer.

The case of *tert*-butyl phenyl ketone was an exception to the general trend. As for the other substrates the proportion of *para*-isomer had increased for the zeolite-catalysed process, but uniquely the proportion of *ortho*-isomer had also increased and in consequence the *meta*-isomer had become the minor product. The product proportions with this substrate are unusual even for traditional nitration of an acylbenzene and this has been attributed to the bulk of the *tert*-butyl group forcing the carbonyl group to twist out of alignment with the benzene ring [41, 42]. It is possible that within the confines of the zeolite pores the twisting out of alignment is further enforced. This substrate would warrant further investigation.

**Table 11** Nitration of deactivated aromatics **4** using nitric acid and TFAA over passivated zeolite H $\beta$  according to Scheme 4

Entry	R	Yield (%) <sup>a</sup>		
		5	6	7
1	CN	–	67	33
2	NO <sub>2</sub>	–	90	8
3	CHO	12	73	15
4	COMe	– <sup>b</sup>	70 <sup>b</sup>	17 <sup>b</sup>
5	COBu	10	50	33
6	COBu <sup>f</sup>	37	26	37
7	CO <sub>2</sub> H	–	78	24
8	CO <sub>2</sub> Me	4	85	10
9	CO <sub>2</sub> Et	8	78	13
10	CO <sub>2</sub> Bu	11	72	14

A mixture of passivated H $\beta$  (Si/Al = 12.5, 0.25 g), nitric acid (0.80 mL, 19 mmol), TFAA (3.50 mL, 25 mmol) and **4** (9.5 mmol) in DCM (20 mL) was refluxed for 4 h

<sup>a</sup> Yields normally calculated by quantitative GC using tetradecane as standard

<sup>b</sup> Yields calculated by <sup>1</sup>H NMR spectroscopy

#### 4 Conclusion

Proton and cation-exchanged forms of zeolites are able to catalyse and improve the *para*-regioselectivity in the nitration reaction of benzonitrile using a nitric acid/acid anhydride/zeolite system. No reaction takes place with the same system in the absence of the zeolite. The catalysed reaction produces only 3- and 4-nitrobenzonitriles in quantitative yield, with no 2-nitrobenzonitrile produced in most cases under the conditions tried. Trifluoroacetic and chloroacetic anhydrides were found to be the most useful of the anhydrides tried. Zeolite H $\beta$  with a Si/Al ratio of 12.5 is the most active of the catalysts tried and also gives a high proportion of 4-nitrobenzonitrile. Furthermore, heating easily regenerates the zeolite, which can be reused at least 6 times to give results similar to those obtained with a fresh sample of the catalyst. Passivation of the zeolite surface by treatment with chlorotrimethylsilane renders the reaction even more prone to produce the *para*-isomer, which is formed in 33% yield, the *para/meta* ratio becoming 0.50.

The zeolite-catalysed process is general for nitration of monosubstituted deactivated aromatic compounds and gives significantly increased proportions of *para*-substituted isomers compared with the results obtained from the traditional mixed acid method. In most cases the proportion of *ortho*-isomer produced is substantially reduced.

Although the reactions described here are not sufficiently selective to render these reactions suitable for commercial application, they nevertheless produce substantially higher proportions of *para*-nitro compounds than has been possible

previously from deactivated substrates. They demonstrate how careful choice of catalyst, reagent, solvent and conditions can have a powerful effect in improving *para*-selectivity even with substrates that normally give very little *para*-product.

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#### References

- Olah GA, Malhotra R, Narang SC (1989) Nitration: methods and mechanisms. VCH, New York
- Schofield K (1980) Aromatic nitration. Cambridge University Press, Cambridge
- Taylor R (1990) Electrophilic aromatic substitution. Wiley, Chichester
- Ingold CK (1969) Structure and mechanism in organic chemistry. Bell, London
- de la Mare PB, Ridd JH (1959) Aromatic substitution: nitration and halogenation. Butterworths, London
- Gigante B, Prazeres A, Marcelo-Curto M, Cornelis A, Laszlo P (1995) J Org Chem 60:3445
- Carvalho B, Laszlo P, Cornelis A, Marcelo-Curto M (1994) PCT Inc Appl WO 94/19310
- Smith K, Musson A, DeBoos GA (1998) J Org Chem 63:8448
- Smith K, Musson A, DeBoos GA (1996) Chem Commun 469
- Smith K, Almeer S, Black SJ (2000) Chem Commun 1571
- Smith K, Almeer S, Peters C (2001) Chem Commun 2748
- Smith K, Almeer S, Black SJ, Peters C (2002) J Mater Chem 12:3285
- Smith K, Ajarim MD, El-Hiti GA (2009) Topics Catal 52:1696
- Kalbasi RJ, Ghiaci M, Massah AR (2009) Appl Catal A 353:1
- Kuba MG, Prins R, Pirngruber GD (2007) Appl Catal A 333:24
- Kuba MG, Prins R, Pirngruber GD (2007) Appl Catal A 333:78
- Peng X, Suzuki H, Lu C (2001) Tetrahedron Lett 42:4357
- Hajipour AR, Ruoho AE (2005) Tetrahedron Lett 46:8307
- Suzuki H, Murashima T (1994) J Chem Soc Perkin Trans 1:903
- Bak RR, Smallridge AJ (2001) Tetrahedron Lett 42:6767
- Almog J, Klein A, Sokol A, Sasson Y, Sonenfeld D, Tamiri T (2006) Tetrahedron Lett 47:8651
- Oxley JC, Smith JL, Moran JS, Canino JN, Almog J (2008) Tetrahedron Lett 49:4449
- Dove MFA, Manz B, Montgomery J, Pattenden G, Wood SA (1998) J Chem Soc Perkin Trans 1:1589
- Yuan Y, Nie J, Zhang Z, Wang S (2005) Appl Catal A Gen 295:170
- Clark JH (2002) Acc Chem Res 35:791
- Clark JH (ed) (1994) Catalysis of organic reactions using supported inorganic reagents. VCH, New York
- Delaude L, Laszlo P, Smith K (1993) Acc Chem Res 26:607
- Smith K (1992) In: Yoshida Z, Ohshiro Y (eds) New aspects of organic synthesis II. Kadonsha, Tokyo and VCH, Weinheim, p 43
- Butters M (1992) In: Smith K (ed) Solid supports and catalysts in organic synthesis. Ellis Harwood, Chichester, p 130
- Smith K (1991) In: Scaros MG, Prunier ML (eds) Catalysis of organic reactions. Marcel Dekker, New York, p 91
- Smith K, El-Hiti GA (2004) Curr Org Synth 1:253
- Smith K, El-Hiti GA (2006) Curr Org Chem 10:1603
- Smith K, Roberts SD, El-Hiti GA (2003) Org Biomol Chem 1:1552
- Smith K, El-Hiti GA, Jayne AJ, Butters M (2003) Org Biomol Chem 1:1560

35. Smith K, El-Hiti GA, Jayne AJ, Butters M (2003) *Org Biomol Chem* 1:2321
36. Smith K, Ewart GM, El-Hiti GA, Randles KR (2004) *Org Biomol Chem* 2:3150
37. Smith K, El-Hiti GA, Hammond MEW, Bahzad D, Li Z, Siquet C (2000) *J Chem Soc Perkin Trans 1*:2745
38. Smith K, Butters M, Paget WE, Goubet D, Fromentin E, Nay B (1999) *Green Chem* 1:83
39. Smith K, Gibbins T, Millar RW, Claridge RP (2000) *J Chem Soc Perkin Trans 1*:2753
40. Vogel AI (1989) *Vogel's textbook of practical organic chemistry*, 5th edn. Longman, Harlow
41. Barker SD, Norris RK, Randles D (1981) *Aust J Chem* 34:1875
42. Moodie RB (1982) *Organic reaction mechanisms* 231