Regioselective nitration of 2- and 4-nitrotoluenes over systems comprising nitric acid, an acid anhydride and a zeolite

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Abstract:
Nitration of 2-nitrotoluene using nitric acid, acetic anhydride and Hβ zeolite produces a 97% yield of 2,4-dinitotoluene along with 3% of 2,6-dinitrotoluene. Nitration of 4-nitrotoluene under similar reaction conditions produces 2,4-dinitrotoluene in 89% yield. When chloroacetic anhydride was used instead of acetic anhydride, nitration of 4-nitotoluene produced a quantitative yield (>99%) of 2,4-nitrotoluene.

Keywords: Regioselective mononitration, nitrotoluenes, zeolite Hβ, shape selectivity, acid anhydrides

Introduction

The products obtained from aromatic nitration are very important as intermediates in the production of many important industrial products, such as pharmaceuticals, dyes, polymers, perfumes, explosives, pesticides and fertilizers. For example, toluene diisocyanate (TDI) and toluenediamine are very important industrial products and can be synthesized from 2,4-dinitrotoluene (2,4-DNT).[1,2] They can be used to produce polyurethane, which is widely used in varnishes and many other applications.[3-5] Traditionally, dinitration of toluene has been conducted using nitric and sulfuric acids to give a mixture of 2,4-DNT and 2,6-dinitrotoluene (2,6-DNT) in around 4:1 ratio. Such a process suffers serious disadvantages, such as low selectivity, production of over-nitration or oxidation by-products, and the requirement for a relatively large quantity of sulfuric acid, which produces toxic waste in the workup step.[6]

There have been many attempts to improve the yield of 2,4-DNT and enhance the 2,4-:2,6-DNT ratio by direct dinitration of toluene using solid catalysts.[7-12] For example, the 2,4-:2,6-DNT ratio could be improved to 9 when the dinitration reaction was carried out using
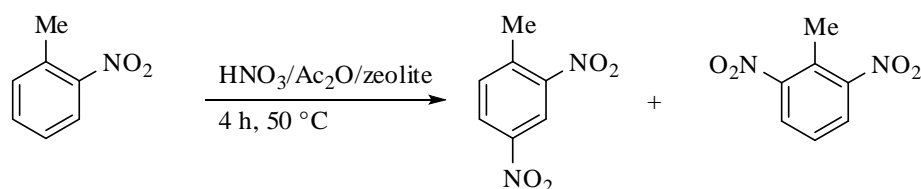
claycop, nitric acid and acetic anhydride, but the method required a large excess of nitric acid and the use of carbon tetrachloride as a solvent.[11] The 2,4-:2,6-DNT ratio was improved to 14 when the reaction was carried out with nitric acid over zeolite Hβ.[12]

We have shown that zeolites and other solid catalysts can play an important role in the enhancement of regioselectivity in nitration processes[13-22] and in many other electrophilic aromatic substitution reactions.[23-31] For example, 2,4-DNT was successfully produced in 96% yield with a 2,4-:2,6-DNT ratio of 70:1 by simple direct dinitration of toluene over a HNO$_3$/acetic anhydride (Ac$_2$O)/trifluoroacetic anhydride (TFAA)/Hβ system in two steps.[14] However, TFAA is toxic, volatile and expensive. Therefore, we have attempted to improve the system to overcome the problems associated with the use of TFAA.[20-22] Indeed, dinitration of toluene (1 molar equivalent) using nitric acid (3.4 molar equivalents) and propanoic anhydride (3.7 molar equivalents) over zeolite Hβ gave 2,4-DNT in 98% yield with a 2,4-:2,6- ratio of 123:1.[20-22] This is easily the most selective quantitative double nitration of toluene ever recorded.

The literature reveals that relatively little attention has been paid to the nitration of mononitrotoluenes.[20,32] Traditionally, when a mixture of sulfuric acid and nitric acid are used the reaction of 2-nitrotoluene (2-NT) produces a 2,4-:2,6-DNT isomer ratio of about 2:1.[14] We have shown that nitration of 2-NT over zeolite Hβ in presence of nitric acid, TFAA and acetic anhydride produced dinitrotoluenes in 98% yield, of which 2,4-DNT was around 94% (the 2,4-:2,6-DNT ratio was 17).[14] However, the reaction required a low temperature (−10 °C) and concerns over the use of TFAA may render it unattractive for commercial processes. We have therefore sought to find a more attractive alternative. We now report the successful nitration of nitrotoluenes over HNO$_3$/acid anhydride/Hβ systems to give predominantly 2,4-DNT.

Results and Discussion

Nitration of 2-NT with nitric acid and acetic anhydride over a zeolite produces two main products, 2,4-DNT, which is the more commercially desirable isomer, and 2,6-DNT. In order to gauge the influence of various zeolites, nitration of 2-NT (35 mmol) was carried out using various quantities of both nitric acid and acetic anhydride (Scheme 1) over 2 g of zeolite HY or Hβ at 50 °C for 4 h. These zeolites were chosen because both have large pores (2-NT might have difficulty entering the pores of small or medium pore zeolites) and have shown high regioselectivity in previous nitration studies.[13-22] The results obtained are recorded in Table 1.

Scheme 1. Nitration of 2-NT over HNO$_3$/Ac$_2$O/zeolite systems.

Table 1. Nitration of 2-nitrotoluene over HNO_3/Ac_2O/zeolite systems according to Scheme 1[a]

Zeolite (SiO_2/Al_2O_3 ratio)	HNO_3 (mmol)	Ac_2O (mmol)	Yield (%)[b]			2,4-:2,6- ratio[c]
			2-NT	2,4-DNT	2,6-DNT	
HY (5.1)	35	50	96	—	—	—
HY (5.1)	70	95	99	—	—	—
HY (5.1)	120	150	89	—	—	—
HY (30)	120	150	63	29	7	4
HY (80)	120	150	75	18	6	3
Hβ (25)	120	150	—	97	3	34

[a] Reaction carried out using 2-NT (35 mmol, 4.8 g), zeolite (2.0 g) and the stated quantities of acetic anhydride and nitric acid for 4 h at 50 °C.
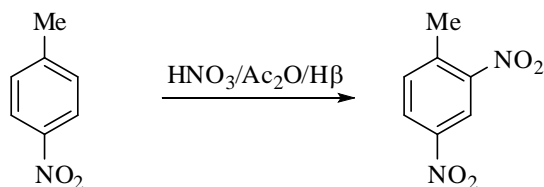[b] Yield was determined by quantitative GC using hexadecane (1 g) as internal standard.
[c] Ratio calculated directly from GC data and not from the rounded figures in the Table.

Table 1 shows that no reaction took place when HY zeolite (SiO_2/Al_2O_3 = 5.1) was used as a catalyst; the starting material was recovered quantitatively even when a large excess of nitrating reagent was used. The results clearly indicated that zeolite HY (SiO_2/Al_2O_3 = 5.1) was not a good catalyst for nitration of 2-NT, presumably because it is not acidic enough to catalyze the reaction. However, use of a more acidic zeolite HY (SiO_2/Al_2O_3 = 30 or 80) under the same conditions was more successful, producing 2,4-DNT in 29 or 18% yield (2,4-:2,6-DNT = *ca.* 4 or 3), respectively. The lower yield and selectivity with the zeolite having the higher SiO_2/Al_2O_3 ratio of the two presumably resulted because this zeolite had so few acidic sites that the rate of reaction was low and the proportion of external surface sites became proportionately significant.

Nitration of 2-NT over zeolite Hβ (SiO_2/Al_2O_3 = 25) led to a quantitative conversion into dinitrotoluenes with a high selectivity for 2,4-DNT (2,4-:2,6-DNT = 34). Despite the increased size of the substrate compared to toluene itself, it was clear that zeolite Hβ remained significantly better than zeolite HY in terms of both activity and selectivity for 2,4-DNT production.[13-22] Therefore, zeolite Hβ was selected as the catalyst for investigation of the nitration of 4-nitrotoluene (4-NT).

Nitration of 4-NT (35 mmol) using nitric acid (35 mmol) and acetic anhydride (50 mmol) over zeolite Hβ (1 g) for 4 h at 50 °C gave only a 63% yield of 2,4-DNT, with 36% of 4-NT remaining. Therefore, the reaction (Scheme 2) was conducted using different proportions of nitrating reagents and catalyst. The results are recorded in Table 2.

Scheme 2. Nitration of 4-nitrotoluene over $HNO_3/Ac_2O/H\beta$ zeolite systems.

Table 2. Nitration of 4-NT over $HNO_3/Ac_2O/H\beta$ zeolite systems according to scheme 2[a]

HNO_3 (mmol)	Ac_2O (mmol)	Zeolite Hβ (g)	Yield (%)[b]	
			4-NT	2,4-DNT
35	50	1	36	63
52	75	1	34	66
70	95	1	30	70
100	130	1	29	70
100	130	2	11	88
120	150	2	11	89

[a] Reaction carried out using 4-NT (35 mmol, 4.8 g), and the stated quantities of zeolite Hβ, acetic anhydride and nitric acid for 4 hours at 50 °C.
[b] Yield determined by quantitative GC using hexadecane (1 g) as internal standard.

It can be seen from Table 2 that increasing the amount of nitrating reagent brought about an increase in the yield of 2,4-DNT, but reached a maximum of around 70% even when the quantity of nitrating reagent was in large excess (100 mmol of nitric acid) if only 1 g of zeolite Hβ was used. However, when more zeolite (2.0 g) was used the yield increased to 89%, but did not improve further. Clearly, 4-NT was less reactive than 2-NT under similar conditions.

In an attempt to increase the yield of 2,4-DNT by nitration of 4-NT, longer reaction times (6 and 8 h) were used, under conditions similar to those that produced 88% of 2,4-DNT, but the yield of 2,4-dinitrotoluene never exceeded 89%. However, when more zeolite (2 g) was used the yield increased to almost 90%, but did not improve further by using even more nitrating agent. It was clear that the majority of the reaction took place within the first 3−4 h. It seems that 89% was the maximum yield of 2,4-DNT that could be achieved from nitration of 4-NT under these conditions. Our attention was therefore turned to use of more active acid anhydrides.

Nitration of 4-NT (35 mmol) with nitric acid (100 mmol) and chloroacetic anhydride (100 mmol) over zeolite Hβ ($SiO_2/Al_2O_3 = 25$, 2.0 g) in dichloromethane (DCM; 10 mL) for 1 h at 50 °C produced a quantitative yield (99.5%) of 2,4-DNT. Chloroacetyl nitrate is more reactive than acetyl nitrate and was able to push the reaction to completion. Nitration of 2-NT using chloroacetyl nitrate under conditions similar to those used for 4-NT gave 2,4-DNT and 2,6-DNT in 94% and 5% yields, respectively (2,4-:2,6-DNT = 19).

Since propionic anhydride had also proven to be more successful than acetic anhydride for double nitration of toluene,[20-22] it was of interest to study nitration of 2-NT and 4-NT using propionic anhydride to see what effect the anhydride would have on the reactivity of the mono-nitro compounds.

Nitration of 2-NT (35 mmol) with nitric acid (70 mmol), propionic anhydride (75 mmol) and zeolite Hβ (2 g) for 4 h at 50 °C gave 2,4-DNT in 95.6% yield along with 4.2% of 2,6-DNT. Nitration of 4-NT under similar conditions gave 2,4-DNT in 96% yield along with 4% of unreacted starting material. These results are intermediate between those obtained using chloroacetic anhydride and those obtained using acetic anhydride.

It has been reported that the relative rates for nitration of 2-NT and 4-NT using the mixed acids method are in the ratio 2.02:1.[32] It was noticed during our studies that 2-NT was more active than 4-NT and it appeared possible that the difference might be greater than that found in the literature. Therefore, it was of interest to check whether the $HNO_3/Ac_2O/H\beta$ system did indeed discriminate better between the 2-NT and 4-NT.

A series of reactions was carried out at 50 °C using various ratios of 2-NT and 4-NT for various reaction times (Table 3). However, under these conditions the reaction of 2-NT was already complete in all cases, even after just 5 minutes. Therefore, in order to get a meaningful comparison, several of the reactions were repeated at room temperature. The results obtained are recorded in parentheses in Table 3.

Table 3. Competition between 2-nitrotoluene and 4-nitrotoluene[a]

NT (mmol)		Time	Components of reaction mixture (mmol)[b]				2,4-:2,6-
2-NT	4-NT	(min)	2-NT	4-NT	2,4-DNT	2,6-DNT	ratio[c]
17.5	17.5	5	0.0 (3.0)[d]	6.8 (12.3)[d]	26.5 (19.0)[d]	0.59 (0.54)[d]	45 (35)[d]
17.5	17.5	10	0.0 (0.84)[d]	5.0 (9.3)[d]	27.8 (24.6)[d]	0.64 (0.56)[d]	43 (43)[d]
17.5	17.5	15	(0.80)[d]	(9.0)[d]	(24.2)[d]	(0.62)[d]	(39)[d]
17.5	17.5	20	0.0	4.4	28.4	0.87	33
17.5	17.5	40	0.0	3.7	28.8	0.71	41
23.3	11.6	20	0.0	2.7	27.8	0.79	35
8.75	26.25	10	0.0	6.1	30.0	0.38	79
8.75	26.25	20	0.0	5.0	31.1	0.31	100
26.25	8.75	10	0.0	4.4	31.2	0.83	38
26.25	8.75	20	0.0	2.8	28.5	0.85	34

[a] Reactions carried out using 2-NT and 4-NT (total amount 35 mmol; proportions as stated), nitric acid (120 mmol, 5.04 mL), acetic anhydride (150 mmol, 14.16 mL) and zeolite Hβ (2.0 g) at 50 °C, unless otherwise indicated, for the stated reaction time.

[b] Product quantities were determined by quantitative GC using hexadecane (1 g) as internal standard.

[c] Ratio calculated directly from GC data and not from the rounded figures in the Table.

[d] Figures in parentheses are for reactions carried out at room temperature.

As can be seen from Table 3, the reaction was very fast in the case of 2-NT even at room temperature. Only 8.6% of 2-NT remained after 5 min and reduced to 2.3% when the reaction time was 15 minutes. On the other hand, the reaction of 4-NT was much slower. Apparent relative rate constants for 4-NT and 2-NT were calculated using Equation 1 (x and y are the final concentrations and x_0 and y_0 are the initial concentrations of 2-NT (x) and 4-NT (y), respectively).[32] The way the experiment was conducted precluded calculation of the true relative rate constants, but the method would underestimate the rate of the faster reaction compared to that of the slower one.

$$k_x/k_y = \log (x/x_0)/\log (y/y_0)$$

Equation 1. Apparent relative rates for 2-NT and 4-NT.

The apparent relative rate ($k_{2\text{-}NT}/k_{4\text{-}NT}$) after 5 min when the reaction was carried out at room temperature was calculated to be 5.0:1. This ratio decreased to 4.8:1 after 10 min and decreased further to 4.6:1 after 15 min. Therefore, the actual relative rate of 2-NT to 4-NT would seem to be greater than 5, which is more than that recorded in the literature (2.02:1) for the reaction with mixed acids.[32] The reason for the difference is not clear but may depend on the way the two compounds fit within the zeolite lattice. The nitrating species may be able to attack the *para*-position of 2-NT relatively easily within the pores, but it may be much more difficult for the nitrating species to attack the *ortho*-position of 4-NT.

Conclusions

Nitration of mononitrotolunenes shows that acetyl nitrate is less reactive than chloroacetyl and propanoyl nitrates. When chloroacetyl nitrate was used for nitration of 2-NT, 2,4-DNT was produced in a 94% yield along with a 5% yield of 2,6-DNT. However, this system produced a 99.5% yield of 2,4-DNT when it was applied to nitration of 4-NT under identical conditions. Propionic anhydride was somewhat more selective for nitration of 2-NT, producing 2,4-DNT in a 96% yield along with a 4% yield of 2,6-DNT. Nitration of 4-NT under identical conditions produced a 96% yield of 2,4-DNT. The ratio of the rate constants for nitration of 2-NT and 4-NT using a $HNO_3/Ac_2O/H\beta$ system was more than double that for the traditional mixed acids method.

Experimental Section

General. Commercial $H\beta$ and HY zeolites were purchased from Zeolyst International and were freshly calcined at 450 °C for a minimum of 6 h prior to use. Nitric acid (100%) was purchased from BDH Laboratory Supplies. Nitrotoluenes and the other chemicals were purchased from Aldrich Chemical Company and used without further purification except for acetic and

propanoic anhydrides, which were distilled. All GC analyses were carried out on a PU 4400 Gas Chromatograph (Philips) using a capillary ZB Carbowax column (30 m, 0.32 mm ID). The GC conditions used for analysis were as follows: 35 °C for 0.5 min, ramped to 240 °C at 20 °C/min and held for 15 min. The injection temperature was 300 °C and the detection temperature 300 °C. Hexadecane was added as an internal standard to allow quantification. All of the expected products from nitration of nitrotoluenes were purchased from Aldrich Chemical Company and used to determine retention times and response factors relative to hexadecane (average from four injections) for each product.

Typical experimental procedure for the nitration of nitrotoluenes using nitric acid, chloroacetic anhydride and zeolite Hβ. Chloroacetic anhydride (17.98 g, 100 mmol) was added to a stirring mixture of nitric acid (6.37 g, 100%, 100 mmol), Hβ (2.0 g, $SiO_2:Al_2O_3 = 25$) and DCM (10 mL), then nitrotoluene (35 mmol) was added dropwise. The flask was equipped with a water condenser fitted with a calcium chloride guard tube and the reaction was heated at 50 °C for 1 h. The reaction mixture was cooled to room temperature, analytical grade acetone (30 mL) was then added and the mixture was stirred for 5 min. The zeolite was removed by suction filtration and washed with copious amounts of acetone. The mother liquors were combined, hexadecane (1.0 g) was added and the mixture was subjected to GC analysis.

Acknowledgments

References and Notes

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