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(54) Title: METHODS FOR THE NITRATION OF AROMATIC COMPOUNDS

(57) Abstract: According to the invention there is provided a method for the nitration of an aromatic compound including the step of reacting the aromatic compound with nitric acid in the presence of an acid anhydride and an aluminosilicate catalyst, in which the acid anhydride is at least one of: $((C_nH_{2n+1})CO)_2O$, where n is 1 to 4 and the moiety C_nH_{2n+1} can be straight or branched chain; $((CH_pCl_q)CO)_2O$, where p is 0 to 2, q is 1 to 3, and p+q = 3; and oxoiane -2, 5-dione, with the proviso that when the acid anhydride is $(CH_3CO)_2O$, the aromatic compound is toluene, 2-nitrotoluene or 4-nitrotoluene, and the nitration is performed to produce 2,4-dinitrotoluene.

METHODS FOR THE NITRATION OF AROMATIC COMPOUNDS

This invention relates to methods for the nitration of aromatic compounds, with particular, but by no means exclusive, reference to the dinitration of toluene to 2,4-dinitrotoluene in high yields and with high regioselectivity.

5   Nitration of aromatic compounds is one of the most important and widely studied chemical reactions. 2,4-Dinitrotoluene (2,4-DNT) is a very important intermediate for the production of industrially important chemicals and is used in the synthesis of polyurethanes, explosives, agrochemicals, pharmaceuticals, fragrances and dyes. The usual commercial production of 2,4-DNT employs the

10   reaction of toluene with nitric acid in the presence of sulphuric acid (so called "mixed acids"). Such dinitration of toluene with mixed acids produces 2,4-DNT and 2,6-dinitritoluene (2,6-DNT) in a ratio of only 4:1 However, separation of such mixtures to provide pure 2,4-DNT is potentially both costly and hazardous, so that for many applications the less desirable mixture of 2,4- and 2,6-DNT is

15   used instead. Production of oxidation by-products is a further disadvantage of the use of mixed acids.

Nitration with mixed acids has the advantage of using cheap and readily available reagents. Consequently, many attempts have been made to improve the mixed acids process by varying the reaction parameters, plant

20   characteristics or product handling. However, these processes still suffer from serious limitations. The selectivity for the desired product is often low, oxidation by-products may be produced and the work-up procedure may lead to the generation of large quantities of corrosive waste acids which are expensive to dispose of or to recycle.

Nitrogen dioxide has been used to polynitrate aromatic compounds at low temperatures in the presence of ozone and a catalyst such as methanesulfonic acid. However, the process has never been applied for the production of 2,4-DNT by dinitration of toluene. Other methods such as nitration using zirconium

5   and hafnium triflates in the presence of nitric acid have been disclosed for the nitration of 2-NT, but the ratio of 2,4-/2,6-DNT was in the range of 2 [Tetrahedron Lett., 39, 1641, 1998, Waller et al.].

An alternative approach would involve the use of solid acid catalysts. The advantage would lie in the easy separation of solid from the product mixture and

10   easy regeneration of the solids. There have been several attempts to improve the process by this approach. One investigation describes a nitration process using a liquid organic solvent, nitric acid and acetic anhydride over Claycop, a reagent consisting of an acidic montmorillonite clay impregnated with anhydrous cupric nitrate [J. Org. Chem., 60, 3445, 1995, Gigante et al.; and WO 9419310].

15   This process provides higher yields of dinitro products with improved selectivity; for example, nitration of toluene in tetrachloromethane gave an 85% yield of dinitrotoluenes with a 2,4-/2,6-DNT ratio of 9. However, the process requires a large excess of nitric acid and the use of carbon tetrachloride as a solvent which makes the process commercially unattractive because the amount of the

20   required products from a given reactor would be low and recovery of the products from large volumes of solvents, particularly environmentally undesirable halogenated solvents such as carbon tetrachloride, would be expensive. Furthermore, in other studies Claycop with acetic anhydride in dichloromethane or tetrachloromethane was found to be neither catalytic nor

regioselective for the nitration of 2-NT [J. Chem. Soc., Perkin. Trans. 2, 847, 1997, Lancaster et al.].

A process for the nitration of aromatic compounds using nitric acid (65%) over zeolite beta has been applied to the synthesis of dinitro compounds [Catal.

5   Today, 60, 275, 2000, Vassena et al.]. For example, nitration of an equimolar mixture of 2-NT and 4-nitrotoluene (4-NT) at a high temperature under simultaneous distillation to remove water gave DNTs in which the 2,4-/2,6-DNT ratio was 94:6. However, the yield of DNTs was low (20%) while other solid catalysts rather than zeolite beta were unstable under the highly acidic

10   conditions and high temperature used (130 °C).

A similar process using nitric acid in the presence of zeolite beta catalysts in an inorganic/organic matrix as a binder was disclosed in US 6620981 B1. Nitration of toluene gave nitrotoluenes (NTs) with 56% conversion and a proportion *o/m/p* of 28/3/68. However, the process requires a high temperature

15   (100-160 °C), with continuous removal of water from the reaction mixture, and has never been applied for the polynitration of toluene.

Aromatic compounds have been nitrated in quantitative yields with high *para*-selectivity in a solvent free process by using a stiochiometeric quantity of nitric acid and acetic anhydride at 0 to 20 °C in the presence of zeolite Hβ

20   [Chem. Commun., 469, 1996. Smith et al.; and WO9636587 A1]. However, successful use of this process to polynitrate aromatic compounds such as toluene has not been disclosed.

Dinitration of toluene with nitric acid and trifluoroacetic anhydride over zeolite Hβ gave 2,4-DNT in 92% yield with a 2,4-/2,6-dinitotoluene ratio of 25 [J.

Chem. Soc., Perkin Trans. 1, 2753, 2000, Smith et al.]. Even greater selectivity (70:1; in 96% yield) was obtained when the reaction was conducted in two stages, with trifluoroacetic anhydride added only in the second stage [J. Chem. Soc., Perkin Trans. 1, 2753, 2000, Smith et al.]. However, such a process is less

5   attractive for commercial production of 2,4-dinitrotoluene because trifluoroacetic anhydride is volatile, toxic and expensive.

There is therefore still a need for a process to produce 2,4-DNT selectively and in high yield, which does not involve the use of exceptionally expensive or toxic reagents, has reasonable energy requirements, avoids use of

10   solvents, eliminates or minimizes the formation of oxidation by-products, and is mild, efficient and safe. The present invention, in at least some of its embodiments, addresses these needs. The present invention is not limited to the production of 2,4-DNT, but rather can be applied to the single or polynitration of a range of aromatic compounds.

15   According to the invention there is provided a method for the nitration of an aromatic compound including the step of reacting the aromatic compound with nitric acid in the presence of an acid anhydride and an aluminosilicate catalyst, in which the acid anhydride is at least one of: $((C_nH_{2n+1})CO)_2O$, where n is 1 to 4 and the moiety C_nH_{2n+1} can be straight or branched chain;

20      $((CH_pCl_q)CO)_2O$, where p is 0 to 2, q is 1 to 3, and p+q = 3; and oxolane-2,5-dione, with the proviso that when the acid anhydride is $(CH_3CO)_2O$, the aromatic compound is toluene, 2-nitrotoluene or 4-nitrotoluene, and the nitration is performed to produce 2,4-dinitrotoluene.

The aromatic compound may be a monocyclic or polycyclic aromatic hydrocarbon, for example benzene, naphthalene, anthracene and biphenyl. The aromatic compound may optionally be substituted by one or more substituents,

5   preferably substituents selected from alkyl, especially C_{1-6}-alkyl and more preferably methyl, ethyl and propyl; alkoxy, especially C_{1-6}-alkoxy and more preferably methoxy and ethoxy; halogen; cyano; nitro; phenyl; hydroxy; amino; formyl; and acyl. The process is particularly suitable for the nitration of a benzene which carries one or two substituents, for example fluorobenzene,

10   chlorobenzene, bromobenzene, toluene, ethylbenzene, *iso*-propylbenzene, *tert*-butylbenzene, benzonitrile, 2-chlorofluorobenzene, 2-fluoroanisole, 2-fluorotoluene, 2-bromotoluene, 3-fluorotoluene, 1,2-difluorobenzene, 2-bromofluorobenzene, 2-nitrotoluene and 4-nitrotoluene.

Preferably, the aromatic compound is toluene, and a dinitration step is performed to produce 2,4-dinitrotoluene. The nitration can occur quickly and

15   regioselectively in high yield.

In other embodiments, the aromatic compound is 2-nitrotoluene or 4-nitrotoluene, and a single nitration step is performed to produce 2,4-dinitrotoluene.

In other embodiments still, the aromatic compound is Ph-X, where Ph is

20   phenyl and X is C_2H_5, C_3H_7, F, OCH_3 or OC_2H_5.

In preferred embodiments, the acid anhydride is propanoic anhydride (propionic anhydride), chloroacetic anhydride or dichloroacetic anhydride. Other examples of suitable acid anhydrides are trichloroacetic anhydride, butyric

anhydride, pentanoic (valeric) anhydride, 2-methylpropionic (iso-butyric) anhydride, trimethylacetic (pivalic) anhydride and oxolane-2,5-dione (succinic anhydride).

Preferably, the aluminosilicate catalyst is a zeolite, especially a zeolite which has a rigid 3-dimensional pore structure. Without wishing to be bound by any particular theory or conjecture, it is believed that the nitration reaction occurs in the confined space of the pores which induces shape selectivity and affects the regioselectivity of the reaction. A Si/Al ratio of from 1 to 1000 is preferred. Preferred zeolites are zeolites with medium to large pore sizes, such as zeolites X, Y, ZSM-5, Mordenite and ß types. Typically, the Si/Al ratio is from 2:1 to 80:1.

The zeolite may be a cation exchanged zeolite. The cation-forms which are most preferred are H^+, Fe^{3+}, Al^{3+}, ammonium, substituted ammonium, rare earth cations and other cations capable of generating acidity. A particularly preferred zeolite is zeolite $H^+\beta$ (also referred to herein as zeolite Hβ). Other cation-exchanged β zeolites might be used, for example, $Fe^{3+}\beta$ and $Al^{3+}\beta$.

Preferably, the method is performed in the absence of a solvent using a liquid acid anhydride. If a solvent is used, it is preferred that this solvent is the acid anhydride itself, ie, the acid anhydride is used in excess. Thus, it is preferred that the method is performed using a reaction system consisting essentially of the aluminosilicate catalyst mixed with the aromatic compound, nitric acid and a liquid acid anhydride, with no additional organic solvent being added to the reaction mixture. Without wishing to be bound by any particular

theory or conjecture, it is believed that the nitric acid and acid hydride react with each other *in situ* to form acyl nitrate, and this acts as the nitrating agent for the aromatic compound. In this way, the need to recover produce from large volumes of solvent is avoided, which might otherwise render the process unattractive for commercialisation.

The method is preferably performed at a temperature in the range -50°C to 100°C, more preferably in the range -20 to 80°C, and most preferably in the range 0°C to 50°C.

Preferably, the ratio of nitric acid to the aromatic compound is in the range 1:1 to 10:1. Preferably, the ratio of nitric acid to acid anhydride is in the range 1:1 to 1:10. More preferably, the ratio of aromatic compound to nitric acid to acid anhydride is in the range 1:1:1 to 1:4:4. It is preferred to utilise only a modest excess of nitric acid and acid anhydride, thereby reducing the amount of waste acid requiring further treatment. It is also advantageous that the method produces very little oxidized product as a waste.

Typically, nitric acid of a concentration in the range 70 to 100% is used, preferably close to 100% because the water present in the nitric acid undesirably hydrolyses the acid anhydride. Dilute nitric acid requires more acid anhydride in the reaction mixture and increases the amount organic acid by-product compared with a more concentrated nitric acid.

It is preferred that the aluminosilicate catalyst is mixed with the nitric acid, followed by the acid anhydride, and then the aromatic compound. This

approach can provide high regioselectivity. However, alternative orders of mixing are also possible.

Typically, the reaction is allowed to continue until complete as judged by an appropriate analytical technique such as gas chromatography or proton

5   nuclear magnetic resonance, and the reaction products are isolated by any convenient means such as extraction or crystallization followed by filtration.

A further aspect of the invention is that the aluminosilicate catalyst may be recycled. Accordingly, the invention provides a process for regeneration and re-use of an aluminosilicate catalyst following use in the nitration of an aromatic

10   compound. The aluminosilicate catalyst regeneration process is preferably performed by heating the catalyst at a temperature of from 20°C to 600°C, more preferably at a temperature of from 100°C to 400°C.

When the aluminosilicate used in the nitration process is removed from the reaction mixture, for example by filtration, the nitrated aromatic compound

15   may be purified by distilling off the relatively volatile organic acid by-product and any unreacted aromatic compound. Alternatively, the organic acid can be removed by washing with a suitable base and subsequently regenerated.

The regenerated aluminosilicate catalyst is suitable for re-use in the nitration process without the addition of fresh aluminosilicate.

20   Whilst the invention has been described above, it extends to any inventive combination or sub-combination of the features set out above or in the following description or claims.

Example 1

Double nitration of toluene

Propionic anhydride (16.90 g, 130 mmol) was added to a stirring mixture of nitric acid (100%; 120 mmol, 5.04 ml) and zeolite Hβ (2.0 g, Si/Al = 12.5)

5   cooled in a bath set at 0 °C and the mixture was stirred for 5 min at constant temperature. Toluene (3.22 g, 35 mmol) was then added dropwise and the mixture was allowed to warm to room temperature. The flask was equipped with a water condenser fitted with a calcium chloride tube and was stirred in a bath set at 50 °C for 4 h. The reaction mixture was cooled to room temperature and

10   analysis by GC indicated that dinitrotoluenes were obtained in 99% yield and the ratio of 2,4-/2,6-DNT was 123:1.

Pure 2,4-DNT (>99% purity by GC) was isolated from the reaction mixture in 94% yield by simply concentrating the mother liquor and recrystallisation from analytical grade diethyl ether.

15   **Examples 2 to 7: Nitration of toluene using liquid anhydrides**

Examples 2 to 7 illustrate the effect of the use of various liquid acid anhydrides on the double nitration of toluene. In the examples 2 to 7, a mixture of toluene (35 mmol, 3.75 ml), nitric acid (120 mmol, 5.04 ml), anhydride (120 mmol) and zeolite Hβ (Si/Al = 12.5; 2.0 g) was stirred in a bath set at 50 °C for

20   the stated period of time. The results are shown in Table 1.

Table 1: The effect of liquid acid anhydride on the nitration of toluene

Example	Anhydride	Time (h)	Yield (%)					2,4-/2,6- Ratio
			2-NT	3-NT	4-NT	2,4-DNT	2,6-DNT	
2	Acetic	4	1.2	2.4	25	71	1.1	65

3	Propionic	4	0	0.9	4.6	94	1	94
4	Butyric	4	7.1	1.3	29	59	2.4	25
5	Valeric	16	1.4	2.6	7.9	83	3	28
6	*Iso*-Butyric	4	22	2.1	44	31	0.7	44
7	Pivalic	4	45	1.3	47	5.5	0	----

Examples 8 to 11: Nitration of toluene using solid anhydrides

Examples 8 to 11 illustrate the effect of the use of various solid acid anhydrides on the double nitration of toluene. In the examples 8 to 11, a mixture of toluene (35 mmol, 3.75 ml), nitric acid (120 mmol, 5.04 ml), anhydride (120 mmol), zeolite Hβ (Si/Al = 12.5; 2.0 g) and dichloromethane (10 ml) was stirred in a bath set at 50 °C for the stated period of time. The results are shown in Table 2.

Table 2: The effect of solid acid anhydride on the nitration of toluene

Example	Anhydride	Time (h)	Yield (%)					2,4-/2,6-Ratio
			2-NT	3-NT	4-NT	2,4-DNT	2,6-DNT	
8	Chloroacetic	4	0	0.2	0	98	2.1	49
9	Dichloroacetic	0.5	0	0	0	98	1.8	54
10	Trichloroacetic	0.5	0	0	7.9	85	6.3	14
11	Succinic	4	0	0.5	0.6	85	8.2	10

Example 12: Nitration of toluene using chloroacetic anhydride in 1,2-dichloroethane as a solvent

A mixture of toluene (35 mmol, 3.75 ml), nitric acid (120 mmol, 5.04 ml), chloroacetic anhydride (120 mmol, 20.52 g), zeolite Hβ (Si/Al = 12.5; 2.0 g) and 1,2-dichloroethane (10 ml) was stirred in a bath set at 50 °C for 2 h. Analysis showed a 97% yield of 2,4-DNT and a 2.3% yield of 2,6-DNT along with 0.9% yield of 4-NT.

Example 13: Two-stage dinitration of toluene using chloroacetic anhydride in dichloromethane

A mixture of toluene (35 mmol, 3.75 ml), nitric acid (120 mmol, 5.04 ml), chloroacetic anhydride (120 mmol, 20.52 g), zeolite Hβ (Si/Al = 12.5; 2.0 g) and dichloromethane (10 ml) was stirred overnight at room temperature in the first step. The reaction mixture was cooled in a bath set to 0 °C and extra fresh chloroacetic anhydride (30 mmol, 5.13 g), nitric acid (30 mmol) and dichloromethane (10 ml) were added in the second step and the reaction mixture was stirred in a bath set at 50 °C for 2 h. Analysis showed a 98% yield of 2,4-DNT and a 1.7% yield of 2,6-DNT.

Example 14: Nitration of toluene using chloroacetic anhydride in a solvent-free system

A mixture of toluene (35 mmol, 3.75 ml), nitric acid (120 mmol, 5.04 ml), chloroacetic anhydride (120 mmol, 20.52 g) and zeolite Hβ (Si/Al = 12.5; 2.0 g) was stirred overnight at room temperature. The reaction mixture was cooled in a bath set to 0 °C and fresh chloroacetic anhydride (30 mmol, 5.13 g) and nitric acid (30 mmol) were added and the reaction mixture was stirred in a bath set at 50 °C for 2 h. Analysis showed a 95% yield of 2,4-DNT and a 4% yield of 2,6-DNT along with 1.4% yield of 4-NT.

Example 15: Two-stage dinitration of toluene using acetic anhydride

A mixture of toluene (35 mmol. 3.75 ml), nitric acid (120 mmol, 5.04 ml), acetic anhydride (150 mmol, 14.16 ml) and Hβ (Si/Al = 12.5; 2.0 g) was stirred overnight at room temperature in the first step. Extra fresh nitric acid (30 mmol, 1.26 ml) and acetic anhydride (37.5 mmol, 3.54 ml) were added in the second step and the reaction mixture was stirred for 2 h in a bath set at 50 °C. Analysis

showed a 88% yield of 2,4-DNT and a 12% yield of 4-NT along with a trace of 2,6-DNT.

Examples 16-19: Effect of quantity of propionic anhydride on dinitration of toluene using propionic anhydride

Examples 16 to 19 illustrate the effect of the use of an excess of propionic anhydride on the double nitration of toluene. In the examples 16 to 19, a mixture of nitric acid (120 mmol), zeolite Hβ (Si/Al = 12.5; 2.0 g) and the stated quantity of propionic anhydride was stirred for 5 min in a bath set at 0 °C. Toluene (3.22 g, 35 mmol) was then added dropwise and the mixture was allowed to warm to room temperature. The flask was equipped with a water condenser fitted with a calcium chloride tube and was stirred in a bath set at 50 °C for 4 h. The results are shown in Table 3.

Table 3: Effect of quantity of propionic anhydride

| Example	EtCO)$_2$O (mmol)	Yields of dinitrotoluenes (%)	Yields (%)		2,4-:2,6-ratio
			2,4-DNT	2,6-DNT	
16	120	95	94	1	93
17	130	98.8	98	0.8	123
18	140	97.9	97	0.9	108
19	160	96.7	96	0.7	137

Examples 20-25: Effect of reaction time on the dinitration of toluene using propionic anhydride

Examples 20 to 25 illustrate the effect of reaction time on the double nitration of toluene using propionic anhydride. In the examples 20 to 25, a mixture of toluene nitric acid (120 mmol, 5.04 ml), propionic anhydride (130

mmol, 16.65 ml) and zeolite Hβ (Si/Al = 12.5; 2.0 g) was stirred for 5 min in a bath set at 0 °C. Toluene (3.22 g, 35 mmol) was then added dropwise and the mixture was allowed to warm to room temperature. The flask was equipped with a water condenser fitted with a calcium chloride tube and was stirred in a bath set at 50 °C for the stated period of time. The results are shown in Table 4.

Table 4: Effect of reaction time on nitration of toluene using propionic anhydride

Example	Time (min)	Yield (%)					2,4-/2,6-Ratio
		2-NT	3-NT	4-NT	2,4-DNT	2,6-DNT	
20	5	0	1.1	15	81	1.1	74
21	15	0	1	13	82	1	82
22	30	0	1.1	11	84	1.1	76
23	60	0	0.9	8	91	0.7	130
24	120	0	0.8	4.8	93	0.9	103
25	240	0	0.4	0.8	98	0.8	123
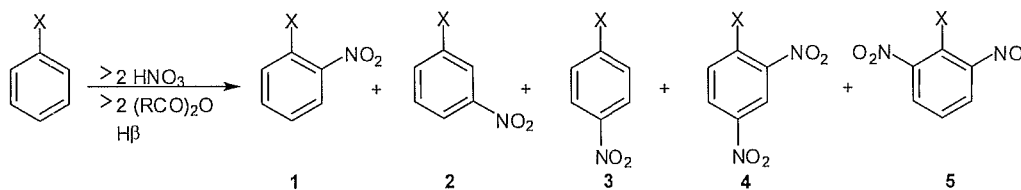
Examples 26-29: Effect of X on the nitration of Ph-X using chloroacetic anhydride

Examples 26 to 29 illustrate the effect of X on the nitration of PhX. The following general procedure was used. A mixture of mono-substituted benzene (35 mmol), nitric acid (120 mmol, 5.04 ml), chloroacetic anhydride (120 mmol, 20.52 g), DCM (10 ml) and zeolite Hβ (Si/Al = 12.5; 2.0 g) was stirred for 4 h in a bath set at 50 °C. The results are shown in Table 5.

Table 5: The effect of X on the nitration of Ph-X

Example	X	Yield (%)					4/5 Ratio
		1	2	3	4	5	
26	Me	0	0.2	0	98	2	49
27	Et	0	0	3.9	95	0	---
28	Pr	0	0	0	96	0	---
29	F	0	0	7.4	57	0	---

Examples 30-32: Effect of X on the nitration of Ph-X using propionic anhydride

Examples 30 to 32 illustrate the effect of X on the nitration of PhX. The following general procedure was used. A mixture of nitric acid (120 mmol, 5.04 ml), propionic anhydride (130 mmol, 16.65 ml) and zeolite Hβ (Si/Al = 12.5; 2.0 g) was stirred for 5 min in a bath set at 0 °C. Mono-substituted benzene (35 mmol), was then added dropwise and the mixture was allowed to warm to room temperature. The flask was equipped with a water condenser fitted with a calcium chloride tube and was stirred in a bath set at 50 °C for 4 h. The results are shown in Table 6.

Table 6: The effect of X on the nitration of Ph-X using propionic anhydride

Example	R	Yield (%)					4/5 Ratio
		1	2	3	4	5	
30	OMe	0	0	0	97	0	---
31	OEt	0	0	0	86	0	---
32	Me	0	0.4	0.8	98	0.8	123

Example 33: Nitration of 2-nitrotoluene using acetic anhydride

A mixture of 2-nitrotoluene (35 mmol, 4.79 ml), zeolite Hβ (Si/Al = 12.5; 2.0 g), nitric acid (120 mmol, 5.04 ml) and acetic anhydride (150 mmol, 14.16 ml) was stirred in a bath set at 50 °C for 4 h. Analysis showed a 97% yield of 2,4-DNT and a 3% yield of 2,6-DNT.

Example 34: Nitration of 4-nitrotoluene using acetic anhydride

A mixture of 4-nitrotoluene (35 mmol, 4.79 ml), zeolite Hβ (Si/Al = 12.5; 2.0 g), nitric acid (100 mmol, 4.20 ml) and acetic anhydride (130 mmol, 12.27 ml) was stirred in a bath set at 50 °C for 4 h. Analysis showed a 88% yield of 2,4-DNT along with 11% of unreacted 4-NT.

Example 35: Nitration of 2-nitrotoluene using chloroacetic anhydride

A mixture of 2-nitrotoluene (35 mmol, 4.79 ml), zeolite Hβ (Si/Al = 12.5; 2.0 g), nitric acid (100 mmol, 4.20 ml) and chloroacetic anhydride (100 mmol, 17.10 g) was stirred in a bath set at 50 °C for 1 h. Analysis showed a 94% yield of 2,4-DNT and a 5% yield of 2,6-DNT.

5   **Example 36: Nitration of 4-nitrotoluene using chloroacetic anhydride**

A mixture of 4-nitrotoluene (35 mmol, 4.79 ml), zeolite Hβ (Si/Al = 12.5; 2.0 g), nitric acid (100 mmol, 4.20 ml) and chloroacetic anhydride (100 mmol, 17.10 g) was stirred in a bath set at 50 °C for 1 h. Analysis showed a 99.5% yield of 2,4-DNT.

10   **Example 37: Nitration of 2-nitrotoluene using propionic anhydride**

A mixture of 2-nitrotoluene (35 mmol, 4.79 ml), zeolite Hβ (Si/Al = 12.5; 2.0 g), nitric acid (70 mmol, 2.94 ml) and propionic anhydride (70 mmol, 12.82 g) was stirred in a bath set at 50 °C for 4 h. Analysis showed a 95.6% yield of 2,4-DNT and a 4.2% yield of 2,6-DNT.

15   **Example 38: Nitration of 4-nitrotoluene using propionic anhydride**

A mixture of 4-nitrotoluene (35 mmol, 4.79 ml), zeolite Hβ (Si/Al = 12.5; 2.0 g), nitric acid (70 mmol, 2.94 ml) and propionic anhydride (70 mmol, 12.82 g) was stirred in a bath set at 50 °C for 4 h. Analysis showed a 96% yield of 2,4-DNT along with 4% of unreacted 4-NT.

20   **Example 39: Recycling of Catalyst**

The zeolite was recovered following extraction of the products from nitration of toluene using nitric acid and propionic anhydride over zeolite Hβ and was then regenerated by heating overnight in air in an oven set at 450 °C.

The method for Example 1 was repeated except that the recovered dry zeolite referred to above was used in place of fresh zeolite Hβ (Si/Al = 12.5) to give nitrotoluenes in 97.5% yield with a 2,4-/2,6-DNT ratio of 195. Further recycling and re-use of the same catalyst gave the results summarised in Table 7.

Table 7: The effect of recycling the zeolite

Cycle No.	Yields of DNTs (%)	Yields of isomers (%)		
		2,4-DNT	2,6-DNT	2,4-/2,6- ratio
1	98.8	98	0.8	123
2	97.5	97	0.5	195
3	96.6	96	0.6	160
4	95.5	95	0.5	190
5	95.9	95	0.9	106
6	95.8	95	0.8	119
7	94.8	94	0.8	118

Examples 40-42: Nitration and dinitration of toluene using zeolite HY

Various silicon to aluminium ratios for zeolite HY were chosen, to see the effect of acid strength and number of active sites on their reactivity. Reactions involved toluene (35 mmol, 3.75 ml), nitric acid (120 mmol, 5.04 ml) and acetic anhydride (150 mmol, 14.16 ml) over zeolite HY (2.0 g) at room temperature overnight. After the first step, the reaction was stopped and extra nitric acid (30 mmol) and acetic anhydride (37.5 mmol) were added and the reaction mixture was stirred for a further 2 hours at 50°C. The results obtained after work up and GC analysis are shown in Table 8.

Table 8: Nitration and dinitration of toluene with zeolite HY

Catalyst Type	Ratio of SiO_2/Al_2O_3	Yield (%)						
		2-NT	3-NT	4-NT	2,4-DNT	2,6-DNT	p/o ratio	2,4-:2,6- ratio
HY	5.1	58	4.1	37	0.0	0.0	0.6	---

| HY | 30 | 14 | 2.2 | 5.1 | 72 | 5.1 | 0.4 | 14 |
| HY | 80 | 30 | 2.1 | 12 | 52 | 5.3 | 0.4 | 13 |

There was no 2,4-DNT produced when zeolite HY (SiO_2/Al_2O_3=5.1) was used. However, 2,4-DNT was produced in 72% yield when dinitration of toluene

5   was carried out over zeolite HY (SiO_2/Al_2O_3=30) and 52% when zeolite HY (SiO_2/Al_2O_3=80) was used.

Experimental Section

Commercial 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

10   purchased from BDH Laboratory Supplies. Other chemicals were purchased from Aldrich Chemical Company and used without further purification except for propanoic anhydride which was distilled over P_2O_5. 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

15   were: 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.

CLAIMS

1.   A method for the nitration of an aromatic compound including the step of reacting the aromatic compound with nitric acid in the presence of an acid anhydride and an aluminosilicate catalyst, in which the acid anhydride is at least one of: $((C_nH_{2n+1})CO)_2O$, where n is 1 to 4 and the moiety C_nH_{2n+1} can be straight or branched chain; $((CH_pCl_q)CO)_2O$, where p is 0 to 2, q is 1 to 3, and p+q = 3; and oxolane -2, 5-dione, with the proviso that when the acid anhydride is $(CH_3CO)_2O$, the aromatic compound is toluene, 2-nitrotoluene or 4-nitrotoluene, and the nitration is performed to produce 2,4-dinitrotoluene.

2.   A method according to claim 1 in which the aromatic compound is toluene, and a dinitration step is performed to produce 2,4-dinitrotoluene.

3.   A method according to claim 1 in which the aromatic compound is 2-nitrotoluene or 4-nitrotoluene, and a single nitration step is performed to produce 2,4-dinitrotoluene.

4.   A method according to claim 1 in which the aromatic compound is Ph-X, where Ph is phenyl and X is C_2H_5, C_3H_7, F, OCH_3 or OC_2H_5.

5.   A method according to any previous claim in which the acid anhydride is propanoic anhydride, chloroacetic anhydride or dichloroacetic anhydride.

6.   A method according to any previous claim in which the aluminosilicate catalyst is a zeolite.

7.   A method according to claim 6 in which the zeolite has a Si/Al ratio of from 1 to 1000.

8.   A method according to claim 8 in which the zeolite is a cation exchanged zeolite.

9.   A method according to claim 8 in which the zeolite is zeolite $H^+\beta$.

10.   A method according to any previous claim which is performed either in the absence of a solvent or using the acid anhydride present as a solvent.

11.   A method according to any previous claim which is performed at a temperature in the range -50°C to 100°C.

12.   A method according to any previous claim in which the ratio of nitric acid to the aromatic compound is in the range 1:1 to 10:1.

13.   A method according to any previous claim in which the ratio of nitric acid to acid anhydride is in the range 1:1 to 1:10.

14.   A method according to any previous claim in which nitric acid of a concentration in the range 70% to 100% is used.

15.   A method according to any previous claim in which the aluminosilicate catalyst is mixed with the nitric acid, followed by the acid anhydride, followed by the aromatic compound.

INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07C201/08   C07C205/06   C07C205/12   ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C07C

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 96/36587 A1 (ZENECA LTD [GB]; DEBOOS GARETH ANDREW [GB]; SMITH KEITH [GB]; MUSSON A) 21 November 1996 (1996-11-21) cited in the application claims 1-18; page 3, lines 10-18;examples 2-18,23 -----	1-15
X	WO 94/19310 A1 (INST NACIONAL DE ENGENHARIA E [PT]; SILVA GIGANTE CARVALHEIRO BARB [PT) 1 September 1994 (1994-09-01) cited in the application claims 1-18; page 5, lines 23-28; page 8, lines 12-17; examples 1-16 ----- -/--	1-15

[X] Further documents are listed in the continuation of Box C.	[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
17 February 2012	02/03/2012

Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer Grammenoudi, S

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INTERNATIONAL SEARCH REPORT

C(Continuation).   DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KEITH SMITH, ET AL.,: "A novel method for the nitration of deactivated aromatic compounds", J.CHEM.SOC.PERKIN TRANS. 1, 2000, pages 2753-2758, XP002669876, cited in the application equations 2,3,5-7; tables 1-7 -----	1-15
X	N. LLWELLYN LANCASTER ET AL.,: "The efficacy of "Claycop" in the dinitration of toluene", J. CHEM. SOC. PERKIN TRANS. 2, 1997, pages 847-848, XP002669877, cited in the application fig. 1, tab. 1,2 -----	1-5, 10-15
X	GIGANTE B ET AL: "MILD AND SELECTIVE NITRATION BY CLAYCOP", JOURNAL OF ORGANIC CHEMISTRY, AMERICAN CHEMICAL SOCIETY, EASTON.; US, vol. 60, no. 11, 2 June 1995 (1995-06-02), pages 3445-3447, XP000499102, ISSN: 0022-3263, DOI: 10.1021/JO00116A034 cited in the application tab. 1,2 -----	1-5, 10-15
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Information on patent family members

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