

(12) **UK Patent Application** (19) **GB** (11) **2 347 409** (13) **A**

(43) Date of A Publication **06.09.2000**

(21) Application No **9904706.0**

(22) Date of Filing **03.03.1999**

(71) Applicant(s)

**The Secretary of State for Defence
(Incorporated in the United Kingdom)
Defence Evaluation & Research Agency, Ively Road,
FARNBOROUGH, Hampshire, GU14 6TD,
United Kingdom**

(72) Inventor(s)

**Ross Wood Millar
Robert Peter Claridge
Simon Patrick Philbin**

(74) Agent and/or Address for Service

**D/IPR Formalities Section (DERA)
Poplar 2, MOD(PE) Abbey Wood #19, BRISTOL,
BS34 8JH, United Kingdom**

(51) INT CL⁷

C07B 43/02 , C01B 21/20 , C07C 201/02 , C07D 305/06

(52) UK CL (Edition R)

**C1A ACD AD31 AM9 APC AVG6 A113 A2B
C2C CDH CMJ CMM C1328 C1562 C20Y C215 C246
C247 C25Y C253 C255 C30Y C330 C332 C470 C472
C621 C629 C639 C708**

(56) Documents Cited

Chemical abstract 75:143705

(58) Field of Search

**UK CL (Edition Q) C1A ACD APC AVG6 A2B
INT CL⁶ C01B 21/20 , C07B 43/02
ONLINE: WPI,EPODOC,JAPIO.CHABS**

(54) Abstract Title

Solid nitrating agent incorporating dinitrogen pentoxide

(57) A solid nitrating reagent comprises either a montmorillonite clay or a zeolite material incorporating an amount, preferably 10-30 wt 90, of gaseous dinitrogen pentoxide. The clay material can be type K10 and suitable zeolites include those designated ZSM-5, zeolite beta, zeolite F720 and zeolite F780 (all H form). The reagent is conveniently prepared by exposing a sample of the montmorillonite clay or zeolite material to gaseous dinitrogen pentoxide contained in a stream of ozonised oxygen at a sub-ambient temperature while agitating the clay or zeolite material. The temperature is in the range of -60 to -20°C. In use the reagent is contacted with a substance to be nitrated in an inert solvent such as hexane or a perfluorocarbon at a temperature of -20 to 15°C. Suitable substances to be nitrated include alcohols, O-silyl ethers and silylamines.

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Solid Nitrating Reagent

The present invention relates to a novel nitrating agent which is effective for carrying out nitrations on heteroatoms while avoiding the use of chlorinated hydrocarbon solvents or highly reactive solvents as the reaction solvent. The nitrating effect derives from use of dinitrogen pentoxide (hereinafter referred to as "DNPO").

Nitration on heteroatoms (oxygen and nitrogen) is commonly carried out by reaction of suitable precursors (alcohols and N-acyl or similar species respectively) with strong acids such as nitric acid in admixture with sulphuric acid or acid anhydrides (e.g. acetic anhydride). Such acid mixtures are highly corrosive, giving rise to handling problems, and the post-reaction liquors are often unstable and difficult to dispose of (for further details see Urbanski, "Chemistry & Technology of Explosives", Vols. 1-3, Pergamon Press, 1967 and Vol. 4, 1984).

In recent developments in nitration chemistry it has been established that DNPO can be used instead of the acid mixtures referred to above to generate nitrate esters and nitramines in excellent yields from precursors such as alcohols or their O-silyl ethers and silylamines respectively. Applicant's British Patent No. 2281562 describes and claims a process for carrying out such reactions and see also Millar, R. W. & Philbin, S. P., *Tetrahedron* 1997, **51** 4371. In an earlier invention of the applicant (European Patent No. 0223440) strained-ring precursors such as epoxides and aziridines were also employed as substrates for reactions with DNPO to generate nitrate esters and nitramines.

The use of these methods has overcome many of the problems inherent in the older "mixed acid" technology, and has permitted nitrations to be carried out under near stoichiometric conditions as well as enabling the recycling of surplus nitrating agent (this refers particularly to the nitrodesilylation chemistry). Consequently the methods have led to markedly improved atom economy in nitrations of this type.

However, in both of these processes using DNPO, a chlorinated hydrocarbon solvent, typically dichloromethane (DCM), is required to act both as reaction solvent and as extraction medium for the removal of the product in an aqueous work-up step. Such solvents are environmentally-unfriendly and create considerable pollution in their manufacture, handling (particularly by inadvertent release into the atmosphere) and disposal.

An aim of the present invention, therefore, is to replace the chlorinated hydrocarbon solvents by less polluting media (so-called "clean" solvents) whilst retaining the advantages of atom economical nitrations using DNPO as referred to above.

Unfortunately few solvents exist which can act as a carrier for DNPO whilst remaining totally inert: apart from chlorinated hydrocarbons other than DCM (which are, of course, also environmentally-unfriendly), choice within the sphere of organic liquids is restricted to a few relatively polar solvents, principally nitromethane and sulpholane (the other possible contender, acetonitrile, reacts slowly with DNPO) and neither of these compounds is suitable for large-scale exploitation on account of hazard and involatility respectively. It appears therefore that new nitrating systems need to be devised in order to arrive at a wholly environmentally friendly nitration methodology.

Finely-divided solids such as clays of the montmorillonite type (designated K10), and to a lesser extent zeolites, have been used as support materials for solid nitrating agents, notably transition metal nitrates such as copper (II) nitrate (the mixture being called 'Claycop') or iron (III) nitrate (called 'Clayfen'). These materials have been used to promote aromatic nitrations with positional selectivity (see, for instance, P. Laszlo, *Preparative Chemistry Using Solid Supports*, Academic Press, 1987; P. Laszlo, *Acc. Chem. Res.*, **26** 607 (1993); K. Smith, A. Musson and G. A. DeBoos, *Chem. Comm.* 1996, 469). However, the conditions employed (known as 'Menke conditions') necessitate the use of aggressive solvents such as acetic anhydride, which is required to generate the active nitrating species.

Applicant has established that, when an inert solvent such as hexane is used with the Claycop reagent (Clayfen was discounted owing to its instability), the nitrating ability of the

solid reagent is greatly reduced and, in the case of alcohol nitrations, good yields of nitrate ester products can only be obtained with a few starting materials (e.g. adamantan-1-ol) and only in the presence of additional oxidant (ozone). Furthermore, no nitramines could be prepared under a variety of conditions. Therefore the known solid nitrating agents based on clay supports appear to be unsuitable for the types of clean syntheses which are being sought.

It has now however been found possible to produce an effective nitrating system by the incorporation of DNPO on to a solid support material comprising a montmorillonite clay or a zeolite. Because DNPO is a powerful nitrating agent which does not require a reactive solvent for activation, this technique provides a more versatile nitrating system and one which is free of any potentially undesirable solvent.

Accordingly the present invention provides, for use as a nitrating reagent, a montmorillonite clay or zeolite material which has incorporated therein dinitrogen pentoxide in an amount which is sufficient to effect nitration.

There is further provided, in accordance with the invention, a method for the preparation of a solid-supported nitration reagent which comprises exposing a sample of a montmorillonite clay or zeolite material to gaseous dinitrogen pentoxide contained in a stream of ozonised oxygen at a sub-ambient temperature while agitating the solid material.

The montmorillonite clay is preferably of the type known as K10, manufactured by Sud-Chemie of Germany but other clays of the type TOT 2:1 (as defined in Smith, K (Ed.), *Solid Supports & Catalysts in Organic Synthesis*, Ellis Horwood, 1992) are also likely to be suitable. Of the zeolites, those designated ZSM-5, zeolite beta, zeolite F720 and zeolite F780 (all H form) (supplied by Zeolyst International Ltd) are suitable. The skilled person will appreciate that it would be a matter of straightforward experimentation to discover which of the available clay and zeolite materials provide the optimum reagent according to the invention in relation to any particular nitration reactions which it is desired to carry out.

The sub-ambient temperature at which the clay or zeolite material is exposed to the gaseous DNPO is preferably a temperature in the range of from -60°C to -20°C , most preferably as low a temperature as possible within this range. The amount of DNPO incorporated in the solid material is typically of the order of 10 to 20% by weight but higher concentrations may be used, eg. 30% or even higher. The amount incorporated can be readily estimated by measuring the gain in weight of the clay or zeolite after the treatment with the gaseous DNPO. Conveniently an exposure time of about 2 hours will be suitable for obtaining a sufficient concentration of DNPO in the solid material but other durations of exposure may be selected in order to produce a desired concentration of DNPO.

The resultant solid nitrating reagent is conveniently referred to by the term "clay-DNPO" or "zeolite-DNPO" depending on the solid material which is used.

The present invention further provides a method for effecting nitration of an organic compound which comprises bringing together a solution of the compound in an appropriate solvent with an effective quantity of the solid nitrating reagent of the invention, allowing reaction to take place and extracting the nitrated product from the mixture.

The solvent is preferably an inert solvent such as, for example, hexane or another non-aromatic hydrocarbon solvent or one of the perfluorocarbons such as perfluoromethylcyclohexane (PP2), perfluorodecalin (PP6) or perfluoroperhydrophenanthrene (PP11). The solvent should be preferably be as anhydrous as possible in order to reduce the likelihood of decomposition of the reaction product through reaction with any (nitric) acid created from any water present in the reaction mixture. For the same reason it is preferred, wherever possible, to keep the solid nitrating reagent also as dry as possible prior to reaction.

Conveniently the solid nitrating reagent may be suspended in the chosen solvent and the organic compound which it is desired to nitrate then added to the suspension. Alternatively, the solid material may be added to a solution of the organic compound with rapid stirring of the liquid to provide effective distribution of the nitrating agent throughout

the liquid. Other methods of effecting the reaction of the DNPO contained within the solid nitrating medium with organic substrates will be readily apparent to the skilled person.

Typically the nitration reaction is carried out at a temperature of from -20°C to 15°C , preferably from around -5 to 0°C , as it is necessary to avoid the use of higher temperatures on account of the relative thermal instability of the DNPO. In fact, it has been observed that this substance, once incorporated into the solid support material, is more stable than in the pure form which provides a further advantage for the nitrating reagent of this invention.

Reactions with the solid nitrating agent of the invention generally take place quite rapidly within a few minutes but for some substrates a longer reaction time, for example of several hours, may be required. Clearly it is well within the scope of experimentation for the skilled addressee to establish an appropriate reaction time in the case of any particular substrate and for any specific nitrating reagent of the invention.

Using hexane as a solvent for the reaction of clay-DNPO, it has been found that good yields of nitrate esters are obtained from a variety of alcohols as substrates, including n-decanol, 2-ethyl-1-hexanol, 2-methyl-2-hexanol, 2-ethyl-1,3-hexanediol and ethane-1,2-diol (ethylene glycol). For all except the last-named alcohol the yields were in excess of 80%. The lower yield of ethyleneglycol dinitrate is accounted for by the difficulty in extracting the product on account of its appreciable solubility in water. Where it may be necessary to wash the product off the solid support this can conveniently be done using an environmentally-friendly solvent such as a perfluorocarbon.

In general the efficiency with which these nitrations can be carried out is in marked contrast to the methods employing the transition metal nitrate systems mentioned previously. For example, with 2-methyl-2-hexanol, Claycop in hexane gives none of the desired nitrate ester, the products instead resulting from dehydration and oxidative cleavage. Moreover, the simplicity of the reaction procedure is noteworthy, with only simple operations such as filtration and evaporation being required, reaction takes place near or slightly below ambient temperature, and no large excess of nitrating agent is required (i.e. the process is atom

economic). Added to this is the feasibility now established by applicant's process of using an environmentally-friendly solvent or solvents, for example the hydrocarbon, hexane, with in certain cases use of an auxiliary solvent such as a perfluorocarbon to wash off the product.

Clay-DNPO has been used to nitrate n-decyl(trimethylsilyl)ether under similar conditions to those employed with the alcohols mentioned above but with a longer (3 hr) reaction time, gave a good yield (84%) of n-decyl nitrate. Likewise N-(trimethylsilyl)morpholine has also been reacted with clay-DNPO under similar conditions to those employed previously except for a longer (18 hr) reaction time and gave 49% of the expected nitramine, N-nitromorpholine, as a pure product. This result contrasts strongly with the Claycop reaction which did not give any of the nitramine, starting from any of the potential precursors viz. free amine, N-trimethylsilyl or N-acetyl derivatives.

Applicant has therefore shown that several compounds containing the energetic moieties nitrate ester and nitramine can be synthesised cleanly and in good to excellent yield using the clay-DNPO system. Aromatic nitration can also be achieved, giving dinitro benzene derivatives, but the advantages in this case are less marked than for the aliphatic species. It will be readily appreciated by the skilled reader that by carrying out the reactions in hexane as solvent, problems relating to the use of non- environment-friendly materials can be avoided. (Although in the examples which follow dichloromethane has been used in small amounts to recover the product, it is anticipated that even this usage will be obviated by use of other more suitable solvents).

The invention will now be further described with reference to the following examples.

Example 1 - Preparation of Clay-DNPO

To an oven dried round bottom flask (100 cm³) fitted with a magnetic follower, K10 montmorillonite clay (6.01 g) was added which had been dried in a vacuum oven (ca.10 mmHg, 30⁰C) for 5 days. The flask was placed onto one of the collection outlets from the DNPO rig and the clay stirred to ensure that tumbling occurred. The flask was then cooled

to -78°C by an external dry ice/acetone bath and DNPO passed through the flask. After 2 h the flask was removed and stoppered and the mass of DNPO deposited determined by the increase in weight. The amount of DNPO deposited was ca. 2 g.

In all of the following examples 2 to 10, where reactions were carried out with clay-DNPO, the material used was prepared in the same manner as in Example 1.

Example 2 - Reaction of Clay-DNPO with 2-Methyl-2-hexanol

To a round bottom flask (100 cm^3) fitted with a magnetic follower, clay-DNPO (2.44 g, ca. 10.7 mmol DNPO) was added and the mixture cooled to -78°C by an external dry ice/acetone bath. n-Hexane (50 cm^3) was added and the resultant suspension was stirred. 2-Methyl-2-hexanol (1.24 g, 10 mmol) was added and the mixture stirred for 2 h at -5°C . The reaction mixture was filtered and the filtrate was neutralised using a saturated sodium hydrogen carbonate solution. The organic layer was removed, dried over magnesium sulphate, filtered and the solvent removed *in vacuo* to afford 2-methyl-2-hexanol nitrate as a pale yellow liquid (1.17 g, 69%).

IR (KBr plates, thin film) $\nu\text{ cm}^{-1}$: 1638 (NO_2 str), 1298 (NO_2 str), 855 (NO_2 str).

Example 3 - Reaction between Clay-DNPO and n-decanol (in n-hexane)

To a round bottom flask (100 cm^3) fitted with a magnetic follower, n-hexane (30 cm^3) and n-decanol (0.47 g, 2.96 mmol) were added and the resultant solution stirred and cooled to between -5 and 0°C by an external dry ice/acetone bath. Clay-DNPO (2.69 g, ca. 3.33 mmol DNPO) was added and the resultant suspension stirred for 30 min at -5 to 0°C . The reaction mixture was then filtered and the filtrate was washed with saturated sodium hydrogen carbonate solution, dried over magnesium sulphate and the solvent removed *in vacuo* to afford n-decanol nitrate as a colourless oil (0.41 g, 68%). The clay was washed with dichloromethane (25 cm^3) and refiltered. The filtrate was washed with sodium

hydrogen carbonate solution, dried over magnesium sulphate and the solvent removed in *vacuo* to afford a second crop of n-decanol nitrate as a pale yellow oil (0.15g, 24.9 %).

Hplc analysis (RP 18, MeCN:H₂O 4: 1) was consistent with an authentic sample of n-decanol nitrate.

IR (KBr plates, thin film) ν cm⁻¹: 2927 (CH str.), 2856 (CH str), 1633 (NO₂ as. str), 1279 (NO₂ sym. str), 863 (ONO₂ str). Lit. ν cm⁻¹: 1632, 1280, 864 (Millar & Philbin, *Tetrahedron* 1997, **53** 4371).

Example 4 - Reaction between Clay-DNPO and n-decanol (in acetonitrile)

To a round bottom flask (100 cm³) fitted with a magnetic follower and thermometer, anhydrous acetonitrile (30 cm³) and n-decanol (0.47 g, 2.96 mmol) were added and the resultant solution stirred and cooled to between -5 and 0°C by an external dry ice/acetone bath. Clay-DNPO (2.59g, ca.3.21 mmol DNPO) was added and the resultant suspension stirred for 30 min at -5 to 0°C. The mixture was filtered and the filtrate was washed with saturated sodium hydrogen carbonate solution, dried over magnesium sulphate and the solvent removed by evaporation at room temperature. This afforded a pale yellow oil which from IR analysis consisted of a mixture of unreacted starting material and n-decanol nitrate.

IR (KBr plates, thin film) ν cm⁻¹: 3346 (OH str), 1635 (NO₂ as. str), 1278 (NO₂ sym. str), 1039(C-OH str), 864 (ONO₂ str).

Example 5 - Reaction between Clay-DNPO and 2-Ethyl-1-hexanol (in n-hexane)

To a round bottom flask (100 cm³) fitted with a magnetic follower and thermometer, freshly distilled n-hexane (30 cm³) and 2-ethyl-1-hexanol (0.39 g, 2.99 mmol) were added and cooled with stirring to between -5 and 0°C. Clay-DNPO (2.58 g, ca. 3.20 mmol DNPO) was added and the reaction mixture stirred for 30 min with cooling. The mixture was filtered and the filtrate was washed with saturated sodium hydrogen carbonate solution, dried over

magnesium sulphate and the solvent removed in *vacuo* to afford a 2-ethyl-1-hexanol nitrate (0.41 g, 78 %) as a colourless oil. The clay was washed with dichloromethane (25 cm³) and refiltered. The filtrate was washed with saturated sodium hydrogen carbonate and dried over magnesium sulphate. The solvent was removed *in vacuo* to afford a second batch of 2-ethyl-1-hexanol nitrate (0.11g, 21 %) as a pale yellow oil.

Hplc analysis (RP18, MeCN:H₂O 4:1) was consistent with an authentic sample.

IR (KBr plates, thin film) ν cm⁻¹: 1632 (NO₂ as. str), 1279 (NO₂ sym. str), 866 (ONO₂ str). Lit. ν cm⁻¹: 1632, 1279, 867 (Millar & Philbin, *Tetrahedron* 1997, **53** 4371).

Example 6 - Reaction between Clay-DNPO and 2-Ethyl-1-hexanol (in acetonitrile)

To a round bottom flask (100 cm³) fitted with a magnetic follower and thermometer, 2-ethyl-1-hexanol (0.39 g, 2.99 mmol) and anhydrous acetonitrile (30 cm³) were added. The resultant solution was stirred and cooled to between -5 and 0 °C. Clay-DNPO (2.50g, ca. 3.10 mmol DNPO) was added and the resultant solution stirred and the temperature kept between -5 and 0 °C for 30 min. The reaction mixture was filtered, and the filtrate was washed with saturated sodium hydrogen carbonate solution, dried over magnesium sulphate and the solvent removed by evaporation at room temperature. This afforded a colourless oil which from IR analysis was a mixture of unreacted starting alcohol and 2-ethyl-1-hexanol nitrate.

IR (KBr plates, thin film) ν cm⁻¹: 3337 (OH str.), 1635 (NO₂ as. str), 1279 (NO₂ sym. str), 1057(C-OH str.), 861 (ONO₂ str).

Example 7 - Reaction between Clay-DNPO and 2-Ethyl-1,3-hexanediol

To a round bottom flask (100 cm³) fitted with a magnetic follower and a thermometer anhydrous n-hexane (30 cm³) and 2-ethyl-1,3-hexane diol (0.52 g, 3.58 mmol) were added and the resultant mixture was stirred and cooled to between -5 and 0 °C by an external dry

ice/acetone bath. ClayDNPO (3.82 g, ca.7.67 mmol DNPO) was added and the resultant suspension stirred for 30 min between -5 and 0°C. The reaction mixture was filtered and the n-hexane was washed with saturated sodium hydrogen carbonate solution, dried over magnesium sulphate and the solvent removed *in vacuo* to afford a colourless oil of 2-ethyl-1,3-hexanediol dinitrate (0.47 g, 55.9 %). The clay was washed with dichloromethane (25 cm³) and the organic layer washed with saturated sodium hydrogen carbonate solution, dried over magnesium sulphate and the solvent removed *in vacuo* to afford 2-ethyl-1,3-hexane diol dinitrate with a minor impurity of a ketone (0.23 g, 27.2 %), a total yield of 83.1 %.

IR (KBr plates, thin film) ν cm⁻¹: 1635 (NO₂ as. str), 1280 (NO₂ sym. str), 866 (ONO₂ str). Lit. ν cm⁻¹: 1647, 1631, 1281, 872, 865 (Millar *et al*, *Tetrahedron* 1993, **49** 7051).

Example 8 - Reaction between Clay-DNPO and Ethylene Glycol

To a jacketed vessel (40 cm³) fitted with a magnetic follower and thermometer, anhydrous ethylene glycol (0.477 g, 7.68 mmol) and anhydrous hexane (25 cm³) were added by syringe and the resultant mixture stirred and cooled between -5 and 0°C by an external Haake water circulator. Clay-DNPO (6.59 g, ca.15.6 mmol DNPO) was added and a small exotherm was observed. The reaction mixture was stirred for 40 min at -3 °C. The reaction mixture was filtered using a Buchner funnel and filter paper. The filtrate was washed with saturated sodium hydrogen carbonate solution (15cm³), dried over magnesium sulphate and the solvent removed by the passage of air to afford ethylene glycol dinitrate as a pale yellow oil (0.02 g, 1.7%). The clay was washed with dichloromethane (15 cm³), filtered and the filtrate washed with sodium hydrogen carbonate solution (15 cm³), dried over magnesium sulphate and the solvent removed by the passage of air to afford ethylene glycol dinitrate as a yellow oil (0.43 g, 36.8%). A small impurity was also present from the IR analysis.

IR (KBr plates, thin film) ν cm⁻¹: 1645 (NO₂ as. str), 1292 (NO₂ sym. str), 1271 (NO₂ sym. str), 898 (ONO₂ str), 844 (ONO₂ str) + 1557 (C-NO₂). Lit. ν cm⁻¹: 1640, 1270, (F. Pristera, *Analyt. Chem.* 1953, **25** 844).

Example 9 - Reaction between Clay-DNPO and n-decyl (trimethylsilyl) ether

To a jacketed vessel fitted with a magnetic follower and thermometer, freshly distilled n-decyl (trimethylsilyl) ether (1.99 g, 8.63 mmol) and n-hexane (30 cm³) were added. The resultant solution was stirred and cooled to between -5 and 0 °C by an external water circulator. Clay-DNPO (4.5g, ca. 9.12 mmol DNPO) was added and the resultant suspension stirred for 3 h between -5 and 0 °C. The reaction mixture was filtered and the filtrate was washed with saturated sodium hydrogen carbonate solution, dried over magnesium sulphate and the solvent removed *in vacuo* to afford n-decanol nitrate as a pale yellow oil (1.48 g, 84%).

IR (KBr plates, thin film) ν cm⁻¹: 1633 (NO₂ as. str), 1280 (NO₂ sym. str), 861 (ONO₂ str) + small carbonyl peak 1729 (CO str). Lit. ν cm⁻¹: 1632, 1280, 864 (Millar & Philbin, *Tetrahedron* 1997 53 4371).

Example 10 - Reaction between Clay-DNPO and N-(trimethylsilyl) morpholine

To a jacketed vessel (100 cm³) fitted with a magnetic follower, thermometer and nitrogen bleed, freshly distilled n-hexane (30 cm³) and N-(trimethylsilyl) morpholine (1.09 g, 6.8 mmol) were added. The resultant mixture was cooled to -5 °C by an external circulator. Clay-DNPO (4.24 g, ca. 8.5 mmol N₂O₅) was added and a small exotherm was observed (ca. 4 °C). Stirring was continued for 2.5 h at -5 °C and the mixture then allowed to warm to room temperature overnight. The reaction mixture was filtered and the filtrate was washed with saturated sodium hydrogen carbonate solution (20 cm³), dried over magnesium sulphate and the solvent removed *in vacuo* to afford a pale yellow oil (0.027g). The residual clay was washed with dichloromethane (3 x 25 cm³) and the organic extracts were combined, neutralised with sodium hydrogen carbonate solution (30 cm³) and dried over magnesium sulphate. The solvent was removed *in vacuo* to afford N-nitromorpholine as a pale yellow crystalline solid (0.44 g, 49%).

IR (KBr disc) ν cm^{-1} : 1519 (NNO₂ as. str.); 1253 (NNO₂ sym. str.); 1117 (CH₂OCH₂ str). Lit ν cm^{-1} (mull): 1524, 1512, 1315, 1254, (Millar & Philbin, *Tetrahedron* 1997, 53 4371).

¹H nmr (60 MHz, CDCl₃, TMS) δ : 3.8 (s). Lit. S(CDCl₃): 3.80 (s) (Millar & Philbin, *Tetrahedron* 1997, 53 4371).

Melting Point: 50.2 °C. (Lit. M. Pt. 50-52 °C, W. Emmons *et al.* ; *J. Org. Chem.* 1958 23, 311).

Example 11 - Reaction between Clay-DNPO and 3-hydroxymethyl-3-methyloxetane (HMMO)

To a round bottom flask (100cm³), fitted with a magnetic follower and thermometer, n-hexane (50cm³) and HMMO (1.05g, 10.2mmol) were added and the resultant mixture stirred and cooled to between -5 and 0°C by an external dry ice/acetone bath. Clay-DNPO (4g, 10.5mmol) was added and the resultant suspension stirred for 30 min. at -5°C. The reaction mixture was filtered and the filtrate was washed with saturates sodium hydrogen carbonate solution and dried over magnesium sulphate. The solvent was removed *in vacuo* to afford a pale yellow oil (0.013g). The clay residue was washed with dichloromethane (25cm³) and filtered. The filtrate was washed with saturated sodium hydrogen carbonate solution and dried over magnesium sulphate. The solvent was removed *in vacuo* to afford a yellow oil (0.69g, ca. 46%).

HPLC analysis using an RP-18 column and a mobile phase of acetonitrile:water (1:1) showed the oil to be a mixture of two products:-

3-(nitratomethyl)-3-methyloxetane (86%) and metriol trinitrate (13%) were both consistent with authentic samples.

Example 12 - Preparation of Zeolite-DNPO

N_2O_5 was supported on zeolite ZSM-5 (supplied by International Zeolyst Ltd.) using an N_2O_5 flow apparatus. N_2O_4 is reacted with ozone in the gas phase and N_2O_5 is deposited on stirred samples of zeolite. N_2O_5 loadings on the zeolite of typically 10-20% were used and the N_2O_5 /zeolite was stored at -60°C .

General Procedure for Nitrations using N_2O_5 /Zeolite

To a stirred mixture of N_2O_5 /zeolite (a stoichiometric equivalence of N_2O_5 to substrate was used) in hexane (ca. 50 ml) under an atmosphere of nitrogen, the substrate (ca. 30mmol) was added keeping the temperature in the range -5°C to 0°C . The reaction mixture was then stirred for typically 1-2 h during which the temperature of the system was allowed to warm to 10 to 15°C . The reaction mixture was then filtered and the filtration residue washed with copious amounts of hexane (ca. 250 ml). The combined organic layers were then quenched with aqueous sodium hydrogen carbonate solution and separated. The hexane layer was then dried over magnesium sulphate, filtered and concentrated *in vacuo* to yield typically a yellow/orange oil.

Example 13 - Reaction between 1-Octanol and Zeolite/DNPO in n-Hexane

To a round bottom flask (100 ml) fitted with a magnetic follower and thermometer, n-hexane (25 ml) was added and cooled to -10°C by an external dry ice/acetone bath. Zeolite(ZSM-5)/DNPO (0.53 g, 56% wt/wt N_2O_5 , Å 2.7 mmol) was added and the resultant suspension stirred. 1-Octanol (0.36 g, 2.7 mmol) was added and a small exotherm was observed, the reaction was stirred for 30 min. between -5 and 5°C . The reaction mixture was filtered and the zeolite was washed with chloroform (15 ml) and the organic layer combined and washed with saturated sodium hydrogen carbonate solution, dried over magnesium sulphate and the solvent removed in *vacuo* to afford a 1-octanol nitrate (0.38 g, 78%) as a yellow oil.

IR (KBr plates, thin film) cm^{-1} : 1632 (NO_2 as. str), 1279 (NO_2 sym. str), 865 (ONO_2 str) + small carbonyl stretch 1729.

Example 14 - Reaction between 2-Methyl-2-hexanol and Zeolite/DNPO in n-Hexane

To a jacketed vessel (100 ml) fitted with a thermometer, stirrer bar and cooled to -5°C by an external Haake circulator 2-methyl-2-hexanol (0.62 g, 5.3 mmol) and n-hexane (20 ml) were added and the resultant mixture stirred. Zeolite (ZSM-5)/DNPO (4.7 g, 14% w/w DNPO Å 6.1 mmol) was added and the suspension stirred for 2 h at -5°C . The zeolite was filtered off and the filtrate was washed with saturated sodium hydrogen carbonate solution, dried over magnesium sulphate and the solvent removed *in vacuo* to afford an unidentified oil (0.003 g). The zeolite was washed with dichloromethane (2 x 20 ml) and the organic extracts were combined, washed with saturated sodium hydrogen carbonate solution, dried over magnesium sulphate and the solvent removed *in vacuo* to afford 2-methyl-2-hexanol nitrate (0.74 g, 86%) as a yellow oil.

IR (KBr plates, thin film) cm^{-1} : 1617 (NO_2 as. str), 1293 (NO_2 sym. str), 870 (ONO_2 str).

When a similar reaction was carried out but with stirring for only 30 min. and using an equimolar amount of DNPO, a 77% yield of 2-methyl-2-hexanol nitrate was obtained.

An authentic sample of 2-methyl-2-hexanol nitrate, prepared by nitration of 2-methyl-2-hexanol using DNPO in dichloromethane, had the following IR spectrum: cm^{-1} (KBr plates, thin film): 1616 (NO_2 asym. str), 1293 (NO_2 sym. str), 869 (ONO_2 str).

Example 15 - Reaction of other alcohols with Zeolite/DNPO in n-Hexane

The following alcohols were reacted by the general method described above:

a) ethylene glycol, b) 2-ethyl-1-hexanol; c) 2-ethyl-1,3-hexanediol and d) 3,3-bis-(hydroxymethyl)oxetane.

(a) The nitration of ethylene glycol proceeded smoothly with a yield of 84%. ^1H Nmr and IR analysis of the product indicated that the reaction had been successful in the production of ethylene glycol dinitrate. HPLC analysis of the product showed the presence of only one compound which had an elution time consistent with the expected product.

IR of product: ν 2972 (C-H), 1639 (NO_2 asym.), 1292, 1271 (NO_2 sym.), 864 (ONO_2); Lit. [F. Pristera, *Analyt. Chem.* 1953, **25** 844]: 1640, 1270 cm^{-1} .

^1H nmr of product: δ 4.8 (s).

(b) The nitration of 2-ethyl-1-hexanol gave a yield of 77%. IR analysis indicated a strong nitrate ester band attributable to 2-ethyl-1-hexanol nitrate, as well as a small hydroxy peak indicating that the reaction had not proceeded through to completion. The IR spectrum also had a peak at 1732 cm^{-1} which is consistent with the stretching frequency of a carbonyl group. It is thought that the nitrating agent may have caused the alcohol to be oxidised to a ketonic species. The nmr spectrum had the expected aliphatic proton signals as well as a broad signal (OH peak) which further confirms the presence of unreacted starting material. The Hplc trace showed the presence of two major compounds.

IR of product mixture: ν 3344 (O-H), 2919 (C-H), 1732 (C=O), 1633 (NO_2 asym.), 1275 (NO_2 sym.), 877 (ONO_2) cm^{-1} . Lit. [R. W. Millar & S. P. Philbin, *Tetrahedron* 1997, **53** 4371] ν cm^{-1} : 1632, 1279, 867.

^1H nmr: δ 0.8 - 1.4 (m); 3.5 (br.s); 4.2 (d). Lit. [*ibid.*] δ : 0.90 (t, 6H); 1.3 (m, 8H); 4.30 (d, 2H).

(c) The nitration of 2-ethyl-1,3-hexanediol gave the dinitrate ester derivative with a yield of 44%. The IR spectrum of the product showed the presence of a nitrate ester group as well as a hydroxy group indicating that unreacted starting material was present. The IR spectrum also had a carbonyl peak which would again represent the formation of an oxidation product. The Nmr spectrum had the expected aliphatic proton signals as well as a broad signal which is consistent with the presence of unreacted starting material. HPLC analysis of the reaction product showed only one major compound which had an elution time consistent with the desired product, 2-ethyl-1,3-hexanediol dinitrate.

IR of product mixture (mainly 2-ethyl-1,3-hexanediol dinitrate): ν 3522 (O-H), 2959 (C-H), 1719 (C=O), 1633 (NO₂ asym.), 1275 (NO₂ sym.), 851 (ONO₂) cm⁻¹.

¹H nmr of product mixture (mainly 2-ethyl-1,3-hexanediol dinitrate): δ 0.9 - 1.5 (m); 2.2 (m); 4.2 (br.s).

(d) The nitration of 3,3-bis(hydroxymethyl)oxetane was carried out by the general method but the reaction yield was only 24%. IR analysis of the reaction product indicated the presence of a nitrate ester group together with a hydroxy peak (indicating unreacted starting material) and a carbonyl peak (indicating the presence of an oxidation product). Nmr analysis gave a spectrum with several peaks some of which are consistent with those expected from the target dinitrate compound, 3,3-bis(nitratomethyl)oxetane. HPLC analysis of the reaction product showed the presence of at least six compounds.

IR of product mixture: ν 3456 (O-H), 2985 (C-H), 1746 (C=O), 1640 (NO₂ asym.), 1275 (NO₂ sym.), 864 (ONO₂) cm⁻¹. Lit. (for 3,3-bis(nitratomethyl)oxetane) [R. W. Millar & S. P. Philbin, *Tetrahedron* 1997, **53** 4371]: 1644, 1278, 867 cm⁻¹.

¹H nmr of product mixture: δ 1.3 (t); 2.0 (s); 4.1 (s); 4.2 (s); 4.5 (s); 4.7 (s). Lit. (for 3,3-bis(nitratomethyl)oxetane) [*ibid.*]: δ 4.65 (s,4H); 4.85 (s,4H).

The general conditions and results for the nitrations described in the examples are set out for convenience in the following table:

**Summary of Nitrate Ester Syntheses Using
Clay-DNPO or HZSM5-DNPO**

| Reagent | Solvent | Yield (Clay) | Yield (Zeol.) | Comments |
|-----------------------------------|--------------|--------------|---------------|--|
| 1-octanol | n-hexane | - | 78 | |
| 2-methyl-2-hexanol | n-hexane | 69 | 86 | Identical to authentic sample (made by DNPO in DCM) |
| n-decanol | n-hexane | 95 | - | |
| n-decanol | acetonitrile | (low) | - | Mixture of nitrate ester and unreacted starting material |
| 2-ethyl-1-hexanol | n-hexane | 99 | 77 | Zeolite run: additional product present (IR 1732cm ⁻¹) |
| 2-ethyl-1-hexanol | acetonitrile | 30 | | Mixture of nitrate ester and unreacted starting material |
| 2-ethyl-1,3-hexane diol | n-hexane | 83 | 44 | Clay run: evidence of C=O str. |
| ethylene glycol | n-hexane | 37 | 84 | Clay run: isolated after DCM wash of clay. Small amount of unknown (IR str 1557 cm ⁻¹) |
| 3,3-bis(hydroxymethyl)oxetane | n-hexane | - | 24 | Multi-product reaction: C=O-containing contaminants (IR 1746cm ⁻¹) |
| n-decyl(trimethylsilyl) ether | n-hexane | 180 | 84 | Evidence of a small amount of carbonyl formation |
| 3-(hydroxymethyl)-3-methyloxetane | n-hexane | 46 | - | Product is mixture of NIMMO and some MTN |
| N-(trimethylsilyl)-morpholine | n-hexane | 49 | (low) | Zeolite product is mixture of nitramine & unchanged starting material |
| N-acetylmorpholine | n-hexane | 58 | - | |

Notes:

All clay-DNPO reactions were carried out between -5 and 0 °C using anhydrous solvents.

All alcohol reactions using clay-DNPO had a run time of 30 min. The trimethylsilyl ether (of n-decanol) was reacted for 180 min.

N-trimethylsilylmorpholine and N-acetylmorpholine were allowed to react for 2.5-3 h.

Zeolite-DNPO reactions were, after addition between -5 and 0°C , stirred for 1-2 h at a reaction temperature of 10 to 15°C .

DCM = dichloromethane; NIMMO = 3-(nitratomethyl)-3-methyloxetane; MTN = metriol trinitrate.

Claims

1. A solid nitrating reagent comprising a montmorillonite clay or zeolite material which has incorporated therein dinitrogen pentoxide in an amount which is sufficient to effect a nitration reaction.
2. A nitrating reagent as claimed in claim 1 containing at least 10% by weight of dinitrogen pentoxide.
3. A nitrating reagent as claimed in claim 2 containing from about 10% to about 30% by weight of dinitrogen pentoxide.
4. A nitrating reagent as claimed in any of claims 1 to 3 wherein the solid material is a montmorillonite clay of the type designated K10.
5. A nitrating reagent as claimed in any of claims 1 to 3 wherein the solid material is a zeolite selected from the types designated ZSM-5, zeolite beta, zeolite F720 and zeolite F780 (all H form).
6. A method for the preparation of a solid-supported nitration reagent which comprises exposing a sample of a montmorillonite clay or a zeolite material to gaseous dinitrogen pentoxide contained in a stream of ozonised oxygen at a sub-ambient temperature while agitating the clay or zeolite material.
7. A method as claimed in claim 6 wherein the sub-ambient temperature is between -60 and -20°C.
8. A method as claimed in claim 6 or claim 7 wherein the solid material is exposed to the gaseous dinitrogen pentoxide for a period of about 2 hours.

9. A method for effecting nitration of an organic compound which comprises bringing together a solution of the compound in an appropriate solvent with an effective quantity of the solid nitrating reagent of claims 1 to 5, allowing reaction to take place and extracting the nitrated product from the mixture.
10. A method as claimed in claim 9 wherein the solvent is an inert, non-polar solvent.
11. A method as claimed in claim 10 wherein the solvent is a non-aromatic hydrocarbon solvent.
12. A method as claimed in claim 11 wherein the solvent is hexane.
13. A method as claimed in claim 10 wherein the solvent is a perfluorocarbon solvent.
14. A method as claimed in claim 13 wherein the solvent is selected from perfluoromethylcyclohexane (PP2), perfluorodecalin (PP6) or perfluoroperhydrophenanthrene (PP11).
15. A method as claimed in any one of claims 9 to 14, wherein the nitration reaction is carried out at a temperature of from -20°C to 15°C .
16. A method as claimed in claim 15 wherein the temperature is from about -5 to 0°C .
17. A method as claimed in any one of claims 9 to 15 wherein the reaction substrate is an alcohol or an O-silyl ether and the product is a corresponding nitrate ester.

18. A method as claimed in any one of claims 9 to 15 wherein the substrate is a silylamine and the product is a corresponding nitramine
19. A solid nitrating reagent substantially as hereinbefore described and with reference to the examples.
20. Use of the nitrating reagent to effect nitration substantially as herein described and with reference to the examples.



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Application No: GB 9904706.0
Claims searched: 1-20

Examiner: C A Clarke
Date of search: 3 June 1999

Patents Act 1977
Search Report under Section 17

Databases searched:

UK Patent Office collections, including GB, EP, WO & US patent specifications, in:
UK CI (Ed.Q): C1A (A2B,ACD,APC)
Int CI (Ed.6): C01B 21/20, C07B 43/02
Other: ONLINE: WPI,EPODOC,JAPIO,CHABS

Documents considered to be relevant:

| Category | Identity of document and relevant passage | Relevant to claims |
|----------|---|--------------------|
| X | CHEMICAL ABSTRACT 75:143705 | 1 |

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| X | Document indicating lack of novelty or inventive step | A | Document indicating technological background and/or state of the art. |
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