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(54) Title of the Invention: **Improved flow synthesis**
Abstract Title: **A method of synthesising an organic high explosive using a flow reactor**

(57) A method of synthesising an organic high explosive, comprising the steps of (i) providing a solution A comprising a nitrating agent, (ii) providing a solution B comprising an explosive precursor reagent, wherein the admixture of solution A and solution B are selected such that they are capable upon formation of the admixture of reacting together to provide the organic high explosive, (iii) determining the critical diameter of the organic high explosive, (iv) wherein the flow reactor comprises a pipe, selecting the internal diameter of the pipe such that it is less than the critical diameter of the organic high explosive, thereby preventing detonation of the formed organic high explosive in said flow reactor, (v) causing the solution A and B to be mixed and passed through the flow reactor to create the admixture, to provide the organic high explosive. Preferably, solution A comprising a nitrating agent comprises nitric acid, nitrites. Preferably, the explosive precursor in solution B is a cycloamine, octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine (TAT), 1,3,5-triacetyl-1,3,5-triazacyclohexanes (TRAT), 1,5-dinitroendomethylene-1,3,5,7-tetraazacyclooctane (DPT), and hexamethylenetetramine. The organic high explosive is preferably a nitramine, more preferably RDX (hexogen) or HMX (octogen). Preferably, the reaction in the above method is temperature-controlled.

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Improved Flow Synthesis

The following invention relates to methods of producing explosives from the direct nitration explosive precursors by flow synthesis. Particularly to a method of producing RDX and HMX.

5   Before the present invention is described in further detail, it is to be understood that the invention is not limited to the particular embodiments described, as such may, of course, vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to be limiting, since the scope of the present invention will be limited only by the appended claims.

10

According to a first aspect of the invention there is provided

A method of synthesising an organic high explosive, comprising the steps of

i) providing a solution A comprising a nitrating agent,

ii) providing a solution B comprising an explosive precursor reagent,

15   wherein the admixture of solution A and solution B are selected such that they are capable upon formation of the admixture of reacting together to provide an organic high explosive,

iii) determining the critical diameter of the organic high explosive,

iv) wherein the flow reactor comprises a pipe, selecting the internal diameter of

20   the pipe such that it is less than the critical diameter of the organic high explosive, thereby preventing detonation of the formed organic high explosive in said flow reactor,

v) causing the solution A and B to be mixed and passed through a flow reactor to create the admixture

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The solution A comprises a nitrating agent, such as for example nitric acid, nitrites and combinations thereof.

The solution B comprises an explosive precursor reagent, explosive precursors are well known in the art, and are often controlled access reagents, as they are readily nitrated with high percentage nitric acid, such as fuming or 99%conc nitric acid.

5

The explosive precursor may be an aromatic compound, phenylamines, cycloamine, toluene, Octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine (TAT), 1,3,5-triacetyl-1,3,5-triazacyclohexanes (TRAT), 1,5-Dinitroendomethylene-1,3,5,7-tetraazacyclooctane (DPT), triazole, and hexamethylenetetramine. The formation of the TAT, TRAT and DPT may require several synthetic steps, but can be safely made using conventional batch techniques as they are not energetic materials.

The solution A and/or B or a solution C which may be mixed at stage ii) further comprises catalysts, strong acids, de-hydrating agents, and acid anhydrides. Strong acids other than nitric acid may be sulphuric acid. De-hyrating agents may be P_2O_5. Acid anhydrides may be acetic acid anhydride or trifluoroacetic anhydride.

20   The nitration reaction is typically exothermic and the flow reactor may be temperature controlled to ensure that the explosive material formed does not run to detonation.

The admixture transitions through the flow reactor, to which a solution D may be added to work up the reactant to provide a precipitate of said explosive material or a salt thereof. The solution D may quench the acid. Solution D, may comprise cooled water, to cause precipitation.

The batch synthesis of explosives is very well regulated due to the explosive hazard. However, the batch pathway for industrial synthesis causes the formation of hundreds of kilos of material to be formed in a reactor. This will cause the building to have a very large safety radius. The use of flow synthesis allows low kilogram production, such that the explosive material may be collected remote from the stored solutions A and/or B and/or C, such as to reduce the hazard of an event. Preferably the location of the collected remote is behind a blast wall or explosive magazine. The use of continuous production of smaller mass of explosive material prevents the build-up of a several hundred kilo batch in one place.

The critical diameter of explosives may be readily characterised, using well defined tests. Publically available sources show that the critical diameter is generally of the order of greater than 1mm, depending on the test used.

The critical diameters of the pure explosive are often modified, by the use of binders to reduce their sensitivity (IM explosives), and the critical diameter of such a composition such as PBX (polymer bonded explosives) may be different to the pure explosive material.

The use of flow synthesis allows the selection of the internal diameter of the pipe used in the flow synthesis, the internal diameter of the flow reactor pipe must be less than the critical diameter of the explosive material being synthesised to mitigate against sustained detonation in the flow reactor. The critical diameter may be determined, and the selection of the diameter of the flow reactor pipe to avoid detonation will improve the safety of the system. The use of more than one flow reactor, or a plurality of flow reactors, each with selected diameters that are less than the critical diameter of the explosive to be manufactured, in parallel, can increase the final output flow, without comprising safety.

Typical large bore tubular reactors used in the industrial synthesis of chemicals may have at least 3-4mm internal diameter pipes. Whilst this allows for very large volume of reagents, the diameter is such, that should the explosive material precipitate out in the pipe and/or cause a blockage, it would allow explosive material to accumulate at a diameter greater than the critical diameter

of the explosive material. This may lead to a large hazard, as the precipitated explosive could sustain detonation.

The industrial synthesis of explosive materials, may preferably have a flow synthesis flow with a pipe having an internal diameter less than 1mm, more preferably less than 500microns, preferably in the range of 100 to 500microns, preferably 250 to 350microns.

According to a further aspect of the invention there is provided an apparatus for carrying out the method of any one of the preceding claims. The apparatus comprising a plurality of flow reactors in parallel, each of said flow reactors comprising a pipe, wherein the internal diameter of the pipe is selected such that it is less than the critical diameter of the organic high explosive

According to a further aspect of the invention there is provided a method of synthesising an organic high explosive, comprising the steps of

i) providing at least one solution, comprising a nitrating agent and an explosive precursor,

ii) causing the solution to be mixed and passed through a flow reactor,

wherein the flow reactor comprises a pipe, wherein the internal diameter of the pipe is selected such that it is less than the critical diameter of the energetic material being formed, thereby preventing detonation of the energetic material in said flow reactor.

The use of flow synthesis provides a facile means of preparing RDX, HMX etc at both laboratory R&D scale of ~100g, and to provide the ability to add further flow reactors to readily scale up production, without the associated dangers of forming +100Kgs of RDX explosive in a single reactor vessel. Further, it also avoids the use of hundreds of litres of highly concentrated acid in a large reactor vessel in a batch process. The use of flow synthesis allows for the continuous

removal and safe stowage of final explosive product material from the flow reactor or flow reactors, to avoid the build-up of large quantities of explosive material. This may allow explosive processing buildings to process a greater mass of explosive and/or associated safety distances to be reduced, as the explosive material may be distributed to safe areas, away from the flow reactor, as it is synthesised.

RDX synthesis

Hexamine was added to the input flow reagent A nitric acid in any wt% up to and including a near saturated solution. The higher the concentration of hexamine in the Input flow reagent A, the more efficient the process. It is highly preferable to dissolve the hexamine in the nitric acid, as short a time as possible before flowing into the reactor, to reduce the likelihood of the nitration reaction starting.

The hexamine may be dissolved in nitric acid with a concentration in the range of from 70% to 92%, more preferably from 88% to 92%., the use of other solvents to aid dissolving the hexamine, may be added.

Preferably input flow reagent A contains only hexamine and nitric acid with a concentration in the range of less and 92%.

The input flow reagent B may comprise 99% concentration nitric acid to ensure the total nitric acid concentration in the flow reactor is at least 92% nitric acid concentration, more preferably input flow reagent B contains only 99% concentration nitric acid.

The use of nitric acid at a concentration below that at which nitration can occur, allows the hexamine starting material to be dissolved, without the nitration reaction starting. This prevents product from precipitating out before it is flowed into the flow reactor, and may prevent blockage of the flow reactor and associated mixing chambers. Further, the use of high percentage concentrations as the dissolving agent for hexamine permits the reaction in the flow reactor to be quickly brought up to the required total nitric acid concentration for nitration to occur. This

avoids the issue of having a diluted concentration of nitric acid concentration in the flow reactor, therefore the input flow reagent B only needs to be a slightly higher concentration of nitric acid, to ensure that the desired range of total nitric acid concentration of greater than 92% is achieved in the flow reactor.

5

To assist in achieving the desirable concentration of nitric acid to start nitration of hexamine, after step ii, the input flow reagents A and B may be premixed in a mixing chamber before entering the flow reactor.

10   It has been found that in step iii) the total nitric acid concentration may be in the range of 90-99% in said flow reactor, more preferably in the range of 93% to 95% nitric acid concentration.

The total nitric acid concentration when input flow reagent A and input flow reagent B contain only nitric acid as the acid and the sole nitration agent, the
15   concentration must be sufficient for nitration to occur, such as for example greater than 92% concentration.

The flow rate of input flow reagent A may be selected from any suitable flow rate with input flow reagent B, to provide a total nitric acid concertation
20   capable of causing nitration of hexamine, such as for example in the range of greater than 92%. The actual flow rate of input flow reagent A may be µL through to millilitres to litres, depending on the capacity of the flow cell.

The flow rate of input flow reagent B may be selected from any suitable
25   flow rate with input flow reagent A to provide a total nitric acid concertation capable of causing nitration of hexamine, such as for example in the range of greater than 92% concentration. The actual flow rate of input flow reagent A may be µL through to millilitres to litres, depending on the capacity of the flow cell.

The ratio of the flow rate Input flow reagent A to Input flow reagent B (A:B) may be B>A, preferably the ratio is greater than 1:3 (A:B), more preferably in the range of (1:4) to (1:10), to ensure the nitric acid total concentration is greater than 92% in the flow reactor. The use of higher concentrations of acid in Input flow reagent B, allows the volume/flow rate of Input flow reagent B to be reduced, ie a lower ratio, which may lead to reducing the quantity of nitric acid being used. This may be caused by using other strong acids, such as for example oleum.

The temperature in the flow reactor needs to be controlled to prevent a highly exothermic reaction from occurring, preferably the temperature is caused to be less than 30°C, preferably between 20°C to 30°C, more preferably between 22°C to 27°C, most preferably at 24°C.The temperature is monitored by water circulators. The flow reactor may be cooled by any suitable means such as for example water circulator or electric coolers.

The reaction in step v, the output mixed flow is quenched, to stop the reaction and to cause precipitation of the RDX product. The output flow may be transferred in to a large volume of quench medium or mixed in a mixing chamber.

Preferably the output mixed flow, which comprises the RDX dissolved in the nitric acid, is mixed with the quench medium via an SOR mixer at the end of the flow reactor. The quench medium may have a pH 7 or less, and may be selected from an aqueous acidic solution or water. The quenching agent may be cooled to induce crystallisation, preferably less than 20°C, preferably in the region of 10°C or less.

The RDX precipitate is filtered and collected and then washed in an aqueous solution, preferably the quenching solution may have a pH 7 or less, preferably water.

The nitration reagent may be selected from at least 70% concentration nitric acid and $NaNO_2$, or containing only 99% concentration nitric acid.

According to a further aspect of the invention there is provided a method of synthesising an organic high explosive, comprising the steps of

i) providing a first solution A

ii) providing a second solution B,

wherein the admixture of solution A and solution B are selected such that they are capable upon formation of the admixture of reacting together to provide an organic high explosive,

iii) causing the solution A and B to be mixed and passed through a flow reactor to create an admixture,

wherein the flow reactor comprises a pipe, wherein the internal diameter of the pipe is selected such that it is less than the critical diameter of the organic high explosive, thereby preventing detonation of the formed organic high explosive in said flow reactor.

Experimental reagents for RDX/HMX

99 % HNO3 was purchased from Honeywell in a 500 mL quantity. Cat. 84392-500ML, Lot. No. I345S.

70 % HNO3 was purchased from Fisher scientific in a 2.5 L quantity. Code: N/2300/PB17. Lot: 1716505.

Hexamine was purchased from Sigma-Aldrich in a 250 g quantity. Cat. 797979-250G, Lot. No. MKCJ7669.

Oleum was purchased from Fisher in a 500 mL quantity. Cat. S/9440/PB08, Lot. No. 1689177.

Experimental
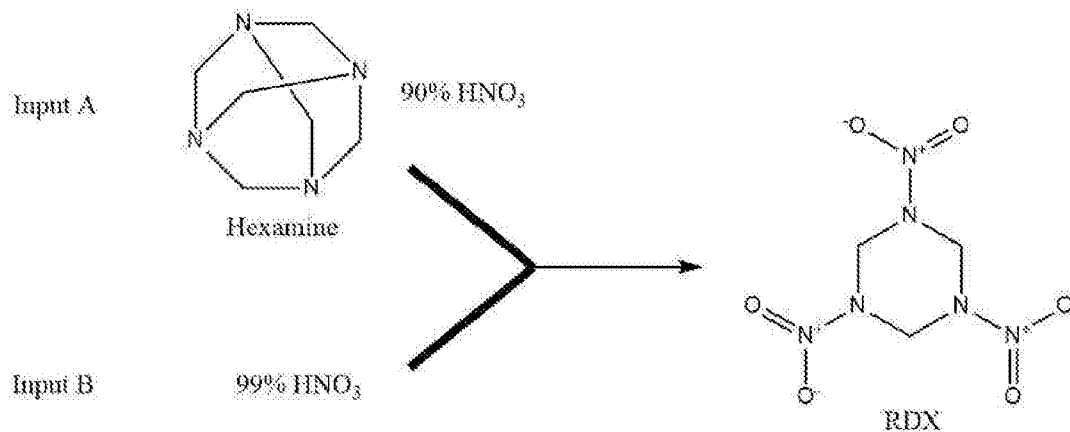
5   The general reaction is shown above, where the input flow reagent A comprises hexamine dissolved in nitric acid, and input flow reagent B comprises the nitrating agent, which may be higher concentration of nitric acid(than input flow reagent A), and/or a further nitrating agent, such as a metal nitrite, such as $NaNO_2$. The input flow reagent A and input flow reagent B are caused to react in
10   the flow reactor to furnish the product RDX.

RDX synthesis using a flow reactor poses more challenging design issues than simply pumping solutions from well-known and quantified batch chemistry. This is mainly due to the fact that the starting material hexamine is solid, and RDX can potentially precipitate out of solution during the reaction. Precipitation of the
15   RDX during the transition through the flow reactor can happen as the acid concentration drops and water content increases, thereby leading to potential blockages in the flow reactor, this could lead to catastrophic events, and so the nitric acid concentration in the flow chemistry.

Before starting the experiment the reactor was prepared by flushing the
20   system with methanol followed by water. Both input systems were then filled with 70 % HNO_3 which was passed through the reactor in order to fully prime the system.

Experiment 1:

Syringe A: Saturated hexamine in 90 % HNO₃ (roughly 1 g in 5 mL).

5   Syringe B: 99 % HNO₃.

Flow reactor used: 3222 Labtrix

Hexamine   RDX
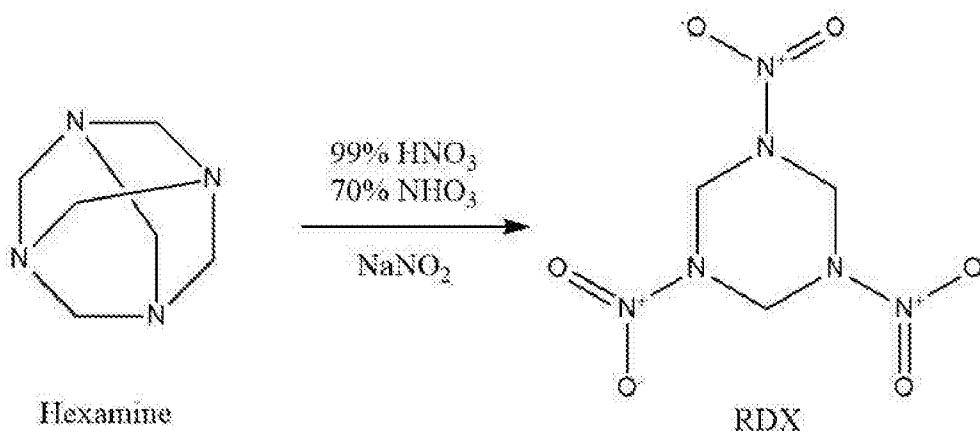
The concentration of the nitric acid in syringe A was 90%conc. The flow
10   rate was set at 1:3 (A:B), however limited product formed. The flow rate of syringe
B, 99 % HNO₃ feed was increased so that the A:B flow ratio was 1:9. When the
sample was collected into water the solution became opaque indicating that RDX
had been produced.

15   Experiment 2 Addition of oleum

Syringe A: 0.5 g hexamine dissolved in 2.5 mL 90 % HNO₃. Solution cooled
during hexamine addition.

Syringe B: 0.95 mL 99 % HNO₃ + 0.05 mL oleum.

20   A series of experiments were carried out aimed at monitoring the influence
of oleum on RDX formation. Experiments produced opaque solutions when

collected into water indicative of RDX formation. The ^{1}H NMR spectrum showed that RDX exists in solution prior to precipitation using water as the quenching agent.

5   Experiment 3 increased oleum addition

Syringe A: 0.5 g hexamine dissolved in 2.5 mL 90 % HNO$_3$. Solution cooled during hexamine addition.

Syringe B: 0.9 mL 99 % HNO$_3$ + 0.1 mL oleum.

10   The increase of oleum by 100%, led to formation of RDX precipitate when collected onto ice. Part of the solution before mixing with ice was collected into d^6-DMSO, the ^{1}H NMR spectrum indicated the formation of RDX.

The use of further acids such as oleum, helps to keep that acid concentration in the reactor at a high level, and may assist in dehydration of the

15   reaction. The use of nitration species such as NaNO$_2$, can allow the use of lower total nitric acid concentrations.

It was found that low acidity in the reactor caused RDX to precipitate from the solution. It is essential to monitor the flow reactor paths for solidified product. Further, whilst it is desirable to increase the acidity of the nitric acid that comprises

20   the hexamine, if the concentration is too high product starts to form, before mixing has commenced, again leading to likelihood of RDX product blocking the flow reactor. Preferably the hexamine is dissolved in the nitric acid, before use, and is not stored long term as a stock solution.

25   HMX example

TAT can be readily synthesised from hexamine via DAPT as an intermediate. The main advantage of going through this route is that an 8-membered ring is formed therefore eliminating the possibility of forming RDX as

a biproduct. The TAT can be directly converted to HMX, using nitration in a flow synthesis arrangement to control the rate of production of explosive material.
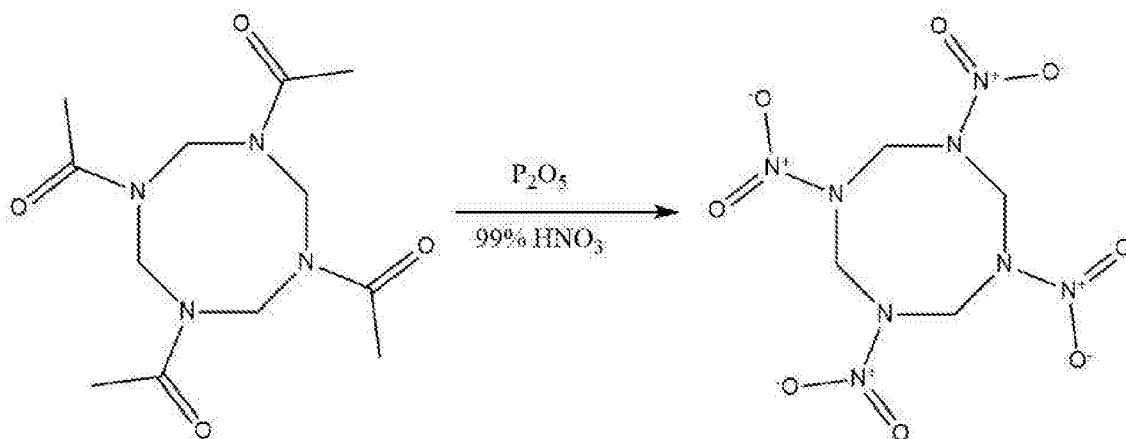
5   Experimental 1

Line A - solution of 100 mg TAT, 1000 mg P_2O_5 and 2 mL of 99 % HNO_3 were premixed in a single solution and passed through a Labtrix reactor. The preferred reaction time of 120 seconds through the flow synthesis reactor provided sufficient time for nitration to occur. The flow synthesis was performed
10   at a temperature greater than room temperature, it was found that a temperature of 75°C provided a temperature which allowed the reaction to proceed, but not sufficient to cause an unwanted explosive event. HMX was isolated, without any RDX contamination being present.

15   Experiment 2 A scaled up Protrix reactor

Line A: 2.0061 g TAT and 20.0357 g of P_2O_5 were dissolved in 40 mL 99 % HNO_3

Line B was used as an emergency flush and was primed with 70 % HNO_3.

Line A and the Protrix were initially primed with 70 % HNO_3 followed by 99 %
20   HNO_3. The reaction mixture was prepared in stages. Initially P_2O_5 is slowly dissolved into a stirred solution of 99 % HNO_3. This solution was kept in an ice bath. This resulted in an opaque-yellow solution. The addition of TAT to this

solution reduced the opacity of the solution however, the reaction mix remained opaque.

Line A was then primed with the reaction mixture.

EXP	TEMP (^0C)	TIME (S)	FLOW A (ML)	P (BAR)	OBSERVATION
0168	75	120	1.66	1.1	Collected for 12 minutes into ice.

5   The solution from the Protrix was left overnight, which resulted in the formation of crystals. These were isolated, washed with water followed by acetone and then analysed using NMR spectroscopy. The ^1H NMR spectrum of experiment 0168 shows that there are multiple species present in the sample. Some of these peaks correspond to unreacted TAT and partially nitrated TAT.

10 These impurities are also observed in the industrial batch synthesis of HMX from TAT and can be removed by boiling the material in acetone followed by recrystallisation. In the 1H NMR spectrum, a peak at 6.02 ppm is characteristic of HMX.

15

Claims

1.   A method of synthesising an organic high explosive in a flow reactor, comprising the steps of

5   i) providing a solution A comprising a nitrating agent,

ii) providing a solution B comprising an explosive precursor reagent,

wherein the admixture of solution A and solution B are selected such that they are capable upon formation of the admixture of reacting together to provide the organic high explosive,

10   iii) determining the critical diameter of the organic high explosive,

iv) wherein the flow reactor comprises a pipe, selecting the internal diameter of the pipe such that it is less than the critical diameter of the organic high explosive, thereby preventing detonation of the formed organic high explosive in said flow reactor,

15   v) causing the solution A and B to be mixed and passed through the flow reactor to create the admixture, to provide the organic high explosive.

2.   A method according to claim 1, wherein the nitrating agent comprises nitric acid, nitrites.

3.   A method according to claim 1 or 2, wherein the organic high explosive is
20   a nitramine.

4.   A method according to claim 3, wherein the nitramine is RDX or HMX.

5.   A method according to any one of the preceding claims, wherein the explosive precursor is an, cycloamine, Octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine (TAT), 1,3,5-triacetyl-1,3,5-triazacyclohexanes (TRAT), 1,5-
25   Dinitroendomethylene-1,3,5,7-tetraazacyclooctane (DPT), and hexamethylenetetramine.

6. A method according to any one of the preceding claims wherein solution A and/or B or a solution C which is mixed at stage v) further comprises catalysts, strong acids, de-hydrating agents, and acid anhydrides.

7. A method according to any one of the preceding claims wherein the flow reactor is temperature controlled.

8. A method according to any one of the preceding claims wherein after the admixture has transitioned through the flow reactor, a solution D is added to work up the reacted admixture to provide a precipitate of said explosive material or a salt thereof.

9. A method according to claim 8 wherein solution D, may comprise cooled water.

10. A method according to any one of the preceding claims wherein the internal diameter of the pipe is less than 500microns.

11. A method according to any one of the preceding claims, wherein the explosive material is collected remotely from the stored solutions A and/or B and/or C, such as to reduce the hazard of an event.

12. A method according to claim 10, wherein the collected remotely is behind a blast wall or within an explosive magazine.

13- Apparatus for carrying out the method of any one of the preceding claims, comprising a plurality of flow reactors in parallel, each of said flow reactors comprising a pipe, wherein the internal diameter of the pipe is selected such that it is less than the critical diameter of the organic high explosive.

Intellectual
Property
Office

Application No:	GB2212531.4	**Examiner:**	Dr S. David Evans
Claims searched:	claims 1-12 (in full) and claim 13 (in part)	**Date of search:**	26 January 2023

Patents Act 1977: Search Report under Section 17

Documents considered to be relevant:

Category	Relevant to claims	Identity of document and passage or figure of particular relevance
X	1, 2, 6-13	Journal of Flow Chemistry, Vol. 5(3), 2015, (Zuckerman, Nathaniel B. et al), "Microreactor flow synthesis of the secondary high explosive 2,6-diamino-3,5-dinitropyrazine-1-oxide (LLM-105)", pages 178-182. See the whole article, but especially the Experimental section at page 181.
X	1, 2, 6, 7, 10-13	Journal of Physics: Conference Series, 1507, 2020 International Conference on Defence Technology (Spring Edition), (Yu Weifei et al), 022030, "Explosive synthesis: novel intrinsically safe method and application with micro-channel reactor", pages 1-8, ISSN: 1742-6588. downloaded for free on 25/01/2023 from https://iopscience.iop.org/article/10.1088/1742-6596/1507/2/022030/pdf). See the entire paper.
X	1, 2, 6, 7, 10-13	CN 107778184 A (INST CHEMICAL MATERIAL CHINA ACADEMY ENGINEERING PHYSICS) See Chem. Abs. Acc. No. 2018:400907 and the whole document, but particularly Figure 1 and Examples 1 to 4.
X	1, 2, 6, 7, 10-13	CN 106800513 A (INST CHEMICAL MAT CHINA ACAD ENG PHYSICS) See WPI Abs. Acc. No. 2017-39483D and the entire document, but especially Figure 1 and Examples 1 to 3.
X	1, 2, 6, 7, 10-13	CN 109824521 A (INST CHEMICAL MATERIAL CHINA ACADEMY ENGINEERING PHYSICS) See WPI Abs. Acc. No. 2019-50051E and the whole document, but especially Figures 1 to 2 and Examples 1 to 3.
X	1, 2, 6, 7, 10-13	CN 109232578 A (INST CHEMICAL MATERIAL CHINA ACADEMY ENGINEERING PHYSICS) See WPI Abs. Acc. No. 2019-13316D and the entire document, but particularly Figure 1 and Examples 1 to 5.
X	1, 2, 6-13	CN 112500357 A (DALIAN INST CHEM & PHYSICS CAS) See WPI Abs. Acc. No. 2021-287062 and the whole document, but particularly Figures 1 to 2 and Example 2.

Intellectual Property Office

X	1, 2, 6, 7, 10-13	CN 107043357 A (INST CHEMICAL MATERIAL CHINA ACADEMY ENGINEERING PHYSICS) See WPI Abs. Acc. No. 2017-56956K and the entire document, but especially Figures 1 to 2 and Embodiments 1 to 3.
A	-	EP 3650443 A1 (FUJIAN YONGJING TECHNOLOGY CO LTD) See the whole document, but particularly the reference to the Protrix® reactor in paragraphs [0091] to [0092].
A	-	CN 110950838 A (UNIV SUN YAT SEN) See the reference to Labtrix® in WPI Abs. Acc. No. 2020-28262L.

Categories:

X	Document indicating lack of novelty or inventive step	A	Document indicating technological background and/or state of the art.
Y	Document indicating lack of inventive step if combined with one or more other documents of same category.	P	Document published on or after the declared priority date but before the filing date of this invention.
&	Member of the same patent family	E	Patent document published on or after, but with priority date earlier than, the filing date of this application.

Field of Search:

Search of GB, EP, WO & US patent documents classified in the following areas of the UKC^X :

Worldwide search of patent documents classified in the following areas of the IPC

B01J; C06B; C07D

The following online and other databases have been used in the preparation of this search report

WPI, EPODOC, INTERNET, CAS ONLINE

International Classification:

Subclass	Subgroup	Valid From
C07D	0251/06	01/01/2006
B01J	0019/00	01/01/2006
C06B	0021/00	01/01/2006
C07D	0257/02	01/01/2006