1

Synthetic Routes to Aliphatic *C*-Nitro Functionality

1.1 INTRODUCTION

The nitro group, whether attached to aromatic or aliphatic carbon, is probably the most widely studied of the functional groups and this is in part attributed to its use as an 'explosophore' in many energetic materials.[1] The chemistry of the nitro group has been extensively reviewed in several excellent works including in a functional group series.[2–8]

A comprehensive discussion of the synthetic methods used to introduce the nitro group into aliphatic compounds, and its diverse chemistry, would require more space than available in this book. While every effort has been made to achieve this, some of these methods are given only brief discussion because they have not as yet found use for the synthesis of energetic materials, or their use is limited in this respect. The nature of energetic materials means that methods used to introduce polynitro functionality are of prime importance and so these are discussed in detail. Therefore, this work complements the last major review on this subject.[9]

The chemical properties of the nitro group have important implications for the synthesis of more complex and useful polynitroaliphatic compounds and so these issues are discussed in relation to energetic materials synthesis.

RCH_2NO_2	$R^1R^2CHNO_2$	$R^1R^2R^3CNO_2$
Primary nitroalkane	**Secondary nitroalkane**	**Tertiary nitroalkane**
$RCH(NO_2)_2$	$R^1R^2C(NO_2)_2$	$R^1R^2CHC(NO_2)_3$
Terminal *gem*-dinitroalkane	**Internal *gem*-dinitroalkane**	**Trinitromethyl**

Figure 1.1

Aliphatic nitroalkanes can be categorized into six basic groups: primary, secondary and tertiary nitroalkanes, terminal and internal *gem*-dinitroalkanes, and trinitromethyl compounds. Primary and secondary nitroalkanes, and terminal *gem*-dinitroalkanes, have acidic protons and find particular use in condensation reactions for the synthesis of more complex and

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functionalized compounds, of which some find application as energetic plasticizers and polymer precursors. Tertiary nitroalkanes and compounds containing internal *gem*-dinitroaliphatic functionality exhibit high thermal and chemical stability and are frequently present in the energetic polynitropolycycloalkanes discussed in Chapter 2. The chemical stability of these various groups is discussed in Section 1.13.

1.2 ALIPHATIC *C*-NITRO COMPOUNDS AS EXPLOSIVES

Nitromethane is not usually regarded as an explosive, but its oxygen balance suggests otherwise, and under certain conditions and with a strong initiator this compound can propagate its own detonation. Nitromethane has been used in combination with ammonium nitrate for blasting. Although this explosive is more powerful than conventional ammonium nitrate-fuel oil (ANFO) it is considerably more expensive. Other simple aliphatic nitroalkanes have less favorable oxygen balances and will not propagate their own detonation.

Polynitroaliphatic compounds have not found widespread use as either commercial or military explosives. This is perhaps surprising considering the high chemical and thermal stability of compounds containing internal *gem*-dinitroaliphatic functionality. In fact, many polynitroaliphatic compounds are powerful explosives, for example, the explosive power of 2,2-dinitropropane exceeds that of aromatic *C*-nitro explosives like TNT. Tetranitromethane, although not explosive on its own, contains a large amount of available oxygen and forms powerful explosive mixtures with aromatic hydrocarbons like toluene. The problem appears to be one of cost and availability of raw materials. Most commercial and military explosives in widespread use today contain nitrate ester, nitramine or aromatic *C*-nitro functionality because these groups are readily introduced into compounds with cheap and readily available reagents like mixed acid (sulfuric and nitric acids mixture). However, sometimes other factors can outweigh the cost of synthesis if a compound finds specialized use. Over the past few decades there has been a demand for more powerful explosives of high thermal and chemical stability. Such criteria are met in the form of polynitrocycloalkanes, which are a class of energetic materials discussed in Chapter 2. These compounds have attracted increased interest in the aliphatic *C*-nitro functionality which may result in the improvement of or discovery of new methods for its incorporation into compounds.

Improved methods for the synthesis of building blocks like 2-fluoro-2,2-dinitroethanol and 2,2-dinitropropanol have resulted in some polynitroaliphatic compounds finding specialized application. Bis(2-fluoro-2,2-dinitroethyl)formal (FEFO) and a 1:1 eutectic mixture of bis(2,2-dinitropropyl)formal (BDNPF) and bis(2,2-dinitropropyl)acetal (BDNPA) have both found use as plasticizers in energetic explosive and propellant formulations.

1.3 DIRECT NITRATION OF ALKANES

Nitroalkanes can be formed from the direct nitration of aliphatic and alicyclic hydrocarbons with either nitric acid[10] or nitrogen dioxide[11] in the vapour phase at elevated temperature. These reactions have achieved industrial importance but are of no value for the synthesis of nitroalkanes on a laboratory scale, although experiments have been conducted on a small scale in sealed tubes.[12–14]

The vapour phase nitration of hydrocarbons proceeds via a radical mechanism[3,15] and so it is found that tertiary carbon centres are nitrated most readily, followed by secondary and primary centres which are only nitrated with difficulty. With increased temperature these reactions become less selective; at temperatures of 410–430 °C hydrocarbons often yield a complex mixture of products. At these temperatures alkyl chain fission occurs and nitroalkanes of shorter chain length are obtained along with oxidation products. An example is given by Levy and Rose[16] who nitrated propane with nitrogen dioxide at 360 °C under 10 atmospheres of pressure and obtained a 75–80 % yield of a mixture containing: 20–25 % nitromethane, 5–10 % nitroethane, 45–55 % 2-nitropropane, 20 % 1-nitropropane and 1 % 2,2-dinitropropane.

The nitration of moderate to high molecular weight alkane substrates results in very complex product mixtures. Consequently, these reactions are only of industrial importance if the mixture of nitroalkane products is separable by distillation. Polynitroalkanes can be observed from the nitration of moderate to high molecular weight alkane substrates with nitrogen dioxide. The nitration of aliphatic hydrocarbons has been the subject of several reviews.[15,17]

Both nitric acid and nitrogen dioxide, in the liquid and vapour phase, have been used for the nitration of the alkyl side chains of various alkyl-substituted aromatics without affecting the aromatic nucleus.[13,18] Thus, treatment of ethylbenzene with nitric acid of 12.5 % concentration in a sealed tube at 105–108 °C is reported to generate a 44 % yield of phenylnitroethane.[13] The nitration of toluene with nitrogen dioxide at a temperature between 20–95 °C yields a mixture of phenylnitromethane and phenyldinitromethane with the proportion of the latter increasing with reaction temperature.[18]

The nitration of aliphatic hydrocarbons with dinitrogen pentoxide[19] and nitronium salts[20] has been described. Topchiev[21] gives an extensive discussion of works related to hydrocarbon nitration conducted prior to 1956.

1.4 ADDITION OF NITRIC ACID, NITROGEN OXIDES AND RELATED COMPOUNDS TO UNSATURATED BONDS

1.4.1 Nitric acid and its mixtures

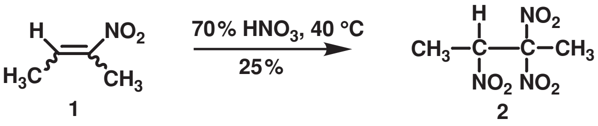


Figure 1.2

Alkenes can react with nitric acid, either neat or in a chlorinated solvent, to give a mixture of compounds, including: *vic*-dinitroalkane, β-nitro-nitrate ester, *vic*-dinitrate ester, β-nitroalcohol, and nitroalkene products.[21–26] Cyclohexene reacts with 70 % nitric acid to yield a mixture of 1,2-dinitrocyclohexane and 2-nitrocyclohexanol nitrate.[23] Frankel and Klager[24] investigated the reactions of several alkenes with 70 % nitric acid, but only in the case of 2-nitro-2-butene (1) was a product identified, namely, 2,2,3-trinitrobutane (2).

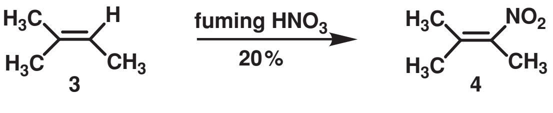


Figure 1.3

The reaction of fuming nitric acid with 2-methyl-2-butene (3) is reported to yield 2-methyl-3-nitro-2-butene (4).[26] The reaction of alkenes with fuming nitric acid, either neat or in chlorinated solvents, is an important route to unsaturated nitrosteroids, which assumedly arise from the dehydration of β-nitroalcohols or the elimination of nitric acid from β-nitro-nitrate esters.[25,27] Temperature control in these reactions is important if an excess of oxidation by-products is to be avoided.

Mixed acid has been reported to react with some alkenes to give β-nitro-nitrate esters amongst other products.[26]

Solutions of acetyl nitrate, prepared from fuming nitric acid and acetic anhydride, can react with alkenes to yield a mixture of nitro and nitrate ester products, but the β-nitroacetate is usually the major product.[28–30] Treatment of cyclohexene with this reagent is reported to yield a mixture of 2-nitrocyclohexanol nitrate, 2-nitrocyclohexanol acetate, 2-nitrocyclohexene and 3-nitrocyclohexene.[29,30] β-Nitroacetates readily undergo elimination to the α-nitroalkenes on heating with potassium bicarbonate.[5] β-Nitroacetates are also reduced to the nitroalkane on treatment with sodium borohydride in DMSO.[31]

Solutions of acetyl nitrate have also been used for the synthesis of α-nitroketones from enol esters and ethers.[30,32]

The reaction of alkynes with nitric acid or mixed acid is generally not synthetically useful. An exception is the reaction of acetylene with mixed acid or fuming nitric acid which leads to the formation of tetranitromethane.[33a] A modification to this reaction uses a mixture of anhydrous nitric acid and mercuric nitrate to form trinitromethane (nitroform) from acetylene.[34] Nitroform is produced industrially via this method in a continuous process in 74 % yield.[34] The reaction of ethylene with 95–100 % nitric acid is also reported to yield nitroform (and 2-nitroethanol).[33b,c] The nitration of ketene with fuming nitric acid is reported to yield tetranitromethane.[35] Tetranitromethane is conveniently synthesized in the laboratory by leaving a mixture of fuming nitric acid and acetic anhydride to stand at room temperature for several days.[33d]

1.4.2 Nitrogen dioxide

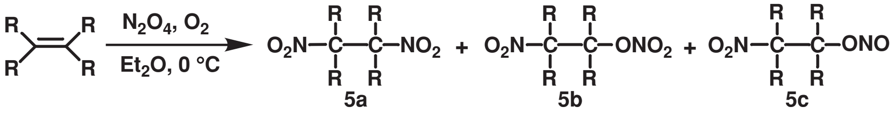


Figure 1.4

The addition of nitrogen oxides and other sources of NO_2 across the double bonds of alkenes is an important route to nitro compounds. Alkenes react with dinitrogen tetroxide in the presence of oxygen to form a mixture of *vic*-dinitro (5a), β-nitro-nitrate ester (5b) and β-nitro-nitrite ester (5c) compounds; the nitrite ester being oxidized to the nitrate ester in the presence of excess dinitrogen tetroxide.[36] A stream of oxygen gas is normally bubbled through the reaction mixture to expel nitrous oxide formed during the reaction and so prevent more complex mixtures being formed. These reactions can be synthetically useful for the synthesis of *vic*-dinitroalkanes because nitrate and nitrous ester by-products are chemically unstable and are readily hydrolyzed to the corresponding β-nitroalcohol on treatment with methanol.

1,2-Dinitroethane and 1,2-dinitrocyclohexane can be formed in this way from the corresponding alkenes in 42 % and 37 % yield respectively.[36a]
The addition of dinitrogen tetroxide across the double bonds of electron deficient fluorinated alkenes is a particularly useful route to *vic*-dinitro compounds where yields are frequently high;[8,37] tetrafluoroethylene gives a 53 % yield of 1,2-dinitro-1,1,2,2-tetrafluoroethane.[38]

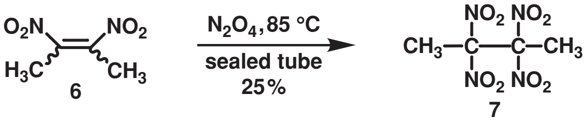


Figure 1.5

The reaction of α-nitroalkenes with nitrogen dioxide or its dimer, dinitrogen tetroxide, has been used to synthesize polynitroalkanes. Thus, the reaction of dinitrogen tetroxide with 2,3-dinitro-2-butene (6) and 3,4-dinitro-3-hexene is reported to yield 2,2,3,3-tetranitrobutane (7, 25 %) and 3,3,4,4-tetranitrohexane (32 %) respectively.[39]

Additions of dinitrogen tetroxide across C–C double bonds are selective. The β-nitro-nitrates formed from terminal alkenes have the nitro group situated on the carbon bearing the most hydrogen and this is irrespective of neighbouring group polarity.[36] Altering reaction conditions and stoichiometry enables the preferential formation of β-nitro-nitrates over *vic*-dinitroalkanes, which, although inherently unstable, provide a synthetically useful route to α-nitroalkenes via base-catalyzed elimination.[40] β-Nitro-nitrates are reduced to the nitroalkane on treatment with sodium borohydride in ethanol.[41] β-Nitro-nitrates also undergo facile hydrolysis to the β-nitroalcohol, and conversion of the latter to the methanesulfonate[42] or acetate,[5] followed by reaction with triethylamine or potassium bicarbonate respectively, yields the α-nitroalkene. The reaction of alkenes with dinitrogen tetroxide in the presence of iodine yields β-nitroalkyl iodides, which on treatment with sodium acetate also yield α-nitroalkenes. 1,4-dinitro-2-butene has been prepared in this way from butadiene.[5] The synthesis of α-nitroalkene has been recently reviewed by Ono.[2]

The reaction of alkenes with nitrogen oxides and other nitrating agents have been extensively discussed by Olah,[3] Topchiev,[21] and in numerous reviews.[43]

The reaction of alkynes with dinitrogen tetroxide is less synthetically useful as a route to nitro compounds. The reaction of 3-hexyne with dinitrogen tetroxide yields a mixture of *cis*- and *trans*-3,4-dinitro-3-hexene (4.5 % and 13 % respectively), 4,4-dinitro-3-hexanone (8 %), 3,4-hexanedione (16 %) and propanoic acid (6 %).[44] 2-Butyne forms a mixture containing both *cis*- and *trans*-2,3-dinitro-2-butene (7 % and 34 % respectively).[44]

1.4.3 Dinitrogen pentoxide

Alkenes react with dinitrogen pentoxide in chlorinated solvents to give a mixture of β-nitro-nitrate, *vic*-dinitro, *vic*-dinitrate ester and nitroalkene compounds.[45a,b] At temperatures between –30 °C and –10 °C the β-nitro-nitrate is often the main product. The β-nitro-nitrates are inherently unstable and readily form the corresponding nitroalkenes.[40] Propylene reacts with dinitrogen pentoxide in methylene chloride between –10 °C and 0 °C to form a mixture of 1-nitro-2-propanol nitrate (27 %) and isomeric nitropropenes (12 %). The same reaction with cyclohexene is more complicated.[45a]

At temperatures between 0 °C and 25 °C the *vic*-dinitrate ester is often observed in the product mixture and can be the major product in some cases.[45c−e] The synthesis of *vic*-dinitrate esters via this route is discussed in Section 3.6.2. Fischer[46] has given a comprehensive review of work relating to the mechanism of dinitrogen pentoxide addition to alkenes.

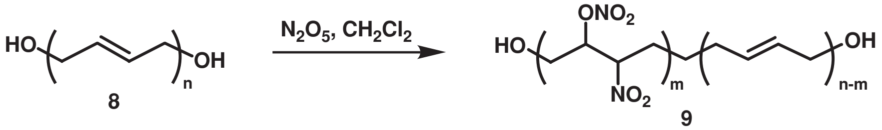


Figure 1.6

Hydroxy-terminated polybutadiene (8) (HTPB) has been treated with dinitrogen pentoxide in methylene chloride. The product (9) is an energetic oligomer but is unlikely to find application because of the inherent instability of β-nitronitrates.[47] Initial peroxyacid epoxidation of some of the double bonds of HTPB followed by reaction with dinitrogen pentoxide yields a product containing *vic*-dinitrate ester groups and this product (NHTPB) is of much more interest as an energetic binder (see Section 3.10).[47]

1.4.4 Nitrous oxide and dinitrogen trioxide

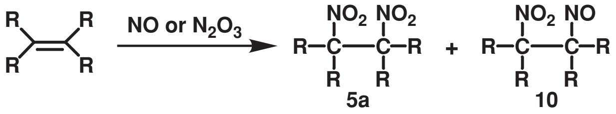


Figure 1.7

The addition of nitrous oxide (NO) or dinitrogen trioxide (N_2O_3) across the double bond of an alkene usually generates a mixture of dinitro (5a) and nitro-nitroso (10) alkanes.[48,49] The reaction of tetrafluoroethylene with dinitrogen trioxide is reported to give 1,2-dinitrotetrafluoroethane and 1-nitro-2-nitrosotetrafluoroethane in 8 % and 42 % yield respectively;[48] the same reaction with nitrous oxide leading to increased yields of 15 % and 68 % respectively.[49] When an excess of nitrous oxide or dinitrogen trioxide is used in these reactions the *vic*-dinitroalkane is usually the main product.[49]

1.4.5 Other nitrating agents

Alkenes react with nitryl chloride to give β-nitroalkyl chlorides, β-chloroalkyl nitrites and *vic*-dichloroalkane products.[50] Nitryl chloride reacts with enol esters to give α-nitroketones.[32b]

A process known as alkene nitrofluorination has been extensively used for the synthesis of β-nitroalkyl fluorides. Reagents used generate the nitronium cation in the presence of fluoride anion, and include: HF/HNO_3,[51] $HF/HNO_3/FSO_3H$,[52] NO_2F,[53] SO_2/NO_2BF_4[54] and HF/pyridine/NO_2BF_4.[55]

A mixture of silver nitrite and iodine reacts with alkenes to give β-nitroalkyl iodides,[56] and therefore, provides a convenient route to α-nitroalkenes.[5] Treatment of alkenes with ammonium nitrate and trifluoroacetic anhydride in the presence of ammonium bromide, followed by treatment of the resulting β-nitroalkyl bromide with triethylamine, is also a general route to α-nitroalkenes.[57]

The reaction of alkenes with nitronium salts proceeds through a nitrocarbocation. The product(s) obtained depends on both the nature of the starting alkene and the conditions used.[3,58]

α-Nitroketones have been synthesized from the reactions of silyl enol ethers with nitronium tetrafluoroborate[59] and tetranitromethane in alkaline media.[60] The reaction of enol acetates with trifluoroacetyl nitrate, generated *in situ* from ammonium nitrate and trifluoroacetic anhydride, also yields α-nitroketones.[61]

1.5 HALIDE DISPLACEMENT

1.5.1 Victor Meyer reaction

One of the most important reactions for the laboratory synthesis of primary aliphatic nitro compounds was discovered by V. Meyer and O. Stüber[62] in 1872 and involves treating alkyl halides with a suspension of silver nitrite in anhydrous diethyl ether. Benzene, hexane and petroleum ether have also been used as solvents for these reactions which are usually conducted between 0 °C and room temperature in the absence of light.

Primary alkyl iodides and bromides are excellent substrates for the Victor Meyer reaction, providing a route to both substituted and unsubstituted nitroalkanes (Table 1.1).[63,65,70,71] The formation of the corresponding nitrite ester is a side-reaction and so the nitroalkane is usually isolated by distillation when possible. The reaction of primary alkyl chlorides with silver nitrite is too slow to be synthetically useful. Secondary alkyl halides and substrates with branching on

$$\text{R—X} \quad + \quad \text{AgNO}_2 \quad \xrightarrow[\text{X = I or Br}]{\text{Et}_2\text{O}} \quad \text{R—NO}_2 \quad + \quad \text{AgX}$$

Table 1.1
Synthesis of nitroalkanes and their derivatives from the reaction of alkyl halides with silver nitrite under the Victor Meyer conditions

Alkyl halide	Yield (%) of nitroalkane	Yield (%) of nitrite ester	Ref.
$CH_3CH_2CH_2Br$	67	19	63
$(CH_3)_2CHBr$	19–26	24–34	64
$CH_3CH_2CH_2CH_2Br$	73	13	65
$CH_3CH_2CHBrCH_3$	19–24	27–37	64
$HOCH_2CH_2I$	62	---	66
$H_2C{=}CHCH_2Br$	55	---	67
ICH_2CO_2Et	77	---	68
p-$O_2NC_6H_4CH_2Br$	75	5	69
p-$MeOC_6H_4CH_2Br$	26	55	69

$$\underset{X = I \text{ or } Br}{XCH_2(CH_2)_nCH_2X} \xrightarrow[\text{or} \atop AgNO_2,\ Et_2O]{NaNO_2,\ DMF \atop \text{phloroglucinol,} \atop (NH_2)_2CO} O_2NCH_2(CH_2)_nCH_2NO_2$$

Table 1.2
Synthesis of dinitroalkanes from the reaction of dihaloalkanes with silver nitrite and sodium nitrite (ref. 75–79)

Homologue	Yield (%) of dinitroalkane		
n =	diiodide/AgNO$_2$	dibromide/AgNO$_2$	dibromide/NaNO$_2$
1	37[75]	20[78]	6[79]
2	46[75]	37[78]	33[79]
3	45[75]	53[78]	29[79]
4	48[75]	---	42[79]
5	60[76]	---	---
6	---	---	---
7	---	---	---
8	50[77]	100[78]	---

the carbon chain give much lower yields of nitro compound.[64] Reactions with such substrates are much slower and nitrite ester formation is much more of a problem. In fact, the nitrite ester and the corresponding alkene can be the main products of the reaction of a secondary alkyl halide with silver nitrite. Consequently, the Victor Meyer reaction is not considered useful for the synthesis of secondary nitroalkanes. Nitrate ester by-products[72,73] can arise from either disproportionation of silver nitrite,[72] a process accelerated by heat and light, or from dehydrohalogenation[64] of the alkyl halide substrate.

The Victor Meyer reaction is remarkably versatile and tolerant of many functional groups, providing a route to arylnitromethanes[69] from benzyl iodides and bromides, α-nitroesters[68] from α-iodoesters, and nitro-substituted epoxides like 1-nitro-2,3-epoxypropane, 1-nitro-2,3-epoxybutane, and 3-nitro-1,2-epoxybutane from the corresponding iodoepoxides[74] (Table 1.1). The Victor Meyer reaction has also been used for the synthesis of numerous α,ω-dinitroalkanes from the corresponding α,ω-diiodoalkanes[75–77] and α,ω-dibromoalkanes[78] where yields of 37–50 % are reported (Table 1.2). 1,5-Dinitropentane (62 %), 1,8-dinitrooctane (64 %) and 1,10-dinitrodecane have recently been synthesized from the corresponding α,ω-diiodoalkanes using water as the reaction solvent.[80] Kornblum[81] has compiled a comprehensive list of reactions illustrating the versatility of the Victor Meyer reaction.

With regard to the mechanism of the Victor Meyer reaction, it is thought that both S_N2 and S_N1 transition states play a role in product ratios.[69,82] Both transition states are known to be highly dependent on the nature of the substrate, the solvent and the reaction conditions used.[83] Which mechanism or combination of mechanisms is operating is important from a practical point of view; the more S_N1 character in these reactions the more nitrite ester formed via attack on an intermediate carbocation. Unsurprisingly, the reaction of silver nitrite with tertiary alkyl halides is not a viable route to tertiary nitroalkanes.[64] The formation of the silver halogen bond is a strong driving force for the Victor Meyer reaction, and consequently, sulfonate esters, and other substrates containing equally good leaving groups, fail to react with silver nitrite.[69]

1.5.2 Modified Victor Meyer Reaction

The synthesis of aliphatic nitro compounds from the reaction of alkyl halides with alkali metal nitrites was discovered by Kornblum and co-workers[84,85] and is known as the modified Victor Meyer reaction or the Kornblum modification. The choice of solvent in these reactions is crucial when sodium nitrite is used as the nitrite source. Both alkyl halide and nitrite anion must be in solution to react, and the higher the concentration of nitrite anion, the faster the reaction. For this reason, both DMF and DMSO are widely used as solvents, with both able to dissolve appreciable amounts of sodium nitrite. Although sodium nitrite is more soluble in DMSO than DMF the former can react with some halide substrates.[86] Urea is occasionally added to DMF solutions of sodium nitrite to increase the solubility of this salt and hence increase reaction rates. Other alkali metal nitrites can be used in these reactions, like lithium nitrite,[87] which is more soluble in DMF than sodium nitrite but is also less widely available.

$$\mathrm{RR'CHNO_2} \;+\; \mathrm{RR'CHONO_2} \xrightarrow{\mathrm{NO_2^-}} \mathrm{RR'CHOH} \;+\; \mathrm{RR'C(NO)NO_2} \qquad \text{(Eq. 1.1)}$$

Figure 1.8

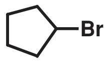
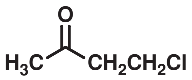
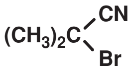
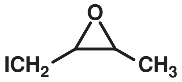
Reaction time is extremely important in avoiding the side reaction illustrated in Eq. (1.1), where the nitroalkane product reacts with nitrite anion and any nitrite ester, formed as by-product, to give a pseudonitrole.[88] The reaction of sodium nitrite with alkyl halides is much faster than this competing nitrosation side reaction, even so, prompt work-up on reaction completion is essential for obtaining good yields.

As a rule, the reaction of primary alkyl iodides with sodium nitrite in DMF takes about 2.5 hours for completion but this is raised to about 6 hours for primary alkyl bromides.[81] The addition of urea cuts these reaction times by approximately half.[80] The reaction of alkyl chlorides with alkali metal nitrites is too slow to be synthetically useful. Secondary alkyl bromides and alicyclic iodides require the addition of a nitrite ester scavenger such as phloroglucinol.[84] Under these conditions secondary nitroalkanes and their derivatives are formed in good yield,[84,85] an advantage over the use of silver nitrite which is generally limited to primary alkyl halides. Nitroalkane products containing electron-withdrawing groups that significantly increase the acidity of the nitro group, i.e. α-nitroesters, are particularly susceptible to nitrosation and also require the addition of a nitrite ester scavenger.[89,90] The reaction of tertiary alkyl halides with sodium nitrite is not a feasible synthetic route to nitro compounds.[84]

The modified Victor Meyer reaction has been used successfully for the synthesis of many substituted and unsubstituted, primary and secondary, nitro compounds from the corresponding alkyl iodides, bromides, sulfonate esters etc. (Table 1.3).[81,84] Arylnitromethanes are synthesized in good yield from benzylic halides if reactions are conducted at subambient temperatures.[84,92] α-Nitroesters[89,90] and β-nitroketones[91] are obtained from the corresponding α-haloesters and β-haloketones. Some substrates containing a strong electron-withdrawing group on the same carbon as the halogen i.e. α-haloketones are destroyed under the modified Victor Meyer conditions and so the use of silver nitrite is preferred.

Silver nitrite gives significantly higher yields of nitro compounds from primary alkyl halides, and consequently, the synthesis of α,ω-dinitroalkanes from the reaction of α,ω-dihaloalkanes with sodium nitrite[79] is inferior to the same reaction with silver nitrite[75–78] (Table 1.2). However, the use of a solvent system composed of DMSO and MEK is reported to considerably improve the yields of α,ω-dinitroalkane when using sodium nitrite.[93]

Table 1.3
Synthesis of nitroalkanes and their derivatives from the reaction of alkyl halides with sodium nitrite under the modified Victor Meyer conditions

Substrate	Solvent	Yield (%) of nitroalkane	Ref.
$CH_3CH_2CH_2CH_2SO_2CH_3$	DMF	46	84
	DMF	57	84
	DMF	47	91
$CH_3CHBrCO_2Et$	DMSO	66	89
$PhCH_2Br$	DMF	55	84
 $(CH_3)_2C(CN)Br$	DMF	52	87
	DMF	70	74

The reaction of α-halocarboxylic acids with sodium nitrite has been used to synthesize nitromethane, nitroethane and nitropropane, although the reaction fails for higher nitroalkanes.[94]

A number of other reactions have been reported which use nitrite anion as a nucleophile, including: (1) reaction of alkyl halides with potassium nitrite in the presence of 18-crown-6,[95] (2) reaction of alkyl halides with nitrite anion bound to amberlite resins,[96] (3) synthesis of 2-nitroethanol from the acid-catalyzed ring opening of ethylene oxide with sodium nitrite,[97] and (4) reaction of primary alkyl chlorides with sodium nitrite in the presence of sodium iodide.[98]

1.5.3 Ter Meer reaction

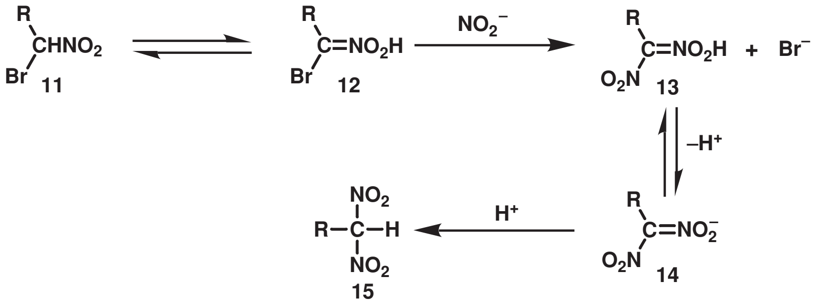


Figure 1.9

The Ter Meer reaction[99] provides a convenient route to terminal *gem*-dinitroaliphatic (15) compounds via the displacement of halogen from terminal α-halonitroalkanes (11) with nitrite anion in alkaline solution. These reactions are believed[100] to go via the tautomeric α-halonitronic acid (12) rather than the α-halonitroalkane (11). The synthesis of internal *gem*-dinitroaliphatic compounds from the corresponding internal α-halonitroalkanes is not possible via this route. The α-halonitroalkane substrates for the Ter Meer reaction are readily obtained from the bromination[62] or chlorination[101] of primary nitroalkanes in alkaline solution, or from the reaction of halogenating agents with oximes followed by oxidation of the resulting α-halonitrosoalkane.[102,103]

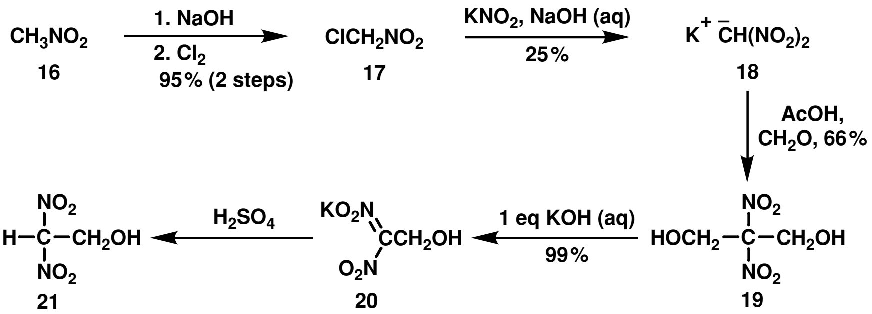


Figure 1.10

The Ter Meer reaction has been used for the synthesis of the potassium salt of dinitromethane (18) by treating chloronitromethane (17) with potassium nitrite in aqueous sodium hydroxide solution.[104] The potassium salt of dinitromethane is a dangerous shock sensitive explosive and should not be isolated; treatment of (18) with formaldehyde in acidic solution forms the more manageable bis-methylol derivative, 2,2-dinitro-1,3-propanediol (19).[104] Partial hydrolysis of (19) with potassium hydroxide, followed by acidification, yields 2,2-dinitroethanol (21).[105] 2,2-Dinitroethanol has also been synthesized from the alkaline bromination of 2-nitroethanol followed by nitrite displacement and subsequent acidification of the resulting potassium 2,2-dinitroethanol.[106] 2,2-Dinitro-1,3-propanediol and 2,2-dinitroethanol are useful derivatives of dinitromethane and find extensive use in condensation and esterification reactions for the synthesis of energetic oligomers and plasticizers.

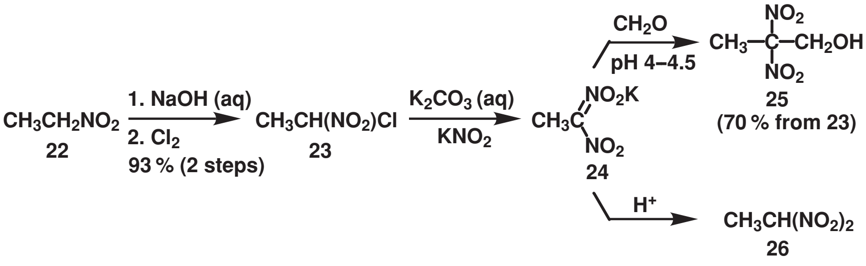


Figure 1.11

Both 1,1-dinitroethane (26) and 1,1-dinitropropane, and their methylol derivatives, 2,2-dinitropropanol (25) and 2,2-dinitro-1-butanol respectively, have been synthesized via the Ter Meer reaction.[99,107] The formal and acetal of 2,2-dinitropropanol in the form of a 1:1 eutectic is an energetic plasticizer and so the synthesis of 2,2-dinitropropanol has been the subject of much investigation.[107] On a pilot plant scale 2,2-dinitropropanol (25) is synthesized in 60 % overall yield from nitroethane (22). Thus, treatment of 1-chloronitroethane (23) with potassium nitrite in aqueous potassium carbonate forms the potassium salt of 1,1-dinitroethane (24), which on acidification, followed by *in situ* reaction with formaldehyde, yields 2,2-dinitropropanol (25). Note, while dinitromethane is unstable at room temperature other terminal *gem*-dinitroalkanes, like 1,1-dinitroethane (26) and 1,1-dinitropropane, are perfectly stable.

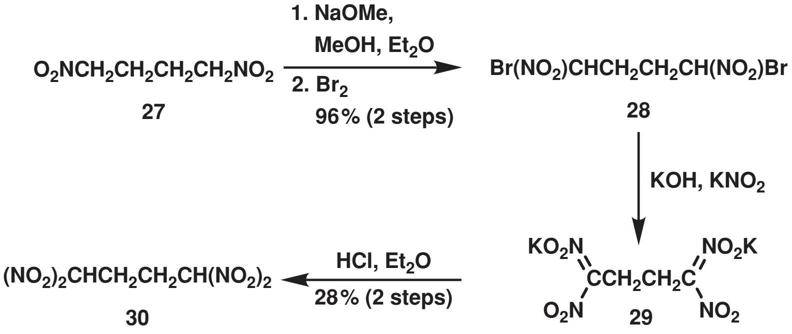


Figure 1.12

The Ter Meer reaction has been used to synthesize $\alpha,\alpha,\omega,\omega$-tetranitroalkanes from the corresponding α,ω-dihalo-α,ω-dinitroalkanes.[108] Thus, treatment of 1,4-dibromo-1,4-dinitrobutane (28) under the Ter Meer conditions yields the dinitronate salt of 1,1,4,4-tetranitrobutane (29); acidification of the latter yields 1,1,4,4-tetranitrobutane (30).[108]

The Ter Meer reaction has not been widely exploited for the synthesis of *gem*-dinitroaliphatic compounds. This is partly because the Kaplan–Shechter oxidative nitration (Section 1.7) is more convenient, but also because of some more serious limitations. The first is the inability to synthesize internal *gem*-dinitroaliphatic compounds; functionality which shows high chemical stability and is found in many cyclic and caged energetic materials. Secondly, the *gem*-nitronitronate salts formed in the Ter Meer reactions often need to be isolated to improve the yield and purity of the product. Dry *gem*-nitronitronate salts are hazardous to handle and those from nitroalkanes like 1,1,4,4-tetranitrobutane are primary explosives which can explode even when wet. Even so, it is common to use conditions that lead to the precipitation of *gem*-nitronitronate salts from solution, a process that both drives the reaction to completion and also provides isolation and purification of the product salt by simple filtration. Purification of *gem*-nitronitronate salts by filtration from the reaction liquors, followed by washing with methanol or ethanol to remove occluded impurities, has been used, although these salts should never be allowed to completely dry.

The choice of base used in the Ter Meer reaction is important for two reasons. First, studies have found that strong bases, such as alkali metal hydroxides, inhibit the reaction and promote side-reactions, whereas the weaker alkali metal carbonates generally give higher yields.[107] Secondly, if the *gem*-nitronitronate salt needs to be purified by filtration it should be sparingly soluble in the reaction solvent and both the reaction solvent and the counterion of the *gem*-nitronitronate salt affect this solubility.[107] Use of the potassium salt is advantageous for aqueous systems where the *gem*-nitronitronate salts are usually only sparingly soluble, whereas the sodium salt can be used for nonaqueous reactions.[107]

It must be emphasized that *gem*-nitronitronate salts should never be stored on safety grounds. These salts readily react with formaldehyde to give the methylol derivatives which are more stable and less hazardous to handle. The latter are often used directly in condensation reactions where treatment with aqueous base forms the *gem*-nitronitronate salt *in situ*.

1.5.4 Displacements using nitronate salts as nucleophiles

Nitronate salts can react with alkyl halides to yield polynitroaliphatic compounds with varying degrees of success. The main by-products of these reactions arise for competitive *O*-alkylation. Alkyl nitrates are formed as by-products when the nitroform anion is used in these reactions.[109]

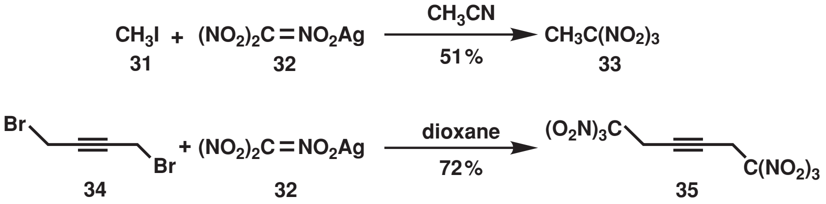


Figure 1.13

Methyl iodide (31) reacts with silver nitroform (32) in acetonitrile to give a 51 % yield of 1,1,1-trinitroethane (33).[109] The potassium salt of nitroform in acetone has been used for the same reaction.[110] Yields between 28 % and 65 % have been reported for the reaction of silver nitroform in acetonitrile with higher molecular weight alkyl iodides.[109] The choice of solvent is important in some reactions, for example, silver nitroform reacts with 1,4-dibromo-2-butyne (34) in solvents like dioxane[111] and acetone[111] to give 1,1,1,6,6,6-hexanitro-3-hexyne (35) in approximately 72 % yield, whereas the same reaction in acetonitrile[109] is reported to give a mixture of compounds.

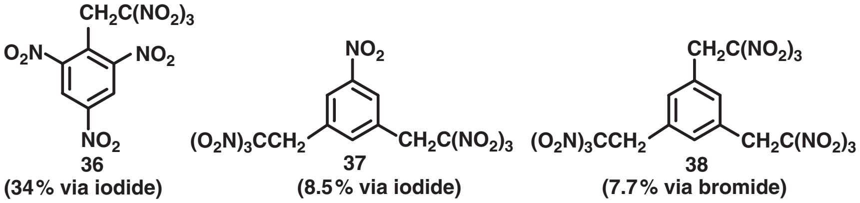
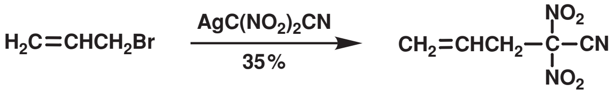


Figure 1.14

Poor to modest yields of trinitromethyl compounds are reported for the reaction of silver nitroform with substituted benzyl iodide and bromide substrates. Compounds like (36), (37), and (38) have been synthesized via this route; these compounds have much more favourable oxygen balances than TNT and are probably powerful explosives.[112] The authors noted that considerable amounts of unstable red oils accompanied these products. The latter are attributed to *O*-alkylation, a side-reaction favoured by an S_N1 transition state and typical of reactions involving benzylic substrates and silver salts. Further research showed that while silver nitroform favours *O*-alkylation, the sodium, potassium and lithium salts favour *C*-alkylation.[113] The synthesis and chemistry of 1,1,1-trinitromethyl compounds has been extensively reviewed.[9,114,115] The alkylation of nitronate salts has been the subject of an excellent review by Nielsen.[116]



$$H_2C{=}CHCH_2Br \xrightarrow[35\%]{AgC(NO_2)_2CN} CH_2{=}CHCH_2{-}\overset{NO_2}{\underset{NO_2}{C}}{-}CN$$

Figure 1.15

The reactions of alkyl halides with the silver salt of dinitroacetonitrile have been shown to be of limited use for the synthesis of polynitroaliphatic compounds.[109,117] These reactions give a mixture of *C*-, *N*- and *O*-alkylation products with product distribution highly dependent on the nature of the substrate.[109,117]

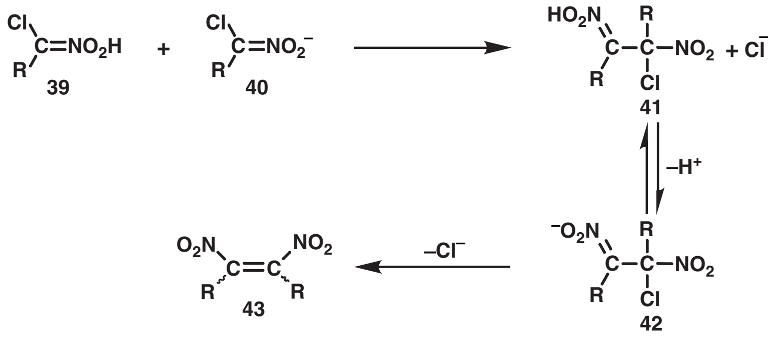


Figure 1.16

The addition of α-chloronitroalkanes to solutions of alkali metal hydroxide has been used for the synthesis of some 1,2-dinitroethylene derivatives (43).[118,119] These reactions involve attack of the nitronate salt (40) on the *aci*-form (39) of the unreacted *gem*-chloronitroalkane followed by formal loss of hydrogen chloride. 2,3-Dinitro-2-butene and 3,4-dinitro-3-hexene (45) are formed in this way from 1-chloro-1-nitroethane and 1-chloro-1-nitropropane (44) respectively.[118]

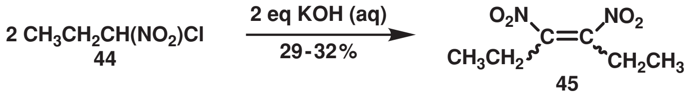


Figure 1.17

In a related reaction to that described above, nitronate salts have been reacted with α-chloronitroalkanes as a route to polynitroaliphatic compounds.[120] 2,3-Dimethyl-2,3-dinitrobutane (48) is formed from the reaction of the nitronate salt of 2-nitropropane (46) with 2-chloro-2-nitropropane (47).[120] A modification to the original process uses nitronate salts in the presence of iodine to form an α-iodonitroalkane *in situ*.[121]

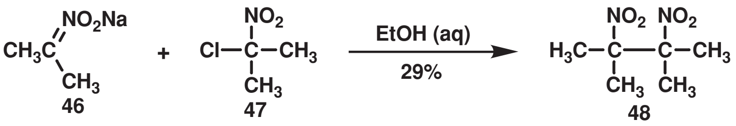


Figure 1.18

1.6 OXIDATION AND NITRATION OF C–N BONDS

1.6.1 Oxidation and nitration of oximes

Methods used for the oxidation or nitration of C–N bonds have found wide use for the synthesis of novel polynitropolycycloalkanes as can be seen in Chapter 2. The conversion of readily available ketone groups to nitro and *gem*-dinitroaliphatic functionality is usually via the oxime and this is an important route used in energetic materials synthesis.

1.6.1.1 Scholl reaction[122]

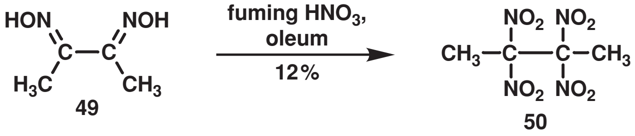
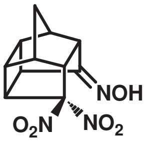
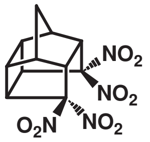
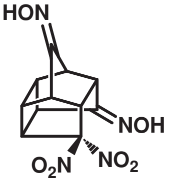
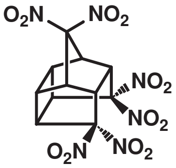
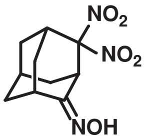
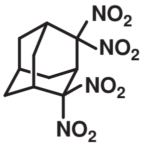
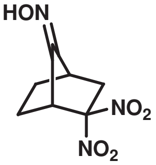
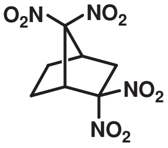


Figure 1.19

One route to *gem*-dinitroalkanes involves the tandem nitration–oxidation of oximes.[122] The nitration of dimethylglyoxime (49) with anhydrous mixed acid is reported to give 2,2,3,3-tetranitrobutane (50) in 12 % yield.[39] However, ammonium nitrate and nitric acid in methylene chloride is a more commonly used reagent, but the product, usually a pseudonitrole, needs treatment with hydrogen peroxide to yield the *gem*-dinitro compound. The nitric acid used in these reactions often contains 12–24 % dissolved dinitrogen tetroxide (‘red fuming nitric acid’) and so the reaction has similarities with the Ponzio reaction (Section 1.6.1.2). Some energetic materials recently synthesized with this reagent are illustrated in Table 1.4 (also see Chapter 2).

Table 1.4
Synthesis of energetic polynitropolycycloalkanes via the Scholl reaction

Oxime	Conditions/reagents	Product	Ref.
	1. 98 % red HNO_3, NH_4NO_3, CH_2Cl_2, reflux 2. 30 % H_2O_2 (aq) reflux 31 % (2 steps)		123
	1. 98 % red HNO_3, urea, NH_4NO_3, CH_2Cl_2, reflux 2. 30 % H_2O_2 (aq) reflux 19 % (2 steps)		124
	98 % HNO_3, urea, CH_2Cl_2, NH_4NO_3 reflux, 29 %		125
	1. 98 % red HNO_3, CH_2Cl_2, urea, NH_4NO_3, reflux 2. 30 % H_2O_2 (aq) reflux 52 % (2 steps)		126

Yields are frequently moderate for Scholl reactions. Aldoximes are not usually compatible with these harsh reaction conditions and are very sensitive to factors such as temperature and reaction time. Consequently, oxidation to the corresponding carboxylic acid is a major side-reaction. However, both the ketoxime (51) and the aldoxime (53) are reported to give good yields of the corresponding *gem*-dinitro compounds, (52) and (54) respectively, on treatment with absolute nitric acid in methylene chloride followed by hydrogen peroxide.[127]

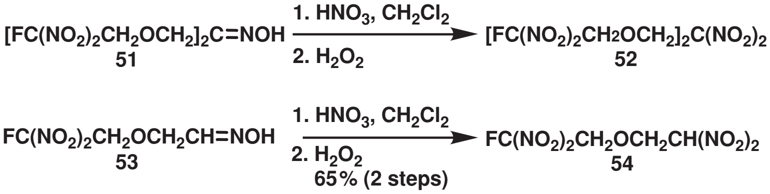


Figure 1.20

The nitration of oximinocyanoacetic acid esters with mixed acid at room temperature yields dinitrocyanoacetic acid esters which are precursors to dinitroacetonitrile and its salts.[128] α-Oximinonitriles can be nitrated to α,α-dinitronitriles with anhydrous nitric acid containing ammonium nitrate, and then subjected to ammonolysis with aqueous ammonia to give the ammonium salt of the corresponding *gem*-dinitroalkane.[129]

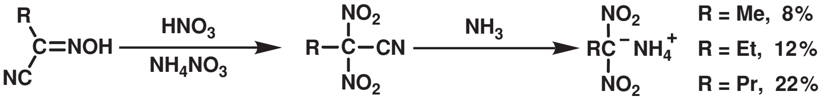
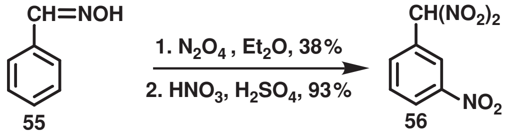


Figure 1.21

A series of α,α-dinitroesters have been synthesized from the reaction of α-oximinoesters with cold nitric acid containing ammonium nitrate, followed by oxidation of the resulting pseudonitroles with oxygen.[130]

1.6.1.2 Ponzio reaction



55

56

Figure 1.22

The Ponzio reaction[131] provides a useful route to *gem*-dinitro compounds and involves treating oximes with a solution of nitrogen dioxide or its dimer in diethyl ether or a chlorinated solvent. The Ponzio reaction works best for aromatic oximes where the synthesis of many substituted aryldinitromethanes have been reported.[132] Compound (56), an isomer of TNT, is formed from the reaction of dinitrogen tetroxide with the oxime of benzaldehyde (55) followed by mono-nitration of the aromatic ring with mixed acid.[133] Yields are usually much lower for aliphatic aldoximes and ketoximes.[134b,135] The parent carbonyl compound of the oxime is usually the major by-product in these reactions.

Dinitrogen pentoxide has also been used to synthesize aryldinitromethanes from arylaldoximes in yields between 20 % and 60 %.[134] Aromatic ring nitration can also occur during these reactions.[134] Dinitrogen pentoxide in chloroform converts α-chlorooximes to the corresponding α-chloro-α,α-dinitro compounds.[135]

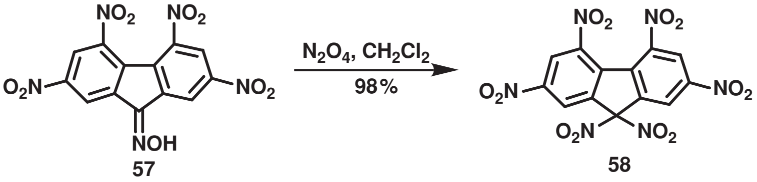


Figure 1.23

Millar and co-workers[136] conducted an extensive reinvestigation into the Ponzio reaction using both dinitrogen pentoxide and dinitrogen tetroxide in different solvents. The mechanism of the Ponzio reaction was studied together with correlations between substrate structure and product yield/purity. The thermally stable explosive 2,4,5,7,9,9-hexanitrofluorene (58) was synthesized from fluoren-9-one in 81 % yield via initial ring nitration with mixed acid, followed by oxime formation and treatment of the resulting product (57) with dinitrogen tetroxide in methylene chloride.[136,137] Millar and co-workers[136] also synthesized 2-(dinitromethyl)-4-nitrophenol, a potential substitute for picric acid, via the reaction of 2-hydroxybenzaldehyde oxime with dinitrogen tetroxide in acetonitrile (21 %). 1,1-Dinitro-1-(4-nitrophenyl)ethane was also synthesized from 4-nitroacetophenone oxime.

1.6.1.3 Peroxyacid oxidation

$$R_2C{=}NOH \xrightarrow[NaHCO_3,\ CH_3CN]{CF_3CO_3H} R_2C{=}NO_2H \rightleftharpoons R_2CHNO_2$$

Figure 1.24

The direct oxidation of an oxime to a nitro group can be achieved with peroxytrifluoroacetic acid, a reagent usually formed *in situ* from the reaction of 90 % hydrogen peroxide with either trifluoroacetic acid or trifluoroacetic anhydride.[138,139] Reactions are commonly conducted in acetonitrile at gentle reflux in the presence of sodium bicarbonate for aliphatic oximes, or alternatively, in the presence of a sodium hydrogen phosphate buffer for aromatic and alicyclic oximes. Urea is frequently added to these reactions to scavenge any oxides of nitrogen formed. Emmons and Pagano[138] used this route to synthesize a number of primary and secondary nitro compounds from the corresponding aldoximes and ketoximes respectively in yields of 40–80 %. This method fails for some sterically hindered oximes.

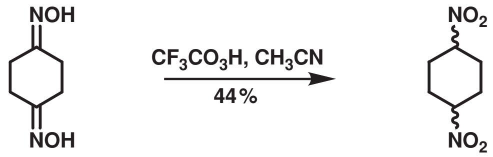
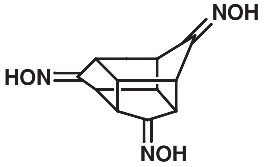
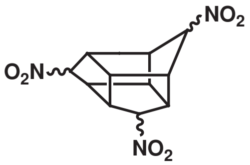
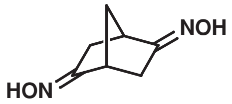
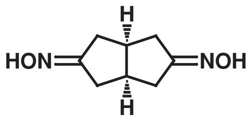
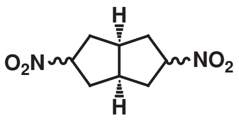


Figure 1.25

Table 1.5
Synthesis of energetic polynitropolycycloalkanes via the oxidation of oximes with peroxytrifluoroacetic acid

Oxime	Conditions/reagents	Product	Ref.
	$(CF_3CO)_2O$, 90% H_2O_2, CH_3CN, $NaHCO_3$, urea 70–75 °C, 35%		123
	$(CF_3CO)_2O$, 90% H_2O_2, CH_3CN, Na_2HPO_4, 75 °C, 65%		141
	$(CF_3CO)_2O$, 90% H_2O_2, CH_3CN, $NaHCO_3$, 75 °C, 60%		141

Nielsen[140] used the same chemistry to synthesize both 1,3- and 1,4-dinitrocyclohexanes from the corresponding dioximes. The peroxytrifluoroacetic acid reagent has been used in reaction routes to a number of highly energetic polynitropolycycloalkanes as illustrated in Table 1.5 (see also Chapter 2).

Some recent advances have been reported in oxime oxidation, including the *in situ* generation of peroxytrifluoroacetic acid from the reaction of urea hydrogen peroxide complex with TFAA in acetonitrile at 0 °C.[142] This method gives good yields of nitroalkanes from aldoximes but fails with ketoximes.

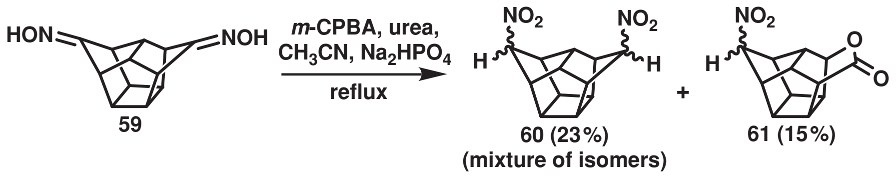


Figure 1.26

Peroxyacids are powerful oxidants and so side reactions are to be expected. Ketones are known to undergo Baeyer–Villiger[143] oxidation to the carboxylic acid ester on treatment with peroxyacids and so these by-products can be observed if oxime hydrolysis occurs during the oxidation. Paquette and co-workers[144] observed such a by-product (61) during the oxidation of the dioxime (59) to the dinitro compound (60) with *m*-CPBA in hot acetonitrile.

Peroxyacetic acid generated *in situ* from sodium perborate and glacial acetic acid has been used for oxime to nitro group conversion.[145] Peroxyimidic acid generated from acetonitrile and hydrogen peroxide has found similar use.[146] An Mo(IV) peroxy complex has been reported for the oxidation of both ketoximes and aldoximes.[147]

1.6.1.4 Halogenation–oxidation–reduction route

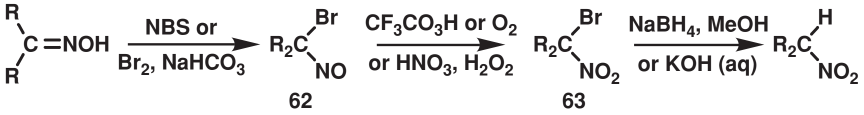


Figure 1.27

A much studied and still widely used reaction for the conversion of oximes to nitroalkanes involves treating the former with a halogen or source of halogen, followed by oxidation of the resulting α-bromonitrosoalkane (62) to an α-bromonitroalkane (63) which is then reduced to a secondary nitroalkane.[102,103,148] Although a lengthy route for this functional group conversion, the reaction proves extremely reliable and finds particular use for sterically hindered substrates.

Initial halogenation of the oxime can use chlorine,[101] hypobromite,[103] bromine,[62a,d] NBS,[103,148] or *N*-bromoacetamide.[148] Oxidation of the α-halonitrosoalkane can be achieved with nitric acid,[103] nitric acid–hydrogen peroxide,[148] atmospheric oxygen,[102] ozone,[149] or a peroxyacid.[140] Reduction of the α-halonitroalkane is achieved with sodium borohydride[103,148] or by catalytic hydrogenation,[149] although potassium hydroxide in ethanol[102] has been used for the conversion.

The original procedure for the bromination–oxidation–reduction route used bromine in aqueous potassium hydroxide, followed by oxidation with nitric acid–hydrogen peroxide and reduction with alkaline ethanol.[102] This procedure was improved by using NBS in aqueous sodium bicarbonate for the initial oxime bromination, followed by oxidation with nitric acid and final reduction of the α-bromonitroalkane with sodium borohydride in methanol. It is possible to convert oximes to nitroalkanes via this procedure without isolating or purifying any of the intermediates. This procedure is reported to give yields of between 10 and 55 % for a range of oxime to nitroalkane conversions.[103,148]

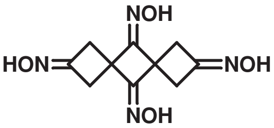
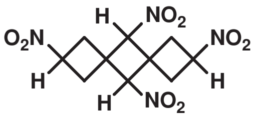
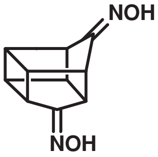
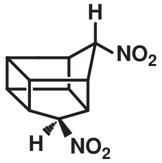
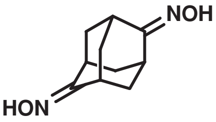
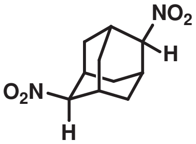
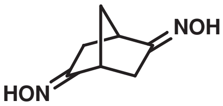
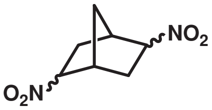
The bromination–oxidation–reduction route has been used in the syntheses of many energetic polynitropolycycloalkanes. Some of these reactions are illustrated in Table 1.6 (see also Chapter 2). A common strategy in these reactions is to use the oxime functionality to incorporate the nitro group, followed by oxidative nitration to *gem*-dinitro functionality via the Kaplan–Shechter reaction. This has been used in the case of 2,5-dinitronorbornane to synthesize 2,2,5,5-tetranitronorbornane.[126]

Research has focused on improving the efficiency of the halogenation–oxidation–reduction route by using reagents that perform the halogenation–oxidation in one step. Hypochlorous acid-hypochlorite[152,153] and hypobromous acid-hypobromite[154] systems have also been explored for the direct conversion of oximes to α-bromonitroalkanes and α-chloronitroalkanes respectively. Some *N*-haloheterocycles[155] have been reported to affect direct oxime to α-halonitroalkane conversion, and on some occasions, the use of NBS[126,152] or the free halogens[156] also leads to α-halonitroalkanes. A mixture of oxone and sodium chloride as a suspension in chloroform is reported as a one-pot method for the direct conversion of oximes to α-chloronitroalkanes.[157]

1.6.2 Oxidation of amines

The direct oxidation of an amino group to a nitro group is a desirable route to nitro compounds. The oxidation of tertiary amines with potassium permanganate has been known for some

Table 1.6
Synthesis of energetic polynitropolycycloalkanes via oxime halogenation

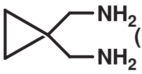
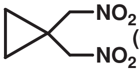
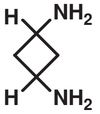
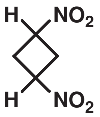
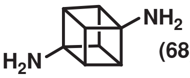
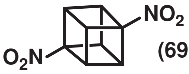
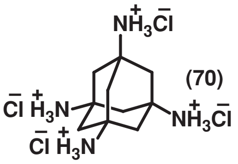
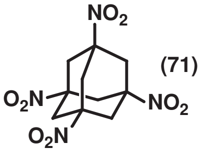
Oxime	Conditions/reagents	Product	Ref.
	1. Cl_2, CH_2Cl_2 2. NaOCl, Bu_4NHSO_4 3. Zn, $NH_2OH.HCl$, THF (aq) 20 % (3 steps)		150
	1. Br_2, DMF, $NaHCO_3$, 2. TFAA, 85 % H_2O_2, 24 % (2 steps) 3. $NaBH_4$, EtOH, 70 %		151
	1. NBS, $NaHCO_3$, dioxane (aq), 24 % 2. $NaBH_4$, THF (aq), 66 %		152
	1. NBS, $NaHCO_3$, dioxane (aq), 36 % 2. $NaBH_4$, EtOH 3. AcOH (aq) 98 % (2 steps)		126

time.[158] These reactions are often conducted in water, or in acetone–water mixtures for higher molecular weight amines.[158] Magnesium sulfate is frequently used as an additive in these reactions to control solution pH. 1,3,5,7-Tetranitroadamantane (71) has been obtained via the permanganate oxidation of the hydrochloride salt of 1,3,5,7-tetraaminoadamantane (70) (Table 1.7). The 45 % yield for this reaction reflects a relative yield of 82 % for the oxidation of each of the four amino groups.[159]

While primary aliphatic amines are converted to nitro compounds on reaction with ozone these reactions are accompanied by numerous by-products.[160] Such side-reactions are largely suppressed by first dissolving the amine onto silica gel followed by passing a stream of 3 % ozone in oxygen through the solid at –78 °C under anhydrous conditions, where yields of between 60 and 70 % are reported.[161] This route has been used to synthesize the energetic cyclopropane (65) from the diamine (64) (Table 1.7).[162]

Amines containing both primary and secondary alkyl groups are oxidized to nitroalkanes with peroxyacetic acid.[163] *m*-Chloroperoxybenzoic acid (*m*-CPBA) in chlorinated solvents at elevated temperature has found similar use.[164] The latter reagent in 1,2-dichloroethane has been used for the synthesis of both 1,3-dinitrocyclobutane (67)[150] (38 %) and 1,4-dinitrocubane (69)[165] from the corresponding diamines, (66) and (68), respectively (Table 1.7); further elaboration of the former allowing the synthesis of 1,1,3,3-tetranitrocyclobutane.[150] Peroxyacetic acid has been used for the oxidation of the tetraamine (70) but the crude product contained some nitroso functionality and needed treating with ozone for full conversion to (71) (Table 1.7).[166] Peroxytrifluoroacetic acid is not effective for the oxidation of aliphatic amines to nitro compounds.[163] The trifluoroacetic acid formed during these reactions protonates the amine

Table 1.7
Synthesis of energetic polynitropolycycloalkanes via amine oxidation

Amine	Conditions/reagents	Product	Ref.
 (64)	O_3 (excess), silica gel, -78 °C 20 - 28%	 (65)	162
 (66)	$ClCH_2CH_2Cl$, *m*-CPBA, reflux 38%	 (67)	150
 (68)	$ClCH_2CH_2Cl$, *m*-CPBA, reflux 40%	 (69)	165
 (70)	1. NaOH (aq) 2. $MgSO_4$, $KMnO_4$ 45% (2 steps)	 (71)	159
	DMDO, $(CH_3)_2CO$, 91%		170

and prevents oxidation, whereas use of a buffer in these reactions results in acylation of the amine.[163] However, peroxytrifluoroacetic acid is an extremely useful reagent for the synthesis of polynitroarylenes from the oxidation of nitroanilines (see Section 4.7.1.5).[167]

Primary, secondary and tertiary aliphatic amines are efficiently converted to nitro compounds in 80–90 % yield with dimethyldioxirane,[168] a reagent prepared[169] from the reaction of oxone ($2KHSO_5$-$KHSO_4$-K_2SO_4) with buffered acetone. Dimethyldioxirane (DMDO) has been used for the synthesis of 1,3,5,7-tetranitroadamantane (71) from the corresponding tetraamine as the tetrahydrochloride salt (70) and is an improvement over the initial synthesis[159] using permanganate anion (Table 1.7).[170] Oxone is able to directly convert some aromatic amines into nitro compounds.[171]

A recent method reported for the oxidation of primary aliphatic amines to nitro compounds uses *tert*-butylhydroperoxide (TBHP) and catalytic zirconium tetra-*tert*-butoxide in presence of molecular sieves.[172]

1.6.3 Nitration of nitronate salts

Nitronate salts and the tautomeric *aci*-form of nitroalkanes, known as nitronic acids, are converted to *gem*-dinitro compounds on treatment with dinitrogen tetroxide.[173–175] Novikov and co-workers[173] synthesized phenyldinitromethane by treating phenylnitromethane with dinitrogen tetroxide in ether and later [174] reported the synthesis of some substituted phenyltrinitromethanes from the direct nitration of the nitronate salts of phenylnitromethanes.

Phenyltrinitromethanes are similarly obtained from the nitration of *gem*-nitronitronate salts with a solution of dinitrogen tetroxide in ether. 1,1,1-Trinitroethane (73) can be formed in this way from the potassium salt of 1,1-dinitroethane (24).[176] Nitrolic acids, the products formed

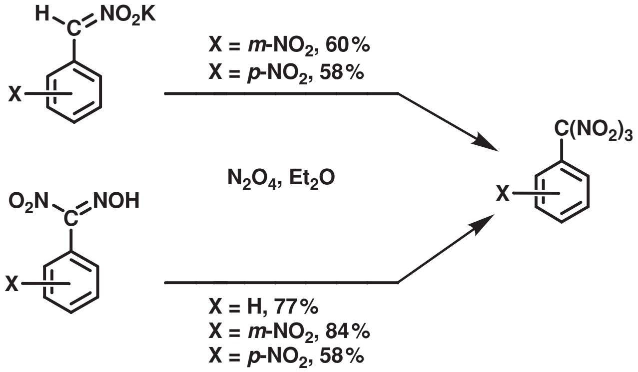


Figure 1.28

by treating primary nitronic acids or their salts (nitronates) with nitrous acid, also undergo nitration to 1,1,1-trinitromethyl compounds.[173,174,177]

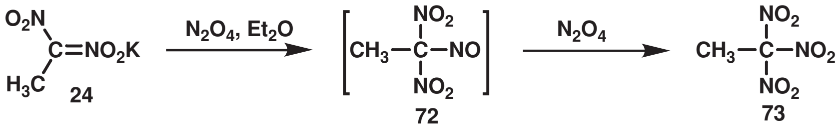


Figure 1.29

Mixed acid or anhydrous nitric acid has been used for the nitration of *gem*-nitronitronate salts to the corresponding 1,1,1-trinitromethyl compounds.[178] A convenient route to hexanitroethane (75) involves treating the dipotassium salt of 1,1,2,2-tetranitroethane (74) with mixed acid; the nitration proceeding via electrophilic addition of the nitronium cation to the bis-nitronitronate ion.[178]

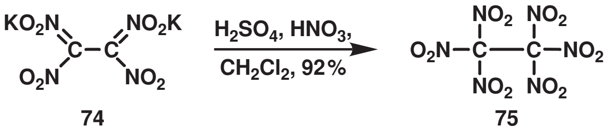


Figure 1.30

Tetranitromethane is an electrophilic source of nitronium cation and has been used in alkaline solution for the nitration of 1,1-dinitropropane to 1,1,1-trinitropropane (32 %), and for nitration of 1-phenyl-3-nitropropane to 1-phenyl-3,3-dinitropropane (32 %) and its further nitration to 1-phenyl-3,3,3-trinitropropane (33 %).[179]

Olsen and co-workers[180] reported the nitration of secondary nitroalkanes to *gem*-dinitro compounds with nitronium tetrafluoroborate in acetonitrile at –40 °C. Yields are lower compared to the Kaplan–Shechter reaction and significant amounts of pseudonitroles are formed, but this is possibly due to impure reagent.

Nitryl fluoride has been used for the nitration of terminal *gem*-dinitro compounds to the corresponding 1,1,1-trinitromethyl compounds.[181]

1.6.4 Oxidation of pseudonitroles

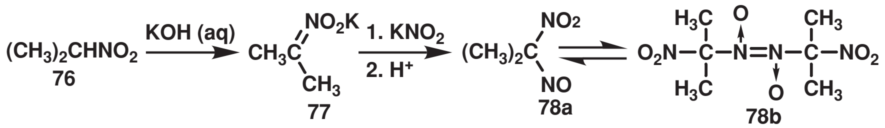


Figure 1.31

The tautomeric nitronic acids of secondary nitroalkanes or their nitronate salts react with nitrous acid or alkali metal nitrites to yield pseudonitroles.[182–184] These pseudonitroles are often isolated as their colourless dimers (78b) but are deep blue in monomeric form (78a). Primary nitroalkanes also form pseudonitroles (80b) but these rapidly isomerise to the nitrolic acid (80a).[182,183] Reactions are commonly conducted by slowly acidifying a mixture containing the nitronate salt and the metal nitrite, during which, the nitronic acid reacts with the nitrite anion. These reactions, first discovered by Meyer,[182] have been used to prepare 2-nitroso-2-nitropropane (78a) and acetonitrolic acid (80a) from 2-nitropropane (76) and nitroethane (22) respectively.[182]

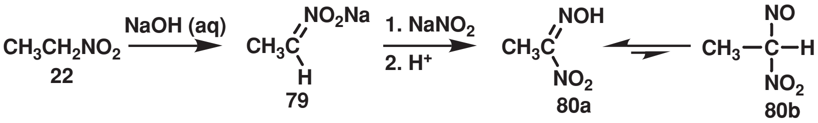


Figure 1.32

Pseudonitrole or nitrolic acid formation can be a side-reaction during the acidification of nitronate salts, particularly if the acid addition is slow. This process has been studied, optimized, and patented as a route to these compounds.[184]

Nitrolic acids undergo oxidation–nitration on treatment with dinitrogen tetroxide to the corresponding trinitromethyl compounds. Dinitroalkanes are obtained on oxidation of pseudonitroles and nitrolic acids with reagents such as chromium trioxide in acetic acid, dichromate, hydrogen peroxide, nitric acid, oxygen, and peroxyacids. Dinitrogen pentoxide in chlorinated solvents has been used for the oxidation of pseudonitroles to internal *gem*-dinitroalkanes.[185] The oxidation of acetonitrolic acid and 2-nitroso-2-nitropropane has been used to synthesize 1,1-dinitroethane[186] and 2,2-dinitropropane[187,188] respectively.

1.6.5 Oxidation of isocyanates

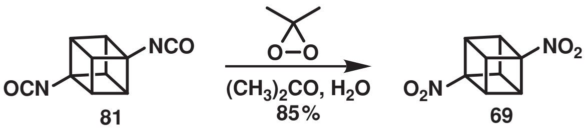


Figure 1.33

Dimethyldioxirane is a powerful oxidant prepared by reacting acetone with $KHSO_5$;[168] the latter is commercially available as a triple salt under the trade name of *oxone*. 1,4-Dinitrocubane

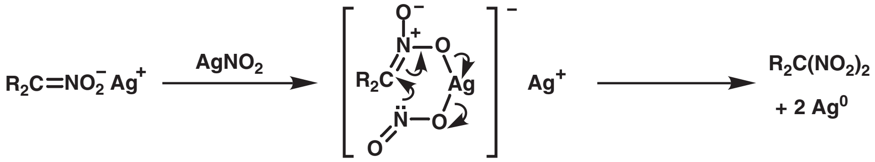
(69) is formed in 85 % yield via the oxidation of the corresponding bis-isocyanate (81) with dimethyldioxirane in wet acetone.[189] Similar chemistry has been used to prepare 1,3,5,7-tetranitrocubane and 1,3-dinitrocubane from the corresponding isocyanates (see Section 2.4).[190] Although dimethyldioxirane is a very efficient reagent for the oxidation of aliphatic isocyanates to nitro compounds, it has been relatively unexplored. These reactions are only limited by the lack of available methods for isocyanate formation and their commercial availability.

1.6.6 Oxidation of nitrosoalkanes

Nitroso compounds are formed during the addition of nitrous oxide,[48,49] dinitrogen trioxide,[48,49] and nitrosyl halides[50] to alkenes, and in some cases, from incomplete oxidation of amines[166] with peroxyacids like peroxyacetic acid. Quenching of carbanions with nitrosyl halides is also a route to nitroso compounds.[190] A full discussion on this subject is beyond the scope of this work and so the readers are directed to the work of Boyer.[191]

Oxidation of aliphatic nitroso functionality is usually facile but is not widely used in energetic materials synthesis. The following reagents have been used in these conversions: oxygen,[192] hydrogen peroxide,[193] nitrous oxide,[194] dinitrogen tetroxide,[195] chromium trioxide,[196] alkaline permanganate,[197] alkaline hypochlorite,[198] ozone,[166] ammonium persulfate,[198] peroxyacids[199] etc.[190]

1.7 KAPLAN–SHECHTER REACTION



82

Figure 1.34 Proposed mechanism for oxidative nitration (ref. 105)

Oxidative nitration, a process discovered by Kaplan and Shechter,[105] is probably the most efficient and useful method available for the synthesis of *gem*-dinitroaliphatic compounds from the corresponding nitroalkanes. The process, which is an electron-transfer substitution at saturated carbon, involves treatment of the nitronate salts of primary or secondary nitroalkanes with silver nitrate and an inorganic nitrite in neutral or alkali media. The reaction is believed[105,200] to proceed through the addition complex (82) which collapses and leads to oxidative addition of nitrite anion to the nitronate and reduction of silver from Ag^{+1} to Ag^0. Reactions proceed rapidly in homogeneous solution between 0 and 30 °C.

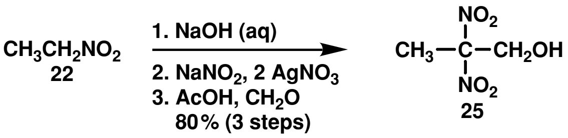


Figure 1.35

A range of primary and secondary nitroalkanes and their derivatives have been converted to the corresponding *gem*-dinitroalkanes via oxidative nitration, including: the conversion of nitroethane, 1-nitropropane, 2-nitropropane and 2-nitro-1,3-propanediol to 1,1-dinitroethane (78 %), 1,1-dinitropropane (86 %), 2,2-dinitropropane (93 %) and 2,2-dinitro-1,3-propanediol (77 %) respectively.[105] The silver nitrate used in these reactions can be recovered quantitatively on a laboratory scale and this has led to a study where oxidative nitration has been considered for the large-scale production of 2,2-dinitropropanol (25) from the nitroethane (22).[107]

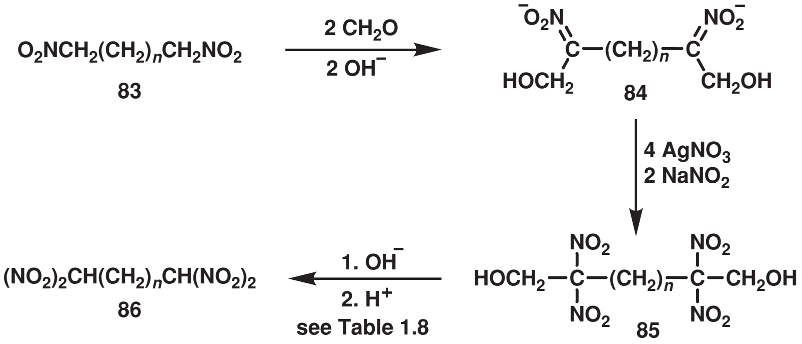


Figure 1.36

Feuer and co-workers[108] used oxidative nitration for the synthesis of $\alpha,\alpha,\omega,\omega$-tetranitroalkanes from the corresponding α,ω-dinitroalkanes (Table 1.8). However, this fails for α,ω-dinitroalkanes in which the nitro groups are not separated by at least three methylene units. Accordingly, oxidative nitration fails for both 1,3-dinitropropane ($n = 1$) and 1,4-dinitrobutane ($n = 2$) and gives a low yield of 1,1,5,5-tetranitropentane ($n = 3$) from 1,5-dinitropentane (Table 1.8). Feuer and co-workers[108] later discovered that the bis-methylol derivatives (84) of α,ω-dinitroalkanes (83) give good yields of product (85) when the separation between nitro groups is two methylene units or greater; the methylol groups can be removed *in situ* via base-catalyzed demethylolation, with loss of formaldehyde, to yield the $\alpha,\alpha,\omega,\omega$-tetranitroalkane (86) (Table 1.8). These reactions still fail for the bis-methylol derivative of 1,3-dinitropropane ($n = 1$) but give a 49 % yield of 1,1,4,4-tetranitrobutane ($n = 2$) after demethylolation of the corresponding bis-methylol derivative, namely, 2,2,5,5-tetranitro-1,6-hexanediol.

Oxidative nitration has a number of advantages over pre-existing routes to *gem*-dinitroalkanes, including:

- Reactions are successful for hindered compounds; 3,3-dinitro-2-butanol is obtained from the oxidative nitration of 3-nitro-2-butanol.[105]
- Oxidative nitration avoids the isolation of *gem*-nitronitronate salts, which are often unstable explosives with a high sensitivity to impact and friction.
- Oxidative nitration has been modified to an electrolytic process.[200]
- Good yields of internal *gem*-dinitroalkanes are attainable, whereas the Ter Meer reaction fails for the synthesis of this class of compounds.
- Oxidative nitration is a one step process from nitroalkane to *gem*- dinitroalkane, whereas the Ter Meer reaction requires two steps (initial halogenation followed by halide displacement with nitrite anion).

Table 1.8
Synthesis of tetranitroalkanes (86) via the oxidative nitration of dinitroalkanes (83) and their bis-methylol derivatives (84)

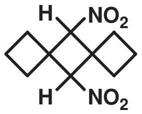
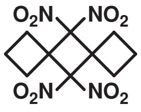
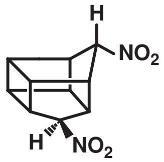
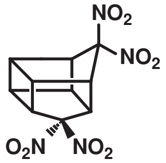
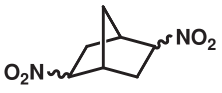
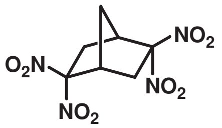
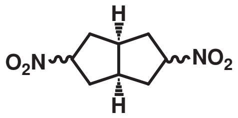
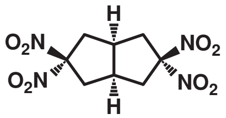
	$(NO_2)_2CH(CH_2)_nCH(NO_2)_2$	
Homologue	Yield (%) of tetranitroalkane (86)	
n =	via the dinitroalkane (83)	via the bis-methylol (84)
1	0	0
2	0	49
3	10	25
4	84	70
5	89	---

Source: Reprinted with permission from C. E. Colwell, H. Feuer, G. Leston and A. T. Nielsen, *J. Org. Chem.*, 1962, **27**, 3598; Copyright 1962 American Chemical Society.

Oxidative nitration is not effective for the synthesis of *gem*-dinitroaliphatic compounds containing an electron-withdrawing group α to the carbon bearing the nitro groups. Oxidative nitration is not successful for the conversion of terminal *gem*-dinitro compounds into 1,1,1-trinitromethyl derivatives.

A major drawback of the Kaplan–Shechter reaction is the use of expensive silver nitrate as one of the reagents, which prevents scale up to an industrial capacity. Urbański and co-workers[201] modified the process by showing that the silver nitrate component can be replaced with an inorganic one-electron transfer agent like ferricyanide anion. In a standard procedure the nitroalkane or the corresponding nitronate salt is treated in alkaline media with potassium

Table 1.9
Synthesis of energetic polynitropolycycloalkanes via oxidative nitration

Substrate	Conditions/reagents	Product	Ref.
	NaOH, $NaNO_2$, $K_3Fe(CN)_6$, $Na_2S_2O_8$, dioxane (aq), 64%		150
	NaOH, $NaNO_2$, $K_3Fe(CN)_6$, MeOH (aq), 65%		151
	NaOH, $NaNO_2$, $K_3Fe(CN)_6$, CH_2Cl_2, H_2O, MeOH 83–91%		141, 126
	NaOH, $NaNO_2$, $K_3Fe(CN)_6$, CH_2Cl_2, H_2O, 76%		141

ferricyanide oxidant in the presence of sodium nitrite. The process was later optimized and its scope expanded by Kornblum and co-workers.[202] In a further modification to this procedure Grakauskas and co-workers[203] showed that a catalytic amount of ferricyanide can be used in conjunction with a stoichiometric amount of persulfate anion as co-oxidant. These modifications often lead to improved yields compared to the original method. The inexpensive reagents used in these reactions, and the high yields frequently obtained, makes this method a very valuable route to *gem*-dinitroaliphatic compounds. The importance of oxidative nitration as a route to *gem*-dinitroaliphatic compounds is reflected in its widespread use for the synthesis of numerous energetic compounds, like those illustrated in Table 1.9. Oxidative nitration has been used in the reported[204] synthesis of a powerful melt-castable explosive, TNAZ (89).

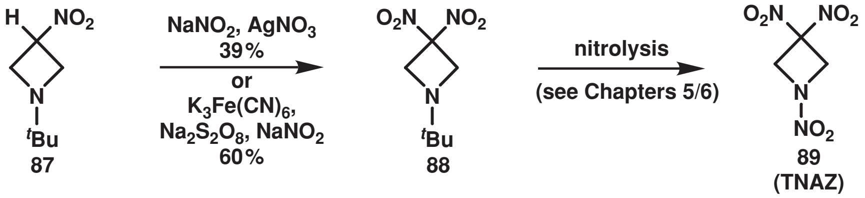


Figure 1.37

1.8 NITRATION OF COMPOUNDS CONTAINING ACIDIC HYDROGEN

1.8.1 Alkaline nitration

The alkaline nitration of compounds containing acidic hydrogen is a valuable route to aliphatic nitro compounds. In these reactions a base is used to remove an acidic proton from the substrate, which is then treated with a source of $-NO_2$. Substrates used in these reactions usually have an electron-withdrawing or resonance-stabilizing group positioned α to a proton(s), and these include: aliphatic and alicyclic ketones, nitriles, carboxylic acid esters, sulfonate esters, *N*,*N*-dialkylamides etc. Proton removal from these substrates may be reversible or irreversible depending on the pK_a of the base compared to the acidity of the substrates proton(s). Bases used for these reactions include: alkali metal alkoxides, sodium hydride, alkali metal amides, lithium bases etc. The nitrating agents range from alkyl nitrate esters to nitrogen oxides.

1.8.1.1 Alkaline nitration with nitrate esters

Alkaline nitration with alkoxide bases and nitrate esters was first explored by Endres and Wislicenus[205] who synthesized phenylnitromethane by treating ethyl phenylacetate with potassium ethoxide in ethanol, followed by addition of ethyl nitrate and hydrolysis–decarboxylation of the resulting α-nitroester with aqueous acid. Phenylnitromethane is synthesized in a similar way via alkaline nitration of benzyl cyanide, followed by treatment of the resulting α-nitronitrile with aqueous base.[206] Wieland and co-workers[207] used alkali metal alkoxides and nitrate esters for the nitration of cyclic ketones but the yields and purity of product are often poor.[208]

Feuer and co-workers[209] conducted extensive studies into alkaline nitration with nitrate esters, exploring the effect of base, time, stoichiometry, concentration, solvent, and temperature on yields and purity. Reactions are generally successful when the substrate α-proton acidity is in the 18–25 pK_a range. Alkoxide bases derived from simple primary and secondary aliphatic alcohols are generally not considered compatible in reactions using alkyl nitrates. Optimum conditions for many of these reactions use potassium *tert*-butoxide and amyl nitrate in THF at −30 °C, although in many cases potassium amide in liquid ammonia at −33 °C works equally well.

Feuer used both reagents to nitrate a number of cyclic ketones (90) to the dipotassium salts of the corresponding α,α'-dinitrocycloketones (91).[210] Although such salts can be isolated it is important to note that α,α'-dinitroketones are intrinsically unstable – direct acidification of these salts causes decomposition with the evolution of nitrogen oxides. In fact, nitro compounds derived from the nitration of active methylene groups are often unstable. This is a direct consequence of having an electron-withdrawing or resonance-stabilizing group α to a potential leaving group; both groups being able to stabilize any anion formed on decomposition.

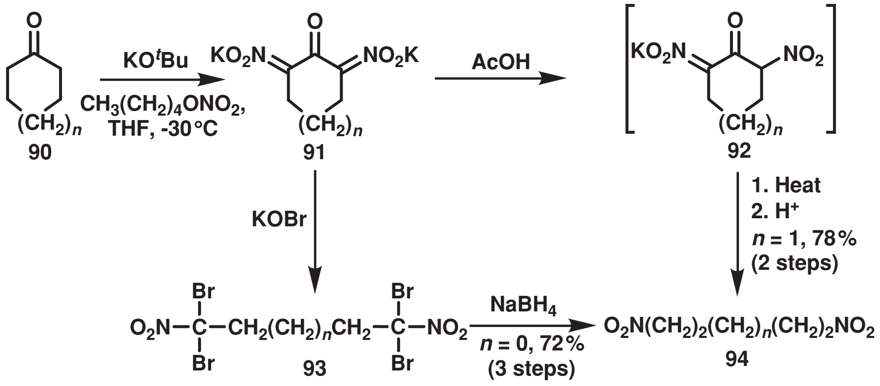


Figure 1.38

The salts of α,α'-dinitrocycloketones (91) are readily converted into α,ω-dinitroalkanes. Klager[211] developed a method whereby the alkali metal salt of the α,α'-dinitrocycloketone (91) is treated with alkaline hypobromite to form the corresponding tetrabromide (93) via a process of ring opening and formal loss of carbon monoxide; selective reduction of the latter with sodium borohydride yields the corresponding α,ω-dinitroalkane (94). Feuer and co-workers[212,213] described an improved method whereby the dipotassium salts of α,α'-dinitrocycloketones (91) are partially acidified with acetic acid to give the corresponding mono-potassium salts (92) which undergo spontaneous hydrolytic ring opening and yield α,ω-dinitroalkanes (94) on further acidification. 1,4-Dinitrobutane (72 %), 1,5-dinitropentane (78 %) and 1,6-dinitrohexane (75 %) have been synthesized from cyclopentane, cyclohexane, and cycloheptane respectively, via these routes.[211–213]

Treatment of acyclic ketones with one equivalent of potassium amide base in liquid ammonia, followed by acidification, yields the α-nitroketone and products resulting from fragmentation.[214] The same reactions with cyclic ketones, again, only using one equivalent of *tert*-butoxide[214] or potassium amide[215] base, generates α-nitrocycloketones and ω-nitrocarboxylic esters. α-Nitrocycloketones derived from the nitration of α,α'-dialkylcycloketones cannot form a stable anion and so cleavage to the ω-nitrocarboxylic ester predominants.[214]

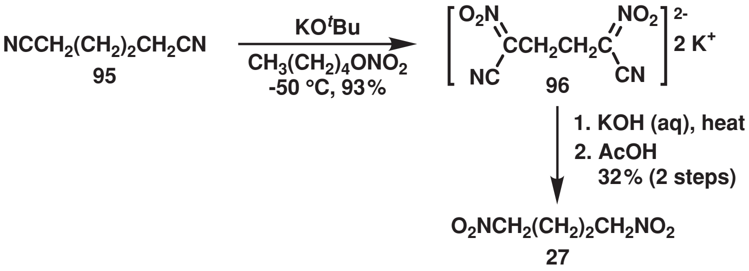


Figure 1.39

Feuer and co-workers[216] extended their studies to the alkaline nitration of α,ω-dinitriles. Nitration with potassium *tert*-butoxide and amyl nitrate in THF at −30 °C yields the corresponding dipotassium salt of the α,ω-dinitro-α,ω-dinitrile. The nitronate salts from these reactions are isolated via methanol-induced precipitation from the aqueous reaction liquors, a process which also separates the product from impurities. These salts undergo hydrolysis on treatment with aqueous potassium hydroxide, and subsequent acidification yields the corresponding α,ω-dinitroalkane. This route has been used to synthesize 1,4-dinitrobutane (27) from apidonitrile (95) in 30 % overall yield.

Feuer and co-workers[217] also nitrated ring-substituted toluenes to the corresponding arylnitromethanes with potassium amide in liquid ammonia. Sulfonate esters[218] and *N*,*N*-dialkylamides[219] undergo similar nitration; the latter isolated as their α-bromo derivatives. Alkaline nitration of ethyl and *tert*-butyl carboxylic esters with potassium amide in liquid ammonia yields both the α-nitroester and the corresponding nitroalkane from decarboxylation.[220]

Treating the dianion of a carboxylic acid with an alkyl nitrate leads to an α-nitrocarboxylic acid which readily undergoes decarboxylation to the corresponding nitroalkane.[221] This method is particularly useful for the synthesis of arylnitromethanes containing electron-donating groups.[221]

1.8.1.2 Alkaline nitration with cyanohydrin nitrates

Acetone cyanohydrin nitrate, a reagent prepared from the nitration of acetone cyanohydrin with acetic anhydride-nitric acid,[222] has been used for the alkaline nitration of alkyl-substituted malonate esters.[222] In these reactions sodium hydride is used to form the carbanions of the malonate esters, which on reaction with acetone cyanohydrin nitrate form the corresponding nitromalonates. The use of a 100 % excess of sodium hydride in these reactions causes the nitromalonates to decompose by decarboxylation to the corresponding α-nitroesters. Alkyl-substituted acetoacetic acid esters behave in a similar way and have been used to synthesize α-nitroesters.[223] Yields of α-nitroesters from both methods average 50–55 %.

In a related reaction arylacetonitriles are nitrated to the corresponding α-nitronitriles, which on alkaline hydrolysis and subsequent acidification, yield arylnitromethanes.[223] This method has been used to convert phenylacetonitrile to phenylnitromethane in 70 % overall yield without the need for intermediate purification.

Acetone cyanohydrin nitrate is, however, of limited use for the nitration of many carbanions and is rapidly destroyed in the presence of alkoxides.[224] Its use for the nitration of weakly basic carbanions such as malonate arises from the perturbation of a side-reaction observed with alkyl nitrates, namely, the carbanion attacking the carbon atom of alkyl nitrate instead of nitrogen, and thus giving alkylation instead of nitration. Alkaline nitrations with acetone cyanohydrin nitrate compliment reactions using alkoxide base and nitrate esters; the latter are generally not applicable to substrates with proton acidities below pK_a 16.

1.8.1.3 Alkaline nitration with tetranitromethane

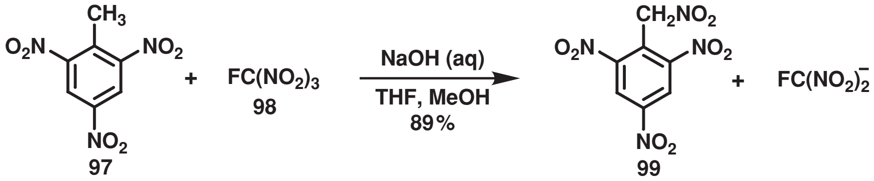


Figure 1.40

The carbon–nitrogen bonds of tetranitromethane are very electron deficient and prone to attack by nucleophiles. Consequently, tetranitromethane and its derivatives behave like nitrating agents in alkaline solution.[179] Fluorotrinitromethane (98) behaves in a similar way and has been used for the nitration of the acidic methyl group of 2,4,6-trinitrotoluene (97) (TNT) to give α,2,4,6-tetranitrotoluene (99) in 89 % yield.[225]

1.8.1.4 Alkaline nitration with nitrogen oxides and related compounds

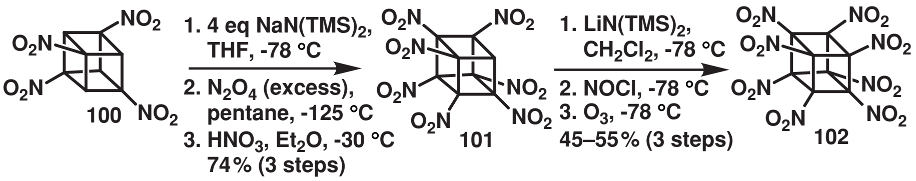
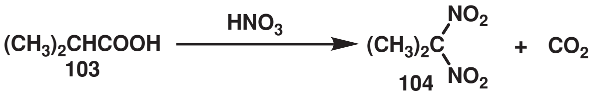


Figure 1.41

Eaton and co-workers[226] synthesis of octanitrocubane (102) (ONC) is a milestone in high-energy materials synthesis. The explosive performance of octanitrocubane is predicted to be very high with a detonation velocity of 9900 m/s.[227] This pioneering synthesis involves, as a key step, the alkaline nitration of 1,3,5,7-tetranitrocubane (100). In this reaction hexamethyldisilazide anion is used to deprotonate positions β to three nitro groups and the resulting tetra-anion is quenched/nitrated with excess dinitrogen tetroxide in pentane to give a 74 % yield of a mixture containing 95 % heptanitrocubane (101) and 5 % hexanitrocubane. This reaction involves nitration of the sodium anion of 1,3,5,7-tetranitrocubane at the melting interface (∼105 °C) between frozen THF and dinitrogen tetroxide in pentane. This is a new nitration technique known as 'interfacial nitration' and probably proceeds via a radical process.[226] Heptanitrocubane (101) is converted to octanitrocubane (102) by further reaction with hexamethyldisilazide anion, followed by quenching with nitrosyl chloride and oxidation with ozone.[226] This example of β-deprotonation-nitration is only feasible because of the combined inductive effect of three nitro groups and the increased sp^2 character of these positions as a result of the strained cubane core. Even then, the low acidity of the β-proton is reflected in the need for a fairly strong base (hexamethyldisilazide in THF ~ pK_a of 25.8[228]).

1.8.2 Acidic nitration

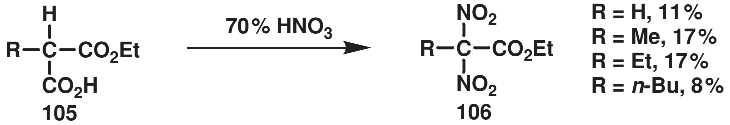
Electrophilic nitrations of aliphatic nitriles,[117] carboxylic acids,[229] carboxylic esters,[230] and β-diketones[231] have been reported. The nitration of 2-alkyl-substituted indane-1,3-diones with nitric acid, followed by alkaline hydrolysis, is a standard laboratory route to primary nitroalkanes.[231]



$$\underset{103}{(CH_3)_2CHCOOH} \xrightarrow{HNO_3} \underset{104}{(CH_3)_2C(NO_2)_2} + CO_2$$

Figure 1.42

Treatment of some carboxylic acids with nitric acid is a route to *gem*-dinitroalkanes, as in the case of *iso*-butyric acid (103), which undergoes nitration-decarboxylation on treatment with nitric acid to give 2,2-dinitropropane (104).[232] Yields are often poor for this type of reaction.



$$\underset{105}{R{-}CH(CO_2H){-}CO_2Et} \xrightarrow{70\%\ HNO_3} \underset{106}{R{-}C(NO_2)_2{-}CO_2Et}$$

R = H, 11%
R = Me, 17%
R = Et, 17%
R = *n*-Bu, 8%

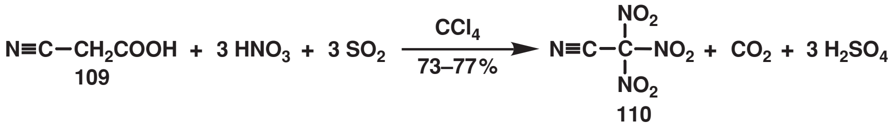
Figure 1.43

The half esters of malonic acid (105) yield α,α-dinitroesters (106) on nitration-decarboxylation with nitric acid, although yields are often poor.[229] Treatment of these α,α-dinitroesters with hydrazine hydrate or alkali metal hydroxides yields the corresponding *gem*-dinitroalkanes.[229]

$$\underset{107}{HO_2CCH_2CO_2Me} \xrightarrow[-5\ ^\circ C\ to\ 5\ ^\circ C,\ 60\%]{20\%\ red\ nitric\ acid} \underset{108}{(NO_2)_2CHCO_2Me} \xrightarrow[90\%]{KOH\ (aq),\ 70\ ^\circ C} \underset{18}{K^+\ {}^-CH(NO_2)_2}$$

Figure 1.44

A potential industrial route to potassium dinitromethane (18) involves treatment of methyl malonate (107) with red fuming nitric acid to give methyl α,α-dinitroacetate (108), followed by hydrolysis-decarboxylation with aqueous potassium hydroxide.[233] Dinitromethane is a precursor to 2,2-dinitroethanol and 2,2-dinitro-1,3-propanediol, both of which are useful in addition and esterification reactions for the production of energetic oligomers and plasticizers.

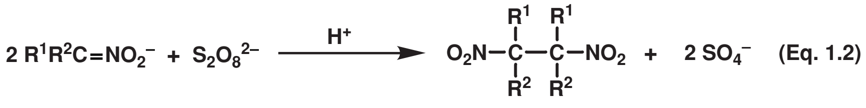


$$\underset{109}{N{\equiv}C{-}CH_2COOH} + 3\,HNO_3 + 3\,SO_2 \xrightarrow[73\text{–}77\%]{CCl_4} \underset{110}{N{\equiv}C{-}C(NO_2)_3} + CO_2 + 3\,H_2SO_4$$

Figure 1.45

Trinitroacetonitrile (110), a precursor to dinitroacetonitrile and its derivatives, can be synthesized from the nitration of cyanoacetic acid (109) with a solution of sulfur dioxide and absolute nitric acid in carbon tetrachloride.[117] This method is particularly attractive because the trinitroacetonitrile can be kept as a solution in carbon tetrachloride without isolation; trinitroacetonitrile is hazardous to handle and its vapours are both toxic and lachrymatory.

1.9 OXIDATIVE DIMERIZATION



$$2\,R^1R^2C{=}NO_2^- + S_2O_8^{2-} \xrightarrow{H^+} O_2N-\overset{R^1}{\underset{R^2}{C}}-\overset{R^1}{\underset{R^2}{C}}-NO_2 + 2\,SO_4^- \quad \text{(Eq. 1.2)}$$

111

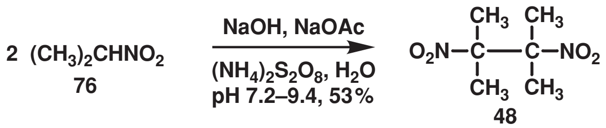
Figure 1.46

Kaplan and Shechter[234] found that certain oxidants react with the nitronate salts of secondary nitroalkanes to yield *vic*-dinitroalkanes (111) in a reaction referred to as oxidative dimerization. These reactions are believed to involve transfer of an electron from the secondary alkyl nitronate to the oxidant with the production of a nitroalkyl radical. The radical can then dimerize to the corresponding *vic*-dinitroalkane (111) (Equation 1.2) or lose nitric oxide to form a ketone via the Nef reaction (Equation 1.3). Unfortunately, formation of the ketone is a major side-reaction during oxidative dimerization and is often the major product.

$$R^1R^2C{=}NO_2^- + 2\,S_2O_8^{2-} + 2\,H_2O \xrightarrow{H^+} R^1R^2C{=}O + 4\,H^+ + NO_3^- + 4\,SO_4^{2-} \text{(Eq. 1.3)}$$

Figure 1.47

Studies into oxidative dimerization have shown that only the persulfate anion is of synthetic value in these reactions. Reaction pH is also crucial; with reactions proceeding fastest when a pH of 7.2–9.4 is maintained.[234] The reaction medium becomes more acidic as the oxidation progresses and needs either buffering or the slow addition of alkali throughout the reaction. If the reaction medium is allowed to become acidic then the starting nitroalkane is regenerated and the Nef reaction predominates.



$$2\ (CH_3)_2CHNO_2 \xrightarrow[\substack{(NH_4)_2S_2O_8,\ H_2O \\ pH\ 7.2\text{–}9.4,\ 53\%}]{NaOH,\ NaOAc} O_2N-\overset{CH_3}{\underset{CH_3}{C}}-\overset{CH_3}{\underset{CH_3}{C}}-NO_2$$

76

48

Figure 1.48

Oxidative dimerization gives reasonable yields of *vic*-dinitroalkanes for some substrates; 2,3-dimethyl-2,3-dinitrobutane (48, 53 %) and 3,4-dimethyl-3,4-dinitrohexane (37 %) are obtained from 2-nitropropane (76) and 2-nitrobutane respectively.[234] However, oxidative dimerization fails to convert 1,1-dinitroethane and trinitromethane into 2,2,3,3-tetranitrobutane and hexanitroethane respectively. Additionally, oxidative dimerisation is not a feasible route for the synthesis of *vic*-dinitroalkanes from primary nitroalkanes. Although oxidative dimerization is limited in scope, and yields are often poor, the starting materials are usually inexpensive.

1.10 ADDITION AND CONDENSATION REACTIONS

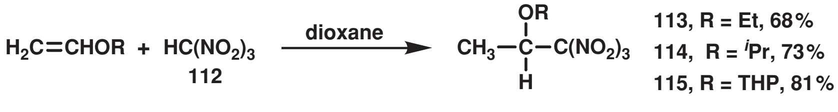
Primary and secondary nitroalkanes, and substrates containing terminal *gem*-dinitroaliphatic functionality, have one or more acidic α-protons, a consequence of inductive and resonance effects imposed by the nitro group. As a result, such compounds can behave like carbanions and participate in a number of addition and condensation reactions which are typical of substrates like ketones, aldehydes, and β-ketoesters. Such reactions are extremely useful for the synthesis of functionalized polynitroaliphatic compounds which find potential use as explosives, energetic oligomers and plasticizers.

Addition and condensation reactions employing nitroform or its methylol derivative, 2,2,2-trinitroethanol, have been used to synthesize a huge number of compounds containing the trinitromethyl group. Such compounds often have a very favourable oxygen balance which contributes to explosive performance. However, compounds containing the trinitromethyl group often exhibit an unacceptably high sensitivity to shock and impact. Kamlet[235] proposed that this high sensitivity was due to the restricted rotation of the C–NO_2 groups. This theory proposes that if rotation is restricted, energy normally dissipated through a combination of bond rotation and bonded atom vibrational modes is more likely to result in bond breaking. In any energetic material the sensitivity to impact is related to the weakest bond(s) in that molecule, and so, in many energetic compounds, the trinitromethyl is the trigger for decomposition. It is not surprising that research in this area rapidly slumped after these findings. The chemistry and synthesis of trinitromethyl containing compounds has been the subject of several excellent reviews.[9,114,115]

2-Fluoro-2,2-dinitroethanol, the methylol derivative of fluorodinitromethane, has been used extensively for the synthesis of fluorodinitromethyl compounds. The fluorine atom is similar in size to that of a proton and so rotation in the fluorodinitromethyl group is much less hindered compared to the trinitromethyl group. Consequently, these compounds are far less sensitive to impact than trinitromethyl compounds but only slightly less energetic. The explosive performance of fluorodinitromethyl compounds has been reviewed.[236]

2-Fluoro-2,2-dinitroethanol is synthesized on a large scale[237] from nitroform in a reaction involving fluorination[238] followed by *in situ* reduction with alkaline hydrogen peroxide[239] in the presence of formaldehyde. The intermediate in this reaction, fluorotrinitromethane, is also synthesized by treating tetranitromethane with potassium fluoride in DMF.[240] Fluorodinitromethane has been synthesized by treating 2,2-dinitro-1,3-propanediol with sodium hydroxide followed by fluorination,[238] or from the direct fluorination of potassium dinitromethane.[233] The salts of fluorodinitromethane are dangerous, and so, its *in situ* formation in addition reactions is greatly preferred. Fluorodinitromethyl compounds have also been synthesized from the fluorination of *gem*-nitronitronate salts.[239a] The synthesis of energetic fluorodinitromethyl compounds has been reviewed.[37,241,242]

1.10.1 1,2-Addition reactions



$$H_2C{=}CHOR + \underset{112}{HC(NO_2)_3} \xrightarrow{\text{dioxane}} CH_3{-}\overset{OR}{\underset{H}{C}}{-}C(NO_2)_3$$

113, R = Et, 68%
114, R = ^{i}Pr, 73%
115, R = THP, 81%

Figure 1.49

The 1,2-addition of nitroform across the double bonds of vinyl ethers has been used to synthesize a large number of α-trinitromethyl ethers; (113–115) have been synthesized from the reaction of nitroform (112) with the corresponding vinyl ethers.[243] The synthesis of α-trinitromethyl ethers from the reaction of an acetal with nitroform involves 1,2-addition via an intermediate oxonium cation; (117) is synthesized in 85 % yield from the reaction of nitroform with the acetal (116).[244] α-Trinitromethyl ethers have been synthesized in a one-pot process from nitroform in the presence of an aldehyde and alcohol, in which case, the acetal is formed *in situ*.[245]

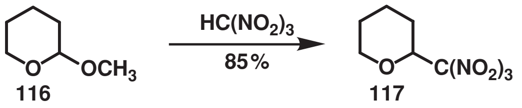


Figure 1.50

Shackelford and co-workers[246] studied the 1,2-addition of 2,2-dinitropropanol, 2,2,2-trinitroethanol, and 2-fluoro-2,2-dinitroethanol across the double bonds of vinyl ethers. These reactions are Lewis acid catalyzed because of the weak nucleophilic character of alcohols which contain two or three electron-withdrawing groups on the carbon β to the hydroxy functionality. Base catalysis is precluded since alkaline conditions lead to deformylation with the formation of formaldehyde and the nitronate salt.

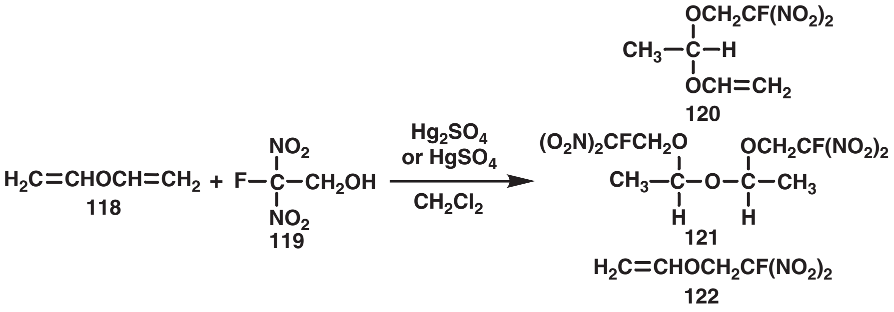


Figure 1.51

The reaction of 2-fluoro-2,2-dinitroethanol (119) with divinylether (118) under different conditions gives three products, namely, the expected vinyl acetal (120) and the bis-acetal (121) from addition of one and two equivalents of 2-fluoro-2,2-dinitroethanol, respectively, and the vinyl ether (122), which results from *trans*-etherification of (118) with loss of acetaldehyde. Shackelford and co-workers[246] found that by altering the nature of the Lewis acid catalyst and the reaction stoichiometry they were able to alter the distribution ratio of these products.

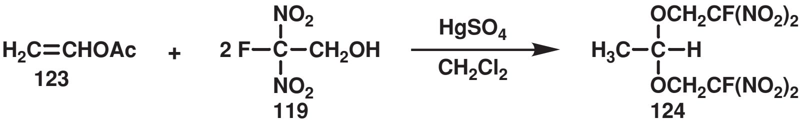


Figure 1.52

The *trans*-etherification of vinyl ethers is not uncommon under Lewis acid catalysis. 1,1-Bis(2-fluoro-2,2-dinitroethyl)ethyl acetal (124) is obtained on reaction of two equivalents of 2-fluoro-2,2-dinitroethanol (119) with vinyl acetate (123) in the presence of mercuric sulfate.[247]

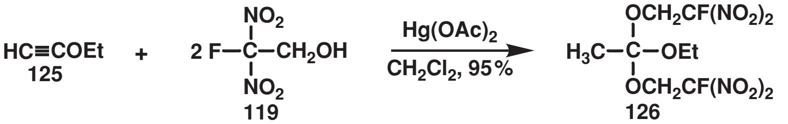


Figure 1.53

The acetylenic bond of propargyl ethers can react with polynitroaliphatic alcohols, as in the case of ethoxyacetylene (125), which reacts with two equivalents of 2-fluoro-2,2-dinitroethanol (119) to give the orthoester (126).[248]

1.10.2 1,4-Addition reactions

1.10.2.1 Michael reaction

Conjugate 1,4-addition of a nucleophile to the double bond of an electron deficient α,β-unsaturated compound is known as the Michael reaction and ranks as one of the most important carbon–carbon bond forming reactions in synthetic organic chemistry. The species undergoing addition to the double bond is known as a Michael donor and includes substrates which are capable of forming carbanions i.e. those with acidic protons. Nitroalkanes are good Michael donors and literature examples of their use in the synthesis of functionalized polynitroaliphatic compounds are extensive.[249–262] These include nitronate anions generated from nitroform, fluorodinitromethane, primary nitroalkanes, secondary nitroalkanes and compounds containing terminal *gem*-dinitroaliphatic functionality. The electron deficient alkene in these reactions is known as the Michael acceptor and includes α,β-unsaturated ketones, aldehydes, carboxylic acids, esters, amides, cyanides etc. Nitroalkenes are excellent Michael acceptors and important from the view of energetic materials synthesis and so these reactions are discussed separately in Section 1.10.2.2.

Michael reactions are base catalyzed and reversible, and so it is common to use either the nitronate salt of the nitroalkane substrate or the nitroalkane in the presence of a catalytic amount of alkali metal hydroxide, alkoxide or amine base.

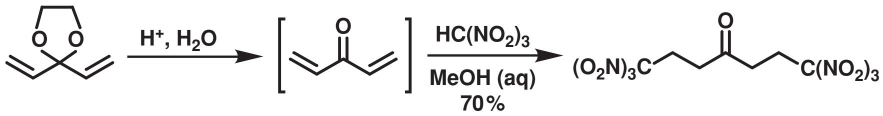


Figure 1.54

The product of a Michael addition depends on the number of acidic protons present in the nitroalkane substrate. Nitroform, which has one acidic proton, can only react with one equivalent of Michael acceptor.[252–258] Nitroform is a strong acid and sufficiently dissociated in solution so that it can be used in addition reactions without a base catalyst. The reaction of nitroform with unsaturated ketones has been investigated by Gilligan and Graff[256] and used to synthesize a number of trinitromethyl-based explosives.

Frankel[258] reported the reaction of nitroform with acrylic acid and its esters. Methyl 4,4,4-trinitrobutyrate (127), the product obtained from nitroform and methyl acrylate, has been used

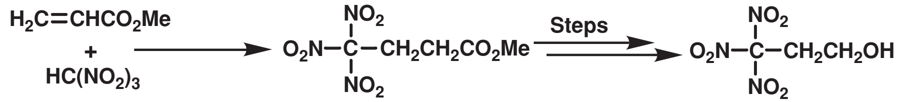


Figure 1.55

for the synthesis of 3,3,3-trinitro-1-propanol (128) through a several step synthesis.[263] 4,4,4-Trinitrobutyric acid has been used for the same purpose.[264] Ross and co-workers[265] reported a number of reactions of nitroform with unsaturated aldehydes.

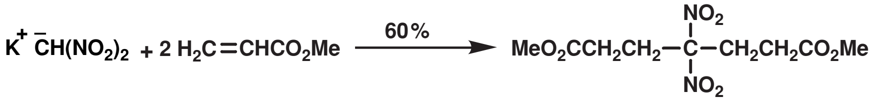


Figure 1.56

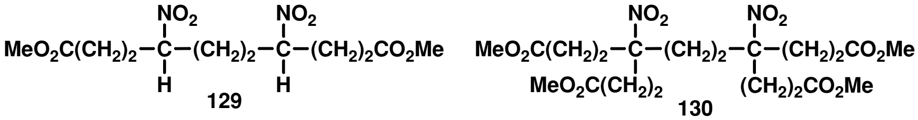


Figure 1.57

Dinitromethane has two acidic protons and reacts with Michael acceptors to form bis-adducts.[251,254,255] Secondary nitroalkanes can only react with one equivalent of Michael acceptor. In the absence of steric effects primary nitroalkanes usually react with two equivalents of Michael acceptor to form bis-adducts. Depending on the reaction stoichiometry, 1,4-dinitrobutane can be reacted with methyl acrylate to form either the bis-adduct (129) or the tetra-adduct (130) in good yield.[249]

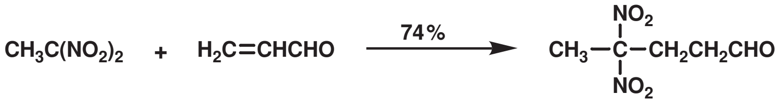


Figure 1.58

Aliphatic compounds containing terminal *gem*-dinitro functionality form adducts with Michael acceptors.[117,253–255,259,260] Of particular interest is the reaction of $\alpha,\alpha,\omega,\omega$-tetranitroalkanes with Michael acceptors.[250] Most $\alpha,\alpha,\omega,\omega$-tetranitroalkanes will react with two equivalents of Michael acceptor to form bis-adducts, like in the case of 1,1,4,4-tetranitrobutane, which reacts with two equivalents of methyl vinyl ketone, methyl acrylate, acrylonitrile etc.[250] The influence of steric effects becomes apparent with $\alpha,\alpha,\gamma,\gamma$-tetranitroalkanes, like 1,1,3,3-tetranitropropane, which can form either mono-adducts or bis-adducts depending on the Michael acceptor used; 1,1,3,3-tetranitropropane will only react with one equivalent of methyl acrylate and the sole product of this reaction is methyl 4,4,6,6-tetranitrohexanoate.[250]

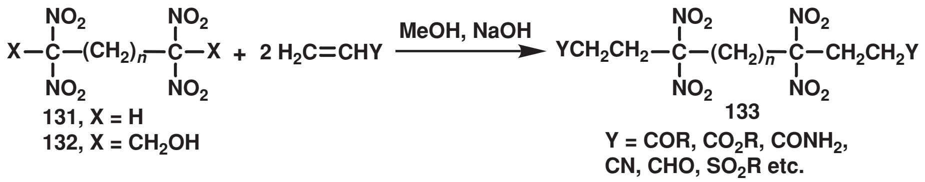


Figure 1.59

Many of the Michael reactions involving the addition of polynitroaliphatic compounds to Michael acceptors use the corresponding methylol derivatives, which are deformylated in the presence of base to give the nitronate anion and formaldehyde. Such procedures are primarily for safety reasons because the nitronate salts of many polynitroaliphatic compounds are shock sensitive explosives. Feuer and co-workers[250] investigated the Michael reactions of numerous α,β-unsaturated compounds with $\alpha,\alpha,\omega,\omega$-tetranitroalkanes (131) and their bis-methylol (132) derivatives. Interest in the Michael adducts derived from $\alpha,\alpha,\omega,\omega$-tetranitroalkanes (133) partly stems from their potential use for the synthesis of energetic oligomers;[250] simple functional group conversion of the terminal appendages giving rise to alcohol, carboxylic acid, isocyanate functionality etc.

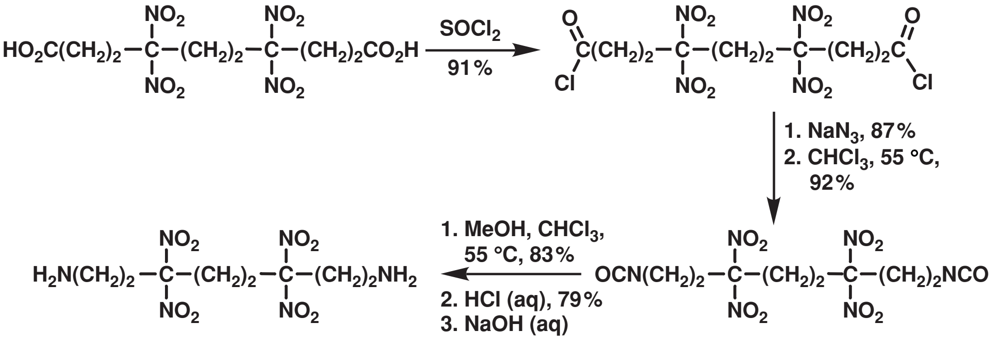


Figure 1.60

The Michael adducts of fluorodinitromethane have attracted interest as energetic plastisizers in both propellant and explosive formulations. Such adducts are usually synthesized by mixing the Michael acceptor with fluorodinitromethane or 2-fluoro-2,2-dinitroethanol in the presence of base.[256,261,262,266] In much the same way, 2,2,2-trinitroethanol can be used as a source of nitroform, and both 2,2-dinitroethanol and 2,2-dinitro-1,3-propanediol used as a source of dinitromethane.

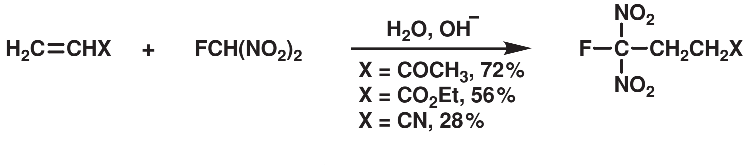
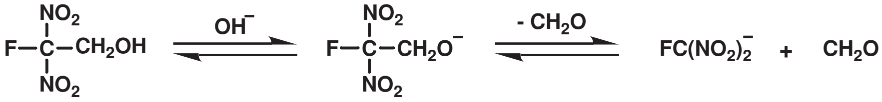


Figure 1.61

The observant may ask, ‘Why does the alkoxide anion of the nitroalcohol not add to the Michael acceptor?’ The addition of alkoxide anions to Michael acceptors is well known, but alcohols with two or more strong electron-withdrawing groups on the β-carbon atom to the alcohol functionality make the corresponding alkoxide a very weak nucleophile. However, there are cases of the 2-fluoro-2,2-dinitroethoxide anion (134) undergoing Michael 1,4-addition with some very reactive Michael acceptors.[261]



$$\underset{119}{F-\overset{NO_2}{\underset{NO_2}{C}}-CH_2OH} \overset{OH^-}{\rightleftharpoons} \underset{134}{F-\overset{NO_2}{\underset{NO_2}{C}}-CH_2O^-} \overset{-\,CH_2O}{\rightleftharpoons} FC(NO_2)_2^- + CH_2O$$

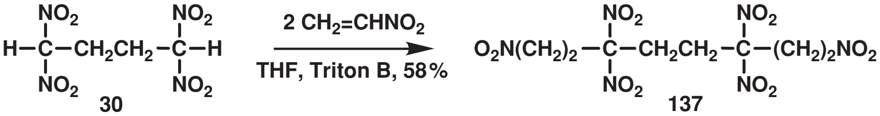
Figure 1.62

1.10.2.2 Additions to nitroalkenes

$$\underset{112}{(NO_2)_3CH} + \underset{135}{CH_2{=}CHNO_2} \xrightarrow{50\%} \underset{136}{(NO_2)_3CCH_2CH_2NO_2}$$

Figure 1.63

The conjugate 1,4-addition of nitronate anions and other nucleophiles to α-nitroalkenes constitutes an important method for the synthesis of polynitroaliphatic compounds.[250,253,258,260,267–269] Nitroform (112) reacts with nitroethene (135) and 2-nitropropene to yield 1,1,1,3-tetranitropropane[258] (136) and 1,1,1,3-tetranitrobutane[267] respectively. A number of examples of additions of 1,1-dinitroethane, 1,1-dinitropropane and 1,1-dinitrobutane to nitroalkenes have been reported.[260,267,269c] Feuer and co-workers[250] reported the synthesis of 1,3,3,6,6,8-hexanitrooctane (137) from the reaction of 1,1,4,4-tetranitrobutane (30) with nitroethene under basic conditions.



$$\underset{30}{H-\overset{NO_2}{\underset{NO_2}{C}}-CH_2CH_2-\overset{NO_2}{\underset{NO_2}{C}}-H} \xrightarrow[\text{THF, Triton B, 58\%}]{2\ CH_2{=}CHNO_2} \underset{137}{O_2N(CH_2)_2-\overset{NO_2}{\underset{NO_2}{C}}-CH_2CH_2-\overset{NO_2}{\underset{NO_2}{C}}-(CH_2)_2NO_2}$$

Figure 1.64

Synthetic routes to α-nitroalkenes have been discussed in previous sections. General routes include: (1) treating β-nitroacetates with alkali metal acetates, carbonates or bicarbonates,[5,268,270] (2) elimination of water from β-nitroalcohols via heating with phthalic anhydride[271] or in the presence of a base,[40,272,273] and (3) degradation of the Mannich products derived from a primary nitroalkane, formaldehyde, and a secondary amine.[274]

Direct Michael addition of secondary nitroalkanes to α-nitroalkenes gives acceptable yields of addition product, however, in general, primary nitroalkanes give much poorer yields of product. Low to moderate yields in both cases are mainly due to the tendency of α-nitroalkenes to polymerize before and during a reaction. More common is the *in situ* generation of the α-nitroalkenes in these addition reactions. Feuer and Miller[268] discovered that 2-nitroalkyl acetates (β-nitroacetates) react with base, in the form of sodium acetate or the sodium salt of a nitroalkane, to generate the corresponding α-nitroalkene. Michael adducts are formed if

Table 1.10 Michael 1,4-addition of nitroalkanes and nitramines with 2-nitroacetates (nitroalkene precursors)

Pseudo acid	Product	Yield (%)
	Michael additions with 2-nitrobutyl acetate	
1-nitropropane	3,5-dinitroheptane	15, 19[a], 13[b]
2-nitropropane	2-methyl-2,4-dinitrohexane	55
1,1-dinitroethane	2,2,4-trinitrohexane	65
ethylene dinitramine	5,8-diaza-3,5,8,10-tetranitrododecane	81
	Michael additions with 3-nitro-2-butyl acetate	
2-nitropropane	2,3-dimethyl-2,4-dinitropentane	33[a,b], 57[b,c]
ethylene dinitramine	4,7-diaza-3,8-dimethyl-2,4,7,9-tetranitrodecane	21
	Michael additions with 1,6-diacetoxy-2,5-dinitrohexane	
2-nitropropane	2,9-dimethyl-2,4,7,9-tetranitrodecane	98
1,1-dinitroethane	3,3,5,8,10,10-hexanitrododecane	94
1-nitraminobutane	5,12-diaza-5,7,10,12-tetranitrohexadecane	88

[a] Solvent was anhydrous THF. [b] 100% excess of the salt of the psuedo acid used (no sodium acetate). [c] Solvent was *tert*-butanol. [d] Equivalent amounts of reactants and sodium acetate used unless otherwise stated. [e] Reactions conducted in aqueous methanol unless otherwise stated.

Source: Reprinted with permission from H. Feuer and R. Miller, *J. Org. Chem.*, 1961, **26**, 1348; Copyright 1961 American Chemical Society.

a nitroalkane or another nucleophile is present during this *in situ* α-nitroalkene formation. 2-Nitrobutyl acetate, 3-nitro-2-butyl acetate and 1,6-diacetoxy-2,5-dinitrohexane are precursors to 2-nitro-1-butene, 2-nitro-2-butene and 2,5-dinitro-1,5-hexadiene respectively. In the presence of sodium acetate these nitroalkene precursors have been used to synthesize a variety of polynitroaliphatic compounds in good to high yield (Table 1.10).[268]

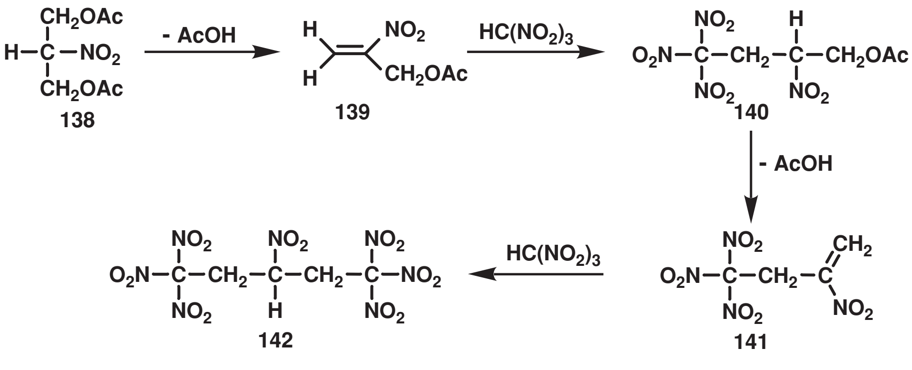


Figure 1.65

Frankel[258] synthesized 2-nitro-3-acetoxy-1-propene (139) by heating 1,3-diacetoxy-2-nitropropane (138) with sodium acetate under reduced pressure. The reaction of 2-nitro-3-acetoxy-1-propene with 1,1-dinitroethane yields 2,2,4,6,6-pentanitroheptane. The same reaction with nitroform provides 1,1,1,3,5,5,5-heptanitropentane (142), a powerful explosive (VOD ~ 9230 m/s) with an excellent oxygen balance.[258,274,275] The synthesis of 1,1,1,3,5,5,5-heptanitropentane from 2-nitro-1,3-propanediol[276] and 2-nitro-1-propen-3-ol[277] has also been reported and involves a similar mechanism.

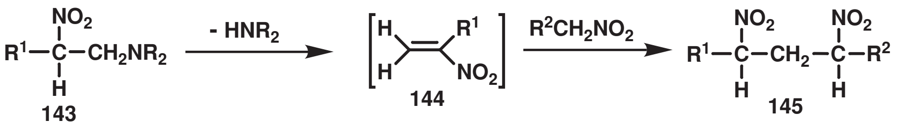


Figure 1.66

Some 1,3-dinitroalkanes (145) have been synthesized from the reaction of nitroalkanes with α-nitroalkenes (144) generated *in situ* from the decomposition of Mannich bases (143) derived from primary nitroalkanes.[274] Reported yields for these reactions are low and the formation of by-products limits the feasibility of the method.

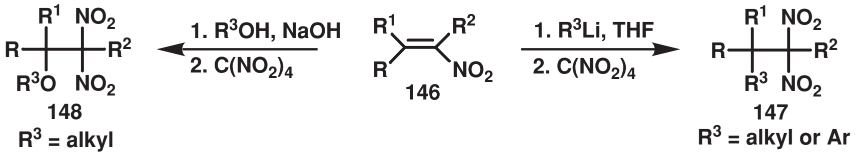


Figure 1.67

Nielsen and Bedford[279] synthesized *gem*-dinitroalkanes (147) from the Michael addition of organolithium reagents to α-nitroalkenes (146) followed by quenching of the resulting nitronate anion with tetranitromethane. The same reaction using alkoxides as bases provides β-alkoxy-*gem*-dinitroalkanes (148).[279]

1.10.2.3 Dinitroethylation

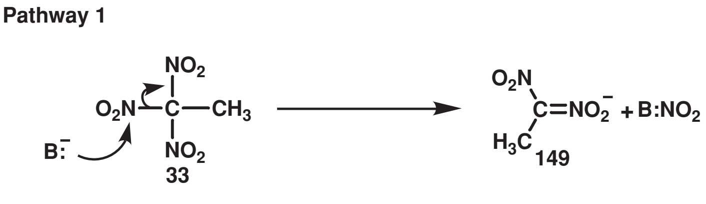


Figure 1.68

Shechter and Zeldin[280] discovered that 1,1,1-trinitroethane (33) can undergo two reactions on treatment with base. First, and typical of the chemistry of 1,1,1-trinitromethyl compounds, the base can attack one of the electron deficient nitro groups of 1,1,1-trinitroethane (33) and form the 1,1-dinitroethane anion (149) (Pathway 1). More unusual is the second reaction where the base abstracts a hydrogen from 1,1,1-trinitroethane (33), followed by formal elimination of nitrous acid and the formation of the reactive intermediate, 1,1-dinitroethene (150), which can react further with any nucleophiles present in a Michael 1,4-addition reaction (Pathway 2).

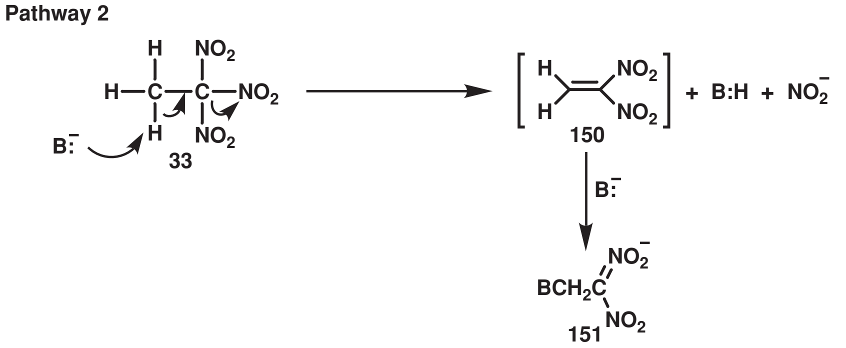


Figure 1.69

Reactions are very dependent on the nature of the base and the reaction conditions used, for example, reaction of 1,1,1-trinitroethane with aqueous potassium hydroxide, or hydroxylamine in methanolic potassium methoxide, gives high yields of potassium 1,1-dinitroethane.[280] However, reaction of 1,1,1-trinitroethane with potassium ethoxide, potassium methoxide and ethanolic potassium cyanide is reported to give 2,2-dinitroethylether, methyl-2,2-dinitroethylether and 3,3-dinitropropionitrile respectively, all in approximately 80 % yield via the 1,4-addition of ethoxide, methoxide and cyanide anion to 1,1-dinitroethene respectively.[280]

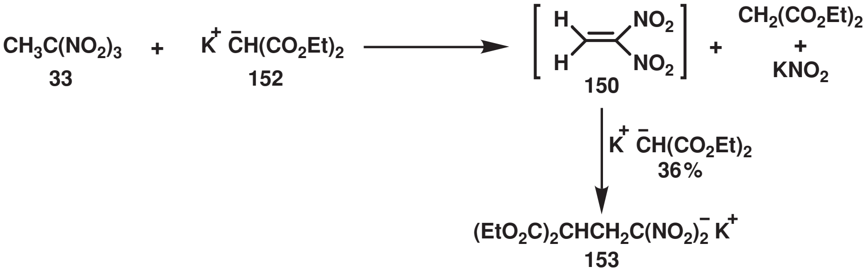


Figure 1.70

Other bases found to react with 1,1,1-trinitroethane via formation of 1,1-dinitroethene include: trimethylamine, guanidine and diethylmalonate anion (152), the latter forming (153) in 36 % yield. Shechter and Zeldin[280] found no correlation as to why some bases react with 1,1,1-trinitroethane so differently to others but noted that simple alkoxides, aliphatic amines, guanidine, cyanide and malonate anions reacted via the 1,1-dinitroethene pathway.

Frankel[281] discovered a similar reaction to the base-induced formation of 1,1-dinitroethene from 1,1,1-trinitroethane; treatment of 2-bromo-2,2-dinitroethyl acetate (154) with potassium

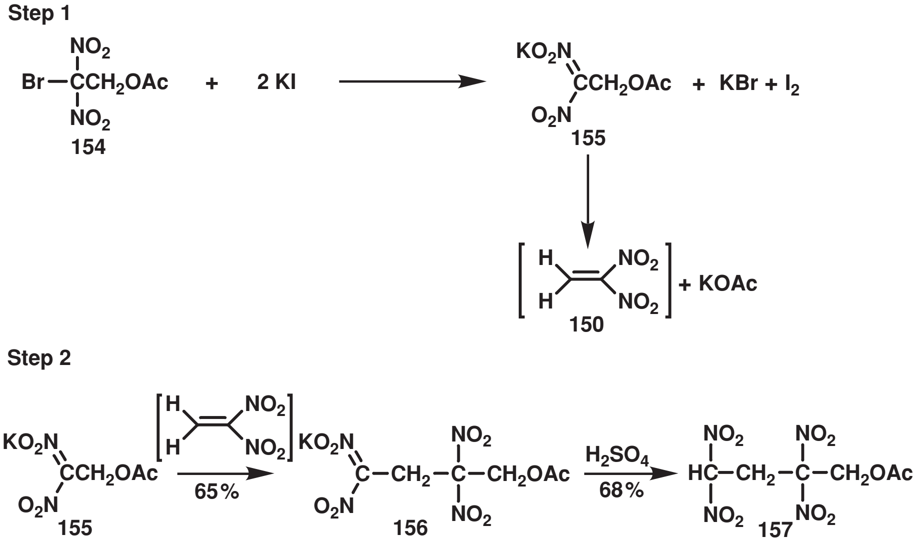


Figure 1.71

iodide gave the potassium salt of 2,2,4,4-tetranitrobutyl acetate (156) in 65 % yield, which on acidification with mineral acid, yielded 2,2,4,4-tetranitrobutyl acetate (157). Frankel[281] explained the unusual result by also postulating the formation of 1,1-dinitroethene, a highly reactive intermediate capable of undergoing Michael type 1,4-addition with any unreacted nitronate anion (155) present in solution. The generality of this reaction, known as 'dinitroethylation', for the synthesis of *gem*-dinitroaliphatic compounds is further illustrated by the formation of the potassium salt of 1,1,3,3-tetranitrobutane when 2-bromo-2,2-dinitroethyl acetate is treated with potassium iodide and the sodium salt of 1,1-dinitroethane.[281]

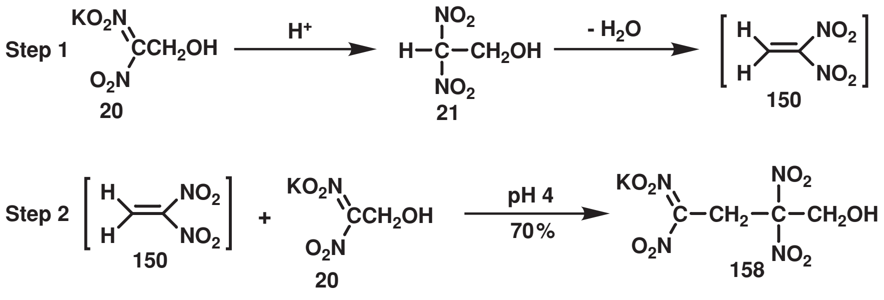


Figure 1.72

The formation of 1,1-dinitroethene (150) as an intermediate also accounts for the formation of potassium 2,2,4,4-tetranitrobutanol (158) when a solution of potassium 2,2-dinitroethanol (20) is partially acidified.[259] Klager and co-workers[259] postulated that 1,1-dinitroethene is formed via elimination of water from 2,2-dinitroethanol and this rapidly undergoes Michael 1,4-addition with any potassium 2,2-dinitroethanol still present in the reaction mixture. Demethylolation of (158) with potassium hydroxide yields the dipotassium salt of 1,1,3,3-tetranitropropane.

1.10.3 Mannich reaction

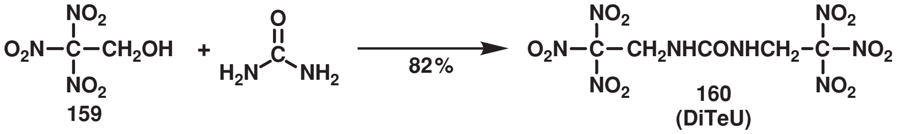
$$\mathrm{R_2NH + CH_2O} \rightleftharpoons \mathrm{R_2NCH_2OH} \rightleftharpoons \mathrm{R_2\overset{+}{N}{=}CH_2 + H_2O} \quad \text{(Eq. 1.4)}$$

$$\mathrm{R_2\overset{+}{N}{=}CH_2 + \overset{-}{C}(NO_2)_3} \rightleftharpoons \mathrm{R_2NCH_2C(NO_2)_3} \quad \text{(Eq. 1.5)}$$

Figure 1.73

The Mannich reaction is an excellent route to polynitroaliphatic amines and their derivatives. β-Nitroalkylamines are formed from the reaction of an amine and aldehyde in the presence of a nitroalkane (Equations 1.4 and 1.5).[282–296] A large number of these reactions use nitroform,[285–287] fluorodinitromethane,[37,256,261,262] or their methylol derivatives, 2,2,2-trinitroethanol[284,291] and 2-fluoro-2,2-dinitroethanol,[37,256,261,262] to synthesize the corresponding trinitromethyl and fluorodinitromethyl derivatives respectively.

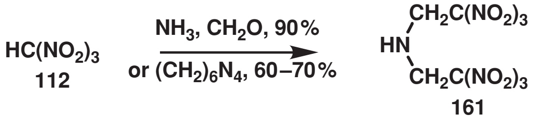
Primary and secondary nitroalkanes, dinitromethane,[282] and terminal *gem*-dinitroaliphatic compounds like 1,1-dinitroethane,[284,288] all contain acidic protons and have been used to generate Mannich products. Formaldehyde is commonly used in these reactions although the use of other aliphatic aldehydes has been reported.[282] The nitroalkane component is frequently generated *in situ* from its methylol derivative, a reaction which also generates formaldehyde. Ammonia,[282,289–291] aliphatic amines,[282–289] hydrazine,[288,289] and even urea[291] have been used as the amine component of Mannich reactions.



$$\mathrm{O_2N{-}C(NO_2)_2{-}CH_2OH} + \mathrm{H_2NC(O)NH_2} \xrightarrow{82\%} \mathrm{O_2N{-}C(NO_2)_2{-}CH_2NHCONHCH_2{-}C(NO_2)_2{-}NO_2}$$

159 160 (DiTeU)

Figure 1.74

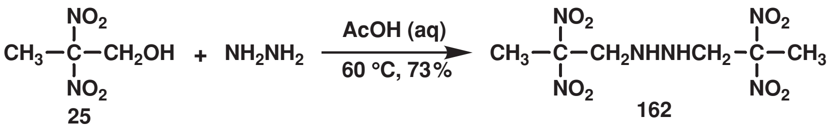


$$\mathrm{HC(NO_2)_3} \xrightarrow[\text{or }\mathrm{(CH_2)_6N_4},\ 60\text{–}70\%]{\mathrm{NH_3, CH_2O},\ 90\%} \mathrm{HN[CH_2C(NO_2)_3]_2}$$

112 161

Figure 1.75

The powerful explosive, bis(2,2,2-trinitroethyl)urea (160) (DiTeU), is synthesized from the reaction of 2,2,2-trinitroethanol (159) with urea, or from the direct reaction of nitroform with formaldehyde and urea.[291] Bis(2,2,2-trinitroethyl)amine (161) has been synthesized from the reaction of 2,2,2-trinitroethanol with ammonia and also from the reaction of nitroform (112) with formaldehyde and ammonia, or hexamine.[291,296]



$$\mathrm{CH_3{-}C(NO_2)_2{-}CH_2OH} + \mathrm{NH_2NH_2} \xrightarrow[60\ ^\circ\mathrm{C},\ 73\%]{\mathrm{AcOH\ (aq)}} \mathrm{CH_3{-}C(NO_2)_2{-}CH_2NHNHCH_2{-}C(NO_2)_2{-}CH_3}$$

25 162

Figure 1.76

Frankel and Klager[289] have reported using the Mannich reaction for the condensation of 2,2-dinitroalkanols with ammonia and hydrazine. This method was used to synthesize 2,2,6,6-tetranitro-4-azaheptane (100 %) and bis(2,2-dinitropropyl)hydrazine (162) (73 %) from the reaction of 2,2-dinitropropanol (25) with ammonia and hydrazine hydrate respectively. This work was later extended to using polynitroaliphatic amines and diamines.[284]

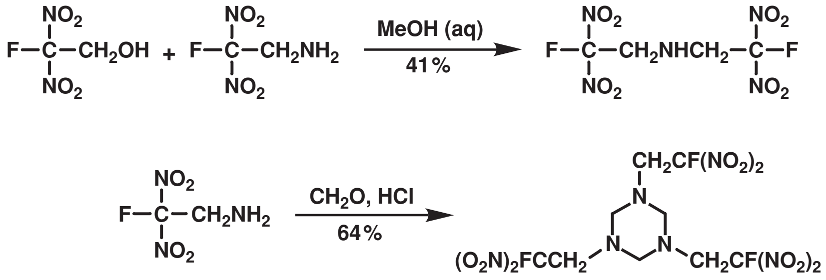
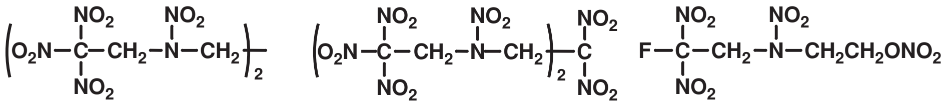


Figure 1.77

Mannich bases derived from polynitroalkanes are usually unstable because of the facile reverse reaction leading to stabilized nitronate anions. The nitration of Mannich bases to nitramines enhances their stability by reducing the electron density on the amine nitrogen through delocalization with the nitro group. The nitration of Mannich bases has been exploited for the synthesis of numerous explosives, some containing both C–NO_2 and N–NO_2 functionality.[293,295,297] Three such compounds, (163), (164) and (165), are illustrated below and others are discussed in Section 6.10.



163 164 165

Figure 1.78

1.10.4 Henry reaction

Polynitroaliphatic alcohols are invaluable intermediates for the synthesis of energetic materials (see Section 1.11). The most important route to β-nitroalcohols is via the Henry reaction where a mixture of the aldehyde and nitroalkane is treated with a catalytic amount of base, or the nitronate salt of the nitroalkane is used directly, in which case, on reaction completion, the reaction mixture is acidified with a weak acid. Reactions are reversible and in the presence of base the salt of the nitroalkane and the free aldehyde are reformed. This reverse reaction is known as demethylolation if formaldehyde is formed.

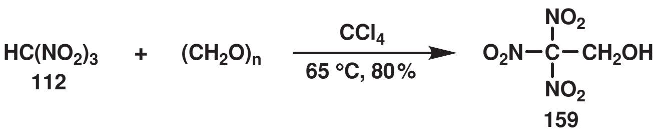


Figure 1.79

Formaldehyde is the most important aldehyde used in Henry reactions in relation to energetic materials synthesis. Nitroform (112) reacts with formaldehyde in the form of trioxane or formalin to yield 2,2,2-trinitroethanol (159).[298,299] The Henry reaction of nitroform with aldehydes other than formaldehyde gives products which are not isolable.

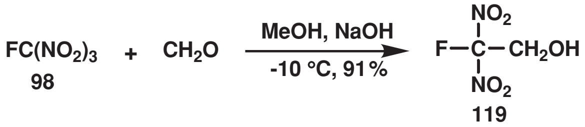


Figure 1.80

2-Fluoro-2,2-dinitroethanol (119) is rarely synthesized from fluorodinitromethane but is reportedly synthesized at Rockwell International, Rocketdyne Division in large quantities from the reaction of fluorotrinitromethane (98) with an alkaline solution of formalin.[300] The same reaction with alkaline hydrogen peroxide and formalin is also used for 2-fluoro-2,2-dinitroethanol production.[239] Unlike nitroform, fluorodinitromethane forms stable products with aldehydes other than formaldehyde.[301–305] Products obtained from the reaction of fluorodinitromethane with dialdehydes contain two hydroxy groups and may find use for the synthesis of energetic polymers.[303–305]

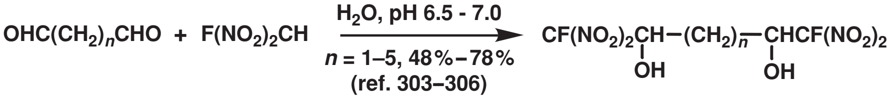


Figure 1.81

Both the Henry reaction and the reverse demethylolation are synthetically useful in the chemistry of polynitroaliphatic compounds. The Henry reaction is commonly used to mask the natural chemistry of an aliphatic nitro or terminal *gem*-dinitro group by removing the acidic α-proton(s). In Section 1.7 we discussed the conversion of α,ω-dinitroalkanes to their bis-methylol derivatives before subjecting them to oxidative nitration and subsequent demethylolation with base, a procedure which results in the formation of $\alpha,\alpha,\omega,\omega$-tetranitroalkanes.[108]

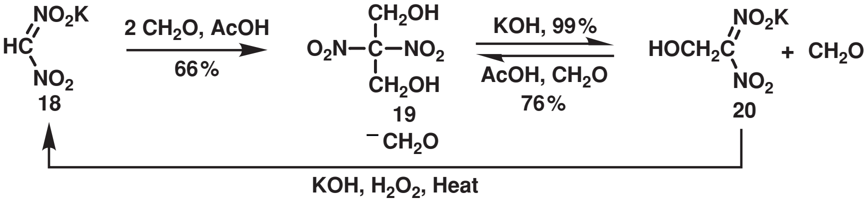
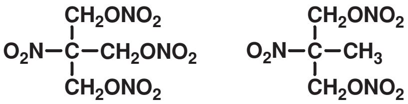


Figure 1.82

Many of the nitronate salts of polynitroaliphatic compounds, particularly salts of *gem*-nitronitronates, exhibit properties similar to known primary explosives. Consequently, the storage of such salts is highly dangerous. Treatment of these nitronate salts with formaldehyde yields the corresponding methylol derivative via the Henry condensation. These methylol derivatives are much safer to store than the parent nitronate salts and are readily converted back to the nitronate on treatment with base. Thus, treatment of the potassium salt of dinitromethane (18) with an excess of formaldehyde in the presence of acetic acid yields the bis-methylol derivative, 2,2-dinitro-1,3-propanediol (19).[104,106] Treatment of 2,2-dinitro-1,3-propanediol (19) with one equivalent of potassium hydroxide leads to demethylolation and yields the potassium salt of 2,2-dinitroethanol (20).[104] Further demethylolation of potassium 2,2-dinitroethanol (20) to potassium dinitromethane (18) is only affected with an excess of base or with hot alkaline hydrogen peroxide solution.[104]

The use of polynitroaliphatic alcohols as sources of the corresponding nitronate anions is common in addition reactions. However, polynitroaliphatic alcohols are useful in their own right. The hydroxy functionalities of 2,2-dinitroethanol, 2,2-dinitro-1,3-propanediol and 2,2-dinitropropanol[107,306] are very versatile and have been extensively used for the synthesis of energetic plasticizers, polymers, explosives and oxidizers in propellants (Section 1.11). Diols obtained from the reactions of $\alpha,\alpha,\omega,\omega$-tetranitroalkanes with formaldehyde are particularly useful for the synthesis of energetic polymers based on ester and carbamate linkages.[108,250,259,281] α, ω-Dinitroalkanes can react with either two or four equivalents of formaldehyde to form diols or tetrols respectively; good yields can be obtained in both cases by varying reaction conditions and the base used.[307]



$\mathrm{O_2N{-}C(CH_2ONO_2)_3}$

166

$\mathrm{O_2N{-}C(CH_3)(CH_2ONO_2)_2}$

167

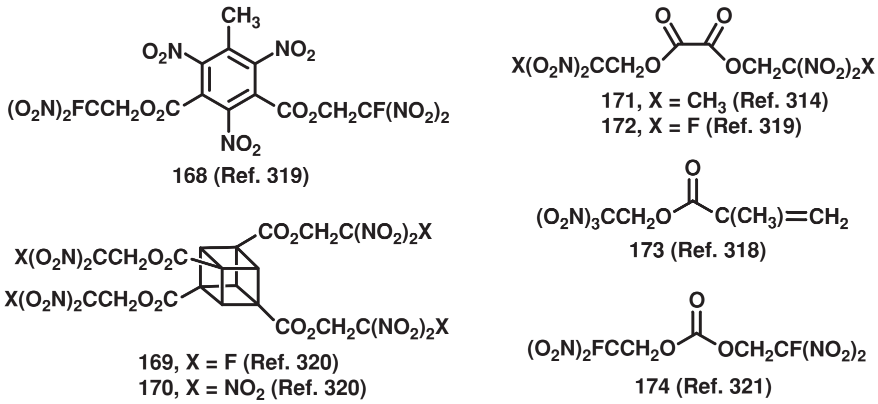
Figure 1.83

Henry reactions have been extensively exploited for the synthesis of nitrate ester explosives. The condensation of nitroalkanes with aldehydes, followed by esterification of the hydroxy groups with nitric acid, leads to a number of nitrate ester explosives (see Chapter 3). The two examples given above (166 and 167) are synthesized from the *O*-nitration of the polyols obtained from the condensation of formaldehyde with nitromethane[308] and nitroethane[309] respectively.

1.11 DERIVATIVES OF POLYNITROALIPHATIC ALCOHOLS

Polynitroaliphatic alcohols containing nitro groups on the carbon β to the hydroxy functionality are less basic than their alkyl counterparts. This decreased basicity of the hydroxy group makes reactions such as esterification, acetal formation and alkylation much slower than usual, and in some cases, these reactions may not proceed without catalysts. To add to the problem, normal base catalysts cannot be used in conjunction with 2,2-dinitroalkanols and 1,1,1-trinitro-2-alkanols because of their facile dissociation in alkaline solution.

The weak nucleophilic nature of polynitroaliphatic alcohols means that reactions often need to be catalyzed by Brønsted acids or Lewis acids. The following methods are commonly used for the esterification of polynitroaliphatic alcohols: (1) heating a solution of the alcohol and acid in the presence of sulfuric acid with Dean–Stark removal of water;[310] (2) using the acid chloride or anhydride in the presence of aluminium chloride;[311,312] (3) reacting the acid and alcohol in the presence of TFAA or PPA as condensing agents;[310,313,314] (4) *trans*-esterification of the methyl ester of the acid component with the alcohol in the presence of sulfuric acid or oleum;[310] (5) using the alcohol and acid chloride in the presence of pyridine, trialkylamines or potassium carbonate;[315,316] (6) reacting the acid chloride and the alcohol without solvent;[298,317,318] and (7) direct esterification of the alcohol with phosphorous trichloride, chlorosulfonic acid or anhydrous nitric acid.[311,314]


168 (Ref. 319)

171, X = CH_3 (Ref. 314)
172, X = F (Ref. 319)

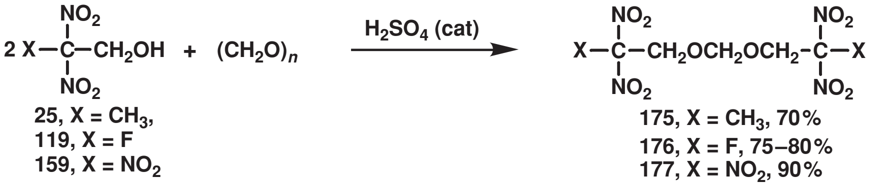
173 (Ref. 318)

169, X = F (Ref. 320)
170, X = NO_2 (Ref. 320)

174 (Ref. 321)

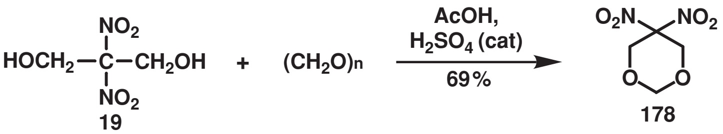
Figure 1.84

A huge number of ester and carbonate derivatives of polynitroaliphatic alcohol have been synthesized; driven by the search for new explosives and energetic plasticizers and oxidizers for propellant and explosive formulations. Most of these are derived from 2-fluoro-2,2-dinitroethanol[319–321] and 2,2,2-trinitroethanol[298,310,311,318] and have excellent oxygen balances. Some examples are illustrated above (168–174) but more comprehensive lists can be found in numerous reviews.[37,114,241,242] Direct esterification of polynitroaliphatic alcohols with nitric acid, mixed acid, or acetic anhydride–nitric acid has been used as a route to mixed polynitroaliphatic–nitrate ester explosives.[311]


25, X = CH_3,
119, X = F
159, X = NO_2

175, X = CH_3, 70%
176, X = F, 75–80%
177, X = NO_2, 90%

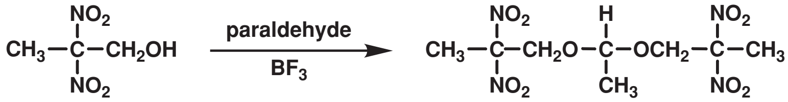
Figure 1.85


19

178

Figure 1.86

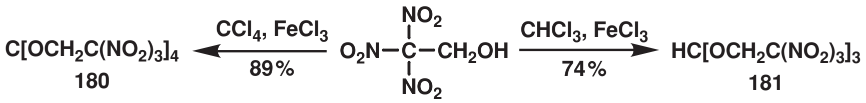
Formals and acetals prepared from the reaction of polynitroaliphatic alcohols with formaldehyde and acetaldehyde have found use as explosive plastisizers for nitrocellulose and in plastic bonded explosives (PBXs). Formals of polynitroaliphatic alcohols are commonly prepared via reaction with trioxane or paraformaldehyde in the presence of sulfuric acid as a condensing agent. Bis(2,2-dinitropropyl)formal (175) is prepared from the reaction of trioxane with 2,2-dinitropropanol (25).[322,323] The reaction of 2,2,2-trinitroethanol (159) and 2,2-dinitro-1,3-propanediol (19) with formaldehyde in the presence of sulfuric acid yields bis(2,2,2-trinitroethyl)formal (177)[322] and the 1,3-dioxane (178)[322,324] respectively. Bis(2-fluoro-2,2-dinitroethyl)formal (176) (FEFO), an energetic plastisizer used in some high energy PBXs, is prepared in 75–80 % yield from the condensation of 2-fluoro-2,2-dinitroethanol (119) with formaldehyde in the presence of concentrated sulfuric acid.[237,312,325–327]



25
179

Figure 1.87

Sulfuric acid cannot be used for the synthesis of acetals and so bis(2,2-dinitropropyl)acetal (179) is prepared from the reaction of paraldehyde with 2,2-dinitropropanol (25) in the presence of boron trifluoride.[322,323] A 50:50 eutectic mixture of bis(2,2-dinitropropyl)formal (175) and bis(2,2-dinitropropyl)acetal (179) has found use as an energetic liquid plastisizer for nitrocellulose.



180
159
181

Figure 1.88

Orthoesters of polynitroaliphatic alcohols have been synthesized in the presence of metal chloride Lewis acid catalysts. Tetrakis(2,2,2-trinitroethyl)orthocarbonate (180) and tris(2,2,2-trinitroethyl)orthoformate (181) are obtained from the reaction of 2,2,2-trinitroethanol (159) with carbon tetrachloride and chloroform, respectively, in the presence of anhydrous ferric chloride.[328,329] Analogous reactions with 2-fluoro-2,2-dinitroethanol have been reported.[329]

The weak nucleophilic nature of polynitroaliphatic alcohols is also reflected in their slow reactions with isocyanates to yield carbamates. These reactions often need the presence of Lewis acids like ferric acetylacetonate or boron trifluoride etherate.[330] The reaction of bifunctional isocyanates with polynitroaliphatic diols has been used to synthesize energetic polymers.[330]

Alkylations and other reactions using polynitroaliphatic alcohols as nucleophiles usually require Lewis acid catalysts. A comprehensive review of the chemistry of fluoronitro compounds, including 2-fluoro-2,2-dinitroethanol, has been given by Adolph and Koppes.[37] Many more examples of the use of polynitroaliphatic alcohols as nucleophiles and in other reactions can be found in numerous reviews.[37,114,241,242]

1.12 MISCELLANEOUS

1.12.1 1,1-Diamino-2,2-dinitroethylenes

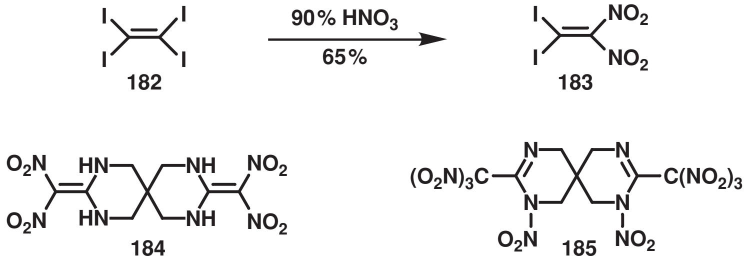


Figure 1.89

The nitration of 1,1,2,2-tetraiodoethylene (182) with 90 % nitric acid provides 1,1-diiododinitroethylene (183) in good yield.[331] Baum and co-workers[331] studied the chemistry of 1,1-diiododinitroethylene and found that displacement of the two vinylic iodide groups is effected by treatment with simple aliphatic amines, diamines and anilines to give 1,1-diamino-2,2-dinitroethylenes in excellent yield. Cyclic products are obtained from the reaction of 1,1-diiododinitroethylene with 1,2-diaminoethane (ethylenediamine), 1,3-diaminopropane and 1,4-diaminobutane. The spirocycle (184) is synthesized from the reaction of 1,1-diiododinitroethylene (183) with 2,2-bis(methylamino)-1,3-diaminopropane.

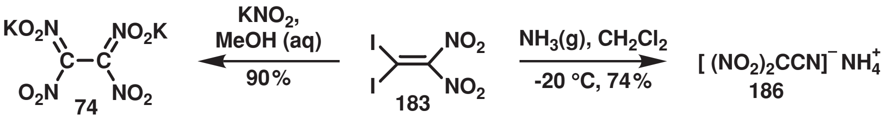


Figure 1.90

The reaction of 1,1-diiododinitroethylene (183) with potassium nitrite in aqueous methanol, and with anhydrous ammonia in methylene chloride, provides a route to the dipotassium salt of 1,1,2,2-tetranitroethane (74) (90 %) and the ammonium salt of dinitroacetonitrile (186) (74 %) respectively.[331]

Further work by Baum and co-workers[332] showed that the nitration of 1,1-diamino-2,2-dinitroethylenes with trifluoroacetic anhydride and nitric acid in methylene chloride yields 1,1,1-trinitromethyl derivatives via addition of nitronium ion to the double bond of the enamine; such treatment also resulting in the *N*-nitration of the products. In this way, trinitromethyl derivatives like (185) and (188) are obtained. Further treatment of these trinitromethyl derivatives with aqueous potassium iodide results in reductive denitration and the formation

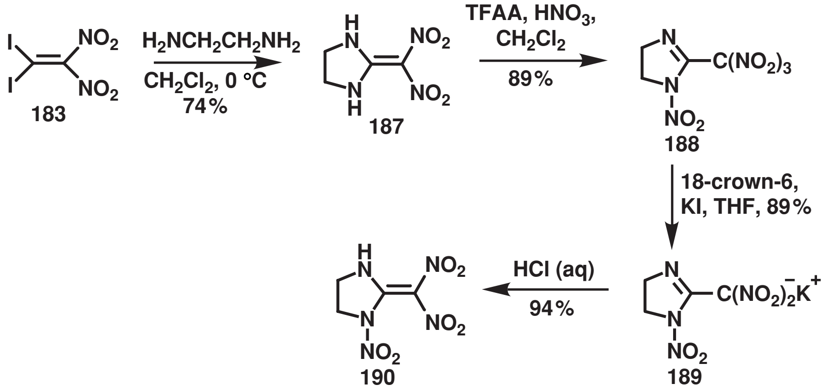


Figure 1.91

of nitronitronate salts (189), which on acidification, yield the *N*-nitro derivatives of the initial 1,1-diamino-2,2-dinitroethylenes (190).

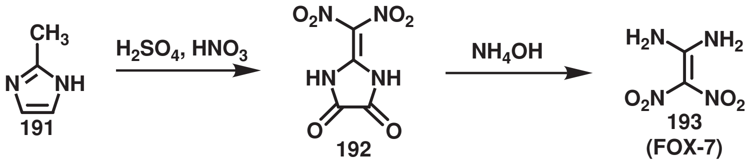


Figure 1.92

1,1-Diamino-2,2-dinitroethylenes have recently attracted interest as energetic explosives. 1,1-Diamino-2,2-dinitroethylene (193) (DADE or FOX-7) is a high energy material with a lower impact sensitivity than HMX and well suited for use in high explosive formulations.[333] FOX-7 (193) was first synthesized by Latypov and co-workers[334] who nitrated 2-methyl-4-nitroimidazole with mixed acid to give a mixture of parabanic acid and 2-(dinitromethylene)-4,5-imidazolidinedione (192), followed by reaction of the latter with aqueous ammonia to yield FOX-7 (193). 2-(Dinitromethylene)-4,5-imidazolidinedione (192) has also been prepared from the low temperature nitration of 2-methylimidazole (191).[335] The condensation of acetamidine hydrochloride with diethyl oxalate in methanol yields a mixture of 2-methylene-4,5-imidazolidinedione and 2-methoxy-2-methyl-4,5-imidazolidinedione; nitration of the latter and subsequent treatment with aqueous ammonia at pH 8–9 also provides FOX-7 in 50 % overall yield.[334] FOX-7 has been synthesized on a pilot plant scale in Sweden[336] by the nitration of 2-methyl-4,6-dihydroxypyrimidine.[337] The conversion of 2-(dinitromethylene)-4,5-imidazolidinedione to FOX-7 has been studied by Cai and co-workers[338] who achieved hydrolysis with water instead of ammonia and also found that hydrolysis with a carboxylic acid produces a larger crystal size which is more suitable for direct use in explosive formulations.

1.12.2 Other routes to aliphatic nitro compounds

A number of routes to aliphatic nitro compounds are not used for energetic materials synthesis but are included here for completeness.

Bachmann and Biermann[339] reported the synthesis of nitroalkanes from the thermolysis of acyl nitrates. The thermolysis of nitrite and nitrate esters over an asbestos catalyst is also reported to yield nitroalkanes.[340]

Olah and co-workers[341] reported the synthesis of nitroalkanes and nitroalkenes from the nitrodesilylation of alkylsilanes and allylsilanes, respectively, with nitronium salts.

Nitroacetylenes are generally unstable and very explosive and so they have been little studied. Schmitt and co-workers[342] used the nitrodesilylation of trialkylsilylacetylenes with both nitronium salts and nitryl fluoride to obtain nitroacetylenes. Dinitrogen pentoxide has also been used for the nitrodesilylation of trialkylsilylacetylenes.[343] Nitrodestannylation of allylsilanes has also been reported.[344]

Diels–Alder reactions using highly reactive polynitroalkenes have been reported. These include cycloaddition reactions with 1,1-dinitroethene,[106,345] 1,1,2,2-tetranitroethylene[346] and various fluoro-1,2-dinitroethylenes.[347]

1.12.3 Selective reductions

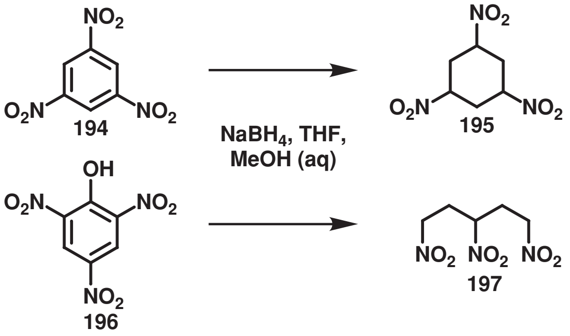


Figure 1.93

Reagents like lithium aluminium hydride and hydrogen over palladium readily reduce the aliphatic nitro group to the corresponding amino group. Sodium borohydride will reduce many functional groups but leaves both aromatic and aliphatic nitro groups intact. Sodium borohydride has been used for the selective reduction of polynitroaliphatic aldehydes,[348] ketones,[348] esters[349] and acid chlorides[310] to the corresponding polynitroaliphatic alcohols. Sodium borohydride has been used for the reduction of the aromatic rings of 1,3,5-trinitrobenzene (194) and picric acid (196) to yield 1,3,5-trinitrocyclohexane[350] (195) and 1,3,5-trinitropentane[351] (197) respectively.

1.13 CHEMICAL STABILITY OF POLYNITROALIPHATIC COMPOUNDS

The stability of polynitroaliphatic compounds to acids, bases and nucleophiles is often linked to the presence of an acidic α-proton(s) which may allow various resonance structures to lead to rearrangement or decomposition. Additionally, the presence of two or more nitro groups on the same carbon atom greatly increases the susceptibility of the carbon–nitrogen bonds to nucleophilic attack.

Table 1.11 Reactions of nitroalkanes and polynitroalkanes with mineral acid

Nitroalkane	Hydrolysis product
RCH_2NO_2	RCOOH
$R^1R^2CHNO_2$	No reaction
$R^1R^2C{=}NO_2H$	$R^1R^2C{=}O$
$R^1R^2C(NO_2)_2$	No reaction
$RCH(NO_2)_2$	RCOOH
$R^1R^2CHC(NO_2)_3$, C-H not activated	No reaction
$R^1R^2CHC(NO_2)_3$, C-H activated	$R^1R^2C{=}O$

Source: Reprinted with permission from J. C. Dacons, M. J. Kamlet and L. A. Kaplan, *J. Org. Chem.*, 1961, **26**, 4371; Copyright 1961 American Chemical Society.

1.13.1 Reactions with mineral acids

Polynitroalkanes are generally stable to mineral acids, although hydrolysis can occur with prolonged heating, depending on the arrangement of the nitro groups within the compound. On treatment with mineral acid primary aliphatic nitro groups are hydrolyzed to the corresponding carboxylic acid via an intermediate hydroxamic acid, whereas secondary nitro groups are unaffected.[352] The presence of an acidic proton in relation to compound stability is illustrated by the inertness of the internal *gem*-dinitroaliphatic group towards hot mineral acids, whereas a terminal *gem*-dinitroaliphatic group is converted to the corresponding carboxylic acid.[352] The same resistance to mineral acid hydrolysis is shown by tertiary nitroalkanes. Trinitromethyl groups are also stable to acid hydrolysis with the exception that an electron-withdrawing group or resonance-stabilizing group is not present on the β-carbon atom. In such cases an acidic proton β to the trinitromethyl group allows acid hydrolysis to lead to the formation of a carbonyl group with the degradation of one carbon atom from the compounds skeleton. A summary of the reactions of nitroalkanes and polynitroalkanes with mineral acid is given in Table 1.11.[352]

Acidification of the nitronate salts of polynitroalkanes can be complicated by the fact that some polynitroaliphatic compounds are unstable, as in the case of dinitromethane and 1,1,2,2-tetranitroethane, where both decompose readily at ambient temperature. The nitronate salts of both primary and secondary aliphatic nitro groups are decomposed to carbonyl compounds on acidification with mineral acid, a synthetic process known as the Nef reaction.[353] *gem*-Nitronitronate salts form the *gem*-dinitroaliphatic compound on acidification with mineral acid.

1.13.2 Reactions with base and nucleophiles

Both primary and secondary aliphatic nitro groups form nitronate salts on reaction with base. Terminal *gem*-dinitroaliphatic groups form the corresponding nitronitronate salts. Internal *gem*-dinitroaliphatic groups lack an acidic proton and cannot form nitronate salts. The nitro groups in compounds containing trinitromethyl groups are especially electron deficient and susceptible to attack by both bases and nucleophiles. The reaction of trinitromethyl compounds with base generates the corresponding *gem*-nitronitronate salt.

The effect of having multiple, powerful electron-withdrawing groups on the same carbon is seen in the extreme case of tetranitromethane with its readiness to lose a nitro group on

Table 1.12 Reactions of nitroalkanes and polynitroalkanes with alkali base

Nitroalkane	Product
$C(NO_2)_4$	$M^+\overline{C}(NO_2)_3$
$HC(NO_2)_3$	$M^+\overline{C}(NO_2)_3$
RCH_2NO_2	Nitronate salt
$R^1R^2CHNO_2$	Nitronate salt
$RCH(NO_2)_2$	Nitronate salt
$R^1R^2C(NO_2)_2$	No reaction
$R^1R^2CHC(NO_2)_3$	$R^1R^2CHC(NO_2)_2^- M^+$

treatment with both base and nucleophile. In fact, treatment of tetranitromethane with alkali hydroxides or aqueous ammonia provides a convenient route to nitroform salts.[354] This electron deficiency of the nitro groups in tetranitromethane finds use in the alkaline nitration of compounds with active methylene groups.[179] The point is further illustrated by the slow decomposition of tetranitromethane in the presence of water, giving nitroform and nitric acid as products. Trinitromethyl groups will also slowly decompose in the presence of hot water. A summary of the reactions of nitroalkanes and polynitroalkanes with alkali base is given in Table 1.12.

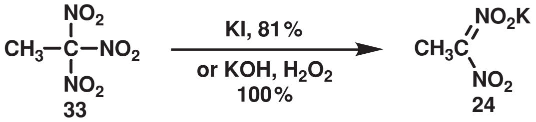


Figure 1.94

As discussed above, the nitro groups of tetranitromethane and trinitromethyl compounds are susceptible to nucleophilic attack. Both potassium iodide[355] and alkaline hydrogen peroxide[356] affect the reductive denitration of trinitromethyl groups to *gem*-nitronitronates; 1,1,1-trinitroethane (33) is quantitatively reduced to potassium 1,1-dinitroethane (24) on treatment with alkaline hydrogen peroxide.[356] Nucleophiles such as potassium fluoride in DMF can displace nitrite anion from tetranitromethane.[357,358] Various nucleophiles, including azide,[359] chloride,[358] fluoride[359] and ethoxide[359] have been used to displace one of the nitro groups from fluorotrinitromethane.

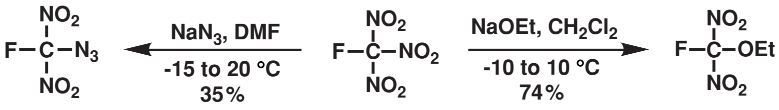


Figure 1.95

The carbon–halogen bonds of 1-halo-1,1-dinitroaliphatic compounds are particularly electron deficient and susceptible to nucleophilic attack. This kind of reaction is synthetically useful in the chemistry of terminal *gem*-dinitroaliphatic compounds. Some *gem*-nitronitronate salts of polynitroalkanes are exceptionally sensitive to mechanical stimuli and explode readily. However, these salts are readily converted into the more predictable 1-halo-1,1-dinitro derivatives, which in turn, are reconverted to the original *gem*-nitronitronate salts on treatment with aqueous potassium iodide.

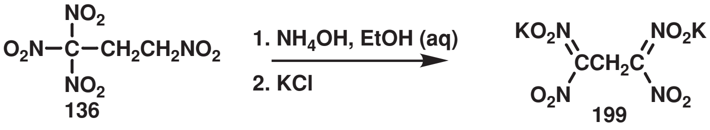


Figure 1.96

In Section 1.10.2.3 we observed that a base can react with 1,1,1-trinitromethyl compounds to either remove an acidic proton or act as a nucleophile to displace a nitro group. Trinitromethyl compounds can also undergo rearrangement reactions is the presence of a base or nucleophile. 1,1,1,3-Tetranitropropane (136) undergoes an internal redistribution of nitro groups on treatment with aqueous alkali or ammonium hydroxide to give 1,1,3,3-tetranitropropane, which is isolated as its sparingly soluble di-potassium salt (199) on adding an aqueous solution of potassium chloride to the reaction mixture.[253,360] This type of rearrangement occurs with other trinitromethyl derivatives of structure (198) and in this way, the potassium salt of 1,1,3,3-tetranitrobutane (201) is obtained from 1,1,1,3-tetranitrobutane (200).[361]

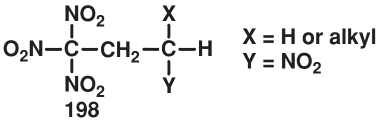


Figure 1.97

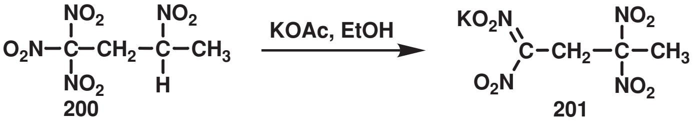


Figure 1.98

2,2,2-Trinitrochloroethane (202) and 2,2,2-trinitroethyl acetate (203) also undergo nitro group rearrangement in the presence of potassium nitrite to give the di-potassium salt of 1,1,2,2-tetranitroethane (74) in both cases.[362]

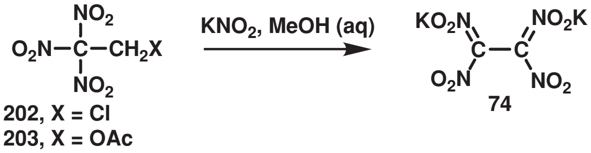


Figure 1.99

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