1

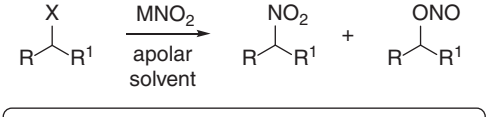
Synthesis of Nitroalkanes

1.1 Synthesis of Nitroalkanes

Simple nitroalkanes ($CH_3(CH_2)_{0–5}NO_2$, *c*-$C_{5,6}H_{9–11}NO_2$, *i*-$PrNO_2$, etc.) are commercially available, while the more complex ones need to be prepared following a variety of synthetic procedure and, in this sense, there are a variety of methods to obtain a large collection of nitroalkanes.

1.1.1 Displacement of Alkyl Halides

Treatment of alkyl halides with metal nitrite is certainly the best known and the most used method for the preparation of nitroalkanes, mainly the primary ones ($R^1 = H$, Scheme 1.1) [1].



Reactivity
Alkyl halide: Primary > Secondary; X: I > Br > Cl

Scheme 1.1 Displacement (nitration) of alkyl halides.

In literature a variety of efficient procedures have been reported using sodium or silver nitrite (M = Ag, Victor-Meyer reaction [2]; M = K or Na Kornblum reaction [3]), anyway the formation of nitroalkanes is accomplished by the formation of alkyl nitrite as by-product, removed via distillation or chromatography. The nitrite is formed because of the ambident nature of the nitrite anion, which bears two different nucleophilic centers. The reaction is typically performed at room temperature adding the halide to a stirred mixture of dimethyl formamide (DMF) and metal nitrite. The use of DMF is due to the ability of this solvent to dissolve the nitrite and to accelerate the reaction of the alkali nitrite with the halide, while minimizing any side reaction such as those reported in Scheme 1.1.

An interesting application of the nitration of alkyl halides has been reported [4] for the preparation of fatty nitroalkanes, mainly the polyunsaturated ones, from

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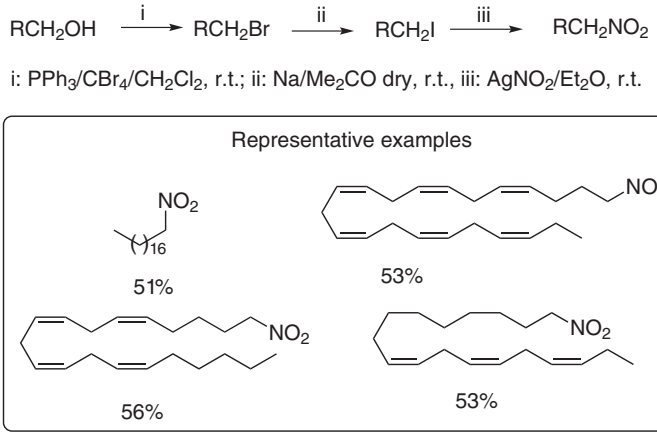
Roberto Ballini and Alessandro Palmieri.

naturally alcohols (Scheme 1.2) through their successive conversion into (i) bromo alkanes, (ii) iodo alkanes (more reactive vs bromo derivatives), and (iii) nitroalkanes with silver nitrite, in Et_2O and at room temperature for three days.



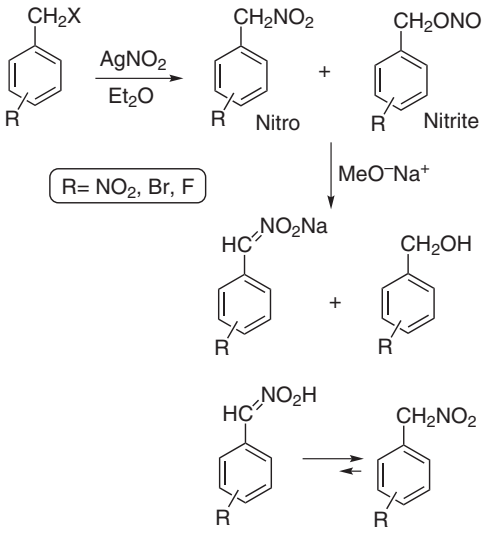
Scheme 1.2 Synthesis of fatty nitroalkanes.

It is important to point out that the need to convert bromo alkanes into the iodo alkanes is due to the fact that, contrary to short-chain bromo alkanes, the longer ones are inert toward the reaction with $AgNO_2$.

Benzylic nitro compounds (aryl nitromethanes) are an important class of nitroalkanes and their preparation shows some drawbacks due to the lack of selectivity, with consequent formation of an amount of nitrite ester. Guillaumet and coworkers [5] reported an improved approach (based on the Victor Meyer reaction) for the synthesis of aryl nitromethanes, minimizing the complex purification process on the basis of the difference in pK_a values between aryl nitromethane and benzyl nitrite ester (side product). In fact, the nitro compound is quite a strong acid ($pK_a = 8–12$) due to the high stability of the formed nitronate. Indeed, the negative charge is delocalized onto the nitro and the aryl group, while the nitrite ester does not bear any acidic proton because the conjugate base is no longer stabilized in any nitro group. This significant acidic difference has been the ideal property to develop a practical purification method usable on large scales.

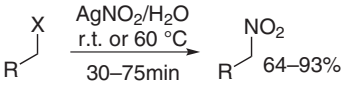
In fact (Scheme 1.3), adding a methanolic solution of sodium methoxide into the filtrate of the reaction, it is possible to observe a precipitate of the formed sodium nitronate that could be simply isolated by filtration. The nitronate, treated with acetic acid and urea, converts into the *aci*-nitro structure through an O-protonation. The latter quickly precipitates in the acidic medium and isomerizes into the target aryl nitromethane in satisfactory yields (>50%) and with the survival of a variety of other functional groups.

However, the nitration of alkyl halides with $AgNO_2$ (Victor Meyer procedure) shows important drawbacks because usually the need of long reaction times and the use of toxic solvents produce important amounts of by-products and require



Scheme 1.3 Aryl nitromethanes synthesis under minimized purification step.

a tedious work-up. Thus, an improved procedure has been developed, in aqueous medium, treating primary alkyl halides with 4 equiv of silver nitrite (r.t. or 60 °C) [6]. The method allows satisfactory to good yields of a variety of primary nitroalkanes, in short reaction times (0.5–1.25 hours, Scheme 1.4). The need of 4 equiv of silver nitrite is due to the fast of the reaction that can minimize the competitive formation of the corresponding alcohol. In addition, the formation of alkyl nitrite is strongly depressed.



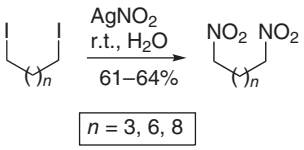
Selected examples:
R = *n*-C_nH_{2n+1}, CH_2=$CH(CH_2)_8$, $AcO(CH_2)_3$, $PhCOCH_2$
X = Br, I.

Scheme 1.4 Nitration of halides with silver nitrite.

Although the method works well with both alkyl bromides and alkyl iodides, the latter often shows higher reactivity, while it fails with secondary halo derivatives. Furthermore, due to the mildness of the reaction conditions, other functionalities such as C=C double bond, ester, imide, and ketones are preserved.

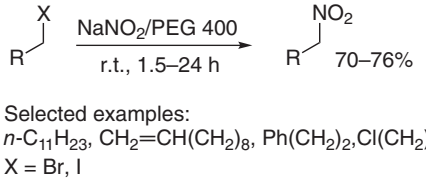
An important application of the above method is the synthesis of α,ω-dinitroalkanes from α,ω-diiodo structures (Scheme 1.5).

Thus, this procedure can be considered as a significant progress in the sustainability of the nitration of halo alkanes. However, a possible drawback consists of the need for a large excess of expensive reagents such as silver nitrite and the formation of the corresponding alcohol due to the competitive action of water vs nitrite.



Scheme 1.5 Nitration of halides with silver nitrite (selected examples).

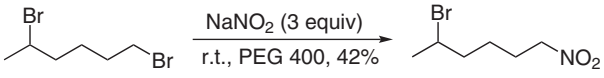
Then, few years later, our group developed an improved eco-friendly nitration of alkyl halides [7], using sodium nitrite in polyethylene glycol (PEG 400) as green reaction medium [8, 9]. Thus, treatment of primary alkyl halides with 1.5–3 equiv of sodium nitrite, at room temperature, in PEG 400 as solvent, allows the chemoselective (other functionalities such as esters, hydroxyl group, C=C double bond, ethers, aromatics, and amides are preserved) formation of primary nitroalkanes (Scheme 1.6). It is important to point out that only traces of alkyl nitrite are observed. In addition, it is relevant that PEG 400, after extraction with cyclohexane, can be recycled at least twice for the same reaction before its disposal as waste.



Scheme 1.6 Nitration of halides under PEG solvent.

Although the procedure works well with both alkyl iodides and bromides, the latter needs larger amounts of sodium nitrite (3 equiv vs 1.5 equiv) and longer reaction times (*ratio* > 3).

With this procedure, the conversion of secondary halo derivatives fails, and this result can be applied to the chemoselective nitration of primary iodides or bromides in the presence of a secondary one (Scheme 1.7).

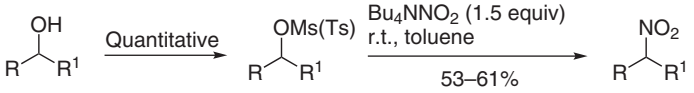


Scheme 1.7 Chemoselective nitration of alkyl halides.

1.2 Nitration of Mesylates and Tosylates

The displacement of alkyl halides with metal nitrite, thanks to the large number of available halides, is the most used procedure for the preparation of nitroalkanes. However, despite the advantages introduced with these methodologies, the search for alternative sources is surely welcomed. In this regard, alcohols are a broad class of

molecules easily available from both commercial and nature sources. The conversion of alcohol into nitroalkanes firstly requires the conversion into the corresponding mesylates or tosylates (usually in quantitative yields) that can be easily converted (Scheme 1.8) into the corresponding nitroalkanes using tetrabutylammonium nitrite (TBAN) in toluene for few hours (2.5 hours for primary compounds and 28–40 hours for the secondary ones) [10].



Selected examples:
R = *n*-C_nH_{2n+1}, $Ph(CH_2)_2$, $CN(CH_2)_4$, $CH_2{=}CH(CH_2)_8$
R^1= H, Me, Et

Scheme 1.8 Nitration of mesylates and tosylates.

The method was realized at room temperature and, after a simple work up, a variety of primary and secondary nitroalkanes can be easily obtained is 41–61% overall yields.

1.3 Oxidation of Nitrogen Derivatives

The oxidation of nitrogen derivatives is a useful alternative to furnish nitroalkanes that are difficult to prepare by the direct nitration of hindered halo derivatives.

1.3.1 Oxidation of Amines

The direct oxidation of primary amines into the corresponding nitro derivatives is very useful for fundamental and industrial applications because it provides targets that may be difficult to obtain via nitration methods.

The pioneering oxidation of primary amines has been performed with various reagents such as ozone [11], $NaMnO_4$ [12], $KMnO_4$ [13], peracetic acid [14], *meta*-chloroperbenzoic acid (MCPBA) [15], and dimethyldioxirane (DMO) [16].

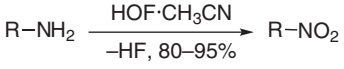
The reactions proceed (Scheme 1.9) via a few intermediates and an efficient oxidant is preferred for a rapid conversion to nitroalkanes. In fact, incomplete oxidation was sometimes observed, with consequent formation of by-products such as nitroso and nitroso-dimers.

Scheme 1.9 Oxidation of primary amines.

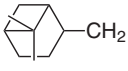
From an environmental point of view, ozonization is also a benign and atom-efficient oxidation process, but an important drawback deals with the safety

since it can lead the formation of unstable and potentially explosive ozonides and peroxides. Moreover, the subsequent quenching step is generally exothermic, thus requiring an efficient temperature control. To overcome the aforementioned disadvantages, few years ago Kappe and coworkers [17] proposed a continuous flow procedure as a valuable alternative to batch protocols for the oxidative conversion of important functionalities, including some primary amines to the corresponding nitroalkanes.

Later, the oxidation of amines has been developed using an alternative and improved oxygen transfer reagent, such as "HOF·CH_3CN complex," simply obtained passing fluorine through acetonitrile. The method (Scheme 1.10) [18] proceeds by dissolving the amine in CH_2Cl_2, then the mixture was cooled to −15 °C and added to the glass reactor containing NaF and HOF·CH_3CN (3 equiv) in cold (−15°C) aqueous CH_3CN.



Selected examples:

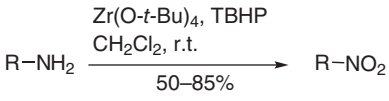
R = *n*-$C_{12}H_{25}$, $PhCH_2$, *c*-C_6H_{11}, 

Scheme 1.10 Oxidation of amines using HOF·CH_3CN.

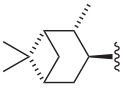
The reaction proceeds for few minutes allowing nitroalkanes in excellent yields. Considering that HOF·CH_3CN cannot be used in a large-scale process due to its instability (half-life = four hours at room temperature), it cannot be packaged and shipped but must be prepared and used immediately. In addition, the oxidation reaction has been performed in batch and all the problems of using concentrated oxidizing media remain. In this context, Sandford and coworkers [19] developed a flow process to solve the above drawbacks. However, for an efficient and selective oxidation, any fluorine gas that enters into the flow channel must be completely consumed before the organic substrate could be added to prevent fluorination and substrate degradation. In addition, the oxidation needs 3 equiv of HOF·CH_3CN to perform the efficient conversion of the ammines to nitroalkanes. Thus, a flow reactor designed specifically for gas–liquid reactions was adapted in order to perform the sequential formation and reaction of HOF·CH_3CN.

Some years before, Krohn and Küpke reported [20] an efficient procedure to convert aliphatic amines into nitro compounds based on a zirconium-catalyzed oxidation of primary amines with *tert*-butyl hydroperoxide (TBHP), in the presence of $Zr(O\text{-}t\text{-}Bu)_4$ as catalyst (Scheme 1.11).

In fact, a solution of amine (10 mmol), in dry CH_2Cl_2, is treated with freshly activated powered molecular sieves (3 Å) and $Zr(O\text{-}t\text{-}Bu)_4$ (1 mmol). After stirring for 30 minutes, a solution of TBHP (59 mmol) in CH_2Cl_2 is added. After complete consumption of the starting material and work-up, good yields of nitroalkanes are obtained. The method works well with a variety of substrates and it is mild enough to preserve other functional groups as acetals and esters.



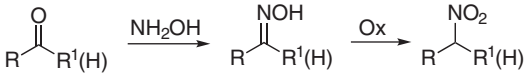
Selected examples:

R = *n*-C_8H_{17}, $(EtO)_2(CH_2)_3$, $(CH_2)_5COOEt$, $PhCHCH_2$, 

Scheme 1.11 Oxidation of amines using Zr(O-*t*-Bu)$_4$.

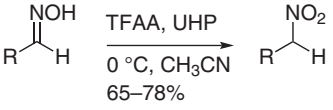
1.3.2 Oxidation of Oximes

Conversion of carbonyl function to nitro group (retro-Nef reaction) [21] is an important method for the preparation of nitro compounds. Such conversion is generally effected via oximes using strong oxidants (Scheme 1.12).

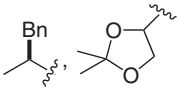


Scheme 1.12 Retro-Nef reaction via oximes.

Following a pioneering procedure performed with CF_3CO_3H [22], there was reported a revised and improved procedure (Scheme 1.13) [23] using peroxytrifluoroacetic acid obtained through reaction of urea–hydrogen peroxide complex (UHP) with trifluoroacetic anhydride (TFAA) in acetonitrile at (0 °C).



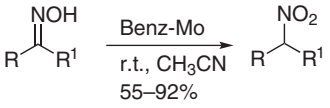
Selected examples:

R = *c*-C_6H_{11}, *n*-C_5H_{11}, *p*-$MeOC_6H_4$, 

Scheme 1.13 Oxidation of oximes with TFAA/UHP.

The procedure allows good yields with aldoximes, while fails to react with ketoximes. On the other hand, ketoximes can be converted into secondary nitroalkanes, following the Olah method [24], oxidizing ketoximes with sodium perborate in glacial acetic acid. However, this procedure failed with aldoximes.

An interesting conversion of both aldoximes and ketoximes to the corresponding nitroalkanes has been realized by a complementary synthetic route of the UHP method. In fact, the oxidation achieved with "Benz-Mo," the Mo(VI) oxidiperoxo complex $[Benz\text{-}MoO(O_2)_2]^-(t\text{-}Bu)_4N^+$ in acetonitrile, affords good yields of both primary and secondary nitroalkanes (Scheme 1.14) [25].

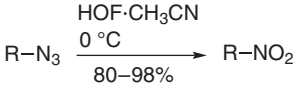


Selected examples:
R= *c*-$C_{12}H_{22}$, Ph; R^1= H, Me, Ph

Scheme 1.14 Oxidation of oximes using Benz-Mo.

1.3.3 Oxidation of Azides

Recently azides have been identified as a new precursor of primary nitroalkanes by oxidation. In this context, Rozen et al. [26] found that the carbon-bonded nitrogen of azides would be nucleophilic enough to interact with the oxygen atom of $HOF{\cdot}CH_3CN$. Thus, thanks to the efficiency of this oxidant, a variety of azides, easily obtainable from alkyl bromides and sodium azide, have been converted into primary nitroalkanes in quantitative or very good yields and in short reaction times (Scheme 1.15).



Selected examples:
R= *c*-C_6H_{11}, *c*-C_5H_9, *n*-$C_{10}H_{21}$, $PhCH_2$, $AcO(CH_2)_5$

Scheme 1.15 Oxidation of azides using $HOF{\cdot}CH_3CN$.

Concerning the use of fluorine, a very corrosive material, it should be used only with the appropriate vacuum line techniques. However, for the occasional user, various premixed mixtures of F_2 in inert gases are commercially available.

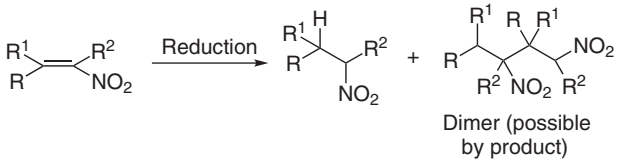
Moreover, as for the oxidation of primary amines, a flow process has been developed [19] and, following this procedure, quantitative yields (<90%) of primary and secondary nitroalkanes were obtained.

1.4 Reduction of Conjugate Nitroalkenes

Conjugated nitroalkenes are a very important class of molecules easily prepared by nitroaldol condensation or direct nitration of the corresponding olefins. Their reduction provides a convenient route to a variety of different functionalities including oximes, carbonyl compounds, hydoxylamines, alkylamines, and nitroalkanes [27, 28].

1.4.1 Reduction of Nitroalkenes into Nitroalkanes

The reduction of conjugate nitroalkenes into nitroalkanes (Scheme 1.16) has been achieved under several distinct protocols; however, often there is a loss of product



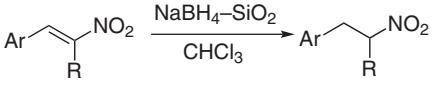
Scheme 1.16 Reduction of nitroalkenes.

due to dimerization caused by the competitive Michael addition of the formed nitronate to another molecule of nitroalkene.

However, because this by-product may be suppressed at reduced pH, the main theme of several reports is the selective reduction of the double bond avoiding the formation of the Michael by-product. Thus, a plethora of reductive methods have been reported. A modified reduction with sodium borohydride in the presence of both silica gel and a mixture of chloroform-propanol as solvent system achieves good results of nitroalkanes (Table 1.1) [29].

Successively, Kabalka et al. [28] proposed three different reductive agents (Table 1.2): (i) trialkylborohydride, (ii) $NaBH_4$ in a mixed MeOH-THF solvents, and (iii) $NaBH_4$ supported on an ion exchange resin, for an effective conversion of nitroalkenes to nitroalkanes.

Table 1.1 $NaBH_4/SiO_2$ reduction of nitroalkenes (selected examples).



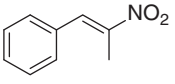
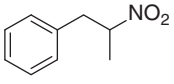
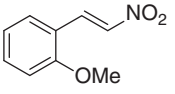
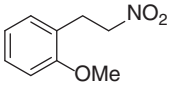
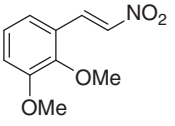
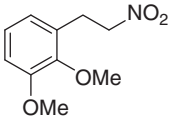
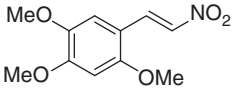
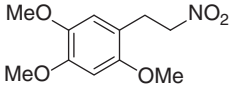
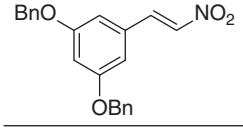
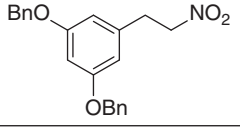
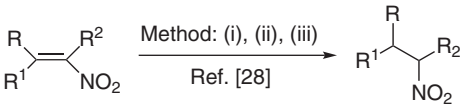
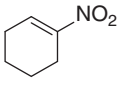
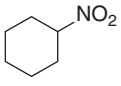
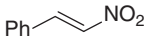
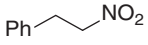
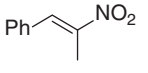
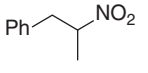
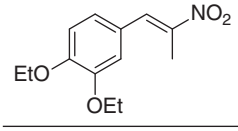
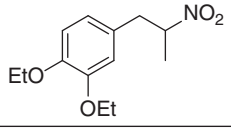
Nitroalkene	Nitroalkane	Yield (%)
		93
		92
		94
		94
		98

Table 1.2 Comparative reduction of nitroalkenes with methods (i)–(iii) (selected examples).



Nitroalkene	Nitroalkane	Yield (%)		
		(i)	(ii)	(iii)
		69	62	80
		78	64	—
		81	82	80
		69	75	83

Later, Vankar and coworkers [30] developed an efficient, chemoselective procedure for the reduction of conjugated nitroalkenes with the use of $NaCNBH_3$ (1 equiv) in methanol (Table 1.3), by the help of Zeolite (H-ZSM-5, [Si:Al = 35 : 1], 0.5 equiv), and a careful control of the pH.

1.4.2 Stereoselective Reduction of Conjugated Nitroalkenes

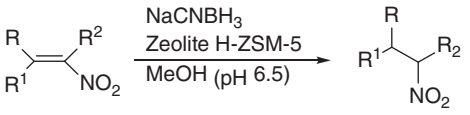
The stereoselective reduction of conjugated nitroalkenes is an important goal and a variety of efficient procedures have been reported [31–36]; however, they seem to be restricted to the reduction of nitrostyrene derivatives. Thus, a survey of the most representative examples is reported in Table 1.4.

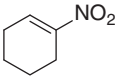
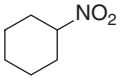
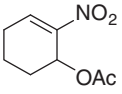
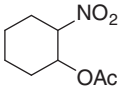
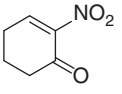
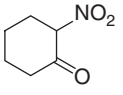
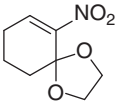
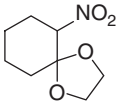
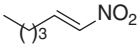
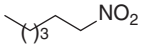
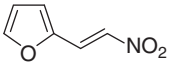
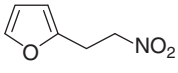
1.4.3 Aldehyde Reductive Nitromethylation

Several decades ago, Wollemberg and Miller developed a useful procedure for the preparation of primary nitroalkanes with an extra atom beginning from aldehydes [37]. The starting point is the nitroaldol (Henry) reaction (Scheme 1.17) of an aldehyde with nitromethane, catalyzed with KF and in the presence of *i*-PrOH as solvent. The formed nitroalkanol is acetylated (acetic anhydride in the presence of 4-dimethylaminopridine as catalyst) and treated with sodium borohydride affording the desired nitroalkane via "one-pot" acetic acid-elimination and C=C double bond reduction.

So, this procedure offers the opportunity to increase the chain length of the starting aldehyde.

Table 1.3 Reduction of nitroalkenes with $NaCNBH_3$ (selected examples).



Nitroalkene	Nitroalkane	Yield (%)
		79
		74
		70
		78
		78
		69

1.5 Nitration of Alkanes

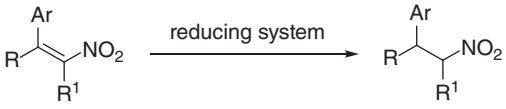
In contrast with the nitration of aromatic hydrocarbons that can easily performed using nitric acid in the presence of sulfuric acid, the selective nitration of aliphatic hydrocarbons is very difficult due to the exceeding low reactivity of the latter.

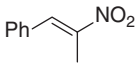
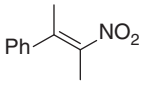
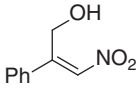
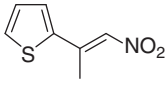
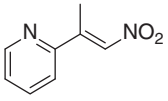
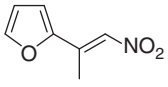
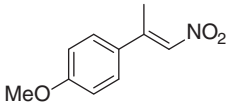
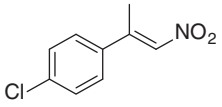
Currently, nitration reactions of aliphatic hydrocarbons are carried out at fairly high temperature using nitrogen dioxide or nitric acid, thanks to a free radical process, involving C—H bond homolysis [38]. Often, under such temperature conditions higher alkanes undergo also cleavage of the C–C skeleton. Thus, Ishii and coworkers [39] developed a milder method for the nitration of light alkanes and alkyl side-chain aromatic compounds with NO_2 and HNO_3 under *N*-hydroxyphthalimide (NHPI) or *N*-acetoxyphtalimide (NAPI) catalysis (Table 1.5).

1.6 Metal-Catalyzed Alkylation or Arylation of Nitroalkanes

Commercially available nitroalkanes can be used as precursors of more complex structures through their alkylation or arylation, performed under metal catalysis.

Table 1.4 Stereoselective reduction of nitroalkenes (selected examples).



Substrate	Reducing system	Yield (%), (ee)
	Baker's yeast, EtOH·H_2O [33]	91 (*S*, 12%)
	Baker's yeast, EtOH·H_2O [33]	72 (*S*, 12%)
	CuF_2/$PhSiH_3$, (*R*)(*S*)-JOSIPHOS, PHMS/PhMe·H_2O [35]	52 (*R*, 90%)
	CuF_2/$PhSiH_3$, (*R*)(*S*)-JOSIPHOS, PHMS/PhMe·H_2O [34]	88 (*R* 92%)
	CuO-*t*-Bu/$PhSiH_3$, (*S*)(*R*)-JOSIPHOS, PMHS/PhMe·H_2O [34]	55 (*S*, 72%)
	CuO-*t*-Bu/$PhSiH_3$, (*S*)(*R*)-JOSIPHOS, PMHS/PhMe·H_2O [34]	72 (*S*, 90%)
	Iridium complex, HCOOH/H_2O, pH 2 [34]	94 (*R*, 92%)
	Iridium complex, HCOOH/H_2O, pH 2 [34]	92 (*R*, 90%)

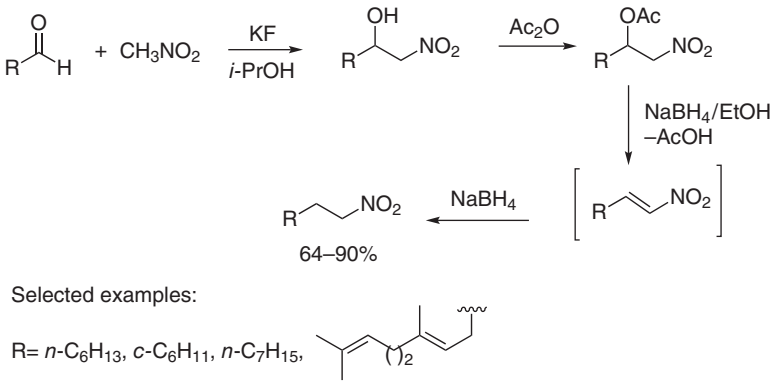
PMHS, polymethylhydrosiloxane.

1.6.1 Nitroalkylation of Aryl Halides

Aryl halides can be converted into "aryl nitromethanes" via a cross-coupling reaction with nitromethane, catalyzed by $Pd_2(dba)_3$, tris(dibenzylideneacetone)dipalladium, as reported in Scheme 1.18 [40].

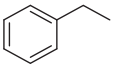
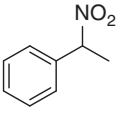
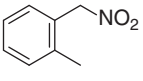
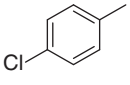
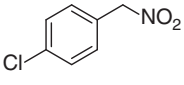
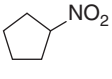
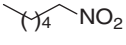
A more general protocol provides the arylation of primary nitroalkanes (different from nitromethane), via Pd-catalyzed reaction with aryl bromide or chlorides (Scheme 1.19) [41].

More detailed applications are reported in Chapter 6.



Scheme 1.17 Reductive nitromethylation of aldehydes.

Table 1.5 Nitration of alkanes (selected examples).

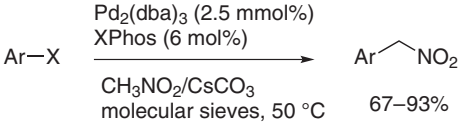
Substrate	Nitrating agent	Nitroalkane	Yield (%)
	NHPI (NO_2)		63
	NAPI (HNO_3)		69
	NAPI (NO_2)		69
	NHPI (HNO_3)		70
	NHPI (NO_2)		54
	NHPI (NO_2)		65

1.6.2 Nitroalkylation of Allylic Esters

Pd catalyzes even the asymmetric allylic alkylation of cyclic allyl esters [42] in the presence of *O*,*N*-bis-trimethylsilylacetamide (BSA) as base and a chiral biphosphine ligand (Table 1.6). The method allows a practical way to primary chiral nitroalkanes with an extra carbon atom.

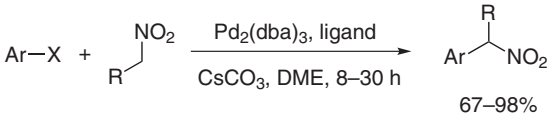
1.6.3 Nitroalkylation of Allylic Alcohols

Unactivated nitroalkenes (mainly nitromethane) can be added to vinyl epoxides, under Pd(0) catalysis, affording nitroalkenols (Scheme 1.20).



Selected examples:
Ar = Ph, *p*-$MeOC_6H_4$, *p*-$CF_3C_6H_4$, *o*-BrC_6H_4, *o*-$NO_2C_6H_4$

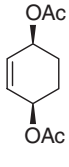
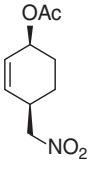
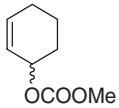
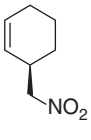
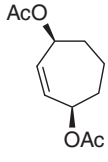
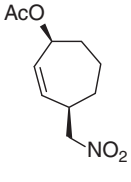
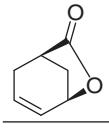
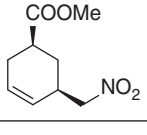
Scheme 1.18 Nitromethylation of aryl halides.

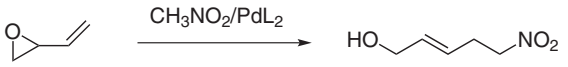


Selected examples:
Ar= Ph, *p*-$MeOOCC_6H_4$, *p*-$MeOC_6H_4$, *p*-$Me_2NC_6H_4$, *o*-$NO_2C_6H_4$
R= Me, Et, $MeOOC(CH_2)_2$
X= Cl, Br

Scheme 1.19 Nitroalkylation of aryl halides.

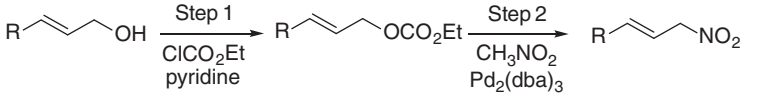
Table 1.6 Asymmetric nitromethylation of cyclic allyl esters (selected examples).

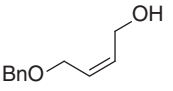
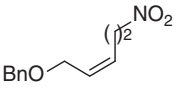
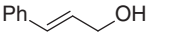
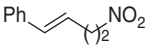
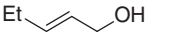
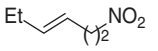
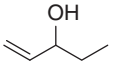
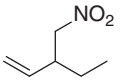
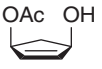
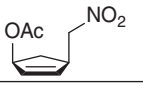
Substrate	Reaction conditions	Nitroalkane	Yield (%), (ee)
	CH_3NO_2/CH_2Cl_2, $Pd_2(dba)_3$, ligand, BSA		82 (99%)
	CH_3NO_2/CH_2Cl_2, $Pd_2(dba)_3$, ligand, Bu_4NCl/BSA		99 (99%)
	CH_3NO_2/CH_2Cl_2, $Pd_2(dba)_3$, ligand, BSA		84 (99%)
	CH_3NO_2/CH_2Cl_2, $Pd_2(dba)_3$, ligand, Bu_4NCl/BSA		74 (99%)



Scheme 1.20 Nitroalkanes addition to vinylepoxides under Pd(0) catalysis.

Table 1.7 Two-step process of nitro alkylation of allylic alcohols (selected examples).



Allylic alcohol	Nitroalkane	Yield (%)
		62
		74
		70
		71
		63

Developing this result, Deardorff et al. [43] reported a two-step process for nitromethylation of allylic alcohols that include (i) the preparation of the corresponding allylic carbonate and (ii) the addition of nitromethane, under $Pd_2(dba)_3$ catalysis.

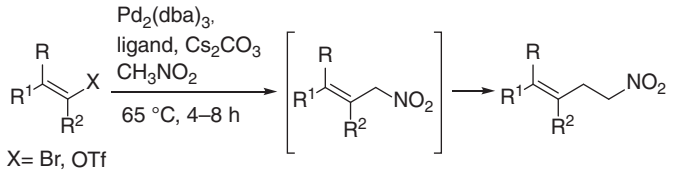
So, this procedure represents a useful method for the synthesis of functionalized nitroalkanes and some of the most representative examples are reported in Table 1.7.

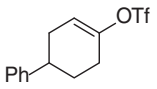
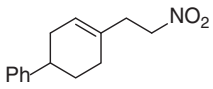
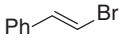
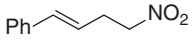
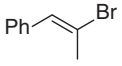
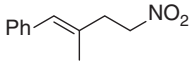
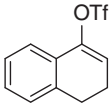
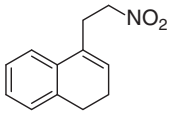
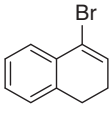
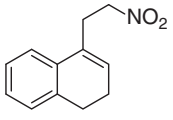
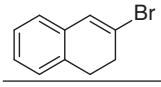
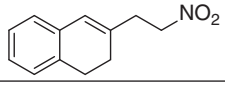
1.6.4 Two-Carbon Homologation of Vinyl Triflates and Bromides

Palladium catalyzes a two-carbon homologation of vinyl bromides (or triflates) via reaction with nitromethane and in the presence of Cs_2CO_3 as base, giving access to homoallylic nitrocompounds (Table 1.8) [44].

The process exploits the anion stabilizing effect and the leaving properties of the nitro group to generate the homoallylic nitro products via a tandem cross-coupling/π-allylation sequence of the alkenyl derivatives with nitromethane. Following this method a variety of homoallylic nitro compounds can be easily obtained.

Table 1.8 Two carbon homologation of vinyl bromides or triflates (selected examples).



Substrate	Nitroalkane	Yield (%)
		76
		69
		69
		74
		83
		93

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