Nitro compounds as useful reagents for the synthesis of dicarbonyl derivatives

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This review is dedicated to Prof. Giuseppe Bartoli on the occasion of his 65th birthday

Abstract

The reaction of functionalized nitroalkanes with electrophiles such as Michael acceptors and aldehydes is one of the most exploited procedures for the synthesis of new carbon-carbon bonds. Conversion of the nitro group in the adduct into a carbonyl derivative usually provides a rapid entry to dicarbonyl systems that are amenable to further synthetic transformation into a plethora of important targets.

Keywords: Conjugate addition, cycloalkanones, dicarbonyl derivatives, Nef reaction, nitroaldol reaction, nitroalkanes

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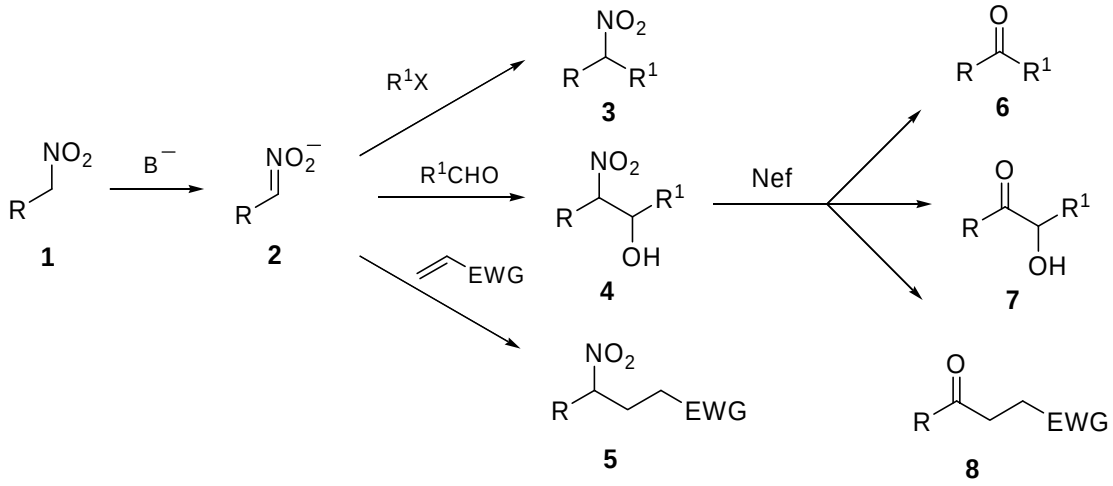
1. Introduction

Polyfunctionalized derivatives containing a dicarbonyl moiety are valuable intermediates in organic synthesis since they can be transformed into a plethora of important target compounds such as cyclopentenones, furans, pyrroles, thiophenes and other heterocyclic systems.[1–8] Classical methods for the synthesis of dicarbonyl derivatives usually involve an addition reaction of a metal enolate with a carboxylic acid ester or with a Michael acceptor. The former procedure is also referred as the Claisen condensation and provides a straightforward entry to 1,3-dicarbonyl derivatives,[9,10] and the latter leads to the formation of 1,5-dicarbonyl frameworks.[11] A viable access to 1,4-dicarbonyl systems using such procedures is not an easy task since it would involve a conjugate addition between an umpoled acyl anion synthon and a Michael acceptor. Nitroalkanes are a valuable source of stabilized carbanions since the high electron-withdrawing power of the nitro group provides an outstanding enhancement of the hydrogen acidity at the α-position (cf. pk_a $MeNO_2$=10).[12–16] Nitronate anions **2** that can be generated from nitroalkanes **1** using a wide range of bases, act as carbon nucleophiles with common electrophiles including haloalkanes,[17] aldehydes,[18,19] and Michael acceptors,[20] leading to carbon-carbon bond formation (Scheme 1).



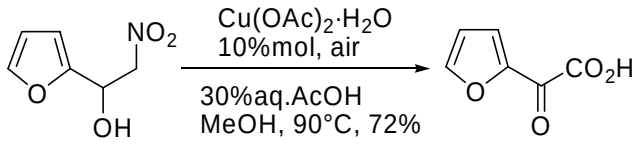
Scheme 1

A further option is represented by the conversion of the nitro group into a carbonyl group, leading to carbonyl derivatives **6-8**, a transformation widely known as the Nef reaction, that ultimately leads to a reversal in the polarity of the neighboring carbon atom from nucleophilic to electrophilic.[21,22] The original procedure for the nitro to carbonyl transformation, as described by Nef, was essentially the hydrolysis in strongly acidic conditions of a nitronate salt produced by basic treatment of a nitroalkane. The harsh conditions in which this conversion is usually carried out (pH < 1) have spurred on the development of alternative methods that can be performed in

oxidative, reductive, as well as almost neutral, conditions. The aim of this review is to discuss the utilization of nitroalkanes as nucleophilic reagents for the synthesis of dicarbonyl derivatives using a strategy involving a nucleophilic addition of the nitro derivative followed by a nitro to carbonyl conversion. Although these procedures are usually accomplished by a two-step synthesis, there are several examples in which this overall transformation can be carried out in a 'one-pot' system thus realizing a more efficient process.

2. 1,2-Dicarbonyl and 1,3-dicarbonyl derivatives

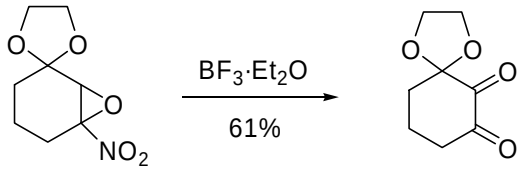
Nitro compounds have been used only occasionally in the synthesis of 1,2- and 1,3-dicarbonyl derivatives. The oxidative Nef reaction carried out on the products of nitroaldol addition such as **9** affords α-keto acids **10** or aldehydes using molecular oxygen in the presence of copper salts (Scheme 2).[23]



9 **10**

Scheme 2

Cyclic nitroalkenes can be converted into α-nitro epoxides **11** using metal salts of *t*-butyl hydroperoxide. Cleavage of the epoxide ring in acidic conditions directly affords 1,2-dicarbonyl derivatives **12** (Scheme 3).[24]



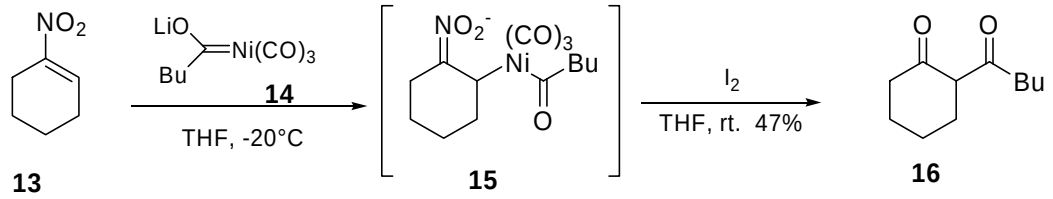
11 **12**

Scheme 3

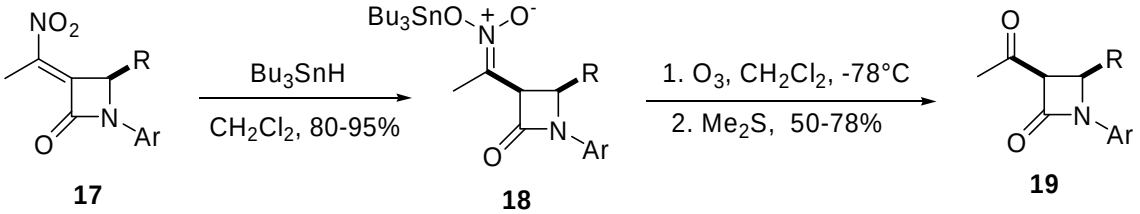
The reaction of the nickel acylate complex **14** with nitroalkenes such as **13** gives the corresponding addition products **15** that, by treatment with iodine, afford the 1,3-dicarbonyl derivatives **16**. Iodine provides cleavage of the nickel adduct and of the nitronate anion in a tandem process (Scheme 4).[25]

The reduction of nitroalkenes such as **17** with Bu_3SnH occurs in neutral conditions, giving the corresponding stannylnitronates **18**.[26] These nitronates can be oxidized to the parent carbonyl

derivatives using ozone at low temperatures. This procedure is particularly effective in the synthesis of β-lactam building blocks **19** (Scheme 5).



Scheme 4



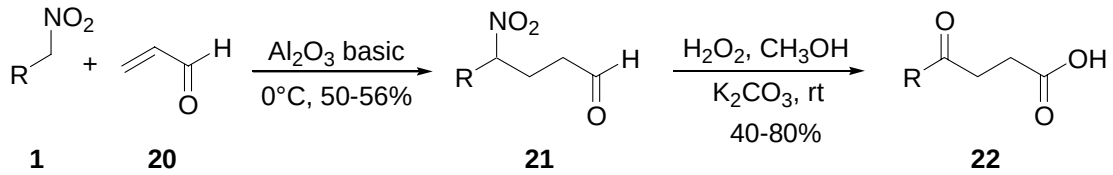
R = Ph, Ar = Ph
R =2,5-$Me_2C_6H_3$, Ar = Ph
R = PhCH=CHMe, Ar = 4-$MeOC_6H_4$

Scheme 5

3. 1,4-Dicarbonyl derivatives

3.1 Synthesis of 1,4-dicarbonyls using a conjugate addition–Nef reaction

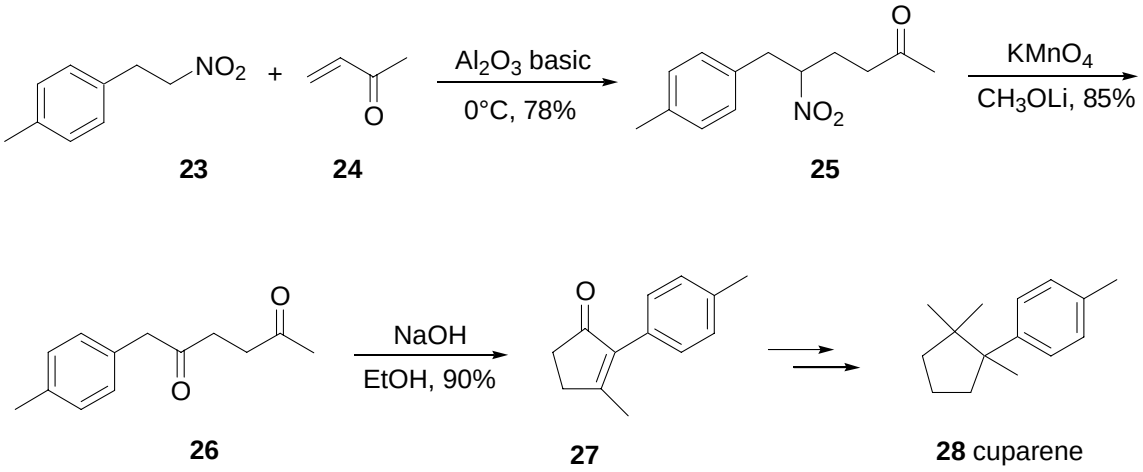
As previously stated, conjugate addition of nitroalkanes to enones and enoates provides a rapid entry to the corresponding γ-nitro carbonyl derivatives that can undergo a Nef reaction giving 1,4-dicarbonyl compounds. This procedure represents one of the most exploited methods to prepare such difunctionalized derivatives that find a number of applications in the synthesis of important target molecules. The Michael addition of nitroalkanes to electron-poor olefins can be realized using basic promoters such as DBU,[27] TMG,[28] triphenylphospine,[29] fluoride salts[30] and hydroxide (alkoxide) anions.[31–34] Besides these procedures that work in homogeneous conditions a number of methods using basic catalysts that operate in heterogeneous systems can be employed profitably to carry out a conjugate addition. Basic alumina is a formidable promoter of such nucleophilic additions that can be accomplished even in solvent-less conditions. Reaction of nitroalkanes **1** with acrolein **20** allows a rapid formation of the adduct **21** that upon oxidative Nef reaction leads to the corresponding 4-oxoalkanoic acid derivative **22** (Scheme 6).[35]



1 **20** **21** **22**

Scheme 6

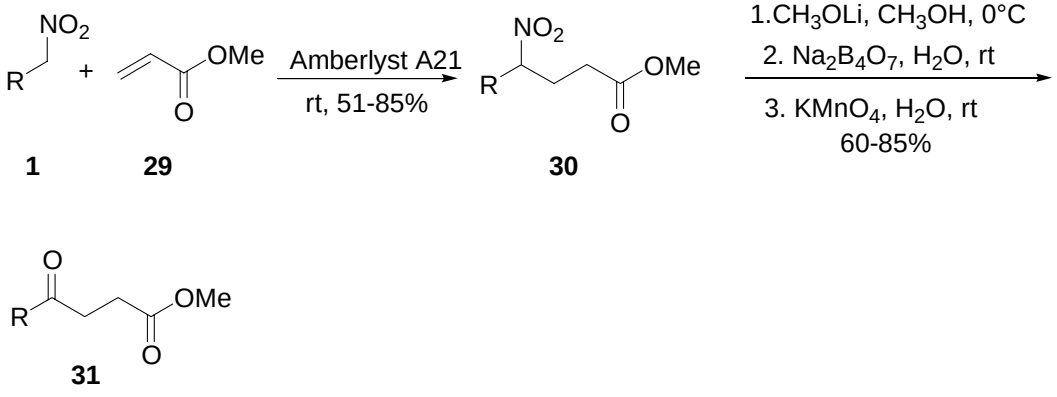
A related procedure provides a rapid synthesis of a functionalized cyclopentenone derivative **27**, an advanced intermediate for the preparation of the sesquiterpene cuparene **28** (Scheme 7).[36]



23 **24** **25** **26** **27** **28** cuparene

Scheme 7

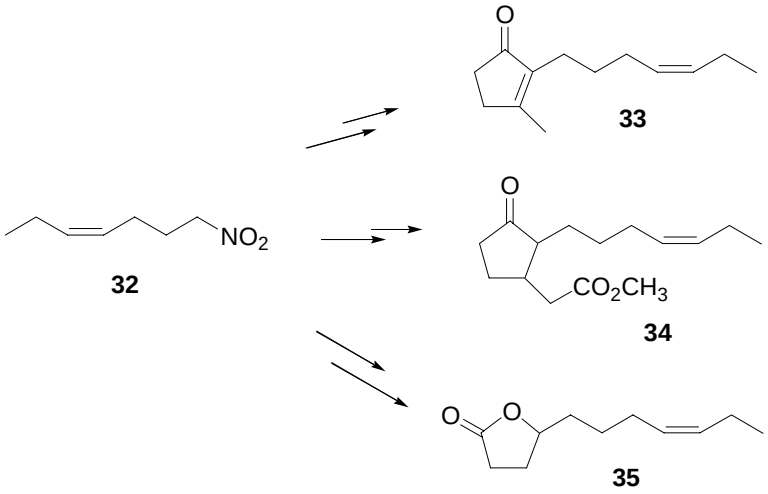
Amberlyst A21 is a macroreticular resin that is particularly efficient in promoting conjugate addition of nitro derivatives **1** to acrylate esters **29** (Scheme 8).[37] The resulting adducts **30** can be easily converted into the 1,4-dicarbonyl compounds **31**.



1 **29** **30** **31**

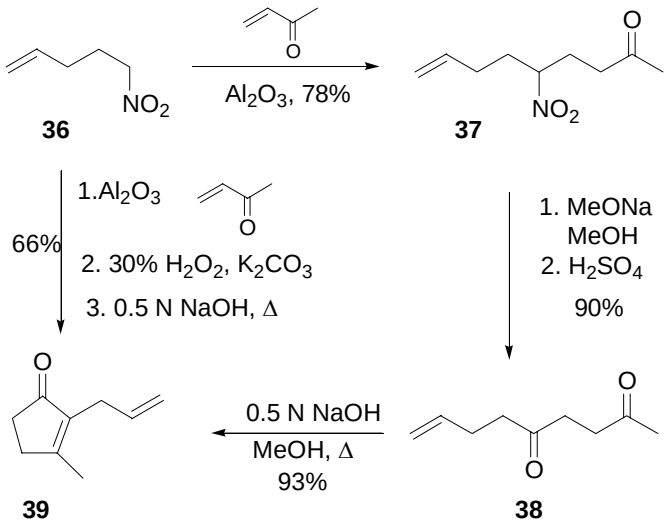
Scheme 8

Following this strategy, a number of synthetically useful five-membered derivatives **33-35** can be finally prepared from the simple and easily available (*Z*)-1-nitro-4-heptene **32** (Scheme 9).[38]



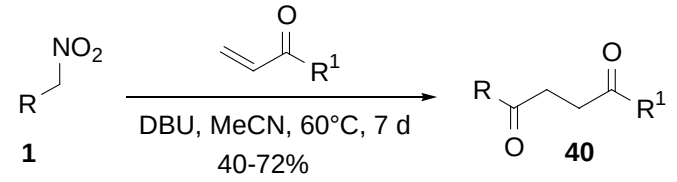
Scheme 9

Allylrethrone **39** is an important component of an insecticidal pyrethroid and its preparation can be realized in three distinct steps, starting from the nitroalkene **36** and methyl vinyl ketone (Scheme 10).[39] The obtained Michael adduct **37** is converted into the diketone **38** by a hydrolytic Nef reaction and is then cyclized to allylrethrone **39** under basic conditions. Alternatively, the same process can be realized in a 'one-pot' reaction, using hydrogen peroxide to carry out the nitro to carbonyl conversion.



Scheme 10

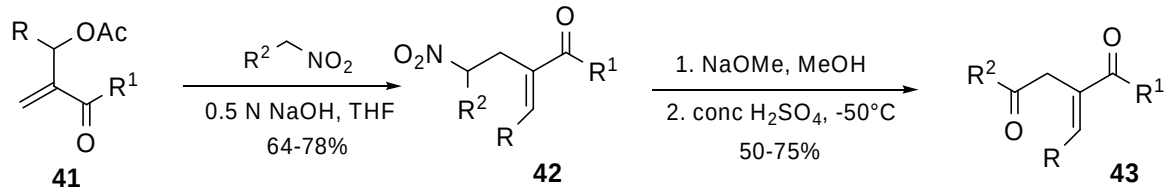
The ability of DBU to promote a conjugate addition of nitroalkanes to enones as well as a Nef reaction on secondary nitroalkanes, can be used in a tandem process that permits the direct synthesis of γ-diketones and γ-keto esters **40** (Scheme 11).[40]



R = *n*-Bu, *n*-C_5H_{11}, $PhCH_2$, $HO(CH_2)_4$
R^1 = Me, OMe

Scheme 11

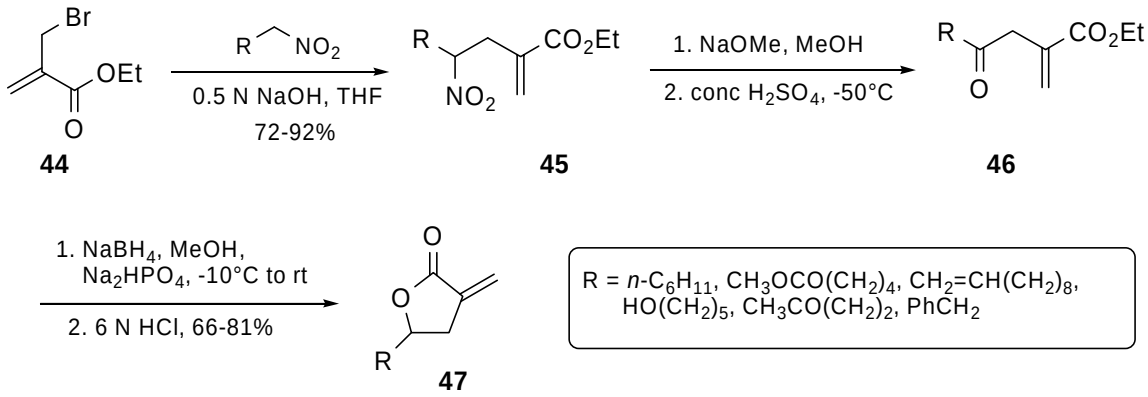
The allylic acetates **41** obtained from the Baylis–Hillman procedure, react with nitroalkanes through a conjugate addition–elimination process that leads to the formation of the unsaturated esters **42**.[41] An hydrolytic nitro to carbonyl conversion on these compounds efficiently affords the (*E*)-alkylidene-1,4-diketones **43** (Scheme 12).



R = Et, *n*-Pr, *i*-Pr, *n*-C_6H_{11} $R^1 = R^2$ = Me, Et

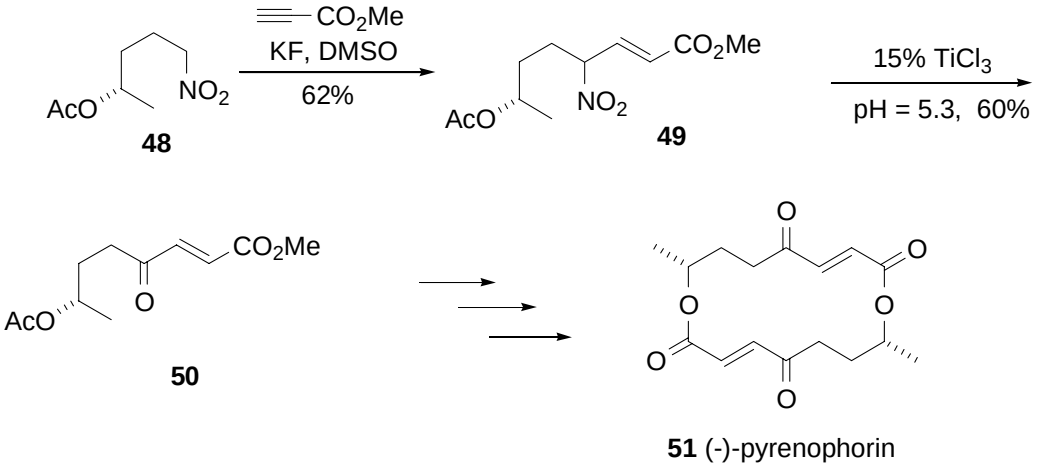
Scheme 12

A related procedure involves ethyl (2-bromomethyl)acrylate **44** as a Michael acceptor that behaves similarly to the acetates **41** in the reaction with nitroalkanes, giving the nitro derivatives **45**. The nitro group is then transformed into keto ester **46** by a procedure involving hydrolytic cleavage. A subsequent reduction with $NaBH_4$ in the presence of Na_2HPO_4 leads to the corresponding alcohol that by a spontaneous lactonization gives *exo*-methylene butyrolactones **47** in good overall yields (Scheme 13).[42]



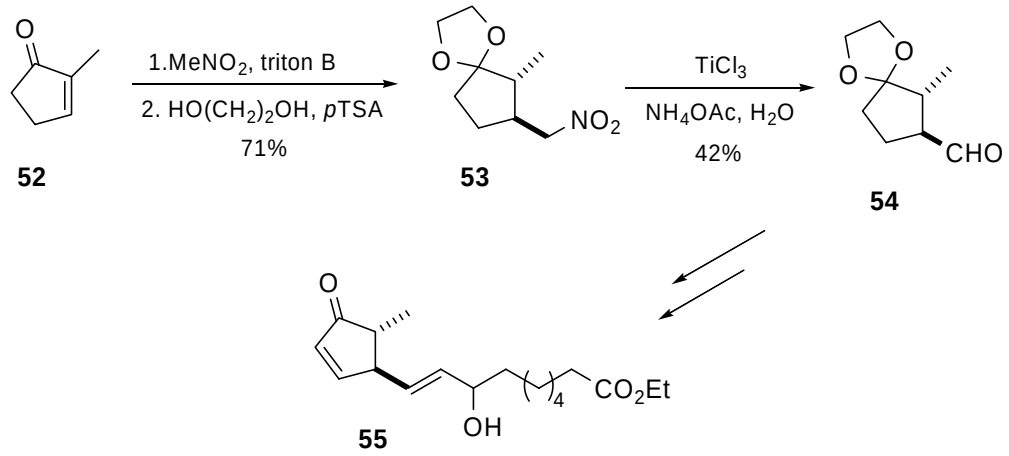
Scheme 13

The enedione system is present in many natural products having an interesting biological activity. Conjugate addition of the chiral nitroacetate **48** to methyl propiolate gives the corresponding adduct **49** that is converted into the enedione **50** by a McMurry reaction involving utilization of $TiCl_3$.[43] This derivative can be converted into optically active (*R*,*R*)-(-)-pyrenophorin **51**, an antifungal macrolide dilactone (Scheme 14).[44] A related strategy is also effective for the total synthesis of macrolide (*R*)-patulolide A.[45]



Scheme 14

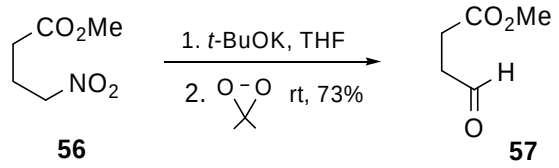
The cyclopentenone unit is a common motif in a wide array of biologically active substances. The cyclopentenone **52** reacts with nitromethane giving a *trans*-substituted nitro derivative that is protected at the carbonyl group as the ketal **53**. A Nef reaction on **53** using $TiCl_3$ gives the aldehyde **54** which is converted into the cyclopentenone **55**, which shows algicidal properties (Scheme 15).[46]



52 **53** **54** **55**

Scheme 15

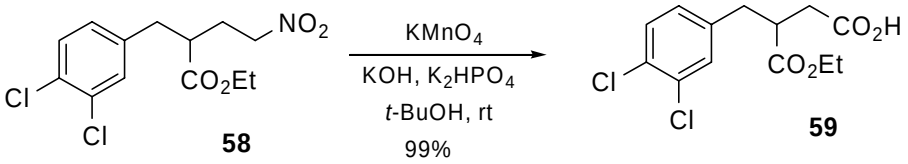
Primary nitroalkanes can be transformed into aldehydes or carboxylic acids depending on the method used to perform the Nef reaction. The aldehydes **57** can be obtained in good yield by oxidation of the potassium nitronate of primary 4-nitro esters **56** using dimethyldioxirane, a reagent that can be prepared readily by reaction of Oxone® with acetone (Scheme 15).[47]



56 **57**

Scheme 16

Buffered permanganate solutions (pH = 11) can oxidize primary nitroalkanes such as **58** into alkanoic acids **59** without affecting other functions such as esters, amides, primary alcohols or acetals (Scheme 17).[48] This procedure is particularly useful in the preparation of monoesters of 2-substituted succinic acids.[49]

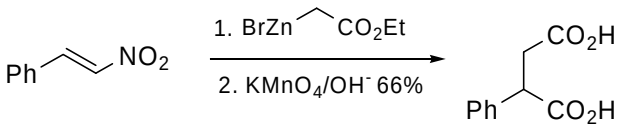


58 **59**

Scheme 17

Conversely, 2-substituted succinic acids **61** can be obtained by reaction of nitroalkenes **60** with Reformatsky reagents obtained from α-bromoesters (Scheme 18).[50] The intermediate adduct

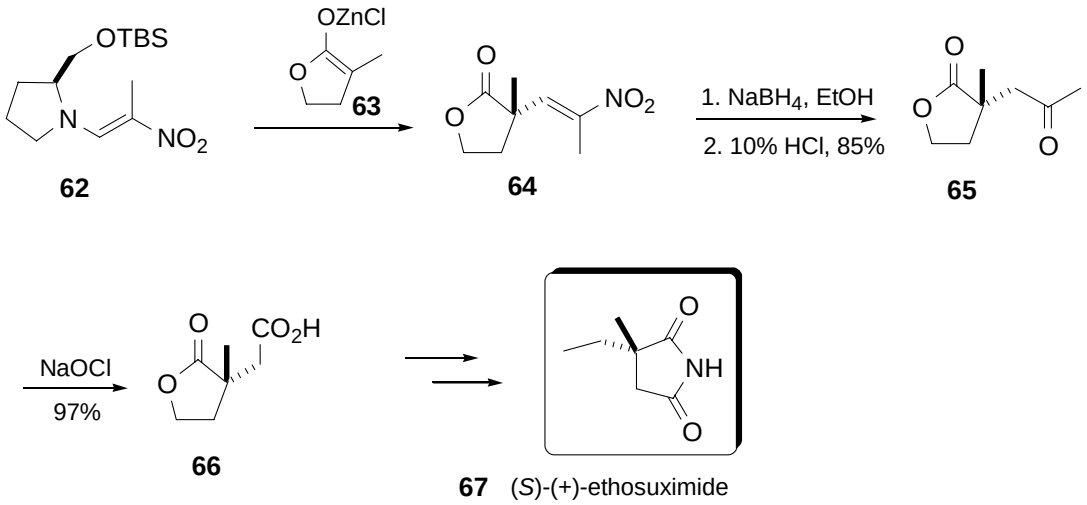
is readily oxidized using alkaline permanganate solution until the introduced ethyl ester function is fully hydrolyzed.



60 **61**

Scheme 18

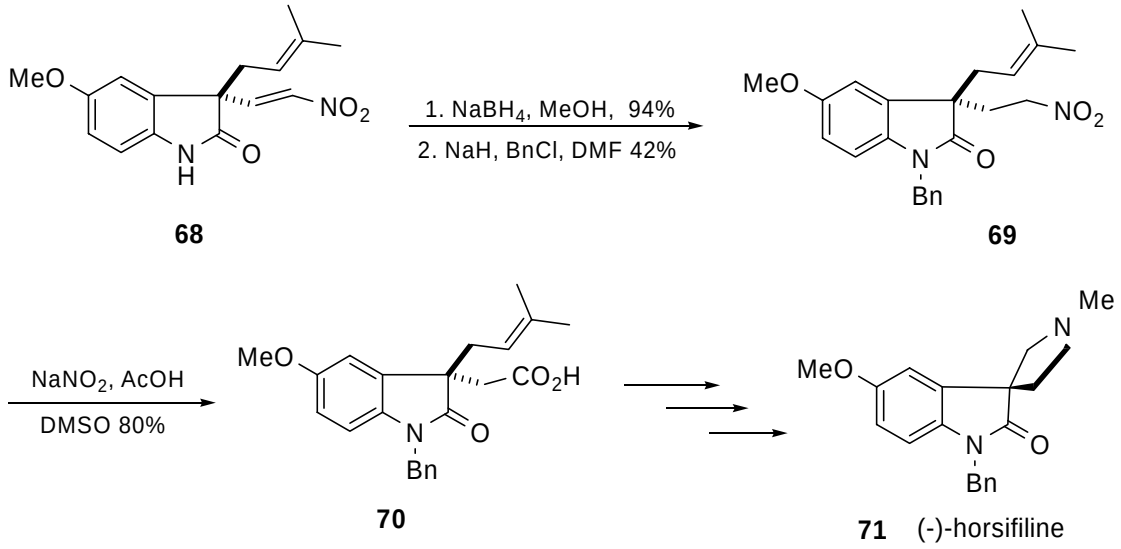
Nitro-olefins can be converted directly into carbonyl derivatives using reductive methods.[51,52] The chiral nitroenamine **62**, obtained from *L*-proline, reacts with the zinc ester enolate **63**, giving the corresponding adduct **64**. The chiral nitroolefin lactone **64** can be transformed into the keto lactone **65** by a tandem nitroolefin reduction–nitronate hydrolysis (Scheme 19). The keto group is cleaved to the parent carboxylic acid **66** by a haloform reaction and ultimately leads to (*S*)-ethosuximide **67**.[53]



62 **64** **65** **66** **67** (*S*)-(+)-ethosuximide

Scheme 19

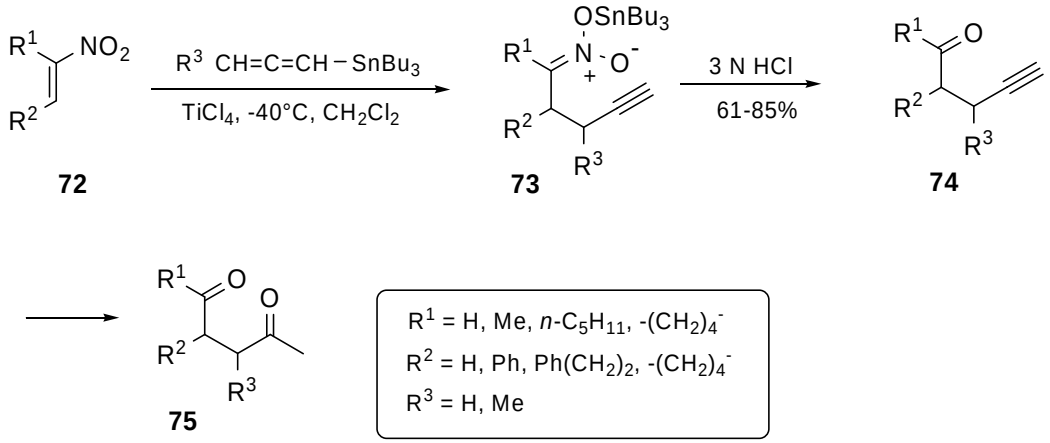
The same strategy can be used in the total synthesis of the oxindole alkaloid (-)-horsfiline **71**. Protection of the indole nitrogen and reduction of nitroolefin **68** affords the nitroalkane **69** that is converted into the carboxylic acid **70** with $NaNO_2$. Further synthetic transformations lead to the preparation of (-)-horsfiline **71** (Scheme 20).[54]



68 **69** **70** **71** (-)-horsifiline

Scheme 20

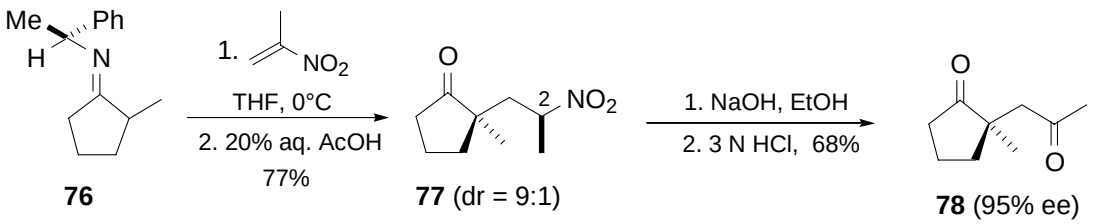
Propargylation of the nitroalkenes **72** can be realized using (tributylstannyl)allenes in the presence of $TiCl_4$.[55] Nitronates **73** obtained as intermediates can be hydrolyzed to the corresponding ketones **74** using 3N HCl. The obtained α-propargylic ketones **74** are precursors of useful building blocks such as the 1,4-diketones **75** (Scheme 21).



72 **73** **74** **75**

Scheme 21

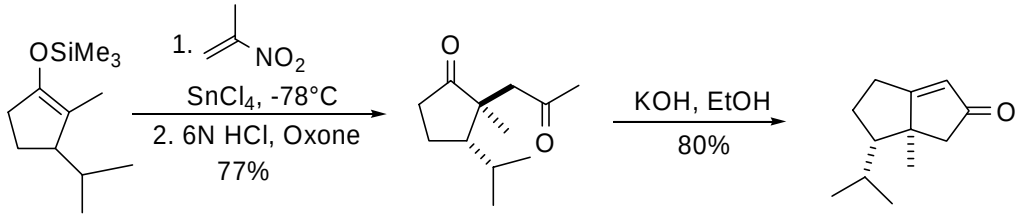
The chiral imine **76** obtained from 2-methylcyclopentanone reacts with 2-nitropropene in a highly regioselective fashion giving a diastereomeric mixture of epimers at C-2, **77**. The subsequent Nef reaction carried out by acidic hydrolysis of the nitronate anion affords the diketone **78** in 95% *ee* (Scheme 22).[56]



76 **77** (dr = 9:1) **78** (95% ee)

Scheme 22

The high reactivity of 2-nitropropene allows its reaction even with the silyl enol ether **79** in the presence of $SnCl_4$ to give the corresponding adduct, which is converted into diketone **80** using Oxone® (Scheme 23).[57] This compound is then transformed by an intramolecular aldol condensation into the bicycloketone **81** that is an important intermediate for the synthesis of polyquinane derivatives.

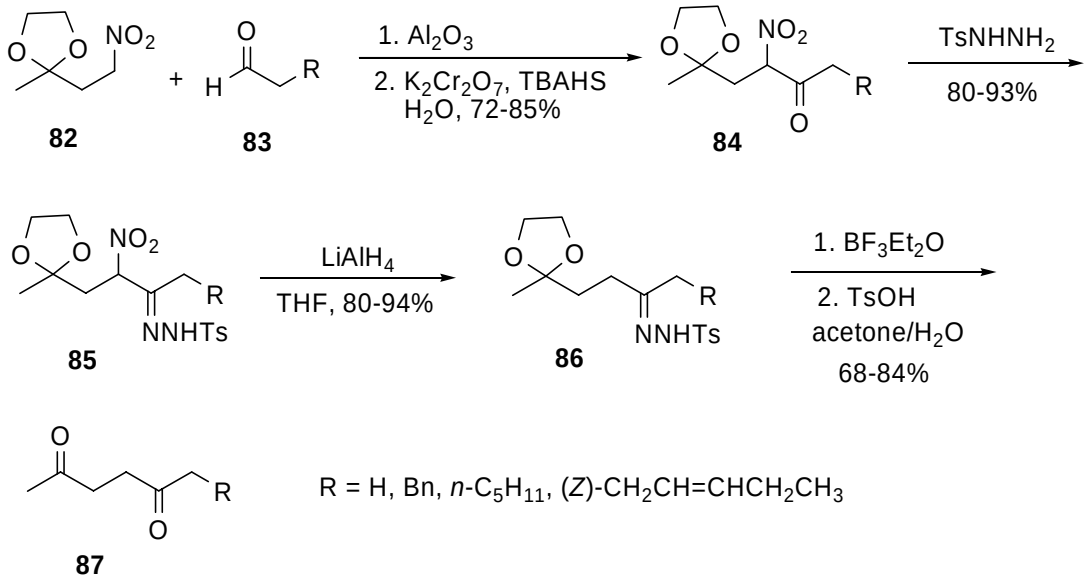


79 **80** **81**

Scheme 23

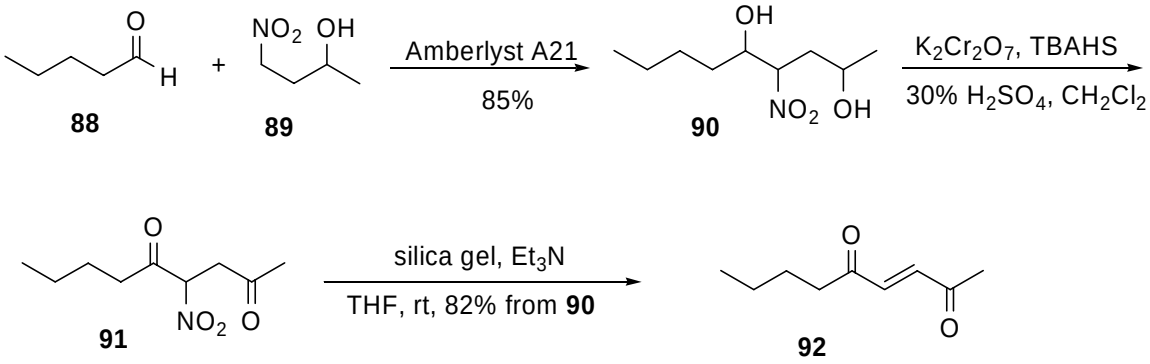
3.2 Synthesis of 1,4-dicarbonyls using a nitroaldol and alkylation reactions

The products obtained from a nitroaldol reaction are usually 1,2-nitro alcohols, unless these derivatives undergo elimination of water under the reaction conditions to afford the corresponding nitroalkenes.[58] At this point, the introduction of a carbonyl group in the molecular framework can be realized by oxidation of the hydroxy group of the nitro alcohol, followed by a reductive denitration in order to eliminate the nitro group. Alternatively, the nitro group in the nitroalkene moiety can be converted directly into a carbonyl group by the usual Nef reaction. Condensation of the nitro dioxolane **82** with aldehydes **83** affords the corresponding nitro alcohols that can be oxidized in a 'one pot' procedure to the parent nitro ketones **84** (Scheme 24).[59,60] This derivative can be denitrated using a procedure that involves its conversion into a tosylhydrazone **85** followed by reduction with $LiAlH_4$.[61] Cleavage of the protecting groups of the obtained compounds **86** in acidic conditions affords the 1,4-diketones **87** in satisfactory overall yield.



Scheme 24

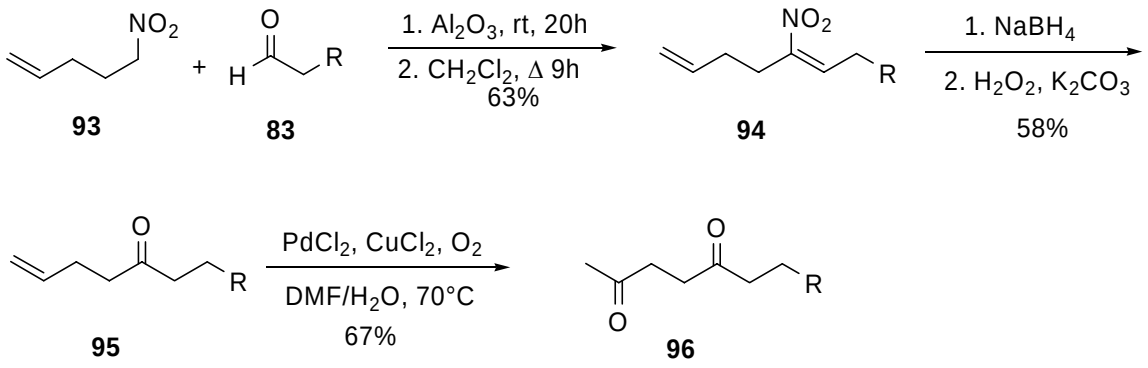
The ability of the nitro group to act as a good leaving group in elimination reactions can be used for the preparation of (*E*)-enediones that are valuable intermediates for the synthesis of biologically active compounds. (*E*)-Non-3-ene-2,5-dione **92** is the main component of the volatile compounds obtained from the cephalic secretion of workers of *Trigona tataira*. Nitroaldol reaction between aldehyde **88** and the nitro alcohol **89** affords the corresponding nitro diol **90** that upon oxidation under phase-transfer conditions of the hydroxy groups, leads to the nitro diketone **91** (Scheme 25).[62,63] Base- assisted elimination of nitrous acid from compound **91** allows the total synthesis of enedione **92** in 70% overall yield.



Scheme 25

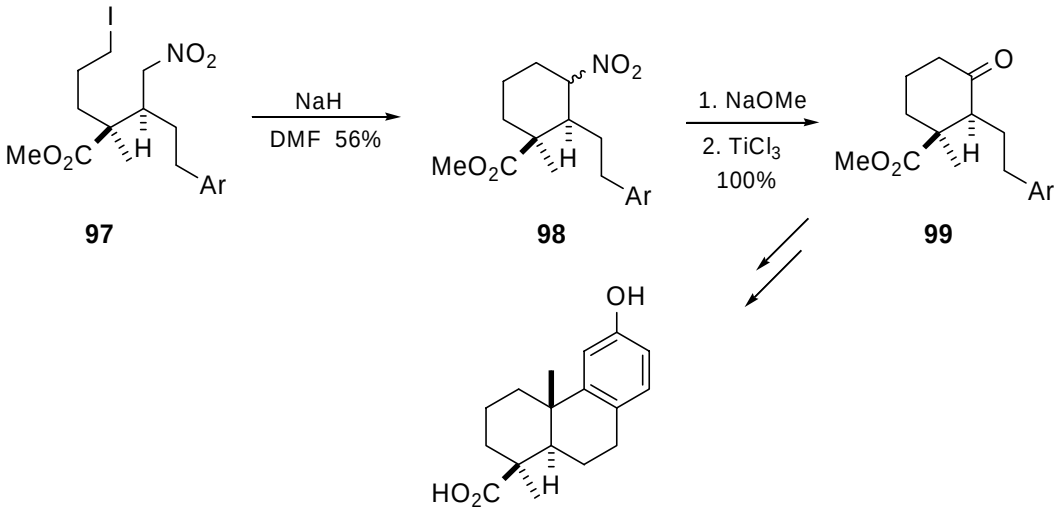
As previously stated, nitroalkenes such as **94** can be obtained directly by a nitroaldol–elimination that can be carried out in a 'one pot' process from nitro derivative **93** and various aldehydes **83** (Scheme 26).[64] Reduction of the nitroalkene double bond using $NaBH_4$ produces an

intermediate sodium nitronate that can be oxidized using hydrogen peroxide in basic conditions to give ketone **95**. The second carbonyl unit can be introduced by a Wacker oxidation using molecular oxygen in the presence of catalytic amounts of $PdCl_2$ and $CuCl_2$ thus affording the 1,4-diketone **96**.



Scheme 26

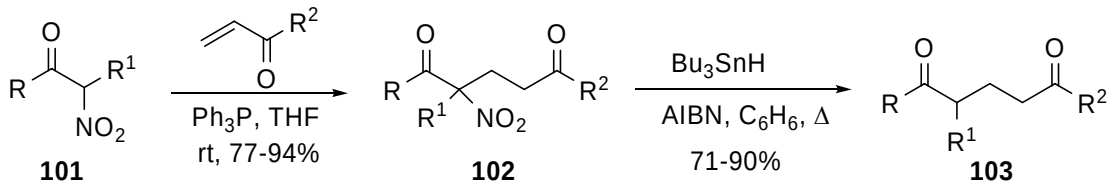
Although C-alkylation of nitronate anions is a less common process than the nitroaldol condensation, it can be particularly effective in intramolecular reactions. Ring-closure, of the nitroiodide **97**, using NaH to generate the nitronate anion, affords the nitrocyclohexane **98** that is converted into the cyclohexanone **99** using $TiCl_3$. (Scheme 27).[65,66] This intermediate can be transformed into (+)-podocarpic acid **100** in a few steps.



Scheme 27

4. 1,5-Dicarbonyl and 1,6-dicarbonyl derivatives

2-Nitro- ketones form the corresponding nitronate anion in weakly basic conditions, as a result of the additional activating effect of the carbonyl group.[67,68] The nitro group in 2-nitro ketones is particularly prone to undergoing a radical-induced denitration using Bu_3SnH, giving rise to the corresponding reduction product.[69] Michael addition of the α-nitro ketones **101** with enones affords the nitro diketones **102** that upon denitration give the 1,5-dicarbonyl derivatives **103**, usually in good yield (Scheme 28).[70,71]

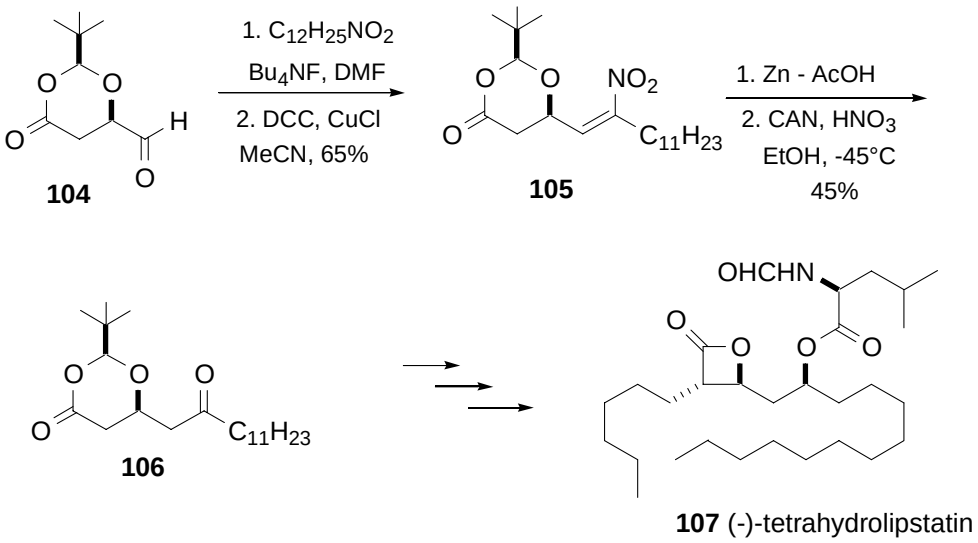


R = Ph, *n*-C_7H_{15}, *n*-Pr, *n*-Bu R^1= H, Me, Et R^2= H, Me

Scheme 28

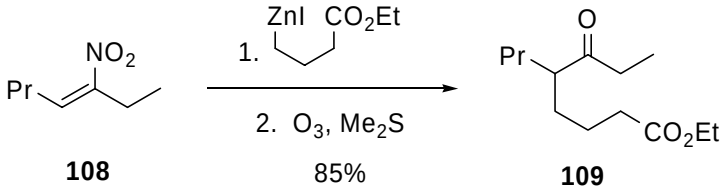
The conjugate addition of 2-nitro ketones is usually carried out in basic conditions,[72] but the easy enolization of these compounds offers the opportunity to realize this process even under solid acidic catalysis by SiO_2.[73]

The nitroaldol condensation can be used to prepare 1,5-dicarbonyl derivatives from 1,4-homologues. Reaction of aldehyde **104** with 1-nitrododecane followed by dehydration gives the nitroalkene **105** (Scheme 29).[74] The nitroalkene **105** is then converted into the ketoester derivative **106**, a pivotal intermediate for the synthesis of the pancreatic lipase inhibitor tetrahydrolipstatin, **107**.



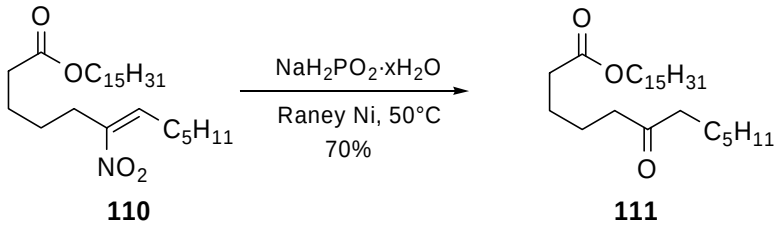
Scheme 29

Organozinc reagents bearing a terminal ester function can be profitably used for the preparation of the 1,6-dicarbonyl compound **109** by reaction with nitroalkenes **108** followed by a Nef reaction (Scheme 30).[75]



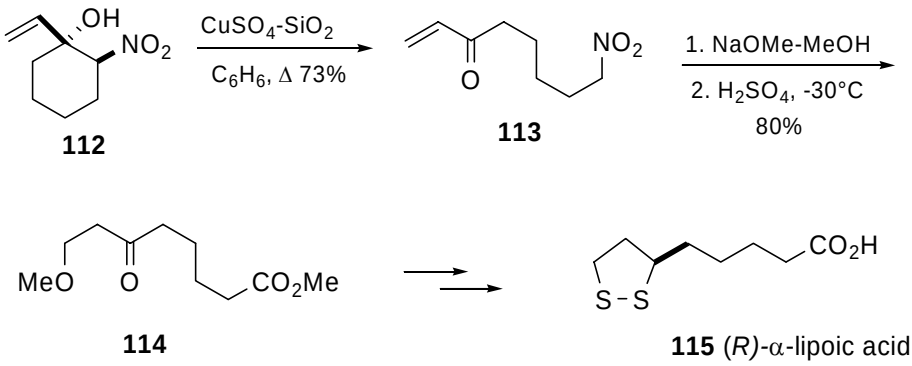
Scheme 30

The nitroalkene **110** is a common product obtained by a nitroaldol–elimination reaction that under a reductive Nef reaction gives the keto ester **111** in satisfactory yield (Scheme 31).[76] The alkyl appendage linked to the keto group can be suitably changed using different aldehydes during the nitroaldol reaction.



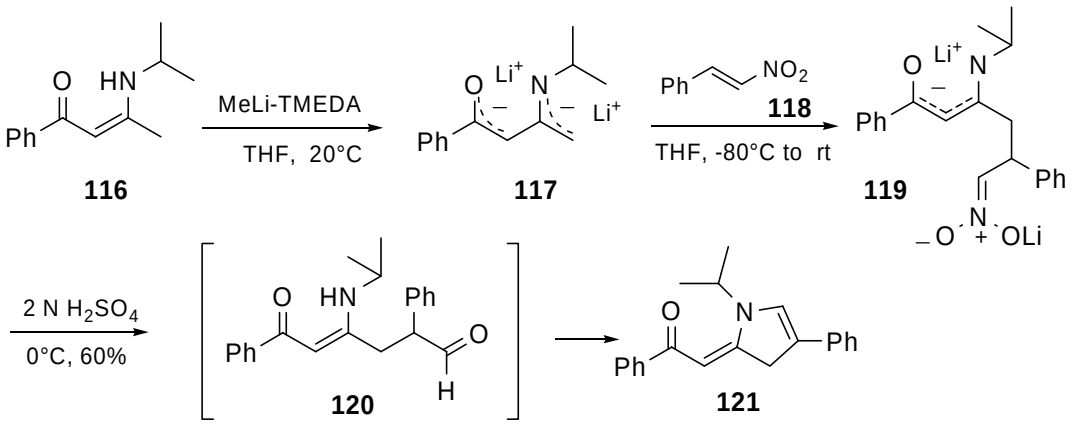
Scheme 31

A retro- nitroaldol reaction on the nitrocyclohexanol **112** gives the open-chain nitro ketone **113** that undergoes a tandem Michael addition-Nef reaction upon reaction with NaOMe, followed by quick acidification with H_2SO_4 to give the keto ester **114**. This derivative is a key intermediate in the synthesis of optically active (*R*)-α-lipoic acid **115** (Scheme 32).[77]



Scheme 32

The dianion of the β-enamino ketone **117**, prepared from **116**, reacts with nitrostyrene **118** at low temperature giving the corresponding nitronate adduct **119**. Upon quenching of this intermediate at 0°C with 2N H_2SO_4, the initially formed aldehyde, **120**, undergoes a rapid cyclization to the dihydropyrrole **121** in 60% overall yield (Scheme 33).[78]

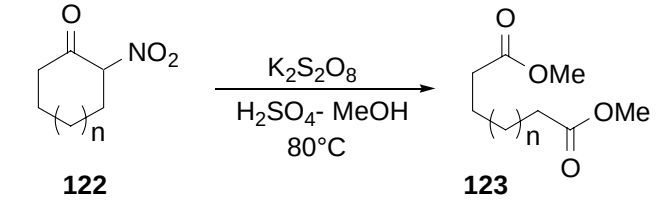


Scheme 33

5. α,ω-Dicarbonyl derivatives by ring cleavage of 2-nitrocycloalkanones

Retro-Claisen condensation of 2-nitrocycloalkanones represents a straightforward route to functionalized terminal nitro esters.[79] Coupling the ring cleavage of the cycle with a Nef reaction allows a direct preparation of α,ω-diester derivatives having an alkyl chain length that depends

on the ring size of the starting 2-nitrocycloalkanone. Potassium persulfate in methanol in the presence of sulfuric acid is able to cleave the 2-nitrocycloalkanones, **122**, giving the corresponding α,ω-dicarboxylic acid methyl esters **123** (Scheme 34).[80] The utilization of hydrogen peroxide in the presence of potassium carbonate starting from compounds **122** allows the preparation of α,ω-dicarboxylic acids and keto acids.[81]

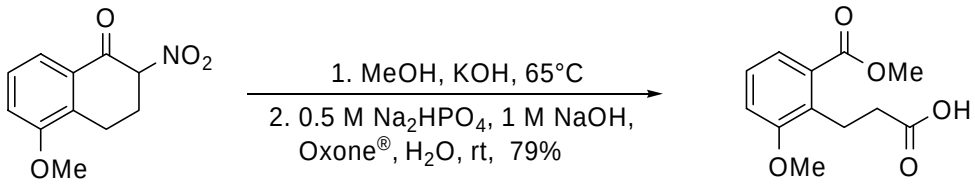


122 **123**

n = 0 (92%); 1 (93%); 2 (90%); 3 (86%); 4 (80%); 5 (81%); 6 (85%); 7 (88%); 10 (78%)

Scheme 34

α,ω-Dicarboxylic acids or their methyl monoesters such as **125** can be obtained regioselectively starting from 2-nitrocycloalkanones **124** using Oxone® in buffered conditions. The carbon atom originally bearing the nitro group is always converted into a free acid function (Scheme 35).[82]

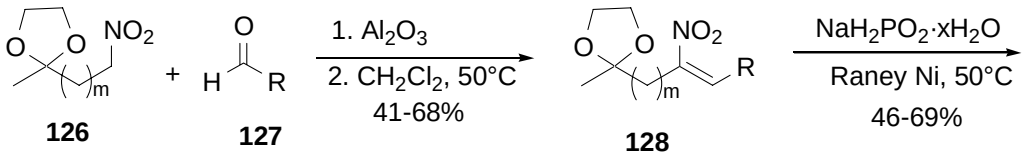


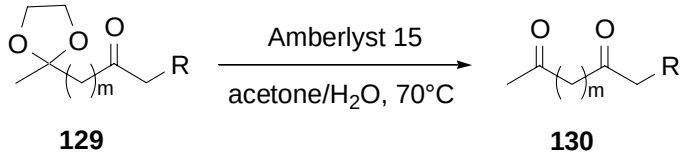
124 **125**

Scheme 35

6. Tunable syntheses of 1,n-dicarbonyl derivatives

Nitro ketones, protected at the carbonyl group as cyclic ketals, can be used as masked 1,n dicarbonyl synthons (n=3–5) for the preparation of various difunctionalized systems. Condensation of the nitro ketals **126** with aldehydes **127** followed by *in situ* elimination affords the nitroalkenes **128**. Such unsaturated derivatives are transformed into ketones **129** and, upon cleavage of the dioxolane ring, are finally converted into 1,n-diketones **130** (Scheme 36).[83]

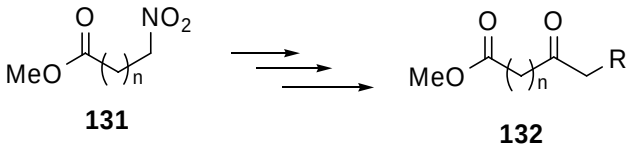




m	R	**130** yield(%)
1	*n*-$C_{10}H_{21}$	90
1	$Ph(CH_2)_2$	87
2	*n*-C_5H_{11}	97
2	*c*-C_6H_{11}	95
3	*n*-C_5H_{11}	90

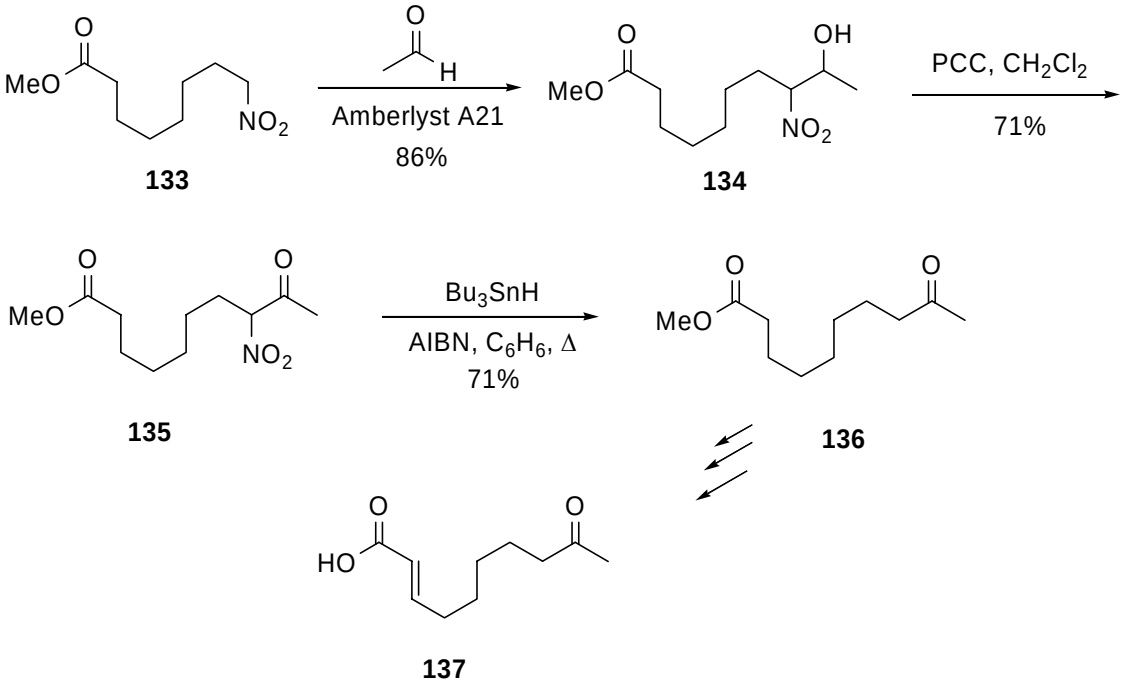
Scheme 36

A related procedure using different nitro esters **131** allows an efficient synthesis of [n+2]-keto esters **132** (n = 1–3) (Scheme 37).[84]



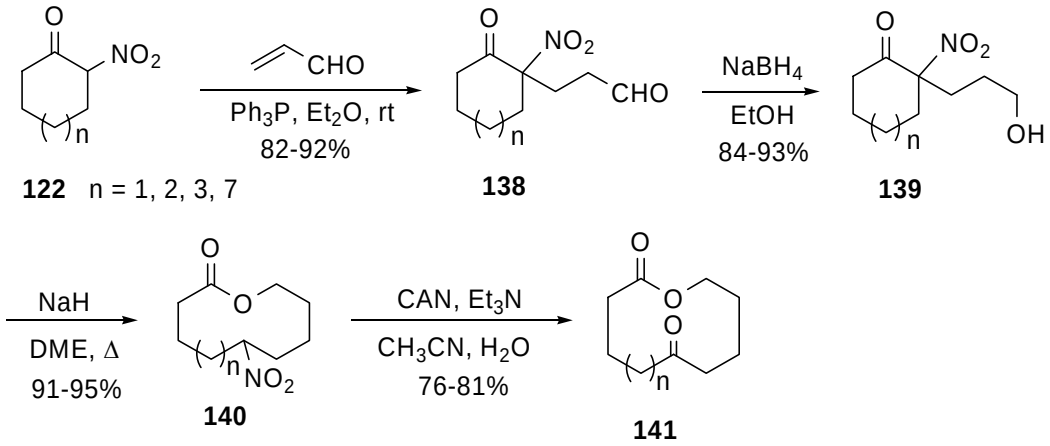
Scheme 37

Methyl 8-nitrooctanoate **133** can be used as starting material for the preparation of (*E*)-9-oxo-2-decenoic acid **137**, an important sex attractant of the queen bee, also implicated as a pheromone of termites (Scheme 38).[85] The overall procedure involves a nitroaldol reaction of **133** with acetaldehyde to give nitro alcohol **134** that is oxidized to the corresponding 2-nitro ketone **135**. Reductive denitration of compound **135** gives the 9-ketoester **136** that is subsequently converted into acid **137** in few steps.



Scheme 38

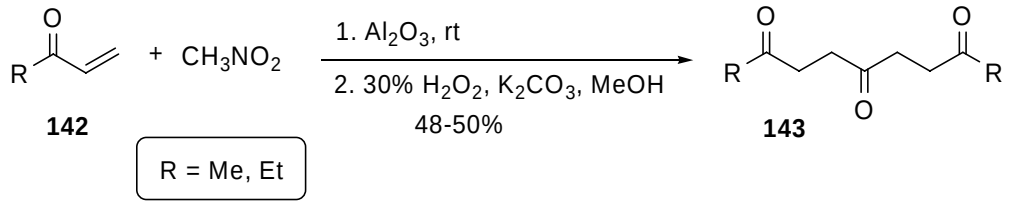
Conjugate addition of 2-nitrocycloalkanones **122** to acrolein gives the corresponding aldehydes **138** that upon reduction with $NaBH_4$ afford alcohols **139** (Scheme 39).[86] An intramolecular retro-Claisen cleavage promoted by NaH allows the preparation of macrolactones **140** that are converted into keto esters **141** by oxidative Nef reaction using cerium ammonium nitrate (CAN).



Scheme 39

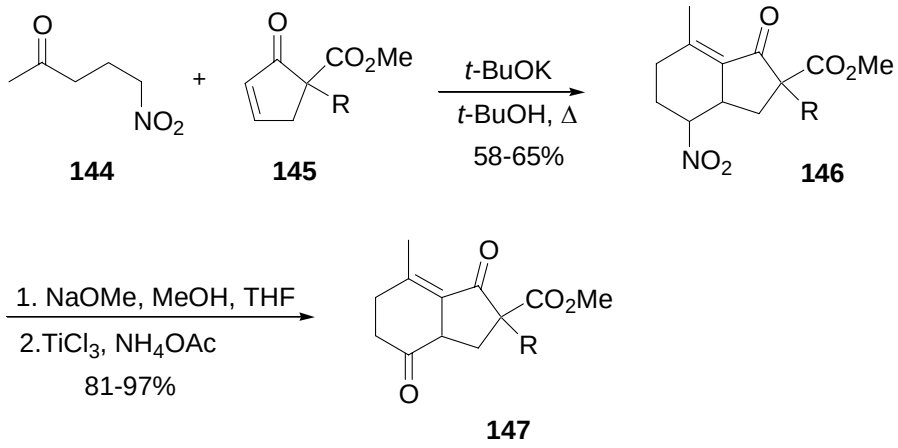
7. Tricarbonyl derivatives

The strategies described above for the preparation of 1,n-dicarbonyl derivatives are often amenable for the synthesis of compounds containing three or more carbonyl groups. Double conjugate addition of nitromethane to enones **142** followed by *in situ* Nef reaction of the resulting adducts provides a straightforward entry to 1,4,7-triketo derivatives **143** (Scheme 40).[87]



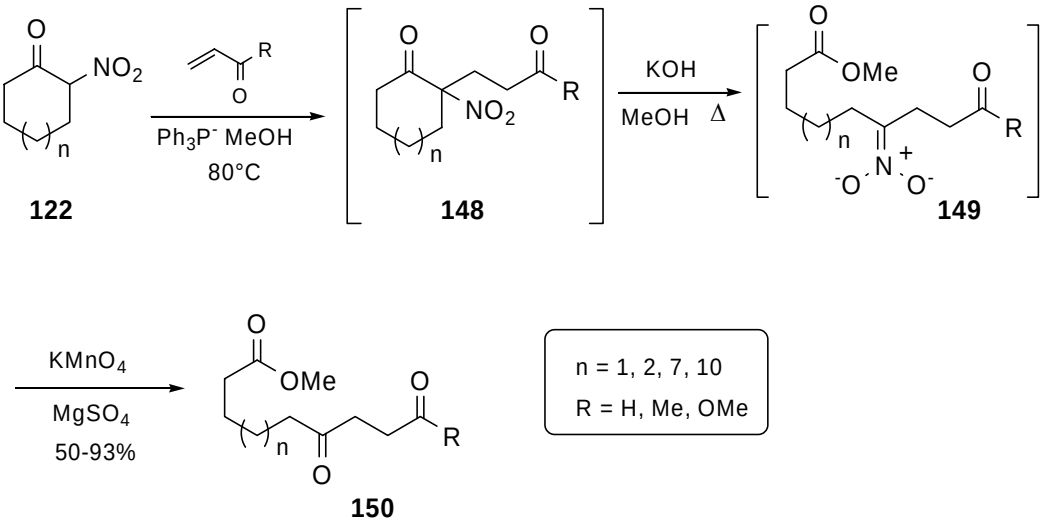
Scheme 40

Reaction of the γ-nitro ketone **144** with cyclic β-ketoesters **145** directly affords bicyclic compounds **146** through a conjugate addition–aldol condensation reaction (Scheme 41).[88,89] These derivatives are important precursors of the germination stimulant strigol and its synthetic analogs.



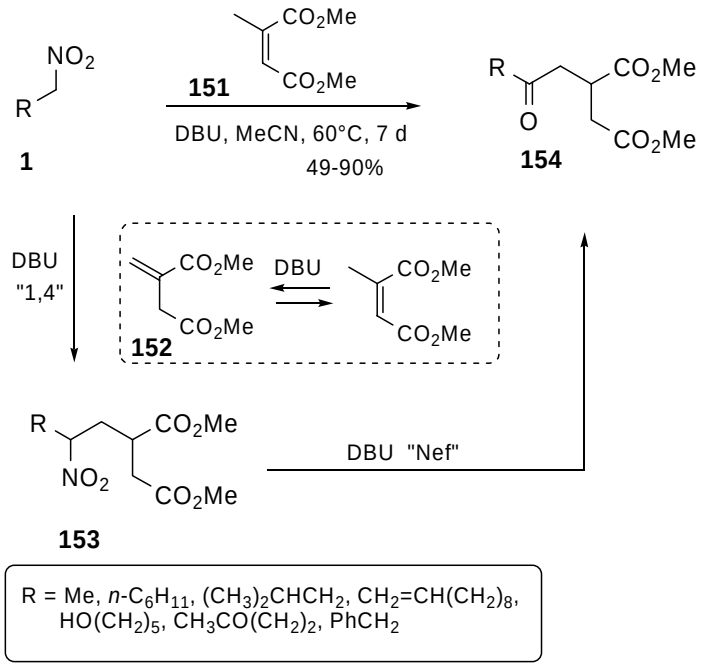
Scheme 41

The 2-nitrocycloalkanones **122** react with enones in the presence of triphenylphospine to give the Michael adducts **148** that, by the simple addition of a methanolic solution of KOH, are cleaved to the corresponding open-chain nitronate anions **149** (Scheme 42).[90,91] These intermediates undergo a Nef reaction using $KMnO_4$ to afford the triketo derivatives **150**. This overall transformation is realized in a 'one-pot' procedure and avoids the isolation of any intermediates.



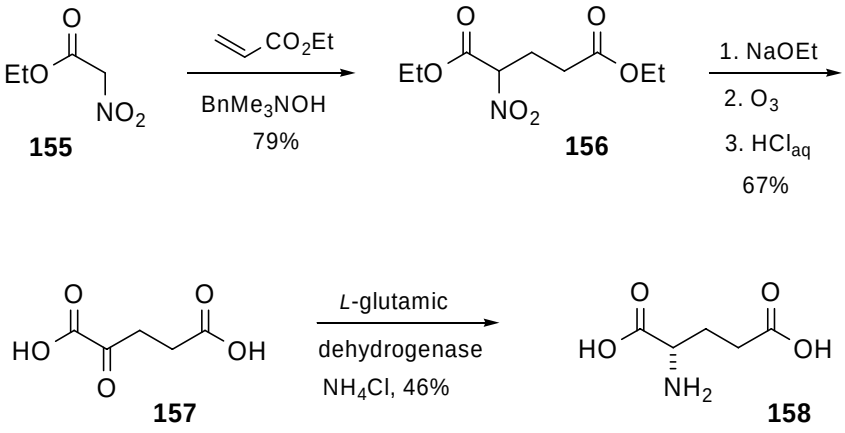
Scheme 42

An unusual behavior can be observed upon reaction of the nitroalkanes **1** with dimethyl citraconate **151** in the presence of DBU. As observed by ^{1}H- NMR analysis, in the presence of DBU there is an equilibrium between **151** and its regioisomer **152** that is probably more reactive towards Michael addition with nitroalkanes. The adducts **153** formed by the usual conjugate addition are therefore subsequently transformed into the keto diesters **154** by a Nef reaction (Scheme 43).[92]



Scheme 43

Stable-isotope- labeled *L*-glutamic acid can be prepared from ^{13}C-enriched compounds, following a strategy involving the conjugate addition of ethyl nitroacetate **155** to ethyl acrylate. Oxidative Nef conversion of the 2-nitroglutarate **156** to diethyl 2-oxoglutarate, and ester hydrolysis, gives 2-oxoglutaric acid **157**. This diacid is transformed into *L*-glutamic acid **158** using the commercially available enzyme glutamic dehydrogenase, in the presence of ammonium ions (Scheme 44).[93]



Scheme 44

8. Conclusions

Many synthetic approaches directed to the preparation of dicarbonyl derivatives enjoy the utilization of nitroalkanes as useful reagents for building up the alkyl framework. Conjugate addition to electron-poor alkenes and nitroaldol condensation are the most exploited procedures to attain this important result. The ability of the nitro group to be converted into a carbonyl group represents the key step of most of the procedures devoted to the preparation of 1,4-dicarbonyl derivatives. This synthetic opportunity is not limited to simple nitroalkanes but can be extended to nitroalkenes, easily obtained by dehydration of the corresponding nitro alcohols. In functionalized reagents such as 2-nitro ketones, the nitro group in the final adduct can be easily removed by reductive denitration or elimination as nitrous acid allowing the preparation of dicarbonyl compounds having a variable distance between the carbonyl groups. All these procedures involving the utilization of nitroalkanes as pivotal reagents for the synthesis of dicarbonyl compounds make the use of these nitrogenated derivatives a formidable tool in organic chemistry.

Acknowledgments

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