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Nitrocyclopropanes: synthesis and properties†

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Abstract. Present knowledge on the methods of synthesis, properties and transformations of nitro- and dinitrocyclopropanes is generalized and described systematically. The main attention is given to the methods of stereoselective cyclopropanation, new approaches to the synthesis of natural compounds and their synthetic analogues with diverse biological activity, in particular, the nitrocyclopropane-based synthesis of aminocyclopropanecarboxylic acids as well as to the construction of energetic compounds. The bibliography includes 112 references.

I. Introduction

Nitrocyclopropanes (NCP) represent a special class of cyclopropanes the molecules of which simultaneously contain strained three-membered rings and nitro groups conventionally referred to as 'energetic' substituents.[1] In the quest for new energetic compounds, NCP of the polyspiran series as well as di- and polynitrocyclopropanes have been of particular interest as the compounds that combine the highest energy content and stability and have recently become easily accessible.[2,3] The strain associated with three-membered rings and the activation due to electron-withdrawing nitro substituents result in the appearance of high and specific reactivity of NCP. This manifests itself in numerous small ring-opening reactions, specific rearrangements and isomerizations, and various complex molecules with the predetermined combination of functional groups can be synthesized based on NCP.[4,5] Nitrocyclopropanes are considered as important building blocks in designing intricate organic molecules due to the multifaceted nature of the nitro group, which not only activates the small ring by its very presence, but can also be converted into other functional groups.[6] Although NCPs pertain to a relatively new class of compounds, their reactions have already found wide use in preparative organic chemistry. Compounds that contain a nitrocyclopropane fragment are the synthetic intermediates in several reactions[4] and can be transformed into various polyfunctionalized compounds.[7] Considerable attention paid to NCP was associated with the fact that nitrocyclopropane fragments were found in several natural compounds.[8–10] For example, the peptide antibiotic hormaomycin includes two nitrocyclopropane fragments.[11,12] Nitrocyclopropanes are the key compounds in the synthesis of recently isolated antibiotic belactosin A, which exhibits anticancer activity,[13] and a new antibiotic Trovafloxacin[14] as well as of cyclopropylamines and quite a number of aminocyclopropanecarboxylic acids known to possess biological activity. Nitrocyclopropane derivatives are especially valuable in the formation of conformationally rigid amino acids and peptides.[15,16]

The present review considers the main methods for synthesis of nitrocyclopropanes, their chemical and thermochemical properties. In NCP under discussion, the nitro group is directly bound to a three-membered ring.

A review[17] covering the literature data on this class of compounds published before 1996 appeared in 1998.

An original recent review in an electronic journal[18] briefly described modern approaches to the NCP synthesis and the most important methods of asymmetric nitrocyclopropanation. However, the latter review did not cover adequately the literature on NCP chemistry, mentioned virtually none of the studies by Russian chemists, contained no data on the synthesis of energetic compounds of the NCP series and provided virtually no information on the synthesis of polycyclic conformationally rigid aminocyclopropanecarboxylic acids based on NCP.

In connection with this, it seemed expedient to survey in more detail the current literature on the NCP chemistry and reflect sufficiently fully the publications in Russian journals.

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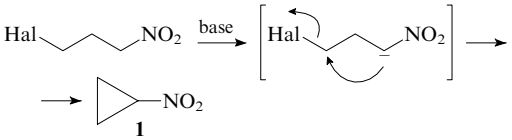
† The review is dedicated to the 100th birthday of Corresponding Member of the USSR Academy of Sciences S S Novikov.

II. Methods of synthesis of nitrocyclopropanes

Despite the considerable angular strain in their three-membered rings, cyclopropanes are formed relatively easily and numerous cyclopropane derivatives were synthesized in different laboratories all over the world. At the same time, nitro-substituted cyclopropanes cannot be considered as easily accessible compounds and, on the whole, the synthesis of cyclic nitro compounds is a more difficult problem than that of their acyclic counterparts. This is explained by the fact that no methods are known so far for the direct introduction of nitro groups into the three-membered ring. Nitration of cyclopropanes with nitrogen oxides or nitric acid was described [19, 20] but is not used in practice due to very low yields. Various intramolecular cyclization reactions and, to a lesser extent, [2 + 1]-cycloaddition reactions are the major methods of NCP synthesis.

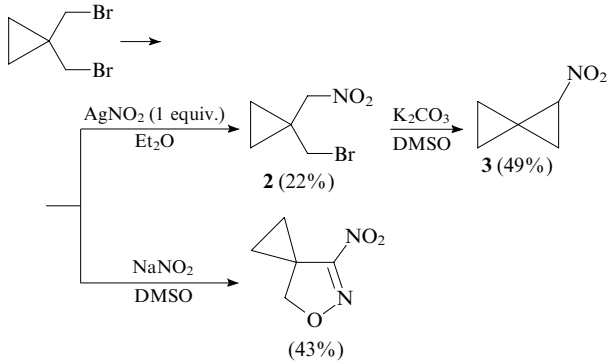
1. Intramolecular 1,3-elimination reactions in the synthesis of nitrocyclopropanes

The first representative of the NCP family, nitrocyclopropane (**1**), has been known since 1953,[19] it is the most accessible and stable compound of this series. The classical scheme of its synthesis is based on 1,3-dehydrohalogenation reactions of 1-halo-3-nitropropanes.[21–24]



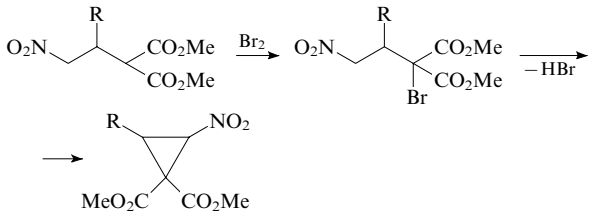
1

However, some NCP derivatives with electron-withdrawing substituents in the small ring were synthesized much earlier [25] and their synthesis was also associated with 1,3-dehydrohalogenation reactions of substituted halonitropropanes. Recently, the intramolecular dehydrohalogenation reaction of 1-bromomethyl-1-nitromethylcyclopropane (**2**) was used [2] in the pioneering synthesis of nitrospiropentane (**3**). The starting nitrobromide **2** was synthesized from 1,1-bis(bromomethyl)cyclopropane and silver nitrite. Note that with $NaNO_2$, irrespective of the reactant ratio, the reaction followed another pathway to afford a single product, nitrooxazaspiro[2.4]heptene.



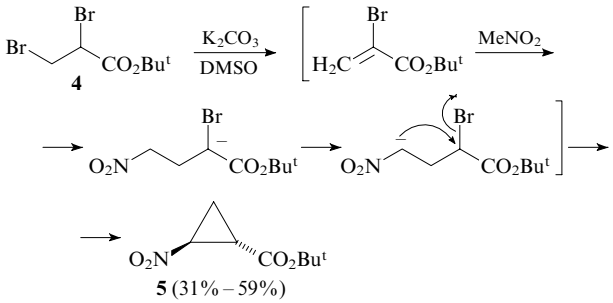
2 (22%) **3** (49%) (43%)

In many versions of NCP synthesis, a 1,3-bromonitropropane fragment established by different methods in the original molecules underwent fast intramolecular cyclization to afford a substituted NCP. The earliest example of this synthesis involved the formation of NCP from α-bromo-γ-nitrodicarboxylates prepared by *in situ* bromination of the corresponding γ-nitrocarboxylates.[26]



R = Pr^n, Ph.

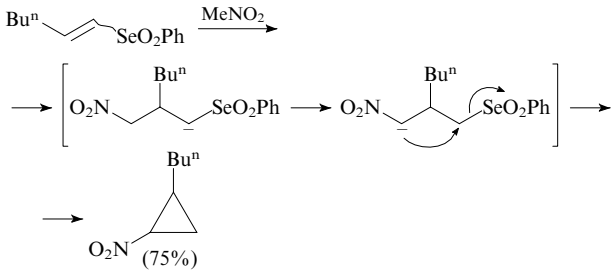
Contemporary methods of NCP synthesis are characterized by performing two-step or more complex reactions as a 'one-pot' process. The substrates suitable for 1,3-cyclization can be obtained under conditions of tandem reactions, which include the Michael addition of nucleophilic reagents containing nitro groups to electrophilic alkenes followed by cyclization. Within the framework of this approach, nitromethane is often used as a building block that supplies the $CHNO_2$ fragment. The reaction of *tert*-butyl 2,3-dibromopropanoate (**4**) with nitromethane can serve as an example.[27] The introduction of compound **4** into a mixture of nitromethane and potash in DMSO afforded *trans*-2-nitrocyclopropanecarboxylate **5**. The reaction proceeded through dehydrobromination of the starting dibromide to yield α-bromoacrylate, which was followed by the Michael addition of nitromethane to the double bond and cyclization of the adduct.



4 **5** (31% – 59%)

The preparative availability of NCP **5** stimulated its use as the precursor for the synthesis of 3-(*trans*-2-nitrocyclopropyl)alanine, the key substrate in the synthesis of hormaomycin and belactosin A possessing antitumour activities.[28, 29]

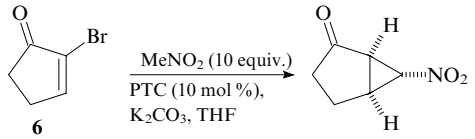
Other examples are known where alkenes containing electron-withdrawing substituents are used as substrates; these substituents activate the double bond favouring easier addition of the nitromethyl anion and in the second stage, *i.e.*, in intramolecular nucleophilic substitution, behave as the leaving groups.[30]



(75%)

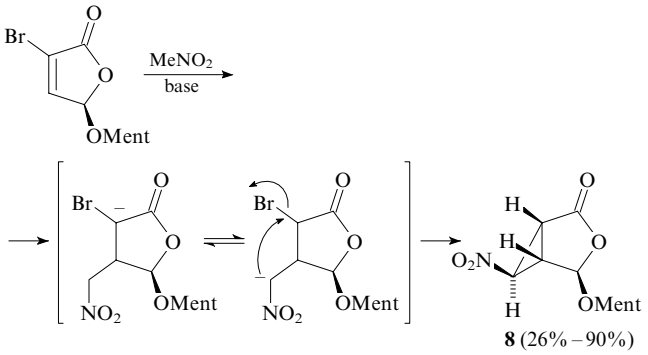
The first asymmetric nitrocyclopropanation in the presence of phase-transfer catalysts (PTC) was reported a decade ago.[31] The reaction of nitromethane (C-nucleophile) with α-bromocyclopentenone (**6**) (the Michael acceptor) in

the presence of potash and a quaternary ammonium salt (PTC) prepared from a chiral amine afforded nitrobicyclohexanone **7** under mild conditions.



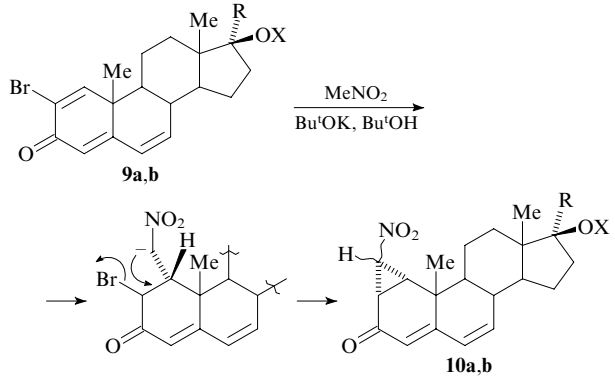
However, the chemical and optical yields of such reactions were low. The use of rubidium carbonate in place of potash increased the yield of NCP **7** to 50% (*ee* 64%).[31] Here, the double bond was additionally activated by the introduction of bromine, which eliminated in the form of an anion in the cyclization.

Such an approach seems promising as evidenced by another remarkable example of the asymmetric synthesis of NCP.[32] The reaction of chiral bromo(menthyloxy)furanone with the nitromethane anion produced enantiomerically pure bicyclic NCP **8**. With alkene : nitromethane : NaH = 1 : 3 : 3 in DMF, the yield of the target compound was 90%. This strategy of NCP synthesis was given the name of Michael Initiated Ring Closure (MIRC), hence, nitromethane is an efficient MIRC reagent, while the addition of a bromine atom as the substituent at the double bond facilitated the cyclopropanation reactions and enhanced their efficiency.



Ment is l-menthyl.

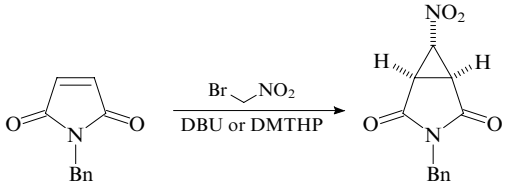
A similar approach was used in the synthesis of NCP of the steroid series.[33]



R = H, X = C(O)Et (**a**); R = Me, X = H (**b**).

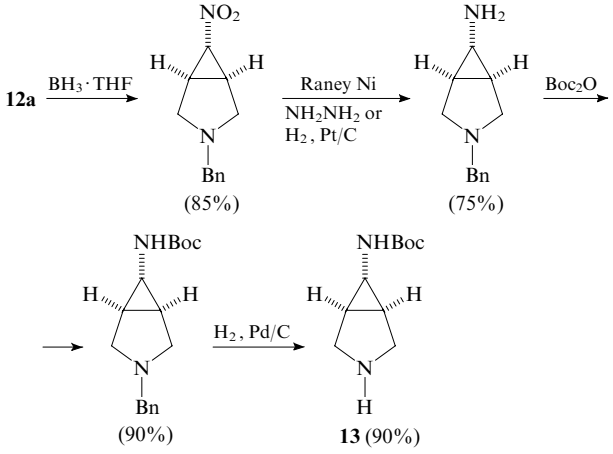
The potassium *tert*-butoxide-assisted addition of nitroalkanes to steroidal 2-bromo-3-oxo-1,4,6-trienes **9** followed by dehydrobromination afforded nitrocyclopropasteroids **10** as the only reaction products albeit in low yields. Nonetheless, these reactions can be used in the synthesis of NCP with non-trivial structures, *e.g.*, fused with the steroid system, which makes them undeniably valuable.

Recently, in a series of studies on the synthesis of polyfunctionalized NCP another combination of the starting reactants has been used, namely, an electrophilic alkene containing one or two electron-withdrawing groups and bromonitromethane. In this case too, the cyclopropanation reactions proceeded as a tandem one-pot process that included the Michael addition and 1,3-dehydrohalogenation. Thus bromonitromethane was used[34] in the cyclopropanation of *N*-benzylmaleimide (**11a**). In this reaction, different bases were assayed; however, the yields of product **12a** remained low and could be increased to 36% when an amidine base, namely, 1,2-dimethyl-1,4,5,6-tetrahydropyrimidine (DMTHP), was employed.



DBU is 1,8-diazabicyclo[5.4.0]unden-7-ene.

This reaction not only allowed the introduction of an NCP fragment to afford bicyclohexane **12a**, but also provided its *cis*-stereochemistry. Moreover, in this study the problem of the nitro group reduction to the amino group with retention of the small ring was solved, which required the preliminary reduction of the five-membered ring of NCP **12a**.

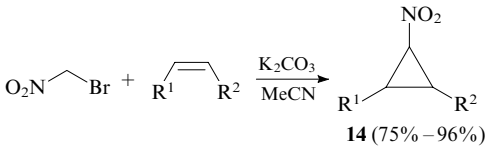


Boc is *tert*-butoxycarbonyl.

6-*exo*-Nitro-3-azabicyclo[3.1.0]hexane (**13**) was the basic starting reactant in the synthesis of the antibacterial drug Trovafloxacin.[35] In this connection, numerous efforts of researchers were directed to optimization of synthesis conditions of compound **13**, investigations into its streochemistry and development of reliable methods for the nitro group reduction.[36–40]

In continuation of these investigations, syntheses of polyfunctionalized NCP **14** by reactions of certain acyclic electrophilic agents containing two electron-withdrawing

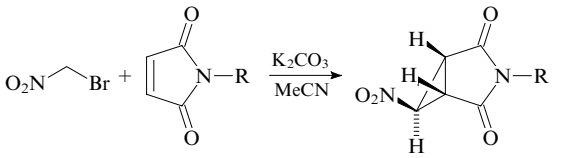
substituents with bromonitromethane in the presence of potash were studied.[41]



14 (75%–96%)

R^1, R^2 = Br, Ac, AcO, CN, 4-$MeC_6H_4C(O)$.

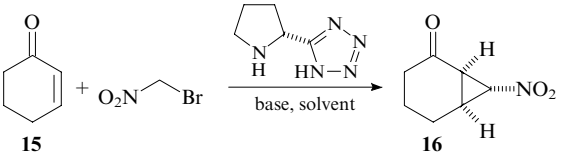
To increase the yield of the reaction products (**14**), it seemed reasonable to add bromonitromethane portionwise to prevent its base-induced resinification. However, the diastereoselectivity of these reactions remained low. *N*-Alkylmaleimides **11a**–**d** with different substituents at the nitrogen were studied as the cyclic electrophilic alkenes. The corresponding 6-nitro-3-azabicyclohexanes **12a**–**d** were synthesized in high yields (65%–82%) and with high diastereoselectivity (up to *de* 100%). This considerable increase in the yield of nitro-3-azabicyclohexanes **12** was of fundamental importance, because they are the key compounds in the synthesis of Trovafloxacin.[35]



11a–**d** **12a**–**d** (65%–82%)

R = Bn (**a**), Me (**b**), Et (**c**), Bu^t (**d**).

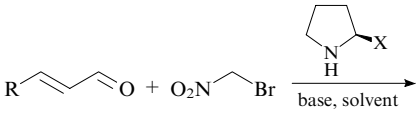
A new enantioselective nitrocyclopropanation reaction of cyclohex-2-enone (**15**) with bromonitromethane in the presence of a chiral organic catalyst was reported.[42]

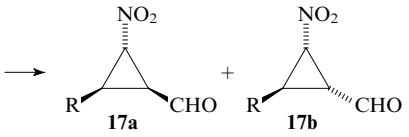


15 **16**

The screening of organic catalysts and bases as well as the optimization of conditions of cyclopropanation reactions made it possible to develop an efficient and enantioselective method for the cyclopropanation of ketone **15**. Using 5-(pyrrolidin-2-yl)-1*H*-tetrazole as the catalyst and morpholine as the base resulted in the desired NCP **16** in the yield of 80% with good enantiomeric excess (*ee* 77%). Moreover, a single recrystallization of this adduct increased the enantiomeric excess to *ee* 98%.

The asymmetric nitrocyclopropanation of α,β-unsaturated aldehydes under the action of bromonitromethane was reported.[43] The reaction proceeded in the presence of chiral amines as the catalysts to afford only two diastereomers **17a**,**b** (of four possible) of 2-nitrocyclopropanecarbaldehyde each with a high degree of enatioselectivity (*ee* 91%–99%).



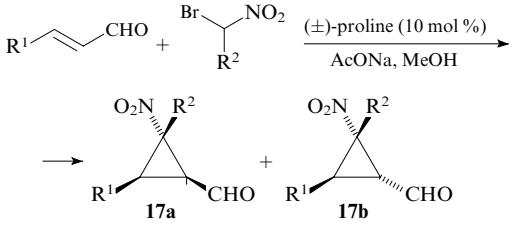


R = Ph, 4-BrC_6H_4, 4-ClC_6H_4, Pr^n, 2-naphthyl;

X = CO_2H, CPh_2OH, CPh_2OSiMe_3, .

This was the first example of enantioselective nitrocyclopropanation of unsaturated aldehydes in the presence of organic catalysts. Compounds **17** formed were later successfully converted to the corresponding β-nitromethylcarboxylates (*ee* 92%) and used in preparation of precursors of synthetic analogues of γ-aminobutyric acid.[43]

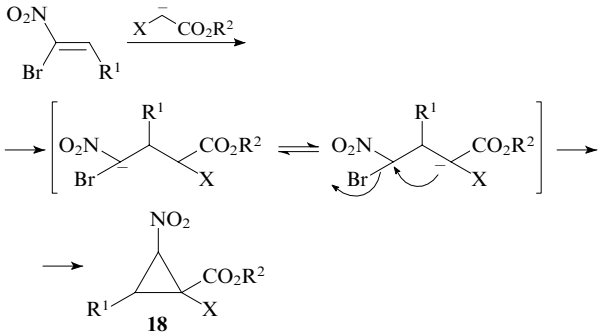
A simultaneously published study[44] was devoted to asymmetric nitrocyclopropanation reactions of unsaturated aldehydes of the aromatic series in the presence of secondary amines as the catalysts. Irrespective of the nature of substituents in their aromatic rings, the starting β-arylacroleins produced NCP **17a**,**b** in 60%–68% yields. 1-Bromo-1-nitroethane (R^2 = Me) and bromo(nitro)phenylmethane (R^2 = Ph) gave good yields of products with high diastereoselectivity. Bromo(nitro)phenylmethane (R^2 = Ph) gave diastereomer **17b** exclusively.



R^1 = Ph: R^2 = Me, Et, Ph, CO_2Et;
R^2 = H: R^1 = Ph, 4-$O_2NC_6H_4$, 4-ClC_6H_4, 4-$MeOC_6H_4$, 4-MeC_6H_4, 3-ClC_6H_4, 2-$MeOC_6H_4$, 2-ClC_6H_4.

Thus, diastereoselectivity of these reactions was largely determined by the structure of the bromo nitro alkane used.

The NCP syntheses that pertain to MIRC processes can be realized in reactions of bromo nitro alkenes with CH-acids. This strategy has been applied earlier.[45]

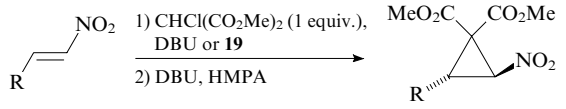


X = CN, CO_2R^2; R^2 = Me: R^1 = Pr^n, Ph, 4-$O_2NC_6H_4$, 3-$O_2NC_6H_4$;
R^2 = Et: R^1 = Me, Pr^n, Ph.

With diethyl malonate used as the CH-acid, the synthesis of NCP **18** included, traditionally, the Michael addition and 1,3-elimination. In addition to diethyl malonate, other CH-acids, namely, indane-1,3-dione, 3-methyl-1-phenylpyrazol-5(4*H*)-one were also studied in this reac-

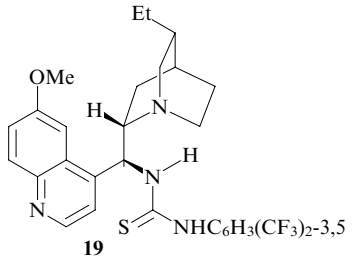
tion, which resulted in NCP with the spiro-structure. Reactions of 1-bromo-1-nitro-2-(4-chlorophenyl)ethene with several CH-acids in the presence of bases proceeded according to the classic scheme (the Michael addition – cyclization).[46]

This approach was used in a new stereoselective one-pot synthesis of substituted NCP **18**.[47] The addition of dimethyl 2-chloromalonate to certain (aryl)nitroalkenes catalyzed by tertiary amines afforded the Michael condensation products that later underwent cyclization into NCP **18** with the high diastereoselectivity under the action of DBU in hexametapol.



18 (64% – 75%, *de* > 98%, *ee* 17% – 47%)

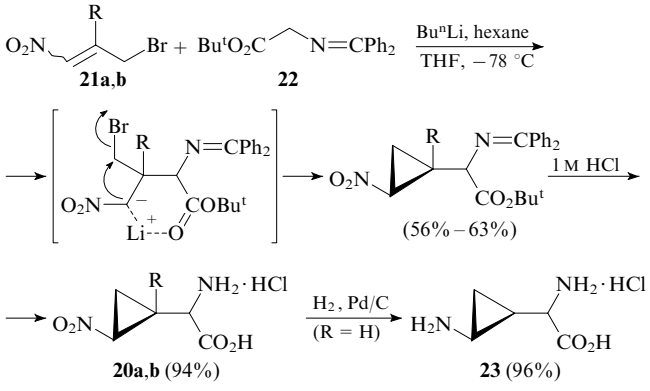
R = Ph, 4-BrC_6H_4, 4-$F_3CC_6H_4$, 2-$O_2NC_6H_4$, 1-naphthyl, 2-thienyl, n-C_6H_{13}.



19

The use of chiral catalyst **19** aimed at asymmetric induction resulted in NCP **18** with low enantioselectivity (*ee* ⩽ 47%).

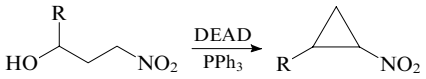
The MIRC strategy has found application in the synthesis of substituted 2-cyclopropylglycines **20**.[48] Bromo nitro alkenes **21** were used as the Michael acceptors, while the lithiated derivative of the glycine equivalent **22** was used as the nucleophile.



R = H (**a**), Me (**b**).

The nitro group in NCP **20a** was reduced to afford diamino carboxylic acid **23**. The latter was isolated in virtually quantitative yield. Amino acid **23** is a conformationally rigid analogue of the natural 2,4-diaminobutanoic acid.[48]

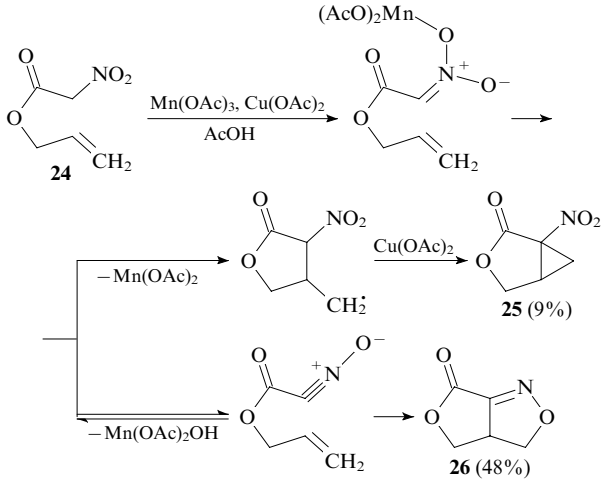
γ-Nitro alcohols were the promising intermediates in the NCP synthesis. Syntheses based on them are feasible because the hydroxyl group could be transformed by any suitable method into a leaving group thus enabling the intramolecular nucleophilic substitution in the carbanion, which usually exists as the nitronate ion. Excellent results in the intramolecular dehydration of γ-nitroalcohols were achieved with the Mitsunobu reagent,[49] *i.e.*, a complex of diethyl azodicarboxylate (DEAD) and triphenylphosphine. It was shown[50] that the Mitsunobu reaction of quite a number of γ-nitro alcohols readily afforded NCP (preferentially, *trans*-isomers) in 75% – 98% yields. The reaction represented a highly efficient intramolecular version of the substitution with formation of a new C – C bond. The competitive O-alkylation was completely absent in the above examples.



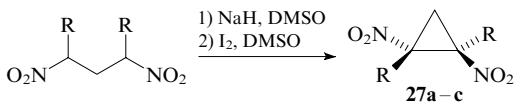
R = n-C_5H_{11}, n-C_6H_{13}, 4-$MeOC_6H_4CH_2$, biphenyl-4-yl, *etc.*

2. Intramolecular oxidative condensation reactions in syntheses of nitro- and 1,2-dinitrocyclopropanes

There are few examples of the use of intramolecular oxidative condensation reactions for the synthesis of NCP; as a rule, these reactions proceeded with low efficiency and were poorly reproducible. Oxidative condensation of allyl nitroacetate (**24**) under the action of trivalent manganese acetate afforded NCP **25** in a yield of merely 9% and furoisoxazoline **26** as the main product.[51]



Several 1,2-dinitrocyclopropanes **27** were synthesized by the intramolecular oxidative condensation of 1,3-dinitropropanes under the action of sodium methylsulfinylmethanide (dimsyl sodium) and iodine in DMSO.[52]



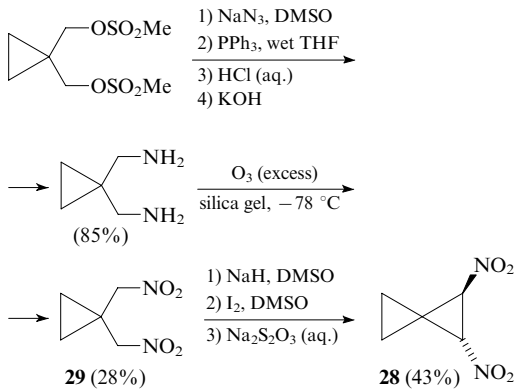
27a – c

R = H (**a**, 24%), Me (**b**, 36%), Et (**c**, 23%).

Exclusively *trans*-isomers of 1,2-dinitrocyclopropanes **27** were synthesized by this method under thermodynamic control where two electronegative nitro groups were located in the antiperiplanar positions with respect to each other.

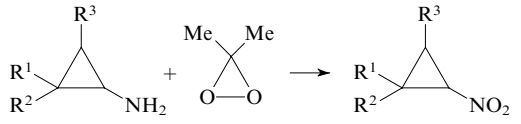
A characteristic feature of dinitrocyclopropanes **27** is relatively high density. Thus for 1,2-dinitrocyclopropane (**27a**), the density reached 1.59 g cm^{-3}.

The oxidative condensation reaction was used[53] in the synthesis of *trans*-1,2-dinitrospiropentane **28** from 1,1-bis(nitromethyl)cyclopropane (**29**) under the action of a base and iodine in DMSO.



3. Oxidation of aminocyclopropanes for the synthesis of nitro-substituted cyclopropanes and spiropentanes

Since the synthesis of aniline, nitro compounds have been considered, as a rule, as the precursors of amines. However, quite a number of nitro-substituted cyclopropanes and spiropentanes are not easily accessible; hence, it was proposed[54,55] to synthesize them by the oxidation of aminocyclopropanes and -spiropentanes that can more easily be prepared from the corresponding carboxylic acids. A newly developed efficient NCP synthesis was carried out by the oxidation of aminocyclopropanes under the action of a dimethyldioxirane (DMDO) in acetone (0.08 mol litre^{-1}). For a series of mono- and diaminocyclopropanes and -spiropentanes, it was shown that under mild conditions the reaction is chemoselective and result in the target NCP in good yields and with retention of small rings.



Nitrocyclopropane	Yield (%)	Nitrocyclopropane	Yield (%)
(**1**) NO$_2$	40	NO$_2$	60
Bu^n NO$_2$	61	NO$_2$ (**3**)	56
NO$_2$	76	O$_2$N NO$_2$ (**30**)	56

It was shown that DMDO oxidizes amine hydrochlorides, which are more stable that the free bases. Particularly, 1,4-diaminospiro[2.2]pentane hydrochloride gave hitherto unknown 1,4-dinitrospiropentane (**30**) with the nitro groups in each of the spiro-linked three-membered rings in a fair yield.

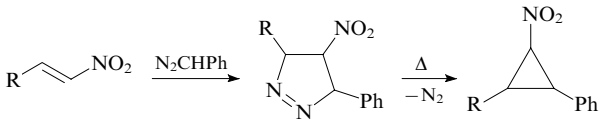
Thus, from the studies discussed above it follows that certain nitro derivatives of alkyl-substituted cyclopropanes and spiropentanes the classic synthesis of which was inefficient or impossible can effectively be synthesized by oxidation of the corresponding aminocyclopropanes and -spiropentanes. At the same time, determination of the scope and limits of this approach requires more extensive studies of aminocyclopropane oxidation reactions.

4. Synthesis of nitrocyclopropanes by [2 + 1] cycloaddition

[2 + 1] Cycloaddition of carbenes or ylides to alkenes is a versatile method of cyclopropane synthesis. This approach is fairly popular for the NCP synthesis, where the nitro group to be introduced into the small ring could be located in both the alkene molecule and the the cyclopropanation reagent.

a. Cyclopropanation of nitroalkenes

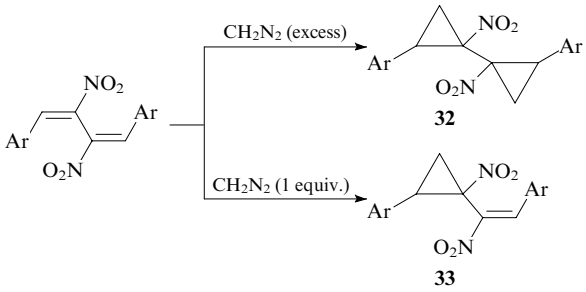
Alkenes containing α-nitro groups are by and large non-reactive in [2 + 1]-cycloaddition reactions of carbenes. Nonetheless, in the 1950s – 1960s, information started to appear on cyclopropanation of α-nitroalkenes in reactions with diazo compounds.[56–62] Recently, the reactions of phenyldiazomethane with ethyl nitroacrylate and β-nitrovinylphosphonate were studied.[63,64] These reactions afforded mixtures of diastereomeric nitrocyclopropanes **31a**,**b** in low yields.



31a,**b** (8% – 12%)

R = CO_2Et (**a**), $P(O)(OCH_2CH_2Cl)_2$ (**b**).

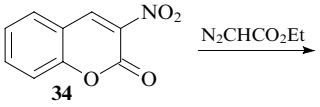
Studies of cyclopropanation of dinitrobuta-1,3-dienes with diazomethane have shown[65] that the reaction carried out in the presence of excess diazomethane in diethyl ether or THF afforded diaryldinitrobicyclopropanes **32** in high yields.

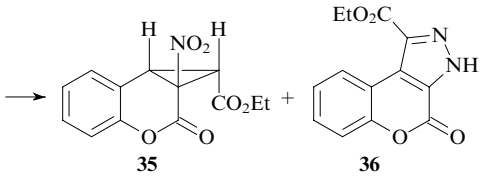


Ar = Ph, 4-MeC_6H_4, 4-MeOC_6H_4, 3-ClC_6H_4, 1-naphthyl, 2-thienyl.

The products represented a mixture of diastereomers (racemic D,L-**32** and *meso*-**32**), which were separated by column chromatography on a chiral phase. The ratio of stereoisomers proved to be dependent on the nature of the aryl substituent in substrates. With 1 equiv. of diazomethane, one double bond in the 1,3-diene system undergoes selective cyclopropanation to vinylnitrocyclopropanes **33**. No pyrazolines were detected in this non-catalyzed butadiene cyclopropanation reaction.

The cycloaddition reaction of ethyl diazoacetate to 3-nitrocoumarin **34** (Ref. 66)

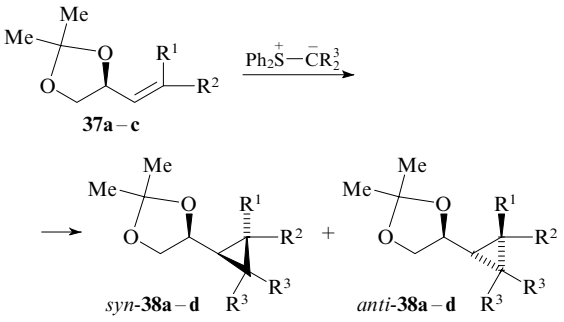




35 **36**

afforded the *endo*-isomeric NCP **35** and substituted pyrazole **36**. The addition of silica gel to the equimolar mixture of nitrocoumarin and ethyl diazoacetate in benzene increased the yield of NCP **35** from 25% to 58%.

However, sulfur ylides proved to be more useful reagents for the cyclopropanation of electrophilic nitroalkenes.[6] This is why attention was focused on the development of approaches to enantiomerically pure NCP. Thus the cyclopropanation reactions of nitroalkenes **37a–c** (bearing chiral dioxolane substituents derived from glyceraldehyde) with sulfur ylides were studied.[67–69] Products **38a–d** were synthesized in yields varying from modest to good.



37a–c

syn-**38a–d** *anti*-**38a–d**

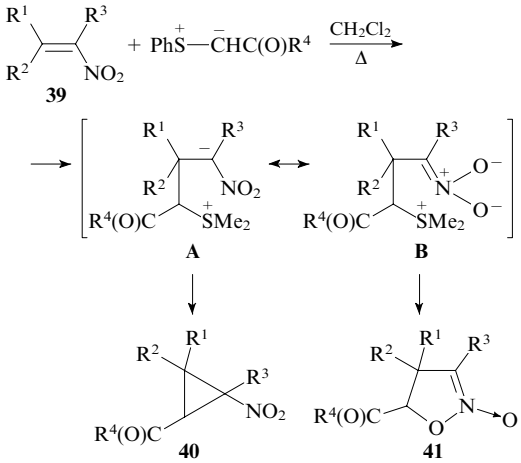
Alkene	Reagent	Product	R^1	R^2	R^3	Yield (%)	Ratio *syn*-**38**:*anti*-**38**
37a	$Ph_2S^+-C^-Me_2$	**38a**	H	NO_2	Me	60	70:30
37b	$Ph_2S^+-C^-Me_2$	**38b**	Me	NO_2	Me	89	>95:5
37c	$Ph_2S^+-C^-Me_2$	**38c**	NO_2	Me	Me	74	94:6
37b	$Ph_2S^+-C^-H_2$	**38d**	Me	NO_2	H	18	50:50
37c	$CHBr_3$–NaOH–TEBA-Cl (see [a])	**38e**	NO_2	Me	Br	24	>95:5

[a] TEBA-Cl is benzyltriethylammonium chloride; in this case, the reaction was carried out at room temperature, in the other cases, it was carried out at −78 °C.

The highest asymmetric induction was observed in reactions of α-methyl-substituted nitroalkenes with sulfonium isopropylide. The addition of dibromocarbene to nitroalkene **37c** under phase-transfer catalysis conditions afforded product **38e** (24%) in a low yield but with high stereoselectivity.

In the cyclopropanation reactions with different sulfur ylides, a wide range of chiral cycloalkenes were tested that have been prepared using the Henry reaction starting from (*R*)-glyceraldehyde, L-serine and the Garner aldehyde.[68] The corresponding NCP were obtained in high yields and with high degrees of diastereoselectivity, they were successfully used in the syntheses of optically active 2-aminocyclopropane-1-carboxylic and 2-(2-aminocyclopropyl)-2-hydroxyacetic acids by the reduction of the nitro groups (catalytic hydrogenation on Pd/C) and the oxidative cleavage of the dioxolane fragments.

The crucial effect of α-substituents in the nitroalkene substrates on the direction of their reactions with sulfur ylides was emphasized.[69]

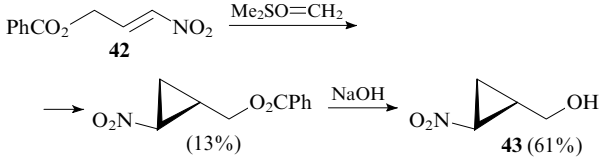


39 **A** **B** **40** **41**

R^1, R^2 = H, Me, Pr^i; $R^1-R^2 = (CH_2)_5$, $(CH_2)_4$; R^3 = H, Me, Et; R^4 = OEt, Ph.

For proton-containing nitroalkenes **39** (R^3 = H), the exclusive formation of NCP **40** was observed; for R^3 = Me, Et, cyclic nitronates **41** were the major reaction products. This difference in the behaviour of nitroalkenes in their reactions with sulfur ylides was explained by the ambident nature of the nitronate anion, which can act as both C-(form **A**) and O-nucleophile (form **B**). The presence of the α-alkyl substituent in the starting substrate enhanced the stability of the nitronate form **B**.

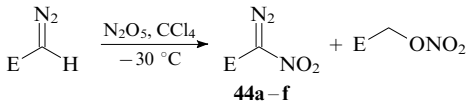
The cyclopropanation of nitroalkene **42** with sulfur ylides was used in the preparation of synthetic precursors of the peptide lactone hormaomicyn.[27] *trans*-2-Nitrocyclopropylmethanol (**43**) was prepared (as a racemate) in six steps, where the reaction of nitroalkene **42** with dimethylsulfoxonium methylide in DMSO played the key role.



42 **43** (61%)

b. Reactions of nitro group-containing carbenes and ylides with alkenes

Nitrodiazomethane and its derivatives served as the source of nitrocarbenes. Nitrodiazomethanes **44** containing an additional electron-withdrawing group (E) were synthesized for the first time by nitration of the corresponding diazomethane derivatives with nitrogen(V) oxide.[70–73]

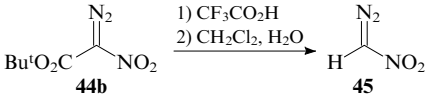


44a–f

E = CO_2Et (**a**), CO_2Bu^t (**b**), CF_3 (**c**), CN (**d**), C(O)Ph (**e**), Ts (**f**).

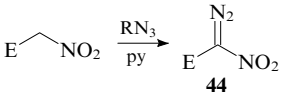
Unsubstituted nitrodiazomethane (**45**) was synthesized from preformed (*tert*-butoxycarbonyl)nitrodiazomethane (**44b**) by hydrolysis followed by decarboxylation.[71] So far

this approach remained the only way for the synthesis of nitrodiazomethane (**45**).

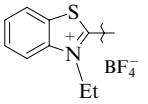
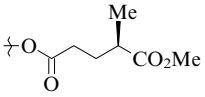


44b **45**

A more convenient method for synthesizing substituted nitrodiazomethanes **44** with electron-withdrawing substituents was the diazo-transfer reaction [73–76] with $CF_3SO_2N_3$ as the source of the diazo group and pyridine as the base. As a rule, high yields of nitrodiazocarbonyl compounds were attained.[75, 76]



44

E	R	Yield (%)	Ref.
CO_2Et	4-$HO_2CC_6H_4SO_2$	8	73
CO_2Et		23 [a]	74
CO_2Et	Tf	92	75
CO_2Bu^t	Tf	90	75
CO_2All	Tf	88	75
CO_2Bn	Tf	96	75
	Tf	68	75
Ac	Tf	83	76
$C(O)Bu^t$	Tf	80	76
C(O)Ad [b]	Tf	93	76

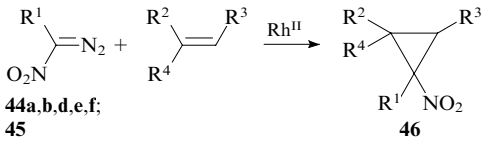
[a] As the base, AcONa was used; [b] Ad is 1-adamantyl.

As was first shown in Refs 76–79, the rhodium carboxylate-catalyzed decomposition of nitrodiazomethane and its derivatives in the presence of alkenes containing electron-donating substituents affords NCP **46**. High yields (up to 85%) were reached with sterically non-hindered terminal alkenes (Table 1).

Table 1. Yields (%) of cyclopropanation products **46** of alkenes with nitrodiazomethane derivatives.[78]

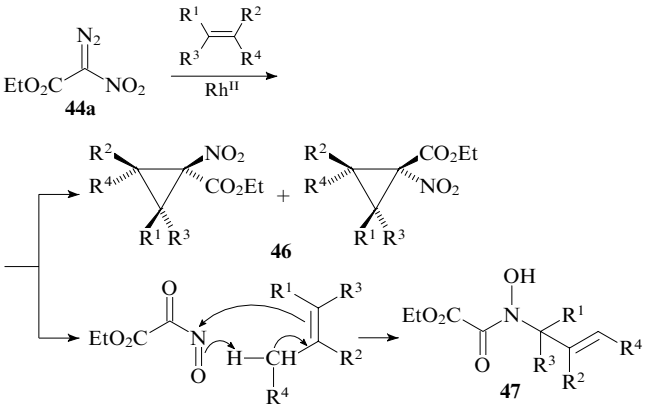
Alkene [a]	Diazo compound (R^1)					
	45 (H)	**44d** (CN)	**44a** (CO_2Et)	**44b** (CO_2Bu^t)	**44e** (COPh)	**44f** (Ts)
Styrene (R^2 = Ph)	54	55	75	83	75	73
Isobutylene ($R^2 = R^4$ = Me)	50	50	75	80	58	72
Hex-1-ene ($R^2 = Bu^n$)	50	55	35	—	—	—
cis-But-2-ene ($R^2 = R^3$ = Me)	50	40	65	59	45	53
Cyclohexene [$R^2 - R^3 = (CH_2)_4$]	30	40	35	30	20	42

[a] Only substituents different from H are shown.



44a,**b**,**d**,**e**,**f**; **45** **46**

The use of sterically hindered alkenes reduced the yields of NCP **46** so that it was isomeric compound **47** containing a hydroxamic acid fragment that was the main product.[78, 79] The formation of this compound was explained [77] by the alkene reaction with an acylnitroso compound, the isomerization product of the nitrocarbene.

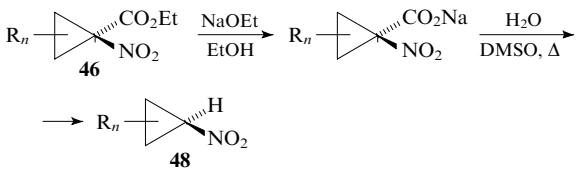


44a **46** **47**

R^1, R^3 = H, Me, Bu^n, Bu^t, Ph, OAc; R^2, R^4 = H, Me, Ph; $R^3 - R^4 = (CH_2)_4$.

It was found [76, 79] that the addition reactions of nitrodiazo esters and nitrodiazo ketones to alkenes proceed in a diastereoselective manner, the presence of bulky groups in the catalyst or the diazo reagent decreasing the diastereoselectivity of the reaction. The use of chiral rhodium- and copper-containing catalysts made it possible to synthesize NCP with moderate enantioselectivity.[80]

The saponification of 1-nitrocyclopropanecarboxylates **46** followed by decarboxylation afforded α-unsubstituted nitrocyclopropanes **48**.[79, 81, 82] This method proved to be more convenient for the preparative synthesis of NCP than the one-step addition of nitrocarbene to alkenes due to the higher stability of nitrodiazo esters **44** and higher yields of the target NCP of the type **48**.



46 **48**

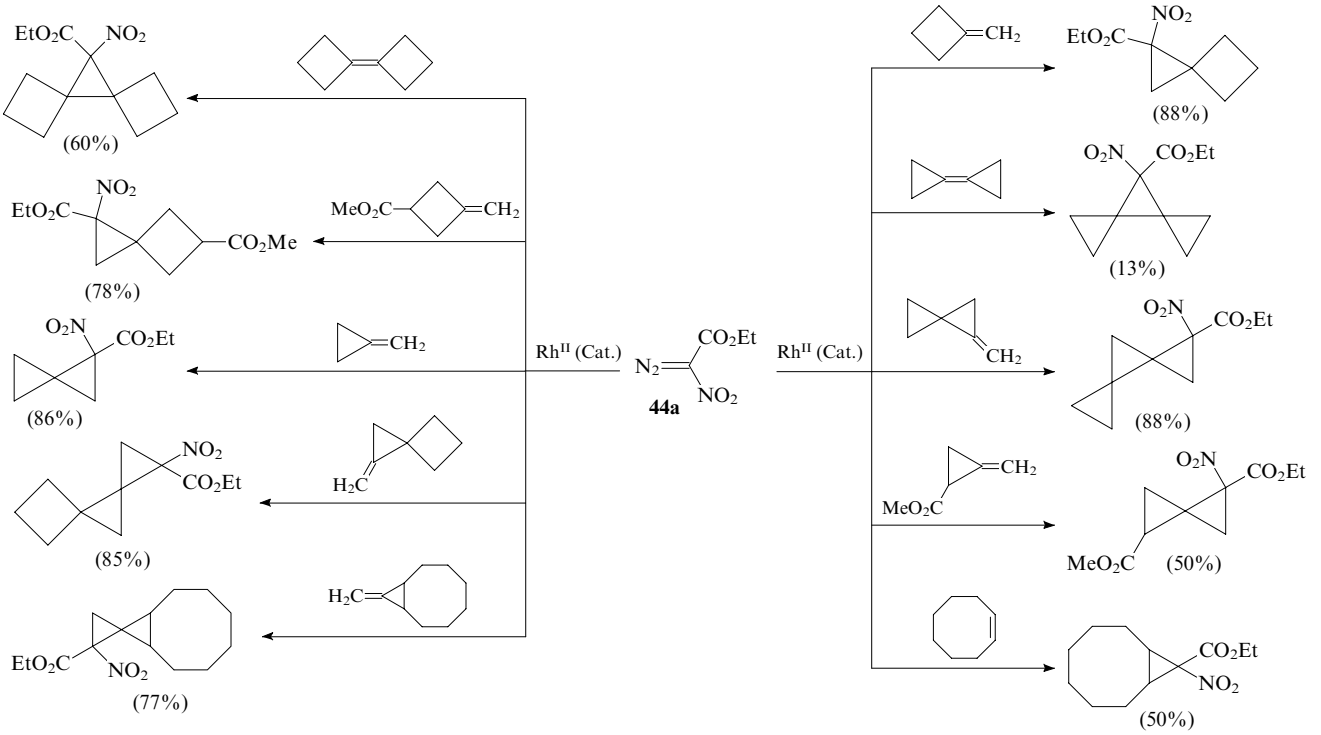
R_n = 2-Ph, 2-Me-2-Ph, 2,2-Me_2, 2,3-Me_2, $(CH_2)_4$, 2-(1-naphthyl), 2-(4-ClC_6H_4).

The reduction of 1-nitrocyclopropanecarboxylates **46** afforded esters of 1-aminocyclopropanecarboxylic acids in high yields.

It was shown that ethyl nitrodiazoacetate (**44a**) readily adds to the sterically non-hindered methylenecyclopropanes and methylenecyclobutanes to form the corresponding ethyl nitrocyclopropanecarboxylates (Scheme 1).[2, 3, 83]

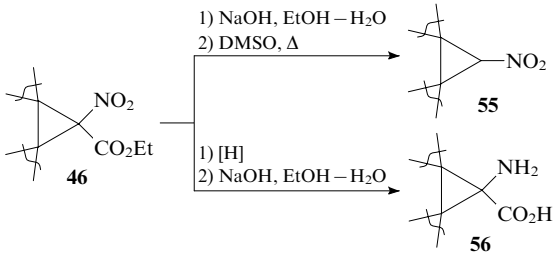
Reactions of vinylcyclopropanes with diazo ester **44a** produced, in addition to 1-nitrocyclopropanecarboxylates **49** and **50**, isoxazoline *N*-oxides **51–53**, which suggests the ability of nitro(ethoxycarbonyl)carbene to react with cer-

Scheme 1

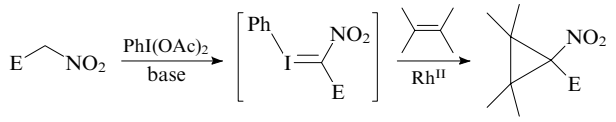


tain alkenes in the resonance 1,3-dipolar form. For alkylidenecyclopropanes with sterically hindered double bonds, the formation of a hydroxamic acid (*e.g.*, compound **54**) was observed in addition to cyclopropanation (Scheme 2).

Saponification and decarboxylation of polyspirocyclic nitrocyclopropanecarboxylates **46** afforded several polyspirocyclic NCP **55**, which represent new energetic compounds,[2,3] while the sequence of reduction and subsequent hydrolysis reactions of polyspirocyclic 1-nitrocyclopropanecarboxylates **46** is a versatile approach to 1-aminocyclopropanecarboxylic acids **56** including those of the triangulane series (Table 2).[83–86]



Iodonium ylides that can be prepared from nitromethanes containing an electron-withdrawing group in the α-position serve as synthetic analogues of nitrocarbenes. A one-pot synthesis of NCP was proposed,[82,87,88] which consisted of the catalytic cyclopropanation of alkenes containing electron-donating substituents with nitromethane or alkyl nitroacetates in the presence of bis(acetoxy)iodobenzene. The addition of iodonium ylides to alkenes derived from nitroacetates occurred with high diastereoselectivity, and chiral rhodium catalysts enable moderate enantiomeric excess of the resulting 1-nitrocyclopropanecarboxylates. The reaction can be represented by the following general scheme, the products are obtained as mixtures of diastereomers with the ratios ranging from 1 : 1 to 99 : 1.



E = CO_2R (R = All, Bn, Pr^i) (64% – 83%), H (24% – 63%).

Scheme 2

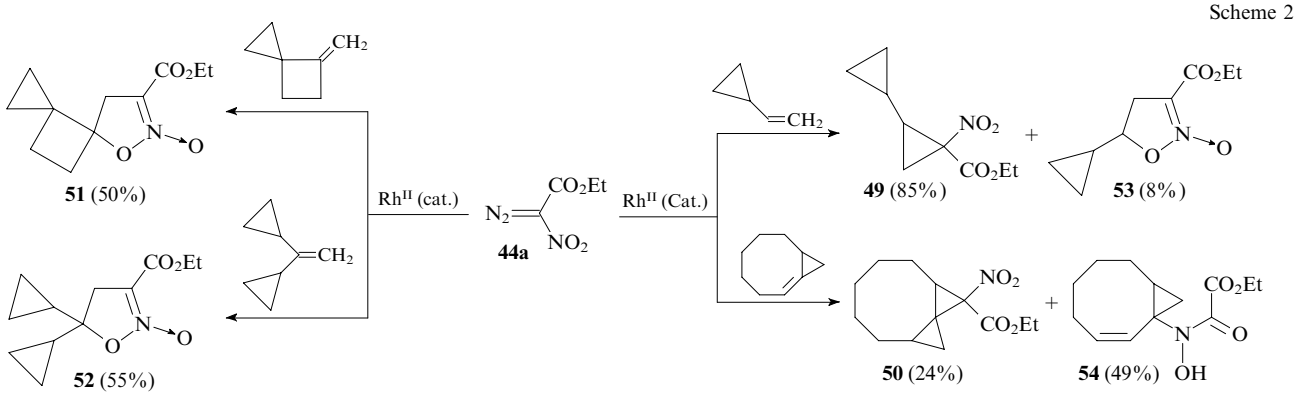
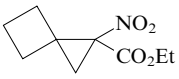
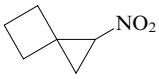
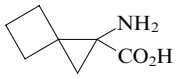
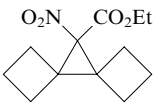
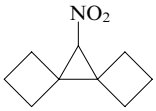
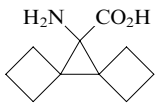
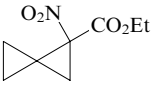
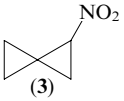
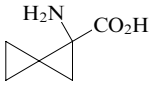
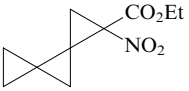
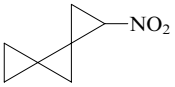
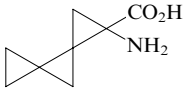
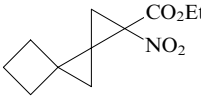
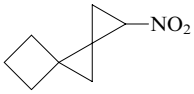
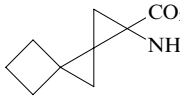
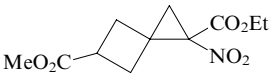
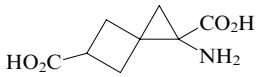
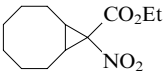
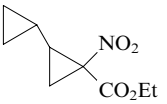
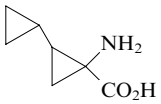
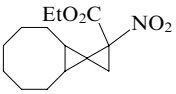
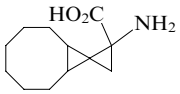
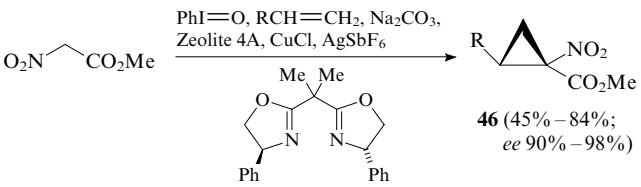


Table 2. Polyspirocyclic NCP **55** and 1-aminocyclopropanecarboxylic acids **56**.

Nitro ester **46**	Nitrocyclopropane **55**	Yield of **55** (%)	Amino acid **56**	Yield of **56** (%)
		82		73
		89		74
	 (**3**)	78		78
		52		82
		56		65
	–	–		51
	–	–		52
	–	–		66
	–	–		78
	–	–		48

An approach to the synthesis of 1-nitrocyclopropanecarboxylates **46** in the enantiomerically pure form was developed.[89] It is based on the asymmetric cyclopropanation of alkenes (styrene, 4-chloro-, 4-methyl-, 4-methoxy- and 4-*tert*-butylstyrene, *etc*.) with phenyliodonium ylides in the presence of copper(I) bis(oxazoline) complexes generated *in situ* (the ratio of diastereomers varied from 82 : 18 to 95 : 5).

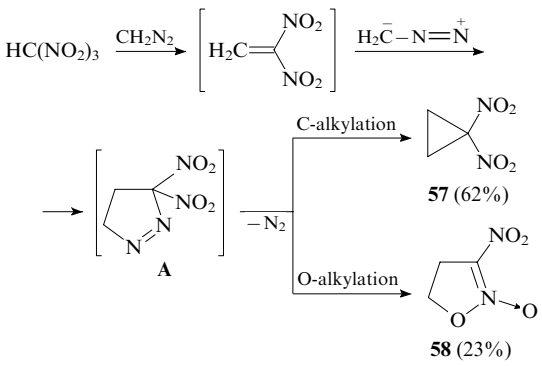


R = Ph, 4-ClC_6H_4, 4-$MeOC_6H_4$, 4-MeC_6H_4, 4-$Bu^tC_6H_4$, *etc*.

5. Synthesis of 1,1-dinitrocyclopropanes

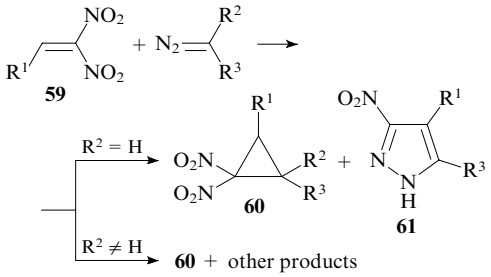
Among dinitrocyclopropanes, only 1,2-disubstituted cyclopropanes synthesized in low yields by oxidative cyclization of 1,3-dinitropropanes have long been known.[1, 90] However, for *gem*-dinitrocyclopropanes, none of synthetic methods discussed above could operate. The literature contains at least three failed attempts to synthesize 1,1-dinitrocyclopropane (**57**).[78, 91, 92]

Reactions of alkynes with nitronates obtained from trinitromethane and diazomethane were shown to afford *gem*-dinitroaziridines and dinitrocyclopropane (**57**) as the side product.[93] Insofar as the latter could solely originate from the reaction of $CH(NO_2)_3$ with diazomethane, this



reaction was studied in detail.[94] It was shown that trinitromethane reacts with diazomethane in the molar ratio 1 : 2 in benzene to afford dinitrocyclopropane (**57**) as the main product. The key step of this reaction is the *in situ* formation of 1,1-dinitroethylene, which further reacts with the second molecule of diazomethane by the [3 + 2] cycloaddition mechanism to form unstable dinitropyrazoline. The latter spontaneously eliminates nitrogen and transforms into either the intramolecular C-alkylation product **57** or the O-alkylation product, *i.e.*, 3-nitroisoxazoline *N*-oxide (**58**). Dinitrocyclopropane (**57**) is a stable compound and can be isolated by column chromatography or by distillation in 60% – 62% yield.

Of fundamental importance was the applicability of this method to the synthesis of analogues of dinitrocyclopropane (**57**). It was found[95] that the reactions of *gem*-dinitroethylenes **59** with diazocarbonyl compounds afforded the corresponding 1,1-dinitrocyclopropanes **60** and nitropyrazoles **61** in different ratios. However, for $R^2 \neq H$, the reaction proceeded less selectively to form a complex mixture of products from which NCP could be isolated in moderate yields only by column chromatography. It was shown that the yield and the ratio of the reaction products of dinitroethylenes **59** with ethyl diazoacetate were virtually independent of the presence of a catalyst, whereas the outcome of the reaction of dinitroalkenes with diazoacetophenone crucially depended on the presence of catalysts. Thus in the presence of $Mo(CO)_6$, dinitrocyclopropanes **60** [R^3 = C(O)Ph] were formed as the main products in high yields.



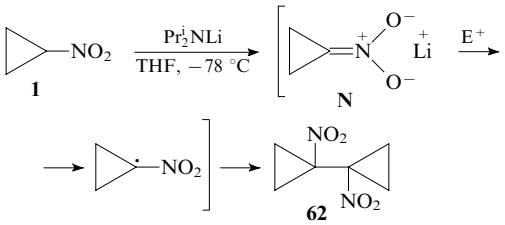
R^1 = H, Ph; R^2 = H, Me, Bn, CO_2Et; R^3 = CO_2Et, Ac, Bz.

On the whole, reactions of 1,1-dinitroalkenes with α-diazocarbonyl compounds represent a rather useful approach to functionalized 1,1-dinitrocyclopropanes **60** of which the most stable and accessible compound was ethyl 2,2-dinitrocyclopropanecarboxylate, a new promising intermediate for the synthesis of different 1,1-dinitrocyclopropane derivatives.[95]

III. Chemical properties of nitrocyclopropanes. Three-membered ring-opening reactions

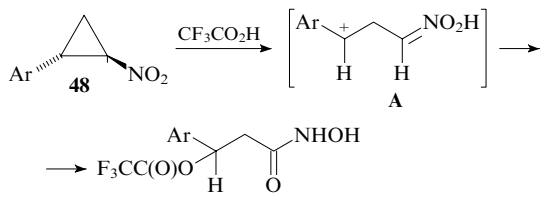
The introduction of the electron-withdrawing nitro group into cyclopropane is known to sharply increase the acidic nature of the adjacent hydrogen atom; a carbanion formed as the result of proton abstraction has sp^2-hybridization.[96] Although the nitro group belongs to the strongest electron-withdrawing substituents and can efficiently stabilize the anionic centre, the CH-acidity was observed to decrease by 10 orders of magnitude on going from 2-nitropropane to nitrocyclopropane.[97] This is rationalized by an increase in the ring strain due to the decreased p character of the carbon – carbon bonds of the cyclopropane ring upon conversion of NCP to the nitrocyclopropyl anion.[17, 98]

Quite a number of transformations typical of NCP were associated with the formation of nitrocyclopropyl anions followed by the opening of the three-membered ring under the action of different reagents. The known reactions of NCP with retention of the small ring are few in number. First of all, these are reactions of the nitro group reduction to the amino group without small-ring opening, *i.e.*, the most important reactions for the synthesis of cyclopropylamines and aminocyclopropanecarboxylic acids. These reactions were considered in the previous section when discussing the synthesis of amino acids and their derivatives. It is reasonable to assume that the nitrocyclopropyl anion **N** generated from an unsubstituted NCP would be more resistant to the electrocyclic ring-opening; this would favour the introduction of a geminal substituent to the nitro group, *i.e.*, the synthesis of a substituted NCP. However, the attempts to prepare α-substituted NCP under the action of bases (*e.g.*, lithium diisopropylamide) and electrophilic reagents resulted only in dimerization of the original nitro compound rather than in substitution.[99] The coupling reaction is quite typical of NCP, it proceeds smoothly and represents a well-known method of preparing unusual dimeric nitrocycloproane molecules such as compound **62**.[1]



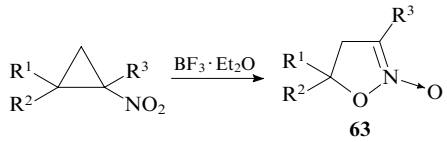
The aldol condensation of NCP with benzaldehyde was successfully carried out under the conditions of generation of nitrocyclopropyl anions from the corresponding sodium cyclopropanecarboxylate in DMSO in the presence of benzaldehyde. Alkyl and aryl derivatives of NCP behaved in the similar fashion.[100] It was found that 2,2- and 2,3-disubstituted NCP formed the nitroaldol adducts only if the starting NCP was introduced into a solution of a base and benzaldehyde. Separation of the cyclopropyl anion generation and alkylation steps resulted in very rapid formation of only the dimeric product.[81] To date, only single publications devoted to these reactions are documented in the literature, they were not actually used in practice for the preparative synthesis of substituted NCP.

Three-membered ring-opening reactions are not typical of NCP, especially in those cases where the ring contains an electron-withdrawing substituent in addition to the nitro group. These doubly activated cyclopropanes are sufficiently resistant against electrophilic reagents. Donor-acceptor cyclopropanes that contain vicinal electron-donating substituents (Ph, two Me, *etc.*) in addition to the nitro group is an exception. In these cyclopropanes, the C – C bond is strongly polarized and prone to heterolysis. From this standpoint, the small-ring electrophilic opening reactions in the NCP induced by bromine or trifluoroacetic acid were interpreted.[78] It was shown[101] that the acid-catalyzed cleavage of 2-aryl-1-nitrocyclopropanes **48** at room temperature proceeds *via* a carbocationic transition state **A**; the nitro group protonation and the C – C bond scission occur simultaneously.



Ar = Ph, 4-$MeOC_6H_4$.

An important factor stimulating this reaction was the strain relief in the molecule that accompanied the three-membered ring-opening. Isomerization of NCP to isoxazoline *N*-oxides **63** catalyzed by boron trifluoride etherate pertains to the same reaction type. The Lewis acid apparently enhanced the electron-withdrawing ability of the nitro group. Similar isomerization proceeds on heating of NCP in DMSO, it is sometimes promoted by silica gel.[102]

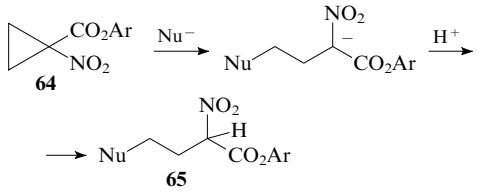


R^1, R^2 = H, Me, Ph; R^3 = CO_2Et, CN.

1. Small-ring nucleophilic opening reactions in NCP

Being a strong electron acceptor, the nitro group polarizes the adjacent C—C bonds and imparts effective electrophilic properties to NCP-substrates in their reactions with nucleophiles. Such reactions are accompanied by small-ring opening to form a carbanion stabilized by the nitro group, which is the most typical chemical transformations of NCP. The NCP that contain an additional electron-withdrawing group are the most active.

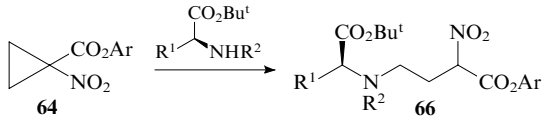
Reactions of 1-nitrocyclopropanecarboxylate **64** with a wide range of C-, N-, O- and S-nucleophiles (Nu^-) to afford γ-substituted α-nitrobutyric acids **65** were studied.[103]



Ar = 2,6-Bu^t_2-4-$MeOC_6H_2$.

Nu	Yield of **65** (%)	Nu	Yield of **65** (%)
CN	81	PhNH	95
$CH(CO_2Me)_2$	83	MeO	96
N_3	89	PhO	71
		PhS	96

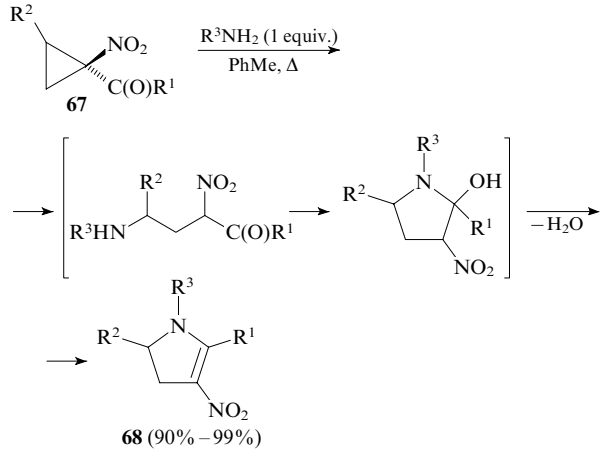
It was noted that soft nucleophiles are more reactive in three-carbon ring-opening. For example, sodium benzenethiolate reacted 15-fold faster than phenolate. The nitro group in the reaction products was reduced to afford (after hydrolysis) a wide range of γ-substituted α-aminobutyric acids.[103] Later, the NCP ring-opening reaction with esters of (*S*)-α-amino acids such as leucine, alanine, proline, phenylglycine, phenylalanine has been described.[104]



Ar = 2,6-Bu^t_2-4-$MeOC_6H_2$; R^2 = H: R^1 = Me, Pr^i, Ph, Bn; R^1-R^2 = $(CH_2)_3$.

Products **66** were reduced with zinc in acetic acid; the subsequent hydrolysis afforded esters of 2-substituted 6-amino-3-azapimelic acids.

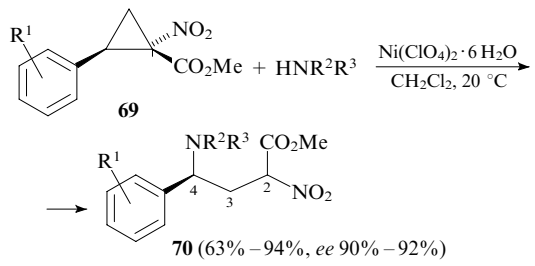
A series of recent studies[105–107] demonstrated the great prospects of the nucleophilic three-membered ring-opening reactions of NCP. 1-Nitrocyclopropyl ketones **67** were studied in reactions with primary amines.[105] Doubly activated NCP **67** underwent a stereoselective reaction with amines (preferentially, aromatic) in boiling toluene to afford 4-nitropyrrolines **68** in high yields.



R^1 = Me, Pr^n, cyclo-C_3H_5, Ph; R^2 = Ph, 4-FC_6H_4, 1-naphthyl; R^3 = Ph, 4-$MeOC_6H_4$, 4-ClC_6H_4, Bn, All, Bu^t.

1-Nitrocyclopropanecarbaldehydes also manifest high activity in reactions with aromatic amines. These reactions included nucleophilic ring-opening and intramolecular condensation steps to form pyrrolines **68** (R^1 = H). This process was favoured by the presence of an aromatic substituent in position 2 of the small ring.

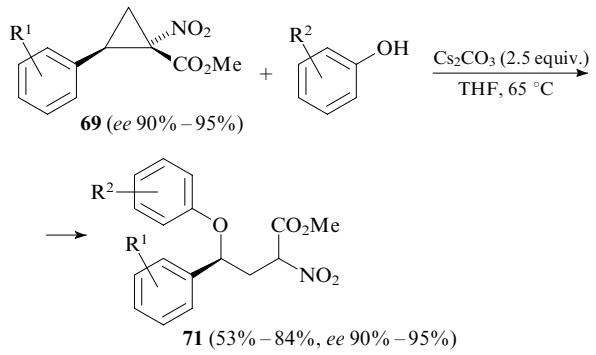
Later, reactions of nucleophilic ring-opening in 1-nitrocyclopropanecarboxylates **69** by amines in the presence of Lewis acids were studied.[106] The ring-opening occurred under mild conditions; nickel perchlorate used as the Lewis acid provided preliminary ionization of the starting NCP for its nucleophilic reaction with amines. In the majority of cases, the reaction proceeded with complete conversion without racemization of the electrophilic site in the cyclopropane ring (C-4 atom in product **70**).



R^1 = H, 4-Cl, 2,3-benzo; R^2 = Alk, Ar; R^3 = Alk, H.

Varying both the Lewis acids and the substituents in position 2 in three-membered rings made it possible to elaborate a general convenient procedure for synthesizing bifunctional compounds **70** that can be used in the synthesis of quite a number of promising biologically active compounds.[106]

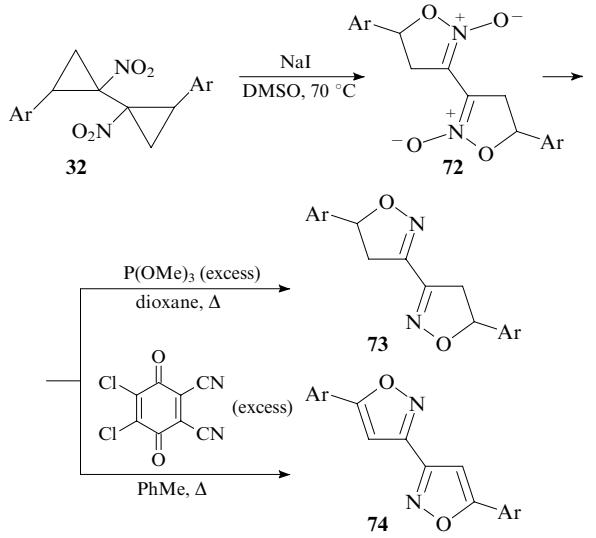
The recently discovered phenol addition to 1-nitropropanecarboxylates **69** should be classified with nucleophilic three-membered ring-opening reactions in NCP.[107]



R^1 = H, 4-Cl, 2,3-benzo; R^2 = Ph, 4-$MeOC_6H_4$, 4-$F_3CC_6H_4$, 3-ClC_6H_4, 2-MeC_6H_4, 2-BrC_6H_4, 2-$MeOC_6H_4$, *etc.*

Reactions with enantiomerically enriched NCP **69** proceeded with complete retention of enantiomeric excesses and the inversion of the absolute configuration of the asymmetric centre in product **71**. 1-Nitro-3-phenoxypropanes were formed in high yields irrespective of the type of substituents in phenols and electrophilic cyclopropanes **69**. The method developed was successfully used in the enantioselective synthesis of certain drugs.[107]

Thermally activated isomerization of NCP to isoxazoline *N*-oxides is well known,[78] as well as the electrophilic ($BF_3 \cdot Et_2O$) and nucleophilic (NaI) catalysis.[103] The NCP isomerization proceeded most efficiently under the action of NaI in DMSO at 70 °C and was accompanied by the nucleophilic three-membered ring-opening with intramolecular O-alkylation.[103] NaI-induced isomerization in DMSO was studied[108] for dinitro(bicyclopropanes) **32**. The corresponding bisnitronates **72** were obtained in high yields. The stereochemical aspects of isomerization were studied and



Ar = 4-MeC_6H_4, 1-naphthyl, 2-thienyl.

the methods for the transformation of bisnitronates **72** into tetrahydro(biisoxazoles) **73** and biisoxazoles **74** were developed.

2. Nucleophilic opening reactions of 1,1-dinitrocyclopropanes. Synthesis of 3-substituted 1,1-dinitropropanes

Synthesis of 1,1-dinitrocyclopropanes **60** was discussed in Section II.5. They are doubly activated cyclopropanes; their reactivity with respect to a wide range of C-, N-, O- and S-nucleophiles was studied. It was shown[109] that dinitrocyclopropane (**57**) reacts with different inorganic salts (KCN, KSCN, NaN_3) to afford stable salts of 1,1-dinitro-3-substituted propanes; acidification of the latter resulted in the corresponding *gem*-dinitropropanes **75a–c** (Table 3).

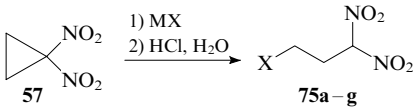
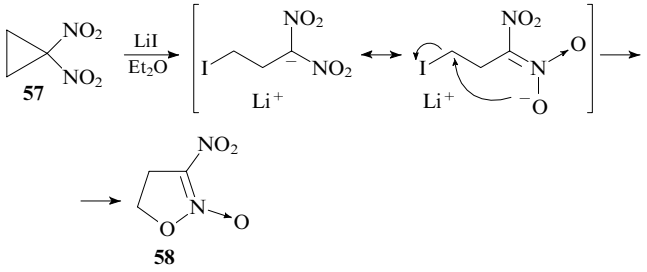


Table 3. Reactions of nucleophilic ring-opening in dinitrocyclopropane **57**.[109]

Compound **75**	MX	Solvent	T/°C	Reaction time/h	Yield (%)
a	NaN_3	MeCN–H_2O (1 : 1)	60	16	52
b	NaCN	MeCN–H_2O (1 : 1)	80	10	54
c	KSCN	MeCN–H_2O (1 : 1)	60	4	75
d	NaOEt	EtOH	boiling	1	84
e	$KOCH_2C{\equiv}CH$	THF	20	24	77
f	$NaS(CH_2)_2Me$	MeOH	20	4	54
g	$NaHC(CO_2Et)_2$	EtOH	boiling	2	82

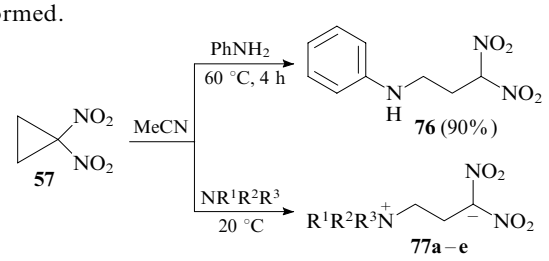
Under the same conditions, the reactions of dinitrocyclopropane (**57**) with alkali metal alcoholates and thiolates afforded propanes **75d–f** with equal ease, while the reaction of lithium iodide in diethyl ether resulted in the rearrangement product, namely, 3-nitroisoxazoline *N*-oxide (**58**) in quantitative yield. The formation of *N*-oxide **58** should be considered as two consecutive nucleophilic substitution reactions in which the iodide anion initiates the small-ring opening.



Cyclopropane **57** underwent three-membered ring-opening with sodium diethyl malonate, which acted as a C-nucleophile, to form dinitroester **75g** (see Table 3).

Amines and nitrogen-containing aromatic heterocycles readily opened the cyclopropane ring. The reaction of compound **57** with aniline afforded neutral product **76**, in

the other cases, zwitter-ionic compounds **77a–e** were formed.



Compound **77**	$NR^1R^2R^3$	Reaction time /h	Yield (%)
a	piperidine	1	67
b	hydrazine	72	48
c	triethylamine	48	79
d	pyridine	24	80
e	4-aminopyridine	24	88

Thus, reactions of 1,1-dinitrocyclopropane (**57**) with various nucleophiles proceeded under mild conditions with cyclopropane ring-opening and the retention of both nitro groups to afford different 3-substituted 1,1-dinitropropanes.

IV. Thermochemical properties of nitro- and dinitrocyclopropanes

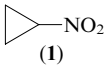
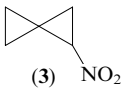
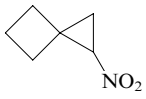
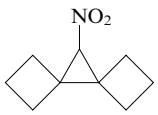
As has already been mentioned in the Introduction, nitrocyclopropanes, including polyspiro derivatives, are highly energetic compounds, their molecules containing simultaneously strained cyclopropane fragments and one or two nitro groups traditionally considered as energetic groups.[1,2] Many nitro compounds are potential explosives, which, on the one hand, makes difficult their experimental studies and, on the other hand, requires knowledge of their thermodynamic properties. For nitrocyclopropane, only the results of quantum chemical calculations of the enthalpy of formation in the gas phase can be found in the literature,[110] it is equal to 26.86 kJ mol^{-1}. Pioneering experimental studies [111,112] provided the combustion energies and the enthalpies of formation of NCP and nitropolyspiro-linked cyclopropanes. Table 4 shows standard thermochemical parameters for nitrocyclopropanes under study. It should be noted that the experimentally found enthalpy of formation of nitrocyclopropane in the gaseous state agrees well with the results of quantum chemical calculations for this compound. Based on the data on enthalpies of formation, the contributions of CNO_2 and $C(NO_2)_2$ groups to the enthalpy were calculated.

By and large, NCP under study are indeed strained compounds with high positive enthalpies of formation. They withstand elevated temperatures, are characterized by storage stability and possess increased densities. The obtained data were used in the determination of reliable increments for nitro- and *gem*-dinitrocyclopropane groups that are of interest for carrying out forecasting calculations and quick estimates of the energetics of strained polycyclic nitro compounds.

* * *

The material considered in this review convincingly reflects considerable success achieved recently in the chemistry of nitrocyclopropanes. Many methods of synthesizing NCP with quite different structures were developed, which has determined their wide use in the preparative organic chemistry. This is true, first of all, for new directions where NCP are used as building blocks in the synthesis of intricate organic molecules such as natural compounds, their synthetic analogues, conformationally rigid polycyclic aminocyclopropanecarboxylic acids with diverse biological activities. Nitrocyclopropanes of the polyspirane (triangulane) series are of interest as a new group of energetic compounds as confirmed by their thermochemical properties determined experimentally.

Table 4. Standard thermochemical characteristics of selected NCP.[a]

Compound	d /g cm^{-3}	$-\Delta_c u^\circ$ /J g^{-1}	$-\Delta_c H^\circ_m$ /kJ mol^{-1}	$\Delta_f H^\circ_m$ (liq.) /kJ mol^{-1}	$\Delta_{vap} H^\circ_m$ /kJ mol^{-1}	$\Delta_f H^\circ_m$ (gas) /kJ mol^{-1}	Ref.
 (**1**)	1.135	21570 ± 35	1877.7 ± 3.1	−17.4 ± 3.1	44.7	27.3	111
 (**57**)	1.423	13570 ± 47	1787.3 ± 7.8	35.1 ± 7.8	52.7	87.8	112
 (**3**)	1.181	27355 ± 39	3094.9 ± 4.4	126.9 ± 4.4	47.7	174.6	111
	1.172	29493 ± 47	3751.7 ± 5.9	104.4 ± 5.9	49.7	154.1	112
	1.211	33114 ± 47	5609.1 ± 7.8	−76.2 ± 7.8	80.3	4.1	112

[a] d is density; $\Delta_c u^\circ$ is standard combustion energy; $\Delta_c H^\circ_m$, $\Delta_f H^\circ_m$ and $\Delta_{vap} H^\circ_m$ are standard enthalpies of combustion, formation and vaporization, respectively.

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References

1. J P Agrawal, R D Hodgson *Organic Chemistry of Explosives* (Chichester, Wiley, 2007)
2. O A Ivanova, N V Yashin, E B Averina, Yu K Grishin, T S Kuznetsova, N S Zefirov *Izv. Akad. Nauk, Ser. Khim.* 2008 (2001) [a]
3. N V Yashin, Candidate Thesis in Chemical Sciences, Moscow State University, Moscow, 2004
4. H U Reissig, R Zimmer *Chem. Rev.* **103** 1151 (2003)
5. M Y Brian, L Pagenkopf *Tetrahedron* **61** 321 (2005)
6. N Ono *The Nitrogroup in Organic Synthesis* (New York: Wiley-VCH, 2001)
7. R Ballini, G Bosica, D Fiorini, A Palmieri, M Petrini *Chem. Rev.* **105** 933 (2005)
8. J Salamn *Top. Curr. Chem.* **207** 1 (2000)
9. W A Donaldson *Tetrahedron* **57** 8589 (2001)
10. T K Chakraborty, V R Reddy *Tetrahedron Lett.* **47** 2099 (2006)
11. K E Brighty, M J Castaldi *Synlett* 1097 (1996)
12. B D Zlatopolskiy, M Radzom, A Zeeck, A de Meijere *Eur. J. Org. Chem.* 1525 (2006)
13. A Asai, A Hasegawa, K Ochiai, Y Yamashita, T Muzukami *J. Antibiot.* **53** 81 (2000)
14. T D Goots, K E Brighty *Med. Res. Rev.* **16** 433 (1996)
15. F Gnad, O Reiser *Chem. Rev.* **103** 1603 (2003)
16. S De Pol, C Zorn, C D Klein, O Zerbe, O Reiser *Angew. Chem., Int. Ed.* **43** 511 (2004)
17. A G Alekseev, V V Razin, in *Sovremennye Problemy Organicheskoi Khimii (Mezhvuz. Sb. Nauch. Tr.)* [Current Problems of Organic Chemistry (Intercollege Collection of Research Works) (St Petersburg: St Petersburg State University, 1998) No. 12, p. 44
18. R Ballini, A Palmieri, D Fiorini *ARKIVOC* (vii) 172 (2007)
19. H B Hass, H Shechter *J. Am. Chem. Soc.* **75** 1382 (1953)
20. A E Stanley, J M Bonicamp, S E Godbey, L M Ludwick *J. Photochem. Photobiol. A* **91** 33 (1995)
21. US P. 3100805; *Chem. Abstr.* **60** P4216 (1964)
22. G M Lampman, D A Horne, G D Hager *J. Chem. Eng. Data* **14** 396 (1969)
23. US P. 3769355; *Chem. Abstr.* **80** 3162 (1974)
24. US P. 3903180; *Chem. Abstr.* **83** 192663 (1975)
25. E P Kohler, P Allen Jr *J. Am. Chem. Soc.* **50** 884 (1928)
26. A S Sopova, O I Yurchenko, V V Perekalin *Zh. Org. Khim.* **1** 1707 (1965) [b]
27. J Zindel, A de Meijere *J. Org. Chem.* **60** 2968 (1995)
28. M Brandl, S I Kozhushkov, K Loscha, O V Kokoreva, D Yufit, A K Howard, A de Meijere *Synlett* 1741 (2000)
29. O V Larionov, T F Savel'eva, K A Kochetkov, N S Ikonnikov, S I Kozhushkov, D S Yufit, J A K Howard, V M Khrustalev, Y N Belokon, A de Meijere *Eur. J. Org. Chem.* 869 (2003)
30. I Kuwajima, R Ando, T Sugawara *Tetrahedron Lett.* **24** 4429 (1983)
31. S Arai, K Nakayama, T Ishida, T Shioiri *Tetrahedron Lett.* **40** 4215 (1999)
32. M C Maestro, M C Barquilla, M R Martin *Tetrahedron: Asymmetry* **10** 3593 (1999)
33. M Kocor, W Kroszczinski *Synthesis* 813 (1976)
34. T F Braish, M Castaldi, S Chan, D E Fox, T Keltonic, J McGarry, J M Hawkins, T Norris, P R Rose, J E Sieser, B J Sitter, H Watson *Synlett* 1100 (1996)
35. T Norris, T F Braish, M Butters, K M De Vries, J M Hawkins, S S Massett, P R Rose, D Santafianos, C Sklavounos *J. Chem. Soc., Perkin Trans. 1* 1615 (2000)
36. US P. 6057455; *Chem. Abstr.* **132** 308241 (2000)
37. US P. 5298629; *Chem. Abstr.* **121** 9156 (1994)
38. Eur. P. 863874; *Chem. Abstr.* **127** 81354 (1997)
39. Eur. P. 818445; *Chem. Abstr.* **128** 140606 (1998)
40. Eur. P. 818446; *Chem. Abstr.* **128** 127930 (1998)
41. R Ballini, D Fiorini, A Palmieri *Synlett* 1704 (2003)
42. H M Hansen, D A Longbootom, S V Ley *Chem. Commun.* 4838 (2006)
43. J Vesely, G-L Zhao, A Bartoszewicz, A Cordova *Tetrahedron Lett.* **49** 4209 (2008)
44. J Zhang, Z Hu, S Zhao, M Yan *Tetrahedron* **65** 802 (2009)
45. A S Sopova, V V Perekalin, O I Yurchenko, G M Arnautova *Zh. Org. Khim.* **5** 868 (1969) [b]
46. E V Trukhin, S V Makarenko, V M Berestovitskaya *Zh. Org. Khim.* **34** 72 (1998) [b]
47. S H McCooey, T McCabe, S J Connon *J. Org. Chem.* **71** 7494 (2006)
48. J Zindel, A de Meijere *Synthesis* 190 (1994)
49. O Mitsunobu *Synthesis* 1 (1981)
50. J Yu, J R Falck *J. Org. Chem.* **57** 3757 (1992)
51. B B Snider, Q L Che *Tetrahedron* **58** 7821 (2002)
52. P A Wade, W P Dailey, P J Carroll *J. Am. Chem. Soc.* **109** 5452 (1987)
53. P A Wade, P A Kondracki, P J Carroll *J. Am. Chem. Soc.* **113** 8807 (1991)
54. Yu A Volkova, O A Ivanova, E M Budynina, E B Averina, in *Materialy XI Mezhdunarodnoi Nauchno-tekhnicheskoi Konferentsii 'Perspektivy Razvitiya Khimii i Prakticheskogo Primeneniya Atsiklicheskikh Soedinenii', Volgograd, 2008* (Proceedings of the XIth International Research and Technical Conference 'Perspectives of Investigation of the Chemistry and Practical Application of Acyclic Compounds', Volgograd, 2008) p. 126
55. Yu A Volkova, O A Ivanova, E M Budynina, E A Revunov, E B Averina *Tetrahedron Lett.* **50** 2793 (2009)
56. A Mustafa, A H E Harhash *J. Am. Chem. Soc.* **76** 1383 (1954)
57. W E Parham, J H G Braxton, J C Serres *J. Org. Chem.* **26** 1831 (1961)
58. G Rembarz, B Erust *Z. Chem.* **7** 421 (1967)
59. J P Marino, T Kaneko *Tetrahedron Lett.* **14** 3971 (1973)
60. F A Gabitov, O V Kreshleva, A L Fridman *Zh. Org. Khim.* **13** 1117 (1977) [b]
61. D Ranganathan, C B Rao, S Ranganathan, A K Mehrotra, R Iyengar *J. Org. Chem.* **45** 1185 (1980)
62. F M Dean, R S Jonson *J. Chem. Soc., Perkin Trans. 1* 2049 (1980)
63. N A Anisimova, N G Makarova, G A Berkova, V M Berestovitskaya *Zh. Org. Khim.* **43** 788 (2007) [b]
64. G A Berkova, N A Anisimova, N G Makarova, L I Deiko, V M Berestovitskaya *Zh. Obshch. Khim.* **76** 156 (2006) [c]
65. T Armaroli, C Dell'Erba, A Gabellini, F Gasparrini, A Mugnoli, M Novi, G Petrillo, C Tavani *Eur. J. Org. Chem.* 1284 (2002)
66. A Bojilova, I Videkova, C Ivanov, N A Rodios, A Terzis, C P Raptopoulou *Tetrahedron* **50** 13023 (1994)
67. G Galley, J Huber, S Anklam, P G Jones, M Patzel *Tetrahedron Lett.* **37** 6307 (1996)
68. J Hubner, J Liebscher, M Patzel *Tetrahedron* **58** 10485 (2002)
69. G Kumaran, G H Kumaran *Synthesis* 1545 (1995)
70. U Schöllkopf, P Tonne, H Schäfer, P Markusch *Justus Liebigs Ann. Chem.* **722** 45 (1969)
71. U Schöllkopf, P Tonne *Justus Liebigs Ann. Chem.* **753** 135 (1971)
72. P E O'Bannon, W P Dailey *Tetrahedron* **46** 7341 (1990)
73. J B Hendrickson, W A Wolf *J. Org. Chem.* **33** 3610 (1968)
74. H Balli, R Llw *Tetrahedron Lett.* **5** 5821 (1966)
75. A B Charette, R P Wurz, T Ollivier *J. Org. Chem.* **65** 9252 (2000)
76. A B Charette, R P Wurz, T Ollivier *Helv. Chim. Acta* **85** 4468 (2002)
77. P E O'Bannon, W P Dailey *Tetrahedron Lett.* **29** 987 (1988)
78. P E O'Bannon, W P Dailey *Tetrahedron* **46** 7341 (1990)
79. P E O'Bannon, W P Dailey *J. Org. Chem.* **54** 3096 (1989)
80. A B Charette, R P Wurz *J. Mol. Catal.* **196** 83 (2003)
81. P E O'Bannon, W P Dailey *J. Org. Chem.* **55** 353 (1990)
82. R P Wurz, A B Charette *J. Org. Chem.* **69** 1262 (2004)

83. N V Yashin, E B Averina, S M Gerdov, T S Kuznetsova, N S Zefirov *Tetrahedron Lett*. **44** 8241 (2003)
84. N V Yashin, E B Averina, Y K Grishin, T S Kuznetsova, N S Zefirov *Synthesis* 279 (2006)
85. N V Yashin, E B Averina, Y K Grishin, T S Kuznetsova, N S Zefirov *Synthesis* 880 (2006)
86. A V Chemagin, N V Yashin, E B Averina, T S Kuznetsova, N S Zefirov *Dokl. Akad. Nauk* **419** 772 (2008) [d]
87. R P Wurz, A B Charette *Org. Lett*. **5** 2327 (2003)
88. H T Bonge, T Hansen *Synlett* 55 (2007)
89. B Moreau, A B Charette *J. Am. Chem. Soc*. **127** 18014 (2005)
90. G A Olah, D R Squire *Chemistry of Energetic Materials* (New York: Academic Press, 1991)
91. V A Tartakovskii, B G Gribov, I A Savost'yanova, S S Novikov *Izv. Akad. Nauk SSSR, Ser. Khim*. 1644 (1965) [a]
92. Y Kai, P Knochel, S Kwiatkowski, J D Dunitz, J F M Oth, D Seebach, H O Kalinowski *Helv. Chim. Acta* **65** 137 (1982)
93. E M Budynina, E B Averina, O A Ivanova, T S Kuznetsova, N S Zefirov *Tetrahedron Lett*. **46** 657 (2005)
94. E M Budynina, E B Averina, O A Ivanova, N V Yashin, T S Kuznetsova, N S Zefirov *Synthesis* 2609 (2004)
95. O A Ivanova, E M Budynina, E B Averina, T S Kuznetsova, Yu K Grishin, N S Zefirov *Synthesis* 2009 (2007)
96. W T Wijnen, H Steinberg, T J Boer *Tetrahedron* **28** 5423 (1972)
97. J E Bartmess, B Wilson, D N Sorensen, J E Bloor *Int. J. Mass Spectrom. Ion Process*. **117** 557 (1992)
98. F G Bordwell, N R Vanier, W S Mathews, J B Hendrickson, P L Skiper *J. Am. Chem. Soc*. **97** 7160 (1975)
99. F G Bordwell, J E Bartness, Y A Hayata *J. Org. Chem*. **43** 3113 (1978)
100. P E O'Bannon, W P Dailey *J. Am. Chem. Soc*. **111** 9244 (1989)
101. W Cao, I Erden, J R Keefe *Angew. Chem., Int. Ed. Engl*. **34** 1091 (1995)
102. R Hanner, D Seebach *Chimia* **39** 356 (1985)
103. D Seebach, R Hanner, T Vettiger *Helv. Chim. Acta* **70** 1507 (1987)
104. T Vettiger, D Seebach *Liebigs Ann. Chem*. 195 (1990)
105. R P Wurz, A B Charette *Org. Lett*. **7** 2313 (2005)
106. O Lifchits, A B Charette *Org. Lett*. **10** 2809 (2008)
107. O Lifchits, D Alberico, I Zakharian, A B Charette *J. Org. Chem*. **73** 6838 (2008)
108. L Bianchi, C Dell'Erba, F Gasparrini, M Novi, G Petrillo, F Sancassan, C Tavani *ARKIVOC* (xi) 142 (2002)
109. E M Budynina, O A Ivanova, E B Averina, T S Kuznetsova, N S Zefirov *Tetrahedron Lett*. **47** 647 (2006)
110. A Burcat *J. Phys. Chem. Ref. Data* **28** 63 (1999)
111. A A Kurskaya, S V Mel'khanova, S M Pimenova, N V Yashin *Zh. Fiz. Khim*. **80** 1972 (2006) [e]
112. S M Pimenova, S V Mel'khanova, V P Kolesov, N V Yashin, T S Kuznetsova *Zh. Fiz. Khim*. **77** 2106 (2003) [e]

[a] — *Russ. Chem. Bull., Int. Ed. (Engl. Transl.)*
[b] — *Russ. J. Org. Chem. (Engl. Transl.)*
[c] — *Russ. J. Gen. Chem. (Engl. Transl.)*
[d] — *Dokl. Chem. (Engl. Transl.)*
[e] — *Russ. J. Phys. Chem. (Engl. Transl.)*