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Recent advances in the catalytic cyclopropanation of unsaturated compounds with diazomethane

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The main achievements and development trends of the past 10–15 years related to the catalytic cyclopropanation of unsaturated compounds with diazomethane are integrated and analyzed. The attention is focused on the most efficient catalysts based on palladium compounds. Data on the effects of substrate structure and nature of catalyst components on the regio- and stereoselectivity of these reactions are systematized. Characteristic features of safe methods for diazomethane generation are considered, including the use of membrane technologies and continuous-flow and *in situ* preparation methods, which have prospects for industrial application.
The bibliography includes 281 references.

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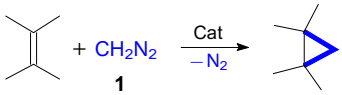
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1. Introduction

Molecules containing a cyclopropane moiety constitute an important class of organic compounds. Despite the high strain energy of the three-carbon ring (27.5 kcal mol^{-1}), these compounds are stable and have a high practical value.[1] Indeed, the cyclopropane moiety is a part of more than 4000 natural compounds[2–13] and more than 100 known pharmaceuticals.[2,3] Cyclopropane derivatives possess a broad spectrum of biological activities[14–17] and participate in important biochemical processes.[18–26] In addition, molecules with three-carbon rings have now become convenient building blocks for the synthesis of various classes of organic molecules.[1,27–30]

Among methods for the construction of cyclopropane ring, direct cyclopropanation of olefins ([2+1]-cycloaddition) is used most often.[1,28–32] One of the methods is cyclomethylenation of unsaturated double bonds (including unactivated ones) with diazomethane in the presence of various catalysts (Scheme 1).[33,34]

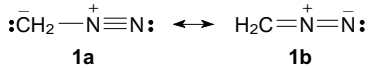
Scheme 1



1

Diazomethane is a linear molecule, the ground state of which is mainly described by two resonance structures: **1a** and **1b**.[34,35]

Structures 1a,b



1a **1b**

Under ambient conditions, diazomethane is a yellow gas (b.p. −23 °C), possessing characteristic spectral properties.[36] The electronic absorption spectrum of diazomethane exhibits two peaks, one at 410 nm and the other (strong) at 270 nm. The IR spectrum of diazomethane also shows an

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intense characteristic absorption band at 2100 cm^{-1}, which corresponds to N≡N triple bond vibrations.

Due to high reactivity, diazomethane is one of the most versatile and useful organic reagents. The only by-product formed upon diazomethane decomposition is N_2. However, extensive use of diazomethane is hampered by its toxicity, high volatility and explosion hazard.[37, 38]

For a long period of time, diazomethane-based methods for the synthesis of cyclopropane derivatives developed slowly and the synthetic potential of this reaction was little studied. In recent years, considerable attention has been paid to the development of safe methods for generation of diazomethane, in particular, using membrane technologies and continuous-flow and *in situ* preparation techniques. On the basis of these approaches, preparative methods for producing gramme amounts of cyclopropanes have been developed. It is especially important that these methods open up prospects for more extensive industrial application of diazomethane in organic synthesis. This is a benefit of catalytic cyclopropanation with diazomethane in comparison with alternative methods (such as Simmons – Smith reaction and the use of various zinc and aluminium carbenoids), which are widely used in organic synthesis, but have little promise for industrial implementation for a number of reasons. The appearance of safe methods for diazomethane generation stimulated studies on the application of diazomethane for catalytic cyclomethylenation of double bonds in olefins to prepare compounds with a cyclopropane ring and on the search for new efficient catalysts for this reaction.

The catalytic cyclomethylenation with diazomethane is especially promising for the preparation of compounds that contain no activating electron-donating or -withdrawing substituents in the three-membered ring, *e.g.*, terpenes, steroids, lipids, antibiotics and other natural and practically valuable compounds.[9, 30, 39] Currently, the introduction of a cyclopropane moiety for the synthesis of these molecules is accomplished using either the Simmons – Smith reaction and related approaches involving aluminium carbenoids[40] or multistep routes including, in particular, the initial introduction of activating substituents to the double bond to be cyclopropanated, subsequent cyclopropanation (Corey – Chaykovsky reaction, *etc.*) and finally transformations of the activating groups. The use of direct catalytic diazomethane cyclopropanation of unactivated double bonds considerably simplifies some of these reactions and increases the yields of products.

The application of catalytic methylenation of olefins with diazomethane in the synthesis of cyclopropanes was fully integrated in only one dedicated review[33] published in 1993. Over the last 15 years, diazomethane was considered only in separate chapters of review publications devoted to the synthesis of cyclopropanes[31, 32, 41] and to organometallic catalysts, particularly those based on palladium[42 – 44] and iron[45 – 47] compounds. Mention should be made of a number of reviews that address the use of diazomethane in the synthesis of particular classes of cyclopropanes, including donor-acceptor cyclopropanes[30] and spirocarbocycles.[43]

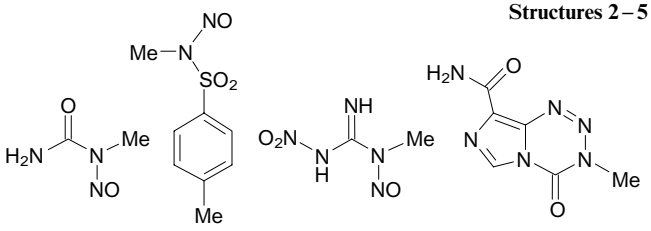
The catalytic cyclopropanation with diazomethane has a limited use in asymmetric synthesis since there are no substituents in the CH_2 group being added. Examples of the application of diazomethane in the asymmetric synthesis of cyclopropanes are considered in a monograph[48] and in several reviews.[2, 49, 50]

Thus, there are actually no review publications on the current state of studies and synthetic potential of the catalytic decomposition of diazomethane for the preparation of cyclopropanes. Therefore, in this review, we systematically describe the data, published mainly over the last 10 – 15 years, on diazomethane generation and use as the cyclomethylenating agent in the synthesis of various classes of organic compounds. Earlier references are included when it is necessary to clarify the details of catalytic cyclopropanation with diazomethane or to demonstrate the key achievements of the preceding period.

2. Sources and generation methods of diazomethane

Diazomethane was first obtained by Pechmann[51] in 1894 from *N*-methyl-*N*-nitrosocarbamate. At present, diazomethane is usually prepared by alkaline hydrolysis of *N*-methyl-*N*-nitroso derivatives of urea, carbamates, sulfonamides and ketones. The most frequently used sources of diazomethane are *N*-methyl-*N*-nitrosourea (**2**) (MNU), *N*-methyl-*N*-nitroso-*p*-toluenesulfonamide (**3**) (diazald) and *N*-methyl-*N*-nitro-*N*-nitrosoguanidine (**4**) (MNNG).[34] Diazald is a commercially available (included in the Sigma-Aldrich catalogue) diazomethane precursor; it is thermally more stable and less toxic than MNU or MNNG.[34, 36] Recently, temozolomide (TMZ) **5** was proposed as one more commercially available non-explosive and non-toxic precursor of diazomethane.[47] For the generation of isotope-labelled (^2H and ^{13}C) diazomethane, efficient methods have been developed for the synthesis of required diazald derivatives,[52] which are now commercially available (Sigma-Aldrich).

Structures 2 – 5



2 **3** **4** **5**

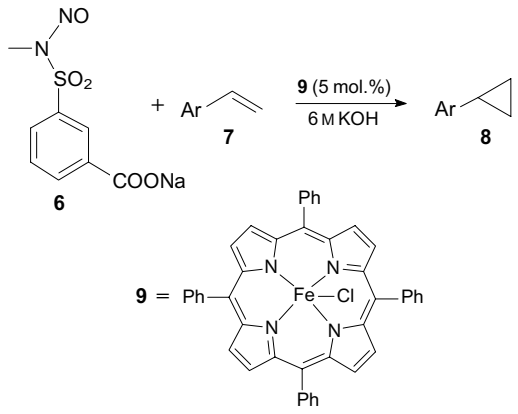
The synthetic versatility of diazomethane is restricted by considerable practical difficulties associated with its preparation and use. Diazomethane solutions are explosive in concentrations of $> 0.6\ M$.[53, 54] Diazomethane gas is explosive in the presence of oxygen even in a concentration of 3.9%, while in an oxygen-free nitrogen atmosphere, the limiting safe concentration of diazomethane is 14.7%.[55] Diazomethane tends to rapidly decompose and to explode on contact with rough surfaces. The synthesis of diazomethane in a laboratory requires special equipment without ground glass joints. One must not use glassware with signs of cracks or other surface defects (*e.g.*, scratches), while sharp edges of glassware should be fire-polished.[38, 51, 56, 57] The exposure to bright light can also induce the detonation of diazomethane. Special laboratory ware kits for the preparation and purification of diazomethane are commercially available (*e.g.* a Sigma-Aldrich kit for the generation from diazald and a Duran kit for the generation from MNNG).

Due to toxicity and explosion hazard, diazomethane is rarely employed in laboratory practice, although it is a highly valuable, highly potent and versatile reagent for the synthesis of many practically useful products. Therefore, in recent years, efforts of researchers have been directed towards the development of safe methods for diazomethane generation and use in organic synthesis.

The first safe method for catalytic cyclopropanation with diazomethane generated *in situ* was developed in 1992.[58] According to this method, *N*-methyl-*N*-nitrosourea (source of diazomethane) was slowly added at 12–18 °C to a two-phase mixture of an olefin solution with a catalyst (0.5 mol.%) in the CH_2Cl_2–Et_2O solvent and a concentrated aqueous KOH solution at such a rate that the resulting diazomethane migrated to the organic phase and completely reacted, without being accumulated, so that the current diazomethane concentration was relatively low. The catalysts efficient for this reaction include $(PhCN)_2PdCl_2$, $[(PhO)_3P]_2PdCl_2$, $Pd(acac)_2$ and $Pd(OAc)_2$. This method was successfully applied for cyclopropanation of various unsaturated compounds.[54, 59–62]

Later, an analogous method was developed for catalytic cyclopropanation of unsaturated compounds with diazomethane generated *in situ* from a water-soluble analogue of diazald **6** (source of diazomethane) on treatment with 6 M KOH.[45] The resulting diazomethane was also transferred to the organic phase of the two-phase system and reacted there with alkenes **7** according to the [2 + 1]-cycloaddition pathway (Scheme 2). The highest yields of cyclopropanes **8** were attained when air-stable iron(III) porphyrin **9** (FeTPPCl) was used as the catalyst, whereas similar rhodium, ruthenium, cobalt, palladium and copper complexes were less active.

Scheme 2



One more safe method for the generation of diazomethane suitable for cyclopropanation reactions is the continuous process giving anhydrous diazomethane in a tube-in-tube reactor.[63] A specific feature of this reactor is an inner tube made of a hydrophobic gas-permeable membrane (Teflon AF-2400). Diazomethane is formed in this inner membrane tube upon alkaline decomposition of diazald and then diffuses across the membrane into the outer tube in which it dissolves in an appropriate organic solvent and undergoes reactions typical of diazomethane, including cyclopropanation (Fig. 1).

This method allows safe reactions with a solution of dry diazomethane to be performed on a laboratory scale. The possibility of scaling up the process was demonstrated in

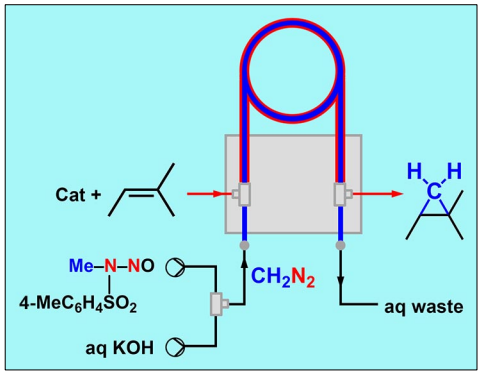
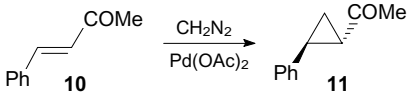


Figure 1. Diagram of the tube-in-tube reactor (aq waste stands for aqueous waste).

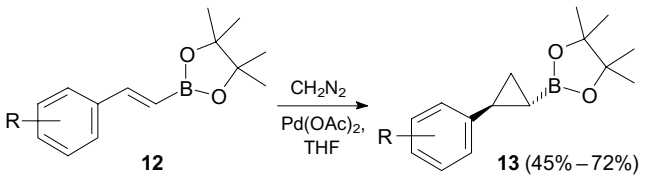
relation to the reaction of 4-phenylbut-3-en-2-one (**10**). In the presence of $Pd(OAc)_2$, the yield of 1-acetyl-2-phenylcyclopropane **11** under non-optimized conditions was 59% (Scheme 3).[63]

Scheme 3



Subsequently, an identical reactor was successfully applied for cyclopropanation of boronic acid esters **12**.[64] The efficiency of this method for the preparation of cyclopropanes **13** was demonstrated for 14 examples (for details, see Section 3.2.3) (Scheme 4). The reactor used in that study was also suitable for scaling-up the synthesis of the target cyclopropane **13a** (R = H) to a capacity of 190 mg per hour.[64]

Scheme 4



Thus, elaboration of the methods for safe generation of diazomethane eliminates the severe limitations hampering the broad use of diazomethane in laboratory practice and industry.

Currently, safe methods for diazomethane generation in a continuous liquid flow have also been developed. According to these methods, a diazomethane source is passed, at a definite rate, through a special chamber, tube or microreactor.[65–70] The generated diazomethane is then collected and used for the subsequent reaction; alternatively, the reaction with the substrate is conducted directly in the flow. The process requires minor amounts of reactants at a time, which makes this method safe. This approach made it possible to implement diazomethane-based syntheses on an industrial scale. The first continuous-flow industrial method for the generation of diazomethane from *N*-methyl-*N*-nitrosourea was developed by the Aerojet company in 1998.[71, 72] One more industrial system for continuous-flow generation

of diazomethane from diazald was devised by Phoenix Chemicals Ltd (50 – 60 tonnes per year).[55] However, the above-indicated processes using diazomethane do not include cyclopropanation. The application of continuous-flow generation of diazomethane for the preparation of cyclopropane derivatives was described only in patents.[73, 74] In view of the synthetic potential of continuous-flow generation of diazomethane, one may expect that in the future, this method would be extended to the laboratory synthesis of cyclopropanes.

3. Catalytic cyclopropanation of unsaturated double bonds

The catalytic decomposition of diazomethane, unlike photochemical or thermal decomposition, is suitable for conducting reactions under mild conditions and for selective synthesis of the target products in high yields. The details of conduction of these reactions and the key catalysts used formerly are considered in a review [33] published in 1993.

3.1. Mechanism of catalytic cyclopropanation of olefins

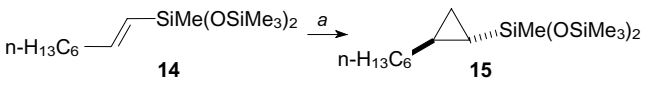
The catalytic cyclopropanation of olefins with diazomethane is one of common methods for the preparation of cyclopropane derivatives. These reactions can occur by two alternative mechanisms, depending on the type of metal in the catalyst (Scheme 5).

The mechanism of reactions catalyzed by Cu-, Fe-, Ru-, Rh- or Co-based catalysts implies the attack by diazomethane on the coordinatively unsaturated site of the catalyst (M) followed by the formation of a metal carbene complex, after elimination of N_2 (Scheme 5 *a*).[49, 75 – 80] Subsequently, this carbene complex undergoes concerted [2 + 1]-cycloaddition with olefin to give a cyclopropane product.

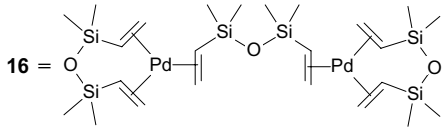
Reactions catalyzed by palladium compounds follow a different mechanism. In this case, the reaction starts with the formation of a complex between low-valent palladium and olefin, which then reacts with a diazo compound to give a metallacyclobutane intermediate, which is then converted to the cyclopropane product (Scheme 5 *b*).[33, 75, 81, 82] Therefore, palladium compounds efficiently catalyze the cyclopropanation of only those olefins that are readily coordinated to palladium. During the reaction, palladium(II) catalysts, such as $Pd(OAc)_2$, $(PhCN)_2 \cdot PdCl_2$ or $Pd(acac)_2$, are first reduced with diazomethane to catalytically active low-valent palladium complexes.[33] The participation of Pd(0) – olefin complexes was detected for the first time back in 1984 in relation to the catalytic cyclopropanation of norbornadiene and cyclooctene in the presence of their π-complexes with $PdCl_2$.[83] The addition of CH_2N_2 caused discolouration of the initially yellow olefin complexes with $PdCl_2$, while further addition of CH_2N_2 induced the usual reaction pathway to give the corresponding cyclopropanes. The zero-valent state of palladium in the reaction was confirmed by utilizing the ability of Pd(0) to form more stable complexes with other ligands, for example, triphenyl phosphite. For this purpose, after $PdCl_2$ was fully converted to the soluble olefin complex and olefin cyclopropanation started, the addition of CH_2N_2 was stopped, and $(PhO)_3P$ was added to the reaction mixture. This resulted in the isolation of the colourless crystalline complex $[(PhO)_3P]_4Pd$.[83]

Later, the participation of Pd(0) complexes as catalytically active species in this reaction was demonstrated for the catalytic cyclopropanation of alkynylsilanes with diazomethane in the presence of $Pd(OAc)_2$.[81] The cyclopropanation of divinyltetramethyldisiloxane resulted in the isolation of the zero-valent palladium complex $[Pd(0)_2(DVTMS)_3]$ (**16**, DVTMS is divinyltetramethyldisiloxane), which proved to be an exceptionally active catalyst for the cyclopropanation of alkenylsilane **14**, providing complete conversion of the substrate at −35 °C within 1 min to give cyclopropane **15** in 96% yield (Scheme 6).[81]

Scheme 6



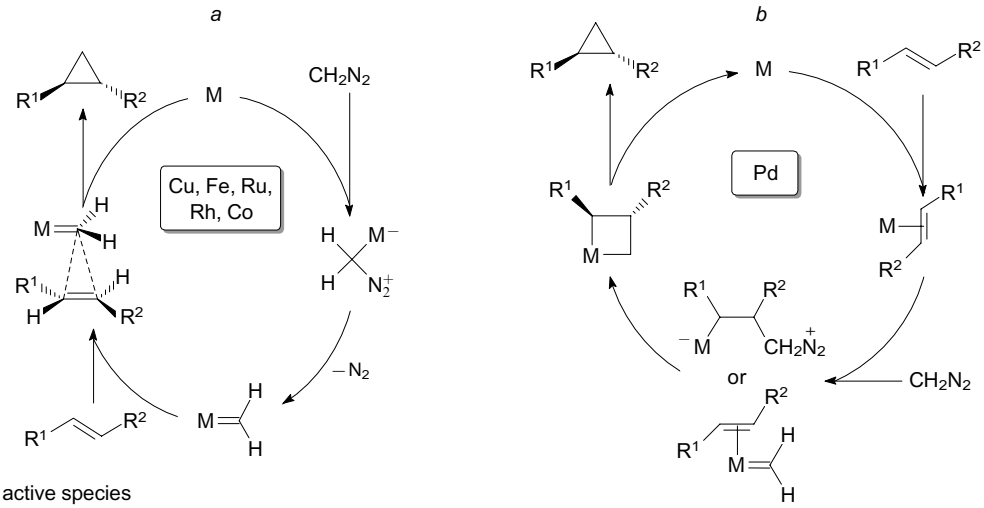
(*a*) CH_2N_2, **16**, Et_2O, −35 °C, 1 min



In addition, catalytically active Pd(0) nanoparticles were also shown to arise in the reaction of cyclohexenone with diazomethane in the presence of $Pd(OAc)_2$.[84]

Apart from palladium compounds, catalysts based on iron complexes have also been actively studied in recent years. These catalysts also proved to be efficient in the

Scheme 5



M is a catalytically active species

catalytic cyclopropanation of alkenes with diazomethane.[45, 46] The catalysts containing no noble metals hold good promise.

Thus, the nature of the metal in the catalyst determines not only the mechanism of catalytic cyclopropanation of olefins with diazomethane, but also the effect of electronic and steric properties of the unsaturated compound on the reaction pathway.

3.2. Palladium-based catalysts for the cyclopropanation of double bonds

Palladium compounds are the most efficient catalysts for diazomethane cyclopropanation of unsaturated double bonds.[33, 42, 54, 58] This gives only cyclopropane derivatives as reaction products, while by-products are formed very rarely.[42, 54, 61] However by no means all types of bonds are suitable for this reaction. Among alkenes, compounds with terminal double bonds are more easily cyclopropanated, whereas alkyl substituents on the double bond sharply decrease or rule out the possibility of cyclopropanation of these substrates.[33] The cyclopropanation rate decreases with decreasing capability of olefins for coordination to palladium (Fig. 2).

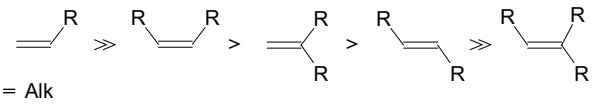
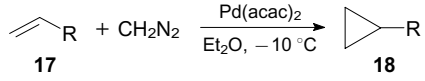


Figure 2. Effect of alkyl substituents on the cyclopropanation rate.

A comparative study of the efficiency of cyclopropanation of a number of alk-1-enes (**17**) with diazomethane (1 equiv.) catalyzed by 1 mol.% $Pd(acac)_2$ was reported.[85] In the series from hex-1-ene to undec-1-ene, somewhat lower yields of cyclopropanes **18** were obtained for oct-1-ene and non-1-ene (Scheme 7).

Scheme 7



17 **18**

R = Bu^n (65%), n-C_5H_{11} (56%), n-C_6H_{13} (39%), n-C_7H_{15} (44%), n-C_9H_{19} (62%), cyclo-C_6H_{11} (41%)

Among unsubstituted C_5-C_8 cycloalkenes, the lowest activity in this reaction was found for cyclohexene. According to a study of competing reactions of cycloalkenes with diazomethane in the presence of $Pd(acac)_2$, the relative reactivities of cyclopentene, cycloheptene and cyclooctene proved to be two orders of magnitude higher than that of cyclohexene (Fig. 3).[86]

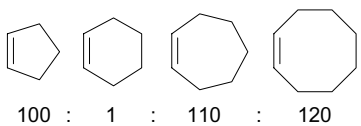
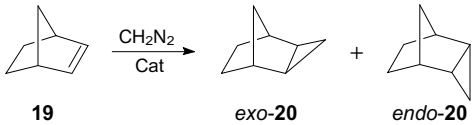


Figure 3. Relative rate of cyclopropanation of cycloalkenes.

The markedly lower reactivity of cyclohexene double bond in the cyclopropanation catalyzed by $(PhCN)_2PdCl_2$ in comparison with cyclooctene and cycloheptene double bonds has been known for long;[83] however, the fact that cyclopentene is two orders of magnitude more reactive than cyclohexene was unexpected.[86] Thus, over the series of unsubstituted cycloalkenes, the reactivity of cyclohexene is abnormally low.

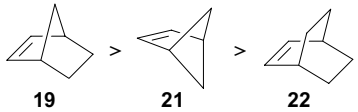
A special place among polycyclic unsaturated compounds is held by norbornene **19**, which is an order of magnitude more reactive towards catalytic diazomethane cyclopropanation than alk-1-enes.[87] The reactivity does not depend significantly on the nature of the palladium catalyst [$Pd(OAc)_2$, $(PhCN)_2 \cdot PdCl_2$, $Pd(acac)_2$ or $(PPh_3)_2 \cdot PdCl_2$], with tricyclooctane *exo*-**20** being formed in high yield in all cases. In the presence of palladium catalysts, norbornene is converted exclusively to *exo*-**20**, whereas the formation of *endo*-**20** as a minor product was detected when Cu- and Rh-based catalysts were used (Scheme 8).[88]

Scheme 8



19 *exo*-**20** *endo*-**20**

The high reactivity of the norbornene double bond is also manifested in the non-catalytic reaction with diazomethane, which occurs as 1,3-dipolar cycloaddition; in this case, norbornene is most reactive out of the series of bicycloalkenes **19**, **21** and **22** (Fig. 4).[89] However, the rate of 1,3-dipolar cycloaddition is much inferior to the rate of catalytic cyclopropanation; therefore, in the presence of at least 0.5 mol.% Pd catalyst, 1-pyrazolines are hardly detected in the products of reaction with diazomethane.



19 **21** **22**

Figure 4. Reactivity of bicycloalkenes towards CH_2N_2.

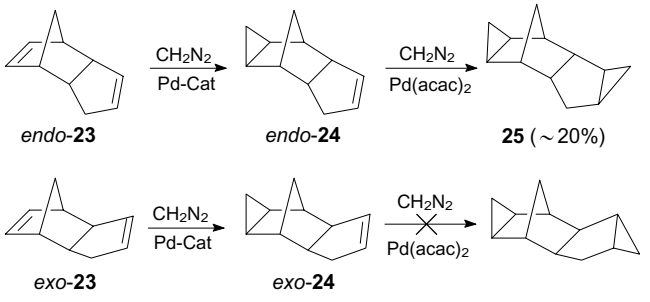
The unusual electronic structure of norbornene and its derivatives has attracted the attention of researchers for many years. Many attempts have been made to account for the abnormally high reactivity of norbornene. One of the recent publications presents an analysis of localized wave functions of norbornene in combination with calculations of NMR parameters, which shows that the electron density distribution in norbornene facilitates the retro-Diels – Alder reaction.[90] Nevertheless, this does not account for all unique properties of norbornene.

Apart from norbornene, interesting trends were revealed for other polycyclic unsaturated compounds containing various types of double bonds. In some cases, a 10- or even 100-fold excess of diazomethane is needed even for the partial cyclopropanation of a trisubstituted endocyclic double bond.[91 – 95]

The diazomethane cyclopropanation of endocyclic double bonds of dicyclopentadiene **23** (for both *endo* and *exo* isomers) in the presence of $Pd(OAc)_2$ or $(PhCN)_2PdCl_2$ is directed only to the norbornene double bond and affords

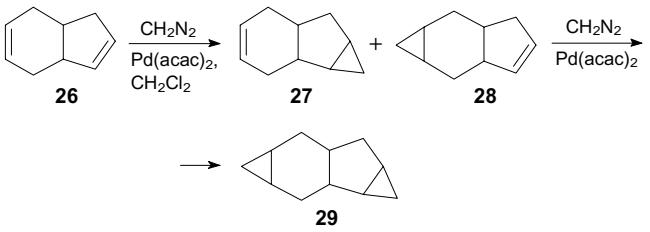
the monoadduct, compound **24** (Refs 58, 62, 96 – 98) (Scheme 9). The cyclopentene moiety remains intact under these conditions. However, when $Pd(acac)_2$ is used as the catalyst, the second double bond in *endo*-**24** can also be partly cyclopropanated to give pentacyclic hydrocarbon **25**, whereas in the case of *exo*-**24**, no products of cyclopropanation of the cyclopentene double bond are detected under the same conditions.[86]

Scheme 9



Among other polycyclic hydrocarbons, worthy of note is 3a,4,7,7a-tetrahydro-1*H*-indene (**26**), in which the cyclopentene moiety is fused with a cyclohexene one. Unlike cyclopentadiene dimers **23**, this compound contains no methylene bridge, which accounts for the specific properties of the norbornene double bond. Unexpectedly, it was found that, depending on the amount of generated diazomethane, the efficient cyclopropanation of either double bond and, moreover, cyclopropanation of both double bonds is possible. As a result, both monoadducts **27** and **28** (as a 3 : 1 mixture) and bisadduct **29** can be obtained (Scheme 10).[86]

Scheme 10



Thus, the geometric and electronic parameters of the double bonds in tetrahydroindene **26**, differing from those of dicyclopentadiene **23**, enable the efficient cyclopropanation of both C=C bonds.

3.2.1. Cyclopropanation of monosubstituted ethenes

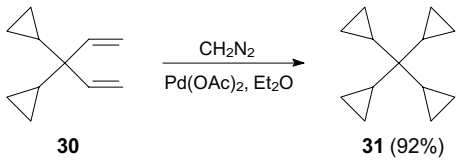
As noted above, the terminal double bond of alkenes is usually readily cyclopropanated to give the corresponding cyclopropane derivatives in high yields.

For example, the $Pd(OAc)_2$-catalyzed cyclopropanation of two bonds of unsaturated dicyclopropyldiethenylmethane (**30**) with a 10-fold excess of diazomethane affords tetra(cyclopropyl)methane (**31**) (Scheme 11).[99,100]

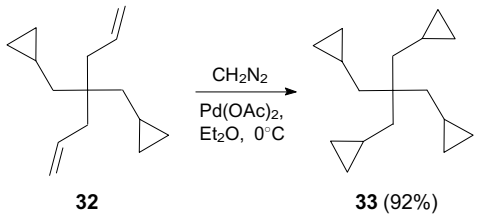
Another similar olefin **32** is also easily converted in the same way to tetrakis(cyclopropylmethyl)methane (**33**) (Scheme 12).[101]

The cyclopropanation of four double bonds of 1,3,5,7-tetravinyladamantane (**34**) with a 10-fold excess of diazomethane afforded 1,3,5,7-tetracyclopropyladamantane (**35**) (Scheme 13).[102]

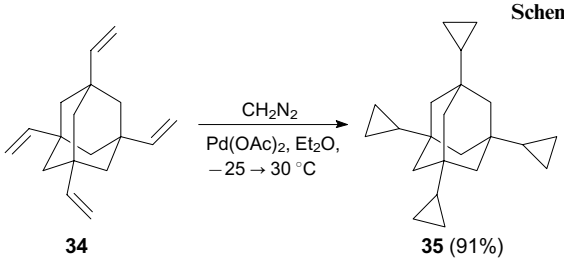
Scheme 11



Scheme 12



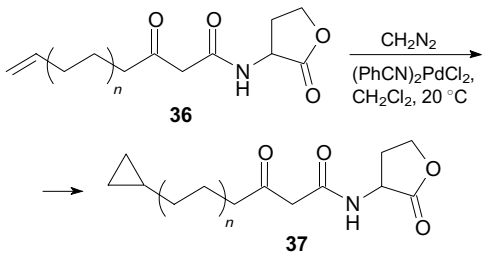
Scheme 13



Similarly to hydrocarbons, unsaturated compounds, in which the terminal double bond is separated from donor or acceptor substituents by two and more CH_2 groups, are easily converted to cyclopropanes in high yields.

This procedure was used to prepare analogues of *N*-(3-oxododecanoyl)-L-homoserine lactone, which induces apoptosis in macrophages. Compounds **36**, in which the terminal double bond is separated from the CO group by five or seven CH_2 groups, are converted to cyclopropane derivatives **37** in 77% ($n = 2$) and 69% ($n = 3$) yields (Scheme 14).[103]

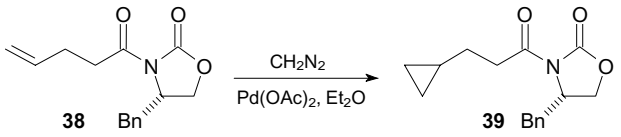
Scheme 14



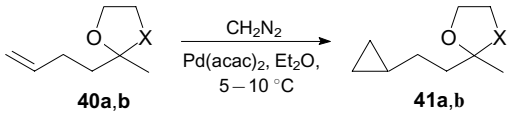
(*S*)-4-Benzyl-3-(pent-4-enoyl)oxazolidin-2-one **38**, in which the terminal double bond is separated from the functional group by two CH_2 groups, reacts with diazomethane in a similar way. This gives cyclopropane **39** as a synthon for the synthesis of a number of physiologically active compounds (Scheme 15).[104]

The diazomethane cyclopropanation of 2-(but-3-enyl)oxazolidine **40a** and 2-(but-3-enyl)-1,3-oxathiolane (**40b**) proceeds smoothly [**40** : CH_2N_2 : $Pd(acac)_2$ = 1 : 3 : 0.02] to give cyclopropanes **41a** and **41b** in 97% and 53% yields, respectively (Scheme 16).[105]

Scheme 15



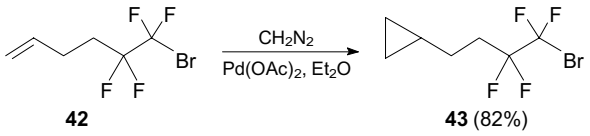
Scheme 16



X = NEt (**a**), S (**b**)

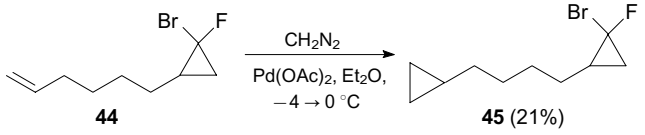
Halogenated compounds, in which the terminal double bond is separated from the halogen atom by several CH_2 groups, are also cyclopropanated with diazomethane. Treatment of 6-bromo-5,5,6,6-tetrafluorohex-1-ene (**42**) with a fivefold excess of diazomethane in the presence of $Pd(OAc)_2$ furnishes (4-bromo-3,3,4,4-tetrafluorobutyl)-cyclopropane **43** (Scheme 17).[106]

Scheme 17



Compound **44**, which also contains a terminal double bond, reacts with diazomethane to give cyclopropanation product **45** in a moderate yield (Scheme 18).[107] However, in this case, an equivalent amount of diazomethane was used; evidently, an excess of CH_2N_2 could increase the yield.

Scheme 18

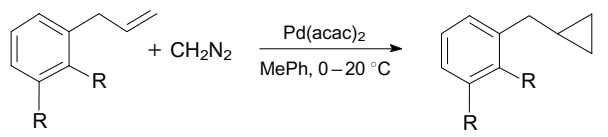


Compounds with an allyl group in which the double bond is separated by one CH_2 group from an aromatic system also successfully react with diazomethane. The reaction of allylbenzene **46** with one equivalent of diazomethane gives cyclopropane **47** in 43% yield;[85] this approximately corresponds to the efficiency of cyclopropanation of styrene (46%). Expectedly, another allylbenzene derivative, 1-allyl-2,3-dimethoxybenzene (**48**), reacts with a twofold excess of CH_2N_2 to afford cyclopropanation product **49** in 82% yield (Scheme 19).[108]

It is also possible to successfully cyclopropanate a more complex functionally substituted allylbenzene **50** by treatment with one equivalent of diazomethane; cyclopropane **51** is thus produced (Scheme 20).[109]

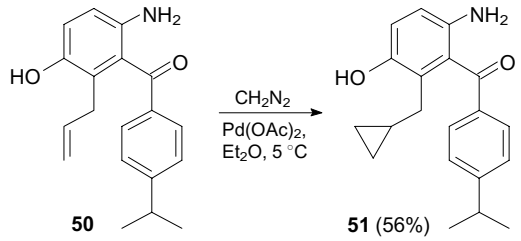
Unlike above examples, the reaction of macrocyclic derivative **52** containing an allylbenzene moiety with diazomethane gives cyclopropane product **53** in only 9% yield (Scheme 21).[110]

Scheme 19

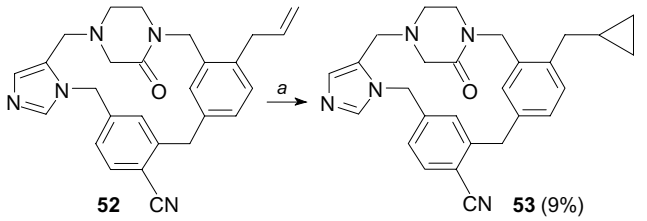


R = H (**46**, 1 : 1), OMe (**48**, 1 : 2)

Scheme 20



Scheme 21

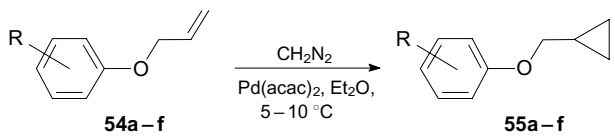


(*a*) CH_2N_2, $Pd(OAc)_2$, $CHCl_3$

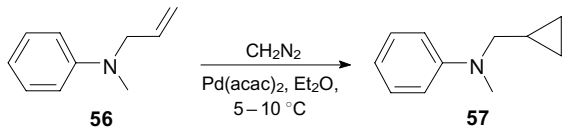
Along with allylbenzene derivatives, (allyloxy)benzenes can also undergo these reactions. Indeed, on treatment with three equivalents of diazomethane, substituted (allyloxy)-benzenes **54a–f** are converted to cyclopropanes **55a–f** in high yields. The cyclopropanation of *N*-allyl-*N*-methylaniline **56** is much less efficient; under similar conditions, *N*-(cyclopropylmethyl)-*N*-methylaniline **57** is obtained in only 36% yield (Scheme 22).[111]

Using isotope-substituted diazald derivatives (D_3C- and ^{13}C-labelled) and (allyloxy)benzene (**54a**) in the presence of $Pd(OAc)_2$ (Et_2O, 0 °C), doubly deuterated and ^{13}C-labelled derivatives of (cyclopropylmethyloxy)benzene **55a** were prepared in 84% and 72% yields, respectively.[52]

Scheme 22

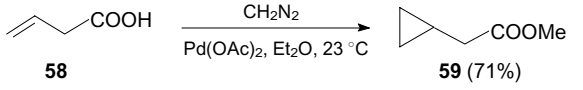


R = H (**a**, 89%), *o*-Me (**b**, 73%), *m*-Me (**c**, 69%), *p*-Me (**d**, 72%), *o*-Br (**e**, 81%), *p*-Br (**f**, 88%)



Among other compounds with an allyl group subjected to diazomethane cyclopropanation, mention should be made of vinylacetic acid **58**, which was allowed to react with a sevenfold excess of diazomethane. In the first step, methylation of acid **58** took place to give the methyl ester, which was cyclopropanated to form methyl 2-cyclopropylacetate (**59**) (Scheme 23).[112]

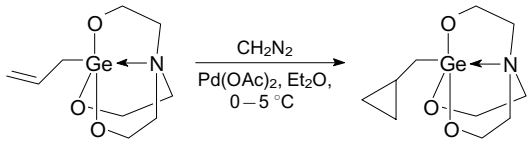
Scheme 23



58 **59** (71%)

The cyclopropanation can also be carried out for allylgermatrane **60**, which reacts with 10 equiv. of diazomethane to give 1-(cyclopropylmethyl)germatrane **61** (Scheme 24).[113]

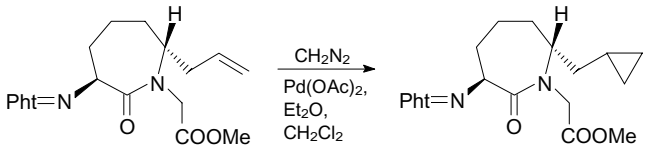
Scheme 24



60 **61** (66%)

The cyclopropanation of an allyl group is used rather often in the targeted syntheses of various practically valuable compounds. Lately, the catalytic cyclopropanation with diazomethane has also been widely used for this purpose. For example, the reaction of allyl-substituted azepan-2-one **62** with a large (~10-fold) excess of diazomethane affords the corresponding cyclopropane derivative **63** in a quantitative yield (Scheme 25).[114]

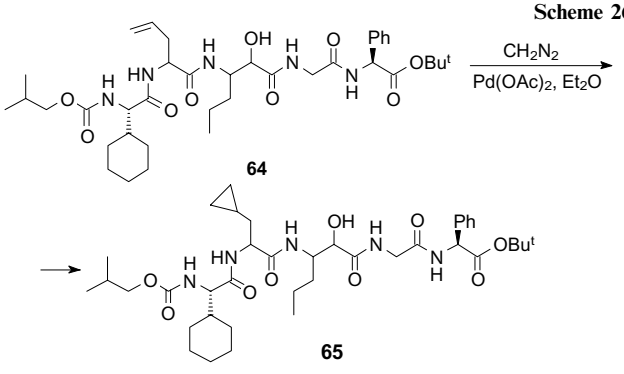
Scheme 25



62 **63** (100%)

A similar method of cyclopropanation of an allyl group was utilized in the synthesis of hepatitis C virus protease inhibitor; in this case, allylic derivative **64** was converted to cyclopropane product **65** in 100% yield (Scheme 26).[115]

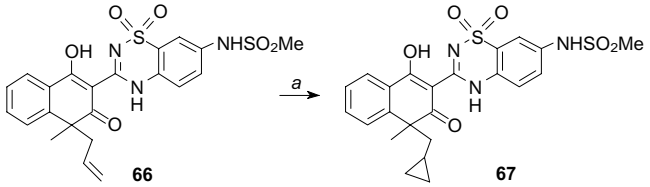
Scheme 26



64 **65**

The same approach was employed in the synthesis of another medication against hepatitis C virus, namely, a polymerase inhibitor. Allylic derivative **66** was converted to cyclopropane product **67**; however, the product yield was moderate, probably, because the reaction was carried out in THF, which is coordinated to the Pd catalyst, thus competing for coordination with the double bond (Scheme 27).[116]

Scheme 27

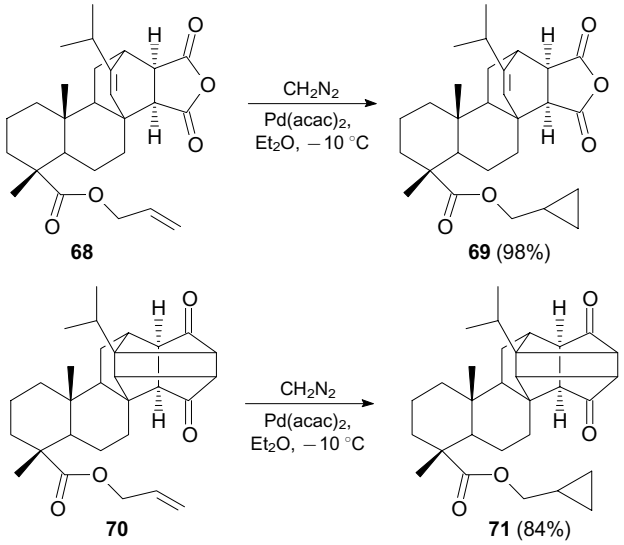


66 **67**

(*a*) CH_2N_2, $Pd(OAc)_2$, THF

Finally, in the syntheses of some other antiviral agents for the treatment of hepatitis C, allyl esters **68** and **70** were allowed to react with three equivalents of CH_2N_2 to give cyclopropane derivatives **69** and **71**, respectively (Scheme 28).[117]

Scheme 28

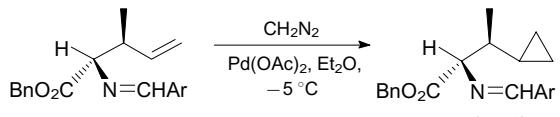


68 **69** (98%)

70 **71** (84%)

The catalytic cyclopropanation was also successfully used as a step in the synthesis of cyclopropane-containing amino acids. For example, the cyclopropanation of the terminal double bond of compound **72** with a threefold excess of diazomethane gave the corresponding cyclopropane **73** (Scheme 29).[118]

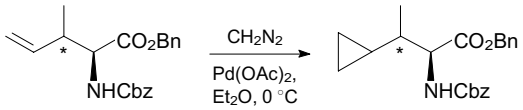
Scheme 29



72 **73** (99%)

The reaction of compound **74** follows a similar route and furnishes 2-amino-3-cyclopropylbutanoic acid derivative **75** (Scheme 30).[119]

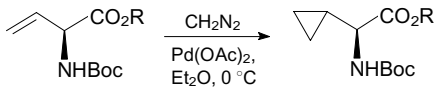
Scheme 30



74 **75** (> 95%)

The cyclopropanation of 2-aminobut-3-enoic acid derivatives **76** with an excess of diazomethane gives 2-amino-2-cyclopropylacetates **77** (Scheme 31).[120, 121]

Scheme 31

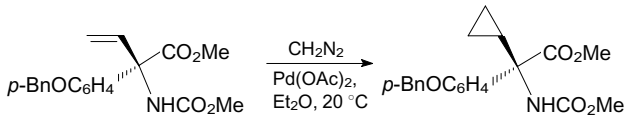


76 **77** (~80%)

R = Et, *p*-MeOC$_6$H$_4$CH$_2$

The reaction of more substituted vinyl acetate **78** with an excess of diazomethane affords cyclopropane **79** in a low yield (Scheme 32) [122] due probably to steric factors.

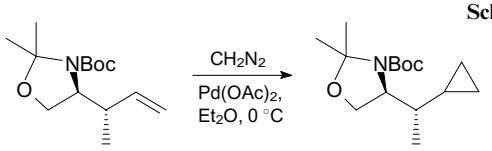
Scheme 32



78 **79** (23%)

One more approach to the synthesis of cyclopropanated amino acids is associated with transformations of oxazolidine derivatives. For instance, allyloxazolidine **80** reacts with a sixfold excess of diazomethane to afford cyclopropane-containing heterocyclic compound **81** in a quantitative yield (Scheme 33).[123, 124]

Scheme 33



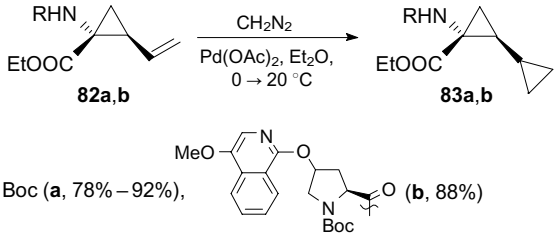
80 **81** (100%)

The bicyclopropane moiety required for the synthesis of a number of practically valuable compounds is often constructed on the basis of vinylcyclopropane, which is cyclopropanated with diazomethane at the double bond; this reaction usually proceeds smoothly and gives products in high yields.

The reaction of vinylcyclopropanes **82** with an excess of diazomethane provided the synthesis of bicyclopropanes **83** (Scheme 34).[125, 126] Compounds **83** are synthons in the synthesis of protease inhibitors meant for the therapy of hepatitis C.[125, 126]

The cyclopropanation of 6-vinylbicyclo[3.1.0]hexan-2-one (**84**), a bicyclic vinylcyclopropane derivative, resulted in the preparation of 6-cyclopropylbicyclo[3.1.0]hexan-2-one (**85**), which is an intermediate in the synthesis of nicotinic acid receptor agonists (Scheme 35).[127, 128]

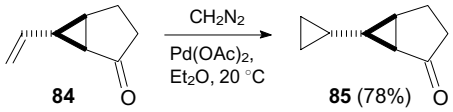
Scheme 34



82a,**b** **83a**,**b**

R = Boc (**a**, 78–92%), (**b**, 88%)

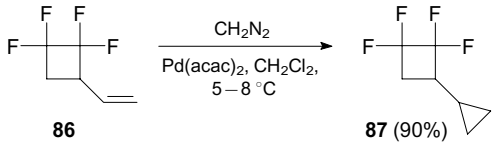
Scheme 35



84 **85** (78%)

Apart from the transformations of vinylcyclopropane derivatives, there are examples of diazomethane reactions with vinylcyclobutanes, which proceed smoothly and give the expected cyclopropylcyclobutanes in high yields. For example, the treatment of 1,1,2,2-tetrafluoro-3-vinylcyclobutane (**86**) with a twofold excess of diazomethane yields 1,1,2,2-tetrafluoro-3-cyclopropylcyclobutane (**87**) (Scheme 36).[129]

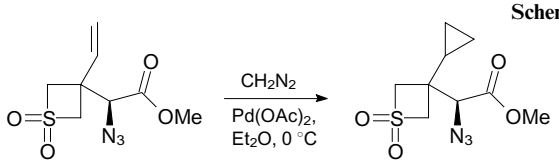
Scheme 36



86 **87** (90%)

One more compound with a four-membered ring, 3-vinylthietane derivative **88**, was used for the synthesis of LpxC inhibitors, which serve for the treatment of cardiovascular diseases. The reaction of compound **88** with five equivalents of diazomethane furnished methyl (*S*)-2-azido-2-(3-cyclopropyl-1,1-dioxidothietan-3-yl)acetate (**89**) (Scheme 37).[130]

Scheme 37



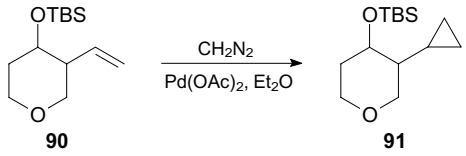
88 **89** (89%)

The double bond of 3-vinyltetrahydro-2*H*-pyran derivative **90** is also cyclopropanated to give the corresponding cyclopropane **91**; however, the reactant ratio and the product yield are not indicated in the publication (Scheme 38).[131]

The cyclopropanation of the terminal vinyl group of 4-vinyl-2,3,4,5-tetrahydro-1*H*-pyrido[4,3-*b*]indole derivative **92** was utilized for the synthesis of indole alkaloids, tetrahydro-γ-carbolines; the reaction with a fivefold excess of diazomethane yielded adduct **93** (Scheme 39).[132]

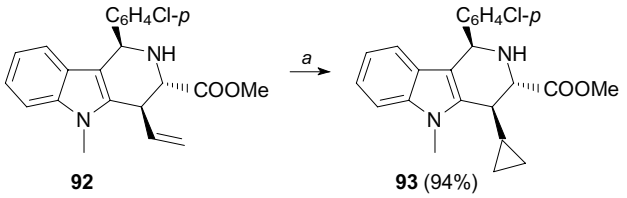
The cyclopropanation of compound **94** on treatment with one equivalent of diazomethane was reported to give

Scheme 38



90 **91**

Scheme 39

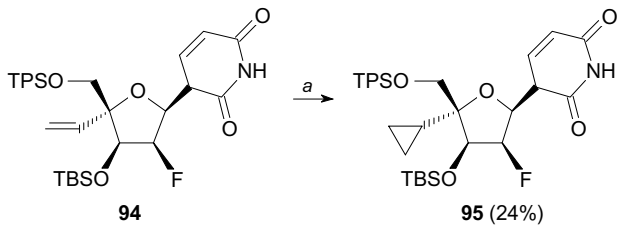


92 **93** (94%)

(*a*) CH_2N_2, $Pd(OAc)_2$, Et_2O, -20 °C

cyclopropyltetrahydrofuran **95** (Scheme 40).[133] The low yield of product **95** does not seem surprising, because of the low amount of diazomethane used and the steric factors. The absence (or no mention in the paper[133]) of adducts formed at the cyclohexenone moiety is more unexpected (see Section 3.2.3). Apparently, this is due to the particular goal of that study, since this reaction was conducted as a part of the total synthesis of a polymerase inhibitor for the treatment of diseases caused by the human respiratory syncytial virus (RSV).

Scheme 40



94 **95** (24%)

(*a*) CH_2N_2, $Pd(OAc)_2$, CH_2Cl_2

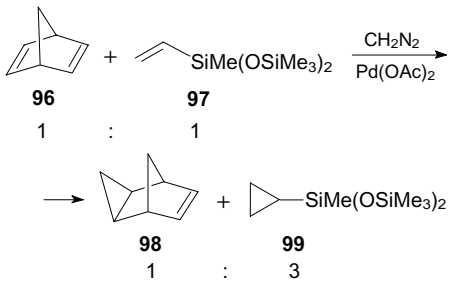
Thus, compounds with a monosubstituted double bond separated from some electron-donating or -withdrawing substituents by at least one sp^3-hybridized carbon atom can be catalytically cyclopropanated almost as efficiently as terminal alkenes.

Assumptions about the electronic effects of substituents present in the starting unsaturated compounds can be made considering the mechanism of their reactions with diazomethane (see Section 3.1). In the presence of Pd catalysts, olefins in which the double bond is readily coordinated to low-valent palladium are efficiently cyclopropanated with diazomethane.[33]

Electron-donating substituents, located directly on the double bond and able to form complexes with palladium, would deactivate the formation of catalytically active π-olefin complexes. Indeed, the cyclopropanation of alkyl vinyl ethers gives products in low yields.[59, 134, 135] Furthermore, the diazomethane cyclopropanation of vinylamine or *N*-vinylaniline catalyzed by palladium compounds is not described in the literature. Most likely, this reaction would have low efficiency if proceeds at all.

Meanwhile, electron-donating substituents that cannot be complexed with palladium would accelerate the reaction. For example, vinylsilanes exhibit abnormally high reactivity in the catalytic cyclopropanation with diazomethane.[81] In particular, it was shown by the method of competing reactions that vinylsiloxane **97** is three times more reactive than norbornadiene **96** (the reaction gives tricyclooctene **98** and cyclopropylsiloxane **99** in 1 : 3 ratio),[81] with the reactivity of norbornadiene being approximately equal to that of norbornene, which usually serves as a reference standard for high reactivity towards cyclopropanation (Scheme 41).[87]

Scheme 41

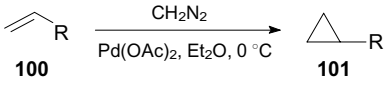


96 : **97**
1 : 1

98 : **99**
1 : 3

Many vinylsilanes **100** react with one equivalent of diazomethane to give cyclopropanes **101** in up to 90% yields, while the use of excess CH_2N_2 results in silyl-substituted cyclopropanes **101** in quantitative yields (Scheme 42).[81]

Scheme 42

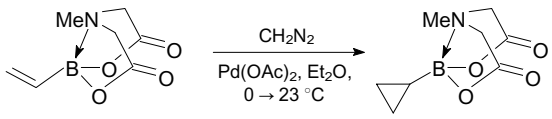


100 **101**

R = $SiEt_3$, $SiMe_2(OEt)$, $SiMe(OEt)_2$, $Si(OEt)_3$, $SiMe(OSiMe_3)_2$, $Si(OSiMe_3)_3$

A vinylic boron compound, vinyl *N*-methyliminodiacetic acid boronate **102**, is also readily cyclopropanated with diazomethane (1.5 equiv.) to give cyclopropane **103** in a high yield (Scheme 43).[136]

Scheme 43

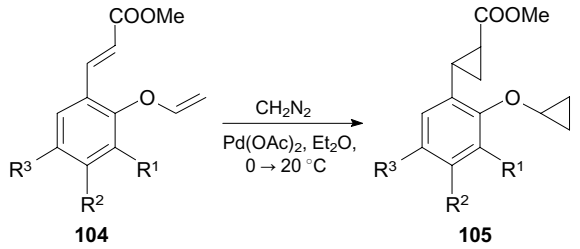


102 **103** (93%)

Unlike alkyl vinyl ethers, which do not form cyclopropane products, aryl vinyl ethers **104**, containing an acrylate moiety, react with an excess of diazomethane to give products **105**, resulting from cyclopropanation of both unsaturated bonds (Scheme 44).[137] It is noteworthy that the cited study[137] presents no data on the relative reactivities of these double bonds and does not indicate the yields of products.

The cyclopropanation of compounds with a terminal double bond bearing an electron-withdrawing substituent with excess diazomethane has variable success, which largely depends on the substituent nature and position. Strong electron-withdrawing substituents sharply accelerate

Scheme 44

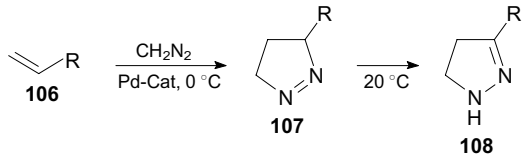


104 **105**

$R^1 = R^2 = R^3 = H$; $R^1 = Me$, $R^2 = R^3 = H$;
$R^1 = Cl$, $R^2 = R^3 = H$; $R^1 = H$, $R^2 + R^3 = (CH)_4$

the competing 1,3-dipolar cycloaddition, giving rise to pyrazolines. For example, direct double bond cyclopropanation of α,β-unsaturated compounds **106** cannot be carried out because of the easy formation of 1-pyrazolines **107**, which readily isomerize under the reaction conditions to 2-pyrazolines **108** (Scheme 45).[85]

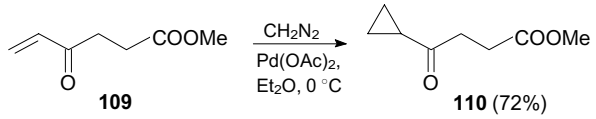
Scheme 45



R = CN (75%), CO_2Me (64%)

However, in the case of a terminal double bond conjugated with a keto group, as, for example, in compound **109**, direct cyclopropanation is possible and gives cyclopropane adduct **110** in a good yield (Scheme 46).[138]

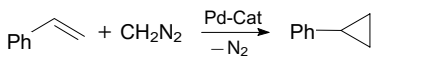
Scheme 46



The role of electronic effects in the cyclopropanation of unsaturated compounds with various reagents (Simmons–Smith reaction, reaction with ethyl diazoacetate, *etc.*) is investigated, most often, using styrene and styrene derivatives with electron-donating or -withdrawing substituents (a series of substituents with increasing Hammett–Taft constants). For olefin cyclopropanation with diazomethane catalyzed by palladium compounds under identical conditions (without excess diazomethane), no dependences of this type were reported.

The reaction of diazomethane with styrene (**111**) is well known and reported in several publications to give product **112** in different yields (depending on the amount of CH_2N_2) (Scheme 47).[85, 139, 140] A common result of these works is that, when the amount of CH_2N_2 is sufficient, the yield of

Scheme 47

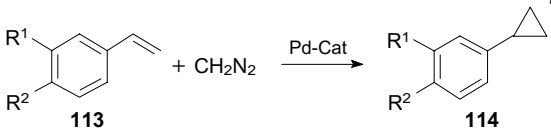


111 **112** (46%–90%)

cyclopropylbenzene **112** is relatively high in the presence of any Pd catalyst.

In the reaction of *p*-methoxystyrene (**113a**) with diazomethane, the yield of *p*-methoxyphenylcyclopropane (**114a**) depends on not only the amount of the diazomethane used, but also the solvent; the yield of cyclopropane **114a** is much higher in THF [139] than in diethyl ether [45] (Scheme 48). With excess diazomethane, 3-nitrostyrene (**113b**) and 3,4-dibromostyrene (**113c**) were converted to cyclopropanes **114b** and **114c** in high yields (see Scheme 48).[139–141]

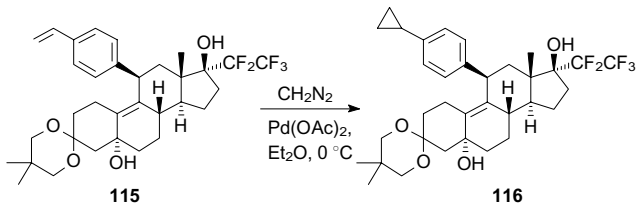
Scheme 48



Compound	R^1	R^2	CH_2N_2 /equiv.	Cat	Solv	Yield (%)
a	H	OMe	1	$Pd(OAc)_2$	Et_2O	9
a	H	OMe	2	$Pd(OAc)_2$	THF	96
b	NO_2	H	3	$Pd(OAc)_2$	Et_2O	99
c	Br	Br	2	$(PhCN)_2PdCl_2$	CH_2Cl_2	90

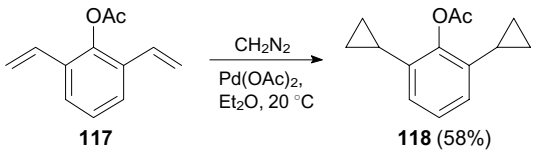
Styrene derivative **115** with a steroid moiety in the *para*-position is also cyclopropanated; the reaction with a large excess of diazomethane results in the formation of cyclopropanation product **116** (Scheme 49).[142]

Scheme 49



Finally, Yao *et al.*[143] described an example of double cyclopropanation of 2,6-divinylphenyl acetate **117** with an excess of diazomethane (4 equiv.) to give 2,6-di(cyclopropyl)phenyl acetate **118** (Scheme 50).[143]

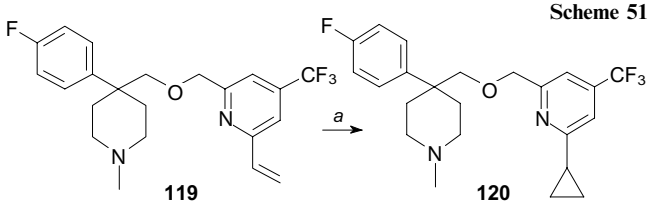
Scheme 50



Apart from styrenes, a number of 2-vinylpyridines used in the synthesis of biologically active compounds for the treatment of depression were also subjected to cyclopropanation with diazomethane.[144] 4-(Trifluoromethyl)-6-vinylpyridine derivative **119** was converted to compound **120**, which exhibited the highest activity (Scheme 51).[144]

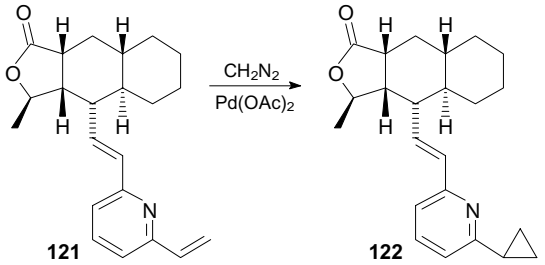
Similarly, the diazomethane cyclopropanation of vinylpyridine **121** afforded cyclopropyl derivative **122**, with the *trans*-disubstituted double bond remaining intact (Scheme 52).[145] However, neither reactant ratio nor the

Scheme 51



(*a*) CH_2N_2, $Pd(OAc)_2$

Scheme 52



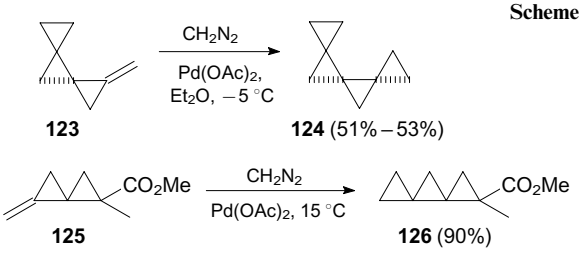
yield of product **122** were indicated in the paper; therefore, it is impossible to evaluate the efficiency of the process.

3.2.2. Cyclopropanation of 1,1-disubstituted ethenes

Among 1,1-disubstituted ethenes, most studied are compounds containing a methylenecyclopropane moiety. The catalytic cyclopropanation of double bonds in this type of compounds is widely used for the synthesis of various spirans and triangulanes. Both unsaturated hydrocarbons and unsaturated compounds containing an electron-withdrawing substituent in the cyclopropane moiety were utilized in these reactions. Although in some cases, the yields of target products (even with excess CH_2N_2 used) were insufficiently high, the reaction was not accompanied by side reactions and the unreacted starting substrate could be recovered.

Thus, 1-methylenedispiro[2.0.2^4.1^3]heptane **123** was treated with a 12-fold excess of diazomethane, which yielded [4]triangulane **124**.[94, 146] Methylenespiro[2.2]pentane derivative **125** was converted to dispiro[2.0.2.1]heptane **126** in a higher yield when a fivefold excess of diazomethane was used (Scheme 53).[147]

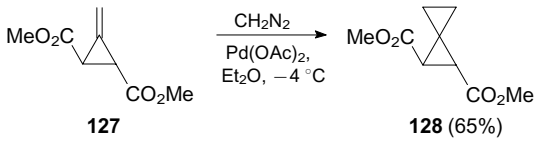
Scheme 53



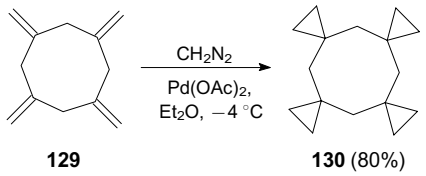
The cyclopropanation of 1-methylenecyclopropane-2,3-dicarboxylate **127** with an excess of diazomethane resulted in the synthesis of spiropentane **128** (Scheme 54).[148] The optically active (*R*,*R*)-(+)-isomer was converted to optically active (1*R*,2*R*)-(−)-bis(methoxycarbonyl)spiropentane **128**.

An interesting example of this type of reaction is the cyclopropanation of all four exocyclic double bonds of

Scheme 54



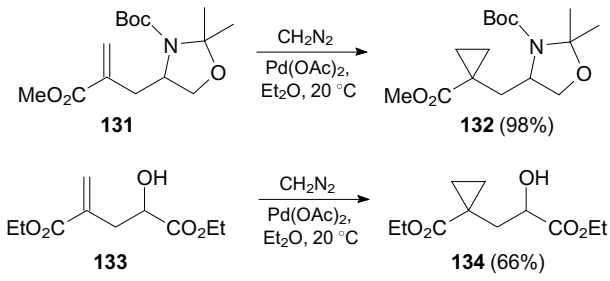
Scheme 55



1,3,5,7-tetramethylenecyclooctane **129** with diazomethane (10 equiv.) giving rise to tetraspirohexadecane **130** (Scheme 55).[149]

The cyclopropanation of 1,1-disubstituted double bonds efficiently proceeds also for a number of aliphatic compounds. For example, 4-methylene-L-glutamic acid derivative **131** containing an electron-withdrawing substituent (CO_2Me) on the double bond was converted to cyclopropane derivative **132** upon the reaction with diazomethane.[150] One more structurally similar compound, diethyl 2-hydroxy-4-methyleneglutarate **133**, was converted to cyclopropane product **134** in a considerably lower yield even when a 30-fold excess of diazomethane was used (Scheme 56).[151] Most likely, in the last-mentioned case, the destruction of the active species of the Pd catalyst could take place even upon the addition of one equivalent of diazomethane, and subsequently the large excess of diazomethane no longer participated in the cyclopropanation reaction, but decomposed to give ethylene gas and cyclopropane.

Scheme 56

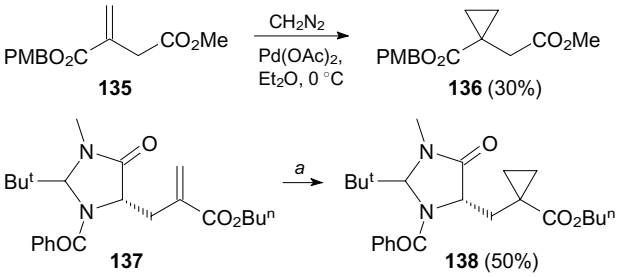


Cyclopropane adducts **136** and **138** were obtained in moderate yields upon the cyclopropanation of itaconic acid **135** and butyl acrylate **137** derivatives with an excess of diazomethane (Scheme 57).[152, 153] In this case, steric factors could apparently have an adverse effect.

Quite successful cyclopropanation of 1,1-disubstituted double bonds with diazomethane (2 eqiuv.) takes place for substrates such as 5-methylenepiperidine-2,3-dicarboxylic acid **139** and 3-(2-methylprop-2-enyl)-2-oxomorpholine-4-carboxylic acid **141**. The corresponding cyclopropane products **140** and **142** are formed in high yields (Scheme 58).[154, 155]

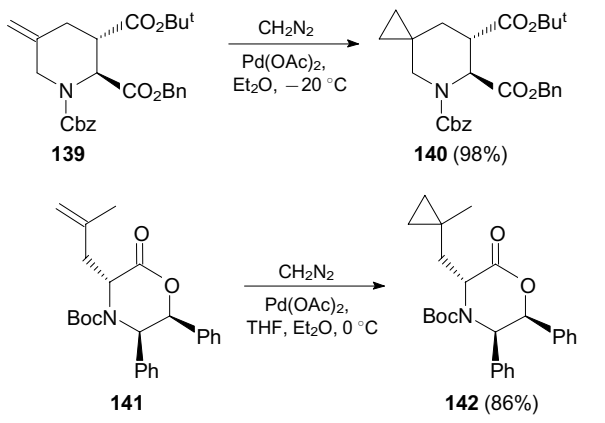
The double bond of 3-methylenepyrrolidin-2-one derivatives **143** and **145** can also be cyclopropanated with an

Scheme 57

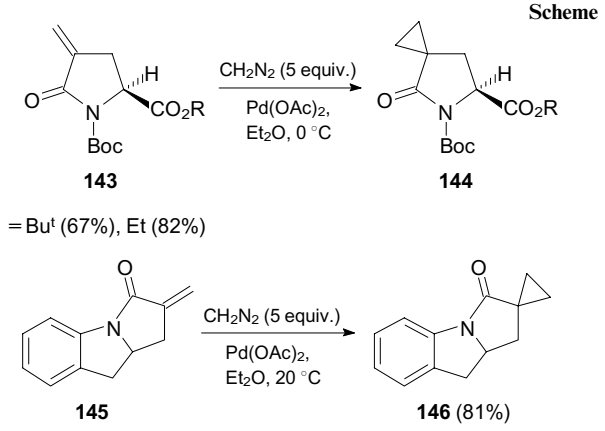


(*a*) CH_2N_2 (9 equiv.), $Pd(OAc)_2$, Et_2O, 0 °C

Scheme 58



Scheme 59

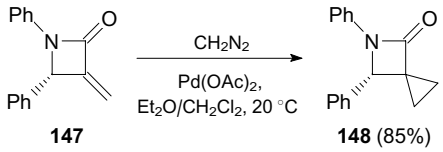


excess of diazomethane to give derivatives **144** and **146** in good yields (Scheme 59).[153, 156, 157]

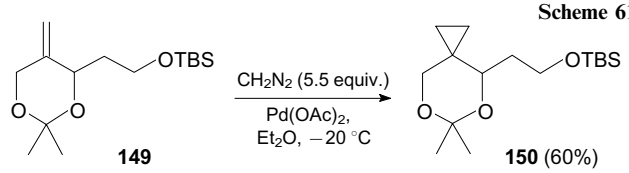
(*S*)-3-Methylene-1,4-diphenylazetidin-2-one **147** reacts with an excess of diazomethane in a similar way to give azaspiro[2.3]hexan-4-one **148** (Scheme 60).[158]

Among other heterocycles, mention should be made of 2,2-dimethyl-5-methylene-1,3-dioxane derivative **149**, which

Scheme 60



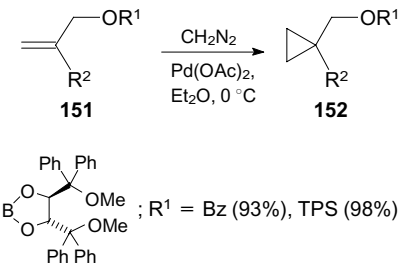
Scheme 61



is cyclopropanated with an excess of diazomethane to give substituted 5,7-dioxaspiro[2.5]octane **150** (Scheme 61).[159]

The cyclopropanation was also performed for alkenylboronic esters **151**, which were allowed to react with a large excess of diazomethane (10 – 12 equiv.) to give 1,1-disubstituted cyclopropanes **152** in high yields (Scheme 62).[160, 161]

Scheme 62



3.2.3. Cyclopropanation of 1,2-disubstituted ethenes

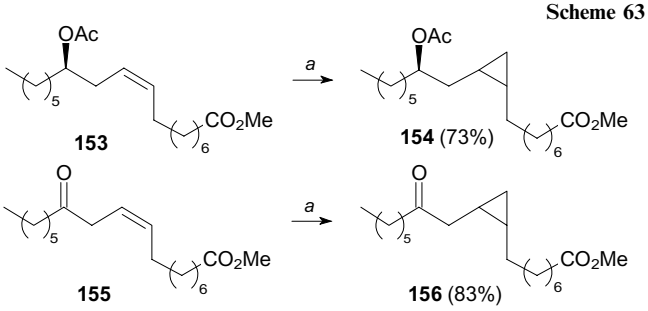
The reactivity difference between *cis*- and *trans*-olefins in the Pd-catalyzed reactions is caused by their different abilities to be coordinated to palladium. As indicated above, most often, *cis* isomers form complexes with palladium somewhat more easily than the corresponding *trans* isomers. However, this difference is slight; therefore, *cis* and *trans* isomers afford cyclopropanation products in nearly equal yields

No examples of the successful cyclopropanation of *cis*- or *trans*-alkenes are known among unsaturated acyclic hydrocarbons with a 1,2-disubstituted double bond. For compounds in which the double bond bears no activating substituents, only a few examples of the successful cyclopropanation have been reported.

For example, ricinoleic acid derivatives **153** and **155**, in which the double bond is separated from functional groups by several CH_2 units, react with an excess of diazomethane ($\sim$20 equiv.) giving rise to *cis*-cyclopropane adducts **154** and **156**, respectively (Scheme 63).[162]

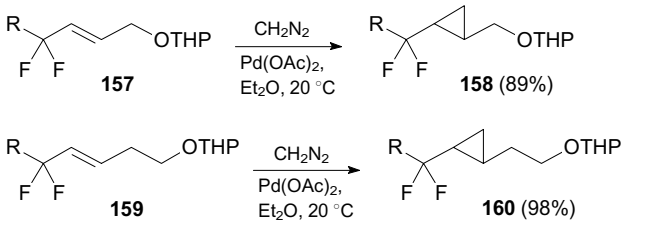
Similarly, diethyl phosphonates **157** and **159**, in which the double bond is also separated from oxygen- and phosphorus-containing groups by CH_2 units, react with

Scheme 63



(*a*) CH_2N_2, $Pd(acac)_2$, Et_2O, 0 °C

Scheme 64



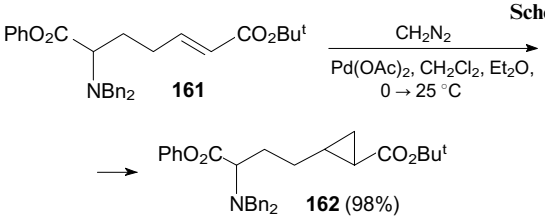
R = P(O)(OEt)$_2$

diazomethane to afford cyclopropanes **158** and **160** in high yields (Scheme 64).[163]

The successful cyclopropanation is mainly provided by the presence of suitable substituents on the double bond — either aromatic or electron-withdrawing ones.

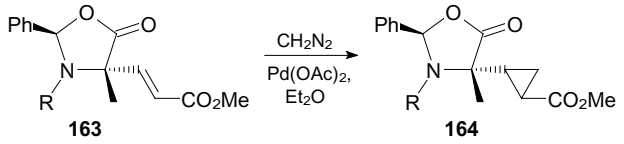
E-β-Substituted acrylic acid ester **161**, in which one electron-withdrawing substituent is located on the double bond, is easily converted to *trans*-cyclopropanecarboxylate **162** under usual conditions of catalytic cyclopropanation (Scheme 65).[164]

Scheme 65



(*E*)-3-(Oxazolidin-4-yl)acrylate derivatives **163** can also be rather smoothly converted to *trans*-disubstituted cyclopropane products **164** (Scheme 66).[165, 166]

Scheme 66



R = Bz (49%), Cbz (67%)

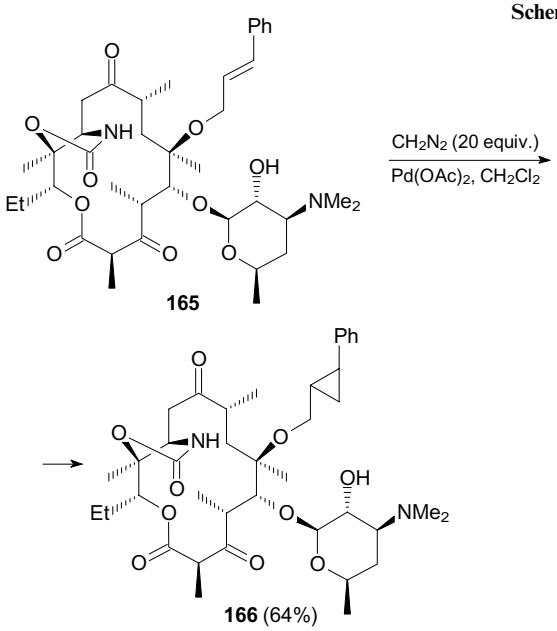
The reaction of erythromycin derivative **165** with a large excess of diazomethane generates *trans*-cyclopropane compound **166** (Scheme 67).[167]

Among 1,2-disubstituted unsaturated compounds, *trans*-cinnamic acid esters **167** containing electron-donating and -withdrawing substituents are most abundant. The catalytic diazomethane cyclopropanation of these compounds can provide the synthesis of phenylcyclopropanecarboxylates **168** in 65% – 99% yields.[30, 137, 168 – 185] Products **168** are formed exclusively as *trans* isomers (Scheme 68). This is, in particular, one of general methods for the synthesis of donor-acceptor cyclopropanes.[30]

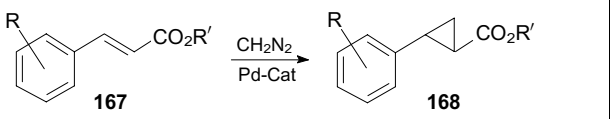
This reaction was also performed for (*E*)- and (*Z*)-3-(2-naphthyl)acrylates **169** and **171**, which were treated with a large excess of diazomethane to be converted to cyclopropanes **170** and **172**, respectively (Scheme 69).[186]

The cyclopropanation of acrylic acid derivatives efficiently proceeds when hetaryl substituents are present on

Scheme 67

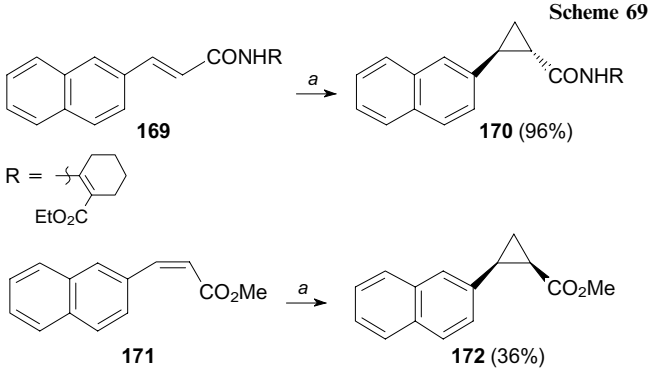


Scheme 68



R = H, 4-Me, 4-MeO, 4-AcO, 4-F, 4-Br, 4-CF_3, 4-CN, 4-NO_2, 2-Br, 2-Thienyl, 3-Thienyl, 2-Furyl, 3-Furyl, *etc.*

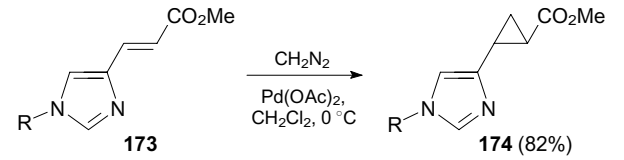
Scheme 69



(*a*) CH_2N_2, $Pd(OAc)_2$, CH_2Cl_2, 0 °C

the double bond. The *trans* isomer of methyl 3-(1*H*-imidazol-4-yl)acrylate **173** reacts with diazomethane to give cyclopropane **174** in a high yield (Scheme 70).[187]

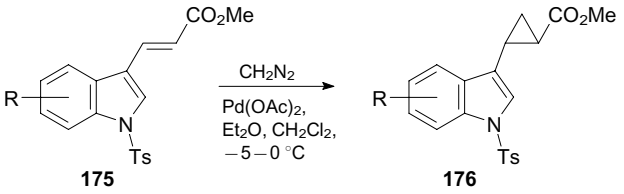
Scheme 70



R = Me_2NSO_2

Derivatives **176**, new biologically active compounds with a cyclopropane moiety, were prepared by the reaction of diazomethane (3–4 equiv.) with *trans*-indolylacrylates **175** (Scheme 71).[188]

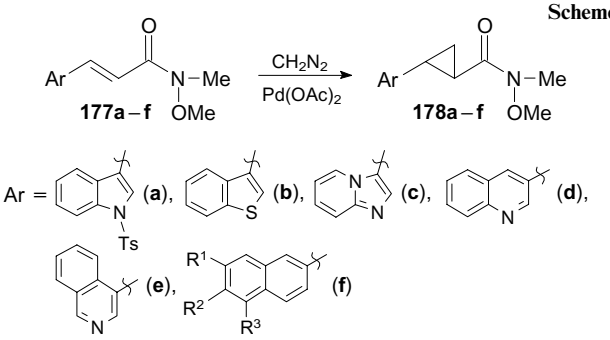
Scheme 71



R = H (70%), 4-OMe (65%), 5-OMe (60%), 5-F (79%)

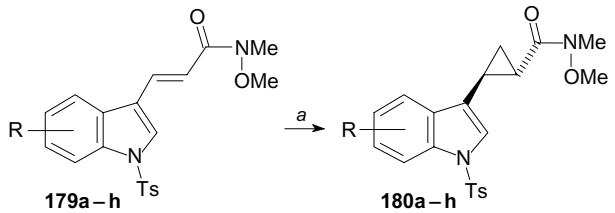
Subsequently, this approach was extended to other hetarylethenes. Using an excess of diazomethane, a number of β-hetarylacrylamides **177a–f** were converted to cyclopropane adducts **178a–f** in 84%–100% yields (Scheme 72).[189]

Scheme 72

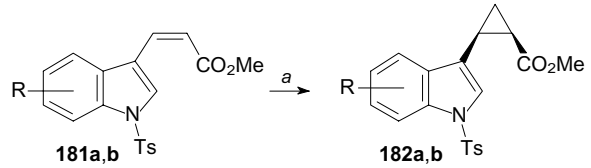


One more study[190] of this series was directed towards the synthesis of analogous cyclopropanes with a substituted indole moiety in the molecule. In this case, too, the selective formation of isomers **180** and **182** takes place upon the cyclopropanation of *cis*- and *trans*-ethenes **179** and **181** with a fivefold excess of diazomethane (Scheme 73).

Scheme 73



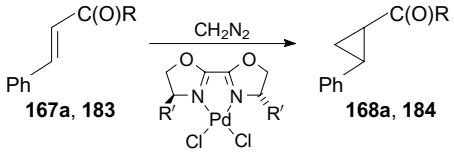
(*a*) CH_2N_2, $Pd(OAc)_2$, CH_2Cl_2, 0 °C;
R = 5-CN (**a**, 54%), 7-CN (**b**, 71%), 6-CN (**c**, 64%), 4-CN (**d**, 78%), 5-F (**e**, 99%), 7-F (**f**, 87%), 6-F (**g**, 95%), 4-F (**h**, 98%)



(*a*) CH_2N_2, $Pd(OAc)_2$, CH_2Cl_2, 0 °C; R = 5-CN (**a**, 82%), 5-F (**b**, 73%)

Other 1,2-disubstituted ethenes, *e.g.*, compound **183**, react with diazomethane similarly to unsaturated esters and their derivatives. These reactions may be directed towards the synthesis of optically active cyclopropanes in the presence of chiral palladium(II) bis(oxazoline) complexes. However, it was found that substrates **167a** and **183** actually give high yields of cyclopropanes **168a** and **184** upon the reaction with diazomethane (2.8 equiv.), but the enantiomeric excess does not exceed 2% (Scheme 74).[185] The formation of racemic products **168a** and **184** is a direct consequence of the cyclopropanation mechanism involving palladium catalysts (see Scheme 5).

Scheme 74

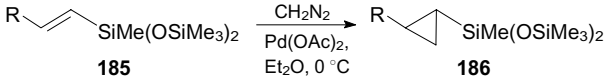


R = Me (**183**, **184**), OMe (**167a**, **168a**); R′ = Bn, Pr^i

Like cinnamic acid derivatives and other 1,2-disubstituted ethenes containing simultaneously electron-donating and -withdrawing substituents, unsaturated compounds with electron-donating substituents such as silyl groups and boronic esters are successfully cyclopropanated with diazomethane.

For instance, alkenylsilanes **185** react with diazomethane to give cyclopropanes **186** in high or even quantitative yields (Scheme 75).[81]

Scheme 75

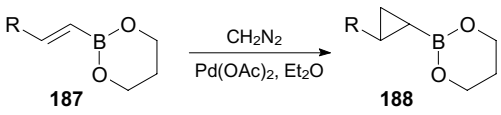


R = C_6H_{13}, Ph, Me_3Si

Alkenylboronic esters and styrylboronates containing a 1,2-disubstituted double bond are also efficiently cyclopropanated with diazomethane.

Thus, 1,3,2-dioxaborinanes **187** with a *trans*-double bond are selectively converted to *trans*-cyclopropanes **188** (Scheme 76).[191–194]

Scheme 76

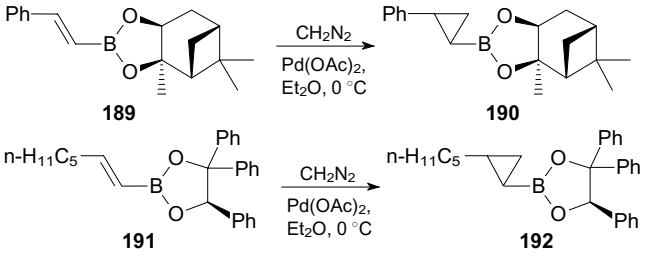


R = Bu^n (75%), n-C_5H_{11} (65%), n-C_6H_{13} (79%), Ph (70%–96%)

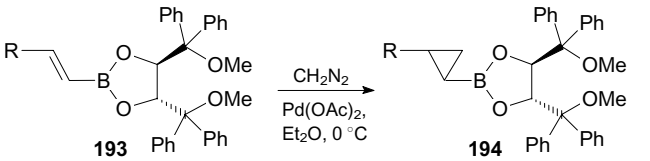
1,3,2-Dioxaborolanes are most widely used in organic synthesis. For example, cyclopropanes **190** and **192** were prepared from esters **189** and **191** in more than 95% yields (Scheme 77).[195]

The cyclopropanation of 4,5-bis(methoxydiphenylmethyl)-1,3,2-dioxaborolane derivatives **193** furnishes cyclopropanes **194** in high yields (95%–98%) (Scheme 78).[161, 193, 195, 196]

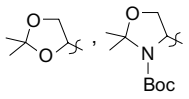
Scheme 77



Scheme 78

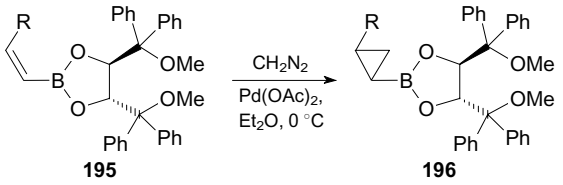


R = n-C_5H_{11}, Bu^n, Bu^t, Ph, $TPSO(CH_2)_3$, $BzOCH_2$, $MOMOCH_2$, $BnOCH_2$, $TBSOCH_2$, $TPSOCH_2$, $HOCH_2$,



Under similar conditions, *cis*-cyclopropylboronic esters **196** were obtained in high yields and with high enantiomeric purity by the reaction of *cis*-substituted chiral boronic esters **195** with an excess of diazomethane (Scheme 79).[160, 161, 197]

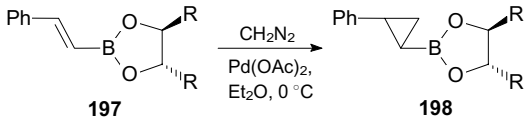
Scheme 79



R = Bu^n (96%), Ph (90%), $MOMOCH_2$ (87%);[197]
R = CH_2OBz (62%) [160, 161]

The cyclopropanation of chiral (*E*)-2-styryl-1,3,2-dioxaborolanes **197** afforded 2-phenylcyclopropylboronic esters **198** (Scheme 80).[198]

Scheme 80

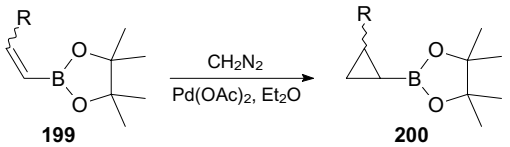


R = CO_2Pr^i (26%, 62% *ee*), $C(O)NMe_2$

A series of *E*- and *Z*-2-alkenyl(styryl)-substituted pinacol boronic esters (4,4,5,5-tetramethyl-1,3,2-dioxaborolanes) **199** were allowed to react with diazomethane, which resulted in the synthesis of *E*- and *Z*-disubstituted cyclopropanes **200** in high yields (Scheme 81).[194, 199, 200]

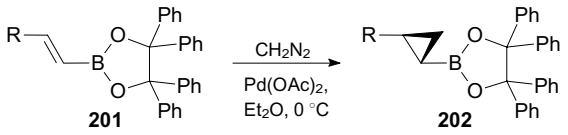
Similarly, 2-alkenyl-substituted (*E*)-4,4,5,5-tetraphenyl-1,3,2-dioxaborolanes **201** were converted to cyclopropanes **202** (Scheme 82).[201]

Scheme 81



R = Ph, Bn, n-C_5H_{11}, 3,4,5-$(MeO)_3C_6H_2$

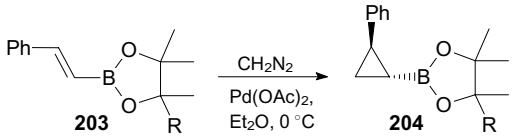
Scheme 82



R =  (70%),  (61%)

Styrylboronate **203** with a polyfluorinated substituent reacts with an excess of diazomethane to give cyclopropane **204** in a quantitative yield (Scheme 83).[202]

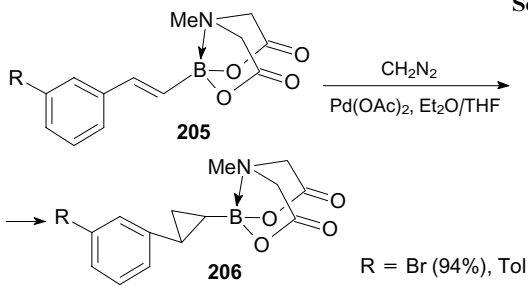
Scheme 83



R = $CH_2Si(CH_2CH_2C_6F_{13}\text{-n})_3$

Finally, *E*-styrylboronic ester derivatives **205** react with diazomethane (2.5 equiv.) yielding the corresponding *trans* isomers of cyclopropanes **206** (Scheme 84).[203]

Scheme 84

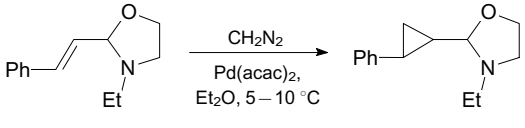


R = Br (94%), Tol (96%)

Among other styryl-substituted heterocycles, 2-styryloxazolidine **207** reacts with diazomethane to be converted to cyclopropane **208** (Scheme 85).[105]

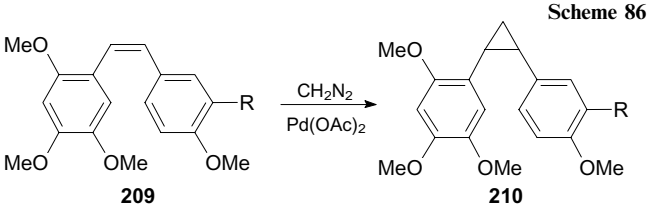
Yet another group of 1,2-disubstituted ethenes that can be catalytically cyclopropanated with diazomethane are *cis*- and *trans*-stilbenes. Thus, *cis*-stilbenes **209** were used to

Scheme 85



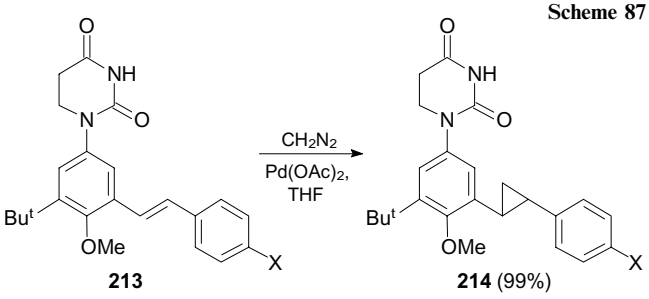
prepare cyclopropanes **210** in satisfactory yields.[204] In the reaction with a large excess of diazomethane, *trans*-stilbenes **211** with various aryl substituents, including structurally complex ones, were converted to *trans*-diarylcyclopropanes **212**, usually in high yields (up to 95%) (Scheme 86).[205–210]

Scheme 86



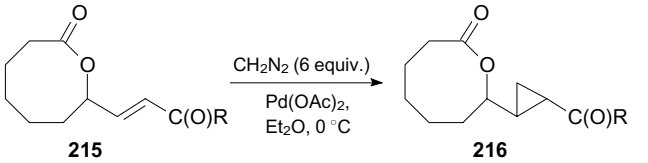
Most diarylcyclopropanes **212** exhibit biological activities. For example, the reaction of stilbene **213** with a 12-fold excess of diazomethane resulted in the synthesis of cyclopropane **214**, which was proposed for the treatment of viral hepatitis C (Scheme 87).[205]

Scheme 87



Among chemical transformations of acyclic1,2-disubstituted ethenes, reactions of diazomethane with acrylic acid derivatives **215** have been reported. The cyclopropanes **216** thus formed were used as intermediates in the synthesis of natural lactones — solandelactones A and B (Scheme 88).[211]

Scheme 88

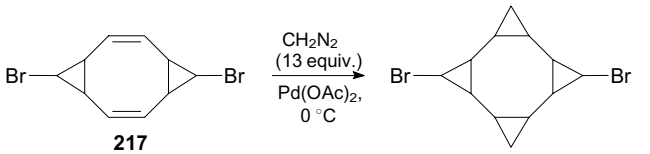


Before passing to a consideration of cycloalkenes, note that the reactivity of their double bond follows approximately the same trends as that of the double bond of similar acyclic derivatives.

In the series of simple cycloalkenes from cyclopentene to cyclooctene, an abnormally low reactivity is inherent in cyclohexene.[83,86] Among polycyclic derivatives, the highest reactivity is characteristic of molecules with a norbornene type double bond [33] (see Section 3.2).

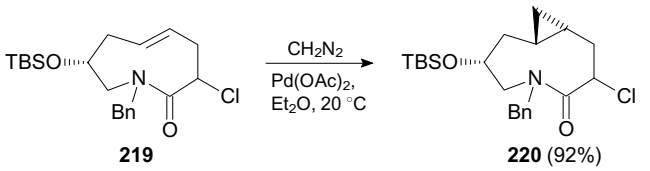
Examples of the successful cyclopropanation of endocyclic double bonds bearing no activating substituents are scanty. The cyclopropanation of 5,10-dibromotricyclo[7.1.0.$0^{4,6}$]deca-2,7-diene **217** with a large excess of diazomethane furnishes cyclooctane **218** with four annulated cyclopropane moieties in the eight-membered ring (Scheme 89).[212]

Scheme 89



One more example is the successful cyclopropanation of the endocyclic *trans*-double bond of substituted (*E*)-1,3,4,7,8,9-hexahydro-2*H*-azonin-2-one **219**, which reacts with diazomethane to give cyclopropane product **220** in a high yield (Scheme 90).[213]

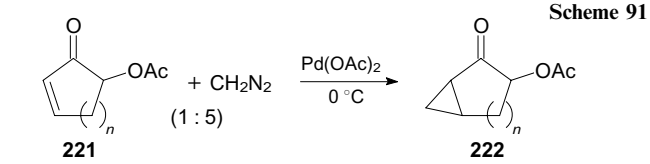
Scheme 90



The cyclopropanation of compounds with endocyclic double bonds is facilitated by the presence of heteroatoms in the ring or functional substituents.

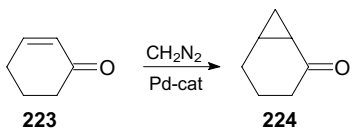
On treatment with an excess of diazomethane, unsaturated cyclic ketones **221** are converted to bicyclic derivatives **222** (Scheme 91).[214] It is noteworthy that in these compounds, like in simple cycloalkenes (cyclopentene and cyclohexene), the double bond in the six-membered ring ($n = 2$) is considerably less reactive than that in the five-membered ring ($n = 1$).

Scheme 91



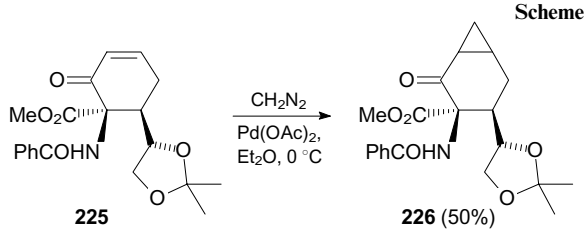
Cyclohexenone **223** reacts with a large excess of diazomethane in the presence of various palladium catalysts to give bicyclo[4.1.0]heptan-2-one (**224**) in a yield of up to 96% (Scheme 92).[185,215,216]

Scheme 92



The reaction of trisubstituted cyclohexenone **225** with an excess of diazomethane also affords cyclopropane product **226** (Scheme 93).[215]

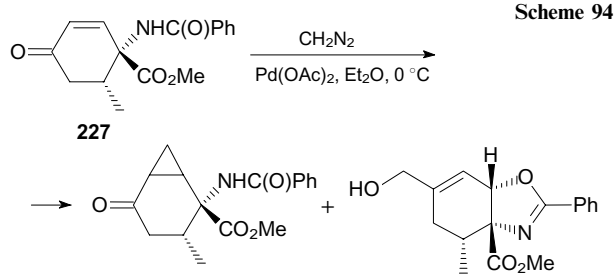
Scheme 93



225 **226** (50%)

When electron-withdrawing groups are located in the allylic position relative to the double bond, as, for example, in compound **227**, the target cyclopropane **228** is formed in a yield of only 8%, while the major product is compound **229** (Scheme 94).[215]

Scheme 94

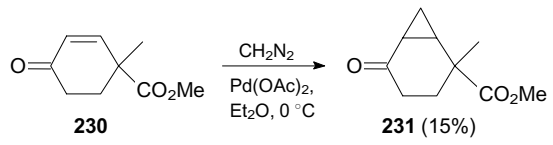


227

228 (8%) **229** (38%)

Another cyclohexenone derivative **230**, in which the methoxycarbonyl group is also located in the allylic position to the double bond, shows low reactivity, similarly to compound **227**. The reaction of **230** with an excess of diazomethane gives cyclopropane derivative **231** in a low yield (Scheme 95).[215]

Scheme 95

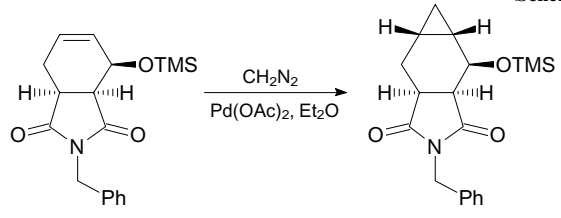


230 **231** (15%)

Compound **232**, containing an electron-donating substituent in the vicinity of the cyclohexene double bond, also reacts with diazomethane to give cyclopropane product **233** (the yield is not indicated) (Scheme 96).[217]

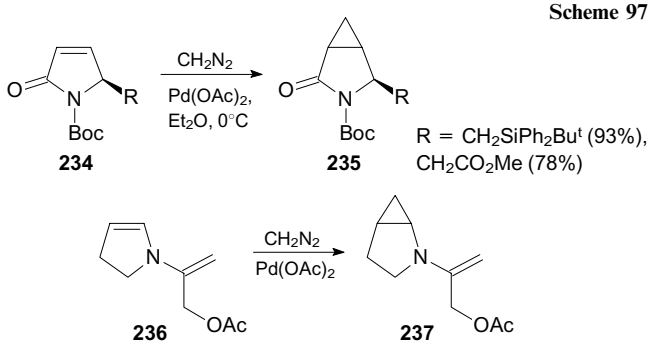
Heterocycles with an endocyclic double bond are also able to react with diazomethane in the presence of palladium compounds. The cyclopropanation of 1,5-dihydro-2*H*-pyrrol-2-one derivatives **234** with a tenfold excess of diazomethane results in the formation of 3-azabicyclo[3.1.0]hexan-2-ones **235**,[218, 219] while similar cyclopropanation of 2,3-dihydro-1*H*-pyrrole **236** gives 2-azabicyclo[3.1.0]hexane derivative **237** (Scheme 97).[220]

Scheme 96



232 **233**

Scheme 97

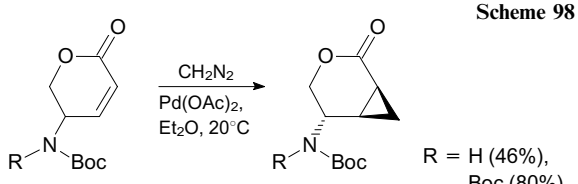


234 **235**

236 **237**

The cyclopropanation of the double bond of 5-amino-substituted 5,6-dihydro-2*H*-pyran-2-ones **238** with diazomethane (5 equiv.) affords cyclopropane products **239** (Scheme 98).[221]

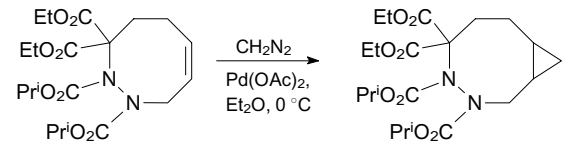
Scheme 98



238 **239**

The addition of diazomethane to the sterically unhindered double bond of one more heterocyclic compound, hexahydro-1,2-diazocine **240**, easily gives cyclopropane **241** (Scheme 99).[222]

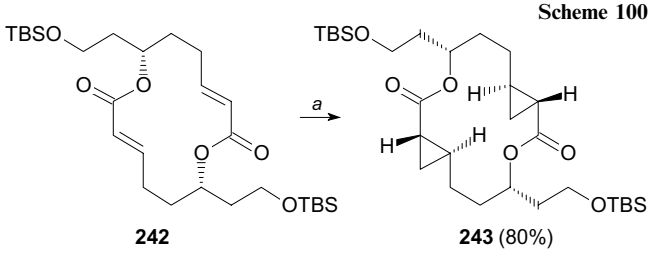
Scheme 99



240 **241** (97%)

Along with the cyclopropanation of *cis*-double bonds, the cyclopropanation of *trans*-double bonds of macrocyclic compounds has been reported. For instance, 14-membered bis-lactone **242** with two *trans*-double bonds forms double

Scheme 100



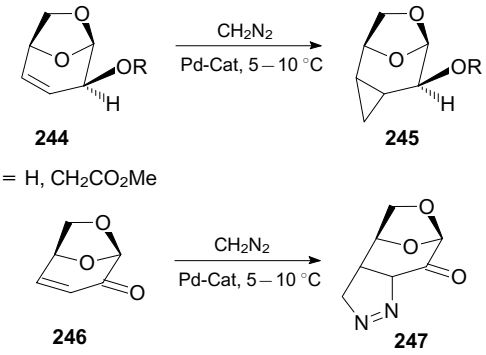
242 **243** (80%)

(*a*) CH_2N_2, $Pd(OAc)_2$, Et_2O, −78 °C

cyclopropanation product **243** upon the reaction with five equivalents of CH_2N_2 (Scheme 100).[223]

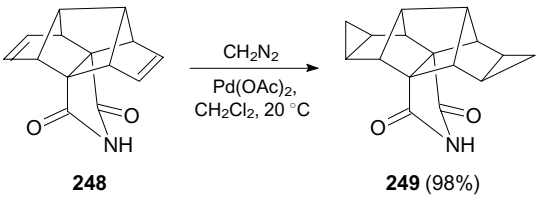
Levoglucosenone derivatives **244** react with two equivalents of CH_2N_2 to furnish cyclopropane adducts **245** in up to 95% yields (Scheme 101).[224] Meanwhile, direct cyclopropanation of the endocyclic double bond of pristine levoglucosenone **246** cannot be carried out under similar conditions because of the easy formation of 1-pyrazoline **247**.[224]

Scheme 101



Among unsaturated polycyclic compounds, a special position is occupied by derivatives containing the norbornene moiety or its heteroanalogue. Like the pristine norbornene, these compounds have high reactivity towards palladium-catalyzed diazomethane cyclopropanation. For example, polycyclic imide **248** readily reacts with an excess of diazomethane to give compound **249**, resulting from cyclopropanation of both norbornene double bonds (Scheme 102).[225, 226]

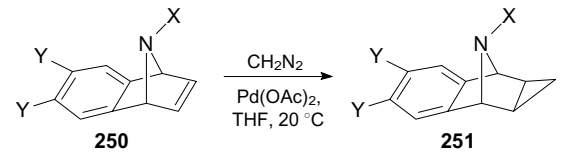
Scheme 102



In addition to norbornene, high activity in these reactions was found for its heteroanalogues. Thus, compounds **250** containing the 7-azabicyclo[2.2.1]hept-2-ene moiety react with a 2.5 – 3-fold excess of diazomethane giving cyclopropanes **251** in 75% – 98% yields (Scheme 103).[227]

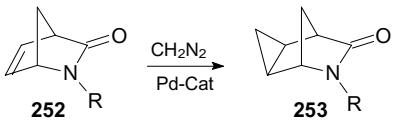
2-Azabicyclo[2.2.1]hept-5-ene derivatives, in particular, amides **252** or ethyl carboxylate **254** also react with an excess of diazomethane in the presence of palladium-based

Scheme 103

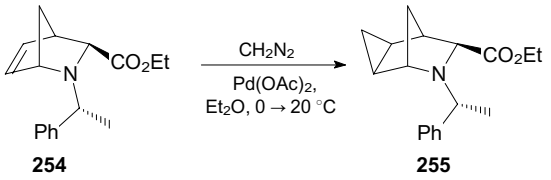


X = Boc, CO_2Me, Cbz, Ts, Ac, C(O)Bu^t, Ph;
Y = Me, Br, MeO; Y – Y is benzo

Scheme 104



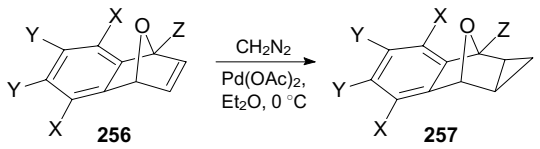
R = H: Pd-Cat = $Pd(OAc)_2$ (52%); R = Boc, Cbz;
Pd-Cat = $Pd(OAc)_2$ (83%), $(PhCN)_2PdCl_2$ (up to 69%)



catalysts giving rise to cyclopropanes **253** and **255** (Scheme 104).[228 – 232]

Apart from aza derivatives, a reasonably high reactivity is also inherent in oxa derivatives of polycyclic compounds. Compounds **256** with a 7-oxabicyclo[2.2.1]hept-2-ene moiety react with an excess of diazomethane (2.6 – 8 equiv.) to be converted to cyclopropane adducts **257** in 64% – 96% yields (Scheme 105).[233 – 236]

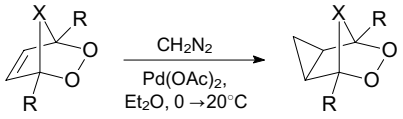
Scheme 105



X = H, Me, OMe, F; Y = H, OMe, F, Br; X + Y = $(CH{=}CH)_2$;
Z = H, Me, Et, Pr, Pr^i, Bu^n, Bu^t, Br, C(O)Me, CO_2Me, CH_2OH

Yet another class of original bicyclic compounds, unsaturated endoperoxides **258**, also give cyclopropanes **259** in 58% – 82% yields when react with diazomethane (up to 20 equiv.) (Scheme 106).[237]

Scheme 106

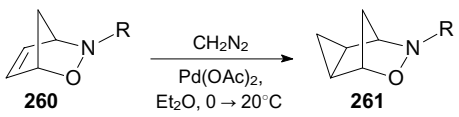


X = O, $(CH_2)_n$
(n = 1, 2);
R = H, Me, Ph

Related molecules **260**, which are obtained by the Diels – Alder reaction from cyclopentadiene and nitroso compounds, rather efficiently react with diazomethane in the presence of $Pd(OAc)_2$ producing annulated cyclopropane products **261** in 73% – 96% yields (Scheme 107).[238]

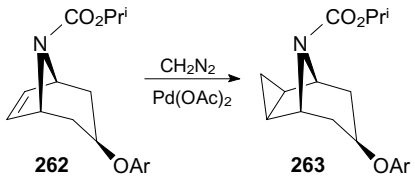
Among the reactions of other bicyclic compounds, the successful cyclopropanation of 8-azabicyclo[3.2.1]oct-6-ene

Scheme 107



R = Boc, Cbz, Bz, BnC(O), PhCH(OH)C(O), $Boc_2NC(O)$,
5-bromopyridin-2-yl

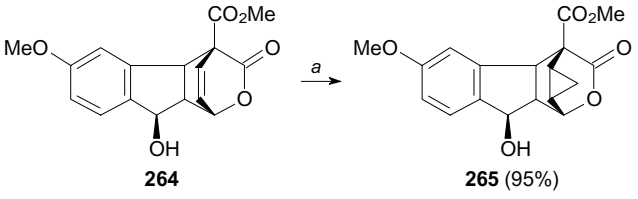
Scheme 108



262 to form cyclopropane derivative **263** has been reported (Scheme 108).[239] In all cases, the annulated three-membered ring (as in the pristine norbornene) points towards the single-atom bridge.

Polycyclic compound **264** containing an oxabicyclo[2.2.2]octene moiety is also cyclopropanated with diazomethane (~10 equiv.), which affords cyclopropane product **265** in a high yield (Scheme 109).[240]

Scheme 109

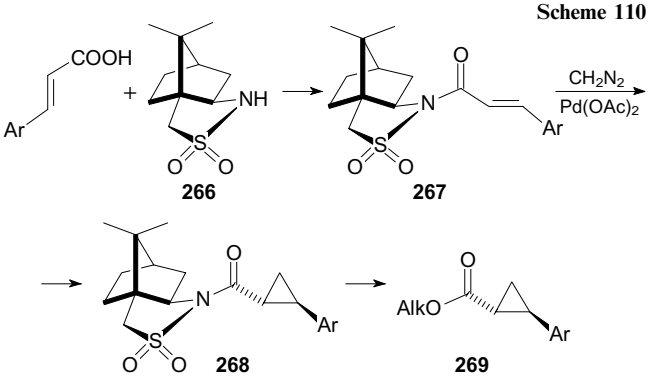


(*a*) CH_2N_2, $Pd(OAc)_2$, Et_2O, 0 °C

As noted above (see Section 3.1), palladium catalysts with chiral ligands, unlike copper, iron, ruthenium, rhodium and other metal compounds, are barely used for the synthesis of optically active cyclopropanes, because the resulting cyclopropane derivatives turn out to be racemic.[185] Nevertheless, this limitation can be circumvented if a chiral ligand is first incorporated into the unsaturated substrate, then cyclopropanation is carried out in the presence of usual palladium compounds (without chiral ligands), and finally the protecting chiral ligand is removed. This synthetic route based on natural chiral bicyclic ligands was utilized to prepare several optically active cyclopropanes.

A chiral ligand, (1*S*)-(−)-camphor-2,10-sultam **266**, was incorporated into cinnamic acid derivatives, which resulted in the formation of chiral unsaturated compounds **267**. The diazomethane cyclopropanation of compounds **267** in the presence of $Pd(OAc)_2$ afforded optically active cyclopropanes **268**. Cyclopropane derivatives **269** with the (1*R*,2*S*)-configuration were obtained in this way in preparative yields (Scheme 110).[241]

Scheme 110



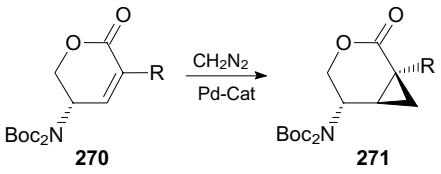
This strategy was also successfully used in the synthesis of some other optically active cyclopropanes from cinnamic acid derivatives.[190, 242 – 244]

3.2.4. Cyclopropanation of polysubstituted ethenes

The currently known examples of the catalytic diazomethane cyclopropanation of trisubstituted double bonds are limited to compounds containing adjacent electron-donating and -withdrawing groups, norbornene derivatives and highly strained molecules with methylenecyclopropane groups. Most often, the cyclopropanation of compounds with a trisubstituted double bond requires even a greater excess of diazomethane than that of disubstituted ethenes, and even in this case, the yields of the cyclopropane products are moderate.

For example, using a large excess of diazomethane, a series of substituted 5,6-dihydro-2*H*-pyran-2-ones **270** were converted to cyclopropanes **271**, the yields of which were not higher than 46% (Scheme 111).[221]

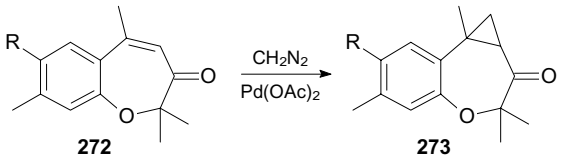
Scheme 111



Pd-Cat = $Pd(OAc)_2$: R = Me (46%), Et (31%), Pr^n (15%);
Pd-Cat = $Pd_2(dba)_3$: R = Pr^n (37%), Bu^n (29%), Ph (0%)

In the reaction with a large excess of diazomethane, 2,2,5-trimethylbenzo[*b*]oxepin-3(2*H*)-one derivatives (**272**) are converted to annulated cyclopropanes **273**, the yields of which are 72% – 90% (Scheme 112).[92, 245, 246]

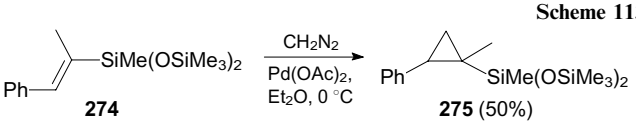
Scheme 112



R = H (85% – 90%), OMe (72%)

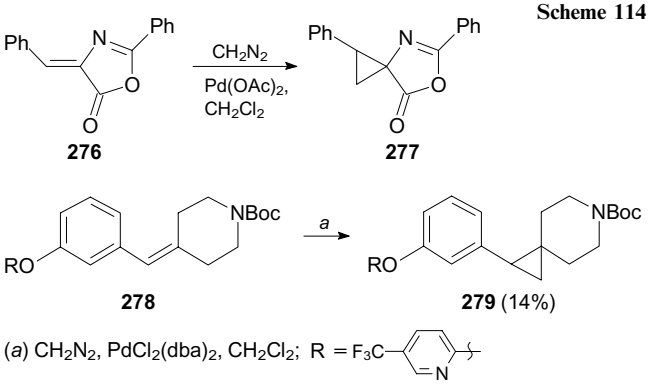
The double bond activation with a silyl group enabled conduction of cyclopropanation for alkenylsilane **274**, which was allowed to react with a fourfold excess of diazomethane, being thus converted to cyclopropane **275** (Scheme 113).[81]

Scheme 113



The catalytic reactions of 4-benzylidene-2-phenyloxazol-5(4*H*)-one **276** and substituted 4-benzylidenepiperidine **278** with diazomethane are examples of the successful cyclopropanation of a substituted exocyclic double bond. These

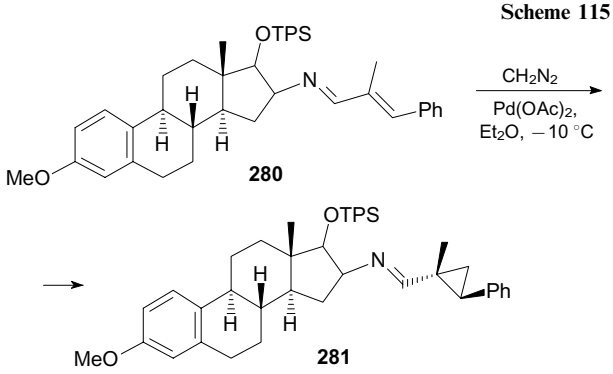
Scheme 114



reactions afforded spiro compounds **277** and **279** (Scheme 114).[247, 248]

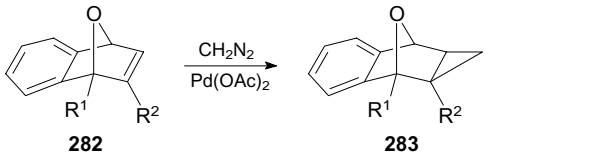
The cyclopropanation has also been reported for α,β-unsaturated aldimine **280**, which was prepared from *O*-silylated steroidal *cis*-amino alcohol and used as a chiral auxiliary for the highly diastereoselective preparation of substituted cyclopropylmethanimine **281** (Scheme 115).[249]

Scheme 115



Among analogous reactions of bicyclic compounds, the cyclopropanation of 7-oxabicyclo[2.2.1]heptenes **282** with a trisubstituted double bond using an excess of diazomethane (2.6–8 equiv.) was reported to give adducts **283** in good yields (Scheme 116).[235]

Scheme 116

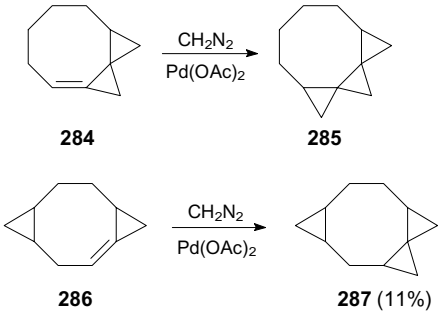


$R^1 = R^2 = Me$ (94%); $R^1 = H$, $R^2 = COOEt$ (72%)

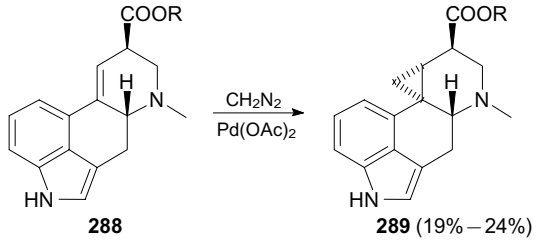
The final example of cyclopropanation of trisubstituted ethenes is the reaction involving the methylenecyclopropane moiety of cyclic compounds **284** and **286**, which makes it possible to prepare, although in a low yield, cyclopropanes annulated to an eight-membered ring (**285** and **287**) (Scheme 117).[250, 251]

Similarly, derivatives containing a cyclopropane moiety annulated to a six-membered ring (**289**) were obtained in moderate yields by the treatment of lysergic acid derivatives **288** with diazomethane (3 equiv.) (Scheme 118).[93]

Scheme 117



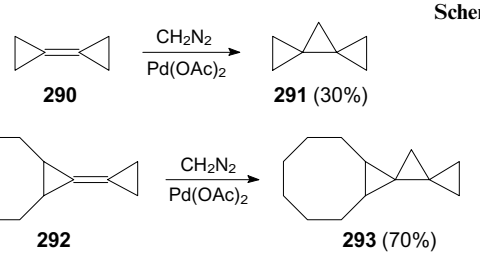
Scheme 118



R = Me, Et, Pr^i

Compounds with a tetrasubstituted double bond were mentioned in the publications [252, 253] dealing with the cyclopropanation of bicyclopropylidene **290** and its derivative **292**. The reaction of these substrates with an excess of diazomethane gives cyclopropanes **291** and **293** (Scheme 119). The former reaction yields up to ten by-products along with dispiroheptane **291**, which is a rare case for Pd-catalyzed cyclopropanation of unsaturated compounds.

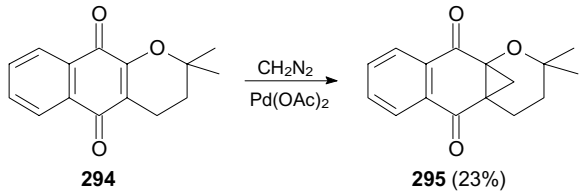
Scheme 119



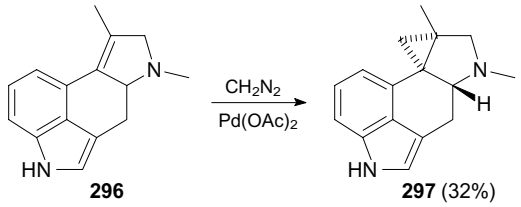
It was shown that the endocyclic tetrasubstituted double bond of 1,4-naphthoquinone derivative **294** can be cyclopropanated with an excess of diazomethane; this gives adduct **295**, although in a low yield (Scheme 120).[254]

A tetrasubstituted double bond was successfully cyclopropanated with the goal to introduce an annulated cyclopropane moiety into some ergot alkaloids.[255] For example, using a tenfold excess of diazomethane, 8-methyl-D-norer-

Scheme 120



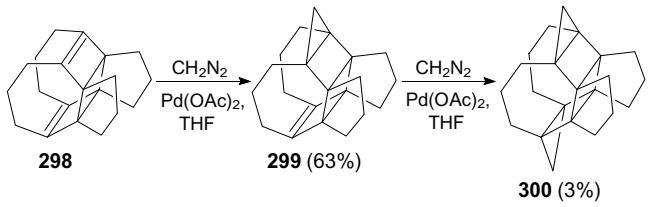
Scheme 121



golene **296** was converted to the alkaloid cycloclavine **297** (Scheme 121).

Finally, among tetrasubstituted unsaturated compounds containing no activating substituents on the double bond, a highly strained cage structure **298** has been described. The cyclopropanation of **298** with an excess of diazomethane (6 equiv.) provided the synthesis of both mono- and bisadducts (compounds **299** and **300**, respectively) (Scheme 122).[91,256]

Scheme 122

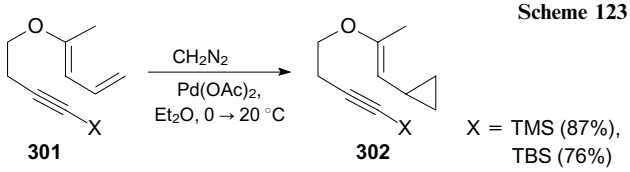


3.2.5. Cyclopropanation of dienes

The relationship, according to which the palladium-catalyzed addition of diazomethane to substituted double bonds, is more difficult than the addition to unsubstituted double bonds is preserved for the cyclopropanation of substituted dienes.[33]

When conjugated dienes have a terminal double bond, exactly this bond is cyclopropanated. Thus, diene ethers **301** react with an excess of diazomethane (5 equiv.) to give vinylcyclopropanes **302** in good yields (Scheme 123).[257]

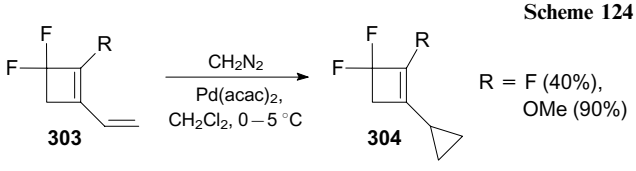
Scheme 123



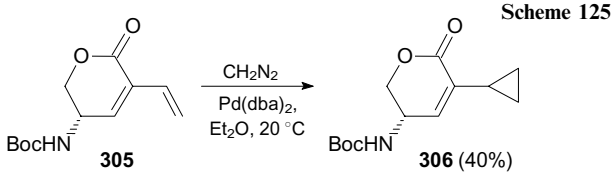
On treatment with a 2 – 3-fold excess of diazomethane, 1-vinylcyclobutenes **303** are also converted exclusively to the products of cyclopropanation of the vinyl group, 1-cyclopropylcyclobutenes **304** (Scheme 124).[129,258]

Despite the presence of the activating carbonyl group and the use of an excess of diazomethane (5 equiv.), the cyclopropanation of conjugated diene **305** involves exclusively the less substituted double bond and affords compound **306** (Scheme 125).[221]

Scheme 124

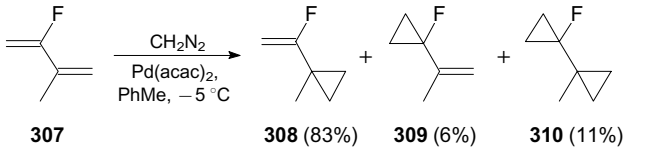


Scheme 125



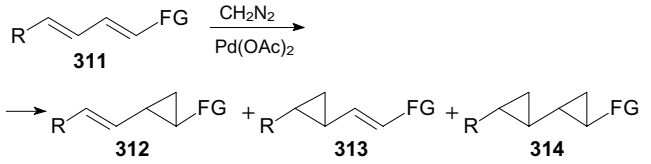
When the starting 1,3-diene molecule contains only disubstituted double bonds, the rate and the site of its reaction with diazomethane are determined by the nature of substituents. For example, 2-fluoro-3-methylbuta-1,3-diene **307**, in which both double bonds are 1,1-disubstituted, is converted to a mixture of cyclopropane adducts, with monoadduct **308** being formed predominantly. In this case, the reaction mixture contains also the products of cyclopropanation of the fluorinated double bond: monoadduct **309** and bisadduct **310**; the conversion of the starting diene **307** is 78% (Scheme 126).[258]

Scheme 126



The regioselectivity of cyclopropanation of double bonds in conjugated dienes containing functional groups (FG) (for example, as in compounds **311**) depends on the nature of these groups (Scheme 127).[259]

Scheme 127

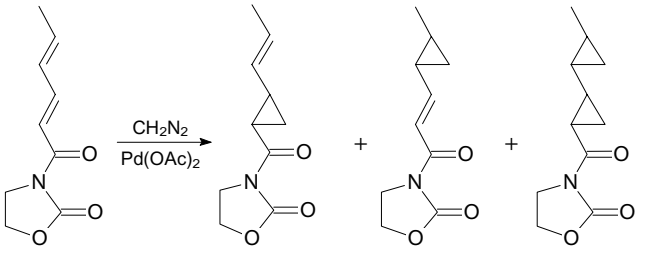


R = Alk, Ar, *etc.*; FG = C(O)Alk, CO_2Alk, C(O)$NAlk_2$, $B(OAlk)_2$, *etc.*

The reactions of ketones and carboxylic acid derivatives usually give mixtures of cyclopropanation products at both double bonds, that is, compounds **312** and **313**, the former being obtained in predominant amounts; the highest regioselectivity is observed for ketones. When 1 equiv. of diazomethane is used, the conversion of diene **315** reaches 90% and the ratio of monoadducts **316** and **317** is ~2 : 1. Under the same conditions, ester **319a** is converted to a mixture of monoadducts **320a** and **321a** in ~4 : 1 ratio. In the case of ketone **319b**, the ratio of monoadducts **320b** and **321b** is 18 : 1; however, the substrate conversion is only 50%. In all cases, bisadducts **318** and **322**, respectively, are also formed (Scheme 128).[259]

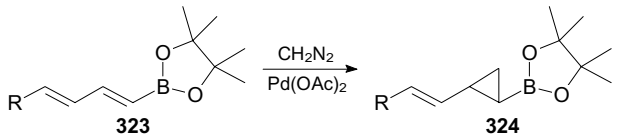
The reaction of 1,3-diene derivatives of boronic esters **323** with diazomethane proceeds regioselectively at the activated double bond adjacent to the boron atom and gives vinylcyclopropyl derivatives **324** in 60% – 70% yields (Scheme 129).[259]

Scheme 128



Compound	R	Yield of **320** (%)	Yield of **321** (%)	Yield of **322** (%)
a	OEt	60	15	10
b	C_5H_{11}	45	2.5	2

Scheme 129



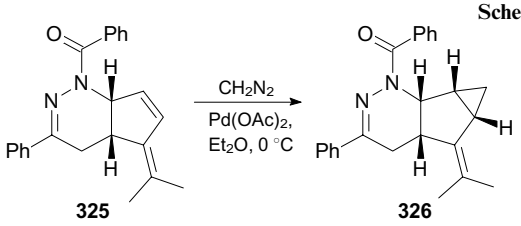
R = n-C_6H_{13}, $PhCH_2CH_2$, $PhCO_2(CH_2)_6$, $TBPSOCH_2CHMe$, (*Z*)-n-$C_8H_{17}CH{=}CH(CH_2)_6$

The high regioselectivity of cyclopropanation stimulated the active use of boronates in organic synthesis in recent years.

Conjugated dienes containing one 1,2-disubstituted bond and one tri- or tetrasubstituted bond usually react with diazomethane to give only products of cyclopropanation of the 1,2-disubstituted double bond, no matter where it is located.

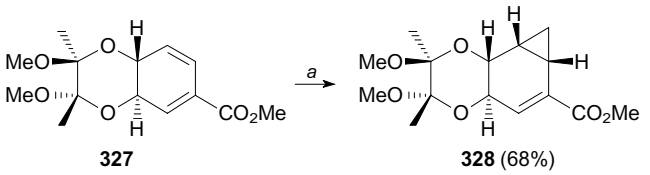
Thus, the reaction of diene **325** with diazomethane (3 equiv.) is directed only at the 1,2-disubstituted endocyclic double bond and results in cyclopropanation product **326** in a quantitative yield (Scheme 130).[260]

Scheme 130



In a similar way, cyclohexadiene **327** reacts only at the less substituted double bond, being converted exclusively to cyclopropane adduct **328**, even when a large excess of diazomethane (22 equiv.) is used (Scheme 131).[261]

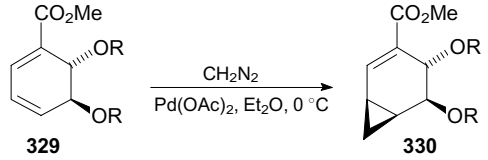
Scheme 131



(*a*) CH_2N_2, $Pd(OAc)_2$, Et_2O, 0 °C

Cyclohexa-1,3-diene-1-carboxylate derivatives **329** also react with an excess of diazomethane (4 equiv.) to give cyclopropanation products exclusively at the 1,2-disubstituted double bond, cyclopropanes **330**, in high yields (Scheme 132).[262]

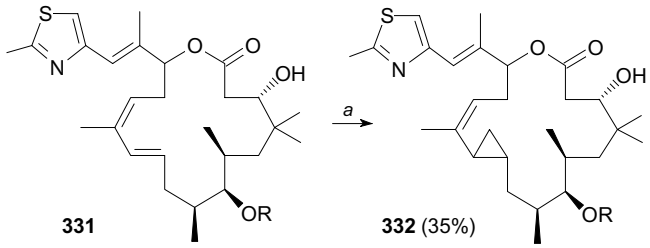
Scheme 132



R = TBS (97%), R–R = CHMe(OMe)CHMe(OMe) (86%)

In macrocyclic diene **331**, cyclopropanation is also directed only to the 1,2-disubstituted *trans*-double bond and affords product **332** (Scheme 133).[263]

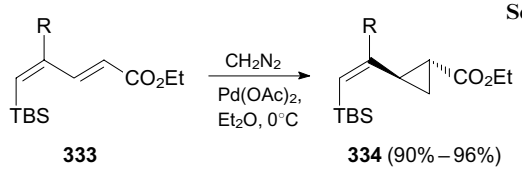
Scheme 133



(*a*) CH_2N_2, $Pd(OAc)_2$, Et_2O, 0 °C; R = Cl_3CCH_2OCO

Despite the activating silyl substituent located at the trisubstituted double bond, acyclic dienes **333** react with an excess of diazomethane (5 equiv.) to give only compounds **334**, resulting from cyclopropanation of the less substituted double bond (Scheme 134).[264]

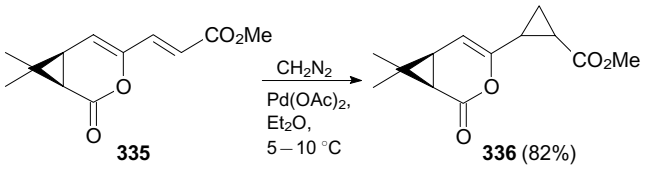
Scheme 134



R = Bu^n, Ph, CH_2OEt

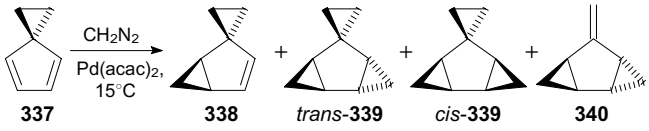
The reaction of lactone **335** with diazomethane also includes the cyclopropanation of only the less substituted double bond, which is furthermore activated by the ester group. When three equivalents of diazomethane are used, only cyclopropane product **336** is obtained (Scheme 135).[265]

Scheme 135



Among cyclic 1,3-dienes, spiro[2.4]hepta-4,6-diene derivatives (**337**) possess a number of unusual properties.[266–268] The catalytic cyclopropanation of spiroheptadiene makes it possible to obtain either monoadduct **338** or bisadduct **339**, depending on the excess of diazomethane used. In the case of exhaustive cyclopropanation with a fourfold excess of diazomethane, the *cis* isomer of **339** was isolated (2% – 5%) in addition to the major *trans* isomer. Moreover, the reaction was accompanied by the side formation of bishomofulvene **340** (1% – 3%). This fact is surprising, as the catalytic cyclopropanation of olefins usually gives no by-products (Scheme 136).[54, 61]

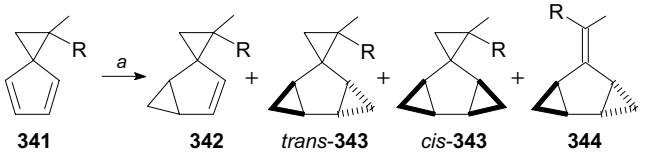
Scheme 136



The use of 1,1,2,2-tetradeuterospiroheptadiene (d_4-**337**) in this reaction demonstrated that, unlike mono- and bisadducts **338** and **339** containing each four deuterium atoms in the molecule, the formed bishomofulvene **340** has only two deuterium atoms, which attests to elimination of one CD_2 group from the initial d_4-**337**.[61]

1-Methyl- and 1,1-dimethylspiro[2.4]hepta-4,6-dienes (**341**) react with diazomethane in a similar way; the double bonds in these hydrocarbons are cyclopropanated less smoothly than the bonds of spiroheptadiene **337**. A high conversion of the substrate is attained when a 8 – 11-fold excess of diazomethane is used; apart from mono- (**342**) and dicyclopropanation (**343**) products, the formation of bishomofulvenes **344** was also detected (3% – 4%). Compounds **344** are formed upon elimination of an unsubstituted methylene group from the spiro cyclopropane ring in the starting compound (Scheme 137).[61]

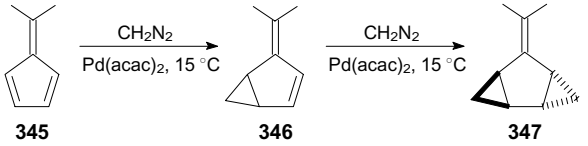
Scheme 137



(*a*) CH_2N_2, $Pd(acac)_2$; R = H, Me

The cyclopropanation of 6,6-dimethylfulvene (**345**) with diazomethane affects only the endocyclic double bonds and gives predominantly, first, monoadduct **346**, which further reacts with diazomethane to be converted to bisadduct **347** as the *trans* isomer. The remaining exocyclic double bond

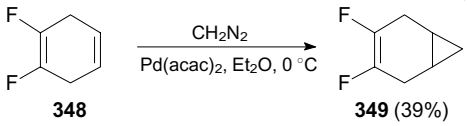
Scheme 138



does not react with diazomethane in the presence of the palladium catalyst (Scheme 138).[61]

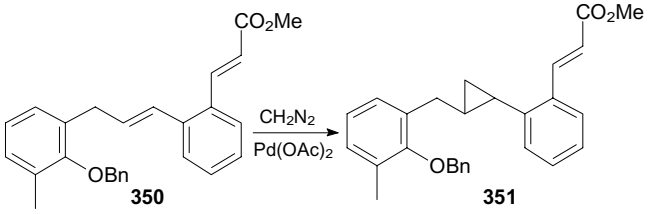
In the case of non-conjugated dienes with different double bonds, the less substituted double bond is also the first to be cyclopropanated. For example, 1,2-difluorocyclohexa-1,4-diene **348** is cyclopropanated with an excess of diazomethane (10 equiv.) only at the unsubstituted double bond; however, the reactivity of this bond is moderate, and 3,4-difluorobicyclo[4.1.0]hept-3-ene **349** is formed in a low yield (Scheme 139).[258]

Scheme 139



An interesting result was noted for the cyclopropanation of substituted *o*-divinylbenzene **350** containing a benzyl substituent on one double bond and an ester group on the other double bond. In this case, unlike cinnamic acid esters, the catalytic cyclopropanation was directed towards the benzyl-substituted double bond and gave cyclopropane **351**, whereas the double bond with the electron-withdrawing CO_2Me group remained intact (Scheme 140).[269]

Scheme 140



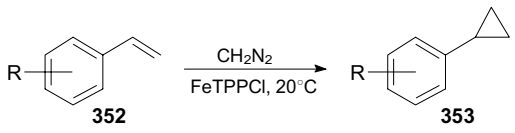
3.3. Other types of catalysts

3.3.1. Iron-based catalysts

In 2012, the iron 5,10,15,20-tetraphenylporphyrin complex FeTPPCl (**9**) was proposed for the first time as an efficient catalyst for diazomethane cyclopropanation.[45] This complex proved to be stable under strongly alkaline conditions used to generate diazomethane *in situ* both from water-soluble diazald derivative **6**[45] and from temozolomide (**5**)[47] under the action of an aqueous 6 M KOH solution. Under these conditions, the cyclopropanation of substituted styrenes **352** (3 equiv. of the source of diazomethane per equiv. of the unsaturated compound) gives high yields of arylcyclopropanes **353** (Scheme 141).[45, 47]

Good product yields were also observed for styrene derivatives with electron-withdrawing and electron-donating substituents.[45, 47] However, substrates with electron-donating substituents reacted faster and gave products in better yields.[47]

Scheme 141

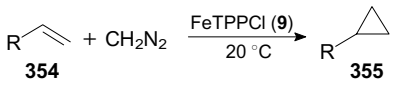


R = 2-OMe (80%,[45] 87%[47]), 4-OMe (89%,[45] 91%[47]), 4-Bu^t (78%),[45] 3-Br (81%),[45] 4-ClCH$_2$ (76%),[45] 3-NO$_2$ (64%),[45] 4-Me (55%),[47] 4-Ph (38%)[47]

Good yields of cyclopropane adducts **355** were also obtained from aryl-substituted 1,3-dienes and enynes **354** with a terminal double bond under the same conditions with FeTPPCl as the catalyst (Scheme 142).[45]

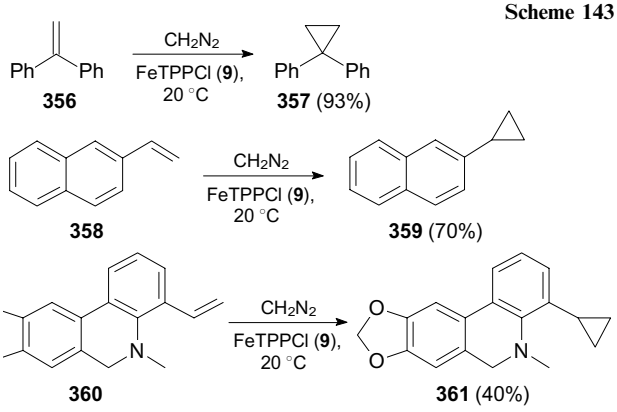
Apart from styrene derivatives, the cyclopropanation was successfully carried out for 1,1-diphenylethylene **356**, vinylnaphthalene **358** and alkaloid **360**, which were converted to cyclopropane derivatives **357**, **359** and **361**, respectively (Scheme 143).[1,47]

Scheme 142

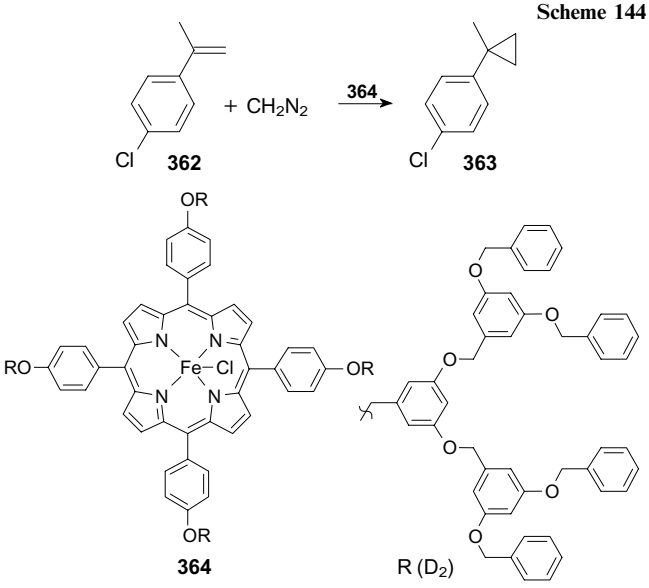


R = 2-MeOC$_6$H$_4$CH=CH (78%), PhCH=CMe (72%), PhC≡C (74%), 4-MeC$_6$H$_4$C≡C (76%)

Scheme 143



Scheme 144



Dendrimers **364** containing an iron porphyrin complex as the catalytically active site and polyether dendrite branches as substituents have been synthesized. The high efficiency of the synthesized catalysts was demonstrated in relation to the model cyclopropanation reaction of 1-chloro-4-(prop-1-en-2-yl)benzene (**362**) giving cyclopropane **363** (Scheme 144 shows only the second generation D_2 branch for compound **364**) (Scheme 144).[270]

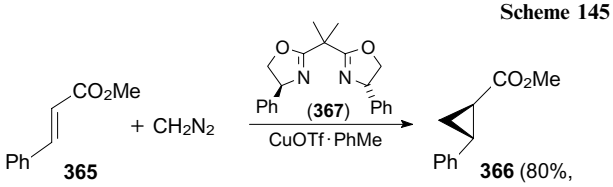
Studies of iron complex-based catalysts for the diazomethane cyclopropanation have been started only recently and, in the future, one should expect new catalysts of this type and data on the cyclopropanation of unsaturated compounds of other classes.

3.3.2. Copper-based catalysts

Copper-based catalysts were among the first to be used for the diazomethane cyclopropanation of unsaturated compounds; therefore, these catalysts have been best studied.[271 – 273] However, due to the very high decomposition rate of diazomethane, low reaction selectivity, usually low yields of cyclopropane products, the need for a large excess of diazomethane and, as a consequence, a large amount of polymethylene by-products, these catalysts are used relatively rarely.

Among copper catalysts, copper complexes with chiral ligands have a limited use for the preparation of optically active compounds.[2,48,49,175] For example, unlike Pd compounds, copper(I) complexes with chiral bis(oxazoline) ligands (**367**) allow enantioselective cyclopropanation of derivatives of cinnamic acid esters **365** with diazomethane. The highest yields of cyclopropanes (up to 80%) are attained for methyl esters **366** (Scheme 145).[175] Sterically hindered esters are formed in lower yields with lower enantioselectivities.

Scheme 145



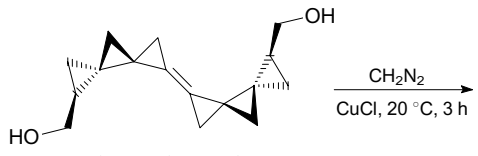
One more current application area of copper catalysts is the cyclopropanation of double bonds that cannot be cyclopropanated in the presence of palladium catalysts such as tri- and tetrasubstituted double bonds.[274 – 278]

Copper(I) chloride (CuCl) was used to catalyze the synthesis of triangulanes.[274] In particular, the cyclopropanation of the tetrasubstituted double bond of diol **368** catalyzed by CuCl (2.67 equiv.) results in the formation of [7]triangulanedimethanol **369** in a low yield despite the large excess of diazomethane (134 equiv.) (Scheme 146).[274]

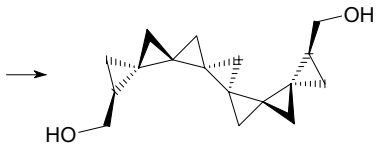
The cyclopropanation of tetrasubstituted double bonds of a different type can be exemplified by the reaction of 1,3-dialkyl-1,3-dihydroimidazol-2-ones **370** and **372** with a large excess of diazomethane (10 equiv.), which gives the expected cyclopropane products **371** and **373** in moderate yields (Scheme 147).[275]

Copper chloride is sometimes used to demonstrate the conceptual possibility of cyclopropanation of also aromatic

Scheme 146

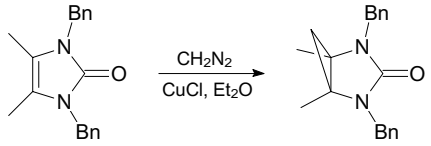


(*E*)-(3*S*,3′*S*,4*R*,4′*R*,5*S*,5′*S*)-**368**

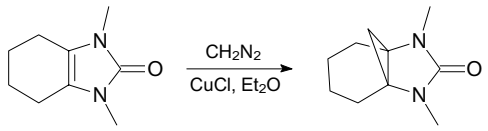


(1*S*,3*R*,4*S*,5*S*,6*S*,7*S*,8*R*,9*S*)-**369** (18%)

Scheme 147



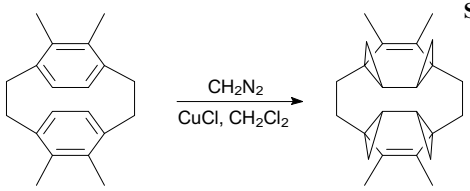
370 **371** (36%)



372 **373** (47%)

double bonds, as for example, in the case of tetramethyl[2.2]paracyclophane **374**. Large excess of diazomethane (21 equiv.) made it possible to obtain the product of cyclopropanation of four double bonds (**375**), although the yield of the product was low (Scheme 148).[279] Compound **375** is the first stable *cis*-bis(σ-homobenzene).

Scheme 148

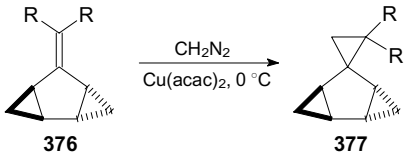


374 **375** (7%)

Finally, mention should be made of the use of $Cu(acac)_2$ as the catalyst of the cyclopropanation of the exocyclic double bond of bishomofulvenes **376**, which cannot be cyclopropanated in the presence of traditional palladium catalysts. The reaction with diazomethane afforded cyclopropane adducts **377** (Scheme 149).[61]

Thus, copper-based catalysts are now used rarely, mainly in those cases where palladium catalysts are inapplicable.

Scheme 149



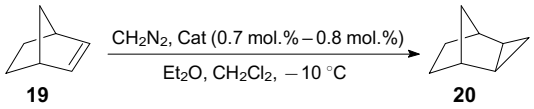
376 **377**

R = H, Me

3.3.3. Catalysts based on miscellaneous metals

Attempts to find effective catalysts for the diazomethane cyclopropanation have been made for a long time. Particular attention was attracted by compounds of metals other than copper or palladium, which are traditionally used in this reaction. In an early systematic study,[85] a number of metals (Co, Ni, Zr, Cr, Rh, Dy, *etc.*) were tested as catalysts, with norbornene **378** being chosen as the model unsaturated compound (norbornene : CH_2N_2 = 1 : 1) (Scheme 150).

Scheme 150



19 **20**

Cat = $Pd(acac)_2$ (72%), $Ni(acac)_2$ (27%), $Cu(acac)_2$ (24%), Ni/C (16%), $Zr(acac)_4$ (15%), $Al(EtCO_2)_3$ (10%), $Cr(acac)_3$ (9%), $VO(acac)_2$ (9%), $Dy(OAc)_2$ (8%), Rh/C (7%), ZrV_2O_7 (6%), $Zn[C_{17}H_{35}CO_2]_2$ (5%), $Co(acac)_3$ (5%), $Cu(OAc)_2$ (3%), $Fe(acac)_3$ (2%), $Ho_2(CO_3)_3$ (2%)

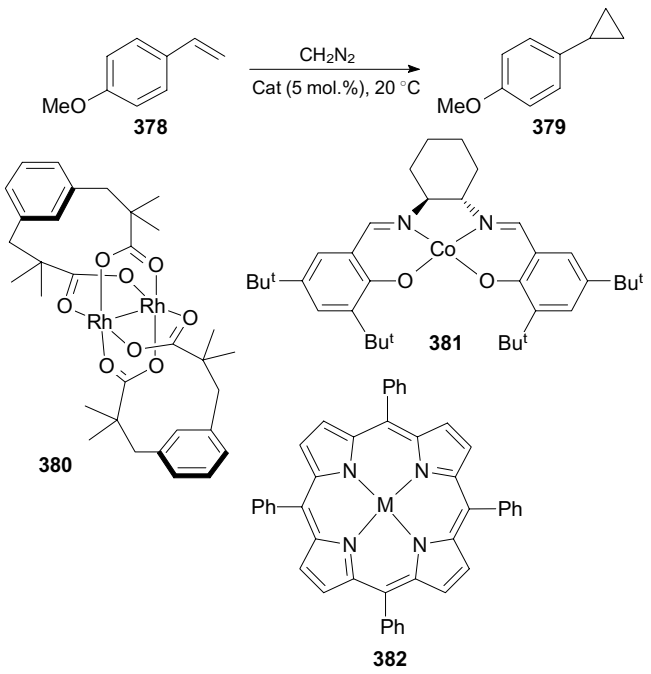
Considering that study[85] from the modern standpoint, based on the accumulated knowledge of the mechanism of diazomethane cyclopropanation catalyzed by various compounds (see Section 3.1), it can be noted that the conclusions drawn in that study are quite reasonable (the highest yield of product **20** was obtained in the presence of palladium catalysts, because norbornene is a very good complexing agent for palladium). Among palladium compounds, the best results were obtained for $Pd(acac)_2$, which is still one of the best catalysts for the cyclopropanation of certain classes of unsaturated compounds with diazomethane.

Compounds of other metals exhibited much lower efficiency.[85] However, the mechanism of cyclopropanation catalyzed by other metals, most likely, differs considerably from the mechanism of action of palladium catalysts. For example, the mechanism may include the intermediate formation of carbene complexes and may be almost unaffected by the degree of complex formation with the double bond of the starting unsaturated compound (see Section 3.1). Therefore, to study the comparative efficiency of the catalysts based on various metals, it is necessary to consider the possible mechanism of action of the chosen catalyst and to take chemically different starting unsaturated compounds for the reaction. For another diazo compound, ethyl diazoacetate, and palladium-based catalysts, the best results were also attained for norbornene (80% – 95% yields), whereas in the presence of platinum compounds, the yield of the cyclopropane product obtained from norbornene was 0% – 20%, while styrene gave the product in 60% – 90% yield.[280, 281] Hence, if only one substrate is taken as the model unsaturated compound, the really efficient catalysts can be overlooked.

In a later study,[45] the search for the best catalysts for the diazomethane cyclopropanation was performed using 4-methoxystyrene (**378**), which was converted to cyclopropane **379**. Diazomethane (3 equiv.) was generated *in situ* by the treatment of diazald analogue **6** with 6 M KOH aqueous solution (Scheme 151).

The following compounds were tested (the value in parentheses is the yield of product **379**): $Cu(OTf)_2$ (0%), $Pd(OAc)_2$ (9%), $Rh_2(OAc)_4$ (0%), $Rh_2C_{17}H_{35}COO)_4$

Scheme 151



(45%), **380** (53%), **381** (23%) and **382** [M = RuCO (93%), Co (33%), FeCl (100%)].[45] A surprising fact is the low yield of cyclopropane **379** with the use of $Pd(OAc)_2$, which may be due to the presence of a two-phase system. Indeed, the efficiency was markedly lower for water-soluble catalysts than for catalysts insoluble in water, but readily soluble in organic solvents. This can be understood by taking into account the details of *in situ* generation of diazomethane from the diazald analogue under the action of concentrated aqueous alkali. In this case, water-soluble metal compounds either pass to the aqueous phase or precipitate. The results obtained by Morandi and Carreira[45] indicate that these studies need to be continued and it is necessary to more thoroughly study the potential of other catalysts, in particular, those based on ruthenium and cobalt, for reactions of chemically diverse unsaturated compounds with a diazomethane solution in diethyl ether or CH_2Cl_2.

4. Conclusion

Analysis of the published data on the cyclopropanation of olefins attests to a considerable progress in the title area of research over the last 10 – 15 years. During this period, new methods for safe generation of diazomethane have been developed, including the use of membrane technologies and continuous-flow and *in situ* generation methods, which eliminate severe limitations on the wide use of diazomethane both in laboratory and in industry and can revive the interest in the diazomethane chemistry.

This review demonstrates the potential of using diazomethane for the synthesis of cyclopropanes by the direct catalytic cyclopropanation of unsaturated compounds. These processes are catalyzed most efficiently by palladium compounds, which ensure high yields of products with a minimized consumption of diazomethane. In recent years, catalysts based on iron compounds have also been actively developed.

The systematic studies of these reactions over this period revealed the regular patterns of cyclopropanation of various double bonds and made it possible to evaluate the efficiency of various catalysts and to propose the mechanisms of their action.

The successful development of this research area would be determined by further search for active and highly selective catalysts for the diazomethane cyclopropanation and further progress in the understanding of the reaction mechanism.

The following acronyms are used in the review:
acac — acetylacetonate,
Boc — *tert*-butyloxycarbonyl protecting group,
Bz — benzoyl,
Bn — benzyl,
Cbz — benzyloxycarbonyl,
cod — cycloocta-1,5-diene,
Diazald — *N*-methyl-*N*-nitroso-*p*-toluenesulfonamide,
DMSO — dimethyl sulfoxide,
DVTMS — divinyltetramethyldisiloxane,
EWG — electron-withdrawing group,
LA — Lewis acid,
MNNG — *N*-methyl-*N*′-nitro-*N*-nitrosoguanidine,
MNU — *N*-methyl-*N*-nitrosourea,
MOM — methoxymethyl,
Naph — naphthyl,
NMR — nuclear magnetic resonance,
R_f — retention factor,
TBS — *tert*-butyldimethylsilyl,
THF — tetrahydrofuran,
THP — tetrahydropyran,
TMZ — temozolomide,
TPS — *tert*-butyldiphenylsilyl.

References

1. O.G.Kulinkovich. *Cyclopropanes in Organic Synthesis*. (Hoboken, NJ: Wiley, 2015)
2. H.Pellissier. *Tetrahedron*, **64**, 7041 (2008)
3. H.Pellissier. *Chiral Sulfur Ligands: Asymmetric Catalysis (RSC Catalysis Series)*. (Cambridge: The Royal Society of Chemistry, 2009)
4. E.Breitmaier. *Terpenes*. (Weinheim: Wiley, 2006)
5. E.Matsumura, M.Matsuda, F.Sato, H.Minami. *Natural Products: Phytochemistry, Botany and Metabolism of Alkaloids, Phenolics and Terpenes*. (Berlin, Heidelberg: Springer, 2013)
6. L.Crombie, M.Elliott. In *Fortschritte der Chemie Organischer Naturstoffe/Progress in the Chemistry of Organic Natural Products/Progrès dans la Chimie des Substances Organiques Naturelles*. (Ed. L.Zechmeister). (Vienna: Springer, 1961). P. 120
7. K.Yamada, M.Ojika, H.Kigoshi. *Angew. Chem., Int. Ed.*, **37**, 1818 (1998)
8. D.L.Boger, D.S.Johnson. *Angew. Chem., Int. Ed. Engl.*, **35**, 1438 (1996)
9. P.Keglevich, A.Keglevich, L.Hazai, G.Kalaus, C.Szantay. *Curr. Org. Chem.*, **18**, 2037 (2014)
10. G.Schmeda-Hirschmann, F.Tsichritzis, J.Jakupovic. *Phytochemistry*, **31**, 1731 (1992)
11. R.Faust. *Angew. Chem., Int. Ed.*, **40**, 2251 (2001)
12. J.Salaün. In *Small Ring Compounds in Organic Synthesis VI*. Vol. 207. (Ed. A.de Meijere). (Berlin, Heidelberg: Springer, 2000). Ch. 1. P. 1
13. Z.Rappoport. *The Chemistry of the Cyclopropyl Group*. Vol. 1. (Chichester, New York, Bisbane, Toronto, Singapore: Wiley, 1987)

14. D.Arlt, M.Jautelat, R.Lantzsch. *Angew. Chem., Int. Ed. Engl.*, **20**, 703 (1981)
15. Y.Katsuda. In *Pyrethroids: From Chrysanthemum to Modern Industrial Insecticide. (Ser. Topics in Current Chemistry*. Vol. 314). (Berlin, Heidelberg: Springer, 2012). P. 90
16. F.Schröder. *Chem. Biodiversity*, **11**, 1734 (2014)
17. A.de Meijere. In *Small Ring Compounds in Organic Synthesis VI*. Vol. 207. (Ed. A.de Meijere). (Berlin, Heidelberg: Springer, 2000)
18. C.D.Poulter. *J. Org. Chem.*, **74**, 2631 (2009)
19. L.A.Wessjohann, W.Brandt, T.Thiemann. *Chem. Rev.*, **103**, 1625 (2003)
20. W.D.Nes. *Chem. Rev.*, **111**, 6423 (2011)
21. J.H.Law. *Acc. Chem. Res.*, **4**, 199 (1971)
22. C.J.Thibodeaux, W.-c.Chang, H.-w.Liu. *Chem. Rev.*, **112**, 1681 (2012)
23. D.F.Iwig, A.Uchida, J.A.Stromberg, S.J.Booker. *J. Am. Chem. Soc.*, **127**, 11612 (2005)
24. G.D.Brown. *Nat. Prod. Rep.*, **15**, 653 (1998)
25. M.J.Garson. *Chem. Rev.*, **93**, 1699 (1993)
26. P.S.Coelho, E.M.Brustad, A.Kannan, F.H.Arnold. *Science*, **339**, 307 (2013)
27. P.Tang, Y.Qin. *Synthesis*, **44**, 2969 (2012)
28. D.Y.K.Chen, R.H.Pouwer, J.-A.Richard. *Chem. Soc. Rev.*, **41**, 4631 (2012)
29. C.Ebner, E.M.Carreira. *Chem. Rev.*, **117**, 11651 (2017)
30. Y.V.Tomilov, L.G.Menchikov, R.A.Novikov, O.A.Ivanova, I.V.Trushkov. *Russ. Chem. Rev.*, **87**, 201 (2018)
31. A.de Meijere, S.I. Kozhushkov. *Sci. Synth.*, **48**, 477 (2009)
32. M.-N.Roy, V.N.G.Lindsay, A.B.Charette. In *Science of Synthesis, 1: Stereoselective Synthesis 1*. Vol. 1. (1st Edn.). (Ed. J.G.de Vries). (Stuttgart: Georg Thieme Verlag, 2011). P. 731
33. Y.V.Tomilov, V.A.Dokichev, U.M.Dzhemilev, O.M.Nefedov. *Russ. Chem. Rev.*, **62**, 799 (1993)
34. H.Zollinger. *Diazo Chemistry II: Aliphatic, Inorganic and Organometallic Compounds*. (Weinheim: VCH, 1995)
35. H.Zollinger. *Diazo Chemistry I: Aromatic and Heteroaromatic Compounds*. (Weinheim: VCH, 1994)
36. M.Regitz, G.Maas. *Diazo Compounds. Properties and Synthesis*. (Orlando: Academic Press, 1986)
37. G.W.Cowell, A.Ledwith. *Quarterly Rev. Chem. Soc.*, **24**, 119 (1970)
38. T.J.de Boer, H.J.Backer. *Org. Synth. Collec.*, **4**, 250 (1963)
39. Z.Časar. *Synthesis*, **52**, 1315 (2020)
40. I.R.Ramazanov, A.V.Yaroslavova, N.R.Yaubasarov, E.N.Gil'manova, U.M.Dzhemilev. *Russ. Chem. Bull.*, **68**, 1869 (2019)
41. A.de Meijere, S.I.Kozhushkov, H.Schill. *Chem. Rev.*, **106**, 4926 (2006)
42. Y.Zhang, J.Wang. *Eur. J. Org. Chem.*, **2011**, 1015 (2011)
43. V.A.D'yakonov, O.A.Trapeznikova, A.de Meijere, U.M.Dzhemilev. *Chem. Rev.*, **114**, 5775 (2014)
44. A.de Meijere. *Handbook of Organopalladium Chemistry for Organic Synthesis*. (New York: Wiley, 2002)
45. B.Morandi, E.M.Carreira. *Science*, **335**, 1471 (2012)
46. J.Kaschel, T.F.Schneider, D.B.Werz. *Angew. Chem., Int. Ed.*, **51**, 7085 (2012)
47. R.L.Svec, P.J.Hergenrother. *Angew. Chem., Int. Ed.*, **59**, 1857 (2020)
48. H.Pellissier, A.Lattanzi, R.Dalpozzo. *Asymmetric Synthesis of Three-Membered Rings*. (Weinheim: Wiley, 2017)
49. H.Lebel, J.-F.Marcoux, C.Molinaro, A.B.Charette. *Chem. Rev.*, **103**, 977 (2003)
50. G.Bartoli, G.Bencivenni, R.Dalpozzo. *Synthesis*, **46**, 979 (2014)
51. H.V.Pechmann. *Ber. Dtsch. Chem. Ges.*, **27**, 1888 (1894)
52. S.W.J.Shields, J.M.Manthorpe. *J. Labelled Compd. Radiopharm.*, **57**, 674 (2014)
53. F.Arndt. *Org. Synth. Collect.*, **2**, 165 (1943)
54. E.V.Shulishov, O.A.Pantyukh, L.G.Menchikov, Y.V.Tomilov. *Tetrahedron Lett.*, **60**, 2043 (2019)
55. L.D.Proctor, A.J.Warr. *Org. Process Res. Dev.*, **6**, 884 (2002)
56. B.Eistert. *Angew. Chem.*, **54**, 124 (1941)
57. J.A.Moore, D.E.Reed. *Org. Synth.*, **41**, 16 (1961)
58. O.M.Nefedov, Y.V.Tomilov, A.B.Kostitsyn, U.M.Dzhemilev, V.A.Dokitchev. *Mendeleev Commun.*, **2**, 13 (1992)
59. Y.V.Tomilov, A.B.Kostitsyn, E.V.Shulishov, A.K.Khusid, O.M.Nefedov. *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, **38**, 2513 (1989)
60. Y.V.Tomilov, A.B.Kostitsyn, V.A.Dokichev, U.M.Dzhemilev, O.M.Nefedov. *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, **38**, 2518 (1989)
61. E.V.Shulishov, O.A.Pantyukh, L.G.Menchikov, Y.V.Tomilov. *Chemistry Select*, **5**, 4046 (2020)
62. C.H.Oh, D.I.Park, J.H.Ryu, J.H.Cho, J.-S.Han. *Bull. Korean Chem. Soc.*, **28**, 322 (2007)
63. F.Mastronardi, B.Gutmann, C.O.Kappe. *Org. Lett.*, **15**, 5590 (2013)
64. H.F.Koolman, S.Kantor, A.R.Bogdan, Y.Wang, J.Y.Pan, S.W.Djuric. *Org. Biomol. Chem.*, **14**, 6591 (2016)
65. H.Yang, B.Martin, B.Schenkel. *Org. Process Res. Dev.*, **22**, 446 (2018)
66. M.Movsisyan, E.I.P.Delbeke, J.K.E.T.Berton, C.Battilocchio, S.V.Ley, C.V.Stevens. *Chem. Soc. Rev.*, **45**, 4892 (2016)
67. M.Struempel, B.Ondruschka, R.Daute, A.Stark. *Green Chem.*, **10**, 41 (2008)
68. M.Struempel, B.Ondruschka, A.Stark. *Org. Process Res. Dev.*, **13**, 1014 (2009)
69. E.Rossi, P.Woehl, M.Maggini. *Org. Process Res. Dev.*, **16**, 1146 (2012)
70. K.J.Hock, R.M.Koenigs. *Chem. – Eur. J.*, **24**, 10571 (2018)
71. Patent US 5854405 (1998)
72. T.G.Archibald. *Chimica Oggi*, **18**, 34 (2000)
73. Patent US 10611704 (2020)
74. Patent WO 2015059290 (2015)
75. M.P.Doyle. *Chem. Rev.*, **86**, 919 (1986)
76. Y.Li, J.-S.Huang, Z.-Y.Zhou, C.-M.Che, X.-Z.You. *J. Am. Chem. Soc.*, **124**, 13185 (2002)
77. C.-M.Che, J.-S.Huang, F.-W.Lee, Y.Li, T.-S.Lai, H.-L.Kwong, P.-F.Teng, W.-S.Lee, W.-C.Lo, S.-M.Peng, Z.-Y.Zhou. *J. Am. Chem. Soc.*, **123**, 4119 (2001)
78. X.Dai, T.H.Warren. *J. Am. Chem. Soc.*, **126**, 10085 (2004)
79. B.F.Straub, P.Hofmann. *Angew. Chem., Int. Ed.*, **40**, 1288 (2001)
80. B.F.Straub, I.Gruber, F.Rominger, P.Hofmann. *J. Organomet. Chem.*, **684**, 124 (2003)
81. G.Berthon-Gelloz, M.Marchant, B.F.Straub, I.E.Marko. *Chem. – Eur. J.*, **15**, 2923 (2009)
82. B.F.Straub. *J. Am. Chem. Soc.*, **124**, 14195 (2002)
83. Y.V.Tomilov, V.G.Bordakov, I.E.Dolgii, O.M.Nefedov. *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, **33**, 533 (1984)
84. O.Illa, C.Rodríguez-García, C.Acosta-Silva, I.Favier, D.Picurelli, A.Oliva, M.Gómez, V.Branchadell, R.M.Ortuño. *Organometallics*, **26**, 3306 (2007)
85. U.M.Dzhemilev, V.A.Dokichev, S.Z.Sultanov, R.I.Khusnutdinov, Y.V.Tomilov, O.M.Nefedov, G.A.Tolstikov. *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, **38**, 1707 (1989)
86. E.V.Shulishov, O.A.Pantyukh, L.G.Menchikov, Y.V.Tomilov. *Mendeleev Commun.*, **30**, 612 (2020)
87. U.M.Dzhemilev, V.A.Dokichev, S.Z.Sultanov, S.L.Khursan, O.M.Nefedov, Y.V.Tomilov, A.B.Kostitsyn. *Bull. Russ. Acad. Sci., Div. Chem. Sci.*, **41**, 1846 (1992)
88. U.M.Dzhemilev, V.A.Dokichev, I.O.Maidanova, O.M.Nefedov, Y.V.Tomilov. *Russ. Chem. Bull.*, **42**, 697 (1993)
89. R.Huisgen, P.H.J.Ooms, M.Mingin, N.L.Allinger. *J. Am. Chem. Soc.*, **102**, 3951 (1980)

90. S.N.Steinmann, P.Vogel, Y.Mo, C.Corminboeuf. *Chem. Commun.*, **47**, 227 (2011)
91. R.Gleiter, G.Pflästerer, H.Irngartinger. *Chem. Ber.*, **126**, 1011 (1993)
92. S.Ghosh, K.Tuhina, D.R.Bhowmik, R.V.Venkateswaran. *Tetrahedron*, **63**, 644 (2007)
93. M.Incze, G.Dornyei, P.Kovacs, O.Egyed, G.Hajos, C.Szantay. *Heterocycles*, **87**, 1553 (2013)
94. A.de Meijere, A.F.Khlebnikov, S.I.Kozhushkov, R.R.Kostikov, P.R.Schreiner, A.Wittkopp, C.Rinderspacher, H.Menzel, D.S.Yufit, J.A.K.Howard. *Chem. – Eur. J.*, **8**, 828 (2002)
95. A.de Meijere, A.F.Khlebnikov, S.I.Kozhushkov, K.Miyazawa, D.Frank, P.R.Schreiner, B.C.Rinderspacher, D.S.Yufit, J.A.K.Howard. *Angew. Chem., Int. Ed.*, **43**, 6553 (2004)
96. Y.-T.Lin, C.-K.Linc, K.-F.Liou, S.-S.Cheng, M.-J.Chang. *J. Chin. Chem. Soc.*, **33**, 341 (1986)
97. A.P.Molchanov, R.R.Kostikov, V.A.Chernyshev. *Zh. Org. Khim.*, **27**, 1648 (1991)
98. A.P.Molchanov, R.R.Kostikov, V.A.Chernyshev. *ChemInform*, **23** (1992)
99. J.E.Anderson, A.de Meijere, S.I.Kozhushkov, L.Lunazzi, A.Mazzanti. *J. Am. Chem. Soc.*, **124**, 6706 (2002)
100. S.I.Kozhushkov, R.R.Kostikov, A.P.Molchanov, R.Boese, J.Benet-Buchholz, P.R.Schreiner, C.Rinderspacher, I.Ghiviriga, A.de Meijere. *Angew. Chem., Int. Ed.*, **40**, 180 (2001)
101. C.V.Ramana, S.M.Baquer, R.G.Gonnade, M.K.Gurjar. *Chem. Commun.*, 614 (2002)
102. S.I.Kozhushkov, D.S.Yufit, R.Boese, D.Blaeser, P.R.Schreiner, A.de Meijere. *Eur. J. Org. Chem.*, 1409 (2005)
103. M.Horikawa, K.Tateda, E.Tuzuki, Y.Ishii, C.Ueda, T.Takabatake, S.Miyairi, K.Yamaguchi, M.Ishiguro. *Bioorg. Med. Chem. Lett.*, **16**, 2130 (2006)
104. G.Butora, G.J.Morriello, S.Kothandaraman, D.Guiadeen, A.Pasternak, W.H.Parsons, M.MacCoss, P.P.Vicario, M.A.Cascieri, L.Yang. *Bioorg. Med. Chem. Lett.*, **16**, 4715 (2006)
105. M.D.Khanova, R.M.Sultanova, R.R.Rafikov, I.P.Baykova, R.Z.Biglova, V.A.Dokichev, Y.V.Tomilov. *Russ. Chem. Bull.*, **57**, 617 (2008)
106. A.Li, A.B.Shtarev, B.E.Smart, Z.-Y.Yang, J.Lusztyk, K.U.Ingold, A.Bravo, W.R.Dolbier. *J. Org. Chem.*, **64**, 5993 (1999)
107. K.N.Sedenkov, E.B.Averin, Y.K.Grishin, T.S.Kuznetsova, N.S.Zefirov. *Russ. Chem. Bull.*, **65**, 1750 (2016)
108. S.Jordi, P.Kraft. *Helv. Chim. Acta*, **101**, e1800048 (2018)
109. L.Widler, E.Altmann, R.Beerli, W.Breitenstein, R.Bouhelal, T.Buhl, R.Gamse, M.Gerspacher, C.Halleux, M.R.John, H.Lehmann, O.Kalb, M.Kneissel, M.Missbach, I.R.Müller, S.Reidemeister, J.Renaud, A.Taillardat, R.Tommasi, S.Weiler, R.M.Wolf, K.Seuwen. *J. Med. Chem.*, **53**, 2250 (2010)
110. C.J.Dinsmore, C.B.Zartman, J.M.Bergman, M.T.Abrams, C.A.Buser, J.C.Culberson, J.P.Davide, M.Ellis-Hutchings, C.Fernandes, S.L.Graham, G.D.Hartman, H.E.Huber, R.B.Lobell, S.D.Mosser, R.G.Robinson, T.M.Williams. *Bioorg. Med. Chem. Lett.*, **14**, 639 (2004)
111. D.O.Ptashko, A.I.Syusina, M.D.Khanova, V.G.Safarova, A.N.Lobov, V.A.Dokichev. *Bash. Khim. Zh.*, **18**, 162 (2011)
112. J.Christoffers, T.Kauf, T.Werner, M.Roessle. *Eur. J. Org. Chem.*, 2601 (2006)
113. G.S.Zaitseva, S.S.Karlov, E.S.Alekseyeva, L.A.Aslanov, E.V.Avtomonov, J.Lorberth. *Z. Naturforsch., B*, **52**, 30 (1997)
114. J.A.Robl, M.P.Cimarusti, L.M.Simpkins, B.Brown, D.E.Ryono, J.E.Bird, M.M.Asaad, T.R.Schaeffer, N.C.Trippodo. *J. Med. Chem.*, **39**, 494 (1996)
115. S.Bogen, A.K.Saksena, A.Arasappan, H.Gu, F.G.Njoroge, V.Girijavallabhan, J.Pichardo, N.Butkiewicz, A.Prongay, V.Madison. *Bioorg. Med. Chem. Lett.*, **15**, 4515 (2005)
116. A.C.Krueger, D.L.Madigan, B.E.Green, D.K.Hutchinson, W.W.Jiang, W.M.Kati, Y.Liu, C.J.Maring, S.V.Masse, K.F.McDaniel, T.R.Middleton, H.Mo, A.Molla, D.A.Montgomery, T.I.Ng, D.J.Kempf. *Bioorg. Med. Chem. Lett.*, **17**, 2289 (2007)
117. G.F.Vafina, M.D.Khanova. *Russ. J. Org. Chem.*, **56**, 346 (2020)
118. L.Wei, Q. Zhu, S.-M.Xu, X.Chang, C.-J.Wang. *J. Am. Chem. Soc.*, **140**, 1508 (2018)
119. Y.Morimoto, M.Takaishi, T.Kinoshita, K.Sakaguchi, K.Shibata. *Chem. Commun.*, 42 (2002)
120. K.O.Hallinan, D.H.G.Crout, W.Errington. *J. Chem. Soc., Perkin Trans. 1*, 3537 (1994)
121. A.R.Howard-Jones, J.M.Elkins, I.J.Clifton, P.L.Roach, R.M.Adlington, J.E.Baldwin, P.J.Rutledge. *Biochemistry*, **46**, 4755 (2007)
122. D.Ma, W.Zhu. *J. Org. Chem.*, **66**, 348 (2001)
123. T.Spangenberg, A.Schoenfelder, B.Breit, A.Mann. *Org. Lett.*, **9**, 3881 (2007)
124. T.Spangenberg, A.Schoenfelder, B.Breit, A.Mann. *Eur. J. Org. Chem.*, **2010**, 6005 (2010)
125. I.S.Young, Y.Qiu, M.J.Smith, M.B.Hay, W.W.Doubleday. *Org. Process Res. Dev.*, **20**, 2108 (2016)
126. L.-Q.Sun, E.Mull, B.Zheng, S.D'Andrea, Q. Zhao, A.X.Wang, N.Sin, B.L.Venables, S.-Y.Sit, Y.Chen, J.Chen, A.Cocuzza, D.M.Bilder, A.Mathur, R.Rampulla, B.-C.Chen, T.Palani, S.Ganesan, P.N.Arunachalam, P.Falk, S.Levine, C.Chen, J.Friborg, F.Yu, D.Hernandez, A.K.Sheaffer, J.O.Knipe, Y.-H.Han, R.Schartman, M.Donoso, K.Mosure, M.W.Sinz, T.Zvyaga, R.Rajamani, K.Kish, J.Tredup, H.E.Klei, Q. Gao, A.Ng, L.Mueller, D.M.Grasela, S.Adams, J.Loy, P.C.Levesque, H.Sun, H.Shi, L.Sun, W.Warner, D.Li, J.Zhu, Y.-K.Wang, H.Fang, M.I.Cockett, N.A.Meanwell, F.McPhee, P.M.Scola. *J. Med. Chem.*, **59**, 8042 (2016)
127. P.D.Boatman, T.O.Schrader, M.Kasem, B.R.Johnson, P.J.Skinner, J.-K.Jung, J.Xu, M.C.Cherrier, P.J.Webb, G.Semple, C.R.Sage, J.Knudsen, R.Chen, A.K.Taggart, E.Carballo-Jane, J.G.Richman. *Bioorg. Med. Chem. Lett.*, **20**, 2797 (2010)
128. P.D.Boatman, B.Lauring, T.O.Schrader, M.Kasem, B.R.Johnson, P.Skinner, J.-K.Jung, J.Xu, M.C.Cherrier, P.J.Webb, G.Semple, C.R.Sage, J.Knudsen, R.Chen, W.-L.Luo, L.Caro, J.Cote, E.Lai, J.Wagner, A.K.Taggart, E.Carballo-Jane, M.Hammond, S.L.Colletti, J.R.Tata, D.T.Connolly, M.G.Waters, J.G.Richman. *J. Med. Chem.*, **55**, 3644 (2012)
129. Y.V.Tomilov, E.V.Guseva, N.V.Volchkov, E.V.Shulishov. *Russ. Chem. Bull.*, **50**, 2113 (2001)
130. F.Cohen, J.B.Aggen, L.D.Andrews, Z.Assar, J.Boggs, T.Choi, P.Dozzo, A.N.Easterday, C.M.Haglund, D.J.Hildebrandt, M.C.Holt, K.Joly, A.Jubb, Z.Kamal, T.R.Kane, A.W.Konradi, K.M.Krause, M.S.Linsell, T.D.Machajewski, O.Miroshnikova, H.E.Moser, V.Nieto, T.Phan, C.Plato, A.W.Serio, J.Seroogy, A.Shakhmin, A.J.Stein, A.D.Sun, S.Sviridov, Z.Wang, K.Wlasichuk, W.Yang, X.Zhou, H.Zhu, R.T.Cirz. *ChemMedChem*, **14**, 1560 (2019)
131. S.Kothandaraman, K.L.Donnely, G.Butora, R.Jiao, A.Pasternak, G.J.Morriello, S.D.Goble, C.Zhou, S.G.Mills, M.MacCoss, P.P.Vicario, J.M.Ayala, J.A.DeMartino, M.Struthers, M.A.Cascieri, L.Yang. *Bioorg. Med. Chem. Lett.*, **19**, 1830 (2009)
132. S.-M.Xu, L.Wei, C.Shen, L.Xiao, H.-Y.Tao, C.-J.Wang. *Nat. Commun.*, **10**, 5553 (2019)

133. G.Wang, J.Deval, J.Hong, N.Dyatkina, M.Prhavc, J.Taylor, A.Fung, Z.Jin, S.K.Stevens, V.Serebryany, J.Liu, Q. Zhang, Y.Tam, S.M.Chanda, D.B.Smith, J.A.Symons, L.M.Blatt, L.Beigelman. *J. Med. Chem.*, **58**, 1862 (2015)
134. Patent US 10364228 (2019)
135. Patent US 10392349 (2019)
136. B.E.Uno, E.P.Gillis, M.D.Burke. *Tetrahedron*, **65**, 3130 (2009)
137. D.Sarkar, S.R.Sahoo. *Synth. Commun.*, **48**, 574 (2018)
138. G.Tang, H.Tian, D.Ma. *Tetrahedron*, **60**, 10547 (2004)
139. D.Dallinger, V.D.Pinho, B.Gutmann, C.O.Kappe. *J. Org. Chem.*, **81**, 5814 (2016)
140. R.Paulissen, A.J.Hubert, P.Teyssie. *Tetrahedron Lett.*, **13**, 1465 (1972)
141. L.G.Tomilova, A.V.Ivanov, I.V.Kostyuchenko, E.V.Shulishov, O.M.Nefedov. *Mendeleev Commun.*, **12**, 149 (2002)
142. C.Möller, W.Bone, A.Cleve, U.Klar, A.Rotgeri, A.Rottmann, M.-H.Schultze-Mosgau, A.Wagenfeld, W.Schwede. *ChemMedChem*, **13**, 2271 (2018)
143. Z.-L.Yao, L.Wang, N.-Q. Shao, Y.-L.Guo, D.-H.Wang. *ACS Catal.*, **9**, 7343 (2019)
144. K.W.Gillman, M.F.Parker, M.Silva, A.P.Degnan, G.O.Tora, N.J.Lodge, Y.-W.Li, S.Lelas, M.Taber, R.G.Krause, R.L.Bertekap, A.E.Newton, R.L.Pieschl, K.D.Lengyel, K.A.Johnson, S.J.Taylor, J.J.Bronson, J.E.Macor. *Bioorg. Med. Chem. Lett.*, **23**, 407 (2013)
145. S.Chackalamannil, Y.Xia, W.J.Greenlee, M.Clasby, D.Doller, H.Tsai, T.Asberom, M.Czarniecki, H.-S.Ahn, G.Boykow, C.Foster, J.Agans-Fantuzzi, M.Bryant, J.Lau, M.Chintala. *J. Med. Chem.*, **48**, 5884 (2005)
146. A.de Meijere, A.F.Khlebnikov, R.R.Kostikov, S.I.Kozhushkov, P.R.Schreiner, A.Wittkopp, D.S.Yufit. *Angew. Chem., Int. Ed.*, **38**, 3474 (1999)
147. Y.V.Tomilov, I.P.Klimenko, E.V.Shulishov, O.M.Nefedov. *Russ. Chem. Bull.*, **49**, 1207 (2000)
148. J.E.Baldwin, D.H.Sakkab. *J. Org. Chem.*, **60**, 2635 (1995)
149. E.B.Averina, K.N.Sedenkova, S.G.Bakhtin, Y.K.Grishin, A.G.Kutateladze, V.A.Roznyatovsky, V.B.Rybakov, G.M.Butov, T.S.Kuznetsova, N.S.Zefirov. *J. Org. Chem.*, **79**, 8163 (2014)
150. O.Ouerfelli, M.Ishida, H.Shinozaki, K.Nakanishi, Y.Ohfune. *Synlett*, **1993**, 409 (1993)
151. X.Liu, Y.Wang, E.Laurini, P.Posocco, H.Chen, F.Ziarelli, A.Janicki, F.Qu, M.Fermeglia, S.Pricl, C.-C.Zhang, L.Peng. *Org. Lett.*, **15**, 4662 (2013)
152. H.C.Shen, F.-X.Ding, S.Raghavan, Q.Deng, S.Luell, M.J.Forrest, E.Carballo-Jane, L.C.Wilsie, M.L.Krsmanovic, A.K.Taggart, K.K.Wu, T.-J.Wu, K.Cheng, N.Ren, T.-Q.Cai, Q.Chen, J.Wang, M.S.Wolff, X.Tong, T.G.Holt, M.G.Waters, M.L.Hammond, J.R.Tata, S.L.Colletti. *J. Med. Chem.*, **53**, 2666 (2010)
153. J.Eacquerra, C.Pedregal, I.Micó, C.Nájera. *Tetrahedron: Asymmetry*, **5**, 921 (1994)
154. J.Zhuo, D.M.Burns, C.Zhang, M.Xu, L.Weng, D.-Q.Qian, C.He, Q.Lin, Y.-L.Li, E.Shi, C.Agrios, B.Metcalf, W.Yao. *Synlett*, **2007**, 0460 (2007)
155. D.D.Staas, K.L.Savage, V.L.Sherman, H.L.Shimp, T.A.Lyle, L.O.Tran, C.M.Wiscount, D.R.McMasters, P.E.J.Sanderson, P.D.Williams, B.J.Lucas, J.A.Krueger, S.Dale Lewis, R.B.White, S.Yu, B.K.Wong, C.J.Kochansky, M.Reza Anari, Y.Yan, J.P.Vacca. *Bioorg. Med. Chem.*, **14**, 6900 (2006)
156. C.M.Moody, D.W.Young. *J. Chem. Soc., Perkin Trans. 1*, 3519 (1997)
157. K.-T.Yip, D.Yang. *Chem. – Asian J.*, **6**, 2166 (2011)
158. X.Wang, F.Meng, Y.Wang, Z.Han, Y.-J.Chen, L.Liu, Z.Wang, K.Ding. *Angew. Chem., Int. Ed.*, **51**, 9276 (2012)
159. S.Fujii, R.Sekine, A.Kano, H.Masuno, C.Songkram, E.Kawachi, T.Hirano, A.Tanatani, H.Kagechika. *Bioorg. Med. Chem.*, **22**, 5891 (2014)
160. J.Pietruszka, G.Solduga. *Eur. J. Org. Chem.*, **2009**, 5998 (2009)
161. J.Pietruszka, A.Witt. *J. Chem. Soc., Perkin Trans. 1*, 4293 (2000)
162. A.M.Davletbakova, I.O.Maidanova, N.Z.Baibulatova, V.A.Dokichev, Y.V.Tomilov, M.S.Yunusov, O.M.Nefedov. *Russ. J. Org. Chem.*, **37**, 608 (2001)
163. G.H.Shen, J.H.Hong. *J. Fluorine Chem.*, **224**, 1 (2019)
164. J.C.Culhane, D.Wang, P.M.Yen, P.A.Cole. *J. Am. Chem. Soc.*, **132**, 3164 (2010)
165. D.Ma, Z.Ma, J.Jian, Z.Yang, C.Zheng. *Tetrahedron: Asymmetry*, **8**, 889 (1997)
166. H.Pajouhesh, K.Curry, H.Pajouhesh, M.H.Meresht, B.Patrick. *Tetrahedron: Asymmetry*, **14**, 593 (2003)
167. Z.Ma, R.F.Clark, A.Brazzale, S.Wang, M.J.Rupp, L.Li, G.Griesgraber, S.Zhang, H.Yong, L.T.Phan, P.A.Nemoto, D.T.W.Chu, J.J.Plattner, X.Zhang, P.Zhong, Z.Cao, A.M.Nilius, V.D.Shortridge, R.Flamm, M.Mitten, J.Meulbroek, P.Ewing, J.Alder, Y.S.Or. *J. Med. Chem.*, **44**, 4137 (2001)
168. S.Ahmad, L.M.Doweyko, S.Dugar, N.Grazier, K.Ngu, S.C.Wu, K.J.Yost, B.-C.Chen, J.Z.Gougoutas, J.D.DiMarco, S.-J.Lan, B.J.Gavin, A.Y.Chen, C.R.Dorso, R.Serafino, M.Kirby, K.S.Atwal. *J. Med. Chem.*, **44**, 3302 (2001)
169. M.Gallant, M.Belley, M.-C.Carrière, A.Chateauneuf, D.Denis, N.Lachance, S.Lamontagne, K.M.Metters, N.Sawyer, D.Slipetz, J.F.Truchon, M.Labelle. *Bioorg. Med. Chem. Lett.*, **13**, 3813 (2003)
170. M.Gallant, N.Chauret, D.Claveau, S.Day, D.Deschênes, D.Dubé, Z.Huang, P.Lacombe, F.Laliberté, J.-F.Lévesque, S.Liu, D.Macdonald, J.Mancini, P.Masson, A.Mastracchio, D.Nicholson, D.A.Nicoll-Griffith, H.Perrier, M.Salem, A.Styhler, R.N.Young, Y.Girard. *Bioorg. Med. Chem. Lett.*, **18**, 1407 (2008)
171. P.L.Minin, J.C.Walton. *Org. Biomol. Chem.*, **2**, 2471 (2004)
172. J.A.Beres, R.D.Crouch Jr. *Org. Prep. Proced. Int.*, **20**, 187 (1988)
173. J.Vallgårda, U.Appelberg, L.-E.Arvidsson, S.Hjorth, B.E.Svensson, U.Hacksell. *J. Med. Chem.*, **39**, 1485 (1996)
174. D.M.Gooden, D.M.Z.Schmidt, J.A.Pollock, A.M.Kabadi, D.G.McCafferty. *Bioorg. Med. Chem. Lett.*, **18**, 3047 (2008)
175. A.B.Charette, M.K.Janes, H.Lebel. *Tetrahedron: Asymmetry*, **14**, 867 (2003)
176. T.-Y.Tsai, T.Hsu, C.-T.Chen, J.-H.Cheng, T.-K.Yeh, X.Chen, C.-Y.Huang, C.-N.Chang, K.-C.Yeh, S.-H.Hsieh, C.-H.Chien, Y.-W.Chang, C.-H.Huang, Y.-W.Huang, C.-L.Huang, S.-H.Wu, M.-H.Wang, C.-T.Lu, Y.-S.Chao, W.-T.Jiaang. *Bioorg. Med. Chem.*, **17**, 2388 (2009)
177. D.Mitra, A.Sengupta, K.Biradha, A.Basak. *Tetrahedron: Asymmetry*, **19**, 2678 (2008)
178. L.-Q.Sun, J.Chen, K.Takaki, G.Johnson, L.Iben, C.D.Mahle, E.Ryan, C.Xu. *Bioorg. Med. Chem. Lett.*, **14**, 1197 (2004)
179. L.-Q.Sun, K.Takaki, J.Chen, L.Iben, J.O.Knipe, L.Pajor, C.D.Mahle, E.Ryan, C.Xu. *Bioorg. Med. Chem. Lett.*, **14**, 5157 (2004)
180. V.M.Tanis, C.Moya, R.S.Jacobs, R.D.Little. *Tetrahedron*, **64**, 10649 (2008)
181. L.Yan, P.Huo, J.J.Hale, S.G.Mills, R.Hajdu, C.A.Keohane, M.J.Rosenbach, J.A.Milligan, G.-J.Shei, G.Chrebet, J.Bergstrom, D.Card, S.M.Mandala. *Bioorg. Med. Chem. Lett.*, **17**, 828 (2007)
182. S.J.Williams, S.C.Zammit, A.J.Cox, D.M.Shackleford, J.Morizzi, Y.Zhang, A.K.Powell, R.E.Gilbert, H.Krum, D.J.Kelly. *Bioorg. Med. Chem. Lett.*, **23**, 6868 (2013)
183. A.Pigott, S.Frescas, J.D.McCorvy, X.-P.Huang, B.L.Roth, D.E.Nichols. *Beilstein J. Org. Chem.*, **8**, 1705 (2012)

184. M.Davi, H.Lebel. *Chem. Commun.*, 4974 (2008)
185. S.E.Denmark, R.A.Stavenger, A.-M.Faucher, J.P.Edwards. *J. Org. Chem.*, **62**, 3375 (1997)
186. O.Bobileva, R.Bokaldere, V.Gailite, I.Kaula, M.Ikaunieks, G.Duburs, R.Petrovska, I.Mandrika, J.Klovins, E.Loza. *Bioorg. Med. Chem.*, **22**, 3654 (2014)
187. I.J.P.De Esch, R.C.Vollinga, K.Goubitz, H.Schenk, U.Appelberg, U.Hacksell, S.Lemstra, O.P.Zuiderveld, M.Hoffmann, R.Leurs, W.M.P.B.Menge, H.Timmerman. *J. Med. Chem.*, **42**, 1115 (1999)
188. S.Vangveravong, A.Kanthasamy, V.L.Lucaites, D.L.Nelson, D.E.Nichols. *J. Med. Chem.*, **41**, 4995 (1998)
189. H.Dalton King, D.J.Denhart, J.A.Deskus, J.L.Ditta, J.R.Epperson, M.A.Higgins, J.E.Kung, L.R.Marcin, C.P.Sloan, G.K.Mattson, T.F.Molski, R.G.Krause, R.L.Bertekap, N.J.Lodge, R.J.Mattson, J.E.Macor. *Bioorg. Med. Chem. Lett.*, **17**, 5647 (2007)
190. R.J.Mattson, J.D.Catt, D.J.Denhart, J.A.Deskus, J.L.Ditta, M.A.Higgins, L.R.Marcin, C.P.Sloan, B.R.Beno, Q.Gao, M.A.Cunningham, G.K.Mattson, T.F.Molski, M.T.Taber, N.J.Lodge. *J. Med. Chem.*, **48**, 6023 (2005)
191. J.P.Hildebrand, S.P.Marsden. *Synlett*, **1996**, 893 (1996)
192. R.Rossi, A.Carpita, A.Ribecai, L.Mannina. *Tetrahedron*, **57**, 2847 (2001)
193. J.E.A.Luithle, J.Pietruszka. *J. Org. Chem.*, **64**, 8287 (1999)
194. J.Pietruszka, A.C.M.Rieche, T.Wilhelm, A.Witt. *Adv. Synth. Catal.*, **345**, 1273 (2003)
195. J.E.A.Luithle, J.Pietruszka, A.Witt. *Chem. Commun.*, 2651 (1998)
196. J.Pietruszka, A.Witt, W.Frey. *Eur. J. Org. Chem.*, **2003**, 3219 (2003)
197. Joachim E.A.Luithle, J.Pietruszka. *Eur. J. Org. Chem.*, **2000**, 2557 (2000)
198. S.-M.Zhou, M.-Z.Deng, L.-J.Xia, M.-H.Tang. *Angew. Chem., Int. Ed.*, **37**, 2845 (1998)
199. G.-H.Fang, Z.-J.Yan, M.-Z.Deng. *Org. Lett.*, **6**, 357 (2004)
200. N.Ty, R.Pontikis, G.G.Chabot, E.Devillers, L.Quentin, S.Bourg, J.-C.Florent. *Bioorg. Med. Chem.*, **21**, 1357 (2013)
201. J.Pietruszka, A.Witt. *Synlett*, **2003**, 0091 (2003)
202. Y.Huang, D.Chen, F.-L.Qing. *Tetrahedron*, **59**, 7879 (2003)
203. E.P.Gillis, M.D.Burke. *J. Am. Chem. Soc.*, **129**, 6716 (2007)
204. R.Fürst, I.Zupkó, Á.Berényi, G.F.Ecker, U.Rinner. *Bioorg. Med. Chem. Lett.*, **19**, 6948 (2009)
205. J.T.Randolph, A.C.Krueger, P.L.Donner, J.K.Pratt, D.Liu, C.E.Motter, T.W.Rockway, M.D.Tufano, R.Wagner, H.B.Lim, J.M.Beyer, R.Mondal, N.S.Panchal, L.Colletti, Y.Liu, G.Koev, W.M.Kati, L.E.Hernandez, D.W.A.Beno, K.L.Longenecker, K.D.Stewart, E.O.Dumas, A.Molla, C.J.Maring. *J. Med. Chem.*, **61**, 1153 (2018)
206. M.Bruncko, W.J.McClellan, M.D.Wendt, D.R.Sauer, A.Geyer, C.R.Dalton, M.A.Kaminski, M.Weitzberg, J.Gong, J.F.Dellaria, R.Mantei, X.Zhao, V.L.Nienaber, K.Stewart, V.Klinghofer, J.Bouska, T.W.Rockway, V.L.Giranda. *Bioorg. Med. Chem. Lett.*, **15**, 93 (2005)
207. A.Thorarensen, B.D.Wakefield, D.L.Romero, K.R.Marotti, M.T.Sweeney, G.E.Zurenko, D.C.Rohrer, F.Han, G.L.Bryant. *Bioorg. Med. Chem. Lett.*, **17**, 2823 (2007)
208. R.C.Schoenfeld, D.L.Bourdet, K.A.Brameld, E.Chin, J.de Vicente, A.Fung, S.F.Harris, E.K.Lee, S.Le Pogam, V.Leveque, J.Li, A.S.T.Lui, I.Najera, S.Rajyaguru, M.Sangi, S.Steiner, F.X.Talamas, J.P.Taygerly, J.Zhao. *J. Med. Chem.*, **56**, 8163 (2013)
209. T.D.Penning, N.S.Chandrakumar, B.B.Chen, H.Y.Chen, B.N.Desai, S.W.Djuric, S.H.Docter, A.F.Gasiecki, R.A.Haack, J.M.Miyashiro, M.A.Russell, S.S.Yu, D.G.Corley, R.C.Durley, B.F.Kilpatrick, B.L.Parnas, L.J.Askonas, J.K.Gierse, E.I.Harding, M.K.Highkin, J.F.Kachur, S.H.Kim, G.G.Krivi, D.Villani-Price, E.Y.Pyla, W.G.Smith, N.S.Ghoreishi-Haack. *J. Med. Chem.*, **43**, 721 (2000)
210. O.Kinzel, C.Steeneck, T.Schlüter, A.Schulz, C.Gege, U.Hahn, E.Hambruch, M.Hornberger, A.Spalwisz, K.Frick, S.Perović-Ottstadt, U.Deuschle, M.Burnet, C.Kremoser. *Bioorg. Med. Chem. Lett.*, **26**, 3746 (2016)
211. N.C.Eichenauer, A.C.M.Nordschild, M.Bischop, D.Schumacher, M.K.W.Mackwitz, R.Tschersich, T.Wilhelm, J.Pietruszka. *Eur. J. Org. Chem.*, **2015**, 5620 (2015)
212. E.B.Averina, E.M.Budynina, Y.K.Grishin, A.N.Zefirov, T.S.Kuznetsova, N.S.Zefirov. *Russ. J. Org. Chem.*, **37**, 1409 (2001)
213. A.Sudau, W.Münch, J.W.Bats, U.Nubbemeyer. *Chem. – Eur. J.*, **7**, 611 (2001)
214. F.D.Özdemirhan, M.Çelik, S.Atli, C.Tanyeli. *Tetrahedron: Asymmetry*, **17**, 287 (2006)
215. C.Rodríguez-García, J.Ibarzo, Á.Álvarez-Larena, V.Branchadell, A.Oliva, R.M.Ortuño. *Tetrahedron*, **57**, 1025 (2001)
216. R.M.Ortuño, J.Ibarzo, A.Alvarez-Larena, J.F.Piniella. *Tetrahedron Lett.*, **37**, 4059 (1996)
217. H.Inagaki, H.Takahashi, M.Takemura. *Bioorg. Med. Chem. Lett.*, **14**, 5193 (2004)
218. R.Nirogi, A.R.Mohammed, A.K.Shinde, S.R.Ravella, N.Bogaraju, R.Subramanian, V.R.Mekala, R.C.Palacharla, N.Muddana, J.B.Thentu, G.Bhyrapuneni, R.Abraham, V.Jasti. *J. Med. Chem.*, **63, 6**, 2833 (2020)
219. A.Gheorghe, M.Schulte, O.Reiser. *J. Org. Chem.*, **71**, 2173 (2006)
220. T.A.Blizzard, F.DiNinno, J.D.Morgan, H.Y.Chen, J.Y.Wu, C.Gude, S.Kim, W.Chan, E.T.Birzin, Y.Tien Yang, L.-Y.Pai, Z.Zhang, E.C.Hayes, C.A.DaSilva, W.Tang, S.P.Rohrer, J.M.Schaeffer, M.L.Hammond. *Bioorg. Med. Chem. Lett.*, **14**, 3861 (2004)
221. R.Risgaard, S.D.Nielsen, K.B.Hansen, C.M.Jensen, B.Nielsen, S.F.Traynelis, R.P.Clausen. *J. Med. Chem.*, **56**, 4071 (2013)
222. I.Duttagupta, K.Goswami, S.Sinha. *Tetrahedron*, **68**, 8347 (2012)
223. R.Chen, L.Li, N.Lin, R.Zhou, Y.Hua, H.Deng, Y.Zhang. *Org. Lett.*, **20**, 1477 (2018)
224. R.A.Novikov, R.R.Rafikov, E.V.Shulishov, L.D.Konyushkin, V.V.Semenov, Y.V.Tomilov. *Russ. Chem. Bull.*, **58**, 327 (2010)
225. E.Torres, M.D.Duque, P.Camps, L.Naesens, T.Calvet, M.Font-Bardia, S.Vázquez. *ChemMedChem*, **5**, 2072 (2010)
226. M.D.Duque, C.Ma, E.Torres, J.Wang, L.Naesens, J.Juárez-Jiménez, P.Camps, F.J.Luque, W.F.DeGrado, R.A.Lamb, L.H.Pinto, S.Vázquez. *J. Med. Chem.*, **54**, 2646 (2011)
227. E.Carlson, W.Tam. *Synthesis*, **48**, 2449 (2016)
228. N.Katagiri, Y.Yamatoya, M.Ishikura. *Tetrahedron Lett.*, **40**, 9069 (1999)
229. Y.Yamatoya, M.Ishikura, N.Katagiri. *Nucleic Acids Symp. Ser.*, **42**, 23 (1999)
230. M.Ishikura, A.Murakami, N.Katagiri. *Heterocycles*, **58**, 317 (2002)
231. R.G.Bhushan, R.Vince. *Bioorg. Med. Chem.*, **10**, 2325 (2002)
232. S.Venkatraman, F.G.Njoroge, W.Wu, V.Girijavallabhan, A.J.Prongay, N.Butkiewicz, J.Pichardo. *Bioorg. Med. Chem. Lett.*, **16**, 1628 (2006)
233. M.McKee, J.Haner, E.Carlson, W.Tam. *Synthesis*, **46**, 1518 (2014)
234. E.Carlson, J.Haner, M.McKee, W.Tam. *Org. Lett.*, **16**, 1776 (2014)
235. E.Carlson, G.Duret, N.Blanchard, W.Tam. *Synth. Commun.*, **46**, 55 (2016)
236. E.Carlson, R.Boutin, W.Tam. *Tetrahedron*, **74**, 5510 (2018)
237. M.A.Emerzian, W.Davenport, J.Song, J.Li, I.Erden. *Adv. Synth. Catal.*, **351**, 999 (2009)
238. C.Ji, M.J.Miller. *Tetrahedron Lett.*, **51**, 3789 (2010)

239. Y.Xia, S.Chackalamannil, W.J.Greenlee, C.Jayne, B.Neustadt, A.Stamford, H.Vaccaro, X.Xu, H.Baker, K.O'Neill, M.Woods, B.Hawes, T.Kowalski. *Bioorg. Med. Chem. Lett.*, **21**, 3290 (2011)
240. T.P.O'Sullivan, H.Zhang, L.N.Mander. *Org. Biomol. Chem.*, **5**, 2627 (2007)
241. J.Vallgårda, U.Appelberg, I.Csöregh, U.Hacksell. *J. Chem. Soc., Perkin Trans. 1*, 461 (1994)
242. L.-Q.Sun, K.Takaki, J.Chen, S.Bertenshaw, L.Iben, C.D.Mahle, E.Ryan, D.Wu, Q.Gao, C.Xu. *Bioorg. Med. Chem. Lett.*, **15**, 1345 (2005)
243. B.Springthorpe, A.Bailey, P.Barton, T.N.Birkinshaw, R.V.Bonnert, R.C.Brown, D.Chapman, J.Dixon, S.D.Guile, R.G.Humphries, S.F.Hunt, F.Ince, A.H.Ingall, I.P.Kirk, P.D.Leeson, P.Leff, R.J.Lewis, B.P.Martin, D.F.McGinnity, M.P.Mortimore, S.W.Paine, G.Pairaudeau, A.Patel, A.J.Rigby, R.J.Riley, B.J.Teobald, W.Tomlinson, P.J.H.Webborn, P.A.Willis. *Bioorg. Med. Chem. Lett.*, **17**, 6013 (2007)
244. J.Chen, B.Levant, C.Jiang, T.M.Keck, A.H.Newman, S.Wang. *J. Med. Chem.*, **57**, 4962 (2014)
245. K.Tuhina, D.R.Bhowmik, R.V.Venkateswaran. *Chem. Commun.*, 634 (2002)
246. A.Roy, K.Tuhina, B.Biswas, R.V.Venkateswaran. *Tetrahedron*, **68**, 6575 (2012)
247. D.Guay, C.Beaulieu, T.J.Reddy, R.Zamboni, N.Methot, J.Rubin, D.Ethier, M.D.Percival. *Bioorg. Med. Chem. Lett.*, **19**, 5392 (2009)
248. M.J.Meyers, S.A.Long, M.J.Pelc, J.L.Wang, S.J.Bowen, M.C.Walker, B.A.Schweitzer, H.M.Madsen, R.E.Tenbrink, J.McDonald, S.E.Smith, S.Foltin, D.Beidler, A.Thorarensen. *Bioorg. Med. Chem. Lett.*, **21**, 6538 (2011)
249. M.Dubs, H.Dieks, W.Günther, M.Kötteritzsch, W.Poppitz, B.Schönecker. *Tetrahedron Lett.*, **43**, 2499 (2002)
250. N.S.Zefirov, T.S.Kuznetsova, O.V.Eremenko, O.V.Kokoreva, G.Zatonsky, B.I.Ugrak. *J. Org. Chem.*, **59**, 4087 (1994)
251. T.S.Kuznetsova, O.V.Eremenko, O.V.Kokoreva, G.V.Zatonsky, N.S.Zefiov. *Russ. Chem. Bull.*, **45**, 1662 (1996)
252. K.A.Lukin, T.S.Kuznetsova, S.I.Kozhushkov, V.A.Piven', N.S.Zefiov. *Zh. Org. Khim.*, **24**, 1644 (1988)
253. T.S.Kuznetsova, E.B.Averina, O.V.Kokoreva, A.N.Zefirov, Y.K.Grishin, N.S.Zefirov. *Russ. J. Org. Chem.*, **36**, 205 (2000)
254. P.F.Carneiro, S.B.do Nascimento, A.V.Pinto, M.d.C.F.R.Pinto, G.C.Lechuga, D.O.Santos, H.M.dos Santos Jr., J.A.L.C.Resende, S.C.Bourguignon, V.F.Ferreira. *Bioorg. Med. Chem.*, **20**, 4995 (2012)
255. M.Incze, G.Dörnyei, I.Moldvai, E.Temesvári-Major, O.Egyed, C.Szántay. *Tetrahedron*, **64**, 2924 (2008)
256. R.Gleiter. *Angew. Chem.*, **104**, 29 (1992)
257. N.F.O'Rourke, K.A.Davies, J.E.Wulff. *J. Org. Chem.*, **77**, 8634 (2012)
258. E.V.Guseva, N.V.Volchkov, Y.V.Tomilov, O.M.Nefedov. *Eur. J. Org. Chem.*, **2004**, 3136 (2004)
259. I.E.Markó, T.Giard, S.Sumida, A.-E.Gies. *Tetrahedron Lett.*, **43**, 2317 (2002)
260. L.Wei, Q.Zhu, Z.-M.Song, K.Liu, C.-J.Wang. *Chem. Commun.*, **54**, 2506 (2018)
261. W.Frey, T.Hausmann, J.Pietruszka. *Z. Kristallogr. – New Cryst. Struct.*, **226**, 595 (2011)
262. T.Hausmann, J.Pietruszka. *Synlett*, **2009**, 3271 (2009)
263. K.Biswas, H.Lin, J.T.Njardarson, M.D.Chappell, T.-C.Chou, Y.Guan, W.P.Tong, L.He, S.B.Horwitz, S.J.Danishefsky. *J. Am. Chem. Soc.*, **124**, 9825 (2002)
264. P.Eilbracht, C.Hollmann, A.M.Schmidt, L.Bärfacker. *Eur. J. Org. Chem.*, **2000**, 1131 (2000)
265. V.G.Kasradze, O.S.Kukovinets, E.V.Salimova, I.I.Gilyazetdinova, M.D.Khanova, A.N.Lobov, F.Z.Galin. *Russ. J. Org. Chem.*, **45**, 1002 (2009)
266. L.G.Menchikov, O.M.Nefedov. *Russ. Chem. Rev.*, **63**, 449 (1994)
267. L.G.Menchikov, O.M.Nefedov. *Russ. Chem. Rev.*, **85**, 205 (2016)
268. L.G.Menchikov, O.M.Nefedov, I.G.Zenkevich. *Russ. Chem. Bull.*, **66**, 491 (2017)
269. M.Belley, M.Gallant, B.Roy, K.Houde, N.Lachance, M.Labelle, L.A.Trimble, N.Chauret, C.Li, N.Sawyer, N.Tremblay, S.Lamontagne, M.-C.Carrière, D.Denis, G.M.Greig, D.Slipetz, K.M.Metters, R.Gordon, C.C.Chan, R.J.Zamboni. *Bioorg. Med. Chem. Lett.*, **15**, 527 (2005)
270. P.Vinš, A.de Cózar, I.Rivilla, K.Nováková, R.Zangi, J.Cvačka, I.Arrastia, A.Arrieta, P.Drašar, J.I.Miranda, F.P.Cossío. *Tetrahedron*, **72**, 1120 (2016)
271. O.M.Nefedov, I.E.Dolgii, Y.V.Tomilov, V.G.Bordakov. *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, **33**, 103 (1984)
272. I.E.Dolgii, K.N.Shavrin, O.M.Nefedov. *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, **36**, 119 (1987)
273. O.M.Nefedov, A.I.Ioffe, L.G.Menchikov. *Khimiya Karbenov*. (The Chemistry of Carbenes). (Moscow: Khimiya, 1990)
274. A.de Meijere, A.F.Khlebnikov, S.I.Kozhushkov, D.S.Yufit, O.V.Chetina, J.A.K.Howard, T.Kurahashi, K.Miyazawa, D.Frank, P.R.Schreiner, B.C.Rinderspacher, M.Fujisawa, C.Yamamoto, Y.Okamoto. *Chem. – Eur. J.*, **12**, 5697 (2006)
275. H.Quast, J.W.Stawitz, B.Mueller. *Heterocycles*, **85**, 2449 (2012)
276. E.E.Schultz, M.M.Shakirov, I.Y.Bagryanskaya, Y.V.Gatilov, G.A.Tolstikov, V.N.Kalinin, H.Schmidhammer. *Russ. J. Org. Chem.*, **39**, 1083 (2003)
277. S.Z.Sultanov, V.A.Dokichev, E.E.Shults, U.M.Dzhemilev, G.A.Tolstikov, O.M.Nefedov. *Russ. Chem. Bull.*, **43**, 509 (1994)
278. A.Arnone, L.Merlini, G.Nasini, O.Vajna de Pava, F.Zunino. *J. Chem. Soc., Perkin Trans. 1*, 610 (2001)
279. D.Wullbrandt, H.Hopf, P.G.Jones. *Eur. J. Org. Chem.*, **2010** 4046 (2010)
280. S.Boverie, F.Simal, A.Demonceau, A.F.Noels, I.L.Eremenko, A.A.Sidorov, S.E.Nefedov. *Tetrahedron Lett.*, **38**, 7543 (1997)
281. R.Bertani, M.Biasiolo, K.Darini, R.A.Michelin, M.Mozzon, F.Visentin, L.Zanotto. *J. Organomet. Chem.*, **642**, 32 (2002)