Synthetic Applications of Vinyl Cyclopropane Opening

Marta Meazza, Hao Guo and Ramon Rios

Vinyl cyclopropanes are amongst the most useful building blocks in organic synthesis. Their easy opening and capacity to generate dipoles have been exploited for the synthesis of cyclopentanes with good yields and sometimes excellent stereoselectivities. In this review we give an overview of their applications, focusing on the present century.

1 Introduction

Vinyl cyclopropanes have attracted much attention due to their versatility and chemical utility. Vinyl cyclopropanes are well known to undergo rearrangement reactions, as donor acceptor cyclopropanes, leading to the synthesis of cyclopentenes, and opening reactions to generate a dipole that can be used in a range of cycloaddition reactions. The first rearrangement of vinyl cyclopropanes was developed by Norman P. Neureiter when he was a research chemist at Humble Oil and Refining. Pyrolysis of 1,1-dichloro-2-vinylcyclopropane rendered 1,1-dichlorocyclopent-3-ene and 2-chlorocyclopentane. This was the start of a huge interest of the organic chemistry community in this scaffold. One year later Vogel, Overberger and Borchert independently reported the thermal rearrangement of vinyl cyclopropanes to obtain cyclopentenes. This last reaction was studied by Flowers, Frey and Wellington some years later.

The interest of this type of rearrangement is clearly based on the possibility to synthesize 5-membered rings. Opposite to their brother cyclohexanes, few synthetic methods were reported. Moreover, the interest for the synthesis of triquinane terpenes which contain this scaffold, made vinyl cyclopropanes a common subject of study and a creative platform for the development of new methodologies leading to cyclopentanes and other carbocycles.

Moreover, the metal catalyzed ring opening of vinyl cyclopropanes has attracted attention thanks to the possibility to use the generated dipoles in several cycloaddition reactions.

In this review, we aim to cover the last methodologies reported in the opening of vinyl cyclopropanes with special focus in the last ten years.

2 Vinyl cyclopropane rearrangements

Despite not being the main focus of this review, vinyl cyclopropane rearrangements have a huge importance in the development of cycloaddition reactions. As stated in the introduction, the rearrangement of vinyl cyclopropanes led to the synthesis of cyclopentanes. Opposite to 6-membered carbocycles that can be easily accessed by Diels Alder or by hydrogenation of benzene rings, 5-membered all carbon rings are difficult to synthesize. The normal [3+2] cyclization requires the use of dipoles that contain at least 1 heteroatom, leading to the synthesis of pyrroles or furanes. For these reasons vinyl cyclopropanes have become one of the most popular starting materials for the synthesis of cyclopentanes.

Probably, one of the earliest examples of the use of vinyl cyclopropanes in total synthesis leading to the formation of cyclopentanes was reported by E. J. Corey in 1975. In their approach to the synthesis of prostenoids, they reported a
thermolysis of vinyl cyclopropane 5 to generate the bicyclic ketone 6 (Scheme 3).

Despite the potentiality of this preliminary report, organic chemists did not study the opening of vinyl cyclopropanes with Pd to generate dipoles until long time after. A synthetic application of vinyl cyclopropanes was reported by Danishefsky in 1972. Vinyl cyclopropane 16 reacts with diethyl malonate sodium salt 17 leading, after quenching, to a two component mixture (5:1, 18:19) of the primary products of the homoconjugate addition (Scheme 7).

Several other groups reported radical openings of vinyl cyclopropanes. Should be highlighted the [3+2] cycloaddition, reported by Feldman, between vinyl cyclopropanes and alkenes using phenyldisulfide, AIBN and trimethylaluminum as catalysts. Burgess reported the opening of vinyl cyclopropanes bearing two electron-withdrawing groups 20, using Pd(0) III as catalyst. Malonates, ketosulfones or disulfones 17 were used as nucleophiles obtaining a mixture of monomer and dimer 21 as products with good yields (Scheme 8).

In 1993, Suzuki and coworkers reported a ring opening polymerization of vinyl cyclopropanes using Pd(0) as catalyst. The vinyl cyclopropane was decorated with two electron-withdrawing substituents 16, showing clearly the formation of the dipole, which then polymerizes 23. The key intermediate is the π-allylpalladium complex 22, which is generated by oxidative addition of Pd(0) to the monomer (Scheme 9).

Some years later, Barrett and coworkers proposed the regioselective ring opening of vinyl cyclopropanes by hydrogenation with Palladium on activated carbon. The reaction follows a similar mechanism of the previous ones. At first coordination of the double bond to palladium 25, followed by insertion into the less hindered bond of the cyclopropane, leads to the formation of the palladacyclobutane 26. Next, the addition of H2 to the palladium 27 and the reductive cleavage of the palladacycle, renders 28 that, after hydrogenation of the double bond, gives the observed product 30 (Scheme 10).

3 Vinyl cyclopropane cycloadditions

3.1 Pd catalyzed reactions

The opening of vinyl cyclopropanes to form dipoles was initially studied by Oda and coworkers in the formation of π-allylic palladium complexes from vinyl cyclopropane derivatives. In this work Oda shows that vinyl cyclopropanes 13 can be easily opened by Pd(II) II, forming allylic Pd complexes and adding a chloro atom at the same time (Scheme 6). The importance of this work relies on the fact that, for the first time, it is clearly showed the potential of vinyl cyclopropanes as synthetic precursors of dipoles.
In 2004, Maffei and coworkers reported an interesting Pd catalyzed vinyl cyclopropane opening with amines. In this work vinyl cyclopropanes, decorated with bisphosphonate unit, reacted with several amines rendering the final compounds in excellent yields (Scheme 11).

Scheme 11

Szabó and coworkers reported a vinyl cyclopropane opening using Pd pincer complexes. The vinyl cyclopropanes react with tetrahydroxydiboron to form trifluoroboron compound (after treatment with KHF$_2$) in excellent yields and regioselectivities (Scheme 12). Soon after, they combined this reaction with a coupling of the corresponding boron compounds with iodobenzenes with excellent results.

Scheme 12

Johnson and coworkers, following their rearrangements with Ni(0), reported a [3+2] cycloaddition, between vinyl cyclopropanes and aldehydes. This reaction is catalyzed by Pd(0) complexes VI to afford tetrahydrofuran derivatives in excellent yields and diastereoselectivities. As shown in Scheme 13, the reaction consists on the formation of π-allyl palladium zwitterion that reacts with the aldehyde in an aldol type mechanism, followed by the intramolecular ring closure between the alcoxide and the allyl palladium complex. A similar reaction was reported by Shi, Xu and Wei where the vinyl cyclopropanes react with isatins. The use of chiral imidazoline-phosphine ligands is crucial to get excellent yields and enantioselectivities.

Scheme 13

An enantioselective palladium catalyzed [3+2] cycloaddition of vinyl cyclopropanes with β,γ-unsaturated α-keto esters was reported by Shi in 2012. In this reaction, Pd(0) complexes VI reacted with the vinyl cyclopropanes, forming the zwitterion that reacts with the unsaturated ketoester to form the corresponding cyclopentane. Chiral imidazoline-phosphines were used as ligands, achieving the final products with good yields and stereoselectivities (Scheme 15).

Scheme 15

Years later, Shi reported a novel cycloaddition between vinyl cyclopropanes and diazo oxindoles. The reaction was efficiently catalyzed by Pd(0) complexes, using chiral imidazoline-phosphines as ligand. The reaction afforded the corresponding oxindole-fused spiropyrazoline in good yields and enantioselectivities. Moreover, they designed a one-pot
cascade reaction adding maleimides. The maleimide reacts with the recent formed dipole to furnish the final multicyclic products, bearing 4 stereocenters, in good yields and stereoselectivities. Later on, the same research group reported a similar reaction using with 2-vinyl-spiroindanones. Again, chiral imidazole-phosphines were the best ligands, achieving the spiro indane derivatives in excellent yields but only moderate enantioselectivities.

A three component coupling between terminal alkynes 50, arynes 52 and vinyl cyclopropanes 16 was reported by Werz in 2015. Initially copper acetylide 51 is generated by deprotonation of the terminal alkyne 50, then it undergoes a nucleophilic attack to the benzene 52, which was generated “in situ” by treatment of 53 with KF, affording the highly nucleophilic intermediate 49. Simultaneously, the vinyl cyclopropane 16 reacts with Pd(0) VI to form the zwitterionic π-allyl palladium complex 35. The allyl complex reacts with the nucleophilic intermediate 49 by the less hindered carbon, forming the desired product 48 and releasing the Pd(0) catalyst VI. The reaction gave the final alkynes products in good yields (Scheme 16).

In 2015 two different groups reported the reaction between vinyl cyclopropanes and nitrostyrenes. In the first paper, vinyl cyclopropanes derived from malonates or malononitriles, react with nitrostyrenes, catalyzed by Pd2(dba)3 using chiral diphosphine ligands. The resulting nitrocyclopentanes were obtained in good yields and enantioselectivities, albeit with low diastereoselectivities. In the second paper, vinyl cyclopropanes derived from 1,3-indanone 16 react with nitrostyrene 60, catalyzed by Pd2(dba)3 VI, using diamine ligands. This time the nitrocyclopentanes 61 were obtained in good yields and stereoselectivities (Scheme 18).

Trost and coworkers reported a formal [3+2] cycloaddition between benzylidene azalactones 54 and racemic vinyl cyclopropanes 16. The reaction was catalyzed by Pd2dba3 VI, using chiral phosphine ligands 58 to induce enantioselectivity. Interestingly, a key aspect to obtain reactivity was the type of substituents in the malonate moiety of the vinyl cyclopropane 16. The authors proposed that the use of trifluoroethylester increases the half-life of the intermediate dipole formed, without losing reactivity. The reaction rendered the spiro azalactone derivatives 55 with good yields and excellent stereoselectivities (Scheme 17, top).

Later, the same research group expanded the scope of the reaction using alkylidene meldrum’s acid 56 DPPBA biphosphine ligands 59 were used, achieving the final spiro cyclopanes 57 in good yields and excellent stereoselectivities (Scheme 17, bottom).

A palladium catalyzed cycloaddition of vinyl cyclopropanes with “in situ” formed imines was reported by Liu in 2015. In this paper arenesulfonyl indoles react with the zwitterion 35 formed by the ring opening of the vinyl cyclopropane 16 by Pd VI, forming the conjugate imine 65. Next, conjugate addition of malonate 66 and subsequent palladium catalyzed allylation, afforded the spiroindolines 68 in good yields and stereoselectivities, using phosphoramidites as ligands (Scheme 19).
A similar reaction was reported by Li and Guo regarding the synthesis of carbocyclic nucleosides. Acrylate derivative 69 reacts with vinyl cyclopropanes 16 under Pd(0) catalysis, using Trost ligand 58 as catalyst. The reaction affords the chiral carbocyclic nucleoside analogues 70, 71 in good yields and moderate to good enantioselectivities (Scheme 20).

A new palladium catalyzed vinyl cyclopropane opening was reported by Hyland in 2015. In this example, vinyl cyclopropanes 16 react with boronic acids 72 in water under Pd(II) catalysis without the need of ligands. In the proposed reaction mechanism, the authors claim that first Pd(II) reacts with the boronic acid 72 to generate Pd(0) nanoparticles. Oxidative addition of the vinyl cyclopropane 16 to the "in situ" generated Pd(0), followed by transmetallation with the boronic acid and reductive elimination, generates the final compounds 78 and 77 in good yields, regio and diastereoselectivities, using mild reaction conditions (Scheme 21).

In 2016 Michelet, Jørgensen and Rios reported, almost at the same time, the formal [3+2] cycloaddition between vinyl cyclopropanes 16 and enals 79. The vinyl cyclopropanes 16 are opened by Pd(0), while the enal 79 is activated by the secondary amine catalyst VIII in a synergistic fashion. The final cyclopentanes 80 and 81, bearing three new stereocenters, were obtained in excellent stereoselectivities (Scheme 22).

Rios and Jørgensen also expanded the scope of this reaction, obtaining the final cyclopentanes 85 and 86 with four new stereocenters while maintaining the excellent control of the stereoselectivity (Scheme 23).
3.2 Rh catalyzed reactions

Wender and coworkers demonstrated the utility of vinyl cyclopropanes by developing an intramolecular [5+2] cycloaddition with alkenes.39,41 The cycloaddition was efficiently catalyzed by Rh(I) X salts in combination of Ag(I) IX affording the cis fused bicycles 88 in good yields (Scheme 24).

In 1999 they reported that, with a careful choice of the substituents in the cyclopropyl moiety and/or through catalyst modifications, an excellent control over the regiochemical outcome of the reaction can be achieved. Concretely, the configuration of the cyclopropyl substituents (cis/trans) determines the final configuration of the cycloheptanes.42 One year later, the same group expanded this concept to intermolecular reactions.43 This time vinyl cyclopropane 89 reacted with alkenes 90 to furnish cycloheptenones 91 in excellent yields. The reaction is catalyzed by Rh(I) salts XI as it is shown in Scheme 25.

Working further on this concept, Wender developed a multicomponent version of this last reaction.44,45 The Rh catalyzed XI reaction between alkenes 90, vinyl cyclopropanes 89 and CO, through an overall [5+2+1] cycloaddition, rendered the final bicyclic octone derivatives 92 in excellent yields (Scheme 26). Years later the same group expanded the scope of the reaction based on computational calculations.46

Wender also developed a closely related reaction consisting in the [5+2] intramolecular cycloaddition between vinyl cyclopropanes and alkenes 93, catalyzed by rhodium X.47,48 The reaction favors the formation of fused rings with a cis fused configuration 94. Importantly, when chiral alkenes are used, the asymmetric information is preserved in the course of the cycloaddition (Scheme 27).

The same year, Wender and coworkers reported the use of this cycloaddition as a key step for the total synthesis of (+)-Dictamnol49 and (+)-Aphanamol.50 Moreover, in 2003 they developed the same reaction but using water as the solvent.51 In 2001, Wender and coworkers reported the first intramolecular [5+2] cycloaddition of vinyl cyclopropanes with alkenes.52-54 For the first time, unactivated vinyl cyclopropanes 95 reacted intermolecularly with alkenes 96 using Rh complexes XI as catalysts. The substitution at the position 1 of the vinyl cyclopropane resulted to be the key to accelerate the reaction, correlating the steric bulkiness of the substrates with the degree of rate enhancement. As it is shown in Scheme 28, good to moderate yields were obtained and with high degree of selectivity when terminal alkenes were used.

Years later, Wender described the first enantioselective [5+2] intramolecular cycloaddition between vinyl cyclopropanes and alkenes.55,56 Chiral diphosphines (BINAP derivatives) were used as Rh ligands affording the final compounds in excellent yields and enantioselectivities. Later on, the same group expanded the scope developing a cascade reaction consisting in an intermolecular [5+2] cycloaddition, followed by a Nazarov cyclization.57,58 Vinyl cyclopropanes 89 reacted with enynes 98 furnishing, in the first instance, a diene that renders, through a Nazarov cyclization, the bicyclic product 99. The [5+2]...
cycloaddition reaction is catalyzed by Rh(I) catalysts XI, while the Nazarov reaction is catalyzed by Ag(I) XII, affording the final bicyclic products 99 in good yields and moderate to excellent diastereoselectivities (Scheme 29).

![Scheme 29]

In 2009, Shintani and Hayashi reported an intramolecular enantioselective [5+2] cycloaddition between alkynyl and vinyl cyclopropane 100, catalyzed by Rh(I) XIII complexes. The use of phosphoramidites 101 as ligands rendered the cycloaddition adducts 102 in excellent yields and enantioselectivities (Scheme 30).

![Scheme 30]

Later, Yu and coworkers reported a similar intramolecular [3+2] cycloaddition between vinyl cyclopropanes and alkenes 100 catalyzed by Rh(I) salts XII, with excellent results. The same group also expanded the reaction by using CO. They reported a homologous Pauson-Khand reaction, based on a Rh(I) XII catalyzed [3+2+1] cycloaddition. As it is shown in Scheme 31, the reaction renders the final products 103 in excellent yields and regioselectivities. Moreover, they demonstrated the value of this methodology by using it as a key step for the synthesis of α-Agarofuran 104. Later on they reported a similar strategy for the formal synthesis of Gracilamine.

![Scheme 31]

Chung and coworkers developed a Rh catalyzed intramolecular [5+2] cycloadditions with vinyl cyclopropanes. NHC carbenes were used as ligands for the first time in this type of reactions. The reactions are extremely fast (10 min) and render the final products in excellent yields (91-98%).

Yu and coworkers described a formal [5+1]/[2+2+1] of 1-yne-vinylcyclopropanes 105 catalyzed by Rh(I) XI. This methodology allows the construction of multifunctional angular tricyclic 5/5/6 scaffolds 113 in a single step. The authors proposed the following mechanism: 1-yne-vinyl cyclopropane 105 and Rh XI generate the intermediate 106 by complexation, cyclopropane cleavage and alkynyl insertion. Migratory insertion of CO into the Rh-C bond 107 and addition of CO render intermediate 108. Next, insertion of the alkene into the Rh-COR bond takes place, forming a tricyclic intermediate 110. This, after another CO insertion 111 and reductive elimination 112, affords the final tricyclic products 113 in good yields (Scheme 32).

![Scheme 32]

A Rh(I) catalyzed [5+1] cycloaddition of vinyl cyclopropanes was reported by Yu. Vinyl cyclopropanes 8 reacted with CO to furnish cyclohexenones in good yields. Careful choice of the Rh catalysts and the reaction conditions, led to the selective formation of α,β-unsaturated cyclohexenones 115 (when [Rh(dppp)]SbF$_6$ XV was used as catalyst and the product was then treated with DBU, Scheme 33 bottom) or to the formation of the β,γ-cyclohexenone 114 as major isomer (when [Rh(dppp)]OTf XIV was used, Scheme 33 top). In 2016 the same research group reported a similar reaction using Fe$_2$(CO)$_3$ as mediator for the synthesis of cyclohexenones.

![Scheme 33]
3.3 Other metals catalyzed reactions

Trost and coworkers reported a similar intramolecular [5+2] cycloaddition between vinyl cyclopropanes and alkynes 100, this time catalyzed by cationic Ruthenium catalysts XVI.69,70 The main characteristics are the mild conditions required (rt, acetone), the excellent chemoselectivity and the high group tolerance. As before, the regioselectivity can be controlled by the choice of substituents and the reaction furnished the products 118 and 119 with complete diastereoselectivity (Scheme 35).

Oshima in 2008, developed a ring opening of vinyl cyclopropanes 16 catalyzed by Ni(0) I with bis(pinacolato)diboron 128 to yield allylic boronates 131.72 The mechanism of the reaction (Scheme 37) is based on the activation of the cyclopropane 16 by the boron compound 128, followed by an oxidative addition of the nickel complex to afford the \( \pi \)-alkyl(oxa-\( \pi \)-allyl)nickel intermediate 129. Transmetalation and reductive elimination provide the final allyl boronate compounds 131 in good yields.

Suginome reported the silylaboration of vinyl cyclopropanes 120 catalyzed by nickel XVII.71 The reaction consists in the cleavage of the vinyl cyclopropane, resulting in the highly regio- and stereoselective formation of 2-borylalkyl-allylsilanes 123. The proposed mechanism consists in the formation of a (silyl)borylNi(II) intermediate 128 via an oxidative addition of Ni to silanoborane. Next, coordination of the Ni complex to the vinyl cyclopropane 120, followed by migratory B-C insertion with cleavage of the C-C bond, renders the allyl nickel species 122. Reductive elimination of the Si-C bond proceeds at the allylic carbon cis group, leading to the high regioselectivity of the final products 123 (Scheme 36).

A nickel catalyzed reaction with vinyl cyclopropanes was reported by Kimura.73 Vinyl cyclopropanes 16 reacted with alkynes 90 and alkyl zinc 132 to generate the final addition products 130 in good yields and stereoselectivities. The reaction starts with the formation of the nickelocene 131 by ring cleavage of the vinyl cyclopropane 16. Next, ZnMe2 132 addition and alkyne insertion in the terminal position of the allyl, lead exclusively to the (E)-vinyl-nickel 133, that undergoes reductive elimination to form the trans-alkene 130 (Scheme 38).
A nickel catalyzed reaction with vinyl cyclopropanes was reported by Louie in 2005. In this paper vinyl cyclopropanes react intramolecularly with the triple bond to form, depending on the nature of the NHC ligand, the 5+2 cycloadduct or the cyclopentane product. Remarkably, when bulkier NHC ligands were used, the major product was the cyclopentane product. The authors propose that a common intermediate is formed in the reaction and, depending on the size of the NHC ligand, reductive elimination or β-hydride elimination take place, to afford the respective final products in good yields (Scheme 39).

Years later, Houk and coworkers studied the reaction performing DFT calculations. Another reaction catalyzed by Ni(cod)_2 was reported by Matsubara and Kurahashi. Vinyl cyclopropanes react with imines in a [3+2]-cycloaddition, to furnish highly substituted pyrrolidines in good to moderate yields and good to excellent diastereoselectivities. The authors explored the use of chiral phosphines to develop an asymmetric version with moderate enantioselectivities.

Another interesting reaction, catalyzed by iron, was reported by Plietker. The combination of the NHC ligand and electron rich ferrate TBAFe is a powerful electron-transfer catalyst that reacts with vinyl cyclopropanes to form allylic substituted products or undergoes a [3+2] cycloaddition depending on the starting materials. The addition of pronucleophiles like cyano ketones, azalactones or cyanoesters took place on the terminal position with excellent control of the diastereoselectivity and very good yields. On the other hand, when the same vinyl cyclopropanes reacted with Michael acceptors, the 5 member rings were furnished in excellent yields, albeit with very low diastereoselectivities.

Krishe and Johnson reported an umpolung reaction with vinyl cyclopropanes. In this work, after the cleavage by the Ir catalyst, nucleophilic iron complexes are used, rendering the final pyrrolidines in good yields albeit in very low diastereoselectivities (Scheme 40).
catalyst, the nucleophilic allymetal species reacted with aldehydes in an enantioselective fashion. Moreover, they coupled this vinyl cyclopropane 16 ring opening with an iridium XXII catalyzed oxidation of alcohols 149 to form the aldehyde “in situ”. The products 150 were obtained in good yields and diastereoselectivities and excellent enantioselectivities (Scheme 44).

![Scheme 44](image)

An intermolecular [5+2] cycloaddition between vinyl cyclopropanes and alkenes, catalyzed by Ir(I) complexes, was reported by Strand in 2015.83 In a fashion similar to the previously reported ones, Ir catalyzes the [5+2] intermolecular cycloaddition and the reaction renders the cycloheptene derivatives in excellent yields. The main advantage to use Ir instead of Rh is the lower cost of the catalyst and the fact that Ir shows catalytic rates 50 times higher.

In 2015 Wang and Huang reported a Rh(III) catalyzed C-H/C-C sequence between aryl rings 151 and vinyl cyclopropanes 16.84 In this reaction Rh XXIII has a dual function: first it activates the aryl group by coordination with a directing group, second it coordinates the vinyl cyclopropane 16, followed by the alkene insertion and β-carbon elimination to cleave the C-C bond of the cyclopropane. The corresponding compounds 152 were obtained in good yields and diastereoselectivities (Scheme 45).

![Scheme 45](image)

Shibata reported a transition metal free coupling reaction of vinyl cyclopropanes 16 with aldehydes 153, catalyzed by tin hydride XXIV.85 The proposed mechanism consists first in the addition of the tin radical to the vinyl cyclopropane 16, to form an intermediate radical which undergoes ring opening and reacts with tin hydride. Next, the organotin reacts with an aldehyde 153 in an aldol fashion to generate alcohol 154 in good yields and moderate to excellent diastereoselectivities (Scheme 46).

![Scheme 46](image)

3.4 Metal-free reactions

A metal free ring opening/cyclization of vinyl cyclopropanes, catalyzed by bromine, was reported by Chandrasekaran.86,87 Vinyl cyclopropanes 155 reacted with Chloramine-T 162 in the presence of a catalytic amount of PTAB 163, affording bicyclic amidines 164. The vinyl cyclopropane 155 undergoes a Ritter-type reaction. First, bromine reacts with the alkene forming the bromonium ion 156, followed by opening of the cyclopropane ring to form the more stable cation 157. Addition of acetonitrile 158 forms the intermediate 159, that reacts with Chloramine-T to form 160. Intramolecular addition of the tosyl amine, through a S$_2$2, renders the final product 164 and regenerates the bromine. Remarkably, the reaction occurs with retention of the configuration of the cyclopropane in excellent yields.

![Scheme 47](image)

An organocatalytic enantioselective ring opening of vinyl cyclopropanes was reported by Maruoka in 2014.88 The reaction consists in an enantioselective radical [3+2] cycloaddition between vinyl cyclopropanes 16 and vinyl ethers 166, catalyzed by thiy radicals 169 derived from binol. The reaction proceeds via addition of the thiy radical to the vinyl cyclopropane, forming radical 165 by ring opening of the cyclopropane. Next, the radical reacts with the vinyl ether to form intermediate 167, that undergoes intramolecular ring closing to form the cyclopentene adduct 168 and regenerate the thiy radical (Scheme 48). After an impressing catalyst optimization, the products were obtained in good to excellent and excellent diastereoselectivities.
Conclusions

Vinyl cyclopropanes have been a useful building block for the development of new synthetic methodologies. The possibility to easily generate dipoles makes these substrates appealing for the development of [3+2] or higher order cycloadditions. In this review we summarized the most recent developments in the field. Organometallic approaches, racemic and enantioselective, have been reported with excellent results. Very recently, synergistic approaches based on the use of organometallic complexes and secondary amine catalysis have proved to be excellent platform to obtain chiral cyclopentanes. In the future, we expect a huge increase of new enantioselective methodologies for the opening of vinyl cyclopropanes. Probably in the next years we will see an explosion of new cycloaddition reactions based on these concepts.

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Notes and references


