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Chemical Transformations of Vinylidenecyclopropanes

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ISSN 2191-5407
ISBN 978-3-642-27572-2
DOI 10.1007/978-3-642-27573-9
Springer Heidelberg New York Dordrecht London

e-ISSN 2191-5415
e-ISBN 978-3-642-27573-9

Library of Congress Control Number: 2011945822

Printed on acid-free paper

Springer is part of Springer Science+Business Media (www.springer.com)

Preface

Vinylidenecyclopropanes (VDCPs), which have strained cyclopropyl group connected with an allene moiety and yet are thermally stable and reactive substances in organic chemistry, are versatile intermediates in organic synthesis. During the past decades, VDCPs have demonstrated special reactivities, which can be tuned by the electronic or steric effects and nature of the substituents on the skeleton. Traditionally, great attention and a lot of effects have been focused on the photo- and thermal-induced chemistry of VDCPs. Recently, we have thoroughly investigated the Lewis acid or Brønsted acid, as well as transition metal, catalyzed/mediated chemistry of VDCPs and have found some new reactions of VDCPs, showing their significant usefulness in organic synthesis. In this volume, we will describe our investigations on the chemistry of VDCPs, including their preparation, their reactivities upon treating with Lewis or Brønsted acid, as well as transition metal catalysts and miscellaneous reactions.

Wenzhou, Shanghai, September 2011

Lixiong Shao
Jianmei Lu
Min Shi

Acknowledgments

The authors are deeply grateful to all the co-workers mentioned in the literatures. Financial support from the Shanghai Municipal Committee of Science and Technology (06XD14005 and 08dj1400100-2), National Basic Research Program of China (973)-2009CB825300, the National Natural Science Foundation of China (21072206, 20472096, 20872162, 20672127, 20821002, 20732008 and 21002072) and the Opening Foundation of Zhejiang Provincial Top Key Discipline (No. 100061200123) are greatly acknowledged.

Contents

Chapter 1
Introduction

Vinylidenecyclopropanes (VDCPs) **1** (Fig. 1.1), which have strained cyclopropyl group connected with an allene moiety and yet are thermally stable and reactive substances in organic chemistry, are versatile intermediates in organic synthesis [1, 2]. The first synthesis of VDCPs **1** can be traced back to 1959 [3]. During the past decades, VDCPs **1** have demonstrated special reactivities, which can be tuned by the electronic or steric effects and nature of the substituents on the skeleton. Thermal, photochemical, Lewis or Brønsted acids, as well as transition metals-catalyzed/mediated skeleton conversions of VDCPs **1** have attracted much attention from mechanistic, theoretical, spectroscopic and synthetic viewpoints [4–7]. For a long period of time, VDCPs **1** were considered as highly unstable compounds, and the traditional investigations were focused mainly on the photo- and heat-induced chemistry of VDCPs **1**. However, during the latest years, VDCPs **1** were found to demonstrate good reactivities and selectivities depending on the nature of the electronic and steric effects of the substituents. It is worthy of noting that more reaction patterns were found for VDCPs **1** with aryl substituent(s) during the recent years. For this guidance, this book intends to collect systematically the widespread knowledge not only regarding synthetic methods, but also including advances on the chemistry of VDCPs **1** bearing at least one aryl substituent on the terminal of the allene or cyclopropyl ring moiety, mainly on the Lewis or Brønsted acid-mediated/catalyzed transformations of VDCPs, transition metal-catalyzed transformations of VDCPs and miscellaneous analogs to update the recent review [8]. In order to minimize the overlap with the recent review, similar mechanisms for some of the corresponding reactions will be overlooked in this book. This book will cover the literature up to the early of year 2011.

Generally, VDCPs **1** are prepared through the reaction of alkenes with in situ produced alkenylidenecarbenes [9–12]. These alkenylidenecarbenes can be formed by treating halogenoalkynes [13–26], halogenoallenes [15, 18, 21, 27–31], polyhalogenocyclopropanes [32–41], and polyhalogenoalkanes [42] with strong bases, also can be generated by heating of diazoallenes [43] and so on [44–53].

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SpringerBriefs in Molecular Science, DOI: 10.1007/978-3-642-27573-9_1,

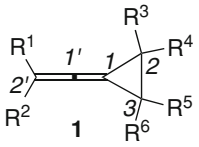
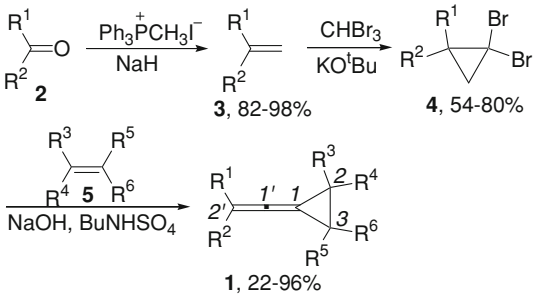


Fig. 1.1 Structure of VDCPs **1**



Scheme 1.1 One of the most popular methods for the synthesis of VDCPs **1**. Reprinted with the permission from [8]. Copyright 2011 American Chemical Society

The method reported by Mizuno and co-workers in 1991[37] is one of the most popular methods to synthesize various VDCPs, and the general route is shown in Scheme 1.1. The general procedure includes a Wittig reaction of the corresponding carbonyl compounds **2** to form alkenes **3** [54–58]. Then, cyclopropanation of alkenes **3** with the in situ generated dibromocarbene gives the 1,1-dibromocyclopropanes **4** [59]. Finally, under phase-transfer conditions, VDCPs **1** can be obtained in acceptable to high yields via the reaction of 1,1-dibromocyclopropanes **4** with various substituted alkenes **5**.

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Chapter 2
Lewis or Brønsted Acid-Mediated Transformations of VDCPs

Abstract Lewis or Brønsted acid-mediated intramolecular rearrangement of VDCPs, and the reactions of VDCPs with acetals, aldehydes, ketones, imines, activated alkenes, nitriles, acyl chlorides, and alcohols are described in this chapter.

Keywords Vinylidenecyclopropanes · Intramolecular rearrangement · Cycloaddition reaction · Ring-opening reaction · Mercury acetate-mediated reaction · Lewis acid-mediated reaction · Brønsted acid-mediated reaction

2.1 Mercury Acetate-Mediated Transformations of VDCPs

Pasto et al. reported the mercury acetate-mediated transformations of VDCPs **1** in 1976 [1–5]. Acetoxymercuration of VDCP **1a** followed by reductive demercuration using a great excess of sodium borohydride produced a complex mixture of the monomeric acetates **8** and **9** (60:40 ratio), dimeric diacetates, and bis(acetoxyalkyl)mercury compounds. Disrotatory ring-opening of an intermediate spiromercurinium ion **6** (or possible cyclopropyl cation **7** as a transition state) is expected to occur with outward rotation of the phenyl group, i.e., in the least sterically congested manner, to produce an allylic cation which then reacts with acetate to produce products **8** and **9**. In addition, **9** can be cleanly rearranged to **8** in the presence of strong protic acid (Scheme 2.1).

In addition to the formation of alcohols **10** and **11**, which correspond to the acetates **8** and **9** formed in acetoxymercuration of VDCP **1a**, hydroxymercuration of **1a** in 50% aqueous tetrahydrofuran (THF) also resulted in the formation of the acetylenic alcohol **12** (small amounts of acetates **8**, **9**, and **13** are also formed) (Scheme 2.2).

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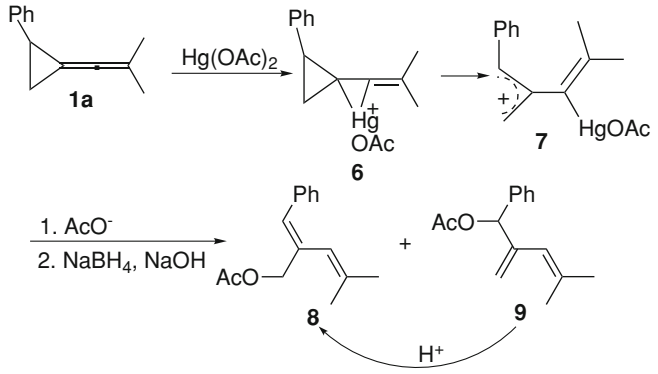
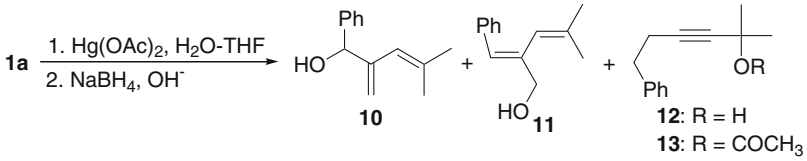
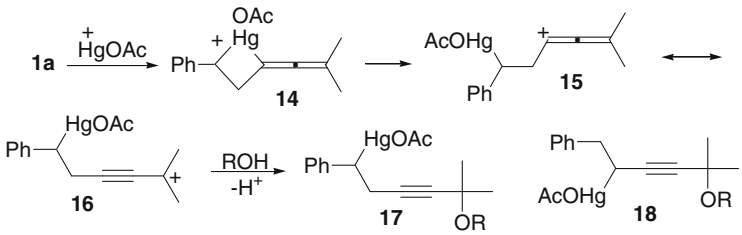


Scheme 2.1 $Hg(OAc)_2$-mediated transformation of VDCP **1a**. Reprinted with the permission from Ref. [1]. Copyright 2011 American Chemical Society

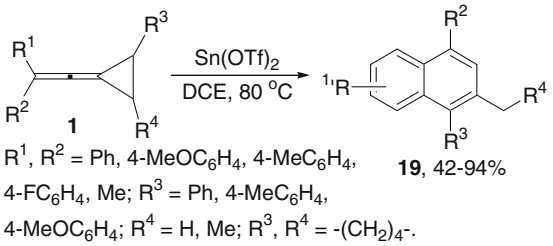


Scheme 2.2 $Hg(OAc)_2$-mediated reaction of VDCP **1a** in aqueous THF. Reprinted with the permission from Ref. [1]. Copyright 2011 American Chemical Society



Scheme 2.3 Plausible mechanism for the $Hg(OAc)_2$-mediated reaction of VDCP **1a**. Reprinted with the permission from Ref. [1]. Copyright 2011 American Chemical Society

The alcohol **12** and acetate **13** may be formed by initial attack by acetoxymercury cation on one of the ring bonds, either as shown to produce **17** or alternatively on the $–CH_2–C=$ bond to give **18**, both of which would be reduced to **12** and **13** (Scheme 2.3) [6, 7].



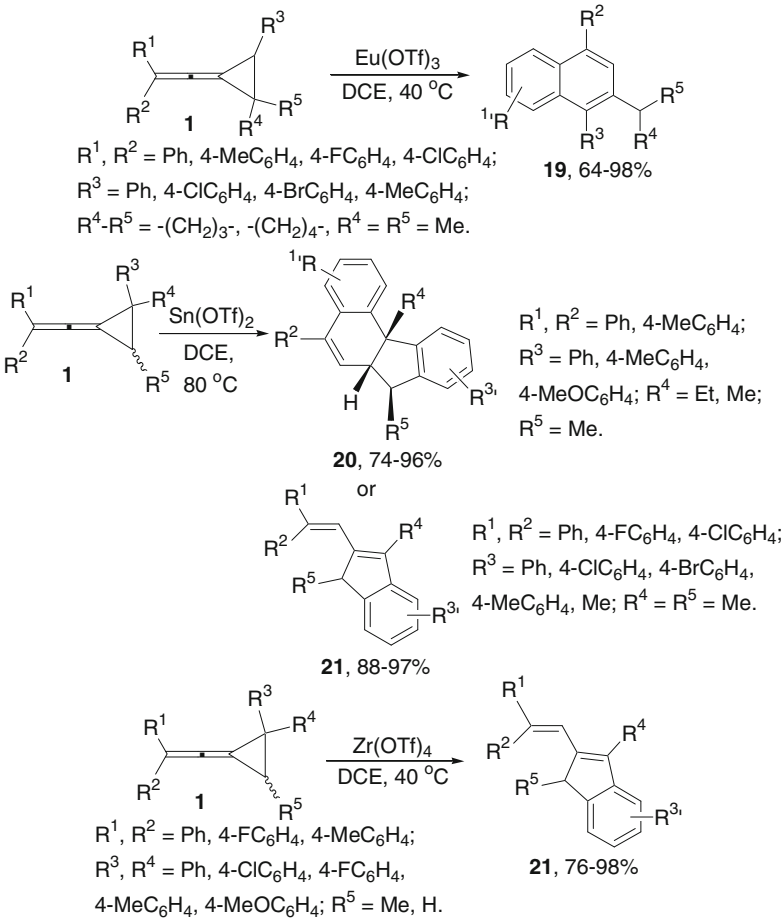
Scheme 2.4 $Sn(OTf)_2$-catalyzed intramolecular rearrangement of VDCPs **1**. Reprinted with the permission from Ref. [1]. Copyright 2011 American Chemical Society

2.2 Lewis or Brønsted Acid-Mediated Intramolecular Rearrangement of VDCPs

During the recent years, Shi et al. have reported a series of Lewis acid-catalyzed rearrangement reactions of VDCPs **1**. For example, in 2005, Shi et al. first found the Lewis acid-catalyzed rearrangement reaction of VDCPs **1**. It was observed that VDCPs **1** could rearrange to naphthalene derivatives **19** in the presence of $Sn(OTf)_2$, in acceptable to high yields under mild conditions (Scheme 2.4) [1, 8].

Based on this pioneering work, Shi et al. investigated thoroughly the Lewis acid-catalyzed rearrangement reactions of VDCPs **1** having three substituents on the corresponding cyclopropyl rings [9–11]. It was found that the reaction products are highly dependent on the substituents on the corresponding cyclopropyl rings and the electronic nature of the aryl groups on VDCPs **1**. For VDCPs **1** bearing two alkyl groups at the C3 position (R^1, R^2, R^3 = aryl; R^4 = H; R^5, R^6 = alkyl), naphthalene derivatives **19** were formed in the presence of Lewis acid $Eu(OTf)_3$ in DCE at 40 °C. For VDCPs **1** in which R^1, R^2, R^3 = aryl and R^4, R^5 = alkyl (*syn*/*anti* isomeric mixture), the corresponding *6a*H-benzo[*c*]fluorine derivatives **20** were obtained in the *syn*-configuration via a double intramolecular Friedel–Crafts reaction using the substrates without electron–withdrawing substituents on aryl groups or the corresponding indene derivatives **21** were formed via an intramolecular Friedel–Crafts reaction as long as one electron-deficient aryl group was attached. For VDCPs **1** in which R^1, R^2, R^3, R^4 = aryl and R^5 = alkyl or H, the corresponding indene derivatives **21** were obtained exclusively via a sterically demanding intramolecular Friedel–Crafts reaction (Scheme 2.5).

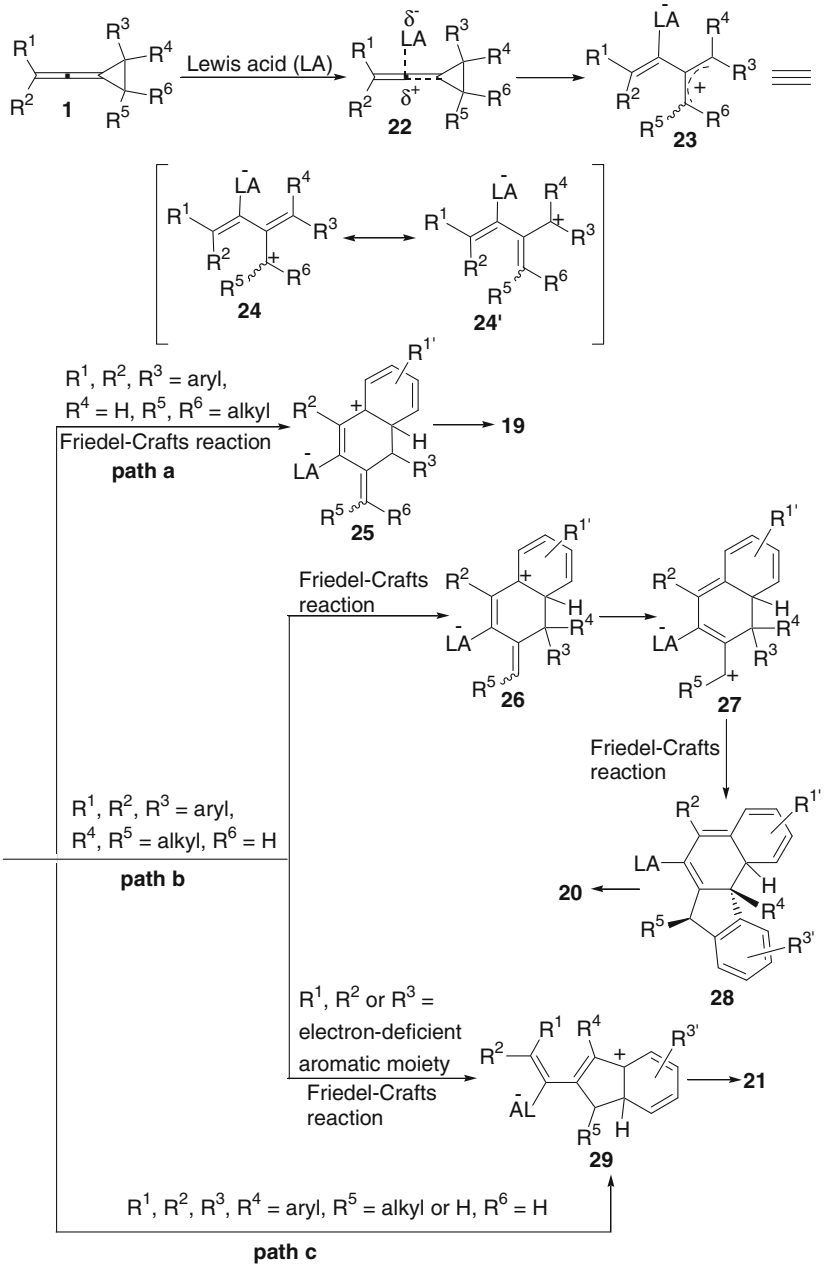
Plausible mechanisms for the formation of naphthalene, *6a*H-benzo[*c*]fluorine, and indene derivatives are shown as below: the coordination of VDCPs **1** to Lewis acid initially gives 1-cyclopropylvinyl cation **22**, a vinyl group stabilized cyclopropyl cation [12–16], which results in the formation of cyclopropyl ring-opened cationic intermediate **23** or its resonance-stabilized zwitterionic intermediate **24** and **24′**, which is stabilized by the aromatic R^3 group in most cases. The intramolecular Friedel–Crafts reaction [17] produces the cyclized intermediate **25**, from which the thermodynamically favored naphthalene derivatives **19** are formed via successive 1,3-carbocation rearrangement, 1,4-proton shift along with release of Lewis acid or deprotonation and 1,3-proton shift (Scheme 2.6, **path a**) [18].



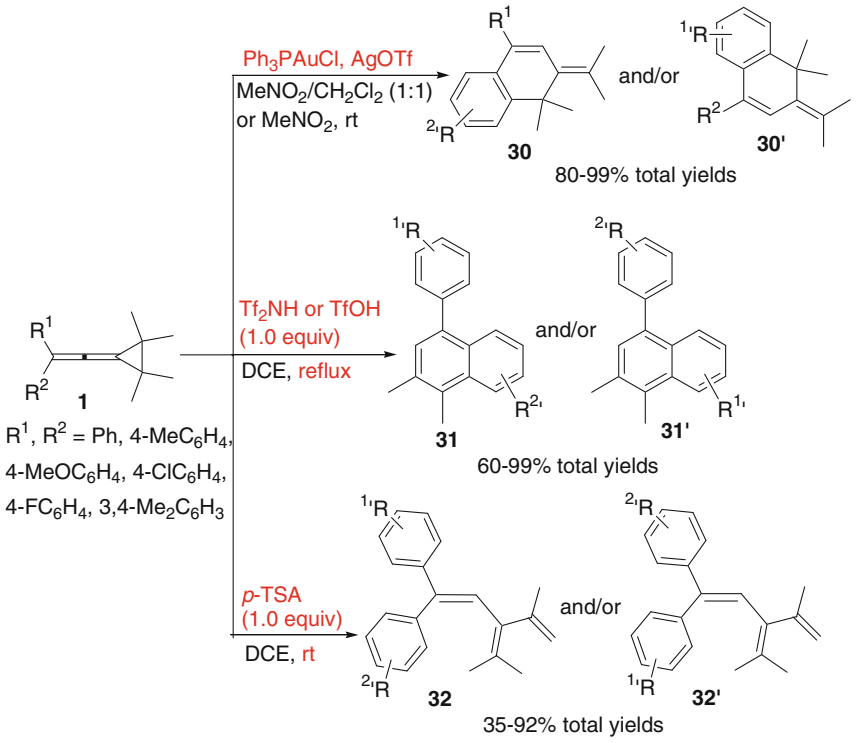
Scheme 2.5 Lewis acid-catalyzed intramolecular rearrangement of VDCPs **1**. Reprinted with the permission from Ref. [1]. Copyright 2011 American Chemical Society

*6a*H-benzo[*c*]fluorine derivatives **20** can be obtained via a double Friedel–Crafts reaction as shown in **path b** in Scheme 2.6. The formation of indene derivatives **21** is illustrated in **path c** in Scheme 2.6.

Using VDCPs **1** with tetramethyl-substituted cyclopropyl ring ($R^3 = R^4 = R^5 = R^6 = Me$), interesting intramolecular rearrangement patterns were found in the presence of different Lewis or Brønsted acid catalyst under different reaction temperature. For example, with soft Lewis acid Au(I) as the catalyst, 2-isopropylidene-1,1-dimethyl-1,2-dihydronaphthalene derivatives **30** and/or **30′** were obtained in good to high yields at room temperature (Scheme 2.7) [19], while with hard Brønsted acid such as Tf_2NH (Tf = trifluoromethanesulfonyl) or toluene-4-sulfonic acid (*p*-TSA) as the catalyst, the corresponding naphthalene



Scheme 2.6 Plausible mechanism for the Lewis acid-catalyzed intramolecular rearrangement of VDCPs **1**. Reprinted with the permission from Ref. [1]. Copyright 2011 American Chemical Society

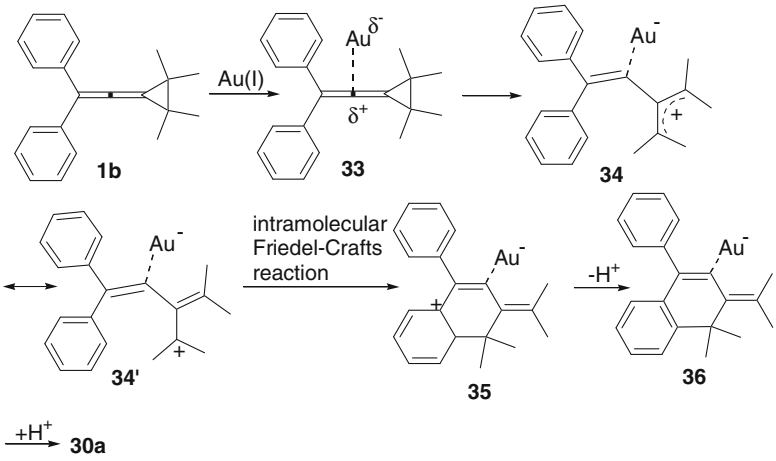


Scheme 2.7 Lewis or Brønsted acid-catalyzed intramolecular rearrangement of VDCPs **1** with tetramethyl groups on the cyclopropyl ring

derivatives **31** and/or **31′** were formed in good to high yields upon heating, along with release of a propene molecule. In addition, in the presence of Brønsted acid such as toluene-4-sulfonic acid (*p*-TSA), the corresponding triene derivatives **32** and **32′** were afforded in moderate to good yields at room temperature (Scheme 2.7) [20]. All ratios of **30** and **30′**, **31** and **31′**, and **32** and **32′** were dependent on the electron character of groups R^1 and R^2.

Plausible mechanism for the formation of products **30** with VDCP **1b** as the model is shown below: first, the corresponding cyclopropyl ring-opened zwitterionic intermediate **34** or the resonance-stabilized zwitterionic intermediate **34′** is formed from the initial zwitterionic intermediate **33**. Then intramolecular Friedel–Crafts reaction with the adjacent aromatic ring takes place to produce zwitterionic intermediate **35**, which affords the corresponding intermediate **36** via deprotonation. Subsequent protonation of intermediate **36** produces the corresponding product **30a** along with the release of Au(I) catalyst (Scheme 2.8).

Plausible mechanism for the formation of products **31** and **32** is shown below: first, protonation of VDCP **1b** by the Brønsted acid regioselectively gives intermediate **37**, which results in the formation of cyclopropyl ring-opened cationic



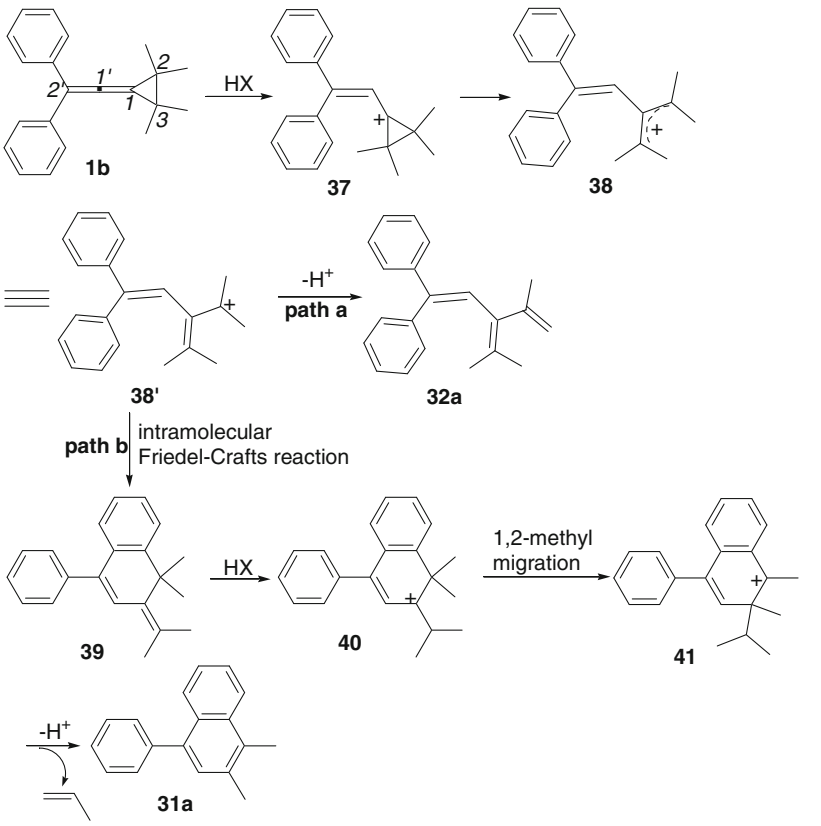
Scheme 2.8 Plausible mechanism for the Au(I)-catalyzed intramolecular rearrangement of VDCP **1b**. Reprinted with the permission from Ref. [19]. Copyright 2011 American Chemical Society

intermediate **38** or **38′**. Then product **32a** will be achieved with release of a proton (Scheme 2.9, **path a**). Alternatively, intermediate **38′** will be transformed to intermediate **39** through an intramolecular Friedel–Crafts reaction (Scheme 2.9, **path b**). Intermediate **39** undergoes subsequent protonation to give intermediate **40**. 1,2-Migration of the methyl group in intermediate **40** gives intermediate **41**, which will produce the final product **31a** with release of a proton and a propene. It is worth noting that this mechanism is postulated on the DFT studies performed with the Gaussian03 program by using the B3LYP method [20].

In the early 2008, Huang et al. reported a Lewis acid $TiCl_4$-mediated ring-expansion reaction of bicyclic VDCPs **1** for the formation of medium- and large-size naphthalenacarbocycle derivatives **42** (Scheme 2.10) [21].

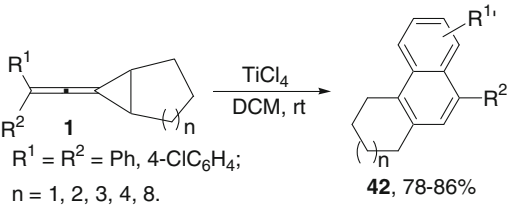
2.3 Lewis or Brønsted Acid-Mediated Reactions of VDCPs with Acetals, Aldehydes and Ketones

Lewis acid $Sc(OTf)_3$-catalyzed reactions of VDCPs **1** with acetals **43** were also established for the preparation of indene derivatives **44** and **45**. This reaction is believed to proceed via regioselective addition of oxonium intermediate to VDCPs **1** and the subsequent intramolecular Friedel–Crafts reaction. It was found that the electronic nature of substituent strongly influenced the reaction results, even leading to different products (Scheme 2.11) [1, 22]. In a word, when R^3, R^4 = aryl, R^5, R^6 = Me or H, indene derivatives **44** can be formed singly; and while $R^3 = R^4 = R^5 = R^6$ = Me, indene derivatives **45** were obtained exclusively.

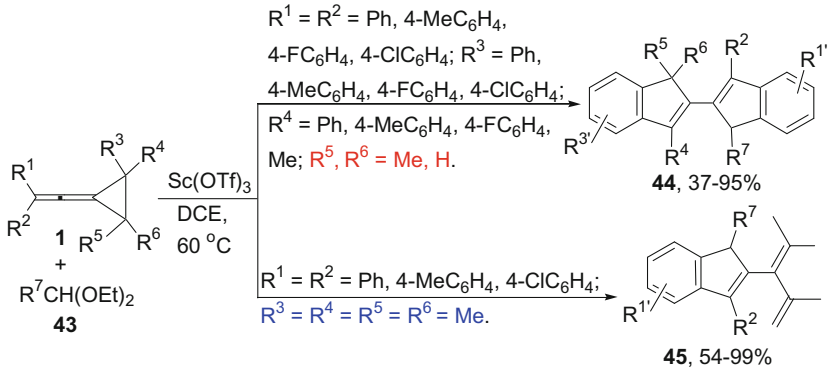


Scheme 2.9 Plausible mechanism for the Brønsted acid-catalyzed intramolecular rearrangement of VDCP **1b**

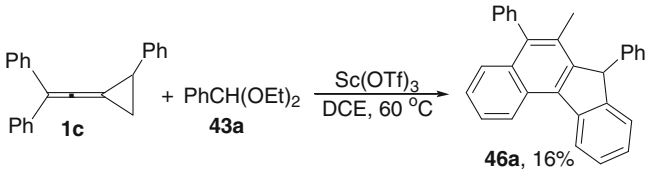
Scheme 2.10 $TiCl_4$-mediated ring-expansion of VDCPs **1**. Reprinted with the permission from Ref. [1]. Copyright 2011 American Chemical Society



Interestingly, the substrate VDCP **1c** with only one phenyl group at the cyclopropyl ring demonstrated a special reactivity under identical reaction conditions. A new product 6-methyl-5,7-diphenyl-7*H*-benzo[*c*]fluorine **46a** along with other unidentified by-products was obtained although the yield (16%) was rather low (Scheme 2.12).



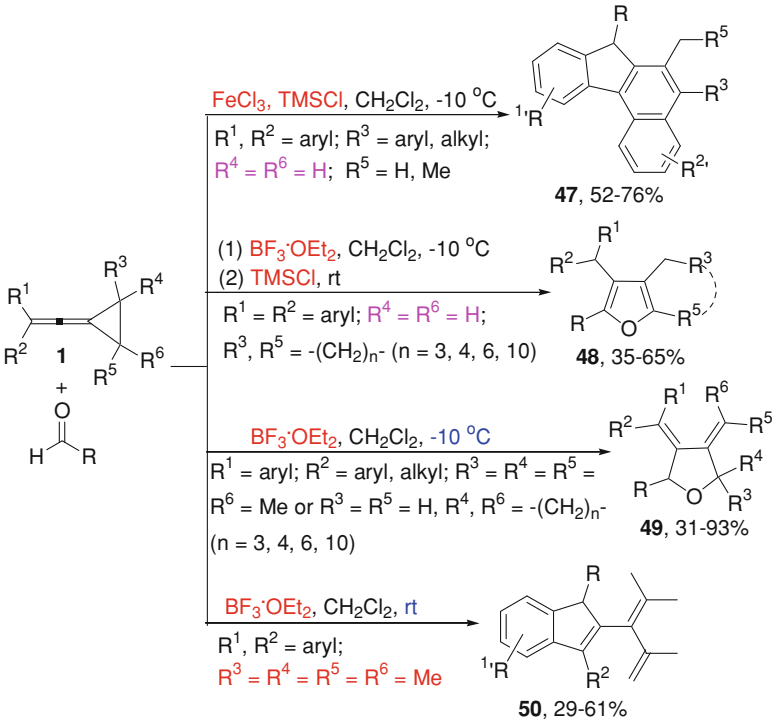
Scheme 2.11 $Sc(OTf)_3$-catalyzed reactions of VDCPs **1** with acetals. Reprinted with the permission from Ref. [1]. Copyright 2011 American Chemical Society



Scheme 2.12 $Sc(OTf)_3$-catalyzed reaction of VDCP **1c** with acetal **43a**. Reprinted with the permission from Ref. [1]. Copyright 2011 American Chemical Society

Huang et al. developed the reactions of VDCPs **1** with aldehydes to provide an efficient and selective method for the synthesis of benzo[*c*]fluorene, tetrahydrofuran, furan, and indene derivatives. A variety of benzo[*c*]fluorene **47**, furan **48**, tetrahydrofuran **49**, and indene derivatives **50** can be obtained selectively depending on the Lewis acid catalysts, the substituents on VDCPs **1**, and the reaction temperature [23–25]. For instance, using $FeCl_3$/TMSCl as the catalyst at −10 °C, benzo[*c*]fluorene derivatives **47** can be obtained in moderate to good yields (R^1, R^2 = aryl, R^3 = aryl, alkyl; $R^4 = R^6 = H$, R^5 = H, Me); first treatment with $BF_3{\cdot}OEt_2$ at −10 °C, then with TMSCl at room temperature, furan derivatives **48** can be achieved in acceptable to moderate yields [$R^1 = R^2$ = aryl; $R^4 = R^6 = H$, R^3, $R^5 = -(CH_2)_n-$ (n = 3, 4, 6, 10)]; using $BF_3{\cdot}OEt_2$ as the catalyst at −10 °C, tetrahydrofuran derivatives **49** can be obtained in acceptable to high yields [R^1 = aryl; R^2 = aryl, alkyl; $R^3 = R^4 = R^5 = R^6$ = Me or $R^3 = R^5 = H$, R^4, $R^6 = -(CH_2)_n-$ (n = 3, 4, 6, 10)]; while using $BF_3{\cdot}OEt_2$ as the catalyst at room temperature, indene derivatives **50** can be formed in low to moderate yields (R^1, R^2 = aryl; $R^3 = R^4 = R^5 = R^6$ = Me) (Scheme 2.13).

Plausible mechanism for the formation of products **47**–**50** is outlined below. Initially, the coordination of aldehydes to Lewis acid (LA) gives intermediate **51**, which adds to VDCPs **1** regioselectively to produce intermediate **52**. Then the

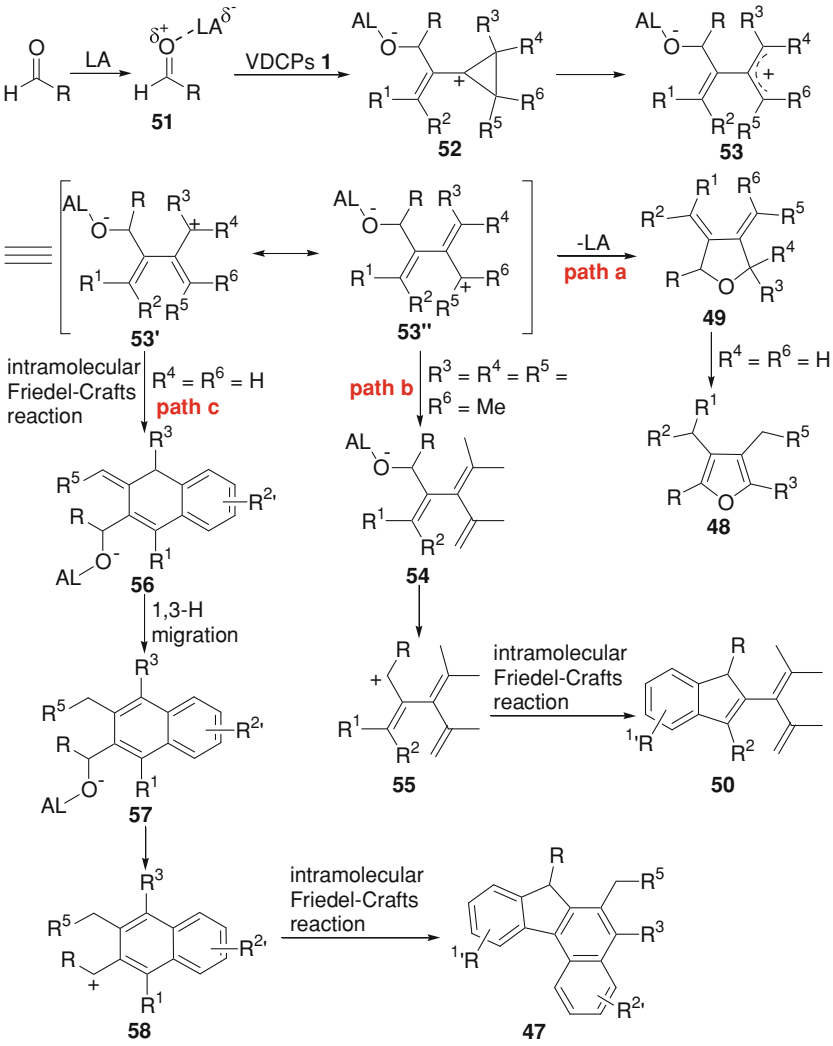


Scheme 2.13 Lewis acid-catalyzed reactions of VDCPs **1** with aldehydes

cyclopropyl ring-opened intermediate **53** or the resonance-stabilized intermediates **53′** and **53″** will be formed. Intramolecular *O*-attack cyclization of intermediate **53′** will afford products **49**. When $R^4 = R^6 = H$, aromatization of **49** will take place to give products **48** (Scheme 2.14, **path a**). When $R^3 = R^4 = R^5 = R^6 = Me$, deprotonation of intermediate **53″** will form intermediate **54**, which then transforms to intermediate **55**. The subsequent intramolecular Friedel–Crafts reaction of intermediate **55** furnishes the indene derivatives **50** (Scheme 2.14, **path b**). In addition, when $R^4 = R^6 = H$, intermediate **53′** undergoes intramolecular Friedel–Crafts reaction to give intermediate **56**. Aromatization of **56** produces the thermodynamically favored naphthalene intermediate **57**, which then transforms to intermediate **58**. Finally, intermediate **58** undergoes another intramolecular Friedel–Crafts reaction to give products **47** (Scheme 2.14, **path c**).

Further studies revealed that using VDCPs **1** with functionalized groups on the cyclopropyl ring shown below as the substrates, their reactions with aldehydes will afford the furo[2,3-*b*]furan derivatives **59** in 37–64% yields (Scheme 2.15).

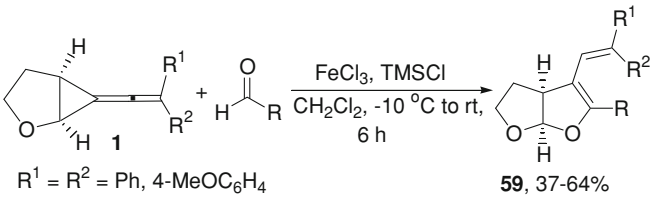
Plausible mechanism for the formation of products **59** is depicted in Scheme 2.16. First, the addition of the Lewis acid-activating aldehydes **51** to VDCPs **1** may occur to give the ring-opened intermediate **60** via proximal cleavage of the cyclopropyl ring. Then an intramolecular cyclization of



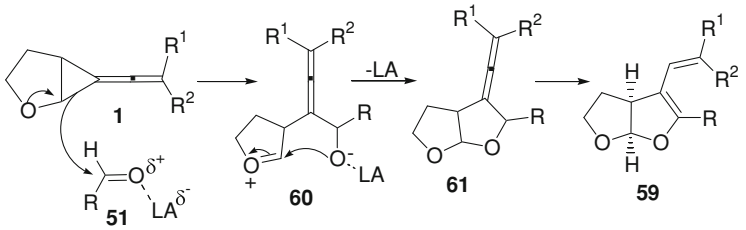
Scheme 2.14 Plausible mechanism for the Lewis acid-catalyzed reactions of VDCPs **1** with aldehydes. Reprinted with the permission from Ref. [25]. Copyright 2011 American Chemical Society

intermediate **60** along with the release of the Lewis acid furnished the [3 + 2] cycloaddition intermediate **61**, which will transform to the final products **59** via 1,3-H shift.

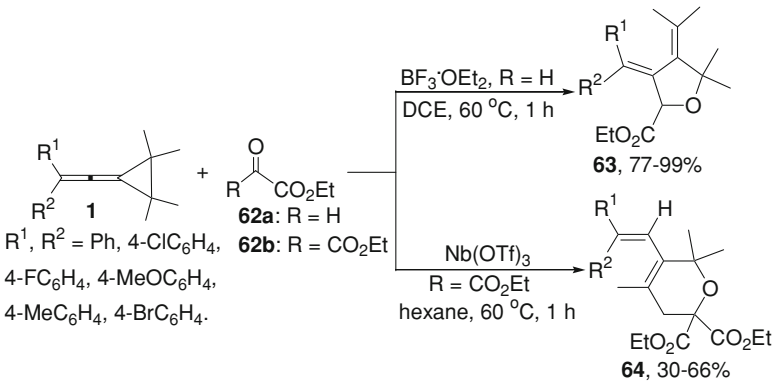
The reactions of VDCPs **1** with activated carbonyl compounds **62** were also investigated and it was found that a number of functionalized tetrahydrofurans **63** and 3,6-dihydropyrans **64** can be formed in moderate to good yields selectively in the presence of different Lewis acids (Scheme 2.17) [26]. In these reactions,



Scheme 2.15 Lewis acid-catalyzed reactions of bicyclic VDCPs **1** with aldehydes

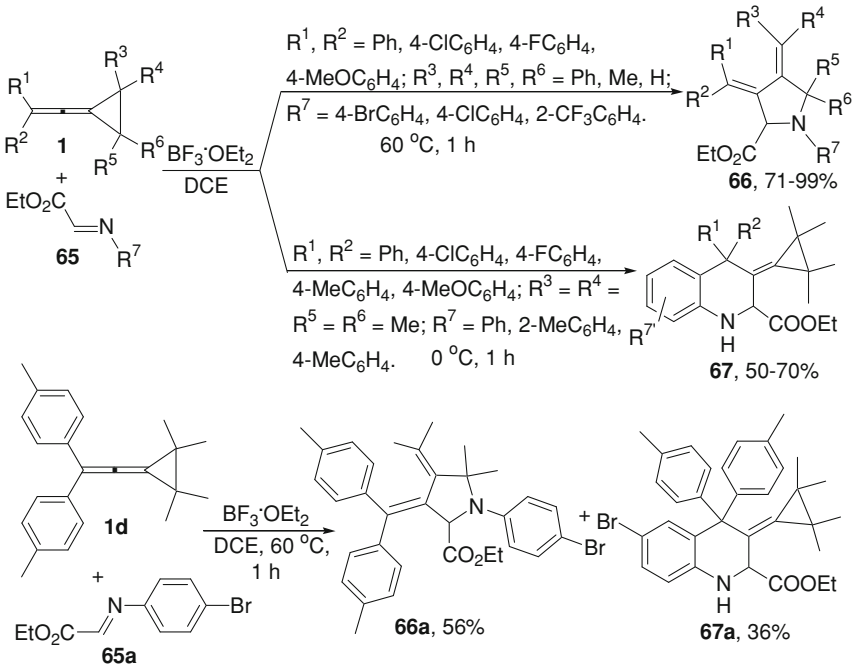


Scheme 2.16 Plausible mechanism for the Lewis acid-catalyzed reactions of bicyclic VDCPs **1** with aldehydes. Reprinted with the permission from Ref. [24]. Copyright 2011 Wiley John and Sons



Scheme 2.17 Lewis acid-catalyzed reactions of VDCPs **1** with activated carbonyl compounds. Reprinted with the permission from Ref. [1]. Copyright 2011 American Chemical Society

tetrahydrofurans **63** were obtained in 77–99% yields in the reactions of VDCPs **1** with oxo-acetic acid ethyl ester **62a** in the presence of $BF_3{\cdot}OEt_2$; however, 3,6-dihydropyrans **64** were formed in 30-66% yields in the reactions of VDCPs **1** with 2-oxo-malonic acid diethyl ester **62b** in the presence of $Nb(OTf)_3$.

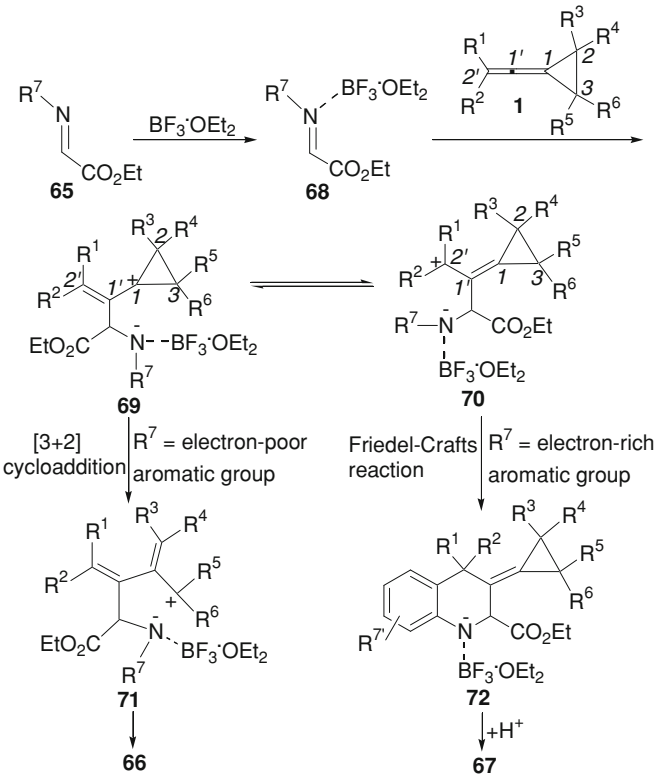


Scheme 2.18 $BF_3{\cdot}OEt_2$-catalyzed reactions of VDCPs **1** with ethyl (arylimino)acetates. Reprinted with the permission from Ref. [1]. Copyright 2011 American Chemical Society

2.4 Lewis or Brønsted Acid-Mediated Reactions of VDCPs with Imines and Their Analogs

The scope of Lewis acid-catalyzed reaction of VDCPs **1** was further extended with respect to a series of ethyl (arylimino)acetates **65**, which led to a facile synthetic protocol of pyrrolidine and 1,2,3,4-tetrahydroquinoline derivatives. A number of pyrrolidine derivatives **66** and 1,2,3,4-tetrahydroquinoline derivatives **67** can be obtained selectively in moderate to good yields by the reaction of VDCPs **1** with ethyl (arylimino)acetates **65** in the presence of Lewis acid $BF_3{\cdot}OEt_2$ depending on the electronic nature of both **65** and R^1 or R^2 aromatic groups of **1** [1, 27–29]. Generally, when R^7 group on **65** is an electron-poor aromatic group, the pyrrolidines **66** will be formed solely; when R^7 is an electron-rich aromatic group, the 1,2,3,4-tetrahydroquinolines **67** will be obtained as the sole products. Meanwhile, if R^1 and R^2 are both electron-rich aromatic groups ($R^1 = R^2 = 4\text{-}MeC_6H_4$ as the example in this case), both of the products **66a** and **67a** can be obtained in spite of R^7 is an electron-poor or -rich group (Scheme 2.18).

Plausible mechanism for the formation of pyrrolidines **66** and 1,2,3,4-tetrahydroquinolines **67** is outlined in Scheme 2.19. First, ethyl (arylimino)acetate **65** is activated by $BF_3{\cdot}OEt_2$ to afford intermediate **68**, which subsequently adds to C1′

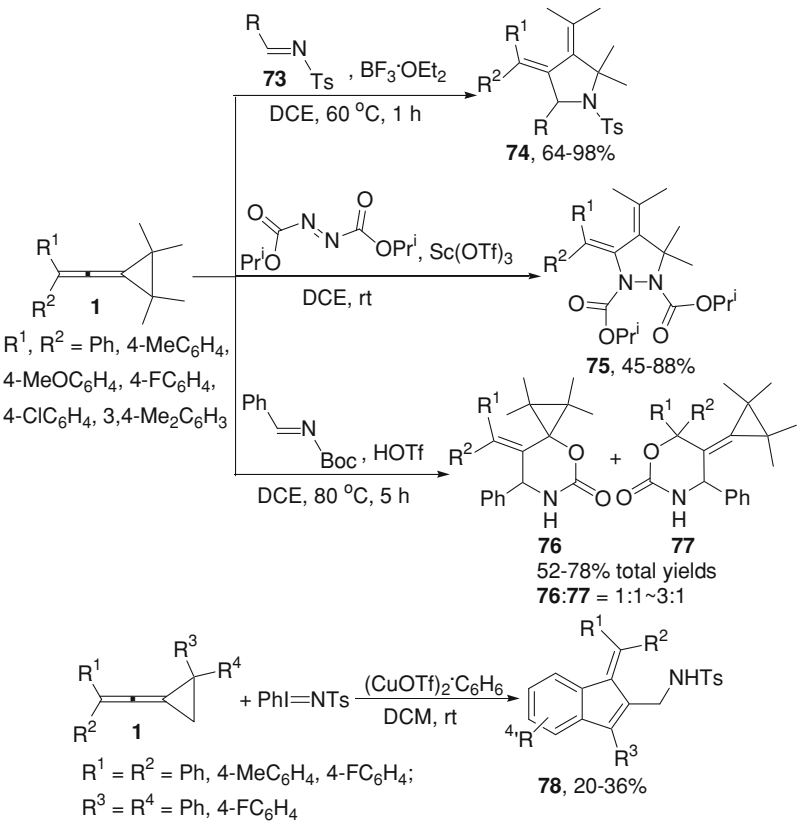


Scheme 2.19 Plausible mechanism for the $BF_3{\cdot}OEt_2$-catalyzed reactions of VDCPs **1** with ethyl (arylimino)acetates. Reprinted with the permission from Ref. [1]. Copyright 2011 American Chemical Society

position of VDCPs **1** to give the corresponding allylic carbocationic intermediates **69** and **70** [30–32]. Intermediate **71**, derived from **69** via a cyclopropyl ring-opening process, undergoes cyclization to give the corresponding [3 + 2] cycloaddition products **66** when R^7 is an electron-poor aromatic group. Alternatively, if R^7 is an electron-rich aromatic group, intramolecular Friedel–Crafts reaction takes place from intermediate **70** to give intermediate **72** [33], which finally furnishes products **67** [34–37].

During the ongoing investigations, Shi et al. found that VDCPs **1** can also react with other activated carbon–nitrogen, nitrogen–nitrogen, and iodine-nitrogen double-bond-containing compounds, such as *N*-toluene-4-sulfonyl (*N*-Ts) imines, diisopropylazodicarboxylate (DIAD), *N*-*tert*-butoxycarbonyl (*N*-Boc) aldimine, and *N*-Ts-iminophenyliodinane in the presence of Lewis or Brønsted acid to afford the corresponding cycloadducts in moderate to high yields (Scheme 2.20) [38].

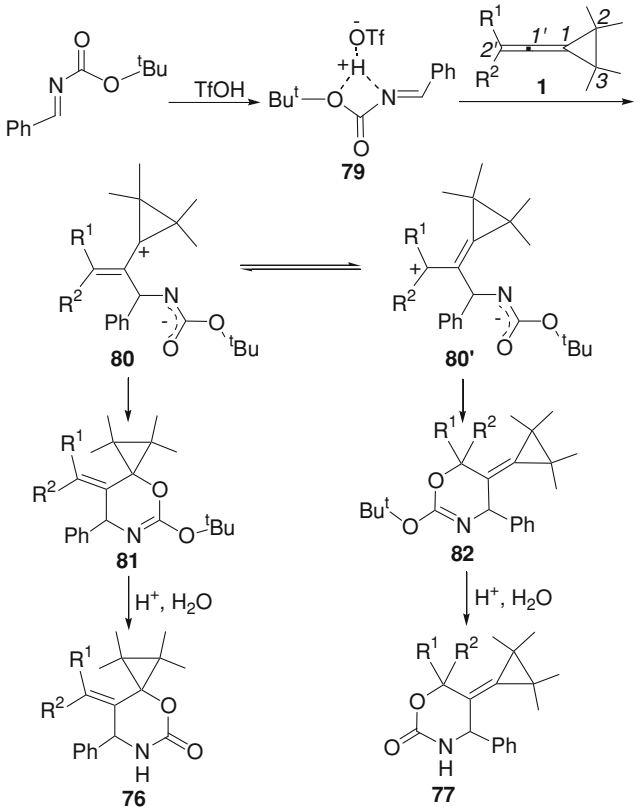
Plausible mechanism for the formation of products **76** and **77** is illustrated in Scheme 2.21. Initially, *N*-Boc aldimine is activated by Brønsted acid TfOH to give



Scheme 2.20 Lewis or Brønsted acid-catalyzed reactions of VDCPs **1** with activated carbon–nitrogen, nitrogen–nitrogen, and iodine-nitrogen double-bond-containing compounds

intermediate **79**, which subsequently adds to the C1′ position of VDCPs **1** selectively to afford the corresponding intermediates **80** and **80′**. Then, ring-closure of intermediates **80** and **80′** affords intermediates **81** and **82**, respectively. Finally, hydrolysis of intermediates **81** and **82** furnishes products **76** and **77**, respectively. It was believed that cyclization of intermediates **80** and **80′** is faster than the cyclopropyl ring-opening reaction in this particular case, so the six-membered products **76** and **77** were formed instead of the [3 + 2] cycloaddition products.

Plausible mechanism for the formation of products **78** is outlined below: initially, intermediate **83** is formed by the reaction of Cu(I) with PhI = NTs according to the general mechanism in the Cu(I)-catalyzed aziridination of olefin [39]. Then, the reaction of intermediate **83** with VDCPs **1** gives the ring-opened zwitterionic intermediate **84** presumably through nucleophilic attack of the cyclopropyl ring on the nitrene species. The allylic rearrangement of zwitterionic intermediate **84** produces intermediate **85**, which undergoes an intramolecular



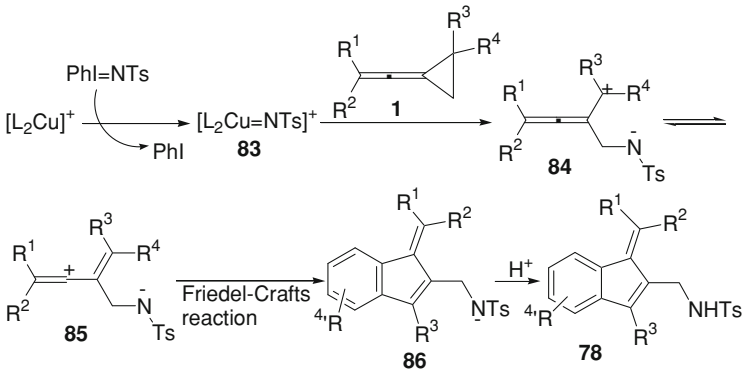
Scheme 2.21 Plausible mechanism for the TfOH-catalyzed reactions of VDCPs **1** with *N*-Boc aldimine

Friedel–Crafts reaction with the R^4 group to generate intermediate **86**. Protonation of intermediate **86** will furnish products **78** (Scheme 2.22).

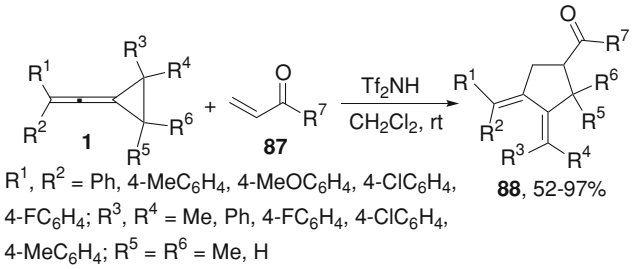
2.5 Brønsted Acid-Mediated Reactions of VDCPs with Activated Alkenes

Further studies showed that VDCPs **1** can also react with activated olefins such as α,β-unsaturated ketones (aldehyde) **87** to give the corresponding [3 + 2] cycloaddition products **88** as the major ones in moderate to high yields (Scheme 2.23) [40].

The formation of products **88** can be rationalized as below with the cycloaddition reaction of VDCP **1b** and methyl vinyl ketone (MVK) as the model: first, MVK is protonated by Tf_2NH to generate intermediate **89a**, which undergoes



Scheme 2.22 Plausible mechanism for the Cu(I)-catalyzed reactions of VDCPs **1** with *N*-Ts-iminophenyliodinane

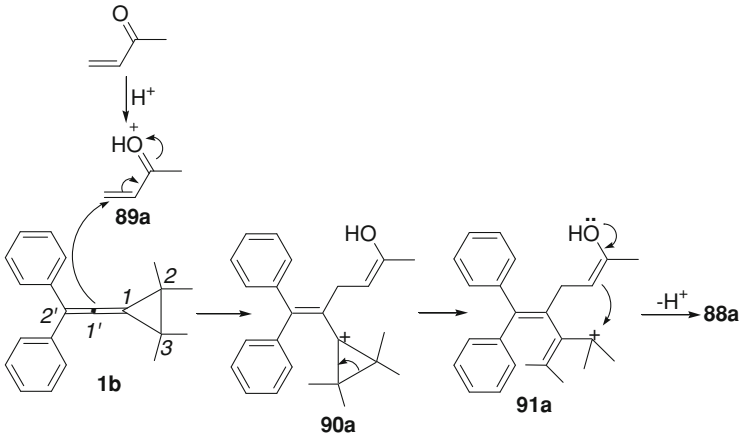


Scheme 2.23 Tf_2NH-catalyzed reactions of VDCPs **1** with activated alkenes

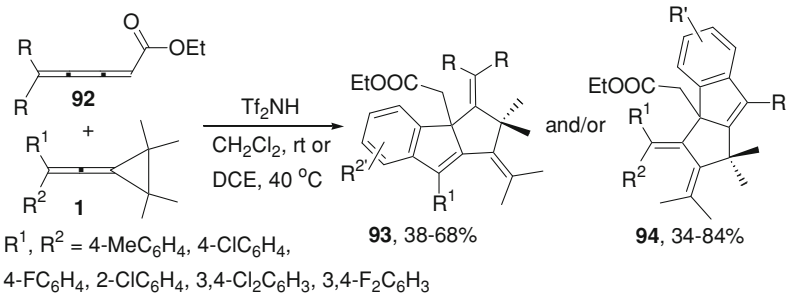
a 1,4-nucleophilic addition reaction with C1′ position of VDCP **1b** to give intermediate **90a**. Subsequently, ring opening of the cyclopropyl ring in intermediate **90a** produces intermediate **91a**. Finally, products **88a** will be achieved from intermediate **91a** through intramolecular nucleophilic attack (Scheme 2.24).

In continuing research, ethyl 5,5-diarylpenta-2,3,4-trienoates **92** were also used as the reaction partner catalyzed by Brønsted acid Tf_2NH. It was found that cascade cycloaddition and Friedel–Crafts reactions of VDCPs **1** were achieved to provide a variety of novel polycyclic ester derivatives **93** and/or **94**, depending on the substituents R^1 and R^2 on VDCPs **1**, in moderate to good yields under mild conditions (Scheme 2.25) [41].

Plausible mechanism for these reactions is shown below: similarly, 5,5-diphenylpenta-2,3,4-trienoate **92a** is first protonated by the Brønsted acid catalyst Tf_2NH to produce intermediate **95a**, which will isomerize to the carbocationic intermediate **97a** via an enolate intermediate **96a**. Subsequently, VDCPs **1** undergoes a nucleophilic attack on intermediate **97a** to generate intermediate **98**, which produces intermediate **99** via the ring opening of the cyclopropyl ring. An intramolecular nucleophilic attack generates an intermediate **100**, which should

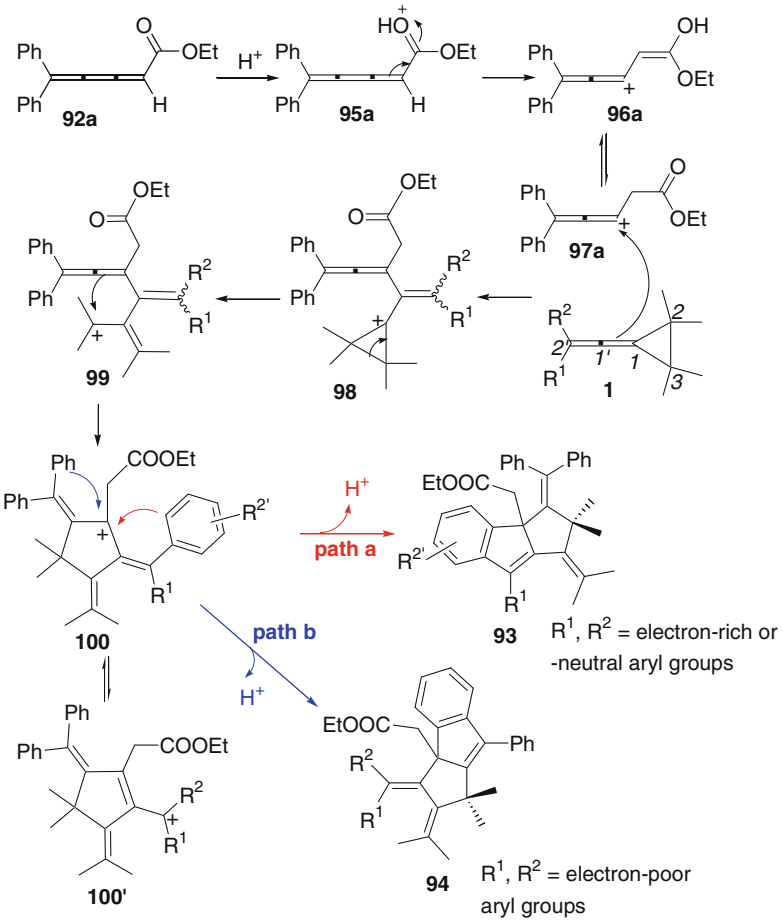


Scheme 2.24 Plausible mechanism for the Brønsted acid-catalyzed reaction of VDCP **1b** with MVK. Reprinted with the permission from Ref. [40]. Copyright 2011 American Chemical Society



Scheme 2.25 Tf_2NH-catalyzed reactions of VDCPs **1** with 5,5-diarylpenta-2,3,4-trienoates **92**

be in equilibrium with intermediate **100′** via allylic rearrangement. It is understandable that the intramolecular Friedel–Crafts reaction is favored for the electron-rich rings of intermediate **100**. Thus, there are two pathways for the intramolecular Friedel–Crafts reaction. For VDCPs **1** bearing moderately electron-donating groups on the phenyl rings or neutral phenyl ring, the intramolecular Friedel–Crafts reaction occurs on the aromatic ring of VDCPs **1** to give the products **93** since R^1 and R^2 are in larger conjugate system which can stabilize the cationic intermediate generated in the Friedel–Crafts reaction (Scheme 2.26, **path a**). On the other hand, for VDCPs **1** bearing electron-withdrawing groups on both of the phenyl rings, the intramolecular Friedel–Crafts reaction occurs on the phenyl ring of 5,5-diphenylpenta-2,3,4-trienoate **92a** to generate products **94** (Scheme 2.26, **path b**).

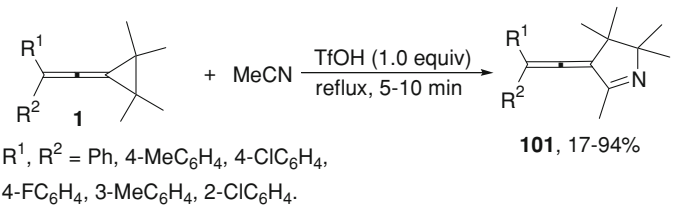


Scheme 2.26 Plausible mechanism for the Brønsted acid-catalyzed reactions of VDCPs **1** with 5,5-diphenylpenta-2,3,4-trienoate **92a.** Reprinted with the permission from Ref. [41]. Copyright 2011 Royal Society of Chemistry

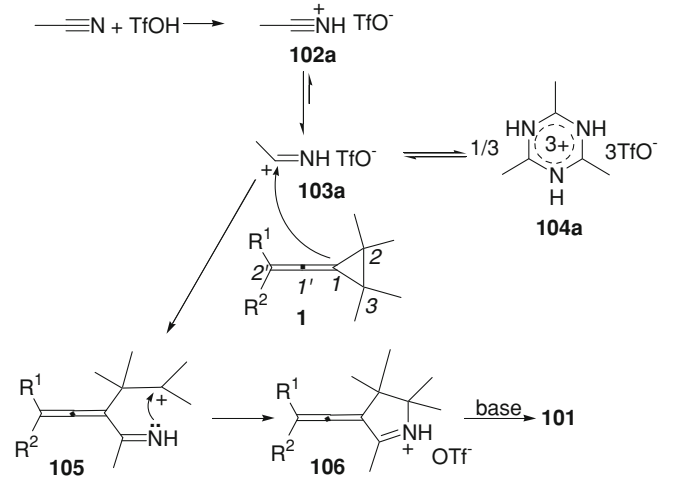
2.6 Brønsted Acid-Mediated Reactions of VDCPs with Nitriles

The Brønsted acid TfOH-catalyzed reactions of VDCPs **1** with MeCN were also investigated in Shi's group and it was reported that the [3 + 2] cycloaddition products, the 3,4-dihydro-2*H*-pyrrole derivatives **101** can be obtained in moderate to excellent yields under reflux within a short time (Scheme 2.27) [1, 42–44]. In these reactions, the four substituents on the cyclopropyl ring of VDCPs **1** should be all methyl groups.

Plausible mechanism for this transformation is outlined in Scheme 2.28. First, there is an equilibrium among intermediates **102a**, **103a**, and **104a** in the reaction



Scheme 2.27 TfOH-catalyzed reactions of VDCPs **1** with acetonitrile. Reprinted with the permission from Ref. [1]. Copyright 2011 American Chemical Society

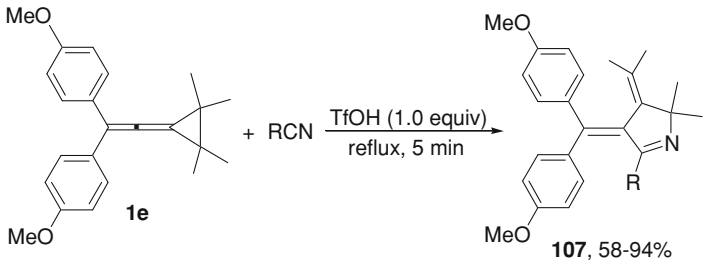


Scheme 2.28 Plausible mechanism for the TfOH-catalyzed reactions of VDCPs **1** with acetonitrile. Reprinted with the permission from Ref. [1]. Copyright 2011 American Chemical Society

of acetonitrile with TfOH according to the previous literatures [45, 46]. Intermediate **103a** undergoes an electrophilic attack to the C1 position of VDCPs **1** to afford the corresponding ring-opened cationic intermediate **105**, which undergoes the subsequent intramolecular cyclization reaction to give cationic intermediate **106**. Treatment of **106** with a base furnishes products **101**.

For strongly electron-donating 4-methoxyphenyl group substituted VDCP **1e** ($R^1 = R^2 = 4\text{-MeOC}_6H_4$, $R^3 = R^4 = R^5 = R^6 = Me$), 3,4-dihydro-2*H*-pyrrole derivatives **107** were formed in moderate to high yields under the same reaction conditions (Scheme 2.29).

Scheme 2.30 shows the plausible mechanism for this [3 + 2] cycloaddition reaction of VDCP **1e** with nitriles mediated by TfOH. Electrophilic attack of intermediate **103** to the C1′ position of VDCP **1e** gives intermediate **108**, which immediately undergoes a ring-opening process to afford intermediate **109**.



Scheme 2.29 TfOH-mediated reactions of VDCP **1e** with nitriles. Reprinted with the permission from Ref. [1]. Copyright 2011 American Chemical Society

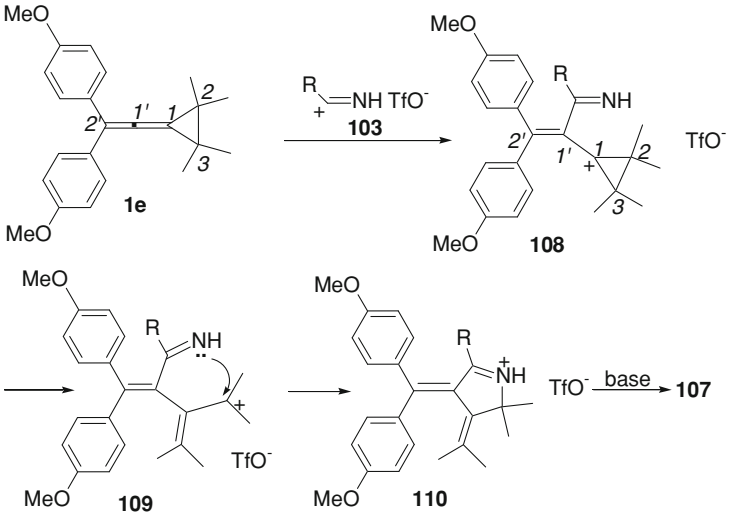
Intramolecular cyclization takes place to give intermediate **110**, which furnishes products **107** by treatment with a base. Maybe the strong electron-donating 4-methoxyphenyl group on VDCP **1e** increases the electron density at C1′ position, facilitating the electrophilic attack of cationic intermediate **103**. Therefore, the reaction takes place in a different pathway.

2.7 Lewis Acid-Mediated Reactions of VDCPs with Acyl Chlorides

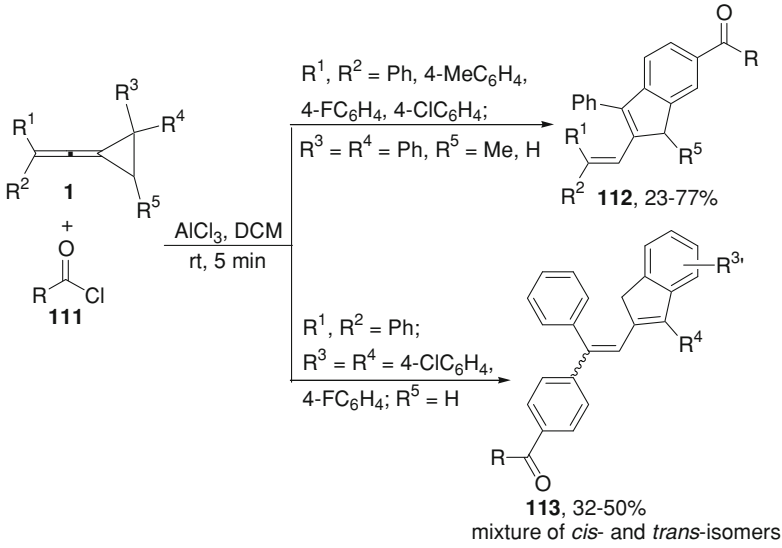
During the investigation on the Lewis acid-mediated chemistry of VDCPs **1**, it was also reported that $AlCl_3$-mediated tandem Friedel–Crafts reaction of VDCPs **1** with acyl chlorides **111** afforded the corresponding products **112** or **113** in moderate to good yields under mild conditions within short reaction time (Scheme 2.31) [1, 47, 48]. The control experiment showed that products **112** and **113** can be derived from the corresponding intramolecular rearrangement products of VDCPs **1**.

2.8 Lewis Acid-Mediated Reactions of VDCPs with Alcohols or Ethers

The reactions between VDCPs **1** and 1,1,3-triarylprop-2-yn-1-ols **114** or their methyl ethers **115** in the presence of Lewis acid were also investigated in Shi's group. 4-Dihydro-1*H*-cyclopenta[*b*]-naphthalene derivatives **116** can be obtained in the reactions of VDCPs **1** with 1,1,3-triarylprop-2-yn-1-ols **114** in the presence of $Zr(OTf)_4$ in DCE at −20 °C; 1,2,3,8-tetrahydrocyclopenta[*a*]indene derivatives **117** can be formed in the reactions of VDCPs **1**, bearing four methyl groups on the cyclopropyl ring, with 1,1,3-triarylprop-2-yn-1-ol methyl ethers **115** in the presence of $Sc(OTf)_3$ in DCE at 40 °C (Scheme 2.32) [49].

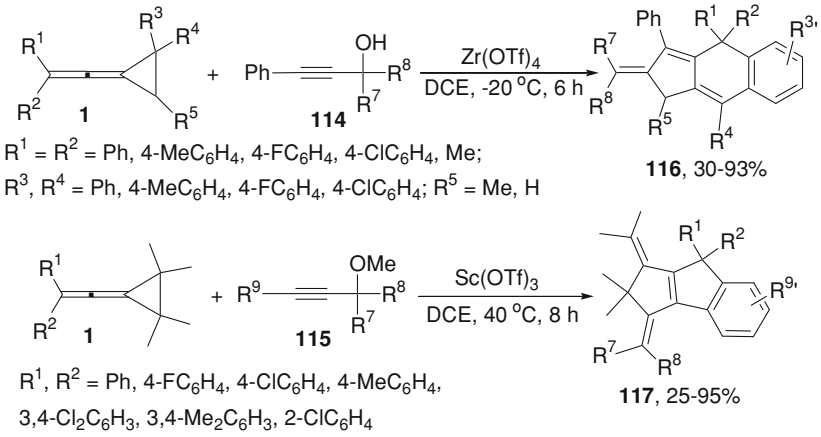


Scheme 2.30 Plausible mechanism for the TfOH-mediated reactions of VDCP **1e** with nitriles. Reprinted with the permission from Ref. [1]. Copyright 2011 American Chemical Society



Scheme 2.31 $AlCl_3$-catalyzed reactions of VDCPs **1** with acyl chlorides. Reprinted with the permission from Ref. [1]. Copyright 2011 American Chemical Society

Plausible mechanism for the formation of products **116** and **117** is outlined below based on Meyer-Schuster rearrangement [50, 51]. In the presence of a Lewis acid,



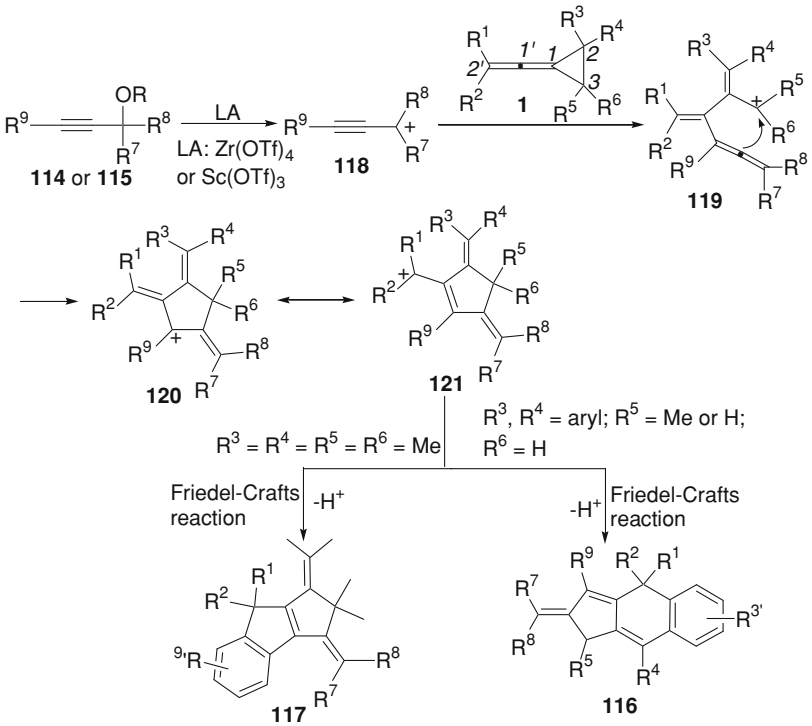
Scheme 2.32 Lewis acid-catalyzed reactions between VDCPs **1** and 1,1,3-triarylprop-2-yn-1-ols or their methyl ethers

propargylic cation intermediate **118** is first produced from 1,1,3-triarylprop-2-yn-1-ols **114** or their methyl ethers **115**. Then nucleophilic attack of C1′ position of VDCPs **1** to intermediate **118**, along with allylic rearrangement affords cationic intermediate **119**. Cyclization of intermediate **119** produces cationic intermediate **120** or its resonance-stabilized intermediate **121**. When $R^3 = R^4 = R^5 = R^6 =$ Me, a Friedel–Crafts reaction with the adjacent aromatic group takes place to afford products **117**. When R^3 and R^4 are both aromatic groups, a Friedel–Crafts reaction with R^3 takes place, presumably due to steric effects, to afford products **116** (Scheme 2.33). In this case, the formation of a stable cationic intermediate **118** is the key step, so when R^7, R^8, or R^9 are aliphatic groups, complex mixtures of products are formed.

Moreover, it was found that for the reactions of VDCPs **1** with **114a**, in which both of R^7 and R^8 are 4-methoxyphenyl groups, a novel functionalized methylenecyclobutene derivatives **122** were achieved in moderate to high yields instead of the 1,2,3,8-tetrahydrocyclopenta[*a*]indene derivatives **117**. This may be because the intermediate formed, cation **123**, produces allyl cationic intermediate **124**, which can be further stabilized by two electron-rich aromatic groups, through an intramolecular proton transfer. Subsequent cyclization and deprotonation afford products **122** (Scheme 2.34).

Encouraged by these results, Shi et al. further explored such cascade electrophilic attack, followed by Friedel–Crafts reaction process of VDCPs **1** with other electrophiles such as enynols **126**. Using $Nd(OTf)_3$ as the catalyst, tricyclic compounds **127** can be formed in acceptable to high yields in these cases (Scheme 2.35) [52].

Plausible mechanism for the formation of tricyclic products **127a** is shown in Scheme 2.36. First, the reaction of enynol **126a** with $Nd(OTf)_3$ generates cationic intermediate **128a**, which can transform to its resonant cationic intermediate **129a**. The reaction of **129a** with VDCP **1b** gives the corresponding cyclopropyl

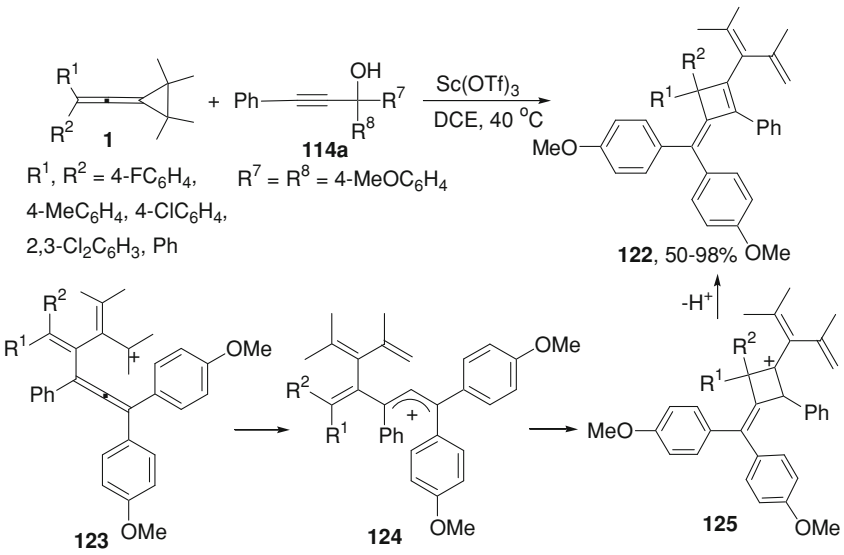


Scheme 2.33 Plausible mechanism for the Lewis acid-catalyzed reactions of VDCPs **1** with 1,1,3-triarylprop-2-yn-1-ols **114** or their methyl ethers **115**

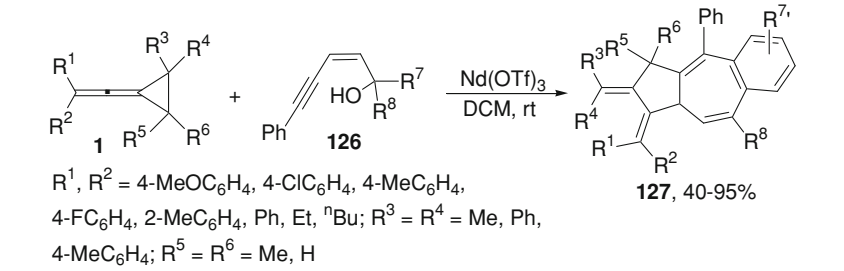
ring-opened π-allylic cationic intermediate **130a**. In this case, the reaction of intermediate **129a** with VDCP **1b** can take place more easily than that of intermediate **128a** presumably because intermediate **129a** is less sterically hindered than intermediate **128a**. Intermediate **130a**, through intramolecular electrophilic attack, affords intermediate **131a**, which undergoes intramolecular Friedel–Crafts reaction to give the final product **127a**.

The reactions were further extended to enol **132a** and dienol **133a**, and the [3 + 2] cycloaddition products **134a** and **135a** were obtained with the reactions of VDCP **1b** (Scheme 2.37).

Plausible mechanism for the formation of products **134a** and **135a** is depicted below: first, treatment of **132a** or **133a** with $Nd(OTf)_3$ gives cationic intermediate **136**, which will transform to its resonant intermediate **137** via allylic rearrangement. Subsequently, the reaction of intermediate **137** with VDCP **1b** affords the cyclopropyl ring-opened π-allylic cationic intermediate **138**, which can either furnish intermediate **139a** (n = 1) or intermediate **140a** (n = 2) via intramolecular electrophilic attack. Nucleophilic attack by the in situ generated H_2O at intermediate **139a** affords the final product **134a**. Alternatively, intermediate **140a** undergoes deprotonation to afford the final product **135a** (Scheme 2.38).

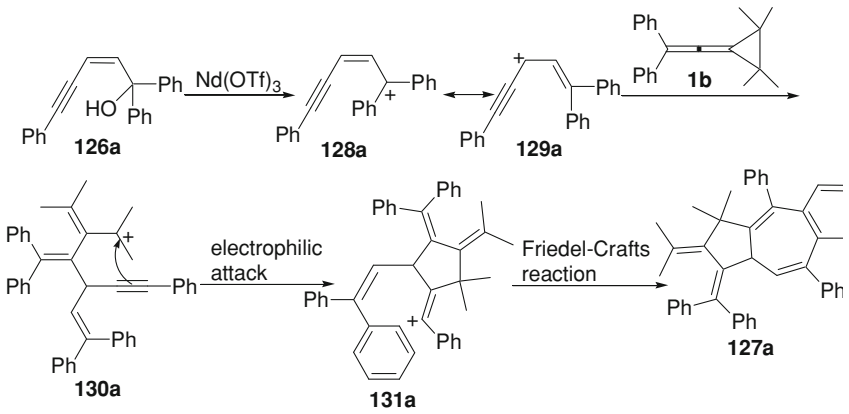


Scheme 2.34 Lewis acid-catalyzed reactions of VDCPs **1** with 1,1,3-triarylprop-2-yn-1-ol **114a**

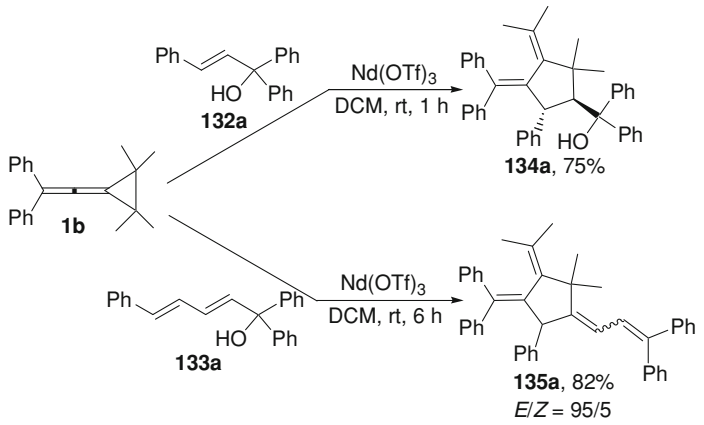


Scheme 2.35 $Nb(OTf)_3$-catalyzed reactions of VDCPs **1** with enynols **126**

When *N*-(4-hydroxy-4,4-diarylbut-2-ynyl)-4-methyl-*N*-prop-2-ynylbenzene-sulfonamides (1,6-diynes) **141** and *N*-allyl-*N*-(4-hydroxy-4,4-diarylbut-2-ynyl)-4-methylbenzenesulfonamides (1,6-enynes) **142** were tested as the partners, the reactions with VDCPs **1** can produce polycyclic compounds **143** and **144** as well as isopropylidene-3,3-diarylcyclobut-1-enyl-methyl derivatives **145** in good to high yields depending on the substituents on VDCPs **1** and substrates **141** and **142** [53]. For instance, Lewis acid $Sn(OTf)_2$ or $BF_3{\cdot}OEt_2$-catalyzed reactions of VDCPs **1**, bearing four methyl groups on the cyclopropyl ring, with 1,6-diynes **141** and 1,6-enynes **142** can afford polycyclic compounds **143** in moderate to high yields; in particular, VDCPs **1** bearing two phenyl groups at one carbon of the cyclopropyl ring produced the corresponding polycyclic compounds **144** in



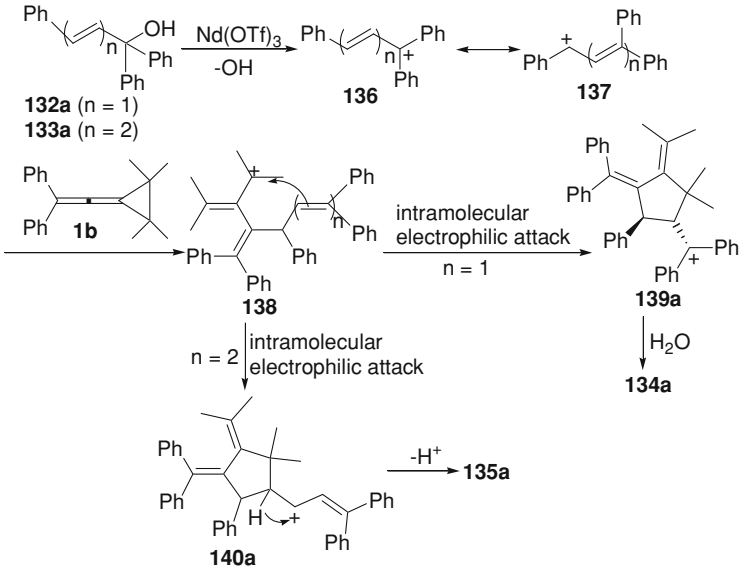
Scheme 2.36 Plausible mechanism for the $Nb(OTf)_3$-catalyzed reaction of VDCP **1b** with enynol **126a**



Scheme 2.37 $Nb(OTf)_3$-catalyzed reactions of VDCP **1b** with enol **132a** and dienol **133a**

51–60% yields. Moreover, the reactions of VDCPs **1** with substrates **141** or **142** bearing strong electron-donating substituents can give products **145** in moderate to high yields (Scheme 2.39).

Plausible mechanism for the formation of products **143** is outlined below based on a cascade rearrangement [54, 55]: Lewis acid (LA)-activating **141** or **142** will give cationic intermediate **146**, which adds to the C1′ position of VDCPs **1** to afford cationic intermediate **147**. Cyclization of intermediate **147** produces



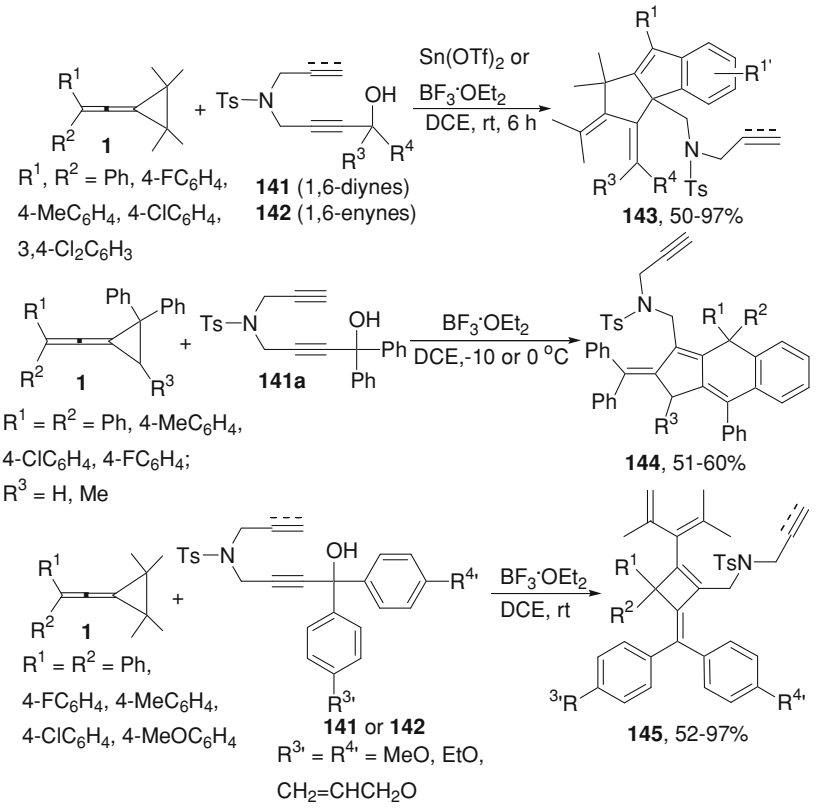
Scheme 2.38 Plausible mechanism for the $Nb(OTf)_3$-catalyzed reactions of VDCP **1b** with enol **132a** and dienol **133a**

intermediate **148**, which affords intermediate **149** via the intramolecular Friedel–Crafts reaction with the adjacent aromatic R^3 group. Aromatization of intermediate **149** furnishes polycyclic compounds **143** (Scheme 2.40).

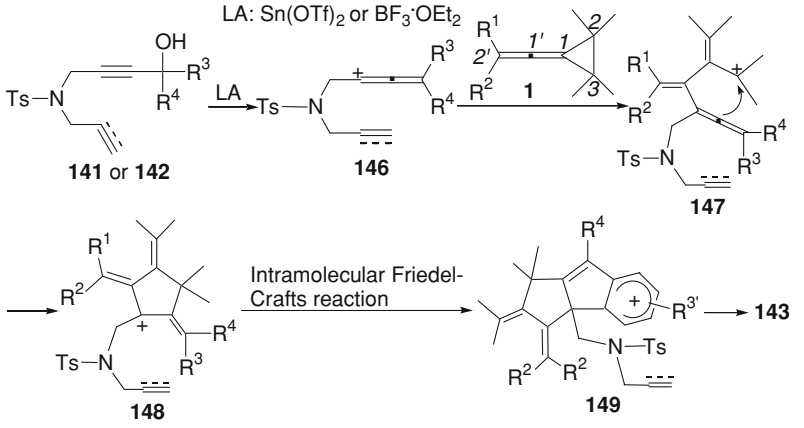
Plausible mechanism for the formation of products **144** is indicated in Scheme 2.41. Similarly, intermediates **146a**, **150** and **151** will be formed in the Lewis acid-catalyzed reactions of **141a** with VDCPs **1**. In this case, the allylic rearrangement of intermediate **151** gives intermediate **152**, which is further stabilized by the two aryl groups and undergoes intramolecular Friedel–Crafts reaction with the adjacent phenyl ring to afford products **144**. The intramolecular Friedel–Crafts reaction with the adjacent phenyl ring of intermediate **152** can take place more easily than that of intermediate **151** since the cyclic cation in intermediate **151** is a sterically tight species which should be more difficult to go through an intramolecular Friedel–Crafts reaction. This is the reason why products **144** were obtained solely in the reactions of VDCPs **1** with two phenyl groups at one carbon of the cyclopropyl ring.

In the case of strong electron-donating groups substituted **141** ($R^3 = R^4 =$ strong electron-donating phenyl rings) were used, similarly, intermediate **154** is formed firstly. Then intermediate **154** will transform to intermediate **155** via an intramolecular proton transfer, which can be stabilized by two electron-rich aromatic groups (R^3 and R^4). Finally, the intramolecular cyclization and deprotonation affords products **145** (Scheme 2.42).

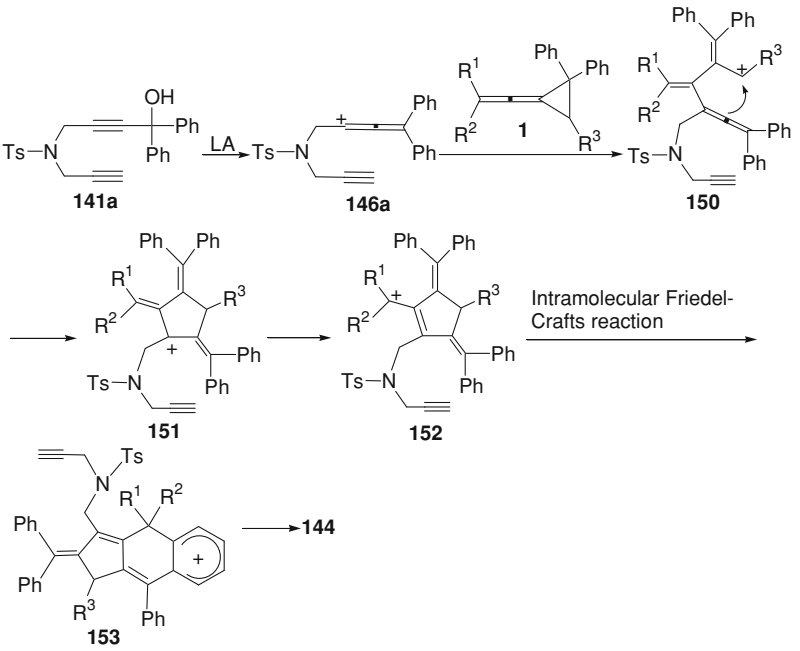
VDCPs **1** can also react with xanthydrol in the presence of $BF_3{\cdot}OEt_2$ to give the corresponding conjugated triene derivatives **157** in moderate to high yields under mild conditions (Scheme 2.43) [56, 57].



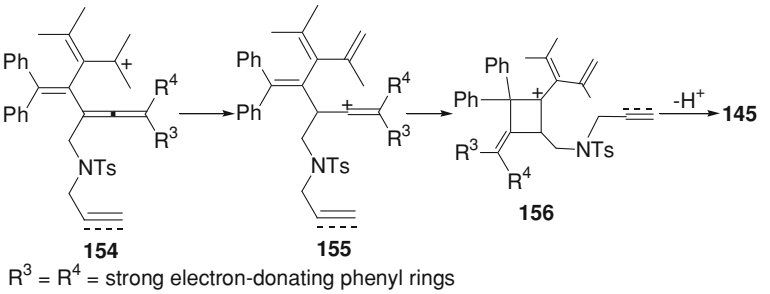
Scheme 2.39 Lewis acid-catalyzed reactions of VDCPs **1** with 1,6-diynes and 1,6-enynes



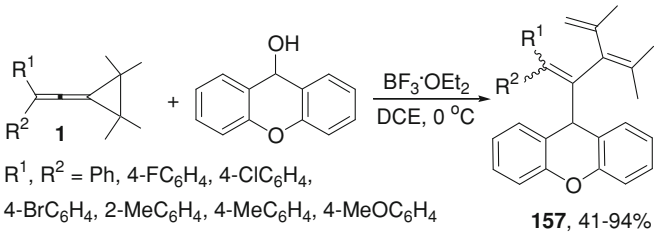
Scheme 2.40 Plausible mechanism for the formation of products **143**



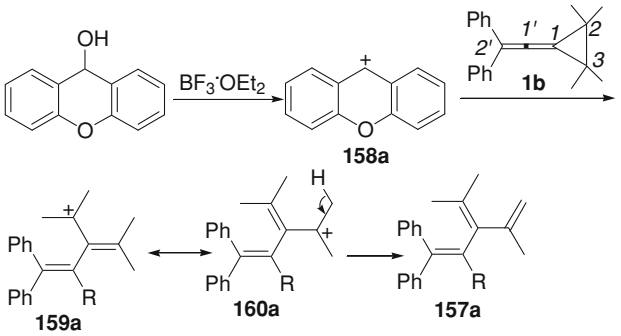
Scheme 2.41 Plausible mechanism for the formation of products **144**



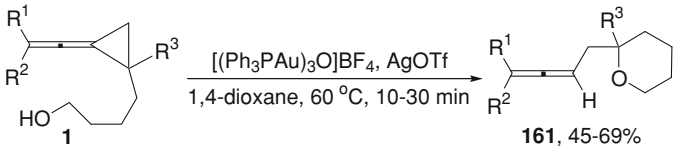
Scheme 2.42 Plausible mechanism for the formation of products **145**



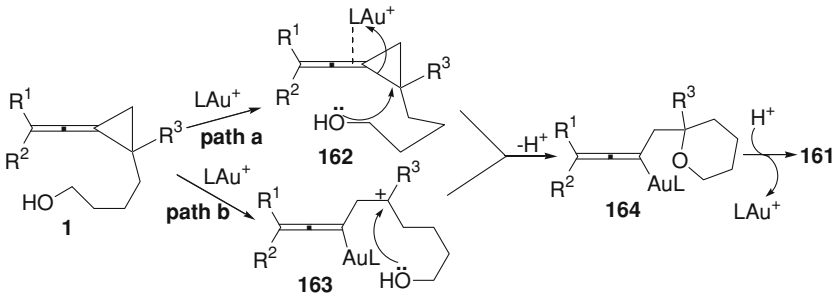
Scheme 2.43 $BF_3{\cdot}OEt_2$-catalyzed reactions of VDCPs **1** with xanthydrol



Scheme 2.44 Plausible mechanism for the $BF_3{\cdot}OEt_2$-catalyzed reactions of VDCPs **1** with xanthydrol. Reprinted from Tetrahedron, Vol 66, Wei Yuan, Min Shi, Reactions of vinylidenecyclopropanes with xanthydrol and xanthenes, Pages 7104–7111, Copyright 2011, with permission from Elsevier

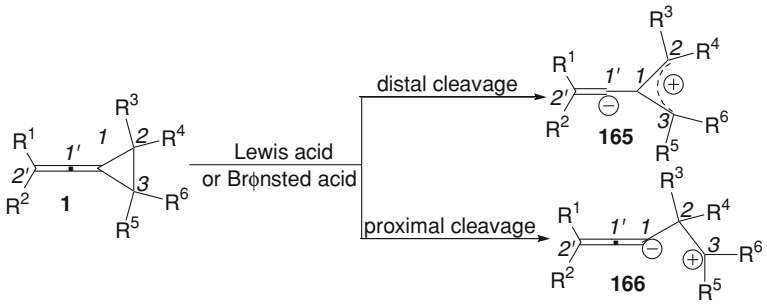


Scheme 2.45 Lewis acid-catalyzed intramolecular ring-opening reaction of VDCPs **1** tethered with alcohol chains



Scheme 2.46 Plausible mechanism for the formation of products **161**. Reprinted with the permission from Ref. [58]. Copyright 2011 American Chemical Society

Plausible mechanism for the reaction of VDCPs **1** with xanthydrol catalyzed by $BF_3{\cdot}OEt_2$ is outlined in Scheme 2.44 using VDCP **1b** as the model. Initially, intermediate **158a** is formed by treatment of xanthydrol with $BF_3{\cdot}OEt_2$, which adds to the C1′ position of VDCP **1b** to give the cyclopropyl ring-opened resonance-



Scheme 2.47 Brief summary for the Lewis or Brønsted acid-mediated reactions of VDCPs **1**. Reprinted with the permission from Ref. [1]. Copyright 2011 American Chemical Society

stabilized intermediates **159a** and **160a** (allylic cation). Deprotonation of intermediate **160a** affords trienes **157a**.

In 2010, an intramolecular ring-opening reaction of VDCPs **1** tethered with alcohol chains was also established. With the combination of $[(Ph_3PAu)_3O]BF_4$ and AgOTf as the catalyst, allene-functionalized tetrahydropyrans **161** can be formed in moderate yields (Scheme 2.45) [58].

Plausible mechanism for the formation of products **161** is shown in Scheme 2.46. First, Au(I) complex is oxidized to L-Au^+ species by cocatalyst AgOTf prior to attacking VDCPs **1**. The subsequent addition/ring-opening processes can occur through two possible pathways: gold cation works as a Lewis acid to activate the allene functionality, affording intermediate **162** (**path a**) [59–62]; Au(I) catalyzes the ring opening via formation of cationic intermediate **163** (**path b**). The intramolecular nucleophilic addition by the hydroxyl group onto the electrophilic carbon centers in intermediates **162** or **163** gives the same intermediate **164**, which produces the corresponding tetrahydropyran derivatives **161** followed by protonation along with the regeneration of Au(I) species for the catalytic cycles.

In summary, the reaction course of VDCPs **1** promoted by Lewis or Brønsted acid can be categorized into the following two patterns: the distal bond and proximal bond cleavage. As can be seen from Scheme 2.47, zwitterionic ions **165** and **166** were formed with these two bond cleavage patterns. To obtain stable zwitterionic ions such as **165** and **166**, the substituents as R^3, R^4, R^5, and R^6 on the cyclopropyl ring cannot be hydrogen atoms at the same time in most cases [1].

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Chapter 3
Transition Metal-Catalyzed Transformations of VDCPs

Abstract Transition metals such as palladium and rhodium-catalyzed transformations of vinylidenecyclopropanes are introduced in this chapter.

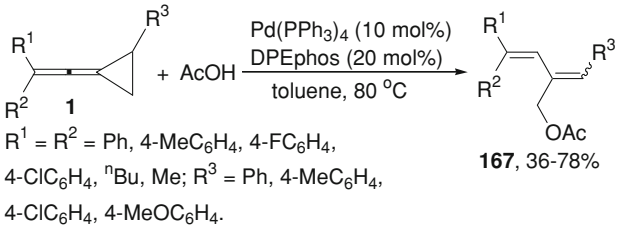
Keywords Vinylidenecyclopropanes · Transition metal · Palladium · Rhodium · Coupling reaction

In 2006, Shi et al. reported that the Pd(0)-catalyzed reactions of VDCPs **1** with acetic acid can proceed efficiently to give the corresponding cyclopropyl ring-opened acetylated dienes **167** in moderate to good yields in the presence of bis[(2-diphenylphosphino)phenyl] ether (DPEphos) ligand under mild reaction conditions (Scheme 3.1) [1–4].

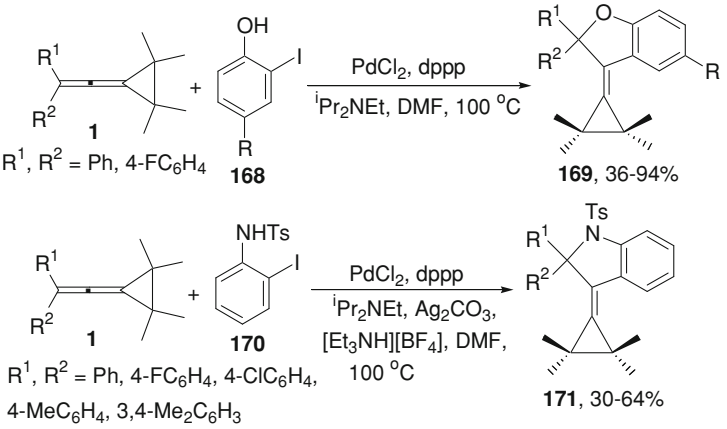
In 2009, Shi and co-workers reported the palladium-catalyzed coupling reactions of VDCPs **1** with 2-iodophenols **168** and *N*-(2-iodophenyl)-4-methylbenzenesulfonamide **170**. For instance, using $PdCl_2$ as the catalyst, and 1,3-bis(diphenylphosphanyl)propane (dppp) as the ligand in the presence of $^{i}Pr_2NEt$, 2,2-diaryl-3-(tetramethylcyclopropylidene)-2,3-(dihydro) benzofuran **169** can be obtained in 36–94% yields. In addition, using $PdCl_2$ as the catalyst, and dppp as the ligand in the presence of $^{i}Pr_2NEt$, Ag_2CO_3 and $[Et_3NH][BF_4]$, 2,2-diaryl -3-tetramethylcyclopropylidene-1-(toluene-4-sulfonyl)-2,3-dihydro-1*H*-indole derivatives **171** can be formed in 30–64% yields (Scheme 3.2) [5].

Treatment of VDCPs **1** with $PdCl_2$ can afford novel dimeric allylpalladium(II) complexes **172** or **173** depending on the substituents attached on the cyclopropyl ring of VDCPs **1**. For example, with VDCPs **1** in which both of R^3 and R^4 are methyl groups, dimeric allylpalladium(II) complexes **172** can be obtained in acceptable to moderate yields; whereas with VDCPs **1** in which R^1, R^2, R^3, and R^4 are aryl groups, dimeric allylpalldium(II) complexes **173** were formed in moderate to good yields as the major products, in which case when R^3 and R^4 as well as R^1 and R^2 are aryl groups bearing electron-donating groups, the $PdCl_2$-catalyzed

L. Shao et al., *Chemical Transformations of Vinylidenecyclopropanes*, SpringerBriefs in Molecular Science, DOI: 10.1007/978-3-642-27573-9_3,



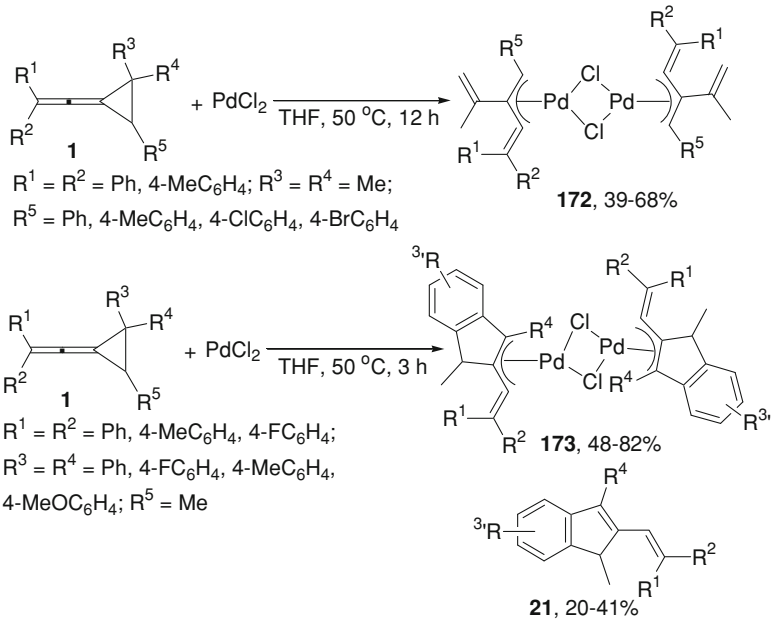
Scheme 3.1 Palladium-catalyzed reactions of VDCPs **1** with acetic acid. Reprinted with the permission from [1]. Copyright 2011 American Chemical Society



Scheme 3.2 Palladium-catalyzed coupling reactions of VDCPs **1** with iodides

rearrangement products **21** will be obtained as the minor products (Scheme 3.3) [6].

On the basis of the above results, plausible mechanism for the formation of dimeric allylpalladium(II) complexes **172** and **173** is outlined in Scheme 3.4. The coordination of $PdCl_2$ with VDCPs **1** produces the initial zwitterionic intermediate **174**, from which the corresponding cyclopropyl ring-opened zwitterionic intermediate **175** is formed. Intermediate **175** can exist as intermediate **176** and its resonance-stabilized intermediate **176′**. As for VDCPs **1** in which both of R^3 and R^4 are methyl groups and R^5 is an aryl group, intermediate **176** is a more reactive species since it bears two alkyl groups R^3 and R^4 at the C2 position, which can be easily transformed to the corresponding intermediate **177** along with the elimination of HCl. Then, the corresponding dimeric allylpalladium(II) complexes **172** are produced from intermediate **177**. On the other hand, for VDCPs **1** in which both of R^3 and R^4 are aryl groups and R^5 is methyl group, intermediate **176′** is more reactive species, which

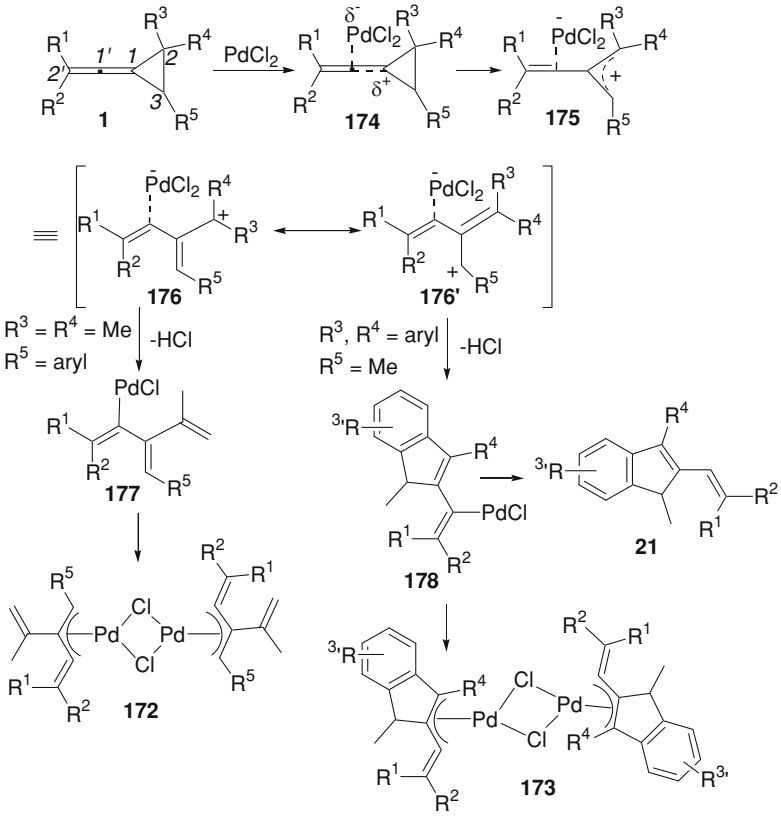


Scheme 3.3 Reactions of VDCPs **1** with $PdCl_2$

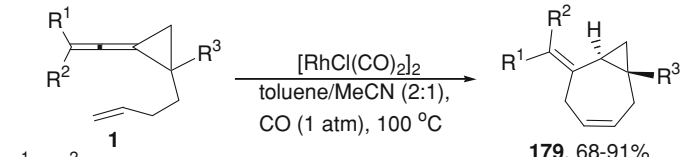
easily undergoes intramolecular Friedel–Crafts reaction with the adjacent aromatic group at the C2 position (R^3 group) to afford the corresponding intermediate **178** along with the elimination of HCl. Intermediate **178** can be transformed to the corresponding dimeric allylpalladium(II) complexes **173** as well as products **21** by protonation. If R^3 and/or R^4 are/is electron-rich aromatic group(s), the intramolecular Friedel–Crafts reaction is facilitated, so the formation of products **21** is favored in these cases.

An efficient catalytic system for the intramolecular ene reaction of alkene moiety attached VDCPs **1** was also established by Shi's group. For example, using $[RhCl(CO)_2]_2$ as the catalyst in co-solvent of toluene and acetonitrile, the reaction was achieved to afford bicycle[5.1.0]octylene derivatives **179** in moderate to high yields (Scheme 3.5) [7].

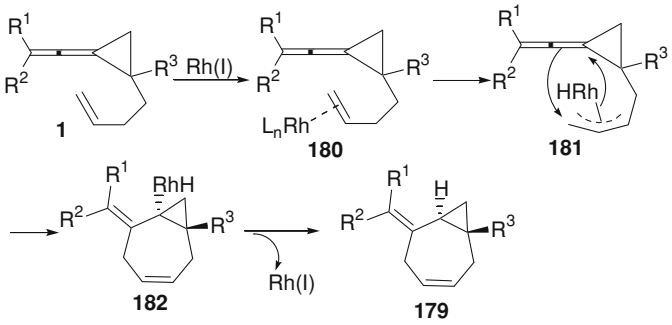
As in a similar mechanism proposed by Taw et al. and Prater et al. [8, 9], plausible mechanism for the formation of products **179** is outlined in Scheme 3.6. First, the terminal alkene in VDCPs **1** can be coordinated to Rh(I) metal center to generate intermediate **180**. Subsequently, the oxidative addition of Rh(I) center into the neighboring allylic C–H bond gives a π-allyl Rh-H species **181** [10–12], which leads to a seven-membered carbocyclic Rh-H species **182** through an intramolecular cycloaddition to the allene moiety. Finally, reductive elimination affords the products **179** along with the regeneration of the Rh(I) catalyst.



Scheme 3.4 Pausible mechanism for the reactions of VDCPs **1** with $PdCl_2$. Reprinted with the permission from [6]. Copyright 2011 American Chemical Society



Scheme 3.5 Rhodium-catalyzed intramolecular ene reactions of VDCPs **1**



Scheme 3.6 Plausible mechanism for the rhodium-catalyzed intramolecular ene reactions of VDCPs **1**. Reprinted with the permission from [7]. Copyright 2011 American Chemical Society

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Chapter 4
Reactions of VDCPs with Electrophiles

Abstract Reactions of vinylidenecyclopropanes with a variety of electrophiles such as diaryl diselenide, iodine, bromine, *N*-fluorodibenzenesulfonimide (NFSI), and *N*-bromosuccinimide are shown in this chapter.

Keywords Vinylidenecyclopropanes · Electrophilic addition · Ring-opening · Rearrangement

An interesting addition reaction of VDCPs **1** with diaryl diselenide **183** catalyzed by iodosobenzene diacetate was first reported by Shi's group. The corresponding addition products **184** could be obtained in moderate to good yields under mild conditions (Scheme 4.1) [1, 2].

Shi et al. also investigated the reactions between VDCPs **1** and *N*-fluorodibenzenesulfonimide (NFSI) and the corresponding fluorinated derivatives **185** can be achieved in good to high yields (Scheme 4.2) [3].

Plausible mechanism for the reactions of VDCPs **1** with NFSI is outlined in Scheme 4.3. Initially, the fluoric cation F^+ and the anionic intermediate $(PhSO_2)_2N^-$ are generated from NFSI under the stardard reaction conditions [4–6]. Then the fluoric cation F^+ adds to the C1′ position of VDCPs **1** to give cationic intermediate **186**. Intermediate **186** can give the cyclopropyl ring-opened cationic intermediate **187**, which can be transformed to the final products **185** via deprotonation.

It was also found that VDCPs **1** can undergo ring-opening reactions upon treatment with iodine or bromine at 0–25 °C in DCE to give the corresponding iodinated or brominated naphthalene derivatives **188** or **189** in low to high yields within 3 h (Scheme 4.4) [1, 7].

In the following research, it was observed that the reactions of VDCPs **1** with equimolar amount of bromine or iodine at low temperature can produce the corresponding addition products **190–192**, depending on the nature of VDCPs, in moderate to good yields at −40 and −100 °C, respectively. In addition, the

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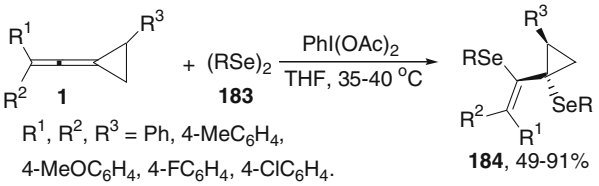
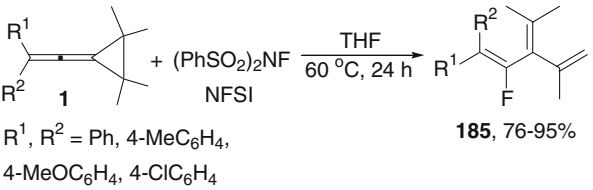
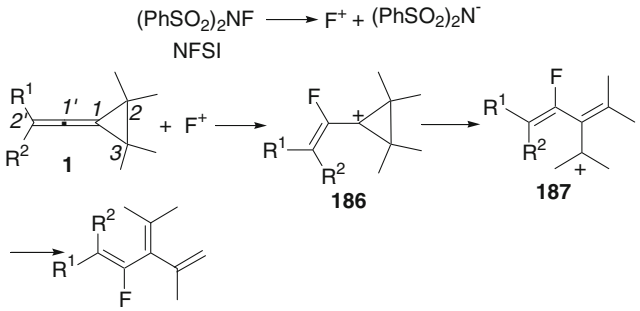


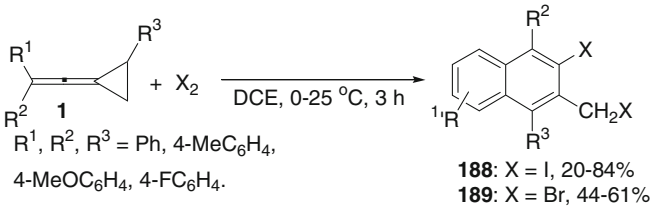
Scheme 4.1 $PhI(OAc)_2$−mediated reactions of VDCPs **1** with diaryl diselenide. Reprinted with the permission from Ref. [1]. Copyright 2011 American Chemical Society



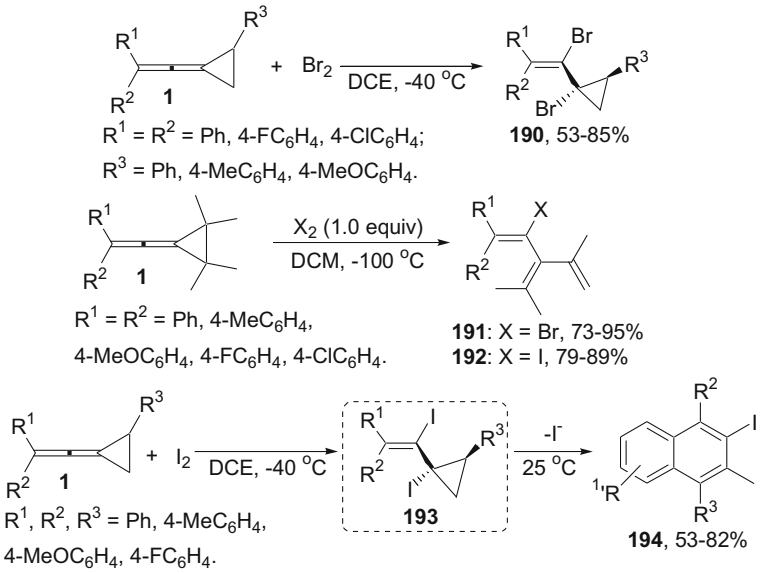
Scheme 4.2 Reactions of VDCPs **1** with NFSI



Scheme 4.3 Plausible mechanism for the reactions of VDCPs **1** with NFSI. Reprinted from Ref. [3]. Copyright 2011, with permission from Elsevier



Scheme 4.4 Reactions of VDCPs **1** with I_2 and Br_2 at 0–25 °C. Reprinted with the permission from Ref. [1]. Copyright 2011 American Chemical Society



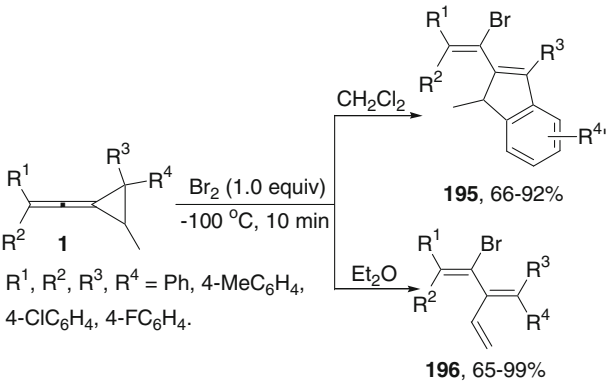
Scheme 4.5 Reactions of VDCPs **1** with I_2 and Br_2 at −40 or −100 °C. Reprinted with the permission from Ref. [1]. Copyright 2011 American Chemical Society

reactions of VDCPs **1** with equimolar amount of iodine gave the corresponding iodinated naphthalene derivatives **194** presumably derived from the corresponding addition products **193** at 25 °C (Scheme 4.5) [1, 8].

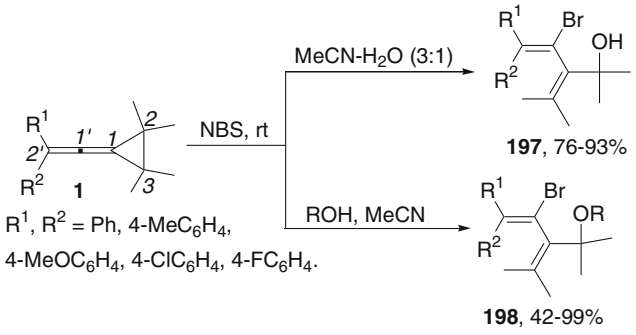
Interestingly, a drastic solvent effect was found to result in different products during the investigation on the reactions of VDCPs **1** with bromine. For example, the brominated indene derivatives **195** were obtained in good to high yields in DCM at −100 °C; however, the brominated conjugate triene derivatives **196** were obtained in diethyl ether at the same temperature (Scheme 4.6) [1, 9].

VDCPs **1** can also undergo hydrobromination or alkoxybromination in the presence of *N*-bromosuccinimide (NBS) and water or alcohols to give the corresponding vinylbromohydrin **197** and vinylbromoalkoxy derivatives **198** in moderate to excellent yields at room temperature (Scheme 4.7) [1, 10].

Huang et al. investigated the halohydroxylation reactions of VDCPs **1** carefully and they found that highly regioselective halohydroxylations of bicyclic VDCPs **1** can be achieved to give four types of products: **199**–**202**, depending on the reaction conditions and the size of the ring of VDCPs **1** [11]. For example, the halohydroxylation reactions of bicyclic VDCPs **1**, in the presence of 1.2 ∼ 1.5 equiv. of *N*-bromosuccinimide (NBS) or *N*-iodosuccinimide (NIS), occur smoothly at room temperature to give the cyclopropyl ring-kept products **199** in moderate to high yields with high regio- and diastereo-selectivity; the reactions between bicyclic VDCPs **1** and 2.0 equiv. of NBS at 100 °C afford products **200** in 48–75% yields by proximal cleavage of the cyclopropyl ring (Scheme 4.8).



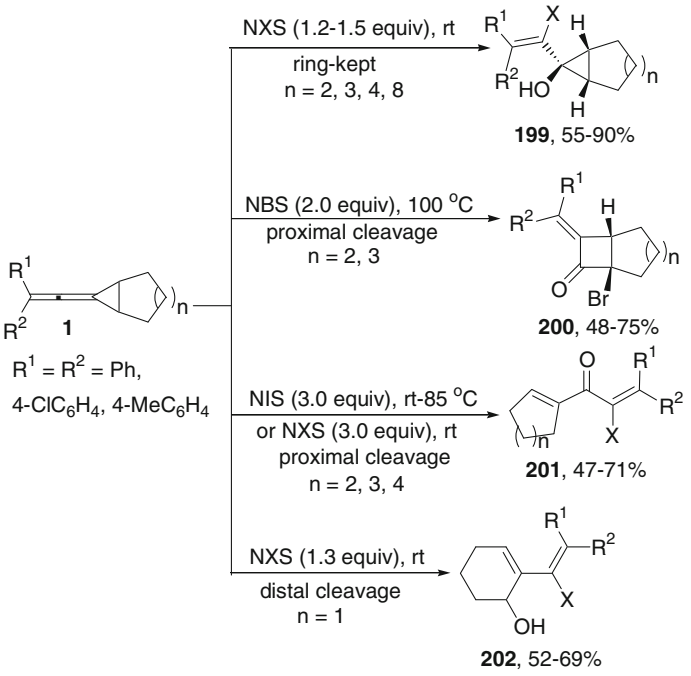
Scheme 4.6 Reactions of VDCPs **1** with Br_2 at −100 °C in different solvents. Reprinted with the permission from Ref. [1]. Copyright 2011 American Chemical Society



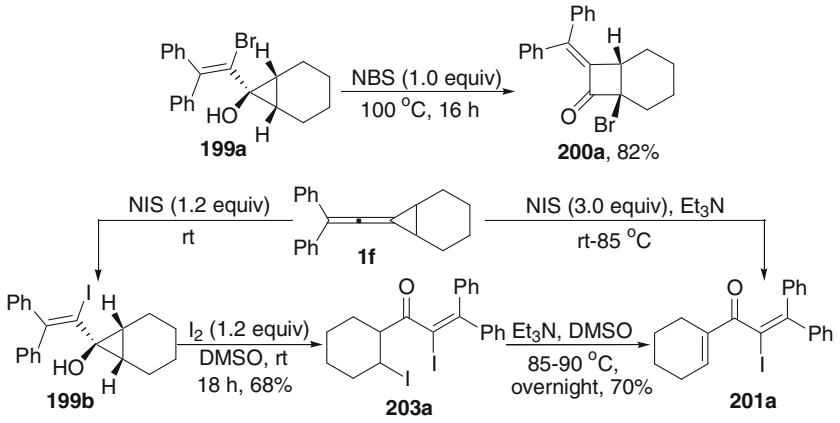
Scheme 4.7 Reactions of VDCPs **1** with NBS. Reprinted with the permission from Ref. [1]. Copyright 2011 American Chemical Society

Further studies showed that treatment of product **199a** with NBS (1.0 equiv.) at 100 °C, the ring-expansion product **200a** can be achieved in 82% yield; treatment of product **199b** with I^+ in DMSO at room temperature for 18 h, intermediate **203a** can be obtained in 68% yield; in addition, further treatment of intermediate **203a** at 85–90 °C in the presence of Et_3N smoothly furnished **201a** in 70% yield (Scheme 4.9).

On the basis of the above control experiments and the obtained intermediate **203a**, plausible mechanism for the formation of products **199–201** is shown in Scheme 4.10 with VDCP **1f** as the model. Initially, X^+ adds to C1′–C1 double bond of VDCP **1f** to give the halonium intermediate **204**, which is selectively attacked by H_2O from the less sterically hindered side to produce the ring-kept halohydroxylation products **199** with high diastereoselectivity. In the presence of another equivalent of NBS at 100 °C, the addition of bromonium ion to the double bond induces ring enlargement to give the dibromocyclobutanone intermediate

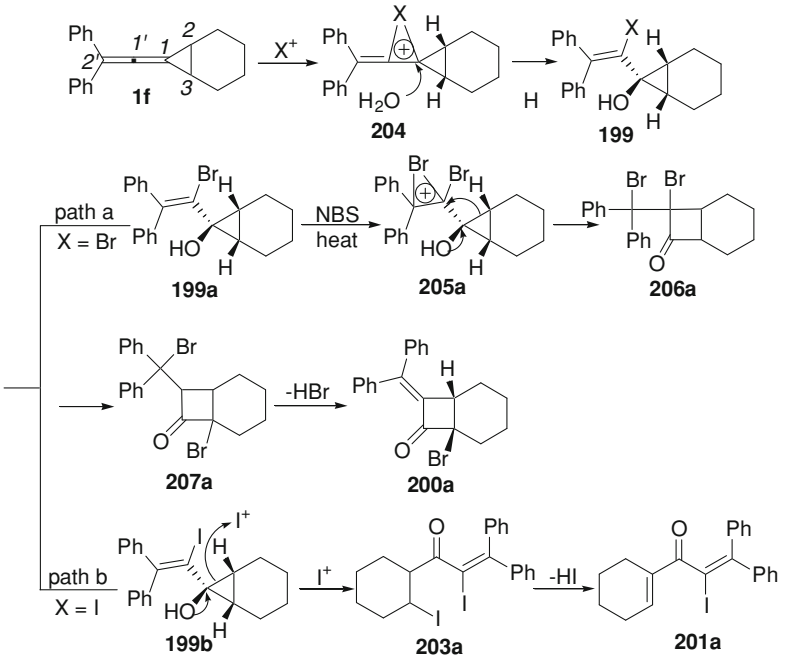


Scheme 4.8 Reactions of bicyclic VDCPs **1** with NBS or NIS

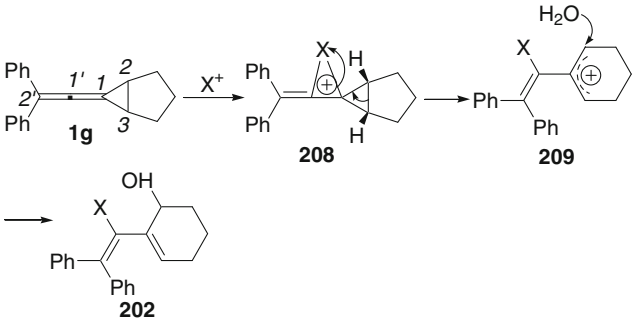


Scheme 4.9 Control experiments for the reactions of bicyclic VDCP **1f** with NBS or NIS. Reprinted with the permission from Ref. [11]. Copyright 2011 Wiley John and Sons

206a. Then a rearrangement occurs with bromine atom migration mediated by HBr to afford intermediate **207a** [12, 13], which eliminates one molecular of HBr to furnish product **200a** (**path a**). However, in the presence of I^+, a different



Scheme 4.10 Plausible mechanism for the reactions of VDCPs **1** with NBS or NIS. Reprinted with the permission from Ref. [11]. Copyright 2011 Wiley John and Sons



Scheme 4.11 Plausible mechanism for the formation of product **202**. Reprinted with the permission from Ref. [11]. Copyright 2011 Wiley John and Sons

electrophilic ring-opening reaction of **199b** occurs with high stereoselectivity to give intermediate **203a**, which eliminates one molecular of HI to achieve product **201a** (**path b**).

Formation of products **202** is proposed in Scheme 4.11 with VDCP **1g** as the model. Initially, X^+ adds to C1′–C1 double bond of VDCP **1g** to give the halonium

ion intermediate **208**, which undergoes a ring-expansion process to afford intermediate **209**. Then attack of H_2O to intermediate **209** furnishes products **202**. Maybe the formation of intermediate **209** as a six-membered ring cation is thermally favored in this case, thus results in the different reaction pattern.

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Chapter 5
Miscellaneous Analogs

Abstract The reactions of vinylidenecyclopropanes (VDCPs) **1**, which cannot be classified into the foregoing chapters, are shown in this chapter. In this chapter, Brønsted base-mediated as well as radical reaction, cycloaddition reaction and oxidation reaction of vinylidenecyclopropanes are displayed.

Keywords Vinylidenecyclopropanes · Brønsted base · Radical reaction · Cycloaddition reaction · Oxidation reaction

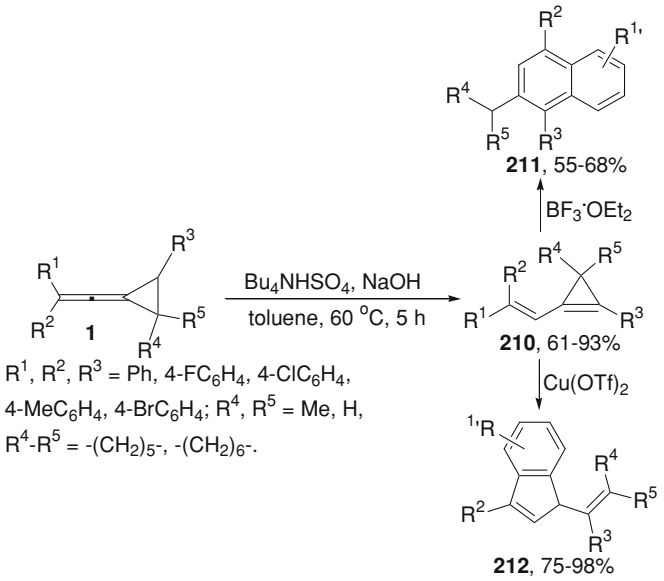
5.1 Brønsted Base-Mediated Transformations of VDCPs

VDCPs **1** can be isomerized to vinylcyclopropenes **210** in good to high yields within 5 h under basic conditions, which can also undergo Lewis acid-catalyzed rearrangement reactions to give the corresponding naphthalenes **211** or indenes **212**, respectively (Scheme 5.1) [1, 2].

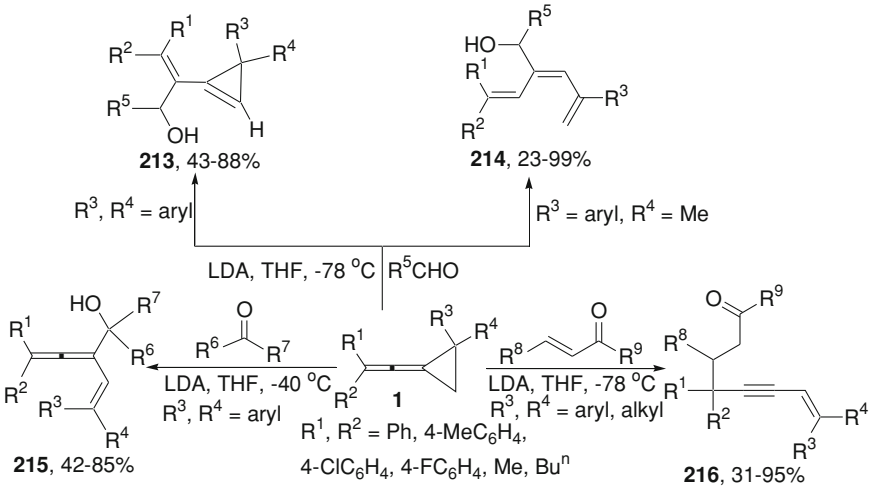
Highly selective addition reactions of VDCPs **1** were realized by treatment with lithium diisopropylamide (LDA) in THF and quenching with aldehydes, ketones, and enones, respectively. A number of vinylcyclopropene derivatives **213**, triene derivatives **214**, allenol derivatives **215**, and 1,3-enyne derivatives **216** can be obtained selectively in moderate to good yields depending on the nature of the R^4 group on the cyclopropyl ring and different electrophiles (Scheme 5.2) [3, 4].

Plausible mechanism for the formation of products **213**–**216** is outlined in Scheme 5.3. Initially, the lithiation of cyclopropyl ring of VDCPs **1** gives the corresponding cyclopropyl carbanion intermediate **217** by treatment with LDA [5]. Intermediate **217** can be transformed to intermediates **218**, **219**, and **220** [6–11]. When both of R^3 and R^4 are aryl groups and aldehydes are used as the electrophiles, vinylcyclopropene derivatives **213** are formed through intermediate **221**

L. Shao et al., *Chemical Transformations of Vinylidenecyclopropanes*, SpringerBriefs in Molecular Science, DOI: 10.1007/978-3-642-27573-9_5,

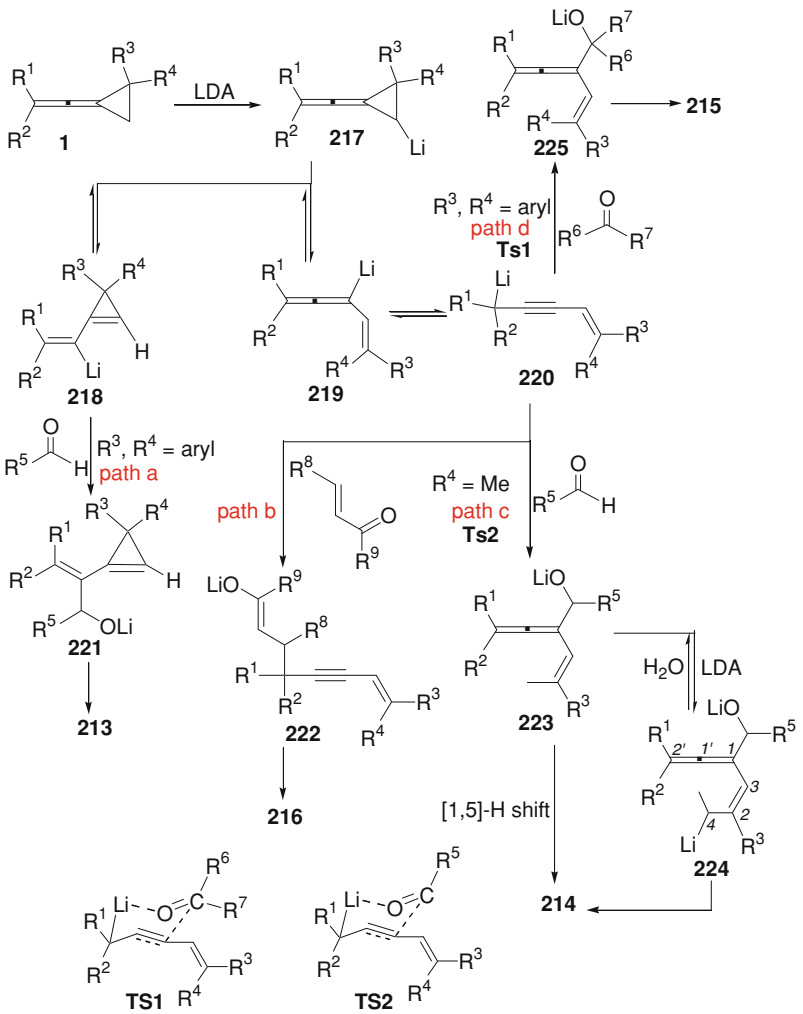


Scheme 5.1 Brønsted base-mediated isomerization of VDCPs **1** and further transformation of the isomerized products. Reprinted with the permission from Ref. [1]. Copyright 2011 American Chemical Society



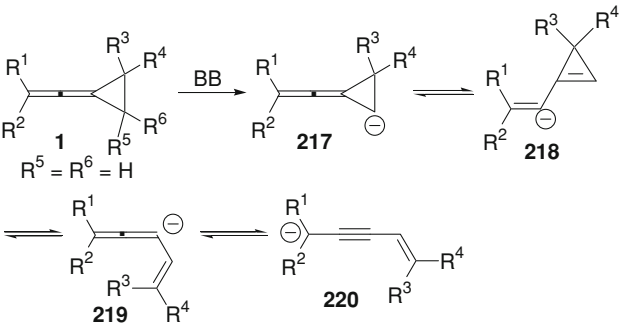
Scheme 5.2 LDA-mediated reactions of VDCPs **1** with aldehydes, ketones, and enones

(**path a**). When ketones are used as the electrophiles, allenol derivatives **215** are obtained by the reaction of intermediate **220** with ketones through intermediate **225** and it is conceivable that a six-membered transition state TS1 is concerned in



Scheme 5.3 Plausible mechanism for the LDA-mediated reactions of VDCPs **1** with aldehydes, ketones and enones

this reaction (**path d**). The different reactivity between aldehydes and ketones may be due to the steric effect of the two electrophiles. When R^4 is methyl and aldehydes are used as the electrophiles, intermediate **223** is formed by the reaction of intermediate **220** with aldehydes through a six-membered transition state TS2, which undergoes a [1,5-H] shift to produce the triene derivatives **214** [12]. When CO_2 was used as the electrophile, similar transformations of VDCPs **1** were achieved. See [13]. Alternatively, intermediate **224** can be formed by lithiation of intermediate **223** (R^4 is methyl), which undergoes a [1,5]-lithium shift to give products **214**. During the two possible pathways, the ambient water can take part in



Scheme 5.4 Brief summary for the Brønsted base-mediated transformations of VDCPs **1**. Reprinted with the permission from Ref. [1]. Copyright 2011 American Chemical Society

the process to partially replace the lithium with proton, which was further confirmed by the deuterium-labeling experiment (**path c**). When enones are used as the electrophiles, intermediate **222** is formed by reaction of intermediate **220** with enones and subsequently 1,3-enyne derivatives **216** are obtained, presumably as the lithiated sp^3 carboanion prefers such Michael addition (**path b**) .When ynones were used as the electrophiles, novel domino carbolithiation reactions of VDCPs **1** were achieved. See [14].

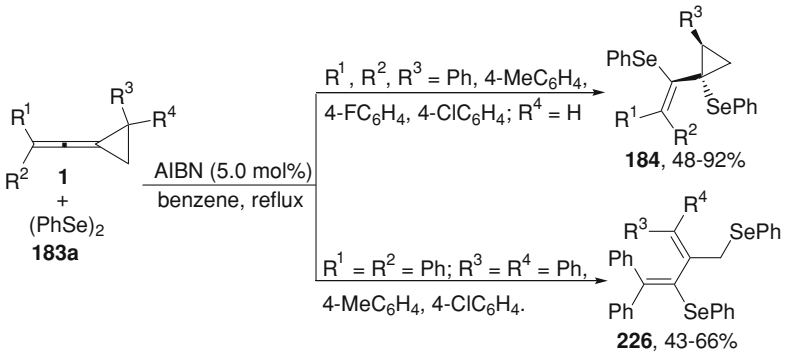
In these reactions, there may be an equilibrium between the lithiated anions such as **217**–**220**. To carry out these reactions smoothly, both of the substituents on one carbon of the cyclopropyl ring of VDCPs **1** should be hydrogen atoms ($R^5 = R^6 = H$); at the same time, R^3 and R^4 can be both aryl or alkyl groups or one of them is an aryl group and the other is an alkyl group, and neither of them can be hydrogen atom (Scheme 5.4).

5.2 Radical Reactions of VDCPs

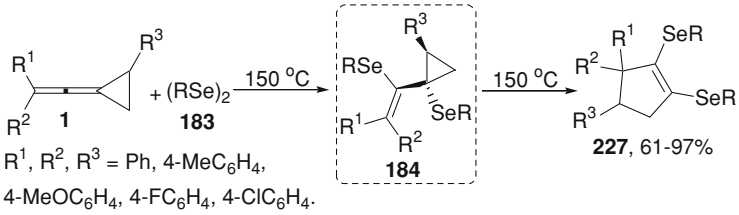
It was found that the reactions of VDCPs **1** with diphenyl diselenide **183a** could also take place in the presence of AIBN to produce the corresponding products **184** or **226** in moderate to good yields under mild conditions (Scheme 5.5) [1, 15].

VDCPs **1** can also undergo the reaction with diaryl diselenide **183** upon heating at 150 °C to give the corresponding 1,2-diarylselenocyclopentene derivatives **227** in moderate to excellent yields, in which the cyclized products are confirmed to be formed from the rearrangement of the normal addition products **184** upon heating (Scheme 5.6) [16].

In 2003, Mizuno et al. reported the cyclopropanation reactions of VDCPs **1** with CHX_3 as the precursor of carbene. It was reported that reactions of diaryl-substituted VDCPs **1** (R^1, R^2 = aryl) with dibromocarbene and dichlorocarbene exclusively gave 1-(dihalomethylene)spiropentanes **228** in moderate to high



Scheme 5.5 AIBN-mediated reactions of VDCPs **1** with diphenyl diselenide. Reprinted with the permission from Ref. [1]. Copyright 2011 American Chemical Society

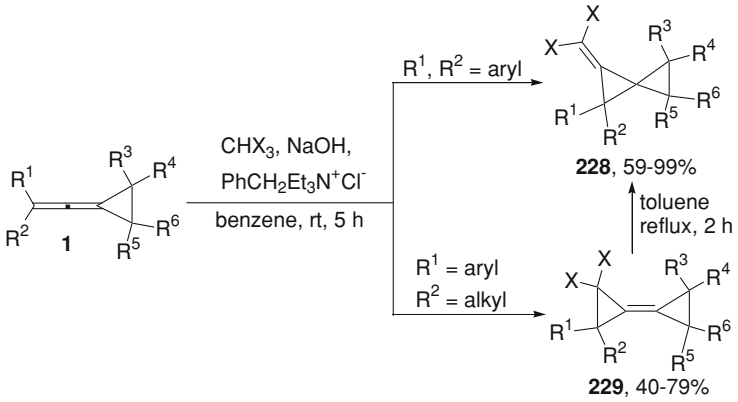


Scheme 5.6 Thermal-induced reactions of VDCPs **1** with diaryl diselenide. Reprinted with the permission from Ref. [1]. Copyright 2011 American Chemical Society

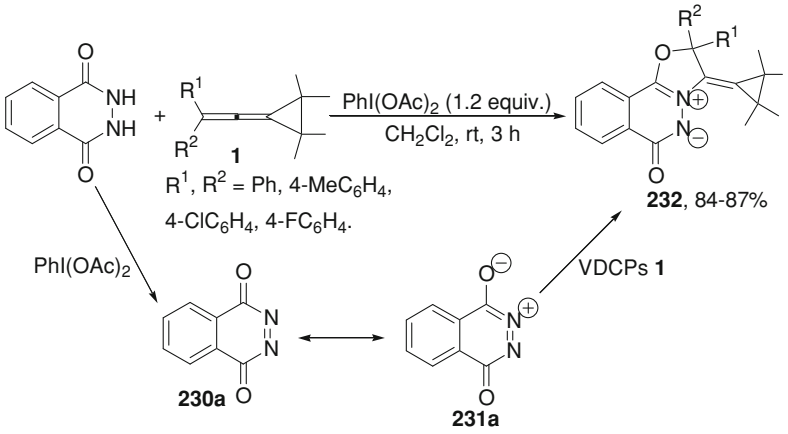
yields, while reactions of monoaryl-substituted VDCPs **1** (R^1 = aryl, R^2 = alkyl) with dihalocarbenes afforded cyclopropylidenecyclopropanes **229** as the major products with the formation of a small amount of **228**. It was also observed that products **229** can be easily converted to products **228** quantitatively in refluxing toluene for 2 h (Scheme 5.7) [17].

5.3 Cycloadditions of VDCPs

Iodobenzene diacetate-mediated reactions of VDCPs **1** with phthalhydrazide can give the corresponding [3 + 2] cycloaddition products **232** in good yields under mild reaction conditions [18]. It was believed that in these reactions, phthalhydrazide was transformed to a 1,3-dipole intermediate in the presence of iodobenzene diacetate. First, iodobenzene diacetate oxidized phthalhydrazide to phthalazine-1,4-dione **230a** [19, 20], which was an equivalent of 1,3-dipole intermediate **231a**. The 1,3-dipole intermediate **231a** reacted with the C1–C1′ double bond of VDCPs **1** to give the corresponding cycloaddition products **232** (Scheme 5.8).



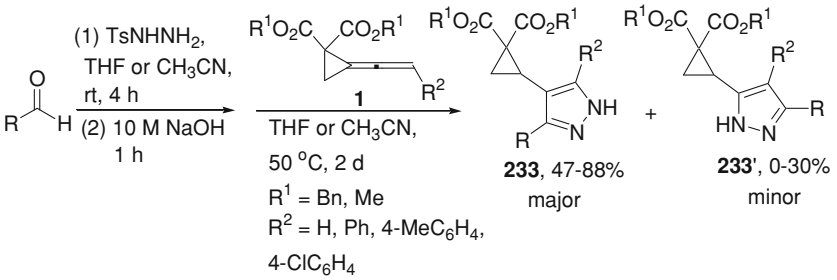
Scheme 5.7 Reactions of VDCPs **1** with dihalocarbenes. Reprinted with the permission from Ref. [1]. Copyright 2011 American Chemical Society



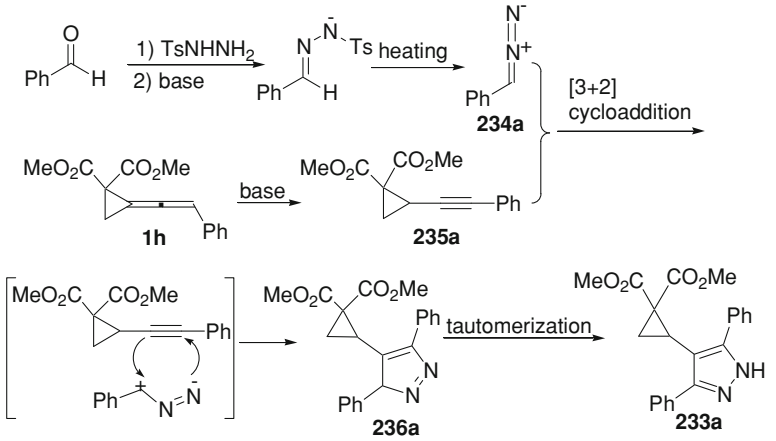
Scheme 5.8 $PhI(OAc)_2$-mediated reactions of VDCPs **1** with phthalhydrazide. Reprinted with the permission from Ref. [1]. Copyright 2011 American Chemical Society

In 2010, Shi et al. reported the 1,3-dipolar cycloaddition reactions of VDCP-diesters **1** with aromatic diazomethanes generated in situ from the corresponding aromatic aldehydes and tosylhydrazine mediated by a base to produce pyrazole derivatives **233** and **233′** in good total yields, with the former as the major, under mild conditions (Scheme 5.9) [21].

On the basis of the above results, plausible mechanism for this [3 + 2] cycloaddition reaction is shown in Scheme 5.10 with the reaction of VDCP **1h** and benzaldehyde as the model. Initially, condensation of tosylhydrazine with benzaldehyde followed by treatment with a base leads to a solution of benzaldehyde tosylhydrazone salt, which upon heating to 50 °C gives phenyl diazomethane



Scheme 5.9 1,3-Dipolar cycloaddition reactions of VDCP-diesters **1**

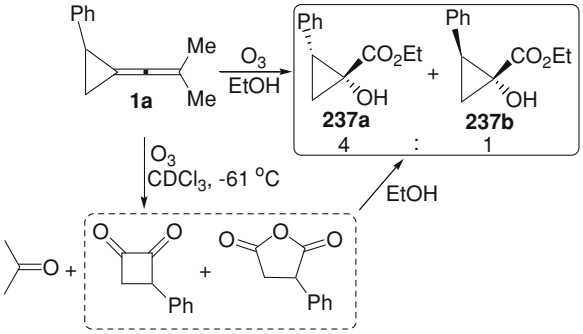


Scheme 5.10 Plausible mechanism for the formation of product **233a**. Reprinted with the permission from Ref. [21]. Copyright 2011 American Chemical Society

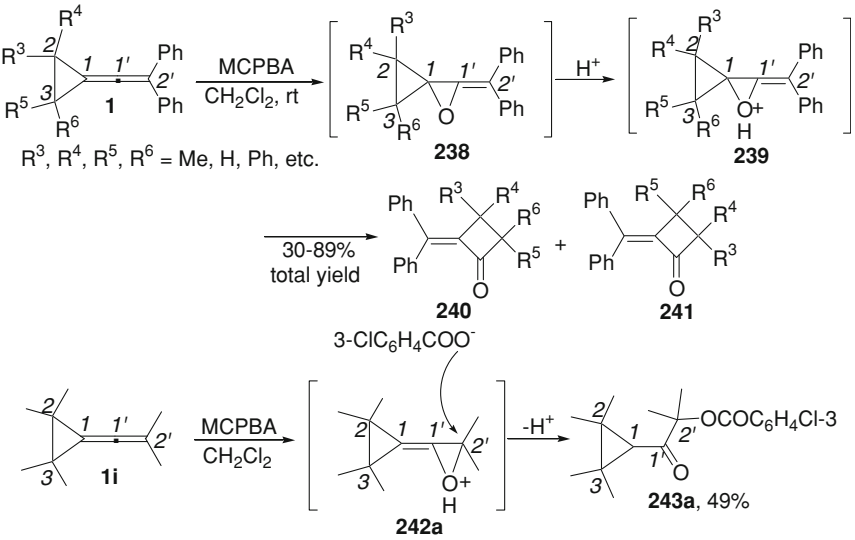
234a. Meanwhile, under the basic condition, VDCP **1h** tautomerizes to its alkyne isomer **235a**, which furnishes intermediate **236a** through [3 + 2] cycloaddition with phenyl diazomethane **234a**. The proton transfer in intermediate **236a** affords the final product **233a**.

5.4 Oxidation Reactions of VDCPs

In 1961, Hartzler et al. reported the ozonolysis reaction of VDCP **1a** in ethanol, in which cyclopropyl hydroxylester **237** was formed in good yield (Scheme 5.11) [1, 22]. Crandall et al. examined this transformation in detail and it was reported that the addition of VDCP **1a** to a saturated solution of ozone (1.0 equiv.) in $CDCl_3$ at −61 °C gave acetone, 3-phenylcyclobutane-1,2-dione and phenylsuccinic



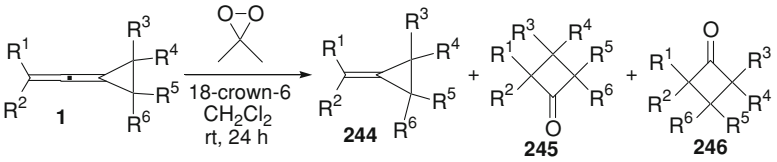
Scheme 5.11 Oxidative reaction of VDCP **1a** with O_3. Reprinted with the permission from Ref. [1]. Copyright 2011 American Chemical Society



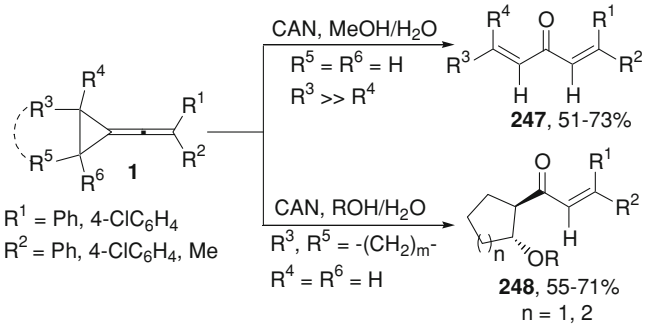
Scheme 5.12 Oxygenation of VDCPs **1** with MCPBA. Reprinted with the permission from Ref. [1]. Copyright 2011 American Chemical Society

anhydride. Treatment of the latter two compounds with excess ethanol can give the esters **237**, which clearly indicates that these two compounds are precursors to the esters (Scheme 5.11) [23].

In 1992, Mizuno et al. reported the regioselective MCPBA-oxidation reactions of VDCPs **1** and the results indicate that the regioselectivity in the epoxidation reactions strongly depends on the substituents on C2′ position of VDCPs **1**. When R^1 and R^2 are both phenyl groups, 2-methylene-cyclobutan-1-ones **240** and **241** are formed singly; when VDCP **1i**, in which R^1 and R^2 are both methyl groups, was used as the substrate, cyclopropyl keto ester derivative **243a** is obtained



Scheme 5.13 Oxygenation of VDCPs **1** with dimethyldioxirane. Reprinted with the permission from Ref. [1]. Copyright 2011 American Chemical Society



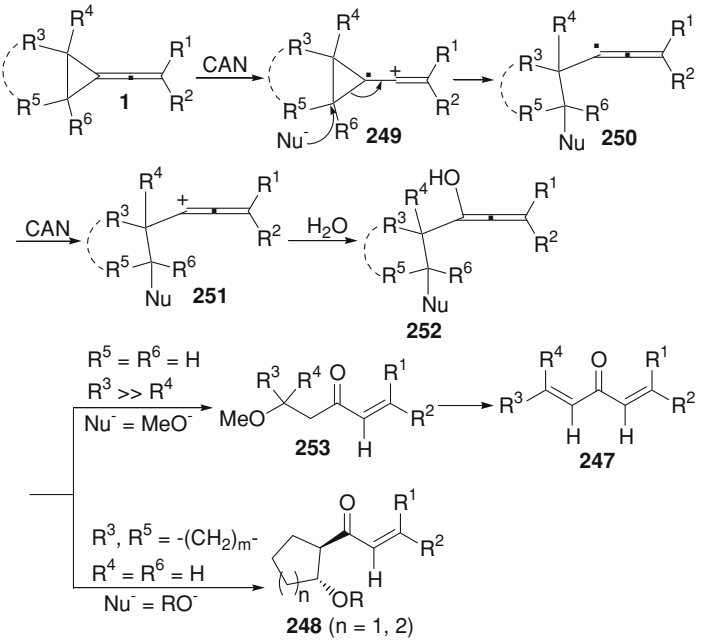
Scheme 5.14 CAN-mediated oxidative rearrangement reactions of VDCPs **1**. Reprinted with the permission from Ref. [1]. Copyright 2011 American Chemical Society

exclusively (Scheme 5.12) [24, 25]. Proposed mechanisms for these transformations are also illustrated in Scheme 5.12. Differences between these two oxidation reactions may be ascribed to the steric and electronic effects of the phenyl groups in C2′ position of VDCPs **1**: it is worthy of noting that phenyl groups at the C2′ position cannot be coplanar with the C1′–C2′ plane for a steric reason.

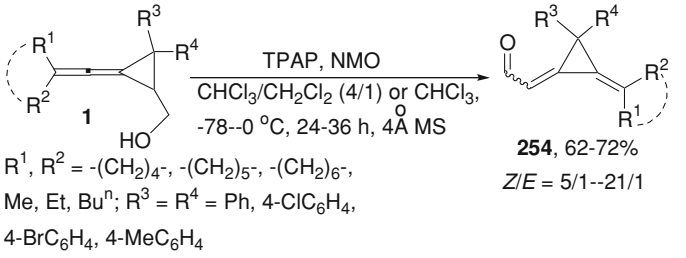
Oxygenation of VDCPs **1** with dimethyldioxirane in CH_2Cl_2 in the presence of 18-crown-6 gave methylenecyclopropanes **244**. Further oxygenation of **244** with dimethyldioxirane gave cyclobutanones **245** and **246** (Scheme 5.13).

In 2008, Huang et al. reported cerium(IV) ammonium nitrate (CAN)-mediated oxidative rearrangement reactions of VDCPs **1**, which resulted in unsymmetrical divinyl ketones **247** and enone derivatives **248** in moderate to good yields with excellent regio- and stereo-selectivities (Scheme 5.14) [26].

Plausible mechanism for these transformations is shown in Scheme 5.15. VDCPs **1**, in the presence of Ce(IV), undergo oxidative electron transfer to afford cationic radical **249**. For a review, see [27]. The following nucleophilic attack of the solvent as MeOH at the cyclopropyl ring may cause the rearrangement to produce the ring-opened radical intermediate **250** [28]. Intermediate **250** can be further oxidized by another molecule of CAN to give cation **251**, which is quenched by water in the solvent to produce intermediate **252**. Subsequent enol rearrangement of the corresponding intermediate **252** affords product **248** or



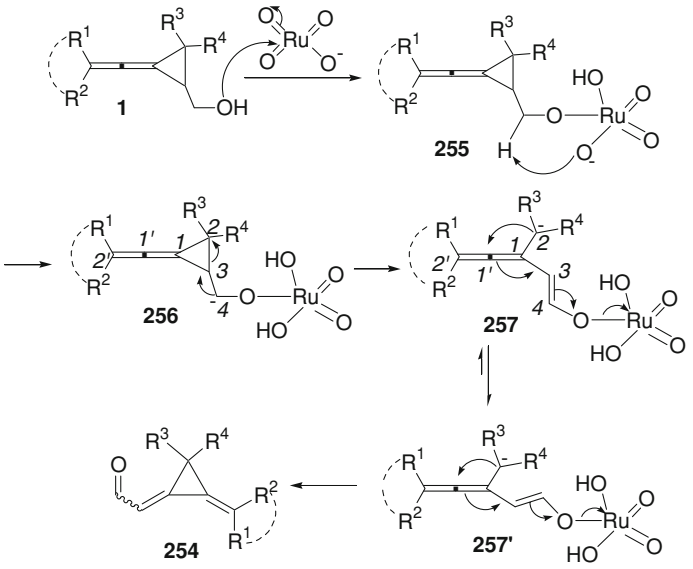
Scheme 5.15 Plausible mechanism for the CAN-mediated oxidative rearrangement reactions of VDCPs **1**. Reprinted with the permission from Ref. [1]. Copyright 2011 American Chemical Society



Scheme 5.16 Oxidative isomerization of VDCPs **1** in the presence of TPAP and NMO

intermediate **253**. Further elimination of a molecule of MeOH from **253** furnishes product **247**. While as for **248**, the *trans*-isomer in a sterically hindered ring does not progress to the corresponding divinyl ketones.

In early 2011, Shi et al. reported that in the presence of tetrapropylammonium perruthenate (TPAP) and 4-methylmorpholine *N*-oxide (NMO), the oxidative isomerization reactions of VDCPs **1** can be achieved to afford dimethylenecyclopropane aldehydes **254** in moderate yields (Scheme 5.16) [29].



Scheme 5.17 Plausible mechanism for the formation of products **254**

Plausible mechanism for the formation of products **254** is outlined below: first, VDCPs **1** reacts with tetrahedral perruthenate ion $Ru^{VII}O_4^-$ to give intermediate **255** [30–32]. After a quick hydrogen migration, the cyclopropyl ring opening of intermediate **256** takes place to afford intermediates **257** and **257′**, which undergoes recyclization to give products **254** (Scheme 5.17). It is plausible that the C3–C4 double bond in intermediate **257** interacts with the sterically large R^2 group, so intermediate **257′** is more stable than intermediate **257**. Therefore, intermediate **257** is assumed to be transformed into **257′** during the reaction, leading to the formation of *Z*-**254** as the major isomer. The electronic effect of the substituents R^3 and R^4 groups may also have some influence on the *Z*/*E* geometric selectivity.

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Chapter 6
Concluding Remarks and Perspectives of VDCPs

During the past years, the chemistry of VDCPs has rapidly developed. VDCPs, especially those with aromatic group(s) on the allene and/or cyclopropyl ring moiety, show diverse reaction patterns in the presence of Lewis acids, Brønsted acids, transition metal catalysts, etc. The chemistry of VDCPs greatly depends on the substituents on the allene and cyclopropyl ring moieties. Lewis or Brønsted acid-mediated chemistry of VDCPs has aroused a renaissance of cationic intermediates. Novel transformations of VDCPs developed during the past years have resulted in the synthesis of aromatic compounds, heterocyclic compounds, and some other useful products. It is believed that with continued investigations in this area, many new reactions and more useful chemistry of VDCPs will be found in the near future.

L. Shao et al., *Chemical Transformations of Vinylidenecyclopropanes*, SpringerBriefs in Molecular Science, DOI: 10.1007/978-3-642-27573-9_6,