# An Evolving Multifunctional Molecular Building Block: Bicyclopropylidene

**Armin de Meijere*[a] and Sergei I. Kozhushkov[a]**

*Dedicated to Professor Hans-Dieter Martin on the occasion of his 60th birthday*

**Keywords:** Bicyclopropylidene / Cross-coupling / Cycloadditions / Organometallic compounds / Spiro compounds

The elucidation of the chemistry of the highly strained and unusually tetrasubstituted alkene bicyclopropylidene (**2**), has proved to be fruitful, both with respect to synthetic applications as a multifunctional $C_6$ building block and for the understanding of certain reaction principles. The different, and steadily improved, methods developed over the last thirty years for the preparation of this unusual alkene, and the more recent methods for the synthesis of functionally substituted as well as spirocyclopropanated derivatives, are presented. The rich chemistry of bicyclopropylidene, beginning with its well-known thermal rearrangement and dimerization, its [2+*n*] cycloadditions with various carbenes, alkenes, 1,3-dipoles, and dienes all the way to its recently developed organometallic chemistry, especially its reactions under the catalysis of palladium and other transition metals, is covered. Some of the peculiar physical properties of bicyclopropylidene (**2**) which explain its unique reactivity, are also discussed. Finally, some synthetically useful chemical transformations of bicyclopropylidene derivatives, for example, synthetic approaches to certain cyclopropanated analogs of natural products, are presented.

## Introduction

When first independently conceived by two separate research groups, bicyclopropylidene (**2**) was mainly of theoretical interest, and the earliest preparations, either by a Simmons−Smith-type monocyclopropanation of the terminal double bond in the extremely sensitive ethenylidenecyclopropane (**1**),[1a,1d] or by a retro-Diels−Alder cleavage of the bisspirocyclopropanated bicyclo[2.2.2]octa-2,5-diene derivative **3**[1b,1c] (Scheme 1), did not even yield enough of this unique tetrasubstituted alkene to permit an extensive investigation of all its bonding properties.

Significant improvements in the preparation of **2** were reported during the following 18 years.[2,3] However, the real breakthrough came with the dramatically improved preparation of 1-cyclopropylcyclopropanol (**5**) from methyl

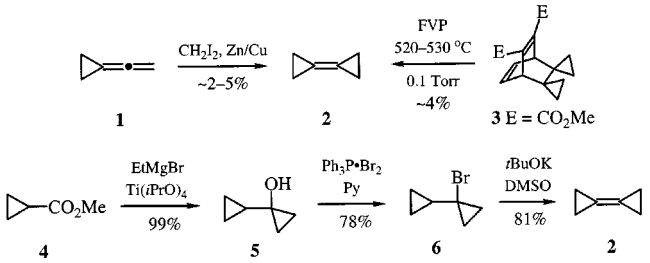
[a] Institut für Organische Chemie der Georg-August-Universität Göttingen,
Tammannstrasse 2, 37077 Göttingen, Germany
Fax: (internat) + 49-(0)551/399-475
E-Mail: Armin.deMeijere@chemie.uni-goettingen.de

*Armin de Meijere, born 1939 in Homberg (Niederrhein), Germany, studied chemistry at the universities of Freiburg and Göttingen and obtained his doctorate (Dr. rer. nat.) at the University of Göttingen under the guidance of Wolfgang Lüttke. Following postdoctoral training under Kenneth B. Wiberg at Yale University in New Haven, CT (USA) he fulfilled the requirements for his "Habilitation" in 1971 at the University of Göttingen. He became Full Professor of Organic Chemistry at the University of Hamburg in 1977, and returned to the University of Göttingen to succeed his former mentor in the chair of Organic Chemistry in October 1989. He has been visiting professor at the University of Wisconsin in Madison, WI, the IBM Research Laboratory in San José, CA, the Technion in Haifa, Israel, Princeton University in Princeton, NJ, the Universitá de Aix-Marseille III, France, the Universitá degli Studi, Firenze, Italy, the Ecole Normale Supérieur, Paris, France, the University of Colorado, Boulder, CO, and the University of Florida, Gainesville, FL. He received a fellowship from the Studienstiftung des Deutschen Volkes, obtained the award "Dozentenstipendium" from the Fonds der Chemischen Industrie in 1972, he was elected a member of the Norwegian Academy of Sciences and Letters in 1992, and in 1996 received the Alexander-von-Humboldt-Gay-Lussac Prize of the French Ministry for Higher Education and Research. In 1997 he was elected as a member of the Braunschweigische Wissenschaftliche Gesellschaft, as an Honorary Professor of the St. Petersburg State University in St. Petersburg, Russia, and nominated as a Fellow of the Japan Society for the Promotion of Science. He is editor or member of the editorial board of a number of scientific journals including Chemical Reviews, periodicals and books. His scientific achievements have been published in over 420 original publications, review articles, and chapters in books. His current research interests include the development of new cascade reactions for the efficient construction of complex skeletons and new small-ring building blocks to be applied in the synthesis of natural and nonnatural compounds, new highly strained polycyclic compounds with interesting properties, as well as the development of new synthetic methodology based on metal-mediated and -catalyzed transformations of organic compounds.*

*Sergei I. Kozhushkov was born in 1956 in Kharkov, USSR. He studied Chemistry at Lomonosov Moscow State University, where he obtained his Doctor degree in 1983 under the supervision of Professor N. S. Zefirov. From 1983 to 1991 he worked at Moscow State University and then at the Zelinsky Institute of Organic Chemistry. In 1991 he joined the research group of Professor A. de Meijere (Georg-August University of Göttingen, Germany) as an Alexander von Humboldt Research Fellow; since 1993 he has worked as a Research Associate, and since 1996 he has held the position of Scientific Assistant. His current research interests focus on the chemistry of highly strained small ring compounds.*

**MICROREVIEWS:** This feature introduces the readers to the authors' research through a concise overview of the selected topic. Reference to important work from others in the field is included.

  1434−193X/00/1223−3809 $ 17.50+.50/0 




Scheme 1. The first and the most efficient preparations of bicyclopropylidene (**2**) (see refs.[1−3,5])

cyclopropanecarboxylate (**4**) by the transformation of an alkoxycarbonyl group into a cyclopropanol fragment with ethylmagnesium bromide in the presence of $Ti(iPrO)_4$, as developed by Kulinkovich et al.[4] The optimized conversion of the alcohol **5** with the triphenylphosphane/bromine reagent to the bromide **6**, and its subsequent dehydrobromination with KO*t*Bu in DMSO, makes the alkene **2** available in every laboratory in synthetically useful quantities of 40−55 g within one week (Scheme 1),[5] and a scale-up of the process poses no problems. An analogous sequence is applicable to prepare substituted, especially spirocyclopropane-annelated, bicyclopropylidenes.[5,6]

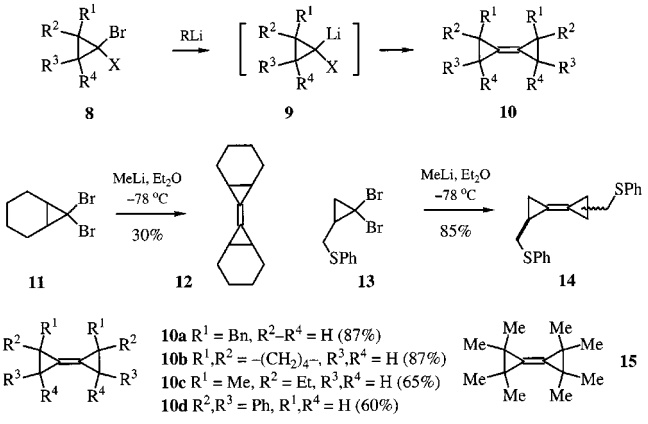
Other approaches to substituted bicyclopropylidenes are by carbene addition to butatrienes and alkenylidenecyclopropanes or by dehalogenative "dimerization" of 1-halo-1-lithiocyclopropanes generated by treatment of 1,1-dihalocyclopropanes with alkyllithium reagents.[6] A large variety of functionally monosubstituted bicyclopropylidenes **7a**−**w** can be prepared directly from bicyclopropylidene (**2**) in moderate to excellent yields by deprotonation with butyllithium in THF at 0 °C and electrophilic substitution of the lithiobicyclopropylidene with appropriate reagents (Scheme 2). Several of these new derivatives **7** could be further transformed with retention of the bicyclopropylidene moiety.[7−10]

A number of di- and oligosubstituted bicyclopropylidenes have been obtained by treatment of the 1,1-dihalocyclopropanes **8** with alkyllithium reagents to generate 1-halo-1-lithiocyclopropanes, so-called cyclopropylidenoids **9**, which undergo reductive "dimerization" (Scheme 3). The first such reaction was reported as early as 1960 by Moore and Ward[11] who obtained the biscyclohexane-annelated bicyclopropylidene **12** in 30% yield. The main shortcomings of this method are its lack of stereoselectivity and the unpredictability of its success, since most monocyclic dibromocyclopropanes are converted into allenes upon treatment with alkyllithium reagents. Yet, in certain cases, such as, for example, the reaction of 1,1-dibromo-2-(phenylthiomethyl)-cyclopropane (**13**) with methyllithium to give 85% of bis-(phenylthiomethyl)bicyclopropylidene **(14)** in 85% yield,[12a] with the (*E*,*E*)-isomer as the main component (its structure has been resolved by X-ray crystal structure analysis[12b]) (Scheme 3), this approach to disubstituted bicyclopropylidenes appears to be very efficient. A significant improvement was eventually made by Neuenschwander et al.[13] who found that copper(II) salts assist the reductive homocoupling of the bromolithiocyclopropanes **9** to give a variety of substituted bicyclopropylidenes of type **10** in reproducible and reasonable yields (see, for example, compounds **10a**−**d**, Scheme 3), albeit as mixtures of diastereomers. The debrominating dimerization of 1,1-dibromotetramethylcyclopropane upon treatment with methyllithium to give the permethylated bicyclopropylidene **15** (Scheme 3) went surprisingly well (41−73% yield),[14] and the yield could not be improved (18−30%)[13c,14a] by running the reaction in the presence of copper(II) salts.




| ElX | $Me_3SiCl$ | PhSSPh | $C_2Cl_6$ | $(CH_2Br)_2$ | $nC_4H_9I$ | $nC_5H_{11}I$ |
|---|---|---|---|---|---|---|
| El | $SiMe_3$ | SPh | Cl | Br | $nC_4H_9$ | $nC_5H_{11}$ |
| Product | **7a** | **7b** | **7c** | **7d** | **7e** | **7f** |
| Yield (%) | 85 | 77 | 73 | 65 | 72 | 80 |
| ElX | $nC_7H_{15}I$ | $Me_2CO$ | oxirane | DMF | DMA | $D_2O$ |
| El | $nC_7H_{15}$ | $CMe_2OH$ | $CH_2CH_2OH$ | CHO | C(O)Me | D |
| Product | **7g** | **7h** | **7i** | **7j** | **7k** | **7l** |
| Yield (%) | 74 | 82 | 50 | 73 | 71 | 80 |
| ElX | $ICH_2CH{=}CH_2$ | $O_2$, AcCl | $O_2$ | $CO_2$ | $Boc_2O$ | |
| El | $CH_2CH{=}CH_2$ | OAc | OH | $CO_2H$ | $CO_2tBu$ | $(CH_2)_3OTHP$ |
| Product | **7m** | **7n** | **7o** | **7p** | **7q** | **7r** |
| Yield (%) | 50 | 32 | 22 | 95 | 69 | 63 |
| ElX | $I(CH_2)_nOTHP$, $n$ = 3–8 | | | | | |
| El | $(CH_2)_4OTHP$ | $(CH_2)_5OTHP$ | $(CH_2)_6OTHP$ | $(CH_2)_7OTHP$ | $(CH_2)_8OTHP$ | |
| Product | **7s** | **7t** | **7u** | **7v** | **7w** | |
| Yield (%) | 85 | 82 | 88 | 68 | 65 | |

Scheme 2. The preparation of functionalized bicyclopropylidene derivatives **7** from bicyclopropylidene (**2**) via lithiobicyclopropylidene (see refs.[6−10])



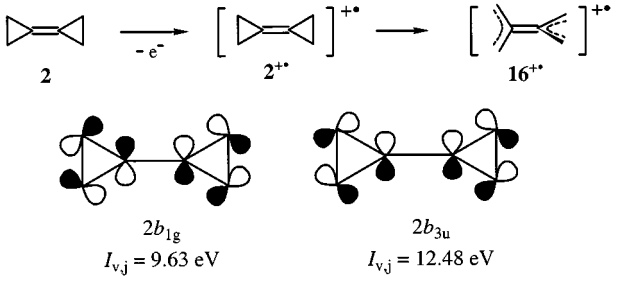

Scheme 3. Synthetic approach to the substituted bicyclopropylidenes **10** by dimerization of cyclopropylidenoids **9** (see refs.[11−14])

## Physical and Bonding Properties of Bicyclopropylidene (2)

Vibrational spectroscopic (IR[1a,1d,2b,2c,15a,15b] and Raman[2a,2c,5b,15]) data of unsubstituted bicyclopropylidene (**2**) have been published by several groups, although with some discrepancies. With respect to its bonding properties, the most relevant vibrational mode is the stretching of the

double bond, which is active only in the Raman spectrum. This band turns out to be very weak: it was first recorded for the octamethylderivative **15** to be at 1848 $cm^{-1}$ [15a] and later also for **2** itself at 1836 $cm^{-1}$.[15c] In the NMR spectra, the alkene **2** shows peaks at $\delta = 1.16$ ($^1H$)[1a,1d,2c,15b] and $\delta = 2.85$ and 110.21 ($^{13}C$) ($CDCl_3$). The $^{13}C-H$ coupling constant of 162.3 Hz indicates an only slightly increased *s*-character of the C−H bond orbitals in comparison with those in cyclopropane itself ($J^{13}_{C,H} = 160.3$ Hz). Thus, the observed facile deprotonation of **2** is not so much due to an enhanced C−H acidity, but a stabilization of the carbanionic character of the formed lithium derivative (see above).

With an oxidation potential of 1.58 V, bicyclopropylidene (**2**) is not as readily oxidized as tetramethylethylene ($E_{ox} = 1.3$ V), yet, upon γ-irradiation of **2** in a $CF_3CCl_3$ matrix at 77 K, a radical cation was formed, the ESR and the corresponding proton ENDOR spectrum of which were analyzed in detail and disclosed that the initially formed radical cation $\mathbf{1}^{+\cdot}$ easily transformed into the tetramethyleneethane radical cation $\mathbf{16}^{+\cdot}$ (Scheme 4).[16]



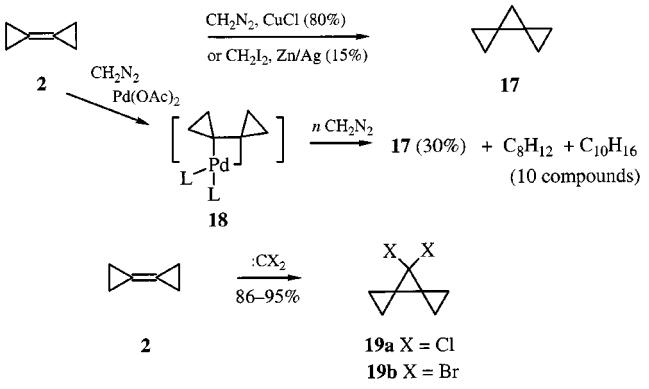

Scheme 4. The tetramethyleneethane radical cation $\mathbf{16}^{+\cdot}$ formed from bicyclopropylidene (**2**) and bonding linear combinations of the Walsh $e_A$ orbitals for **2** (see refs.[16,17])

The photoelectron spectrum of bicyclopropylidene (**2**) reveals the lowest ionization energy (π-$IE_v$) band at 8.93 eV, which corresponds to a significantly higher HOMO energy (by 0.64 eV) than that of methylenecyclopropane. The split between the bonding linear combinations of the Walsh $e_A$ orbitals of 2.85 eV ($2b_{3u} - 2b_{1g}$) (Scheme 4), and the value of −2.14 eV for the resonance integral between linked 2*p* atomic orbitals of the adjacent cyclopropane rings in **2**, indicate a significant electronic interaction between the two cyclopropyl groups, a fact that justifies the description of **2** as a "bishomobutatriene".[15b,17] This, and its high-lying HOMO, are responsible for its uniquely enhanced reactivity towards a wide range of electrophiles and cycloaddends.

Several independent structural analyses for the unsubstituted bicyclopropylidene (**2**)[18] disclose a consistent difference between longer distal [1.534(2) Å at 245 K] and shorter proximal [1.467(1) Å at 245 K] bonds in the cyclopropane rings due to changes in hybridization, especially of the doubly bonded carbon atoms, which cause an increased angular strain[6b,19,20] and a length of 1.304(2) Å for the central double bond. The experimentally determined heat of formation [$\Delta H^0_f(g)$] for bicyclopropylidene (**2**) is equal to 77.5 kcal/mol,[21] from which the strain energy was calculated to be 77.4 kcal/mol.

## [2 + *n*] Cycloadditions

The cyclopropanation of bicyclopropylidene (**2**) under Gaspar−Roth or modified Simmons−Smith conditions gave dispiro[2.0.2.1]heptane ([3]triangulane, **17**) in 80[22] and 15% yield,[2a] respectively (Scheme 5). The palladium(II) acetate-catalyzed cyclopropanation of **2** with diazomethane, however, gave a number of products resulting, apparently, from insertion of one or more methylene units into an initially formed palladacyclobutane **18** (Scheme 5).[3d,23]

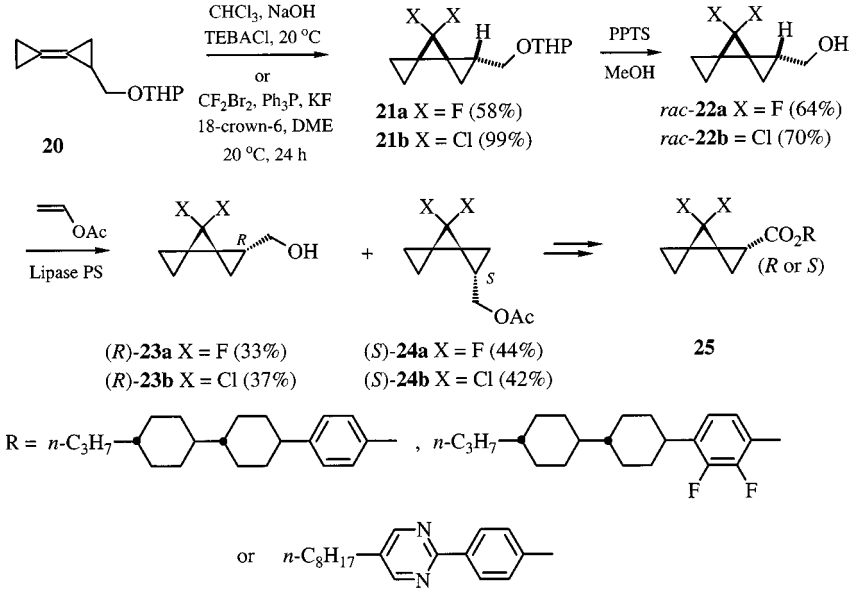



Scheme 5. The addition of methylene and dihalocarbenes to bicyclopropylidene (**2**) (see refs.[2a,3d,22,23−26])

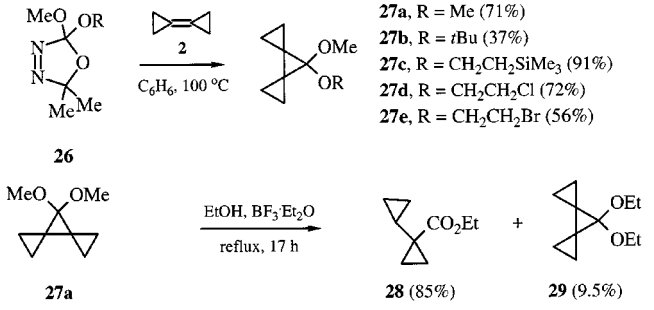
The addition of dichloro-[14a,24] and dibromocarbenes generated from $PhHgBr_3$ [25] or bromoform[26] gave the corresponding 7,7-dihalotrispiro[2.0.2.1]heptanes **19** in 86−95% yields (Scheme 5). Such trispiroheptane derivatives may actually possess practically useful properties. For example, the addition of dichloro- and difluorocarbenes to the bicyclopropylidene derivative **20** (Scheme 6) has recently been applied for the preparation of the optically active dispiro[2.0.2.1]heptane derivatives **25** as novel ferroelectric liquid crystalline compounds.[27]

Bicyclopropylidene (**2**) cleanly reacts with several dialkoxycarbenes generated in situ from the corresponding 2,2-dialkoxy-$\Delta^3$-1,3,4-oxadiazolines of type **26** to afford the dialkyl acetals of [3]triangulan-7-one **27** (Scheme 7).[28] The partially successful transacetalization of the dimethyl acetal **27a** upon heating under reflux in excess ethanol in the presence of boron trifluoride−diethyl ether indicates that a 7-alkoxydispiro[2.0.2.1]heptyl cation must be a reasonably stable species in spite of its extreme angle strain (Scheme 7).[28]

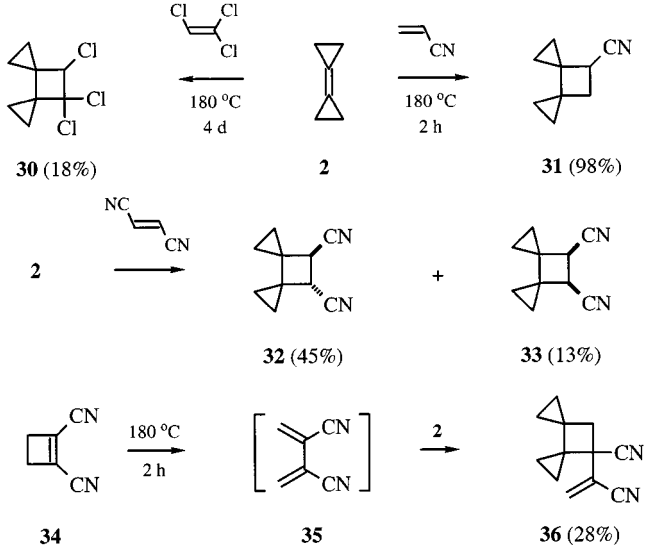
Bicyclopropylidene (**2**) reacts with electron-deficient cycloaddends in different ways, depending on the substrate. Trichloroethylene and acrylonitrile undergo cycloaddition to **2** at elevated temperatures yielding the corresponding [2+2] adducts **30** and **31**, respectively. Fumaronitrile upon reaction with **2** gives rise to both *trans*- (**32**) and *cis*-7,8-dicyanodispiro[2.0.2.2]octanes (**33**). The cyanovinyldispiro[2.0.2.2]octane derivative **36** was isolated from the reaction of **2** with 1,2-dicyanocyclobutene (**34**). Apparently, **43** at 180 °C undergoes ring-opening to **35**, and then **2** adds across one of the double bonds of **35** to give **36** (Scheme 8).[29,30] The capto-dative substituted alkenes **39**



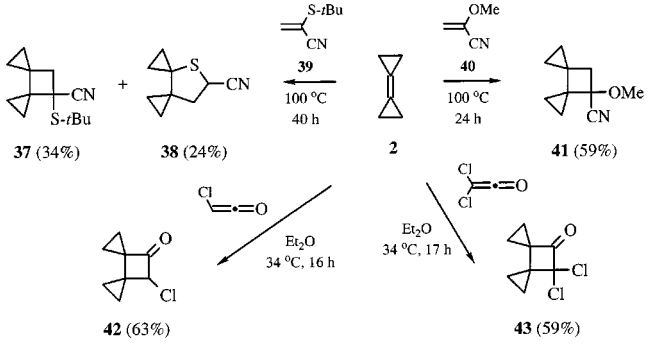

Scheme 6. The preparation of ferroelectric liquid crystalline compounds **25** by dihalocarbene addition to bicyclopropylidene derivative **20** (see ref.[27])




Scheme 7. The cycloaddition of dialkoxycarbenes to bicyclopropylidene (**2**) (see ref.[28])




Scheme 8. [2+2] Cycloaddition reactions of bicyclopropylidene (**2**) with substituted ethenes (see refs.[29,30])



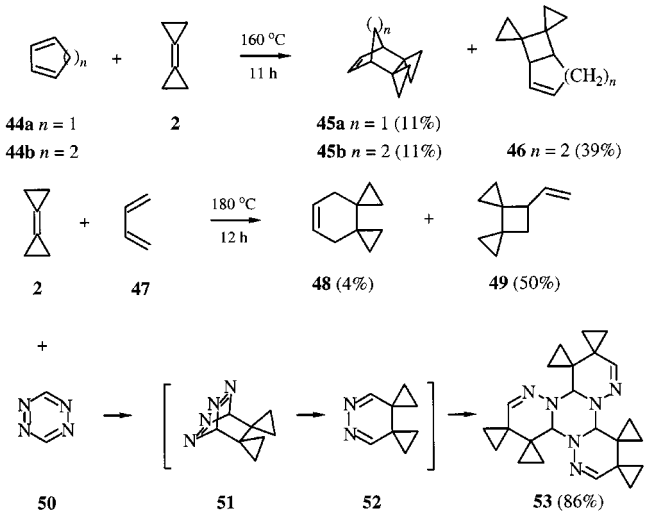

Scheme 9. The cycloaddition of bicyclopropylidene (**2**) to captodative substituted alkenes **39** and **40**, as well as chloro- and dichloroketene (see refs.[29–31])

and **40** also undergo formal [2+2] cycloadditions with **2** to yield compounds **37**, **38** and **41**, respectively (Scheme 9).[31] All of the above-mentioned [2+2] cycloadducts presumably arise via intermediate 1,4-diradicals in a stepwise manner.[29,31] However, the cycloadducts **42** and **43** of **2** to chloro- and dichloroketene most likely arise from a concerted [$\pi 2_s + \pi 2_a$] cycloaddition reaction (Scheme 9).[29,30]

Bicyclopropylidene (**2**) is capable of undergoing cycloadditions by different modes, depending on the nature of the cycloaddend. Whereas cyclopentadiene (**44a**) gives the [4+2] cycloadduct **45a** only, the reactions with 1,3-cyclohexadiene (**44b**) and 1,3-butadiene (**47**) lead to mixtures of the [4+2] adducts **45b** and **48**, and the [2+2] cycloadducts **46** and **49**, with an increasing proportion of the latter, in this order (Scheme 10).[29,32a] This indicates that all these cycloadditions of **2** onto hydrocarbon dienes occur stepwise via 1,4-diradicals.

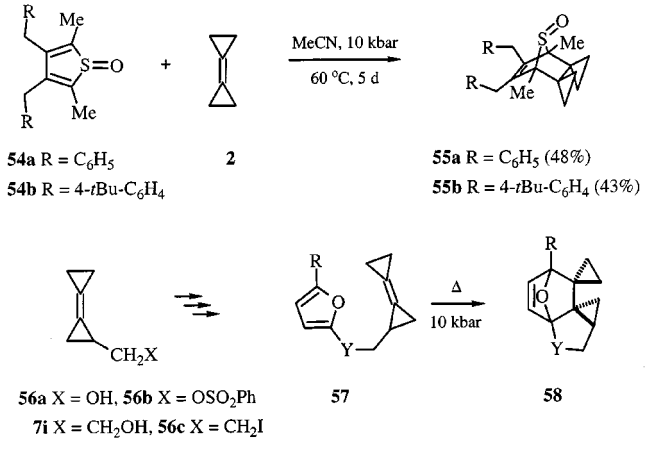
The reaction of bicyclopropylidene (**2**) with 1,2,4,5-tetrazine (**50**), a diene with inverse electron demand, affords two stereoisomeric products of type **53** and trimers of the 8,9-diazadispiro[2.0.2.4]deca-7,9-diene (**52**), obviously formed via the normal [4+2] cycloadduct **51** (Scheme 10).[29]

Bicyclopropylidene (**2**) does not undergo an intermolecular Diels–Alder reaction with furan or 2-methoxyfuran even at high pressure. It does, however, add to the thi-




Scheme 10. Different modes of cycloaddition of dienes to bicyclopropylidene (**2**) (see refs.[29,32a])

ophene *S*-monoxides **54**, under a pressure of 10 kbar, to yield the [4+2] cycloadducts **55** as single diastereomers.[32b] Intramolecular cycloadditions of compounds **57**, with a furan tethered to a bicyclopropylidene unit, are also easily brought about under high pressure (10 kbar) and give cycloadducts **58** stereoselectively in yields ranging from 32 to 95% (Scheme 11).[10]

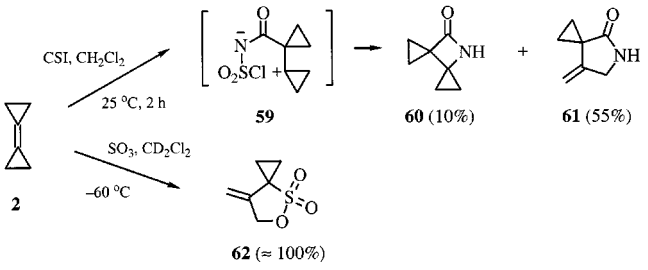



| R | H | MeO | H | H |
|---|---|---|---|---|
| Y | $CH_2$ | $CH_2$ | $CH_2O$ | $Me_2SiO$ |
| Yield of **58** (%) | 32 | 95 | 46 | 83 |

Scheme 11. Inter- and intramolecular Diels–Alder reactions of bicyclopropylidene (**2**) and its derivatives **57** (see refs.[10,32b])

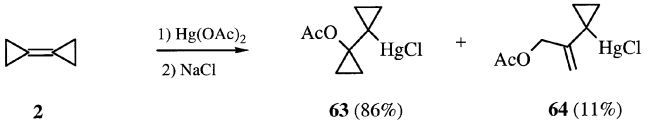
## Electrophilic and Radical Additions

Chlorosulfonyl isocyanate with **2** gives the expected β-lactam **60** only as a minor product, the principal product being the γ-lactam derivative **61**. It is reasonable to assume that the formation of the 1,4-zwitterionic intermediate **59** is responsible for the formation of **61** (Scheme 12).[29,30] Sulfonation of **2** with $SO_3$ also proceeds with ring opening of one of the cyclopropyl groups to give the spirocyclopropane-γ-sultone **62** in quantitative yield (Scheme 12).[33]




Scheme 12. Reactions of bicyclopropylidene (**2**) with chlorosulfonyl isocyanate (CSI) and $SO_3$ (see refs.[29,30,33])

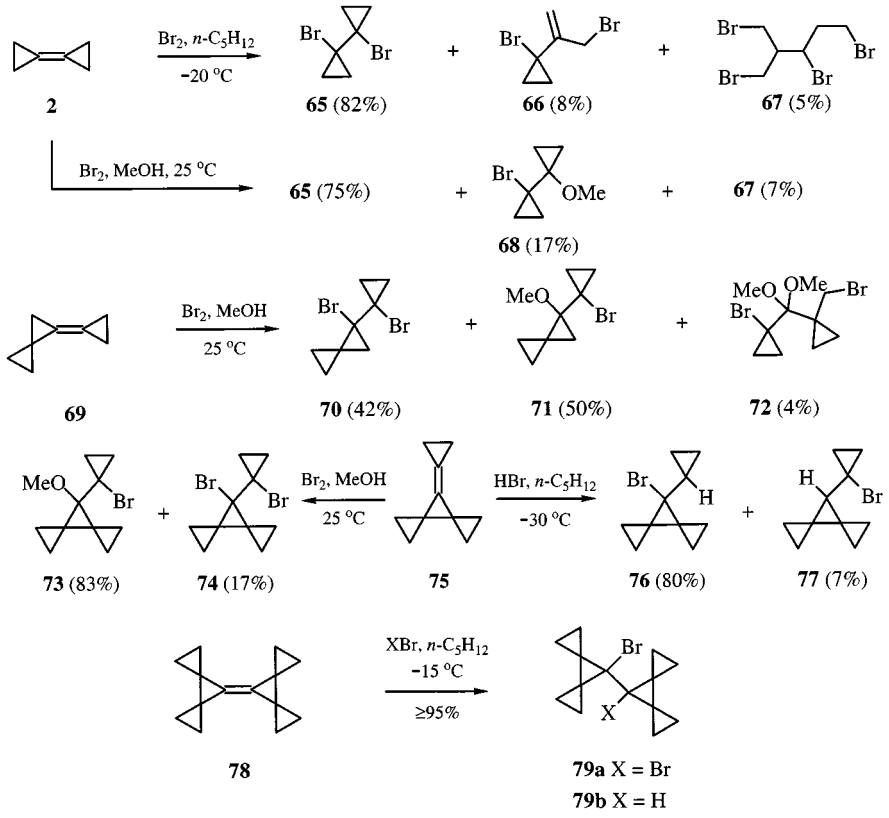
However, most other additions of electrophiles and radicals to bicyclopropylidene (**2**) predominantly give products in which both rings are retained and the only minor by-product arises by cyclopropyl-to-allyl cation (radical) rearrangement. Apparently, the cyclopropyl substituent on the cationic or radical center can efficiently stabilize an intermediate cyclopropyl cation or radical and prevent them from undergoing ring opening.[6] For example, the addition of mercuric acetate to **2** leads to a mixture of **63** and **64** in a ratio of 8:1 and a total yield of 97%. Apparently, the bicyclopropyl derivative **63** is formed by the usual 1,2-acetoxymercuration without ring opening of the intermediate 1-cyclopropylcyclopropyl cation, and the minor product **64** is formed by cyclopropyl-to-allyl cation rearrangement (Scheme 13).[34]



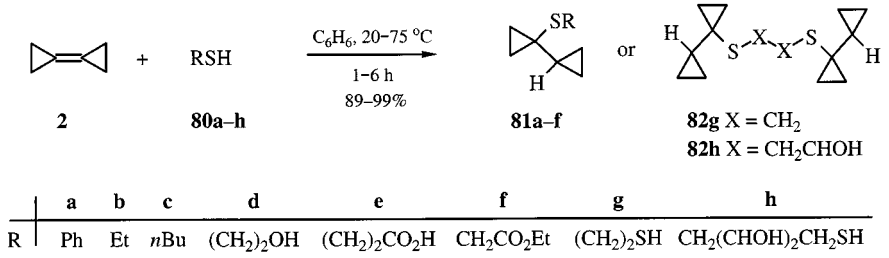

Scheme 13. Oxymercuration of bicyclopropylidene (**2**) (see ref.[34])

Bromine additions to bicyclopropylidene (**2**), as well as the spirocyclopropanated bicyclopropylidenes **69** and **75** have been performed in methanol at 25 °C. An increasing number of spiroannelated three-membered rings was found to stabilize the intermediate cyclopropyl cations against ring opening (Scheme 14).[35] Thus, the bromination and hydrobromination of the di- and tetraspirocyclopropanated bicyclopropylidenes **75** and **78** proceeds with complete retention of all cyclopropane rings (Scheme 14).[26c,35a,36]

In full accord with this, the addition of thiols **80a–h** to the double bond of bicyclopropylidene (**2**) in benzene proceeds rapidly at 20 to 75 °C, in the absence of catalysts or radical initiators, to give products **81a–h** almost quantitatively with complete retention of both three-membered rings (Scheme 15).[37] The addition of thiols to the *n*-alkylbicyclopropylidenes **7e–g** does not proceed stereoselectively, although in all cases the thioester function adds to the double bond with retention of the cyclopropane ring to give interesting new compounds containing bicyclopropyl fragments.[37] Apparently, the intermediate 1-(1′-alkylthiocyclopropyl)cyclopropyl radicals in this radical addition to **2** undergo ring opening far less rapidly than ordinary cyclopropylmethyl radicals.



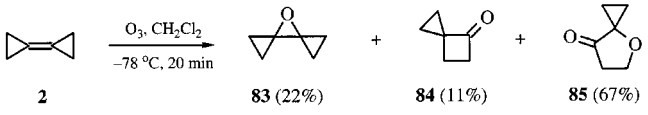

Scheme 14. Bromination and hydrobromination of bicyclopropylidene (**2**) and the spirocyclopropanated bicyclopropylidenes **69**, **75**, **78** (see ref.[35])




Scheme 15. Radical addition of thiols and dithiols **80** to bicyclopropylidene (**2**) (see ref.[37])

## 1,3-Dipolar Cycloadditions

The reaction of **2** with ozone gives rise to a mixture of the epoxide **83**, spiro[2.3]hexan-4-one (**84**) and 4-oxaspiro[2.4]heptan-7-one (**85**). While **83** and **84** apparently arise by 1,3-ring closure and cyclopropylcarbinyl-to-cyclobutyl ring enlargement of an intermediate 1,3-zwitterion formed by oxygen abstraction from a 1,5-zwitterion en route to a primary ozonide, respectively, the major product **85** must be formed from an oxy-analog of a cyclopropylmethyl-to-homoallyl cation rearrangement of an intermediate 1,5-zwitterion formed by heterolytic ring opening of the primary ozonide between two oxygen atoms (Scheme 16).[29,30]

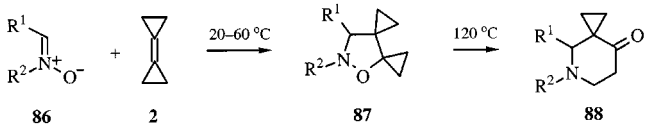



Scheme 16. Ozonolysis of bicyclopropylidene (**2**) (see refs. [29,30])

Nitrones **86** react at ambient or slightly elevated temperature (60 °C) with bicyclopropylidene (**2**) to give the bis(spirocyclopropane)-annelated isoxazolidines **87**. Heating of the cycloadducts **87** in xylene solution at 110−125 °C leads to a clean rearrangement with homolytic opening of the spirocyclopropane ring in the 5-position (adjacent to the N−O bond) to give the spirocyclopropane-annelated piperidones **88** after ring reclosure. The same sequence of cycloaddition and rearrangement can be achieved in a single operation with considerable benefit for the reaction yield by heating a nitrone **86** and **2** in xylene solution at 120 °C (Scheme 17).[38−41]

This reaction has also been applied for the preparation of aza analogs with the basic skeleton and functional groups of the extremely cytotoxic sesquiterpenes illudin and ptaquiloside, and some of these simple azaanalogs have indeed been found to exhibit DNA-cleaving abilities.[41]

1,3-Dipolar cycloadditions of the nitrile oxides **89** onto **2** give much poorer yields of cycloadducts **90** than those of

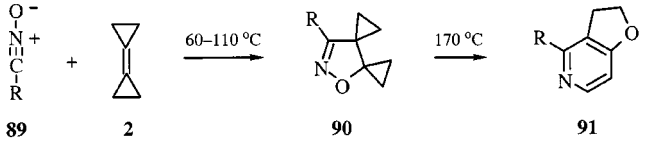



**86** **2** **87** **88**

| $R^1$ | $R^2$ | Yield of **87** (%) | Yield of **88** (%) (one-pot yields in parentheses) |
|---|---|---|---|
| Me | Ph | 93 | 63 (61) |
| Me | $CO_2Et$ | 34 | 61 (54) |
| $-(CH_2)_3-$ | | 42 | 60 (25) |
| $-(CH_2)_2-CMe_2-$ | | 80 | 76 (80) |
| $-(CH_2)_4-$ | | 37 | 68 (48) |
| *o*-$CH_2CH_2C_6H_4-$ | | 73 | 50 (73) |

Scheme 17. 1,3-Dipolar cycloadditions of nitrones **86** to bicyclopropylidene (**2**) (see refs.[38,41])

nitrones **86**. The cycloadditions of **89** to **2** require higher temperatures and unfavorably compete with the dimerization of the nitrile oxides to furoxanes. However, stable nitrile oxides **89** with bulky substituents R that hamper dimerization, can be used favorably. The thermal rearrangements of the 5-spirocyclopropane-annelated isoxazolines **90** always require higher temperatures than those of the isoxazolidine counterparts. Under these conditions the second cyclopropane ring is also cleaved to give the furopyridines **91** (Scheme 18).[38–40]



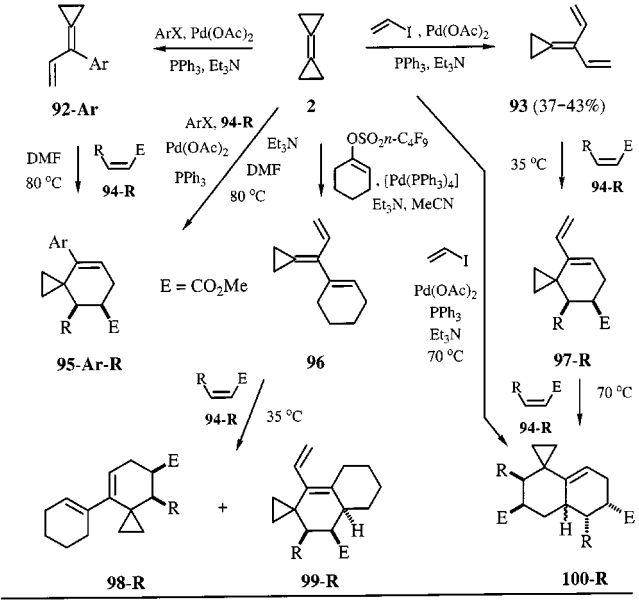

**89** **2** **90** **91**

| R | Yield of **90** (%) | Yield of **91** (%) |
|---|---|---|
| Me | 10 | 0 |
| Ph | 40 | 44 |
| 2,4,6-$Me_3C_6H_2$ | 67 | 44 |
| $Ph_3C$ | 17 | 21 |

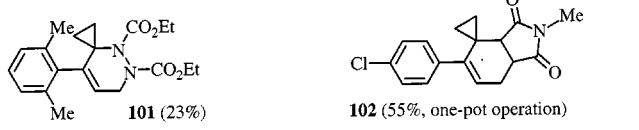
Scheme 18. 1,3-Dipolar cycloadditions of nitrile oxides **89** to bicyclopropylidene (**2**) (see refs.[38–40])

## Metal-Catalyzed Reactions of Bicyclopropylidene (2)

Coupling of **2** with iodobenzene under Heck reaction conditions gives the phenyl-substituted diene **92-Ph** which was isolated in up to 78% yield.[42,43] When heated at 80 °C in DMF or MeCN with various dienophiles **94-R** (R = H, *cis*-$CO_2Me$, *trans*-$CO_2Me$), **92-Ph** and its analogs **92-Ar**, obtained from **2** and other haloarenes, cleanly give the spiro[2.5]octene derivatives **95-Ar** (Scheme 19). The Heck coupling of iodoarenes and bicyclopropylidene (**2**) can be carried out in the presence of the dienophiles **94-R** to give the spiro[2.5]octenes **95-Ar-R** in a single operation in 41–100% yield (Scheme 19).[42,43] It is quite remarkable that the carbopalladation of **2** apparently proceeds more rapidly than that of methyl acrylate **94-H**, as the coupling even in the presence of **94-H** gives only a trace of methyl cinnamate which results directly from the reaction of the latter with iodobenzene. With the enantiomerically pure *N*-acryloyl-(*S*)-camphorsultam, the corresponding spiro[2.5]octene derivative was obtained as a single enantiomer. Vinyl iodide coupled to **2** gives the rather sensitive and reactive cross-conjugated triene **93** in 37–43% isolated yield. When a dienophile **94-R** was added to the reaction mixture prior to workup, the corresponding monoadducts of type **97** were isolated in 15–65% yield. Heating a mixture of **2**, vinyl iodide and a dienophile **94-R** in the presence of the palladium catalyst gives the corresponding bisadducts **100** resulting from a domino Diels–Alder addition to the cross-conjugated triene **93** (Scheme 19).[42,43] The aryl-substituted dienes **92-Ar** were also trapped in Diels–Alder reactions with diethyl azodicarboxylate and *N*-methylsuccinimide to yield the heterocyclic products **101** and **102**, respectively, in the latter case even more efficiently without isolation of the intermediate **92-Ar** (Scheme 19).[43a,43c]




| Substrate | Dienophile **94-R** R | Product | Yield (%) |
|---|---|---|---|
| PhI | H | **95-Ph-H** | 100 |
| PhBr | H | **95-Ph-H** | 59 |
| PhI | $CO_2Me$ | **95-Ph-$CO_2Me$** | 97 |
| *p*Tol-I | $CO_2Me$ | **95-Tol-$CO_2Me$** | 99 |
| 4-Pyr-I | H | **95-4-Pyr-H** | 81 |
| 4-Pyr-I | $CO_2Me$ | **95-4-Pyr-$CO_2Me$** | 60 |
| 2-Bromothiophene | H | **95-2-Thienyl-H** | 88 |
| $C_6H_9ONf$ | $CO_2Me$ | **98-$CO_2Me$, 99-$CO_2Me$** | 41 |
| $C_2H_3I$ | H | **97-H** | 63 |
| $C_2H_3I$ | H | **100-H** | 59 |
| $C_2H_3I$ | $CO_2Me$ | **97-$CO_2Me$** | 60 |
| $C_2H_3I$ | $CO_2Me$ | **100-$CO_2Me$** | 49 |

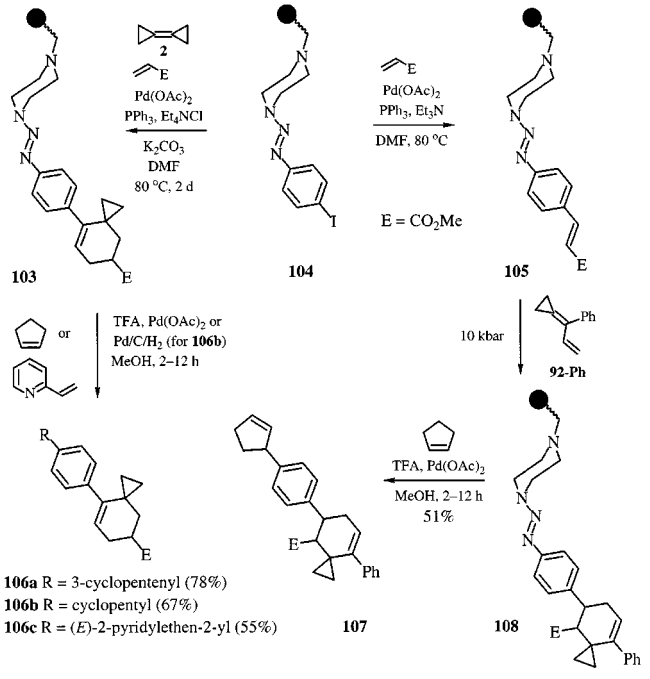


**101** (23%) **102** (55%, one-pot operation)

Scheme 19. Domino Heck–Diels–Alder reactions of bicyclopropylidene (**2**) (see refs.[42,43])

When carried out in the solid phase with the iodoaryltriazenyl-substituted Merrifield resin **104**, this unusual three-component reaction was extended by a further dimension

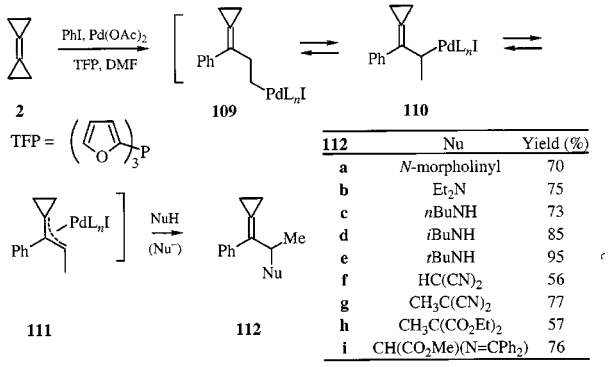
(Scheme 20).[43a] The subsequent deprotection of the coupling-cycloaddition products **103** which, in the first instance, leads to a diazonium ion, can be combined with another Heck-type coupling with an alkene to result in the products **106** in good yields. A further permutation is offered by the possibility of first coupling the resin-bound triazenylphenyl iodide **104** with methyl acrylate and then using the product under high pressure in a domino Heck−Diels−Alder reaction with bicyclopropylidene and iodobenzene to give the coupling-cycloaddition product **108**, and terminating with another Heck coupling upon removal from the resin (Scheme 20; the diene **92-Ph** is already the result from the Heck coupling of **2** and PhI).[43a] This novel five-component reaction is a Heck−Heck−Diels−Alder−Heck sequence, carried out in two steps.



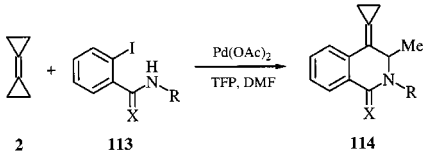

Scheme 20. Heck−Diels−Alder−Heck and Heck−Heck-Diels−Alder−Heck sequential reactions of bicyclopropylidene (**2**) on a polymer support (see refs.[43a])

The coupling of **2** with iodobenzene under Heck reaction conditions in the presence of the more basic trisfurylphosphane ligand, which is known to retard β-hydride elimination, apparently leads to a rearrangement of the σ-homoallyl- **109** to a σ-allylpalladium intermediate **110** which was efficiently trapped with various nitrogen and carbon nucleophiles to yield the methylenecyclopropane derivatives **112**. An intramolecular version of the latter could also be carried out, albeit with lower yields (Scheme 21).[43c]

A nickel(0)-catalyzed [2+2] cycloaddition of cyclobutene to bicyclopropylidene (**2**) provides an access to the bis-(spirocyclopropane)-annelated bicyclo[2.2.0]hexane derivative **115**, which was of interest for mechanistic studies of the bicyclo[2.2.0]hexane to 1,5-hexadiene rearrangement. The main product, 1,5-cyclooctadiene (**116**), was mostly formed by dimerization of cyclobutene and subsequent rearrangement (Scheme 22).[2d,44]

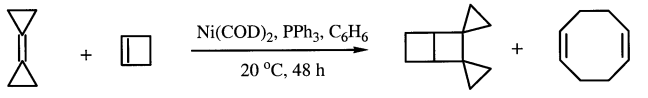



| 112 | Nu | Yield (%) |
|---|---|---|
| a | *N*-morpholinyl | 70 |
| b | $Et_2N$ | 75 |
| c | *n*BuNH | 73 |
| d | *i*BuNH | 85 |
| e | *t*BuNH | 95 |
| f | $HC(CN)_2$ | 56 |
| g | $CH_3C(CN)_2$ | 77 |
| h | $CH_3C(CO_2Et)_2$ | 57 |
| i | $CH(CO_2Me)(N{=}CPh_2)$ | 76 |




| 114 | X | R | Yield (%) |
|---|---|---|---|
| a | O | H | 17 |
| b | O | *i*Pr | 29 |
| c | $H_2$ | Bn | 31 |

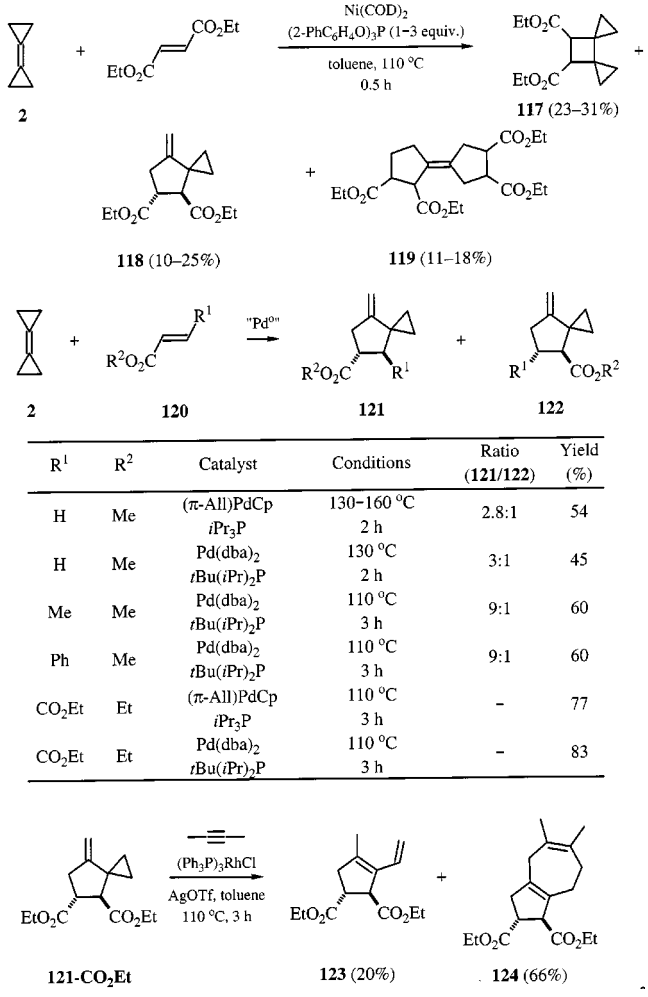
Scheme 21. Heck coupling of aryl iodides with bicyclopropylidene (**2**) followed by rearrangement of the σ-homoallyl to a π-allylpalladium intermediate and its trapping with nucleophiles (see refs.[43a,43c])




Scheme 22. Nickel(0)-catalyzed [2+2] cycloaddition of cyclobutene to bicyclopropylidene (**2**) (see refs.[2d,44])

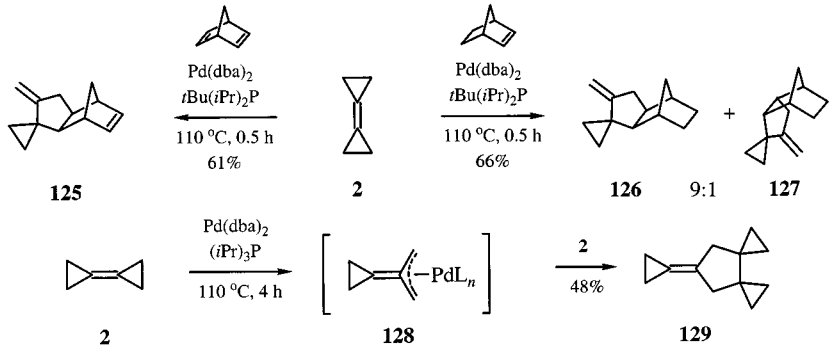
Bicyclopropylidene (**2**) also reacts with electron-deficient alkenes under nickel(0) catalysis, for example with diethyl fumarate and $Ni(COD)_2$, to give the [2+2] cycloadduct **117** as the main component in the product mixture.[45] Under palladium(0) catalysis, a formal [3+2] cycloaddition of electron-deficient (Scheme 23) or strained alkenes can be achieved exclusively (Scheme 24).[45] With unsymmetrically substituted alkenes of type **120**, two regioisomeric products were obtained, and the isomer **122** bearing the alkoxycarbonyl group adjacent to the spiro atom was the minor component in all cases. The product **121-$CO_2$Et** from **2** and diethyl fumarate can be further transformed in a rhodium-catalyzed reaction with 2-butyne to yield the bicyclo[5.3.0]-decadiene derivative **124** with a five-seven-membered ring combination as the main product.[45] Norbornadiene and norbornene react with **2** in a similar manner to give the formal [3+2] cycloadducts **125** and **126**, **127**, respectively, the latter as a 9:1 mixture of *exo*- (**126**) and *endo*- (**127**) isomers. In the absence of another activated alkene, one molecule of bicyclopropylidene (**2**), after the opening of a distal bond, undergoes a formal [3+2] cycloaddition to a second molecule of **2** to give 8-cyclopropylidenedispiro-[2.0.2.3]nonane (**129**) (Scheme 24).[43b]

Bromobicyclopropylidene (**7d**) reacts with the chlorozinc compound **131**, generated by metal exchange from lithiated ethyl *N*-(diphenylmethylene)glycinate, under $PdCl_2$(dppf) catalysis to give the substituted diene **135** formed by an unprecedented type of ring opening (Scheme 25).[46] An analogous ring opening was observed in the coupling of 2-bro-



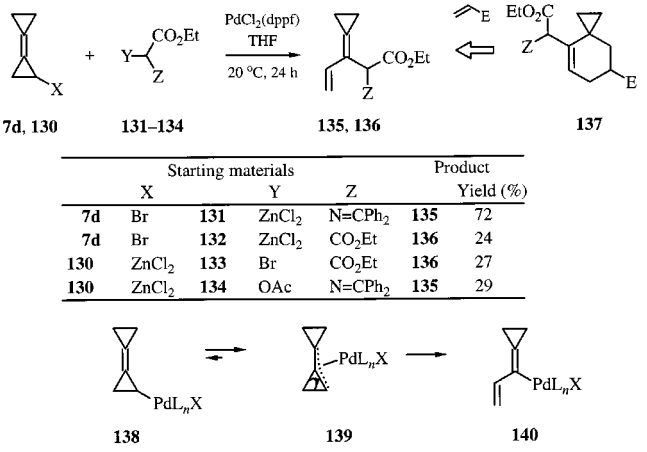

| $R^1$ | $R^2$ | Catalyst | Conditions | Ratio (**121**/**122**) | Yield (%) |
|---|---|---|---|---|---|
| H | Me | (π-All)PdCp<br>$iPr_3P$ | 130–160 °C<br>2 h | 2.8:1 | 54 |
| H | Me | $Pd(dba)_2$<br>$tBu(iPr)_2P$ | 130 °C<br>2 h | 3:1 | 45 |
| Me | Me | $Pd(dba)_2$<br>$tBu(iPr)_2P$ | 110 °C<br>3 h | 9:1 | 60 |
| Ph | Me | $Pd(dba)_2$<br>$tBu(iPr)_2P$ | 110 °C<br>3 h | 9:1 | 60 |
| $CO_2Et$ | Et | (π-All)PdCp<br>$iPr_3P$ | 110 °C<br>3 h | – | 77 |
| $CO_2Et$ | Et | $Pd(dba)_2$<br>$tBu(iPr)_2P$ | 110 °C<br>3 h | – | 83 |

Scheme 23. Reactions of bicyclopropylidene (**2**) with electron-deficient alkenes under nickel(0) and palladium(0) catalysis (see ref.[45])




Scheme 24. Palladium-catalyzed codimerization of bicyclopropylidene (**2**) with strained alkenes (see refs.[43b, 45])

momethylenecyclopropane under $Pd(dppa)_2$ catalysis, and of bromobicyclopropylidene (**7d**) with organometallic derivatives of diethyl malonate **132** under $PdCl_2$(dppf) catalysis.[46] Upon reversal of the polarities of the reactants, i.e. treatment of bicyclopropylidenylzinc chloride (**130**) with the bromomalonate **133** or O′Donnell′s acetoxyglycine derivative **134** under palladium catalysis, the same products were formed, but in lower yields. Most probably, a bicyclopropylidenylpalladium halide **138**, formed in the initial stages of these reactions, undergoes ring opening via the π-allylpalladium complex **139** to give the σ-dienylpalladium complex **140**, and this, in turn, couples with the derivative of the CH-acidic substrates.




| Starting materials | | | | | Product | |
|---|---|---|---|---|---|---|
| | X | | Y | Z | | Yield (%) |
| **7d** | Br | **131** | $ZnCl_2$ | N=$CPh_2$ | **135** | 72 |
| **7d** | Br | **132** | $ZnCl_2$ | $CO_2Et$ | **136** | 24 |
| **130** | $ZnCl_2$ | **133** | Br | $CO_2Et$ | **136** | 27 |
| **130** | $ZnCl_2$ | **134** | OAc | N=$CPh_2$ | **135** | 29 |

Scheme 25. Palladium-catalyzed cross-coupling of bicyclopropylidene derivatives with metallated or brominated CH-acidic compounds accompanied by an unprecedented ring opening (see ref.[46])

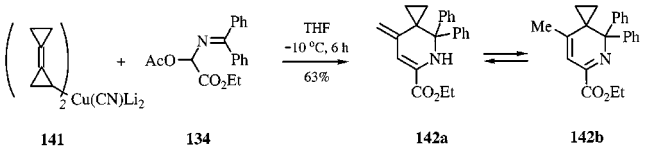
In analogy to the aryl-substituted 1,3-dienes **92-Ar**, the vinylmethylenecyclopropanes **135/136** should react with dienophiles and thus open up access to the correspondingly substituted spiro[2.5]octene derivatives **137**.

Another interesting example of an unusual transformation of bicyclopropylidene (**2**) is the reaction of the higher-order cuprate **141**, derived from **2**, with the electrophilic glycine cation equivalent **134**, which produces the methylenetetrahydropyridine derivative **142a** (Scheme 26).[47] In solution, compound **142a** exhibits a tautomeric equilibrium with **142b**.

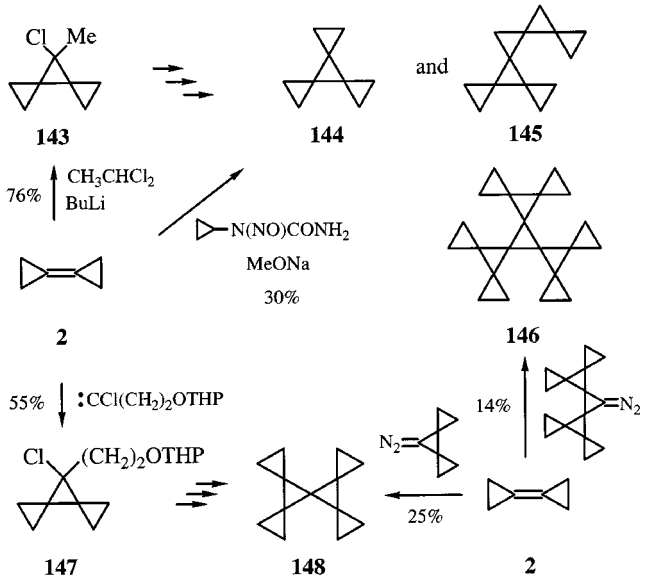
Stable complexes of platinum, titanium,[48] and cobalt[48] with a bicyclopropylidene ligand have been obtained, showing that **2** is a remarkably good ligand despite being a tetrasubstituted alkene.

## Higher Triangulanes from Bicyclopropylidene

The addition of different carbenes to bicyclopropylidene (**2**) (Scheme 27), or functionalized bicyclopropylidenes, has been used as a key step in the synthesis of a number of the theoretically interesting branched triangulanes.[49] This




Scheme 26. Reaction of the higher-order cuprate **141** derived from **2**, with O′Donnell′s acetoxyglycine derivative **134** occurring with opening of a three-membered ring (see ref.[33])

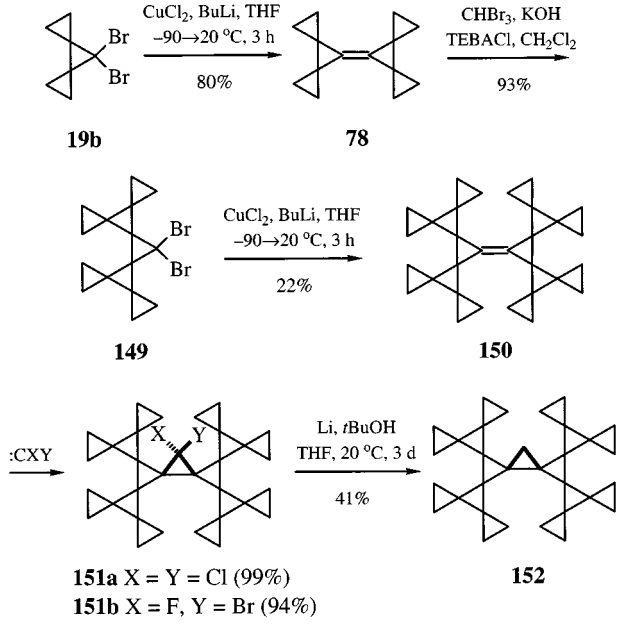



Scheme 27. The preparation of some branched triangulanes utilizing carbene cycloadditions onto bicyclopropylidene (**2**) (see refs.[26c,50–52])

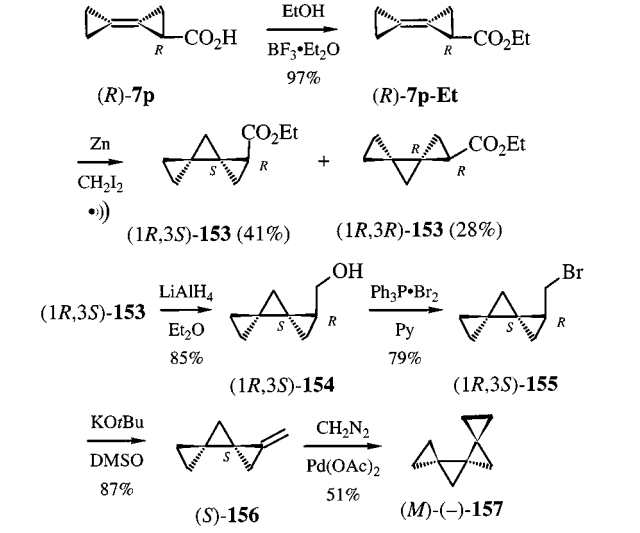
methodology was, for example, applied in the preparation of [3]rotane (**144**)[22,50] and the highly strained oligospirocyclopropanated [3]rotanes **145**, **146** and **148** (Scheme 27).[51,52]

The copper(II) chloride-assisted reductive coupling of 7-bromo-7-lithiocyclopropanes, generated from 7,7-dibromodispiro[2.0.2.1]heptane (**19b**), the dibromocarbene adduct of bicyclopropylidene (**2**), yields the perspirocyclopropanated bicyclopropylidene **78** (80% isolated),[4a,4c,53] making this exotic hydrocarbon[26c,36] easily available in preparatively useful quantities (Scheme 28). It is really spectacular that the dibromide **149**, the dibromocarbene adduct of **78**, can be "dimerized" again to give the third-generation bicyclopropylidene **150**. Reductive dechlorination of its dichlorocarbene adduct **151a** leads to the hydrocarbon **152** (Scheme 28) which, with its 15 spirofused cyclopropane rings, sets a new record for hydrocarbons consisting solely of spirofused cyclopropane rings.[14a,53]

(*M*)-(−)-Trispiro[2.0.0.2.1.1]nonane [(*M*)-(−)-**157**] — the first enantiomerically pure unbranched [4]triangulane — has been prepared from enantiomerically pure bicyclopropylidenecarboxylic acid [(*R*)-**7p**], with the cyclopropanation under Simmons–Smith conditions of its ethyl ester (*R*)-**7p-Et** as a key step (Scheme 29).[54] In spite of the fact that [4]triangulane has no chromophore which would lead to any significant absorption above 200 nm, it has a remarkably high specific rotation even at 589 nm with $[\alpha]_D^{20}$ = −192.7 ($c$ = 1.18, $CHCl_3$). Its outstanding rotatory power is in line with its helical arrangement of sigma bonds, as evidenced by the perfect agreement of the experimental and the computed specific rotation.




Scheme 28. The preparation of the branched [15]triangulane **152** (see refs.[14a,53])

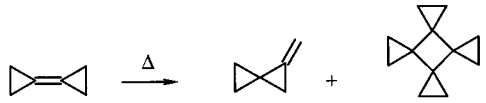



Scheme 29. The cyclopropanation of the enantiomerically pure ester (*R*)-**7p-Et** as a key step in the preparation of enantiomerically pure (*M*)-[4]triangulane [(*M*)-**157**] (see ref.[54])

## Miscellaneous

Bicyclopropylidene (**2**) undergoes a clean rearrangement to methylenespiropentane (**158**) when passed through a hot tube at 330 °C.[55] In view of the ready availability of **2**, this rearrangement constitutes the most convenient preparative approach to **158**.[55b] When heated in a closed vessel as a pure compound[1a,1d] or in solution (50% in toluene),[56] a

substantial fraction of **2** dimerizes to yield [4]rotane (**159**) (Scheme 30).[29]



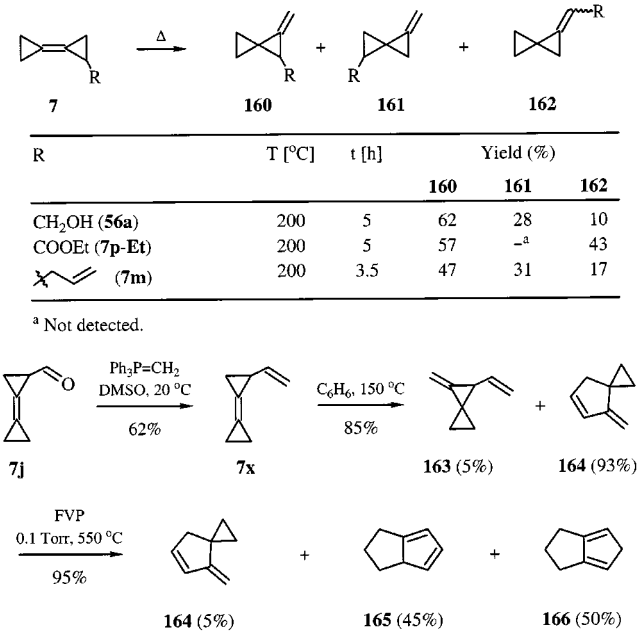
**2** **158** **159**

| T [°C] | t [h] | Conditions | **158** (%) | **159** (%) |
|---|---|---|---|---|
| 230 | – | flow pyrolysis | no reaction | |
| 330 | – | flow pyrolysis | 85 | – |
| 210 | 4 | sealed ampoule | 55 | 35 |
| 170 | 84 | 50% soln in toluene, sealed ampoule | 18 | 68 |

Scheme 30. Thermal transformations of bicyclopropylidene (**2**) under various conditions (see refs.[1a,1d,29,55,56])

As a rule, although with several exceptions, the thermal rearrangements of functionally substituted bicyclopropylidenes of type **7** yield mixtures of compounds (Scheme 31).[55b,57] The ethenyl-substituted bicyclopropylidene **7x**, prepared by Wittig olefination of the aldehyde **7j**, undergo a multistep rearrangement via 2-ethenyl-1-methylenespiropentane (**163**) and 4-methylenespiro[2.4]hept-5-ene (**164**) to eventually yield a 1:1 mixture of the two bicyclo[3.3.0]octadienes **165** and **166**.[55b]

In protic solvents, the alkylbicyclopropylidenes **7e,f** can be smoothly reduced with lithium to give a mixture of *cis*- and *trans*-2-substituted bicyclopropyl derivatives almost quantitatively. The stereoselectivity of these reductions with dissolved lithium is strongly affected by the solvent and the temperature — it is highly *trans*-stereoselective in liquid ammonia at −35 °C (Scheme 32). Utilizing this reactivity,



**7** **160** **161** **162**

| R | T [°C] | t [h] | Yield (%) | | |
|---|---|---|---|---|---|
| | | | **160** | **161** | **162** |
| $CH_2OH$ (**56a**) | 200 | 5 | 62 | 28 | 10 |
| COOEt (**7p-Et**) | 200 | 5 | 57 | –[a] | 43 |
| (**7m**) | 200 | 3.5 | 47 | 31 | 17 |

[a] Not detected.



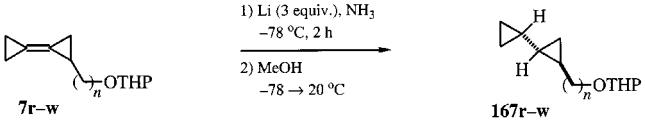
**7j** **7x** **163** (5%) **164** (93%)



**164** (5%) **165** (45%) **166** (50%)

Scheme 31. Thermal rearrangement of the 2-substituted bicyclopropylidenes **56a**, **7p-Et**, **7m** and ethenylbicyclopropylidene (**7x**) (see refs.[55b,57])

the THP-protected (bicyclopropylidenyl)alkanols **7r**−**w** were reduced to the *trans*-bicyclopropyl derivatives **167r**−**w** (Scheme 32) which, after deprotection, were oxidized to bicyclopropyl-substituted fatty acids. The latter were investigated for their biological activity and degradation[9] or applied to prepare liquid crystalline compounds with bicyclopropyl-substituted side chains.[58]



**7r–w** **167r–w**

| *n* | 3 | 4 | 5 | 6 | 7 | 8 |
|---|---|---|---|---|---|---|
| Product | **167r** | **167s** | **167t** | **167u** | **167v** | **167w** |
| Yield (%) | 64 | 88 | 83 | 87 | 67 | 75 |

Scheme 32. *trans*-Stereoselective reduction of the double bonds in the THP-protected (bicyclopropylidenyl)alkanols **7r**−**w** (see ref. [9])

The higher-order cuprate generated from lithiobicyclopropylidene and $[CuIBu_3P]_4$ can be oxidatively dimerized to give an 80% yield of bis(bicyclopropylidenyl) **168** as a 1.6:1 mixture of *meso*- and *d,l*-diastereomers (Scheme 33).[14a]

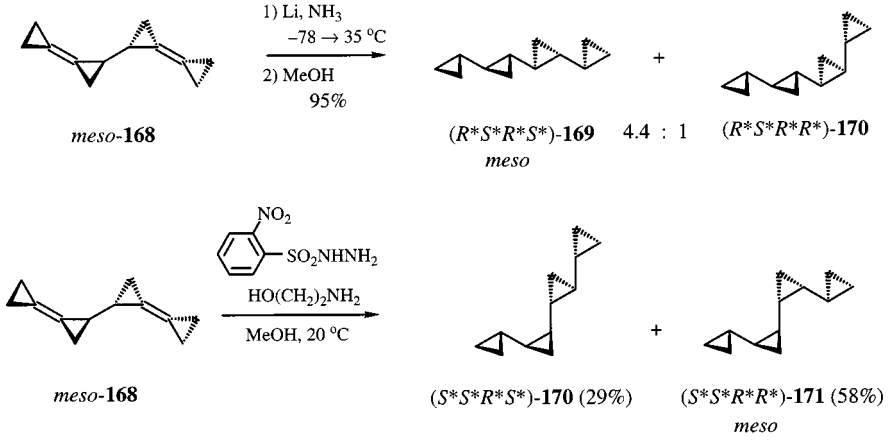
The reduction of *meso*-bis(bicyclopropylidenyl) (*meso*-**168**) with lithium in liquid ammonia gives an almost quantitative yield of the two diastereomeric quatercyclopropyls *trans,trans*-**169** and *cis,trans*-**170** in a ratio of 4.4:1 (Scheme 34).[14a] On the other hand, reduction of *meso*-**168** with the diimine generated from 2-nitrobenzenesulfonyl hydrazide gives the *cis,cis*-quatercyclopropyl (**171**) as the main product (isolated by chromatography) along with the *cis,trans*-diastereomer **170** (Scheme 34).[14a]

Bicyclopropylidene derivatives have also been used to prepare bicyclopropylidene analogs of biologically active methylenecyclopropane derivatives. Two particularly interesting examples are the naturally occurring 3-(2-methylenecyclopropyl)alanine (**172**), so-called hypoglycine A, and 1-amino-2-methylenecyclopropane-1-carboxylic acid (methylene-ACC) (**173**), which both show a strong hypoglycemic effect (Figure 1).[59]

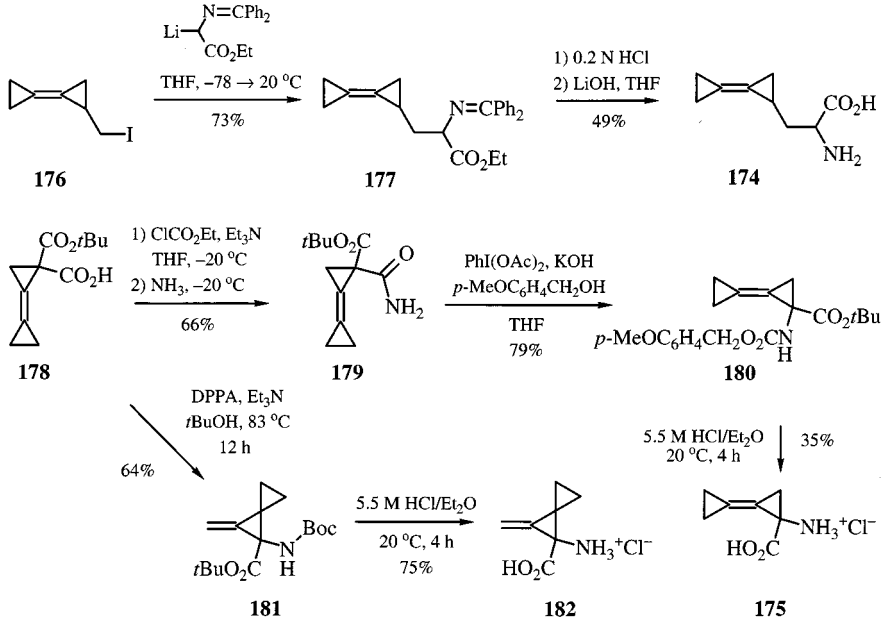
Since the more highly strained bicyclopropylidene (**2**), a cyclopropanated analog of methylenecyclopropane, is even more reactive than the latter, it is to be expected that analogs **174** and **175** of the amino acids **172** and **173**, containing a bicyclopropylidenyl moiety, would also exhibit biological activities. While these amino acids **174** and **175**, as well as the methylenespiropentane amino acid **182**, have been prepared recently (Scheme 35),[8] their biological activities have still not been tested.

**2** *meso*-**168** 1.3 : 1 *d,l*-**168**

Scheme 33. Synthesis of *meso*- and *d,l*-bis(bicyclopropylidenyl) *meso*- and *d,l*-**168** (see ref.[14a])




Scheme 34. Reduction of the double bonds in *meso*-bis(bicyclopropylidenyl) (*meso*-**168**) under various conditions to yield quatercyclopropyls **169**−**171** (see ref.[14a])




Scheme 35. Preparation of bicyclopropylidene and methylenespiropentane analogs **174**, **175** and **182** of biologically active amino acids with a methylenecyclopropane moiety (see ref.[8])

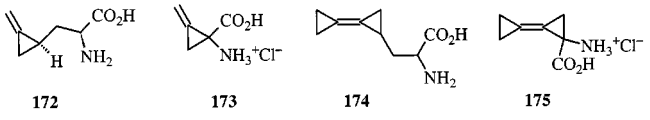



Figure 1. Biologically active methylenecyclopropane amino acids and their bicyclopropylidene analogs (see refs.[8,59])

## Conclusion

The presented results illustrate the broad synthetic applicability of bicyclopropylidene (**2**) and its derivatives in organic synthesis, especially towards the preparation of new cyclopropyl-containing compounds. Nevertheless, there is a huge unexplored area of bicyclopropylidene chemistry in view of modern organometallic chemistry, and there is a broad scope for the preparation and synthetic application of new bicyclopropylidene derivatives.

[1] [1a] P. Le Perchec, J.-M. Conia, *Tetrahedron Lett*. **1970**, 1587−1588. − [1b] A. de Meijere, Habilitationsschrift, Universität Göttingen, **1971**. − [1c] A. de Meijere, *Chem. Ber*. **1974**, *107*, 1702−1713. − [1d] J. M. Denis, P. Le Perchec, J.-M. Conia, *Tetrahedron* **1977**, *33*, 399−408.

[2] [2a] J. M. Denis, C. Girard, J.-M. Conia, *Synthesis* **1972**, 549−550. − [2b] A. J. Schipperijn, Recl. Trav. Chim. Pays-*Bas* **1971**, *90*, 1110. − [2c] A. J. Schipperijn, P. Smael, Recl. Trav. Chim. Pays-*Bas* **1973**, *92*, 1121−1133. − [2d] D. Kaufmann, A. de Meijere, Chem. *Ber*. **1984**, *117*, 3134−3150.

[3] [3a] L. Fitjer, J.-M. Conia, *Angew. Chem*. **1973**, *85*, 347−349; *Angew. Chem. Int. Ed. Engl*. **1973**, *12*, 332−334. − [3b] A. H. Schmidt, U. Schirmer, J.-M. Conia, *Chem. Ber*. **1976**, *109*, 2588−2595. − [3c] W. Weber, A. de Meijere, *Synth. Commun*. **1986**, *16*, 837−845. − [3d] K. A. Lukin, T. S. Kuznetsova, S. I. Kozhushkov, V. A. Piven′, N. S. Zefirov, *Zh. Org. Khim*. **1988**, *24*, 1644−1648; *J. Org. Chem. USSR (Engl. Transl.)* **1988**, *24*, 1483−1486.

[4] Reviews: [4a] O. G. Kulinkovich, A. de Meijere, *Chem. Rev*. **2000**, *100*, 2789−2834. − [4b] B. Breit, *J. Prakt. Chem*. **2000**,

*342*, 211−214. − [4c] F. Sato, H. Urabe, S. Okamoto, *Synlett* **2000**, 753−775.

[5] [5a] A. de Meijere, S. I. Kozhushkov, T. Spaeth, N. S. Zefirov, *J. Org. Chem*. **1993**, *58*, 502−505. − [5b] A. de Meijere, S. I. Kozhushkov, T. Spaeth, *Org. Synth*. **2000**, in press.

[6] Reviews: [6a] A. de Meijere, S. I. Kozhushkov, A. F. Khlebnikov, *Zh. Org. Khim*. **1996**, *32*, 1607−1626; *Russ. J. Org. Chem. (Engl. Transl.)* **1996**, *32*, 1555−1575. − [6b] A. de Meijere, S. I. Kozhushkov, A. F. Khlebnikov, *Top. Curr. Chem.* **2000**, *207*, 89−147.

[7] A. de Meijere, S. I. Kozhushkov, N. S. Zefirov, *Synthesis* **1993**, 681−683.

[8] M. Brandl, S. I. Kozhushkov, D. S. Yufit, J. A. K. Howard, A. de Meijere, *Eur. J. Org. Chem*. **1998**, 2785−2795.

[9] S. Löhr, C. Jacobi, A. Johann, G. Gottschalk, A. de Meijere, *Eur. J. Org. Chem*. **2000**, 2979−2989.

[10] T. Heiner, S. I. Kozhushkov, M. Noltemeyer, T. Haumann, R. Boese, A. de Meijere, *Tetrahedron* **1996**, *52*, 12185−12196.

[11] W. R. Moore, H. R. Ward, *J. Org. Chem.* **1960**, *25*, 2073−20XX. For the first, but unverified, communication on the preparation of a bicyclopropylidene derivative, see: E. P. Kohler, S. F. Darling, *J. Am. Chem. Soc.* **1930**, *52*, 424−432.

[12] [12a] J. Arct, L. Skattebøl, *Acta Chem. Scand*. **1982**, *B 36*, 593−598. − [12b] C. Rømming, *Acta Chem. Scand*. **1981**, *A 35*, 725−726.

[13] [13a] M. Borer, T. Loosli, M. Neuenschwander, *Chimia* **1991**, *45*, 382−386. − [13b] T. Loosli, M. Borer, I. Kulakowska, A. Minder, M. Neuenschwander, P. Engel, *Helv. Chim. Acta* **1995**, *78*, 1144−1165. − [13c] M. Borer, T. Loosli, A. Minder, M. Neuenschwander, P. Engel, *Helv. Chim. Acta* **1995**, *78*, 1311−1324. − [13d] M. Borer, M. Neuenschwander, *Helv. Chim. Acta* **1997**, *80*, 2486−2501. − [13e] R. Huwyler, X. Li, P. Bönzli, M. Neuenschwander, *Helv. Chim. Acta* **1999**, *82*, 1242−1249.

[14] [14a] M. von Seebach, Dissertation, Universität Göttingen, **2000**. − [14b] H. W. Anderson, PhD Thesis, Massachusetts Institute of Technology, Cambridge, Massachusetts, **1972**. − [14c] A. de Meijere, M. von Seebach, S. Zöllner, S. I. Kozhushkov, V. N. Belov, R. Boese, J. Benet-Buchholz, D. S. Yufit, J. A. K. Howard, *Eur. J. Org. Chem*. **2000**, to be submitted.

[15] [15a] R. C. Lord, C. J. Warrey, *Spectrochim. Acta* **1973**, *A30*, 915−921. − [15b] A. Hofland, T. J. de Boer, Recl. Trav. Chim. Pays-*Bas* **1987**, *106*, 558−562. − [15c] A. de Meijere, F. Seyed-Mahdavi, M. Spickermann, unpublished results.

[16] [16a] F. Gerson, A. de Meijere, X.-Z. Qin, *J. Am. Chem. Soc*. **1989**, *111*, 1135−1136. − [16b] F. Gerson, R. Schmidlin, A. de Meijere, T. Späth, *J. Am. Chem. Soc*. **1995**, *117*, 8431−8434.

[17] [17a] R. Gleiter, R. Haider, J.-M. Conia, J.-P. Barnier, A. de Meijere, W. Weber, *J. Chem. Soc., Chem. Commun*. **1979**, 130−132. − [17b] R. Gleiter, J. Spanget-Larson, in *Advances in Strain in Organic Chemistry, Vol. 2* (Ed.: B. Halton), JAI Press Ltd, London, **1992**, pp. 143−189.

[18] [18a] M. Trætteberg, A. Simon, E. M. Peters, A. de Meijere, *J. Mol. Struct*. **1984**, *118*, 333−343. − [18b] J. S. A. M. de Boer, C. H. Stam, Recl. Trav. Chim. Pays-*Bas* **1993**, *112*, 635−638. − [18c] R. Boese, T. Haumann, P. Stellberg, in *Advances in Molecular Structure Research, Vol. 1* (Eds.: M. Hargittai, I. Hargittai), JAI Press Ltd, London, **1995**, pp. 202−226, and references therein.

[19] R. Boese, in *Advances in Strain in Organic Chemistry, Vol. 2* (Ed.: B. Halton), JAI Press Ltd, London, **1992**, pp. 191−254.

[20] R. Boese, T. Haumann, E. D. Jemmis, B. Kiran, S. I. Kozhushkov, A. de Meijere, *Liebigs Ann*. **1996**, 913−919.

[21] V. P. Kolesov, S. M. Pimenova, V. A. Lukyanova, T. S. Kuznetsova, M. P. Kozina, *J. Chem. Thermodynamics* **1998**, *30*, 1455−1464.

[22] L. Fitjer, J.-M. Conia, *Angew. Chem*. **1973**, *85*, 349−350; *Angew. Chem. Int. Ed. Engl*. **1973**, *12*, 334−335.

[23] K. A. Lukin, N. S. Zefirov, *Dokl. Akad. Nauk. SSSR* **1989**, *305*, 631−634; *Dokl. Chem. (Engl. Transl.)*. **1989**, *305*, 104−106.

[24] K. A. Lukin, A. A. Andrievskii, N. S. Zefirov, *Dokl. Akad. Nauk. SSSR* **1991**, *321*, 521−523; *Dokl. Chem. (Engl. Transl.)* **1991**, *321*, 353−355.

[25] L. Fitjer, J.-M. Conia, *Angew. Chem*. **1973**, *85*, 832−833; *Angew. Chem. Int. Ed. Engl*. **1973**, *12*, 761−762.

[26] [26a] K. A. Lukin, N. S. Zefirov, *Zh. Org. Khim.* **1987**, *23*, 2548−2552; *J. Org. Chem. USSR (Engl. Transl.)* **1987**, *23*, 2249−2252. − [26b] K. A. Lukin, N. S. Zefirov, D. S. Yufit, Yu. T. Struchkov, *Tetrahedron* **1992**, *45*, 9977−9984. − [26c] S. Zöllner, Dissertation, Universität Hamburg, **1991**.

[27] [27a] K. Miyazawa, D. S. Yufit, J. A. K. Howard, A. de Meijere, *Eur. J. Org. Chem*., in press. − [27b] K. Miyazawa, Dissertation, Universität Göttingen, **2000**.

[28] A. de Meijere, S. I. Kozhushkov, D. S. Yufit, R. Boese, T. Haumann, D. L. Pole, P. K. Sharma, J. Warkentin, *Liebigs Ann*. **1996**, 601−612.

[29] A. de Meijere, I. Erden, W. Weber, D. Kaufmann, *J. Org. Chem*. **1988**, *53*, 152−161.

[30] W. Weber, I. Erden, A. de Meijere, *Angew. Chem*. **1980**, *92*, 387−388; *Angew. Chem. Int. Ed. Engl*. **1980**, *19*, 387−388.

[31] A. de Meijere, H. Wenck, F. Seyed-Mahdavi, H. G. Viehe, V. Gallez, *Tetrahedron* **1986**, *42*, 1291−1297.

[32] [32a] D. Kaufmann, A. de Meijere, *Angew. Chem*. **1973**, *85*, 151−152; *Angew. Chem. Int. Ed. Engl*. **1973**, *12*, 159−160. − [32b] T. Thiemann, D. Ohira, Y. Li, T. Sawada, S. Mataka, K. Rauch, M. Noltemeyer, A. de Meijere, *J. Chem. Soc., Perkin Trans. 1* **2000**, in press.

[33] [33a] R. M. Schonk, C. W. Meijer, H. H. Bakker, S. Zöllner, H. Cerfontain, A. de Meijere, Recl. Trav. Chim. Pays-*Bas* **1993**, *112*, 457−461. − [33b] R. M. Schonk, B. H. Bakker, H. Cerfontain, *Phosph. Sulf. Sil. Relat. Elem*. **1991**, *59*, 173−176 and 467−470.

[34] T. S. Kuznetsova, S. I. Kozhushkov, K. A. Lukin, Yu. K. Grishin, D. V. Bazhenov, A. S. Koz′min, N. S. Zefirov, *Zh. Org. Khim*. **1991**, *27*, 78−83; *J. Org. Chem. USSR (Engl. Transl.)* **1991**, *27*, 67−71.

[35] [35a] T. Späth, Dissertation, Universität Göttingen, **1995**. − [35b] T. Späth, S. I. Kozhushkov, T. Fiebig, M.-F. Ruasse, M. Dodin, K. Albrecht, Y. Apeloig, A. de Meijere, J. Org. *Chem.* **2000**, to be submitted.

[36] S. Zöllner, H. Buchholz, R. Boese, R. Gleiter, A. de Meijere, *Angew. Chem*. **1991**, *103*, 1544−1546; *Angew. Chem. Int. Ed. Engl*. **1991**, *30*, 1518−1520.

[37] S. I. Kozhushkov, M. Brandl, A. de Meijere, Eur. *J. Org. Chem*. **1998**, 1535−1542.

[38] A. Brandi, A. Goti, S. I. Kozhushkov, A. de Meijere, *J. Chem. Soc., Chem. Commun*. **1994**, 2185−2186.

[39] A. Goti, B. Anichini, A. Brandi, S. I. Kozhushkov, C. Gratkowski, A. de Meijere, *J. Org. Chem*. **1996**, *61*, 1665−1672.

[40] B. Anichini, A. Goti, A. Brandi, S. I. Kozhushkov, A. de Meijere, *Synlett* **1997**, 25−26; F. M. Cordero, I. Barile, A. Brandi, S. I. Kozhushkov, A. de Meijere, *Synlett* **2000**, 1034−1037.

[41] [41a] A. Goti, B. Anichini, A. Brandi, A. de Meijere, L. Citti, S. Nevischi, *Tetrahedron Lett*. **1995**, *36*, 5811−5814. − [41b] C. Zorn, B. Anichini, A. Goti, A. Brandi, S. I. Kozhushkov, A. de Meijere, L. Citti, *J. Org. Chem*. **1999**, *64*, 7846−7855, and references cited therein.

[42] S. Bräse, A. de Meijere, *Angew. Chem*. **1995**, *107*, 2741−2743; *Angew. Chem. Int. Ed. Engl*. **1995**, *34*, 2545−2547.

[43] [43a] A. de Meijere, H. Nüske, M. Es-Sayed, T. Labahn, M. Schroen, S. Bräse, *Angew. Chem*. **1999**, *111*, 3881−3884; *Angew. Chem. Int. Ed*. **1999**, *38*, 3669−3672. − [43b] H. Nüske, S. Bräse, S. I. Kozhushkov, A. de Meijere, *Chem. Eur. J.* **2000**, in preparation. − [43c] H. Nüske, Dissertation, Universität Göttingen, **2000**.

[44] D. Kaufmann, A. de Meijere, *Tetrahedron Lett*. **1979**, 779−782.

[45] P. Binger, P. Wedemann, S. I. Kozhushkov, A. de Meijere, *Eur. J. Org. Chem*. **1998**, 113−119.

[46] M. Brandl, S. I. Kozhushkov, S. Bräse, A. de Meijere, *Eur. J. Org. Chem*. **1998**, 453−457.

[47] S. I. Kozhushkov, M. Brandl, D. S. Yufit, R. Machinek, A. de Meijere, *Liebigs Ann./Recueil* **1997**, 2197−2204.

[48] J. Foerstner, S. I. Kozhushkov, P. Binger, P. Wedemann, A. de Meijere, H. Butenschön, *J. Chem. Soc., Chem. Commun*. **1998**, 239−240.

[49] Reviews: [49a] A. de Meijere, S. I. Kozhushkov, *Chem. Rev.* **2000**, *100*, 93−142. − [49b] A. de Meijere, S. I. Kozhushkov, in *Advances in Strain in Organic Chemistry, Vol. 4* (Ed.: B. Halton), JAI Press Ltd., London, **1995**, pp. 225−282.

[50] [50a] N. S. Zefirov, K. A. Lukin, S. I. Kozhushkov, T. S. Kuznetsova, A. M. Domarev, I. M. Sosonkin, *Zh. Org. Khim*. **1989**, *25*, 312−319; *J. Org. Chem. USSR (Engl. Transl.)* **1989**, *25*, 278−284. − [50b] I. Erden, *Synth. Commun*. **1986**, *16*, 117−121.

[51] N. S. Zefirov, S. I. Kozhushkov, B. I. Ugrak, K. A. Lukin, O.

V. Kokoreva, D. S. Yufit, Yu. T. Struchkov, S. Zoellner, R. Boese, A. de Meijere, *J. Org. Chem*. **1992**, *57*, 701−708.
[52] S. I. Kozhushkov, T. Haumann, R. Boese, A. de Meijere, *Angew. Chem*. **1993**, *105*, 426−429; *Angew. Chem. Int. Ed. Engl*. **1993**, *32*, 401−403.
[53] M. von Seebach, S. I. Kozhushkov, R. Boese, J. Benet-Buchholz, D. S. Yufit, J. A. K. Howard, A. de Meijere, *Angew. Chem*. **2000**, *112*, 2617−2620; *Angew. Chem. Int. Ed.* **2000**, *39*, 2495−2498.
[54] A. de Meijere, A. F. Khlebnikov, R. R. Kostikov, S. I. Kozhushkov, P. R. Schreiner, A. Wittkopp, D. S. Yufit, *Angew. Chem*. **1999**, *111*, 3682−3685; *Angew. Chem. Int. Ed.* **1999**, *38*, 3474−3477.
[55] [55a] D. Faber, Dissertation, Universität Göttingen, **1996**. − [55b] D. Faber, S. I. Kozhushkov, V. Bagutskii, A. de Meijere, unpublished results.
[56] H.-D. Beckhaus, C. Rüchardt, S. I. Kozhushkov, V. N. Belov, S. P. Verevkin, A. de Meijere, *J. Am. Chem. Soc*. **1995**, *117*, 11854−11860.
[57] K. A. Lukin, N. S. Zefirov, *Zh. Org. Khim*. **1991**, *27*, 1358−1361; *J. Org. Chem. USSR (Engl. Transl.)* **1991**, *27*, 1187−1190.
[58] K. Miyazawa, S. Löhr, A. de Meijere, *Mol. Cryst. Liq. Cryst*. **2000**, in press.
[59] [59a] J. E. Baldwin, R. M. Adlington, D. Bebbington, A. T. Russell, *Tetrahedron* **1994**, *50*, 12015−12028, and references cited therein. − [59b] M.-T. Lai, L.-D. Liu, H.-W. Liu, *J. Am. Chem. Soc*. **1991**, *113*, 7388−7397. − [59c] M.-T. Lai, H.-W. Liu, *J. Am. Chem. Soc.* **1992**, *114*, 3160−3162. − [59d] N. Kurokawa, Y. Ohfune, *Tetrahedron Lett*. **1985**, *26*, 83−84. − [59e] K. Li, W. Du, N. L. S. Que, H.-W. Liu, *J. Am. Chem. Soc*. **1996**, *118*, 8763−8764.

Received July 10, 2000
[O00346]