The Chemistry of Highly Strained Oligospirocyclopropane Systems†

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I. Introduction

By now it should be common knowledge that the chemical properties of systems containing three-membered rings may be profoundly different from those of acyclic analogues and of corresponding derivatives of larger cycloalkanes.[1,2] The pronounced tendency to undergo ring-opening reactions is a consequence of the ring strain and the peculiar type of bonding in cyclopropane. An even more enhanced chemical reactivity of a cyclopropane moiety may be observed when either the cyclopropyl group is conjugated with appropriate electronically active substituents[3−5] or its overall strain[6] is increased by incorporation into an oligocyclic molecule in such a way that it shares an atom (spirofusion) or two (annelation) with another small ring, especially another cyclopropane.

† Dedicated to Professor Wolfgang Lüttke on the occasion of his 80th birthday.

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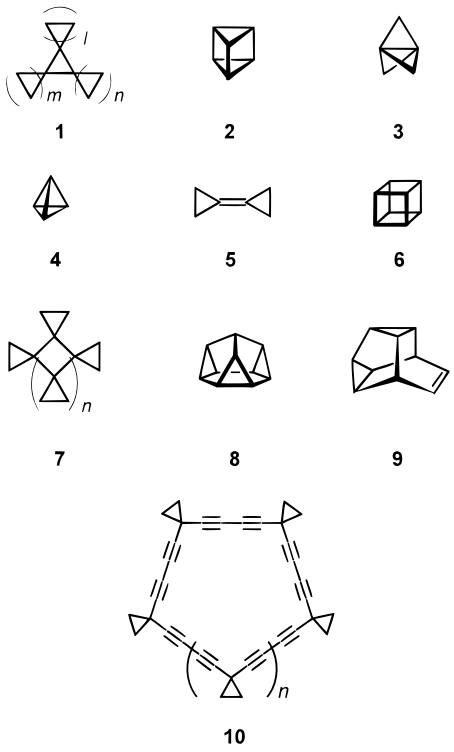
Understanding the influence of strain in organic molecules upon their reactivity is of fundamental importance not only as a theoretical exercise, but also for experimental application, since the concept of strain and strain energies provides a basis that helps to correlate the structures, stabilities, and reactivities of molecules,[1,2] at least for certain types of reactions. A quantitative assessment of strain and strain energies (SE) can only be made by taking the difference between the enthalpy of formation ΔH(g) of the substance under consideration (theoretically calculated or experimentally determined) and that of a hypothetical strain-free model.[1] Basically, there are two approaches based on either an additivity scheme of (i) bond energies (BE) or (ii) group increments (GI) (for details see refs 1 and 2). In many cases, the total SE of a polycycle only slightly differs from the sum of SE's of their constituting monocycles.[7] This rule even holds for such hydrocarbons as cubane[8] (**6**, Chart 1) (SE_{exp} = 161.7 versus ΣSE_{cycl} = 161.4 kcal/mol[9,10]), cyclic oligomers of cyclopropylidene [*n*]rotanes **7**[11] with $n \geq 4$,[12] diademane **8**[13] (108.6 vs 107.3 kcal/mol[14]), snoutene **9**[13] (78.3 vs 75.6 kcal/mol[15]), and

Chart 1



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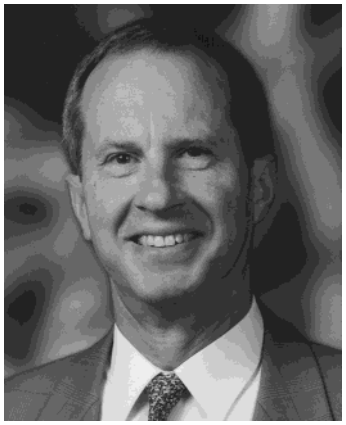


Armin de Meijere was born in 1939 in Homberg (Niederrhein), Germany. He studied chemistry at the universities of Freiburg and Göttingen and obtained his doctorate (Dr. Rer. Nat.) at the University of Göttingen under the guidance of Wolfgang Lüttke. Following postdoctoral training under Kenneth B. Wiberg at Yale University in new Haven, CT, he obtained 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 as Professor of Organic Chemistry in October 1989. He is currently Dean of the Faculty of Chemistry at the University of Göttingen. He has been a visiting professor at the University of Wisconsin in Madison, WI, the IBM Research Laboratory in San Jose, CA, the Technion in Haifa, Israel, Princeton University in Princeton, NJ, the University of Aix-Marseille III, the Università degli Studi, Firenze, Italy, the Ecole Normale Supérieur, Paris, France, the University of Colorado, Boulder, CO, and the University of Florida, Gainsville, FL. He received a fellowship from the Studienstiftung des Deutschen Volkes, obtained the award "Dozentenstipendium" from the Fonds der Chemischen Industrie in 1972, and was elected a member of the Norwegian Academy of Sciences and Letters in 1992, and in 1996 he 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 Japan Society for the Promotion of Science. He is Editor or member of the editorial board of a number of scientific journals, periodicals, and books. His scientific achievements have been published in over 400 original publications, review articles, and chapters in books. His current research interests include the development of new small-ring building blocks and their application in the synthesis of natural and non-natural compounds; new highly strained polycyclic compounds with interesting properties; and preparation and applications of organometallic complexes and catalysts in organic synthesis.

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 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. Since 1996 he has held a position of a Scientific Assistant. His current research interests focus on the chemistry of highly strained small-ring compounds.

"exploded" [*n*]rotanes **10**.[16] Yet for several hydrocarbons the total SE of the molecule significantly exceeds the sum of SE's of its components. This is particularly true for the whole family of hydrocarbons that consist of spiroannelated cyclopropane rings only—the so-called linear- and branched[*n*]-triangulanes (**1**) as well as their cycloannelated analogues,[11b,17] triprismane (**2**)[18] (149.4 vs 137 kcal/mol[19]), [1.1.1]-propellane (**3**)[20] (104.2 vs 84.4 kcal/mol[21]), tetrahedrane (**4**)[22] (140.8 vs 112.5 kcal/mol), and bicyclopropylidene (**5**) (77.4 vs 56.2 kcal/mol[23]). No matter whether a hydrocarbon exhibits a total strain that does or does not follow the additivity schemes, its thermal stability and chemical reactivity does not simply correlate with its total strain energy nor with its number of small-ring subunits and their mode of junction (spirofused or annelated).

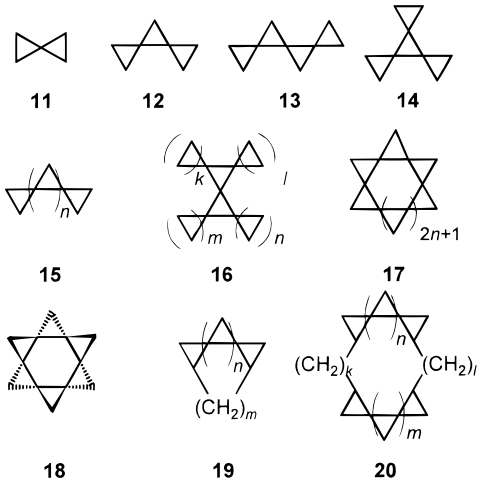
This review is focused on the family of highly strained [*n*]triangulanes **1**, their cycloannelated analogues and functional derivatives. All of these hydrocarbon skeletons are relatively stable toward heating and a variety of chemical reagents despite their high overall strain energies. This compilation is intended to summarize old and new developments for this class of compounds and in particular includes the most recent results. However, it would be impossible in this article to present a comprehensive review on spiropentane (**11**) and all of its derivatives (827 compounds), as in the period of over 100 years since the first preparation of spiropentane **11**[24] spirocondensed three-membered ring systems have been the subject of numerous investigations.

II. Triangulanes: Nomenclature, Classification, and Stereoisomerism

The two known theoretical models describing the unique bonding in cyclopropane are essentially equal and can be transformed into each other.[25−27] The spiroannelation of two or more cyclopropane rings in a molecule, which is accompanied by an additional increase in strain, causes even more changes in the hybridization and thus the electronic structure. This in turn can lead to remarkable changes in physical and chemical properties. A number of theoretical studies were focused primarily on the quantitative estimation of structural[21,28−35a] and energetic[10,21,28,29a,30,32,33,35−39] parameters as well as the bonding properties[21,28,29a,30,33a,37,40−43] in such hydrocarbons. It has only been during the past 30 years that synthetic approaches to hydrocarbons such as **12**,[44,45,47,50] **13**,[46,50] and **14**,[46−50] consisting of three and four spirocondensed cyclopropane units, have been elaborated. Eventually such hydrocarbons were termed triangulanes,[51] and several synthetic strategies for the preparation of higher members in this family of hydrocarbons have been proposed.[51−57]

The whole class of triangulanes can be subdivided into three subclasses according to their structure

Chart 2



(Chart 2): the unbranched[*n*]triangulanes (UTs) **15**[51] (other names linear[*n*]-triangulanes, LTs,[52] or chain-[*n*]triangulanes, CHTs[58]), the branched[*n*]triangulanes (BTs) **16**,[52−57] and cyclo[*n*]triangulanes (CTs) **17**. Thus, spiropentane (**11**), according to this definition, is unbranched[2]triangulane ([2]UT), [3]rotane **14**[11] is the only possible branched[4]triangulane ([4]BT, other rotanes cannot be called triangulanes), and "davidane" **18** is cyclo[6]triangulane ([6]CT).[59] It has also been proposed to name compounds of type **19** and **20** "cyclosubstituted[*n*]triangulanes" (CSTs),[59,62−65] although the term "cycloannelated[*n*]-triangulanes" (CATs) would be more appropriate. Up to now, several synthetic approaches to UTs and BTs have been successful. The first members of the CAT family of type **19** ($n = 0$, $m = 2$, 3) have been known since 1962,[66] and more than 20 years later several compounds of type **19** and **20** with more than two spirocyclopropane units were eventually prepared.[67−70] Only the cyclo[*n*] triangulanes remain elusive, as there is no communication yet reporting the successful preparation of any CT. Two points can be made in advance: (i) A cyclic triangulane can only be constructed with an even number of three-membered rings and a planar central ring[35a] and (ii) according to various calculations [8]CT would be the most realistic and straightforward synthetic target,[35a,39] yet and [10]CT and [6]CT ("davidane") **18** should not be impossible despite their excessive strain due to the additional angle distortion in their spiropentane subunits.

The stereochemical features of triangulanes are sufficiently intriguing and thus deserve special consideration. The elucidation of possible stereoisomeric triangulanes is not straightforward for the higher members of the family, because the number of geometrical isomers grows rapidly with an increasing number of three-membered rings and many of the diastereomers are chiral. Thus, the molecule of trispiro[2.0.2.1]heptane ([3]UT) **12**, being achiral itself, has two enantiotopic positions: attachment of a fourth spirocyclopropane ring in either position a or b in **12** will lead to two enantiomeric [4]UTs (*M*)- and (*P*)-**13** (Scheme 1).[51,71] Essentially, the C_2-symmetric molecule of **13** is a section of a helix, and therefore, the stereochemical descriptors for helicenes

Scheme 1

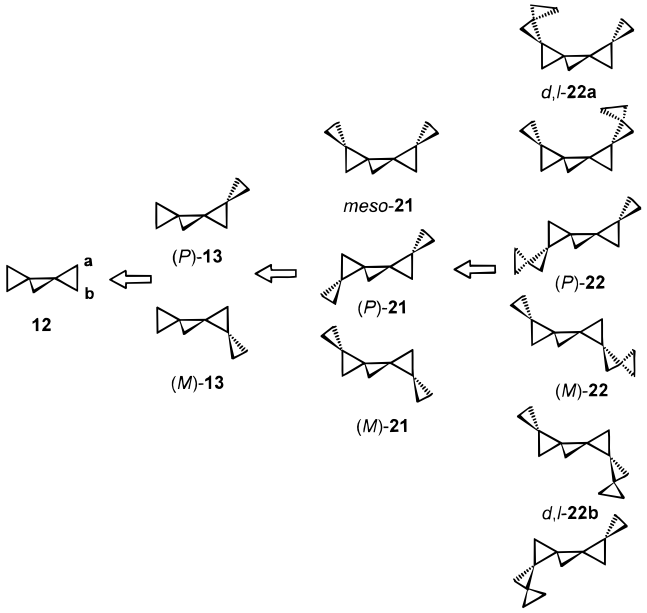


Table 1. Number of Enantiomeric Pairs (N_1) and Number of Achiral Stereoisomers (N_2) of [*n*]UTs with Increasing Number (*n*) of Three-Membered Rings

	n								
	2	3	4	5	6	7	8	9	10
N_1	0	0	1	1	3	4	10	16	36
N_2	1	1	0	1	0	2	0	4	0

can logically be applied for **13** and extended unbranched[*n*]triangulanes.

Although [4]triangulane **13** has no chromophore which would lead to any significant absorption above 200 nm, full valence space single excitation configuration interaction treatment (SCI) computations at the B3LYP/6-31G(d) level of theory predicted for (*M*)-[4]triangulane **13**, even at 589 nm, the remarkably high specific rotation of $[\alpha]_D^{20} = -208.0$.[71] The rotatory strength of (*M*)-[5]triangulane **21** should be about twice as large as that of (*M*)-[4]triangulane **13**, whereas the rotatory strength of (*M*)-[6]triangulane **22** was calculated to be only slightly larger than that of **21**. These outstanding rotatory powers are in line with the helical arrangements of σ bonds in [*n*]-triangulanes, which justifies calling them σ-[*n*]helicenes in analogy to the well-known π-[*n*]helicenes consisting of annelated aromatic subunits.

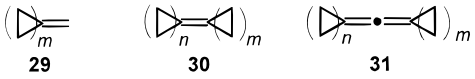
The stereochemical interrelations for the UTs have been examined from an algebraic−combinatorial point of view on the basis of abstract configuration theory;[72] a similar approach has been developed for the characterization of polybenzoid hydrocarbons.[73] Two main problems have been resolved by graph theory:[51] (i) the enumeration of possible stereoisomeric UTs, i.e., general equations to calculate the number of isomers have been obtained (see Table 1), and (ii) the construction of the generation tree to represent the interrelations between the stereoisomerism of UTs and their key synthetic precursors, the methylene[*n*]triangulanes. An analogous systematization of CTs and CATs is also in progress.[74]

III. Synthesis of Triangulanes

A. Synthetic Methods to Assemble Oligospirocyclopropanes

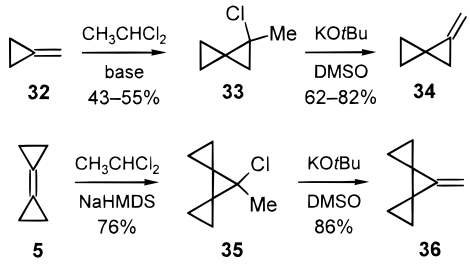
For the assembly of triangulane skeletons it is essential to select a set of standard chemical transformations compatible with cyclopropane chemistry, which can be applied in a repetitive fashion and permits one to perform two main structural transformations: the extension of an [*n*]triangulane chain (eq 1) and the termination by functional group removal (eq 2) or double bond cyclopropanation (eq 3). The majority of possibilities for such transformations has been elaborated on during the last 30 years and applied in preparations of the simple [2]-, [3]-, and [4]triangulanes.[44−50] Second, an appropriate sequence of transformations has to be elaborated on to achieve the desired skeleton. As a starting material, one can use a methylenetriangulane **29**, a bicyclopropylidene derivative **30**,[23] or an allene **31** (Chart 3). The best preparative method for the extension of a linear oligospirocyclopropane chain turned out to be the addition of chloromethylcarbene to a methylenecyclopropane as published by Binger et al. in 1974.[75] The cycloaddition of chloromethylcarbene to methylenecyclopropane **32** itself,[76] its derivatives of type **29**,[50,51,54] or bicyclopropylidenes **30**[12,49,50,54] in general and the parent **5** in particular[49,50] followed by dehydrochlorination with potassium *tert*-butoxide in DMSO gives the corresponding chain-extended methylene[*n*]triangulanes in moderate to good yields (Scheme 2). For the termination step in building an [*n*]triangulane chain, several reactions have been tested. Historically the first one[24] was the reductive ring closure by treatment of a 1,3-dihaloalkane with sodium metal; other reducing agents (Zn, Mg, RLi, etc.) have since been introduced and used with better success.[77] The preparation of spiropentane (**11**) from tetrakis(bromomethyl)methane (**39**) by this nowadays so-called Gustavson reaction was drastically improved by Applequist et al.,[78] who first used zinc dust in the presence of the disodium salt of ethylenediaminetetraacetic acid to trap the zinc bromide formed and thus prevent ring expansion and ring opening occurring at the stage of the intermediate 1,1-bis(bromomethyl)cyclopropane which would give methylenecyclobutane (**40**) and 2-methyl-1-butene (**41**).[79] The best results in such ring closures of 1,3-dihaloalkanes were achieved applying an electrochemical cathodic reduction.[80] The reductive ring closure was also applied in the first preparation of methylenespiropentane (**34**),[44a] 7-methylenedispiro[2.0.2.1]heptane (**36**), and 7-cyclopropylidenedispiro[2.0.2.1]heptane (**42**).[48,81,82] Nevertheless, in many cases this cyclization is accompanied by ring-opening and ring-expansion reactions of cyclopropanes[50,83,84] and cannot be recommended as a general procedure (Scheme 3).

Chart 3



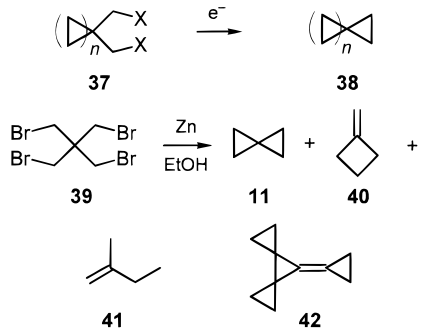
29 30 31

Scheme 2



32 33 34 5 35 36

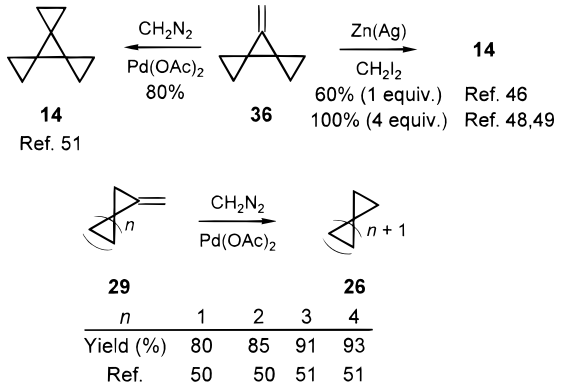
Scheme 3



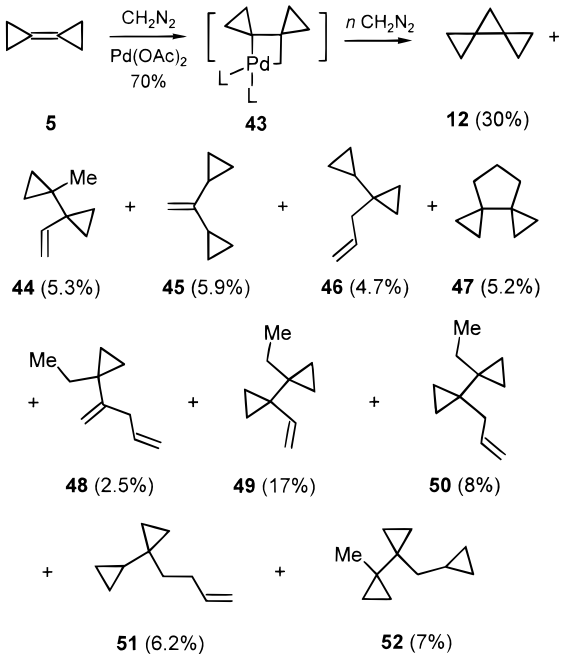
37 38 39 11 40 41 42

The most common methodology for the termination step is by cyclopropanation of the double bond in a methylene[*n*]triangulane **29** or cyclopropylidenetriangulane **30** with a methylene donor or a dihalocarbene transfer reagent and subsequent reduction. Methylene can be transferred to alkenes using diazomethane in the presence of a catalyst (e.g., CuCl, CuBr, CuOTf, $Pd(OAc)_2$, $[Rh(OAc)_2]_2$, etc.)[85] or with diiodomethane/zinc−copper or zinc−silver couple (Simmons−Smith reagent).[86] Every variant has its scope and limitations.[87] According to recent experience, diazomethane in the presence of $Pd(OAc)_2$[88] gives best results for the cyclopropanation of terminal double bonds in compounds of type **29**[50−56] (normally conversion is almost quantitative and isolated yields are about 80−90%). Sometimes, the Simmons−Smith reaction[86,87] gives comparable yields (Scheme 4).[48,49,55] For an internal double bond as in bicyclopropylidenes (cyclopropylidenetriangulanes) **30** and dicyclopropylidenemethane derivatives **31**, the use of CH_2N_2/$Pd(OAc)_2$ gives a number of products resulting from insertion of several methylene units into the initially formed palladacycle **43**,[89,90] as, e.g., observed in the attempted cyclopropanation of bicyclopropylidene (**5**)

Scheme 4

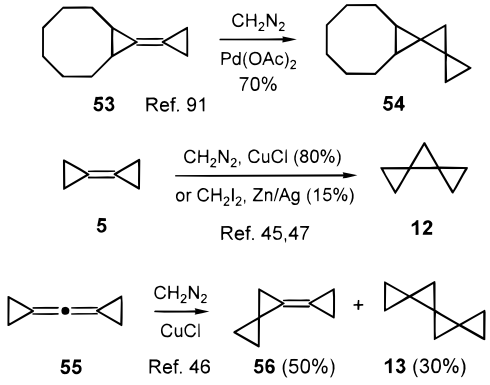


Scheme 5



itself (Scheme 5).[89a] However, this oligomethylenation was not observed in the recently performed cyclopropanation of the fused bicyclopropylidene derivative **53** (Scheme 6).[91] Also, the Gaspar–Roth protocol (CH_2N_2/CuCl)[92a] can be applied for the cyclopropanation of bicyclopropylidenes **30** and allenes of type **31** as well as allenes containing no three-membered rings,[92b–94] albeit the yields often leave much to be desired. The Simmons–Smith reaction, especially when accelerated by ultrasonication,[71] has also

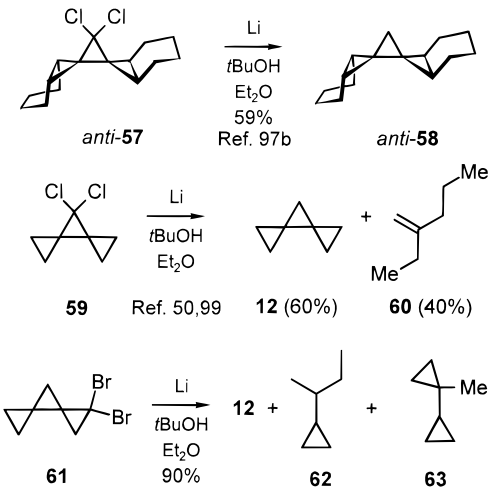
Scheme 6



been shown to be applicable for the cyclopropanation.[44,95]

Another possible terminating transformation is by addition of a dihalocarbene to compounds of type **29**–**31**[23,96] with subsequent reductive removal of the halogens using Zn/AcOH,[95] Na/ROH,[97a,d] $LiAlH_4$,[98] Zn/ROH,[98] Bu_3SnH,[98] or Li/tBuOH[50,95,97b] (Scheme 7). In

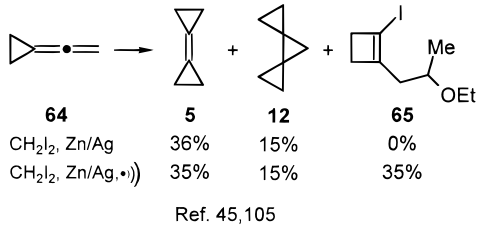
Scheme 7



some cases,[50,97a,99] partial reductive ring opening of the oligospirocyclopropane skeleton has been reported, but triangulane **12** was obtained exclusively upon reductive dehalogenation of **59** under the same conditions, yet at a lower temperature.[100]

One more reaction to be mentioned in this context is the cyclopropanation of ethenylidenecyclopropanes such as **64** and related allenes with the Simmons–Smith reagent. Normally it provides mixtures of mono- and dicyclopropanated products such as **5** and **12** in low to moderate yields.[11a,101–104] Surprisingly, the application of ultrasound in the case of allene **64** only complicated the situation in that it led to the formation of the 1-iodocyclobutene derivative **65** (Scheme 8).[105] The authors rationalize this as result-

Scheme 8



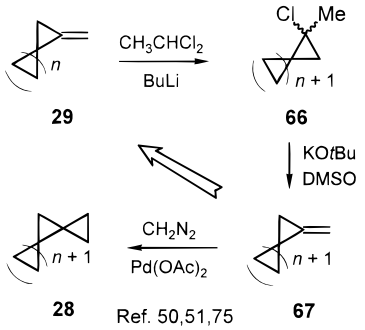
ing from the addition of an ethoxyethyl radical to the allene **64** followed by radical ring expansion of a new type and subsequent trapping of an iodine atom. It was found, however, that the yields of biscyclopropanated products from allenes of type **64** in Simmons–Smith cyclopropanations can be substantially improved using diiodomethane/trimethylaluminum as a reagent.[106]

B. Synthesis of Unbranched Triangulanes (UTs)

For the preparation of unbranched[*n*]triangulanes (UTs), two main strategies have been proposed and

examined. The first one includes step by step extension of the oligocyclopropane chain starting from methylenecyclopropane (**32**) itself and terminating with a cyclopropanation of the extended methylene-[n + 1]triangulane **67** using CH_2N_2/$Pd(OAc)_2$ (Scheme 9).[50,51] Along this route, [3]**12**, [4]**13**, [5]**21**, and [6]UT

Scheme 9

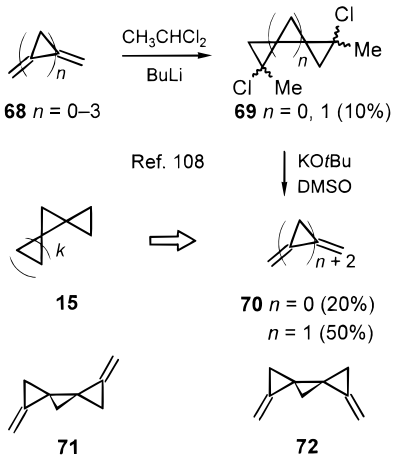


n	Yield of **66** (%)	**67** (%)	**28** (%)
0	45	82	80
1	40	75	85
2	85	75	91
3	60	82	93

22 have been prepared in good to excellent yields, and individual stereoisomers have been separated and characterized for [6]UT **22**. The main drawback of this methodology is, however, the lack of stereoselectivity: a mixture of all possible isomers is normally obtained, and the separation of individual compounds can be tedious (for example, it was not possible at all for [5]UT **21**).

Another possible approach utilizes the same sequence of transformations but starts with a bis-(methylene)triangulane of type **68**, extending the chain in both directions at the same time (Scheme 10).[107] The termination step was not examined in this

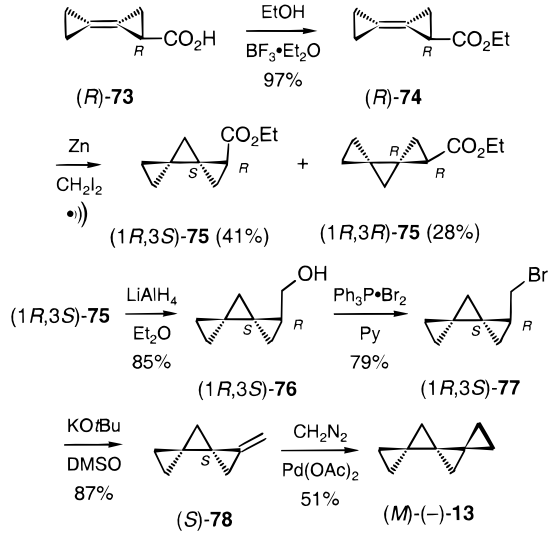
Scheme 10



case. This approach appears to give better results in terms of stereoselectivity; for example, diene **68** (n = 3) was obtained predominantly as the *anti*-isomer **71** (ratio **71**/**72** = 9:1). On the other hand, starting materials such as dimethylenecyclopropane **68** (n = 1)[108] or dimethylenespiropentane **68** (n = 2)[107] were never prepared on a large scale. These compounds **68** (n = 1, 2) possess a limited stability, and allene as well as ethenylidenecyclopropane **64** were shown to give mainly monoadducts with chloromethylcarbene.[109]

The first enantiomerically pure unbranched [4]triangulane—(*M*)-(−)-trispiro[2.0.0.2.1.1]nonane (**13**)[71]—was prepared starting from racemic bicyclopropylidenecarboxylic acid *rac*-**73**.[110] The optical resolution of *rac*-**73** with dehydroabietylamine furnished (*S*)-(+)-**73** and (*R*)-(−)-**73**. The ethyl ester (*R*)-**74** of the latter was cyclopropanated to give ethyl (1*R*,3*R*)- and (1*R*,3*S*)-[3]triangulane-1-carboxylates (1*R*,3*R*)-**75** and (1*R*,3*S*)-**75**. (1*R*,3*S*)-**75** was converted into (*M*)-(−)-**13** with an enantiomeric excess of 99% via reduction to the alcohol *exo*-(1*R*,3*S*)-**76**, conversion to the bromide *exo*-(1*R*,3*S*)-**77**, its subsequent dehydrobromination to (*S*)-1-methylene[3]triangulane (*S*)-**78**, followed by cyclopropanation in 6% overall yield starting from *rac*-**73** (Scheme 11). As mentioned

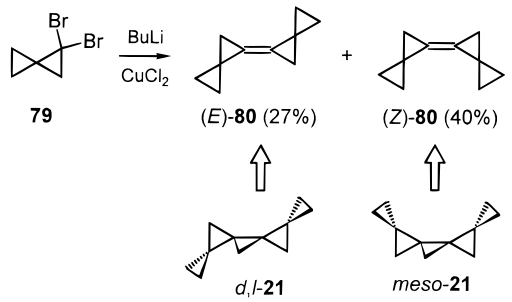
Scheme 11



above, [4]triangulane **13** has no chromophore which would lead to any significant absorption above 200 nm. Nevertheless, it has a remarkably high specific rotation even at 589 nm with $[\alpha]_D^{20} = -192.7$ (c = 1.18, $CHCl_3$), as predicted by computations at the B3LYP/6-31G(d) level of theory.[71]

Another prospective approach to stereoselective preparations of UTs might start by applying the recently reported efficient dimerization of cyclopropylidenoids generated from 1,1-dibromocyclopropanes and alkyllithiums in the presence of $CuCl_2$[111] to 1,1-dibromotriangulanes. In fact, dibromospiropentane **79** could be formally dimerized in this way to yield the bisspirocyclopropanated bicyclopropylidenes (*E*)- and (*Z*)-**80** in a preparatively acceptable yield (Scheme 12).[112] The alkenes (*E*)- and (*Z*)-**80** could easily be separated by low-temperature crystallization. Their cyclopropanation should give selectively [5]UTs D,L-**21** and *meso*-**21**, which could not be separated when they were obtained as a mixture.[51]

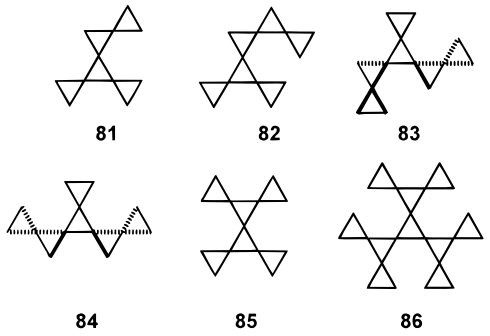
Scheme 12



C. Synthetic Approaches to Branched Triangulanes (BTs)

The simplest and most highly symmetrical branched triangulane (BT) [3]rotane **14** was prepared along several routes as mentioned above.[46−50] For the construction of a branched triangulane framework it is essential to have a convenient way for chain branching. Five different strategies have been elaborated to solve this problem, and at least one of them has successfully been applied to each of the BTs **81**−**86** (Chart 4).

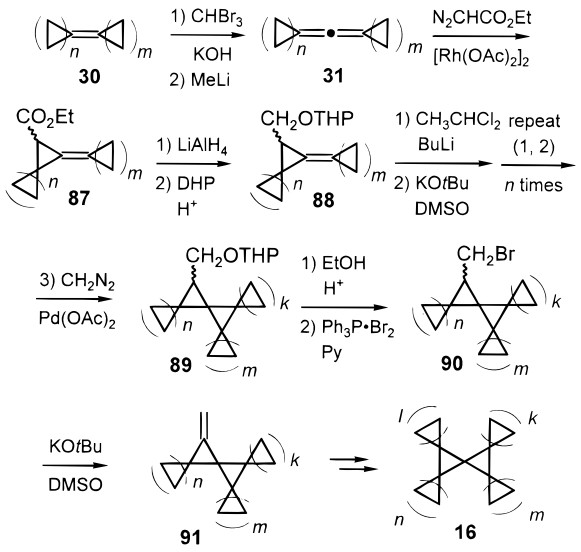
Chart 4



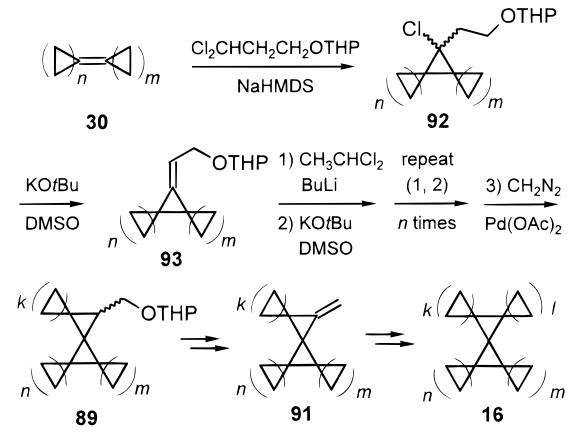
The first approach makes use of two main principles: First, a methylenecyclopropane moiety [e.g., **30** ($m \neq 0$, $n = 0$)] can easily be transformed into an ethenylidenecyclopropane fragment [e.g., **31** ($m \neq 0$, $n = 0$)] by the cycloaddition of dibromocarbene and subsequent treatment of the resulting dibromotriangulane with an alkyllithium reagent.[113] Second, the resulting allene normally adds only 1 equiv of chloromethylcarbene or ethoxycarbonylcarbene; the latter adds selectively to the terminal double bond.[52,53,109] The same sequence applied to a bicyclopropylidene **30** ($m,n \neq 0$) will lead to a dicyclopropylidenemethane **31** ($m,n \neq 0$) and further to a branched methylenetriangulane **91**, which eventually is cyclopropanated to a branched triangulane **16** (Scheme 13). This strategy has been used to synthesize BTs **83**, **84** (6% overall yield in 11 steps), and **85** (5% overall yield in nine steps).[52,53,56] In several cases the key transformation of the dibromotriangulane to the corresponding allene resulted in a mixture of products (see below).

The second strategy is based upon the addition of substituted chloroethylcarbenes to methylenecyclopropanes or bicyclopropylidenes as depicted in Scheme 14. Its synthetic potential has been demonstrated by the preparation of the BT hydrocarbons **83**−**85**.[54]

Scheme 13

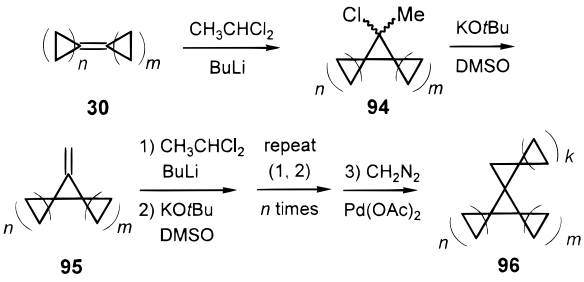


Scheme 14



The common shortcoming of these two strategies is that both rely on uncomfortably complicated multistep preparations. The third possible approach is also multistep but appears to be more convenient. It utilizes the same sequence of operations as that used for the synthesis of UTs[49−51] (Scheme 9) starting from a bicyclopropylidene derivative (Scheme 15). This

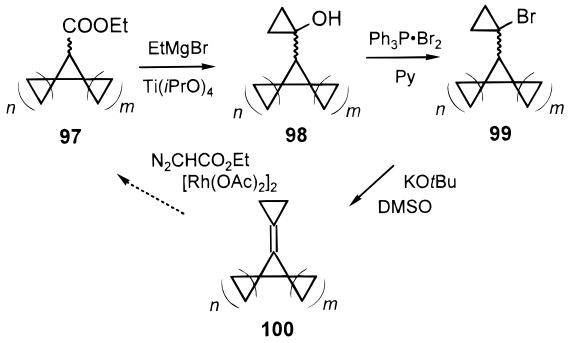
Scheme 15



approach then relies on the accessibility of an appropriate bicyclopropylidene of type **30**. Along this route, compounds **81** (17% overall yield in five steps) and **82** (10% overall yield in seven steps) have been obtained starting from bicyclopropylidene (**5**).[54] A versatile general approach to bicyclopropylidene (**5**) itself and various cyclopropylidenetriangulanes has

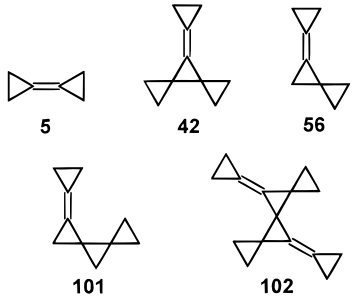
been developed,[114] based upon the transformation of an alkoxycarbonyl group into a cyclopropanol fragment with ethylmagnesium bromide in the presence of Ti(*i*PrO)$_4$ as developed by Kulinkovich et al.[115] The cyclopropylcyclopropanols **98** resulting from a cyclopropanecarboxylate **97** can be transformed to 1-bromocyclopropylcyclopropane derivatives **99**, which are then dehydrobrominated to the cyclopropylidenetriangulane **100**. Since an alkoxycarbonylcarbene addition onto a bicyclopropylidene creates a new cyclopropanecarboxylate of type **97** (Scheme 16), the whole

Scheme 16



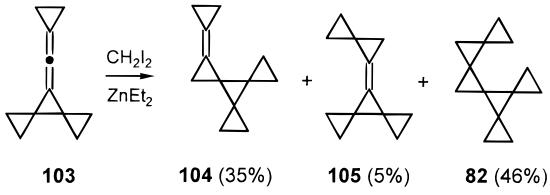
sequence can be applied in a repetitive fashion. This allows the preparation of a large variety of compounds with a bicyclopropylidene moiety on a preparative scale. Applying this sequence, the triangulane synthetic precursors **5**, **42**, **56**, **101**, and **102** (Chart 5) to various BTs have been prepared in good

Chart 5



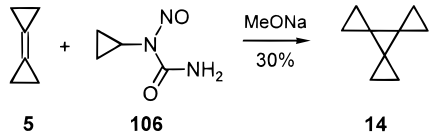
to excellent yields.[114] This third methodology is superior to the other two, as, e.g., by applying it to the bicyclopropylidenes (*E*)- and (*Z*)-**80** one would have a stereoselective route to the BTs **83** and **84** which were previously only obtained as a mixture. The [6]BT **82**, along with the bicyclopropylidenes **104** and **105**, has also been prepared applying the Simmons−Smith reaction to the allene **103** (Scheme 17).[55]

Scheme 17



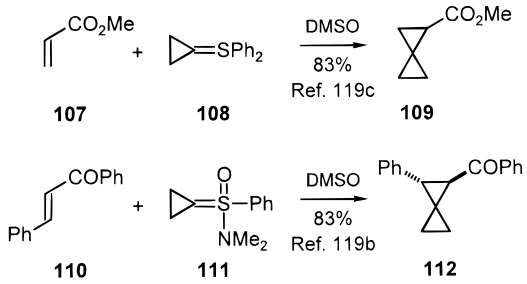
The fourth strategy is the most convergent one, as two building blocks of comparable size are attached to each other to form the final BT molecule. The first successful application of this strategy was the preparation of [3]rotane (**14**) by the reaction of in situ generated diazocyclopropane with bicyclopropylidene (**5**) (Scheme 18).[47] Several synthetic equivalents of

Scheme 18



cyclopropylidenes have been investigated in detail.[92b,116−120] The most commonly applicable method is the in situ generation of a diazocyclopropane (**113**) from the corresponding *N*-nitrosocyclopropylurea by treatment with a base. The reaction of a dibromocyclopropane with an alkyllithium reagent in the presence of an internal or external double bond[118] has been applied mainly for the preparation of cycloannelated[*n*]triangulanes (see below).[66−70] Sulfonium- and sulfoxoniumcyclopropylides **108** and **111**[119] have found a limited application in oligospirocyclopropane chemistry, e.g., for the preparation of the spiropentane derivatives **109** and **112** (Scheme 19). The highly

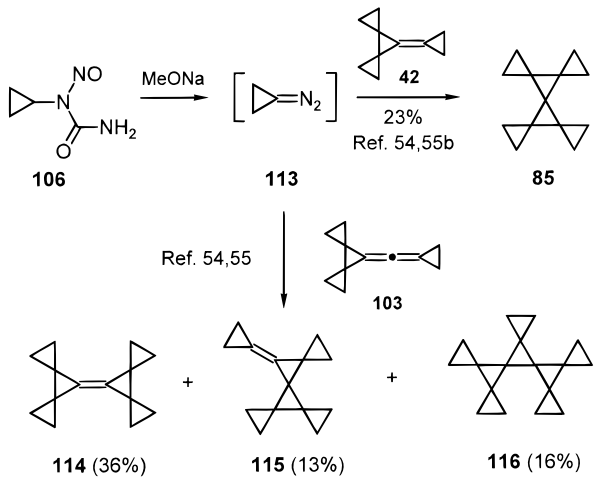
Scheme 19



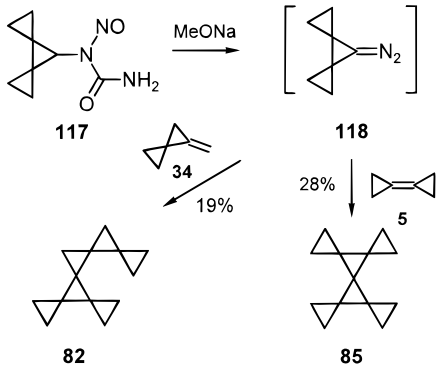
convergent building block method has been applied to make C_{2v}-[6]BT **85**[54,55b] and C_{2v}-[8]BT **116** (Scheme 20).[54,55b] Comparable results were achieved with in situ generated 7-diazodispiro[2.0.2.1]heptane (**118**) (Scheme 21).[57,121]

The competing 1,3-dipolar cycloadditions of diazocyclopropane (**113**) and spirocyclopropanated

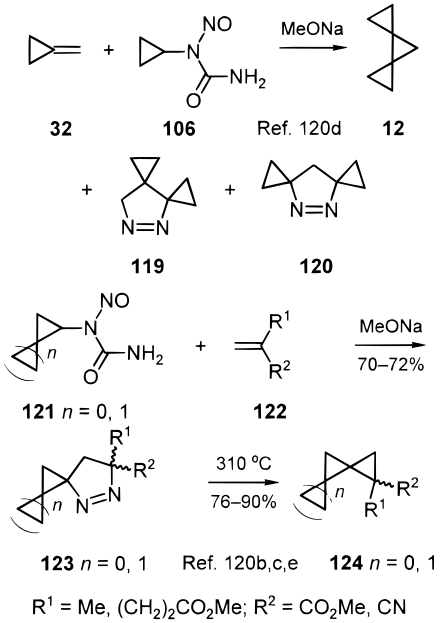
Scheme 20



Scheme 21



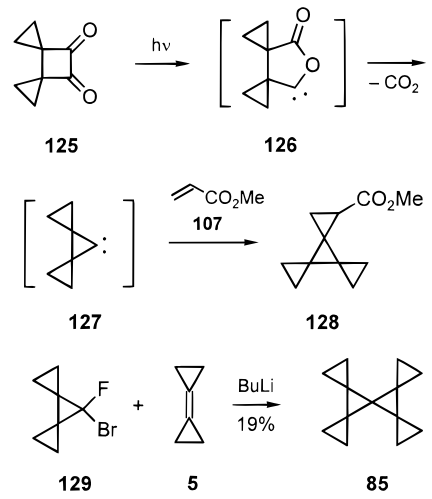
Scheme 22



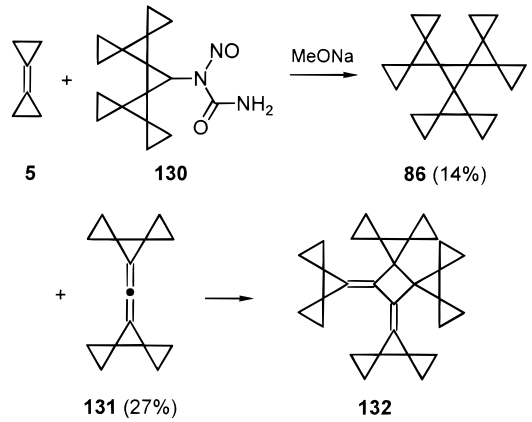
diazocyclopropanes onto the double bond of, e.g., methylenecyclopropane to yield 1-pyrazolines **119** and **123**[120] is probably the main reason for the low yields in most applications of the block method (Scheme 22). With electronegative substituents, such pyrazolines **123** yield UT derivatives **124** under pyrolysis conditions.[120] It remains to be tested whether such pyrazolines as **119** and **123** can be photolyzed to give triangulanes without ring opening.

Nevertheless, the other known methods to generate a cyclopropylidene synthetic equivalent have no advantages.[122] Thus, the originally reported possibility of generating and trapping dispiro[2.0.2.1]hept-7-ylidene (**127**) by photolysis of dispiro[2.0.2.2]octane-7,8-dione (**125**) via **126**[123] (Scheme 23) has later been questioned by an independent authentic preparation of methyl [3]rotanecarboxylate (**128**) via Cu-catalyzed addition of methyl diazoacetate onto 7-methylene[3]-triangulane (**36**)[48] and the generation of **127** from 7-bromo-7-fluoro[3]triangulane (**129**) in the presence of bicyclopropylidene (**5**) did not lead to an improved yield of the [6]BT **85**;[100] nevertheless, in the presence of $CuCl_2$ the yield of **85** dramatically increased up to 65%. Despite the moderate to low yield and possible difficulties in separating the mixtures of final products, this block method has apparent advantages as it is much shorter in many cases than the linear

Scheme 23



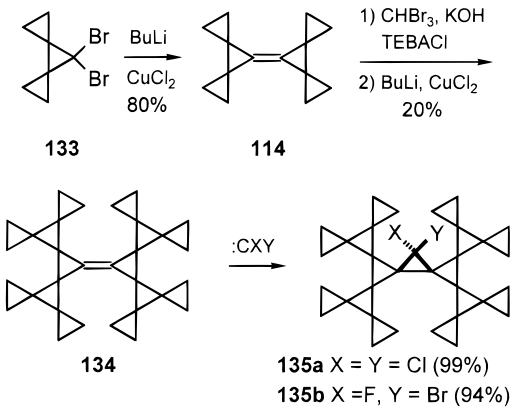
Scheme 24



strategies discussed above. Moreover, for certain cases the convergent approach is the only applicable one, as demonstrated by the successful preparation of the completely spirocyclopropanated [3]rotane **86**, the C_{3h}-symmetric [10]-BT (Scheme 24).[57] The allene **131**, which was formed as the major product by ring opening of the cyclopropylidene intermediate derived from **130**, dimerized spontaneously to produce the interesting diene **132**.[57,124]

The most recent approach to BTs is essentially an extension of the block method based upon the efficient dimerization of cyclopropylidenoids generated from dibromotriangulanes (see above).[111] It is spectacular that this new method could also successfully be applied to 7,7-dibromodispiro[2.0.2.1]heptane (**133**), the dibromocarbene adduct of bicyclopropylidene (**5**), to yield the perspirocyclopropanated bicyclopropylidene **114** (80% isolated), making this exotic hydrocarbon—a superbicyclopropylidene—which had previously been prepared along a tedious 14-step sequence (cf. Scheme 20) easily available in preparatively useful quantities (Scheme 25).[112] It is even more spectacular that the dibromocarbene adduct of **114**[57] can be "dimerized" again to give the "supersuperbicyclopropylidene" **134**. The addition of dihalocarbenes onto this alkene yielded the dihalo[15]BTs **135**—the largest BTs known up to now.

Scheme 25



133 **114** **134**

135a X = Y = Cl (99%)
135b X =F, Y = Br (94%)

D. Cycloannelated Triangulanes (CATs)

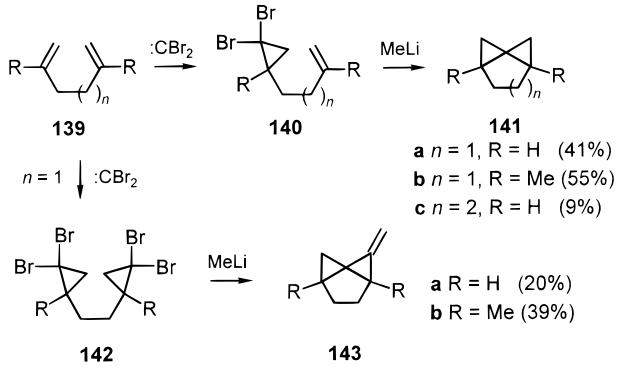
Considering possible preparations of cycloannelated[*n*]triangulanes (CATs) **137** in general, one may conceive two different approaches: One of them uses an intramolecular cheletropic cycloaddition of a cyclopropylidene or cyclopropylidenoid as in **136** as the key step, the other sequentially generates annelated spiropentane units on preexisting cyclic framework **138** (Chart 6).

Chart 6

136 **137** **138**

The feasability of the first strategy was actually demonstrated by Skattebøl as early as 1962. The cycloaddition of 1 or 2 equiv of dibromocarbene to the α,ω-dienes **139a**−**c** and subsequent treatment of the resulting dibromocyclopropane derivatives **140** and **142** with methyllithium at −78 °C gave the two- and three-carbon bridged spiropentanes **141a**−**c** (*n* = 1, 2) and methylenespiropentane derivatives **143a**,**b**, respectively (Scheme 26).[66] During the first 15 years

Scheme 26



139 **140** **141**

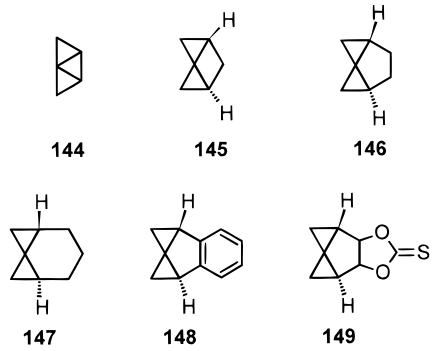
a *n* = 1, R = H (41%)
b *n* = 1, R = Me (55%)
c *n* = 2, R = H (9%)

142 **143**

a R = H (20%)
b R = Me (39%)

after their preparation, these CATs **141** and **143** have received surprisingly little attention. Their renaissance was due to further developments by Brinker et al.[67,68] and Wiberg et al.[70] Not surprisingly, the smallest conceivable cycloannelated spiropentane, the hydrocarbon **144**, turned out to be unstable even at −55 °C.[70f,g] The unsubstituted hydrocarbon **145** still remains unknown. A thermochemical study for **146**,[125] photoelectron spectroscopic investigations of **146** and **148**,[126] and structure analyses of **146**, **148** (prepared similarly in 33% yield[67b]), and **149** have been reported (Chart 7).[70e,127] Brinker et al. were

Chart 7

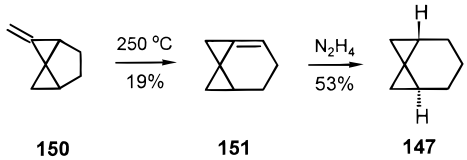


144 **145** **146**

147 **148** **149**

unable to reproduce Skattebøl's preparation of **147** (≙**141c**, Scheme 26).[128a] Eventually, this hydrocarbon was authentically prepared indirectly starting from Skattebøl's bridged methylenespiropentane−CST **150** (≙**143a**, Scheme 26) by thermal isomerization and reduction with diimide (Scheme 27).[128b] Functionally

Scheme 27

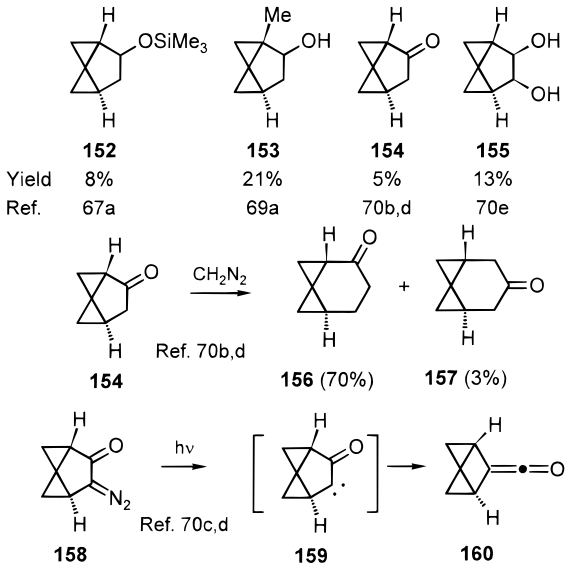


150 **151** **147**

substituted CATs **152**−**155** were also obtained applying Skattebøl's method but in much lower yield (Scheme 28).[67a,69,70b−e] Carbon skeletons of type **147** and **145** were constructed by ring expansion and ring contraction of two-carbon bridged spiropentane derivatives **154** and **158**, respectively.[70b−d]

The first step of the other possible approach to CATs is cyclopropanation of a cycloalkene **161** (*n* = 0) to a bromobicyclo[*m*.1.0]alkane **162** (*n* = 0) by

Scheme 28

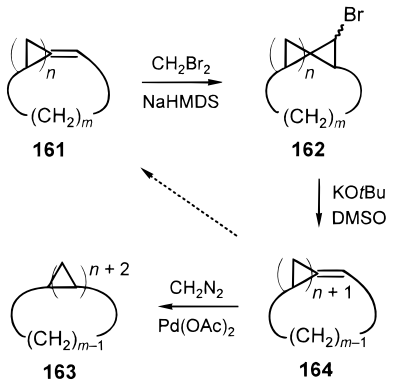


	152	**153**	**154**	**155**
Yield	8%	21%	5%	13%
Ref.	67a	69a	70b,d	70e

154 **156** (70%) **157** (3%)

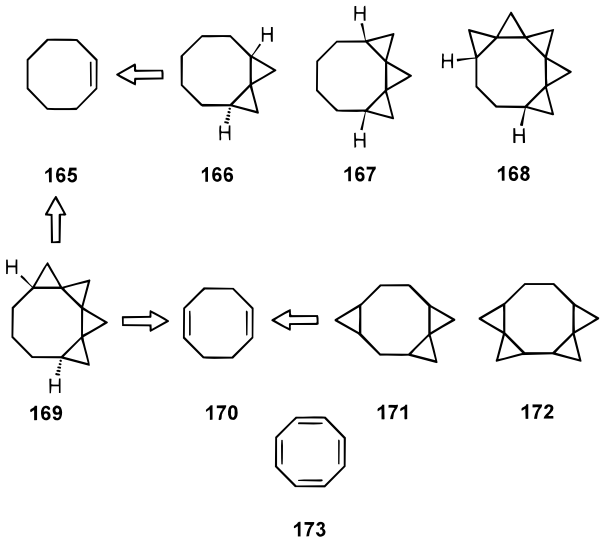
158 **159** **160**

Scheme 29



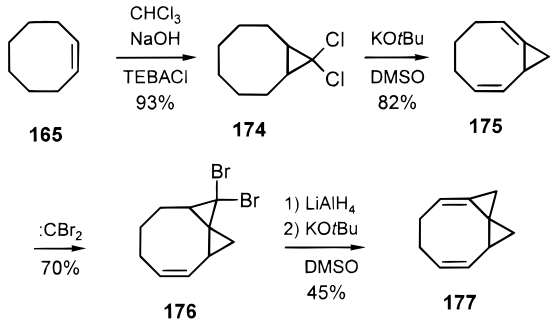
means of bromocarbene addition followed by dehydrobromination and isomerization to a cycloannelated methylenecyclopropane **164** ($n = 0$) (Scheme 29).[129] With this, the same sequence of transformations can be repeated over and over again. A simple methylenation of any bridged methylenetriangulane **164** ($n \geq 0$) will lead to the corresponding cycloannelated triangulane **163** ($n \geq 0$). This multistage strategy has been realized starting from cyclooctene (**165**), cyclooctadiene (**170**), and cyclooctatetraene (**173**) (Scheme 30).[62−65] The CATs **166**−**169** and **171** and **172** were

Scheme 30



successfully prepared in overall yields (based on the starting alkene) of 33% (**166**), 10% (**167**), 16% (**171**), and 9% (**172**)[62,63b] (the yields of several last steps in the preparations of **168** and **169** were not reported[63a]). Hydrocarbons **171** and **172** were obtained as 4:1 mixtures of diastereomers. The preparation of some CATs from cyclooctatetraene (**173**) has also been reported.[64,65a] The CAT analogous to **166**, but with a nine-membered central ring, was also prepared by cyclopropanation of a corresponding cycloannelated methylenecyclopropane of type **161** with CH_2N_2/$Pd(OAc)_2$.[65b] Dienes **175**[130a] and **177**[130b] could be prepared rather efficiently from cyclooctene (**165**) (Scheme 31), but their potential application toward the construction of cycloannelated[*n*]triangulanes has not been probed any further. It is an open question if CTs can be also obtained along this pedestrian

Scheme 31

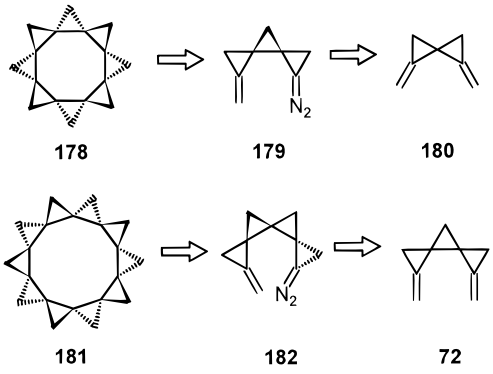


route, as the higher strained bridged methylene[*n*]triangulanes **164** and intermediate cyclopropene derivatives should add *tert*-butanol on the dehydrobromination step.[129−131]

E. Along the Route to Cyclotriangulanes (CTs)

No workable concepts to prepare [8]CT **178** and [10]CT **181** have been published so far. The most highly convergent syntheses would be by dimerization of an in situ generated enantiomerically pure diazotriangulane **179** and **182**, respectively (Scheme 32).[130a] But this would require a feasible access to the

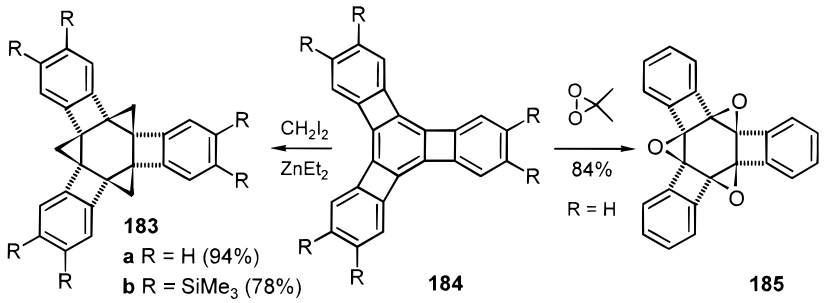
Scheme 32



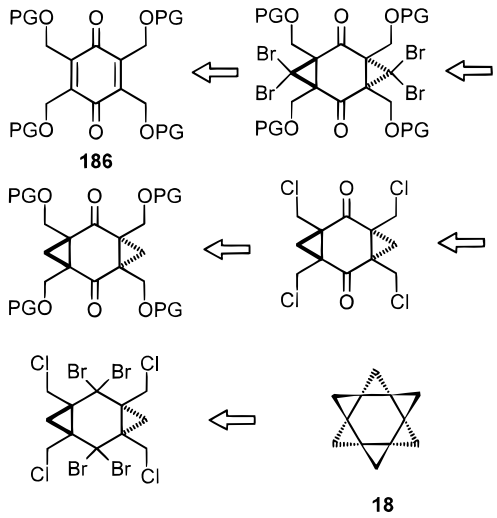
appropriate enantiomeric precursors to **179** and **182** or other feasible cyclopropylidene precursors.

As mentioned above, the [6]CT "davidane" **18** might be rather unstable according to theoretical predictions of its overall strain.[35a,39,132] However, the nature is often more complicated than theoretical predictions, and quite a few more highly strained molecules than **18** have been prepared and found to be perfectly stable (see Introduction). The closest relatives of **18**—two derivatives of all-*cis*-[2.1.2.1.2.1]-hexaannulane **183** and a heteroanalogue **185**—have been successfully prepared[133] by Simmons−Smith cyclopropanation and epoxidation, respectively (Scheme 33), of tris(benzocyclobutadieno)benzene **184**[134] and turned out to be relatively stable. The triepoxide **185**, like benzenetriepoxide, could be heated to 180 °C before it underwent rearrangement with [$\sigma^2 + \sigma^2 + \sigma^2$] cycloreversion of the heptacyclic core structure. A possible synthetic approach to davidane **18** may be based on the known *trans*-selective 2-fold dicyclopropanation of tetrasubstituted quinones with dibromocarbene[135a] which would predetermine the correct geometry of the target. After reductive debromin-

Scheme 33



Scheme 34

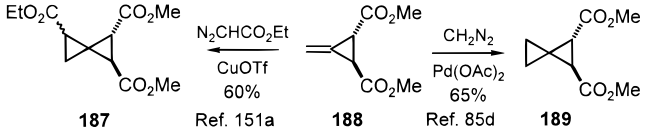


ation[135b] and several transformations which appear to be realizable (Scheme 34), a 4-fold cyclization upon treatment with an alkyllithium reagent analogous to that applied in the high-yielding preparation of the extremely strained [1.1.1]propellane (**3**)[20b,c] might lead to the hydrocarbon **18**.

F. Substituted Triangulanes

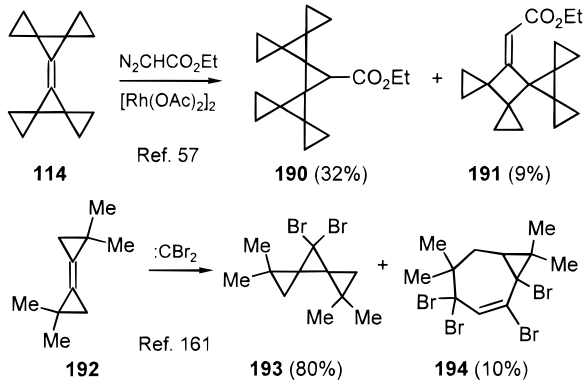
In general, substituted triangulanes can be produced via cycloaddition of a substituted carbene (or cyclopropylidene) to an allene, a methylenetriangulane, or a bicyclopropylidene as well as by starting with a correspondingly substituted methylenetriangulane[76] or bicyclopropylidene[23] in any of the above-discussed preparations. This latter approach does not need special consideration. Reactions of this type as well as their products—tetra- and dibromotriangulanes (for examples, see refs 46, 52, 53, 55, 57, 66, 67, 96a,b, 98b, 99, 122a, and 136−141), oligochlorotriangulanes,[96a,b,97a,d,98c,136,139a,141−147] mono- and oligoalkyl(aryl)-triangulanes[44b,65b,93,98b,103a,b,116d,117b,c,118,122b,148−152]—are sufficiently well documented. The abundance of experimental material, especially for spiropentane, the simplest unbranched triangulane [2]UT (**11**), makes it virtually impossible to present a concise and simple systematization within the scope of a limited review. Cycloadditions of different carbenes onto bicyclopropylidene (**5**) and its derivatives have recently been reviewed.[23] Mono- and oligoalkoxycarbonyltriangulanes were prepared by cycloaddition of alkyl diazoacetates onto methylenecyclopropane derivatives or cyclopropanation of alkoxycarbonyl-substituted methylenecyclopropanes.[48a,52,53,94,101,103b,114,120,143,153−159] Examples for both types of transformations are shown for Feist's ester **188** (Scheme 35). Dibromo- and ethoxycarbonyltri-

Scheme 35



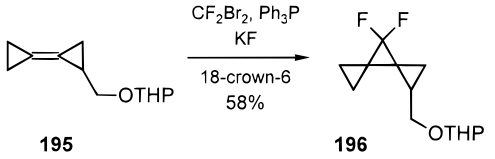
angulanes have been widely used in the preparations of higher members in the triangulane family (see above). It is noteworthy, however, that sterically congested tetraspirocyclopropanated bicyclopropylidenes such as **114**, when reacted with ethyl diazoacetate in the presence of $[Rh(OAc)_2]_2$, can yield byproducts such as **191** by ring expansion[57,160] (cf. also refs 48b and 81). A similar behavior was observed upon dibromocarbene addition to the sterically congested tetramethylbicyclopropylidene **192** (Scheme 36).[161]

Scheme 36



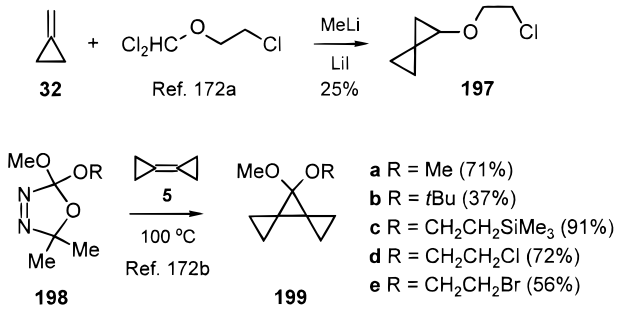
The addition of monohalocarbenes onto methylenecyclopropanes proceeded in low to moderate yields;[62−65,140b,162,163] therefore, monohalotriangulanes (mainly halospiropentanes) were better prepared by monoreduction of dihalocarbene adducts.[98a,131,164−166a] Chlorospiropentane itself was obtained by direct chlorination of spiropentane (**11**).[166b] Fluoro derivatives of triangulanes are limited to oligofluorospiropentanes which were prepared by cyclopropanation of fluorinated methylenecyclopropanes[167] and allenes[168] or difluorocarbene addition onto methylenecyclopropanes[143,167,169a] and allenes.[170] The chemistry of some fluorinated [3]triangulanes such as **196** is now being studied (Scheme 37).[171]

Scheme 37



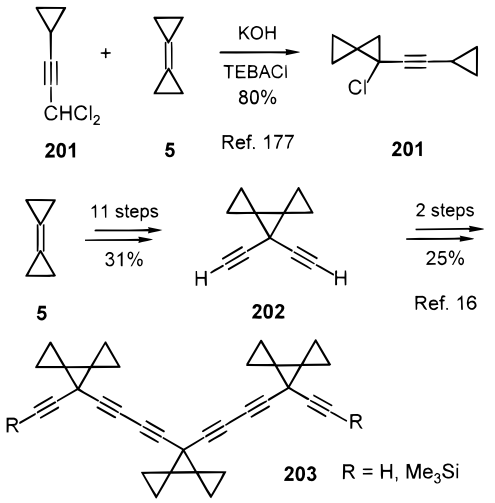
The cycloadditions of chloroethoxycarbene onto methylenecyclopropane (**32**)[172a] or dialkoxycarbenes generated in situ from the corresponding 2,2-dialkoxy-Δ^3-1,3,4-oxadiazolines of type **198** onto bicyclopropylidene (**5**)[172b] afforded the protected spiropentanol **197** and the dialkyl acetals of dispiro[2.0.2.1]heptanone **199**, respectively (Scheme 38).

Scheme 38



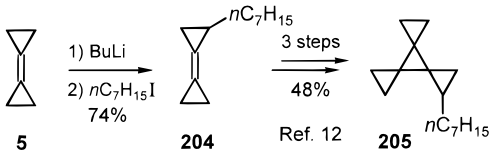
Spiropentyl alcohols[90,102a,106,154,173,174] and ketones[119a,c] may also be prepared by direct cyclopropanation of methylenecyclopropyl- and allenylalkanols (ketones) with methylene or cyclopropylidene. Vinyl-substituted spiropentane derivatives were obtained by transformations of spiropentanes with other functional groups[90,175] and, in low yields, by cyclopropanation of vinylallenes[93a] or spirocyclopropanation of butadiene.[176] While the chloro-substituted ethynylspiropentane **201** was prepared in one step by direct cyclopropanation of methylenecyclopropane (**32**),[177] a more complicated multistep synthesis had to be developed to obtain 7,7-diethynyl[3]triangulane (**202**) and its dehydrotrimer **203** (Scheme 39).[16]

Scheme 39



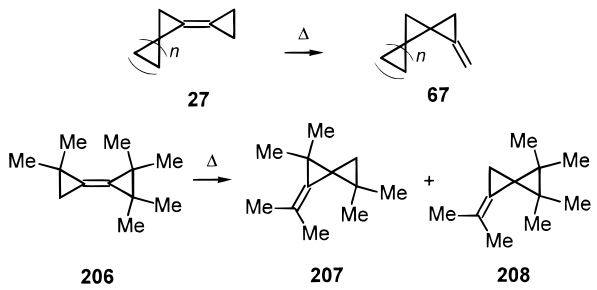
n-Heptyl[4]BT **205** has been prepared from *n*-heptylbicyclopropylidene (**204**), which was obtained by electrophilic alkylation of deprotonated bicyclopropylidene (**5**) (Scheme 40).[12]

Scheme 40



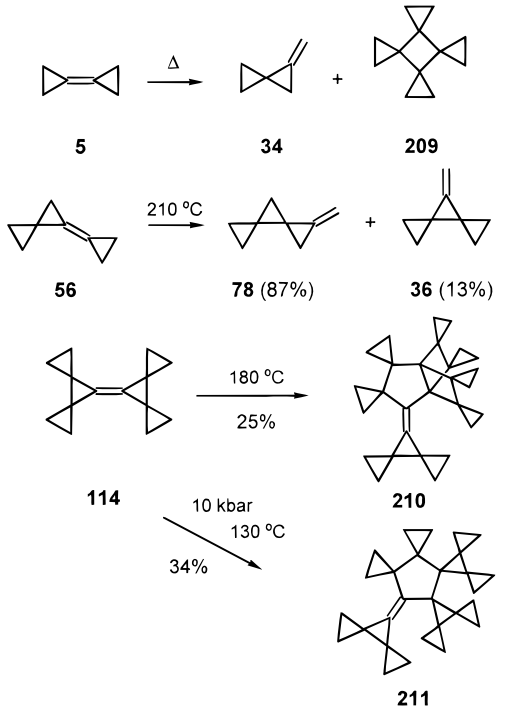
One general method for the preparation of methylene[*n*]triangulanes has been discussed above (for a brief summary see also ref 76c). Another approach to methylene[*n*]triangulanes of type **67** is by thermal reorganization of bicyclopropylidenes of type **27** (Scheme 41). Crandall et al. showed for the first time

Scheme 41

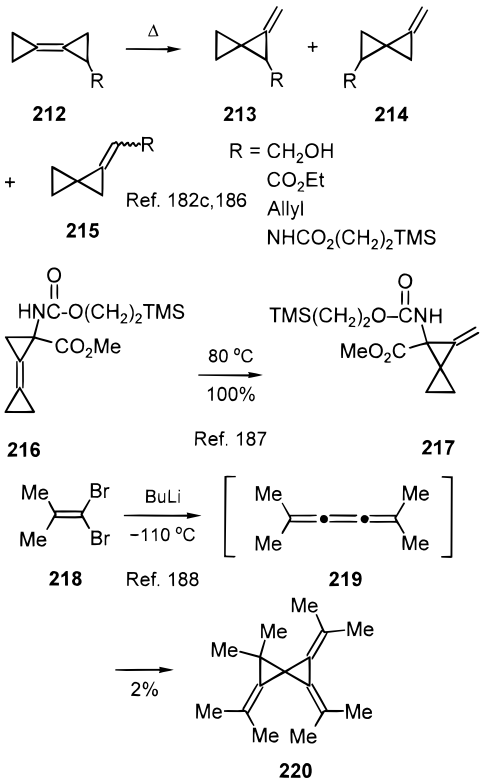


that hexamethylbicyclopropylidene **206** rearranges at 400 °C in a flow pyrolysis system to yield a 10:1 mixture of two isomeric hexamethylmethylenespiropentanes **207** and **208** (Scheme 41).[44b,178] Analogous transformations have also been reported for a number of oligoalkylbicyclopropylidenes[44a,179] and 1,1-dideuteriobicyclopropylidene.[180] The mechanistic and kinetic aspects of these rearrangements as well as subsequent transformations of the resulting methylenespiropentanes to dimethylenecyclobutane derivatives at higher temperatures have been reviewed.[181] Bicyclopropylidene (**5**) undergoes a clean rearrangement to methylenespiropentane (**34**) when heated to 330 °C in a flow system (85% yield);[182] when the rearrangement was performed in the gas phase in a static reactor for kinetic measurements, it was found to be reversible.[182b] When heated in a closed vessel as a pure compound[11a,183] or in solution (50% in toluene),[14] a substantial fraction of **5** dimerizes to yield up to 68% of [4]rotane (**209**) (Scheme 42).[184] The thermolysis of monospirocyclopropanated bicyclopropylidene **56** leads to a mixture of both possible isomeric products **78** and **36**,[47] but prolonged heating of the sterically congested perspirocyclopropanated bicyclopropylidene **114** gave, along with polymeric materials, two different rearranged dimerization products **210** or **211**, depending on the conditions (Scheme 42).[185] As a rule, the thermal rearrangements of functionally substituted bicyclopropylidenes of type **212** yield mixtures of products (Scheme 43).[156b,182c,186] But the methoxycarbonyl-substituted carbamate **216** underwent a clean regioselective isomerization to give **217** as a single product.[187] Yet one more method of preparing oligomethylenetriangulanes should be mentioned: Upon treatment of 1,1-dibromo-2-methylpropene (**218**) with butyllithium at −110 °C, the unique triisopropylidenedimethyl-

Scheme 42



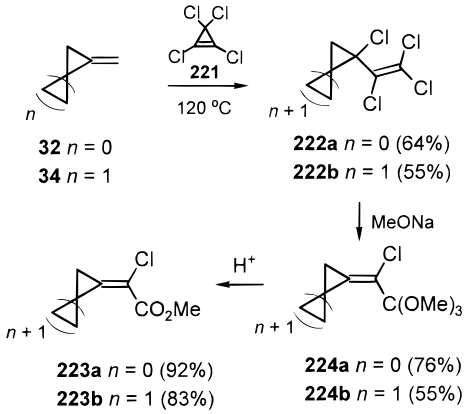
Scheme 43



spiropentane (**220**) was formed by addition of isobutylidene to in situ generated tetramethylbutatriene (**219**), albeit in very low yield (Scheme 43).[188]

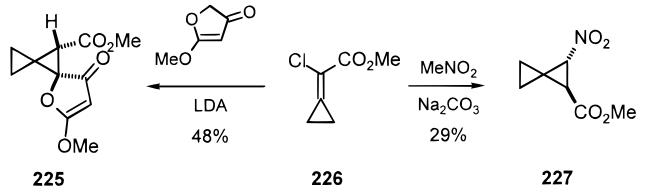
Tetrachlorocyclopropene (**221**), upon heating to 120 °C in the presence of methylenecyclopropane (**32**) or methylenespiropentane (**34**), yields 1-chloro-1-(trichloroethenyl)triangulanes **222a**,**b**,[130a,189,190] which after heating with sodium methoxide in methanol followed by acidic hydrolysis of the ortho esters **224a**,**b** were transformed into the highly functionalized methyl-

Scheme 44



ene[*n*]triangulanes **223a**[165,190] and **223b**[130a] (Scheme 44) (for a review on the chemistry of such compounds see ref 191). Apart from showing a variety of interesting and preparatively useful chemical properties (see below and ref 191), these compounds as well as the parent methyl 1-chloro-1-cyclopropylideneacetate (**226**) were applied in the preparation of substituted triangulanes via sequences of Michael addition followed by Intramolecular Ring Closure (MIRC) reactions. This type of transformation has been developed as a general synthetic approach toward substituted cyclopropane derivatives.[5] The normal MIRC reactions were observed in Michael additions of carbon nucleophiles with additional C−H acidic protons and a leaving group in the α-position of the acceptor. In these cases the intramolecular nucleophilic substitution of chlorine with a newly formed nucleophilic carbon center led to the formation of the second cyclopropane ring to form spiropentane derivatives **225** and **227** as single diastereomers (the structure of **225** has been verified by X-ray crystal structure analysis) (Scheme 45).[192] Albeit the products are

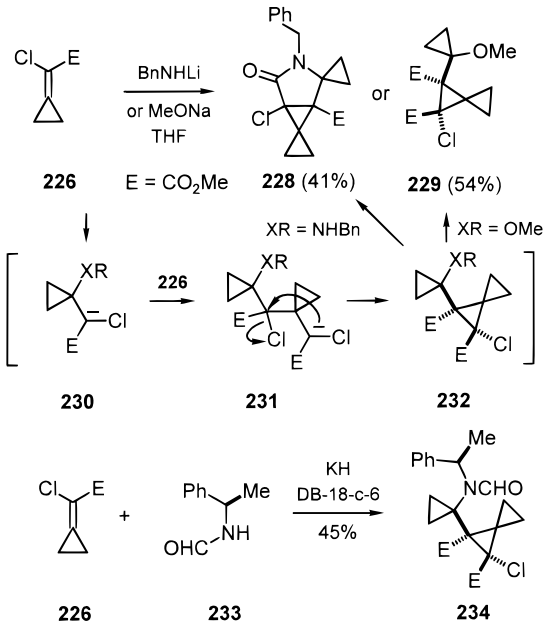
Scheme 45



obtained in moderate to low yield only, these results are of principal importance, as these methods permit one to stereoselectively prepare simple oligo-substituted triangulanes which are not easily available by any other route. In the presence of an excess of the chloroester **226** or if the first Michael intermediate contains another appropriately located acceptor-activated double bond, the reaction may proceed with two consecutive Michael additions followed by ring closure through intramolecular nucleophilic displacement. Analogously to the established abbreviation MIRC, this sequence of transformations has been termed a Michael Michael Addition Ring Closure (MIMIRC) reaction.[191] Spiropentane derivatives are formed from the acrylate **226**, when 2 equiv of **226** react with 1 equiv of a nucleophile under aprotic conditions. Thus, the formation of the unique spiro-

pentanecarboxylate derivatives **228** and **229** was incidentally observed when methyl 2-chloro-2-cyclopropylideneacetate (**226**) was treated with lithium benzylamide and sodium methoxide, respectively, in anhydrous THF.[165,193] The sequence of events leading to the spiropentane moiety (Scheme 46) apparently

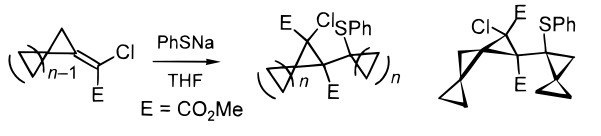
Scheme 46



starts with a Michael addition to **226** leading to an α-chloroenolate intermediate **230** which, under the aprotic conditions, adds again to a molecule of **226** to give the new α-chloroenolate intermediate **231**. γ-Chlorine elimination from the latter produces a spiropentane derivative **232** which, in the case of sodium methoxide (X−R = OMe), corresponds to the final product **229** (54% yield). With the benzylamino substituent, intermediate **232** (X−R = NHBn), by the appropriate arrangement of benzylamino and methoxycarbonyl substituents, undergoes an intramolecular lactamization to form the azabicyclo[3.1.0]hexane-1-carboxylate skeleton **228** with an annelated spiropentane moiety and a β-amino acid amide feature as a single product in 41% yield. The anion generated from *N*-(1-phenylethyl)formamide (**233**) reacted with the chloroester **226** in the same MIMIRC mode to give the spiropentane derivative **234** (Scheme 46).[194a]

The analogous transformation of the chloroester **226** and its spirocyclopropanated analogue **223a** with sodium thiophenolate in anhydrous THF gave the spiropentane **235** and [3]triangulane derivative **236** in 45% and 30% yield, respectively (Scheme 47).[130a,194b] No MIMIRC product was isolated from the same reaction of the chlorodispiroheptylideneacetate **223b**

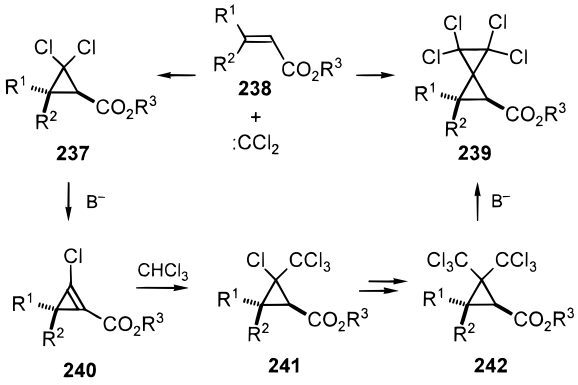
Scheme 47



with thiophenolate.[130a] The product **236** from **223a** was obtained as a single diastereomer with (1*S**,2*R**,1′*R**) configuration (according to X-ray crystal structural data).

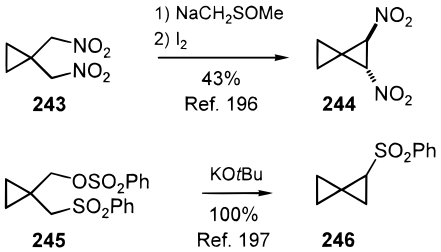
Some more reactions which uniquely lead to spiropentane derivatives should also be mentioned. For instance, tetrachlorospiropentanes **239** may be prepared by the reaction of Michael acceptors (alkenes) **238** activated by electron-withdrawing groups with dichlorocarbene generated from chloroform under basic conditions (Scheme 48).[147] These spirocyclopropanations are believed to proceed by two sequences of consecutive dehydrochlorination and trichloromethide addition of the initially formed dichlorocarbene adduct **237** via the intermediates **241** and **242**. A γ-dechlorination of the latter, probably initiated by nucleophilic attack at one of the six chlorine substituents, would then form the tetrachlorospiropentanecarboxylate **239**. Among the other γ-eliminations leading to spiropentanes, the preparation of oligodeuteriospiropentanes,[195] dinitrospiropentane **244**,[196] and benzenesulfonylspiropentane (**246**)[197] are also worthy to be mentioned (Scheme 49).

Scheme 48



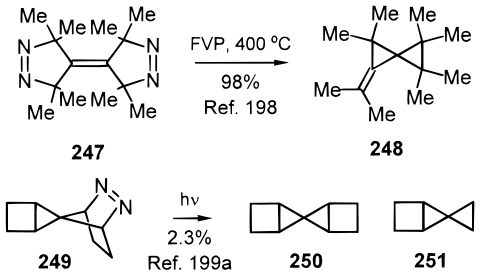
R^1	R^2	R^3	Yield (%)	Ref.
Ph	H	Me	48	147a
Me	Me	Me	57	147b
Me	H	*t*Bu	40	147c
H	H	*t*Bu	80	147d

Scheme 49



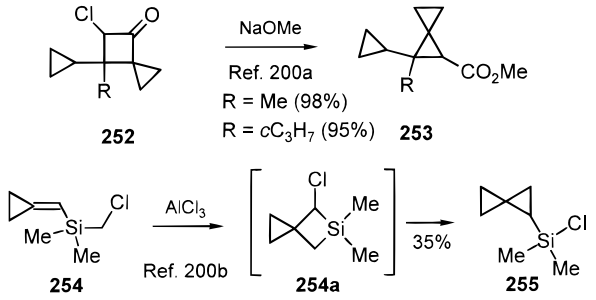
A less common approach to spiropentane is that based on the thermal or photochemical ring contraction of 1-pyrazolines (see also Scheme 22[120]). Thus, upon flash vacuum pyrolysis of the diazo compound **247** at 400 °C, only isopropylidenehexamethylspiropentane (**248**) and not the conceivable octamethylbicyclopropylidene was formed (Scheme 50).[198] Spiropentanes **250**[199a] and **251**[9,199b,c] were also pre-

Scheme 50



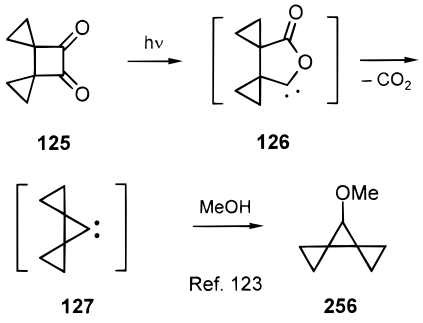
pared by this method in low yields. A spiropentane moiety may also be constructed by contraction of a four- to a three-membered ring, and this is sometimes achieved in excellent yields (Scheme 51).[200a] The

Scheme 51



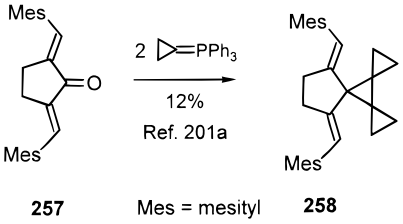
transformation of the (chloromethyldimethylsilyl)-methylenecyclopropane **254** under the action of $AlCl_3$ also occurs with ring contraction of the first formed intermediate 4-chloro-5,5-dimethyl-5-silaspiro[2.3]-hexane **254a**.[200b] Another unique formation of a triangulane has been observed in the photochemical conversion of dispiro[2.0.2.2]octanedione **125**. When irradiated in methanol solution, the dispiro[2.0.2.1]-heptylidene **127** formed by ring enlargement to **126** and fragmentation undergoes insertion into the OH bond of methanol (Scheme 52).[123] An interesting but

Scheme 52



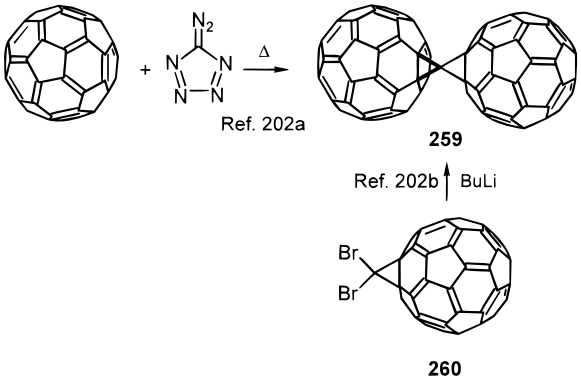
low yielding assembly of a triangulane skeleton by use of the cyclopropylidenephosphorane Wittig reagent on the peculiar 2,5-di(mesitylmethylene)cyclopentanone **257** has also been reported.[201] Apparently, the first equivalent of the reagent underwent a normal Wittig olefination of **257**, but the resulting cyclopropylidenecyclopentane derivative must have reacted with a second molecule of the ylid which acted as a cyclopropanating agent to give **258** (Scheme 53). Traces of spiropentane fused to two C_{60} fullerene units, i.e., the bis(C_{60}-fullereno)spiropentane **259**,

Scheme 53



could be isolated upon photochemical decomposition of diazotetrazole in the presence of C_{60} fullerene[202a] and also detected by MALDI-TOF mass spectrometric analysis in the reaction mixture from dibromomethyno-C_{60}-fullerene **260** and butyllithium[202b] (Scheme 54).

Scheme 54



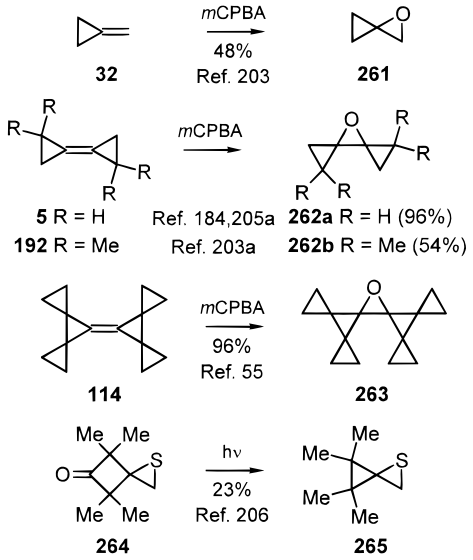
G. Heterotriangulanes

The simplest oxatriangulanes—oxaspiropentanes—can be readily prepared by straightforward epoxidation of methylenecyclopropanes[203a–c] and by reaction of sulfonium cyclopropylides with carbonyl compounds.[203e] In particular, the oxaspiropentane derivatives produced by the latter method have found a widespread application in organic synthesis.[203e,204] Among the higher oxatriangulanes, the 7-oxa[3]-triangulanes **262a**,**b** and the branched oxa[7]-triangulane **263** have been obtained by epoxidation from bicyclopropylidenes **5**, **192**, and perspirocyclopropanated bicyclopropylidene **114** (Scheme 55).[55,203,205] In contrast to methylenecyclopropane (**32**), bicyclopropylidene (**5**) reacts with *m*CPBA spontaneously at 0 °C within 5 min.[184] Only one example of a thiaspiropentane derivative has been reported. Compound **265** was obtained in low yield (23%) by ring contraction of 1-thia-4,4,6,6-tetramethylspiro[2.3]-hexanone **264** (Scheme 55).[206]

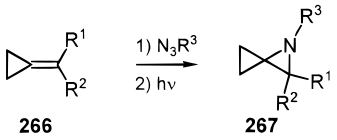
The most common approach to azaspiropentanes **267** starts with 1,3-dipolar cycloaddition of an azide to a methylenecyclopropane **266** followed by photochemically induced ring contraction (Scheme 56).[207,208] An alternative access was encountered in the Diels–Alder trapping of in situ generated azaspiropentenes with appropriate dienes.[209]

A completely different approach to functionally substituted azaspiropentanes has recently been elaborated.[193,210] It was found that Michael adducts of primary amines to the α-chloroacrylate **226**[191] upon treatment with triethylamine in methanol cyclize to

Scheme 55

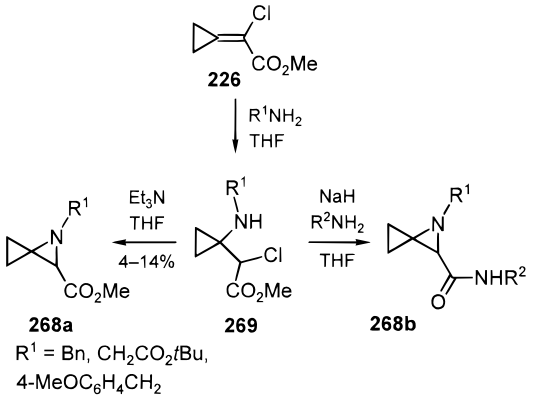


Scheme 56



R^1	R^2	R^3	Yield (%)	Ref.
H	H	Ph	63	207
H	H	CO_2Me	35	207
H	Ph	Ph	38	208
Ph	Ph	Ph	46	208

Scheme 57



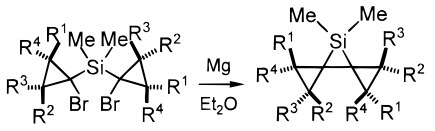
give azaspiropentanecarboxylates **268**, albeit in low yields (4−14%, Scheme 57). The low yields of the esters **268** may be attributed to their limited stabilities. The more stable amides **268b** can be isolated upon treatment of **269** with a second equivalent of a primary amine or ammonia in the presence of sodium hydride in preparatively more viable yields (Scheme 57 and Table 2). The esters and amides **268a**,**b** are essentially protected forms of a spirocyclopropanated derivative of aziridinecarboxylic acid,[211] which has been incorporated into interesting peptidomimetics.

The method of cyclopropane ring closure by reductive 1,3-dehalogenation applied to the 1,3-dibromides **270** (cf. refs 44a, 48, 81, and 82) turned out to be successful to afford the 7-sila[3]triangulanes **271**—

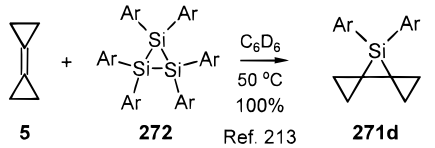
Table 2. Synthesis of Azaspiropentane Carboxamides 268b from Methyl 2-Chloro-2-cyclopropylideneacetate (226) via β-Amino-α-chloroesters 269

entry	R^1	R^2	yield (%)
1	*n*Bu	*n*Pr	22
2	*n*Bu	H	16
3	Bn	Bn	59
4	Bn	4-$MeOC_6H_4CH_2$	47
5	Bn	(Ph)(Me)CH	47
6	Bn	H	48
7	4-$MeOC_6H_4CH_2$	4-$MeOC_6H_4CH_2$	27
8	(Ph)(Me)CH	Bn	36
9	(Ph)(Me)CH	(Ph)(Me)CH	27
10	$PhCH_2CH_2$	H	33
11	*n*Pr	H	12

Scheme 58



	R^1	R^2	R^3	R^4	Yield (%)	Ref.
a	$-(CH_2)_4-$		H	H	80	212a,b
b	H	Me	H	Me	62	212b
c	H	Me	Me	H	45	212a



the first stable derivatives of silacyclopropane (Scheme 58).[212] A stable 7-sila[3]triangulane **271d** could also be obtained in quantitative yield by cycloaddition of a stabilized silylene which was formed in situ by thermally induced fragmentation of the corresponding trisilacyclopropane **272** (Scheme 58).[213]

IV. Selected Physical Properties of Triangulanes

A. Spectral Data

Spiropentane ([2]UT, **11**), the first member in the triangulane family, has been thoroughly studied by various spectroscopic techniques: infrared, Raman,[24a,214] NMR spectroscopy,[215] mass spectrometry,[216] and photoelectron spectroscopy;[126,217] microwave spectroscopy has been applied for spiropentyl chloride **273**.[218] NMR data for **12**−**14**,[47,50,220] IR and UV for **12** and **14**,[47] and the PE spectrum of **14**[219] have also been investigated. The spectroscopic data of the higher UTs and BTs as well as those of their derivatives have been reported along with their respective preparations.

The ^{13}C NMR data of triangulanes are the most informative ones, as they relate to structural differences[221] better than any other spectroscopic data. The vast increase in reported ^{13}C NMR spectra in recent years[51−57] prompted an attempt to work out an empirical additivity scheme for ^{13}C NMR chemical shifts in triangulanes,[222] which reveals the correla-

tion between triangulane structures and ^{13}C NMR chemical shifts. According to this approach, three types of carbon atoms can be distinguished in a triangulane molecule: CH_2 groups of terminal three-membered rings (A), CH_2 groups of internal fragments (B), and spiroatoms (C). Chemical shifts of type A carbons are in the range 2.5−7.4 ppm, type B carbon signals appear between 10.2 and 14.0 ppm, and type C signals between 13.5 and 23.4 ppm. The influence of the neighboring cyclopropane rings on the chemical shift depends on the relative distance from any particular position in a molecule and can be expressed in corresponding increments for the atoms of type A and B (two different groups of increments for A and B have been proposed). The influence of a three-membered ring five bonds away is negligibly small. For carbon atoms of type C, only the number of neighboring spiroatoms plays a role.[222] This increment scheme has been used for the configurational assignment of stereoisomeric triangulanes which are frequently encountered, for example the diastereomers of [5]UT *meso*- and (*M*)/(*P*)-**21** (Chart 9, calculated values are given in parentheses).

Chart 8

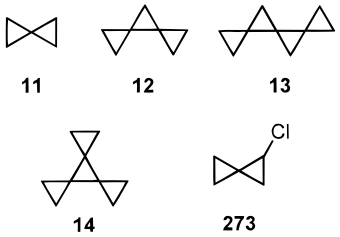
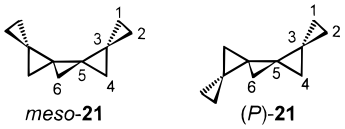


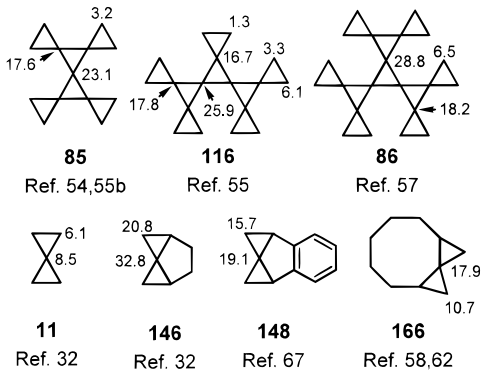
Chart 9



C-1	7.1 (6.8)	C-1	4.3 (4.2)
C-2	5.1 (5.1)	C-2	4.8 (4.8)
C-3	14.1 (14.0)	C-3	13.8 (14.0)
C-4	12.9 (12.5)	C-4	11.0 (11.2)
C-5	19.5 (20.2)	C-5	18.7 (18.4)
C-6	11.4 (11.6)	C-6	11.2 (11.6)

This additivity scheme, however, does have essential shortcomings: (i) it can practically be used only with the molecular models in hand, (ii) the chemical shifts of the spiroatoms cannot be predicted with a reasonable accuracy, and (iii) the spectral data of several BTs, which were prepared after the design of the scheme, are not included in the data basis and therefore such skeletons as **85**, **116**, and **86** (Chart 10) are not covered. Even the spectral data of spiropentane (**11**) do not fit into the scheme. For several of the cycloannelated[*n*]triangulanes—CATs **146**, **148**, and **166**—the signals in the ^{13}C NMR spectra for all types of carbons in the spiropentane fragments were observed at consistently lower field relative to those in UTs and BTs, and this effect increased with increasing total strain in the molecule (Chart 10).

Chart 10



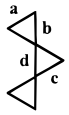
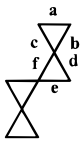
In the EI mass spectrum of spiropentane (**11**) recorded at 70 eV,[216] the parent peak is that of the $[C_5H_7]^+$ ion at $m/z = 67$ [M − 1]. The spectrum recorded at 15 eV shows the main peak at $m/z = 40$ [M − 28], a fragment ion formed through the loss of ethylene from the molecular ion. The higher triangulanes have not been studied in detail by mass spectrometry. In most cases, the molecular ions of [3]- to [6]triangulanes can hardly be observed in EI spectra taken at 70 eV and are even weak at 12 eV. Chemical ionization, however, does produce spectra showing molecular ion peaks of reasonable intensity even for the higher members of the [*n*]BT family such as **85**, **116**, and **86** ($n = 6$, 8, and 10).

B. Bonding Properties and Molecular Structures

Considering the electronic and bonding properties of triangulanes, two basic questions have to be addressed. The first one concerns the bonding in a three-membered ring as a building block of triangulanes in general, and the second relates to the MO interactions of adjacent cyclopropanes spiroannelated in a triangulane skeleton. The first question has been discussed in many contexts and summarized often.[2,223,224] The most frequently applied bonding model for cyclopropanes is that originally proposed by Walsh.[25−27] Better consistency with the PE spectroscopic data of many cyclopropane derivatives is obtained with an improved model with approximately 20% radial contribution to the tangential cyclopropane orbitals.[26c,d,223] Cremer[2] added support to the idea of σ-delocalization by analyzing the properties of the electron density distribution (EDD) in three-membered rings, which lead to a phenomenon called σ-aromaticity.[2b]

The bonding properties in oligospirocyclopropane assemblies have not been assessed at a comparably high level of theory except for the (*M*)-[4]triangulane (*M*)-**13**.[71] The hybridization in spiropentane (**11**) has been analyzed on the basis of $^{13}C-H$[215c,225a] and $^{13}C-{}^{13}C$[225b] coupling constants. In the latter case the distal and proximal bonds in **11** have been found to be $C(sp^{3.81})-C(sp^{3.81})$ and $C(sp^{3.81})-C(sp^{2.86})$ hybridized, respectively. The hybridization in UTs **11**, **12**, and **14** was also examined using the method of maximum overlap (MMO)[40,42,43] assuming C−C bond lengths of 1.54 Å and C−H bond lengths of 1.08 Å; the corresponding values for **11** were $sp^{3.82}$ and $sp^{3.90}-sp^{3.00}$.

Table 3. Calculated and Experimentally Determined Bond Lengths in UTs 11−13 (all values in Å)

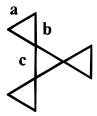
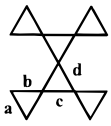
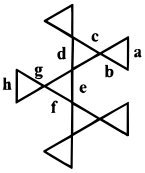
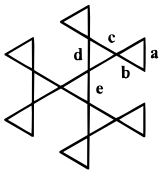
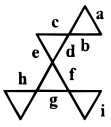
Compound	Method of Investigation	Length of C–C Bond				Ref
 (D_{3h})	6-31 G*	1.497				229
	X-ray (94 K)	1.499(1)				231
 **11** (D_{2d})	IMOA	**a** 1.511	**b** 1.495			29b
	MM2	**a** 1.534	**b** 1.480			33
	MM2	**a** 1.530	**b** 1.479			19a
	MM3	**a** 1.515	**b** 1.483			19a
	MNDO	**a** 1.529	**b** 1.509			229
	MINDO/3	**a** 1.490	**b** 1.503			30
	CFF:PEF 404	**a** 1.551	**b** 1.489			31
	STO-3G	**a** 1.514	**b** 1.486			28
	3-21G	**a** 1.529	**b** 1.482			32
	4-21G	**a** 1.534	**b** 1.487			232
	4-21G*	**a** 1.518	**b** 1.478			232
	4-31G	**a** 1.517	**b** 1.481			32
	6-31G	**a** 1.513	**b** 1.479			21
	6-31G*	**a** 1.517	**b** 1.475			229
	GIS	**a** 1.524	**b** 1.477			229
	Electron Diffr.	**a** 1.519(3)	**b** 1.469(1)			230
	X-ray (110 K)	**a** 1.527(1)	**b** 1.477(1)			127
 **12** (C_{2v})	IMOA	**a** 1.520	**b** 1.493	**c** 1.494	**d** 1.467	29a
	MM2	**a** 1.537	**b** 1.478	**c** 1.502	**d** 1.456	33
	MINDO/3	**a** 1.490	**b** 1.504	**c** 1.498	**d** 1.514	30
	6-31G*	**a** 1.517	**b** 1.475	**c** 1.492	**d** 1.455	229
	GIS	**a** 1.524	**b** 1.477	**c** 1.500	**d** 1.454	229
	X-ray (120 K)	**a** 1.531(1)	**b** 1.485(1)	**c** 1.506(2)	**d** 1.464(1)	229
 **13** (C_2)	MM2	**a** 1.537	**b** 1.478	**c** 1.478		33
		d 1.500	**e** 1.503	**f** 1.456		
	6-31G*	**a** 1.517	**b** 1.475	**c** 1.476		229
		d 1.493	**e** 1.493	**f** 1.455		
	GIS	**a** 1.524	**b** 1.477	**c** 1.477		229
		d 1.500	**e** 1.500	**f** 1.454		
	X-ray (120 K)	**a** 1.527(1)	**b** 1.476(1)	**c** 1.480(2)		229
		d 1.501(1)	**e** 1.502(1)	**f** 1.458(1)		

For triangulanes **12** and **14**, the iterative maximum overlap approximation method (IMOA) was applied for the same purpose.[29] The values of $sp^{3.76}$ (distal bond), $sp^{3.58}$−$sp^{3.03}$ (proximal bond), and $sp^{2.96}$ (the bonds between two spiroatoms) have been obtained for [3]rotane (**14**). The calculations for [3]UT **12** showed similar results. Despite differences in the actual results, different theoretical models all predict an increasing s-character in the sequence: distal bond, proximal bond, and bond between spiroatoms. The magnitude of C−C bond overlaps increases in the same sequence.[29] The same conclusion—relative weakening of distal and strengthening of proximal bonds as well as bonds between spiroatoms—has been drawn for compounds **11**−**14** from simple MM2 calculations.[33]

Photoelectron spectra (PES) have been recorded and interpreted for spiropentane (**11**),[126,217] [3]rotane **14**,[219] and the bridged spiropentanes **146** and **148**.[126] According to their interpretation, the resonance integral between linked 2p atomic orbitals of the adjacent cyclopropane rings in **14** is equal to −2.05 eV and the hybridization of the spiroatoms is close to sp. As a result of the PES investigation a "qualitative Walsh-type model" for the valence orbitals of **11**, constructed with the basis orbitals of the central carbon atoms (2s, $2p_x$, $2p_y$, and $2p_z$) and two ethylene fragments contributing with their π and π^* MOs, has been suggested by Gleiter et al.[126] (for another models see also refs 225b and 226). In the PE spectrum of **146**, the first six bands are shifted by 0.6−1.1 eV to lower ionization energies in comparison with **11**. The spectrum of **148** disclosed essentially no interaction between the valence MOs of the spiropentane moiety and the aromatic ring.

The experimental electron density distribution (EDD) maps of **11**, **14**,[127,227,228] as well as of **12** and **13**[228b,229] show some asymmetry with the maxima being more pronouncedly shifted outside the ring along the proximal and distal bonds. The electron density in the centers of the three-membered rings is increased. This can be interpreted as an argument

Table 4. Calculated and Experimentally Determined Bond Lengths in BTs 14, 82, 85, 86, and 116 (all values in Å)

Compound	Method of Investigation	Length of C–C Bond				Ref
 **14** (D_{3h})	IMOA	**a** 1.520	**b** 1.494	**c** 1.468		34,29a
	MM2	**a** 1.538	**b** 1.477	**c** 1.475		33
	MNDO	**a** 1.530	**b** 1.510	**c** 1.495		227
	MNDO	**a** 1.529	**b** 1.511	**c** 1.494		229
	MINDO/3	**a** 1.489	**b** 1.506	**c** 1.510		30
	AM1	**a** 1.507	**b** 1.483	**c** 1.657		227
	CFF:PEF 304	**a** 1.598	**b** 1.487	**c** 1.519		31
	CFF:PEF 404	**a** 1.555	**b** 1.483	**c** 1.504		31
	6-31G*	**a** 1.518	**b** 1.475	**c** 1.471		229
	GIS	**a** 1.524	**b** 1.477	**c** 1.477		229
	X-ray	**a** 1.496(1)	**b** 1.500(4)	**c** 1.465(4)		233
	X-ray (120 K)	**a** 1.525(2)	**b** 1.477(1)	**c** 1.475(2)		229
 **85** (D_{2d})	MNDO	**a** 1.529	**b** 1.511	**c** 1.496	**d** 1.469	229
	6-31G*	**a** 1.517	**b** 1.476	**c** 1.471	**d** 1.472	229
	GIS	**a** 1.524	**b** 1.477	**c** 1.477	**d** 1.477	229
	X-ray (140 K)	**a** 1.532(3)	**b** 1.486(3)	**c** 1.476(3)	**d** 1.481(2)	54,235b
 **116** (C_{2v})	MNDO	**a** 1.528	**b** 1.495	**c** 1.511	**d** 1.497	229
		e 1.498	**f** 1.498	**g** 1.510	**h** 1.529	
	6-31G*	**a** 1.517	**b** 1.477	**c** 1.470	**d** 1.474	229
		e 1.477	**f** 1.472	**g** 1.477	**h** 1.517	
	GIS	**a** 1.524	**b** 1.477	**c** 1.477	**d** 1.477	229
		e 1.477	**f** 1.477	**g** 1.477	**h** 1.524	
	X-ray (190 K)	**a** 1.516(3)	**b** 1.475(3)	**c** 1.471(2)	**d** 1.472(4)	55
		e 1.483(7)	**f** 1.471(4)	**g** 1.472(4)	**h** 1.512(8)	
 **86** (D_{3h})	MNDO	**a** 1.528	**b** 1.511	**c** 1.498		229
		d 1.495	**e** 1.500			
	6-31G*	**a** 1.517	**b** 1.476	**c** 1.469		229
		d 1.475	**e** 1.477			
	GIS	**a** 1.524	**b** 1.477	**c** 1.477		229
		d 1.477	**e** 1.477			
	X-ray (120 K)	**a** 1.529(1)	**b** 1.481(1)	**c** 1.476(2)		57
		d 1.479(1)	**e** 1.484(1)			
 **82** (C_s)	6-31G*	**a** 1.517	**b** 1.476	**c** 1.492	**d** 1.456	229
		e 1.493	**f** 1.472	**g** 1.471	**h** 1.475	
		i 1.518				
	GIS	**a** 1.524	**b** 1.477	**c** 1.500	**d** 1.454	229
		e 1.500	**f** 1.477	**g** 1.477	**h** 1.477	
		i 1.524				
	X-ray (120 K)	**a** 1.530(1)	**b** 1.483(1)	**c** 1.506(1)	**d** 1.460(2)	229
		e 1.509(1)	**f** 1.480(1)	**g** 1.482(1)	**h** 1.485(1)	
		i 1.532(1)				

favoring the predicted surface delocalization of σ-electrons (σ-aromaticity).[2]

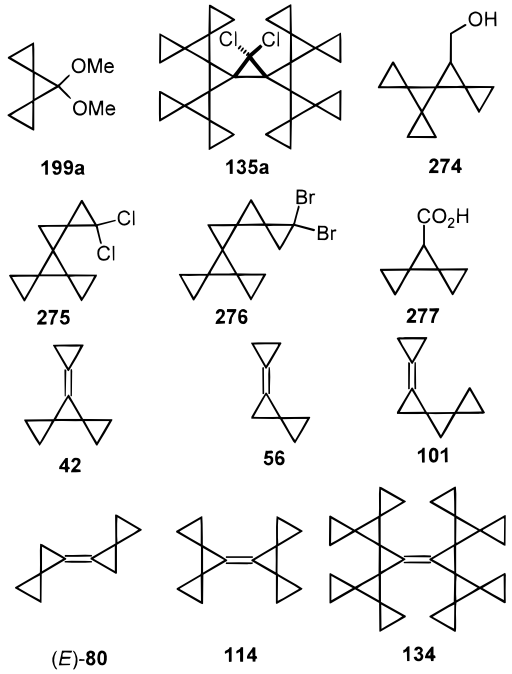
The determination of precise values for the parameters describing the shape and size of a molecule is of crucial importance in organic chemistry. Exact structure determination of triangulanes has been of constant interest starting with the first examination of spiropentane (**11**) in 1945 by gas-phase electron diffraction[24b] followed by a microwave spectroscopic investigation of spiropentyl chloride **273** in 1966.[218] The first reasonably accurate structure determination of **11** by electron diffraction was reported in 1968.[230] The structures of compounds **11**−**14** were also the object of numerous theoretical investigations frequently going ahead of the experimental determinations.

A comparison of calculated and experimentally determined bond lengths for UTs **11**−**13** and BTs **14**, **82**, **85**, **86**, and **116** is presented in Tables 3 and 4.

Except for the MINDO/3 method, all theoretical calculations predict a lengthening of the distal bonds of type a and shortening of the proximal bonds b as well as central bonds in completely spirocyclopropanated hydrocarbons such as **14**. This phenomenon would result from a partial release of the additional angle strain at the spiroatoms[33] and hybridization

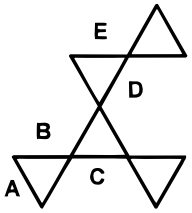
changes.[54,227,228,234] In the last 10 years a large number of X-ray crystal structures for functionally substituted spiropentanes,[142a,143,169b] higher BTs **82**,[229] **85**,[54,235b] **86**,[57] and **116**[55] (Table 4), substituted BTs **135a**,[112] **199a**,[172b] **274**,[54,235a] **275**,[136,235c] **276**,[136] and **277**,[236] and synthetic precursors of triangulanes **42**, **56**, **101**,[229] **114**,[55] (*E*)-**80**, and **135**[112] (Chart 11) have

Chart 11



been reported (for reviews, see refs 23b and 228). A comparison of the structures **14**, **85**, **86**, and **116** shows a consistent difference between longer distal and shorter proximal bonds in the outer spirocyclopropane units and also a gradual small but observable lengthening of the C−C bonds in the central rings upon consecutive spirocyclopropanation of a cyclopropane ring on going from **14** (1.475 Å) to **85** (1.481 Å), **116** (1.483 Å), and **86** (1.484 Å). This might be attributable to an additional electronic interaction in terms of a spiroconjugation between the outer rings and the central three-membered rings.[57] The substituents cause some distortion in the adjacent cyclopropane rings in **275**−**277** but not in **274**. Any abnormally short intermolecular contacts have not been found.

The abundance of experimental data prompted the development of a general increment scheme (GIS) for the quantitative prediction of different C−C bond lengths in triangulanes in general. Allen's proposal[237] to describe the geometries of substituted cyclopropanes, when applied to functionally substituted spiropentanes,[143] gave satisfactory results, but in the case of triangulanes[136] this approach overestimated the bond lengths in trispiro-substituted fragments. A second proposed additivity scheme (general increment scheme, GIS),[229] which differs from the first one only in the values of the basic parameters and increments, gives better overall results (see Tables 3 and 4). In both schemes, all bonds are divided into five categories depending on their relative position in a molecule, the number and locations of the spiroannelated three-membered rings as, e.g., in **81**: distal (**A**), proximal (**B**), distal−proximal−proximal (**C**), proximal−proximal (**D**), and distal−proximal (**E**).



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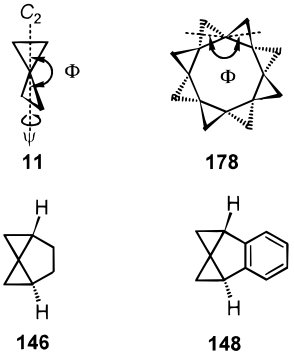
Assuming that the influences of all cyclopropanes and double bonds are additive and independent of each other, in the latter scheme (GIS)[229] the structures can be described using an initial value of 1.5008 Å for the C−C bond length in a cyclopropane unit and an increment of +0.0227 Å for each "distal" and −0.0234 Å for each "proximal" spirocyclopropane in the estimation of the actual bond length. A comparison of the bond lengths estimated according to this scheme and the experimentally determined ones is presented in Tables 3 and 4. In essence, this additivity scheme reduces the variety of triangulane structures to a description with only four bond lengths, namely, 1.454, 1.477, 1.500, and 1.524 Å. A bond of type D is better reproduced in the other additivity scheme.[136] Basically, such an increment scheme can describe the main tendencies in triangulane geometries but not the subtle effects. (For the influence of an attached double bond on the geometry of a triangulane skeleton, see refs 23b and 229).

The structures of CATs such as **146** deserve special attention. On the basis of STO 6-31G* calculations it was predicted[32] that the deformation of a spiropentane skeleton does not require excessive energy, yet its deformation through bending of the angle Φ should be more facile than through twisting (τ) around the C_2 axis (Chart 12). (For a short account

Chart 12



of calculated geometries and energetic parameters in such compounds, see also ref 70d.) This prediction has been supported experimentally.[127] In the crystal, spiropentane (**11**) is slightly deformed with Φ = 179.6° and τ = 90.2° due to packing effects. By bridging two non-spiroatoms as in **146**, bending or twisting or both must occur.[32] The X-ray structure analysis of **146** revealed Φ = 154.0° and τ = 80.0°.[127]

Table 5. Comparison of Thermochemical Data for 11−14, 21, 146, 205, and 251 According to Theoretical and Experimental Investigations (all values in kcal/mol)

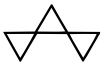
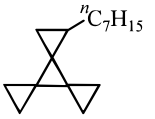
Compound	Method	ΔH_f° (g)	SE	Ref
 C_3H_6	exp.	12.74	28.13[a]	10,240
 **11**	MM2	43.97		35b
	MM2	43.96	63.3[b], 64.0[c], 63.31[d]	33a
	MM2	44.34		19a
	MM3	43.83		9
	MM3	44.15		19a
	MM/2ER W	44.45		9
	MINDO/3	28.7	45.6[b]	30,37b
	SR	44.0		241
	SCF MO	58.0	75.2	37a
	STO-3G	43.8	63.7[c]	28
	3-21G	48.60		32
	4-31G	45.50	65.4[c]	28
	4-31G	44.08		32
	6-31G*	42.62	61.4[e]	21
	AM1	50.82		39
	RM3	42.94		39
	exp.	41.77±0.31	62.59±0.31	238a
	exp.	44.23±0.18	65.05±0.18[a]	238b
 **12**	MM2	76.0	99.8[b], 100.42[d]	33
	MMX 88	76.0		51
	MINDO/3		69.9[b]	30
	AM1	83.51		39
	RM3	70.63		39
	exp.	72.27±0.83	98.52±0.83[d]	239
 **13**	MM2	108.0	136.2[b], 137.5[d]	33
	MM2	111.2	142.0[a]	12
	MM3	102.3	133.1[a]	12
	MMX 88	107.9		51
	AM1	116.8		39
	RM3	98.4		39
	exp.	102.6±1.6	134.28±1.6[a]	239
	exp.	106.57±0.19	138.25±0.19[a]	12
 **14**	MM2	109.19	137.1[b], 139.3[c], 138.38[d]	33
	MM2	109.2	140.0[a]	12
	MM3	101.2	132.0[a]	12
	MINDO/3		95.21	30
	AM1	117.35		39
	RM3	99.23		39
	exp.	101.1±1.17	132.18±1.17[a]	239
	exp.	105.91±0.32	137.59±0.32[a]	12
 **21**	MMX 88	139.85		51
	AM1	150.12		
	RM3	129.19		
	exp.	129.83±1.62[f]	166.94±1.62[a]	239

Table 5 (Continued)

Compound	Method	ΔH_f° (g)	SE	Ref
 **205**	MM2	68.71	138.44[a]	12
	MM3	62.34	132.08[a]	12
	exp.	64.99±0.69	134.7±0.69[a]	12
 **146**	6-31G*	59	80[e]	32
	exp.	55.5	80.6	125
 **251**	MM3	67.18	92.3	9
	MM/2ER W	67.67	92.8	9
	exp.	68.85	93.9	9

[a] GI method according to Schleyer.[10] [b] GI method according to Benson.[242] [c] Homodesmotic BE method according to George.[243] [d] BE method according to Allinger.[244] [e] GI method according to Wiberg.[21,32] [f] A 3:1 mixture of *meso*-**21** and (*P*),(*M*)-**21** was used in the combustion.

In phenylene-bridged spiropentane **148**, the bending is even greater ($\Phi = 151.4°$) whereas the twisting is less ($\tau = 85.2°$) and the "tensile spring" of the spiropentane unit in **148** lengthens the proximal C−C bond in the benzene ring. These experimental results indicate that cyclo[*n*]triangulanes such as [8]CT **178** or even [10]CT **181** and "davidane" **18** are not unreasonable targets for synthesis. According to calculations [HF/6-31G(d) method],[132] the deformation of the spiropentane units in **178** is predicted to be only minimal with angles $\Phi = 178.8°$ and $\tau = 87.6°$ and bond lengths of 1.494 and 1.456 Å, respectively. The corresponding values for "davidane" **18** and [10]-CT (**181**) are equal to $\Phi = 165.5°$, $\tau = 78.4°$ and $\Phi = 174.2°$, $\tau = 87.3°$, respectively.[132]

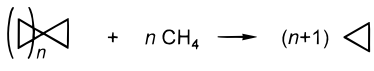
The most comprehensive theoretical treatment of structural and energetic properties of triangulanes is contained in a doctoral thesis.[132a]

C. Thermochemical Properties

The concept of strain[6] and strain energies provides a basis that helps to correlate structures, stabilities, and reactivities of molecules.[1,2] A quantitative estimation of SEs in triangulanes has been attempted in a number of detailed theoretical investigations. However, the main attention was paid to spiropentane (**11**), the only triangulane for which an experimental value was available until recently (see Table 5). Two different measurements of the enthalpy of formation ΔH(g) for spiropentane (**11**) have been reported;[238] however, the second value of 44.23 kcal/mol[238b] is now generally accepted. In the two most recently published experimental investigations,[12,239] the enthalpies of formation for UTs **12**, **13**, and **21** and BT **14** have been determined by measuring their heats of combustion in a microcalorimeter; these values and the strain energies (SE) derived from them are compared with values from different calculations (Table 5). Apparently the semiempirical MINDO/3 method vastly underestimates the strain energies of such compounds. AM1 and RM3 methods demonstrate over- or underestimation, respectively. Higher level ab initio calculations give better results, but simple molecular mechanics calculations with both the MM2 and MM3 parameter sets give surprisingly good results for triangulanes **11**−**14** and **205**. The enthalpies of formation for **11**−**14** can be evaluated quite satisfactorily using the isodesmic reactions leading to separated rings[245] in a modification for spirocompounds[28] (Scheme 59; for a definition of the terms "isodesmic" and "homodesmotic", see ref 1, p 7).

On top of the question of whether the total strain energy of a triangulane somehow correlates to its thermal stability, it is interesting to note that any spirojunction of two cyclopropane rings leads to additional strain. Dewar et al. stressed for the first time that the strain energy of spiropentane (**11**) should be more than twice that of cyclopropane,[37a] i.e., the spirojunction of two cyclopropane rings should lead to additional strain. In fact, the experi-

Scheme 59[a]



38

Compound	**11** (*n* = 1)	**12** (*n* = 2)	**13** (*n* = 3)	**14**
ΔH_{RS}° [a]	43.37	74.0	104.63	104.63
ΔH_f° (g)$_{exp.}$	44.23	72.27	106.57	105.91

[a] Calculated with ΔH(g) (C_3H_6) = 12.74 kcal/mol; ΔH(g) (CH_4) = −17.89 kcal/mol.[240]

mental values of SE for spiropentane (**11**) (65.1 kcal/mol[238b]) and cyclopropane (28.1 kcal/mol[10]) based on the same strain-free model[10] lead to an excessive incremental strain energy of $\Delta SE = 8.9$ kcal/mol (65.1 $-$ (2 $\times$ 28.1)). Apparently, the same excess increment should be applicable *n* times for a triangulane with *n* spirocarbon atoms with $\Delta SE = 8-10$ kcal/mol, as predicted by MM2 calculations.[33] The recently performed AM1 and RM3 calculations estimated this value to be 11.9 ± 0.7 or 5.9 ± 0.5 kcal/mol per spiro atom, respectively (calculations were performed up to [10]UT and [10]BT).[39] The values of ΔSE, calculated on the basis of experimentally determined ΔH(g) for **12**$-$**14**,[239] are equal to 7.1 kcal/mol for **12** {[98.52 $-$ (3 $\times$ 28.13)]/2}, 7.3 kcal/mol for **13**, and 6.6 kcal/mol for **14** and **21**. This seems to indicate that ΔSE would indeed depend on the number of spiro atoms as well as their position in a molecule. Tatevskii et al.[246] proposed eq 4 to evaluate ΔH(g) in triangulanes in which *k* denotes the number of CH_2 fragments and *m* the number of spirocarbon atoms.[239]

$$\Delta H(g) = k \times 4.24 + m \times 25.39[\text{kcal/mol}] \quad (4)$$

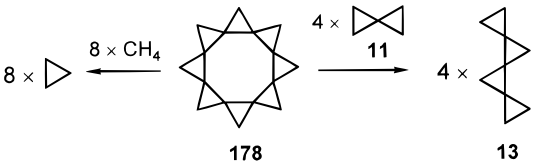
The later published data, however, show that the difference SE $-$ [4 $\times$ SE(C_3H_6)] is equal to 25.7 kcal/mol for **13** and 25.1 kcal/mol for **14**, corresponding to an excess increment ΔSE of 8.6 and 8.4 kcal/mol per spirojunction, respectively.[12] The mean value for **13** and **14** is 8.5 kcal/mol per spirocarbon atom, within the limits of error, essentially the same as that for **11**. These results indicate that all types of spiro atoms in [*n*]triangulanes contribute the same additional strain and that a general additivity scheme can be applied to calculate total strain energies for such compounds. Assuming that this additivity scheme also holds for higher [*n*]triangulanes, one can assess their SEs according to eq 5.

$$SE = n \times 28.1 + (n - 1) \times 8.6[\text{kcal/mol}] \quad (5)$$

In this equation the mean value for the whole series **11**, **13**, and **14** should be applied; *n* denotes the number of cyclopropane units (every [*n*]triangulane has (*n* $-$ 1) spirocarbon atoms). Such an additivity phenomenon was not observed for spirocyclopropanated cyclobutanes and higher [*n*]rotanes, and the excess strain increment is only 2.4 ± 0.5 kcal/mol for [4]rotane (**209**) and even smaller for not fully spirocyclopropanated cyclobutanes.[12]

Turning again to the concept of a cyclic [8]triangulane **178**, it is possible to estimate its ΔH(g) according to a ring-separation reaction or according to a homodesmotic reaction with spiropentane (**11**), as proposed by Boese and Haumann[132] (Scheme 60),

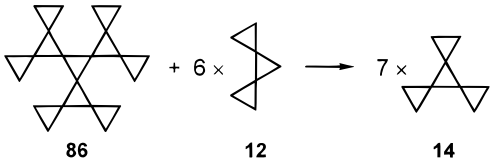
Scheme 60



to be equal to 245.1 and 231.6 kcal/mol, respectively (as calculated at the 6-31G* level of theory, ΔH of this homodesmotic reaction is 1.89 kcal/mol[132]). HF/6-31G(d) calculations yield a value of 237.0 kcal/mol.[132a] According to eq 5, the SE of **178** is equal to 293.6 kcal/mol, which is close to the results of HF/6-31G(d) calculations accounting for the enhanced increment of a spirocarbon atom in the case of a cyclic triangulane.[132a]

In view of these values, the thermodynamic driving forces for thermal reorganizations of triangulanes ought to be strong. Surprisingly, however, many of the known triangulanes enjoy a remarkable thermal stability. For example, the thermal rearrangement of spiropentane (**11**) is observed only at temperatures above 350 °C and requires an activation energy of 57.6 kcal/mol[247] which is considerably lower than that of a thermal isomerization of a simple cyclopropane derivative (e.g., 65.2 kcal/mol[181]). The [10]triangulane **86**, which is thermally stable up to 250 °C,[57] according to eq 5 would possess a total SE of 358.4 kcal/mol. Using the homodesmotic reaction in Scheme 61,

Scheme 61



the predicted ΔH(g) is 274.2 kcal/mol. For comparison, cubane (**6**) with its strain energy between 157[248a] and 161 kcal/mol[248b] and ΔH(g) between 148.7[248a] and 158.8 kcal/mol[248b] is thermally stable up to 220 °C.[8b] The [*n*]triangulanes therefore present another convincing example for the well-known fact that total strain energy of a molecule and kinetic instability do not correlate at all.

Therefore, as far as thermal stability is concerned, higher aggregates of spiropentane units would have every chance to exist. Model calculations[132a] show that four spiropentane units **A** can be linked to construct [8]CT **B** without significant angular distortions. Two [8]CTs in turn linked in a spiro fashion by four three-membered rings form a sort of cube ([20]pentacyclotriangulane **C**), and five such cubes can be linked through common triangular faces to give a toroid structure, [80]triacontacyclotriangulane **D** (Figure 1). A carbon network comprising only spiro-linked three-membered rings is therefore conceivable.[57] Whether such a network can actually be realized is a matter of the future.

A rather promising and quite realistic route to reasonably large aggregates of spirocyclopropane rings relies on the new methodology of dimerizing copper cyclopropylidenoids generated from 1,1-dibromotriangulanes. This allows one to construct a whole family of dendritic molecules consisting of spiro-annelated three-membered rings with a central double bond, which in turn can probably be used to prepare higher order branched [*n*]triangulanes (Figure 1).[112]

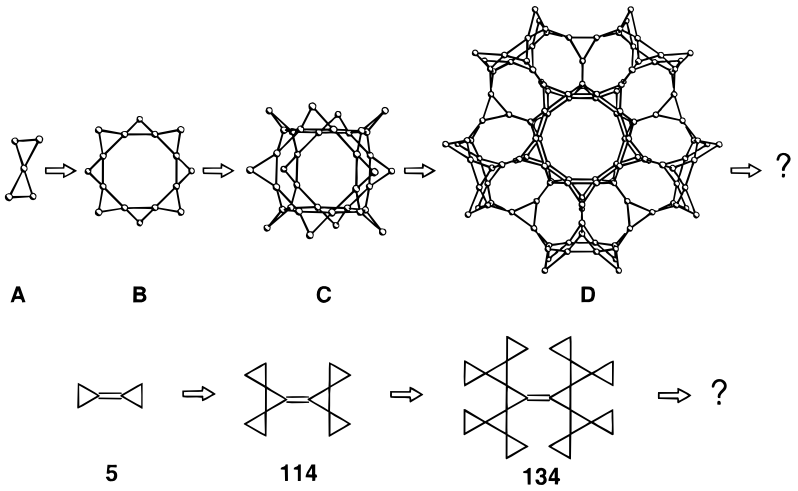


Figure 1.

V. Chemical Transformations of Triangulanes

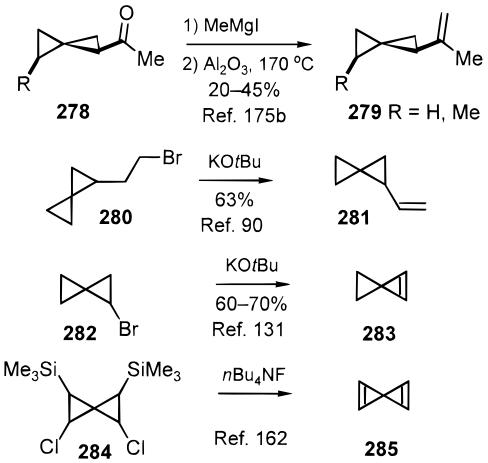
Up until now, little is known about the chemical properties of triangulanes. Most literature reports are limited mainly to the chemistry of spiropentane (**11**) and of substituted spiropentanes, in particular to their thermal rearrangements. The chemistry of substituted triangulanes can formally be divided into two big sections: (i) reactions with retention of the triangulane skeleton and (ii) reactions accompanied by ring opening or ring enlargement of one or more rings.

A. With Retention of the Skeleton

The simplest reactions with retention of the oligospirocyclopropane skeleton are ordinary functional group interconversions such as reduction of an alkoxycarbonyl to a hydroxymethyl group[94,101,151a,155a,158,174,249] and vice versa,[106,154] oxidation of a hydroxyl group to an oxo group[158,173a] and vice versa,[173a] hydrolysis of an ester,[57,143,153,158,165] transformation of an acid to an acid chloride followed by Curtius rearrangement,[57,153,165,249,250a] reduction of an oxime to an amine,[102b,250b] conversion of a formyl to a dichloromethyl group,[158] reduction of a *gem*-dichloride or *gem*-dibromide,[97d,98b,145] etc., which all have been performed on triangulane skeletons. This type of conversion does not involve the chemical uniqueness of triangulanes but has been used along the route to higher triangulanes (see section III) or for the preparation of functionally substituted oligospirocyclopropanes.

Different methods had to be used to generate vinylic side chains as in **279** and **281**[90,175b] or double bonds in the three-membered rings of spiropentane.[131,162] While the former **279** and **281** could be obtained by dehydratation of the methylmagnesium iodide adduct on the carbonyl substituent in **278** and dehydrobromination of a β-bromoethyl derivative **280**, respectively, the highly strained and unstable spiropentene **283** and spiropentadiene **285** were generated by dehydrobromination of bromospiropentane **282** and 2-fold dechlorosilylation of a bischlorobis(trimethylsilyl)spiropentane **284** (Scheme 62). The diene could only be isolated as its Diels−Alder adduct with cyclopentadiene in 10% yield.[162]

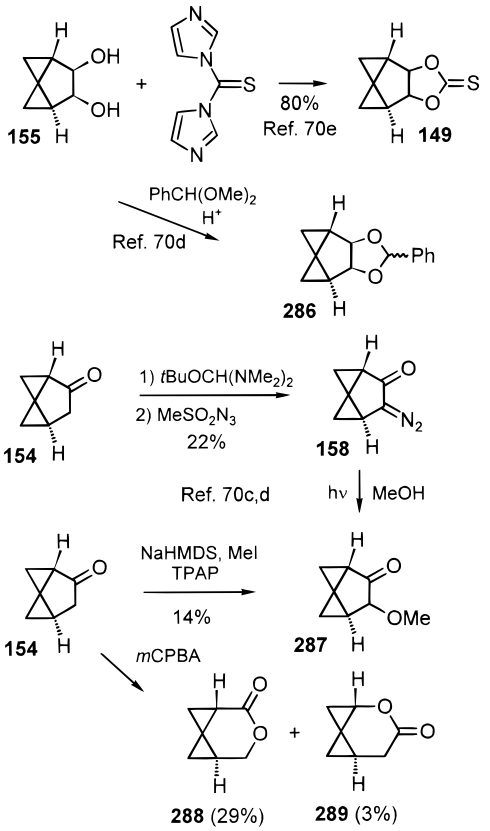
Scheme 62



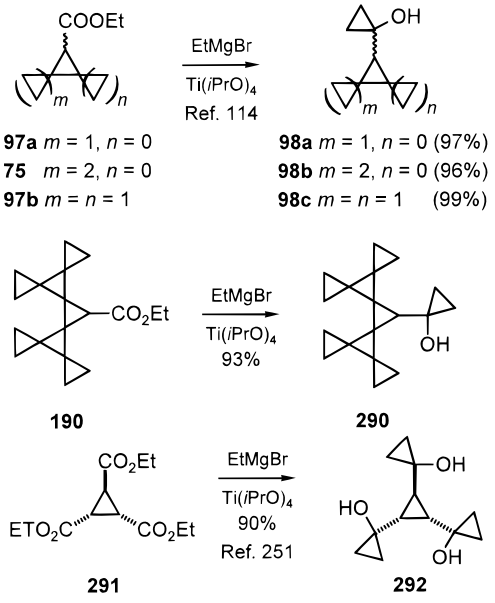
Only a limited number of transformations without destruction of their spiropentane systems have been reported for CATs with a tricyclo[4.1.0.0^{1,3}]heptane skeleton (**146**); several examples are shown in Scheme 63 (see also Schemes 27 and 28).[70] The transformation of ethyl [*n*]triangulanecarboxylates with ethylmagnesium bromide in the presence of Ti(*i*PrO)$_4$ (Kulinkovich reaction,[115] see also Scheme 16) to give (1′-hydroxycyclopropyl)triangulane derivatives **98** in excellent yield (Scheme 64) deserves special mentioning.[114,251] Another remarkable observation is the through-space activation of C−H bonds in (diisopropylamino)carbonyl[3]triangulanes **293** and **294**.[159] The aminocarbonyl-group-directed metalation of C−H bonds on strained hydrocarbon skeletons with magnesium amides has been developed by Eaton et al. as a powerful method for functionalization.[252] This methodology is applicable to [3]UTs and causes through-space activation and stereospecific functionalization of C−H bonds separated from the activating center by three or even four C−C bonds (Scheme 65). This methodology may obviously be applied for the preparation of oligosubstituted higher triangulanes.

A Grignard reagent can be easily prepared from spiropentyl chloride (**273**), and it reacts quite normally with ethyl chloroformate and isocyanates.[153,250a] Less effective was the direct lithiation of spiropentanecarboxylic acid (**300**) and *tert*-butyl 1-chlorospiro-

Scheme 63



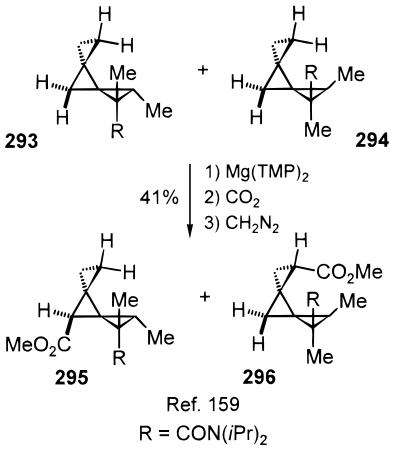
Scheme 64



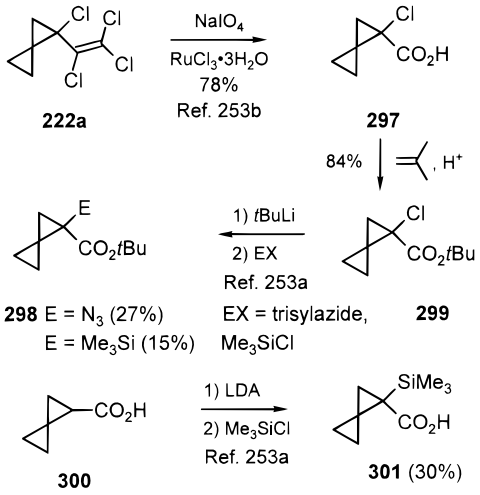
pentanecarboxylate (**299**) (Scheme 66).[253a] The α-chloroester **299** was prepared via oxidation of 1-chloro-1-(trichloroethenyl)spiropentane (**222a**) (Scheme 66) followed by esterification.

The higher order cuprate **302** of type $R_2Cu(CN)Li_2$[254] derived from bromospiropentane (**282**) reacts with O'Donnells acetate **303**[255]—an electrophilic glycine equivalent—to yield the protected spiropentylglycine **304** (Scheme 67).[165] The reaction of an analogous cuprate prepared from methylenespiropentane (**34**) to a certain extent occurred with an unusual mode of opening of one three-membered ring

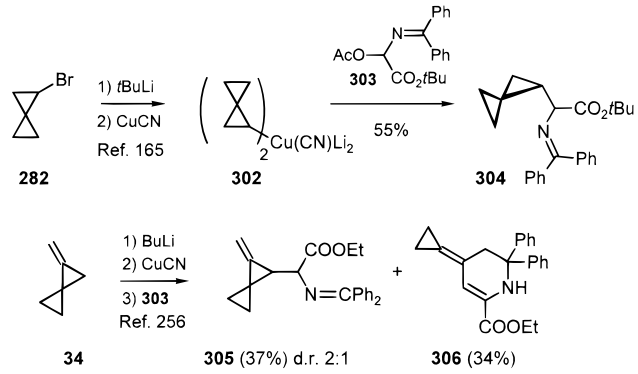
Scheme 65



Scheme 66



Scheme 67

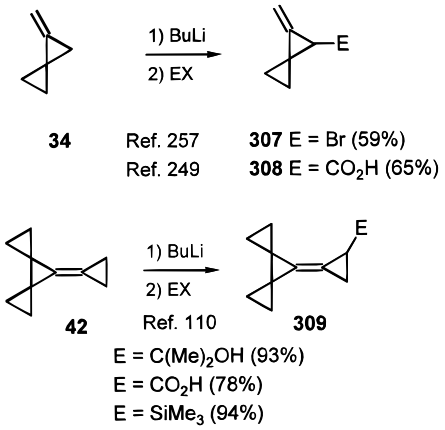


and thus gave a mixture of (methylenespiropentyl)-glycine **305** and the rearrangement product **306** (Scheme 67).[256]

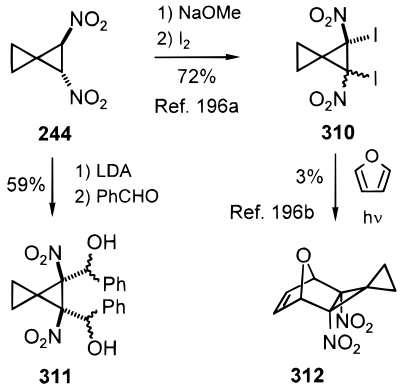
A large variety of functionally monosubstituted triangulanes can be prepared directly from methylenetriangulane or cyclopropylidenetriangulane in moderate to excellent yields by deprotonation with butyllithium in THF at 0 °C and electrophilic substitution of the lithiated hydrocarbon with appropriate reagents (Scheme 68).[110,249,257]

Dinitrospiropentane (**244**) with its first pK_a = 18.6−21.6 can be doubly deprotonated and functionalized even more easily (Scheme 69).[196a] Photolysis

Scheme 68



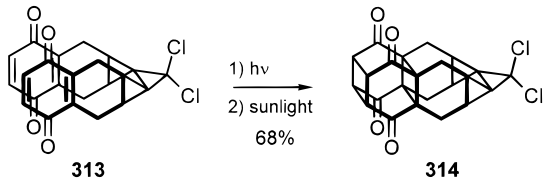
Scheme 69



of the diiodide **310** in the presence of furan afforded the formal Diels−Alder adduct **312** of the in situ formed intermediate 1,2-dinitrospiropentene.[196b]

Intramolecular [π^2s + π^2s] cycloaddition reactions in the bis-*p*-benzoquinone-annelated 7,7-dichlorotriangulane **313** have been used for the construction of a tube-like molecule **314** (Scheme 70).[141a] Another

Scheme 70

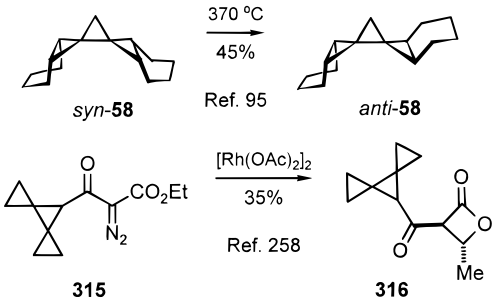


interesting transformation with conservation of the triangulane skeleton is the thermal *syn*−*anti* interconversion of a [3]triangulane fused with two six-membered rings *syn*-**58** to *anti*-**58** (Scheme 71).[95] Unfortunately, the interesting mechanistic aspects of this rearrangement have not been investigated.

The α-diazo-*β*-ketoester **315** upon $[Rh(OAc)_2]_2$-catalyzed decomposition in the presence of alkenes gave, as the only isolated product, the *β*-lactone **316**, apparently from intramolecular insertion of an intermediate ethoxycarbonylcarbene (Scheme 71).[258]

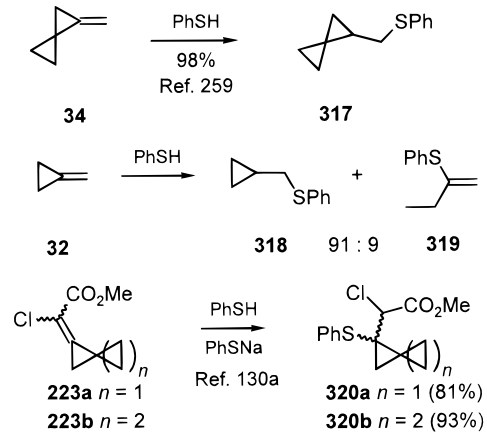
The different types of addition reactions onto the double bonds in methylene- and cyclopropylidenetriangulanes are of special interest, as they may proceed with retention of the oligospirocyclopropane moiety as well as with ring opening. Surprisingly, the

Scheme 71



additions of thiophenol onto the double bonds of bicyclopropylidene (**5**) and methylenespiropentane (**34**) proceed quantitatively in benzene at 20 °C in the absence of catalysts or radical initiators; **34** gave exclusively the anti-Markovnikov adduct **317** with complete retention of both three-membered rings. For comparison, methylenecyclopropane (**32**) gave 9% of the ring-opened compound **319** in addition to the anti-Markovnikov adduct **318** (Scheme 72).[259] The

Scheme 72



2-chloro-2-triangulanylideneacetates **223** with their highly polarized double bonds react rapidly with thiophenol in terms of a Michael addition, also without ring opening to yield triangulanes **320** with a thiophenyl group on their cyclopropane rings[130a] (Scheme 72). Like the parent alkyl 2-chloro-2-cyclopropylideneacetates **226**,[191] the acrylates **223a**,**b** exhibit a vastly enhanced reactivity as Michael acceptors.[191] The double bond in **223a**−Bn can be reduced with $NaBH_4$ absorbed on silica gel (Scheme 73).[165] The Michael additions of various nitrogen nucleophiles (Scheme 73 and Table 6)[165,190,253a] yielded

Scheme 73. For Details, see Table 6

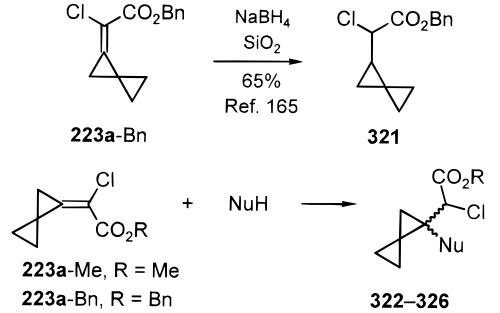
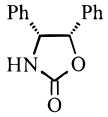
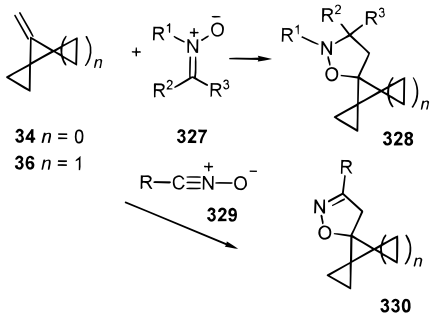


Table 6. Michael Addition of Nitrogen Nucleophiles onto Alkyl 2-Chloro-2-spiropentylideneacetates 223a

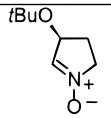
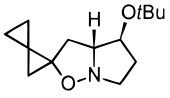
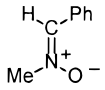
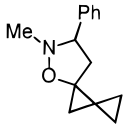
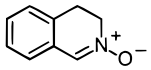
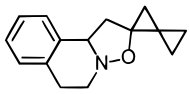
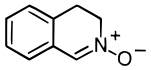
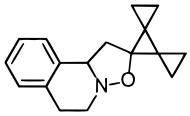
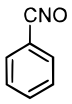
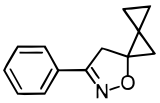
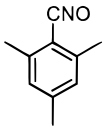
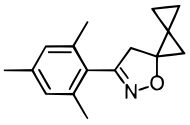
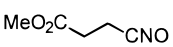
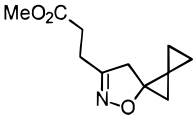
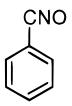
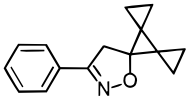
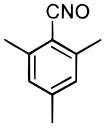
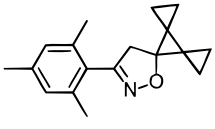
Entry	Starting Material	NuH	Product	Yield (%)	Ref
1	**223a**-Bn	Bn_2NH	**322**	88	253a
2	**223a**-Me	$PH_2C{=}NH$	**323**	96	190
3	**223a**-Bn	$PH_2C{=}NH$	**324**	98	253a
4	**223a**-Me		**325**	74–85	165,253a
5	**223a**-Bn		**326**	74–91	165,253a

Scheme 74. For Details, see Table 7



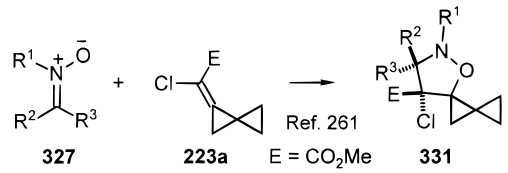
useful intermediates **321**−**326** for the preparations of nonnatural amino acids containing spiropentyl groups (see below). The 1,3-dipolar cycloaddition of various nitrones **327** and nitrile oxides **329** to methylenespiropentane (**34**) and 7-methylenedispiro[2.0.2.1]-heptane (**36**) under relatively mild conditions (40 or

Table 7. Cycloadditions of Nitrones 327 and Nitrile Oxides 329 to Methylenespiropentane (34) and 7-Methylenedispiro[2.0.2.1]heptane (36)

Nitrone or Nitrile Oxide	Alkene	Cycloadduct	Yield (%)	Ref
	**34**		57	260c
	**34**		48	260c
	**34**		44	260c
	**36**		51	260c
	**34**		64	260a,c
	**34**		95	260a,c
	**34**		44	260b,c
	**36**		54	260c
	**36**		93	260c

60 °C) established the possibility to synthesize new spirocyclopropane-annelated nitrogen heterocycles (Scheme 74 and Table 7).[260] The yields of 5-spirocyclopropaneisoxazolidines **331**, obtained upon cycloaddition of nitrones **327** to the polarized double bond of chlorospiropentylideneacetate **223a**, were even better (Scheme 75).[261] One of the basic reactions—

Scheme 75

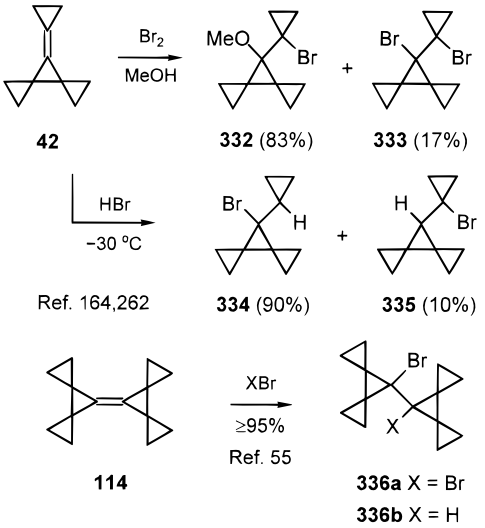


327 **223a** **331**

327	R^1	R^2	R^3	Yield of 331 (%)
a	*o*-$CH_2CH_2C_6H_4$–		H	93
b	–$(CH_2)_3$–		H	58
c	Me	H	Ph	68

the electrophilic addition of bromine onto the double bond of an alkene—has also been investigated for methylene- and cyclopropylidenetriangulanes. An increased number of spiroannelated three-membered rings was found to stabilize the intermediate cyclopropyl cations against ring opening; bromine additions to 7-cyclopropylidenedispiro[2.0.2.1]heptane (**42**) performed in methanol at 25 °C proceed with complete retention of all cyclopropane rings (Scheme 76),[164,262] and so did the bromination as well as the hydrobromination of di- and tetraspirocyclopropanated bicyclopropylidenes **42** and **114** (Scheme 76).[55,164,262]

Scheme 76

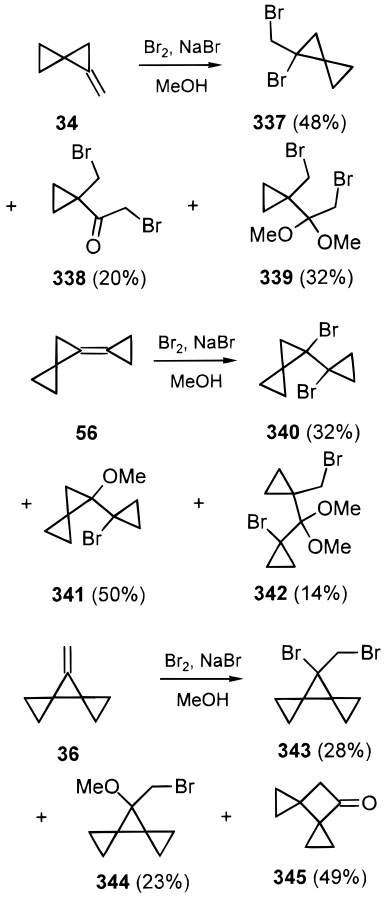


42 **332** (83%) **333** (17%) **334** (90%) **335** (10%) **114** **336a** X = Br **336b** X = H

B. With Ring Opening

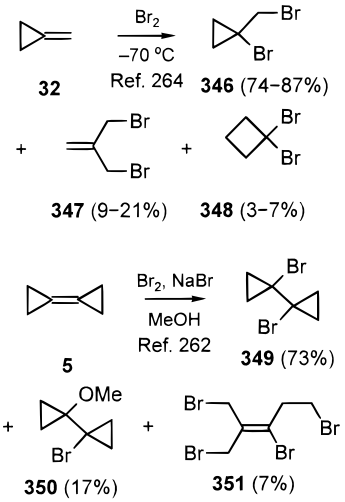
For the first, reactions of oligospirocyclopropanes accompanied by ring opening comprise numerous examples in which a cationic center is intermediately generated directly on a cyclopropane moiety or in the α-position of a side chain. Thus, bromine additions to methylenetriangulanes **34** and **36** and cyclopropylidenetriangulane **56** when performed in methanol

Scheme 77



34 **337** (48%) **338** (20%) **339** (32%) **56** **340** (32%) **341** (50%) **342** (14%) **36** **343** (28%) **344** (23%) **345** (49%)

Scheme 78



32 **346** (74–87%) **347** (9–21%) **348** (3–7%) **5** **349** (73%) **350** (17%) **351** (7%)

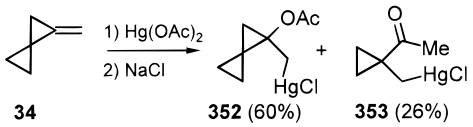
at 25 °C in the presence of sodium bromide were all accompanied to a certain extent by ring-opening or ring-enlargement reactions (Scheme 77),[164,262] which can be attributed to the intermediate formation of cyclopropyl or cyclopropylcarbinyl cations.[263] For comparison, partial ring opening has been observed in the chlorination and bromination reactions of methylenecyclopropane (**32**) even at −70 °C (Scheme 78),[264] but bicyclopropylidene (**5**) reacts with bromine in the presence of NaBr at room temperature to give only 7% of the ring-opened product **351**.[164,262] Apparently, an increase of the number of adjacent three-membered rings leads to an increased stability of the

Table 8. Rate Coefficients (k_{Br_2}) of Bromine Addition to Alkenes 5, 32, 34, 36, 42, and 56 and π-Ionization Energies (π-IE$_v$)

Alkene	k_{Br_2} [mol^{-1}·l·s^{-1}]	log k_{Br_2}	IE [eV]
32	$(3.66\pm0.09)\times10^2$	2.56	9.57
34	$(5.90\pm0.27)\times10^3$	3.77	9.10
5	$(4.70\pm0.05)\times10^4$	4.67	8.93
36	$(1.95\pm0.10)\times10^5$	5.29	
56	$(1.63\pm0.04)\times10^6$	6.21	8.70
42	$(3.42\pm0.11)\times10^7$	7.53	8.50

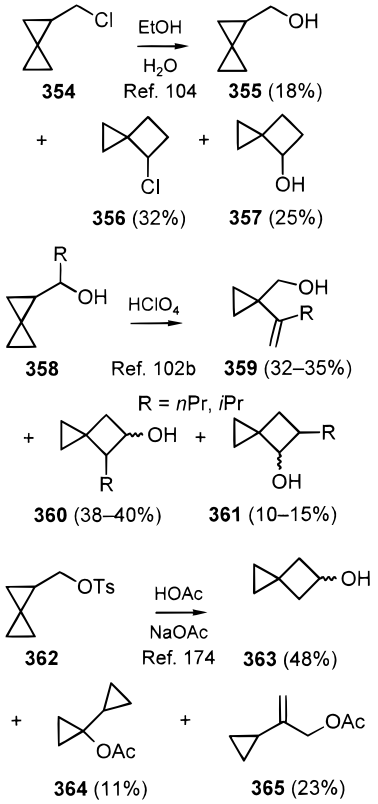
intermediate cyclopropyl cations, which makes them less prone to undergo ring-opening reactions. However, the recently determined kinetic data for the bromination of methylenetriangulanes **34** and **36** and cyclopropylidenetriangulanes **42** and **56** as well as bicyclopropylidene (**5**) and methylenecyclopropane (**32**) in methanol at 25 °C disclose that the addition of Br_2 onto the double bonds in these alkenes proceeds essentially with the same rate as bromination of the corresponding oligomethylated ethylenes. The bromination rate increases with an increasing number of spiroannelated three-membered rings, and the rate of bromination correlates with the π-ionization energies of the molecules (Table 8).[262] The addition of mercuric acetate to **34** proceeded predominantly by the usual 1,2-acetoxymercuration without ring opening of the intermediate spiropentyl cation to give adduct **352**,[265] but a competing addition across the C−C single bond of the spiropentane moiety resulting in **353** was also observed (Scheme 79).

Scheme 79

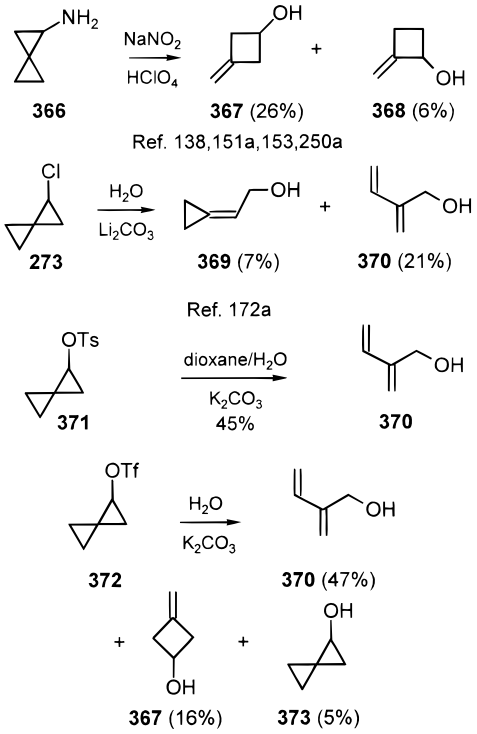


By generating a cationic center in the α-position to a spiropentyl fragment upon solvolysis, a ring expansion was the predominant reaction pathway (Scheme 80).[102b,104,174] Spiropentyl cation, when generated by deamination of spiropentylamine (**366**), underwent a rearrangement with ring opening and ring expansion of both cyclopropanes (Scheme 81).[138,151a,153,250a] Opening of both rings, but with formation of 2-(hydroxymethyl)butadiene (**370**) as the

Scheme 80

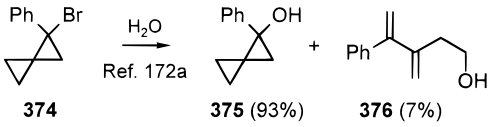


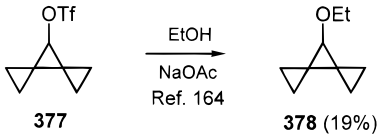
Scheme 81

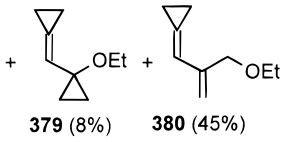


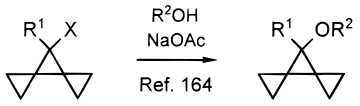
main rearrangement product, was also observed upon solvolysis of the chloride **273**, tosylate **371**, and triflate **372**.[172a] All reactions have been investigated in great detail with regard to their mechanisms and the structures of the respective intermediates. The kinetic data for the solvolysis of spiropentyl chloride (**273**) ($k = 7.1 \times 10^{-5}$ s^{-1} versus 1.4×10^{-5} s^{-1} for chlorocyclopropane)[266] and spiropentylmethyl chlo-

Scheme 82







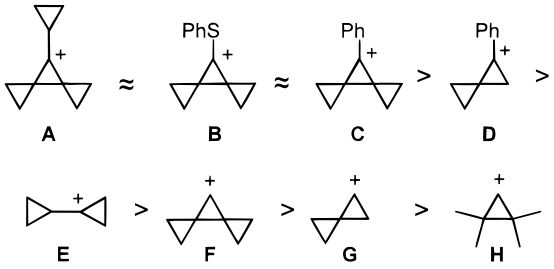


R^1	R^2	X	Yield **382** (%)
Ph	Me	Br	90
SPh	Me	Cl	100
SPh	Ac	Cl	100
cC_3H_5	Me	Br	87

ride (**354**)[104] showed that the second three-membered rings have only an insignificant influence upon the rates in comparison with the corresponding cyclopropyl derivatives.

Compounds with adjacent cyclopropylcation-stabilizing groups such as phenyl in **374**[172a,263] or spirocyclopropane fragments in **377**[164] upon solvolysis gave an increased yield of the oligospirocyclopropane moieties (Scheme 82). The accumulated experimental evidence allows one to estimate the relative stabilities of variously substituted and spirocyclopropanated cyclopropyl cations, as shown in Scheme 83, and

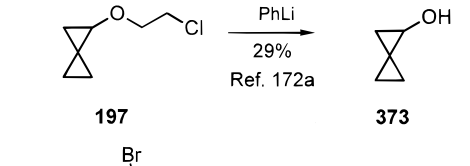
Scheme 83

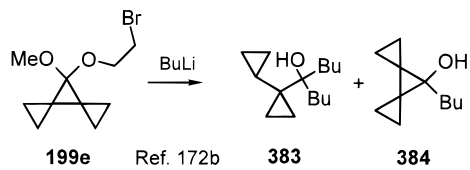


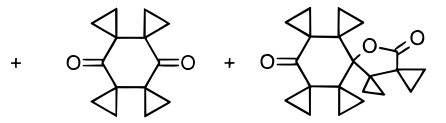
calculations performed at the RHF/6-31G* level of theory also confirm this order.[262]

Applying the method of Schöllkopf et al.[267] to the chloroethyl ester **197** allows one to prepare spiropentanol **373**, albeit in low yield (Scheme 84).[172a] Contrary to this, the attempted deprotection of acetals **199** predominantly gave products with ring opening. Thus, treatment of **199e** with *n*-butyllithium gave only 10% of 7-*n*-butyldispiroheptan-7-ol **384** and the three products **383**, **385**, and **386** which had formed with opening of the central cyclopropane ring (Scheme 84).[172b] All of these products apparently arose from the intermediately formed dispiro[2.0.2.1]-

Scheme 84



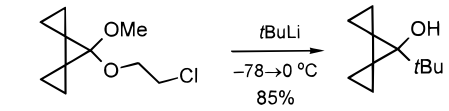


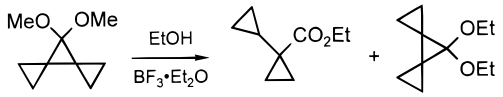


T [°C]	Yield of **383** (%)	**384** (%)	**385** (%)	**386** (%)
−78	15	10	8	0
−110	7	10	15	26

heptan-7-one. Only in the product **384** and a few other reactions was the triangulane skeleton conserved. For example, treatment of **199d** with *tert*-butyllithium afforded in high yield 7-*tert*-butyldispiro-[2.0.2.1]heptan-7-ol (**387**), and attempted transacetalization of the dimethyl acetal **199a** succeeded partially with retention of the skeleton when it was boiled in excess ethanol in the presence of boron trifluoride etherate (Scheme 85).[172b]

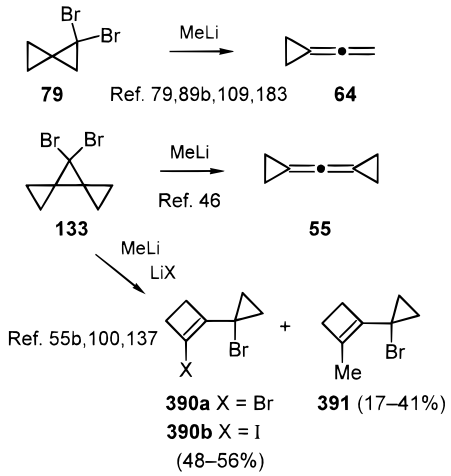
Scheme 85





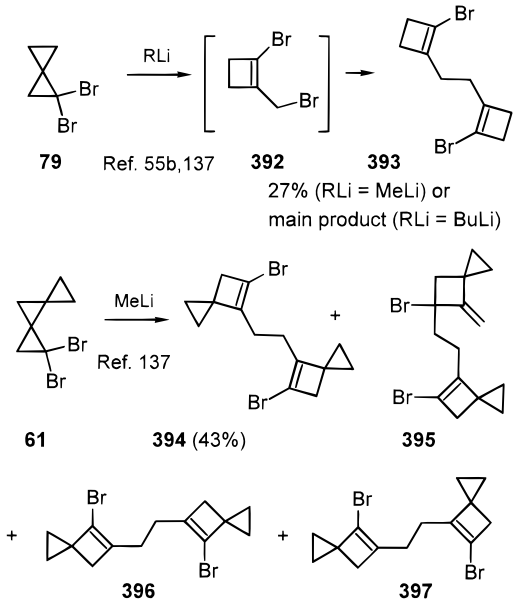
Some special attention should be paid to the chemical behavior of *gem*-dibromotriangulanes. Ring opening of the carbenes generated by treatment of *gem*-dibromocyclopropanes with alkyllithium reagents (RLi) is a widely used preparative route to allenes[113] and has been successfully applied in the preparation of BTs (Scheme 13). The accepted mechanism includes lithium-bromide exchange to yield a bromolithiocarbenoid which α-eliminates LiBr above −90 °C, and the resulting cyclopropylidene rapidly undergoes an electrocyclic ring opening to the corresponding allene. Known side reactions are electrophilic substitution on the bromolithiocarbenoid[268] and inter- or intramolecular insertion or cycloaddition of the cyclopropylidene moiety.[66,67,118] This reaction has been shown to give good results in producing ethenylidenecyclopropane (**64**) (35% yield) from **79**[89b,109,183] and bis(cyclopropylidene)methane (**55**) from **133**[46,234] (Scheme 86). The originally reported yield of 85% in

Scheme 86

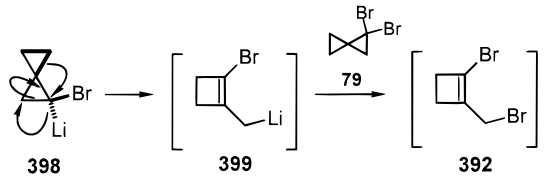


the latter transformation[46] could not be reproduced, at least not when carried out at −40 to −55 °C with methyllithium containing lithium bromide or iodide. The allene **55** was isolated in only 20−21% yield[55b,137] along with the cyclobutene derivatives **390a**,**b** and **391** (the formation of **391** was reported only in refs 55b and 100). When the reaction was performed at 0 °C, **55** (60%), **390a** (10%), and **390b** (11%) were isolated.[137] The treatment of dibromospiropentane (**79**) with alkyllithiums at −50 °C resulted in the formation of **393** with presumed intermediacy of 1-bromo-2-(bromomethyl)cyclobutene (**392**). Similarly, when 1,1-dibromodispiro[2.0.2.1]heptane (**61**) was treated with methyllithium, a mixture of at least four products, with the 1,2-bis(bromospiro[2.3]hexenyl)ethane **394** predominating, was obtained (Scheme 87). No satisfactory account of these unusual reactions has been proposed. The idea that the starting dibromide **133** rearranges under the action of LiBr[55b] has not been supported experimentally.[137] On the other hand, such a reorganization can hardly occur at the intermediate cyclopropylidene. More likely the rearrangement would proceed at the bromolithiocarbenoid species **398** to form a (bromocyclobutenyl)-

Scheme 87

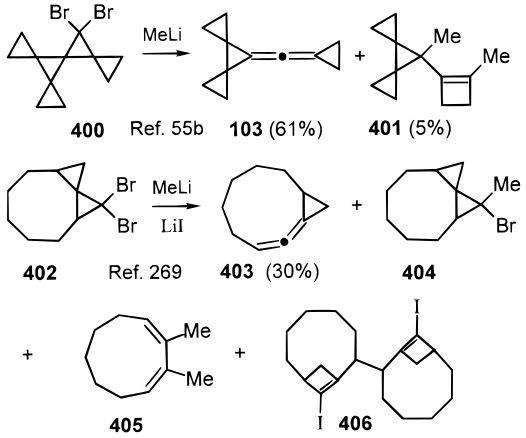


Scheme 88

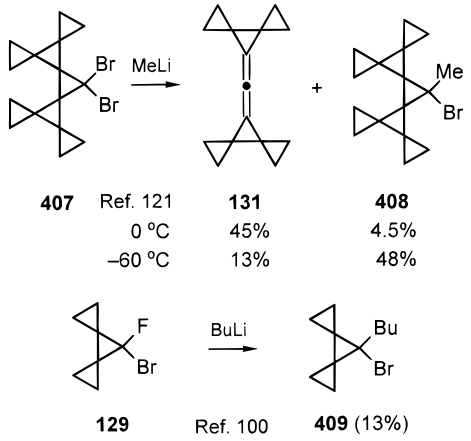


methyllithium intermediate of type **399** (Scheme 88, cf. also ref 79). For the higher dibromo-BTs and dibromo-CATs, e.g., **400** and **402**, this type of rearrangement has been observed only to a smaller extent (Scheme 89[55b,269]) or not at all, as for **407** and 7-bromo-7-fluoro[3]triangulane (**129**) (Scheme 90).[55b,100,121]

Scheme 89

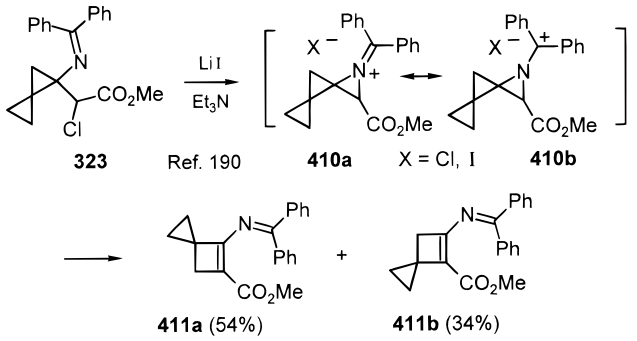


Scheme 90

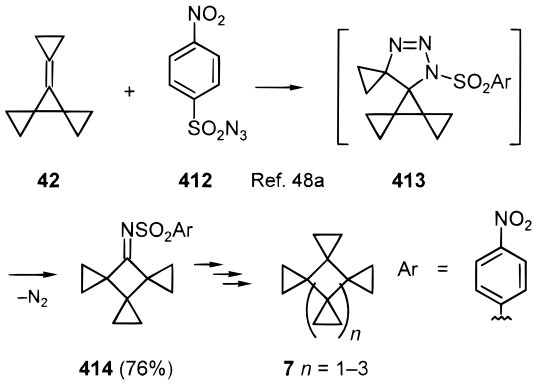


An interesting rearrangement of the diphenylmethyleneimine Michael adduct **323** of the chloroester **223a** has been reported (Scheme 91).[190] The key step in this rearrangement is believed to be the lithium-iodide-induced reorganization of the azatriangulane intermediate **410**, which is analogous to the frequently reported rearrangement of oxaspiropentanes to cyclobutanones (see below). The 1,3-dipolar cycloaddition of *p*-nitrobenzenesulfonyl azide (**412**) onto dispirocyclopropanated bicyclopropylidene **42** has been used as the key step in a general procedure with repetitive steps for the preparation of [*n*]rotanes **7** (Scheme 92).[48a] Upon heating the cycloadducts **328** and **330** of nitrones and nitrile oxides, respectively,

Scheme 91

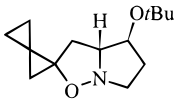
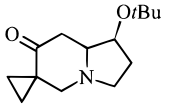
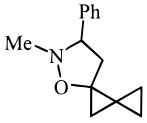
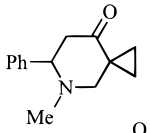
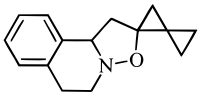
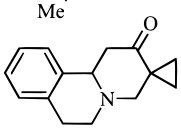
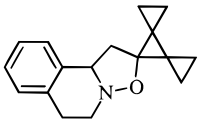
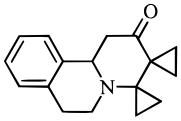
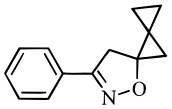
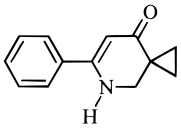
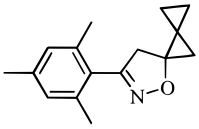
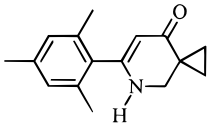
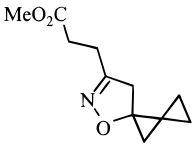
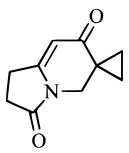
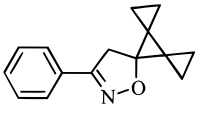
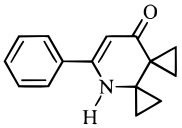
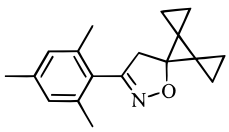
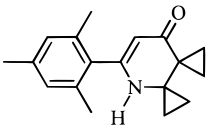


Scheme 92

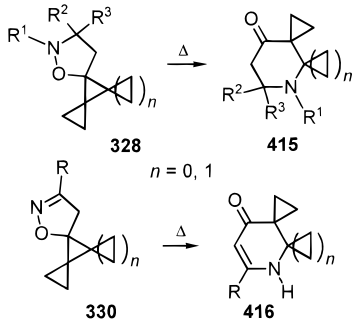


onto methylenetriangulanes (for their preparation see Scheme 74), dissolved in a high-boiling aromatic solvent at 125−163 °C, they underwent rearrangements with opening of one of the two cyclopropane rings to give 5-spirocyclopropane-tetrahydropyrid-4-ones **415** and 5-spirocyclopropane-dihydropyrid-4-ones **416** in moderate to very good yields (Scheme

Table 9. Thermal Rearrangements of the Cycloadducts 328 and 330 of Nitrones and Nitrile Oxides onto Methylene[*n*]triangulanes

Starting Material		Product		Yield (%)
	**328a**		**415a**	40
	**328b**		**415b**	40
	**328c**		**415c**	32
	**328d**		**415d**	34
	**330a**		**416a**	70
	**330b**		**416b**	92
	**330c**		**416c**	66
	**330d**		**416d**	53
	**330e**		**416e**	73

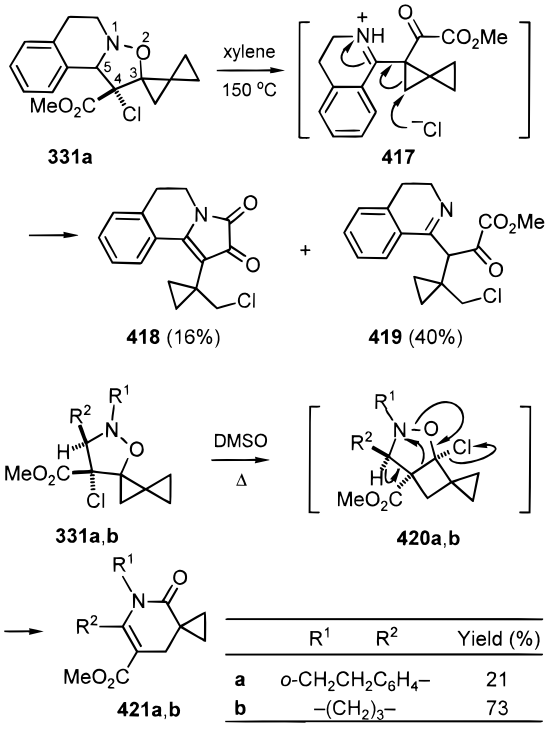
Scheme 93



93 and Table 9).[260] Compounds **415** may also be prepared in a one-pot procedure in essentially the same yields by heating a mixture of the alkene and the respective nitrone at a temperature at which the thermal rearrangement of the primary adducts occurs. Spirocyclopropane ring opening occurs with high regio- and chemoselectivity. Mechanistically, this rearrangement is believed to start with a homolytic N−O bond cleavage followed by the oxy-analogue of the well-known rapid ($k \approx 10^8$ s^{-1}) cyclopropylmethyl radical to homoallyl radical ring opening[270] and intramolecular recombination of radicals. In contrast to 1,3-dipolar cycloadducts onto methylenetriangulane derivatives without functional groups, the thermal behavior of compounds of the type **331** with polar substituents strongly depends on the polarity of the solvent as well as the nature of substituents R^1−R^3 and their rearrangements proceed in a completely different way. Thus, only reversible isomerization at the C^4 center of the isoxazolidine ring was observed for isoxazoloisoquinoline **331a** upon heating in toluene (110 °C, 3 h). However, at 150 °C in xylene, compound **331a** underwent a reorganization into the dehydroisoquinoline **419** and its cyclic amide **418**,[261] presumably via intermolecular nucleophilic attack with ring opening of the intermediate **417** with its doubly activated cyclopropane as a key step (Scheme 94).[4] When heated in DMSO, the isoxazolidines **331a**,**b** rearranged in a completely different way. Whereas the isomerization of **331a** proceeded only at 150 °C with considerable decomposition of the starting material and consequently gave a low yield of benzoquinolizinone **421a** (21%), a fast and clean reorganization of the isoxazolidine **331b** occurred at 100 °C in DMSO to give the hexahydroindolizin-5-one **421b** in 73% yield (Scheme 94).[261] The mechanism of this reaction is still not clear, but the key step probably occurs in the cyclobutane derivative of type **420** which is formed from **331** via a cationic cyclopropylmethyl to cyclobutyl rearrangement.[271] From the spiropentyl derivative **331b**, such a cyclobutane derivative **420b** could be prepared in 94% yield by stirring it in dichloromethane solution in the presence of Al_2O_3 at 20 °C. Upon heating in DMSO at 100 °C for 2 h, **420b** quantitatively isomerized into **421b**.[261b]

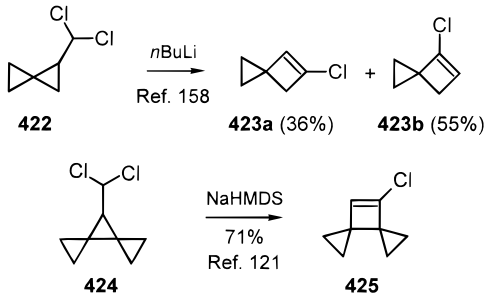
When a carbenoid center is generated in the α-position of a spiropentyl unit as in **422** or of a [3]-UT as in **424**, rapid ring enlargement to a cyclobutene fragment occurs, as is well-known for cyclopropylcarbenes. These intermediate carbenoids could

Scheme 94



	R^1	R^2	Yield (%)
a	*o*-$CH_2CH_2C_6H_4$–		21
b	–$(CH_2)_3$–		73

Scheme 95

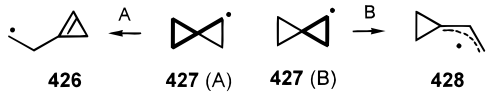


not be trapped with alkenes (Scheme 95).[121,158] The carbene generated by base-induced degradation of spiropentylcarbaldehyde tosylhydrazone behaves analogously.[158] However, successful additions of chlorocyclopropylcarbene generated from (dichloromethyl)cyclopropane by treatment with potassium *tert*-butoxide[272] or from 3-chloro-3-cyclopropyldiazirine by photolysis[273] to alkenes have been reported.

Oxidation of spiropentane (**11**) with photochemically generated singlet oxygen was accompanied by ring opening of one or two cyclopropane rings to give a complex mixture of products.[274] The photochemical decomposition of spiropentane (**11**) has been investigated at 25 °C[275] as well as at 386 °C[195b] and found to result in the formation of a mixture of simple unsaturated hydrocarbons (ethene, ethyne, propene, propyne, allene, etc.). In contrast, reaction of **11** with methylene generated by photochemical decomposition of diazomethane proceeds with retention of the spiropentane moiety to give methylspiropentane.[276]

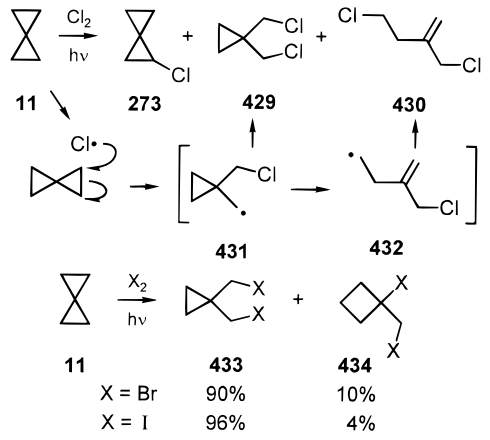
The C−H bond dissociation in **11** with an enthalpy of activation of 99 kcal/mol[277] affords the spiropentyl radical **427**. This radical is interesting in that it is simultaneously a cyclopropyl radical (B) and a cyclopropylmethyl radical (A) (Scheme 96). The rigid

Scheme 96



perpendicular orientation of the SOMO and the C(1)-C(3) bond in **427** prevents overlap, and this impedes the opening of type B to give a cyclopropylmethyl radical **428**. Ring opening of type A to give the highly strained cyclopropenylethyl radical **426** is also retarded due to the very poor overlap of the SOMO with the C(3)-C(4) bond, and thus, the corresponding rate constant was found to be 10^3 s^{-1} at 270 K[278] while for the cyclopropylmethyl radical it is $k = 4.6 \times 10^7$ s^{-1}.[270] Therefore, the spiropentane skeleton is frequently retained in radical substitution reactions of **11**. For instance, the photochlorination of **11** in the vapor phase (Scheme 97) gave spiropentyl chloride

Scheme 97



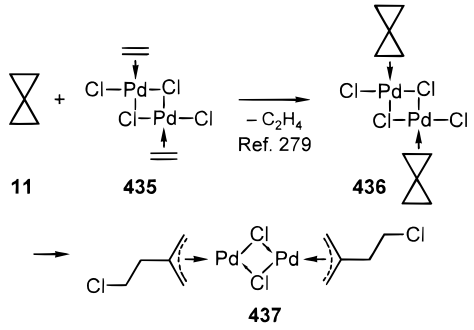
273 as the main product (yield 35−43%)[166b] (see also Scheme 72). No other products derived from spiropentyl radical **427** were detected. But a direct attack of a chlorine atom with simultaneous opening of a distal C−C bond (a so-called S_H2 reaction) does play an important role leading to the formation of **429** and **430**.[166b,278] In solution, this S_H2 attack becomes the predominant pathway[278] and the products **429** and **430** are formed in 54−96% yield. Bromination and iodination of **11** proceeds at least partially via an ionic mechanism, as indicated by the composition of the product mixtures (Scheme 97).[278]

Spiropentane (**11**) also undergoes a reaction with the ethenepalladium dichloride complex **435** in which both rings are opened to give the 2-(2-chloroethyl)-π-allylpalladium chloride complex **437** (Scheme 98),[279] and it polymerizes under the action of Ziegler-type catalysts or Lewis acids, also with opening of both three-membered rings.[280]

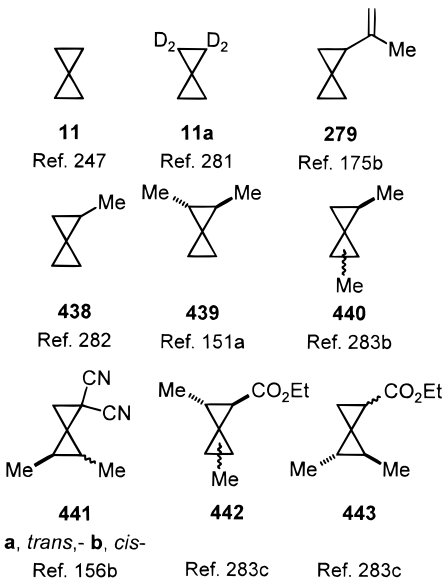
The thermal decompositions of spiropentane (**11**) and its derivatives **279** and **438**−**443** (Scheme 99) have received a good deal of attention (for a review, see ref 181).

The thermal isomerization of **11** was found to occur as a first-order reaction in the temperature range 360−400 °C with $k = 4.13 \times 10^{-4}$ s^{-1} (at 380 °C) and an activation energy $E_a = 57.57$ kcal/mol (preexponential factor $\log A = 15.56$).[247] The activation energy for the rearrangement of **11** is significantly smaller

Scheme 98

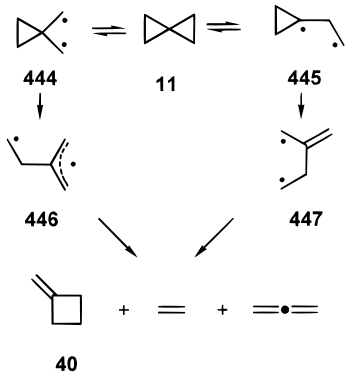


Scheme 99

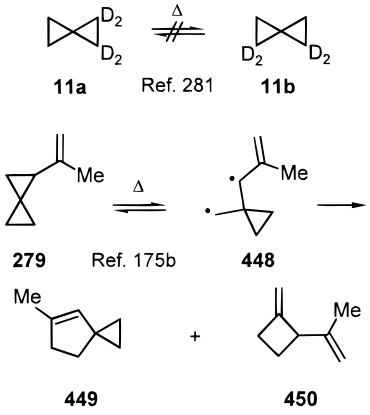


than that for the rearrangement of cyclopropane to propene (65.2 kcal/mol[181]), and this fact has been attributed to the additional strain energy in **11**.[1,224] On the other hand, the activation energy for the rearrangement of **11** is about 10 kcal/mol higher than the bond dissociation energy of its distal C−C bond.[181] This indicates that the initial bond cleavage is not the rate-determining step. The reaction leads mainly to methylenecyclobutane (**40**) along with small quantities of ethylene and allene (the conversion of **11** at 355 °C was 80% in 27 h[139]). It is believed that the initial step is a C(1)-C(2) bond rupture to form the diradical **444** which opens the second ring to give **446**, rather than the rupture of the C(1)-C(3) bond to produce **445** and then **446** or **447** (Scheme 100).[281] A computational study of this rearrangement at the 3-21G and 6-31G* levels of theory also indicated an initial distal bond cleavage.[284] The contamination of **40** with allene and ethylene appeared to be somewhat larger than could be expected as arising through fragmentation of chemically activated methylenecyclobutane (**40**),[247] but a detailed examination of the pressure dependence of the product composition[282] could not support an undoubtedly direct formation of allene from **11** (see also ref 181). Similar results have been obtained for methylspiropentane (**438**).[283] No degenerate rearrangement was found for **11**, as 1,1,2,2-tetradeuteriospiropentane (**11a**) did not equilibrate with 1,1,4,4-tetradeuteriospiropentane (**11b**) (Scheme 101).[281] A concerted rearrangement of **11** to

Scheme 100



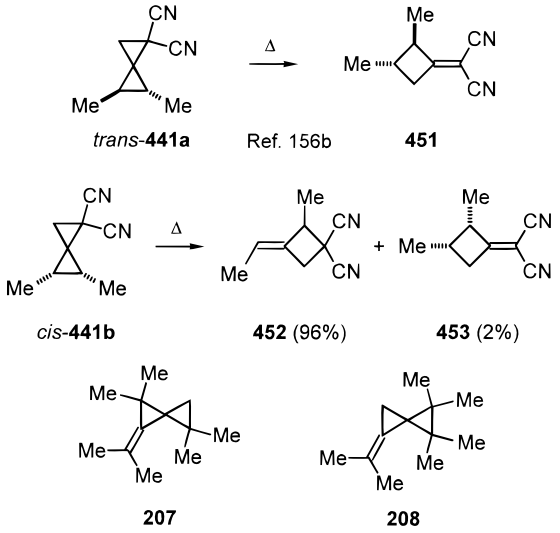
Scheme 101



40 has also been proposed.[282] The real pathway for the structural isomerization of substituted spiropentanes definitely varies depending on the nature of substituents on the spiropentane moiety (for a detailed discussion, see ref 181). For example, the isopropenyl derivative **279** was found to thermally undergo unimolecular rearrangement to 5-methylspiro[2.4]hept-4-ene (**449**) and 2-isopropenyl-1-methylenecyclobutane (**450**), both arising from initial reversible C(1)-C(2) bond fission. Diene **450** can result from a 1,2-alkyl shift with ring enlargement as known for the cyclopropylcarbinyl radical rearrangement.[175b]

The thermal rearrangement of 1,1-dicyano-4,5-dimethylspiropentane **441** yields different products depending on the configuration of the starting material: the *trans*-isomer, *trans*-**441a**, yields only **451** after initial C(1)-C(2) bond cleavage and with retention of the configuration of the migrating group (Scheme 102).[156b] For the *cis*-isomer, *cis*-**441b**, the first step must have been a C(1)-C(3) bond fission, as **452** was formed as the main product. While 1,1-difluorospiropentane upon heating at 340 °C gave a mixture of (difluoromethylene)cyclobutane and 2,2-difluoromethylenecyclobutane,[167b] the pyrolysis of 1,1,2,2-tetrafluorospiropentane was more complicated, as reversible isomerization to 1,1,4,4-tetrafluorospiropentane[167c] and difluorocarbene extrusion[167c,169a] were also observed. Methylenespiropentane (**34**) rearranges to give a 7:1 mixture of 1,2- and 1,3-dimethylenecyclobutanes (8% conversion after 10 h at 300 °C)[44a,179c] or 3-methylene-1,4-pentadiene at 510 °C.[44a] Similar results have been obtained for the hexamethyl-substituted methylenespiropentanes **207**

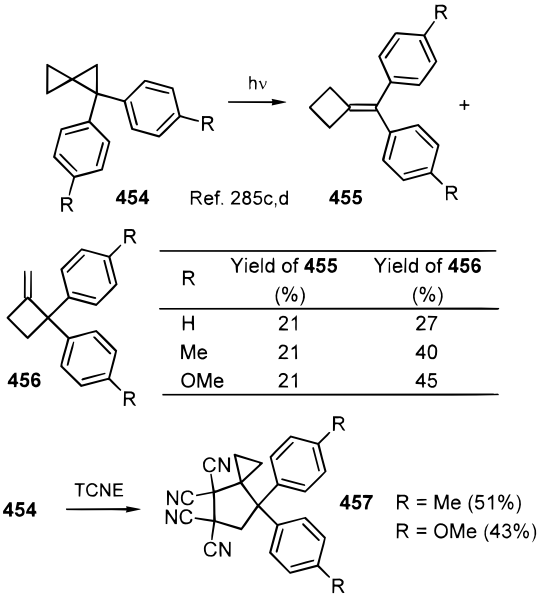
Scheme 102



and **208**.[44b,178] The detailed mechanism of these transformations has been discussed.[181]

Cation radicals generated by photolysis of 1,1-diarylspiropentanes **454** in the presence of anthraquinone completely rearrange to the thermodynamically more stable (diarylmethylene)cyclobutanes **455** and the less stable 2,2-diaryl-1-methylenecyclobutanes **456** in a concerted and stepwise manner, respectively.[285a,b] Acetone-sensitized photolysis led to essentially the same products (Scheme 103) but

Scheme 103

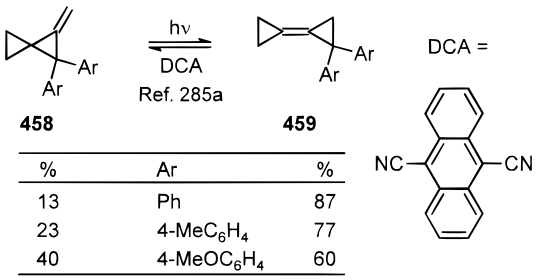


R	Yield of **455** (%)	Yield of **456** (%)
H	21	27
Me	21	40
OMe	21	45

via diradical intermediates similar to those shown in Scheme 100. Upon photolysis of electron donor−acceptor complexes of **454** with tetracyanoethylene (TCNE), the adducts of TCNE onto **454** were also formed,[285c,d] and the thermal reactions of **454** with TCNE result in the formation of **457** as single products (Scheme 103).[285d]

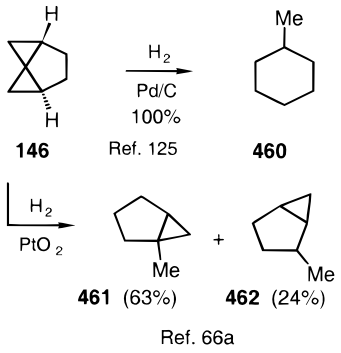
A remarkable reorganization was observed for 2,2-diarylmethylenespiropentanes **458** after photoinitiated electron transfer from 9,10-dicyanoanthracene (DCA) leading to the reversible formation of 2,2-

Scheme 104



%	Ar	%
13	Ph	87
23	4-MeC_6H_4	77
40	4-$MeOC_6H_4$	60

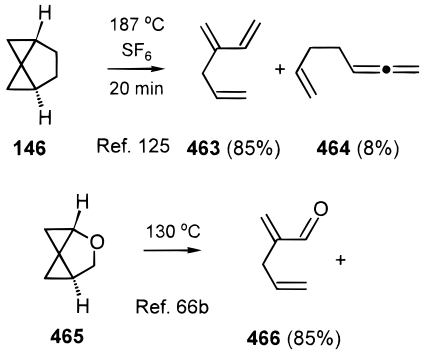
Scheme 105



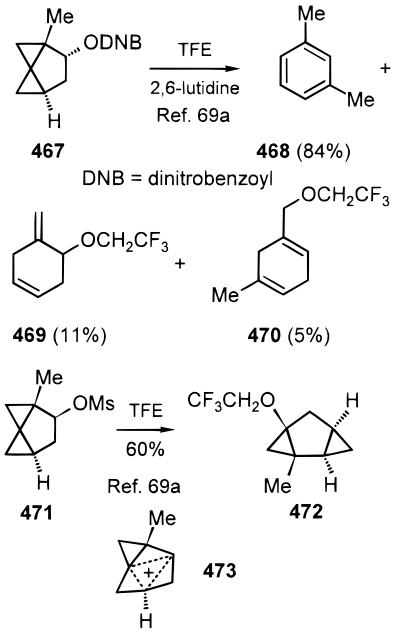
diarylbicyclopropylidenes **459**, the proportion of which decreases with an increase of the electron-donating ability of the aryl substituents (Scheme 104).[285a] The corresponding thermal interconversion of methylenespiropentane (**34**) and bicyclopropylidene (**5**) is also reversible, yet the equilibrium is much more on the side of **34** (see Schemes 41−43). The experimentally determined standard heats of formation ΔH(g) for methylenespiropentane (**34**) and bicyclopropylidene (**5**) are 75.5 and 77.5 kcal/mol, respectively.[23]

The spiropentane moiety in CATs containing the tricyclo[4.1.0.0^{1,3}]heptane skeleton is even more inclined to ring opening. The hydrogenation of **146** proceeds, depending on the catalyst, with opening of one or both cyclopropane rings to give two isomeric methylbicyclo[3.1.0]hexanes **461** and **462**[66a] or methylcyclohexane (**460**)[125] (Scheme 105); the heat of hydrogenation of the latter reaction has been measured to derive the standard heat of formation ΔH(g) of **146**. Compared to that of **11**, the thermal stabilities of **146**[125] and its oxa analogue **465**[66b] are considerably lower: complete destruction of tricyclo[4.1.0.0^{1,3}]heptane moieties was observed upon heating of **146** and **465** to 187 and 130 °C, respectively (Scheme 106, cf. also Scheme 27). The solvolysis of *trans*-dinitrobenzoate **467** in buffered anhydrous 2,2,2-trifluoroethanol (TFE) yielded *m*-xylene (**468**) and the trifluoroethyl esters **469** and **470**. In contrast, *cis*-mesylate **471** under these conditions affords the tricyclo[4.1.0.0^{2,4}]heptane derivative **472**[69a] which has been interpreted to indicate the intermediate formation of the trishomocyclopropyl cation **473**[286] (Scheme 107).

Scheme 106

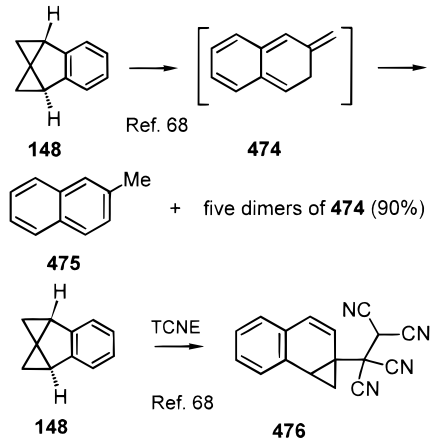


Scheme 107

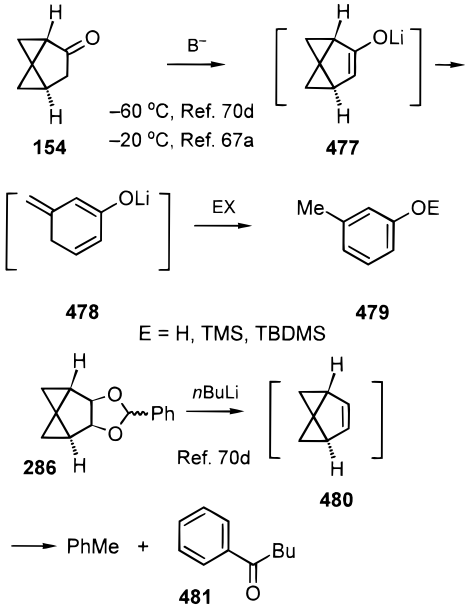


Cycloannelated[*n*]triangulanes (CATs) with a double bond in a tricyclo[4.1.0.0^{1,3}]heptane moiety are particularly unstable. Thus, the benzoannelated tricycloheptane **148** underwent a retro-Diels−Alder reaction even at 30 °C and reacts with TCNE at room temperature (Scheme 108).[68] The enolate **477** generated from the ketone **154** under the action of LDA[67a] or LiHMDS[70d] undergoes ring opening even more easily (Scheme 109). The intermediate **478** was observed spectroscopically.[70d] The formation of toluene and valerophenone **481** upon reaction of the acetal **286** with butyllithium was also explained as resulting from rearrangement in the intermediate tricyclo[4.1.0.0^{1,3}]hept-2-ene (**480**) (Scheme 109).[70d]

Scheme 108

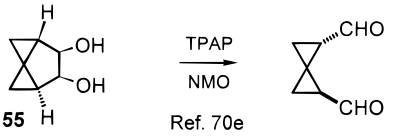


Scheme 109



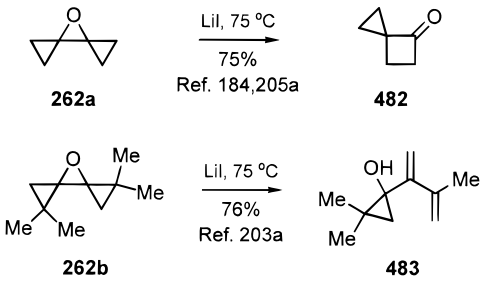
The vicinal diol **155**, however, can be oxidatively cleaved with complete retention of a spiropentane moiety (Scheme 110).[70e]

Scheme 110



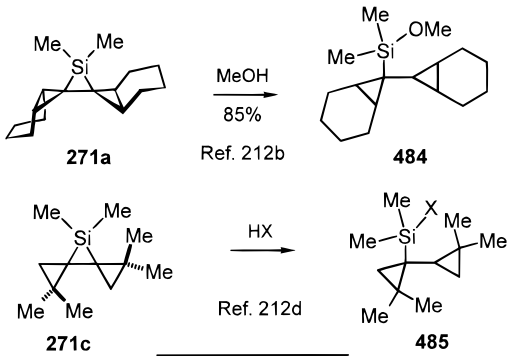
The lithium iodide and other Lewis-acid-catalyzed reorganization of oxa[2]triangulanes (oxaspiropentanes) to cyclobutanones has found widespread application in organic synthesis.[11a,174,203−205a] The 7-oxa-[3]triangulane (7-oxadispiro[2.0.2.1]heptane, **262a**) is remarkably more stable toward lithium iodide than oxaspiropentanes; its isomerization could be effected only at 75 °C.[184,205a] Under the same conditions, the sterically congested 1,1,5,5-tetramethyloxa[3]triangulane **262b** does not give a cyclobutanone but instead rearranges to 2,2-dimethyl-1-(3-isoprenyl)-cyclopropanol (**483**) (Scheme 111).[203a] The labile C−Si

Scheme 111



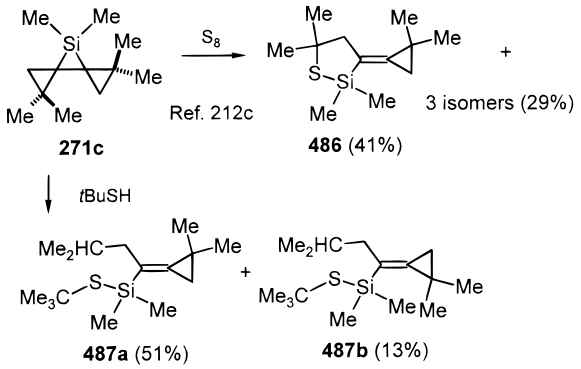
bond in 7-sila[3]triangulanes **271** can readily be attacked by different species. The reactions which presumably proceed via ionic intermediates yield silyl-substituted bicyclopropyl derivatives of the type **484** and **485** with retention of both three-membered carbocyclic rings (Scheme 112).[212a,b,d] In transformations via radical intermediates, however, a cyclopropylcarbinyl to butenyl rearrangement of one three-membered carbocyclic ring occurred to eventually give the methylenecyclopropane derivatives **486** or **487**, depending on the reagent (Scheme 113).[212c]

Scheme 112



X	Yield (%)
$OCMe_3$	80
OPh	83
NEt_2	57
$NiPr_2$	62
OAc	88
O_2CCMe_3	87

Scheme 113



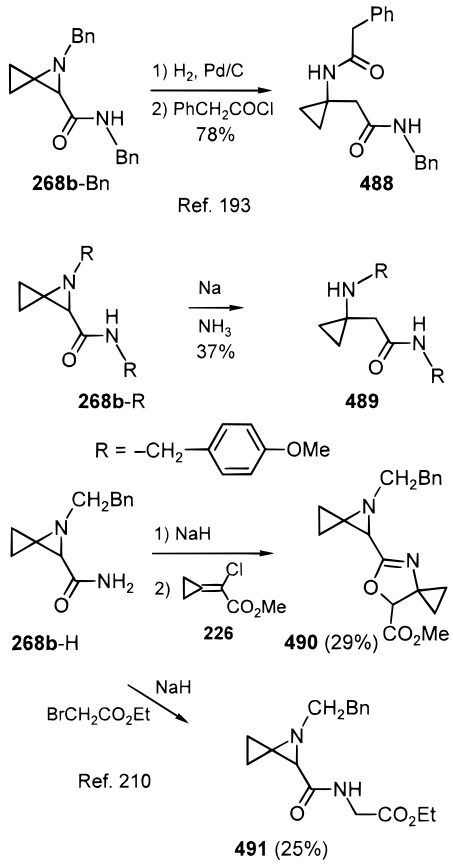
Aza[2]triangulanes (azaspiropentanes) **268b** underwent chemical transformations with as well as without opening of their aziridine moiety, but most products were isolated only in moderate to low yield (Scheme 114).[193,210]

VI. Triangulanes with Properties of Potential Practical Applicability

As triangulanes combine high strain energies with relatively high thermal stabilities, one obviously possible use has been conceived quite some time ago, e.g., spiropentane (**11**) had been proposed as a high-energy aviation fuel.[287] But no essential progress has been achieved in this context during the past decades.

A growing number of cyclopropyl group containing compounds, naturally occurring or prepared in the laboratory, are known to exhibit influences on biological systems. This ranges from antifungal and insecticidal activities to neurochemical and enzyme inhibitory activities.[288] To the best of our knowledge, no spiropentane derivatives or higher oligospirocyclopropane aggregates have been isolated from

Scheme 114



natural products. Nevertheless, some of the synthetically accessed substituted spiropentanes have demonstrated biological activities. Thus, compound **492** showed an analgetic activity,[289] compounds **493** and **497** were found to be effective pesticides against *Phaedon cochleariae* and *Tetranychus urticae*,[290] spiropentane derivative **494** appeared to be a powerful insecticide against *Anthonomus grandis*,[291] and the esters **495**[292] and **496**[293] as well as their analogue **498**[294] possess insecticidal and acaricidal activities (Chart 13). Yet none of these compounds has been put into practical use.

Some spiropentane derivatives are known to be potent enzyme inhibitors controlling key biological processes. For example, spiropentylacetic acid (**499**) (Chart 14)[106] irreversibly inactivates pig kidney medium-chain acyl-CoA dehydrogenase (MCAD) and *Megasphaera elsdenii* short-chain acyl-CoA dehydrogenase (SCAD).[154] These actions proceed with cleavage of one of the three-membered rings by way of a cyclopropylcarbinyl to butenyl radical rearrangement,[270] as demonstrated in a detailed mechanistic investigation.[154] The spiropentylcarboxamide (*Z*)-**500** inhibits mammalian β-lactamase renal dipeptidase (dehydropeptidase I) but only with a moderate activity.[295]

Most of the known naturally occurring amino acids containing a cyclopropyl group and the nonnatural cyclopropyl analogues of natural amino acids exhibit interesting biological activities.[288,296] Two particularly interesting specimens in this group of natural products are 3-(2′-methylenecyclopropyl)alanine (**501**), so-called hypoglycine A,[297] occurring in unripe ackee

Chart 13

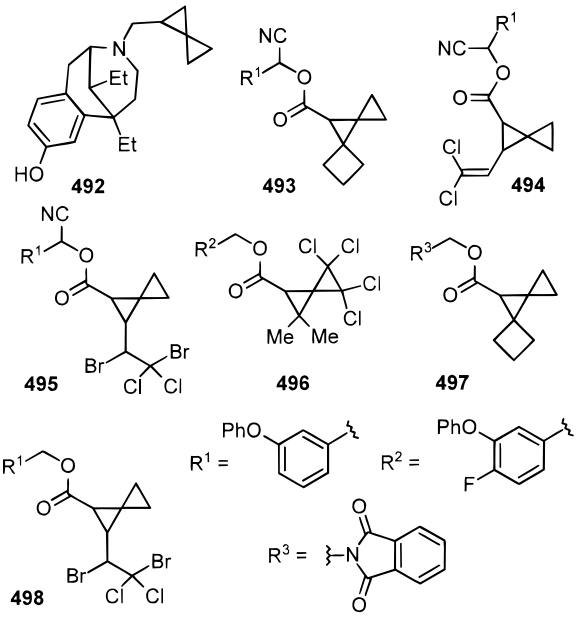
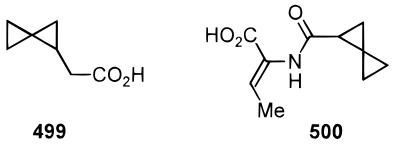
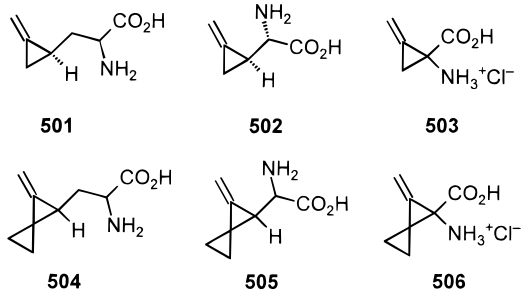


Chart 14



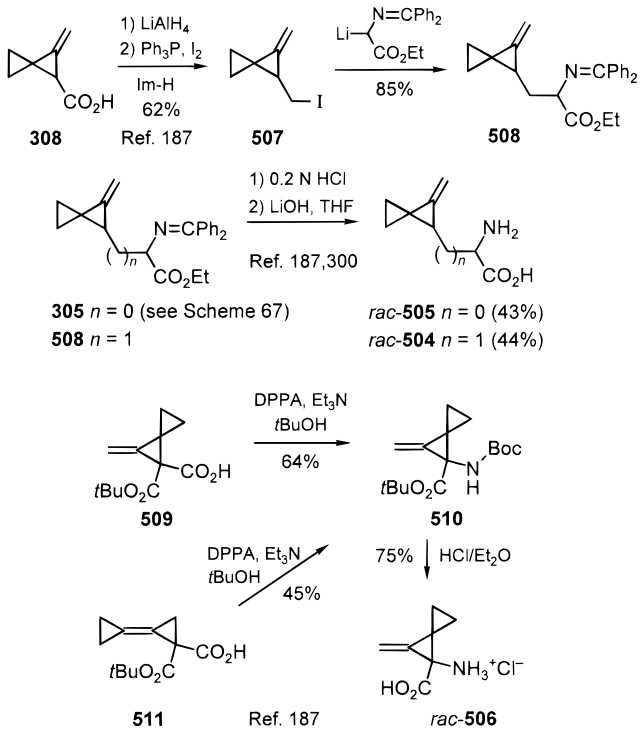
plums, and 2-(2′-methylenecyclopropyl)glycine (**502**), which has been isolated from lychee fruits,[298] because both show a strong hypoglycemic effect. The irreversible inactivation of ACC deaminase caused by the action of 1-amino-2-methylenecyclopropane-1-carboxylate (methylene-ACC) (**503**) has also recently been reported.[299] Most likely the enzyme inhibitory effects of **501**−**503** are associated with the presence of the reactive methylenecyclopropane unit in these molecules (Chart 15).[76] In close analogy, the highly

Chart 15



strained methylenespiropentyl units, functionalized as in the amino acids **504**−**506**, might show biological effects as well. Therefore, racemic methylenespiropentyl-substituted alanine (*rac*-**504**) and glycine (*rac*-**505**) were synthesized applying coupling reactions with the two glycine equivalents of O'Donnell as key steps (Schemes 67 and 115).[187,256,300] The amino acid *rac*-**506** was obtained via Curtius degradation of the monoesters **509** and **511** (in the last case the reaction was accompanied by a bicyclopropylidene to methylenecyclopropane rearrangement, cf. section 3.F)

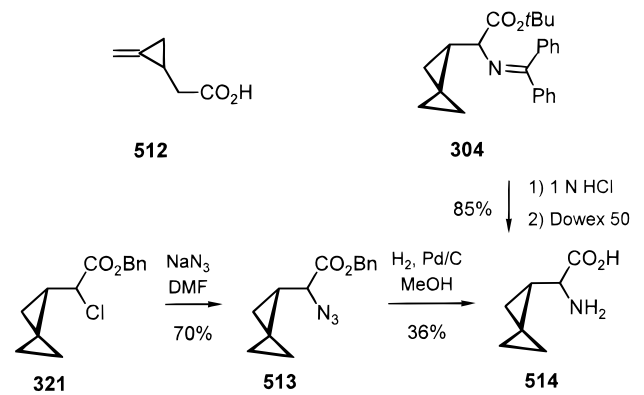
Scheme 115



followed by deprotection (Scheme 115). The biological testing of the amino acids **504**−**506** is still in progress.

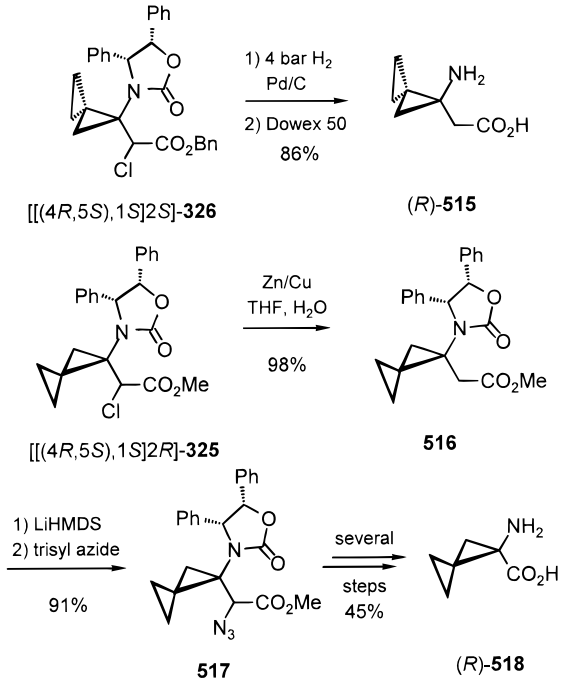
Since three-membered rings have a number of chemical properties in common with a C=C double bond,[3] it appeared to be interesting to prepare the spiropentyl analogues of **501** and **502** and to test their potential physiological activities. At least such an anticipated similarity has been found between (spiropentyl)acetic acid (**499**)[106,154] and (methylenecyclopropyl)acetic acid (**512**), which is believed to play a crucial role in the biological action of hypoglycine A (**501**).[297] Racemic spiropentylglycine (**514**) has been synthesized by nucleophilic substitution of the chlorine in the Michael adduct **321** (for its preparation see Scheme 73) with an azide group followed by hydrogenolytic deprotection of the resulting azide **513**. An alternative approach to **514** was achieved by simple deprotection of the precursor **304**, the preparation of which was discussed above (see Scheme 67) (Scheme 116).[165,253a] Enantiomerically pure[301] (1′-aminospiropentyl)acetic acid [(*R*)-**515**] and 1-aminospiropentanecarboxylic acid [(*R*)-**518**] were obtained

Scheme 116

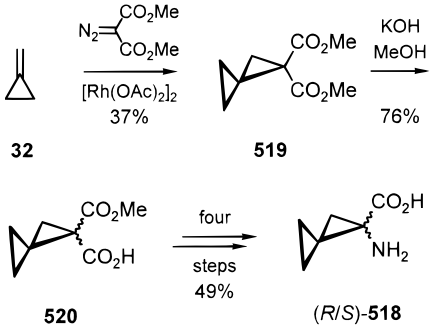


from the enantiomerically pure Michael adducts **325** and **326** of (4*R*,5*S*)-4,5-diphenyloxazolidine-2-one to methyl 2-chloro-2-spiropentylideneacetates **223a**-Me and **223a**-Bn (Scheme 117; for the preparation of **325** and **326** see Scheme 73 and Table 6).[165,253a] Racemic 1-aminospiropentanecarboxylic acid (*R*/*S*-**518**) was prepared by rhodium-catalyzed addition of dimethyl diazomalonate to methylenecyclopropane (**32**) and subsequent Curtius degradation of the halfester **520** (overall yield 14%) (Scheme 118).[165,253a]

Scheme 117

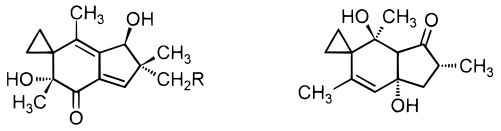


Scheme 118



Several natural products containing a cyclopropane ring exhibit their biological activity through a process of ring opening resulting in an alkylation of a nucleophilic group in a substrate, e.g., an enzyme. Among these are compounds such as the illudins **521a**,**b**[302−304] and ptaquiloside **522**,[305] three sesquiterpenes isolated from mushrooms and bracken fern, respectively (Chart 16). The extreme general cytotoxicity of these compounds has hampered their development as an anticancer drug for a long time. Heterocycles of type **415** and **416** prepared by thermal rearrangement of substituted triangulanes **328** and **330** (Scheme 93 and Table 9), which essentially contain the aza-analogous skeletons of **521** and **522**,

Chart 16



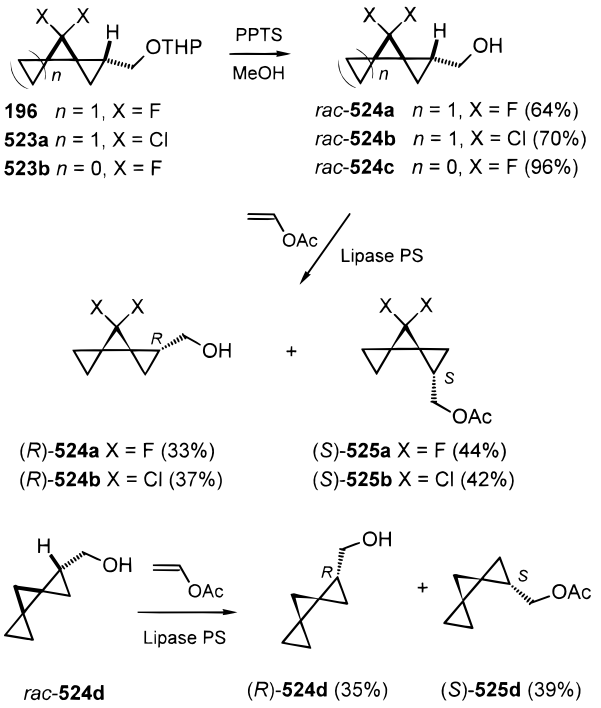
521 a Illudin S (R = OH)
b Illudin M (R = H)

522 Ptaquiloside

have been tested with respect to their activity in cleaving a DNA plasmid. Albeit the activities shown by these compounds were only moderate, it is sufficient to entitle these easily accessible compounds a promising class of aza-analogues of the natural compounds such as illudins and ptaquiloside possessing the same essential spirocyclopropane functionality.[260c]

The rigid [2]- and [3]triangulane units might possess appropriate features to be incorporated into liquid crystaline materials. Several derivatives of type **526** and **528** have recently been prepared in racemic as well as in enantiomerically pure form, the latter after enzymatic resolution of alcohols **524** (Scheme 119). Transformations to the final product

Scheme 119



196 *n* = 1, X = F
523a *n* = 1, X = Cl
523b *n* = 0, X = F

rac-**524a** *n* = 1, X = F (64%)
rac-**524b** *n* = 1, X = Cl (70%)
rac-**524c** *n* = 0, X = F (96%)

(*R*)-**524a** X = F (33%)
(*R*)-**524b** X = Cl (37%)

(*S*)-**525a** X = F (44%)
(*S*)-**525b** X = Cl (42%)

rac-**524d**

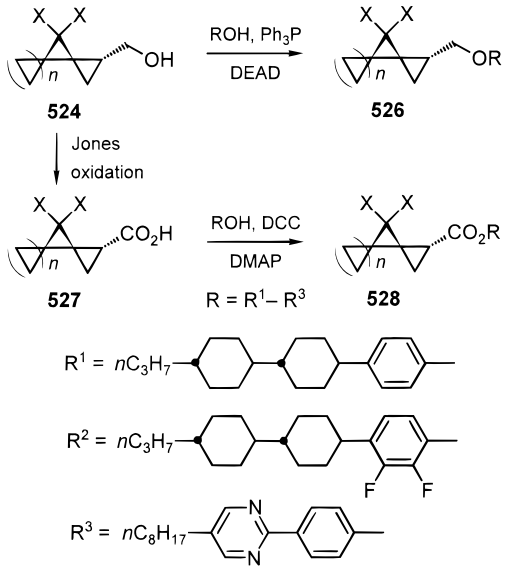
(*R*)-**524d** (35%)

(*S*)-**525d** (39%)

were carried out by a set of standard operations (Scheme 120 and Table 10).[306] The isomeric 6,6-difluoro[3]triangulane derivatives were obtained as well. Among the compounds prepared (Table 10), the esters *rac*-**528a** as well as (*R*)/(*S*)-**528c** exhibited the best liquid crystalline properties, as the 7,7-difluoro-[3]triangulane moiety induces a larger positive dielectric anisotropy $\Delta\epsilon$ than the ordinary nonpolar liquid crystals (for example, 4,4′-dialkyldicyclohexyls). Enantiomerically pure compounds **528c** also demonstrated ferroelectric properties and very high helical twisting powers (HTP).[306]

At last, [3]triangulanes of type **529** and **530** (Chart 17) possessing spatially close surfaces have recently

Scheme 120



524

526

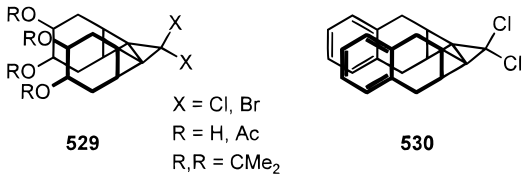
527

528

Table 10. Preparation of Liquid Crystalline Triangulane Derivatives

starting material	*n*	X	R	product	yield (%)
rac-**524a**	1	F		*rac*-**527a**	72
(*R*)-**524a**	1	F		(*R*)-**527a**	79
(*S*)-**524a**	1	F		(*S*)-**527a**	71
rac-**524b**	1	Cl		*rac*-**527b**	69
(*R*)-**524b**	1	Cl		(*R*)-**527b**	80
(*S*)-**524b**	1	Cl		(*S*)-**527b**	83
rac-**524c**	0	F		*rac*-**527c**	42
rac-**524d**	1	H		*rac*-**527d**	80
(*R*)-**524d**	1	H		(*R*)-**527d**	80
(*S*)-**524d**	1	H		(*S*)-**527d**	72
rac-**524a**	1	F	R^1	*rac*-**526a**	57
rac-**524b**	1	Cl	R^1	*rac*-**526b**	46
rac-**524c**	0	F	R^1	*rac*-**526c**	47
rac-**527a**	1	F	R^1	*rac*-**528a**	74
rac-**527a**	1	F	R^2	*rac*-**528b**	89
(*R*)-**527a**	1	F	R^3	(*R*)-**528c**	95
(*S*)-**527a**	1	F	R^3	(*S*)-**528c**	84
rac-**527b**	1	Cl	R^1	*rac*-**528d**	61
(*R*)-**527b**	1	Cl	R^3	(*R*)-**528e**	69
(*S*)-**527b**	1	Cl	R^3	(*S*)-**528e**	76
rac-**527c**	0	F	R^1	*rac*-**528f**	74
(*R*)-**527d**	1	H	R^3	(*R*)-**528g**	63
(*S*)-**527d**	1	H	R^3	(*S*)-**528g**	73

Chart 17



529
X = Cl, Br
R = H, Ac
R,R = CMe_2

530

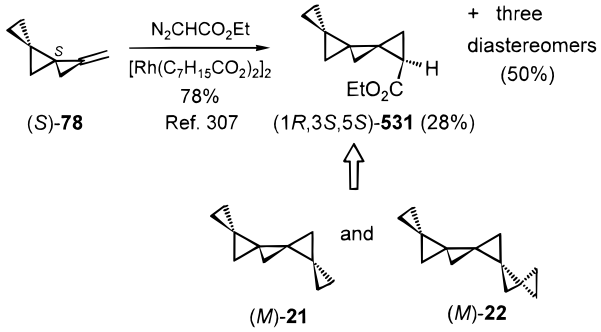
been published as precursors to "tunable" molecular clefts.[141b] For example, compound **529** (X = Cl, R = H) forms 1:1:1 complexes with D-ribose and sodium ions.

VII. Conclusions and Further Perspectives

In only a decade, the rather limited chemistry of spiropentane has evolved into the much wider field of higher [*n*]triangulanes and their derivatives. Is

there anything left to be done? Yes. Indeed, there is a huge unexplored area of triangulane chemistry opening up, thanks to recent developments in organic synthesis, and in the not too distant future, there will be a broad assortment of new triangulanes, especially with respect to stereoselectively functionalized derivatives and their interesting physical properties. For example, the outstanding specific rotation of enantiopure (*M*)-[4]triangulane [(*M*)-dispiro[2.0.0.2.1.1]-nonane, (*M*)-**13**] (Scheme 10)[71] prompts the immediate development of possible enantioselective approaches to higher analogues of this first *σ*-[*n*]helicene. It should, in principle, be possible to prepare enantiomerically enriched or pure [5]- and [6]triangulanes (*M*)-**21** and (*M*)-**22** (Scheme 121) from the same

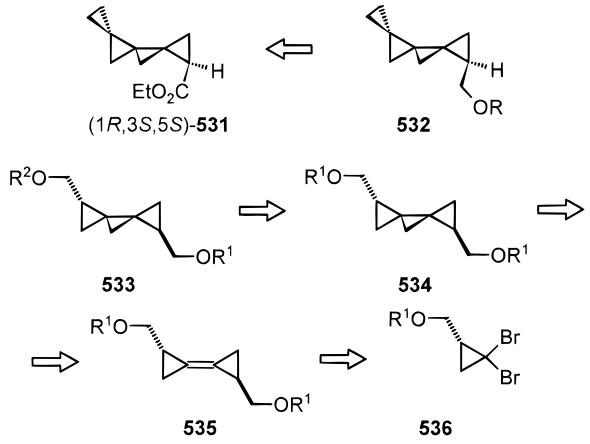
Scheme 121



synthetic precursor as that used for (*M*)-**13**, i.e., methylene[3]triangulane (*S*)-**78**, since the position of the methylene group predetermines any further extension of the helix. Thus, the addition of ethoxycarbonylcarbene, generated by decomposition of ethyl diazoacetate in the presence of dirhodium tetraoctanoate, to (*S*)-**78** affords a mixture of four diastereomeric esters **531** (78% overall yield) in a ratio of 26:15:26:33. The major diastereomer can be isolated by simply distilling off the other three over a concentric tube column, and it possesses the appropriate (1*R*,3*S*,5*S*) configuration, as determined by X-ray crystal structure analysis of the corresponding acid (Scheme 121).[307] It should be possible to prepare the *σ*-[*n*]helicenes (*M*)-**21** and (*M*)-**22** from (1*R*,3*S*,5*S*)-**531** in a number of synthetic transformations for which the feasibility has already been established in triangulane chemistry. The design of an executable route to the enantiopure *σ*-[7]- and *σ*-[8]helicenes is obviously an even more challenging problem.

Triangulane derivatives such as (1*R*,3*S*,5*S*)-**531** in enantiomerically pure form may be used for the preparation of novel liquid crystalline materials of type **532** with a "banana shaped" end group (Scheme 122; for possible definitions of R and a set of chemical operations, see also Scheme 120). Potentially mesogenic novel core units for "banana shaped" liquid crystals may be constructed starting from bifunctional [3]triangulane derivatives **534** which should be accessible by dimerization of copper cyclopropylidenoids generated from 1,1-dibromocyclopropanes **536**[111,112] and subsequent cyclopropanation of the thus obtained bicyclopropylidene derivatives **535**. Appropriate chemical transformations of the side chains in **534**, possibly with enzymes, may lead to

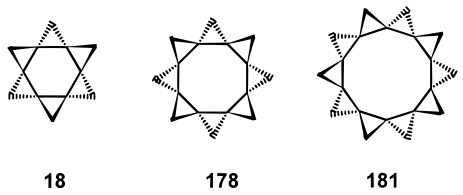
Scheme 122



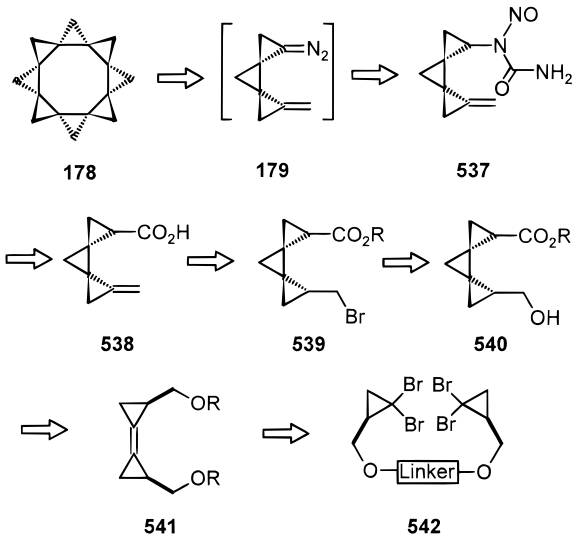
optical resolution of these intermediates (Scheme 122).

Another intriguing and challenging synthetic task, which is not only of theoretical interest,[308] is the preparation of davidane (cyclo[6]triangulane) **18** and its higher analogues cyclo[8]- **178** and cyclo[10]-triangulane **181** (Chart 18). While the most straightforward strategies toward these hydrocarbons, as discussed above (see section III.E), do not appear unrealistic, none has yet been successfully executed. However, now that the basic methodology for the preparation of enantiopure [*n*]triangulane derivatives has been developed,[71] the chances to at least achieve the synthesis of **178** and possibly even **181** look better than before (Scheme 123). Although two identical molecules of the chiral key carbene precursor **179** have to react with each other, the whole sequence

Chart 18



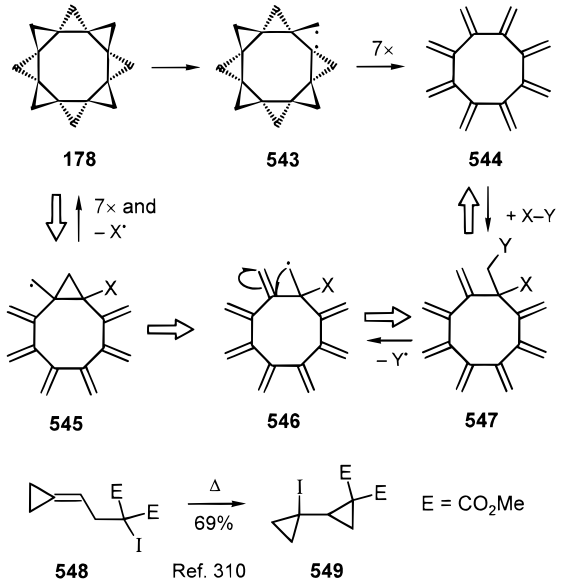
Scheme 123



can be carried out with the racemates, as the target molecule **178** has C_{4v} symmetry.

Although the total strain energy in cyclo[8]-triangulane **178** would be in excess of 290 kcal/mol,[12] it would probably be rather stable toward thermal isomerization. The required activation energy to cleave a carbon−carbon bond in one of the three-membered rings would not be much lower than that for homolytic opening of a simple cyclopropane derivative.[181,247] Once such a cleavage occurs, it would yield the intermediate diradical **543** which, in a zipper mode, would probably open all seven remaining cyclopropane rings by repeated cyclopropylmethyl to butenyl radical rearrangements[270] to finally give the [8]radialene **544** (Scheme 124).[309] On the other

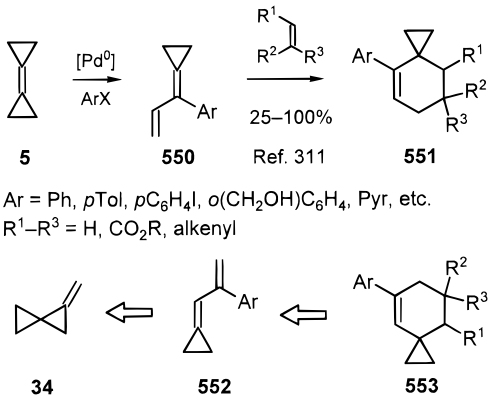
Scheme 124



hand, it would be interesting to test the idea of a homoallyl radical of type **546**, generated from an appropriate derivative **547** from [8]radialene **544**, undergoing a zipper mode cyclization to eventually yield cyclo[8]triangulane **178** (Scheme 124). The basic 3-*exo-trig* ring closure of a homoallyl to a cyclopropylmethyl radical has indeed been observed in the atom-transfer rearrangement of the (2-cyclopropylideneethyl)iodomalonate **548** to the bicyclopropyl derivative **549**.[310]

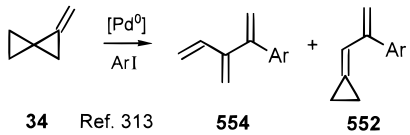
The possible zipper mode ring opening of methylene[*n*]triangulanes upon palladium-catalyzed cross-coupling reactions with aryl halides (or alkenyl halides), which proceeds with consecutive cyclopropylmethyl- to homoallylpalladium rearrangements,[311] also opens up interesting perspectives. Since bicyclopropylidene (**5**) was discovered to rapidly cross couple with alkenyl and aryl halides under palladium catalysis with opening of one three-membered ring to give cross-conjugated trienes and dienes **550**, respectively (Scheme 125),[311,312] methylenespiropentane (**34**), an isomer of bicyclopropylidene (**5**), might be expected to behave similarly. However, the coupling-rearrangement reaction of **34** would yield the diene **552**, a regioisomer of **550**. When carried out in the presence of a dienophile, the cross-

Scheme 125

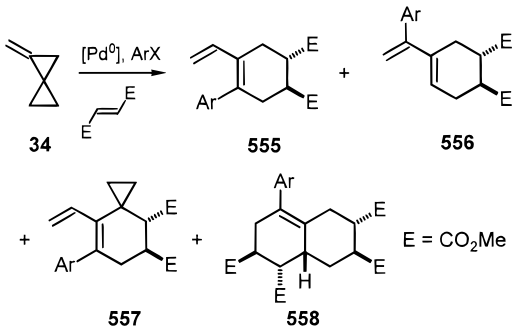


coupling rearrangement of **5** is immediately succeeded by a Diels−Alder cycloaddition to yield spiro[2.5]octene derivative **551**; the expected corresponding products from **34** would be regioisomers of **551**, spiro[2.5]octene derivatives **553** (Scheme 125). Indeed, methylenespiropentane (**34**) does react with aryl halides under palladium catalysis to give dienes **552** but only as a minor product.[313a] The major products are cross-conjugated trienes **554**,[314] which are particularly interesting in that they are able to undergo domino-Diels−Alder reactions[315] with added dienophiles such as dimethyl fumarate to yield bicyclic bisadducts, e.g., **558** (Scheme 126).[313b] An extrapola-

Scheme 126



Ar	(%)	(%)
Ph	32	6
4-I-C_6H_4	17	5
3-Pyridyl	22	8
2-($HOCH_2$)-C_6H_4	18	6

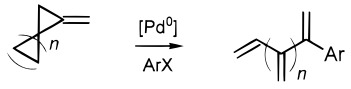


Ar	Yield of **555**–**557** (%)	Yield of **558** (%)
Ph	27	29
2-thienyl	48	17

tion of these reactions of **34** to higher methylene[*n*]-triangulanes **29** would open new routes to cross-conjugated oligoenes **559** (Scheme 127).[314]

For quite a while it appeared as if the perspirocyclopropanated [3]rotane **86** would be the ultimate

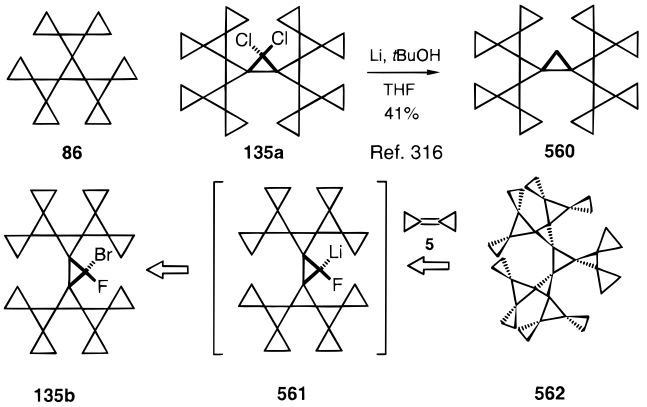
Scheme 127



29 **559**

achievable branched triangulane.[57] But recent success in preparing the dichlorocarbene adduct **135a** (Scheme 25) from the "super-super-bicyclopropylidene" **134**[112] fuels new hope that the limits for generating even higher aggregates of spiroannelated cyclopropane rings can be pushed forward still further. Reductive dechlorination of **135a** led to the hydrocarbon **560** (Scheme 128),[316] which, with its 15

Scheme 128



86 **135a** Ref. 316 **560**

135b **561** **562**

spirocyclopropane rings, already sets a new record. Taking the steric congestion around the central ring in **135** and the relative sizes of a chlorine and a spiroannelated cyclopropane ring into account, it does not appear completely impossible that a carbenoid **561** generated from the recently prepared bromofluorocarbene adduct **135b** could be trapped by bicyclopropylidene (**5**) to yield **562**, an aggregate of 18 spirocyclopropane rings (Scheme 128). With the latest synthetic methodology[316] it would now even be possible to prepare gram quantities of the highly branched [15]triangulane **560** and determine its heat of combustion in order to fully establish the proposed scheme of strain additivities in all sorts of [*n*]-triangulanes.[12]

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