3-Heteroquadricyclanes in Organic Synthesis

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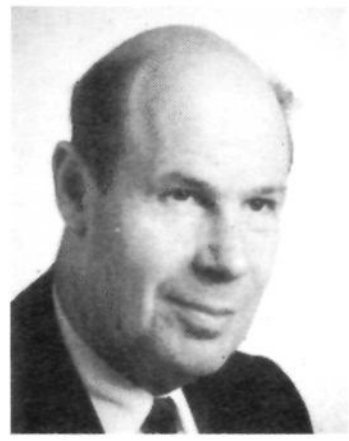
Received October 17, 1988 (Revised Manuscript Received April 13, 1989)

Contents



Werner Tochtermann was born in Pforzheim, Germany, in 1934. He studied chemistry at the Universities of Münster and Heidelberg. In 1960 he received his doctoral degree under the direction of Georg Wittig. After postdoctoral work as an assistant to his academic teacher, he started his own research on seven-membered-ring systems. In 1965 he was appointed Privatdozent at the University of Heidelberg. He joined the Fachbereich Organische Chemie und Makromolekulare Chemie at the Technische Hochschule Darmstadt in 1972. Since 1976 he has been Professor of Chemistry at the University of Kiel. His research activities cover the field of synthetic organic chemistry in general. At present his special interest is focused on the chemistry of polycyclic compounds, large-ring chemistry, and the reactivity and chiroptical properties of boat-shaped arenes.

Gesa Olsson was born in Lübeck, FRG, in 1960. She received her diploma degree in 1984 and her doctoral degree in 1988 from the University of Kiel working under the direction of Werner Tochtermann. She was involved in research on chiral bridged oxepines and [*n*]paracyclophanes, annelated tetrahydrofurans, and mechanistic photochemical investigations. After a short postdoctoral period, she joined the plant protection department of the Schering Co., West Berlin, in November 1988.

I. Introduction

In 1966 Prinzbach and co-workers[1] described the synthesis of the first heteroquadricyclane, 1,5-dicarbomethoxy-3-oxaquadricyclane (**1**);[2] 2 years later they reported the synthesis of several 3-azaquadricyclanes.[3] Since then, these highly strained systems[4] have been the subject of a great number of synthetic, mechanistic, spectroscopic, and theoretical investigations. The reasons for these fascinating developments have been the easy availability of many derivatives and their tendency to undergo manifold, often highly selective, reactions, especially in the oxygen series.

This review deals in its first two sections with the synthesis and the spectroscopic and structural properties of 3-oxo- and 3-azaquadricyclanes. In the third section an overview of the different reaction types of heteroquadricyclanes is given. The last section illustrates some of the very different applications of the title compounds. Syntheses that proceed via heteroquadricyclanes and/or their thermal rearrangement products are outlined there.

The literature until 1987 has been fully covered, along with some contributions published in 1988. Carbocyclic quadricyclanes and their heterosubstituted derivatives are not dealt with here.[5]

II. Synthesis of 3-Heteroquadricyclanes

The synthesis of 3-oxaquadricyclanes usually starts with the Diels–Alder reaction of furans with alkynes to

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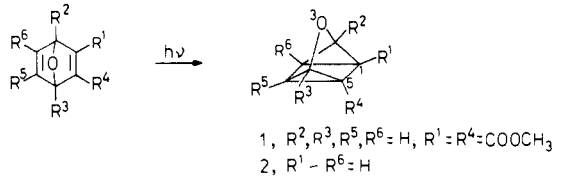

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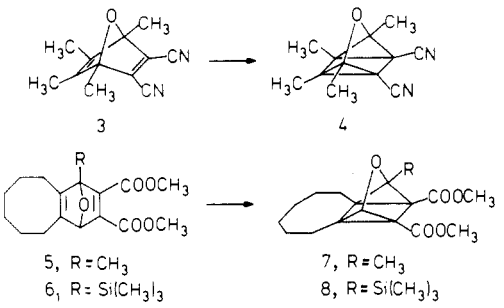

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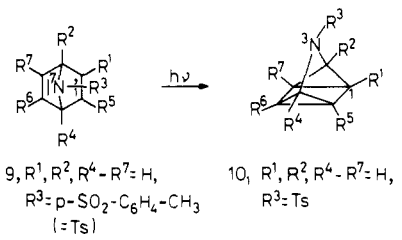

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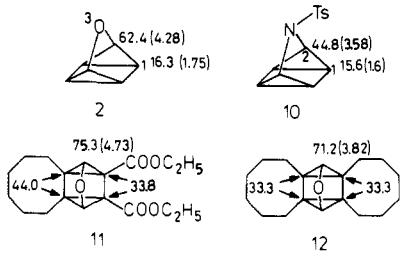

give 7-oxanorbornadienes. Although furans with a great variety of substitution patterns can be used for this cycloaddition, the method is clearly limited because of the relatively low reactivity of alkynes toward furans. Only alkynes having either strong electron-withdrawing substituents (e.g., dimethyl acetylenedicarboxylate, dicyanoacetylene, and hexafluorobutyne) or ring strain (e.g., arynes and cycloalkynes, especially cycloctyne and its derivatives) give good to excellent yields. Thus the synthesis of the parent compound, 3-oxaquadricyclane (**2**, Scheme I)[6] could only be accomplished by using vinylene carbonate as the alkyne equivalent and by converting its cycloadduct with furan to 7-oxanorbornadiene, according to Corey and Winter.[7] The use or development of suitable alkyne equivalents[8] in order to increase the scope of the oxanorbornadiene synthesis would be highly desirable.

7-Oxanorbornadienes with suitable chromophores (e.g., $COOCH_3$) are selectively transformed into 3-oxaquadricyclanes by direct photoexcitation with filtered UV light, usually at low temperatures with ether as solvent.[9] For oxanorbornadienes that absorb only at short wavelengths (R = H, alkyl, CF_3, etc.) or that show partial overlap of the absorptions with the photoproducts, a sensitized excitation with acetone can be used. In most cases the yields are good to excellent, despite some side reactions, such as cycloreversion to give the starting material or di-π-methane rearrangement[10] to give hydroxyfulvenes (see section IV.D), especially upon sensitized excitation.[11] Thus the parent compound **2** was isolated in 90–95% yield.[9] It has also been reported that the highly substituted oxanorbornadienes **3**, **5**, and **6** afford oxaquadricyclanes **4**, **7**, and **8** on simple exposure to sunlight (Scheme 2).[12,13]

The corresponding conversion of the 7-azanorbornadienes to the 3-azaquadricyclanes raises more problems than in the oxygen series. First of all, only pyrroles with strongly electron-withdrawing groups on the nitrogen atom are sufficiently reactive as dienes in Diels–Alder reactions. Therefore most 3-azaquadricyclanes known hitherto contain NSO_2R groups, though a few examples have NCOOR or $^+NR_2$. Moreover, 7-azanorbornenes often under an easy [4 + 2] cycloreversion,[14] so that the use of suitable olefinic dienophiles as alkyne equivalents or precursors is also limited. Consequently, the synthesis of *N*-*p*-tosyl-7-azanorbornadiene (**9**) could only be achieved in moderate yield by a multistep reaction sequence.[14]

On the other hand, the photoisomerization **9** → **10** is usually performed in the same way as in the oxygen series (high-pressure UV lamp, Pyrex filter, ether as solvent) either by direct or by acetone-sensitized excitation (Scheme 3). Yields as high as 94% (e.g., for **10**) have been reported by Prinzbach and co-workers.[14] The photoreaction and work-up procedures have to be carried out at low temperatures because many azaquadricyclanes are thermally very unstable and undergo isomerization to azepines (see section IV.A,B).

III. Spectroscopic and Structural Properties of Heteroquadricyclanes

In 3-oxa- and 3-azaquadricyclanes the cyclopropane carbon atoms and the protons attached to them show very characteristic chemical shifts and coupling constants. This is demonstrated in Scheme 4 for the selected compounds **2**,[9] **10**,[14] **11**,[15,16] and **12**.[17] The first numbers are the ^{13}C NMR data: the ^1H NMR shifts are given in parentheses. It thus follows that the formation of the heteroquadricyclanes and their thermolysis to give heteropines (see section IV.A,B) can be easily monitored by ^1H NMR spectroscopy.

In the IR spectra of the quadricyclic compounds cyclopropane C–H stretching vibrations in the range 3070–3090 cm^{-1} are detected. The UV spectra show only end absorption near 220 nm if there are no other chromophores present (**2**: $\epsilon_{220} = 35$ in methanol[9]).

Hogeveen and Nusse[18] have reported a detailed NMR spectroscopic study for 2,4-octano-1,5-dicarbomethoxy-3-oxaquadricyclane (**13**). Temperature-dependent ^1H NMR spectra revealed by line-shape analysis two different conformational interchanges of the octano bridge in solution, their free enthalpies of activation being $\Delta G^{\ddagger}_{203} = 10.6$ and $\Delta G^{\ddagger}_{183} = 9.4$ kcal/mol. The first one was ascribed to a swinging **13I** ⇌ **13II** of the octamethylene chain over the oxygen atom; the second was ascribed to a conformational change of the pseudorotation type in the 11-membered ring formed by the methylene chain, two bridgehead carbons, and the oxygen (Scheme 5).

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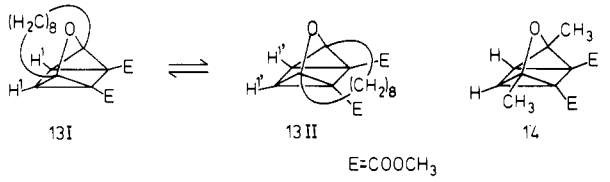

With the same compound **13** an X-ray structural analysis has been undertaken.[19,20] However, the structure could only be refined to a final *R* value of 0.129. The angles in the four-membered ring on the base possesses values between 89 and 92°; the inner cyclopropane angles are also quite normal and lie in the range 56–62° (for a further discussion, see section IV.B).

IV. Reactions of Heteroquadricyclanes

A. Thermal Isomerization

A characteristic and most useful feature (vide infra) of the highly strained 3-oxa- and 3-azaquadricyclanes is their tendency to isomerize under thermolytic conditions. As we shall outline in the forthcoming sections, this skeletal rearrangement proceeds in most cases in a highly regioselective manner, thus providing a new route to a great number of different classes of compounds.

The half-life periods for a variety of heteroquadricyclanes have been measured by Prinzbach and co-workers,[1,6,9,14,21] Hogeveen and Nusse,[22] and our group.[17] In general, azaquadricyclanes are more labile than the corresponding oxygen compounds.[3,14] Some aza derivatives rearrange rapidly below 0 °C, sometimes even at temperatures as low as −80 °C.[14] On the other hand, the kinetic parameters in the oxygen series are usually determined in the temperature range between 70 and 140 °C.

The kinetic stability of all tetracyclic compounds is highly dependent on their substitution patterns. On the basis of the data known at the present time, no general conclusions can be reached, although there are some consistent trends. For instance, in most,[9] but no in all,[17] cases carbomethoxy groups lead to a decrease in kinetic stability; chlorine substituents have an even larger effect in the same direction in the nitrogen series,[14] while trifluoromethyl groups exhibit a very small influence in oxaquadricyclanes.[9]

The reaction rates are considerably increased when intramolecular cycloadditions are possible.[9] These effects may be due to changes in the ground states of the strained tetracyclic compounds. The first step of the thermolysis can be considered to be highly exothermic (vide infra), so that the corresponding early transition states resemble the ground states. In line with these considerations Hogeveen and Nusse[18,22] suggested that the difference in the rates of thermal decomposition of **14** and **13** (**14**:**13** = 0.006:1) results because **13**, which has an 11-membered ring, is at a rather higher energy than **14**.

In most cases the thermolysis of 3-hetereoquadricyclanes leads in excellent yields to oxepines and 1-substituted 1*H*-azepines, which show respectively in solution the classical valence isomerism with the corresponding arene oxides and arene imines.[23] Several mechanistic pathways for this $3\sigma \rightarrow 3\pi$ isomerization

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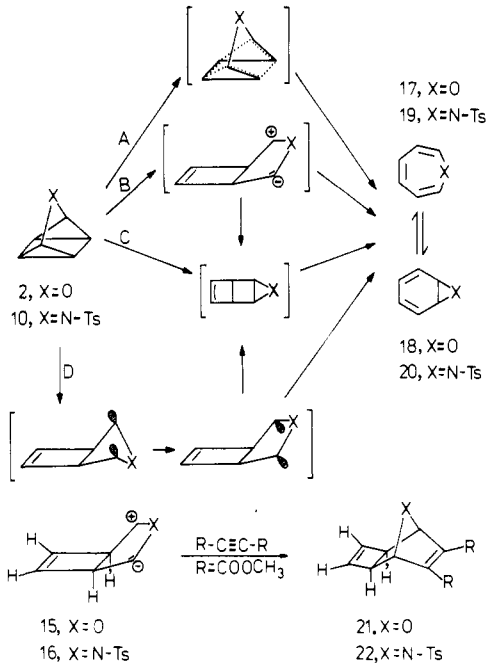

were originally considered (Scheme 6).[21]

Experimental evidence,[9,14,17,21,22] as well as the MO considerations of Haselbach and Martin,[24] are in favor of the two-step mechanism (B). The isomerization starts with a 1,3-dipolar cycloreversion to give carbonyl ylide **15** (X = O) or azomethine ylide **16** (X = N-Ts). This reaction constitutes a special access to these nonstabilized 1,3-dipolar species.

The same mechanistic pathway was independently observed by Tanny and Fowler.[25] Using Schleyer's value of 101 kcal/mol for the ring strain of quadricyclane,[4,26] Huisgen[27] has estimated a release of 63 kcal/mol of strain energy for the process **2** → **15** (X = O). In the second step the seven-membered-ring systems **17** and **19** are formed by a 1,5-electrocyclic ring opening[27] of intermediates **15** and **16**. The 1,3-dipoles could be trapped by Prinzbach and co-workers with dimethyl acetylenedicarboxylate as dipolarophile to give cycloadducts **21** and **22**.[6,9,14,28]

The intermediacy of dipoles **15** and **16** also explains the thermal behavior of similarly substituted oxa- and azaquadricyclanes: According to Haselbach and Martin,[24] azomethine ylides **16** are more stable by about 6 kcal/mol than carbonyl ylides **15**. This roughly corresponds to the differences in kinetic stabilities of related tetracyclic oxygen and nitrogen compounds.[14] On the other hand, process B in Scheme 6 is highly unfavorable for carbocycles, even if the intermediate is considered to be a diradical.[24,25] The special nature of the 3-heteroquadricyclanes with respect to their thermal behavior is manifested by the comparison with carbocyclic analogues. The prototypical quadricyclic carbanion (**2**, X = $\bar{C}H^-$ instead of O) is not known. There are, however, experimental observations that can be interpreted in terms of a cycloreversion that is rapid even below −50 °C.[29] In contrast, quadricyclanes are generally isomerized to norbornadienes[5,24,30] by initial homolysis of an internal bicyclopentane bond. The situation with 3-methylene and 3-keto derivatives is somewhat more complicated. These compounds can be used for the synthesis of heptafulvenes and tropones.[30]

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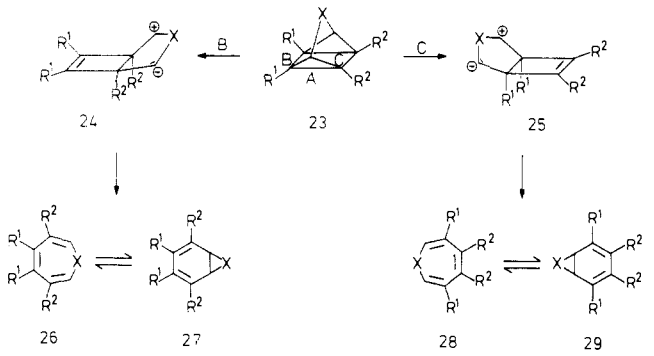

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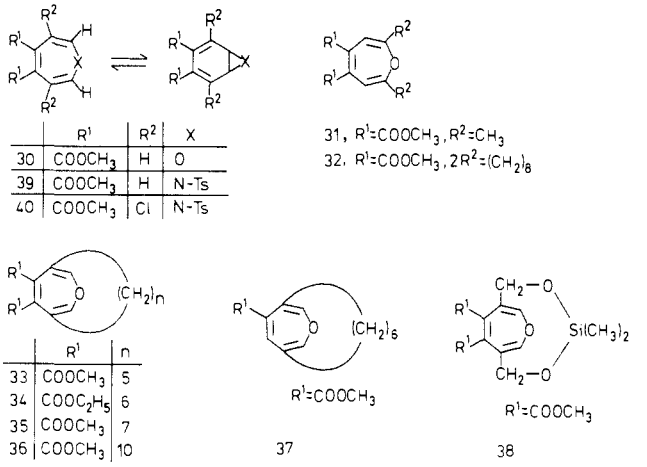

	R^1	R^2	X
30	$COOCH_3$	H	O
39	$COOCH_3$	H	N-Ts
40	$COOCH_3$	Cl	N-Ts

31, R^1=$COOCH_3$, R^2=CH_3
32, R^1=$COOCH_3$, $2R^2$=$(CH_2)_8$

	R^1	n
33	$COOCH_3$	5
34	$COOC_2H_5$	6
35	$COOCH_3$	7
36	$COOCH_3$	10

37: R^1=$COOCH_3$

38: R^1=$COOCH_3$

B. Regioselectivity of the Heteroquadricyclane Cycloreversion

Heteroquadricyclanes **23** with different substituents R^1 and R^2 on the cyclobutane ring can give two different 1,3-dipoles **24** and **25** (Scheme 7). Cleavage of the bonds B leads to **24** and finally to heteropine/benzene oxide/imine isomer **26**/**27**; bond breaking of C gives rise to **25** and **28**/**29**. It is of mechanistic interest as well as of synthetic importance that in most cases the $3\sigma \rightarrow 3\pi$ isomerization occurs with high regioselectivity and gives predominantly or even exclusively one of the two possible isomeric systems. For example, heteroquadricyclanes in which R^1 are ester groups (e.g., R^1 = $COOCH_3$) always prefer pathway B to give intermediates and products with a maleic ester partial structure.

In the oxaquadricyclane series bond B is a cyclopropane bond between a typical donor and a π-acceptor substituent.[9] Using the concept of donor–acceptor-substituted cyclopropanes,[31] one may easily understand the preferential cleavage of this bond in these cases. MNDO calculations for *cis*- and *trans*-2-hydroxycyclopropanecarboxylic acid indicate this bond to be longer and therefore more easily activated than the other ones.[31]

Despite the limited quality of the data, the same conclusion can be drawn from the X-ray structural analysis of the octano derivative **13** (bond lengths for B: 1.56 and 1.535 Å; bond lengths for C: 1.485 and 1.505 Å).[20] This "ester effect" enables, for instance, the preparative synthesis of oxepines **30**,[1,9,21] **31** and **32**,[18,22] **33–36**,[15,32–35] **37**,[36] and **38**[37] and azepines **39–40** (Scheme 8).

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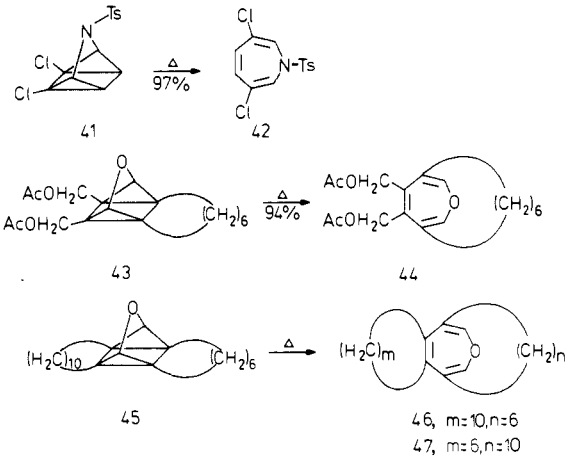

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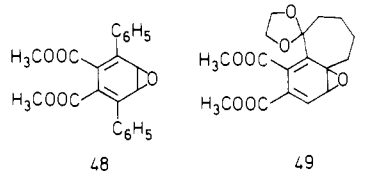

It is much more difficult to explain other substituent effects on the regioselectivity of the heteroquadricyclane thermolysis. In the presence of two trifluoromethyl groups in the oxaquadricyclane framework or of two chloro substituents in azaquadricyclane **41**, the C–C bonds of the cyclopropane rings opposite to the substituents are predominantly cleaved. For example, 3,6-dichloro-1-((4-methylphenyl)sulfonyl)-1*H*-azepine (**42**) is isolated from **41** in 97% yield.[14] Other surprising examples are the conversions **43** → **44**[17] in high yield and the formation of an 86:14 ratio of isomers **46** and **47**[17] from **45** (Scheme 9).

Many of these seven-membered-ring systems exist in solution in equilibrium with the corresponding arene oxides[38] or arene imines. However, there are also examples that prefer one form. This holds for 3,6-alkanooxepines **33**[32] and **34**[39] with short pentamethylene and hexamethylene bridges. In these cases the benzene oxides (n = 5, 6) could not be detected.[32,33,39] The opposite situation was found for **48**[40] and for **49**,[41] at least in the crystalline state (Scheme 10).

In summary, the thermolysis of heteroquadricyclane provides a general synthesis of oxepines/arene oxides and azepines/arene imines.[9,14] Since these interesting classes of cyclic compounds can also be obtained by using the alternative approach of Vogel and co-workers,[23,38,42] organic chemists currently have two different preparative methods with a broad scope of application at their disposal.

C. Further Cycloadditions of 3-Heteroquadricyclanes

The trapping reaction of dipoles **15** and **16** with dimethyl acetylenedicarboxylate can be considered at least formally as an attack of the dienophile at the positions 2 and 4 of the heteroquadricyclane. In this context these heterocycles behave like bishomofurans and bishomopyrroles, respectively.[28,30]

In the course of their systematic studies, Prinzbach and co-workers also found other types of cycloadditions.

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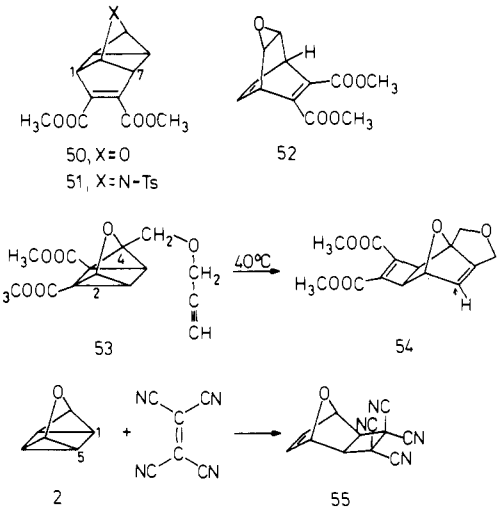

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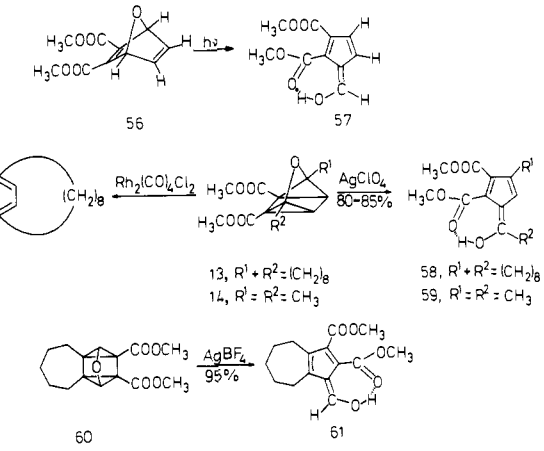


7-Oxanorbornadiene and 7-*N*-*p*-tosylazanorbornadiene also react with dimethyl acetylenedicarboxylate to give [2 + 2 + 2] adducts of the types **50** and **51**, which are formally addition products to the C-1–C-7 bond of heteroquadricyclanes (Scheme 11).[9,14] When 3-oxaquadricyclane (**2**) was heated with dimethyl acetylenedicarboxylate to 100 °C, a 1:1 mixture of adduct **21** to dipole **15** and of Diels–Alder adduct **52** to benzene oxide was isolated.[9,23]

Oxaquadricyclanes like **53** with suitable bridgehead substituents were constructed in order to facilitate an intramolecular cycloaddition. The quantitative formation of tetracyclic compound **54** at relatively low temperatures ($t_{1/2}$ = 8.1 min for **53** at 82 °C) was interpreted preferably in terms of a concerted symmetry-allowed [$_{\pi}2 + {}_{\sigma}2 + {}_{\sigma}2$] addition of the alkyne part to C-2/C-4 of **53**.[9] An exceptional pathway is observed in the addition of tetracyanoethylene to C-1/C-5 of **2** to give **55**.[43] The assumption of a concerted [$_{\pi}2 + {}_{\sigma}2 + {}_{\sigma}2$] addition to the bishomocyclobutadiene unit of **2** is supported here also by the observation that this reaction does not require the elevated temperatures necessary to generate the corresponding carbonyl ylide **15**.[43]

The structure of a dimer of 1,5-dicarboxymethoxy-3-oxaquadricyclane (**1**) formed by standing at room temperature for 2 months was elucidated by Deslongchamps and Kallos.[44] Its formation can be explained by assuming a cycloaddition of the corresponding carbonyl ylide to C-1/C-5 of a second molecule of this tetracyclic compound.

In summary, the strained heteroquadricyclanes have the possibility of undergoing various types of cycloadditions depending on their substitution pattern and their reaction partners.

Kaupp and Prinzbach[45] have carried out a systematic comparative investigation of the reactivity of various carbocyclic quadricyclanes and their hetero analogues toward a series of dienophiles.

D. Reactions of Heteroquadricyclanes with Metal Catalysts: Synthesis of Fulvene and Benzene Derivatives

The isolation of 6-hydroxyfulvenes by thermolysis and CuCl-catalyzed rearrangement of oxaquadricyclanes was reported first in 1969.[40] In a detailed study Stusche and Prinzbach[11] showed that 6-hydroxyfulvenes are also formed directly from substituted 7-oxanorbornadienes in yields between 5 and 55% on acetone-sensitized photoexcitation via the di-π-methane rearrangement.[10] For example, **56** affords **57** in 38% yield (Scheme 12).

According to McCulloch and co-workers.[46] oxanorbornadienes also isomerize rapidly in the presence of iodine. The reaction is initiated by light. Oxaquadricyclanes having bridgehead methyl substituents undergo slow photoisomerization to the same fulvenes. In 1971 the Canadian group reported on the synthesis of hydroxyfulvene **59** by treatment of oxaquadricyclane **14** with concentrated sulfuric acid.[47]

The best yields, however, are obtained by the silver salt catalyzed rearrangement[11] of oxaquadricyclanes: For example, treatment of **13**, **14**, and **60** with $AgClO_4$ or $AgBF_4$ gives fulvenes **58**, **59**, and **61** in yields between 80 and 95%.[22,48] Reaction of **13** and **14** with catalytic amounts of $Pd(C_6H_5CN)_2Cl_2$ or $[Rh(CO)_2Cl]_2$[49] leads to product mixtures. The main products with the palladium catalyst are again fulvenes **58** (45%) and **59** (70%).

From a synthetic point of view it is noteworthy that **14** is deoxygenated in 35% yield to give dicarbomethoxy[8]paracyclophane **62**.[22] From their kinetic and mechanistic investigations Hogeveen and Nusse[22] have drawn the conclusion that the different catalysts can cleave the bonds of the cyclopropane rings and of the C–O–C fragment as well, depending on the initial attack of the metal.

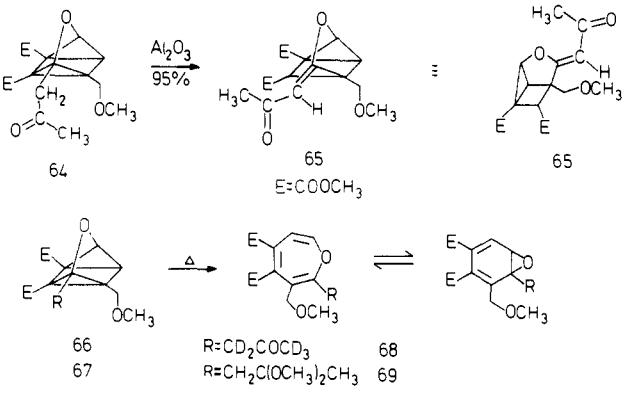
Photoisomerization of benzazanorbornadienes to benzaminofulvenes has also been reported.[50] The use of $PdI_2((C_6H_5)_3Sb)_2$ led to a clearn $2\sigma \rightarrow 2\pi$ isomerization of **2** and **10** in high yield at room temperature[9,14] to give the corresponding heteronorbornadienes.

E. Selective Bond Cleavages of Heteroquadricyclanes

In contrast to the formation of hydroxyfulvenes with sulfuric acid described above, oxaquadricyclane **14** undergoes a selective cleavage of one cyclopropyl bond in combination with a formal proton shift when it is treated with trichloroacetic acid; 3-oxatricycloheptane **63** is obtained in 75% yield (Scheme 13).[22] The same reaction also occurs with octane derivative **13**. It was suggested that oxatricycloheptane **63** is also the primary product of the sulfuric acid catalyzed reaction of **14** and

SCHEME 13

SCHEME 14



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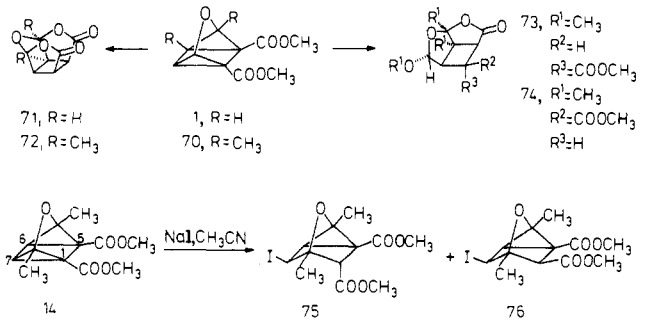


that it is converted subsequently to hydroxyfulvene **59**.

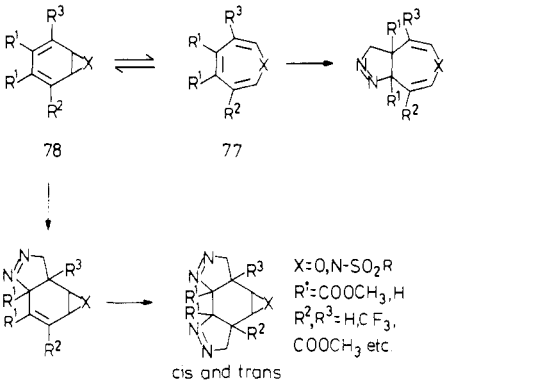
Oxatricycloheptanes are also formed under very mild conditions when the substituent on C-2 has an activated methylene group in the α position: Thus isomer **65** is formed in 95% yield on simple filtration of **64** over alumina with ethyl acetate (Scheme 14). It is noteworthy that **65** is also the main product (48%) of the thermolysis of **64** in boiling toluene.[51]

The system **64** represents a nice example of the general behavior of the heteroquadricyclane family. In this highly strained system the activation barriers for the different strain-releasing reactions are very similar, so that a slight change in the substitution pattern can lead to the preferential formation of other products. In the present case, deactivation of the methylene group reactivity in **66** or **67**, either by deuteration or by acetalization, leads again to oxepine/benzene oxides **68** and **69** as the "normal" main products of the thermolysis.[51]

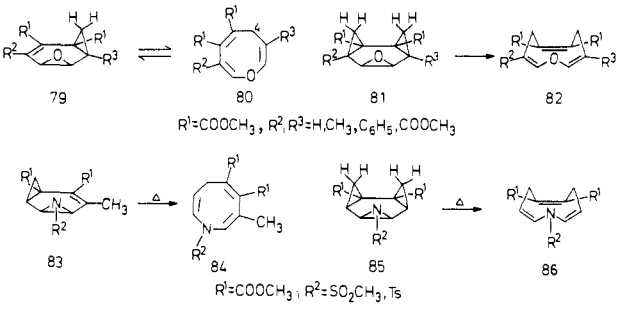
Remarkable acid-catalyzed transformations with cyclopropyl bond cleavages of oxaquadricyclane diesters **1** and **70** were reported by Wenkert and co-workers.[52] Exposure of the latter to refluxing aqueous methanolic hydrochloric acid produced bislactones **71** and **72**, while a reaction of **70** at room temperature afforded monolactones **73**/**74** (Scheme 15).

A nucleophilic cleavage of the C-1–C-7 bond of dicarbomethoxyoxaquadricyclane **14** under very mild conditions was observed by Nelsen and Calabrese.[53] Stirring of **14** with sodium iodide in acetonitrile at room temperature led to a 4:1 mixture of endo and exo isomers **75** and **76**. On catalytic hydrogenation the C-1–C-7 and C-5–C-6 bonds of 1,5-dicarbomethoxy-3-oxaquadricyclane are cleaved to give the corresponding known 7-oxanorbornane derivative.[44]

SCHEME 16



SCHEME 17



V. Syntheses via Heteroquadricyclanes and Heteropines

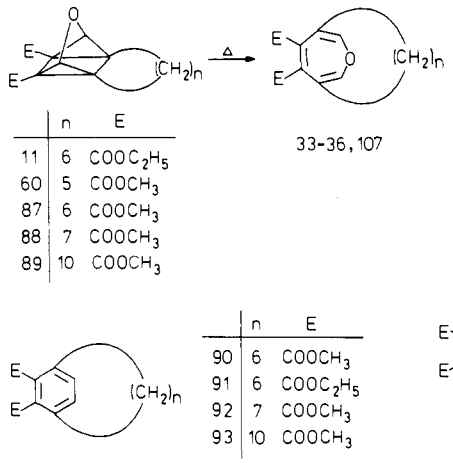
A. General Remarks

3-Heteroquadricyclanes have been used for the synthesis of a great variety of different classes of compounds. Most examples take advantage of the transformation of furans or pyrroles to oxepines or azepines via the tetracyclic intermediates. The seven-membered rings or their valence isomers are then converted to the final products. In this section the usefulness of the heteroquadricyclane → heteropine sequence for this purpose is outlined.[54]

B. Synthesis of Bis- and Tris-σ-homobenzene Derivatives and Eight- and Nine-Membered Heterocycles

The valence tautomeric oxepine/benzene oxide and azepine/benzene imine systems **77**/**78** add 1 or 2 mol of diazomethane to give mono- or bispyrazolines, respectively (Scheme 16).[55] Photolysis of these adducts affords *cis*-oxabis-σ-homobenzenes, *cis*- and *trans*-oxatris-σ-homobenzenes, and the corresponding aza analogues.[55] The strained *cis*-σ-homobenzenes **79**, **81**, **83**, and **85** were prototypes of a rapidly expanding class of bis- and tris-σ-homobenzenes which undergo the preparatively valuable $[_\pi 2 + _\sigma 2 + _\sigma 2]/[_\sigma 2 + _\sigma 2 + _\sigma 2]$cycloreversion reactions to give 4*H*-oxocines **80**, dihydroazocines **84**, dihydrooxonines **82**, or dihydroazonines **86**, respectively (Scheme 17). Prinzbach and his group have published detailed investigations in this field, including stereochemical and mechanistic aspects and the

SCHEME 18



influence of various substituents.[55,56]

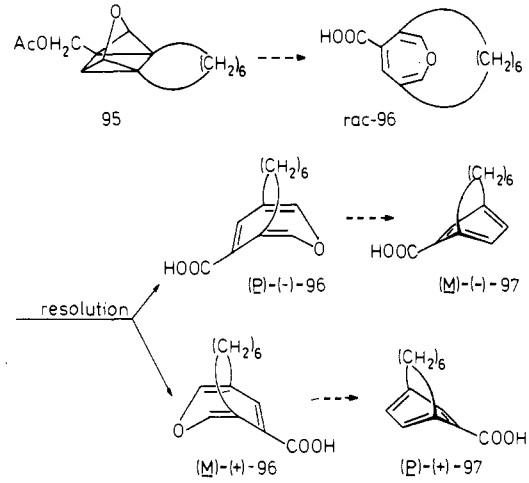
C. Synthesis of Oxepinophanes, Cyclophanes, and Medium and Large Rings

In section IV.A it was pointed out that the influence of substituents, especially of carbomethoxy groups, on the course of the 3-oxaquadricyclane thermolysis leads to the regioselective formation of 3,6-bridged oxepines **33–38** from 6,7-annelated oxaquadricyclane precursors.[15,17,32-37] Annelation in the 2,4-positions leads to the 2,7-bridged oxepine **32**.[22] This synthesis of ansa compounds has a large scope: it includes heterobridged systems as **38**[37] and fails only when there are fewer than five bridging atoms.[57] In particular, 4,5-dicarbethoxy-3,6-hexanooxepine **34** can be easily synthesized on a multigram scale[15,33]via oxaquadricyclane **11** obtained from 3,4-dicarbethoxyfuran and cyclooctyne.[58] A new approach to [*n*]paracyclophanes[5] **90–93** could be developed from oxepine precursors. Heptano and decano derivatives **35** and **36** undergo deoxygenation in one step either with McMurry's reagent[34] or with [Rh-$(CO)_2Cl]_2$.[35] These reactions probably proceed via the corresponding arene oxides.[38] In contrast, no valence tautomerism could be detected in the pentano and hexano series. Compound **34** was found to be stable even against sulfuric acid in ethanol under reflux![39] However, deoxygenation to [6]paracyclophane **91** could be realized in a two-step procedure. Transannular addition of bromine to **34** gave dibromo epoxide **94**, which on subsequent treatment with a modified McMurry reagent afforded **91** in 61% yield (Scheme 18).[33,59]

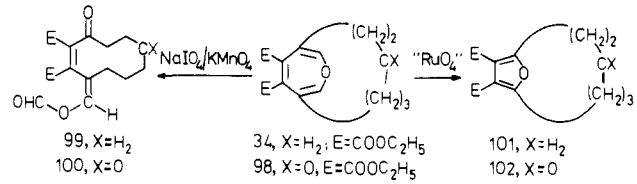
The oxaquadricyclane → oxepine approach makes disubstituted [6]- and [7]paracyclophanes **90–92** available in amounts that can be used in further preparations.[33,34] These boat-shaped benzene derivatives represent interesting borderline cases. On one hand, they are typically aromatic benzene derivatives with respect to their spectroscopic properties; on the other hand, they very easily undergo the addition and cycloaddition reactions characteristic of alkenes and alkadienes.[33,34]

Oxaquadricyclane **95** was the starting material for the synthesis of the enantiomeric (*P*)-(−)- and (*M*)-(+)-4-carboxy-3,6-hexanooxepines [(*P*)-**96** and (*M*)-**96**] and the (*M*)-(−)- and (*P*)-(+)-8-carboxy[6]paracyclophanes [(*M*)-**97** and (*P*)-**97**] (Scheme 19).[36,60] The absolute configurations of these compounds, which show interesting chiroptical properties, were determined by X-ray

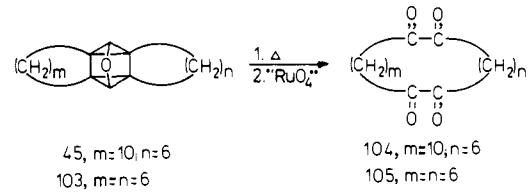
SCHEME 19



SCHEME 20



SCHEME 21



structural analysis of a camphanoyl derivative of 4-(hydroxymethyl)-3,6-hexanooxepine.[61]

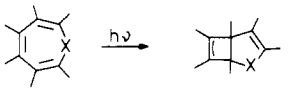
Attempted synthesis of [5]paracyclophanes from oxepines **33** and **38** have thus far failed.[32,37] For shorter bridged [*n*]paracyclophanes the photochemical Dewar benzene approach of Bickelhaupt and Tobe must be used.[62,63]

The above synthesis of paracyclophanes via oxepines takes advantage of the easy reduction of the latter. The synthetic usefulness of oxepinophanes is demonstrated by the results of their oxidation. Treatment of **34** and **98** with sodium metaperiodate/potassium permanganate according to Lemieux and von Rudloff[64] affords highly functionalized ten-membered-ring systems **99** and **100**[15,65] by cleavage of one carbon–carbon double bond (Scheme 20). It is noteworthy that in the case of **98** the bond nearer the carbonyl group is cleaved in a regioselective manner, probably because of less transannular shielding of this bond.[65]

The sequence **98** → **100** can also be used for a new approach to hydroazulene lactones (see section V.G). The oxidation of oxepinophanes **34** and **98** with ruthenium tetraoxide, generated in situ according to the method of Sharpless and co-workers,[66] produces [6]-(2,5)furanophanes **101** and **102** in yields of up to 56%. The mechanism of this surprising ring contraction is not clear at the present time.[48,65] Enol ester **100** is also oxidized to **102** and therefore may be an intermediate.

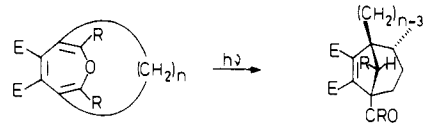
An oxidation with ruthenium tetraoxide[66] was also used for a new approach to macrocyclic bis-α-diketones:

SCHEME 22



106, X=N-R

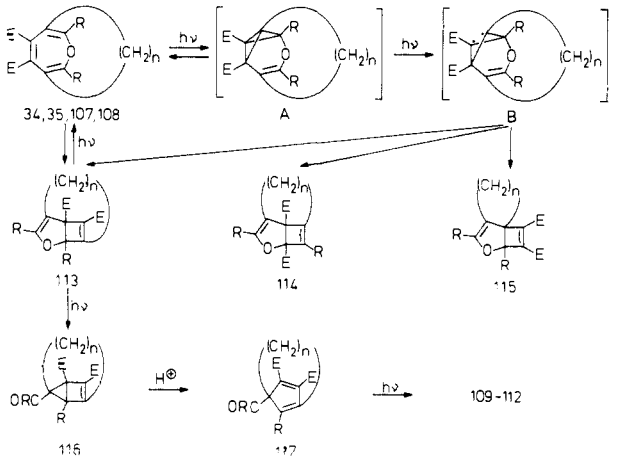
SCHEME 23



	n	R	E
34	6	H	$COOC_2H_5$
35	7	H	$COOCH_3$
107	6	H	$COOCH_3$
108	6	D	$COOCH_3$

	n	R	E
109	6	H	$COOC_2H_5$
110	7	H	$COOCH_3$
111	6	H	$COOCH_3$
112	6	D	$COOCH_3$

SCHEME 24



34,35,107,108 A B 113 114 115 116 117 109-112

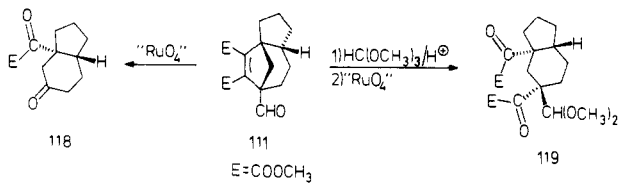
Bisannelated oxaquadricyclanes **45** and **103** give on thermolysis 4,5-annelated 3,6-bridged oxepines (see section IV.B), all double bonds of which are cleaved to afford monocyclic tetracarbonyl derivatives[7] **104** and **105** in 30–40% yield (Scheme 21).[67]

D. The Photochemistry of Heteropines: Synthesis of Polycyclic Compounds

The symmetry-allowed disrotatory photochemical ring closure[68] of oxepine and azepine derivatives to give 2-oxa- and 2-azabicyclo[3.2.0]hepta-3,6-dienes **106** was first studied by Paquette and co-workers (Scheme 22).[69] Many examples of this photoisomerization are known at the present time.[55,61,70] 4,5-Dicarbalkoxy-3,6-hexano- and -heptanooxepines **34**, **35**, **107**, and **108** represent a remarkable exception. Irradiation of these ansa compounds produces tricyclic aldehydes **109–112** in yields between 30 and 65% (Schemes 23 and 24).[70]

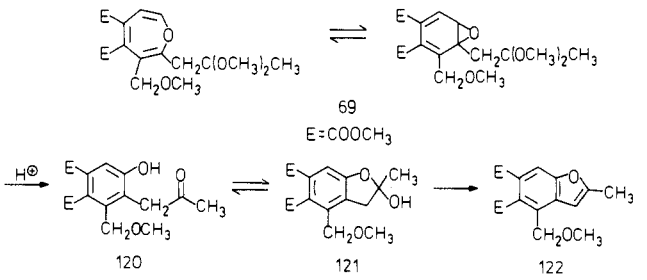
It could be shown that this rearrangement proceeds via dihydrofurans **113–115**, cyclopropanecarbaldehydes **116**, and cyclopentadienecarbaldehydes **117** as intermediates. In order to explain the occurrence of rearranged dihydrofurans, bicyclobutanes A and cyclobutane-1,3-diyl radicals B were suggested as intermediates.[70] The photochemical rearrangement **107** → **111** can be used for a new approach to a highly functionalized *trans*-hexahydroindanes **118** and **119** by oxidative cleavage of the C=C double bond of aldehyde **111** (Scheme 25).[71]

SCHEME 25



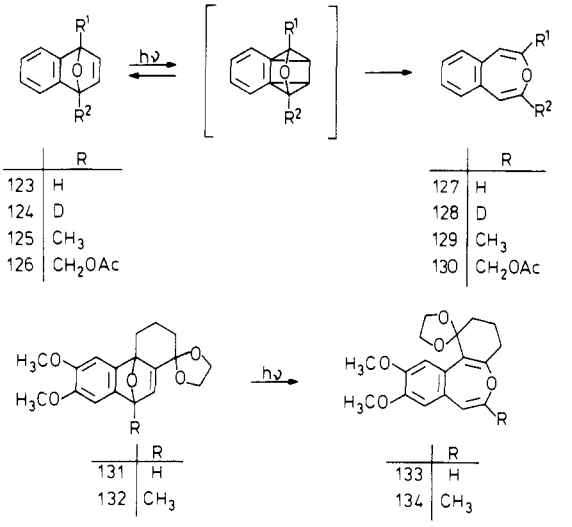
118 111 E=$COOCH_3$ 119

SCHEME 26



69 E=$COOCH_3$ 120 121 122

SCHEME 27



	R
123	H
124	D
125	CH_3
126	CH_2OAc

	R
127	H
128	D
129	CH_3
130	CH_2OAc

	R
131	H
132	CH_3

	R
133	H
134	CH_3

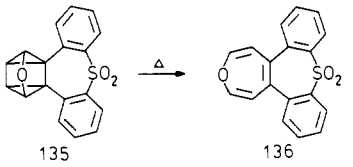
With esters of optically active secondary alcohols this photorearrangement shows chiral induction and produces enantiomerically pure aldehydes **111**.[71] The synthesis of optically active α-keto esters **119** via oxaquadricyclane **87** again demonstrates the large scope of oxaquadricyclane transformations.

E. Synthesis of Benzofurans, Benzoxepines, and Related Compounds

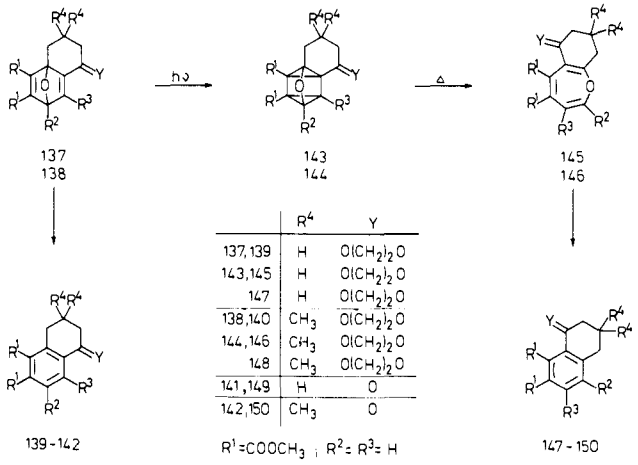
As was shown in section IV.E oxepine/benzene oxide **69** is the main product of the thermolysis of oxaquadricyclane **67** (R = $CH_2C(OCH_3)_2CH_3$). Treatment of **69** with *p*-toluenesulfonic acid in ether leads to benzofuran **122** in 70% yield. Phenol **120** and hemiacetal **121** are intermediates in this reaction sequence (Scheme 26).[51]

Irradiation of benzoannelated oxanorbornadienes **123–126**, easily available from benzyne and furans, leads to rearranged benzoxepines **127–130**, albeit in low yields between 5 and 10% (Scheme 27).[72–74] Ziegler and Hammond have shown that this reaction proceeds via nonisolable oxaquadricyclane intermediates.[72] The analogous reactions with benzazanorbornadienes (**123**, NCOOR instead of O)[50,73] and epoxyphenanthrenes **131**/**132**[74,75] give somewhat better yields (**133**/**134**:

SCHEME 28



SCHEME 29



	R^4	Y
137,139	H	$O(CH_2)_2O$
143,145	H	$O(CH_2)_2O$
147	H	$O(CH_2)_2O$
138,140	CH_3	$O(CH_2)_2O$
144,146	CH_3	$O(CH_2)_2O$
148	CH_3	$O(CH_2)_2O$
141,149	H	O
142,150	CH_3	O

25–33%). In the case of the thiepine *S,S*-dioxide system oxaquadricyclane **135** can be isolated. It rearranges cleanly to thiepinooxepine **136** [$t_{1/2}$(20 °C) ~ 6 h in $CHCl_3$] (Scheme 28).[73]

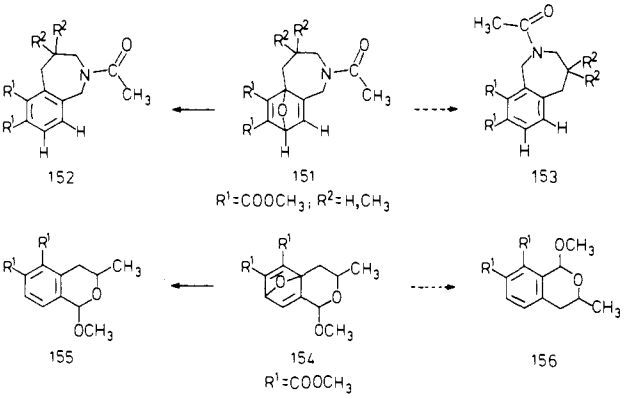
F. Transpositions of Carbonyl and Other Groups in Ring Systems via Oxaquadricyclanes

According to the mechanism discussed in section IV.A, the 7-heteronorbornadiene → 3-heteroquadricyclane → 1-heteropine sequence is accompanied by a skeletal rearrangement. Carbon atoms that are in an α position to one another in the starting material migrate into β positions in the final product and vice versa. This fact can be used to bring about transpositions of carbonyl and other groups[76] in ring systems. In this way it is possible to synthesize isomeric compounds from one and the same starting material. The general procedure is outlined in the Scheme 29 by the reaction sequence **139** ← **137** → **143** → **145** → **147**.[75]

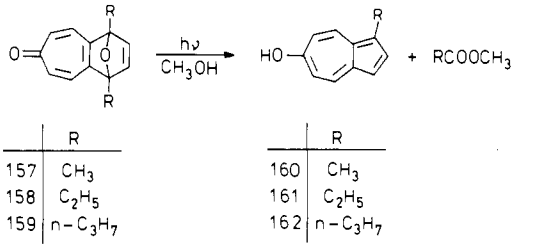
On one hand, oxanorbornadienes **137** and **138** can be deoxygenated by known methods to give tetralone diesters **139** and **140** without any migration of the substituents. On the other hand, irradiation of **137** and **138**, thermolysis of **143** and **144**, and subsequent deoxygenation of **145** and **146** lead to an isomeric tetralone skeleton in which the carbons bearing R^2–R^4 and Y have moved into other positions relative to the carbomethoxy-substituted carbon atoms. In summary, the conversion of **138** to **148** is equivalent to a combined 1,2-transposition of the dimethylmethylene group and a 1,4-transposition of the protected carbonyl function.[75] This sequence was also applied to the synthesis of isomeric phenol derivatives.[75,77]

The transposition concept via isolable oxaquadricyclanes has a unique application in that it allows a shift of heteroatoms in ring systems that is otherwise not possible. This was demonstrated by the synthesis of isomeric benz[*c*]azepines[78] and isochromane derivatives.[79] The reaction sequences **152** ← **151** → **153** and **155** ← **154** → **156** imply the 1,3-transposition of an amide function and the 1,2-transposition of an acetal oxygen, respectively (Scheme 30).

SCHEME 30



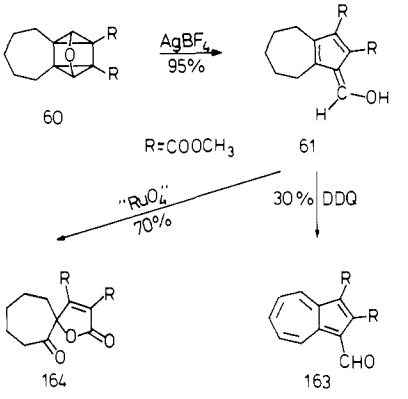
SCHEME 31



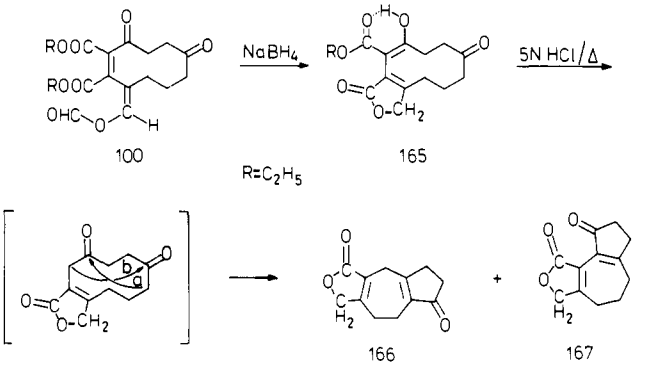
	R
157	CH_3
158	C_2H_5
159	n-C_3H_7

	R
160	CH_3
161	C_2H_5
162	n-C_3H_7

SCHEME 32



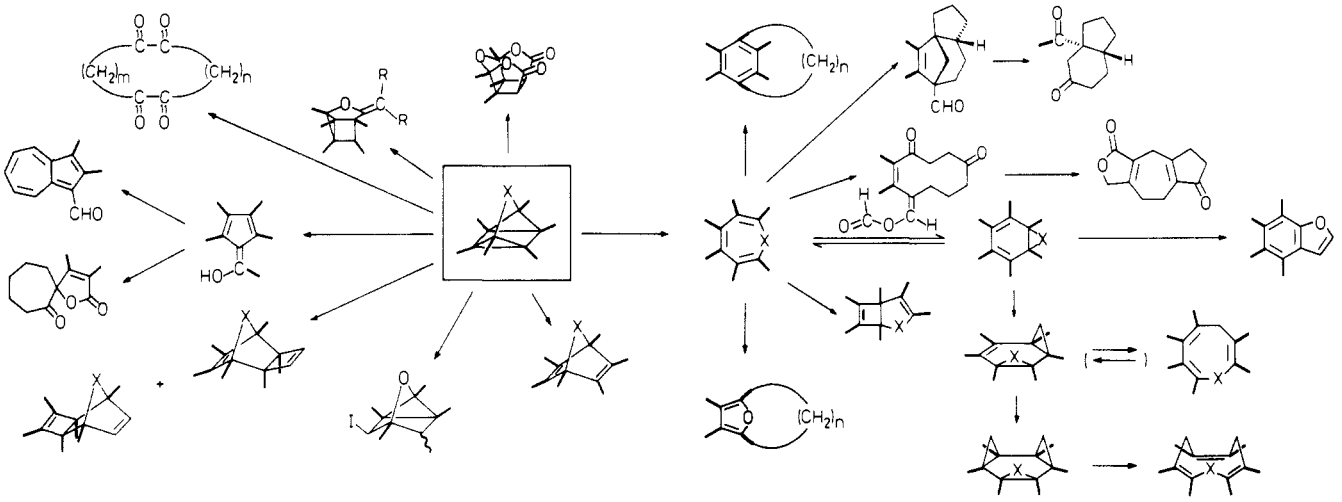
SCHEME 33



G. Synthesis of Azulene Derivatives and Related Compounds

The syntheses described so far in section V.B–F took advantage of the rearrangement of the heteroquadricyclanes to the seven-membered heteropines.

SCHEME 34



The alternative rearrangement of 3-oxaquadricyclanes to 6-hydroxyfulvenes (section IV.D) offers a new approach to azulene derivatives.

Irradiation of oxanorbornadienes **157–159**, readily available from 4,5-dehydrotropone and furans in methanol, gives 6-hydroxyazulenes **160–162** in high yield (Scheme 31).[80] The proposed mechanism involves the formation of a carbene intermediate from the corresponding oxaquadricyclane via a diradical, subsequent addition of methanol, and elimination of $RCOOCH_3$ to give **160–162**.[80]

Another route to substituted azulenes starts with the silver ion catalyzed isomerization of oxaquadricyclane **60** to hydroxyfulvene **61**. Compound **61** can be dehydrogenated with DDQ or NBS to azulenecarbaldehyde **163** (Scheme 32).[48] Several azulenes have been synthesized by selective reactions with the aldehyde group.

A remarkable rearrangement to butenolide **164** takes place in about 70% yield when hydroxyfulvene **61** is oxidized with ruthenium tetraoxide.[48]

Finally, it should be noted that cyclodecadienedione **100** obtained via the oxaquadricyclane route (section V.C) can be converted in a two-step sequence to a 1:1 mixture of hydroazulene lactones **166** and **167**, which are easily separated.[65] Lactone **166** has the framework of naturally occurring sesquiterpene lactones (Scheme 33).[81]

VI. Conclusion

The present review has the aim of demonstrating the broad scope of possible transformations of 3-oxa- and 3-azaquadricyclanes and to invite organic chemists to use these highly strained compounds for synthetic purposes. Scheme 34 gives an overview on the reactions described so far.

We noted earlier that in particular the formation of oxaquadricyclanes by irradiation of oxanorbornadienes fails only in a few cases.[9,17] It is apparent, however, that at present the clearest need in this area is the development of syntheses of new starting materials, such as suitable furans, pyrroles[82] and other heterodienes, reactive alkynes, or their equivalents. Prinzbach and co-workers have discussed this aspect earlier and recently in detail.[9,14,30]

At this point we note that the publication of an easy, multigram synthesis of only one valuable compound, namely cyclooctyne, by Brandsma and Verkruijsse in 1978[58] stimulated new developments in the field of oxaquadricyclane chemistry.[15,17,32–36,59,61,65,70,71] Therefore we are looking with optimism into the future.[83]

Acknowledgments. Financial support of our own contribution by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie is gratefully acknowledged. For correspondence and helpful comments we are indebted to Professor Horst Prinzbach. We thank Mrs. V. Sadowski and Dr. M. C. L. Gerry for proofreading the manuscript.

VII. References

(1) Prinzbach, H.; Arguelles, M.; Druckrey, E. *Angew. Chem.* **1966**, *78*, 1057; *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 1039. Druckrey, E.; Arguelles, M.; Prinzbach, H. *Chimia* **1966**, *20*, 432.
(2) This compound and methyl derivatives thereof were reported in 1967 also by: Payo, E.; Cortes, L.; Mantecon, J.; Rivas, C.; De Pinto, G. *Tetrahedron Lett.* **1967**, 2415. Payo, E.; Cortes, L.; Mantecon, J.; Rivas, C. *Acta Cient. Venez.* **1967**, *18*, 130; *Chem. Abstr.* **1969**, *70*, 3681d.
(3) Prinzbach, H.; Fuchs, R.; Kitzing, R. *Angew. Chem.* **1968**, *80*, 78; *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 67.
(4) von R. Schleyer, P.; Williams, E. J.; Blanchard, K. R. *J. Am. Chem. Soc.* **1970**, *92*, 2377.
(5) For recent reviews, see: Meier, H. In *Methoden der organischen Chemie (Houben-Weyl), Photochemie I*; Thieme: Stuttgart, 1975; Vol. IV/5a, p 222. Greenberg, A.; Liebman, J. F. *Strained Organic Molecules*; Academic Press: New York, 1978. Cristol, S. J. *Tetrahedron* **1986**, *42*, 1617.
(6) Prinzbach, H.; Babsch, H. *Angew. Chem.* **1975**, *87*, 772; *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 753.
(7) Corey, E. J.; Winter, R. A. E. *J. Am. Chem. Soc.* **1963**, *85*, 2677. Corey, E. J. *Pure Appl. Chem.* **1967**, *14*, 19.
(8) Hall, R. G.; Tripett, S. *Tetrahedron Lett.* **1982**, *23*, 2603. De Lucchi, O.; Lucchini, V.; Pasquato, L.; Modena, G. *J. Org. Chem.* **1984**, *49*, 596. De Lucchi, O.; Modena, G. *Tetrahedron* **1984**, *40*, 2585. Carr, R. V. C.; Williams, R. V.; Paquette, L. A. *J. Org. Chem.* **1983**, *48*, 4976. Mirsadeghi, S.; Rickborn, B. *J. Org. Chem.* **1985**, *50*, 4340.
(9) Prinzbach, H.; Bingmann, H.; Markert, J.; Fischer, G.; Knothe, L.; Eberbach, W.; Brokatzky-Geiger, J. *Chem. Ber.* **1986**, *119*, 589 and references cited therein.
(10) Zimmerman, H. E. In *Rearrangements in Ground and Excited States*; De Mayo, P., Ed.; Academic Press: New York, 1980; p 131.
(11) Stusche, D.; Prinzbach, H. *Chem. Ber.* **1973**, *106*, 3817.
(12) Hall, R. H.; Harkema, S.; Den Hertog, H. J.; Van Hummel, G. J.; Reinhoudt, D. N. *Recl. Trav. Chim. Pays-Bas* **1981**, *100*, 312.
(13) Tochtermann, W.; Goepfert, A., unpublished results. Goepfert, A. Diplomarbeit Universität Kiel, Kiel, FRG, 1988.
(14) Prinzbach, H.; Bingmann, H.; Fritz, H.; Markert, J.; Knothe, L.; Eberbach, W.; Brokatzky-Geiger, J.; Sekutowski, J. C.; Krüger, C. *Chem. Ber.* **1986**, *119*, 616 and references cited therein.

(15) Tochtermann, W.; Rösner, P. *Tetrahedron Lett.* **1980**, *21*, 4905; *Chem. Ber.* **1981**, *114*, 3725.
(16) According to recent ^{13}C NMR studies, the original assignment of signals to the tetrasubstituted cyclopropane carbons has to be interchanged.[13]
(17) Vagt, U.; Haase, M.; Konusch, J.; Tochtermann, W. *Chem. Ber.* **1987**, *120*, 769.
(18) Hogeveen, H.; Nusse, B. J. *Tetrahedron Lett.* **1976**, 699.
(19) Hogeveen, H.; Nusse, B. J. *J. Organomet. Chem.* **1979**, *171*, 237.
(20) Spek, A. L. *Cryst. Struct. Commun.* **1978**, *7*, 159. Similar differences were recently found in the X-ray structures of 11 and 87. Tochtermann, W.; Vogt, C.; Peters, E.-M.; Peters, K.; von Schnering, H. G., unpublished results.
(21) Eberbach, W.; Perroud-Arguelles, M.; Achenbach, H.; Druckrey, E.; Prinzbach, H. *Helv. Chim. Acta* **1971**, *54*, 2579.
(22) Hogeveen, H.; Nusse, B. J. *J. Am. Chem. Soc.* **1978**, *100*, 3110.
(23) Review: Vogel, E.; Günther, H. *Angew. Chem.* **1967**, *79*, 429; *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 385.
(24) Haselbach, E.; Martin, H.-D. *Helv. Chim. Acta* **1974**, *57*, 472.
(25) Tanny, S. R.; Fowler, F. W. *J. Am. Chem. Soc.* **1973**, *95*, 7320.
(26) Hall et al. (Hall, H. K., Jr.; Smith, C. D.; Baldt, J. H. *J. Am. Chem. Soc.* **1973**, *95*, 3197) give a value of 78.7 kcal/mol for the strain energy of quadricyclane.
(27) Huisgen, R. *Angew. Chem.* **1980**, *92*, 979; *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 947.
(28) Prinzbach, H.; Arguelles, M.; Vogel, P.; Eberbach, W. *Angew. Chem.* **1967**, *79*, 1103; *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 1070. Prinzbach, H.; Fuchs, R.; Kitzing, R.; Achenbach, H. *Angew. Chem.* **1968**, *80*, 699; *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 727.
(29) Stapersma, J.; Kuipers, P.; Klumpp, G. W. *Recl. Trav. Chim. Pays-Bas* **1982**, *101*, 213.
(30) For a comparison of quadricyclanes and their heterocyclic analogues, see: Prinzbach, H. *Pure Appl. Chem.* **1968**, *16*, 17. Syntheses with 3-methylene- and 3-ketoquadricyclanes: Babsch, H.; Fritz, H.; Prinzbach, H. *Tetrahedron Lett.* **1975**, 4677. Prinzbach, H.; Babsch, H.; Fritz, H. *Tetrahedron Lett.* **1976**, 2129. Bingmann, H.; Beck, A.; Fritz, H.; Prinzbach, H. *Chem. Ber.* **1981**, *114*, 1679. Beck, A.; Bingmann, H.; Kagabu, S.; Knothe, L.; Hädicke, E.; Prinzbach, H. *Chem. Ber.* **1983**, *116*, 1963. Schweikert, O.; Netscher, T.; Knothe, L.; Prinzbach, H. *Chem. Ber.* **1984**, *117*, 2027.
(31) Recent reviews: Reissig, H.-U. In *The Chemistry of the Cyclopropyl Group*; Rappoport, Z., Ed.; Wiley: Chichester, 1987; Chapter 8. Reissig, H.-U. *Top. Curr. Chem.* **1988**, *144*, 73. Brückner, C.; Reissig, H.-U. *Chem. Ber.* **1987**, *120*, 617.
(32) Jessen, J. L.; Schroeder, G.; Tochtermann, W. *Chem. Ber.* **1985**, *118*, 3287.
(33) Liebe, J.; Wolff, C.; Krieger, C.; Weiss, J.; Tochtermann, W. *Chem. Ber.* **1985**, *118*, 4144.
(34) Hunger, J.; Wolff, C.; Tochtermann, W.; Peters, E.-M.; Peters, K.; von Schnering, H. G. *Chem. Ber.* **1986**, *119*, 2698.
(35) Tochtermann, W.; Haase, M. *Chem. Ber.* **1984**, *117*, 2293.
(36) Tochtermann, W.; Vagt, U.; Snatzke, G. *Chem. Ber.* **1985**, *118*, 1996.
(37) Jenneskens, L. W.; Kostermans, G. B. M.; Ten Brink, H. J.; De Wolf, W. H.; Bickelhaupt, F. *J. Chem. Soc., Perkin Trans. 1* **1985**, 2119.
(38) Recent review: Shirwaiker, G. S.; Bhatt, M. V. *Adv. Heterocycl. Chem.* **1984**, *37*, 67.
(39) Rösner, P.; Wolff, C.; Tochtermann, W. *Chem. Ber.* **1982**, *115*, 1162.
(40) Prinzbach, H.; Vogel, P. *Helv. Chim. Acta* **1969**, *52*, 369.
(41) Epe, B.; Rösner, P.; Tochtermann, W. *Liebigs Ann. Chem.* **1980**, *1889*.
(42) Vogel, E.; Altenbach, H.-J.; Drossard, J.-M.; Schmickler, H.; Stegelmeier, H. *Angew. Chem.* **1980**, *92*, 1053; *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 1016. Altenbach, H.-J.; Blech, B.; Marco, J. A.; Vogel, E. *Angew. Chem.* **1982**, *954*, 789; *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 722. For 1*H*-azepines, see also: Hafner, K. *Angew. Chem.* **1963**, *75*, 1041; *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 165.
(43) Nishida, S.; Imai, T.; Hamatsu, K.; Tsuji, T.; Murakami, M. *J. Chem. Soc., Chem. Commun.* **1983**, 1191.
(44) Deslongchamps, P.; Kallos, J. *Can. J. Chem.* **1967**, *45*, 2235.
(45) Kaupp, G.; Prinzbach, H. *Chem. Ber.* **1971**, *104*, 182.
(46) Bansal, R. K.; McCulloch, A. W.; Rasmussen, P. W.; McInnes, A. G. *Can. J. Chem.* **1975**, *53*, 138.
(47) McCulloch, A. W.; Stanovnik, B.; McInnes, A. G. *Can. J. Chem.* **1971**, *49*, 241.
(48) Tochtermann, W.; Pahl, A.; Peters, E.-M.; Peters, K.; von Schnering, H. G. *Chem. Ber.* **1988**, *121*, 493.
(49) Bruggink, A.; Hogeveen, H. *Tetrahedron Lett.* **1972**, 4961.
(50) Kaupp, G.; Perreten, J.; Leute, R.; Prinzbach, H. *Chem. Ber.* **1970**, *103*, 2288.
(51) Glombik, H.; Wolff, C.; Tochtermann, W. *Chem. Ber.* **1987**, *120*, 775. See also: Hasenrück, K.; Martin, H. D. *Synthesis* **1988**, 569.
(52) Wenkert, E.; McPherson, C. A.; Sanchez, E. L.; Webb, R. L. *Synth. Commun.* **1973**, *3*, 255. Wenkert, E.; Craveiro, A. A.; Sanchez, E. L. *Ibid.* **1977**, *7*, 85.
(53) Nelsen, S. F.; Calabrese, J. C. *J. Am. Chem. Soc.* **1973**, *95*, 8385.
(54) In ref 37 Bickelhaupt and his group have used the term "Prinzbach–Tochtermann sequence" for the transformation of furans to oxepines.
(55) Prinzbach, H.; Kaupp, G.; Fuchs, R.; Joyeux, M.; Kitzing, R.; Markert, J. *Chem. Ber.* **1973**, *106*, 3824. Prinzbach, H.; Stusche, D.; Breuninger, M.; Markert, J. *Ibid.* **1976**, *109*, 2823. Prinzbach, H.; Stusche, D.; Markert, J.; Limbach, H.-H. *Ibid.* **1976**, *109*, 3505.
(56) For the synthesis of the related trioxa- and triaza-tris-σ-homobenzenes (benzene trioxides and triimines), see: Vogel, E.; Altenbach, H.-J.; Sommerfeld, C.-D. *Angew. Chem.* **1972**, *84*, 986; *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 939. Schwesinger, R.; Prinzbach, H. *Angew. Chem.* **1972**, *84*, 990; *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 942. Schwesinger, R.; Fritz, H.; Prinzbach, H. *Chem. Ber.* **1979**, *112*, 3317. Keller, R.; Schwesinger, R.; Fritsche, W.; Schneider, H.-W.; Hunkler, D.; Prinzbach, H. *Ibid.* **1979**, *112*, 3347. Schwesinger, R.; Breuninger, M.; Gallenkamp, B.; Müller, K.-H.; Hunkler, D.; Prinzbach, H. *Ibid.* **1980**, *113*, 3127 and references cited therein. For S,S,S and O,N,C systems, see: Kagabu, S.; Kaiser, C.; Keller, R.; Becker, P. G.; Müller, K.-H.; Knothe, L.; Rihs, G.; Prinzbach, H. *Chem. Ber.* **1988**, *121*, 741. Zipperer, B.; Müller, K.-H.; Gallenkamp, B.; Hildebrand, R.; Fletschinger, M.; Burger, D.; Pillat, M.; Hunkler, D.; Knothe, L.; Fritz, H.; Prinzbach, H. *Chem. Ber.* **1988**, *121*, 757.
(57) Tochtermann, W.; Pahl, A., unpublished results. Pahl, A. Diplomarbeit Universität Kiel, Kiel, FRG, 1985.
(58) Brandsma, L.; Verkruijsse, H. D. *Synthesis* **1978**, 290.
(59) Liebe, J.; Wolff, C.; Tochtermann, W. *Tetrahedron Lett.* **1982**, *23*, 171.
(60) *rac*-8-Carboxy[6]paracyclophane was first synthesized by: Tobe, Y.; Kakiuchi, K.; Odaira, Y.; Hosaki, T.; Kai, Y.; Kasai, N. *J. Am. Chem. Soc.* **1983**, *105*, 1376.
(61) Beitz, G.; Vagt, U.; Tochtermann, W. *Tetrahedron Lett.* **1985**, *26*, 721. Tochtermann, W.; Olsson, G.; Vogt, C.; Peters, E.-M.; Peters, K.; von Schnering, H. G. *Chem. Ber.* **1987**, *120*, 1523.
(62) [5]Paracyclophanes: Jenneskens, L. W.; De Kanter, F. J. J.; Kraakman, P. A.; Turkenburg, L. A. M.; Koolhaas, W. E.; De Wolf, W. H.; Bickelhaupt, F.; Tobe, Y.; Kakiuchi, K.; Odaira, Y. *J. Am. Chem. Soc.* **1985**, *107*, 3716. Tobe, Y.; Kaneda, T.; Kakiuchi, K.; Odaira, Y. *Chem. Lett.* **1985**, 1301. Kostermans, G. B. M.; De Wolf, W. H.; Bickelhaupt, F. *Tetrahedron Lett.* **1986**, *27*, 1095; *Tetrahedron* **1987**, *43*, 2955.
(63) [4]Paracyclophanes: Kostermans, G. B. M.; Bobeldijk, M.; De Wolf, W. H.; Bickelhaupt, F. *J. Am. Chem. Soc.* **1987**, *109*, 2471. Tsuji, T.; Nishida, S. *J. Chem. Soc., Chem. Commun.* **1987**, 1189; *J. Am. Chem. Soc.* **1988**, *110*, 2157.
(64) Lemieux, R. U.; von Rudloff, E. *Can. J. Chem.* **1955**, *33*, 1701. von Rudloff, E. *Ibid.* **1955**, *33*, 1714.
(65) Tochtermann, W.; Luttmann, K.; Peters, E.-M.; Peters, K.; von Schnering, H. G. *Tetrahedron Lett.* **1987**, *28*, 2521. Tochtermann, W.; Luttmann, K., unpublished results. Luttmann, K. Dissertation Universität Kiel, Kiel, FRG, 1987.
(66) Carlsen, P. H. J.; Katsuki, T.; Martin, V. S.; Sharpless, K. B. *J. Org. Chem.* **1981**, *46*, 3936.
(67) Tochtermann, W.; Haase, M.; Dibbern, R. *Tetrahedron Lett.* **1988**, *29*, 189.
(68) Woodward, R. B.; Hoffmann, R. *Angew. Chem.* **1969**, *81*, 797; *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 781.
(69) Paquette, L. A.; Barrett, J. H. *J. Am. Chem. Soc.* **1966**, *88*, 1718.
(70) Sczostak, A.; Sönnichsen, F.; Tochtermann, W.; Peters, E.-M.; Peters, K.; von Schnering, H. G. *Tetrahedron Lett.* **1985**, *26*, 5677. Tochtermann, W.; Olsson, G.; Sczostak, A.; Sönnichsen, F.; Frauenrath, H.; Runsink, J.; Peters, E.-M.; Peters, K.; von Schnering, H. G. *Chem. Ber.* **1989**, *122*, 199.
(71) Tochtermann, W.; Sönnichsen, F.; Schlösser, U., unpublished results. Sönnichsen, F.; Schlösser, U. Dissertationen Universtität Kiel, Kiel, FRG, 1988.
(72) Ziegler, G. R.; Hammond, G. S.; *J. Am. Chem. Soc.* **1968**, *90*, 513. Ziegler, G. R. *Ibid.* **1969**, *91*, 446.
(73) Prinzbach, H.; Würsch, P.; Vogel, P.; Tochtermann, W.; Franke, C. *Helv. Chim. Acta* **1968**, *51*, 911. The recent synthesis of 8*H*-3-Oxaheptalen-8-one in which the seven-membered rings are fused in the same way as in **136** probably proceeds via an oxaquadricyclane intermediate, too: Nakazawa, T.; Ishihara, M.; Jinguji, M.; Yamaguchi, M.; Yamochi, H.; Murata, I. *Chem. Lett.* **1988**, 1647.
(74) Tochtermann, W.; Timm, H.; Diekmann, J. *Tetrahedron Lett.* **1977**, 4311.
(75) Tochtermann, W.; Timm, H. *Tetrahedron Lett.* **1978**, 2145. Tochtermann, W.; Köhn, H. *Chem. Ber.* **1980**, *113*, 3249.

(76) Reviews: Morris, D. G. *Q. Rev., Chem. Soc.* **1982**, *11*, 397. Kane, V. V.; Singh, V.; Martin, A. *Tetrahedron* **1983**, *39*, 345.
(77) Tochtermann, W.; Timm, H. *Heterocycles* **1978**, *11*, 327.
(78) Tochtermann, W.; Heuer, M. *Chem. Ber.* **1982**, *115*, 2125.
(79) Glombik, H.; Tochtermann, W. *Chem. Ber.* **1984**, *117*, 2422.
(80) Nakazawa, T.; Ashizawa, M.; Jinguji, M.; Yamaguchi, M.; Murata, I. *Chem. Lett.* **1986**, 2045.
(81) Review: Ayer, W. A.; Browne, L. M. *Tetrahedron* **1981**, *37*, 2199.
(82) Diels–Alder reactions of *N*-aminopyrrole derivatives with reactive alkynes are known: Schultz, A. G.; Shen, M.; Ravichandran, R. *Tetrahedron Lett.* **1981**, *22*, 1767. Shen, M.; Schultz, A. G. *Tetrahedron Lett.* **1981**, *22*, 3347.
(83) A new approach to the 3-oxaquadricyclane system by intramolecular photochemical [2 + 2 + 2 + 2] cycloaddition of a polycyclic compound was recently observed: Prinzbach, H.; Wollenweber, M., unpublished results. Wollenweber, M. Diplomarbeit Universität Freiburg/Brsg., Freiburg, FRG, 1988.