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Dressel, Jurgen

THROUGH-BOND INTERACTION OF TWO MUTUALLY PERPENDICULAR PI-RIBBONS THROUGH A CYCLOBUTANE RELAY

The Ohio State University

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To my wife, Linda, and my parents
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I want to thank my parents, who dared the sacrifices involved with allowing me a thorough education; my wife, Linda, who shared with me the ups and downs of a graduate student's wife and was the source of light and comfort in darker hours; Professor Herbert Mayr (then at the Friedrich Alexander-Universität of Erlangen-Nurnberg), who was able to ignite my enthusiasm for organic chemistry; Drs. Heiner Jendralla, Yuji Miyahara and Ho-Shen Lin, mentors and friends at the same time, who introduced me to the art of observation and their philosophies of science; Professor Leo Paquette, my preceptor, who had enough tolerance for the follies of a young, unseasoned mind and pulled me out of many dead end streets; Professors Swenton, Shechter and Hart for inspiring lectures; Christian Schade, Jeff Romine, Howard Rosenzweig and Dan Cheney, friends, with whom I have spent many happy hours inside and outside of chemistry; other friends like Mark Okazaki, Jesus Ezquerra, Dennis St. Laurent, Ting Zhong Wang and Clifford Lau without whose unselfish help this dissertation could not have been completed; my wife Linda, and Philipp Wadsworth for their help with the structural formulae; Dr. Marc-Andre Poupart
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PUBLICATIONS AND PRESENTATION


FIELDS OF STUDY

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CHAPTER I

PREFACE

Have you ever tried to explain to a fellow natural scientist, or even worse, to somebody who has only rudimentary, if any, knowledge of chemistry, why you are doing what you are doing?

What kept me going during my dissertational research was the beauty and simplicity of the highly symmetrical tricyclo[5.5.0.02/8]dodeca-3,5,9,11-tetraene (already the monstrosity of the awkward, though functional, name dampens the enthusiasm). I wanted to see that its $\text{D}_{2d}$ symmetry reduces the proton decoupled $^{13}\text{C}$ NMR spectrum to only three lines (the entire synthesis proved to be a lesson in group theory). On a more rational basis, theoreticians fill the journals with more and more calculations from which they derive models for reality, and if they are worthwhile models, they make predictions. However, the fascination of chemistry lies in the fact that it is an experimental science: the chemist can conceive an 'intelligent' experiment and then go into the laboratory and find evidence for the correctness of the model or disprove it (intentionally,
I avoid 'prove' the model. Day by day, organic chemists synthesize new compounds that help man fight diseases, increase crops, make hitherto uninhabitable areas habitable. However, whenever they develop a synthetic strategy, whenever they form or break bonds, they base their decisions on knowledge and models acquired and elucidated by chemists who do basic research.
CHAPTER II

INTRODUCTION

This work describes the successful synthesis of tricyclic, polyunsaturated hydrocarbons in which the 1 and 3 positions of one face as well as the 2 and 4 positions of the opposite face of a cyclobutane ring are connected by \( \pi \)-ribbons. The planes that are described by the two \( \pi \)-ribbons are perpendicular to each other (Figure 1).

Photoelectron spectroscopy and UV spectroscopy are to serve as probes of the extent to which these \( \pi \)-ribbons communicate through the cyclobutane relay \( \sigma \)-orbitals.

The third chapter presents the evidence that exists for spiroconjugation, the interaction of \( \pi \)-ribbons with cyclobutane rings, as well as how the concept of interaction of
mutually perpendicular π-ribbons through a cyclobutane relay evolved from spiroconjugation, a special form of through-space interaction.

Chapter IV provides a rationale for why the synthetic scheme of stepwise belting of an all-trans tetrasubstituted cyclobutane was chosen over other possible approaches.

The ensuing chapters describe the actual syntheses of the \([4^{1,4,4^{1,4}}] (1)\), \([4^{1,4,2^{1,2}}] (2)\), and \([4^{1,4,4^{2,3}}] (3)\) through-bond conjugated tricycles, their thermal and photochemical behavior, and their spectral properties.
CHAPTER III

HISTORICAL BACKGROUND

In 1967, Simmons and Fukunaga predicted theoretically that two mutually perpendicular, conjugated π-systems (π-ribbons) should interact with each other through space, if they were connected by a spirocarbon\(^1\) (Figure 2). They estimated that the overlap integral \(S_{\text{spiro}}\) of this 'spiro-conjugation\(^2\) would amount to about 20% of the overlap integral \(S_{\pi\pi}\) of two adjacent p-orbitals in benzene (distance of 1.48Å). Depending on the π-ribbon size, spiroconjugation would affect the energy levels of the unoccupied molecular orbitals, of the occupied molecular orbitals, or of both. The following qualitative orbital interaction diagram is
taken from reference (2) for three cases that have been studied theoretically and/or experimentally (Figure 3-5).

**Figure 3:** FMO's of 4

Spiro[2.2]penta-1,4-diene (4) belongs to the $D_{2d}$-symmetry group. The orbitals are labeled using the mirror planes $\sigma_1$ and $\sigma_2$ as symmetry elements.

**Figure 4:** FMO's of 5
Figure 5: FMO's of 6

In (1,1)spirene (4), only the etheno bridge LUMO's can interact with each other in a symmetry-allowed fashion, thereby decreasing the HOMO-LUMO gap. Symmetry allowed interaction in (2,1)spirene (5) is weak. It lowers the HOMO, and therefore simultaneously increases the HOMO-LUMO gap. In (2,2)spirene (6), the butadiene bridge HOMOs can interact with each other, thereby raising the HOMO and reducing the HOMO-LUMO gap.

At the same time as Simmons, Hoffmann considered spiroconjugation as one mode of interacting two allyl fragments and predicted an overlap for [3,3]spirarene (7) that
is one-fifth as efficient as in the other alternative, viz. benzene\(^4\) (Figure 6).

**Figure 6:** FMO's of 7

Gleiter described the utility and the rudimentary principles of photoelectron spectroscopy (PES) to study electronic phenomena\(^5\): photons from a helium discharge lamp [He(I)\(\alpha\)-line=21.21eV] eject electrons from the valence orbitals of the vaporized sample. From the known energy of the light source (\(h\nu\)) and the measured kinetic energy of the emitted electrons (\(E_{\text{kin}}\)), the vertical ionization potential \(I_{\text{vj}}\) can be calculated:

\[
I_{\text{vj}} = h\nu - E_{\text{kin}} = -\varepsilon_j
\]

If the effects of electron correlation and electron reorganization are neglected, the orbital energy \(\varepsilon_j\) can be approximated by the negative value of the ionization potential \(I_{\text{vj}}\) (Koopmans' theorem)\(^6\). Photoelectron spectroscopy therefore serves as direct method of measuring the energies
of occupied orbitals and therefore electronic effects that influence them. Indeed, Semmelhack and Heilbronner found evidence for spiroconjugation in the UV and PE spectra of \((2,2)\)spirene \((6)^7,8\), Figure 7:

**Figure 7:** UV and PE Spectral Data for 6, 8 and 9

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<td>UV: (\lambda_{\text{max}}/\text{nm})</td>
<td>270 (^9)</td>
<td>253</td>
<td>240 (^10)</td>
</tr>
<tr>
<td>PE: (I_{\nu,1}[-e(\text{HOMO})]/\text{eV})</td>
<td>7.99</td>
<td>8.10</td>
<td>8.60</td>
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<tr>
<td>(I_{\nu,2}[-e(\text{SUBHOMO})]/\text{eV})</td>
<td>9.22</td>
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As expected from the qualitative MO scheme (compare Figure 5), the degeneracy of the butadiene HOMO's of the two bridges is destroyed, and the new HOMO lies at a higher energy level (lower ionization potential) than a reference compound (7) that shows no spiroconjugation. The reduction of the HOMO-LUMO gap is displayed in the bathochromic shift of the UV absorption from 253 nm (in 8) to 270 nm (in 6).

Gordon et al. also rationalized the increased rate of dimerization of 6 with the reduced HOMO-LUMO gap and antibonding interaction between the dienophile LUMO and the spiroconjugated HOMO of the diene. Whereas 6 dimerizes
200 times faster than 7 at 50°C, both react with electron deficient dienophiles like dimethyl acetylenedicarboxylate with comparable rates [at 34°C = τ₁ (6) = 320 s, τ₁ (8) = 410 s]⁹. The smaller HOMO-LUMO gap makes the HOMO(dieneophile)-LUMO(diene) interaction energetically significant (Figure 8).

The resonance structure 11 of spiro[5.5]undeca-1,4,6,9-tetraene-3,8-dione (10) is isoelectronic with (2,2)spirene (6) if the oxygen atoms are ignored (Figure 9). Therefore its LUMOs are also degenerate and localized on the

---

**Figure 8:** FMO Scheme of Diels-Alder Reaction of 6

---

**Figure 9:** Resonance Structures of 10
respective cyclohexadienone moieties. In agreement with the qualitative orbital scheme of 6 (Figure 5), Gerson et al. did not observe a delocalization of the negative charge over both rings in the ESR spectrum of radical anion 12, when 10 was reduced electrochemically. The major splitting pattern was very similar for 12 and 13.

(Obviously contact ion pair formation of the radical anion with the counter cation will destroy the degeneracy and hinder delocalization)

Spiroconjugation in (2,1)spirene (5) is more ambiguous. Semmelhack et al. found no rate enhancement for the hydroxide-catalyzed tritium exchange of 14 in comparison to the Figure 10: Rates of Deprotonation for 14, 16, 17 and 18.
partially saturated reference compounds 16 to 18 (Figure 10). The anion 15 resulting from deprotonation of 14 is isoelectronic to 5 and should be stabilized by spiroconjugation.

Generation of the allyl anion 15 and its analogs by polarography also showed no increased stability for 15 as would be evident from a less negative half-wave potential (Figure 11).

Figure 11:  Half-wave Reduction Potentials for 19, 20, 21 and 22

\[
\begin{align*}
E^*_f \text{ (vs SCE)}/V & \quad -1.68 & -1.58 & -1.63 & -1.61 \\
\end{align*}
\]

Although the dialkylated (2,1)spirene 23 displays a hypsochromic shift from 257 nm (for 24) to 241 nm in the UV, as expected from the increased HOMO-LUMO gap in the qualitative MO scheme (Figure 4), the photoelectron spectra reveal a destabilization for 23 in comparison to 25 (Figure 12).

Dürr and Gleiter explained their observation by a transfer of electron density from the cyclopropene n orbital
Figure 12: UV and PE Spectral Data for 23, 24, 25 and 9

UV: $\lambda_{\text{max}}/\text{nm}$

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Figure 13: FMO's of 5
to the C\textsubscript{1\texttext{,}4}-C\textsubscript{4\texttext{,}7}-\sigma-\text{orbital of the cyclopentadiene moiety} [\sigma*(b\textsubscript{2})] (Figure 13). Since the butadiene HOMO also has high coefficients at positions 4 and 7, an increased charge density at carbons 4 and 7 would raise the HOMO energy of 23.

This charge transfer would also explain Semmelhack's reduction and deprotonation results (vide supra).

There are conflicting reports about the nature and function of the cyclopropane ring in 24 (a reference for the UV spectrum of 5) and its dialkylated form 25 (a reference for the PE Spectrum of 23). Whereas Clark and Fiato explain the abnormal downfield shift of the cyclopropyl protons in 24 in the $^1\text{H}$ NMR (60 MHz, CCl\textsubscript{4}, $\delta$ 1.62 ppm, compare spiro [4.2]heptane: $\delta$ 0.37 ppm) with the $\pi$-complex 26 as being an important resonance structure\textsuperscript{18}, Chiang and Wilcox cannot reconcile their observed electron diffraction pattern of 24 with equal or nearly equal bond lengths C\textsubscript{1}-C\textsubscript{4}, C\textsubscript{4}-C\textsubscript{5} and C\textsubscript{5}C\textsubscript{6}\textsuperscript{10}. With C\textsubscript{4}-C\textsubscript{5}=1.341Å and C\textsubscript{5}-C\textsubscript{6}=1.469Å, the geometry of 24 resembles isolated double and single bonds (1.339Å and 1.483Å, respectively).
In the case of (2,2)spirene (6), Heilbronner et al. indicated\(^8\) that the HOMO energy of cyclopentadiene (9) was a better reference point for the two highest occupied MO's in 6 than the HOMO of 8 because "in 8 this orbital is destabilized by the alkyl moieties, whereas in 6 the relative inductive influence of the two cyclopentadiene units on each other is about zero". On the assumption that the relative inductive influences of the cyclopentadiene and cyclopropene moieties are also about zero, the UV absorption of cyclopentadiene (9) might be a better reference point than the absorption of 24 to assess the potential spiroconjugation of 23. Then, even the UV spectrum shows no signs of a stabilizing spiroconjugation, i.e. a widening of the HOMO-LUMO gap: 9: 240 nm; 23: 241 nm.

Most pieces of evidence therefore point to the conclusion that spiroconjugation is too weak a stabilizing factor in (2,1)spirene (5) to override the destabilization by charge transfer.

Semiempirical CNDO/2 calculations assess spiroconjugation in spirenes as weak in comparison to the spirarenes\(^19\); however, when Gordon et al compared CNDO/2 and MINDO/3 results with the experimental PES data of 3, they found the CNDO/2 estimate for the \(\varepsilon\text{(SUBHOMO)}\) to be too large by 82\% and the MINDO/3 estimate to be too small by 32\%\(^{11}\). Only after adjustments of the core resonance integral \(\beta_{\text{spiro}}\),
were reasonable values for the HOMO splitting of (2,2)spirene (6) obtained. For (2,1)spirene (2), the modified MINDO/3\textsuperscript{11} as well as ab initio STO-3G calculations\textsuperscript{20} only predict a weak stabilization.

In summary, convincing evidence for spiroconjugation has only been found for (2,2)spirene, not for (2,1)spirene.

Figure 14: FMO's of Cycloalkenes and 1,3-Cycloalkadienes in Comparison to Walsh Orbitals of Cyclobutane and Cyclopropane
In spiroconjugation, the spirocarbon spacer poses a limit to the proximity of the termini of the mutually perpendicular π-ribbons and consequently to the overlap and extent of through-space interaction. Therefore, Gleiter and coworkers suggested in 1977/8 to replace the insulating spirocarbon by a suitable relay through which the π-ribbons could communicate more efficiently, viz., a cyclobutane ring\textsuperscript{21,22}. The cyclobutane ring fulfills all criteria for efficient molecular orbital overlap\textsuperscript{23}: (1) according to their PE spectra, the cyclobutane Walsh orbitals\textsuperscript{23,24} lie relatively close in energy to the molecular orbitals of cyclic alkenes or 1,3-alkadienes (E\textsubscript{r}-E\textsubscript{s} in third term, Ref. 29; \textbf{Figure 14}), (2) the puckered cyclobutane ring has the same D\textsubscript{2d} symmetry as the two mutually perpendicular π-ribbons with π=π' (for π≠π', the cyclobutane obviously also contains the symmetry elements of C\textsubscript{2v}, a subgroup of D\textsubscript{2d}); (3) in contrast to spiroconjugation, the cyclobutane relay orbitals are only one C-C single bond removed from the π-ribbon termini, allowing for more pronounced overlap (~2.5Å vs. 1.5Å, R\textsubscript{k,1} in second term\textsuperscript{29}).

Hoffmann had already discussed through-bond interaction\textsuperscript{35}. For example, in 1,4-diazabicyclo[2.2.2]octane (27, DABCO), the non-bonding lone pairs on nitrogen can interact through the σ and σ*-orbitals of the ethano bridges (\textbf{Figure 15}).
PES actually showed this interaction to be quite significant: the HOMO and the SUBHOMO of DABCO (27) are separated by 2.13 eV\textsuperscript{36-38}.

That sp\textsuperscript{2}-carbons can interact with cyclobutanes has been demonstrated by the PES of vinylcyclobutane\textsuperscript{39} (29, Figure 16).

When one tries to reproduce the ionization potentials obtained by photoelectron spectroscopy with theoretical calculations like ZDO (zero differential overlap)\textsuperscript{40}, for both vinylcyclopropanes (e.g. 28) and vinylcyclobutanes
(e.g. 29) a resonance integral $\beta$ of $-1.9$eV seems to be most appropriate. However, the actual interaction integrals $H_{\pi\omega}$ ($\pi$ stands for the vinyl $\pi$-orbitals, $\omega$ for the Walsh orbitals of cyclopropane or cyclobutane) consist of the resonance integral $\beta$ as well as the coefficients $C_\pi$ and $C_\omega$ of the atomic orbitals in the corresponding wave functions. "The difference in the interaction integrals should be a measure of the difference in the ability of the particular ring to stabilize a $\pi$-system"$^5$.

Cyclopropane $H_{\pi\omega}=\beta \cdot C_\pi \cdot C_\omega=1.9 \cdot 0.707\cdot (2/\sqrt{6})=-1.1$eV

Cyclobutane $H_{\pi\omega}=\beta \cdot C_\pi \cdot C_\omega=1.9 \cdot 0.707 \cdot 0.5=0.67$eV

Clearly, cyclopropane can interact more strongly with adjacent $\pi$-systems than cyclobutane.

Both termini of a $\pi$-ribbon can interact in three different ways with a cyclobutane ring (Figure 17):
(1) by twofold connection with the 1-position of cyclobutane as in 30$^{42}$; (2) by connection with the 1- and the 2-positions as in 31$^{43}$ and 32$^{44}$; or (3) by connection with the
Figure 17: Modes of Interaction of One $\pi$-Ribbon with Cyclobutane

1- and the 3-positions as in 33 and 34. Whereas the PE spectra are difficult to interpret conclusively in 30, connectivities II and III reveal significant interaction between the cyclobutane Walsh orbitals and the $\pi$-ribbon.
In more complex systems, reliable PE assignments can only be made when a series of closely related compounds is studied, e.g. as in the case of 34:

\[ \text{35} \quad \text{36} \]

The PE spectra of 35 and 36 are not complicated by through-bond interaction, and the peaks can therefore be easily assigned. Correlation of these peaks with 34 allows assignment of the PES of 34 and therefore assessment of the extent of interaction between the cyclobutane ring and the butadiene moiety. Whereas semiempirical MINDO/3 and Extended Hückel calculations reproduce the experimentally observed ionization potentials poorly, the ZDO-model gives excellent results. The cis-butadiene π-orbital energies as well as the cyclobutane Walsh orbital energies before interaction can be secured from PES data. After the mutual inductive effects are accounted for, and a certain value for the resonance integral $\beta$ is assumed, the Schroedinger equation and thus the secular determinants can be solved to give the eigen values, i.e. energy levels of the orbitals after interaction. These theoretical values determine the ranking of the MO's and therefore aid assignment of the experimental PE spectra. In 34, repulsive four electron
interaction of the butadiene MO's with the cyclobutane Walsh orbitals pushes the $\varepsilon(\pi_2)$ and $\varepsilon(\pi_1)$ orbitals of the butadiene bridge up from -8.4eV and -10.9eV to -8.3 and -10.2eV, respectively\textsuperscript{46}.

Nelson and Gillespie rationalized the fact that radical anion 37 shows an eight times larger $\beta$-hyperfine splitting $a_H$ with H$_5$ than semidione 38\textsuperscript{48}, by interaction of the naphthalene/semidione SOMO with occupied Walsh orbitals of the cyclobutane ring (Figure 18)\textsuperscript{49}. Symmetry-allowed

**Figure 18:** FMO's of 37 and 38

![FMO's of 37 and 38](image)

(only the $\alpha$-coefficients of the naphthalene/semidione-SOMO are shown).
interaction between the naphthalene SOMO and the $a_2$ Walsh orbital generates high spin density in the cyclobutane carbon-carbon bonds, affected by the relatively big coupling with $H_5$. In contrast, the semidione SOMO could interact with the occupied $b_2$-Walsh orbital that contains little spin density in the cyclobutane C-C bonds, resulting in a small coupling with $H_5$.

This closes the logical loop started on page 15. When two π-ribbons are connected to a cyclobutane ring instead of only one, different connectivity patterns are again possible. I mention only two in which representatives have actually been synthesized and investigated (Figure 19). While categories IV and V both displayed through-bond interaction of the two π-ribbons through the cyclobutane ring in the PE spectra, my research has concentrated on category VI, where the π-ribbons are perpendicular to each other.

Tricyclo[3.3.0.0$^2,6$]octa-3,7-diene (42), synthesized already in 1969 by Meinwald and Tsuruta$^{51}$, and by Zimmermann, Robbins and Schantl$^{52}$, surprises by the dramatic bathochromic shift in its UV spectrum to a $\lambda_{\text{max}}$ of 300 nm (compare monounsaturated 43: 250 nm).
Figure 19: Interaction of Two \( \pi \)-Ribbons with Cyclobutane

\[ \begin{align*}
\pi & \quad \text{and} \quad 1-2 \\
\text{and} & \quad 3-4 \\
\text{syn} & \quad \text{anti}
\end{align*} \]

\[ \begin{align*}
\pi & \quad \pi \\
\pi & \quad \pi
\end{align*} \]

\[ \begin{align*}
\pi & \quad \pi \\
\pi & \quad \pi
\end{align*} \]

\[ \begin{align*}
\pi & \quad \pi \\
\pi & \quad \pi
\end{align*} \]

\[ \begin{align*}
\pi & \quad \pi \\
\pi & \quad \pi
\end{align*} \]
This fact triggered theoreticians like Gleiter and Kobayashi$^{53}$, and Hoffmann$^{35}$ to speculate on conjugation of the etheno bridges through the cyclobutane Walsh orbitals. Unfortunately, the thermal instability of 42 [it rearranges to semibullvalene (44) with an estimated halflife of 10 min at room temperature] precluded the determination of its occupied MO levels by PES. As in the case of 34, the orbital energy pattern of 43 could be explained within the ZDO model by a resonance integral $\beta = -1.9$eV between the cyclobutane Walsh orbitals and the etheno bridge.
The only other examples of cyclobutanes where the 1,3- and 2,4-positions are connected by mutually perpendicular \(\pi\)-ribbons (class VI) were found to be 45-48. Unfortunately, the electronic spectra of bisanhydride 45\textsuperscript{55,56} and bisnaphtho-cyclobutane 47\textsuperscript{57} were not recorded. Therefore, no clue to through-bond interaction exists.

Comparison of the through-space interaction of mutually perpendicular \(\pi\)-ribbons (spiroconjugation) with the through-

Figure 20: EH FMO's of 42

bond interaction through a cyclobutane-relay led Gleiter, Bischof, and Haider to develop the following molecular orbital schemes\textsuperscript{22} from the \(\pi\)-orbitals of ethylene and buta-
diene and the Walsh orbitals of cyclobutane. The reduced HOMO-LUMO gap in the MO scheme of 42 would explain the bathochromic UV shift.

Figure 21: EH FMO's of 2

The through-bond interaction in 2 is calculated to be weakly stabilizing but might be overridden by extraneous effects as demonstrated for 5.

In 1, the butadiene LUMO's are expected to remain unaffected and degenerate, since their mutual interaction is orthogonal. The butadiene HOMO's can interact with each other through the filled $b_1$-Walsh orbital. Since all participating orbitals are filled, their interaction is
destabilizing, raising the $\epsilon$ (HOMO) and reducing the HOMO-LUMO gap. Through-bond interaction is predicted to be more severe than through-space interaction, resulting in a higher HOMO and a smaller HOMO-LUMO gap for 1 (compare Figure 5).
In addition, the symmetry order of the HOMO and the SUBHOMO in 6 is opposite that of 1 (a$_2$ and b$_1$).

Of the theoretically discussed through-bond conjugated hydrocarbons, only the [2.2]system 42 and a tetrabenzio analog of 1, viz., 48, had been prepared and investigated. Since both 1 and 48 have the same D$_{2d}$ symmetry, their orbital patterns look very similar. However, the poor resolution of the PE spectrum of 48 prevented a closer analysis of its electronic structure. The LUMOs of 48 remain degenerate and localized in the respective bridges as in 1 according to calculations by the PPP model$^{47}$.

Müllen and Huber found evidence for this in the ESR spectrum of the radical anion of 48, generated electrochemically or by a potassium mirror in dimethoxyethane at -70 to -90°C$^{59}$. With $^+$NBu$_4$ as a countercation (see 55), the

![Chemical Structures](image)

$x^+::^+$NBu$_4$ 55
K$^+$ 56

57
ESR splitting pattern resembled that of the 9,10-dihydro-phenanthrene radical anion 57, i.e., the negative charge was localized in one bridge. With $K^+$ as countercation (56) the electron seemed to couple with sets of four protons, i.e. the negative charge appeared to be delocalized over the whole molecule. However, Mullen and Huber explained this by invoking a larger solvation sheath around the smaller, more highly charged $R^+$, reducing the charge density in the solvated cation $K(DME)_x^+$ and weakening the Coulomb attraction to the radical anion. This looser ion pair would facilitate transfer of the charge from one side of the molecule to the other and thereby resemble a completely delocalized radical anion.

As suspected before, the evidence from spiroconjugation suggested that the through-space interaction was more noticeable for $\pi$-ribbons with an equal number of $\pi$-electrons than with $\pi$-ribbons of different size. Therefore, to investigate the effects of potential through-bond interaction of $\pi$-ribbons through a cyclobutane ring, a tricycle with $n=n'$ was chosen as first target with the greatest promise to find a significant effect, namely 1.
CHAPTER IV

SYNTHETIC STRATEGY

Each retrosynthetic analysis for tricyclo[5.5.0.0²,⁸]-dodeca-3,5,9,11-tetraene (1) must ultimately face the question concerning the timing of four-membered ring installation. Scheme 2 shows the disconnections that we and other groups have considered.

a) Disconnection I: Intramolecular Crosscycloaddition:

Cyclodecane→Tricyclo[5.5.0.0²,⁸]dodecane

Scheme 1: Expected Photocyclization of 58
Scheme 2: Retrosynthetic Analysis of 1
Intramolecular photocyclization of a suitably substituted cyclododeca-1,6-diene (58) is expected to lead to the linear 6-4-6-tricyclic system 60, not to the crosscyclized tricyclo[5.5.0.0^2,8]dodecane (59). The pathway followed during photocyclization depends heavily on ring size. Srinivasan reported that mercury-sensitized photolysis of cycloocta-1,5-diene (61) yielded the product of cross-

Scheme 3: Photocyclization of 1,5-Dienes 61 and 65
photocyclization (63), not the linear 4-4-4-tricycle 64\textsuperscript{60,61} (Scheme 3). The open-chain hexa-1,5-diene (65) afforded bicyclo[2.1.1]hexane (67) in 10\% yield under the same conditions\textsuperscript{62,63} (Scheme 3). However, when the double bonds are separated by one more methylene group, the parallel cycloadduct predominates\textsuperscript{64} (70 to 72) or is formed to the exclusion of the cross cyclo-adduct (74 to 76)\textsuperscript{65}.

Scheme 4: Photocyclization of 1,6-Dienes 70 and 74

\[\text{70} \quad \xrightarrow{\text{hv}} \quad \text{72} + \text{73}\]

\[\text{74} \quad \xrightarrow{\text{hv}} \quad \text{75} \quad \xrightarrow{\text{X: H}_2\text{O}} \text{76}\]
Srinivasan explained the photosensitized cyclization by a stepwise pathway. One double bond is excited to the triplet state, one radical center cyclizes onto the second double bond to form preferentially a five-membered ring, and the second σ-bond is ultimately formed. There are

Scheme 5: Photocyclization of 1,6-Dienes 70 and 74
exceptions to this empirical 'Rule of Five' \textsuperscript{65-68}. Heathcock and Badger found substantial amounts of crosscycloaddition product 78 after the irradiation of dienone 77\textsuperscript{69} (Scheme 5), and Yoshihara et al. isolated β-copaene (82) as a minor byproduct in the photolysis of germacrene D (81) to (-)β-bourbonene (83). In the photolysis of 1,8-divinylnaphthalene (84), Meinwald and Young obtained predominantly the cross cycloadduct 85\textsuperscript{71}. Possibly these observations reflect a competing cyclization from the excited singlet state - in contrast to Shani's (75) and Srinivasan's (70) photosensitized cycloadditions [acetone and Hg(\textsuperscript{3}P\textsubscript{1}) as photosensitizers, respectively]\textsuperscript{72}.

Interestingly, while Nelson and Gillespie observed the crosscycloaddition product 92 only as a minor product in the photolysis of 91, pyrolysis afforded 92 almost quantitatively. The same was true for 95\textsuperscript{78}. Mitchell and Sondheimer obtained the dinaphtho analog of a \textsuperscript{[3\textsuperscript{1},3\textsuperscript{1},3\textsuperscript{1},3]} through-bond conjugated system, 47, as a very minor component in the Wittig condensation of 1,8-naphthalenedicarboxaldehyde (96) with bisylide 97\textsuperscript{79}. Wittig and Skipka synthesized the tetrabenzo analog of tricyclo[5.5.0.0\textsuperscript{2,8}]-dodeca-3,5,9,11-tetraene (1), i.e. 48, by pyrolysis of 98\textsuperscript{80}.

All of these examples demonstrate that cross photocycloaddition can be achieved if a five-membered ring is formed leading to the supposed biradical intermediate.
Scheme 6: Crosscyclization of 91, 95, 96 + 97 and 98

91 \[ \text{hv} \quad 2.4 \quad 400 \text{C} \quad 95\% \]

95 \[ 375-410^\circ C \]

major

96 \[ 97 \]

CHO CHO PPh\textsubscript{3} & \text{PPh\textsubscript{3}} \]

\[ \text{CHO} \quad \text{CHO} \quad \text{PPh}_3 \quad \text{PPh}_3 \]

\[ 96 \quad 97 \quad \text{reflux, 3 h} \quad 47:0.1\% \quad + \]

isomer

98 \[ 310^\circ C \quad 7 \text{ min} \]

48

99
The 'Rule of Five' can be extended by one carbon, if one of the double bonds is conjugated with another double bond, a carbonyl group, or an aromatic ring system (84,98), although the extent of cross-cyclization and normal cyclization varies unpredictably. In completely conjugated systems, where the residual double bonds are chemically neutralized as aromatic rings, even pyrolysis leads to cross-cyclization, probably as in the photolysis via biradical intermediates.

b) Disconnection II: Intramolecular Nucleophilic Substitution:

Bicyclo[4.4.0]decane → Tricyclo[4.4.0.0\(^2,7\)]decane

Scheme 7: Heathcock's Entry into Tricyclo[4.4.0.0\(^2,7\)]decanes

\[
\begin{align*}
100 & \xrightarrow{\text{Na}^+\text{CH}_2\text{SCH}_3, \text{DMSO}, 75^\circ\text{C}, 3h} 101 \\
& \rightarrow 102
\end{align*}
\]
In their synthesis of (+)-copaene (103) and (±)-ylangene (104), Heathcock et al. used intramolecular nucleophilic substitution within 100 to form the four-membered ring and generate the tricyclo[4.4.0.0^{2,7}]decane skeleton of 102\textsuperscript{81} (Scheme 7).

Gleiter and his research group are currently pursuing the synthesis of a derivative of tricyclo[5.5.0.0^{3,8}]dodeca-3,5,9,11-tetraene (1), the methyltetraene 105, using

Scheme 8: Borden's Ring Expansion Sequence

Heathcock's tricyclic intermediate 102 followed by a ring expansion sequence\textsuperscript{82}. Borden utilized this strategy in his synthesis of bicyclo[4.1.1]octa-3,5-diene (34) (Scheme 8,
for a similar strategy leading to the parent-tetraene 1, see Appendix A)\(^{83-85}\).

c). Disconnection III: Simultaneous Belting: Cyclobutane to Tricyclo[5.5.0.0^{2,8}]dodecane.

In their attempt to synthesize truncated tetrahedrane (110), Woodward, Scott\(^{86}\), and Brousseau\(^{87}\) envisioned tetraene 1 as a precursor. They planned to doubly cyclize an all trans tetra-substituted cyclobutane. However, when

**Scheme 9: Attempted Acyloin Condensation of 111**
they subjected tetraester 111 to the acyloin condensation conditions, they could not isolate any tricyclic 112 (Scheme 9), although the acyloin condition had proven to be of great value in belting the 1- and the 3-position of a cyclobutane (Scheme 10):

Scheme 10: Russell's Acyloin Condensations of 113, 115 and 117

Chasey believed that he had some evidence for the bisthiocarbonate 119 or 120 resulting from reductive ethanolysis of the crude acyloin condensation product followed by reaction with bisimidazolithionocarbonate in acetonitrile/pyridine.
Reaction of the tetrabromide 121 with sodium sulfide in HMPA did not yield the desired 1,3- and 2,4-bridged disulfide 122, but instead the 1,2- and 3,4-bridged disulfide 123\(^{87}\) (Scheme 11).

Scheme 11: Brousseau's Sulfide Ring Closure
This illustrates an interesting point about cyclobutane. Unsubstituted cyclobutane is not flat ($D_{4h}$) but puckered$^{91-93}$ ($D_{2d}$) by 35° with a barrier to planarity of about 1.5 kcal/mol as determined by IR$^{94}$ and Raman spectroscopy$^{149}$.

Figure 23: Puckered Cyclobutane

The puckering destroys the equivalency of the geminal substituents and differentiates axial and equatorial positions. An all-trans tetrasubstituted cyclobutane is therefore expected to prefer the all-equatorial conformation 121e to avoid the repulsive 1,3-transannular interactions experienced in the all-axial conformation 121a. Thus, whenever 1,2-bridging is geometrically feasible, an all trans, symmetrically tetra substituted cyclobutane is liable to form a 1,2 over a 1,3 bridge. Only, when the bridge size becomes too short to form the 1,2 bridge, then 1,3 bridging predominates. For example, after refluxing in acetic anhydride, only the 1,3;2,4-bridged bisanhydride 45 could be isolated from tetraacid 49, not the 1,2;3,4 bridged isomer 50$^{55,56,95}$ (Scheme 12).
Scheme 12: Anhydride Formation from 49

Other cyclization procedures that Chasey tried like 'Dieckmann' condensation of tetraacid 124 with barium oxide, anhydride formation from 124 followed by pyrolysis, or Thorpe-Ziegler reaction of tetranitrile 125, were to no avail.
That simultaneous double cyclization procedures with long bridges (like the sulfide formation) failed to give the wanted 1,3- and 2,4-bridging can be rationalized on the basis of the conformational bias of the all-trans tetrasubstituted cyclobutane. Why the alternative cyclization leading to the tricyclo[4.4.0.0²,⁷]decane skeleton was unsuccessful remains unexplained.

d) Disconnection IV: Stepwise Bridging. Cyclobutane to Bicyclo[4.1.1]octane to Tricyclo[5.5.0.0²,⁸]dodecane.

To divide the double cyclization into two separate bridging steps, an all trans tetrasubstituted cyclobutane precursor is needed, the substituents of which should not be identical as in 111 or 121, but differentiated in the 1,3 and the 2,4 positions.

Scheme 13: Stepwise Bridging
In this way, the system (126) can only bridge the 1- and 3-positions and avoids the complication of competing 1,2-bridging. The stepwise belting scheme offers the additional opportunity to prepare tricyclic systems with unsymmetrical bridge sizes from common intermediates, an invaluable asset for the study of mutually perpendicular π-ribbons consisting

Scheme 14: Divergent Synthesis of \([m^a, b, n^c, d]\) Through Bond Conjugated Systems
of different numbers of sp²-carbons around the cyclobutane ring (Scheme 14).

A cyclobutane precursor that fulfills these conditions was found in ε-truxillic acid (132)⁵⁶. The product of the first bridging, bicyclic bis(tetrahydropyran)ether 48¹³³, proved to be versatile enough to allow elaboration of the [⁴¹,⁴,⁴¹,⁴], [⁴¹,⁴,²¹,²], and [⁴¹,⁴,⁴²,³] through-bond conjugated hydrocarbons 1, 2 and 3 (Scheme 15).

Scheme 15: Divergent Synthesis of 1, 2 and 3
CHAPTER V

TRICYCLO[5.5.0.02,8]DODECA-3,5,9,11-TETRAENE (1)

A. Synthesis

That the stepwise belting scheme for the synthesis of the tricyclo[5.5.0.02,8]dodecane-skeleton works, was demonstrated by Chasey's synthesis of tricyclo[5.5.0.02,8]dodeca-4,10-diene (128). A significant portion of the synthesis has already been discussed by Chasey. The present discussion will consequently be limited to the new advances and ancillary key observations.

Several bottlenecks had to be removed from Chasey's reaction sequence to permit the synthesis of tricyclo[5.5.0.02,8]dodeca-3,5,9,11-tetraene (1) in those amounts necessary for its physico-chemical study (Scheme 16). Specifically, the steps where improvement was desirable were the solid state photolytic dimerization of trans-cinnamic acid (134), ruthenium tetroxide oxidation of the phenyl substituents in 137, the acyloin condensations, and conversion of the vicinal diols into double bonds.
Scheme 16: Modification of Chasey’s Synthesis of 128

134 \[ \text{Ph} \overset{\text{CO}_2\text{H}}{\longrightarrow} \overset{\text{h} \downarrow}{\text{H}_2\text{O}} \longrightarrow \overset{\text{Ph}}{\text{CO}_2\text{H}} \]

135 \[ \overset{\text{Ph}}{\text{HO}_2\text{C}} \overset{\text{Ph}}{\text{CO}_2\text{H}} \]

132 \[ \overset{\text{Ph}}{\text{CO}_2\text{H}} \]

136 \[ \overset{\text{Ph}}{\text{OH}} \overset{\text{OH}}{\longrightarrow} \overset{\text{Ph}_3\text{PBr}_2}{\longrightarrow} \overset{\text{Br}}{\text{Ph}} \overset{\text{Br}}{\text{Ph}} \]

137 \[ \overset{\text{Ph}}{\text{Br}} \overset{\text{Br}}{\text{Ph}} \]

138 \[ \overset{\text{Ph}}{\text{HO}} \overset{\text{Br}}{\text{Ph}} \overset{\text{Br}}{\text{Ph}} \]

139 \[ \overset{\text{THPO}}{\text{Br}} \overset{\text{NaCN}}{\longrightarrow} \overset{\text{CN}}{\text{ThPO}} \overset{\text{CH}_2\text{N}_2}{\longrightarrow} \overset{\text{CO}_2\text{Me}}{\text{ThPO}} \]

140 \[ \overset{\text{THPO}}{\text{CN}} \overset{\text{KOH}}{\longrightarrow} \overset{\text{CN}}{\text{THPO}} \]

141 \[ \overset{\text{THPO}}{\text{CO}_2\text{Me}} \overset{\text{H}_2\text{O}}{\longrightarrow} \overset{\text{CO}_2\text{Me}}{\text{THPO}} \]

142 \[ \overset{\text{THPO}}{\text{OH}} \overset{\text{CSiCl}_2}{\longrightarrow} \overset{\text{S}}{\text{THPO}} \]

143 \[ \overset{\text{THPO}}{\text{S}} \overset{\text{Me}_3\text{PBr}_2}{\longrightarrow} \overset{\text{PPh}_3}{\text{Br}} \]

144 \[ \overset{\text{Br}}{\text{Br}} \overset{\text{NaCN}}{\longrightarrow} \overset{\text{NC}}{\text{Br}} \overset{\text{NC}}{\text{Br}} \]

145 \[ \overset{\text{1. KOH}}{\text{NC}} \overset{\text{2. H}_2\text{O}^+}{\longrightarrow} \overset{\text{MeO}_2\text{C}}{\text{Br}} \overset{\text{3. CH}_2\text{N}_2}{\longrightarrow} \overset{\text{MeO}_2\text{C}}{\text{Br}} \]

146 \[ \overset{\text{1. Na/K[1:4]}\text{TMSCl}}{\text{MeO}_2\text{C}} \overset{\text{2. H}_2\text{O}}{\longrightarrow} \overset{\text{3. LAH}}{\text{MeO}_2\text{C}} \]

147 \[ \overset{\text{HO}}{\text{OH}} \overset{\text{CSiCl}_2}{\longrightarrow} \overset{\text{S}}{\text{148}} \overset{\text{148}}{\longrightarrow} \overset{\text{128}}{\text{128}} \]
To limit the number of regioisomers, the photodimerization of trans-cinnamic acid (134) is performed in the solid state. Farnum and Mostahari's photolysis using a suspension of trans-cinnamic acid (134) in water proved far superior to Griffin's original procedure. The laborious deposition of the acid on the walls of a graduated cylinder was avoided and the scale of the reaction could be increased from 0.09 mol to 0.95 mol. In this way, cleaner material became available in large quantity, an especially important for the beginning of an extended reaction sequence. After five days of irradiation, 45 to 86 g of α-truxillic acid (135) could be obtained (versus 6.2 g in three days with the old procedure). Although Chasey had observed lower yields in larger scale ruthenium tetroxide oxidations of diphenyl dibromide 137, the scale of the reaction could presently be increased without problems from 1.43 mmol to 100 mmol, while simultaneously increasing the yield from 47 to 70% following reduction of the intermediate diacid with borane-THF complex.

The rate enhancement that Carlson et al. and Chakraborti and Ghatak observed upon adding acetonitrile as a cosolvent for the oxidation could not be reproduced in our system. Sodium metaperiodate as a cooxidant for the ruthenium dioxide or ruthenium trichloride catalyst left the reaction incomplete.
The saponification of bisnitrile 140 proceeded more cleanly when the reaction mixture was heated to higher temperatures, i.e., 140-150°C instead of 100°C. In this manner, the overall yield for the alcohol protection and carbon homologation of dibromo diol 138 into di-THP diester 141 rose from 39% to 76%. It was found more convenient to effect the Schräpler-Rühlmann-modified acyloin condensation with sodium-potassium (1:1) alloy/trimethylsilyl chloride/ether/room temperature instead of sodium/trimethylsilyl chloride/refluxing toluene. Thus, no mercury seal was necessary, the liquid sodium-potassium alloy could be handled with a mineral-oil coated syringe, and the combination of a compressed air-driven high-speed motor, a Hersberg stirring rod, and a Morton flask generated the fine metal dispersion necessary for the success of the ring closure. Surprisingly, coupling of the diester seemed to occur instantaneously and made high dilution unnecessary. For example, 86g (0.20 mol) of diester 141 could be reacted in only 350 mL of ether.

We had expected that the all-trans substitution plan of the cyclobutane ring of 141 would prefer the all-equatorial conformation so as to minimize mutual 1,3-diaxial repulsion of the tetrahydropyranoxyethyl methyl groups (compare page 41; Figure 24). If so, a reduction in the rate of cyclization should have been observed.
Since the reductive ethanolysis of the intermediate bissilyl enol ether with sodium borohydride and refluxing ethanol proved problematic, the solvolysis and reduction steps were separated.

In the hydrolysis, a compromise in acidity (\(\sim p\text{H} = 5\), phosphate buffer) was found where the hydrolysis seemed to proceed faster and the acid labile THP protecting groups were unaffected. Fluoride ion accelerated the subsequent desilylation.

In his synthesis of bicyclo[4.1.1]octa-2,4-diene (34), Volz had observed\(^{105}\) only cis-diol 149 as the product of the reductive ethanolysis of bissilyl enol ether 118 (Scheme 17). In contrast, Chasey noticed\(^{90}\) that both cis and trans-diol (142c and t) were formed when bissilyl enol ether 150 was subjected to the same reaction conditions. In this study, reduction of the acyloin 151 with an excess of
Scheme 17: Reduction of Acyloins to Diols 149 and 142

- 118 $\xrightarrow{\text{NaBH}_4, \text{ethanol reflux}}$ 149
- 150 $\xrightarrow{\text{H}_2\text{O}}$ 151
- 142 $\xrightarrow{\text{LiAlH}_4, \text{THF, } 0^\circ\text{C}}$ 152
- 153c, 153t
lithium aluminum hydride in anhydrous THF gave only cis-diol 142c. Because the chiral centers introduced by the THP-groups made differentiation between the cis- and the trans-diols difficult, the reduction product was deprotected with para-toluenesulfonic acid in ethyl acetate (55°C, 7h) or with acid washed Dowex-50 resin in methanol (room temperature, 1h). The resulting tetraol displayed 7 lines in its broadband-decoupled 75 MHz $^{13}$C NMR spectrum, as expected uniquely for the $C_2$ symmetry of cis diol 153c (Figure 24). The transdiol 153t possesses $C_2$-symmetry and should therefore exhibit only 5 carbon signals (Scheme 17).

The hydride probably deprotonates the hydroxyl group of the acyloin prior to reduction of the carbonyl function. The resulting aluminate 152 could theoretically serve two functions: (a) it could deliver a hydride atom intramolecularly to the carbonyl group, thereby giving rise to the trans diol 142t. Lansbury et al. explained the exclusive formation of trans diol 180 in the reduction of diketone 178 this way$^{106,107}$ (Scheme 24); (b) the bulky aluminate could merely serve as a blocking group, sterically shielding the proximal face of the molecule against intermolecular attack by a second hydride. Force field calculations (MMP2) and semiempirical quantum mechanical calculations (MINDO/3)$^{46}$ on bicyclo[4.1.1]octane (35) suggest that the four-carbon bridge can adapt a more or less ideal chair conformation
Figure 24: 13C NMR of 142c
Scheme 17: Lansbury's Reduction of Diketone 178

Together with the cyclobutane ring. The aluminate would probably prefer the equatorial position (see 152e), and the 7-endo hydrogen would hinder β-approach of an incoming hydride. α-Attack then leads to the cis diol.

Scheme 18: Reduction of β-Hydroxy Ketone 154
Akhtar and Marsh used the steric bulk of an aluminate or borate to explain the $\beta$-reduction followed by cholestane-5-$\alpha$-ol-3-one 154 with sodium borohydride/diglyme and lithium aluminum hydride/ether versus the preferential $\alpha$-reduction seen with sodium borohydride/methanol (Scheme 18).

Obviously, this analysis does not explain the different selectivities observed by Chasey and Volz.

Earlier attempts to convert a vicinal cis diol directly into a diene had either failed or delivered the diene in low yields and poor purity (consult Volz, Hagedorn, and Chasey for attempted conversion of diols 149, 154 and 155 into their respective dienes).

Additionally, the presence of a diene unit in close proximity to the cyclobutane ring was anticipated to introduce sensitivity in subsequent manipulations. Therefore, Volz and Chasey had found the intermediate conversion of the vicinal diol into an olefin advantageous. Thus, the question of whether the vicinal diol was cis or trans became crucial for the ensuing olefination.
For example, the Corey-Winter olefination\textsuperscript{111} proceeds stereospecifically and in smaller cyclic systems requires the vicinal hydroxyl groups to be cis-oriented.

On the other hand, the Vedejs modification\textsuperscript{112} of this reaction is tolerant of mixtures of cis and trans diols (Scheme 19).

Since the cis diol could be formed exclusively, the longer Vedejs methodology could be avoided. In 1982, Corey and Hopkins published\textsuperscript{113} an improved version of the Corey-

\begin{scheme}
\textbf{Scheme 19: Olefination of Vicinal Diols}
\end{scheme}
Winter olefination wherein thiophosgene and 4-dimethylamino pyridine (methylene chloride, 0°C, ~2h) are combined to promote thiocarbonate formation. With the more nucleophilic 1,3-dimethyl-2-phenyl-1,3-diazaphospholidine, the sulfur extrusion-decarboxylation temperature can be lowered from ..°C (refluxing triethylphosphite) to 40-50°C. On a large scale, this step actually proved to be highly exothermic. Neat phospholidine had to be used as reaction medium because dilution with THF slowed the reaction down. For workup, Corey and Hopkins adsorbed the reaction mixture onto silica gel and eluted the product with ether. On a larger scale, it was found more convenient simply to partition the reaction mixture between water and ether.

In contrast to the Vedejs modification deployed by Chasey, the Corey-Hopkins procedure left the di-THP ether functionalities of 133 completely untouched.

In Chasey's hands, dialdehyde 156 obtained by reduction of the dinitrile 140 with diisobutylaluminum hydride did not undergo deoxygenative coupling to olefin 156 with low valent titanium. McMurry had already found in his synthesis of civetone, that ethyleneglycol ketals do not survive the coupling conditions. Only when he resorted to the catechol ketal 159 was the carbonyl protecting group left intact. Interestingly, the THP ethers in 142 did survive the McMurry procedure. Cis diol 142, the presumed
intermediate of the McMurry coupling\textsuperscript{116} could be olefinated in 70% yield with titanium trichloride/potassium/

Scheme 20: Deoxygenation with Titanium(0)

Chasey

\[
\begin{array}{c}
\text{THPO} \\
\text{CHO} \\
\text{THPO} \\
\text{CHO}
\end{array}
\xrightarrow{\text{TiCl}_3.K} 
\begin{array}{c}
\text{THPO} \\
\text{CHO}
\end{array}
\]

156 \rightarrow 133

Mc Murry

\[
\begin{array}{c}
\text{CHO} \\
\text{CHO}
\end{array}
\xrightarrow{\text{TiCl}_3.K} 
\begin{array}{c}
\text{CHO}
\end{array}
\]

\[
\begin{array}{c}
\text{CHO}
\end{array}
\]

\[
\begin{array}{c}
\text{CHO}
\end{array}
\]

R = \text{CH}_2 \text{CH}_2 \quad 157 \rightarrow 158

159 \quad 160

\[
\begin{array}{c}
\text{OH} \\
\text{OH}
\end{array}
\xrightarrow{\text{TiCl}_3.K \text{DME reflux} \quad 70\%} 
\begin{array}{c}
\text{OH}
\end{array}
\]

142 \rightarrow 133
dimethoxyethane (DME)/reflux. Thus, the capricious thio-carbonate formation step (yields ranged from 43 to 89%) could be circumvented, reducing the original two-step vici-nal diol-olefin conversion sequence to only one (Scheme 20).

Although McMurry coupling would shorten the reaction scheme considerably (by 10 steps if applied twice), there are two drawbacks. Firstly, it requires the intermediacy of a potentially labile dialdehyde; secondly, the intramolecular coupling requires high dilution and slow addition (in a typical example 150 mg are added over 40 h) making the acquisition of large amounts of material difficult. In an effort to accelerate the deoxygenation, diol 147 was sonicated with titanium trichloride/potassium/dimethoxyethane in the temperature range 40-60°C.

Although sonication accelerates many heterogeneous reactions admirably, in this case no dramatic rate enhancement was observed. Even when the titanium was pre-formed under the usual conditions (refluxing dimethoxyethane), addition of the diol followed by sonication led mostly to recovery of starting material. Therefore, the acyloin route was maintained; though longer it consists mostly of simple, fast, and high yielding reactions.

The second chain homologation sequence, i.e. direct bromination of the THP ether 133, nucleophilic substitution with sodium cyanide in DMSO, saponification with
potassium hydroxide/methanol/water/140-150°C overnight, acidification, and diazomethane esterification proceeded in 93% overall yield after Kugelrohr distillation of diester 146. On this occasion, the acyloin condensation worked better with an excess of lower melting sodium/potassium alloy (1:4, mp -11°C), followed by the same hydrolysis and reduction as in the first acyloin condensation. Again, only cis diol was obtained as evidenced by the 9-line $^{13}$C NMR pattern (broadband decoupled).

The Corey-Hopkins olefination of diol 147 proved to be more problematic. Although the diol was barely soluble in methylene chloride, the thiocarbonate could be efficiently
formed in this solvent. However, adsorption of the reaction mixture on silica gel led to partial hydrolysis of thiocarbonate 148 to carbonate 161, and prolonged exposure to basic alumina (activity III) led via 'pinacol-pinacolone' rearrangement to ketone 162 (Scheme 21). Florisil was therefore the adsorbent of choice.

Figure 25: Some Symmetry Elements of 128

Sulfur extrusion and decarboxylation to give the crystalline diene 128, mp 41.5-43.5°C, proceeded smoothly. For the first time, the high $D_{2d}$-symmetry of the target molecule was
evident from its simple $^1$H NMR and $^{13}$C NMR spectra (Figure 25).

(C$_2'$ and C$_2''$ are perpendicular to the main axis C$_2$ and bisect the 90° angle between symmetry planes $\sigma_1$ and $\sigma_2$).

The latter shows only three different carbon signals. Again, as in the olefination of the first bridge, direct deoxygenation of vicinal diol 147 with titanium trichloride THF complex/potassium in refluxing dimethoxyethane avoided the complications of thiocarbonate formation. In a very clean reaction, diene 128 could be isolated in 77% yield.

Volz had shown earlier$^{46,105}$ that double allylic bromination followed by reductive debromination was successful in transforming olefin 36 into diene 34. The reagents
used for the debromination were apparently a combination of Sondheimer's and Vogel's conditions (Scheme 22).

Scheme 22: Conversion of Monoenes into Dienes

Volz, 1976\(^{46,105}\):

\[
\text{NBS (2.8 eq)} \rightarrow \text{AIBN} \rightarrow \text{Zn/Cu} \rightarrow \text{DMF} \rightarrow \text{18%}
\]

Sondheimer et al., 1966:

\[
\text{Zn} \rightarrow \text{DMF, RT 100%}
\]

Vogel et al, 1971:

\[
\text{KI acetone 50%}
\]

Allylic bromination of diene 128 with 4.0-4.7 equivalents of N-bromosuccinimide (NBS), and a catalytic amount of azobisisobutyronitrile (AIBN) under irradiation with a sunlamp afforded a plethora of stereoisomeric bromides 164. When this mixture was treated with freshly prepared zinc-
copper couple in anhydrous DMF at room temperature under argon for 12 h, tetraene 1, tetraene bromide 165, and tetraene dibromide 166 were produced and separated by reverse-phase HPLC (C18, 90% methanol/water) (Scheme 23).

Scheme 23: Conversion of 128 into 1

![Scheme 23: Conversion of 128 into 1](image)

During all manipulations involving tetraene 1 or its bromo derivatives, high temperatures (50°C and higher) and exposure to UV light (e.g. ceiling light) had to be avoided, as will be discussed in Section B.

Tricyclo[5.5.0.0²,8]dodecatetra-3,5,9,11-ene (1), a soft white solid, mp 33.5-34.5°C with a strong musty odor,
could be easily identified: (1) by the simplicity of its $^{13}$C NMR spectrum—the three carbon signals reflect the high $D_{2d}$-symmetry of the molecule (compare diene 128, p. 10), and (2) by the resemblance of the olefinic portion of its $^1$H NMR spectrum to that of Volz's bicyclo[4.1.1]octa-2,4-diene 34 (AA'BB'XX' pattern; Figure 26,27).

Figure 26: NMR Comparison of 1 and 34

![Diagram of molecules 1 and 34]

<table>
<thead>
<tr>
<th>$^1$H NMR</th>
<th>300 MHz, CDCl$_3$</th>
<th>400 MHz, CDCl$_3$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$H_1$</td>
<td>2.60-2.50 (m)</td>
<td>2.96 (m)</td>
</tr>
<tr>
<td>$H_2$</td>
<td>6.03-5.92 (m)</td>
<td>6.22 (m)</td>
</tr>
<tr>
<td>$H_3$</td>
<td>5.80-5.70 (m)</td>
<td>5.87 (m)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>$^{13}$C NMR</th>
<th>75 MHz, CDCl$_3$</th>
<th>100 MHz, C$_6$D$_6$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$C_1$</td>
<td>32.95</td>
<td>35.18</td>
</tr>
<tr>
<td>$C_2$</td>
<td>134.39</td>
<td>138.55</td>
</tr>
<tr>
<td>$C_3$</td>
<td>123.11</td>
<td>124.21</td>
</tr>
</tbody>
</table>

The proton signals of tetraene 1 were assigned by homodecoupling, and the carbon signals were tentatively assigned using bicyclo[4.1.1]octa-2,4-diene 34 for comparison. The
$^{13}$C NMR spectrum of the latter has recently been completely characterized by Christl and Herzog. 125.

The regiochemistry of tetraene bromide 165 could be determined by the coupling pattern of its olefinic protons. The reliability of the coupling pattern is confirmed by comparison with that observed for 3-bromobicyclo[4.1.1]octa-2,4-diene (167) 125 (Figure 27).

Figure 27: $^1$H NMR Comparison of 165 and 167

![H NMR Comparison of 165 and 167](image)

<table>
<thead>
<tr>
<th></th>
<th>165</th>
<th>167</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>H NMR</strong></td>
<td>300 MHz, CDCl$_3$</td>
<td>400 MHz, CDCl$_3$</td>
</tr>
<tr>
<td><strong>H$_2$</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>H$_3$</strong></td>
<td>6.21 (ddd, $J_3,1=7.6$, $J_3,3=2.0$, $J_3,5=0.7$ Hz)</td>
<td></td>
</tr>
<tr>
<td><strong>H$_4$</strong></td>
<td>5.55 (ddd, $J_4,3=11.1$, $J_4,5=7.6$, $J_4,6=0.7$ Hz)</td>
<td>6.05 (ddd, $J_4,3=11.6$, $J_4,5=1.8$, $J_4,6=0.8$ Hz)</td>
</tr>
<tr>
<td><strong>H$_5$</strong></td>
<td>6.04 (br dd, $J_5,3=11.1$, $J_5,6=8.2$ Hz)</td>
<td>6.16 (br dd, $J_5,3=11.6$, $J_5,6=8.2$, $J_5,7=0.7$ Hz)</td>
</tr>
</tbody>
</table>

Tetraene dibromide (166) could not be obtained completely pure and its identity was inferred from its $^1$H NMR spectrum. As an interesting side aspect, tricyclo[5.5.0.0$^{2,8}$]dodecataetra-3,5,9,11-ene (1) has the same $D_{2d}$ symmetry as allene.
The $C_2$-symmetric dibromide is therefore also chiral\textsuperscript{126} (Figure 28).

**Figure 28:** Chirality of 166

Gerlach and Müller actually obtained another molecule with $C_2$ symmetry in optically active form, viz. $(+)-(5S)$-1,6-spiro[4,4]nonadiene \textsuperscript{126}.

Different amounts of N-bromosuccinimide or different bromination temperatures did not change the result of allylic bromination and reductive debromination. According to analytical TLC, the plethora of allylic bromides converged to 2, 165, and 166 instantaneously after exposure to
zinc copper couple in dimethylformamide. When the reduction was allowed to proceed at room temperature for almost 4 days, only tetraene 1 could be isolated in 57% yield. Potassium iodide and iodine did not seem to have any effect on the outcome of the reaction and could therefore be omitted. It was of crucial importance to exclude any oxygen during the preparation of the zinc-copper couple and the reductive debromination. Deactivated zinc-copper couple required longer reduction times and higher temperatures. Metalation of the vinyl bromides 165 and 166 seemed to be the rate-determining step (Scheme 24).

Scheme 24: Metalation of 165 and 166

As expected, the vinyl bromides can be more efficiently metalated and protonated under Seebach's conditions (2 equivalents of tert-butyllithium, THF, -78°C, 5 min, then
methanol, -78°C). Actually, the simplest and fastest procedure for converting the allylic bromides into tetraene 1 was with tert-butyllithium (Scheme 25).

Scheme 25: Reductive Debromination of 164

Two alternatives are advanced to explain the occurrence of tetraene bromide 165 and tetraene dibromide 166. One possibility involves overbromination to the penta- and hexabromide followed by fast 1,4- and 1,2-reductive bromination and slow insertion of zinc into the vinyl bromide-carbon bond. Although allylic rearrangements during allylic radical brominations are common, Engman and Byström did not report any vinyl bromides or geminal dibromo-mides as products of exhaustive allylic bromination (Scheme 26). Apparently, radicals α to bromine are disfavored, as are vicinal dibromides, the former probably due to the destabilization of the allylic radical by the electronegative
bromine, the latter due to the steric repulsion of two vicinal bromine atoms. Additionally, Volz isolated only bicyclo[4.1.1]oct-3-ene (163) after reaction of 2,5-dibromo-bicyclo[4.1.1]oct-3-ene (36) with 2.6 equivalents of N-bromo-succinimide in 85% yield, a finding that could be
reproduced in the allylic bromination of chlorosulfone 239 to 285 (compare Chapter , p. , Scheme 27).

This, together with the fact that no 4-bromo tricyclo-[5.5.0.0^{2,8}]dodecatetra-3,5,9,11-ene (181) as well as no 3-bromo tricyclo[5.5.0.0^{2,8}]dodecatri-4,9,11-ene (183, from underbromination) was found according to GC/MS, makes overbromination unlikely.

Scheme 27: Allylic Bromination of 178

The second possibility is that some residual base (e.g. zinc hydroxide or bromide ion) dehydrobrominated tetrabromide 164 to 165 and 166.

When the mixture of allylic tetrabromides was treated with potassium tert-butoxide in THF, all the different spots
on TLC corresponding to the diastereomeric allylic tetra-
bromides converged into essentially one UV-active spot, again instantaneously. Although the mass recovery was poor (38%) and the obtained tetraenedibromide impure due to its propensity to polymerize, only one regioisomer was observed. This is additional evidence for the high regiospecificity of the bisallylic bromination.

**Scheme 28: Dehydrobromination of 164**

In retrospect the ease with which dibromo chlorosulfone 285 eliminated hydrogen bromide to provide 289 makes this alternative even more plausible (also see p. ).

Chasey synthesized **exo-syn-**7,8-diphenylbicyclo[4.1.1]-octa-2,4-diene (185)\(^{90,98}\) by double dehydrobromination of
trans-dibromide 185 under the modified conditions developed by King and Paquette\textsuperscript{131} (Scheme 29).

**Scheme 29: Dehydrobromination of Vicinal trans-Dibromides**

\[
\begin{array}{c}
\text{Ph} \quad \text{Br} \\
\text{HMPA,110} \text{C} \\
\text{7 h}
\end{array}
\xrightarrow{\text{Li}_2\text{CO}_3,\text{LiCl}}
\begin{array}{c}
\text{Ph} \\
\text{HMPA,110} \text{C}
\end{array}
\]

In contrast to that, Volz saw only debromination when he treated trans-3,4-dibromobicyclo[4.1.1]octane 187 with potassium tert-butoxide in THF or DMSO, and no reaction at all with 1,5-diazabicyclo[5.4.0]undecene (DBU) in refluxing THF (Scheme 29).

In agreement with what Chasey had already observed for exo,syn 7,8-diphenylbicyclo[4.1.1]oct-3-ene (188)\textsuperscript{90}, pyridinium bromide perbromide in glacial acetic acid and carbon
tetrachloride proved to be superior to bromine in brominating the double bonds of diene 128. As expected, both possible diastereomers, the $S_4$-symmetric (4$R^*$,5$R^*$,10$S^*$,11$S^*$) and the $D_2$-symmetric (4$S^*$,5$S^*$,10$S^*$,11$S^*$) tetrabromides (189)\textsuperscript{132,133} were present in almost equal amounts. The ratio of diastereomers was 54:46 according to the $^{13}$C NMR spectrum, which displayed two closely spaced sets of 3 carbons each (Scheme 30).

Scheme 30: Bromination/Dehydrobromination of 128 to 1

Only 189 ($D_2$) is chiral, since 189 ($S_4$) contains an improper rotation axis (Figure 29).
Figure 29: 189(S₄) and 189(D₂)

Treatment of the tetrabromides with potassium tri-phenylmethide, a base advocated by Anton and Crabtree for dehydrobromination of monobromides, simply resulted in electron transfer to give diene 128 cleanly. DBU in DMF up to 105°C led to slow decomposition.

Fortunately, one of the few solvents in which the tetrabromide 189 was soluble was THF. Thus, when 189 was
treated with potassium tert-butoxide in THF at room temperature, 68% of tetraene 1 were isolated in excellent purity. No traces of the possible debromination products 128 or 190 could be detected by $^1$H NMR.

So far the bromination-dehydrobromination of diene 1 leading to tetraene 34 has been found to be the cleanest and most highly yielding one.

For reliable assignment of the ionization potentials in the photoelectron spectrum of 1, the partially saturated tricyclo[5.5.0.0$^2$,8]dodeca-3,5-diene (191) and the completely saturated tricyclo[5.5.0.0$^2$,8]dodecane (192) were required.

Exposure of a methanolic solution of diene 128 to 1 atm of hydrogen in the presence of 5% palladium on carbon resulted in basically instantaneous and clean conversion to 192 in 93% yield after bulb to bulb distillation.

To arrive at diene 191, unsaturated diol 147 was hydrogenated under the same conditions (99%) to give highly crystalline diol (193), a compound poorly soluble in most solvents.
In agreement with earlier observations\textsuperscript{105}, double mesylation followed by treatment with potassium tert-butoxide in THF at room temperature was not a suitable route for the conversion of the vicinal diol 193 into the diene 191. According to GC/MS, the desired diene 191 was present in the reaction mixture but only in dismal amounts and admixed with several other components.

Scheme 31: Conversion of 147 into 191

Therefore diol 193 was transformed into diene 191 by sequential McMurry deoxygenation to olefin 194 (78%), bromination with pyridinium bromide perbromide to dibromide
195 (80%), and finally double dehydrobromination with potassium tert-butoxide in THF (83%) (Scheme 31).
B) Thermal and Photochemical Rearrangement

Already during the monitoring of the formation of tetraene 1 by analytical GC, two peaks were noticed in the C\textsubscript{12} hydrocarbon range (using \textit{trans,trans,trans}-cyclododeca-1,4,8-triene as reference). The integration ratios depended markedly on the injection port temperature of the GC. Under controlled conditions (C\textsubscript{6}D\textsubscript{6}, 102°C, sealed NMR tube), the D\textsubscript{2d} symmetric tetraene 1 rearranged cleanly and quantitatively (according to \textit{1}H NMR, 300 MHz) into an unsymmetric C\textsubscript{12} hydrocarbon as evident from the 12-line-pattern in the broadband-decoupled 75 MHz \textit{13}C NMR spectrum \[\tau_{1/2}(102^\circ\text{C})=63\text{ min, } k(102^\circ\text{C})=1.8\cdot10^{-4}\text{ s}^{-1}\]. The new hydrocarbon could be isolated in 50% yield by preparative GC as a volatile, mobile, colorless oil with an intensive olefinic odor. The integration ratio of 2:1 for the olefinic and aliphatic portions of the \textit{1}H NMR spectrum indicated that a tricyclic ring system had been preserved during the rearrangement. The very characteristic dddd pattern centered at \(\delta 4.94\) ppm (CDCl\textsubscript{3}) opened the door for the final structure elucidation. When the proton spectrum was compared with those of the known (CH)\textsubscript{12} valence isomers (see Appendix B), the centers of its chemical shifts were found to be superimposable upon those of tricyclo[5.5.0.0\textsubscript{2,10}]dodeca-3,5,8,11-tetraene (196), a compound that had been synthesized earlier in this
Figure 30: 1H NMR of 1, 300 MHz, CDC13
group by Kukla. Homonuclear proton decoupling allowed specific assignment of most of the $^1$H NMR signals.

$^1$H-NMR (300 MHz, CDCl$_3$) $\delta$ 6.40 (dd, $J_{11,12} = 5.7$ Hz, $J_{11,10} = 2.9$ Hz, H$_{11}$), 6.08 (ddd, $J_{12,11} = 5.7$ Hz, $J_{12,1} = 3.0$ Hz, $J_{12,9} = 1.0$ Hz, H$_{12}$), 6.04-5.87 (series of m, H$_3$-6,9), 4.94 (dddd, $J_{8,9} = 9.4$ Hz, $J_{8,7} = 3.5$ Hz, $J_{8,1} = 1.8$ Hz, $J_{8,10} = 0.7$ Hz, H$_8$), 2.91-2.83 (m, H$_7$), 2.83-2.79 (m, H$_2$), 2.77-2.72 (m, H$_{10}$), 2.45-2.41 (m, H$_1$).

$^1$C-NMR (75 MHz, CDCl$_3$) 141.05, 134.58, 132.99, 132.08, 129.34, 127.08, 125.27, 122.36, 50.46, 44.21, 41.59, 38.25.

The $^1$H NMR spectrum of 196 shows many similarities to that of bicyclo[3.2.1]octa-2,6-diene (197) that was assigned by Brown and Occolowitz,

$^1$H NMR (100 MHz, CCl$_4$) $\delta$ 6.10 (q, H$_7$), 5.89 (br, H$_2$), 5.58 (q, H$_6$), 5.10 (br d, H$_3$), 2.58 (br, H$_{1,5}$), 2.21 (complex d, $J = H_{exo}$), 1.90 (dd, $J = Hz$, H$_{5,syn}$), 1.76 (d, H$_{endo}$) 1.68 d, H$_{anti}$). (The authors did not report any coupling constants; although q stands for quartet, only a dd makes sense for their absorption, unless the coupling constants for three different
indicates a change in appearance of the peak; but no coupling constant was extractable due to the complexity of the coupling pattern.

**Figure 31:** Homodecoupling (\(^1\)H) of 196 (300 MHz, CDCl\(_3\))
protons happen to be identical.) Especially striking are the upfield shifts of H_{196} (in 196) to $\delta$ 6.40 ppm and of H_{197} (in 197) to $\delta$ 6.10 ppm, and the downfield shift of H_{8} (m, 196) to $\delta$ 4.94 ppm and of H_{3} (in 197) to $\delta$ 5.10 ppm.

That 196 was identical with Kukla's hydrocarbon was also shown by comparing the 300 MHz $^1$H-NMR spectrum (CDCl$_3$) of 196 with that of material synthesized by Kukla's method$^{137}$ (Scheme 32).

Scheme 32: Synthesis of 196 by Kukla's Method

Woodward's research group wanted to synthesize truncated tetrahedrane (110) via several electrocyclic
rarrangements using tetraene 1 as an advanced intermediate\textsuperscript{86,87}.

Scheme 33: Woodward's Strategy to Truncated Tetrahedrane (204)

In hindsight, this plan was probably doomed because the desired rearrangement products stemming from thermally allowed [1,5] alkyl migration to give 202 and Cope rearrangement to 203 are thermodynamically less stable than the precursor 1, as predicted by forcefield calculations derived from Allinger's MMP2\textsuperscript{141} program using geometries preoptimized by Still's MODEL program\textsuperscript{142} (a variation of Allinger's MM2\textsuperscript{143,145,147}; see Figures 33-36 for stereoviews of 1, 196, 202, 203 as calculated by MODEL).
Obviously, the heats of formation of the different (CH)_{12} valence isomers have to be treated with caution, because the force field calculations do not consider electronic interactions, like the through-bond-interaction in tetraene 34 that is predicted to be destabilizing by the semiempirical MINDO/3 program. The puckering angle of 28.5°C for unsubstituted cyclobutane, as determined by Allinger's MM2 force field program, was close to the experimental value of 35°C, although the calculation
Figure 33: Stereoview of 1
Figure 34: Stereoview of 196
Figure 35: Stereoview of 202
Figure 36: Stereoview of 203
underestimated the energy barrier to ring inversion by 0.6 kcal/mol (0.9 kcal/mol instead of 1.5 kcal/mol).^94,147

From among the calculated (CH)_{12} valence isomers, 196 is indeed the thermodynamic sink. The thermodynamic instability of the theoretical [1,5-C] shift isomer 202 is underlined by the failure of several research groups to synthesize this molecule (Scheme 34).

Scheme 34: Scott's Attempt to Synthesize 202

![Scheme 34](image)

The propensity of this type of skeleton to relieve strain by rearrangement is known (Scheme 35):

Two mechanisms are theoretically possible for this formal [1,3-C] migration: (1) a concerted pathway and (2) a stepwise pathway going through biradical intermediate 212 (Scheme 36).

To accept the concerted [1,3] allyl migration as a viable alternative needs some explanation. According to the
Masamune et al.\textsuperscript{149}, Katz et al.\textsuperscript{150}, 1970:

\[ \begin{align*}
\text{208} & \xrightarrow{[3,3c]} \text{RT} \quad \text{209} \\
1' & \quad \quad 2' \\
2 & \quad \quad 3 \\
1 & \quad \quad 3'
\end{align*} \]

Vedejs et al., 1977\textsuperscript{151}:

\[ \begin{align*}
\text{210} & \xrightarrow{[1,3c]} \text{50}^\circ\text{C} \quad \text{211} \\
1 & \quad \quad 2 \\
1' & \quad \quad 2' \\
1 & \quad \quad 3 \\
1 & \quad \quad \text{CO}_2\text{Et}
\end{align*} \]

**Scheme 35:** Thermal Rearrangement of 208 and 210

Woodward-Hoffmann rules\textsuperscript{152}, thermal [1,3] allyl shifts are only symmetry allowed, if the migrating center inverts its stereochemistry during the migration. This would lead to a hydrocarbon (213) that is very strained according to molecular models (Scheme 36).

When Berson and co-workers\textsuperscript{154-158} tried to explain why certain systems seem to favor retention of stereochemistry of the migrating center during thermally initiated [1,3]
Scheme 36: Mechanistic Options for Thermal Rearrangement of 1 into 196

\[
\begin{align*}
\text{[1,3c]} \\
\text{[\tau^1_2 \rightarrow \sigma^{-1}_3]} \quad \text{retention} \\
\end{align*}
\]

homolysis of \( C_1 - C_1 \)

\[
\begin{align*}
[1,3c] \\
[\tau^1_2 \rightarrow \sigma^{-1}_3] \quad \text{inversion} \\
\end{align*}
\]

\[
\begin{align*}
213 \\
\end{align*}
\]

Scheme 37: Thermal Rearrangement of 214

\[
\begin{align*}
\Delta & \quad \text{inversion} \\
\text{retention} \\
12 : 88
\end{align*}
\]
allyl migration (e.g. 214, Scheme 37), he suggested interaction of subjacent orbitals as a stabilizing factor.

The reason, why concerted reactions proceed faster, i.e., with a lower energy of activation, than their radical counterparts, is that they preserve bonding interactions in the transition state. Berson argued that, although weak, symmetry-allowed interaction between the migrating center and both the doubly occupied molecular orbital subjacent to the SOMO and the LUMO of the allyl fragment would stabilize

**Figure 37:** FMO Schemes of [1,3-C]Migrations
the transition state and make it preferable to the biradical intermediate. Therefore the 'thermally forbidden', concerted [1,3-C] migration should be considered as an alternative to the biradical pathway (Figure 37).

One way to differentiate a concerted [1,3-C] from a mechanism involving a biradical intermediate is to take advantage of the high symmetry of tetraene 1 and follow an isotopic label through the rearrangement. Tetraene dibromide 166 was the precursor of choice (Scheme 38).

Scheme 38: Deuteration of 166

![Scheme 38: Deuteration of 166]

The $D_{2d}$ symmetry of 1 makes positions 3, 6, 9 and 12 fully equivalent. Therefore, instead of breaking differentiated cyclobutane bonds, tetraene 1-$d_2$ can be considered tetradeuterated in those positions.
When a solution of dideuterated tetraene 1-\(d_2\) in carbon tetrachloride was thermolyzed at 110-115°C in a sealed NMR tube for 5 h, the proton-decoupled 77 MHz \(^2H\) NMR spectrum showed only four signals of almost equal height (Scheme 39).

Scheme 39: Thermal Rearrangement of 1-\(d_2\)
Figure 38: $^2\text{H}$ NMR of $1-\text{d}_2$

Figure 39: $^2\text{H}$ NMR of 196-'d$_2$' from Thermal Rearrangement of $1-\text{d}_2$
Figure 40: $^1$H NMR of 196 and $^2$H NMR of 196-$^2$d$_2$ in CCl$_4$

$^1$H NMR (500 MHz, CCl$_4$)

$\delta$ 6.4 ($H_{11}$), 6.08 ($H_{12}$),
6.02–5.86 ($H_{6,9}$),
4.87 ($H_8$), 2.87 ($H_7$),
2.83 ($H_5$), 2.76 ($H_{10}$),
2.47 ($H_3$)

$^2$H NMR (77 MHz, CCl$_4$)

$\mu$ 6.08 ($D_{12}$), 5.99, 5.92,
5.87 ($D_{3,6,9}$) in peak
height
ratio 1:1.24:1.11:1.30

Since $^2$H NMR chemical shifts correspond closely to $^1$H NMR shifts and since the $^1$H NMR spectrum of tetraene had been assigned by homodecoupling, the deuterated positions were readily identified.

The secondary kinetic deuterium isotope effect resides within the error limits of detection and can therefore be ignored to a first approximation (compare Scheme 36).

Of the two alternatives only the concerted [1,3-C] shift is reconcilable with the deuterium scrambling pattern (compare Scheme 39).

Surprisingly, irradiation of tetraene 1 led to the same rearranged isomers in addition to another (CH)$_{12}$-valence
isomer, tentatively assigned as trans fused bicyclo[6.4.0]-dodeca-2,4,6,9,11-pentaene (217) (Scheme 40).

Scheme 40: Photochemical Rearrangement of 1

In 217, the aliphatic absorption at relatively low field (δ 3.53-3.59 ppm) indicated the presence of a doubly allylic methine proton. Since no other aliphatic absorption except those belonging to 196 were present, a C₂ or C₅-symmetric molecule seemed probable.

The higher vinyl to aliphatic proton ratio suggested the transformation of a ring connection into a double bond, i.e. opening of the tricyclic structure to a bicyclic one.

Attempted isolation of the second component (217) by preparative GC (T_{inj} = 250°C, T_{col} = 190°C, t_{ret} = 11-13
min) only resulted in thermal rearrangement to a new compound, 1,2-benzocycloocta-1,3,7-triene (219) (Scheme 41).

Scheme 41: Thermal Rearrangement of 217

![Scheme 41](image)

Observed for 217: $^1$H-NMR (300 MHz, CDCl$_3$) $\delta$ 7.23-7.16 (m, 2H), 7.16-7.09 (m, 2H), 6.54 (d, $J_{4,5} = 11.9$ Hz, $H_6$), 6.00-5.90 (m, $H_5$), 2.33 (m, $H_6$).

The synthesis of 219 was first reported by Wittig et al.$^{159}$ Its $^1$H NMR spectrum was recorded by Meier et al.$^{160}$ and Farnum et al.$^{161}$ and was in good agreement with our observed spectrum.

Farnum et al. (1982)$^{161}$: $^1$H-NMR (250 MHz, CDCl$_3$) $\delta$ 7.22 (m, 2H), 6.25 (d, $J = 12.3$ Hz, 2H), 5.92 (m, 2H), 2.29 (m, 4H).

The peak at $\delta$ 6.25 ppm in Farnum's spectrum must be a typographical error because it deviates from our and Meier's peaks as well as Buchanan and McCarville's spectrum of the dideuterated compound 219-d$_2$ ($\delta$ 6.52 ppm (d, $J = 11.9$ Hz)).$^{162}$
Only two of the known \((CH)_{12}\) valence isomers fit the \(^1H\) NMR fingerprint of the second photolytic rearrangement product, viz., the \textit{cis}- and \textit{trans}-bicyclo[6.4.0]dodeca-2,4,6,9,11-pentaenes \((220)\) and \((217)\) \(^{163}\) (Figure 41).

**Figure 41:** Röttele et al.'s \(^1H\) NMRs of 217 and 220

\[
\begin{align*}
217 \ (C\textsubscript{1}) & \quad 5.80 \text{ (m, 10H)}, \ 3.43 \ ('s', \ 2H) \\
220 \ (C\textsubscript{8}) & \quad 5.78 \text{ (m, 10H)}, \ 3.47 \ ('s', \ 2H)
\end{align*}
\]

Röttele and co-workers studied the thermal and photochemical interconversion of [12]annulene valence isomers \(^{163,164}\) (Scheme 42).

Due to its thermal instability, 220 can be excluded and 217 confirmed as the second photorearrangement product.

The origin of 219 can then be explained by two consecutive, thermally allowed \([1,5-H]\) migration with extended conjugation and aromaticity as the driving forces (Scheme 43).

Exposure of 217 \([\lambda_{\text{max}}=252 \text{ nm (6000)}]\) \(^{163}\) to short-wave length
irradiation (254 nm) opens a pathway that finally leads to the ultimate thermodynamic sink of benzene dimers, i.e., benzene.

When tetraene 1 was irradiated with light of long wavelength (366 nm) in methylene chloride-d$_2$ (only the starting material 1 absorbs light, whereas products 196 and 217 remain unaffected), 217 does not funnel into benzene
(compare Scheme ..). The fact that the integration ratio of all (CH)$_{12}$ hydrocarbons combined and an arbitrary internal standard, CDHCl$_2$, stayed constant during the irradiation, suggests that the conversion of 1 into 196 and 217 was quantitative (Table 1).

At the same time, the ratio 196:217 stayed fairly constant, i.e., they do not seem to be derived from each other, but stem directly from 1 or a common intermediate.

As expected, the photochemical rearrangement in chloroform-d$_1$ took longer because, due to its higher wavelength UV cutoff, chloroform-d$_1$ absorbs a bigger portion of the incoming light (Table 2). The apparent loss of material as evident from the ratio (1+196+217+218):standard is probably due to the equilibration of 217 into the other valence isomers (221, 220, 222, compare Scheme 42) that are not accounted for. The shorter wavelength irradiation (254 nm) can excite photolysis product 217 and trigger further rearrangements that finally lead to the thermodynamic sink

Scheme 44: Photosensitized Irradiation of 196
**Table 1:** Irradiation of 1 at λ 366 nm in CD$_2$Cl$_2$.

<table>
<thead>
<tr>
<th>Δt/min</th>
<th>1 2.58-2.50 (4H)</th>
<th>196 2.88-2.69 (3H)</th>
<th>217 3.53-3.49 (2H)</th>
<th>CDHCl$_2$ 5.32</th>
<th>196:197</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
<td>0</td>
<td>0</td>
<td>0.81</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>72</td>
<td>18</td>
<td>10</td>
<td>0.95</td>
<td>1.8</td>
</tr>
<tr>
<td>11</td>
<td>55</td>
<td>30</td>
<td>15</td>
<td>1.05</td>
<td>2.0</td>
</tr>
<tr>
<td>24</td>
<td>24</td>
<td>53</td>
<td>24</td>
<td>0.88</td>
<td>2.2</td>
</tr>
<tr>
<td>51</td>
<td>0</td>
<td>65</td>
<td>35</td>
<td>0.86</td>
<td>1.9</td>
</tr>
</tbody>
</table>
Table 2: Irradiation of 1 at $\lambda$ 254 nm in CLCl$_3$.

<table>
<thead>
<tr>
<th>$\Delta t$/h</th>
<th>$\delta$/ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 2.60-2.50</td>
</tr>
<tr>
<td></td>
<td>196 2.92-2.72</td>
</tr>
<tr>
<td></td>
<td>217 3.56-3.43</td>
</tr>
<tr>
<td></td>
<td>218 7.36</td>
</tr>
<tr>
<td></td>
<td>(1+196+217+218): standard 1.31-118</td>
</tr>
<tr>
<td></td>
<td>196: standard 0.31</td>
</tr>
<tr>
<td></td>
<td>217: standard 0.21</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>0</th>
<th>100</th>
<th>0</th>
<th>0</th>
<th>0</th>
<th>1.11</th>
<th>0</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>52</td>
<td>28</td>
<td>19</td>
<td>0</td>
<td>1.10</td>
<td>0.31</td>
<td>0.21</td>
</tr>
<tr>
<td>14</td>
<td>0</td>
<td>45</td>
<td>25</td>
<td>1</td>
<td>0.80</td>
<td>0.50</td>
<td>0.28</td>
</tr>
<tr>
<td>64</td>
<td>0</td>
<td>35</td>
<td>12</td>
<td>9</td>
<td>0.68</td>
<td>0.39</td>
<td>0.13</td>
</tr>
</tbody>
</table>
benzene. The decrease in intensity is much more dramatic for 217 than it is for 196 upon prolonged irradiation. The only photorearrangement known for 196 is photosensitized (Scheme 44).\textsuperscript{137}

When deuterium labeled tetraene 1-\textsubscript{d\textsubscript{2}} was photolyzed in methylene chloride-\textsubscript{d\textsubscript{2}} at room temperature with long wavelength light, only four of the twelve possible positions in 196 showed deuterium incorporation, all with the same intensity (Scheme 45).

Scheme 45: Photochemical Rearrangement of 1-\textsubscript{d\textsubscript{2}}

That is, both thermal and photochemical rearrangements of 1 seem to go via a concerted [1,3-\textsubscript{C}] migration. In
Figure 42: $^2$H NMR of photolysis products of 1-d$_2$
Compare $^1$H NMR (300 MHz, CD$_2$Cl$_2$ 6/ppm:

![NMR spectrum diagram]
contrast to the thermolysis, however, the photolytic [1,3-C] is allowed to proceed with retention of the migrating center according to the Woodward-Hoffmann rules\textsuperscript{153}. In the second product, 217, the label is scrambled over all positions with a predominance at $\delta$ 5.56 ppm. This is in agreement with a mechanism involving an open [12]annulene, that can recylize by thermal disrotatory six electron, photochemical conrotatory six electron, thermal conrotatory eight electron, and photochemical disrotatory eight electron electrocyclic ring closures to give 217.
Scheme 46: Summary: Thermal and Photochemical Rearrangement of 1

Scheme 46 involves the thermal and photochemical rearrangement of 1. The reaction pathways include bond homolysis and involve compounds 196, 212, 217, 220, and 222. The reaction pathways are as follows:

1. **Thermal Reaction:**
   - 1 → 196
   - 1 → 217

2. **Photochemical Reaction:**
   - 1 → 196
   - 1 → 220
   - 1 → 222

The compound 218 is actually observed and identified in the scheme.
C) Photoelectron and UV Spectra

The Gleiter group in Heidelberg, West Germany, our theoretical collaborators, recorded the photoelectron spectra of tetraene 1, diene 191 and hydrocarbon 192 (Scheme 44; for the spectra, see Appendix B, Figures 82-84)\(^{165,166}\).

**Figure 44:** 1, 191 and 192

Assignments to the absorptions have clearly demonstrated three features that are in good agreement with the theoretical calculations (MINDO/3\(^{22}\), see Figure 45; for the partial MO schemes of 1 and 6 see page 27, Figure 22 and page 7, Figure 5, respectively).

1) The energy of the HOMO rises from -9.2 to -8.06eV, to -7.56eV, as the cisoid butadiene 225 is incorporated into a cycloheptane skeleton (226)\(^{168}\); an additional methano bridge initiates the interaction between a cyclobutane ring and one \(\pi\)-ribbon (34); a second, still saturated four carbon bridge spans the remaining apices of the cyclobutane ring (191), and, finally, through-bond interaction of the two \(\pi\)-ribbons through the cyclobutane relay is switched on (1).
(2) As in the case of [4.4]spirononatetraene (6), the
degeneracy of the butadiene HOMO is broken; without any
communication, each butadiene HOMO would be expected to have
the same energy; however, due to the through-bond inter-
action, they are split.
3) On the assumption that the size of the HOMO-SUBHOMO gap, i.e. the extent to which the degeneracy of the orbitals is broken, is an indicator for the size of interaction, then through-bond interaction (as in 1) appears to be stronger than spiroconjugation (as in 6):

1: \[ \varepsilon(\text{HOMO}) - \varepsilon(\text{SUBHOMO}) = 1.44\text{eV} \]

6: \[ \varepsilon(\text{HOMO}) - \varepsilon(\text{SUBHOMO}) = 1.23\text{eV} \]

A similar trend that was seen for \( \varepsilon(\text{HOMO}) \) in the PE spectra can be observed for the electronic spectrum (Figure 46). In going from butadiene 225\textsuperscript{168} to tetraene 1, the \( \lambda_{\text{max}} \) with the highest extinction coefficient shifts from 217 nm to 318 nm. This trend is understandable when one remembers that the butadiene LUMO's remain largely unaffected by the interaction with the cyclobutane Walsh orbitals. Therefore, an increase of \( \varepsilon(\text{HOMO}) \) translates into a decreased HOMO-LUMO gap \([\varepsilon(\text{LUMO})-\varepsilon(\text{HOMO})]\) and a reduced transition energy \( E \) or longer wavelength absorption. Again, through-bond interaction wins out over spiroconjugation. 1: 318 nm, 6: \( \lambda_{\text{max}} = 270 \text{ nm} \).

Interestingly, both photoelectron and UV spectroscopy yield very similar HOMO-SUBHOMO gaps.

\textbf{PES:} \[ \varepsilon(\text{HOMO}) - \varepsilon(\text{SUBHOMO}) = -7.56\text{eV} - (-9.00)\text{eV} = 1.44\text{eV} = \Delta I(i,j) \]

\textbf{UV:} \[ E_{0,0} (1) - E_{0,0} (2) = 5.04\text{eV} - 3.50\text{eV} = 1.54\text{eV} = \Delta E(i,j) \]
Previously, Heilbronner and coworkers had observed the same phenomenon for [4.4]spirononatetraene (6)\(^8\). There, \(\Delta E(i,j)\) was 1.19 eV to 1.28 eV, and \(\Delta I(i,j)\) was 1.23 eV; \(\Delta E(i,j)\) and
\( \Delta I(i,j) \) were therefore identical within the limits of error.

\[
\Delta^1E(i,j) = \Delta I(i,j) + (J_{ik} - J_{jk}) + 2(K_{jk} - K_{ik})^8
\]

Therefore the energetic difference of the electronic transitions \( [\Delta^1E(i,j)] \) and the difference of the ionization potentials \( [\Delta I(i,j)] \) will only be the same, if the terms of the Coulomb integrals \( J_{ik} - J_{jk} \) and the exchange integrals \( 2(K_{jk} - K_{jk}) \) are equal to 0 (usually not the case), i.e., if electronic motion is independent from nuclear motion (Figure 47). For 1 the Coulomb integral term and the exchange integral term must be very similar.

**Figure 47:** Electronic Transitions and Ionization, when the Coulomb-Integrals and the Exchange Integrals are equal to 0
D) Reduction of Tetraene 1

While PE-spectroscopy revealed information about the occupied orbitals of tetraene 1, specifically their ionization potentials, one-electron reduction to the radical anion would theoretically show the charge distribution in the LUMO by the hyperfine coupling pattern in the ESR spectrum. The ESR spectrum could answer the question whether the LUMO of 1 is delocalized over the whole molecule or localized in one diene bridge (Figure 48).

**Figure 48:** Radical Anion of 1

\[
\begin{array}{c}
\text{or}
\end{array}
\begin{array}{c}
\text{or}
\end{array}
\]

Gleiter's extended Hückel calculations\(^{22}\) predicted the latter: the LUMO of 1 is degenerate and resembles the LUMO of isolated butadienes (compare page 27, Figure 22; Figure 49).

**Figure 49:** Degenerate LUMOs of 1
Therefore the ESR spectrum of the racial anion 1 should only display $\beta$-hyperfine splitting with two pairs of 2 identical hydrogens, not two pairs of 4 identical hydrogens as expected for the completely delocalized case.

The only spiroconjugated case investigated by ESR spectroscopy, $12^{13}$, showed the negative charge to be localized largely in one $\pi$-ribbon (Figure 50).

Figure 50: ESR Hyperfine Splitting Constants in Radical Anions 12 and 13 Long Range ESR Hyperfine Splitting Constants in the Radical Anions of 37 and 38

Comparison with the dienone 13 demonstrates that only a small portion of the extra charge density leaked into the second ring.

In the class of compounds where one $\pi$-ribbon can interact with a cyclobutane ring, Nelson and Gillespie studied radical anion 37$^{49}$ (Figure 51).

They took the fact that the ethano bridge hydrogens couple relatively strongly (1.20 Gauss) with the excess electron as evidence for interaction of the naphthalene
bridge with the Walsh orbitals of cyclobutane. In contrast to that, Russell, Whittle, and Kaeske reported only a very small long-range hyperfine splitting (0.15 G) with the ethano bridge hydrogens in semidione \(38^{48}\).

The example that comes closest to tetraene 1 is tetra-benzo derivative 48. As has been discussed earlier, (compare page 28) Müllen and Huber found that the ESR spectrum of 48 depended on the reduction conditions (Figure 52)\(^{59}\).

With potassium as countercation (56), the negative charge seemed to be completely delocalized over the two biphenyl bridges, because the ESR spectrum showed coupling with three quadruplets of identical protons. Not so with tetra-\(\text{n-}\)butylammonium ion (55): there the spectrum resembled very much that of 9,10-dihydrophenanthrene (57), where the electron appeared to be completely localized in one biphenyl
Müllen and Huber explained this difference with the different sizes of the countercations.

The behavior of 56 could be rationalized in terms of a SOMO (former LUMO of the neutral species) that spans the whole molecule, or by a rapidly equilibrating radical anion, in which the charge resides only for a short time in one of the biphenyl bridges and quickly transfers into the other bridge intramolecularly\textsuperscript{171}. This phenomenon resembles the intramolecular electron transfer in mixed valence metal complexes\textsuperscript{172,173}. For example, in the Creutz-Taube ion (227) a pyrazine bridge facilitates the exchange of an
electron between the two ruthenium atoms of different oxidation states. One can draw the analogy between the metal complex where the pyrazine ligand serves as an electronic mediator between ruthenium (II) and ruthenium (III), and the radical anion of tetraene 1, where the cyclobutane with its high-lying Walsh orbitals can serve as a mediator between the neutral butadiene bridge (formal oxidation level 0) and the monoreduced butadiene bridge (formal oxidation level -1; Figure 53).

Figure 53: Analogy of Creutz-Taube Ion (227) and Radical Anion of 1

Harriman and Maki estimated\textsuperscript{174} the frequency of intramolecular electron transfer of monoreduced nitrophenyl compounds 9 that are bridged by methano-, ethano-, oxo- and thio-bridges. Analysis of the ESR lineshape yielded the following electron transfer rates, $\nu(s^{-1})$ (Figure 54).

When Müllen and Huber\textsuperscript{175} reduced tetraene 1 with potassium in THF or dimethoxyethane at -78°C, they obtained an intensively red solution. However, instead of the ESR
Figure 54: Intramolecular Electron Transfer Rates in Rates in 228

X -nothing- -CH2- -S- -O- -CH2-CH2-

v/s.\(^{-1}\) \(\approx 10^8\) \(\approx 10^8\) 9-10\(^6\) 3-10\(^6\) 2-10\(^6\)

spectrum of 1, they recorded a spectrum of another paramagnetic species that had formed apparently by instantaneous rearrangement of 1. Assisted by the corresponding ENDOR resonances they could interpret the ESR spectrum in terms of the following hyperfine coupling constants:

- 1H 0.0270 mT
- 3H 0.0525 mT
- 1H 0.0630 mT
- 1H 0.2475 mT
- 1H 0.3735 mT
- 1H 0.4650 mT
- 1H 0.5295 mT
- 1H 0.5775 mT
- 1H 1.0800 mT

From a calculation of the spin populations (McLachlan, McConnell), the number of hydrogens, and symmetry considerations they suggested structure 229 as rearrangement product.
The ESR spectrum disappeared again upon prolonged metal contact, but not due to the formation of a diamagnetic species (e.g. a dianion), because even the NMR signals of the starting material just disappeared during the reduction, without producing new signals.

Reoxidation with oxygen or iodine yielded broad absorptions in the olefinic region of the NMR spectrum, but after filtration through alumina no definite product could be identified.

Protonation of the reduction mixture with methanol led to product mixtures that contained higher molecular weight compounds according to mass spectroscopy, possibly oligomers or polymers.

Obviously without additional evidence, structure 229 remains conjecture. However, one could imagine the following scenario to arrive at 229 (Scheme 47).

Although extended Hückel calculations indicate that the LUMOs of 1 are localized in the diene bridges, they could
enter into symmetry-allowed interaction with antibonding cyclobutane Walsh orbitals. The flat projection of the cyclobutane Walsh orbitals demonstrate the antibonding character in the cyclobutane carbon-carbon bonds (Figure 55). Occupation of those LUMO's with additional electrons would therefore weaken the Cyclobutane Bonds and trigger rearrangement by rupture of the cyclobutane ring to give a dihydroheptalene radical anion (230) (Scheme 47).
E. Summary

Tetraene 1 was obtained by bromination and dehydrobromination of Chasey's diene 128. The improved, optimized synthetic scheme (counting the best yields, the 26-step sequence afforded 1 in 4.4% overall yield starting from trans-cinnamic acid) made available quantities of 1 sufficiently large to permit its physico-chemical study.

The light-sensitive tetraene is relatively stable at room temperature in diluted form. Dimerization (polymerization) does, however, occur slowly when stored in neat condition.

At elevated temperatures (100°C), 1 rearranges to Kukla's hydrocarbon (196) by a concerted [1,3]carbon migration that is forbidden by the Woodward-Hoffmann rules. Photolysis with long wavelength light (366 nm) leads to the same (CH)_{12} valence isomer 196 by a concerted reaction pathway, in addition to bicyclo[6.4.0]pentaene (217).

Photoelectron spectroscopy shows the raising of the HOMO energy and the splitting of the formerly degenerate butadiene HOMO's that was expected from through-bond conjugation of the mutually perpendicular \( \pi \)-ribbons through the cyclobutane relay orbitals. The dramatic bathochromic shift in the UV absorption confirms the reduced HOMO-LUMO gap. In
comparison to the corresponding spiroconjugated (through-space) conjugated tetraene (6), the stronger HOMO-SUBHOMO splitting (PES) and the reduced HOMO-LUMO gap (UV) demonstrate that the cyclobutane relay is suitable to enhance interaction of the mutually perpendicular $\pi$-ribbons.

One-electron reduction of 1 does not lead to the radical anion of 1 but to skeletal rearrangement.
A) **Synthesis**

In applying the only other approach to the tricyclo\[5.3.0.0^{2,8}\]decane skeleton, Gleiter et al.\textsuperscript{175} synthesized ketone 235 by photolysis of \textit{cis,cis}-2,7-cyclodecadienone (231) (Scheme 48).

**Scheme 48:** Gleiter's Synthesis of 235
In contrast to Heathcock's trans,trans-2,7-cyclodecadienone (77) that cross-cyclizes to the tricyclo[4.4.0.0^2,8]decane skeleton (compare page 34, Scheme 5), 231 photoisomerizes to 232, then cross-cyclizes to 235 in accord with Srinivasan's 'Rule of Five' (compare page 35). Recently, Gleiter and co-workers were able to photocyclize 236 to 237\textsuperscript{176,177}, a result that theoretically would enable them to elaborate concurrently a two-carbon and a four-carbon bridge. However, attempts to convert the photoproduct into the target triene 2 have been unsuccessful up to now\textsuperscript{177} (vide infra) (Scheme 49).

Scheme 49: Gleiter's Photocyclization of 236 to 237
Strategy I

Scheme 50: Strategy I to 2

Carlson and May demonstrated\textsuperscript{178} that the strained bicyclo-[2.1.1]-hex-2-enes 248 and 33 can be synthesized by Ramberg-Bäcklund methodology\textsuperscript{179} (Scheme 51).

Scheme 51: Carlson and May's Synthesis of 248 and 33

\( R = \text{Me} \) 248 40%  
\( R = \text{H} \) 33 68%
Experimentally, cyclization of the earlier intermediate dibromide 144 with anhydrous sodium sulfide in hot HMPA\(^{180}\) yielded the tricyclic sulfide 238 almost quantitatively. Care had to be taken to avoid any moisture during the \(\alpha\)-chlorination of 238 with N-chlorosuccinimide (NCS) in hot carbon tetrachloride to avoid hydrolysis of \(\alpha\)-chloro sulfide 249 to mercaptan aldehyde 250 (Scheme 52).

Scheme 52: Hydrolysis of 249

![Scheme 52: Hydrolysis of 249](image)

Selective oxidation of 249 to chloro sulfone 239 was complicated by the fact that the intermediate chloro sulfoxide 251 stained only very weakly on TLC plates with the common staining solutions (phosphomolybdic acid, \textit{para}-anisaldehyde, iodine). Also, excess \textit{meta}-chloroperbenzoic acid (MCPBA) readily over-oxidized 239 to epoxides 252 and 253; these epimers were readily separable by MPLC (Scheme 53). Interestingly, an incomplete oxidation showed only one of the two possible chloro sulfoxide diastereomers (251) to be present. Consequently, only one of them was formed, or both
Scheme 53: Oxidation of 249

were formed, and one of them reacted faster to the chloro sulfone than the other. It was not necessary to change the solvent from carbon tetrachloride to methylene chloride after the α-chlorination of sulfide 238, since oxidation of α-chloro sulfide 249 proceeded as well in carbon tetrachloride (although MCPBA was not as soluble). It was sufficient simply to filter off the succinimide. Solvent change only increased the danger of hydrolysis of 249. The α-chlorination could also be performed in methylene chloride (it was actually instantaneous at room temperature because NCS was soluble in methylene chloride), but the solubility of the resulting succinimide made its removal difficult
after the reaction. Since monoperphthalic acid offered no advantage in the control and selectivity of the oxidation of 249 to 239, buffer-washed MCPBA (99% purity) proved to be more convenient.

The usual Ramberg-Bäcklund conditions (potassium tert-butoxide, THF) instantaneously transformed 239 into the very volatile diene 240. The hydrocarbon was isolated by washing most of the THF out of the pentane solution with water, rotary evaporation of the bulk solvent at room temperature/150 mm Hg, careful evacuation (room temperature/25 mm Hg), and ultimately trapping of the diene selectively at 40°C/0.05 mm Hg. At this pressure and temperature, no residual THF condensed according to $^1$H NMR. In the $^1$H NMR

Figure 56: $^1$H NMR of Bicyclo[2.1.1]hex-2-enes

![Chemical structures](image)

6, 7.13 (t, $J=2.2$ Hz, $H_9$); 2.58 (t, $J=2.2$ Hz, $H_1, 8$).

6.07 (t, $J=2$ Hz, $H_2$).

6.0 (t, $J=2.0$ Hz, $H_1$).

3.76 (t, $J=2$ Hz).
spectrum of 240, the vinyl protons $H_9, H_{10}$ and the bridgehead protons $H_1, H_8$ appear as two triplets, a feature seemingly characteristic of bicyclo[2.1.1]hex-2-enes (Figure 56). Both the vicinal coupling $J_{9,8}$ and the allylic $W$-coupling $J_{10,8}$ happen to be identical in the isolated AA'XX' spin system\textsuperscript{182,183}.

Diene 240 is surprisingly temperature sensitive. It rearranges to a completely asymmetric hydrocarbon (10 signals in $^{13}$C NMR) on the preparative GC column ($T_{\text{inj}} = 180^\circ \text{C}$, $T_{\text{col}} = 150^\circ \text{C}$, $T_{\text{det}} = 180^\circ \text{C}$, $t_{\text{ret}} = 10-14 \text{ min}$). The $^1\text{H}$ NMR spectrum pointed to 3,6-dihydroisobullvalene (261) as the product of a formal [1,3-$\text{C}$] migration, possibly via a biradical intermediate (260) (Scheme 54, see Appendix B, Figure for $^1\text{H}$ NMR and $^{13}$C NMR of 261).

Scheme 54: Thermal Rearrangement of 240 into 261
Bicyclo[2.1.1]hex-2-enes are well preceded to undergo [1,3] carbon migrations, in principle, retro-vinyl


![Scheme 55](image)

(The difference to 100% was accounted for by CH₂-migration)
cyclopropane-cyclopentene rearrangements. When Roth and Friedrich investigated the stereochemistry of the migrating carbon in 5-substituted bicyclo[2.1.1]hex-2-enes, they found a predominance of inversion, as expected by the Woodward-Hoffmann rules if the rearrangement follows a concerted, thermally allowed pathway. The minor retention might be explained by a competing stepwise biradical mechanism (Scheme 55).

However, as in the rearrangement of tricyclo[3.3.-0.0^2,6]octa-3,7-diene (42) to semibullvalene (268) (Scheme 56), inversion is geometrically impossible for 240. Therefore, both systems probably follow a radical mechanism (compare Chapter VB, for thermal rearrangement of 1).

Scheme 56: Thermal Rearrangement of 42 into 240

When 261 was heated even higher (preparative GC: T_{col} ≥ 170°C), two additional hydrocarbons started to appear. In the ^1H NMR spectrum, the vinyl H/aliphatic H ratio changed from 4:8 (as in 240 and 261) to 6:6; in the ^13C NMR spectrum, the sp2-C/sp3-C ratio changed from 4:6 (as in 240
Figure 58: $^1$H NMR of 269

Figure 59: $^1$H NMR of 270

Figure 57: $^1$H NMR of 268
Figure 60: $^1$H NMR of Mixture of 268 and 270.
and 261) to 6:4, indicating that the tricyclic diene structure was converted into a bicyclic triene structure during the rearrangement. The close spacing of the two sets of 10 signals in the $^{13}$C NMR spectrum hinted at structurally related $C_{10}H_{12}$ isomers. The $^1$H NMR spectrum of the mixture looked very similar to those of tetrahydroazulenes 268-270 that had been characterized earlier by Heger and Grimme.$^{186,187}$ (Figure 57-59).

Based on comparison of the $^1$H NMR spectra and the probable mechanism for the second rearrangement (Scheme 57), structures 268 and 270 are considered to be the rearrangement products.

**Scheme 57: Thermal Rearrangement of 261 into 268 and 270**

![Scheme 57: Thermal Rearrangement of 261 into 268 and 270](image)

Inspection of molecular models shows that, in addition to being activated by hyperconjugation with the adjacent double bond, the migrating hydrogen lies in very close proximity to the opposing double bond, ideally positioned for the electrocyclic rearrangement. Again, there is ample
precedence for 1,5-hydrogen shifts in systems in which one of the double bonds of the participating diene is substituted by a cyclopropane ring, e.g.,

Kusacek and Musso, 1970:

Glass, Zirnea and Winstein, 1963:

Paquette and Detty, 1978:

Mironov et al. established that 1,3-cycloheptadienes equilibrate rapidly above 120°C (Scheme 58), explaining the mixture of tetrahydroazulenes 268 and 269. This thermal instability of diene 240, i.e. the propensity of the cyclobutane carbon-carbon bonds to break homolytically, also might explain why no material containing an
intact bicyclo[2.1.1]hex-2-ene moiety (according to $^1$H NMR) was isolated from the attempted allylic bromination of 240 (Scheme 59).

The radical center $\alpha$ to the bicyclo[2.1.1]hex-2-ene offered a splendid opportunity to relieve the considerable ring strain. The literature precedence for allylic radical bromination $\alpha$ to strained ring systems was ambiguous. Paquette, Philips, and Wingard reported that allylic bromination of 278 followed by dehydrobromination afforded
279 smoothly, whereas in the case of triene 280 the same sequence (with two equivalents of N-bromosuccinimide) led to a wild mixture of compounds for no obvious reason (Scheme 60).

Scheme 60: Allylic Bromination of 278 and 280

As in the synthetic scheme of tetraene 1, a possible alternative to allylic bromination-reductive debromination was bromination of diene 240 followed by double dehydrobromination, and then reductive debromination of the resulting dibromide 263.

Dehydrobromination of the trans dibromide on the two carbon bridge to give the vinyl bromide would certainly
require more drastic conditions because it has to be a syn elimination. Wiberg and Ubesax had shown\(^{183}\) that reductive dehalogenation of trans-2,3-dichlorobicyclo[2.1.1]hexanes (e.g., 284) afforded bicyclo[2.1.1]hex-2-enes (e.g., 255) in excellent yield (Scheme 62), although the sodium phenanthrenide should probably be displaced by a metalating reagent like tert-butyllithium to avoid radical anion rearrangements, as seen for 1 (compare Scheme 47, page 110; Scheme 62).
However, bromination of 240 with pyridinium bromide perbromide in an acidic medium did not yield the anticipated tetrabromide 282, but instead a mixture of compounds that turned into black baseline material, whenever purification was attempted. An intermediate bromonium or hydronium ion like 281 probably initiated the decomposition and destruction of the bicyclo[2.1.1]hexane moiety. Here, milder conditions (pyridine as solvent, lower reaction temperature) might have led to a more positive result.
Strategy II.

Scheme 63: Strategy II to 2

To circumvent generation of a radical center α to the bicyclo[2.1.1]hex-2-ene unit during the allylic bromination, the halogenation was tried one step earlier, at the chloro sulfone stage. Paquette and Houser previously demonstrated

Scheme 64: Allylic Bromination of Sulfone 285
that the sulfone functionality does not interfere with the allylic radical bromination of double bonds\textsuperscript{196} (Scheme 64).

Ramberg-Bäcklund ring contraction with one equivalent of potassium tert-butoxide was expected to be very fast according to the rapid transformation of 230 into diene 240, and could be followed by reductive debromination of 241.

Indeed, allylic bromination of 239 yielded a mixture of allylic dibromides 285 (2\textsuperscript{3}=8 theoretically possible isomers) that could not be separated into clean components by preparative TLC (silica gel, 30\% ethyl acetate/petroleum ether), but was clearly recognizable as desired product by \textsuperscript{1}H NMR integration. However, base treatment of dibromo chloro sulfone 285 demonstrated that dehydrobromination was even faster than the Ramberg-Bäcklund reaction. When 285 was titrated with 1.6 M potassium tert-butoxide/THF until no more starting material was left according to analytical TLC, or alternatively, when 285 was heated to 70°C with an excess of anhydrous potassium carbonate in 2-propanol, two UV-active compounds were isolated by MPLC that were very close in \( R_F \) (silica gel, 20\% ethyl acetate/petroleum ether) to the starting material, suggesting already that something different from a nonpolar dibromide like 241 had been formed. The vinyl region of both UV light-sensitive isomers were almost superimposable with tetraene dibromide 166; both fractions gave the correct mass (\( M^+ \)) and the expected
isotope pattern in the mass spectrum for 288 and 289 (Scheme 65).

Scheme 65: Base Treatment of 285

\[
\begin{align*}
\text{Cl} & \quad \text{KOH}\text{Bu} \\
\text{O}_2\text{S} & \quad \text{THF} \\
\text{285} & \quad \text{or} \\
\text{xs K}_2\text{CO}_3 & \quad \text{iPrOH} \\
\end{align*}
\]

Consideration of the dipole moments suggested the assignment given. Initially, the fact that even an excess of potassium carbonate in hot 2-propanol only affected dehydrobromination made us wonder whether the steric constraints imposed by the rigid diene bridge made Ramberg-Bäcklund ring contraction sluggish or even impossible. However, when 285 was later treated with an excess of potassium tert-butoxide/THF, GC/MS revealed a mixture of the three possible lumibullvalene bromide isomers 290-292, as expected from mechanistic considerations\textsuperscript{197} (vide infra). Solvation of the deprotonated α-chloro sulfone by the protic solvent 2-propanol might be the reason for the different behavior in the two
base systems. Previously, Paquette, Philips, and Wingard had observed that α-chloro sulfone 293 would exchange the α and α’ protons when placed in sodium deuteroxide/deuterium oxide/dioxane/reflux/days, but not undergo Ramberg-Bäcklund ring contraction, whereas the latter would occur at much milder conditions with potassium tert-butoxide/THF/0°C/5h. They explained this reactivity difference by solvation.

Strategy III.

Scheme 66: Strategy III to 2
To transform the overoxidation problem of 239 to 252/253 into an asset, 252/253 might be treated with base to achieve both the Ramberg-Bäcklund ring contraction and the epoxide allylic alcohol rearrangement, possibly in one pot. Direct dehydration with Burgess or Martin's reagent might be risky, because the α-double bond would stabilize the incipient positive charge of an E1 mechanism and could therefore trigger skeletal rearrangement. An alternative route would be allylic oxidation to enone followed by tosylhydrazone formation and treatment with an alkyl lithium (Shapiro reaction). Young and Borden had used this sequence for transforming enone into the dimethyl substituted bicyclo[4.1.1]octa-2,4-diene (Scheme 67).

Scheme 67: Borden's Conversion of 296 into 297 by Shapiro Reaction

α-Chlorination of sulfide 238 followed by oxidation with an excess of MCPBA yielded 252 and 253 in an 87%
overall yield after MPLC (silica gel, 90% ethyl acetate/petroleum ether). Chasey opened epoxide 298 with lithium diisopropylamide in ether to allylic alcohol 299.

Scheme 68: Chasey's Epoxide-Allylic Alcohol Rearrangement of 298

However, Crandall and Apparu concluded in their review\textsuperscript{198} that lithium diethylamide was the best compromise between a bulky amide base (that minimizes the danger of nucleophilic attack on the epoxide) and a slim amide base (that can easily coordinate with the endo oxygen lone pair of a cyclic epoxide). The coordination is believed to be necessary for a six-membered ring transition state of the epoxide opening. A non-coordinating solvent like benzene also seems to aid this coordination, and addition of HMPA minimizes α-deprotonation that leads to isomerization to the ketone\textsuperscript{203} (Scheme 69).
Scheme 69: Mechanism of Epoxide- Allylic Alcohol Rearrangement

Scheme 70: Conversion of 238 to 300
When 253 was reacted with lithium diethylamide in ether/benzene/HMPA (5:15:1) at room temperature for 5.5 h and then at 50°C for 8.5 h, the only material that was isolated resembled more hydrated lumibullvalene (300) in its \(^1\)H NMR spectrum than the expected dienol 294. Only one stereoisomer seemed to be formed, hinting to a concerted [1,3-C] migration of apex carbon 1 or 8 from carbon 5 or 7, respectively, to yield 300 endo or 300 exo. (see Appendix B for rearrangement scheme, Scheme 70).

However, at this point, the poor mass balance and the lack of further evidence cannot exclude a biradical pathway or migrations of carbons 2 and 7 into the bicyclo[2.1.1]hex-2-ene moiety (migration of carbon 2 into the bicyclo[2.1.1]-hex-2-ene double bond to give 38a and 38b is considered unlikely, because bonds C\(_1\)C\(_7\) and C\(_7\)C\(_8\) are probably activated/elongated by interaction of the double bonds C\(_5\)C\(_6\) and C\(_8\)C\(_1\) through the cyclobutane ring, in contrast to bonds C\(_2\)C\(_1\) and C\(_2\)C\(_8\)).

Monitoring the reaction by TLC did not tell clearly whether such high reaction temperatures or long reaction
times were necessary to drive the reaction to completion. Based on the assumption that the Ramberg-Bäcklund ring contraction is the first step, analysis could be facilitated by trying to separate the two steps of the sequence, e.g.,

**Scheme 71: Two Step Scheme for Conversion of 252/253 to 294**

by affecting the Ramberg-Bäcklund reaction with potassium tert-butoxide/THF at low temperature (Scheme 71). Alkoxides are notoriously sluggish in rearranging epoxides, and the tert-butoxide anion should be bulky enough to avoid nucleophilic epoxide opening. However, this route was not explored in greater detail, because more promising avenues opened in the meantime.
Strategy IV

Scheme 72: Strategy IV to 2

Strategy II demonstrated that the allylic protons $\alpha$ to the bromines were more acidic than the protons $\alpha'$ to the $\alpha$-chloro sulfone, since dehydrobromination occurred faster than Ramberg-Bäcklund ring contraction (compare p. 136). An alternative 1,3-butadiene equivalent to the bisallylic dibromide is the trans-vicinal dibromide. There the protons $\alpha$ to the bromines are not as activated, additionally, the saturated four carbon bridge in 304 is expected to adopt a

Figure 61: Most Stable Conformations of 35, 191, 304
similar chair conformation as 35 (calculated by MINDO/3)\textsuperscript{46} and 191 (calculated by MMP2\textsuperscript{204}) (Figure 61).

Therefore, dehydrobromination to the vinyl bromide should not be a problem if the bromines assume axial positions. Thus, Ramberg-Bäcklund ring contraction and double dehydrobromination could possibly be done in one pot to give 2.

Although 304 could be secured by bromination of α-chloro sulfone 239, it proved to be more efficient to brominate sulfide 238 before α-chlorination and oxidation,

\textbf{Scheme 73: Synthesis of 304}
because the low-yielding, selective oxidation was avoided (Scheme 73). Initial attempts to effect ring contraction and double dehydrobromination of 304 with potassium tert-butoxide at room temperature only resulted in the recovery of lumibullvalene (209)\textsuperscript{205}, the rearrangement product expected for triene 3. An attempt to simplify the isolation of the volatile C\textsubscript{10} hydrocarbon and at the same time to keep the reaction temperature low enough to avoid rearrangement failed. The only material recovered from reaction of 304 with freshly sublimed potassium tert-butoxide in refluxing dimethyl ether (bp-26°C) was diene 240 and another compound displaying the typical bicyclo[2.1.1]hex-2-ene \textsuperscript{1H} NMR pattern that was tentatively defined as dibromide 305. Since starting material 304 did not show any residual absorption in the vinyl region of the \textsuperscript{1H} NMR, 240 could not have come from unbrominated chloro sulfone 239, but only from debromination of dibromide 305. When a solution of 304 in THF-d_g was treated at -78°C with an excess of freshly sublimed potassium tert-butoxide and warmed to -30°C in an NMR probe, all absorptions due to the \(\alpha\)- and \(\alpha'\)-protons of the \(\alpha\)-chloro sulfone 304 disappeared, and instead the characteristic bicyclo[2.1.1]hex-2-ene signals were visible at low field. The sample was warmed up in 10° increments, and vinyl proton absorptions due to 240 slowly grew in.
Only at 0°C did double dehydrobromination to 2 become competitive (Scheme 74).

Scheme 74: Reaction of 304 with KO\textsuperscript{t}-Bu/THF-d\textsubscript{8}

At room temperature, signals of lumibullvalene (209) slowly appeared and replaced the peaks stemming from 2 in less than 10 min at 40°C. Thus, according to the \textsuperscript{1}H NMR experiment, the Ramberg-Bäcklund ring contraction was basically instantaneous below -30°C (when 304 was titrated
with potassium tert-butoxide, dibromide 305 could actually be isolated and characterized). Whereas debromination set in already at low temperatures, the rate of dehydrobromination was accelerated only at 0°C.

At room temperature triene 2 rearranged to other valence isomers that were identified after closer inspection as isobullvalene (208) and lumibullvalene (209) by comparison with the original spectra (as will be elaborated in Section B; Scheme 75).

Scheme 75: Thermal Rearrangement of 2 to 208 and 209

A compromise between competing debromination at lower temperature and rearrangement at higher temperature was found when the reaction was conducted and worked up at 0°C (Scheme 76).

Volz observed debromination as the only mode of action when he tried to dehydrobrominate 187 with potassium tert-butoxide in DMSO\textsuperscript{105} (page 73, Scheme 29).
Scheme 76: Reaction of 304 with KO^t-Bu at Different Temperatures

![Chemical structure](image)

| Me₂O (-26°C) | 100 | 0 | 0 | 0 | 100:0 |
| THF (0°C) from | 14 | 71 | 14 | 0 | 14:86 |
| to | 15 | 77 | 8 | 0 | 15:85 |

The only other examples of debromination of vicinal trans-dibromides were found in the propellane series. There it is more understandable, because deprotonation in the neopentyl position is sterically hindered for the bulky tert-butoxide base.

All the other reactions involving trans-4,5-dibromo-bicyclo[4.1.1]octane substructures resulted in dehydrobromination to the 1,3-dienes (185, 189, 195, and 307).
In the chair conformation of bicyclo[4.1.1]octane, both dehydrobromination and debromination seem to have an almost ideal antiperiplanar relationship between axial proton and axial bromide or between two axial bromides, respectively. One (more or less) plausible mechanism is nucleophilic attack of a tert-butoxide ion on one of the bromines.

Scheme 77: Mechanism for Debromination vs. Dehydrobromination
to form the olefin, bromide ion, and **tert**-butylhypobromite (Scheme 77).

For some reason, the free energy of activation at low temperature must be higher for the dehydrobromination ($\Delta G^\neq_a$) than for the debromination ($\Delta G^\neq_b$), perhaps because transition state 309 senses more of the strain being imparted to the system than does transition state 311. The strong temperature dependence of the dehydrobromination:debromination ratio hints to a significant entropy term. Since the number of particles on the reactant and product side is the same for both pathways, any entropic cause must be sought in the degree of organization within the transition state itself.

Triene 2, contaminated with about 15% of diene 240 and varying amounts of isobullvalene (208), condensed as a white solid at -78°C and melted on warming to 0°C to a clear colorless liquid.

$^1$H-NMR (300 MHz, CDCl$_3$, 263K) $\delta$

- 7.28 (t, $J_{9,8} = J_{9,1} = 2.3$ Hz, $H_{9,10}$), 6.34-6.24 (m, $H_{3,6}$), 6.24-6.15 (m, $H_{4,5}$), 3.56-3.43 (m, $H_{2,7}$), 1.17 (t, $J_{1,10} = J_{1,9} = 2.3$ Hz, $H_{1,8}$). (assigned by homodecoupling).
$^{13}$C-NMR (75 MHz, CDCl$_3$, 263K) 149.36, 136.26, 126.69, 78.37, 29.61 ppm.

UV (cyclohexane, 293K, $\lambda_{\text{max}}^{207}$): 258 (sh), 266 (sh), 274, 284, 296 (sh).

Again, the bicyclo[2.1.1]-hex-2-ene moiety of 2 displayed the characteristic pattern of two triplets with a coupling constant of $J = 2.3$ Hz (compare p. 124), but this time its vinylprotons ($H_9, H_{10}$) experienced a record deshielding to $\delta 7.28$ ppm, and its bridgehead protons ($H_1, H_8$) were shifted upfield to $\delta 1.17$ ppm. In the $^{13}$C NMR spectrum, carbons 9 and 10 were shifted downfield to 149.36 ppm, carbons 2 and 7 upfield to 29.61 ppm, and the residual bridgehead carbons were deshielded to 78.37 ppm (the $^{13}$C NMR-assignments are tentative, correlation of the spectra see ch. ). The vertical electronic transition ($\lambda_{\text{max}}$) of 274 nm resembles those seen with bicyclo[4.1.1]octa-3,5-

Figure 62: UV Spectrum of 2, 34 and 175

![Image of UV Spectrum](image-url)
diene (34) and tricyclo[5.3.3.0.2,8]decadiene (175), although the hypsochromic shift of 9nm versus 175 can be interpreted as evidence for the weakly stabilizing through-bond interaction of the monoene and diene bridges through the cyclobutane ring (compare page 26, Figure 21; Figure 62).
Strategy V.

Scheme 78: Strategy V to 2

By introduction of the diene bridge at an earlier stage, the complication of competing debromination could be avoided. At the same time, the last step (the Ramberg-Bäcklund reaction) could be performed at a lower temperature than required for the dehydrobromination, thereby minimizing thermal rearrangement of 2 to 208 and 209. Double debromination of dibromo sulfide with potassium tert-butoxide/THF at room temperature afforded the smelly, low melting sulfide 311 in excellent yield (94%). Subsequent α-chlorination and oxidation to 312 proceeded sluggishly in only 45% yield after MPLC. Without any problems, diene
chloro sulfone 312 underwent facile ring contraction to triene 2, that could be obtained in 92% purity (8% of 208), when the reaction was worked up at -10 to 0°C. Interestingly, diene 312 did not equilibrate with the benzylideneacetone iron tricarbonyl complex 313 to give the protected diene 314\textsuperscript{208,209}. Instead the BDA iron complex only decomposed to liberate the ligand (Scheme 79).

Scheme 79: Attempted Complexation of 312 to 314

The iron tricarbonyl moiety has been used to protect unstable dienes from rearranging. Brookhart could remove the protecting group under mild conditions, e.g., 317 (Scheme 80).
More forcing procedures like iron pentacarbonyl or diiron enneacarbonyl were not tried.

The outcome of the different strategies (for a summary, see Scheme 81) shows that tricyclic sulfide 238 was a very versatile intermediate, from which many attacks on the target molecule 2 could be initiated. The final, successful one confirmed that it was advisable to wait with the introduction of the highly strained bicyclo[2.1.1]hex-2-ene moiety until the very last moment in the synthesis. Any earlier installment provoked complications in further manipulations or premature rearrangement to alleviate the strain. Instead lengthening the bridge by one more atom reduced the internal ring strain to a bearable level. Again, the Ramberg-Bäcklund ring contraction demonstrated its power to form strained rings cleanly under mild conditions and in high yields for thermally labile and acid sensitive molecules.
Scheme 81: Summary of Approaches from 144 to 52
B) Thermal Rearrangement

When a solution of triene 2 in chloroform-d, was allowed to warm to 20°C, 2 rearranged into the valence isomer isobullvalene (208). After a short induction period, signals of a third hydrocarbon lumibullvalene (209), grew in and finally replaced 2 quantitatively. The structure of isobullvalene (208) was deduced by comparison with the $^1$H NMR spectrum recorded by Hojo, Seidner and Masamune$^{149}$, and by Katz, Cheung and Acton$^{150}$.

Ref. (149): $^1$H NMR (100 MHz, CDCl$_3$, -40°C) $\delta$ 6.17-5.57 (series of m), 5.43-5.35 (d), 3.87-3.69 (m), 2.09-1.39 (series of m).

Observed$^{211}$: $^1$H NMR (300 MHz, CDCl$_3$, 20°C) $\delta$ 5.98 (dd, $J = 11.1$, $^3$
3.9 Hz, 1H), 5.83 (dd, J = 11.6, 6.0 Hz, 1H), 5.77 (d, J = 8.6 Hz, 1H), 5.69 (d, J = 5.6 Hz, 1H), 5.67-5.61 (m, 1H), 5.35-5.31 (m, 1H), 3.78-3.70 (m, 1H), 2.00-1.93 (m, 1H), 1.80-1.72 (m, 1H), 1.57-1.48 (m, 1H).

The same authors had already reported that isobullvalene (208) rearranges to lumibullvalene (209) at room temperature. Again, the spectral features of 209 were in good agreement with those first determined by Jones\textsuperscript{205}.

![Diagram of 209]

Ref. 205: \textsuperscript{1}H NMR (100 MHz) \(\delta\)

6.57 (dd, J = 5.9, 3.0 Hz), 5.81 (t, J = 3.0 Hz), 5.51 (dd, J = 5.9, 2.0 Hz), 3.10 (br s), 2.48 (br s).

Observed: \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}) \(\delta\) 6.67 (dd, J\textsubscript{9,10} = 5.7 Hz, J\textsubscript{9,8} = 2.8 Hz, H\textsubscript{6,7}), 5.96-5.89 (m, H\textsubscript{6,7}), 5.60 (dd, J\textsubscript{10,9} = 5.7 Hz, J\textsubscript{10,1} = 2.1 Hz, H\textsubscript{10,3}), 3.20-3.15 (m, H\textsubscript{1,2}), 2.48-2.45 (m, H\textsubscript{5,8}).

\textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}) 145.46, 133.36, 129.40, 60.30, 41.62 ppm.
The $^{13}$C NMR spectrum nicely demonstrates the $C_2$ symmetry of lumibullvalene (209): the $C_2$ axis reduces the number of distinct carbon atom signals to five. Already Jones remarked that homodecoupling of the $^1H$ NMR was not sufficient to assign all proton chemical shifts because the rigid structure of 209 could create long-range couplings of significant size$^{205,212}$.

**Figure 63 Homodecoupling pattern for 209 (300 MHz, CDCl$_3$)**

<table>
<thead>
<tr>
<th>affected proton</th>
<th>$H_a$</th>
<th>$H_b$</th>
<th>$H_c$</th>
<th>$H_d$</th>
<th>$H_e$</th>
<th>$\delta$/ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>$J$/Hz</td>
<td>6.69</td>
<td>5.92</td>
<td>5.60</td>
<td>3.17</td>
<td>2.46</td>
<td>$\delta$/ppm</td>
</tr>
</tbody>
</table>

It was difficult to determine the effect that irradiation of the vinyl protons had on the aliphatic protons because of the complexity of the coupling pattern. However, the coupling constant $J_{a,c} = 5.7$ Hz, a typical value for
vicinal vinyl protons with a cis relationship, suggests the remaining vinyl proton \( H_b \) to be \( H_{6,7} \). This would rationalize the enormous simplification of the \( H_b \) signal, when \( H_e \) is decoupled, \( H_a \) and \( H_e \) form an AA'XX' system in which \( H_b \) couples strongly with the vicinal \( H_e \) and the

Scheme 82: Katz and Cheung's labeling of 208
allylic $H_e$. Previously, Katz and Cheung suggested\(^{214}\) $H_e$ to be $H_{5,8}$ because deuteration of isobullvalene as in 208-$d_1$ reduced the intensity of $H_e$ by 50% in the lumibullvalene rearrangement product (209-$d_1$, Scheme 82). Whereas exclusive labeling of $H_e$ in lumibullvalene (209-$d_1$) was in line with a concerted Cope rearrangement, homolytic opening of isobullvalene to biradical 321-$d_1$ would have scrambled the label into both the aliphatic positions ($H_d$ and $H_e$ 209-$d_1$). Finally, comparison of lumibullvalene (209) with other molecules that contain the bicyclo[3.2.1.]octa-2,6-diene moiety such as bicyclo[3.2.1]octa-2,6-diene (197)\(^{140}\) itself or tricyclo[5.5.0.0\textsuperscript{2,10}]dodeca-3,5,8,11-tetraene (196) (compare page 80) shows that $H_7$ is usually more deshielded than $H_6$, suggesting the proper assignment for lumibullvalene 209 to be: $H_a$ (δ 6.69 ppm) = $H_{4,9}$ and $H_c$ (δ 5.60 ppm) = $H_{3,10}$.

![Chemical Structures](image)
All the previous considerations led to the $^1$H NMR assignment for 209, given on p. 27.

The signal intensity of triene 2 decreased with a first-order rate constant of $k_1 = 1.55 \cdot 10^{-4} \text{s}^{-1}$ in the $^1$H NMR spectrum at $20^\circ\text{C}$, corresponding to a half-life of $\tau_1(20^\circ\text{C}) = 74 \text{ min}$ (see Table 1). Coincidentally, exactly the same rate constant was calculated for the Cope rearrangement of isobullvalene (208) to lumibullvalene (209) from the known activation parameters$^{149}$ (Appendix E).

With the rate constants $k_1$ and $k_2$ in hand, the time dependence of the concentrations of 2, 208, and 209 can be simulated mathematically (see Appendix E for a derivation of the rate laws). The computed time dependencies of concentrations [2], [208] and [209] agreed reasonably well with the experimental values (Figure 63, Table 3), indicating that the mechanistic assumptions for the thermal rearrangement of 2 to 208 and 209 were valid.

The thermal rearrangement of 2 to 209 can occur by three different mechanisms (Scheme 83):

1. concerted, thermally 'forbidden' (according to the Woodward-Hoffmann rules) [1,3-C] migration of a cyclobutane apex into the two carbon bridge (compare with concerted [1,3-C] shift of tetraene 1, page 88).

2. concerted, thermally 'allowed' [1,5-C] migration of a cyclobutane apex into the four carbon bridge.
Figure 63: Thermal Rearrangement of 2 (CDCl₃, 20°C)
Scheme 83: Mechanistic Options for Thermal Rearrangement of 2
Table 3. Thermal Rearrangement of 2 to 208 and 209 (CDCl₃, 0°C): (compare p. for experimental and Appendix E for computational procedure; the values in parentheses are calculated from the rate equations derived in Appendix E).

<table>
<thead>
<tr>
<th>t/min</th>
<th>[2]</th>
<th>[208]</th>
<th>[209]</th>
<th>ln[2]</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>90 (90.0)</td>
<td>10 (10)</td>
<td>0 (0)</td>
<td>4.500</td>
</tr>
<tr>
<td>10</td>
<td>81 (82.0)</td>
<td>17 (16.7)</td>
<td>2 (1.3)</td>
<td>4.394</td>
</tr>
<tr>
<td>20</td>
<td>73 (74.7)</td>
<td>24 (22.2)</td>
<td>3 (3.1)</td>
<td>4.290</td>
</tr>
<tr>
<td>30</td>
<td>67 (68.1)</td>
<td>27 (26.6)</td>
<td>6 (5.3)</td>
<td>4.205</td>
</tr>
<tr>
<td>40</td>
<td>60 (62.0)</td>
<td>31 (30.0)</td>
<td>8 (8.0)</td>
<td>4.094</td>
</tr>
<tr>
<td>50</td>
<td>(56.5)</td>
<td>(32.6)</td>
<td>(11.0)</td>
<td></td>
</tr>
<tr>
<td>60</td>
<td>50 (51.5)</td>
<td>36 (34.5)</td>
<td>13 (14.0)</td>
<td>3.912</td>
</tr>
<tr>
<td>70</td>
<td>45 (46.0)</td>
<td>38 (35.8)</td>
<td>17 (17.3)</td>
<td>3.807</td>
</tr>
<tr>
<td>80</td>
<td>42 (42.8)</td>
<td>39 (36.6)</td>
<td>19 (20.6)</td>
<td>3.738</td>
</tr>
<tr>
<td>90</td>
<td>38 (39.0)</td>
<td>39 (36.9)</td>
<td>23 (24.1)</td>
<td>3.637</td>
</tr>
<tr>
<td>100</td>
<td>34 (35.5)</td>
<td>40 (37.0)</td>
<td>26 (27.5)</td>
<td>3.526</td>
</tr>
<tr>
<td>110</td>
<td>31 (32.4)</td>
<td>39 (36.7)</td>
<td>30 (30.9)</td>
<td>3.434</td>
</tr>
<tr>
<td>120</td>
<td>29 (29.5)</td>
<td>38 (36.2)</td>
<td>33 (34.3)</td>
<td>3.367</td>
</tr>
<tr>
<td>130</td>
<td>26 (26.9)</td>
<td>38 (35.5)</td>
<td>37 (37.6)</td>
<td>3.258</td>
</tr>
<tr>
<td>∞</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>100 (100)</td>
<td></td>
</tr>
</tbody>
</table>
(3) homolysis of a cyclobutane bond followed by recombination within the biradical 321.

All three mechanisms could be differentiated by a suitably placed label. Because isobullvalene (208) was known to rearrange stereospecifically to lumibullvalene (209) in a concerted [3,3]sigmatropic shift (compare p. 158), the fate of a deuterium label during the rearrangement of 24 to 209 would reveal the mechanism.

Paquette, Philips, and Wingard demonstrated 195 that α-chlorosulfone 322 undergoes proton-deuterium exchange in protic solvents. Even episulfone 323 can be deprotonated by potassium tert-butoxide/tert-butanol-d₄ before it extrudes sulfur dioxide²¹⁵⁻²¹⁷ (Scheme 84).

**Scheme 84:** H/D-Exchange in 322 and 323
Therefore in the case of dibromo chlorosulfone 304, we had a compound in hand that could be labeled in situ under the Ramberg-Bäcklund reaction conditions. And indeed, when 304 was slowly (over 1 h) warmed up from -78°C to 0°C with potassium tert-butoxide/tert-butanol-d₁ (formed in situ from potassium tert-butoxide and deuterium oxide), integration of the vinyl protons H₉,₁₀ corresponded to only 1.54 protons instead of 2, i.e. 0.46 D had been incorporated during the equilibration (Scheme 85).

Scheme 85: H/D-Exchange in 304

Since H₉ and H₁₀ are equivalent due to the C₂ᵥ symmetry of 2, the partially deuterated 2 (probably a mixture of 2, 2-estone, and 2-estone) can be considered as deuterated in both positions.
Scheme 86: Thermal Rearrangement of $2\text{-}d_2$: Mechanistic Options
The following labeling patterns are expected from the three different mechanisms [compare absolute assignment of $^1$H NMR of lumibullvalene (209), page 156; Scheme 86]

<table>
<thead>
<tr>
<th>mechanism</th>
<th>labeled position in 109</th>
<th>intensity ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>$H_a : H_c$</td>
<td>1:1</td>
</tr>
<tr>
<td>II</td>
<td>$H_c : H_d$</td>
<td>1:1</td>
</tr>
<tr>
<td>III</td>
<td>$H_a : H_c : H_b$</td>
<td>1:2:1</td>
</tr>
</tbody>
</table>

The ratios are expected when the secondary kinetic isotope effects are ignored. The usual secondary $\frac{k_H}{k_D}$ (-1.1) probably lies within the error limits of the $^1$H NMR integration. While the deuterium incorporation in the product can be determined only with difficulty by $^1$H NMR (only 23% incorporation), $^2$H NMR makes the assignment easy.

When the deuterated triene 2-$d_1$ was completely rearranged in carbon tetrachloride, the proton decoupled $^2$H NMR spectrum showed three absorptions at $\delta$ 6.63, 5.58 and 3.18 with an intensity ratio of 1.0:2.1:1.0 as expected for option III, the stepwise biradical mechanism.

$^2$H NMR (77 MHz, $CCl_4$, reference: $CDCl_3$, $\delta$ 7.26 ppm) $\delta$ 6.63 ($D_a$), 5.57 ($D_c$), 3.13 ($D_d$).
Compare $^1$H NMR (300 MHz, CCl$_4$) $\delta$

6.63 ($H_a$), 5.87 ($H_b$), 5.58 ($H_c$),
3.18 ($H_d$), 2.50 ($H_e$).

Although this ratio could also be explained by two competing concerted [1,3] and [1,5] shifts (options I and II) which happen to have the same rate constants, this possibility seems to be highly unlikely, because the thermally allowed concerted pathway (II) should have a much more favorable energy of activation than the thermally forbidden one (I).

Figure 64: $^2$H NMR of 209-d
As in the case of the tetraene (compare p.), the force-field calculations (MMP2) yield heats of formation ($\Delta H^o$) for the C$_{10}$H$_{10}$ valence isomers that are in good agreement with the experimental observations (Figure 65).

**Figure 65:** Heats of Formations ($\Delta H^o$) of 2, 208 and 298

Obviously, the force-field calculations do not take into account of the consequences of electronic interaction. It is interesting to note that, according to the MMP2 program, the energetic order of structure types changed in going from the C$_{12}$ to the C$_{10}$ hydrocarbons. In the methine dodecamers the semibullvalene type structure was even higher (compare Figure 32, page 83) in energy than the through-bond
FIGURE 66: Stereoview of 2
FIGURE 67  Stereoview of 208
Figure 68: Stereoview of 209 (MMP2)
conjugated system 1, whereas in the class of the methine decamers 208 settled energywise between 2 and 209. This reflects the immense strain encountered in the bicyclo-[2.1.1]hex-2-ene moiety of 2, as well as the additional strain of one etheno unit, that makes it difficult to build molecular models of 202. This raises the question, why the biradical derived from 2 does not immediately collapse to the energetic sink 209, especially since the higher coefficient of the central carbon of the pentadienyl SOMO should make overlap and bond formation even more kinetically favorable to give 209. The answer probably lies in the principle of least motion\textsuperscript{218}: the termini of the allyl and the pentadienyl radicals lie in much closer proximity making bond formation at these positions kinetically favorable. The cyclopropane ring ties the etheno and the diene bridge of the isobullvalene (208) together so that they are close enough to relieve the strain of 206 by a Cope rearrangement to 209.

Within the series of tricyclic hydrocarbons which allow interaction of two mutually perpendicular π-ribbons through a cyclobutane ring the thermal lability, i.e., the propensity to rearrange, decreases from the [2\textsuperscript{1,2},2\textsuperscript{1,2}] (42), to the [4\textsuperscript{1,4},2\textsuperscript{1,2}] (2) and finally to the [4\textsuperscript{1,4},4\textsuperscript{1,4}] (1) system, an order that is in line with the expected decrease in ring strain (Figure 69).
Figure 69: Thermal Lability of 42, 2 and 1

Given the thermal lability of 2, it is not surprising that Gleiter et al. only isolated the rearrangement product.

Scheme 87: Shapiro-Reaction of Bicyclo[2.1.1]hexan-2-ones
lumibullvalene (209), from the Shapiro reaction of ketone 325\textsuperscript{177} (Scheme 87).

What is surprising is that such mild conditions (0°C) were sufficient to introduce the last double bond in such high yield (assuming 209 was formed with the intermediacy of 2), while it took Meinwald and Uno 15 h at room temperature to achieve the same in much lower yield in the seemingly less strained bicyclo[2.1.1]hex-2-ene (33)\textsuperscript{220}.

If the Shapiro reaction actually worked at 0°C, the isolation of 209 might simply reflect the work-up conditions (room temperature?)\textsuperscript{275}. 
C. Summary

Triene 2 could be synthesized in five steps from the advanced intermediate 144. It proved to be most useful to leave the tricycle at an intermediate level of strain, where the cyclobutane is bridged by a three- and a four-atom bridge, to introduce the butadiene unsaturation first and only then contract the three-atom sulfide linkage by the extremely powerful Ramberg-Bäcklund reaction. All other attempts to incorporate the bicyclo[2.1.1]hex-2-ene moiety at an early stage of the synthetic route either met with complete failure or complications.

The odorous, colorless oily 2 could not be stored at room temperature or even at -15°C, because it rearranged by a biradical pathway via isobullvalene (208) to lumbullvalene (209).

While the slight hypsochromic shift in the UV spectrum indicates, if anything, a widened HOMO-LUMO gap (as expected from a weakly stabilizing through-bond interaction\textsuperscript{22}), the PE spectra still await recording and critical evaluation.
CHAPTER VII

9,10-DIMETHYLENETRICYCLO[5.3.0.0²,8]DECA-3,5-DIENE

A) Introduction

Not only the termini of a π-ribbon but also its central carbons, can be connected to the cyclobutane ring (Figure 70). And these mutually perpendicular conjugated polyene bridges should still communicate with each other through the cyclobutane ring. Diene 42, triene 2, and tetraene 1 can be considered as typical representations of class I through-bond conjugated systems \([n^1,n.m^1,m]\). Triene 327 could be isolated as the monoadduct of N-phenyltriazolinedione to tetraene 328\(^{221}\), but was not studied for any potential through-bond conjugative effects by spectroscopic methods. Both 327 and the target compound, tetraene 3, formally belong to the hybrid class II, in which one of the π-ribbons is connected by its termini, the other one by its central carbons to the cyclobutane ring.

Bisanhydride 45 and tetraene 328\(^{221}\) are representatives of class IV: both π-ribbons are connected to the cyclobutane ring by its central carbons. Again, unfortunately no
Figure 70: Modes of Interaction between n-Ribbons and a Cyclobutane Ring Geometric and FMO Difference of [21.2], [42.3], and [41.4] Bridge

1. \( \pi \)
2. \([41.4, 21.2]\)
3. \([41.4, 41.4]\)
4. \([41.4, 42.3]\)
5. \([42.3, 42.3]\)
6. \([52.4, 52.4]\)
spectroscopic data are available for 45, while tetraene 328 will be discussed later.

The 2,3-connected 1,3-butadiene actually constitutes a compromise between an etheno bridge and a butadiene bridge that is connected by its termini. While the geometric constraints are very similar for the \([2^{1,2}]\) and the \([4^{2,3}]\)-

\[
\text{Scheme 71 Geometric and FMO Difference of } [2^{1,2}], [4^{2,3}], \text{ and } [4^{1,4}]\text{Bridge ..........}
\]

\[
\begin{align*}
\text{[2^{1,2}]} & \quad \text{[4^{2,3}]} & \quad \text{[4^{1,4}]} \\
\end{align*}
\]

\[
\begin{align*}
d_{1,2} & \quad -1.34 \AA^{222} & \quad -1.48 \AA^{222} \\
\varepsilon(\psi_2)/eV & \quad -8.61(a_2)^{223} & \quad -8.40(a)^{46} \\
\varepsilon(\psi_1)/eV & \quad -9.6(b_1)^{53} & \quad -11.1 \; (b_1) & \quad -10.90 \; (b_1) \\
\end{align*}
\]

(\(\varepsilon\) entails only inductive effect of cyclobutane ring, not conjugation with its Walsh orbitals).
bridge (\(-1.34\text{\AA} \text{ vs } -1.48\text{\AA}\))\textsuperscript{222}, the energy levels of the molecular orbitals of \([4^2,3]\)\textsuperscript{223} are much more similar to those of the \([4^1,4]\textsuperscript{46}\) bridge, and the symmetries of the FMO's of both \([4^2,3]\) and \([4^1,4]\) are opposite to those of the etheno bridge \([2^1,2]\) (Figure 71).

The study of systems like \([4^2,3,4^1,4]\) (1) or \([4^2,3,4^2,3]\) (3 or 56) would therefore offer a unique chance to learn about the extent to which geometric strain, energy levels of the participating molecular orbitals, and symmetry of the MOs affect through-bond interaction of mutually perpendicular π-ribbons through a cyclobutane relay.

Electronic interaction between the \([4^2,3]\) π-ribbon and the Walsh orbitals of cyclobutane had been suspected very early. In 1971, Borden and Gold obtained 1,2,5,6-tetramethyl-3,4,7,8-tetramethylenetricyclo[3.3.0.0\(2^1,6\)]octane (328) by pyrolysis of 1,2,5,6-tetramethyl-3,4,7,8-tetramethylenecycloocta-1,5-diene (329) (Scheme 88)\textsuperscript{221}. The temperature of 380°C is high enough to cleave tricyclo [3.3.0.0\(2^2,6\)]octane (63) back to cycloocta-1,5-diene (61)\textsuperscript{224}. The doubly unsaturated analog of 63, tricyclo[3.3.0.0\(2^2,6\)]octa-3,7-diene (42), rearranges to semibullvalene (44) at an even lower temperature (Scheme 88).

Borden, Gold, and Young took the high thermal stability of 328 in contrast to the lability of 42 to be an indication that the butadiene bridges of 328 interact in a stabilizing
manner with the cyclobutane ring, whereas the etheno bridges interact with it in a destabilizing manner$^{225}$. Obviously, one has to remember that the shorter $C_3C_4$-bond in 42 (-1.34Å) will produce more strain than the longer $C_2C_3$ bond of a 1,3-butadiene in 328 (-1.48Å)$^{222}$. One could also imagine that 328 minimizes the eclipsed interactions of the vicinal methyl groups, i.e., similarly to the tertiary-butyl groups in tetrakis-(tert-butyl)tetrahedrane (331) the
ring strain in 283 is compensated for by the van der Waals repulsion of the alkyl substituents in 329.

The same problem, how to differentiate steric from electronic effects, was encountered when Borden, Gold, and Jorgensen tried to attribute the sluggishness of 3 in Diels-Alder reactions to this electronic stabilization. Even the assignment of the photoelectron spectrum was complicated by the effect of the methyl groups. An unambiguous answer can therefore only be expected from the parent compound.

Jorgensen and Borden compared the interaction of butadiene ribbons and ethylene bridges with cyclobutane rings by Extended Hückel calculations (EH). Whereas the π-bond order \((P_{12})\) between carbons C\(_1\) and C\(_2\) is slightly negative and repulsive, \(P_{12}\) is positive in 337, i.e., the interaction between the butadiene moiety and the cyclobutane ring contributed to the σ-bonding between carbons C\(_1\) and C\(_2\). As might be expected, the benzene ring of benzobicyclo-
[2.1.1]hex-2-ene (254) adopts an intermediate position. The stabilizing/destabilizing effect of an etheno/butadiene bridge is more pronounced for a cyclopropane ring (338 vs. 339) and less pronounced for a cyclopentane (340 vs. 341). Interestingly, the way the π-ribbon is connected to the cyclobutane ring is also important. Whereas the 1,3-connection (33) results in a weakly destabilizing π-bond order, $P_{12}$ becomes positive when the etheno bridge is connected in 1,2 fashion (31) (Figure 72).

Isodesmic reactions provide a computational tool to get information about thermodynamic stabilization, e.g., 337 and ethylene combined are thermodynamically more favorable than 33 and butadiene (Scheme 89).

Scheme 89: Isodesmic Reaction Transforming 33 into 337

When Hogeveen, Huurdeman, and Kok observed the dramatic rate differences in the Diels-Alder reactions of the 2,3-dimethylenetetramethylbicyclo[2.1.1]hexane (342) and
Figure 72: Bond Orders Between Small Rings and π-Ribbons

$P_{1,2} = -0.007$

33

254

237

338

0.036

0.078

339

0.089

340

341

0.059

31

0.073
the 3,4-dimethylenetetramethyltricyclo[3.1.0.0^{2,6}]hexane (343) with tetracyanoethylene (TCNE), they believed to have strong evidence for the stabilizing interaction of the butadiene bridge and the cyclobutane ring versus the destabilizing interaction of the butadiene bridge with a bicyclobutane moiety. However, again most of the effects seemed to be due to the steric hindrance of the endo-methyl groups that block the approach of a dienophile more effectively in 342 than in 343. The parent compounds of 342 and 343, 337^{235}, and 344^{236}, were much closer in reactivity (Figure 73).

Interestingly, when C_2 and C_3 of the butadiene bridge are connected to the 1- and 3-positions of the cyclobutane ring as in 337, the system absorbs UV light at substantially lower wavelength (238.5 nm)^{236} than a system where no significant interaction is expected (like 347:252 nm)^{237}. Even more dramatic is the effect, when 337 is compared to 34, where the termini of the butadiene bridge are connected to the cyclobutane (277 nm)^{46} (Figure 74).

In the photoelectron spectra, 34^{46} displays a higher HOMO than 337^{238} (Figure 75).

The fact that the 1,3-butadiene HOMO (a_2) has higher coefficients at the termini (Figure 76) might explain why interaction of the butadiene a_2 with the corresponding a_2 cyclobutane-Walsh orbitals is stronger in 34 than in 337.
Figure 73: Diels-Alder Reactivity of $[4^2,3]$Systems with TCNE

<table>
<thead>
<tr>
<th>Compound</th>
<th>$k_{rel}$ (20°C)</th>
<th>$k_{rel}$ (1°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>342</td>
<td>1</td>
<td>850</td>
</tr>
<tr>
<td>337</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>344</td>
<td></td>
<td>30</td>
</tr>
<tr>
<td>341</td>
<td>2.5•10$^5$</td>
<td>5.1•10$^5$</td>
</tr>
<tr>
<td>345</td>
<td>1.2•10$^6$</td>
<td></td>
</tr>
<tr>
<td>346</td>
<td></td>
<td>3.1•10$^7$</td>
</tr>
<tr>
<td>343</td>
<td></td>
<td>1,400</td>
</tr>
</tbody>
</table>

Figure 74: UV Absorptions of $[4^2,3]$Systems

<table>
<thead>
<tr>
<th>Compound</th>
<th>$\lambda_{max}$/nm</th>
</tr>
</thead>
<tbody>
<tr>
<td>342</td>
<td>240</td>
</tr>
<tr>
<td>337</td>
<td>238.5</td>
</tr>
<tr>
<td>341</td>
<td>248</td>
</tr>
<tr>
<td>347</td>
<td>252</td>
</tr>
<tr>
<td>34</td>
<td>277</td>
</tr>
</tbody>
</table>
The higher HOMO of 26 might also reduce the HOMO-LUMO gap and cause the strong bathochromic shift in the UV spectrum, whereas the only weakly destabilized HOMO of 337 might explain the slight hypsochromic shift. Obviously, without
information about the effect of the interaction on the LUMO this remains speculation. The bigger coefficients of the MO of butadiene at the central carbons should enhance interaction with the $b_1$ Walsh orbital of cyclobutane in 337 and explain the stronger splitting of the $b_1$ levels relative to 34 (Figure 76).

Gleiter's MINDO/3 calculations of 9,10-dimethylene-tricyclo[5.3.0.0²,8]deca-3,5-diene (3)²² predicted the effect of through-bond interaction on the FMO's to be intermediate between 332 and tetraene 1.
B) Synthesis

The 2,3-dimethylenebicyclo[2.1.1]hexane moiety of 332 was considered the crucial part because with the synthesis of 1 and 2 a lot of experience had already been acquired on the other half of the molecule, the bicyclo[4.1.1]octa-3,5-diene moiety.

Different synthetic approaches have been chosen for the introduction of vicinal dimethylene moieties into strained rings: Scheme 90: Synthetic Approaches to Vicinal Dimethylene Moieties

Griffin and Peterson, 1963:

\[
\begin{align*}
\text{Br} & \quad \text{Br} \\
\text{Br} & \quad \text{Br} \\
\text{Br} & \quad \text{348} \\
\end{align*}
\]

\[\xrightarrow{\text{NaOEt/EtOH}}\]

\[0^\circ \text{C}, 36\text{h}\]

\[50\%\]

\[
\begin{align*}
\text{Br} & \quad \text{Br} \\
\text{349} \\
\end{align*}
\]

Borden and Gold, 1971:

\[329 \quad \xrightarrow{380^\circ \text{C}}\]

\[328\]
Scheme 90 (continued):

1. Br₂ (1 eq)  
-80°C  
2. NEt₃  
-80°C → RT  
60%

352 → 343

353

PyHBr₃  
0°C  
69%

353 → 342

354

hν  
-30°C  
36%

354 → 337

355

Cl  
KOBu  
DMSO  
28%

355 → 344
Of all the methodologies, Capozzi and Hogeveen's seemed to be the most intriguing one because it was most compatible with our strategy of belting an all-trans tetrasubstituted cyclobutane in stepwise fashion (Scheme 91).

Scheme 91: Synthetic Strategy to 3

The unsaturated, bicyclic di-THP ether 133 could be crafted into diketone 356. Since its two carbonyl functions are locked into a syn-configuration by the rigid bicyclo-[4.1.1]hexane skeleton, 356 should be ideally set up for McMurry coupling. With Capozzii and Hogeveen's mild
bromination conditions, 357 could be capable of tetrabromination and possibly tetradehydrobromination, all in one pot. An alternative route to 3 via acyloin condensation of diester 358 followed by oxidative workup to diketone 359, double methylenation, and olefin/diene transformation was considered, but not implemented.

For the deprotection of the di-THP ether 133, Beier and Mundy's method\textsuperscript{243} using an acid-washed Dowex-50 ion exchange

Scheme 92: Deprotection and Oxidation of 133
resin (methanol, room temperature, 1h) proved to be far superior to that of Miyashita, Yoshikoshi, and Grieco (para-toluene sulfonic acid, ethanol, 55°C, 26h): the former afforded diol under milder conditions, faster, and in higher yields.

Problems like lactone formation were anticipated with chromium trioxide-based oxidants during the oxidation of 358 to diacid 359. For example, Trost et al. oxidized diol 363 cleanly to lactone 364 with Collin's reagent (Scheme 93).

Scheme 93: Trost's Oxidation of Diol 363

Schröder and Griffith introduced an alternative reagent for oxidizing primary alcohols to carboxylic acids in the presence of functionalities like double bonds (Scheme 94).

When catalytic amounts of ruthenium trichloride hydrate are treated with an alkaline solution of potassium persulfate, potassium ruthenate (K₂RuO₄) immediately forms,
reminiscent of ruthenium tetroxide (RuO₄) in its golden orange color, but due to its lower oxidation level (+6 instead of +8) less aggressive than the latter.

Although diol 358 was only marginally soluble in methylene chloride, the oxidation proceeded cleanly in the biphasic reaction mixture to diacid 359, a white solid, that slowly deteriorated to a tan solid at room temperature and was best used immediately. During the oxidation, the color of the reaction mixture was not a good indicator for completion of the process. When an oxidation was worked up immediately after it had turned from dark-brown to its original golden-yellow (2.3 h instead of 5h) by quenching the excess oxidant with sodium sulfite, acidification, and diazomethane esterification, substantial amounts of half-oxidized alcohol ester 362 were recovered (Scheme 92). Surprisingly, some epimerized diester 361 could also be
isolated and was easily distinguishable from $C_{2v}$-symmetric exo,exo-diester$^{360}$ by its reduced $C_s$ symmetry (Figure 77).

Scheme 95: Wiberg's Epimerization of 367/368

KOH, methanol reflux, 85%

Cyclobutyl esters are not expected to be very acidic because the ring strain that is introduced into the system by enolization should retard proton abstraction. However,

Figure 77: Symmetries of 360 and 361

$^{13}$C NMR 6 lines 9 lines
Wiberg reported the base induced epimerization/saponification of bicyclo[2.1.1]hex-5-yl ester 38, although under more drastic conditions (Scheme 95).

Potassium carbonate in methanol did not equilibrate at room temperature. The epimerization could also have taken place at the intermediate aldehyde oxidation level, the α-proton of which is more acidic than that of the ester. In less basic media (half-saturated sodium bicarbonate: pH ~8; phosphate buffer pH ~8), the oxidation potential of potassium persulfate was not high enough to oxidize ruthenium trichloride to potassium ruthenate.

Carboxylic acids can be converted into the corresponding methyl ketones by methylation of the acid chloride

Scheme 96: Griffin and Hager's Conversion of a Carbocyclic Acid into a Methyl Ketone

![Scheme 96 Diagram]
with lithium dimethylcuprate or other organometallic reagents (ref. 206, page 439). Griffin and Hager tackled\textsuperscript{55} a very similar problem by resorting to Wolfram and Brown's method\textsuperscript{247} (Scheme 96). However, a more direct and faster method was desirable, namely direct treatment of the diacid with an excess of methyllithium, or better deprotonation and methyllithium addition to the lithium carboxylate\textsuperscript{248}, e.g.\textsuperscript{249}, Scheme 97:

Scheme 97: Paquette's Conversion of 375 into 376

\[
\begin{align*}
\text{CO}_2H & \quad \text{CO}_2H \\
\text{LiH} & \quad 94\% \\
\text{MeLi} &
\end{align*}
\]

Scheme 98: Addition of Methyllithium to 359

\[
\begin{align*}
\text{HO}_2C & \quad \text{HO}_2C \\
\text{LiH, THF} & \quad \text{rt, 0.5h} \\
\text{MeLi} & \quad 0^\circ \text{to RT} \\
\text{HCl/NH}_4\text{Cl} & \quad 53\% \\
\end{align*}
\]
However, 356 was always accompanied by varying amounts of overaddition products 377 and 378 (Scheme 98).

To avoid the capricious potassium ruthenate oxidation as well as the unpredictable and separation intensive methyllithium addition, a different approach to diketone 356 was explored. Swern oxidation\textsuperscript{250-252} of diol 358 afforded dialdehyde 379 cleanly. While chromatography (MPLC, silica gel) led to a recovery of only 17\% of the theoretical amount of 379, the yield could be boosted to 91\% when the

**Scheme 99:** Conversion of 358 into 380
dialdehyde was isolated by bulb to bulb distillation. As expected, addition of methyllithium\textsuperscript{253} afforded both diastereomers of the diol, 380(C\textsubscript{5}) and 380(C\textsubscript{2}). The diols were highly crystalline and very poorly soluble in methylene chloride (the solvent for the subsequent Swern oxidation) (Scheme 99).

When the highly crystalline diketone 356 was subjected to the usual McMurry conditions\textsuperscript{115} (potassium, refluxing dimethoxyethane, titanium trichloride-tristetrahydrofuran complex, rigorous exclusion of oxygen and moisture) ca. 13\% of not completely pure diene 357 was isolated (by preparative GC), in addition to the pinacol intermediate 381 (Scheme 100).

\textbf{Scheme 100: McMurry Coupling of 356}

![McMurry Coupling of 356](image-url)
The \(^1\)H NMR spectra of 356 and 357 showed very similar absorption patterns, although the methyl protons were obviously shifted upfield in 357 from \(\delta 2.13\) to 1.84 (300 MHz, CDCl\(_3\)). Since neither yield nor purity of the McMurry coupling could be improved, the detour via pinacol 381 was tried. And indeed, Corey, Danheiser, and Chandrasekaran's pinacol coupling procedure\(^{255}\) with a titanium (II) species generated in situ from titanium tetrachloride and magnesium amalgam yielded the cis diol 381c cleanly. Again, the symmetry of the molecule helped to assign the configuration: the trans diol 381t has \(C_2\) symmetry and should therefore contain six different carbons, whereas cis diol 381c has only \(C_5\) symmetry and nine distinct carbons.

When the pinacol (381) was subjected to the McMurry deoxygenation conditions, very clean product 357 was obtained although in low yield (12\%), together with unreacted starting material (33\%). Whether the steric crowding in the dimethyl substituted bicyclop2.1.1)hexane is the reason for the inefficient McMurry coupling remains unknown. Although this olefination method can be used to prepare very sterically demanding alkenes, yields are usually very modest at best in these cases.

Nevertheless, the planned Capozzi and Hogeveen bromination /dehydrobromination \(^{240}\) (pyridinium bromide perbromide
in pyridine) was tried, and a UV active, non-volatile compound was formed that was identified as dibromodiene 382. No tetrabromide 383 and very little, if any tetraene 3 could be detected (Scheme 101).

Scheme 101: Bromination of 357

The fact that the secondary trans dibromide does not eliminate in the basic solvent suggests that maybe the bis-tertiary dibromide is never formed on the other side of the molecule, due to steric crowding. Instead, the initially-formed bromonium ion might immediately eliminate a proton to give the allylic bromide. Elimination of the second equivalent of hydrogen bromide should then be fast (Scheme 102). Initially, we feared that this bromination/dehydrobromination was only applicable to Hogeveen's bicyclo[2.1.1]hex-2-ene 353, where the apical methyl groups block the attack of an incoming bromide on the bromonium ion completely, and a
tremendous repulsive interaction is relieved on introduction of the sp$^2$-carbon.

Since the olefination to diene 357 remained extremely inefficient an alternative route to 3 had to be sought. Pinacol 381 was still deemed a worthy precursor. Bromination to 387 avoided the isolation of an additional volatile C$_{12}$ hydrocarbon. Although tertiary mesylates can be prepared in strained small rings like cyclobutane by mesylation with sulfene$^{256}$, they are very unstable (Scheme 103). Therefore it was not very surprising, that attempted isolation of the dimesylate only led to black tar.
Scheme 103: Preparation of Tertiary Mesylates

Scheme 104: Transformation of 381 into 3
However, when the sulfone formation conditions and Hogeveen's bromination/dehydrobromination idea, i.e. formation of a good leaving group in situ and immediate trapping/elimination by the basic solvent pyridine, were combined, 382 could be directly obtained from the dibromodiol 387. Dehydrobromination of the vicinal trans dibromide to the tetraene 3 with potassium tert-butoxide in THF proceeded then without any complication (Scheme 104).

Tetraene 3 proved to be fairly stable, and was easily recognizable by its $^1$H NMR spectrum: the typical AA'BB'XX' pattern of the butadiene termini which are connected to the cyclobutane and the typical 2,3-dimethylenebicyclo[2.1.1]-hexane moiety whose vinyl and bridgehead protons do not couple with each other but appear just as sharp singlets.

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$

$$6.13-5.97 \text{ (m, } 4\text{H}_3\text{-6}), 5.23 \text{ (s, } 2\text{H}_{11,12}), 4.94 \text{ (s, } 2\text{H}_{11,12}), 2.80-2.70 \text{ (m, } 2\text{H}_2\text{-7}), 1.75 \text{ (s, } 2\text{H}_1\text{-8})$$

Contracting the apices of the cyclobutane by a short bridge (as in 50) or widening them by the diene bridge (as in 51) does not have any marked difference on the chemical shift of the exo methylene protons. However, H$_1$ experiences a dramatic
upfield shift to $\delta$ 1.75 ppm similar to triene 2. (compare to diene 240).

**Figure 78:** $^1$H NMR Correlations of Molecules Containing 2,3-Dimethylelenebicyclo[2.1.1]hexane moiety
CHAPTER VIII

CONCLUSION

The stepwise belting scheme of an all-trans tetrasubstituted cyclobutane ring has been successfully applied to three representative hydrocarbons (1, 2, 3), the mutually perpendicular π-ribbons of which can interact with each other through the cyclobutane relay.

The dramatic bathochromic shift in the UV spectrum of 1 and its significant splitting of the butadiene HOMO degeneracy (as observed by photoelectron spectroscopy) support the theoretical prediction that the Walsh orbitals of cyclobutane can serve as a relay between the two π-
ribbons and enhance their interaction relative to through-space interaction (as in 6). Hydrocarbons 2 and 3 still await spectroscopic scrutiny.

Deuterium labeling indicates that upon heating to 100°C 1 undergoes a concerted [1,3-C] migration to 196 that is thermally forbidden by the Woodward-Hoffmann rules, whereas 2 rearranges to isobullvalene (208) at room temperature via a biradical intermediate. The photocyclic rearrangement of 1 to 196 is also concerted.

Currently under investigation are electron diffraction studies on tetraene 1 and suitable reference compounds (191 and 192). They could provide experimental evidence concerning whether the cyclobutane bonds (C1-C2) are elongated by through-bond interaction as indicated by comparison of force-field and semi-empirical calculations. While the former (MMP2) ignores electronic effects, it does predict a cyclobutane bond length of 1.55Å; the latter (MINDO/3) which does consider electronic effects, results in a slightly longer bond length (1.57Å)22,257.
**EXPERIMENTAL**

Instrumentation:

<table>
<thead>
<tr>
<th>Technique</th>
<th>Equipment</th>
</tr>
</thead>
<tbody>
<tr>
<td>IR</td>
<td>Perkin Elmer 1320 Infrared Spectrophotometer (standard $\tilde{\nu} = 1601 \text{ cm}^{-1}$ for polystyrene)</td>
</tr>
<tr>
<td>NMR $^1$H</td>
<td>Bruker WM 300 (internal standard: $\delta$ 7.26 for chloroform-$d_1$, $\delta$ 7.15 for benzene-$d_6$, unless specified otherwise)</td>
</tr>
<tr>
<td>NMR $^{13}$C</td>
<td>Bruker WP 80 and Bruker WM 300 (internal standard: 77.00 ppm for chloroform-$d_1$, 128 ppm for benzene-$d_6$, unless specified otherwise)</td>
</tr>
<tr>
<td>NMR $^2$H</td>
<td>Bruker 500 (internal standard: $\delta$ 7.26 for chloroform-$d_1$, $\delta$ 5.28 for methylene chloride-$d_2$)</td>
</tr>
<tr>
<td>UV</td>
<td>Hewlett Packard 8451A Diode Array Spectrometer</td>
</tr>
<tr>
<td>MS</td>
<td>EI: Kratos MS-30 (70eV)</td>
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<td></td>
<td>CI: Finnigan 4021 with INCOS Data System</td>
</tr>
<tr>
<td>GC/MS</td>
<td>Hewlett Packard 5790A Series GC with 5790A Series Mass Selective Detector</td>
</tr>
<tr>
<td></td>
<td>or VG 70-250S</td>
</tr>
</tbody>
</table>
mp  Thomas Hoover melting point apparatus (uncorrected)

Elemental Analysis  Scandinavian Microanalytical Laboratory, Herlev, Denmark

GC  preparative: Varian Aerograph Series 2700 (thermal conductivity detector)
    analytical: Carlo Erba Instrumenzione Mod. 180
              Varian Gaschromatograph 3300 (both with flame ionization detectors)

HPLC  Perkin Elmer Series 2 Liquid Chromatograph with Perkin Elmer LC 25 RI Detector

HPLC  Fluid Metering FMI model RP Lab Pump with Waters Associates Differential Refractometer R403 and Electronic Unit, and Gilson Micro fractionator

Purification of chemicals as well as flash chromatography were performed according to literature procedures. The inert atmosphere set-up is described in Appendix D.

The Experimentals leading from cinnamic acid (134) to the synthesis of tricyclo[5.5.0.0^{2,8}]dodeca-4,8-diene (128) only contain those analytical data that are not provided by Chasey\textsuperscript{90}. We thank Dr. Kurt Loening from Chemical Abstracts, Columbus, Ohio, for naming the compounds.
Figure 79: Guide to Experimental (1)
Figure 80: Guide to Experimental (2)
Figure 81: Guide to Experimental (3)
2-c,4-t-Diphenyl-1,3-t-cyclobutanedicarboxylic Acid (α-Truxillic Acid) (135)\textsuperscript{96}.

A 6L Erlenmeyer flask equipped with a $\mathbb{S}$ 60/50 joint to accommodate a water-jacketed Pyrex photochemical reactor, a $\mathbb{S}$ 24/40 joint to accommodate a mechanical cone stirrer, and another $\mathbb{S}$ 24/40 joint to permit the addition of reagents was filled with trans-cinnamic acid (145 g, 0.95 mol) and 1 L of water. The trans-cinnamic acid (134, less dense than water) was suspended by rapid stirring, and another 3.5 L of water were added at a reduced stirring speed. The suspension was irradiated with a 450 W medium-pressure Hanovia lamp for five days. The yellowish reaction product (denser than water) was suction-filtered and the unreacted starting material was removed by trituration with 1 L of ether and 400 mL of 95% ethanol. Evacuation of the solid at 90°C and 25 mmHg left 44.8 - 85.5g (31-59%, lit.\textsuperscript{96} 41-45%) of α-truxillic acid.
2-t,4-t-Diphenyl-1-t,3-c-cyclobutanedicarboxylic Acid (ε-Truxillic acid, 132)\textsuperscript{56,90}

\[
\begin{align*}
\text{Ph} & \quad \text{CO}_2\text{H} \\
\text{Ph} & \quad \text{CO}_2\text{H}
\end{align*}
\]

\(\alpha\)-Truxillic acid (135, 15.0 g, 51 mmol), potassium hydroxide pellets (60 g, 1.07 mol) and reagent grade sand (75.0 g) were finely ground under nitrogen in a glove bag. The mixture was firmly pressed into a 250 mL Erlenmeyer flask, and the vessel was fitted with a 2-hole stopper. Under a continuous flow of nitrogen, the flask was submersed in a hot Wood's metal bath and kept between 290 and 330°C for 3-3.5 h. The mixture melted partially and turned green-yellow. After being cooled to room temperature, the solid mass was dissolved in water by heating on a steam bath and then filtered through a Buchner funnel. The filtrate was diluted to 300 mL with water, acidified with 80 mL of concentrated hydrochloric acid, stirred for 15 min, and cooled to 0°C. The cold suspension was filtered through a sintered Buchner funnel. The off-white, cheesy solid was triturated with ethyl acetate (5x100mL). The combined yellow ethyl acetate phases were dried over magnesium sulfate and the solvent was removed by rotary evaporation. Recrystallization from ethyl acetate/hexane yielded 13.2 g (88\% average yield) of a light-brown crystalline solid, mp 178-180°C (lit.\textsuperscript{90} 66\%, mp 192°C) \textsuperscript{1H}
NMR (60 MHz, CDCl$_3$) $\delta$ 11.2 (s, 2H), 7.35 (s, 10H), 4.05 (t, $J = 9$ Hz, 2H), 3.35 (t, $J = 9$ Hz, 2H).

N-Methyl-N-nitrosourea (415).

A 5-L three-necked, round bottomed flask equipped with a reflux condenser and an overhead stirrer was filled with 506 g (7.55 mol) of methylamine hydrochloride, 1.5 kg (25 mol) of urea and 2 L of water. The yellow solution was heated to mild reflux for 3 h, then boiled vigorously for 15 min. After cooling to 0°C, 550 g (7.97 mol) of sodium nitrite was added. Concentrated sulfuric acid (500 g, 5.00 mol) and ice (3 kg) were equally distributed between three 4-L beakers. The beakers were cooled in an ice/methanol mixture. With vigorous mechanical stirring, the cold (0°C) clear yellow N-methylurea/sodium nitrite solution was added via addition funnels at such a rate that the temperature of the reaction mixture stayed in the range of 0-5°C (to prevent acid-catalyzed denitrosylation). After the addition, the product that floated on top of the solution was separated by suction filtration. The beige solid was triturated with 250 mL of ice water to remove the acid and filtered again. Finally, drying in a desiccator over potassium hydroxide pellets for 6 h under
oil pump vacuum gave 580-780 g (75-92%) of a pale yellow solid. The product was stored in an amber glass bottle in the refrigerator. [The glassware was subsequently cleaned in a potassium hydroxide/methanol bath in the hood in order to decompose the highly carcinogenic N-methyl-N-nitrosourea].

Dimethyl 2-t,4-t-Diphenyl-1-r,3-c-cyclobutanedicarboxylate

(416)

\[
\begin{align*}
\text{Ph} & \quad \text{CO}_2\text{Me} \\
\text{Ph} & \quad \text{CO}_2\text{Me}
\end{align*}
\]

N-Methyl-N-nitrosourea (20.6 g, 0.193 mol) was added in small portions to a cold (0°C) vigorously stirred mixture of 40% aqueous potassium hydroxide solution (70 mL) and ether (200 mL) at such a rate that the temperature did not exceed 5°C. The yellow ethereal phase was decanted and dried over potassium hydroxide at 0°C for 30 min (the flask was not stoppered!). Three more ethereal diazomethane solutions were prepared in the same manner. These were slowly poured into a solution of diacid 132 (59.2 g, 0.200 mol) in methanol (200 mL) at room temperature, until the yellow color persisted and vigorous nitrogen evolution ceased. The excess diazomethane
was back-titrated with glacial acetic acid until the yellow color disappeared. Usually about 4 to 4.5 equivalents of N-methyl-N-nitrosourea were consumed. Filtration and evaporation of the solvent yielded 62.3 to 64.8 g (96-100%) of a brown, viscous, sweet-smelling, clear liquid (lit. mp 64°C).

2-t,4-t-Diphenyl-1-x,3-g-cyclobutanedimethanol (136)\textsuperscript{90}

Under nitrogen, a solution of diester 416 (221 g, 0.682 mol) in anhydrous THF (300 mL) was added to a suspension of lithium aluminum hydride (55.8 g, 1.47 mol) in anhydrous THF (700 mL) at such a rate as to maintain reflux. After 11 h of heating, the grey suspension was cooled to room temperature and 300 mL of saturated aqueous sodium sulfate solution was added slowly until the vigorous hydrogen evolution ceased and the heavy aluminates precipitated to leave a clear yellow supernatant. THF (600 mL) had to be added to allow for efficient stirring. The suspension was filtered, and the aluminates were leached with THF (3x600 mL). The combined organic phases were evaporated. To remove the last traces of THF, diethyl ether was added and evaporated to leave 178 g (96%) of white yellowish, solid diol 136 (lit.\textsuperscript{90} 100%).
1,3-c-Bis(bromomethyl)-2,4-t-diphenycyclobutane (137)\textsuperscript{90}

Under a blanket of nitrogen, bromine (120 mL, 2.34 mol) was added dropwise to a cold (0°C) solution of triphenylphosphine (600 g, 2.27 mol) in 3 L of methylene chloride, until a drop was no longer discolored (some triphenylphosphine dibromide precipitated as a white solid). Diol 136 (214 g, 0.800 mol) was dissolved in 0.9 L of methylene chloride and added within 30 min. After another 30 min at 0°C, the clear yellow solution was stirred at room temperature for 20 h, then the solvent was evaporated. The remaining solids were triturated with a total volume of 4 L of petroleum ether. Evaporation of the organic extracts and recrystallization from petroleum ether (poorly soluble)/chloroform (very soluble) yielded 254 g (81%) of highly crystalline, pale yellow dibromide 137, mp 58.5-62.5°C. After a second recrystallization, the melting point\textsuperscript{19} increased to 62.5-63.5°C (lit. 81% mp: 54-55°C).
A 5-L three-necked, round-bottomed flask equipped with an overhead stirrer, a reflux condenser and a 500 mL addition funnel was charged with dibromide 137 (40 g, 0.10 mol), ruthenium dioxide hydrate (purchased from Engelhardt, 1.5 g, ca. 8.2 mmol), and 300 mL of methylene chloride. With vigorous stirring ca. 4 L of Chlorox solution (0.76 M aqueous sodium hypochlorite, 3.0 mol) was added at such a rate that the methylene chloride was maintained at reflux, (the oxidation is initially very exothermic and usually takes 7-8 h). The end-point was reached, when the solution no longer changed color from golden-orange (ruthenium tetroxide) to black (ruthenium dioxide) within a five-minute period. The ruthenium tetroxide was extracted with methylene chloride (5x200 mL) and quenched with ether. The volume of the aqueous phase was reduced to ca. 1 L on a rotary evaporator. Then, 100 mL of concentrated hydrochloric acid was added to precipitate the diacid (caution: chlorine gas evolution), and the remainder of the aqueous solvent was removed by filtration. The solid was taken up in 800 mL of ether, the organic phase was dried over magnesium sulfate, decolorized
with charcoal, and filtered through a Celite pad. Evapora-
tion of the ether yielded the dicarboxylic acid as a white
paste that was directly utilized in the ensuing reduction.
Under a nitrogen atmosphere and with vigorous stirring by a
Hershberg stirrer, borane-THF complex (1.3 L of 1M, 1.3 mol)
was added within 1.5 h to a cold (0°C) solution of the
diacid (from four oxidation runs) in anhydrous tetrahydro-
furan (200mL). Stirring was continued for 1 h at 0°C, then
for 4 h at room temperature (when polymeric intermediates
were formed, stirring was continued until these dissolved).
The pale yellow reaction mixture was poured onto crushed ice
(500 g) and stirred overnight. The solution was neutralized
with sodium carbonate. The solvent was rotary evaporated,
and the still hot two-phase system was extracted with 1.8 L
of boiling chloroform. Drying of the solution over mag-
nesium sulfate, filtration, and evaporation yielded a
yellow, tacky solid. For recrystallization purposes, this
solid was suspended in 400 mL of methylene chloride and
completely dissolved with chloroform at the boiling point.
Petroleum ether was added until the solution turned cloudy.
Yield: 85 g (70%) of pale yellow, small, hard crystals
(lit.90 47%).
2-t,4-t-Bis[[tetrahydro-2H-pyran-2-yl]oxy]methyl]-1-t,3-g-cyclobutanediacetic Acid (418)\textsuperscript{90}.

Diol 417 (50 g, 0.17 mol), pyridinium tosylate (6.15 g, 24.5 mmol), and dihydropyran (83 g, 1.0 mol) were dissolved in 1 L of methylene chloride and stirred at room temperature for 20 h.

The yellow, cloudy reaction mixture was washed with water (3x200 mL) and brine (200 mL). Drying over magnesium sulfate and evaporation of the solvent yielded 81.9 g of an orange oil. This crude protected dibromide 139 was dissolved in 200 mL of anhydrous dimethylsulfoxide under argon. When 66.6 g (1.36 mol) of freshly ground sodium cyanide was added, the solution turned orange and heated up. After 6.5 h of heating at 90-100°C in an oil bath, the dark brown solution (solidification occurred on cooling) was partitioned between 500 mL of water and 200 mL of ether. The aqueous phase was extracted with a total volume of 1.3 L of ether, and the combined ether phases were washed with water (100 mL), brine (2x150 mL), then dried over magnesium sulfate. Evaporation of the solvent yielded 62.7 g of a brown oil 140. Aqueous potassium hydroxide solution (372 g of potassium hydroxide in 450 mL of water) was slowly added to a solution of the crude dinitrile 140 in 450 mL of
methanol. A highly exothermic reaction was noted and ammonia was evolved. The orange emulsion was heated to reflux for 15 h in a sand bath. After evaporation of the methanol, the water-insoluble material was extracted with 200 mL of ether. The aqueous phase was cooled to 0°C, diluted with 200 mL of water, and acidified to pH 4/5 with concentrated hydrochloric acid. The voluminous precipitate was extracted with a total of 1.5 L of ether. Washing with brine, drying over magnesium sulfate, and evaporation of the solvent left 54.4 g (80% yield starting from diol 417) of a pale yellow solid (mp 120-121°C). The mp could not be raised by recrystallization (lit. 90% 0.95x0.86x0.43 = 35%).

Dimethyl 2-t,4-t-Bis[[tetrahydro-2H-pyran-2-yl]oxy]methyl]-1-t,3-c-cyclobutanediacetate (141)

\[
\begin{align*}
\text{THPO} & \quad \text{CO}_2\text{Me} \\
\text{THPO} & \quad \text{CO}_2\text{Me}
\end{align*}
\]

Method A: Compare 416 (quantitative yield).

Method B^{267}:

The 250 mL distillation flask of a diazomethane generator (no ground joints, glassware wrapped with
insulating tape) was filled with a solution of 26 g of potassium hydroxide in 35 mL of water and 130 mL of 95% ethanol, completely submerged in an oil bath and heated to 65°C. N-methyl-N-nitroso-p-toluenesulfonamide (Diazald, 86.0 g, 10.4 mol) was dissolved in 800 mL of ether. A 500 mL separatory funnel was filled with the filtered Diazald solution and mounted on the distillation apparatus so that its stem was directly above the potassium hydroxide solution. A 2-L Erlenmeyer flask filled with a suspension of 43.8 g (0.10 mol) of crude diacid 418 in 100 mL of ether was connected air-tight to the distillation apparatus. Unreacted diazomethane and nitrogen were allowed to exit through a solution of glacial acetic acid in ether (via the vacuum adapter). The Diazald solution was added to the potassium hydroxide solution at such a rate that only a minimum amount of ether accumulated in the distillation flask. The excess diazomethane was quenched with acetic acid. Drying of the solution over sodium carbonate, filtration, evaporation of the ether, and chromatography (230x60 mm silica gel, 50% ether/petroleum ether) afforded 44.5 g (95%) of a yellow viscous oil.
(3R,4S,7Sn,8Sn)-7,8-Bis[[tetrahydro-2H-pyran-2-yl]oxy]-methyl]bicyclo[4.1.1]octane-3,4-diol (142).

Under an atmosphere of argon, anhydrous ether (250 mL) was placed into a 1-L three-necked Morton flask equipped with an Allen condenser and a Hershberg stirrer. With rapid stirring, 60 mL of a sodium/potassium (1:1) alloy were injected. The apparatus was equipped with a 250-mL pressure equalizing addition funnel filled with trimethylsilyl chloride (freshly distilled from calcium hydride, 135 mL, 1.05 mol), and a 250-mL Hershberg addition funnel filled with diester 141 (86 g, 0.20 mol) in anhydrous ether (total volume of the solution: 150 mL). At the maximum speed of the compressed air stirrer, both solution were added within 4 h (exothermic reaction). Stirring was continued for 12 h before the purple solids were allowed to settle for 4 h. A 1-L three-necked round bottomed flask was equipped with a 500-mL pressure equalizing addition funnel topped by an Allen condenser, charged with potassium dihydrogen phosphate (5.4 g), potassium fluoride dihydrate (7.5 g), water (200 mL), and methanol (150 mL), and flushed with argon. The supernatant acyloin condensation-solution was transferred by cannula (15 gauge) into the vigorously stirred hydrolysis
vessel by applying a weak vacuum (the hydrogen evolved by the hydrolysis of unreacted sodium potassium alloy regulated the rate of transfer automatically). The acyloin condensation residue was triturated with anhydrous ether (3x50 mL) and finally decomposed by sequential injection of 2-propanol (100 mL), methanol (100 mL), and water (100 mL) while venting the hydrogen into a brisk flow of argon. With vigorous magnetic stirring of both phases, the hydrolysis mixture was heated to 70°C for 10 h. During that time most of the ether collected in the addition funnel. The residual ether and methanol were removed on a rotary evaporator, 300 mL of ether was added, and the aqueous phase was saturated with sodium chloride. Extraction with more (2x100 mL) ether, drying of the combined ether phases over magnesium sulfate, and evaporation yielded 105 g of a pale yellow paste. Reduction with lithium aluminum hydride (5.7 g, 0.15 mol) in anhydrous THF (150 mL) at 0°C for 30 min, hydrolysis with saturated aqueous ammonium-chloride solution, and Soxhlet-extraction of the insolubles with THF for 12 h yielded 80 g of a yellow, viscous oil. Flash chromatography of 0.26 g of this crude oil on (180x20 mm silica gel with 80% ethyl acetate/petroleum ether, 5-6 psi) afforded 0.17 g of pale yellow oil that spontaneously solidified. Accordingly, the total yield was ca. 52.3 g (71%, usually 65-73%) (lit. 90 82%).
Preparation of Sodium/Potassium (1:1) Alloy\textsuperscript{268}.

Potassium (39.2 g, 1g-atom) and sodium (23.0 g, 1g-atom) were cut into small pieces (cubes of 1 cm) and placed in a 200-mL glass bottle filled with 50 ml of mineral oil. Some of the sodium and potassium pieces were mechanically fused with a glass rod and then left standing at room temperature. After ca. 2 h all cubes had fused. The alloy can be stored under mineral oil and syringed out for use with a dry glass syringe, the piston of which is coated with a film of mineral oil (density of alloy \( \sim 1g/mL \), mp 11°C).

\[(3-\text{R},4\text{S},7\text{Sn},8\text{Sn})-3,4\text{-Dihydroxybicyclo[4.1.1]octane-7,8-dimethanol}\ (153).\]

Method A\textsuperscript{244}:

\[
\text{The Bis(tetrahydropyranyl) ether 142 (91.6 mg, 0.248 mmol), pyridinium tosylate (13 mg, 0.05 mmol), and 2 mL of absolute ethanol were stirred at 55°C for 26 h. The solvent was rotary evaporated, the residue was dissolved in ethyl acetate, filtered through a short plug of silica gel to remove the catalyst, evaporated again, and purified by MPLC (25% methanol/ethyl acetate, silica gel). A glassy}
\]
solid (42.8 mg, 86%) was isolated and recrystallized from acetone to give colorless plates, mp 126.5-127.5°C.

**Method B**:243

Bis(tetrahydropyranyl)ether 142 (100 mg, 0.269 mmol), Dowex 50x4-400 acid-treated resin (45 mg) and 2 mL of methanol were stored at room temperature for 15 h. The colorless suspension was filtered through Celite, rotary evaporated, and evacuated (Kugelrohr, 0.01 mm Hg, 60°C) to leave 59 mg of a colorless oil (theory: 54 mg; only minor impurities by 75 MHz $^{13}$C-NMR).

IR (KBr, cm$^{-1}$) 3640-3060 (br s), 3030 (w), 2920 (br s), 1380 (m), 1035 (s), 1020 (s).

$^1$H NMR (300 MHz, methanol-$d_4$, reference MeOH: δ 4.77 ppm) δ 4.11 (t, $\nu = 5.1$ Hz, 2H), 3.55 (dd, $\nu = 8.3, 5.9$ Hz, 4H), 2.74-2.62 (m, 1H), 1.90-1.70 (m, 7H).

$^{13}$C NMR (75 MHz, methanol-$d_4$, reference: CD$_3$-OD: 49.00 ppm) 74.63, 66.88, 66.82, 44.74, 44.49, 36.71, 36.21 ppm.

MS m/z calcd for C$_{10}$H$_{12}$O (M$^+$-3H$_2$O): 148.0888; obsd. 148.0915; 149 (2%), 148(6), 119 (18), 107 (20), 93 (40), 83 (60), 79 (61), 67 (57), 55 (100).

Elemental analysis: calcd for C$_{10}$H$_{18}$O$_4$: C: 59.39, H: 8.97; found: C: 59.57; H: 8.96.
Cyclic O,O-[(3R,4S,7Sn,8Sn)-7,8-Bis[[tetrahydro-2H-pyran-2-yl]oxy]methyl]bicyclo[4.1.1]oct-3,4-ylene] Thiocarbonate

Freshly sublimed 4-dimethylaminopyridine (sublimation: 0.35 mm Hg, 110°C; 7.90 g, 64.8 mmol) and diol 142 (10.0 g, 27.0 mmol) were dissolved in 100 mL of anhydrous methylene chloride under nitrogen and cooled to 0°C. An 85% thiophosgene solution in carbon tetrachloride (2.5 mL, 32.4 mmol) was slowly injected with vigorous stirring. The intensively orange-red emulsion quickly faded, and a solid precipitated. After one night at 0°C, 100 mL of ether was added dropwise at 0°C to precipitate as much 4-dimethylaminopyridine hydrochloride as possible. The suspension was filtered through a sintered glass funnel, and the solids were washed with ether (3x50 mL). The combined filtrates were evaporated and chromatographed on a silica gel column (60x60 mm, ether) to give 13.0 g of a pale yellow, viscous oil (theoretical yield: 11.1 g). No further purification was necessary for the olefination. A purified sample displayed the following spectrum: $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 5.28-5.21 (m, 2H), 4.54-4.50 (m, 2H), 3.91-3.75 (m, 4H), 3.57-3.43 (m, 4H), 2.44-2.35 (m, 2H), 24.19-2.10 (m, 5H), 1.84-1.49 (m, 13H).
2,5-Dimethyl-1-phenyl-2,5-diaza-phospholidine \(^{269}\).

\[
\text{bp} 0.75 \ 85-100^\circ C \ \text{(lit.} 269 \ \text{bp} 0.7 \ 90-95^\circ C) \ \text{bp} \]

\( ^1H \text{ NMR (60 MHz, CDCl}_3 \ \delta \)

7.5-7.2 (m, 5H), 3.1 (d, \( \delta = 4 \text{ Hz,} \)

4H), 2.6 (d, \( \delta = 14 \text{ Hz,} \)

6H).

\[2,2'-(\{7_{S_n} , 8_{S_n} \}-\text{Bicyclo}[4.1.1] \text{oct-3-en-7,8-ylenebis(methyl-}

\text{eneoxy)} \text{bis[tetrahydro-2H-pyran]}(133)\] \(^{113}\).

**Method A:**

The 2,5-dimethyl-1-phenyl-2,5-

diazaphospholidine (9.8 mL, 54 mmol) was added to the crude thiocarbonate

143 (13 g, max. 27 mmol) under an atmosphere of nitrogen. After a short induction

period, the initially pale yellow solution turned orange-yellow, a highly exothermic reaction started, and gas was evolved. After overnight stirring at room temperature, another 3 mL of phospholidine was added, and the mixture was heated to 40°C for 1 h. The reaction mixture was dissolved in 150 mL of methylene chloride, adsorbed on 30 g of silica gel, and poured onto a column packed with 100 g of silica
gel. At first, the thiophospholide eluted with methylene chloride to be followed by the reaction product with ether/petroleum ether (1:1). Rotary evaporation yielded a colorless oil that solidified in the freezer (7.85 g, 86.5% from diol 142), mp 35.5°-38.5°C.

IR (neat, cm⁻¹): 3035-2800 (br s), 1135 (s), 1115 (s), 1075 (s), 1050 (s), 1025 (br s).

¹H NMR (300 MHz, CDCl₃) δ 5.56 (br s, 2), 4.65-4.54 (m, 2H), 4.00-3.80 (series of m, 4H), 3.66-3.56 (m, 2H), 3.56-3.42 (m, 2H), 2.27 (s, 4H), 2.13 (br t, J = 10 Hz, 2H), 2.01 (td, J = 6.0, 2.0 Hz, 2H), 1.88-1.42 (series of m, 20H).

MS m/z calcd for C₁₅H₂₄O₃ (M⁺-dihydropyran): 252.1725, obsd. 252.1710; 259 (0.6%); 252 (1.6); 234 (0.8); 168 (6); 150 (1.3); 132 (3); 91 (11); 85 (100); 79 (8); 67 (12).
(7Sn,8Sn)-7,8-Bis(bromomethyl)bicyclo[4.1.1]oct-3-ene (144)

Triphenylphosphine (12.3 g, 46.9 mmol) was dissolved in 100 mL of methylene chloride under nitrogen and cooled to 0°C. Bromine (2.4 mL, 46.9 mmol) was added with a pipette until one drop of bromine was no longer discolored. The excess bromine was reacted by adding a few crystals of triphenylphosphine.

Bis(tetrahydropyranyl)ether 133 (7.15 g, 21.3 mmol) was dissolved in 20 mL of methylene chloride and added dropwise at 0°C. After 5 min, the mixture was allowed to warm to room temperature and stirred for 2.5 h. The intensively yellow, clear reaction mixture was adsorbed onto 50 mL of silica gel and packed on top of 800 mL of silica gel. Flash chromatography (petroleum ether, 5 psi, 250 mL fractions) yielded 5.1 g (82%) of pale yellow crystals in fractions 8-18.

Colorless crystals obtained by MPLC (petroleum ether, silica gel) melted at 63.5-66.0°C (lit. mp 63.5-65.0°C).

^H NMR (300 MHz, CDCl₃) δ 5.57 (s, 2H), 3.61 (d, J = 8.6 Hz, 4H), 2.32 (d, J = 0.9 Hz, 4H), 2.25-2.10 (m, 4H).
A reaction mixture consisting of dry DMSO (100 mL), crude dibromide 144 (5.10 g, 17.5 mmol), and finely ground sodium cyanide (3.42 g, 69.9 mmol) was heated to 70-100°C for 2 h with the exclusion of moisture. After being cooled to room temperature, the mixture was partitioned between water (200 mL) and ether (100 mL). The aqueous phase was extracted with ether (3x100 mL). The combined organic phases were washed with water (50 mL) and brine (50 mL), filtered through a magnesium sulfate cone, and evaporated to leave 3.85 g of a yellow, partially crystalline material (theoretical yield 3.25 g, lit. 90 98%) that could be used without further purification. An analytically pure sample was obtained by MPLC (30% ethyla cetate/petroleum ether), and subsequently recrystallized from methanol: mp 71.5°C (lit. 90 mp 66°C).

$^1$H NMR (300 MHz, CDCl$_3$) δ 5.62 (s, 2H), 2.66 (d, J = 8.7 Hz, 4H), 2.36 (s, 4H), 2.25 (br s, 2H), 2.15 (td, J = 8.6, 1.3 Hz, 2H).

Elemental analysis: calcd. for C$_{12}$H$_{14}$N$_2$: C: 77.38; H: 7.58; found: C: 77.13; H:7.56.
Dimethyl \( (7\text{sn},8\text{sn}) \)-Bicyclo[4.1.1]oct-3-ene-7,8-diacetate (146).

Method A: By Saponification of Bisnitrile 145

A heterogeneous mixture of crude dicyanide 145 (3.85 g, max. 17.5 mmol), methanol (40 mL), and aqueous potassium hydroxide solution (50 mL, from 37 g of potassium hydroxide and 45 mL of water) was refluxed vigorously in a sand bath (140-150°C). After 10 h, the methanol was evaporated and the aqueous phase was extracted with ether (discarded), cooled to 0°C, and acidified with concentrated hydrochloric acid (42 mL), and extracted again with ether (5x100 mL). Evaporation of the ether phases after drying over magnesium sulfate yielded a green-brown solid. A suspension of the solid in 100 mL of ether was esterified with diazomethane (from Diazald). The diester was purified by flash chromatography (380x30 mm of silica gel, 15% ethyl acetate/petroleum ether, 8 psi, 25 mL fractions, fraction 9-17) to give 3.58 g of a mobile yellow oil (81% from dibromide 144; lit. 46% from dinitrile). 

\(^{1}\text{H NMR (300 MHz, CDCl}_3\) \( \delta \) 5.57 (br s, 2H), 3.64 (s, 6H), 2.66 (d, \( J = 8.3 \text{ Hz}, 4\text{H} \)), 2.32-2.23 (m, 4H), 2.15-2.06 (m, 2H), 2.04 (br s, 2H).
Method B: By Jones Oxidation of Diol 419²⁷⁴.

A solution of diol 419 (50 mg, 0.26 mmol) in acetone (10 mL) was cooled to 0°C. Under vigorous stirring with a Hershberg stirrer, Jones reagent [1 M, CrO₃ (1.0 g, 10.0 mmol) in H₂SO₄ (1.0 mL), then filled up to 10 mL with water] was added dropwise. The mixture had to be warmed to room temperature to achieve a reasonable reaction rate. After the addition of 1 mL, a red-orange color persisted. The turbid, almost colorless supernatant solution was pipetted out, the coagulated green, chromate residues were triturated with ether (5 mL), and the combined organic phases were rotary evaporated. The chromate salts and the evaporation residues were separated between water (10 mL) and ether (10 mL). The aqueous phase was saturated with sodium chloride and extracted with ether (2x5 mL). The combined ether phases were washed with brine (5 mL), and esterified with ethereal diazomethane. Evaporation of the solvents yielded 34 mg (52%) of a colorless, clear, mobile oil after MPLC (20% ethyl acetate/petroleum ether, silica gel).
cis-Tricyclo[5.5.0.0^2,8]dodec-10-ene-4,5-diol (147).

A dry, 1-L three-necked Morton flask equipped with an Allen conden­ser, a Hershberg stirrer, and a 24/40 15-cm straight extension piece was charged with 350 mL of ether (freshly distilled from sodium/benzophenone). Under a dynamic nitrogen atmosphere and with rapid stirring by a compressed air high-speed stirrer, 3 mL of sodium/potassium (1:4) alloy was injected. After 30 min, the alloy had become a very fine, grey-white dispersion. Two dry, nitrogen-flushed 30-mL syringes were filled with an ethereal solution of dry trimethylsilyl chloride (5 mL, 40 mmol, freshly distilled from calcium hydride, diluted to 30 mL with anhydrous ether), and an ethereal solution of diester 146 (0.50 g, 0.20 mmol, total volume 30 mL) respectively, and then mounted on a dual syringe pump. The tips of the 30-cm needles were placed directly above the dispersion. Both solutions were added simultaneously within 3 h. The dark grey suspension was stirred for another 3 h. Hydrolysis as for diester 141: potassium dihydrogen phosphate (5.4 g), potassium fluoride dihydrate (7.5 g), water (200 mL), and methanol (200 mL) at 70°C for 24 h; workup with ether (100 + 2x70 mL), brine (50
mL), then drying over magnesium sulfate. Reduction as for lithium aluminum hydride (0.25 g, 6.6 mmol) in anhydrous THF, 10 min at 0°C, then quenching with saturated aqueous ammonium chloride solution and Soxhlet extraction with THF. The pasty solid left after rotary evaporation was triturated with ether (4x3 mL) and filtered through a sintered glass funnel. The amorphous residue amounted to 0.16 g of 147, the combined ether phases were separated by MPLC (ethyl acetate, silica gel) to give 0.09 g of 147 and 0.05 g of open chain diol 419. Therefore the yield was 0.25 g (81%) of 147, mp 152-156°C (lit. 148-153°C) after recrystallization from ethyl acetate and 0.05 g (16%) of 419 mp 94.0-94.5°C, with a cis:trans ratio of 147 higher than 92:8 according to 20 MHz 13C NMR.

(7Sn,8Sn)-Bicyclo[4.1.1]oct-3-ene-7,8-diethanol (419).

\[
\begin{align*}
\text{IR (CDCl}_3): & \quad 3620 \text{ (m)}, 3700-3200 \text{ (br w)}, 3000 \text{ (w)}, 2930 \text{ (s)}, 2890 \text{ (s)}, 2820 \text{ (m)}, 1420 \text{ (m)}, 1050 \text{ (s)}, 1030 \text{ (s) cm}^{-1}.
\end{align*}
\]

\[
\begin{align*}
^1\text{H NMR (300 MHz, CDCl}_3) & \delta 5.55 \text{ (br s, 2H)}, 3.61 \text{ (t, J = 6.8 Hz, 4H)}, 2.23 \text{ (br d, J = 1.9 Hz, 4H)}, 2.04-1.88 \text{ (m, 6H)}, 1.80-1.68 \text{ (m, 2H)}, 1.32 \text{ (s, 2H)}. 
\end{align*}
\]
MS calcd for C₁₂H₂₀O₂ (M⁺) 196.1463 found: 196.1509
(1.3%), 194 (1.0), 147 (11), 134 (14), 105 (43), 91 (100),
79 (71), 67 (49), 55 (28).

(7SN,8SN)-Bicyclo[4.1.1]oct6-3-ene-7,8-diacetaldehyde (420)
Method A: By oxidation of diol 419

Under argon, a solution of
diol 419 (55 mg, 0.28 mmol) in hot chloroform (2 mL) was added to a stirred suspension of ground, activated 3Å molecular sieves (0.28 g) and pyridinium chlorochromate (0.36 g, 1.7 mmol) in dry methylene chloride (2 mL). After 30 min, the supernatant solution was decanted from the dark red-black gum and the latter was extracted with ether (3x2 mL). The combined organic phases were filtered through 60x10 mm Florisil grade A and eluted with 20 ml of ether to yield 11 mg (20%) of a colorless oil.

IR (CDCl₃, cm⁻¹) 3000 (w), 2900 (m), 2880 (m), 2820 (m), 2720 (m), 1720 (s), 1420 (m).

¹H NMR (300 MHz, CDCl₃) δ 9.68 (t, J = 1.6 Hz, 2H), 5.65-5.50 (m, 2H), 2.80 (dd, J = 8.1, 1.5 Hz, 4H)m, 2.31 (br s, 4H), 2.21 (br t, J = 6.9 Hz, 2H), 2.02 (br s, 2H).
MS m/z: calcd for C_{12}H_{16}O_{2} (M^+): 192.1146, obsd. 192.1130 (2%), 148 (42), 135 (28), 119 (29), 105 (30), 91 (88), 79 (100), 67 (84).

**Method B:** By reduction of dinitrile 145.

Under argon, dinitrile 145 (100 mg, 0.537 mmol) was dissolved in 4 mL of anhydrous benzene and cooled to 10°C in an ice bath. Diisobutylaluminum hydride (1M in hexanes, 1.2 mL, 1.2 mmol) was injected dropwise; the intensively yellow, clear solution was stirred at room temperature for 6 h. The mixture was then cannulated into vigorously stirred 5% aqueous sulfuric acid (rinsed with 2x5 mL of anhydrous ether), stirred until all solids had dissolved (ca. 10 min), and extracted with ether (3x3 mL). The combined organic phases were washed with brine (3 mL), dried over magnesium sulfate, filtered, and rotary evaporated to leave 75 mg (73%) of a pale, yellow oil, that was pure by $^1$H NMR.

Cyclic O,O-cis-Tricyclo[5.5.0.0^{2,8}]dodec-10-en-4,5-ylene Thiocarbonate (148).

Under argon, the diol (100 mg, 0.515 mmol) and 4-dimethylamino-pyridine (151 mg, 1.24 mmol, sublimed) were dissolved in 3 mL of anhydrous methylene chloride and
cooled to 0°C. Thiophosgene/carbon tetrachloride (85%, 0.06 mL, 0.62 mmol) was injected dropwise. The orange-red suspension that formed was stirred for 3 h at 0°C, then warmed up to room temperature and adsorbed on 3 g of basic alumina (activity III). Chromatography on 12 g of basic alumina (activity III) with ether afforded 84 mg (72%) of pale yellow crystals, mp 155-156°C (lit. 90 77%, mp 148-153°C).

IR (CDCl₃, cm⁻¹): 3010 (w), 2920 (m), 2805 (w), 1295 (s), 1280 (s).

¹H NMR (300 MHz, CDCl₃) δ 5.63-5.48 (m, 2H), 5.28-5.18 (m, 2H), 2.47-2.14 (series of m, 9H), 2.07 (br s, 2H), 1.85-1.77 (m, 1H).

When chromatographed on silica gel, the thiocarbonate hydrolyzed to a mixture of cis- and (supposed) trans-carbonate.

Cyclic cis-Tricyclo[5.5.0.0²,8]dodec-10-en-4,5-ylene Carbonate (161c).

MPLC (18% ethyl acetate/-petroleum ether, silica gel) yielded a white solid, mp 122-125°C (lower Rf).

IR (CDCl₃, cm⁻¹) 2920 (m), 1800 (s), 1025 (m).
$^1$H NMR (300 MHz, CDCl$_3$) δ 5.61-5.54 (m, 2H), 5.11-5.04 (m, 2H), 2.40-2.06 (series of m, 11H), 1.81-1.80 (m, 1H).

$^{13}$C NMR (75 MHz, CDCl$_3$) 154.6, 125.50, 124.93, 80.85, 41.05, 39.12, 37.71, 33.38, 33.63, 32.91 ppm.

MS m/z calcd for C$_{13}$H$_{16}$O$_3$ (M$^+$) 220.1100, obsd: 220.1111 (19), 166 (23), 158 (28), 143 (54), 129 (62), 117 (51), 105 (35), 91 (100), 79 (86), 67 (74).

Cyclic trans-Tricyclo[5.5.0.0$^{2,8}$]dodec-10-en-4,5-ylene Carbonate(161t).

MPLC (18% ethyl acetate/-petroleum ether, SiO$_2$) yielded a pale yellow solid, mp 130-148°C (higher R$_F$).

IR (CDCl$_3$, cm$^{-1}$) 2920 (m), 1805 (s), 1045 (s).

$^1$H NMR (300 MHz, CDCl$_3$) δ 4.78-4.73 (m, 2H), 2.48-2.42 (m, 2H), 2.30 (br s, 4H), 1.78-1.70 (m, 2H).

When exposed overnight to basic alumina activity III in addition to cis- and trans-carbonate 161, ketone 162 could be isolated.
Tricyclo[5.5.0.0^2,8]dodec-10-en-4-one (162).

MPLC on silica gel (16% ethyl acetate/petroleum ether, silica gel) yielded a volatile, colorless oil.

IR (CDCl₃, cm⁻¹) 3010 (w), 2990 (m), 2830 (w), 1690 (s).

¹H NMR (300 MHz, CDCl₃) δ 5.58 (br s, 2H), 2.71 (t, J = 6.9 Hz, 2H), 2.58 (d, J = 4.0 Hz, 2H), 2.39-2.23 (m, 4H₃,6), 2.19-2.12 (m, 3H), 2.09-2.03 (m, 1H), 1.89 (5d, J = 6.9, 3.5 Hz, 2H).

¹³C NMR (75 MHz, CDCl₃) 213.87, 125.542, 47.82, 40.97, 39.65, 35.34, 33.38, 28.96 ppm.

MS m/z calcd. for C₁₂H₁₆O (M⁺): 176.1201, obsd. 176.1205 (75), 148 (78), 134 (30), 119 (43), 105 (39), 91 (100), 79 (93), 69 (52).
Tricyclo[5.5.0.0²,8]dodeca-4,10-diene (128).

Method A: From Thiocarbonate (148)

Under argon, a suspension of thiocarbonate 148 (87 mg, 0.37 mmol) in 0.5 mL of 1,3-dimethyl-2-phenyl-diazophosphalidine was stirred at 48°C for 3.5 h, and left standing at room temperature overnight. The homogeneous reaction mixture was diluted with pentane (3 mL), adsorbed on silica gel, and flash chromatographed (120x20 mm silica gel, pentane, 2 psi, 10 mL/fraction, fraction 5-8) to leave 42 mg (71%) of a white solid after rotary evaporation (room temperature, 100 mmHg), mp 41.5-43.5°C.

Method B: By deoxygenation of diol 147.

Under argon, a 500 mL Schlenk flask was charged with titanium trichloride-tetrahydrofuran complex (23 g, 62 mmol) and potassium (9.6 g, 0.25 mol) by Schlenk technique and equipped with a reflux condenser and stir bar. After the addition of anhydrous dimethoxyethane (200 mL, freshly distilled from sodium/potassium/benzophenone under argon) the stirred mixture was heated to reflux for 1 h. Diol 147 (1.00 g, 5.15 mmol) was dissolved in hot, anhydrous
dimethoxyethane (total 30 mL) and added by cannula to the reduction mixture that had been removed from the oil bath. After 18 h of reflux, the black suspension was cooled to room temperature, diluted with 200 mL of distilled pentane, and decanted onto a glass frit covered with Celite under a brisk flow of argon. Suction was applied at such a rate that the filter residue was always covered with solvent in order to avoid contact of the unreacted potassium with the humid air and ignition of the solvent vapors. The filter residues were rinsed with distilled pentane (200 mL), and the combined clear colorless filtrates were washed with water (250 mL). The aqueous phase was extracted with pentane (100 mL) and the combined organic phases were washed with water (2x100 mL) and brine (100 mL). The bulk of the solvent was rotary evaporated at 150 mm Hg/room temperature, the rest at 60 mm Hg. After evacuation at 20 mm Hg for 10 min, the material was twice distilled bulb to bulb (0.05 mm Hg 50°C, receiver cooled to -78°C) to yield 0.64 g (77%) of a white, soft solid, homogeneous by GC and 1H NMR.
Tricyclo[5.5.0.0²,8]dodecane (192).

A 50-mL Schlenk flask filled with diene (224 mg, 1.40 mmol) and 5% palladium on carbon (118 mg) was evacuated and flushed with argon, then charged with methanol. After 1 h of vigorous stirring in an atmospheric hydrogenator, capillary GC showed that no starting diene 128 (130°C, diene 128:t<sub>ret</sub> = 5.96 min, 192:6.24 min) was left. After the mixture had settled for 24 h, the supernatant solution was decanted and filtered through a cotton plug. The granular black residue was washed with distilled pentane (30 mL), and the combined filtrates were washed with water (20 mL). The aqueous phase was extracted with pentane (2×10 mL), the combined pentane phases were washed with water (2×10 mL) and brine (10 mL) and rotary evaporated (60 mm Hg, room temperature). The remaining colorless oil was taken up in pentane (2 mL), dried over magnesium sulfate, filtered, rotary evaporated, and distilled by Kugelrohr after evacuation (10 min, 20 mm Hg, room temperature; then 0.05 mm Hg, 50°C, receiver bulb cooled to -78°C) to yield 214 mg (93%) of a white solid that melted below room temperature.

IR (CDCl₃, cm⁻¹) 2915 (s), 2865 (m), 2845 (m), 1465 (w), 1455 (w), 1440 (w).
$^{1}H$ NMR (300 MHz, CDCl$_3$) 6 2.05-1.98 (m, 4H), 1.73-1.63 (m, 8H), 1.63-1.50 (m, 8H).

$^{13}$C NMR (75 MHz, CDCl$_3$) 40.08, 30.55, 25.46 ppm.

MS m/z calcd. for C$_{12}$H$_{20}$ (M$^+$): 164.1565, obsd. 164.1599 (42), 165 (9), 149 (24), 121 (75), 109 (50), 93 (66), 82 (93), 67 (100).

(4R$^*$,5R$^*$,10S$^*$,11S$^*$)- and (4S$^*$,5S$^*$,10S$^*$,11S$^*$)-4,5,10,11-Tetrabromotricyclo[5.5.0.0$^{2,8}$]dodecane (189).

Diene 128 (20 mg, 0.13 mmol) was dissolved in 4 mL of carbon tetrachloride and 4 mL of glacial acetic acid. After the addition of pyridinium bromide perbromide (recrystallized from glacial acetic acid, 88 mg, 0.29 mmol), the suspension was stirred at room temperature for 1.5 h and then partitioned between 10 mL of carbon tetrachloride and 10 mL of water. The organic phase was washed with 10 mL of saturated aqueous sodium bicarbonate solution, dried over magnesium sulfate, filtered, and evaporated to leave 54 mg (90%) of a white solid, mp. 236-238°C (dec.), that was poorly soluble in carbon tetrachloride, cold chloroform, or ether, and very soluble in
benzene or tetrahydrofuran. According to $^{13}$C NMR, the ratio of the two possible diastereomers was 54:46.

IR (KBr, cm$^{-1}$) 2910 (s), 2840 (w), 1430 (m), 1110 (s), 750 (s), 635 (s).

$^1$H NMR (300 MHz, benzene-$d_6$) $\delta$ 3.96-3.85 (m, 4H), 2.12-2.00 (m, 4H), 1.65-1.52 (m, 4H), 0.94-0.90 (m, 4H).

$^{13}$C NMR (75 MHz, benzene-$d_6$) major (54%): 56.08; 41.66; 39.24. minor (46%); 56.17; 41.48; 39.42 ppm.

MS m/z calcd for C$_{12}$H$_{15}$Br$_8$ (M$^+$-HBr$_2$): 318.9520, obsd 318.9501. 321 (10%), 319 (25), 317 (12), 239 (26), 237 (23), 91 (100), 79 (97).

Preparation of 83% Zinc Copper-Couple (Modified Procedure by McMurry and Kees)$^{115}$.

The McMurry/Kees procedure was modified to allow convenient manipulation under oxygen-free conditions. The apparatus consisted of a Schlenk-type glass frit with two Teflon stopcocks and two male $\frac{24}{40}$ joints, a 1 L one-necked round-bottomed flask as receiver for the washing solutions, and a 100-mL Schlenk-type round-bottomed flask as reaction flask (containing stirring bar). All solvents and solutions were purged with argon for 15 min before use. Under an atmosphere of argon, zinc dust (5.0 g, 77 mmol) was filled into the Schlenk flask, stirred with 40 mL of 3%
hydrochloric acid for 3 min and filtered. In the same way, the zinc was sequentially treated with more 3% hydrochloric acid (2x40 mL), water (3x40 mL), 2% aqueous cuprous sulfate solution (4x40 mL, 3.2 g of cuprous sulfate pentahydrate, 13 mmol, in 160 mL water), water (2x50mL), acetone (2x50 mL), and ether (2x50 mL). After evacuation, the purple zinc-copper couple was stored under argon. It had to be manipulated in the glove box, since its reactivity decreased significantly when exposed to air.

**Tricyclo[5.5.0.0\(^{2,8}\)]dodeca-3,5,9,11-tetraene (1).**

**Method A: By Allylic Bromination-Reductive Debromination**

Under argon, a stirred solution of diene 128 (105 mg, 0.644 mmol), N-bromosuccinimide (516 mg, 2.9 mmol, recrystallized from water) and azobisisobutyronitrile (17 mg, 0.10 mmol, recrystallized from benzene) in 12 mL of dry carbontetrachloride was irradiated with a sun lamp for 1.5 h. During that time, the inner temperature of the reaction mixture rose to 56°C, and all of the N-bromosuccinimide (denser than carbon tetrachloride) was converted into succinimide (lighter than the solvent). Filtration of the suspension through silica gel (35x20 mm, carbon tetrachloride) and evaporation of the
solvent at 50°C (to prevent frothing) yielded 304 mg of a bromide mixture as a white paste. No attempt was made to separate the multitude of possible isomers but instead the mixture was used as such.

For the subsequent manipulations, exposure to UV light had to be avoided. Therefore ceiling lights were shut off, and the reaction apparatus was wrapped in aluminum foil. Daylight did no harm.

I. Reductive Debromination with Zinc-Copper-Couple

In the glove box (argon), 83% zinc-copper-couple (83% w/n, 0.50 g) was added to the bromide mixture (145 mg, max. 0.305 mmol) under argon, dimethylformamide (5 mL, freshly distilled from calcium hydride under argon) was injected, and the suspension was stirred at room temperature. After 1 h, no starting material remained according to TLC and, after 3.9 days no tetraene bromide remained according to GC (1.7mx1.5 mm 3% OV101 on 100-120 Gaschrom Q, 30 mL He/mm, 120°C, retention times: tetraene 196: 2.07 min, tetraene 1: 2.73 min, and tetraene bromide: 6.33 min.) The reaction mixture was distributed between water (3 mL) and redistilled pentane (4mL), and the combined pentane phases were washed with water (3x3 mL). Drying over magnesium sulfate, removal of the solvent in a lyophylizer (760 to 20 mm Hg, receiver cooled to -78°C) and sublimation of the residue (room
temperature 0.03-0.01 mm Hg, trapped in V-tube at -78°C)
yielded 27 mg (57% from diene) of colorless, musty-smelling
plates, mp 33.5-35.5°C.

IR (neat, cm⁻¹) 3020 (br, s), 2940 (br, s), 1580 (s),
1370 (s), 1280 (s), 1050 (3), 825 (8), 780 (s), 665 (br, s).

¹H NMR (300 MHz, CDCl₃) δ 6.03-5.92 (m, 4H₃,6,9,12),
5.80-5.70 (m, 4H₄,5,10,11), 2.60-2.50 (m, 4H₁,2,7,9),
(assigned by homodecoupling).

¹³C NMR (75 MHz, CDCl₃) 134.39, 123.11, 32.93 ppm.

UV [cyclohexane, s_{max}/nm (ε)] 228 (8900), 318 (3000).

MS m/z calcd for C₁₂H₁₂ (M⁺) 156.0939, obsd. 156.0926
(56), 155 (52), 141 (37), 128 (50), 115 (55), 91 (100), 78
(50).

II. Reductive Debromination with tert-Butyllithium

Under argon, the bromide mixture (165 mg, max, 0.328
mmol) was dissolved in anhydrous THF (5 mL) and
cooled to -78°C. tert-Butyllithium (1.6M in pentane, 0.87
mL, 1.4 mmol) was injected dropwise. After 10 min, the
dark-red reaction mixture was quenched with 0.1 mL of
methanol at -78°C, warmed to room temperature, and washed
with brine (2x3mL). The solution was diluted with redistil-
led pentane (5 mL), and dried over magnesium sulfate. After
evaporation of the solvent (bulk at 160 mmHg, rest at 30
mmHg), sublimation (45°C, 0.03 mmHg) afforded 28.5 mg (53% from diene) of tetraene 1.

Method B: By Bromination-Dehydrobromination

Under argon, potassium-tert-butoxide (1.6M in THF, 0.60 mL, 0.96 mmol) was injected into a cold (0°C) solution of the tetrabromide 186 (56 mg, 0.12 mmol) in anhydrous THF (5 mL). The orange-brown suspension was warmed to room temperature and stirred for 30 min. The reaction mixture was then partitioned between 10 mL of water and 10 mL of redistilled pentane. The organic phase was washed with water (5 mL) and half-saturated aqueous ammonium chloride solution (2x5 mL), dried over magnesium sulfate, filtered through 20x10 mm of Florisil, and evaporated at 0°C and 120 mmHg until only about 1-2 mL of liquid was left. The residue was evacuated briefly in a Kugelrohr distillation apparatus at room temperature/30 mm Hg/2 min to remove most of the THF, then Kugelrohr distilled into a bulb cooled to -20 to -35°C. Resublimation at room temperature/0.02 mm Hg yielded 13 mg (68%) of a white semisolid containing only minimal impurities, especially no solvent or diene by 300 MHz ¹H NMR. When a sample was stored for prolonged times (even at -15°C) in base-washed glassware, a brittle solid formed that was insoluble in all solvents tried (compare 165).
3-Bromotricyclo[5.5.0.0^{2,8}]dodeca-3,5,9,11-tetraene (165).

Again all manipulations were done with exclusion of direct ceiling lights. In incomplete reductive debromination with zinc-copper-couple, tetraene bromide could be isolated by reversed phase HPLC (250x4.6mm C_{18} (5 μm Zorbax 008), 90% methanol/water 1.5 mL/min, 165: retention time 8.23 min, compare tetraene: 7.62 min). The combined fractions were extracted with distilled pentane (3x10 mL), the pentane phases were washed with water (3x10 mL) and brine (5 mL), then dried over magnesium sulfate. After evaporation of the solvent, the residue was distilled at 0.01 mm Hg and ~60°C. The ^1H NMR signals were assigned by homo-decoupling techniques.

IR (CDCl$_3$, cm$^{-1}$) 3040 (s), 2960(s), 2850 (w), 1595 (w), 1580 (s), 1275 (m), 1065 (m), 825 (m), 680 (s).

^1H NMR (300 MHz, CDCl$_3$) δ 6.21 (ddd, $\delta_{4,5} = 7.6$ Hz, $\delta_{4,2} = 2.0$ Hz, $\delta_{4,6} = 0.7$ Hz, 1H$_6$), 6.04 (br dd, $\delta_{6,5} = 11.1$ Hz, $\delta_{6,7} = 8.2$ Hz, 1H$_6$), 6.00-5.90 (m, 2H$_9,12$), 5.82-5.73 (m, 2H$_{10,11}$), 5.55 (ddd, $\delta_{5,6} = 11.1$ Hz, $\delta_{5,4} = 7.6$ Hz, $\delta_{5,7} = 0.7$ Hz, 1H$_5$), 2.92 (br dd, $\delta_{2,7} = 4.8$ Hz, $\delta_{2,4} = 2.0$ Hz, 1H$_2$), 2.76-2.67 (m, 2H$_{18}$), 2.56 (ddd, $\delta_{7,6} = 8.2$ Hz, $\delta_{7,2} = 4.8$ Hz, $\delta_{7,5} = 0.7$ Hz, 1H$_7$).
$^{13}$C NMR (75 MHz, CDCl$_3$) 135.06, 132.94, 127.61, 125.15, 123.53, 122.07, 44.57, 33.75, 32.86 ppm.

MS m/z calcd for C$_{12}$H$_{11}$Br$_{1}$ (M$^+$): 236.0024, obs. 236.0023 (7), 234 (7), 171 (17), 169 (21), 155 (100), 128 (23), 115 (18), 91 (19).

UV (cyclohexane; $\lambda_{\text{max}}$/nm, $\varepsilon$): 234 (6850), 244 (sh, 4780), 324 (2210).

3,9-Dibromo[5.5.0.0$^{2,8}$]dodeca-3,5,9,11-tetraene (166)

(All manipulations were performed with protection from light).

**Method A:** As By-Product of Reductive Debromination of 164.

Under the same HPLC conditions used for 165, dibromo tetraene 166 eluted with a retention time of 10.07 min. The isolated material was still relatively impure.

**Method B:** By Dehydrobromination of 164.

Under argon, crude tetrabromide 164 (0.12 g, max. 0.25 mmol), prepared from diene 128 (40 mg, 0.25 mmol) according to the procedure on p. , was dissolved in anhydrous THF (3 mL), cooled to 0°C and treated with potassium tert-butoxide/THF (1.6 M, 0.6 mL, 4 mmol). After 15 min at 0°C, the dark brown mixture was partitioned between pentane (10 mL) and
water (10 mL). The aqueous phase was extracted with pentane (5 mL), and the combined organic phases were washed with water (2x5 mL), and brine (5 mL). After rotary evaporation, pentane (3 mL) was added, and the material seemed to polymerize. The suspension was dried over magnesium sulfite, filtered, and rotary evaporated to leave 71 mg of a dark brown oil. Flash chromatography (1 g of TLC grade silica gel, pentane, 20 drops/fraction, 3 psi, fractions 5-8) yielded 30 mg (38%) of a pale yellow oil that still had a strong tendency to polymerize (this dimerization/polymerization characteristic seemed to increase in going from 1 to 165 to 168) and contained impurities according to $^1$H NMR.

$^1$H NMR (300 MHz, CDCl$_3$) δ 6.23 (dd, $J_{4,5}$ = 7.6 Hz, $J_{4,2}$ = 1.7 Hz, 2H$_4$), 6.03 (dd, $J_{6,5}$ = 11.3 Hz, $J_{6,1}$ = 8.5 Hz, 2H$_6$), 5.58 (dd, $J_{5,6}$ = 11.1 Hz, $J_{5,4}$ = 7.6 Hz, 2H$_5$), 3.05 (dd, $J_{2,1}$ = 5.8 Hz, $J_{2,4}$ = 1.4 Hz, 2H$_2$), 2.70 (dd, $J_{1,6}$ = 8.4 Hz, $J_{1,2}$ = 5.6 Hz, 2H$_1$).

$^{13}$C NMR (75 MHz, CDCl$_3$) 135.88, 126.04, 125.57, 122.51, 45.14, 33.58 ppm.
Thermal Rearrangement of 1 to Tricyclo[5.5.0.0²,10]dodeca-
3,5,8,11-tetraene (196).

A: In Chloroform-$_d_1$.

Tetraene 1 (2 mg, 0.01 mmol) in 0.5 mL of chloroform-$_d_1$ was sealed in an NMR tube, completely submersed in an oil bath, and kept at 80°C. The progress of the rearrangement was followed by $^1$H NMR. Tetraene 1 rearranged with a half life of 7h.

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 6.40 (dd, $J_{11,12} = 5.7$ Hz, $J_{11,10} = 2.9$ Hz, 1H$_{11}$), 6.08 (ddd, $J_{12,11} = 5.7$ Hz, $J_{12,1} = 3.0$ H, $J_{12,9} = 1.0$ Hz, 1H$_{12}$), 6.04-5.87 (series of m, 5H$_3$-6,9'), 4.94 (ddddd, $J_{8,9} = 9.4$ Hz, $J_{8,7} = 3.5$ Hz, $J_{8,1} = 1.8$ Hz, $J_{8,10} = 0.7$ Hz, 1H$_8$), 2.91-2.83 (m, 1H$_7$), 2.83-2.79 (m, 1H$_2$), 2.77-2.72 (m, 1H$_{10}$), 2.45-2.41 (m, 1H$_1$) (assigned by homo-decoupling).

$^{13}$C NMR (75 MHz, CDCl$_3$) 141.05, 134.58, 132.99, 129.34, 127.08, 125.27, 122.36, 50.46, 44.21, 41.59, 38.25 ppm.
B. In Benzene-$d_6$.

Tetraene 1 (7 mg, 0.05 mmol) was dissolved in 1 mL of benzene-$d_6$ in a 5 mm medium-walled NMR tube fitted with a $\S$ 19/35 male joint. After 5 freeze pump-thaw-cycles (liquid nitrogen, 0.05 mm Hg), the tube was sealed, wrapped in aluminum foil, completely submersed in an oil bath, and heated at 102°C. The progress of reaction was followed by 300 MHz $^1$H NMR integration (in time intervals the sample was removed from the oil bath, quickly cleaned and cooled with petroleum ether and measured).

1: $^1$H NMR (300 MHz, C$_6$D$_6$) $\delta$ 5.90-5.80 (m, 4H); 5.76-5.68 (m, 4H); 2.63-2.56 (m, 4H).

196: $^1$H NMR (300 MHz, C$_6$D$_6$) $\delta$ 6.29 (dd, $\gamma$ = 8.8, 2.9 Hz, 1H), 5.82-6.07 (series of m, 6H), 5.02-4.96 (m, 1H), 2.82-2.75 (m, 1H), 2.73-2.67 (m, 1H), 2.52-2.46 (m, 1H), 2.42-2.37 (m, 1H).

For this purpose, the probe was immediately cooled to room temperature and measured.

<table>
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<th>elapsed time/h</th>
<th>integral/mm (%)</th>
<th>ratio</th>
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<td>1 (2.63-2.56 ppm; 4H)</td>
<td>57 (100)</td>
<td>53:124 = 0.4274</td>
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<tr>
<td>196 (2.37-2.52 ppm; 4H) and 2.67-2.82 ppm; 4H)</td>
<td>0 (0)</td>
<td>54:133 = 0.4779</td>
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<tr>
<td>(7.15 ppm): 1n %</td>
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<td>(6.4-4.8 ppm)</td>
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<td>0.00</td>
<td>57 (100)</td>
<td>53:124 = 0.4274</td>
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<td>0.50</td>
<td>30 (56)</td>
<td>54:133 = 0.4779</td>
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<tr>
<td>1.00</td>
<td>17 (32)</td>
<td>38:112 = 0.3392</td>
</tr>
<tr>
<td>2.08</td>
<td>5 (9)</td>
<td>49:114 = 0.4298</td>
</tr>
<tr>
<td>4.08</td>
<td>0 (0)</td>
<td>44:114 = 0.3860</td>
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</table>
Thermal Rearrangement of 1-\(\text{d}_2\).

Tetraene 1-\(\text{d}_2\) (4 mg, 0.03 mmol) was dissolved in carbon tetrachloride (0.5 mL, spectrophotometric grade) and sealed into an NMR tube after four freeze-pump-thaw cycles. Completely protected from light by aluminum foil, the solution was thermolyzed in an oil bath at 110-115°C for 5h. 1-\(\text{d}_2\): \(\text{^2H NMR [77 MHz, CCl}_4\text{, reference: } \delta (\text{CDCl}_3) 7.26 \text{ ppm}] \delta 6.01\).

\(\text{196-d}_x\): \(\text{^2H NMR [77 MHz, CCl}_4\text{, reference: } \delta (\text{CDCl}_3) 7.26 \text{ ppm, proton-decoupled}] \delta 6.06 (1.00), 5.97 (1.24), 5.91 (1.11), 5.86 (1.30)\).

Photolytic Rearrangement of 1:

A. NMR experiment in methylene chloride-\(\text{d}_2\) (366 nm).

A solution of 1 (ca. 4 mg, 0.03 mmol) in methylene chloride-\(\text{d}_2\) (1 mL) was sealed into an NMR tube after four freeze-pump-thaw cycles. No rearrangement occurred within 10 min, when the sample was irradiated through an uranium glass filter with a TLC hand lamp (8 W mercury vapor, long wave range: transmission maximum 366 nm). Without filter, 1 rearranged completely within 51 min according to \(\text{^1H NMR (300 MHz) (Table 1, p. )}\). In addition to \(\text{196 (65%)}\), \(\text{217 (35%)}\) was tentatively identified as the second product.
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$^1$H NMR (300 MHz, CD$_2$Cl$_2$) δ 6.39 (dd, $J = 5.6$, 2.9 Hz, 1H), 6.06 (dd, $J = 5.9$, 3.0 Hz, 1H), 6.00-5.87 (series of m, 5H), 4.91-4.85 (m, 1H), 2.88-2.82 (m, 1H), 2.82-2.76 (m, 1H), 2.75-2.69 (m, 1H), 2.43-2.36 (br s, 1H).

$^1$H NMR (300 MHz, CD$_2$Cl$_2$) δ buried under 6.00-5.87 (4H), 5.87-5.83 (m, 2H), 5.83-5.78 (m, 2H), 5.55-5.48 (m, 2H), 3.53-3.49 (m, 2H).

B. Preparative Scale Irradiation of 1 in Pentane (366 nm).

A solution of 1 (11 mg, 0.071 mmol) in pentane (10 mL) in a Pyrex test tube was carefully evacuated and flushed with argon. After irradiation (2 h) with a long wavelength hand TLC lamp (366 nm transmission maximum), rotary evaporation (room temperature, 100 mm Hg) and preparative GC (5 m x 4 mm 10% SE 30 Chromosorp P, 60 ml He/min, injection port: 250°C, column:190°C, detector:220°C) yielded three components: 1) 2.4 mg (22%) of 196 ($t_{ret} = 9-11$ min), 2) 2.7 mg (25%) of a mixture ($t_{ret} = 11-13$ min), 3) 1.8 mg (17%) of 219 (79% pure, $t_{ret} = 13-15$ min) as colorless oils with strong musty odors.
\(^1\)H NMR (300 MHz, CD\(_2\)Cl\(_2\)) \(\delta\)

7.23–7.16 (m, 2H), 7.16–7.09 (m, 2H), 6.54 (d, \(J = 11.9\) Hz, 2H), 6.00–5.90 (m, 2H), 2.33 ('t', \(J = 2.8\) Hz, 4H).

C. NMR-Scale Irradiation of 1-\(d_2\) in methylene chloride (366 nm).

An NMR solution of 1-\(d_2\) (5 mg, 0.03 mmol - 87% deuterated in positions 3 and 9) in methylene chloride (spectrophotometric grade) was prepared as in A and irradiated at 366 nm for 54 min. According to \(^2\)H NMR, all of the starting material (1-\(d_2\)) was replaced by 196-\(d_x\) and 217-\(d\).

196-\(d_x\): \(^2\)H NMR [77 MHz, CH\(_2\)Cl\(_2\), reference: \(\delta\) (CD\(_2\)Cl\(_2\)) 5.32 ppm, proton-decoupled] \(\delta\) 6.11 (D\(_{12}\)), 6.03, 5.98, 5.93 (D\(_{1,6,9}\)).

217-\(d_x\): \(^2\)H NMR [77 MHz, CH\(_2\)Cl\(_2\), reference: \(\delta\) (CD\(_2\)Cl\(_2\)) 5.32 ppm, proton decoupled] \(\delta\) 5.83 (1.7), 5.75 (1.6), 5.56 (3.3), 3.50 (1.0).
3,9-Dideuteriotricyclo[5.5.0.0²,8]dodeca-3,5,9,11-tetraene 1-d₂.

(All manipulations were performed with protection from light.)

Crude dibromide 166 (30 mg, max 0.096 mmol) was rotary evaporated into a flame-dried flask with anhydrous benzene and dissolved in anhydrous THF (3 mL) under argon. At -78°C, tert-butyllithium/pentanes (1.5 M, 0.67 mL, 1.0 mmol) was injected dropwise. After 5 min the dark red solution was quenched with 99.8% deuterium oxide (0.15 mL, 7.5 mmol) at -78°C, warmed to room temperature, and partitioned between pentane (10 mL) and water (10 mL). The aqueous phase was extracted with pentane (5 mL), the combined organic phases were washed with water (2x5 mL) and brine (5 mL), rotary evaporated, redissolved in pentane (3 mL), dried over magnesium sulfate, filtered, and again rotary evaporated. Condensation into a V-tube (dry ice/2-propanol trap, 0.05 mm Hg, gentle heating with heat gun) afforded 4 mg (27%) of a white solid, that melted slightly below room temperature, was about 73% pure by GC, and ca. 87% deuterated in positions 3 and 9. The material was used as such.
\textsuperscript{1}H NMR [300 MHz, CDCl\textsubscript{3}, C\textsubscript{6}D\textsubscript{6}-insert as lock, \(\delta\) (CDCl\textsubscript{3}) 7.26 ppm from \textsuperscript{2}H NMR as internal standard] \(\delta\) 6.05-5.95 (m, 2.26 H\textsubscript{3,6}), 5.80-5.72 (m, 4H\textsubscript{4,5}), 2.65-2.58 (m, 4H\textsubscript{1,2}).

\textsuperscript{2}H NMR [77 MHz, CDCl\textsubscript{3}, reference: \(\delta\) (CDCl\textsubscript{3}) 5.32 ppm] \(\delta\) 6.00 (D\textsubscript{3,9}).

\textsuperscript{2}H NMR [77 MHz, CH\textsubscript{2}Cl\textsubscript{2}, reference: \(\delta\) (CD\textsubscript{2}Cl\textsubscript{2}) 5.32 ppm] \(\delta\) 6.01 (D\textsubscript{3,9}).

MS m/z calcd for C\textsubscript{12}H\textsubscript{10}D\textsubscript{2} (M\textsuperscript{+}): 158.1060, obsd. 158.1062 (60), 157 (163), 142 (31), 129 (37), 116 (40), 92 (100), 79 (52).

cis-Tricyclo[5.5.0.0\textsuperscript{2,8}]dodecane-4,5-diol (193).

Diol 147 (0.58 g, 3.0 mmol) was dissolved in hot methanol (10 mL) in a 50-mL Schlenk flask. Under argon, 116 mg of 5\% palladium on carbon was added, and the black suspension was stirred vigorously under hydrogen in an atmospheric hydrogenator for 1.3 h until no starting material was left according to TLC (developed twice with 40\% ethyl acetate/petroleum ether, silica gel, unsaturated diol: \(R_F = 0.31\), stains purple with anisaldehyde staining solution, saturated diol: \(R_F = 0.36\), stains brown). The mixture was filtered through Celite and
the filter residue was mixed with THF to afford 0.58 g (99%) of a white solid, mp. 157-170°C after rotary evaporation.

$^1$H NMR (300 MHz, CDCl$_3$) δ 4.23 (t, $J = 5.4$ Hz, 2H), 2.63-2.57 (m, 1H), 2.05-1.89 (series of m's, 8 or 9H), 1.73-1.50 (series of m's, 8 or 9H).

$^{13}$C NMR (75 MHz, CDCl$_3$) 73.94, 40.82, 40.10, 38.32, 35.16, 30.50, 25.22, 25.12 ppm.

MS m/z calcd. for C$_{12}$H$_{20}$O$_2$ ($M^+$): 196.1464, obsd. 196.1471 (3); 178, (12), 160 (15), 149 (28), 134 (40), 121 (40), 107 (35), 95 (77), 81 (80), 67 (100), 55 (75), 41 (43).

Tricyclo[5.5.0.0$^{2,8}$]dodec-4-ene (194).

(Compare deoxygenation of diol 147 to diene 128)

Titanium trichloride-tristetrahydrofuran complex (13 g, 35 mmol), potassium (5.4 g, 0.14 mol), anhydrous dimethoxyethane (100 mL) contained in a 250-mL Schlenk flask fitted with a reflux condenser was heated at reflux for 1.25 h. Diol 193 (0.56 g, 2.9 mmol) was added in 20 mL of anhydrous dimethoxyethane and refluxed for 25.5 h, diluted with petroleum ether (100 mL), rinsed with pentane (100 mL), washed with water (200 mL), and extracted with petroleum ether (50 mL). The combined
organic phases were washed with water (2x100 mL) and brine (50 mL), dried over magnesium sulfate, rotary evaporated (150-60 mmHg, room temperature), evacuated (20 mmHg, room temperature, 10 min) and distilled bulb to bulb (0.03 mmHg, 30-40°C, receiver cooled to -78°C) to give 0.36 g (78%) of a clear, colorless oil with a faint olefinic odor.

IR (neat, cm\(^{-1}\)) 3000 (w), 2910 (br s), 2840 (m), 2810 (m).

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \& 5.56 (br s, 2H), 2.30-2.23 (m, 4H), 2.10 (br s, 2H), 1.99 (br s, 2H), 1.76-1.70 (m, 4H), 1.62-1.56 (m, 4H).

\(^1\)C NMR (75 MHz, CDCl\(_3\)) 125.86, 40.71, 38.46, 33.92, 30.25, 25.46 ppm.

MS m/z calcd. for C\(_{12}\)H\(_{18}\) (M\(^+\)): 162.1417, obsd.; 162.1413 (22), 147 (12), 133 (42), 121 (23), 105 (28), 91 (65), 79 (100), 67 (46), 55 (21).

**trans-4,5-Dibromotricyclo[5.5.0.0\(^2\)8]dodecane** (195).

A mixture of olefin 194 (0.35 g, 2.2 mol), pyridinium bromide perbromide (0.74 g, 2.4 mmol), glacial acetic acid (10 mL), and carbon tetrachloride (10 mL) was stirred at room temperature for
2.3 h, then diluted with more carbon tetrachloride (10 mL). The suspension was sequentially washed with water (20 mL), aqueous sodium sulfite solution (10 mL), and saturated aqueous sodium bicarbonate solution (10 mL). The colorless, clear, organic phase was dried over magnesium sulfate, filtered, and rotary evaporated. A volatile nonpolar impurity was removed by MPLC (petroleum ether, silica gel) to give 0.57 g (80%) of a pale yellow solid, mp 64.0-65.0°C.

IR (CDCl₃, cm⁻¹) 2910 (s), 2850 (m), 2840 (m), 1435 (m).

¹H NMR (300 MHz, CDCl₃) δ 4.64-4.50 (m, 2H), 2.80-2.68 (m, 2H), 2.30-2.15 (m, 2H), 2.06-1.95 (m, 4H), 1.73-1.46 (two br s, 8H).

¹³C NMR (75 MHz, CDCl₃) 57.49, 42.98, 40.07, 39.98, 29.77, 24.89.

MS m/z calcd. for C₁₂H₁₈⁷⁹Br₈¹Br (M⁺): 321.9754, obsd. 321.9728 (0.7), 324 (0.4), 320 (0.4), 161 (100), 91 (50), 79 (42), 67 (43).
Tricyclo[5.5.0.0^2,8]dodeca-3,5-diene (191).

Under argon, a solution of dibromide 195 (0.48 g, 1.5 mmol) in anhydrous THF (2 mL) was treated with 1.6 M potassium tert-butoxide/THF (3.8 mL, 6 mmol) at room temperature. After 3 h of stirring, the brown-orange reaction mixture was partitioned between pentane (20 mL) and water (20 mL). The aqueous phase was extracted with pentane (10 mL), the combined organic phases were washed with water (2x10 mL) and brine (10 mL), and rotary evaporated (60 mmHg, room temperature). The residue was evacuated (20 mmHg, room temperature, 10 min), then distilled twice in a Kugelrohr apparatus (0.05 mmHg, 50 °C, receiver cooled with dry ice/2-propanol) to give 200 mg (83%) of a colorless oil, homogeneous by GC.

IR (neat, cm\(^{-1}\)) 3015 (m), 2980 (s), 2850 (m), 2830 (m).

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \delta 6.26-6.14 (m, 2H\(_3\),6), 5.83-5.75 (m, 2H\(_4\),5), 2.48 (br d, \(J_{2,3} = 6.9\) Hz, 2H\(_2\),7), 2.15-2.07 (m, 2H\(_7\),8), 1.79-163 (two m's, 8H\(_9\)-12).

\(^13\)C NMR (75 MHz, CDCl\(_3\)) 137.77, 123.23, 40.91, 33.24, 30.33, 24.97.

MS m/z calcd. for C\(_{12}\)H\(_{16}\) (M\(^+\)): 160.1260; obsd.: 160.1256
A 100 mL three-necked round bottomed flask equipped with a distillation apparatus was charged with finely ground sodium sulfide monohydrate (4.04 g, 16.8 mmol) and HMPA (50 mL). Under a vacuum of 30 mm Hg, the stirred suspension was slowly (to avoid bumping) heated to 140°C until all the water had distilled over. After cooling to room temperature, the vacuum was released to argon, and the distillation apparatus was replaced by a rubber septum. The dibromide (1.65 g, 5.61 mmol) in anhydrous HMPA (10 mL) was cannulated into the reaction flask. After 2.75 h at 110°C, the mixture was cooled to room temperature and partitioned between water (70 mL) and petroleum ether (50 mL). The aqueous phase was extracted with 50 mL of petroleum ether and the combined organic phases were washed twice with 50 mL of water, dried over magnesium sulfate, and evaporated. The residue was distilled by Kugelrohr at 60°C/0.02 mm Hg to afford 908 mg (99%) of a colorless liquid that crystallized in the
freezer. Bulb to bulb resublimation yielded a strong-smelling, analytically pure, white solid, mp 28°C.

IR (neat, cm\(^{-1}\)) 3000 (m), 2960-2840 (s), 2820 (m), 1440 (w), 1420 (m), 1255 (m), 1155 (m), 1075 (w), 925 (m), 855 (m), 655 (s).

\(^1\)H NMR (300 MHz, CDCl\(_3\)) δ 5.56-5.52 (br s, 2H\(_4\)), 3.30 (d, \(\text{J}_{9,8} = 3.0\) Hz, 4H\(_9\)), 2.39-2.35 (br s, 2H), 2.34-2.29 (m, 4H\(_3\)), 2.23-2.17 (m, 2H) (assigned by homo-decoupling).

\(^13\)C NMR (75 MHz, CDCl\(_3\)) 126.11, 40.46, 38.53, 37.44, 23.47 ppm.

MS m/z calcd for C\(_{15}\)H\(_{14}\)S (M\(^+\)) : 166.0817, obsd 166.0845, (100%), 119 (28), 105 (23), 99 (28), 91 (56), 85 (23), 79 (42).


9-Chloro-10-thiatricyclo[5.4.0.0\(^2,8\)]undec-4-ene 10,10-Dioxide (239).

Sulfide 238 (503 mg 3.03 mmol) was α-chlorinated with N-chloro-succinimide (recrystallized from benzene, 406 mg, 3.03 mmol) in 10 mL of anhydrous carbon tetrachloride and filtered as described
The clear, colorless solution heated up considerably when treated with 99% meta-chloroperbenzoic acid (99%, 0.84 g, 5.76 mmol). After 18.5 h of stirring at room temperature under argon, the thick slurry was partitioned between 20 mL of dichloromethane and 30 mL of saturated aqueous potassium carbonate solution:saturated aqueous sodium sulfite solution:water (6:6:18). The aqueous phase was extracted with dichloromethane (2x10 mL). The combined organic phases were dried over magnesium sulfate, evaporated, and chromatographed on 140x20 mm flash-silica gel with 20% ethyl acetate/petroleum ether (applied in dichloromethane for better solubility, 10 mL fractions) to yield 443 mg (63%) of a white solid in fractions 9 to 17, mp 117-121°C (after MPLC with 40% ethyl acetate/petroleum ether on silica gel).

IR (CDCl₃, cm⁻¹) 3010 (w), 2880 (m), 2820 (w), 1350 (s), 1140 (s).

¹H NMR (300 MHz, CDCl₃) δ 5.59 (m, 2H₄,₅), 5.29 (d, J = 4.3 Hz, 1H), 3.79 (d, J = 3.4 Hz, 2H), 2.94-2.84 (m, 1H), 2.72-2.65 (m, 1H), 2.57-2.42 (series of m, 5H), 2.42-2.34 (m, 1H).

¹³C NMR (75 MHz, CDCl₃) 125.13, 124.69, 83.39, 66.57, 45.68, 39.19, 36.98, 36.91, 31.86, 31.68 ppm.
MS m/z calcd. for C_{10}H_{13}\text{ClO}_{2}\text{S} (M^+): 232.0324, obsd. 232.0340, 235 (1%), 234 (2), 233 (1), 232 (4), 197 (2), 166 (5), 91 (100), 79 (83), 67 (41).

Occasionally, chloro sulfoxide 251 was observed as a by-product that could only be stained on analytical TLC in high concentrations. The sulfoxide was purified by MPLC (80% ethyl acetate/petroleum ether, silica gel).

9-Chloro-10-thiatricyclo[5.4.0.0\textsuperscript{2,8}]undec-4-ene 10-Oxide (251).

\[
\begin{align*}
\text{IR (CDCl}_3, \text{ cm}^{-1}) & \quad 3000 (w), 2910 (m), 2880 (m), 2820 (w), 1420 (m), 1035 (s). \\
\text{\textsuperscript{1}H NMR (300 MHz, CDCl}_3) & \quad 5.65-5.52 (m, 2H), 5.04 (dd, J = 3.8, 1.2 Hz, 1H), 3.99 (dd, J = 13.5, 2.7 Hz, 1H), 3.08 (ddd, J = 13.5, 3.9, 1.3 Hz, 1H), 1.35, 1.28 (series of m, 5H), 2.57 (t, J = 3.9 Hz, 1H), 2.52-2.28 (series of m, 5H), 2.22-2.13 (m, 1H). \\
\text{\textsuperscript{13}C NMR (75 MHz, CDCl}_3) & \quad 125.28, 125.05, 85.10, 61.81, 46.43, 39.68, 38.57, 37.11, 32.25, 31.67 ppm. \\
\text{MS m/z calcd. for C}_{10}\text{H}_{13}\text{ClO}_{2}\text{S} (M^+) & \quad 216.0376, \text{obsd: } 216.0364, 218 (35%), 217 (3), 216 (8), 199 (27), 181 (24), 167 (26), 153 (15), 131 (94), 91 (100).
\end{align*}
\]
Tricyclo[5.3.0.0^2,8]deca-4,9-diene (240).

A solution of chloro sulfone 239 (434 mg, 1.86 mmol) in anhydrous THF (5 mL) was cooled to 0°C under argon, treated with potassium tert-butoxide (1.6 M in THF, 1.7 ml, 2.8 mmol) and warmed to room temperature. After 1.8 h, another 4 mL of potassium tert-butoxide solution (6.4 mmol) was added to drive the reaction to completion. Partitioning of the thick, orange-brown slurry between 20 mL of water and 20 mL of distilled pentane, extraction of the aqueous phase with distilled pentane (2x10 mL), and washing of the combined organic phases with water (2x20 mL) and brine (10 mL) was followed by filtration through 40x20 mm of neutral alumina (activity I). The eluate was concentrated to ca. 5 mL at 0°C/150 mmHg, most of the THF was removed by brief evaporation in a Kugelrohr distillation apparatus at 0°C/40 mmHg/5 min, and the diene was distilled bulb-to-bulb at room temperature/0.1-0.2 mm Hg and trapped in an ethylene glycol/dry ice cooling bath kept at -45 to -50°C. Redistillation at room temperature /0.1-0.05 mm Hg yielded 201 mg (82%) of a mobile, pale blue liquid, that was pure by ^1H NMR and did not contain any solvent.
$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.13 (t, $J_{9,8} = J_{9,1} = 2.2$ Hz, 2H$_{9,10}$), 5.58 (br s, 2H$_{4,5}$), 2.91 (br s, 2H$_{2,7}$), 2.58 (t, $J_{1,10} = J_{1,9} = 2.2$ Hz, 2H$_{2,8}$), 2.45 (d', $J = 1.8$ Hz, 4H$_{3,6}$).

$^{13}$C NMR (75 MHz, CDCl$_3$) 147.65, 126.87, 78.49, 50.43, 32.10 ppm.

MS m/z calcd for C$_{10}$H$_{12}$ (M$^+$): 132.0939; obsd 132.0946 (15%), 131 (19), 117 (85), 104 (24), 91 (80), 78 (100), 65 (44).

During an attempt to purify diene 240 by preparative GC (5mx4mm 10% SE30 Chromosorb P, 60 mL He/min), 240 rearranged to isomeric hydrocarbons 261, 268 and 270 in ratios depending on the column temperature: 170°C: 20.8:1:2.5; 230°C: 1:2.4:3.6. All isomers left the GC with a distinct odor and a blue tinge. Structure 261 was tentatively assigned by NMR, while structures 268 and 270 were assigned as a mixture by comparison with original $^1$H NMR spectra.

2a,2b,3,6,6a,6b-Hexahydrocycloprop[cd]azulene (261).

$^1$H NMR (300 MHz, CD$_2$Cl$_2$) $\delta$

6.77-5.66 (m, 2H), 5.66-5.54 (m, 1H), 5.47-5.36 (m, 1H), 3.28-3.18 (br s, 1H), 2.78-2.65 (m, 1H), 2.47-2.33 (m, 1H), 2.29-2.14 (m, 1H), 2.14-2.00 (m, 1H), 2.00-1.92
(m, 1H), 1.62-1.52 (m, 1H), 1.47-1.34 (m, 1H).

$^{13}$C NMR (75 MHz, CDCl$_3$) 138.33, 130.39, 129.34, 128.72, 44.99, 31.11, 28.96, 23.69, 22.45.

cis-1,3a,8,8a-Tetrahydroazulene (268) and cis-1,3a,4,8a-Tetrahydroazulene (270).

Mixture: $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 6.15-5.62 (series of m, 6H, 268 and 270), 3.50-3.43 (m, 1H, 268), 3.11-2.99 (m, 1H, 270), 2.92-2.78 (m, 1H, 268 and 270), 2.68-2.55 (m, 1H, 268 and 270), 2.36-1.90 (series of m, 3H, 268 and 270).

$^{13}$C NMR (75 MHz, CDCl$_3$) (from mixture):

268: 136.01, 134.52, 132.86, 128.75, 127.67, 125.25, 50.64, 50.25, 41.22, 33.42.

270: 136.87, 135.33, 133.73, 128.60, 127.38, 123.72, 52.06, 44.11, 40.69, 30.80.
9-Chloro-3,6-dibromo-10-thia-tricyclo[5.4.0.0^2,8]undec-4-ene 10,10-Dioxide (285).

Chlorosulfone 239 (25.5 mg, 0.109 mmol), N-bromosuccinimide (41 mg, 0.23 mmol) and azobisisobutyronitrile (3.6 mg, 0.022 mmol) in anhydrous carbon tetrachloride (4 mL) were irradiated under argon with a sun lamp for 2.3 h. After being cooled to room temperature, the colorless suspension was filtered through a short Florisil column using 30% ethyl acetate/petroleum ether as eluant to leave 46.3 mg of a colorless oil. Usually this mixture was used directly for further reaction. For characterization, the material was purified by preparative TLC (30% ethyl acetate/petroleum ether) to give two UV active components.

Fr.1: \( R_F = 0.65-0.53 \), 15.8 mg (37.1%) of a white solid, a mixture of at least two isomers.

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \& 5.80 (br s, 4H), 5.33 (d, \( \bar{J} = 3.6 \text{ Hz}, 1H \)), 5.31 (d, \( \bar{J} = 3.9 \text{ Hz}, 1H \)), 5.14-5.04 (m, 4H), 3.90-3.84 (m, 4H), 3.32-3.29 (m, 2H), 3.10-3.05 (m, 2H), 2.88-2.83 (m, 2H), 2.78-2.70 (m, 1H).
Fr.2: \( R_F = 0.47-0.41 \), 10.2 mg (23.9\%) of colorless oil probably only 1 diastereomer.

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \& 5.81 (d, \( J = 1.9 \) Hz, 2H), 5.26 (d, \( J = 3.9 \) Hz, 1H), 5.04-4.96 (m, 2H), 3.91 (d, \( J = 3.3 \) Hz, 2H), 3.32 (t, \( J = 4.7 \) Hz, 1H), 3.06 (t, \( J = 4.7 \) Hz, 1H), 3.05-3.00 (m, 1H), 2.52 (dd, \( J = 6.0, 4.0 \) Hz, 1H).

3-Bromo-9-chloro-10-thia-tricyclo[5.4.0.0\(^2,8\)]undeca-3,5-diene 10,10-Dioxide (288,289).

Dibromide 289 (4.5 mg, 12 \( \mu \)mol) in 1.5 mL of anhydrous THF was cooled to 0\(^\circ\)C under argon, treated with potassium tert-butoxide (1.6 M in THF, 7 \( \mu \)l, 12 \( \mu \)mol) and warmed to room temperature. After 12 h, more potassium tert-butoxide solution (4 \( \mu \)l, 6 \( \mu \)mol) was injected, until no starting material was left according to analytical TLC. The solvent was rotary evaporated and the residue was taken up in 20\% ethyl acetate/petroleum ether and filtered through a pipet filled with Florisil (2 cm, 5x1 mL off 20\% ethyl acetate/petroleum ether). The eluate was chromatographed by MPLC (20\% ethyl acetate/petroleum ether, silica gel; sensitive to UV light) to give 2 fractions.
Fraction 1: \( R_F = 0.42 \), 1.0 mg (28%) of a yellow oil.

\(^1\text{H} \text{NMR (300 MHz, CDCl}_3\text{)} \delta 6.48 (\text{dd, } \text{J} = 6, 1 \text{ Hz, } 1\text{H}), 6.27 (\text{dd, } \text{J} = 10, 9\text{ Hz, } 1\text{H}), 5.83 (\text{dd, } \text{J} = 10, 6 \text{ Hz, } 1\text{H}), 5.40 (\text{d, } \text{J} = 5.1 \text{ Hz, } 1\text{H}), 3.85-3.79 (\text{m, } 2\text{H}), 3.66 (\text{dd, } \text{J} = 5, 1\text{Hz, } 1\text{H}), 3.07 (\text{dd, } \text{J} = 9, 6\text{Hz, } 1\text{H}), 2.50 (\text{dd, } \text{J} = 6, 4 \text{ Hz, } 1\text{H}), 2.40-2.35 (\text{m, } 1\text{H}).

\text{MS m/z calcd for } \text{C}_{10}\text{H}_{10}\text{Br}_{81}\text{ClO}_3\text{S (M\textsuperscript{+}): 309.9253, obsd. 309.9256, 312 (4), 310 (13), 308 (10), 165 (20), 129 (1100), 84 (97).}

Fraction 2: \( R_F = 0.24 \), 0.6 mg (17%) of a white solid.

\(^1\text{H} \text{NMR (300 MHz, CDCl}_3\text{)} \delta 6.45 (\text{dd, } \text{J} = 7, 2 \text{ Hz, } 1\text{H}), 6.22 (\text{ddd, } \text{J} = 11.5, 6.5, 2 \text{ Hz, } 1\text{H}), 5.83 (\text{dd, } \text{J} = 11, 7 \text{ Hz, } 1\text{H}), 5.31 (\text{d, } \text{J} = 4.5 \text{ Hz, } 1\text{H}), 3.83-3.79 (\text{m, } 2\text{H}); 3.41-3.34 (\text{m, } 2\text{H}), 2.51 (\text{dd, } \text{J} = 6, 4.5 \text{ Hz, } 1\text{H}), 2.38 (\text{dd, } \text{J} = 6.5, 3.5 \text{ Hz, } 1\text{H}).

\text{MS m/z calcd. for } \text{C}_{10}\text{H}_{10}\text{Br}_{81}\text{ClO}_3\text{S (M\textsuperscript{+}): 309.9253, obsd. 309.9279, 312 (3), 310 (9), 308 (8), 165 (23), 129 (100), 115 (31).}
Bromolumibullvalene (290-292).

Under argon, a solution of dibromide (7 mg, 18 μmol) in anhydrous THF (1 mL) was cooled to 0°C and treated with 1.6 M potassium tert-butoxide/THF (0.5 mL, 0.8 mmol) for 40 min. The reaction mixture was quenched with water (10 mL). Extraction of the mixture with pentane (10+2x5 mL), washing of the combined organic phases with water (2x5 mL) and brine (5 mL), drying over magnesium sulfate, and rotary evaporation left 3 mg of an odorous oil. After flash chromatography (0.96 g TLC-grade silica gel, pentane, 5 psi, 0.2 mL/fraction, fraction 7-9) and distillation (0.05-0.03 mm Hg, warmed with heat-gun), 1.5 mg (30%) of a colorless oil was obtained that consisted of a 42:50:8 mixture of three lumibullvalene monobromide isomers according to GC/MS and ¹H NMR: (300 MHz, CDCl₃) δ 6.81-6.77 (m), 6.66-6.62 (m), 6.62-6.52 (m), 6.14-6.04 (m), 5.87-5.81 (m), 5.76-5.69 (m), 3.39-3.34 (m), 3.27-3.17 (m), 3.14-3.08 (m), 2.77-2.72 (m), 2.71-2.52 (m); t_{ret} = 8.814 min (area 42): calcd. for C₁₀H₇⁹Br(M⁺) 207.99 obsd.: 208.00 (15); 210 [1.3, M⁺(⁸¹Br)], 128 (100). t_{ret} = 8.889 min (area 50): calcd. for C₁₀H₇⁹Br(M⁺) 207.99 obsd.: 208.00 (1.4); 210 [1.5, M⁺(⁸¹Br)], 128 (100). t_{ret} = 9.140 min: M⁺(⁷⁹Br) and M⁺(⁸¹Br) were not registered, but the
decomposition pattern was very similar to the faster components: 128 (100).

10-Chloro-5-oxa-11-thiatetra
cyclo[6.4.0.0^{2,9}.0^{4,6}]dodecane
11,11-Dioxide (252-253).

Sulfide 238 (51.7 mg, 0.311 mmol) was filtered through basic alumina (activity I) (20x3 mm) with carbon tetrachloride (4 mL) and heated under argon with N-chloro-
succinimide (41.7 mg, 0.311 mmol) to 70°C for 25 min. After being cooled to room temperature, the supernatant solution was cannulated through a dry, cotton plugged pipet into a dry, argon-flushed flask (with 3x1 mL of anhydrous carbon tetrachloride) to avoid hydrolysis of the water-sensitive chloro sulfide. The solvent was replaced with anhydrous methylene chloride (5mL), and the solution was cooled to 0°C. Then the solution was treated with meta-chloroperbenzoic acid (243 mg of 85%, ca 1.12 mmol and 100 mg of 99%, 0.58 mmol), washed with potassium dihydrogen phosphate/dipotassium hydrogen phosphate buffer, pH 7.5). After 4 h at room temperature, the reaction mixture was partitioned between 19 mL of saturated aqueous sodium sulfite solution:saturated aqueous sodium carbonate solution:water (3:3:13) and 10 mL of methylene chloride.
The pale yellow organic phase was washed with 5 mL of brine, dried over magnesium sulfate and evaporated. The residue was purified by MPLC (90% ethylacetate/petroleum ether, silica gel) to give:

Fraction 1: \((2R^*,4S^*,6R^*,8S^*)-10\text{-Chloro-5-oxa-11-thiatetra} \text{cyclo[6.4.0.0}^{2,9}.0^{4,6}] \text{dodecane 11,11-Dioxide (252).}

\[ R_F = 0.62 \text{ (silica gel, 80\% ethylacetate/petroleum ether)} \]
35.3 mg (46\%) of white solid, mp 138-145°C.

\[ \text{IR (CDCl}_3, \text{ cm}^{-1}) 2970 (m), 2910 (m), 2830 (w), 1425 (m), 1325 (s), 1205 (m), 1115 (s). \]

\[ ^1H \text{ NMR (300 MHz, CDCl}_3) 5.25 (d, J_{10,9} = 3.8 \text{ Hz, } 1H_{10}), 3.66 (d, J_{12,1} = 3.5 \text{ Hz, } 2H_{12}), 3.36 (\text{br s, } 2H_4,6), 2.84-2.80 (m, 1H_9), 2.78-2.70 (m, 1H_2), 2.64 (dd, J_{7,7} = 16.4 \text{ Hz, } J_{7,8} = 4.2 \text{ Hz, } 1H_7), 2.63 (dd, J_{3,3} = 16.3 \text{ Hz, } J_{3,2} = 4.6 \text{ Hz, } 1H_3), 2.54-2.47 (m, 1H_8), 2.35 (dd, J_{g,1} = 5.2 \text{ Hz, } J_{9,10} = 4.4 \text{ Hz, } 1H_9), 2.17 (dt, J_{3,3} = 16.1 \text{ Hz, } J_{3,2} = J_{3,4} = 2.9 \text{ Hz, } 1H_3), 2.12 (dt, J_{7,7} = 16.2 \text{ Hz, } J_{7,6} = J_{7,8} = 3.0 \text{ Hz, } 1H_7) \text{ (assigned by homo-decoupling).} \]

\[ ^{13}C \text{ NMR (75 MHz, CDCl}_3) 82.79, 66.62, 57.22, 57.11, 47.40, 39.27, 36.39, 28.78, 28.66 \text{ ppm.} \]

\[ \text{MS m/z calcd for } C_{10}H_{14}^{37}ClO_3S (M+H^+) 251.0323, \text{ obsd. } 251.0315 (1.5), 249 (3.5), 171 (2.5), 149 (23), 105 (88), 91 (100), 79 (81), 65 (69). \]
Fraction 2: (2R*,4R*,6S*,8S*)-10-Chloro-5-oxa-11-thiatetra-
cyclo[6.4.0.0²,9.0⁴,6]dodecane 11,11-Dioxide (253).

R_f = 0.40 m (silica gel, 80% ethyl acetate/ petroleum
ether), 31.7 mg (41%) of colorless oil.

IR (CDCl₃, cm⁻¹) 2975 (m), 2910 (m), 2830 (w), 1425 (m), 1320 (s),
1210 (m), 1115 (s), 1010 (m), 800 (m).

¹H NMR (300 MHz, CDCl₃) δ 5.15 (d, J₁₀.₉ = 3.9 Hz, 1H₁₀), 3.76 (d,
J₁₂,₁ = 3.4 Hz, 2H₁₂), 3.37 (br s, 2H₄,6), 3.01 (t, J₉,₁ =
J₉,₁₀ = 4.9 Hz, 1H₉), 2.76-2.70 (m, 1H₂), 2.63 (dd, J₇₇ =
11.1 Hz, J₇,₈ = 4.7 Hz, 1H₇), 2.57 (dd, J₃,₃ = 10.9 Hz, J₃,₂
= 4.6 Hz, 1H₃), 2.54-2.47 (m, 1H₈), 2.28-2.12 (series of m,
3H₁,₃,₇) (assigned by homo-decoupling).

¹³C NMR (75 MHz, CDCl₃) 83.15, 66.13; 57.14; 57.10,
41.73, 38.81, 38.23, 36.40, 28.72, 28.56 ppm.

MS m/z calcd for C₁₀H₁₄ClO₃S (M+H⁺): 251.0322, obsd.
251.0329 (1.7%), 249 (2.7), 184 (2.0), 171 (11.2), 149 (15),
105 (100), 91 (91), 79 (67), 65 (42).
10-Hydroxytricyclo[5.3.0.0^4,8]deca-2,5-diene (300).

Under argon, a solution of diethylamine (52 µL, distilled from calcium hydride) in anhydrous ether (3mL) was cooled with an ice bath. After the injection of 1.6 M n-butyllithium/hexanes (0.32 mL, 0.51 mmol), the colorless clear solution was warmed to room temperature for 5 min. HMPA (0.20 mL, 1.1 mmol) was added to the suspension, then the yellow, cloudy solution was cooled to 0°C. Epoxy chlorosulfone 252/253 (31.7 mg, 0.127 mmol) dissolved in anhydrous benzene (3x1 mL) was cannulated in. After 5.5 h at room temperature, the dark orange, clear solution was heated to 50°C for 8.5 h, then cooled to room temperature, poured onto water (10 mL), and extracted with ether (3x5 mL). The combined organic phases were washed with water (2x5 mL; the tip of a spatula with ammonium chloride broke up the emulsion), dried over magnesium sulfate, filtered, rotary evaporated, and purified by MPLC (20% ethyl acetate/petroleum ether, silica gel) to leave ca. 2 mg (11%) of a white sticky solid after sublimation (0.01 mm Hg, room temperature), mp 54-56°C.

^1H NMR (300 MHz, C₆D₆) δ 6.35 (dd, J = 5.7, 2.7 Hz, 1H), 5.82 (ddd, J = 9.0, 5.3, 1.0 Hz, 1H), 5.63 (dd, J = 5.7, 3.1 Hz, 1H), 5.18 (dd, J = 9.2, 5.7 Hz, 1H), 4.26 (br d, J = 4.9 Hz, 1H).
MS m/z calcd for M+: 148.0888, obsd 148.0911 (10%), 130 (58), 115 (45), 104 (59), 91 (100), 78 (63).

trans-4,5-Dibromo-10-thiatricyclo[5.4.0.0^2,8]undecane (306).

Sulfide 238 (396 mg, 2.39 mmol) and pyridinium bromide perbromide (recrystallized from glacial acetic acid, 804 mg, 2.63 mmol) in carbon tetrachloride (6 mL) and glacial acetic acid (6 mL) were stirred at room temperature for 1 h and then partitioned between 20 mL of water and 20 mL of carbon tetrachloride. The organic phase was washed with 10 mL of saturated aqueous sodium bicarbonate solution, dried over magnesium sulfate, evaporated, and evacuated at 0.01 mm Hg/50°C/3 h to leave 722 mg (93%) of an off-white solid. This material could be used as such. Flash chromatography on silica gel with 10% ethyl acetate/petroleum ether afforded a white solid, mp 116.5-117.5°C.

IR (CDCl₃, cm⁻¹) 2920 (s), 2850 (m), 1435 (m), 1245 (m).
\(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta 4.58-4.46 \text{ (m, 2H)}, 3.28-3.16 \text{ (m, 4H)}, 2.84 \text{ (dt, } J = 15, 4.5 \text{ Hz, 2H)}, 2.39 \text{ (br s, 4H)}, 2.33 \text{ (br dd, } J = 15, 8.5 \text{ Hz, 2H}).

\(^13\)C NMR (75 MHz, CDCl\(_3\)) 56.15, 41.83, 40.04, 37.79, 35.63 ppm.

MS m/z calcd for C\(_{16}\)H\(_{18}\)\(^8\)Br\(^7\)Br\(^9\)S (M\(^+\)): 325.9162, found: 325.9137 (36), 328 (18), 324 (18), 247 (25), 245 (24), 213 (6), 211 (7), 166 (50), 165 (52), 131 (100), 105 (74), 91 (98).

\((2R^*,4R^*,R^*,7S^*)\)-4,5-Dibromo-9-chloro-10-thiatricyclo-[5.4.0.0\(^2\),8]undecane 10,10-Dioxide (304).

Method A: By Bromination of 239.

Chlorosulfone 239 (15.6 mg, 66.9 \(\mu\)mol) and pyridinium bromide perbromide (recrystallized from glacial acetic acid, 22 mg, 70 \(\mu\)mol) in carbon tetrachloride (0.5 mL) and glacial acetic acid (0.5 mL) were stirred at room temperature for 30 min and then separated between carbon tetrachloride (1.5 mL) and water (1 mL).

The organic phase was washed with half-saturated aqueous potassium carbonate solution (2x1 mL) and brine (1 mL),
dried over magnesium sulfate and evaporated to give 23.5 mg of a colorless oil that still contained about 14% starting material according to 60 MHz $^1$H NMR. The mixture was therefore resubmitted to the bromination conditions [0.3 mL of carbon tetrachloride, 0.3 mL of glacial acetic acid, 3.1 mg (10.1 μmol) of pyridinium bromide perbromide (10.1 μmol); 4 h 40 min] to yield after work-up and MPLC (30% ethyl acetate/petroleum ether, silica gel) 23.2 mg (88%) of a colorless, frothing oil.

**Method B: By α-Chlorination and Oxidation of Dibromide**

Sulfide 238 (722 mg, 2.1 mmol) and N-chlorosuccinimide (297 mg, 2.21 mmol) in anhydrous carbon tetrachloride (10 mL) were heated to 90°C under argon for 10 min. After being cooled to room temperature, the reaction suspension was filtered through a dry, cotton-plugged Pasteur pipet with exclusion of moisture and cooled to 0°C. *meta*-Chloro per benzoic acid (99%, 950 mg, 5.52 mmol) was added to 0°C, and the mixture was stirred for 2 h at room temperature. The reaction mixture was partitioned between saturated aqueous potassium carbonate solution, aqueous sodium sulfite solution and water (1:1:3) and chloroform to yield after drying over magnesium sulfate and careful rotary evaporation 730 mg (84%) of a white frothy foam that was pure by TLC.
IR (CDCl₃, cm⁻¹) 2920 (w), 1325 (s), 1125 (s).

¹H NMR (300 MHz, CDCl₃) δ 5.23 (d, J = 4.0 Hz, 1H), 4.75-4.65 (m, 2H), 3.73 (d, J = 4.2 Hz, 2H), 3.20-3.14 (m, 1H), 3.05-2.84 (series of m, 4H), 2.75-2.71 (m, 1H), 2.62-2.45 (series of m, 2H).

¹³C NMR (75 MHz, CDCl₃) 80.99, 80.89, 64.02, 63.95, 53.49, 53.38, 44.14, 44.10, 40.27, 40.14, 38.79, 38.68, 36.23, 36.11, 35.98, 35.53 ppm.

MS (Cl,CH₄) m/z calcd. for C₁₀H₁₃⁷⁹Br₈¹Br₅Cl₂S (M⁺): 391.87 obsd. 392.66 (35), 395 (21), 391 (18), 233 (100).

10-Thiatricyclo[5.4.0.0²,8]undeca-3,5-diene (311).

Under argon, a solution of dibromide 306 (179 mg, 0.550 mmol) in anhydrous THF (7 mL) was cooled to 0°C and treated with potassium tert-butoxide (1.6 M in THF, 1.0 mL, 1.6 mmol). After being stirred for 35 min at room temperature, the solution was separated between 20 ml of water and 20 ml of pentane. The organic phase was washed with water (2x10 mL) and saturated aqueous ammonium chloride solution (10 mL), dried over magnesium sulfate, and evaporated. Bulb to bulb distillation (0.01 mmHg, 50°C) left 85 mg (94%) of a white, intensively smelly
solid that melted at 33.0-35.5°C after two more sublimations.

IR (CDCl₃, cm⁻¹) δ 3020 (m), 2920 (s), 2840 (m), 1360 (m), 1235 (m), 1005 (m), 860 (m), 670 (s).

¹H NMR (300 MHz, CDCl₃) δ 6.22-6.11 (m, 2H₃,6), 5.91-5.83 (m, 2H₄,5), 3.33-3.22 (m, 4H₉,11), 2.75-2.68 (m, 2H₂,7), 2.05-1.99 (m, 2H₁,8) (assigned by homodecoupling).

¹³C NMR (75 MHz, CDCl₃) 135.88, 124.44, 42.03, 34.29, 29.36 ppm.

MS m/z calcd. for C₁₂H₁₂S(M⁺): 164.0660; obsd 164.0667, 165 (6%), 164 (47), 117 (46), 91 (100).

9-Chloro-10-thiatricyclo[5.4.0.0²,8]undeca-3,5-diene 10,10-Dioxide (312).

Sulfide (311) (23.4 mg, 0.143 mmol) dissolved in anhydrous carbon tetrachloride [4 mL, filtered through basic alumina (activity I) together with sulfide] was heated to 85°C under argon for 1.3 h with N-chlorosuccinimide (19.1 mg, 0.143 mmol, recrystallized from benzene). After cooling the mixture to room temperature, 99% meta-chloroperbenzoic acid (50 mg, 0.25 mmol) was added in three portions, and stirring at room temperature was continued overnight. The mixture was diluted with 10 mL
of carbon tetrachloride, washed with 10 mL of saturated aqueous potassium carbonate solution:saturated aqueous sodium sulfite solution:and water (2:1:7). The aqueous phase was extracted with 2 mL of carbon tetrachloride and the combined organic phases were dried over magnesium sulfate. Solvent evaporation yielded 28.2 mg of a tan solid, MPLC of which (30% ethylacetate/petroleum ether, silica gel) afforded 14.9 mg (45%) of a white sticky solid, mp 160-165°C.

IR (CDCl₃, cm⁻¹) 3030 (w), 2940 (w), 1330 (s), 1320 (s), 1120 (s).

¹H NMR (300 MHz, CDCl₃) δ 6.27-6.11 (m, 2H₃), 6.05-5.95 (m, 2H₄,5), 5.32 (d, J₉,8 = 4.0 Hz, 1H₉), 3.83-3.72 (m, 2H₆,7), 3.33 (dd, J₇,6 = 8.3 Hz, J₇,2 = 5.8 Hz, 1H₇), 3.05 (dd, J₂,3 = 8.4 Hz, J₂,7 = 5.8 Hz, 1H₂), 2.32 (dd, J₈,1 = 6.1 Hz, J₈,9 = 4.1 Hz, H₁), 2.23-2.15 (m, 1H₁) (assigned by homodecoupling).

¹³C NMR (75 MHz, CDCl₃) 132.92, 132.01, 125.95, 125.35, 80.90, 62.55, 40.37, 38.57, 35.98, 27.76 ppm.

MS m/z calcd for C₁₀H₁₁³⁷ClSO₂ (M⁺) 232.0139, obsd 232.0139 (3%), 230 (5), 131 (72), 115 (56), 103 (28), 91 (100), 77 (39), 65 (30), 51 (34).
Tricyclo[5.3.0.0²,8]deca-3,5,9-triene (2).

Method A: From 304.

While at 0°C, under argon, and protected from direct light, 1.5 mL of 1.6 M potassium tert-butoxide/THF (2.4 mmol) was injected dropwise into a solution of dibromide 304 (100 mg, 0.25 mmol) in anhydrous THF (3 mL). After 1 h of stirring, the black reaction mixture was partitioned between cold, distilled pentane (10 mL) and cold water (10 mL) using chilled glassware, in the cold room (2-4°C). The orange organic phase was washed with water (2x5 mL), and filtered through a pipet filled with 2 cm of Florisil that had been equilibrated with cold pentane. The solvent was rotary evaporated (0°C, 70 mm Hg) and the brown residue was distilled in a Kugelrohr apparatus (distillation flask cooled to 0°C, receiver flask cooled to -40°C, 0.05 mm Hg) after brief evacuation (20 mm Hg, 0°C, 2 min). Redistillation (distillation flask cooled to 0°C, receiver V-tube cooled to -40°C) afforded a colorless oil with a strong musty odor, that consisted of a mixture of triene 2, diene 240 and isobullvalene (208) in a ratio of 10:2:1 according to ¹H NMR (263 K) in high yield.

¹H NMR (300 MHz, CDCl₃) δ 7.28 (t, J₉,₈ = J₉,₁ = 2.3 Hz, 2H₉,₁₀), 6.34-6.24 (m, 2H₃,₆), 6.24-6.15 (m, 2H₄,₅), 3.56-
3.49 (m, 2H$_2$,7), 1.17 (t, J$_{1,10}$ = J$_{1,9}$ = 2.3 Hz, 2H$_{1,8}$) (assigned by homodecoupling).

$^{13}$C NMR (75 MHz, CDCl$_3$): 149.36, 136.26, 126.29, 78.37, 29.61.

**Method B: From 312.**

A solution of diene 312 (16 mg, 69 µmol) in anhydrous THF (1 mL) was cooled to -10°C and treated with 1.6 M potassium tert-butoxide/THF (88 µL, 0.14 mmol). After 10 min, the solution was quenched at -10°C with cold brine: water (1:1, 2 mL), and stirred vigorously with cold distilled pentane (2+2x1 mL). To separate the phases, the lower aqueous phase was withdrawn by pipet and transferred into another cold flask. In the same manner, the combined organic phases were washed with cold brine:water (1:1, 2x1 mL) and brine (1 mL), and rotary evaporated (-10°C, 60 mm Hg) to a volume of ca. 0.3 mL. After the addition of ca. 50 mg of magnesium sulfate, the remaining solvent was rotary evaporated (0°C, 30 mmHg). Distillation by the Kugelrohr technique as before furnished an 11:1 mixture of triene 2 and isobullvalene 208 in good yield.
Thermal Rearrangement of 2.

An NMR tube containing a cold (-78°C) solution of 2 in chloroform-d$_1$ was equilibrated in the 300 MHz NMR instrument at 293 K for 10 min. Then spectra were collected in 10 min intervals (eight scans took 37 sec) and integrated always using the same amplitude. The following absorptions were chosen for integrations: 2 = δ 6.37-6.16 (4H), 208 = δ 5.33 (1H), 209 = δ 6.67 (2H). The sum of the integrals of each scan was normalized to 100. The slope of ln[2] = f(t) yielded the rate constant $k = 1.55 \cdot 10^{-4}$ s$^{-1}$, corresponding to a half-life of $\tau_{1/2} = 74$ min at 20°C (Table 3, p. ).

Thermal Rearrangement of 2-d$_2$.

A solution of dibromo chlorosulfone 304 (93 mg, 0.24 mmol) and 99.8% deuterium oxide (2.9 µL, 2.9 mmol) in anhydrous THF (1.5 mL) was cooled to -70°C, treated with 1.6 M potassium tert-butoxide/ THF (3.6 mL, 5.8 mmol) and slowly warmed to 0°C within 1 h. After another hour at 0°C, the reaction mixture was worked up with water and pentane at 0°C as described in Method B (of triene 2 synthesis).
According to 300 MHz \(^1\)H NMR (CDCl\(_3\), 263 K), the hydrocarbon mixture consisted of triene 2, diene 240 and isobullvalene (208) in a ratio of 53:43:4 with a deuterium incorporation of about 30% in the 9- and 10-positions of the diene and triene. Careful evaporation of the CDCl\(_3\) and condensation into a V-tube (room temperature, 0.05 mm Hg) yielded about 6 mg (19%) of material that was dissolved in carbon tetrachloride and heated, until all was converted into lumibullvalene (209). 77 MHz \(^2\)H NMR in CCl\(_4\) with \(\delta\) (CDCl\(_3\)) 7.26 ppm as standard revealed the presence of three deuterium signals at 3.32, 5.7 and 6.77 ppm in a ratio of 1:2:1.

\((7_\text{sn}, 8_\text{sn})\) -Bicyclo[4,1,1]oct-3-ene-7,8-dimethanol (358).

**Method A:** (Compare 142)

Bis(tetrahydropyranyl)ether 133 (98.5 mg, 0.293 mmol) yielded 40.5 mg (82%) of diol 358 after MPLC (ethyl acetate, silica gel). After recrystallization from chloroform, the white solid melted at 98.5-100.0°C.

IR (CDCl\(_3\)) 3605 (m), 3600-3100 (br w), 3000 (w), 2880 (s), 2815 (m), 1420 (w), 1070 (m), 1020 (s).

\(^1\)H-NMR (300 MHz, CDCl\(_3\)) \& 5.59 (br s, 2H), 3.81 (d, \(J =\)


7.0 Hz, 4H), 2.29 (s, 4H), 2.14 (br s, 2H), 2.05-1.87 (m, 4H).

\[ \text{MS } m/z \text{ calcd for } C_{10}H_{16}O_2 (M^+) : 168.1146; \text{ obsd.:} \]
168.1147 (1%); 119 (22), 109 (39), 91 (77), 79 (100), 67 (72).

**Method B**: Bis(tetrahydropyranyl) ether 133 (2.98 g, 8.84 mmol) was stirred with acid-washed Dowex 50x4-400 resin (0.5 g) in 13 mL of methanol at room temperature. After 1 h, the mixture was filtered through Celite. The filtrate was rotary evaporated and evacuated (room temperature, 0.03 mmHg) to leave 1.82 g of a clear, pale yellow oil (theoretical yield: 1.49 g). Purification by MPLC (ethyl acetate, silica gel) afforded 1.36 g (91%) of a white solid.

(7\text{sn},8\text{sn})-Bicyclo[4.1.1]oct-3-ene-7,8-dicarboxylic Acid
(359).

A solution of diol 358 (400 mg, 2.38 mmol) in dichloromethane was added to the golden orange solution of ruthenium trichloride hydrate (27 mg, \(~0.10 \text{ mmol}), potassium persulfate (3.4 g, 14 mmol), and potassium hydroxide (5.2 g, 93 mmol) in water (140 mL). After 5 h of vigorous stirring, the dark-brown
reaction mixture had turned orange again. The excess oxidant was quenched with sodium thiosulfate (1.89 g, 15 mmol). The aqueous phase was saturated with sodium chloride. Residual organic impurities were extracted with ether (2x50 mL), and the aqueous phase was acidified at 0°C with concentrated hydrochloric acid (20 mL, 0.24 mol). Extraction with ether (3x50 mL), drying over magnesium sulfate, and rotary evaporation afforded 411 mg (87%) of a white solid, that turned tan at room temperature (decomposition above 250°C).

IR (RBr, cm⁻¹): 3800-2300 (br, m), 1695 (s), 1425 (m), 1325 (m), 1290 (m), 1220 (m).

¹H NMR (300 MHz, acetone-d₆, reference CD₃COCD₂H δ 2.04 ppm) δ 5.65 (br s, 2H), 3.13 (br s, 2H), 2.51 ('t', J = 2.1 Hz, 2H), 2.38 ('d', J = 1.7 Hz, 4H).

¹³C NMR (75 MHz, acetone-d₆, reference CD₃COCD₃ 29.8 ppm) 175.63, 126.23, 45.49, 38.22, 33.92 ppm.

MS m/z calcd. for C₁₀H₁₂O₄ (M⁺): 196.0735, obsd.: 196.0755 (2.6), 197 (1.6), 179 (11), 160 (127), 150 (23), 105 (80), 79 (82), 67 (100).
Dimethyl (7\textsubscript{n},8\textsubscript{n})-Bicyclo[4.1.1]oct-3-enedicarboxylate(360)\textsuperscript{246}.

A suspension of diol 358 (0.50 g, 3.0 mmol) in dichloromethane (25 mL) was added to a vigorously stirred, golden orange suspension of ruthenium trichloride hydrate (39 mg), potassium persulfate (6.5 g, 28 mmol), and potassium hydroxide (10.0 g, 179 mmol) in water (100 mL). After 2.3 h, the dark brown suspension had turned clear and golden-orange again. The excess oxidant was quenched with sodium sulfite (3.5 g) by stirring for 30 min. Concentrated hydrochloric acid (30 mL) was added over 10 min at 0°C, and the resulting black suspension was extracted with ether (100 mL). After being saturated with sodium chloride, the aqueous phase was extracted with more ether (2 x 50 mL). The combined organic phases were washed with brine (50 mL), dried over magnesium sulfate, filtered and rotary evaporated to yield 0.50 g of a pale yellow, sticky solid. Esterification with ethereal diazomethane, followed by MPLC with 80% ethyl acetate/petroleum ether on silica gel yielded 108 mg of a pale yellow mobile oil as the more polar fraction that proved to be alcohol ester 362 (18%). The less polar fraction was again submitted to MPLC (20% ethyl acetate/petroleum ether, silica
gel) to give 53 mg of impure endo,exo-diester 361 as first fraction and 260 mg (39%) of exo,exo-diester 360 as second fraction (after Kugelrohr distillation, 70-100°C, 0.03 mm Hg) as long, colorless needles, mp 33-36°C. MPLC of the endo,exo-diester 361 (10% ethyl acetate/petroleum ester, silica gel) and peak shaving followed by Kugelrohr distillation resulted in 31 mg (4.6%) of a colorless, mobile oil.

Methyl (7s\textsubscript{n}, 8s\textsubscript{n})-8-Hydroxymethyl-bicyclo[4.1.1]oct-3-enecarboxylate(362).

\[
\text{IR (neat, cm}^{-1}) \ 3660-3140 \text{ (br, m), 3000 (m), 2960 (s), 2920 (s), 2880 (s), 2820 (m), 1730 (s), 1430 (m), 1275 (m), 1210 (s), 1030 (m).}
\]

\[
\text{\textsuperscript{1}H NMR (300 MHz, CDCl}_3\text{) } \delta 5.54 \text{ (s, 2H), 3.67 (d, J = 7.7 Hz, 2H), 3.62 (s, 3H), 2.98 (brs, 1H), 2.59-2.50 (m, 3H), 2.46-2.16 (br AB, 4H), 1.88-1.80 (m, 1H).}
\]

In CDCl\textsubscript{3}, the \textsuperscript{13}C NMR spectrum showed only seven instead of the theoretical eight signals; in C\textsubscript{6}D\textsubscript{6}, all eight peaks appeared.

\[
\text{\textsuperscript{13}C NMR (75 MHz, CDCl}_3\text{) 176.48, 125.41, 64.38, 51.57, 43.93, 35.80, 33.75 ppm; \textsuperscript{13}C NMR (75 MHz, C}_6\text{D}_6\text{) 176.36, 125.88, 64.61, 51.39, m 44.58, 44.38, 36.35, 34.16 ppm.}
\]
MS m/z calcd. for C_{11}H_{16}O_3 (M^+): 196.1099, obsd.: 196.1083 (1), 178 (3), 137 (28), 119 (57), 105 (41), 91 (71), 79 (80), 67 (66).

**Dimethyl (7s\textsubscript{n}, 8s\textsubscript{n})-Bicyclo[4.1.1]oct-3-ene-dicarboxylate (360).**

IR (CH\textsubscript{2}Cl\textsubscript{2}, cm\textsuperscript{-1}) 3000 (w), 2970 (m), 2880 (m), 2820 (w), 1725 (s), 1430 (m), 1200 (br, m).

\(^1\text{H} NMR (300 MHz, CDCl\textsubscript{3})\) δ 5.60 (br s, 2H), 3.67 (s, 6H), 3.09 (br s, 2H), 2.52 (t, J = 2.0 Hz, 2H), 2.39-2.30 (m, 4H).

\(^1\text{C} NMR (75 MHz, CDCl\textsubscript{3})\) 174.91, 125.22, 51.64, 44.86, 37.45, 33.10 ppm.

MS m/z calcd. for C_{12}H_{16}O_4 (M^+): 224.1049, obsd. 224.1034 (7), 225 (1), 170 (8), 151 (3), 133 (33), 105 (100), 79 (47), 69 (79).
Dimethyl (7\textsubscript{sn}, 8\textsubscript{sn})-Bicyclo[4.1.1]oct-3-enedicarboxylate (361).

\[
\text{IR (neat, cm}^{-1}\text{)} 3000 (w), 2950 (m), 2870 (w), 2820 (w), 1725 (s), 1430 (m), 1225 (s), 1165 (s), 1105 (m), 1045 (m).
\]

\[
\text{\textsuperscript{1}H NMR (300 MHz, CDCl}{}_{3}\text{)} \delta 5.56-5.45 (m, 2H), 3.70 (s, 3H), 3.64 (t, J = 8.4 Hz, 1H), 3.58 (s, 3H), 3.08-2.97 (m, 2H), 2.81-2.66 (m, 2H), 2.51-2.47 (m, 1H), 2.37-2.22 (m, 2H).
\]

\[
\text{\textsuperscript{13}C NMR (75 MHz, CDCl}{}_{3}\text{)} 175.41, 172.35, 125.86, 51.71, 50.84, 44.57, 40.19, 38.37, 30.95.
\]

\[
\text{MS m/z calcd. for C}_{12}\text{H}_{16}\text{O}_{4} (M^+) : 224.1049, \text{obsd. 224.1028 (3), 225 (1), 193 (36), 164 (51), 160 (95), 133 (52), 132 (46), 131 (49), 111 (89), 105 (100), 91 (43).}
\]

(7\textsubscript{sn}, 8\textsubscript{sn})-7, 8-Diacetylbicyclo[4.1.1]oct-3-ene (356).

Diacid 359 (411 mg, 2.10 mmol) was added to a suspension of lithium hydride (53 mg, 7.6 mmol) in anhydrous THF (10 mL) and stirred at room temperature for 30 min. After cooling to 0°C, 1.5 M
methyllithium in ether (7.8 mL, 11.8 mmol) was injected dropwise over 5 min. The yellow suspension was stirred at room temperature for 10 h, diluted with more anhydrous THF (10 mL), and stirred for another 10 h. For hydrolysis, the reaction mixture was added by cannula to a vigorously stirred solution of water (40 mL), 10% aqueous hydrochloric acid (20 mL), and saturated aqueous ammonium chloride solution (10 mL). After neutralization with sodium carbonate, the THF was removed by rotary evaporation. The aqueous phase was extracted with ether (3x50 mL). Drying of the organic phases with magnesium sulfate, filtration, and rotary evaporation afforded 404 mg of a yellow oil that spontaneously crystallized. Purification by MPLC (50% ethyl acetate/petroleum ether, silica gel) yielded 210 mg (53%) of diketone that crystallized as white, colorless needles, mp 102-104°C. A sample of analytical purity was obtained by preparative GC (1.1 m x 4 mm 5% SE-30 on Chromosorp W 60-80, 60 ml He/min, 120°C).

IR (CDCl₃, cm⁻¹) 3000 (w), 2940 (w), 2880 (m), 2820 (w), 1700 (s), 1420 (m), 1355 (s), 1275 (m), 1215 (m), 1180 (m).

¹H NMR (300 MHz, CDCl₃) & 5.66 (br s, 2H), 3.16 (br s, 2H), 2.56 (t, J = 2.1 Hz, 2H), 2.41 (br d, J = 1.7 Hz, 4H), 2.13 (s, 6H).
$^{13}$C NMR (75 MHz, CDCl$_3$) 208.15, 125.57, 53.15, 35.65, 33.30, 27.11 ppm.

MS $m/z$ calcd. for C$_{12}$H$_{16}$O$_2$ (M$^+$): 192.1150, obsd. 192.1165 (3), 193 (4) 177 (14), 150 (16), 149 (16), 135 (100), 107 (34), 92 (56), 79 (35), 71 (35).

Anal. calcd. for C$_{12}$H$_{16}$O$_2$: C: 74.97, H: 8.39; found: C: 75.39, H: 8.27.

In addition to the diketone, varying amounts of over addition products were observed as more polar components.

(7$_{SN}$,8$_{SN}$)-8-(1-Hydroxy-1-methylethyl)bicyclo[4.1.1]oct-3-en-7-yl Methyl Ketone (377).

White solid, mp 94.0-95.5°C; IR (CDCl$_3$, cm$^{-1}$) 2970 (m), 2930 (m), 2875 (m), 2820 (w), 1690 (s), 1190 (m).

$^1$H NMR (300 MHz, CDCl$_3$) 8 5.66 (br s, 2H), 2.87 (br s, 2H), 2.53-2.49 (m, 1H), 2.38 (br AB, $J_{AB} = 18.4$ Hz, 2H), 2.27 (br AB, $J_{BA} = 18.3$ Hz, 2H), 2.13 (s, 3H), 1.66-1.62 (m, 1H), 1.12 (s, 6H).

$^{13}$C NMR (75 MHz, CDCl$_3$) 211.70, 125.77, 69.75, 52.69, 51.58, 34.28, 33.75, 27.11, 26.90 ppm.

Mass spectrometry by electronic ionization (70eV) did
not give any parent peak, or an m/z resulting from dehydration.

\[
\text{MS } m/z \text{ calcd. for } C_{12}H_{17}O_2 (M^+-CH_3): 193.1229, \text{ obsd.: 193.1247 (24), 107 (32), 92 (79), 43 (100).}
\]

\[
\text{MS (Cl, CH_4) } m/z \text{ calcd. for } C_{13}H_{21}O_2 (M+H^+): 209.15 \text{ obsd. 209.08.}
\]

\((7S_n,8S_n)-\alpha,\alpha,\alpha',\alpha'-\text{Tetramethylbicyclo[4.1.1]oct-3-ene-7,8-dimethanol (378).}\)

Soft, white needles.

IR (CDCl_3, cm\(^{-1}\)) 3360 (br w), 2970 (m), 2930 (m), 2870 (m), 2810 (m), 1700 (br w), 1420 (w), 1365 (w), 1150 (w).

\(^1\)H NMR (300 MHz, CDCl_3) \(\delta\)
\[
5.61 \text{ (br s, 2H), 4.13 \text{ (br s, 2H), 2.77-2.68 \text{ (m, 2H), 2.21 \text{ (br 'd', } J = 1.6 \text{ Hz, 4H), 1.62 \text{ (t, } J = 2.9 \text{ Hz, 2H), 1.17 \text{ (s, 12H).}}}
\]

\[
\text{MS } m/z \text{ calcd. for } C_{13}H_{21}O_2 (M^+-CH_3): 209.1542, \text{ obsd.: 209.1537 (10), 191 (41), 105 (74), 92 (77), 82 (84), 43 (100).}
\]
(7\textsubscript{s}, 8\textsubscript{s})-Bicyclo[4.1.1]oct-3-ene-7,8-dicarboxaldehyde (379).

Under argon, a solution of freshly distilled oxalyl chloride (0.78 mL, 9.0 mmol) in methylene chloride (40 mL) was cooled to -65°C. Anhydrous DMSO (1.3 mL, 18 mmol) was injected dropwise (exo-thermic reaction; gas evolution). After stirring for 20 min at -65°C to -60°C, a solution of diol 358 (0.50 g, 3.0 mmol) in hot methylene chloride (total 25 mL, 358 badly soluble) was added slowly by cannula. After another 20 min at -60°C to -65°C triethylamine (56 mL, 42 mmol, stored under argon over potassium hydroxide) was injected and the mixture was warmed up to room temperature over 4 h. The suspension was washed with water (2x50 mL) and brine (50 mL), dried over magnesium sulfate, filtered and rotary evaporated. Bulb to bulb distillation (70-85°C, 0.03 mm Hg) afforded 0.44 g (90%) of a pale yellow oil that was 98% pure according to GC.

IR (CDCl\textsubscript{3}, cm\textsuperscript{-1}) 3010 (w), 2920 (m), 2880 (m), 2720 (w), 1710 (s).

\textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}) \delta 9.84 (s, 2H\textsubscript{9}), 5.89 (br s, 2H\textsubscript{3}), 3.26 (br s, 2H\textsubscript{7}), 2.66 (t, 2H\textsubscript{1}), 2.50-2.43 (m, 4H\textsubscript{2}).
$^{13}\text{C NMR}$ (75 MHz, CDCl$_3$) 201.17, 125.25, 52.58, 33.17, 32.26 ppm.

MS m/z calcd for C$_{13}$H$_{13}$O$_2$ (M+H$^+$): 165.0915, obsd. 165.0917.

(7$^{sn}$,8$^{sn}$)-α,α'-Dimethylbicyclo[4.1.1]oct-3-ene-7,8-dimethanol (380).

Under argon, a solution of dialdehyde 379 (0.44 g, 2.7 mmol) in anhydrous ether (10 mL) was cooled to -35°C and treated with methyl-lithium (1.5 M in ether, 5 mL, 7.5 mmol). After 10 min at -35°C the clear solution was allowed to warm to -10°C and transferred by cannula to a stirred saturated aqueous ammonium chloride solution (20 mL). The aqueous phase was extracted with ether (3x25 mL) and the combined colorless, clear, organic phases were dried over magnesium sulfate, filtered and rotary evaporated to leave 0.45 g (98%) of a pale yellow solid that was poorly soluble in most solvents.
9,10-Dimethyltricyclo[5.3.0.0^{2,8}]deca-4,9-diene (357).

Method A: From Diol 381

Titanium trichloride-tris-tetrahydrofuran complex (0.19 g, 0.51 mmol) and potassium (86 mg, 2.2 mmol) were weighed into an oven-dried 25-mL Schlenk flask under argon by the Schlenk technique. The flask was equipped with a reflux condenser and stir bar and all joints were secured by springs or wire. After the addition of dimethoxyethane [7 mL, freshly distilled from Na/K (1:1)/benzophenone under argon], the blue suspension was refluxed for 1.5 h. A solution of the diol in anhydrous dimethoxyethane was added by cannula, and the black suspension was refluxed for another 18 h. After cooling to room temperature, the titanium residues were precipitated with pentane (15 mL). The supernatant solution was siphoned off by cannula and filtered through a cotton plug. The residue was triturated with more pentane (2x5 mL). The combined organic phases were washed with water (3x10 mL), dried over magnesium sulfate, rotary evaporated (0°C, 100-60 mm Hg), and purified by preparative GC (1.1mx4mm 5% SE30 on Chromosorp W 60-80, 80°C t_{ret} = 4 min) to give 1 mg (12%) of a colorless oil.
IR (CDCl₃, cm⁻¹) 3020 (w), 2920 (s), 2880 (m), 2820 (w), 1455 (w), 1420 (w).

¹H NMR (300 MHz, CDCl₃) 5.55 (br s, 2H), 2.85-2.82 (br s, 2H), 2.45-2.33 (m 4H), 2.31 (s, 2H), 1.84 (s, 6H).

¹³C NMR (75 MHz, CDCl₃) 147.48, 126.99, 74.41, 54.33, 32.18, 12.97 ppm.

MS m/z calcd. for C₁₂H₁₆(M⁺): 160.1252, found: 160.1240 (7), 161 (16), 119 (16), 107 (46), 105 (46), 91 (100), 77 (43).

The combined aqueous phases and trituration residue were extracted with ether (40 mL total). The organic phase was washed with water (20 mL) and brine (10 mL), dried over magnesium sulfate, filtered, and rotary evaporated. The resulting brown oil afforded 3.3 mg (33%) of starting material after flash chromatography (1 g of TLC grade silica gel, 40% ethyl acetate/petroleum ether, 4-5 psi, 0.2 mL/fraction).

Method B: From Diketone 356.

In the same apparatus, titanium trichloride-tristetrahydrofuran (0.41 g, 1.1 mmol), and potassium (0.17 g, 4.4 mmol) were refluxed in anhydrous dimethoxyethane (7 mL) for 1 h. At room temperature, diketone 356 (24 mg, 0.13 mmol) dissolved in anhydrous dimethoxyethane (3 mL) was added by cannula. The reaction mixture was refluxed for 15 h and
worked up in analogous fashion to give 2.3 mg (13%) of dione (less pure) and 1.5 mg (7%) of diol.
cis-9,10-Dimethyltricyclo[5.3.0.0\(^2,8\)]dec-4-ene-9,10-diol (381).

A suspension of magnesium powder (70-80 mesh, 50 mg, 2.1 g-atom) and mercuric chloride (16 mg, 0.057 mmol) was stirred under argon in anhydrous THF (2 mL) at room temperature for 15 min. The cloudy supernatant solution was siphoned off with a syringe, the dark amalgam was washed with anhydrous THF (3×3 mL) and finally suspended in more anhydrous THF (3 mL). After cooling to -15 to -10°C, freshly distilled titanium tetrachloride was injected dropwise in a very exothermic reaction. Diketone 356 (50 mg, 0.26 mmol) in anhydrous THF (3 mL) was added rapidly by cannula at -10°C. After 7 h stirring at 0°C, no starting material was left by TLC (40% ethyl acetate/petroleum ether, silica gel). The pitch black mixture was stirred with saturated aqueous potassium carbonate solution (0.5 mL) for 15 min at 0°C. A blue-black, granular precipitate settled. After the addition of ether (total 20 mL), the supernatant solution was suction filtered through Celite. The clear, colorless filtrate was washed with brine (7 mL), dried over magnesium sulfate, filtered, and rotary evaporated, redissolved in ether, and dried with more magnesium sulfate. MPLC (50% ethyl acetate/petroleum
ether, silica gel) afforded 38 mg (76%) of a white crystalline solid, mp 119-121°C.

IR (CDCl₃, cm⁻¹) 3600 (m), 3600-3160 (m, br), 3000 (m), 2940 (s), 2860(m), 1380 (s), 1130 (s), 1065 (m).

¹H NMR (300 MHz, CDCl₃) δ 5.64-5.50 (m, 2H), 3.01 (br s, 2H), 2.74-2.66 (m, 1H), 2.60-2.53 (m, 2H), 2.53-2.45 (m, 2H), 2.13 (s, 2H), 2.04-1.94 (m, 1H), 1.41 (s, 6H).

¹³C NMR (75 MHz, CDCl₃) 127.01, 125.99, 78.77, 56.54., 44.58, 42.21, 30.72, 30.58, 21.90.

MS: EI (70eV) m/z calcd. for C₁₂H₁₆O (M⁺-D₂O): 176.1201, obsd. 176.1228 (6), 177 (5), 151 (46), 137 (100), 127 (97), 123 (88), 97 (79), 93 (94), 81 (61), 79 (69).

Cl (CH₄) m/z calcd. for C₁₂H₁₃O₂ (M⁺): 194.14, obsd. 194.06.

(4R*,5R*,9R*,10S*)-4,5-Dibromo-9,10-dimethyltricyclo-
[5.3.0.0²,8]decane-9,10-diol (387).

A solution of diol 381 (28 mg, 0.14 mmol) in pyridine (1 mL) was cooled to 0°C and treated with portions of pyridinium bromide perbromide (48 mg, 0.15 mmol).

After 1 h at room temperature, the pale yellow suspension was separated between water (10 mL) and ether (10 mL). The organic phase was washed with water.
(2x5 mL) and brine (5 mL), dried over magnesium sulfate, filtered, and rotary evaporated. The residual pyridine was removed in high vacuum, and the remaining solids were purified by MPLC (50% ethyl acetate/petroleum ether, silica gel, applied in methylene chloride) to yield 33 mg (66%) of a white, hard crystalline solid, mp 159-162°C (dec).

IR (CDCl₃, cm⁻¹) 3600 (m), 3600-3160 (m, br), 2940 (br s), 1420 (s), 1375 (s), 1160 (s), 1135 (br s).

¹H NMR (300 MHz, CDCl₃) δ 4.73-4.63 (m, 2H), 3.04 (dt, J = 16.0, 3.4 Hz, 1H), 2.97 (dt, J = 16.1, 3.5 Hz, 1H), 3.13-2.90 (br s, 2H), 2.72-2.66 (m, 1H), 2.59 (s, 2H), 2.59-2.39 (series of m, 2H), 2.00-1.92 (m, 1H), 1.39 (s, 6H).

The ¹³C NMR did not resolve all the peaks for the two possible diastereomers.

¹³C NMR (75 MHz, CDCl₃) 77.88, 77.80, 55.62, 55.34, 54.81, 54.76, 44.86, 42.90, 34.65, 34.60, 22.0.

No parent mass was obtainable by MS.
**trans-4,5-Dibromo-9,10-dimethylenetetracyclo[5.3.0.0\textsuperscript{2,8}]decane** (382).

**Method A: By Bromination-Didehydrobromination of Diene 357.**

A solution of diene 357 (1.5 mg, 9.4 µmol) in pyridine (0.5 mL) was stirred with pyridinium bromide perbromide (8.6 mg, 28 µmol) at 0°C for 30 min, then at room temperature for 30 min. The yellow, clear solution was diluted with pentane (10 mL) and washed with cold 5% aqueous hydrochloric acid (3x5 mL). The clear, colorless organic phase was dried over sodium carbonate, filtered, and rotary evaporated. The residue was filtered through a pipet filled with Florisil (benzene as an eluant) to leave material (too little to weigh reliably), the \textsuperscript{1}H NMR of which was compatible with the proposed product (382).

**Method B: By Dehydration of Diol 387.**

Diol 387 (8.1 mg, 23 µmol) was rotary evaporated into a dry flask with anhydrous benzene. Under argon, the pyridine solution (anhydrous, 2 mL) of 287 was cooled to -40°C. Sequentially, mesityl chloride (8 µL, 0.1 mmol) and anhydrous triethylamine (14 µL, 0.1 mmol) were injected. The
solution was warmed from -40°C to 0°C during 0.5 h, and from 0°C to room temperature during 1.25 h. Since some starting material was left according to TLC, the procedure was repeated with the same amounts of reagents. Then the reaction mixture was partitioned between ether (10 mL) and cold 5% aqueous hydrochloric acid (5°C, 10 mL). The organic phase was washed with more cold acid (2x5mL) and saturated aqueous sodium bicarbonate solution (5 mL), dried over magnesium sulfate, filtered, and rotary evaporated. The residual oil was triturated with pentane/ether (3:1), the triturates were filtered through silica gel (pentane as eluant) and rotary evaporated to leave 2.2 mg (30%) of diene.

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \& 5.13 (s, 2H), 4.91 (s, 2H), 4.77-4.72 (m, 2H), 3.32 (s, 2H), 3.11-3.02 (m, 2H), 2.57-2.45 (m, 2H), 2.21-2.15 (m, 2H).

MS m/z calcd. for C\(_{12}\)H\(_{15}\)\(^{79}\)Br\(^{81}\)Br (M+H\(^+\)): 318.9519, obsd. 318.9528 (8), 321 (4), 317 (5), 264 (9), 219 (41), 157 (54), 131 (45), 91 (36), 69 (100).
9,10-Dimethyleneetricyclo[5.3.0.0²,⁸]deca-3,5-diene (3)

Dibromide 382 (1 mg, 3 μmol) was rotary evaporated into a dry flask with anhydrous benzene, then dissolved in anhydrous THF (1 mL) under argon. At 0°C, 20 μL (1.6 M, 32 μmol) of potassium tert-butoxide/THF was injected. After 10 min, another 10 μL of base were added and the reaction mixture was immediately quenched with water (2 mL) at 0°C. Extraction with pentane (2+2x1 mL), washing of the combined organic phases with water (2x1.5 mL) and brine (1.5 mL), rotary evaporation, and flash chromatography (0.33 g of TLC grade silica gel, 5 psi, 10 drops/fraction, pentane) left 0.7 mg of a musty smelling oil after evacuation (room temperature 30 mmHg, 2 min). Again, the injection port temperature dependence of the peak ratio (two peaks) suggested a modest thermal lability of the product.

^1H NMR (300 MHz, CDCl₃) δ 6.13-5.97 (m, 4H), 5.23 (s, 2H), 4.94 (s, 2H), 2.80-2.70 (m, 2H), 1.75 (s, 2H).
APPENDIX A

Heathcock Approach to 1

There are several drawbacks to Heathcock's synthetic scheme. When he looked for a suitable precursor for the intramolecular substitution, epoxide 396 seemed to be the ideal choice, because opening of the epoxide would leave with the formed alcohol 397 a handle for further elaboration of this three-carbon bridge (Scheme 106). However, direct treatment of the Wieland-Miescher ketone-derived enone 395 with meta-chloroperbenzoic acid resulted in a low yield (40%) because Baeyer-Villiger oxidation turned out to be a serious side reaction. The latter could be avoided by a protection-deprotection sequence of the carbonyl function. But the approach trajectory for the intramolecular nucleophilic substitution did not seem to be correct for the epoxide. A number of bases did not touch keto epoxide 396. The only thing alcoholates like sodium methoxide or benzyl alcoholate did were epoxide opening, albeit in a regio-specific fashion (398). This proved to be the solution to the problem. The resulting secondary alcohol could be converted into a leaving group that underwent cyclization...
like a charm (399 to 400). The trans relationship of the tosylate and the protected alcohol functionality solved an additional problem: E2 elimination. Bearing the problems that Heathcock encountered in mind, as well as the desire to
synthesize the parent tetraene 1 and not the methyl substituted tetraene 105 the following synthetic scheme is suggested (Scheme 107).

Evan's and Wiberg's synthesis of bicyclic enone 402 might be improved by utilizing Birch and Dastur's observation that dichloromaleic anhydride catalyzes the isomerization of 3,6-dihydroanisole to 5,6-dihydroanisole. Vinylmagnesium bromide addition to 402 will probably give a mixture of epimers that should, however, be separable after anionic oxy-Cope rearrangement. Schultz's rediscovery of Rapoport's formal addition of 'methylhypo-bromide' to a methyl enol ether should convert 405 stereoselectively (in analogy to the epoxidation) to the β-bromo ketal 406 (β=face of decalin). Heathcock's cyclization had worked for both tosylate or bromide as a leaving group. Therefore, no problems are expected in the conversion of 406 to 407, especially since one β proton lies syn to the bromide and the β' side is completely substituted (reducing the β-elimination problem). The dissymmetry of 407 could either be used for elaboration into asymmetric through-bond conjugated tricycles or broken by hydrolysis to the C₂-symmetric diketone 408. The Borden ring expansion sequence can now be applied to both bridges of 408 simultaneously, and the resulting bis(enone) can be subjected to 1,2-reduction to arrive at bis(allylic alcohol) 411. As an
Scheme 107: Proposed Synthesis of 1

1. TMSCl, Et3N, DMF
2. CH2Cl2, Zn/Cu

1. FeCl3, DMF
2. NaOAc, MeOH

LiAlH4

POCl3

Py
alternative to Borden's dehydration that requires refluxing tetrachloroethane (bp 83°C) and would therefore thermally rearrange product, tetraene 1, I would consider dehydration with phosphoryl chloride in pyridine.
APPENDIX B

Spectral Data

Figure 80: Photo Electron Spectrum of 1
Figure 83: Photoelectron Spectrum of 191
Figure 84: Photoelectron spectrum of $^{192}$
APPENDIX C

Rearrangement of 294 to 300

* = hydroxylated methylene group
- = most likely reaction pathway
The tricyclo[5.3.0.0^{2,8}]decane skeleton of 294 probably rearranges by a stepwise, biradical pathway (as 2), and not by a concerted mechanism (like II, III, IV, Vb). Homolysis option I is considered unlikely, because the transient biradical has only one allylic stabilization [based on Tsang's resonance energy of the isobutenyl radical (12 kcal mol^{-1})]. Gajewski had estimated the resonance energy of the allyl radical to be 10 kcal mol^{-1}. This leaves only option V, or specifically Va or Vc. Already the biradical derived from 2 did not immediately close to the lumibullvalene skeleton, but (maybe due to the Principle of Least Motion) at first to isobullvalene 208. Option Vc is therefore also unlikely, making 300 the most probable product, since the ease with which isobullvalene derivatives undergo Cope rearrangement is well established.
APPENDIX D

Derivation of Rate Laws for Thermal Rearrangement of 2

For \( A_0 = B_0 = C_0 = 0 \) the time dependence of \( A, B, C \) is derived in:

\[
\begin{align*}
- \frac{dA}{dt} &= k_1 A \iff \frac{dA}{A} = -k_1 dt \\
&\iff \int_{A_0}^{t} \frac{dA}{A} = -\int_{0}^{t} k_1 dt \iff [\ln A]_{A_0}^{t} = -[k_1 t]_{0}^{t} \\
&\iff \ln A = -k_1 t \iff A = A_0 e^{-k_1 t} \tag{1} \\
\frac{dB}{dt} &= k_1 A - k_2 B \tag{2} \\
(1) \text{ into (2)}: \Rightarrow \frac{dB}{dt} &= k_1 A_0 e^{-k_1 t} - k_2 B - e^{k_2 t}
\end{align*}
\]

333
\[ \implies e^{k_2 t} \frac{dB}{dt} + k_2 e^{k_2 t} B = k_1 A_0 e^{(k_2 - k_1) t} \]  
(3)

\[ \frac{g}{f} \quad \frac{df}{dg} \quad \frac{dg}{f} \]

\[ d(fg) = df \cdot g + f \cdot dg \]  
(4)

(4) into (3): \[ \frac{d}{dt} (e^{k_2 t} B) = k_1 A_0 e^{(k_2 - k_1) t} \]  
(5)

I. \( k_1 \neq k_2 \): 

\[ k_1 A_0 \quad [e^{(k_2 - k_1) t}]_0^t \]

\[ t \frac{d}{dt} (e^{k_2 t} B) dt = k_1 A_0 e^{(k_2 - k_1) t} \]

\[ \implies [e^{k_2 t} B]_0^t = \frac{k_1 A_0}{k_2 - k_1} [e^{(k_2 - k_1) t}]_0^t \]

\[ \implies e^{k_2 t} B - B_0 = \frac{k_1 A_0}{k_2 - k_1} [e^{(k_2 - k_1) t} - 1] \]

\[ \implies B = \frac{k_1 A_0}{k_2 - k_1} (e^{-k_1 t} - e^{-k_2 t}) + B_0 e^{-k_2 t} \]  
(6)

\[ A + B + C = A_0 + B_0 + C_0 \implies C = A_0 - A + B_0 - B + C_0 \]  
(7)

(1), (6) into (7):

\[ C = A_0 [1 - e^{-k_1 t} - \frac{k_1}{k_2 - k_1} (e^{-k_1 t} - e^{-k_2 t})] + B_0 (1 - e^{-k_2 t}) + C_0 \]

\[ = A_0 [1 + \frac{1}{k_2 - k_1} (-k_2 e^{-k_1 t} + k_1 e^{-k_1 t} - k_1 e^{-k_1 t} + k_1 e^{-k_2 t})] + \]

\[ + B_0 (1 - e^{-k_2 t}) + C_0 \]

\[ C = A_0 \left[ 1 + \frac{1}{k_2 - k_1} (k_1 e^{-k_2 t} - k_2 - k_1 t) \right] + B_0 (1 - e^{-k_2 t}) + C_0 \]  
(8)
II. \( k_1 = k_2 = k : \Rightarrow \) (5) \( \frac{d}{dt} (e^{k_1 t} B) = kA_0 \mid ^t_0 \)

\[ \iff [e^{k_1 t} B]_0 = [kA_0 t]_0 \]

\[ \iff e^{k_1 t} B - B_0 = kA_0 t \]

\[ \iff B = e^{-k_1 t} (kA_0 t + B_0) \quad (9) \]

(1), (9) into (7):

\[ \Rightarrow C = A_0 (1 - e^{-k_1 t} - kte^{-k_1 t}) + B_0 (1 - e^{-k_1 t}) + C_0 \]

\[ C = A_0 [1 - e^{-k_1 t} (1 + kt)] + B_0 (1 - e^{-k_1 t}) + C_0 \quad (10) \]

\[ B_{\max}: \quad \frac{dB}{dt} = 0 = -ke^{-k_1 t} (kA_0 t + B_0) + kA_0 e^{-k_1 t} \mid _{ke^{-k_1 t}} \]

\[ \iff 0 = -kA_0 t - B_0 + A_0 \]

\[ \iff t_{\max} = \frac{A_0 - B_0}{kA_0} \quad (11) \]

For \( k_1 = k_2 = 1.55 \cdot 10^{-4} \text{ s}^{-1} = 9.3 \cdot 10^{-3} \text{ min}^{-1} \); \( A_0 = 90; \) \( B = 10; \) \( C_0 = 0 \)

into (1):

\[ A = 90 \cdot e^{-9.3 \cdot 10^{-3} \text{ min}^{-1} \cdot t} \quad (12) \]

(9):

\[ B = e^{-9.3 \cdot 10^{-3} \text{ min}^{-1} \cdot t} (9.3 \cdot 10^{-3} \text{ min}^{-1} \cdot 90 \cdot t + 10) \]

\[ B = e^{-9.3 \cdot 3 \text{ min}^{-1} \cdot t} (0.837 \text{ min}^{-1} \cdot t + 10) \quad (13) \]

\[ A + B + C = 100 \quad \iff C = 100 - A - B \quad (14) \]

\[ t_{\max} = \frac{90 - 100}{9.3 \cdot 10^{-3} \cdot 90} \text{ min} = 96 \text{ min} \]

\[ B_{\max} = B(t_{\max}) = 37.0 \]
Calculation of $k_2$ at 20°C according to Ref. 149

$\Delta H^\# = 19.3 \text{ kcal mol}^{-1} = 8.07 \cdot 10^{-4} \text{ J mol}^{-1}$; $\Delta S^\# = -10 \text{ eu} = -42 \text{ JK}^{-1} \text{ mol}^{-1}$; $T = 293 \text{ K}$; $k = 1.38 \cdot 10^{-23} \text{ JK}^{-1}$; $h = 6.63 \cdot 10^{34} \text{ Js}$; $R = 8.31 \text{ J mol}^{-1} \text{ K}^{-1}$

$\Delta G^\# = \Delta H^\# - T \cdot \Delta S^\# = 9.30 \cdot 10^{4} \text{ J mol}^{-1}$

$k = \frac{kT}{h} \exp \left( - \frac{\Delta G^\#}{RT} \right) = 1.57 \cdot 10^{-4} \text{ s}^{-1}$

$\tau_{1/2} = \frac{\ln 2}{k} = 4.41 \cdot 10^{3} \text{ s} = 74 \text{ min}$
APPENDIX E

Inert Atmosphere Set-up

The described inert atmosphere set-up traces its origin to the research groups of E.J. Corey, Wolfgang Oppolzer, and A.I. Meyers (Figure 82) with the help of Dr. Ho-Shen Lin.

Special Features:

1. The necessary overpressure valve (adjusted to an overpressure of ~ 100 mm Hg) allowed inert atmosphere reactions to proceed under a positive argon pressure, something that was very convenient for low temperature reactions and Schlenk-type manipulations. Greased joints had to be wired to or secured by springs.

2. The Tygon tubing was filled with methylene chloride and soaked overnight. The resulting tubing was stiffer and did not collapse under house vacuum.
Figure 88: Inert Atmosphere Set-Up

- Dryerite
- Sulfur
- House-vacuum
- Oilpump
- Ar or N₂
3. Rubber tubing served as connection between glass and Tygon tubing. This connection had the advantage that it could be pulled off glass tubing several times without jeopardizing the safety of the connection. By hardening the Tygon tubing in liquid nitrogen it could be easily pushed into the rubber tubing.

4. An extra connection for house vacuum/oil pump vacuum avoided the many joints (and potential leaks) of the double manifold. With a liquid nitrogen trap (that was more efficient and less messy than a dry ice/2-propanol trap) vacuums of 0.05-0.01 mmHg could be routinely achieved.

5. Separate connection for solvent stills avoided exposure of the reactions to solvent vapors. The additional stopcock allowed convenient cannulation by positive argon pressure.
REFERENCES AND NOTES


3. Simmons and Fukunaga\(^1\) defined \((m,n)\)spirenes as spirocycles with two polyene bridges that contain \(m\) and \(n\) etheno units, i.e. \(2m\) and \(2n\) conjugated sp\(^2\)-carbons, respectively. Hoffmann\(^4\) defines \([m.n]\)spirarenes, more closely to the spirocycle nomenclature, as spirocycles with two polenyl bridges that contain \(m\) and \(n\) sp\(^2\)-carbons, respectively.

\[
\begin{align*}
\text{(m,n) spirene} & & \text{[m.n] spirarene} \\
& & \\
\end{align*}
\]


The values reported in the original publication of the synthesis of 6 were slightly different.

$6: \text{UV } [\lambda_{\text{max}}(\epsilon), \text{EtOH}]: 2.76 \text{ nm (1120)}, 218 \text{ nm (5350)}. \quad 8: \text{UV } [\lambda_{\text{max}}(\epsilon), \text{EtOH}]: 254 \text{ nm (2750)}. $


12. Semmelhack, Foos, and Katz did not present any evidence for a dimer of 6, but just measured the rate of disappearance of 6 during heating.


14. Prof. Mülten, personal communication.


Hoffmann and Davidson developed the molecular orbitals of cyclobutane by interacting the group orbitals of four methylene moieties with each other, i.e., in the same way Walsh had developed the orbitals of cyclopropane. Already earlier Salem and Wright had obtained a similar set of molecular orbitals for cyclobutane with the same qualitative energy pattern following the Förster-Coulson-Moffitt description for cyclopropane. Heilbronner et al. cautioned against the use of Walsh orbitals and argued in favor of the Förster-Coulson-Moffitt basis orbitals to rationalize the electronic properties of cyclopropane. Whether the same caveat holds for cyclobutane is not known.


Klopman and Salem derived an expression for the energy (ΔE) gained and lost when the orbitals of one reactant overlap with those of another:

\[
\Delta E = - \sum_{ab} \left( q_a + q_b \right) \beta_{ab} S_{ab} + \sum_{k<l} \frac{Q_k Q_l}{R_{kl}}
\]

- First term
- Second term
- Third term

\[ q_a, q_b \] electron populations (electron demittes) in AO's a and b
\[ \beta, S \] resonance and overlap integrals
\[ Q_k, Q_l \] local total charges on atoms k and l
\[ \varepsilon \] local dielectric constant
\[ R_{kl} \] distance between atoms k and l
\[ C_{ra} \] coefficient of AO a in MO r, where r refers to the MO on one molecule and a refers to that on the other
\[ E_r \] energy of MO r
39. For a review of photoelectron spectra of compounds containing cyclobutane and cyclopropane rings, see Ref. 5.
40. Gleiter advocates the ZDO model as most suitable to interpret photoelectron spectra. ZDO neglects all three center and four center electron repulsions.
47. The different semiempirical MO treatments are explained in ref. 41, p. 496 ff.


The only evidence the authors offered that only the bisanhydride 45 with the connectivity 1-3 and 2-4 was formed from tetraacid 49 instead of the bianhydride 50 with connectivity 1-2 and 3-4 (that is admittedly seems to be more strained according to molecular models) was methanolysis, followed by diazomethane etherification to the known tetraester 51. 'All attempts to prepare 52 from the readily available cage anhydride 45 failed', however, 45 can only give 53 due to the $C_2$-symmetry of intermediate 54, whereas 50 could possibly yield both regioisomers 53 and 52. This provides additional evidence that the bisanhydride formed from tetraacid 49 indeed 45.

66. Srinivasan, R., Abstracts, 156th National Meeting of the American Chemical Society, San Francisco, California, April 1968, p. 89P.


72. Precursor 87, if capable of ring expansion into the tricyclo[5.5.0.0^2.8]doedecane skeleton by Borden's methodology, might be accessible from photocyclization of the unknown 2,7-cyclodeca-diene-1,5-diene 88. Dienedione 87 could be secured by base or rhodium trichloride catalyzed isomerization of 3,8-cyclodecadiene-1,6-dione 89 or reduction-allylic oxidation of dibromodiene-diol 90.


82. Prof. Gleiter, private communication.


89. Russell et al. did not characterize any of their acyloin condensation products; for an experimental procedure for 118, see Ref. 46.


91. For a review of cyclobutane stereochemistry, see: Moriarty, R.M. Top. Stereochem. 1974, 8, 271.

92. For a comprehensive review of the geometry of cyclobutane and its derivatives by spectroscopic methods (electron diffraction, IR, near-IR, Raman, NMR) and calculations (CNDO/2, ab initio), see: Cotton, F.A.; Frenz, B.A. Tetrahedron 1974, 30, 1587.


95. For an experimental procedure, see Ref. 87.


The activation barrier for ring inversion of puckered cyclobutane is relatively small, only 1.48 kcal mol$^{-1}$ in comparison to the 10.8 kcal mol$^{-1}$ for the ring inversion of the cyclohexane chair. However, Bauld et al. estimated that the experimental strain energy of cyclobutane, 26.4 kcal mol$^{-1}$, consists only of less than 6.75 kcal mol$^{-1}$ Baeyer strain (ring strain), whereas the rest is made up by 1,3-diaxial interaction. A cis-1,3-disubstituted cyclobutane should therefore show a strong preference for the diequatorial conformation, and even more so a trans,trans,trans-1,2,3,4-tetrasubstituted cyclobutane.


110. The transformation of vicinal diols into olefins is reviewed in Block, E. Org. React. 1984, 30, 457.


Few molecules with $S_4$ symmetry are known. Other examples of molecules with $S_4$ symmetry are:
133. McCasland and Proskow actually synthesized the optically inactive $S_4$ symmetric meso-trans-trans-3,4,3',4'-tetramethylspiro-(1,1')-bipyroloidinium-2-toluenesulfonate and its chiral $D_2$-symmetric diastereomer.

\[ [\alpha]^{30}_{D}(H_2O) = +19.88^\circ \]

no optical rotation


135. Rautenstrauch, V.; Scholl, H.-J.; Vogel, E. Angew. Chem. 1968, 80, 278.

136. For a review on the use of DBU and DBN as bases, see: Oediger, H.; Möller, F.; Eiter, K. Synthesis 1972, 591.

137. Interestingly, already the different conformers of 192 have the same symmetry behavior as 189.


144. The utility and limitation of force-field programs have been reviewed in Burkert, U.; Allinger, N.L. Molecular Mechanics; ACS Monograph 177, American Chemical Society: Washington, D.C., 1982.


152. I use concerted and electrocyclic, or stepwise and biradical-like as synonymous expressions, although this is not necessarily true: concerted reaction can have a discrete local energy minimum between educt and product on the energy surface. see: Baldwin, J.E.; Andrist, H.; Pinschmidt, R.K., Jr. *Acc. Chem. Res.* 1972, *5*, 402.


165. The interpretations and complete assignment of the photoelectron spectra with the help of semiempirical and ab initio calculation methods is still in progress.

166. In more complex structures like 1, a safe interpretation of photoelectron spectra is only possible when the assignments are compared to those of analogs, like 191 and 192.


170. a) Conversion of wavelength $\lambda$/nm into $E$/eV

$$E = h\nu = \frac{hc}{\lambda}$$

$$E = \lambda^{-1}(6.63 \cdot 10^{-34} \text{Js} \cdot 3.00 \cdot 18 \text{ms}^{-1}) = \lambda^{-1}1.99 \cdot 10^{-25} \text{Jm}$$

$$e = 1.60 \cdot 10^{-19} \text{C} \Rightarrow 1 \text{J} = 6.25 \cdot 10^{18} \text{eV}; \{\lambda\} = \lambda \cdot 10^9 \text{m}^{-1}$$

$$\Rightarrow E = \{\lambda\}^{-1}1.24 \cdot 10^3 \text{eV}$$

b) To make a comparison possible, the vertical transitions from the vibrational ground state of the electronic ground state ($\nu=0$) to the vibrational ground state of the electronic excited state ($\nu'=0$) are chosen, i.e. the onset values of the UV absorptions (= longest wavelength of a peak in the UV spectrum).

171. The intermolecular equilibration is highly unlikely, because at such low temperatures (-80°C) diffusion is slow, especially when one remembers the low concentration of radical anions that is actually present in the sample. Prof. Mullen, private communication.


Prof. Müllen, private communication.


Pomerantz found that the $^1$H NMR of benzo bicyclo-[2.1.1]hex-2-ene can be simulated well by computer, when the coupling constant between the bridgehead proton $H$ and the endo proton $H_A$ is set equal to 0.

\[
\]

In a number of 5-substituted bicyclo[2.1.1]hex-2-enes Wiberg and Ubersax observed that the vinyl protons always appeared as a sharp triplet with $J_{2,1}=2$ Hz, $J_{2,4}=1.5$ Hz.

\[
X=H, \ Y=CO_2Me, \ CH_2OH, \ CH_2OAc, \ CH_2CH_2OH
\]

\[
X=CH_2OH, \ Y=H
\]


188. We thank Prof. Grimme for kindly providing us with copies of the 1H NMR spectra of tetrahydroazulenes 268-270 as well as of the relevant pages out of Heger's dissertation dealing with their structure proof.


This scheme was developed after the elucidation of the thermal rearrangement of 2.


201. For a review, see: Shapiro, R.H. Org. React. 1976, 38, 26.


204. I want to thank Dr. Marc-André Poupart for his kind help with the force-field calculations (MODEL, MMP2).


207. To record the UV spectrum, an aliquot of cold, concentrated solution of 2 in cyclohexane was syringed into the cuvette filled with cyclohexane and preequilibrated at room temperature. The spectrum was recorded with a 1 s-pulse of a photodiode array UV spectrometer. The signal centered at 247 nm which had a partially resolved vibrational fine structure, decayed when the solution was left at room temperature. The ε could not be determined because the original weight of the sample was not known.


211. The \(^1\text{H}\) NMR spectrum of 46 was recorded after 30 min at 20°C. The rearrangement had proceeded to a mixture 2:240:209:208 = 50:15:8:27.

212. Since Kukla did not elaborate on his absolute assignment of the \(^1\text{H}\) NMR spectrum of 209, and since the absolute assignment will be of crucial importance to the determination of the mechanism of the thermal rearrangement, the important steps will be mentioned here.


218. Hine formulated the 'principle of least motion' this way: "These elementary reactions will be favored that involve the least change in atomic position and electronic configuration" Hine, J. J. Org. Chem. 1966, 31, 1236.


230. A plan to synthesize 332 by acyloin condensation of tetraester 333 followed by oxidative work-up and tetramethylation had to be abandoned, because Griffin and Hager reported that dissolving metal reduction of 333 leads to cleavage of the cyclobutane ring instead of ring closure.

231. Although EH calculations cannot be trusted quantitatively, their real value lies in the qualitative results they provide. Gimarc, B.M. Molecular Structure and Bonding, Academic: New York, NY, 1979; p. 216.
232. \[ P_{ij} = \sum_v \gamma_v c_{\mu v} c_{\nu j}, \] \[ \gamma_v: \text{number of electrons in molecular} \]
orbital \( \mu, c_{\mu i}, c_{\mu j}: \text{coefficient of MO}_{\mu} \) at atom i and j.

\[ \text{e.g. } P_{12}(\text{ethylene}) = 1, P_{12}(\text{butadiene}) = 0.894, \]
\[ P_{23}(\text{butadiene}) = 0.447. \]


254. Although the reaction seemed to be cleaner with zinc-copper couple according to GC, only trace amounts of diene 357 were observed. Since the polymeric titanium trichloride itself is very awkward to handle and very sensitive to oxygen and moisture due to its high surface area as an amorphous solid, the hard crystalline free-flowing, less sensitive titanium trichloride-tristetrahydrofuran complex was preferred. Preparation: Manzer L.E. Inorg. Synth. 1982, 21, 135.


257. Mislow and co-workers observed that empirical force-fields predict a shorter central bond length in 393 [d(C=C]=1.57Å] than was later found by X-ray (1.64Å). They attributed this elongation to through-bond interaction, an electronic effect that is not picked up by force-fields. Dougherty, D.A.; Houshshell, W.D.; Schlegerl, H.B.; Bell, R.A.; Mislow, K. Tetrahedron Lett. 1976, 1976, 3479.
258. Mislow and co-workers calculated a similar discrepancy for the still elusive $\pi,\pi'$-dibenzene 394 which they attributed to through-bond interaction.

\[
d(C_1-C_2): \text{force-field (EFF)}: 1.543\text{Å} \\
\text{MINDO/3} : 1.595\text{Å} \\
\text{Gaussian 70 ab inito} : 1.596\text{Å} \\
(\text{STO-3G})
\]


264. Rapoport, H.; Lovell, C.H.; Rast, H.R.; Warren, H.E.,


267. ALDRICH procedure; DeBoer, T. J.; Barker, H.J.; Org.

268. I want to thank Dr. Yugi Miyahara for suggesting his
very useful, safe, and convenient procedure.

1028.


271. For a review of PCC/PDC oxidation, see: Piancatelli,

2647.

Chem. 19878, 43, 4172.


275. A study of the experimental that was not available in
ref. 177 reveals that the methyllithium was added to
the tosyl-hydrozone of 325 at 0°C, but the reaction
was stirred at room temperature for 16 h.
Gleiter, R.; Zimmermann, H.; Sander, W.; Hauck, M.
submitted for publication.