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Synthesis of cyclopentadienyl derivatives: Stereoelectronic effects in the Diels-Alder cyclocondensation reaction

García, José Gabriel, Ph.D.
The Louisiana State University and Agricultural and Mechanical Col., 1990
Synthesis of Cyclopentadienyl Derivatives.
Stereoelectronic Effects in the Diels-Alder Cyclocondensation Reaction

A Dissertation

Submitted to the Graduate Faculty of the Louisiana State University and Agricultural and Mechanical College in partial fulfillment of the requirements for the degree of Doctor of Philosophy in The Department of Chemistry

by

José Gabriel García
B.S. Universidad Iberoamericana, 1983
M.S. Louisiana State University, 1986
December, 1990
To the García Guajardo family,

Juan Manuel
Maria Perla

Maria Esther
Juan Manuel
Maria Perla
Catalina
Maria Teresa
Ana Maria
Luis Miguel
Science is teaching man to know and reverence truth, and to believe that only as far as he knows and loves it can he live worthily on earth, and vindicate the dignity of his spirit.

Moses Harvey
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ABSTRACT

This dissertation is divided into three chapters. Chapter one describes attempts to synthesize bis-monosubstituted cyclopentadienyl compounds as probes for complexation to transition metals. Prior to the attempted synthesis of bis-monosubstituted cyclopentadienyl compounds, the syntheses of two different organic frameworks bearing a C₂-symmetry axis is described; namely, the 1,3-dioxolane-2,2-dimethyl and the 1,1'-binaphthyl frameworks.

Chapter two describes the attempts to synthesize monofulvene derivatives as model compounds for the synthesis of difulvenes. Also, chapter two describes the attempts to synthesize different difulvene derivatives, that for the most part bear a C₂-symmetry axis, as model compounds for cyclopentadienyl-derivative anions to be complexed to transition metals. The syntheses of several different frameworks bearing C₂-symmetry axis, such as 1,5-disubstituted-trans-decalin, 2,7-disubstituted-tricyclo[5.3.3.0^{6,10}], 1,3-dioxolane-2,2-dimethyl, and 2,2'disubstituted-1,1-binaphthyl, are presented.

Chapter three describes attempts to synthesize tricyclo[9.3.0.0^{4,8}]tetradeca-4,7,11,14-tetraene via two different routes as suggested by retrosynthetic analysis; namely, via a thermal rearrangement of a bis-spirocyclopentadiene derivative and via Diels-Alder cyclocondensation of an electron deficient diene with cyclooctadiene. The Diels-Alder cyclocondensation reaction used in the first step of one of these synthetic methods is examined in order to find out the origin of the dienophile π-stereoselectivity, by a combination of structural techniques and reactant modifications.
CHAPTER ONE.

Attempted Synthesis of Cyclopentadiene Derivatives

1.1 Introduction.

Chiral cyclopentadienyl ligands are starting to be recognized as potential chiral auxiliaries in asymmetric organometallic reactions.\textsuperscript{1-12} Despite their promise, only a few chiral cyclopentadienyl ligands (in which mainly cyclopentadienes with one chiral substituent is involved)\textsuperscript{13-26} have been prepared compared to the many other examples of chiral ligands in the literature.\textsuperscript{27}

1.1.1 Retrosynthetic analysis.

The purpose of the retrosynthetic analysis is to take a molecule and break it down by a series of disconnections that leads us to possible simple starting materials.

It is difficult to look at a complex molecule as \(1A\) and identify it with simple starting materials. A retrosynthetic analysis shows a systematic (not the only one) approach in finding the shortest possible route in synthesizing a molecule as complex as it may be.

It is desirable to disconnect \(1A\) in a symmetric fashion as shown in figure 1.1 leading to synthon \(1B\), since complexation of a transition metal by \(\textit{bis-}\eta^5\)-cyclopentadienides is well preceded.\textsuperscript{13-26} \(1B\) can be thought as a product from a functional group interconversion of \(1C\) by a double \(S_N2\) attack of cyclopentadienyl anion on the carbons bearing the leaving group.

The stereochemical outcome of a variety of catalytic or stoichiometric\textsuperscript{28-30}
transformations in which new stereocenters are formed should be controlled by chiral
cyclopentadienyl ligands to transition metals. Hence, it was interesting to synthesize
such ligands. It was then thought of a bridged chiral ligand having a $C_2$-symmetry
axis (compounds of the type depicted by 1A) as shown in figure 1.1, due to its
inherent advantages.2

![Chemical structures](image1.png)

Fig. 1.1 Retrosynthetic analysis of 1A

Two organic moieties, namely 1,3-dioxolane-2,2-dimethyl-4,5-$trans$-disubstituted and 1,1'-binaphthyl-2,2'disubstituted frameworks shown in figure 1.2
were chosen as potentially good systems due to their synthetic accesibility$^{31,32}$ as well
as the ready availability of each enantiomer.$^{27,31,32}$

![Chemical structures](image2.png)

Fig. 1.2 Organic frameworks chosen (having a $C_2$ symmetry axis)
Figure 1.3 Attempted synthesis of bis-monosubstituted cyclopentadienyl ligand bearing the 2,2-dimethyl-1,3-dioxolane-4,5-trans-disubstituted framework
The strategy is based upon the bis-monoalkylation of the cyclopentadiene by several methods. Figures 1.3 and 1.13 depict the synthetic approaches to the target systems.

There are some indirect ways of synthesizing substituted cyclopentadienyl compounds (building the ring from the corresponding open chain, followed by chemical interconversions upon obtaining the corresponding unsaturated ring) such as the old method by Borsche & Menz\textsuperscript{33} shown in figure 1.4, or the more recent method by Skatebøl\textsuperscript{34-37}

![Fig. 1.4 Borsche and Menz synthesis of Cp](image)

shown in figure 1.5. For the purposes of this work, it was thought that a more direct approach (in which cyclopentadiene is used as a reactant) would be more convenient in order to shorten the synthesis. Some methods concerning the alkylation by a cyclopentadienyl moiety have been described in the literature, namely, the use of the lithium or sodium salt of

![Fig. 1.5 Skatebøl synthesis of Cp](image)

cyclopentadiene by Vollhardt \textit{et al.},\textsuperscript{2} the more recent use of the potassium salt of cyclopentadiene by Shirokii \textit{et al.},\textsuperscript{38} the use of the thallium salt of cyclopentadiene by
Corey et al.,\textsuperscript{39} the use of the dilithium salt of ferrocene by Osgerby & Pauson,\textsuperscript{40} the use of ferrocene in the presence of acid on diazo-compounds by Kasahara et al.,\textsuperscript{41} the use of the Cp-Cu.SMe\textsubscript{2} complex by Rosenblum et al.\textsuperscript{42} and the use of the Cp-Cu.PBu\textsubscript{3} complex by Nilsson et al.\textsuperscript{43}
1.2 Results and Discussions.

1.2.1 Attempted synthesis of bis-(monosubstituted)-cyclopentadienyl ligands bearing 2,2-dimethyl-1,3-dioxolane-4,5-trans-disubstituted framework.

Different methods applied to the synthesis of the target molecules 1.7 (see figure 1.3) and 1.16 (see figure 1.13) were tried; namely, changing the nature of the leaving group in the 2,2-dimethyl-1,3-dioxolane-4,5-trans-disubstituted framework, and changing the nature of the nucleophile.

1.2.1.1 Use of Different Leaving Groups.

The synthesis of the required framework, 2,2-dimethyl-1,3-dioxolane-4,5-trans-disubstituted, namely, the diester compound 1.1, was accomplished in only one step by treating the diethyl L-tartrate with 2,2-dimethoxy propane in the presence of catalytic amounts of acid in good yield as shown in figure 1.6. Reduction of compound 1.1 in sodium borohydride afforded the corresponding di-alcohol 1.2 in fairly good yields (see figure 1.6). The di-tosylate compound 1.3 was successfully prepared in good yields by treating compound 1.2 with p-toluenesulfonyl chloride in pyridine at 0°C. Attempts to synthesize the corresponding bis-monosubstituted-cyclopentadienyl compound 1.7 by direct alkylation of compound 1.3 with sodium cyclopentadienide were unsuccessful, affording a tricyclic compound 1.6 as shown in figure 1.7.
Fig. 1.6. Attempted synthesis of a bis-monosubstituted cyclopentadienide 1.7

Apparently, deprotonation of the already inserted cyclopentadienyl moiety occurs faster than the second alkylation, allowing the intermediate to have an intramolecular alkylation forming the corresponding tricyclic compound 1.6. See figure 1.7.

Fig. 1.7. Speculative route leading to 1.6 in the attempted synthesis of 1.7

The di-tosylate compound 1.3 was successfully converted in fairly good yields into
the corresponding di-bromide derivative 1.4 by treatment of 1.3 with lithium bromide in refluxing DMSO, as shown in figure 1.8. Compound 1.4 (bearing a better leaving group than compound 1.3) was expected to have a better chance of being attacked by the second cyclopentadienyl anion prior to the deprotonation of the already inserted cyclopentadienyl moiety. Attempts to synthesize 1.7 by treating 1.4 with sodium cyclopentadienide were unsuccessful as shown in figure 1.8, obtaining the tricyclic compound 1.6. Apparently the process shown in figure 1.7 is independent of the nature of the leaving group. In order to corroborate this assertion, the corresponding di-iodide compound 1.5 was prepared in good yields from the dibromide compound 1.4 on treatment with sodium iodide in refluxing acetone.

![Chemical structures and reactions](image)

Fig. 1.8. Different routes followed in the attempted synthesis of 1.7.

Compound 1.6 is formed instead

Attempts to synthesize compound 1.7 by treating 1.5 with sodium
cyclopentadienide were unsuccessful, obtaining once more the tricyclic compound 1.6 as shown in figure 1.9.

![Synthesis of cyclopentadienyl thallium](image)

Fig. 1.9. Formation of compound 1.6 in lieu of compound 1.7

1.2.1.2 Use of Different Nucleophiles

Knowing that the nature of the leaving group in the substrate does not influence the alkylation by the cyclopentadienyl anion, different cyclopentadienides were prepared to be tested as potentially better nucleophilic alkylating agents, namely, sodium cyclopentadienide, lithium cyclopentadienide, cyclopentadienyl thallium and 1,1'-di-lithium ferrocenyledene-N,N,N',N'-tetramethyl-ethylene diamine (FCDL) complex.

Cyclopentadienyl thallium was prepared by treating cyclopentadiene with thallium acetate in the presence of potassium hydroxide (see figure 1.10).

![Synthesis of cyclopentadienyl thallium](image)

Fig. 1.10. Synthesis of cyclopentadienyl thallium

The di-bromide compound 1.4 and the corresponding di-iodide 1.5 were unreactive toward cyclopentadienyl thallium (see figure 1.11).
A last attempt to synthesize compound 1.7, was treating the dibromide compound 1.4 with FCDL complex, prepared as depicted in figure 1.12. No reaction was detected to occur under the reaction conditions.
Figure 1.13 Grignard and Ullmann routes applied to the synthesis of 2,2'-bis-bromomethyl-1,1'-binaphthyl 1.14
1.2.2 Attempted synthesis of bis-(monosubstituted)-cyclopentadienyl ligands bearing 1,1'-binaphthyl-2,2'-

bis(methylene) framework

Two methods were applied to the synthesis of the 1,1'-binaphthyl-2,2'-bis-(methylene) framework towards the synthesis of target molecule 1.16, namely, Ullmann and Grignard couplings. Figure 1.13 shows schematically both routes.

1.2.2.1 Synthesis via Ullmann Coupling

Synthesis via Ullmann coupling started by converting 1-bromo-2-methyl naphthalene, in good yield, into the corresponding 1-bromo-2-bromomethyl naphthalene 1.8 by reaction with N-bromo succinimide in the presence of peroxide. Further oxidation of 1.8 in the presence of a mixture of acetic acid-hydrobromic acid in hexamethylene tetraamine afforded the corresponding 1-bromo-2-naphthaldehyde 1.9 in fairly good yield. The conversion into the corresponding 1-bromo-2-naphthoic acid 1.10 was successfully achieved by oxidation of the former in the presence of potassium permanganate in acetone. Esterification to the corresponding methyl ester 1.11 was performed in good yield by refluxing the corresponding acid 1.10 in methyl alcohol in the presence of catalytic amounts of acid. Ullmann coupling of the corresponding methyl, 1-bromo-2-naphthanoate 1.11 in order to achieve the desire framework, namely, 2,2'-bis-(methylcarboxylate) 1,1'binaphthyl 1.12 was successfully performed in fairly good yield by heating it with cupper/bronze. Reduction of 1.12 into the corresponding 2,2-bis-(methylene-hydroxide) 1.13 was successfully performed by treatment with lithium aluminum hydride in ether. The
corresponding 2,2'-bis-(methylene-bromide) 1.14 was prepared in fairly good yield by heating the corresponding 2,2'-bis-(methylene-hydroxide) 1.13 with a mixture of acetic acid-hydrobromic acid as shown in figure 1.13.

1.2.2.2 Synthesis via Grignard Coupling

Synthesis via Grignard coupling was successfully performed, in good yield, by treating 1-bromo-2-methyl naphthalene with its grignard derivative in the presence of bis-triphenyl nickel chloride catalyst as shown in figure 1.13. The resulting 1,1'-binaphthyl-2,2'-dimethyl 1.15 was further interconverted into the corresponding 2,2'-bis-(methylene-bromide) 1.14 in very good yield by the treatment with N-bromo succinimide in the presence of benzoyl peroxide.

There is no doubt on the efficiency of the Grignard route over the Ullmann coupling not only because it is possible to prepare the same compound 1.14 from the same starting material 2-bromo-1-methyl naphthalene in only 2 steps as opposed to 7 steps, but also to the fact of the high yields involved in these two simple reactions.

1.2.2.3 Direct alkylation by cyclopentadienyl anion

Attempts to synthesize compound 1.16 (figure 1.14) from the corresponding 1,1'-binaphthyl-2,2'-bis-(methylene-bromide) 1.14 were unsuccessful as shown in figure 1.14. 1,1'-binaphthyl-2,2'-bis-(methylene-bromide) 1.14 was treated with cyclopentadienyl lithium, from which the corresponding spiro compound 1.17 was isolated. This results once more support the idea of deprotonation occurring faster than alkylation.
1.2.2.4 Use of ferrocene-dilithium salt as nucleophile

Attempts to synthesize compound 1.18 shown in figure 1.16 by treating 1,1'-binaphthyl-2,2'-bis-(methylen bromide) 1.14 with FCDL.
complex were unsuccessful, affording compound 1.19 (see figure 1.17).

Another attempt to synthesize compound 1.16 by a different approach than the previously described, involved the treatment of 1,1'-binaphthyl-2,2'-bis-(methylenebromide) 1.14 with a cyclopentadienyl copper dimethyl sulfide complex (prepared by treating copper(I) bromide dimethyl sulfide complex with the lithium salt of cyclopentadienyl anion in THF at -78°C). The result was that the pentacyclic compound 1.19 was formed as seen in figure 1.18.

1.2.2.5 Use of $\text{CpCu.S(Me)}_2$ as nucleophile

Another attempt to synthesize compound 1.16 by a different approach than the previously described, involved the treatment of 1,1'-binaphthyl-2,2'-bis-(methylenebromide) 1.14 with a cyclopentadienyl copper dimethyl sulfide complex (prepared by treating copper(I) bromide dimethyl sulfide complex with the lithium salt of cyclopentadienyl anion in THF at -78°C). The result was that the pentacyclic compound 1.19 was formed as seen in figure 1.18.
1.2.3 Attempted Synthesis of a bis-(monosubstituted) cyclopentadienyl ligand bearing the 1,1'-binaphthyl-2,2'-disubstituted framework.

In continuing the synthesis of compounds having a $C_2$-Symmetry bearing the binaphthyl framework, another system was thought to be of great interest because of its peculiarity of having the two cyclopentadienyl moieties well oriented to be complexed by a metal. Such a system is depicted by compound 1.20, shown in figure 1.19.

The attempt to synthesize compound 1.20 started with the treatment of 2-naphthol with hydrazine monohydrate at high temperature in a closed system forming in fairly
good yield 2,2'-diamino-1,1'-binaphthyl 1.21, from which a diazonium salt was prepared; namely, the tribromo mercurate 1.22 by treatment of 1.21 with sodium nitrite in the presence of mercuric bromide/potassium bromide or zinc bromide/potassium bromide. Attempts to synthesize compound 1.20 from 1.22 by treatment with ferrocene in the presence of DMSO, or in the presence of acetic acid, or with FCDL complex were unsuccessful, as depicted in figure 1.20.

Fig. 1.20. Attempted synthesis of compound 1.20
1.3 Conclusions

Retrosynthetic analysis is a great tool in helping to decide the best synthetic route to a molecule as complex as it may look.

Synthesis toward the target molecules 1.7 and 1.16 was for the most part successful in building the C2-symmetric framework.

The key step, the bis-cyclopentadienylation of both molecular frameworks, was unfruitful due to intramolecular cyclization by the anion of the already inserted cyclopentadienyl unit, leading to 1,2-disubstituted cyclopentadienyl compounds in lieu of the bis-(monosubstituted)-cyclopentadienyl compounds 1.7 and 1.16.
1.4 Experimental Section

General Procedures. Melting points are uncorrected. $^1$H NMR and $^{13}$C NMR spectra were measured at 200 MHz respectively on a Bruker AC 200 spectrometer. Chemical shifts are reported in ppm (δ) downfield from tetramethylsilane. IR spectra were recorded with a Perkin Elmer 283B Infrared spectrophotometer. MS were recorded on Hewlett Packard 5985A mass spectrometer.

Materials and Methods. Cyclopentadiene was freshly cracked from dicyclopentadiene. Dichloromethane and hexane were distilled from calcium hydride under argon atmosphere. Tetrahydrofuran was distilled from potassium under argon atmosphere and ether was distilled from a sodium/potassium amalgam under argon atmosphere. Other reagents were used as received from commercial sources.

\[ \begin{align*}
\text{OCH}_3 & + \text{HO} \xrightarrow{\text{TosOH}} \text{COOCH}_2\text{CH}_3 \\
\text{OCH}_3 & \quad \text{HO} \xrightarrow{\text{TosOH}} \text{COOCH}_2\text{CH}_3
\end{align*} \]

(1.1)

1.4.1 Synthesis of Diethyl 2,3-$O$-isopropylidene-L-tartrate (1.1)

This compound was prepared by the method of Carmack and Kelley.\textsuperscript{31} A benzene solution (200 ml) of diethyl-L-tartrate (88 mL, 0.51 mol) and 2,2-dimethoxy propane (64 mL, 0.52 mol) together with $p$-toluensulfonic acid (0.25 g) was refluxed while and until 200 mL of the resulting methanol-benzene azeotrope is removed. $p$-Toluensulfonic acid is neutralized with 0.5 g of potassium carbonate. The solvent and
unreacted 2,2-dimethoxypropane were removed under reduced pressure, and the product mixture was distilled as a clear light-yellow liquid (100 g, 80%) bp 90-103°C (0.08 mm Hg). $^1$H NMR (CDCl$_3$) $\delta$ 1.32 (t, 6H), 1.50 (s, 6H), 4.30 (q, 4H), 4.78 (s, 2H).

1.4.2 Synthesis of 2,3-0-isopropyldene-L-threitol (1.2).

This compound was prepared by the method of Carmack & Kelley.$^{31}$ An ethanol solution (100 mL) of 1.1 (50 g, 0.20 mol) was added dropwise to a stirring ethanol solution (350 mL) of sodium borohydride (23.6 g, 0.62 mol). The addition is at a rate that a moderate reflux and gas evolution were maintained. The mixture is then refluxed for 2 h, cooled to r.t. and concentrated to a thick slurry under reduced pressure followed by cooling to 0°C. The mixture is diluted in chloroform (250 mL) and water (75 mL), then dropwise added under vigorous stirring, and filtered. The filter cake was rinsed with chloroform (3 x 50 mL), filtrate and rinses were combined, dried over magnesium sulfate, filtered and concentrated under reduced pressure. The product mixture was distilled as a clear colorless liquid (20 g, 62%). bp 95-105°C (0.05 mm Hg). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 1.43 (s, 6H), 2.66 (broad s, 2H), 3.75 (dd, 4H), 3.99 (t, 2H).
1.4.3 Synthesis of 1,4-ditosyl-2,3-O-isopropylidene-L-threitol (1.3)

This compound was prepared by the method of Rubin et al.,44 A pyridine solution (118 ml) of 1.2 (18.8 g, 0.12 mol) is cooled to 0°C and p-toluensulfonyl chloride powder (49 g, 0.26 mol) was slowly added maintaining the temperature below 5°C. When the addition is complete, the resulting mixture is stirred at 0°C for 14 h, then hydrolyzed at 0°C by dropwise addition of water. The resulting slurry was filtered and the cake washed with ice-cold water. The white powder was recrystallized from ethanol as fine needles (50 g, 89%). mp 79-82°C. $^1$H NMR (CDCl$_3$) $\delta$ 1.30 (s, 6H), 2.46 (s, 6H), 4.05 (broad s, 2H), 7.54 (q, 8H).

1.4.4 Synthesis of 2,3-O-isopropylidene-1,4-dibromo-L-threitol (1.4)

This compound was prepared by the method of Townsend et al.,45 A DMSO solution (125 ml) of lithium bromide (1.1 g, 0.01 mol) and 1.3 (12.2 g, 26 mmol) were heated under argon atmosphere at 60°C overnight. The product was poured into ice water and extracted with ether (3 x 50 mL), the combined extracts were washed
with water, dried over magnesium sulfate, filtered, and concentrated under reduced pressure. The product was distilled as a clear colorless liquid (4.7 g, 79%) bp 60-70°C (0.2 mm Hg). 4.7 g (63%). ¹H NMR (CDCl₃) δ 1.47 (s, 6H), 3.55 (d, 4H), 4.16 (t, 2H).

1.4.5 Synthesis of 2,3-O-isopropylidene-1,4-diiodo-L-threitol (1.5).

This compound was prepared by the method described by Vogel.⁴⁶ An acetone solution (20 ml) of 1.4 (1.0 mL, 7.6 mmol) and sodium iodide (2.3 g, 15 mmol) was stirred overnight at r.t. under argon atmosphere, followed by heating to reflux for 18 h. The product was concentrated under reduced pressure and distilled as a clear amberish liquid, bp 80-85°C (0.1 mm Hg). 1.69 g (58%). ¹H NMR (CDCl₃) δ 1.47 (s, 6H), 3.37 (d, 4H), 3.84 (t, 2H).

1.4.6 Synthesis of cyclopentadienyl thallium (I).

This compound was prepared by the method of Madhavan et al.⁴⁷ An aqueous solution (100 ml) of potassium hydroxide (10 g) was stirred at 25°C, then thallium acetate (4 g, 15 mmol) was added followed by the fast addition of 1,3-cyclopentadiene.
The mixture is vigorously stirred for 1 min, the white precipitate formed was filtered, washed with ethanol and dried in a dessicator (wrapped in aluminum foil to prevent it from light exposure) over calcium sulfate.

1.4.7 Attempted synthesis of 2,3-O-isopropylidene-1,4-bis-(cyclopentadiene)-L-threitol (1.7).

1.4.7.1 Cyclopentadienyl lithium method

This attempt was done by following a modified method of Vollhart & Halterman. A THF solution (30 ml) of cyclopentadiene (4 mL, 48 mmol) was treated under argon atmosphere at 0°C with a 1.6 M solution of n-butyl lithium (30 mL, 48 mmol). Upon addition, the mixture is allowed to warm up to room temp., and a solution of 1.3 (11.2 g, 24 mmol) in THF (30 mL) was quickly added. The resulting mixture is refluxed for 2 h, filtered, concentrated under reduced pressure, and recrystallized from ethanol affording a pale yellow solid (3.4 g, 74%) mp. 44-46°C. 

\[ ^1H\text{NMR (CDCl}_3\text{)} \delta 6.30 (b, 6H), 3.78 (d, 4H), 2.92-2.75 (m, 4H), 2.54-2.38 (m, 2H), 1.46 (s, 6H). MS: 192 (M^+), 177, 117(100), 105, 91, 78, 43. \]

1.4.7.2 Cyclopentadienyl thallium method/THF

This attempt was done by following the method of Conway & Rausch. A THF suspension (10 ml) of cyclopentadienyl thallium (0.08 g, 0.3 mmol) was treated under
argon atmosphere at room temp. with 1.4 (0.04 g, 0.15 mmol). After 2 h, more 1.4 (0.1 mL, 0.76 mmol) was added followed by the addition of cyclopentadienyl thallium (0.41 g, 1.52 mmol). The resulting mixture is stirred overnight, filtered, concentrated under reduced pressure, affording a pale yellow liquid (1.4).

1.4.7.3 Cyclopentadienyl thallium method (CH$_3$CN)

This attempt was done by following the method of Conway & Rausch.$^{48}$ A CH$_3$CN solution (20 ml) of 1.4 (1.46 g, 3.8 mmol) and cyclopentadienyl thallium (2.36 g, 8.8 mmol) was stirred for 5 days, filtered, concentrated under reduced pressure, affording a pale yellow liquid (1.4).

\[
\begin{align*}
\text{Br} & \quad \text{CH}_3 \\
\text{Br} & \quad \text{CH}_2\text{Br}
\end{align*}
\]

(1.8)

1.4.8 Synthesis of 1-bromo-2-bromomethyl-naphthalene (1.8).

This compound was prepared by the method of Newman & Kosak.$^{49}$ A carbon tetrachloride solution (60 ml) of 1-bromo-2-methyl-naphthalene (50 g, 0.23 mol), N-bromo-succinimide (42 g, 0.23 mol) and benzoyl peroxide (0.24 g) was refluxed for 3 h. The warm product was diluted with carbon tetrachloride (80 mL) and filtered. The filtrate was concentrated under reduced pressure and recrystallized from ethanol affording a clear slightly yellow powder (57 g, 81%). $^1$H NMR (CDCl$_3$) $\delta$ 4.85 (s, 3H), 7.45-7.90, 8.28-8.45 (m, 6H).
1.4.9 Synthesis of 1-bromo-2-naphthaldehyde (1.9).

This compound was prepared by the method of Newman & Kosak.\(^49\) A chloroform solution (200 ml) of 1.8 (45 g, 0.15 mol) is put to reflux, then hexamethylene tetraamine (24 g, 0.17 mol) is slowly cannulated in. The resulting salt is cold filtered followed by heating to reflux with a 50% aq. solution of acetic acid (325 mL) for 1.5 h. Concentrated HCl (55 mL) is slowly added and the mixture refluxed for 10 min. The precipitate is filtered and recrystallized from ethanol yielding fine clear needles (14 g, 40%). \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 10.68 (s, 1H), 8.60-8.40 (m, 1H), 8.00-7.61 (m, 5H).

1.4.10 Synthesis of 1-bromo-2-naphthoic acid (1.10).

This compound was prepared by Dr. Mark L. McLaughlin in our laboratories.
1.4.11 Synthesis of methyl, 1-bromo-2-naphthanoate (1.11).

This compound was prepared by the method of Hall & Turner.\textsuperscript{50} A methyl alcohol solution (37 ml) of 1-bromo-2-naphthoic acid (11 g, 4.4 mmol) and concentrated sulfuric acid (1 mL) was refluxed for 4 h. The product was concentrated under reduced pressure and poured into water, then extracted with ether. The ethereal solution was washed with a saturated solution of sodium bicarbonate, washed with water and dried over magnesium sulfate, finally it is filtered and concentrated under reduced pressure affording a white powder (8.2 g, 70%). \textsuperscript{1}H NMR (CDCl\textsubscript{3}) \( \delta 4.03 \) (s, 3H), 7.50-8.0, 8.40-8.55 (m, m, 6H).

1.4.12 Synthesis of dimethyl 1,1'-binaphthyl-2,2'-dicarboxylate (1.12).

This compound was prepared by the method of Hall & Turner.\textsuperscript{50} Activation of Cu/bronze (Fuson & Cleveland):\textsuperscript{51} An acetone (102 mL) solution (2%) of Iodine (1.7 g) was mixed with cupper/bronze (8.2%) for 10 min. The product is filtered,
removed, washed with a 1:1 solution of hydrochloric acid: acetone (41 mL total), and stirred until a slurry is formed. The product is filtered, washed with acetone, and dried under vacuum until use (it must be used almost immediately).

A mixture of the just activated Cu/bronze with methyl, 1-bromo-2-naphthanoate (8.15 g, 3.1 mmol) was heated up to 270-280°C for 20 min. The warm product (~60°C) was diluted with toluene (40 mL) and filtered while still warm. The filtrate was concentrated under reduced pressure and recrystallized from ethanol affording a clear light beige solid (7.5 g, 65%) mp 157-159°C. $^1$H NMR (CDCl$_3$) δ 3.5 (s, 6H), 7.09 (d, 2H), 7.23 (t, 2H), 7.52 (t, 2H), 7.95 (d, 2H), 8.10 (q, 4H).

1.4.13 Synthesis of 2,2'-bis-(hydroxymethyl)-1,1'-binaphthyl (1.13).

This compound was prepared by the method of Hall & Turner.$^{50}$ An ether solution (45 ml) of 1.12 (1.85 g, 5 mmol) was poured slowly into an ether solution (35 mL) of lithium aluminum hydride (0.5 g). The resulting mixture was refluxed for 30 min. The product was quenched with cold water and the resulting slurry was dissolved by adding a 2N sulfuric acid solution. The ethereal solution is separated and concentrated under reduced pressure. The product obtained is recrystallized from ethanol affording a white solid (0.8 g, 51%) mp 189-191°C. $^1$H NMR (CDCl$_3$) δ 1.61 (s, 4H), 2.93 (broad s, 2H), 7.00-8.10 (m, 12H).
1.4.14 Synthesis of 2,2'-bis-bromomethyl-1,1'-binaphthyl (1.14).

This compound was prepared by the method of Hall & Turner. A glacial acetic acid solution (10 ml) of 1.13 (0.4 g, 1.3 mmol) is brought to boiling temp. Boiling hydrobromic acid (3 mL) was slowly added. The resulting solution was stirred for 15 min, followed by the addition of excess boiling hydrobromic acid (2 mL). The boiling is continued for 0.5 h. Upon cooling, filtering, and recrystallizing, a pale yellow solid was obtained (0.46 g, 80%) mp 149-151°C. $^1$H NMR (CDCl$_3$) $\delta$ 4.25 (s, 4H), 7.00-8.10 (m, 12H).

1.4.15 Synthesis of 2,2'-bis-methyl-1,1'-binaphthyl (1.15)

This compound was prepared by the method of Maigrot & Mazaleyrat. A 1:1 ether:benzene solution (60 ml) of 1-bromo-2-methyllnaphthalene (17 g, 7.5 mmol) is
slowly added at room temp. under argon atmosphere to a stirring mixture of magnesium turnings (2 g, 82 mmol), and 1,2-dibromoethane (3 drops) in ether (4 mL), at such a rate as to maintain a gentle reflux. Upon addition, the resulting mixture is refluxed for 1 h, and added slowly under argon atm. to a vigorously stirring ether solution (50 mL) of 1-bromo-2-methylnaphthalene (14.8 g, 6.7 mmol) and bis-triphenylphosphine nickel chloride (0.5 g, 0.8 mmol). Upon addition, the resulting mixture is refluxed for 24 h. The resulting solution is then hydrolyzed with water followed by a 20% hydrochloric acid. The product is extracted with ether, washed with water, dried over magnesium sulfate, filtered, concentrated under reduced pressure, and distilled affording a glassy-yellowish very thick oily liquid (12.6 g, 67%) bp 180°C (high vacuum). $^1$H NMR (CDCl$_3$) δ 2.08 (s, 6H), 7.00-8.00 (m, 12H).

1.4.16 Synthesis of 2,2'-bis-bromomethyl-1,1'-binaphthyl (1.14)

This compound was prepared by the method of Maigrot & Mazaleyrat. A carbon tetrachloride solution (140 ml) of 1.15 (21.4 g, 76 mmol), N-bromo succinimide (29.8 g, 16.7 mmol) and benzoyl peroxide (0.3 g) is refluxed under argon atmosphere overnight. The resulting misture is filtered while still warm. The product is concentrated under reduced pressure, diluted in a 1:3 toluene:hexane solution (30 mL), concentrated under reduced pressure, and recrystallized from ethanol affording, after a
white solid (29 g, 87%) mp 149-151°C. $^1$H NMR (CDCl$_3$) $\delta$ 4.25 (s, 4H), 7.00-8.10 (m, 12H).

1.4.17 Attempted synthesis of 2,2'-bis-(methylene cyclopentadienide)-1,1'-binaphthyl (1.16)

1.4.17.1 Use of Cyclopentadienyl-sodium$^{1,2,3}$

A THF solution (10 ml) of 1.14 (0.59 g, 1.4 mmol) is slowly cannulated at room temp. under argon atmosphere into a THF solution (10 mL) of washed NaH (0.08 g, 3.5 mmol) and cyclopentadiene (0.3 mL, 3.5 mmol). A white-beige precipitates out almost immediately, and the mixture is stirred for 20 min. The resulting mixture is filtered, and the product (filtrate) quenched with ice cold water and extracted with ether. The combined extracts were washed with water, with a saturated NaCl solution, and again with water, then dried over magnesium sulfate, filtered and concentrated under reduced pressure affording a pale yellow solid which is further dried over high vacuum. Spiro 1.17 (0.22 g, 46%) mp 122-125°C. $^1$H NMR (CDCl$_3$) $\delta$ 1.13 (b s, impurities), 2.08 (d, 2H), 2.83 (d, 2H), 6.31 (s, 4H), 7.10-7.30, 7.34-7.54, 7.84-7.98 (m,m,m, 12H). MS: 344 (M$^+$), 279, 277, 276, 265(100), 264, 263, 141, 77, 66, 65, 63.
1.4.17.2 Ferrocene-dilithium salt

Preparation of ferrocenyledene dilithium TMEDA salt.\textsuperscript{52}

A dry hexane solution (2 ml) of TMEDA (0.6 mL, 3.6 mmol) is stirred under argon atmosphere at room temp. A 1.6 M solution of n-Butyl-lithium (2.3 mL, 2.1 mmol) is slowly added and the resulting mixture is stirred for 20 min. A hexane solution (30 mL) of ferrocene (0.34 g, 1.7 mmol) is added over a period of 30 min. The resulting mixture is stirred at room temp. overnight, and compound 1.14 (0.6 g, 1.4 mmol) is slowly added into it. The resulting mixture is stirred overnight, filtered and the product recrystallized from ethanol affording mainly unreacted 1.14.

\[ \text{HO} \rightarrow \text{NH}_2\text{NH}_2\cdot\text{H}_2\text{O} \rightarrow \text{NH}_2 \text{NH}_2 \]

(1.21)

1.4.18 Synthesis of 2,2'-Diamino-1,1'-binaphthyl (1.21)

This compound was prepared by the method of Brown \textit{et al.}\textsuperscript{53} A mixture of 2-hydroxy-naphthalene (13 g, 0.09 mol) and hydrazine monohydrate (2.5 mL, 0.05 mol) is heated to 180°C in a parr bomb for 74 h. The resulting mixture is dissolved in a hot 4:1 methanol:hydrochloric acid solution (500 mL). The product is washed with ether, and the aqueous layer neutralized with a strong sodium hydroxide solution until clear precipitation occurred, followed by filtration and then it is dried under high vacuum affording a slightly brown solid (5.9 g, 46%) mp 187-189°C. $^1$H NMR (CDCl$_3$) $\delta$
3.18 (s, 4H), [6.88 (d), 7.23 (t), 7.38-7.62 (m), 8.01 (d), 8.18 (d), 12H].

1.4.19 Attempted synthesis of 2,2'-[(1,1'-ferrocenyl)-1,1'-binaphthyl (1.19).

\[
\begin{align*}
\text{NH}_2 & \quad \text{NaNO}_2/\text{HgBr}_2 \\
\text{NH}_2 & \quad \text{N}_2^+\text{HgBr}_3^- \\
\text{N}_2^+\text{HgBr}_3^- & \quad (1.22)
\end{align*}
\]

1.4.19.1 Synthesis of 2,2'-bis-(diazonium tribromo-mercurate)-1,1'-binaphthyl (1.22)

This compound is prepared by the method of Brown et al.\textsuperscript{53} To a cold (-5 to -10°C) concentrated sulfuric acid solution (195 ml), potassium nitrate (7.2 g, 85 mmol) is slowly added with continuous stirring. The resulting mixture is brought to room temp. until complete dissolution. The resulting solution is cooled to -8°C. Then a pyridine solution (35 mL) of 2,2'-diamino-1,1'-binaphthyl (5.1 g, 18 mmol) is dropwise added maintaining the temp. below -5°C. The resulting black molasses is stirred for 2 h.

The quenching of the reaction is carried out by slowly adding pieces of ice maintaining the temp. around 0°C, then an aqueous solution (130 mL) of urea (5.1 g, 85 mmol) is very slowly added keeping the temp. below -5°C. The resulting mixture is allowed to stir for 45 min (time at which no more gas is evolved from the reaction).
Then an ice cold aqueous solution (41 mL) of mercuric bromide (18.2 g) and potassium bromide (18.5 g) is added dropwise maintaining the temp. below -5°C. The resulting mixture is allowed to stir for 45 min and the yellow-brown solid (5.1 g) product is filtered and washed with dry methanol followed by dry ether and used immediately.

1.4.19.1.1 Ferrocene-Glacial acetic acid route

A glacial acetic acid solution (30 mL) of ferrocene (0.8 g, 4.3 mmol) was placed under argon atmosphere and put under continuous stirring. Then, the previously and fresh diazonium salt prepared is slowly added. The resulting mixture is stirred at room temp. for 3 h, followed by heating to 40°C for 4 h. The resulting dark-red solution is quenched with ammonium hydroxide until pH neutral, then the product is extracted with ether, dried over magnesium sulfate, filtered and dried under high vacuum affording ferrocene and the hydrolysis product of the diazonium salt.

1.4.19.1.2 Dilithium salt of ferrocene route

The diazonium salt is prepared as described above.

A THF solution (8 mL) of the just prepared diazonium salt (0.5 g, 0.4 mmol) was placed under argon atmosphere and put under continuous stirring at -78°C. Then, a THF solution (7 mL) of dilithium salt ferrocene (0.2 g, 0.4 mmol) is slowly added. The resulting mixture is stirred for 1 h. The resulting dark-red solution is quenched with concentrated sodium hydroxide solution, then the product is extracted with ether, dried over magnesium sulfate, filtered and dried under high vacuum affording ferrocene and the hydrolysis product of the diazonium salt.
CHAPTER TWO.
Synthesis of Fulvene Derivatives

2.1 Introduction.

Fulvenes are hydrocarbons with odd-membered rings that are fully unsaturated and crossed-conjugated via an exocyclic double bond, as shown in figure 2.1. Many of these unsaturated compounds are not isolable due to high reactivity with oxygen or tendencies to polymerize.54

![Fig. 2.1. Tri-, penta-, hepta- and nona-fulvenes.]

That fulvenes interest many people and are synthetically useful compounds is evidenced by the fact that they have been the subject of investigation ever since the discovery of this class of compounds at the turn of the century.55,56 Fulvenes function as ligands in stable transition metal complexes analogous to other highly unsaturated organic moieties such as cyclobutadiene.54

Continuing the study towards the preparation of chiral cyclopentadienyl ligands as potentially good ligands to a transition metal, different types of pentafulvenes (a category within fulvenes describing a cyclopentadiene with an exocyclic double bond), were targeted for synthesis. These molecules were potential synthons for the preparation of chiral organometallic compounds.
2.1.1 Retrosynthetic analysis.

The purpose of the retrosynthetic analysis as it has been described in chapter one, is to take a molecule and break it down by a series of disconnections that leads us to possible simple starting materials.

A retrosynthetic analysis shows a systematic (not the only one) approach in finding the shortest possible route in synthesizing a molecule as complex as it may be.

It is desirable to disconnect 2A in a symmetric fashion as shown in figure 2.2, leading to synthons 2B by a functional group interconversion (FGI). Another FGI on 2B would lead to the corresponding dicarbonyl derivative 2C.

Several methods of cyclopentadiene addition to carbonyl compounds have been reported.\textsuperscript{55,56} The formation of a pentafulvene from a carbonyl compound is shown in figure 2.3.

When fulvenes are treated with alkyl or aryl lithium reagents, a potential monosubstituted $\eta^5$-cyclopentadienyl anion is formed which could then be complexed to a transition metal.\textsuperscript{55,56} (See figure 2.4)
Figure 2.3 Formation of a pentafulvene from a cyclopentadienyl anion and a carbonyl compound.

Figure 2.4 Monosubstituted cyclopentadienyl anion, derived from a pentafulvene, complexed to a transition metal.
2.2 Results.

As model reactions for the preparation of metal complexes bearing a bridged cyclopentadienyl moiety having \( C_2 \) symmetry, some mono and difulvenes (as synthon compounds) were synthesized.

2.2.1 Synthesis of Monofulvenes.

When 2-adamantanone is treated in solution in methanol with cyclopentadiene in the presence of pyrrolidine, the corresponding monofulvene derivative compound 2.1 is obtained in modest yield as shown in figure 2.5. Recrystallization made possible its characterization by X-ray structural analysis\(^5\). Figure 2.6 shows the Ortep diagram of 2.1.

![Fig. 2.5 Synthesis of 9-(2,4-cyclopentadien-1-ylidene)tricyclo[3.3.1.1.3,7]decane 2.1](image)

Monofulvene 2.2 derived from the bicyclo[2.2.1]hepta-2-one was successfully prepared by treatment with cyclopentadiene and pyrrolidine (see figure 2.7). Similarly, the monofulvene derivative 2.3 was also successfully synthesized from the corresponding bicyclo[3.3.1]nonan-9-one (see figure 2.8).
Figure 2.6 ORTEP diagram of 9-(2,4-cyclopentadienide-1-ylidene)tricyclo[3.3.1.1^{3,7}]decane
Recrystallization of monofulvene 2.3 permitted its characterization by X-ray crystal structure analysis.\textsuperscript{58} Figure 2.9 shows the ortep diagram for 2.3.

**2.2.2 Synthesis of Difulvenes.**

Compound 2.4 was prepared in low yields from the corresponding diketone (2,6-hexadione) by treatment, in methanol, with cyclopentadiene in the presence of pyrrolidine as depicted in figure 2.10.
Figure 2.9 ORTEP diagram of 9-(2,4-cyclopentadiene-1-ylidene)bicyclo[3.3.1]nonane 2.3
Attempts to synthesize difulvene 2.7 started with the preparation of bicyclo[4.4.0]deca-2,7-dione 2.5 by oxidation of the corresponding 2,7-dihydroxibicyclo[4.4.0]decane, which was performed in fairly good yields using chromic acid as seen in figure 2.11. Transformation of 2.5 into the corresponding trans isomer 2.6 was successfully performed by treatment of 2.5 with hydrochloric acid in fairly good yield. Recrystallization of 2.6 permitted its characterization by X-ray crystal structure analysis. Figure 2.12 shows the Ortep diagram of 2.6.

Attempts to synthesize difulvene 2.7 from the corresponding trans-diketone, by the known methodology, were unsuccessful. Difulvene 2.7 is probably formed under the reaction conditions, but due to the high tendency of these compounds to decompose or readily polymerize, it undergoes polymerization even at freezing temperatures, since it is detected immediately after the reaction takes place (during the first hour) by $^1$H NMR spectroscopy, but when it is stored at freezing temperature, a bright yellow powder precipitates out. This yellow powder has the $^1$H NMR of a polymer. The signals are broad but at the same chemical shifts of the initial compound signals. No further characterization of this polymer was performed.

The synthesis of difulvene 2.9 started as follows; (see figure 2.13). First, the successful photochemically induced $\pi^{2s} + \pi^{2s}$ cycloaddition-dimerization of cyclopentenenone afforded tricyclo[5.3.0.0$^{2,6}$]deca-3,8-dione 2.8 in fairly good
Figure 2.12 ORTEP diagram of trans-1,6-bicyclo[4.4.0]deca-2,7-dione 2.6
Attempts to synthesize the corresponding difulvene 2.9 were unsuccessful obtaining a bright yellow powder which by $^1$H NMR spectroscopy showed to be a polymeric material.

\[ \text{hv} \overset{}{\rightarrow} \begin{array}{c}
\text{Cyclopentadiene} \\
\text{Pyrroldine} \\
\text{methanol}
\end{array} \]

**Fig. 2.13** Attempted synthesis of 2,7-*bis*(2,4-cyclopentadiene-1-ylidene) tricyclo[5.3.0.0$^6,1^0$]decane 2.9

Attempts toward the synthesis of difulvene 2.12 started from the Diels-Alder $\pi^4$s+$\pi^2$s cycloaddition of cyclopentadiene to benzoquinone in very good yield affording tricyclo[6.2.1.0$^2,7$]undeca-4,9-diene-3,6-dione 2.10 as seen in figure 2.14.

\[ \text{hv} \overset{}{\rightarrow} \begin{array}{c}
\text{pentacyclo[5.4.0.0$^2,6$.0$^3,10$.0$^5,9$]} \\
\text{undecane-8,11-dione 2.11}
\end{array} \]

**Fig. 2.14** Synthesis of pentacyclo[5.4.0.0$^2,6$.0$^3,10$.0$^5,9$] undecane-8,11-dione 2.11

Photochemically induced $\pi^2$s+$\pi^2$s intramolecular cycloaddition of 2.10 afforded in fairly good yield the corresponding diketone 2.11 (see figure 2.14).
Attempts to synthesize difulvene 2.12 from the corresponding diketone 2.10 were unsuccessful, affording compound 2.13 (see figure 2.15), which was mainly characterized by $^1$H NMR and $^{13}$C NMR since preliminary attempts to recrystallize the compound were unsuccessful. The pyrrolidine protons H7 and H8 (see figure 2.16 for numbering system) were assigned by their chemical shifts as a triplet at 2.91 ppm for H7 and a multiplet at 1.85-1.74 ppm for H8.
From the $^1$H-$^1$H-COSY experiment, H3 was located at 2.55 ppm (broad multiplet) because of its coupling to 4 different protons, namely H4, H6, H1, and H2. Spin-spin homodecoupling as well as $^1$H-$^1$H-COSY experiments suggested that proton H4 be assigned at 2.68 ppm (broad multiplet) because of its couplings to H3 and H5 respectively. H5 is assigned at 2.78 ppm (doublet) because of its coupling to H4 (by $^1$H-$^1$H-COSY). $^{13}$C NMR DEPT and $^{13}$C-$^1$H correlation experiments distinguished between primary and secondary carbons in 2.13, hence, knowing that H3 is attached to C3 (44.04 ppm), H4 is attached to C4 (41.87 ppm) and H5 is attached to C5 (44.88 ppm), the only tertiary C left is C6 (55.61 ppm) leading to the assignment of H6 at 2.81 ppm (doublet). Also, 90° pulse DEPT experiment showed inverted peaks for the 3 methylene carbons (C1; 47.75 ppm, C7; 42.97 ppm and C8; 24.48 ppm) attached to H1-H2 (1.52 and 1.85 ppm respectively), H7, and H8 respectively. H1-H2 protons correlated to C1. NOE experiments permitted the distinction between H1 and H2. Irradiation at 1.85 ppm showed an increase in the inverted signal assigned to H6.

The structure was confirmed by x-ray structural analysis after a successful recrystallization of an analytical sample. Figure 2.17 shows a pluto diagram for 2.13.

Synthesis toward difulvene 2.17 started by treating ethyl-2-oxocyclopentane with potassium metal and ethyl 4-bromobutyrate in toluene to afford in fairly good yield the diester 2.14 as shown in figure 2.18.
Figure 2.17 Pluto diagram of 3,8-bis(pyrrolidyl)pentacyclo[8.2.1.1^{3,8}.0^{2,7}.0^{4,9}.0^{5,10}.]-3,8-epoxyundecane 2.13
Fig. 2.18 Attempted synthesis of 1,6-\textit{bis}(2,4-cyclopentadiene-1-ylidene)spiro[4.4]nonane 2.17

The diester 2.14 was successfully converted into the carboxylic acid derivative 2.15 by hydrolysis and \textit{in-situ} decarboxylation of 2.14. Intramolecular cyclization of 2.15 in the presence of a polyphosphoric acid:acetic acid mixture afforded spiro[4.4]nonan-1,6-dione 2.16. Attempts to synthesize the corresponding difulvene 2.17 by treating 2.16 with cyclopentadiene in the presence of pyrrolidine were unsuccessful, giving a bright yellow polymeric material which was not further characterized.

The synthesis toward difulvene 2.21 started by the successful preparation in very good yield of the dimethyl ester compound 2.18 from dimethyl-L-tartrate and dimethoxy propane in the presence of $p$-toluensulfonic acid as shown in figure 2.19. Conversion of the dimethyl ester 2.18 into the corresponding \textit{bis}-pyrrolidyl amide 2.19 was successfully performed in very good yield. Recrystallization of 2.19 permitted its characterization by X-ray crystal structure analysis$^{60}$. Figure 2.20 shows the Ortep diagram of 2.19. Compound 2.19 was then interconverted in good yield into the corresponding \textit{bis}-methylketone 2.20. Attempts to synthesize difulvene
Figure 2.19 Attempted synthesis of difulvene compound 2.21
Figure 2.20 ORTEP diagram of 4,5-bis(pyrrolidinamide)-2,2-dimethyl-1,3-dioxolane 2.19
by treating \( 2.20 \) with cyclopentadiene in the presence of pyrrolidine were unsuccessful, obtaining a bright yellow powder, which by \(^1\text{H}\) NMR spectroscopy showed to be a polymeric material. No further characterization of this polymer was performed.

![Chemical structure](image)

**Fig. 2.21** Attempted synthesis of \( 2,2\text{-}\text{bis}(2,4\text{-cyclopentadiene}-1\text{-ylidene})\)-1,1'-binaphthyl \( 2.23 \)

The synthesis toward difulvene \( 2.23 \) started by treating \( 2,2\text{-}\text{bis}-\text{bromomethyl}-1,1\text{-}\text{bynaphthyl} \ 1.14 \) (whose preparation is described in the previous chapter. See figure 1.13) with 2-nitro-2-propyl sodium in ethanol-DMSO solution affording in fairly good yield the corresponding \( \text{bis}-\text{aldehyde} \ 2.22 \) as shown in figure 2.21. Attempts to prepare the corresponding difulvene \( 2.23 \) by treating \( 2.22 \) with cyclopentadiene in the presence of pyrrolidine were unsuccessful resulting in the formation of a bright yellow polymer.
2.3 Conclusions

Retrosynthetic analysis is a great tool in helping to decide the best synthetic route to a molecule as complex as it may look.

Synthesis toward the target monofulvene molecules 2.1, 2.2 and 2.3 was successful. These compounds were found to be very stable. The two solid monofulvenes 2.1 and 2.3 were successfully recrystallized and their structures were confirmed by X-ray crystal structure determination.

Synthesis of difulvenes in general was for the most part unsuccessful in building the fulvene functionality. Difulvene 2.4 was the only compound stable long enough to be fully characterized. Difulvenes 2.7, 2.9, 2.17, 2.21, and 2.23, were found to be very unstable molecules due to their extreme reactivity, polymerizing even at lower temperatures; therefore, they were not fully characterized.

From the synthesis toward difulvenes 2.7 and 2.21, diketone 2.6, and the diamide 2.19 were fully characterized and their structures confirmed by X-ray crystal structure determination.

Spectroscopic evidence suggests that difulvene 2.12 was not even formed under the reaction conditions. Polycyclic compound 2.13 was formed instead. Its structure was determined by NMR spectroscopy and confirmed by X-ray crystal structure determination.
2.4 Experimental Section

General Procedures. Melting points are uncorrected. $^1$H NMR and $^{13}$C NMR spectra were measured at 200 MHz on a Bruker AC 200 spectrometer. Chemical shifts are reported in δ or ppm downfield from tetramethylsilane. IR spectra were recorded with a Perkin Elmer 283B Infrared spectrophotometer. MS were recorded on Hewlett Packard 5985A mass spectrometer. High-resolution MS were obtained from the Midwestern Regional Mass Spectroscopy Facility at the Univ. of Nebraska-Lincoln. Elemental analysis for all new compounds were obtained from Desert Analytics (Tucson, AR) or Oneida Research Services, Inc. (Whiteboro, NY).

Materials and Methods. Cyclopentadiene was freshly cracked from dicyclopentadiene (Aldrich). Methanol, ethanol, toluene, benzene, and chloroform, reagent grade were used as received.

\[\text{Cyclopentadiene \xrightarrow{\text{Pyrrolidine, methanol}} \text{9-(2,4-cyclopentadien-1-ylidene)tricyclo[3.3.1.1^{3,7}]decane}} (2.1)\]

2.4.1 Synthesis of 9-(2,4-cyclopentadien-1-ylidene)tricyclo[3.3.1.1^{3,7}]decane (2.1)

This compound was prepared by the method of Stone & Little. A 1:1 methanol:dichloromethane solution (7 ml) of 2-adamantanone (1.6 g, 10.7 mmol) is stirred under argon atmosphere at 25°C. Cyclopentadiene (0.7 mL, 10.7 mmol) is added followed by the quick addition of pyrrolidine (0.9 mL, 10.7 mmol). The resulting solution is stirred for 4 h., quenched with glacial acetic acid (1 mL) and the
product extracted with ether. The combined extracts were washed with water, dried over magnesium sulfate, filtered, and concentrated under reduced pressure to afford a bright-yellow solid, mp 88-89°C (ref. mp 91-92°C) \(^{62}\) (1.08 g, 51.4%). \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 6.58 (dd broad, 4H), 3.31 (broad, 2H), 2.56 (broad, 2H), 2.01 (broad, 10H); \(^{13}\)C (CDCl\(_3\)) \(\delta\) 28.22, 36.98, 37.28, 40.17, 119.40, 130.40, 135.74, 167.32; MS, m/z (relative intensity) 199 (M\(^+\) + 1), 198 (100), 155, 115, 91, 77.

2.4.2 Synthesis of 2-(2,4-cyclopentadiene-1-ylidene)bicyclo[2.2.1]heptane (2.2)

This compound was prepared by the method of Stone & Little.\(^{61}\) A methanol solution (17 ml) of bicyclo[3.2.1]heptane-2-one (5 g, 45.5 mmol) is stirred under argon atmosphere at 25°C. Cyclopentadiene (2.8 mL, 45.5 mmol) is added followed by the quick addition of pyrrolidine (3.6 mL, 46 mmol). The resulting solution is stirred for 3 h., quenched with glacial acetic acid (3 mL) and the product extracted with ether. The combined extracts were washed with water, dried over magnesium sulfate, filtered, and concentrated under reduced pressure to afford a bright-yellow liquid, bp 50-55°C (@ high vacuum)(1.2 g, 17%). \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 6.50 (m, 4H), 3.37 (broad, 1H), 2.50 (b, 2H), 1.97-1.18 (b, 6H); \(^{13}\)C (CDCl\(_3\)) \(\delta\) 27.65, 29.00, 36.00, 38.73, 39.06, 44.21, 120.71, 120.78, 129.06, 130.19, 135.86, 163.51; MS,
2.4.3 Synthesis of 9-(2,4-cyclopentadiene-1-ylidene)bicyclo[3.3.1]nonane (2.3)

This compound was prepared by the method of Stone & Little. A methanol solution (5 ml) of bicyclo[3.3.1]nonane-9-one (0.5 g, 5 mmol) is stirred under argon atmosphere at 25°C. Cyclopentadiene (2 mL, 24 mmol) is added followed by the quick addition of pyrrolidine (2 mL, 24 mmol). The resulting solution is stirred for 2 h., precipitating a bright-yellow solid which is filtered and dried under vacuum. Bright yellow crystals sublime at 30-40°C (high vacuum) mp 48-49°C (0.6 g, 65.8%). $^1$H NMR (CDCl$_3$) $\delta$ 6.54 (dd, 4H), 3.22 (broad, 2H), 2.20-1.83 (m broad, 8H), 1.67-1.50 (m broad, 4H); $^{13}$C (CDCl$_3$) $\delta$ 21.69, 34.81, 37.34, 119.19, 130.55.


2.4.4 Synthesis of 2,5-bis(2,4-cyclopentadiene-1-ylidene)hexane (2.4)

This compound was prepared by the method of Stone & Little. A methanol
solution (35 ml) of 2,5-hexadione (5 mL, 43 mmol) is stirred under argon atmosphere at 25°C. Cyclopentadiene (5.6 mL, 85 mmol) is added followed by the quick addition of pyrrolidine (7.1 mL, 84 mmol). The resulting solution is stirred for 15 min, quenched with glacial acetic acid (6 mL) and the product extracted with ether. The combined extracts were washed with water, dried over magnesium sulfate, filtered, concentrated under reduced pressure and distilled under high vacuum affording a clear bright-yellow viscous liquid, bp 70-90°C (0.08 mm Hg) (1.79 g, 20%). ¹H NMR (CDCl₃) δ 2.26 (s, 6H, 2 CH₃), 2.75 (s, 4H, 2 CH₂), 6.48 (s, 8H, Cp-H); ¹³C (CDCl₃) δ 20.96 (2 CH₃), 36.75 (2 CH₂), 120.03 (2 olefinic C), 120.78 (2 olefinic C), 131.25 (4 olefinic C), 143.02 (2 quat. C), 151.53 (2 quat. C); MS, m/z (relative intensity) 210(M⁺), 195 (100), 180, 167, 105, 77; HR-MS, m/z (M⁺) C₁₆H₁₈ Calcd. 210.1413; Obsd. 210.1416; C₁₅₁₃CH₁₈ Calcd. 211.1440; Obsd. 211.1439. IR (neat) 3130, 3080, 2970, 2940, 2920, 2870, 1645, 1625, 1478, 1468, 1440, 1380, 1095, 860 cm⁻¹.


2.4.5 Synthesis of bicyclo[4.4.0]deca-2,7-dione (2.5)
This compound was prepared by the method of Peet & Cargill; Kleinfelter & Schleyer. A 5:1 acetone:dichloromethane solution (600 ml) of Decalin-1,5-diol (10 g, 59 mmol) is stirred at 25°C. 8N solution of Chromic acid (60 mL) is slowly added not allowing a yellow-amber precipitate to remain for extended periods of time keeping the temperature between 20 and 30°C. The resulting heterogeneous mixture is stirred overnight, mixed with sodium bisulfite, decanted, and concentrated under reduced pressure affording a white solid which is recrystallized from dichloromethane affording water clear crystals, mp 163-165°C (7.4 g, 76%). \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 2.46-2.38 (m broad, 2H), 2.37-2.24 (m broad, 4H), 2.20-2.10 (m broad, 4H), 1.81-1.58 (m broad, 4H); \(^1^3\)C NMR (CDCl\(_3\)) \(\delta\) 24.35, 24.91, 41.14, 55.44, 209.77.

2.4.6 Synthesis of bicyclo[4.4.0]trans-1,6-deca-2,7-dione (2.6)

This compound was prepared by the method of Hamon & Richards. A chloroform suspension (60 ml) of decalin-1,5-dione (4 g, 24 mmol) is stirred under argon atmosphere at 25°C. Anhydrous hydrochloric acid is slowly bubbled in changing the suspension into a clear solution. The bubbling is continued for 10 min. followed by argon bubbling for 15 min. The resulting solution is concentrated under reduced pressure affording a white powder which is recrystallized from dichloromethane affording water clear crystals, mp 170-172°C (2.8 g, 70%). \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 2.46-2.38 (m broad, 2H), 2.37-2.24 (m broad, 4H), 2.20-2.10 (m broad, 4H), 1.81-1.58
2.4.7 Attempted Synthesis of 2,7-bis-(2,4-cyclopentadiene-1-ylidene)bicyclo[4.4.0]decane (2.7)

This compound was attempted to be prepared by the method of Stone & Little. A 5:1 methanol:dichloromethane solution (12 ml) of trans-decalin-1,5-dione (1.5 g, 9 mmol) is stirred under argon atmosphere at 25°C. Cyclopentadiene (3 ml, 45 mmol) is slowly added followed by the quick addition of pyrrolidine (3.8 mL, 45 mmol). The resulting solution is stirred overnight, quenched with glacial acetic acid (2.7 mL), diluted with water and extracted with ether. The combined extracts are washed with brine, then water, dried over magnesium sulfate, filtered and concentrated under reduced pressure yielding a bright yellow solid which is passed through an alumina column (using hexane as eluent) affording a bright yellow oily material which polymerizes even at 0°C. Oily material before it polymerizes: $^1$H NMR (CDCl$_3$) $\delta$ 6.74-6.41 (b, 8H), 3.38-3.18 (b, 2H), 2.95-2.72 (b, 4H), 2.40-1.20 (b, 12H); $^{13}$C NMR (CDCl$_3$) $\delta$ 27.25, 27.54, 28.83, 45.05, 119.45, 120.25, 131.33, 158.11; MS, m/z (relative intensity) 262 (M$^+$), 85, 71, 57(100), 43.
2.4.8 Synthesis of tricyclo[5.3.0.0²,6]deca-3,8-dione (2.8)

This compound was prepared by the method of Eaton. Cyclopentenone (2 g, 25 mmol) was placed in an NMR tube and irradiated from 15 GE germicidal lamps (3500 Å) of white light in a Rayonet photochemical reactor for 90 H, 20 min. yielding white crystals and a yellow solution. The crystals are recrystallized from carbon tetrachloride and sublimed under high vacuum at 115-120°C giving clear crystals. mp 110-112°C (1.0 g, 50%): ^1^H NMR (CDCl₃) δ 2.90-2.05 (m); ^1^3^C (CDCl₃) δ 27.77, 35.85, 37.10, 49.22, 219.21; MS, m/z (relative intensity) 164 (M⁺), 108, 94, 79(100), 54.

2.4.9 Attempted synthesis of 3,8-bis-(2,4-cyclopentadiene-1-ylidene)tricyclo[5.3.0.0²,6]decane (2.9)

This compound was prepared by the method of Stone & Little. A methanol solution (8 ml) of tricyclo[5.3.0.0¹.⁵]decane-5,10-dione (0.87 g, 5.3 mmol) is stirred under argon atmosphere at 25°C. Cyclopentadiene (3.5 ml, 53 mmol) is slowly added followed by the quick addition of pyrrolidine (4.4 mL, 53 mmol). The resulting solution is stirred 1/2 H, and put under ice yielding a bright yellow solid which slowly polymerizes even at 0°C. mp 160-180°C (dec.): ^1^H NMR (CDCl₃) δ 6.45 (dd, 8H), 3.11 (broad, 4H), 2.90-2.53 (broad, 8H); ^1^3^C (CDCl₃) δ 40.59, 41.21, 44.33, 53.14,
124.79, 127.94, 131.76, 132.94, 142.94; MS, m/z (relative intensity) 260 (M⁺), 130(100), 115, 77.

2.4.10 Synthesis of tricyclo[6.2.1.0²,7]undeca-4,9-diene-3,6-dione (2.10)

This compound was prepared by the method of Wasserman.⁶⁷ A tetrahydrofuran solution (10 ml) of benzoquinone (0.87 g, 8.1 mmol) is stirred under argon atmosphere at 25°C. Cyclopentadiene (0.6 ml, 8 mmol) is slowly added. The resulting solution is stirred overnight, and concentrated giving a yellowish solid which upon recrystallization from hexane afforded clear-greenish needles (1.0 g, 73%): ¹H NMR (CDCl₃) δ 6.60 (s, 2H), 6.08 (t, 2H), 3.57 (t, 2H), 3.22 (t, 2H), 1.55 (qt, 2H); ¹³C (CDCl₃) δ 48.35, 48.79, 135.29, 142.06, 199.39.

2.4.11 Synthesis of pentacyclo[5.4.0.0²,6³,1⁰0⁵,9]undeca-8,11-dione (2.11)
This compound was prepared by the method of Cookson, Crundwell & Hudec.\(^6\) A deutero-chloroform solution (1 ml) of tricyclo[6.2.1.0\(^2\)7] undecane-4,9-diene-3,6-dione (0.31 g, 2 mmol) is put in an NMR tube and irradiated with 15 bulbs of white light in a photochemical reactor for 20 H. 10 min. yielding a dark amber solution, which upon concentration and then sublimation (100-110°C at @ 0.5 mm Hg) gave a fine white powder-crystalline material. mp 240-242°C (0.2 g, 64\%): \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 3.4-2.6 (m, 8H), 2.15-1.82 (q, 2H); \(^13\)C (CDCl\(_3\)) \(\delta\) 38.71, 40.44, 48.22, 44.62, 54.70, 211.99.

2.4.12 Attempted Synthesis of 3,8-bis-(2,4-cyclopentadiene-1-ylidene)pentacyclo[5.4.0.0\(^2\)6.0\(^3\)10\(^5\)9]undecane (2.12)

This compound was attempted to be prepared by the method of Stone & Little.\(^6\) A methanol solution (5 ml) of pentacyclo[5.4.0.0\(^2\)6.0\(^3\)10\(^5\)9] undecane-8,11-dione 2.11 (1 g, 5.7 mmol) is stirred under argon atmosphere at room temp. Cyclopentadiene (4.7 ml, 57 mmol) is slowly added followed by the quick addition of pyrrolidine (4.7 mL, 57 mmol). The resulting solution is stirred for 2.5 H. The white solid formed is filtered and dried under vacuum overnight. The mother liquor is neutralized with glacial acetic acid (5 mL), diluted in water, extracted with ether, the organic layer dried over magnesium sulfate, filtered and concentrated under reduced pressure yielding an amber liquid which turned out to be dicyclopentadiene. The white
powder formed is recrystallized from ethanol affording fine white needles. 2.13, mp 163-165°C (0.42 g, 25%). ¹H NMR (CDCl₃) δ 1.52 (dt, 1H), 1.74-1.84 (m, 8H), 1.85 (dt, 1H), 2.55 (broad m, 2H), 2.68 (broad m, 2H), 2.78 (d, 2H), 2.81 (d, 2H), 2.91 (t, 8H). ¹³C NMR (CDCl₃) δ 24.48, 41.87, 42.97, 44.04, 44.88, 47.75, 55.61, 106.26. IR (thin film, in cm⁻¹): 2984 (b), 2920 (m), 2880 (s), 2845 (m), 1388 (m), 1347 (m), 855 (m). HRMS: M⁺ (Calcd., Obsd) C₁₉H₂₆N₂O (298.2049, 298.2043), C₁₈¹³CH₂₆N₂O (299.2090, 299.2074), C₁₅H₁₈NO (228.1415, 228.1381), C₁₄H₁₈N (200.1474, 200.1431), C₁₁H₁₄N (160.1155, 160.1121), C₉H₁₂N (134.1001, 134.0965).

2.4.13 Synthesis of 2-oxo-(1-carboethoxy-1'-ethylbutyrate) cyclopentane (2.14)

This compound was prepared by the method of Bachman & Struve.⁶⁹ A toluene suspension (250 ml) of potassium (12.5 g, 0.32 mol) is put under ice. Ethyl 2-oxocyclopentane carboxylate (50 g, 0.32 mol) is slowly added. The resulting solution is warmed up to 25°C and allowed to stir for 1 h. Upon cooling back to 0°C, Ethyl 4-bromobutyrate (50 g, 0.26 mol) is added. The resulting mixture is refluxed overnight. A 15% aqueous HCl solution (300 mL) is added, the organic layer is then extracted, washed with water, dried over magnesium sulfate, filtered, concentrated under reduced pressure and distilled under high vacuum (@ 100-120°C) affording a water clear liquid, (19.4 g, 74%). ¹H NMR (CDCl₃) δ 4.12 (q, 4H), 2.40-2.18 (m, 4H), 2.08-
1.82 (m broad, 4H), 1.74-1.50 (m broad, 4H), 1.26 (t, 6H).

2.4.14 Synthesis of 2-oxo-1-cyclopentanebutyric acid (2.15)

This compound was prepared by the method of Bachman & Struve. A concentrated HCl solution (12 ml) of 2.14 (7 g, 27 mmol) is put under reflux for 2 h. Excess HCl is removed under reduced pressure, and the brown residue dissolved in benzene. The pH is raised with sodium carbonate solution to approx. 10. The aqueous solution is extracted, acidified with HCl (until pH 2) and extracted with ether. The organic layer is dried over magnesium sulfate, filtered, and concentrated under reduced pressure yielding a light amber semi-viscous liquid (1.43 g, 32%). bp 130-150°C (0.1 mm Hg). 1H NMR (CDCl₃) δ 2.46-1.18 (m).

2.4.15 Synthesis of spiro[4.4]nona-1,6-dione (2.16)

This compound was prepared by the method of Gerlach & Müller. An acetic acid solution (51 ml) 2.15 (7.5 g, 44 mmol) is heated together with polyphosphoric
acid (25 g) for 5 h. The resulting mixture is poured into ice/water and extracted with benzene. The organic layer is washed with a saturated solution of sodium bicarbonate, dried over magnesium sulfate, concentrated under reduced pressure and distilled under aspirator pressure (@ 90-120°C) affording a water clear liquid (2.5 g, 37%). $^1$H NMR (CDCl$_3$) $\delta$ 2.50-1.75 (m broad); $^{13}$C NMR (CDCl$_3$) $\delta$ 19.70, 34.30, 38.41, 164.64, 218.61.

![Chemical Structure](image)

**2.4.16 Attempted synthesis of 1,6-bia-(2,4-cyclopentadiene-1-ylidene)spiro[4.4]nonane (2.17)**

This compound was attempted to be prepared by the method of Stone & Little. A methanol solution (2 ml) of 2.16 (200 mg, 1.3 mmol) is stirred under argon atmosphere at room temp. Cyclopentadiene (0.9 ml, 13 mmol) is slowly added followed by the quick addition of pyrrolidine (1.1 mL, 13 mmol). The resulting solution is allowed to stir overnight, neutralized with glacial acetic acid (1 mL), diluted in water, and extracted with ether. The organic layer dried over magnesium sulfate, filtered and concentrated under reduced pressure yielding an amber liquid which polymerizes quickly on standing (even at low temperatures).
2.4.17 Synthesis of 4,5-*bis*-methyl-2,2-dimethyl-1,3-dioxolane-4,5-*trans*-bis-carboxylate (2.18)

This compound was prepared by the method of Musich & Rapoport. A benzene solution (80 ml) of dimethyl-L-tartrate (33 g, 0.19 mol) and 2,2-dimethoxy propane (35 mL, 0.28 mol) together with *p*-toluensulfonic acid (0.17 g) was refluxed in a soxhlet apparatus for 6 h. Potassium carbonate (0.20 g) is added and the resulting mixture allowed to cool to room temp. overnight, filtered, concentrated unde reduced pressure, and extracted with ether. The organic layer is then washed with borax, water, dried over magnesium sulfate, filtered, concentrated under reduced pressure and distilled under high vacuum (@80-85°C) affording a water-clear liquid (33.4 g, 81%).

\[
^1\text{H NMR (CDCl}_3) \delta 1.48 (s, 6H), 3.84 (s, 6H), 4.30 (q, 4H), 4.72 (s, 2H).
\]

2.4.18 Synthesis of 4,5-*bis*-pyrrolidylamide-2,2-dimethyl-1,3-dioxolane (2.19)

This compound was prepared by a modified method of Klein *et al.* Seebach *et*
A pyrrolidine solution (25 mL) of 2.18 (2.6 g, 12 mmol) is refluxed for 24 h. The resulting solution is concentrated giving a yellowish solid which is recrystallized from ethanol. mp 153-155°C (3.15 g, 89%). $^1$H NMR (CDCl$_3$) $\delta$ 1.47 (s, 6H), 1.93-1.84 (m, 4H), 1.99-1.94 (m, 4H), 3.48 (t, 4H), 3.77-3.64 (m, 4H), 5.09 (s, 2H); $^{13}$C NMR (CDCl$_3$) $\delta$ 23.57, 25.61, 25.92, 46.20, 46.53, 76.27, 111.66, 166.48. HRMS: M$^+$ (Calcd, Obsd.): C$_{14}$H$_{24}$N$_2$O$_4$ (297.1778, 297.1766), C$_{15}$H$_{24}$N$_2$O$_4$ (296.1732, 296.1738), C$_{10}$H$_{16}$NO$_3$ (198.1145, 198.1133), C$_7$H$_{10}$NO$_2$ (140.0731, 140.0708), C$_5$H$_8$NO (98.0461, 98.0469).

$^{2.4.19}$ Synthesis of 4,5-trans-bis-acetyl-2,2-dimethyl-1,3-dioxolane (2.20)

This compound was prepared by the method of Briggs et al.$^{74}$ A 3M magnesium bromide solution (15 mL, 45 mmol) is slowly added to a chilled THF solution (60 mL) of 2.19 (4.5 g, 15 mmol). The resulting solution is allowed to stir for 1 h, poured into water followed by addition of ammonium chloride until complete dissolution of the precipitated salt. The resulting solution is extracted with DCM. The organic layer is washed with water, dried over magnesium sulfate, filtered, concentrated under reduced pressure and distilled at high vacuum (@ 60-65°C) affording a pale yellow clear liquid (1.55 g, 55%). $^1$H NMR (CDCl$_3$) $\delta$ 1.45 (s, 6H), 2.32 (s, 6H), 4.58 (s, 2H). $^{13}$C NMR (CDCl$_3$) $\delta$ 26.43, 26.53, 81.67, 112.43, 206.44.
2.4.20 Attempted synthesis of 4,5-trans-bis-1-(2,4-cyclopentadien-1-ylidene)ethyl-2,2-dimethyl-1,3-dioxolane (2.21)

This compound was attempted to be prepared by the method of Stone & Little.\textsuperscript{61} and Olah et al.\textsuperscript{62} A methanol solution (10 ml) of 2.20 (1 g, 7.6 mmol) is stirred under argon atmosphere at room temp. Pyrrolidine (6.2 mL, 76 mmol) is slowly added followed by the quick addition of cyclopentadiene (6.2 ml, 76 mmol). The resulting solution is allowed to stir overnight, neutralized with glacial acetic acid (6 mL), diluted in water, and extracted with ether. The organic layer dried over magnesium sulfate, filtered and concentrated under reduced pressure yielding an amber liquid which polymerizes quickly on standing (even at low temperatures).

2.4.21 Synthesis of 1,1'-binaphthyl-2,2'-bis-naphthaldehyde (2.22)
This compound was prepared by the method of Miyano et al. An ethanol solution (35 mL) of 2-nitropropane (3.3 g, 37 mmol) and sodium (0.6 g, 26 mmol) under argon atmosphere is slowly added at 25°C to a DMSO solution (30 mL) of 2,2'-bis-bromomethyl-1,1'-binaphthyl (2.2 g, 5 mmol). The resulting solution is stirred for 3 h at 25°C, followed by heating at 80-100°C for 4 h and allowed to cool to 25°C overnight. The resulting solution is poured into ice-cold water, extracted with DCM, washed with 2M HCl, 1M sodium carbonate, water, dried over magnesium sulfate, filtered and concentrated under reduced pressure affording a yellowish solid (1.2 g, 77%). $^1$H NMR (CDCl$_3$) $\delta$ 8.21-7.10 (m broad), 9.64 (s).

2.4.22 Attempted synthesis of 1,1'-binaphthyl-2,2'-bis-(2,4-cyclopentadien-1-ylidene) (2.23)

This compound was attempted to be prepared by the method of Stone & Little. A methanol solution (2 ml) of 2.22 (1 g, 3.2 mmol) is stirred under argon atmosphere at 25°C. Pyrrolidine (3 mL, 35 mmol) is slowly added followed by the quick addition of cyclopentadiene (3 ml, 36 mmol). A white powder precipitates out almost immediately after the addition is complete. The reaction mixture is allowed to stir overnight, neutralized with glacial acetic acid (2 mL), forming a dark amber gummy material (2.22a) which is separated by filtration. The mother liquor is diluted in water, and
extracted with ether. The organic layer dried over magnesium sulfate, filtered and concentrated under reduced pressure yielding an amber foamy material which polymerizes as a bright yellow solid (2.22b) upon dryness.

2.22a: $^1$H NMR (CDCl$_3$) δ 8.05-7.72 (m, broad), 7.50-6.85 (m, broad), 6.58 (d, 4H), 6.47 (d, 4H); MS m/z (rel. intensity): 406 (C$_{32}$H$_{22}$), 344, 277, 276, 138, 137, 82, 80, 55, 44(100), 41.

2.22b: $^1$H NMR (CDCl$_3$) δ 8.05-7.72 (m, broad), 7.50-6.85 (m, broad), 6.58 (d, 4H), 6.47 (d, 4H).
CHAPTER THREE.
Synthesis of Tricyclo[9.3.0.0^{4,8}]tetradeca-4,7,11,14-tetraene

3.1 Introduction.

Tricyclo[9.3.0.0^{4,8}]tetradeca-4,7,11,14-tetraene (figure 3.1) is potentially an important precursor to chelating bis-cyclopentadienyl metal complexes that could be used as asymmetric catalysts.\textsuperscript{6,7,8,10,18,19} Also, two and three dimensional polymers (of the type shown in figures 3.2 and 3.3) which could exhibit electrical conductivity,\textsuperscript{76} could be prepared from this target molecule.

\begin{figure}[h]
\centering
\includegraphics[width=0.5\textwidth]{fig31.png}
\caption{Tricyclo[9.3.0.0^{4,8}]tetradeca-4,7,11,14-tetraene.}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=0.5\textwidth]{fig32.png}
\caption{Model of the structure (monomer) of a possible 2D conductive polymer.}
\end{figure}
3.1.1 Retrosynthetic analysis.

The purpose of the retrosynthetic analysis as it has been described in the previous chapters is to take a molecule and break it down by a series of disconnections that leads us to possible simple starting materials.

A retrosynthetic analysis shows a systematic (not the only one) approach in finding the shortest possible route in synthesizing a molecule as complex as it may be.

Breaking of tricyclo[9.3.0.0^4,8]tetradeca-4,7,11,14-tetraene can be done in several different ways. Two of the most symmetric breakings are going to be analyzed, namely, via thermal functional group interconversion (A), and via Diels-Alder cyclocondensation (B) as it is depicted in figure 3.4.

3.1.1.1 Analysis via thermal interconversion (A).

Retrosynthetic analysis A starts with a thermal rearrangement$^3$ of A.1 giving the
Figure 3.4 Retrosynthetic analysis of the monomer leading to the possible conductive polymer
tricyclic-di-spiro compound A.2 which might be formed from synthon A.3 by a
(bis)-nucleophilic attack of cyclopentadienyl anion.² Functional group interconversion
of A.3 leads to the oxaspiro compound A.4 by an opening of the ether ring with boron
reagents,⁷⁷-⁷⁹ and finally A.4 can be formed from the simple starting materials
cyclopentadiene and diethylene glycol¹³ as shown in figure 3.4.

3.1.1.2 Analysis via Diels-Alder Cyclocondensation (B).

Retrosynthetic analysis B starts with a functional group interconversion⁸⁰-⁸³ of
tricyclo[9.3.0.0⁴,8]tetradeca-4,7,11,14-tetraene leading to B.1 (a 5,7,12,14-
tetrasubstituted tricyclo[9.3.0.0⁴,8]tetradecane) which through a series of functional
group interconversions⁸⁴-⁸⁶ leads to B.2 (pentacyclo[12.2.1.1⁶,⁹]0²,1³,1⁵,1⁰]octadeca-
7,15-diene). Further functional group interconversions⁸⁷-⁹⁰ transforms B.2 into the
synthon compound B.3. Retro-Diels-Alder transformation⁹¹,⁹² of B.3 leads to
simple, commercially available starting materials, such as 1,5-cyclooctadiene and
hexasubstituted cyclopentadienes⁹³-⁹⁵ as shown in figure 3.4.

3.1.2 Diels-Alder Cyclocondensation Reaction.
A Brief Introduction.

Otto Diels and Kurt Alder⁹⁶,⁹⁷ were already able to identify essential characteristics
of the [4+2]-cycloaddition:
1) The addition reactions take a stereospecific course resulting in a cis addition.
2) In the case of cyclic dienes the endo principle is often followed.
3) Unsymmetrical substituted reactants combine regiospecifically to give the
cycloadduct.  

4) With maleic anhydride, valued in those days as the most reactive test dienophile, electron releasing groups in the diene accelerate the reaction, while electron withdrawing groups in the diene retard it.

The Diels-Alder cyclocondensation reaction has developed into one of the most important organic reactions, from both an experimental and a theoretical point of view, and the concepts of its mechanism were most strongly influenced by the Woodward-Hoffmann rules. A great amount of experimental and theoretical studies has been published on the Diels-Alder reactions, including reviews which facilitate general access to it; however, the mechanism of this reaction is still in controversy.

The preparative potential of the [4+2]-Diels-Alder cyclocondensation reaction (which was discovered more than 60 years ago) has not been exhausted yet. The almost unlimited possibility to vary the diene- and the dienophile- components provides in many cases the simplest access to cyclic derivative compounds. The possibility of using cyclic compounds, heterodiienes and heterodienophiles opens up access to one-pot syntheses to monocyclic, bicyclic and polycyclic carbo- and heterocycles. The high preparative value of [4+2]-Diels-Alder cycloadditions follows, not only from the mostly very high yields, but also from the stereo-, diastereo-, enantio- and generally regiospecific course of the reaction.

3.1.2.1 Stereoelectronic Effects in the Diels-Alder Cyclocondensation Reaction.

Through-space and through-bond orbital interactions as a classic concept was introduced by Hoffman, Imamura and Hehre in 1968. DABCO and pyrazine (figure
3.5) are examples in which nitrogen non-bonding orbitals interact through three σ bonds.\textsuperscript{139} Hoffmann et al's model calculations\textsuperscript{138} suggest that:

1) The energy level ordering of the orbitals resulting from through-\(n\)-bonds interactions depends on the parity of the number \(n\), of the relaying σ bonds; Thus, the parity rule suggests that through-space and through-\(n\)-bonds interactions reinforce each other for even values of \(n\) but are mutually antagonistic for odd values of \(n\),

2) For a given value of \(n\), the extent of through-\(n\)-bonds, depends on the geometry of the σ relay and is maximized for an all trans arrangement of σ bonds.\textsuperscript{138,140,141} For example, interactions through-4-bonds is predicted, by the trans effect, to diminish along the series: \(tt > tc > cc\) (arrangement of σ bonds), see figure 3.6,

3) Interactions through-\(n\)-bonds are attenuated slowly with increasing \(n\) and may be significant for \(n=8\), as suggested by extended Hückel calculations and in contrast to through-space effects.\textsuperscript{139}
3.1.2.1.1. Through-Bond Orbital Interactions.

There is experimental evidence\textsuperscript{139,142-144} by means of photoelectron spectroscopy\textsuperscript{145} that the \textit{parity} rule for orbital interactions through-\textit{n}-bonds is valid for at least values of \textit{n}=1-4. There is one example of orbital interactions through 8 \textit{a} bonds.\textsuperscript{146}

As an example, in the \textit{itt} model shown in figure 3.7, the \textit{a}, \textit{a} mixing occurs primarily through overlap of the \textit{a} molecular orbital (MO) with that part of the \textit{a} MO which is contributed by the atomic orbital (AO) on the carbon adjacent to the \textit{a} bond as shown by the "solid" lines in figure 3.7. All \textit{trans} planar conformation of \textit{a} bonds maximizes the \textit{a} level of interaction.\textsuperscript{139} Any deviations from this conformation will result in weakening the vicinal \textit{a},\textit{a} antibonding interactions, resulting in the reduction of the \textit{a} level of interaction, \textit{i.e.} the extent of through-bond interaction. Planar \textit{cis} arrangement of \textit{a} bonds greatly reduce through-bond interactions because \textit{cis} vicinal \textit{a},\textit{a} interactions become bonding; \textit{e.g.} the overlap between \textit{a}\textsubscript{23} and \textit{a}\textsubscript{45} in the model depicted in figure 3.7 is bonding when the dihedral angle C2-C3-C4-C5 = 0°.\textsuperscript{139} Quantitative methods have been developed, in order to explain in more detail such orbital interactions, by Weinhold,\textsuperscript{141,147} Heilbronner\textsuperscript{148,149} and coworkers. Balaji \textit{et al.}\textsuperscript{142} provides the first unequivocal evidence that through-\textit{n}-bond orbital interactions can operate over large distances (7Å if measured direct or 9Å if traced through the
connecting $\sigma$ bonds), and that indeed through-$n$-bonds interactions involving $\pi$ MO's of the dienes are very long-range, \textit{e.g.} for values of $n$ as large as 16 or, equivalently, for an inter-$\pi$-orbital separation of 21Å \cite{150,151}. Miller \textit{et al.}\cite{150,151} have provided some amazing examples of long-range intramolecular interaction occurring over large distances.

![Diagram of orbitals](image)

\textbf{Fig. 3.7} \textit{ttt} model showing the $\pi,\sigma$ mixing of orbitals

The through-$n$-bond orbital interaction idea has not until recently enjoyed much popularity. This is largely on the account of the widely held belief that the coupling between $\sigma$ and $\pi$ orbitals is too weak to be considered, however, as it has been mentioned above, there is literature evidence based upon different type of studies that clearly indicate that such a belief is unjustified, and that through-$n$-bond orbital interactions are energetically far from being insignificant even for double bonds that are separated by distances of up to 7.5Å.

The work to be described herein will deal with experimental details that would hopefully lead to an understanding of the Diels-Alder cyclocondensation reaction by studying the factors that affect the stereochemical output. One of such factors to be considered is the through-$n$-bond orbital interaction. Results concentrating for the most part all the attention to the $\pi$-face of the diene have been published\cite{152-155}, contrary to the system that is going to be described in this work, namely, the dienophile.
Because of the nature of the dienes employed in this work, namely, dienes with a C₂-symmetry axis, the attention is focused, in a unique way, in the nature of the dienophile. The model shown in figure 3.7, in which there are 4 saturated carbons (C₂-C₃-C₄-C₅) between the double bonds (C₁ & C₆), applies very well to the framework of the system to be described in this work.

3.1.2.1.2. Through-Space Orbital Interactions.

A through-space orbital interaction is simple to analyze when there is a direct spatial overlap of two functional groups. Norbornadiene is a good example to visualize through-space orbital interactions: The delocalized combinations after interactions are shown in figure 3.8, identified by their proper symmetry designations (S:symmetric, A:antisymmetric). The π levels are defined as shown in figure 3.9.

![Fig. 3.8 Norbornadiene showing the orbitals and their symmetries](image)

Some specific consequences of the interactions are the following:

1) The ionization potential of norbornadiene should be smaller in magnitude than that of a model norbornene. This is confirmed by Bishof et al.¹⁵⁶

2) Either removing one electron from SA to form the radical cation or adding one to form the radical anion should promote bond formation between C₂ and C₆ or C₃ and C₅. Therefore, the extent and sign of orbital interaction have direct chemical
and physical consequences.

Fig. 3.9 \( \pi \)-levels in norbornadiene

Another example illustrating the through-space orbital interaction is that of the \textit{cis} and \textit{trans} isomers of an azo compound (figure 3.10). In the \textit{cis} isomer one would expect a dominant through-space orbital interaction, with the S combination at lower energy. This is confirmed by various calculations on the system.\textsuperscript{140} The interesting case is the \textit{trans} isomer. The first inclination is to say that the overlap between the two hybrids is small since they are pointing away from each other. The actual value of this overlap is sizable, and probably even somewhat larger than the corresponding vicinal \textit{cis} overlap.\textsuperscript{157}

Fig. 3.10 \textit{Cis} and \textit{trans} conformations of azo-compounds

Balaji \textit{et al.}\textsuperscript{142} report the evidence of a large through-space orbital interaction in
tetracyclo[6.2.1.1^{3,6}0.2.7]dodecane\textsuperscript{158} (TCDD in figure 3.11) as well as evidence for through-space orbital interaction by a hyperconjugative interaction between the $\pi$ MO's and the orbitals of the intervening methylene groups in hexacyclo[10.2.1.1^{15,8}3,10^4,90^2,11]tetradecane\textsuperscript{159} (HCTD in figure 3.11) as well as in octacyclo[14.2.1.1^{17,10}5,12^3,14^0,2,15^0,4,130^6,11]octadecane.\textsuperscript{159} (OCOD in figure 3.11). This through-space orbital interaction that Paddon-Row termed laticyclic hyperconjugation\textsuperscript{159} is depicted in figure 3.11.

Experimental results are going to be described in order to find out whether this particular type of long-range through-space orbital interaction plays a role in determining the stereochemical output of the Diels-Alder cyclocondensation reaction.

The uniqueness of this work is the fact, as described earlier, that the attention is focused in the nature of the dienophile as opposed to the nature of the diene.

\begin{figure}
\centering
\includegraphics[width=\textwidth]{structures.png}
\caption{Structures of TCDD, HCTD and OCOD}
\end{figure}

Eventhough laticyclic hyperconjugation as a through-space orbital interaction involving $\pi^*$ MO's and orbitals of the methylene bridging groups are possible, Balaji
et al.\textsuperscript{142} suggest, based in experimental work using electron transmission spectroscopy, that they (through-space orbital interactions) are much less important than the C-C $\sigma$ through-$n$-bonds interactions.
3.2 Results

3.2.1 Synthesis \textit{via} Thermal Rearrangement.

As a model reaction and because of being a precursor in the synthesis of neutral compounds that are believed to be active antitumor drugs due to the presence of a chelating organic hydrophilic moiety together with a lipophilic cyclopentadienyl ligand making this compounds (shown in figure 3.12) more permeable through the cell membrane.\textsuperscript{160,161} 2,2'-iminobisethanol 3.1 was converted into the corresponding 2,2'-(p-toluensulfonylimino) \textit{bis}ethyl di(p-toluenesulfonate) 3.2 in very good yield by treatment with \textit{p}-toluensulfonfyl chloride in pyridine at 0°C.

\begin{center}
\textbf{Fig. 3.12} Model of a neutral chelated metallocene compound as a possible antitumor agent
\end{center}

Compound 3.2 was further interconverted into the corresponding N-(\textit{p}-toluensulfonyl)-8-azaspiro[4.5]deca-1,3-diene 3.3 in poor yield (15-25\%) by treatment with sodium cyclopentadienide in hexamethylphosphoramid (HMPA) as shown in figure 3.13.
Successful recrystallization of 3.3 permitted its characterization by X-ray structural analysis. Figure 3.14 shows an ORTEP diagram of 3.3.

Knowing that the insertion of a cyclopentadienyl unit on a bis-substituted compound to give the corresponding spiro derivative can be accomplished successfully in fair yields, the synthesis of tricyclo[9.3.0.0^2\text{4},8]\text{4,7,11,14}-tetradeca-4,7,11,14-tetraene started by converting diethylene glycol in very good yield into the corresponding ditosylate derivative compound 3.4 by treatment with p-toluensulfonyl chloride in pyridine at low temperature. Compound 3.4 was then treated with sodium cyclopentadienide in order to afford the oxa-spiro cyclopentadienyl derivative compound 3.5 as depicted in figure 3.15.

Several attempts were tried to maximize the yield by using solvents like dimethyl formamide (DMF) or hexamethylphosphoramid (HMPA) in different concentrations as shown in figure 3.16. The best condition found for such reaction was when HMPA is used as a solvent in the following concentrations: [NaH]: 1.0-2.5 M, [3.4]: 0.4-0.8 M giving a yield of 27-30%. Compound 3.5 was then transformed into the
Figure 3.14 ORTEP diagram of N-\((p\text{-toluensulfonyl})\)-8-azaspiro\([4.5]\)deca-1,3-diene 3.3
Figure 3.16 Effect of the concentration of reactants upon %yield obtained in the synthesis of 8-oxaspiro[4.5]decane-1,3-diene 3.5
corresponding opened bromo-alcohol derivative 3.6 by making use of dimethyl-boron bromide as

![Chemical Reaction Diagram](image)

**Fig. 3.17** Attempted synthesis of 1-(2-O-p-toluensulfonyl)-1-(2-bromoethyl)-cyclopenta-2,4-diene (3.7)

depicted in figure 3.17. Compound 3.6 was found to be very reactive since even at the time of distilling over in the collecting flask (0°C) it started to decompose (see figure 3.18).

![Speculative Routes Diagram](image)

**Fig. 3.18** Speculative routes followed by 3.6

Attempts to interconvert 3.6 into the corresponding mono(p-toluensulfonyl) derivative 3.7 in the receiving flask during distillation were unsuccessful giving a mixture of compounds that were not identified as compound 3.7 by $^1$H NMR spectroscopy.
3.2.2 Synthesis via Diels-Alder Cyclocondensation.

The synthesis of tricyclo[9.3.0.0⁴,8]tetradeca-4,7,11,14-tetraene via Diels-Alder cycloaddition started by preparing 1,1-dimethoxy-2,3,4,5-tetrachlorocyclopentadiene 3.8 from the corresponding hexachlorocyclopentadiene, in good yields, by refluxing it in a potassium hydroxide-methanol solution overnight. The next step is a Diels-Alder cycloaddition of compound 3.8 with 1,5-cyclooctadiene (COD). The reaction takes place exothermically at 130-140°C affording a mixture of two stereoisomers, namely, the endo-endo anti (3.9) and endo-endo syn (3.10) 1,6,7,8,9,14,15,16-octachloro-17,17,18,18-tetramethoxypentacyclo[12.2.1.1⁶,90²,13⁰5,10]octadeca-7,15-dienes in fairly good yield (88%) as shown in figure 3.19. The separation of both isomers is carried out by washing the mixture thoroughly with ether while filtering. 3.9, which is insoluble in ether, remains as a fine white powder. Evaporation of the filtrate results in pure 3.10. Successful recrystallization of both isomers permitted their characterization by X-ray crystal structure determination. Figures 3.20 and 3.21 show ORTEP diagrams of 3.9 and 3.10 respectively.

As part of the synthesis following a side route toward tricyclo[9.3.0.0⁴,8]tetradeca-4,7,11,14-tetraene via the intermediate pentacyclo[12.2.1.1⁶,90²,13⁰5,10]octadecane, as shown in figure 3.22, the cycloaddition of COD to hexachlorocyclopentadiene (HCCP) resulted in a mixture of two stereoisomers, analogous to 3.9 and 3.10, namely, the endo-endo anti 3.11 and endo-endo syn 3.12 1,6,7,8,9,14,15,16,17,17,18,18-dodecachloropentacyclo[12.2.1.1⁶,90²,13⁰5,10]octadeca-7,15-diene in good yields (90-95%) as depicted in figure 3.23. The separation of both 3.11 and 3.12 is carried out similarly to that of 3.9 and 3.10. Successful recrystallization of both isomers permitted their characterization by X-ray
Figure 3.19 Diels-Alder cyclocondensation reaction of DMTCCP with COD

Figure 3.19 Diels-Alder cyclocondensation reaction of DMTCCP with COD
Figure 3.20 Pluto diagram of endo-endo-anti-1,6,7,8,9,14,15,16-octachloro-17,17,18,18-tetramethoxy pentacyclo[12.2.1.1^{6,9}.0^{2,13}.0^5,10.]octadeca-7,15-diene 3.9
Figure 3.21 Pluto diagram of *endo-endo-syn*-1,6,7,8,9,14,15,16-octachloro-17,17,18,18-tetramethoxy pentacyclo[12.2.1.1^6.9.0^2.13.0^5.10.]octadeca-7,15-diene 3.10
Figure 3.22 Reaction scheme for the synthesis of pentacyclo[12.2.1.1^{6,9}.0^{2,13}.0^{5,10}]octadeca-7,15-diene
Figure 3.23 Diels-Alder cyclocondensation reaction of HCCP with COD
Figure 3.24 Pluto diagram of *endo-endo-anti*-1,6,7,8,9,14,15,16,17,17,18,18-dodecachloro pentacyclo[12.2.1.1<sup>6,9</sup>.0<sup>2,13</sup>.0<sup>5,10</sup>]octadeca-7,15-diene 3.11
Figure 3.25 ORTEP diagram of $\text{endo-endo-syn-1,6,7,8,9,14,15,16,17,17,18,18-dodecachloro}$ \(\text{pentacyclo[12.2.1.1^{6,9}.0^{2,13}.0^{5,10}.]octadeca-7,15-diene} \text{ 3.12}$
crystal structure analysis.\textsuperscript{164} Figures 3.24 and 3.25 depict Pluto and ORTEP diagrams of 3.11 and 3.12 respectively.

### 3.2.2.1 Detailed study of the Diels-Alder Cyclocondensation Reaction

Preliminary results of the Diels-Alder cycloaddition to form compounds 3.9 and 3.10 suggested a ratio of stereoisomers to be in the vicinity of 1:4 \textit{syn:anti}. Formation of compounds 3.11 and 3.12 showed the ratio of \textit{syn:anti} being in the vicinity of 1:4. Attempts to detect retro-Diels-Alder by heating pure and separate samples of 3.9, 3.10, 3.11 & 3.12 in an NMR tube under argon atmosphere at 250°C failed. These results suggest that equilibration of stereoisomers does not take place. In order to study the cycloaddition in more detail and to try to understand the type of process involved, the corresponding monoadducts 3.13 and 3.14 were successfully synthesized, as shown in figure 3.26. Successful recrystallization of 3.13 permitted its characterization by X-ray crystal structure analysis\textsuperscript{165} showing the stereochemistry of the eight-membered ring being in the twisted-boat conformation. Figure 3.27 shows an ORTEP diagram of 3.13.

A set of experiments that could be monitored by $^1$H NMR was designed, namely cycloaddition of COD with 4 eq. of HCCP and with 4 eq. of DMTCCP respectively; cycloaddition of 3.13 with 3 eq. of HCCP and 3 eq. of DMTCCP respectively; and finally, cycloaddition of 3.14 with 3 eq. of HCCP and 3 eq. of DMTCCP respectively as shown in figure 3.28.
Fig. 3.26 Synthesis of the Diels-Alder monoadducts 3.13 and 3.14

$^1$H NMR spectroscopy of the cycloadditions showed no difference in ratio of isomer formations giving a constant value of 1:4 ratio for syn:anti stereoisomers regardless of the substrate or dienophile employed. Apparently, because of the different solubilities of both isomers (due to their difference in polarities), one of the isomers precipitates in the NMR tube, thus, changing the detectable ratio of the stereoisomers when the preliminary results were obtained.

$^1$H NMR monitoring of the cycloadditions was done by performing the reactions neat inside an ampule sealed with a septum under argon atmosphere and continuous stirring at 133-140°C. After 3 h of stirring, the reaction mixtures are dissolved in CDCl$_3$ and the ratio of both stereoisomers is determined by calculating the area of the relative intensities of the methoxy signals (when appropriate), otherwise, by the relative intensities of the H1 and H3 signals, since their chemical shifts vary from one stereoisomer to the other in the order of 0.2 to 0.7 ppm, as shown in figure 3.29.

By performing the $^1$H NMR study on the above described cycloadditions, the "mixed" Diels-Alder diadduct was separated; namely, the endo-endo-anti-
Figure 3.27 ORTEP diagram of endo-1,10,11,12,13,13-hexachlorotricyclo[8.2.1.0^2,9.]trideca-7,11-diene 3.13
Figure 3.28 Reaction scheme for the formation of the Diels-Alder diadducts via cyclooctadiene and via the corresponding monoadducts showing the ratio of stereoisomers
Fig. 3.29 Chemical shifts for stereoisomers 3.9, 3.10, 3.11 and 3.12
1,6,7,8,9,14,15,16,17,17-decachloro-18,18-dimethoxypentacyclo
[12.2.1.16,9,02,13.05,10]octadeca-7,15-diene 3.15. Successful recrystallization permitted the determination of the crystal structure of 3.15. Figure 3.30 shows a Pluto diagram of 3.15.

In order to find out whether steric effects (due to the bulkiness of the methoxy or chlorine units in the bridge-head position of the norbornene unit) play a meaningful role in the stereoselectivity of the cycloaddition; COD was reacted with 1,2,3,4-tetrachloro-1,3-cyclopentadiene (TCCP, in which two hydrogens are occupying the place of either the methoxyls or the chlorine units) monoadduct 3.13 was reacted with TCCP and also, monoadduct 3.14 was reacted with TCCP (see figure 3.31). These cycloadditions were not clean reactions because of the formation of a non-isolable tar-like residue bringing the yield down to below 55%; therefore, a complete study was not reliable on NMR spectroscopy.

However, compounds 3.16, 3.17, and 3.18 were successfully synthesized, separated and fully characterized from the above cycloadditions. Successful recrystallization permitted their characterization by X-ray crystal structure analysis. Figures 3.32, 3.33 and 3.34 show ORTEP diagrams of 3.16, 3.17 and 3.18 respectively.

Quantitative molecular mechanics calculations (MM2) performed in the macromodel system on the diadducts 3.10, 3.12 (boat compounds), and 3.9, 3.11 (chair compounds) are summarized (and compared to quantitative X-ray data) in figures 3.35 and 3.36 respectively. MM2 results for compound 3.10 are in agreement with the experimental data from X-ray. On the other hand, X-ray data for 3.12 shows a discrepancy to the MM2 results. Apparently, the lattice energy for an almost perfect boat conformation in 3.12 is smaller than the required to obtain a twisted boat conformation, allowing it to remain as a perfect boat.
Figure 3.30 Pluto diagram of 1,6,7,8,9,14,15,16,17,17-decachloro-18,18-dimethoxypentacyclo [12.2.1.1^{6,9}.0^{2,13}.0^{5,10}]octadeca-7,15-diene 3.15
Figure 3.31 Reaction scheme for the formation of the Diels-Alder diadducts 3.16, 3.17, and 3.18
Figure 3.32 ORTEP diagram of *endo-endo-anti*-1,6,7,8,9,14,15,16-octachloro pentacyclo[12.2.1.1<sup>6</sup>.0<sup>2</sup>.1<sup>3</sup>.0<sup>5</sup>.10.]octadeca-7,15-diene 3.16
Figure 3.33 ORTEP diagram of endo-endo-anti-1,6,7,8,9,14,15,16,17,17-decachloro pentacyclo[12.2.1.1^6,9.0^2,13.0^5,10]octadeca-7,15-diene 3.17
Figure 3.34 ORTEP diagram of endo-endo-anti-1,6,7,8,9,14,15,16-octachloro-17,17-dimethoxy pentacyclo[12.2.1.1^{6,9}.0^{2,13}.0^{5,10}]octadeca-7,15-diene 3.18
Twisted boat conformation of 3.10 is more stable than its parent compound in the twisted chair conformation (3.9) by 11.1 KJ/mol. These results are rather striking since such energy difference does not seem to contribute in changing the ratio of stereoisomer formation. On the other hand, 3.12 (twisted boat conformation) is less stable than 3.11 (chair conformation) by 8.4 KJ/mol.

![Diagram of molecular structure]

<table>
<thead>
<tr>
<th> </th>
<th>X-Ray*</th>
<th>MM2</th>
<th>X-Ray</th>
<th>MM2</th>
</tr>
</thead>
<tbody>
<tr>
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</tr>
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<td>2.3</td>
<td>-27.4</td>
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<tr>
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<td>-5.4</td>
<td>1.1</td>
<td>3.6</td>
</tr>
<tr>
<td>$\theta_4$</td>
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<td>28.1</td>
<td>0.7</td>
<td>-27.4</td>
</tr>
</tbody>
</table>

*Two independent molecules in the unit cell

Fig. 3.35 Quantitative MM2 data compared to that of X-ray for 3.9 and 3.11
Fig. 3.36 Quantitative MM2 data compared to that of X-ray for 3.10 and 3.12

Figures 3.37 and 3.38 depict the qualitative MM2 calculation results compared to those of X-ray for compounds 3.10, 3.12 and 3.9, 3.11 respectively.

Quantitative molecular mechanics calculations (MM2) performed in the macromodel system from crystallographic data on the monoadducts 3.13 and 3.14 in their chair and boat forms suggest, that 3.13 in the chair conformation is less stable than the boat conformation by 3 KJ/mol. This result is in agreement with the actual conformation adopted in the crystalline state (boat conformation, see figure 3.27). Similarly, 3.14 is suggested to be less stable in the chair conformation than in the boat conformation by 0.9 KJ/mol.

In order to find out whether there is some steric effect of the hydrogens α to the cyclooctene double bond in the monoadduct in both chair and boat conformations and
Figure 3.37 Comparison of qualitative MM2 and X-ray data for 3.10 and 3.12
Figure 3.38 Comparison of qualitative MM2 and X-ray data for 3.9 and 3.11
Figure 3.39 PCMODEL drawing of the interaction between the monoadduct in the chair conformation and the incoming electron deficient diene. Total relative energy: 27.84 KJ/mol
Figure 3.40 PCMODEL drawing of the interaction between the monoadduct in the boat conformation and the incoming electron deficient diene. Total relative energy: 26.51 KJ/mol
the incoming electron-deficient diene (to give the corresponding Diels-Alder diadduct), PCMODEL calculations showed that both transition states are energetically similar, with the transition state when the monoadduct is in the boat conformation being more stable than the corresponding chair transition state by 1.3 KJ/mol. Both transition states are depicted in figures 3.39 and 3.40.

The suggestion by Vogel et al.\textsuperscript{169} that stereoselectivity is governed by the relative stabilities of the diastereisomeric diadducts does not appear to be true with compounds \ref{eq:3.9}, \ref{eq:3.11} and \ref{eq:3.10}, \ref{eq:3.12} respectively as suggested by MM2 calculations.

The fact that both boat conformations in \ref{eq:3.13} and \ref{eq:3.14} are more stable than their corresponding chair conformations as suggested by MM2 calculations, together with the fact that steric interactions, as suggested by PCMODEL calculations on the intermediates, do not play a meaningful role in controlling dienophile face selectivity, suggests that there might be some kind of long range through space $\pi-\sigma^*-\pi$ intramolecular electronic interaction\textsuperscript{138,140,142,146,170-173} as mentioned in the introductory section of this chapter and as depicted in figure 3.41 (for comparison purposes, see figure 3.7). There is theoretical and experimental evidence for trans $\pi-\sigma^*-\pi$ conjugation being more effective than cis $\pi-\sigma^*-\pi$ conjugation,\textsuperscript{139,142-146} thus explaining the difference in stereoselectivities encountered in which the diadduct formed in excess is the endo-endo-anti (chair) stereoisomer.
In order to corroborate the long range through space intramolecular electronic interaction, compound 3.14 was successfully reduced to the corresponding endo-12,12-dimethoxy-tricyclo[8.2.1.0^2,8]dodeca-5-ene (3.19) as it is depicted in figure 3.42. Compound 3.19 was reacted with HCCP and DMTCCP respectively in a 1:3 equivalent ratio at 133-140°C for 3 h under inert atmosphere (as shown in figures 3.43 and 3.44) followed by the determination, by $^1$H NMR, of the boat:chair isomer ratio of the final products 3.20:3.21 and 3.21:3.22 respectively. Under the reaction

![Diagram](image_url)

**Fig. 3.42** Synthesis of endo-13,13-dimethoxy-tricyclo[8.2.1.0^2,8]trideca-5-ene (3.19)
Figure 3.43 Diels-Alder cyclocondensation reaction of 3.19 with HCCP
Figure 3.44 Diels-Alder cyclocondensation reaction of 3.19 with DMTCCP
Figure 3.45 ORTEP diagram of *endo-endo-anti*-1,14,15,16,17,17-hexachloro-18,18-dimethoxy pentacyclo[12.2.1.1^6.9.0^2.13.0^5.10.]octadeca-7,15-diene 3.20
Figure 3.46 ORTEP diagram of \textit{endo-endo-anti-1,14,15,16-tetrachloro-17,18,18-tetramethoxy pentacyclo[12.2.1.1^6.9.0^2.13.0^5.10.]octadeca-7,15-diene} 3.22
conditions only 5-7% of boat isomers were detected. This greater selectivity (12-14:1 anti:syn) of 3.19 compared to that of 3.13 and 3.14 (4:1 anti:syn) is consistent with a more effective $\pi-\sigma^*-\pi$ overlap in the anti orientation since the more electron rich norbornene double bond of 3.19 donates more electron density towards the cyclooctene subunit, thus stabilizing the chair conformer over the boat conformer than that of 3.13 or 3.14. The endo-endo isomers 3.20 and 3.22 were characterized by spectroscopic techniques. Successful recrystallization of 3.20 and 3.22 permitted their characterization by X-ray crystal structure analysis. Figures 3.45 and 3.46 show the ORTEP diagrams of 3.20 and 3.22 respectively.

Recrystallization of 3.22 in ethanol resulted in the formation of endo-endo-anti-9,14,15,16,18,18-hexachloro-17,17-diethoxypentacyclo[12.2.1.16*9.12*13.05,10]octadeca-7,15-diene 3.24 in which the methoxy groups are interchanged by ethoxy groups as it is depicted in figure 3.47. Compound 3.24 was fully characterized by spectroscopic techniques and its structure was confirmed by X-ray crystal structure analysis. Figure 3.48 shows an ORTEP diagram of 3.24.

![Fig. 3.47 Formation of endo-endo-anti-9,14,15,16,18,18-hexachloro-17,17-diethoxypentacyclo[12.2.1.16*9.12*13.05,10]octadeca-7,15-diene 3.24 during recrystallization of 3.20](image)

In order to establish whether the Diels-Alder cyclocondensation reaction is
Figure 3.48 ORTEP diagram of endo-endo-anti-1,14,15,16,17,17-hexachloro-18,18-diethoxy pentacyclo[12.2.1.1^{6,9}.0^{2,13}.0^{5,10}].octadeca-7,15-diene 3.24
Figure 3.49 Reaction scheme for the Diels-Alder cyclocondensation reaction of the monoadducts 3.13 and 3.14 with DPIBF showing the ratio of stereoisomers.
Figure 3.50 Pluto diagram of 15,16-benzo-18,18-dimethoxy-1,14-diphenyl-6,7,8,9-tetrachloro-17-oxapentacyclo[12.2.1.1^6^9.0^2^13.0^5^10.]octadeca-7-ene 3.25
dependent upon the type of diene employed, a more reactive diene than the three already used dienes, namely, 1,3-diphenylisobenzofuran (DPIBF) was reacted with monoadducts 3.13 and 3.14 in a 1:3 equivalent ratio respectively. $^1$H NMR study of these reactions shows that the ratio of the endo-endo products (the only ones detected) remains constant (1:4 boat:chair, see figure 3.49), in agreement with previous experiments when HCCP and DMTCCP are used as the electron deficient dienes. (For comparison see figure 3.28).

The stereochemistry of the four different compounds isolated from the above described experiment, namely, the endo-endo-anti 3.25, 3.27 and the endo-endo-syn 3.26, 3.28 was determined by $^1$H NMR spectroscopy and comparison with similar compounds such as 3.9, 3.15, 3.16, 3.17, and 3.18 (see figures 3.19, 3.28, 3.32, 3.33, and 3.34). The ratio of boat:chair isomers was determined by the relative intensity of the methoxy signals in the case of 3.25 and 3.26 and by the relative intensity of the methylene protons in the case of 3.27 and 3.28. Compounds 3.25 and 3.27 were separated from the mixture and characterized by spectroscopic techniques. Successful recrystallization of 3.25 permitted its characterization by X-ray crystal structure analysis. Figure 3.50 depicts the Pluto diagram of 3.25 and figure 3.51 depicts compound 3.27 with the stereochemistry as determined by NMR spectroscopy.
Compound 3.19 was hydrolyzed to the corresponding ketone derivative, compound 3.29, under sulfuric acid-ether conditions in fairly good yields as depicted in figure 3.52. Successful recrystallization permitted its characterization by X-ray crystal structure analysis.

Figure 3.53 shows the ORTEP diagram of 3.29. It is interesting that the cyclooctene subunit in compound 3.29 adopts the twisted-boat conformation, analogous to the conformation adopted by the cyclooctene subunit in compound 3.13 (see figure 3.27). This result is in agreement with the notion of long-range electronic interaction (already described in the introductory section of this chapter). There is evidence\textsuperscript{174,175} that the
π* of the carbonyl interacts with the electron rich double bond of the norbornene subunit, having a destabilizing effect via through-space orbital interaction with the σ*
orbital at the methylene-methylene bond in the cyclooctene ring (see figure 3.54) increasing thus the population of the boat stereoisomer which could actually be stabilized by through-space orbital interaction between the π-HOMO of the cyclooctene subunit and the σ orbital of the ring fusion bond.

![Diagram of molecular orbitals](image)

**Fig. 3.54** Compound 3.29 showing the interaction between π* of the carbonyl
and the π-HOMO of norbornene

Compound 3.29 was reacted with 3 eq. of HCCP and DMTCCP respectively, under neat condition and argon atmosphere at 133-140°C for 3 h. The results obtained from this particular reaction show that not only the endo-endo-anti diadduct (D) is formed (by NMR spectroscopy data comparison with compounds 3.11 and 3.12 -see figure 3.29 for comparison-, D: doublet of doublets at 2.82 ppm for H1, multiplet at 1.10-0.88 ppm for H2 and a triplet at 6.45 ppm for the vinylic protons), but also an endo-endo-endo-triadduct: 1,8,9,10,11,18,19,20,21,23,23-dodecachloro-22-oxoheptacyclo [16.2.1.13,16.18.11.02,17.04,15.07,12.]trieicosa-9,19-diene (T') is formed as shown in figure 3.55 (by reaction of the norbornenone double bond with another mol of the electron deficient diene). Successful separation and recrystallization
Figure 3.53 ORTEP diagram of tricyclo[8.2.1.0^{2,9}].trideca-5,11-diene 3.29
permitted its characterization by X-ray crystal structure analysis (figure 3.74 shows a Pluto diagram of T). Therefore, the attempt on obtaining a ratio for only the endo-endo stereoisomers was unfruitful. In order to find out whether the cyclooctene double bond is more reactive than the norbornone double bond, equimolar amounts of 3.29 are reacted with HCCP, it is also found that the reaction mixture contains T together with D and also 3.29 in an approximate ratio of 2:6:1 T:D:3.29 (as determined by the relative intensities of the vinylic signals in the case of D [triplet at 6.45 ppm] and 3.29 [triplets at 6.46 and 5.75 ppm] and the norbornanone protons in T [doublet of doublets at 2.98 ppm] by $^1$H NMR spectroscopy).

In order to have a better understanding as of what would be the type of stereoelectronic effect responsible for such molecular behaviour observed in this particular Diels-Alder cyclocondensation reaction, compound 3.29 was reduced, via Wolff-Kishner reduction, to the corresponding hydrocarbon 3.30 (as depicted in figure 3.56) in very low yields (5-15%). An alternative route toward the synthesis of 3.30 proved to be more successful, namely, via reduction of 3.19 with sodium in refluxing ethanol. The % yield is in the vicinity of 65% and is made only in two steps from COD, as shown in figure 3.56.

Analogous to the cyclocondensation reaction of 3.29 with HCCP and DMTCCP respectively, cyclocondensation reaction between 3.30 with 3 eq. of HCCP and DMTCCCP respectively, shows that not only the endo-endo-anti diadduct (DD) is formed (by NMR spectroscopy data comparison with compounds 3.11 and 3.12 -see figure 3.29 for comparison-, DD: doublet of doublets at 2.79 ppm for H1, multiplet at 0.90-0.70 ppm for H2 and a triplet at 6.05 ppm for the vinylic protons), but also probably (by NMR spectroscopy data comparison with D) the endo-endo-endo-triadduct (TT) is formed as shown in figure 3.57 (by reaction of the norbornene double
Figure 3.55 Diels-Alder cyclocondensation reaction of 3.29 with HCCP
Figure 3.56 Synthesis of tricyclo[8.2.1.0^2,9.]trideca-5,10-diene 3.30
bond with another mol of the electron deficient diene). Therefore, the attempt on obtaining a ratio for only the endo-endo stereoisomers was again unfruitful. In order to find out whether the cyclooctene double bond is more reactive than the norbornene double bond, equimolar amounts of 3.30 are reacted with HCCP, it is also found that the reaction mixture contains TT together with DD and also 3.30 in an approximate ratio of 2:6:1 TT:DD:3.30 (as shown in figure 3.57 and determined by the relative intensities of the vinylic signals in the case of DD [triplet at 6.05 ppm] and 3.30 [triplets at 6.10 and 5.72 ppm] and the norbornene protons in TT [doublet of doublets at 2.95 ppm] by $^1$H NMR spectroscopy, analogous to the ratio found for T:D:3.29).

Compounds D, DD, T, and TT, are currently under further investigation in order to be fully characterized.

Compound 3.30 was then selectively hydrogenated at the norbornene double bond using a P2-nickel catalyst to form compound 3.31 as depicted in figure 3.58. Compound 3.31 was then reacted with HCCP and DMTCCP under the conditions described earlier and shown in figure 3.58. The results are that only the endo-endo diadducts are formed, namely, the endo-endo-anti and the endo-endo-syn stereoisomers. The ratio of these stereoisomers is approximately 2.5-3.0:1 anti:syn, as determined by NMR spectroscopy, based upon the intensity of the methoxy signals (when DMTCCP is used): a singlet at 3.59, 3.52 ppm for the endo-endo-anti stereoisomer and 3.61, 3.53 ppm for the endo-endo-syn stereoisomer - see figure 3.29 for comparison-; and based upon the intensity of the H1 signals (when HCCP is used): a doublet of doublets at 2.89 ppm for the endo-endo-anti stereoisomer and 3.10 ppm for the endo-endo-syn stereoisomer - see figure 3.29 for comparison-.

These results show that there is indeed a longe-range through-bond and through-space stereoelectronic effect induced by the norbornene double bond over the cyclooctene double bond that has an effect on the stereoselectivity of the Diels-Alder
Figure 3.57 Diels-Alder cyclocondensation reaction of 3.30 with HCCP
Figure 3.58 Synthesis of endo-tricyclo[8.2.1.0^{2,9}]trideca-5-ene 3.31. Diels-Alder cyclocondensation reaction of 3.31 with HCCP and DMTCCP.
cyclocondensation reaction.

Continuing the work towards the synthesis of tricyclo[9.3.0.0^4,8]tetradeca-4,7,11,14-tetraene, compound 3.9 was then successfully reduced in yields up to 65\% to the corresponding de-chlorinated compound 3.32 when sodium metal in refluxing tert-butanol was used as shown in figure 3.59.

![Fig. 3.59 Synthesis of endo-endo-anti-17,17,18,18-tetramethoxypentacyclo[12.2.1.1^6,9.0^2,13.0^5,10]octadeca-7,15-diene 3.32](image)

Successfull recrystallization of 3.32 permitted its characterization by X-ray crystal structure analysis. Figure 3.60 shows the ORTEP diagram of 3.32. In an attempt to improve the yield on this reduction, sodium sand was employed, as opposed to sodium metal in a tert-butyl alcohol:THF mixture, affording compound 3.32 in very low yield (5-10\%). Hydrolysis of compound 3.32 in gentle refluxing acetic acid:water 4:1 mixture afforded the corresponding di-ketone derivative 3.33 as depicted in figure 3.61.

![Fig. 3.61 Synthesis of endo-endo-anti-17,18-dioxopentacyclo[12.2.1.1^6,9.0^2,13.0^5,10]octadeca-7,15-diene 3.33](image)
Figure 3.60 ORTEP diagram of 17,17,18,18-tetramethoxypentacyclo\([12.2.1.1^{6,9}.0^{2,13}.0^{5,10}]\)octadeca-7,15-diene 3.32
Successful recrystallization permitted its characterization by X-ray crystal structure analysis. Figure 3.62 shows the ORTEP diagram of 3.33. Attempts to hydrolyze compound 3.32 using a sulfuric acid:water mixture failed by giving a polymeric material which was not fully characterized. Attempts to obtain compound 3.33 via hydrolysis of 3.9 followed by reduction as depicted in figure 3.63 were unsuccessful since no hydrolysis product of 3.9 was detected. Some polymeric material was formed and the yield of recovery of starting material was as high as 80-85%.

Attempts to reduce compound 3.33 via Wolff-Kishner reduction by heating 3.33 up to 200°C in the presence of potassium hydroxide:diethylene glycol:hydrazine monohydrate mixture afforded the corresponding hydrocarbon 3.34 in very low yields (15-25%) as depicted in figure 3.64. However, when 3.33 is treated first with hydrazine monohydrate to form the corresponding di-hydrazone 3.35 followed by treatment with potassium hydroxide:diethylene glycol suspension, the yield of compound

Fig. 3.63 Attempted side route in the synthesis of endo-endo-anti-17,18-dioxopentacyclo[12.2.1.16,9.02,13,05,10]octadeca-7,15-diene 3.33 from 3.9
Figure 3.62 ORTEP diagram of 17,18-dioxopentacyclo[12.2.1.1^{6,9}.0^{2,13}.0^{5,10}]octadeca-7,15-diene 3.33
3.34 was improved up to 60-70% (see figure 3.65). Figure 3.66 depicts compound 3.34 showing the stereochemistry as determined by different NMR experiments such as $^1$H NMR, $^1$H-$^1$H-COSY, $^{13}$C and $^1$H-$^{13}$C correlation.

![Chemical structure 3.33 to 3.34](image)

**Fig. 3.64** One pot-two step synthesis of endo-endo-anti-pentacyclo[12.2.1.16'.9.02.13.05.10]octadeca-7,15-diene 3.34 from 3.33

Attempts to obtain compound 3.34 by complete reduction of compound 3.11 either with sodium sand or sodium metal were unsuccessful with very low yields (1-3%) as shown in figure 3.67. Another methodology to obtain compound 3.34 was the

![Chemical structure 3.33 to 3.34 with overall yield](image)

**Fig. 3.65** Two step synthesis to endo-endo-anti-pentacyclo[12.2.1.16'.9.02.13.05.10]octadeca-7,15-diene 3.34 from 3.33
treatment of 3.11 with zinc/acetic acid, from which compound 3.16 was obtained. Unfortunately, due to solubility problems, the yields were not higher than 5% (see figure 3.67) and the reduction of 3.16 in the presence of sodium metal to obtain compound 3.34 were only fair (approx. 22%) as depicted in figure 3.67.

Fig. 3.66 Drawing of endo-endo-anti-pentacyclo[12.2.1.1^6.9.0^2.13.0^5.10]octadeca-7,15-diene 3.34 showing the stereochemistry as determined by NMR spectroscopy.

It is interesting that the majority of the compounds analyzed thus far by X-ray crystal structure analysis are found to adopt either twist-boat or chair conformations (except in compound 3.12, in which the conformation adopted is more of a perfect boat!). See figure 3.25.

Conformations adopted by saturated cyclooctane systems have been studied in detail. From the theoretical as well as from the experimental point of view, the conformations adopted by the majority of compounds (bearing the cycloctane or cyclooctene subunits) described in this chapter are indeed interesting for being so unusual. The closest examples of a saturated cyclooctane system being in the chair or twist-boat conformation have been described by Umehara et al. and Okumoto et al. with the only difference that the literature cyclooctane systems bear two carbonyl groups, e.g. two sp^2 carbons.

Attempts to oxidize compound 3.32 and 3.34 via three different methods, namely potassium permangante in refluxing acetone, ruthenium trichloride with sodium
Figure 3.67 Side routes toward the synthesis of pentacyclo[12.2.1.1<sup>6,9</sup>.0<sup>2,13</sup>.0<sup>5,10</sup>.10]octadeca-7,15-diene 3.34
periodate in carbon tetrachloride-acetonitrile, and ozonolysis in dichloromethane at -78°C in order to obtain the corresponding tetraacid derivatives have thus far failed as depicted by the dotted arrows in figures 3.68 and 3.69 respectively.

Figure 3.68 Attempted oxidations of 3.32

In all cases, the corresponding starting materials 3.32 and 3.34 have not been found to be present in the reaction mixture indicating that some sort of reaction (still uncertain) takes place. Unfortunately, none of the products corresponding to the tetraacid derivatives have been able to be extracted from the reaction mixtures. These oxidations are currently under further investigation.

Figure 3.69 Attempted oxidations of 3.34

In continuing the study toward the synthesis of the possible 3D-conductive polymer shown in figure 3.3, cyclooctatetraene was reacted with HCCP in order to obtain the expected diadduct 3.36, as depicted in figure 3.70.
Contrary to what was expected, compound 3.37 was formed instead in fairly good yield (see figure 3.71). There is literature evidence\textsuperscript{181,182} for this behaviour of cyclooctatetraene (COT). At least two unrelated compounds that bear the same molecular framework as the one found in 3.37 have been synthesized by two other groups\textsuperscript{181,182}. The path followed by COT in this particular Diels-Alder cyclocondensation reaction has also been studied\textsuperscript{182} and its application to the formation of compound 3.37 could be described as follows (see figure 3.73):

1) COT undergoes equilibrium in order to form bicyclo[4.2.0]octa-2,4,7-triene 3G. It has been reported that 3G is formed in very low concentrations.\textsuperscript{182} Compound 3G could then react with one equivalent of HCCP forming the monoadduct 3H.

2) COT could react with one equivalent of HCCP forming a different (than 3H) monoadduct 3I which would then undergo an intramolecular Diels-Alder cyclocondensation forming the already described monoadduct 3H.

Monoadduct 3H undergoes a second Diels-Alder cyclocondensation reaction with another equivalent of HCCP forming the final product, diadduct 3.37. See figure 3.73. Successfull recrystallization permitted its characterization by X-ray crystal structure analysis\textsuperscript{183}. Figure 3.72 shows the ORTEP diagram of 3.37 looking from

\begin{figure}[h]
\centering
\includegraphics[width=0.5\textwidth]{fig3.70}
\caption{Expected compound 3.36 from the cyclocondensation of COT with HCCP}
\end{figure}
above and a side view.

Fig. 3.71 Formation of endo-endo-1,5,6,7,8,14,15,16,17,17,18,18-dodecachloro hexacyclo[12.2.1.1^{5,8}.0^{2,13}.0^{3,12}.0^{4,9}]octadeca-6,10,15-triene 3.37 when cyclooctatetraene is reacted with HCCP
Figure 3.72 ORTEP drawings of above and side views of endo-endo-1,5,6,7,8,14,15,16,17,17,18,18-dodecachlorohexacyclo[12.2.1.15,8.12,13.03,12.04,9.]octadeca-6,10,15-triene 3.37
Figure 3.73 Reaction pathways followed in the Diels-Alder reaction between cyclooctatetraene (COT) and hexachlorocyclopentadiene (HCCP) forming the diadduct 3.37
Figure 3.74 Pluto diagram of 1,8,9,10,11,18,19,20,21,23,23-dodecachloro-22-oxo heptacyclo[16.2.1.1^3,16.1^8,11.0^2,17.0^4,15.0^7,12.]tricicosa-9,19-diene T
3.3 Conclusions

Retrosynthetic analysis is a great tool in helping to decide the best synthetic route to a molecule as challenging and complex as it may look.

Synthesis of tricyclo[9.3.0.0^{4,8}]tetradeca-4,7,11,14-tetraene via Diels-Alder cyclocondensation reaction, although it remains unfinished, proved to be a better route than the thermal rearrangement route.

An entire set of new and interesting compounds adopting peculiar conformations, were synthesized and characterized by different spectroscopic techniques. A considerable amount of compounds were successfully recrystallized and their crystal structures solved by X-ray crystal structure analysis.

Saturated cyclooctane systems were found to adopt for the most part chair, boat, and twisted boat conformations.

Cyclooctene systems were found to adopt twisted boat conformations. These data are in agreement with what is suggested by MM2 calculations.

Stability of the product as suggested by MM2 calculations, steric effects as suggested by PCMODEL calculations on the transition states, and the difference in the ratio of stereoisomers found for the different Diels-Alder cyclocondensation reactions are strong evidence suggesting that the effects involved in controlling the stereoselectivity of these reactions are of stereoelectronic nature.

The double bond in the norbornene unit (in the corresponding monoadducts) does seem to have an effect of stereoelectronic nature (a mixture of through-bond and through-space orbital interactions) on the behaviour of the cyclooctene double bond, thus playing an important role in deciding the stereochemical output of the Diels-Alder cyclocondensation reaction.
3.4 Experimental Section

General Procedures. Melting points are uncorrected. $^1$H NMR and $^{13}$C NMR spectra were measured at 200 MHz on a Bruker AC 200 spectrometer. Chemical shifts are reported in $\delta$ or ppm downfield from tetramethylsilane. IR spectra were recorded with a Perkin Elmer 1760x FT-IR infrared spectrometer. MS were recorded on a Hewlett Packard 5985A mass spectrometer. High-resolution MS were obtained from the Midwestern Regional Mass Spectroscopy Facility (University of Nebraska-Lincoln). Elemental analysis were obtained from Desert Analytics (Tucson, AR) or Oneida Research Services, Inc. (Whiteboro, NY).

Materials and Methods. Cyclopentadiene was freshly cracked from dicyclopentadiene (Aldrich). Methanol, ethanol, toluene, benzene, and chloroform, reagent grade were used as received. Hexane was distilled from calcium hydride. Tetrahydrofuran and ether were distilled from sodium-potassium alloy.

![Chemical Reaction](image)

3.4.1 Synthesis of 2,2\(^\prime\)-(p-toluensulfonylimino)bis-ethyl-di(p-toluensulfonate) (3.2)

This compound was prepared by the method of Searle & Geue.\textsuperscript{184} A pyridine solution (138 ml) of diethanolamine (13.8 mL, 0.14 mol) is stirred at room temp. $p$-Toluensulfonyl chloride (81.9 g, 0.43 mol) is slowly added maintaining the
temperature below 5°C. The resulting solution-suspension is stirred for 2 h, quenched by dropwise addition of a 5M HCl solution (270 mL) keeping the temperature below 10°C. The reaction mixture is allowed to warm up to r.t. for 3 h and the mother liquors decanted. The brown paste thus obtained is recrystallized from methanol affording pale yellowish needles, mp 81-83°C (64.5 g, 81.2%). $^1$H NMR (CDCl$_3$) $\delta$ 2.43 (s, 3H), 2.46 (s, 6H), 3.37 (t, 4H), 4.11 (t, 4H), 7.46 (q, 4H), 7.56 (q, 8H); $^{13}$C (CDCl$_3$) $\delta$ 21.51, 21.65, 48.45, 68.26, 127.25, 127.94, 130.00, 132.39, 135.26, 144.15, 145.18.

3.4.2 Synthesis of N-($p$-toluenesulfonyl)-8-azaspiro[4.5]deca-1,3-diene (3.3)

An HMPA solution (70 ml) of previously washed sodium hydride (37 g, 77 mmol) is stirred under argon atmosphere at room temp. Cyclopentadiene (2.9 mL, 35 mmol) is added. The resulting solution is stirred for 30 min, followed by a slow addition (20 min) of a HMPA solution (50 mL) of 3.2 (20 g, 35 mmol). The resulting mixture is allowed to sit at room temperature overnight, then hydrolyzed with ice-cold water and the resulting solid is recrystallized from 2,2,4-trimethylpentane affording white crystals, 3.3 mp 106-108°C (2.6 g, 26%). $^1$H NMR (CDCl$_3$) $\delta$ 1.68 (t, 4H), 2.47 (s, 3H), 3.19 (t, 4H), 6.30 (q, 4H), 7.52 (q, 4H); $^{13}$C (CDCl$_3$) $\delta$ 21.52, 30.55, 45.48, 54.36, 127.68, 129.79, 133.38, 142.02, 143.47; HRMS, m/z C$_{16}$H$_{19}$NO$_2$S$^{32}$S: Calcd.: 289.1148, Obsd.: 289.1132; C$_{15}$H$_{19}$NO$_2$S$^{32}$S: Calcd.: 290.1167, Obsd.:
This compound was prepared by the method of Townsend et al.\textsuperscript{45} and Carmack & Kelley.\textsuperscript{31} A pyridine solution (378 ml) of diethylene glycol (71 mL, 0.74 mol) is vigorously stirred (mechanical stirring) at 0°C. p-Toluensulfonyl chloride (310 g, 1.6 mol) is slowly added over a period of 11 h keeping the temperature below 3°C. Upon addition of the substrate, the resulting white suspension is allowed to stir overnight (from 0°C to r.t.). The suspension is then filtered and washed with a minimum amount of ether and dried under aspirator vacuum overnight affording a white crystalline solid, which is recrystallized from ethanol affording transparent needles, 3.4 mp 85-87°C (148 g, 48%). \textsuperscript{1}H NMR (CDCl\textsubscript{3}) \textsuperscript{8} 2.48 (s, 6H), 3.62 (t, 4H), 4.08 (t, 4H), 7.59 (q, 8H); \textsuperscript{13}C (CDCl\textsubscript{3}) \textsuperscript{8} 21.87, 68.99, 69.30, 128.16, 130.15, 133.10, 145.48.
A hexamethylene phosphoramide (HMPA) suspension (70 ml) of a freshly washed, with hexane, 50% dispersion of sodium hydride (7.6 g, 0.16 mol) is stirred under argon atmosphere at room temp. Cyclopentadiene (5 mL, 0.06 mol) is slowly added. The resulting grey suspension is stirred for 15 min, followed by the automatic injection of an HMPA solution (80 mL) of 3.4 (25 g, 0.06) over a period of 16 h. Upon addition of the substrate, the resulting deep wine-red suspension is allowed to stir for 3 h. The resulting suspension is hydrolyzed by pouring it into ice-cold water, and the product extracted with ether. The combined organic extracts are washed with a 5% aqueous HCl until pH neutral, dried over magnesium sulfate, filtered and concentrated under reduced pressure affording a slightly bright yellow liquid which is distilled under aspirator vacuum yielding a water-clear liquid, 3.5 bp 85-100°C (25-20 mm Hg) (2.5 g, 30%). $^1$H NMR (CDCl$_3$) δ 1.61 (t, 4H), 3.83 (t, 4H), 6.31 (d, 2H), 6.55 (d, 2H); $^{13}$C (CDCl$_3$) δ 31.32, 54.47, 66.82, 129.23, 142.83; HRMS, C$_9$H$_{12}$O: Calcd.: 136.0904, Obsd.: 136.0886; $^{13}$C$_8$H$_{12}$O: Calcd.: 137.0908, Obsd.: 137.0924; C$_8$H$_{10}$: Calcd.: 106.0756, Obsd.: 106.0780; C$_8$H$_9$: Calcd.: 105.0712, Obsd.: 105.0703; C$_7$H$_7$: Calcd.: 91.0527, Obsd.: 91.0550; IR (neat) 2940, 2920, 2857, 1472, 1446, 1383, 1248, 1135, 1110, 1048, 950, 840, 740 cm$^{-1}$.

Anal. Calcd. for C$_9$H$_{12}$ (%): C, 79.37; H, 8.88; O, 11.75. Found: C, 78.75; H, 8.81; O, 12.52.

3.4.5 Attempted Synthesis of 1-(2-Hydroxyethyl)-1-(2-bromoethyl)-2,4-cyclopentadiene (3.6)
A dichloromethane solution (5 ml) of 3.5 (1.48 g, 11 mmol) and dry triethylamine (0.36 mL, 1.6 mmol) is stirred under argon atmosphere at room temp. A 2.67M DCM solution (8.3 mL) of dimethylboron bromide\(^{77-79}\) (22.2 mmol) is slowly added. The resulting solution is allowed to stir overnight, then hydrolyzed by pouring a saturated sodium bicarbonate solution (50 mL). The product is extracted with DCM (50 mL) and the combined organic extracts washed with a 5% aqueous HCl solution, followed by water until pH neutral, then dried over magnesium sulfate and then distilled under high vacuum yielding a pale yellowish liquid which polymerizes on standing (even at low temp.), bp 70-72°C (0.3-0.4 mm Hg) (1.45 g, 66%). \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 2.01 (dd, 4H), 2.33 (dd, 4H), 3.15 (dd, 4H), 3.45 (dd, 4H), 6.34 (m, 4H); MS, m/z (relative intensity) 218, 216 (M\(^+\)), 137, 123, 110, 109, 95, 93, 91, 83, 82, 81, 79 (100), 78, 77, 67, 65, 55, 53, 51.

\[\text{3.4.6 Synthesis of 1,1-dimethoxy-2,3,4,5-tetrachlorocyclopenta-diene (3.8)}\]
This compound was prepared by the method of Newcomer & McBee,\textsuperscript{93} and McBee \textit{et al.}\textsuperscript{94} A freshly prepared hot methanol solution (400 mL) of potassium hydroxide (112 g, 2 mol) is slowly added to a methanol solution (375 mL) of hexachlorocyclopentadiene (205 g, 0.75 mol) to maintain a gentle reflux. The resulting mixture is stirred at room temp. overnight. The resulting precipitate is filtered (115 g) and the solution concentrated under reduced pressure, washed with water (5 x 200 mL), dried over magnesium sulfate and distilled under high vacuum (@ 75-90°C) affording a clear pale-yellow liquid, 3.8 (140.4 g, 71%). \textsuperscript{1}H NMR (CDCl\textsubscript{3}) \( \delta \) 3.37 (s, 6H, 2 CH\textsubscript{3}); \textsuperscript{13}C (CDCl\textsubscript{3}) \( \delta \) 51.76, 104.64, 128.42, 129.30.

3.4.7 Synthesis of \textit{endo-endo-(anti \& syn)-1,6,7,8,9,14,15,16-octachloro-17,17,18,18-tetramethoxypentacyclo [12.2.2.1\textsuperscript{6,9}.0\textsuperscript{2,3}.13.0\textsuperscript{5,10}]octadeca-7,15-dienes (3.9 \& 3.10).}

These compounds were prepared by the method of Akhter \textit{et al.}\textsuperscript{91} A neat solution of 1,1-dimethoxy-2,3,4,5-tetrachlorocyclopentadiene (200 g, 0.76 mol) with 1,5-cyclooctadiene (27.3 g, 0.25 mol) is slowly heated (oil bath) under continuous stirring
and argon atmosphere. The solution is stirred at 165-170°C (oil bath temp.) for 1 h. A yellowish powder precipitates in the reaction flask. The resulting mixture is cooled to 0°C, filtered and washed with ether to afford a fine white powder (103 g, 65% pure anti stereoisomer 3.9). A sample was recrystallized from slow cooling of xylenes. mp 356-358°C (dec.) . $^1$H NMR (CDCl$_3$) $\delta$ 3.58 (s, 6H), 3.52 (s, 6H), 2.67 (d, 4H), 2.10 (d, 4H), 0.80 (t, 4H); $^{13}$C (CDCl$_3$) $\delta$ 128.6, 111.3, 79.1, 52.7, 51.9, 51.6, 21.9; HRMS: [M-Cl] $\text{C}_{22}\text{H}_{24}\text{Cl}_7\text{O}_4$ Calcd: 596.9489, Obsd: 596.9501; C$_{22}$H$_{24}$Cl$_6$ClO$_4$ Calcd: 598.9465, Obsd: 598.9465 FT-IR: 2982.3, 2949.9, 2909.4, 2845, 1606.8, 1471.1, 1289.2, 1197, 1110.2, 993, 953.4 cm$^{-1}$. From the ether extract a white powder was obtained after evaporation of solvent mp 219-222°C (25 g, 16% pure syn stereoisomer 3.10) Total %yield: 81%. $^1$H NMR (CDCl$_3$) $\delta$ 3.66 (s, 3H), 3.56 (s, 3H), 2.85 (d, 4H), 1.94 (d, 4H), 1.38 (dd, 4H); $^{13}$C (CDCl$_3$) $\delta$ 129.04, 111.62, 79.35, 52.82, 51.83, 46.64, 19.96 ppm; HR-MS: [M+-Cl]: C$_{22}$H$_{24}$Cl$_7$O$_4$ Calcd: 596.9494, Obsd: 596.9504; C$_{22}$H$_{24}$Cl$_6$ClO$_4$ Calcd: 598.9467, Obsd: 598.9475; C$_{22}$H$_{24}$Cl$_5$Cl$_2$O$_4$ Calcd: 600.9439, Obsd: 600.9451; FT-IR: 2950.1, 2844.4, 1604.3, 1451.4, 1198.5, 1174.6, 1107.9, 983.6 cm$^{-1}$.

![Diagram](image1)

![Diagram](image2)

3.4.8 Synthesis of endo-endo-(anti & syn)

1,6,7,8,9,14,15,16,17,17,18,18-dodecachloropentacyclo [12.2.1.16.9.02.13.05.10]octadeca-7,15-dienes (3.11 & 3.12)
These compounds were prepared by modification of a method by Akhtar et al. A neat solution of hexachlorocyclopentadiene (60.6 g, 222 mmol) with 1,5-cyclooctadiene (10 g, 93 mmol) is slowly heated (oil bath) under continuous stirring and argon. When the oil bath temp. reached 180-185°C the heating was removed. The resulting dark powder is recrystallized from xylenes affording clear brown crystals (a mixture of both endo-endo isomers) (56.6 g, 94%). endo-endo-anti-1,6,7,8,9,14,15,16,17,18,18-dodecachloropentacyclo[12.2.1.16\textsuperscript{6}.9.0\textsuperscript{2}.13.0\textsuperscript{5}.10]octadeca-7,15-diene, 3.11: mp >360°C. \textsuperscript{1}H NMR (CDCl\textsubscript{3}) \(\delta\) 2.87 (dd, 4H), 2.24 (d, 4H), 0.87 (d, 4H); \textsuperscript{13}C (CDCl\textsubscript{3}) \(\delta\) 130.8, 82.7, 51.4, 29.8, 22.9; MS, m/z (relative intensity) 653 (M\textsuperscript{+}), 297, 295, 276, 274, 272(100), 270, 237, 235. HR-MS, m/z (M\textsuperscript{+}) C\textsubscript{18}H\textsubscript{12}\textsuperscript{35}Cl\textsubscript{10}\textsuperscript{37}Cl\textsubscript{2} Calcd. 651.714206; Obsd. 651.7142; C\textsubscript{18}H\textsubscript{12}\textsuperscript{35}Cl\textsubscript{9}\textsuperscript{37}Cl\textsubscript{3} Calcd. 653.71253; Obsd. 653.7111. FT-IR: 2941.1, 1601.5, 1463.3, 1283.3, 1168.2, 1001.5, 911.7 cm\textsuperscript{-1}.

endo-endo-syn-1,6,7,8,9,14,15,16,17,18,18-dodecachloropentacyclo [12.2.1.16\textsuperscript{6}.9.0\textsuperscript{2}.13.0\textsuperscript{5}.10] octadeca-7,15-diene, 3.12: mp >320°C (subl.). \textsuperscript{1}H NMR (CDCl\textsubscript{3}) \(\delta\) 3.00 (dd, 4H), 2.06 (d, 4H), 1.48 (d, 4H); \textsuperscript{13}C (CDCl\textsubscript{3}) \(\delta\) 131.2, 82.9, 46.3, 29.8, 20.7; MS, m/z (relative intensity) 653 (M\textsuperscript{+}), 297, 295, 276, 274, 272(100), 270, 237, 235. HR-MS, C\textsubscript{18}H\textsubscript{12}\textsuperscript{35}Cl\textsubscript{10}\textsuperscript{37}Cl\textsubscript{2} Calcd. 651.714206; Obsd. 651.7142; C\textsubscript{18}H\textsubscript{12}\textsuperscript{35}Cl\textsubscript{9}\textsuperscript{37}Cl\textsubscript{3} Calcd. 653.7112; Obsd. 653.7111. FT-IR: 2970.2, 1604.3, 1168.2, 1006.7, 917.9 cm\textsuperscript{-1}. 
3.4.9 Synthesis of endo-1,10,11,12,13,13-hexachlorotricyclo[8.2.1.0².⁹]trideca-5,11-diene (3.13).

This compound was prepared by modification of a method of Eaton et al. A neat solution of hexachlorocyclopentadiene (20 g, 73 mmol) with 1,5-cyclooctadiene (63.4 g, 587 mmol) is slowly heated (oil bath) under continuous stirring and argon atmosphere to 144-150°C and allowed to stir for 10 h. The resulting suspension is cooled to 0°C and filtered affording a white solid which is washed with ether and determined to be 3.11. The filtrate is concentrated under reduced pressure and distilled under high vacuum @ 100-110°C to remove COD. The residue (a pale yellowish paste) is washed with methanol and filtered affording a fine white powder. 3.13 mp 54-57°C (21.4 g, 81.8%). $^1$H NMR (CDCl₃) δ 5.78 (t, 2H), 2.93 (q, 2H), 2.53-2.25 (m, 2H), 2.21-1.95 (m, 4H), 1.70-1.42 (m, 2H) ; $^{13}$C (CDCl₃) δ 131.55, 131.14, 83.07, 50.28, 25.59, 24.66 ; HRMS: C₁₃H₁₂$^{35}$C₅$^{37}$Cl Calcd. 379.9045, Obsd. 379.9037; C₁₃H₁₂$^{35}$C₄$^{37}$Cl₂ Calcd. 379.9043, Obsd. 379.9038. FT-IR: 2943.4, 2890.7, 2846.7, 1606.8, 1473, 1279.5, 1162.8, 1073.6, 1011.4 cm⁻¹.
3.4.10 Synthesis of *endo*-13,13-dimethoxy-1,10,11,12-tetrachloro-
tricyclo[8.2.1.0\textsuperscript{2,9}]trideca-5,11-diene (3.14).

This compound was prepared by the method of Eaton *et al.*\textsuperscript{185} A neat solution of 1,1-dimethoxy-2,3,4,5-tetrachlorocyclopentadiene (10 g, 38 mmol) with 1,5-
cyclooctadiene (41 g, 380 mmol) is slowly heated (oil bath) under continuous stirring
and argon atmosphere to 150-160°C and allowed to stir for 1 h. The resulting solution
is diluted with ether (no precipitate is formed), concentrated under reduced pressure,
and distilled under high vacuum @ 100-110°C to remove COD. The residue is washed
with ether and filtered affording a fine white powder determined to be 3.9. The filtrate
is concentrated under reduced pressure and then distilled under high vacuum @ 150-
170°C affording a thick pale yellowish clear liquid. 3.14 (10.7 g, 76%). \textsuperscript{1}H NMR
(CDCl\textsubscript{3}) \textsuperscript{δ} 5.78 (t, 2H), 3.61 (s, 3H), 3.56 (s, 3H), 2.73 (m, 2H), 2.48-2.28 (m,
2H), 2.18-1.93 (m, 4H), 1.57-1.33 (m, 2H).
3.4.11 Synthesis of *endo-endo-anti*-1,6,7,8,9,14,15,16,17,17-decachloro-18,18-dimethoxypentacyclo[12.2.1.1^6.9.0^2.13.0^5.10]octadeca-7,15-diene (3.15).

This compound was prepared by modification of a method of Akhtar *et al.* A neat solution of 1,1'-dimethoxy-2,3,4,5-tetrachlorocyclopenta-2,4-diene (2.1 g, 7.9 mmol) with 3.13 (1 g, 2.6 mmol) is slowly heated (oil bath) under continuous stirring and argon atmosphere at 133-140°C for 3 h. The resulting suspension is cooled to 0°C and filtered affording a white solid which is washed with ether affording a white powder. (1.1 g, 66% chair + 16% boat); 3.15 mp 283-284°C. $^1$H NMR (CDCl$_3$) $\delta$ 3.59 (s, 3H), 3.52 (s, 3H), 2.86 (d, 2H), 2.68 (d, 2H), 2.17 (q, 2H); $^{13}$C (CDCl$_3$) $\delta$ 130.70, 128.80, 111.56, 82.73, 78.98, 52.74, 51.81, 51.64, 51.35, 22.83, 21.93. HRMS: C$_{20}$H$_{18}^{35}$Cl$_{10}$O$_2$ Calcd. 639.8203, Obsd. 639.8169; C$_{20}$H$_{18}^{35}$Cl$_9^{37}$ClO$_2$ Calcd. 641.8171, Obsd. 641.8146; FTIR: 2952.1, 1603.7, 1476.1, 1296.1, 1198.5, 1107.1, 992.5, 846.1, 756.1 cm$^{-1}$. 
3.4.12 Synthesis of endo-endo-anti-1,6,7,8,9,14,15,16,17,17-decachloro-18,18-dimethoxypentacyclo [12.2.1.16'.9.02'.13.05'.10]octadeca-7,15-diene (3.15)

This compound was prepared by modification of a method of Akhtar et al. A neat solution of hexachlorocyclopentadiene (2.2 g, 81 mmol) with 3.14 (1 g, 2.7 mmol) is slowly heated (oil bath) under continuous stirring and argon atmosphere at 133-140°C for 3 h. The resulting suspension is cooled to 0°C and filtered affording a white solid which is washed with ether affording a fine white powder. 3.15 mp 283-284°C (1.03 g, 59% of anti stereoisomer).

3.4.13 Synthesis of 1,2,3,4-tetrachlorocyclopenta-1,3-diene.

This compound was prepared by the method of Roedig. A glacial acetic acid solution (150 mL) of hexachlorocyclopentadiene (68.5 g, 0.251 mol) is vigorously stirred at 15°C. Then zinc dust (40 g) is slowly added keeping the temperature between 16-25°C. The resulting suspension is treated with warm water (40-50°C) and filtered
affording a yellow crystalline material which upon recrystallization from methanol gave big rectangular clear crystals. mp 61.5-62.5°C (28.6 g, 56%). $^1$H NMR (CDCl$_3$) $\delta$ 3.38 (s, 2H); $^{13}$C (CDCl$_3$) $\delta$ 127.98, 125.37, 46.95.

![Chemical structure](image)

3.4.14 Synthesis of endo-endo-anti-1,6,7,8,9,14,15,16 octachloropentacyclo[12.2.1.1$^6$.9.0$^2$.13$.0^5$.10]octadeca-7,15-diene (3.16)

This compound was prepared by modification of a method of Akhtar et al.$^{91}$ A neat solution of 1,2,3,4-tetrachlorocyclopentadiene$^{95}$ (2 g, 9.8 mmol) with 1,5-cyclooctadiene (265 mg, 2.5 mmol) is slowly heated (oil bath) under continuous stirring and argon atmosphere to 120-130°C and allowed to stir for 3 h. The resulting paste is cooled to 0°C and filtered affording a white solid which is washed with hexane followed by ether. 3.16 mp 312-315°C (dec.) (460 mg, 35.7%). $^1$H NMR (CDCl$_3$) $\delta$ 2.64 (d, 4H), 2.44 (d, 2H), 2.40 (d, 2H), 2.21 (d, 4H), 0.80 (t, 4H); $^{13}$C (CDCl$_3$) $\delta$ 132.1, 66.4, 63.2, 55.4, 23.0; HRMS, C$_{18}$H$_{16}^{35}$Cl$_7^{37}$Cl Calcd. 513.8733; Obsd. 513.8726; C$_{18}$H$_{16}^{35}$Cl$_6^{37}$Cl$_2$ Calcd. 515.8703; Obsd. 515.8695. FT-IR: 2941, 2906.2, 1591.3, 1290.8, 1469.5, 1226.7, 1126, 1037.6, 944.4 cm$^{-1}$. 


3.4.15 Synthesis of \textit{endo-endo-anti}-1,6,7,8,9,14,15,16,17,17-decachloropentacyclo[12.2.1.16,9.02,13.05,10]octadeca-7,15-diene (3.17)

This compound was prepared by modification of a method of Akhtar et al.\textsuperscript{91} A neat solution of 1,2,3,4-tetrachlorocyclopenta-1,3-diene (1.6 g, 7.9 mmol) with 3.13 (1 g, 2.6 mmol) is slowly neatened (oil bath) under continuous stirring and argon atmosphere at 105-110°C for 2.5 h. The resulting suspension is cooled to 0°C and filtered affording a white solid which is washed with small amounts of ether affording a fine white powder. 3.17 mp >285°C (dec.) (0.6 g, 39.5%). $^1$H NMR (CDCl$_3$) $\delta$ 2.88 (d, 2H), 2.67 (d, 2H), 2.45 (q, 2H), 2.24 (d, 4H), 1.0-0.8 (m, 4H); $^{13}$C (CDCl$_3$) $\delta$ 132.10, 130.70, 82.70, 73.29, 63.04, 55.14, 51.40, 23.01, 22.72, 20.55. HRMS: C$_{18}$H$_{14}$Cl$_{35}$Cl$_{37}$ Calcd. 581.7968, Obsd. 581.7928; C$_{18}$H$_{14}$Cl$_{35}$Cl$_{37}$Cl$_2$ Calcd. 583.7932, Obsd. 583.7906; C$_{18}$H$_{14}$Cl$_{35}$Cl$_{37}$Cl$_3$ Calcd. 585.7898, Obsd. 585.7884. FT-IR: 2950.4, 2914.3, 2253.8, 1603.6, 1471.4, 1290.4, 1261.2, 1167, 1078.5, 908.8 cm$^{-1}$. 
3.4.16 Synthesis of *endo-endo-anti*-17,17-dimethoxy-1,6,7,8,9,14,15,16-octachloropentacyclo[12.2.1.1<sup>6</sup>.9<sup>2</sup>,13<sup>5</sup>,10<sup>2</sup>]octadeca-7,15-diene (3.18)

This compound was prepared by modification of a method of Akhtar *et al.*<sup>91</sup> A neat solution of 1,2,3,4-tetrachlorocyclopenta-1,3-diene (0.82 g, 4 mmol) with 3.14 (0.5 g, 1.3 mmol) is slowly heated (oil bath) under continuous stirring and argon atmosphere at 110-115°C for 2 h. The resulting yellow paste is cooled to 0°C and filtered affording a white solid which is washed with ether. 3.18 mp >305°C (dec.) (0.33 g, 53.5%). $^1$H NMR (CDCl<sub>3</sub>) $\delta$ 3.59 (s, 3H), 3.52 (s, 3H), 2.65 (t, 4H), 2.42 (q, 2H), 2.14 (t, 4H), 0.90-0.65 (m, 4H); $^{13}$C (CDCl<sub>3</sub>) $\delta$ 132.10, 128.65, 111.58, 79.10, 73.41, 63.12, 55.28, 52.70, 51.97, 51.61, 22.79, 22.15. HRMS: C<sub>20</sub>H<sub>20</sub>Cl<sub>2</sub>O<sub>2</sub> Calcd. 573.8947, Obsd. 573.8933; C<sub>20</sub>H<sub>20</sub>Cl<sub>6</sub>O<sub>2</sub> Calcd. 575.8920, Obsd. 575.8901. FT-IR: 2949.6, 2909, 1646, 1594.6, 1472.1, 1291.5, 1196.2, 990.7, 909.5 cm<sup>-1</sup>. 
3.4.17 Synthesis of endo-endo-anti-1,6,7,8,9,14,15,16-octachloropentacyclo[12.2.1.16,9.02,13.05,10]octadeca-7,15-diene (3.16)

This compound was prepared by the method of Grieco. A glacial acetic acid solution (15 mL) of 3.11 (10 g, 15.3 mmol) is vigorously stirred at 0°C. Zinc powder (12 g, 183.8 mmol) is slowly added (over a 2 h period) keeping the temperature below 10°C. The resulting mixture is stirred overnight, and extracted with DCM. The combined organic extracts are washed with brine, water, dried over magnesium sulfate, filtered, and concentrated under reduced pressure giving a pale yellowish paste which is further washed with ether. Upon evaporation of the ethereal filtrate, a fine white powder forms. 3.16 mp 312-315°C (dec.) (0.5 g, 6.4%).
3.4.18 Synthesis of endo-endo-(anti & syn)-15,16-benzo-18,18-dimethoxy-1,14-diphenyl-6,7,8,9-tetrachloro-17-oxapentacyclo[12.2.1.1^{6,9}.0^{2,13}.0^{5,10}]octadeca-7-ene (3.25 & 3.26)

This compounds were prepared by modification of a method of Akhtar et al. A neat solution of 3.14 (0.7 g, 1.9 mmol) with 1,3-diphenylisobenzofuran (0.51 g, 1.9 mmol) is slowly heated (oil bath) under continuous stirring and argon atmosphere to 133-140°C and allowed to stir for 2 h. The resulting suspension is cooled to 0°C, filtered, and washed with a 1:1 hexane:ether solution affording a bright green yellowish powder. 3.26 (boat stereoisomer) (1.03 g, 84.5% total). 3.25 (chair stereoisomer) mp 253-255°C: $^1$H NMR (CDCl$_3$) $\delta$ 7.74 (d, 4H), 7.6-7.4 (m, 6H), 7.25 (q, 4H), 3.57 (s, 3H), 3.56 (s, 3H), 3.21 (d, 2H), 2.53 (d, 2H), 2.2-1.9 (m, 4H), 1.4-1.3 (m, 2H), 1.10 (t, 2H); $^{13}$C (CDCl$_3$) $\delta$ 146.42, 137.20, 128.60, 128.42, 128.03, 127.67, 126.40, 121.42, 111.29, 90.31, 79.17, 52.64, 52.06, 51.50, 48.92, 47.19, 43.77, 25.18, 22.13. HRMS: (M-3Cl) $C_{35}H_{32}O_{3}^{35}Cl_{3}$ Calcd. 605.1414, Obsd. 605.1426; $C_{35}H_{32}O_{3}^{35}Cl_{2}^{37}Cl$ Calcd. 607.1370, Obsd. 607.1414; (M-[H$_2$O-2Cl])
C_{35}H_{30}O_2^{35}Cl_3^{37}Cl \text{ Calcd. } 624.0972, \text{ Obsd. } 624.0972; \ C_{35}H_{30}O_2^{35}Cl_2^{37}Cl_2 \text{ Calcd. } 626.0974, \text{ Obsd. } 626.0955. \text{ FT-IR: } 3064.4, 3029.5, 2950.4, 2937.5, 2909.3, 2866.7, 2844.6, 2249.4, 1604, 1499.2, 1474.3, 1458.4, 1447, 1363.5, 1305.7, 1277.8, 1198.9, 1156.7, 1110.7, 1013.7, 989.7 \text{ cm}^{-1}.

\begin{figure}
\centering
\includegraphics[width=0.5\textwidth]{fig}
\caption{Structure of the compound.}
\end{figure}

3.4.19 Synthesis of endo- endo-(anti & syn)-15,16-benzo-1,14-diphenyl-6,7,8,9,18,18-hexachloro-17-oxapentacyclo[12.2.1.1^{6}.9.0^{2}.13.0^{5}.10]octadeca-7-ene (3.27 & 3.28)

This compound was prepared by modification of a method of Akhtar et al.\textsuperscript{91} A neat solution of 3.13 (0.13 g, 0.34 mmol) with 1,3-diphenylisobenzofuran (0.3 g, 1.1 mmol) is slowly heated (oil bath) under continuous stirring and argon atmosphere to 133-140°C and allowed to stir for 2 h. The resulting suspension is cooled to 0°C, filtered, and washed with a 1:1 hexane:ether solution affording a bright green yellowish powder. (0.17 g, 76.8% both isomers); 3.27 (chair stereoisomer) \text{ mp } 154-155°C. \text{ }^1\text{H NMR (CDCl}_3\text{) } \delta 7.68-7.62 \text{ (m, 4H), 7.48-7.39 \text{ (m, 6H), 7.22-7.20 \text{ (m, 2H), 7.11-7.07 \text{ (m, 2H), 3.12 \text{ (dd, 2H), 2.64 \text{ (dd, 2H), 2.07 \text{ (t, 4H), 1.25 \text{ (m, 4H); } ^13\text{C (CDCl}_3\text{) } \delta 146.18, 137.23, 128.50, 128.33, 127.96, 127.57, 126.57, 121.43,}{
117.05, 90.27, 82.77, 51.49, 48.88, 46.83, 43.77, 25.10, 23.01. HRMS: 
\[ \text{C}_{33}\text{H}_{26}\text{O}^{35}\text{Cl}_{6} \text{ Calcd.} 648.0129, \text{ Obsd.} 648.0084; \text{ C}_{33}\text{H}_{26}\text{O}^{35}\text{Cl}_{3}^{37}\text{Cl} \text{ Calcd.} 650.0099, \text{ Obsd.} 650.0058; \]
FT-IR: 3062.5, 3027.6, 2940.0, 2935.7, 2865.6, 
1663.2, 1603.4, 1448.8, 1316.6, 1279.6, 1075.9, 1012.3, 987.9, 927.3, 908.2 cm\(^{-1}\).

3.14 (18.1 g, 48.7 mmol) dissolved in THF (100 mL) is slowly cannulated in and allowed to reflux for 30 h. The resulting suspension is cooled to 0°C and filtered. The filtrate is then treated with ice and extracted with DCM. The combined organic extracts are washed with brine, water, dried over magnesium sulfate, filtered and concentrated under reduced pressure followed by distillation under high vacuum @ 100-110°C to affording a pale green-yellowish liquid. 3.19 (8.38 g, 73.2%). \( ^1\text{H NMR (CDCl}_3 \) \( \delta 6.11 \text{ (t, 2H), 5.73 (t, 2H), 3.24 (s, 3H), 3.10 (s, 3H), 2.74-2.65 (m, 2H), 2.58-2.42 (m, 2H), 2.34-2.18 (m, 2H), 2.08-1.91 (m, 2H), 1.81-1.62 (m, 2H), 1.53-1.31 (m, 2H); }^{13}\text{C (CDCl}_3 \) \( \delta 133.17, 132.04, 118.53, 52.16, 51.61, 49.73, 42.53, 30.40, 25.98. \)

3.4.20 Synthesis of endo-13,13-dimethoxytricyclo[8.2.1.0\(^2.9\)]trideca-5,11-diene (3.19)

This compound was prepared by the method of Eaton et al.\(^{185}\) A THF suspension (127 mL) of sodium metal (18.9 g, 820 mmol) with absolute ethanol (23 mL) is refluxed under continuous stirring and argon atmosphere. 3.14 (18.1 g, 48.7 mmol) dissolved in THF (100 mL) is slowly cannulated in and allowed to reflux for 30 h. The resulting suspension is cooled to 0°C and filtered. The filtrate is then treated with ice and extracted with DCM. The combined organic extracts are washed with brine, water, dried over magnesium sulfate, filtered and concentrated under reduced pressure followed by distillation under high vacuum @ 100-110°C to affording a pale green-yellowish liquid. 3.19 (8.38 g, 73.2%). \( ^1\text{H NMR (CDCl}_3 \) \( \delta 6.11 \text{ (t, 2H), 5.73 (t, 2H), 3.24 (s, 3H), 3.10 (s, 3H), 2.74-2.65 (m, 2H), 2.58-2.42 (m, 2H), 2.34-2.18 (m, 2H), 2.08-1.91 (m, 2H), 1.81-1.62 (m, 2H), 1.53-1.31 (m, 2H); }^{13}\text{C (CDCl}_3 \) \( \delta 133.17, 132.04, 118.53, 52.16, 51.61, 49.73, 42.53, 30.40, 25.98. \)
3.4.21 Synthesis of endo-endo-anti-17,17-dimethoxy-6,7,8,9,18,18-hexachloropentacyclo[12.2.1.16\(>9.0^2\),13.05,10]octadeca-7,15-diene (3.20).

This compound was prepared by modification of a method of Akhtar et al. A neat solution of 3.19 (283 mg, 1.2 mmol) with hexachlorocyclopentadiene (416 mg, 1.5 mmol) is slowly heated (oil bath) under continuous stirring and argon atmosphere at 133-140°C for 3 h. The resulting yellow paste is cooled to 0°C and dissolved in CDCl₃. Upon evaporation of solvent, the residue is washed with ether and dissolved in hot hexane. Upon cooling of the solvent, crystals grew over a 3 day period. 3.20 mp 169-172°C (0.49 g, 79.9%). ¹H NMR (CDCl₃) δ 6.06 (t, 2H), 3.22 (s, 3H), 3.10 (s, 3H), 2.84-2.74 (m, 4H), 2.69 (t, 2H), 2.51-2.32 (m, 2H), 2.17-1.96 (m, 2H), 1.88-1.67 (m, 2H), 1.04-0.81 (m, 2H); ¹³C (CDCl₃) δ 132.53, 130.63, 117.72, 82.89, 54.64, 52.00, 51.69, 51.49, 49.79, 42.50, 26.70, 23.52. HRMS: C_{20}H_{22}{^{35}}Cl_{6}O_{2} Calcd. 503.9752, Obsd. 503.9751; C_{20}H_{22}{^{35}}Cl_{4}{^{37}}ClO_{2} Calcd. 505.9717, Obsd. 505.9721; C_{20}H_{22}{^{35}}Cl_{4}{^{37}}Cl_{2}O_{2} Calcd. 507.9711, Obsd. 507.9696. FT-IR: 2951.7, 2933.4, 2904.6, 2864.8, 2830.1, 2361.0, 2342.4, 1774.6, 1604.9, 1471.7, 1283.3, 1166.4, 1101.0, 1064.5, 908.0 cm⁻¹.
3.4.22 Synthesis of endo-endd-anti-17,17,18,18-tetramethoxy-
6,7,8,9-tetrachloropentacyclo[12.2.1.1^6.9^2.13.0^8,10]

tetradeca-7,15-diene (3.22).

This compound was prepared by modification of a method of Akhtar et al. A
neat solution of 3.19 (222 mg, 1 mmol) with 1,1-dimethoxy-2,3,4,5-
tetrachlorocyclopenta-2,4-diene (373 mg, 1.4 mmol) is slowly heated (oil bath) under
continuous stirring and argon atmosphere at 133-140°C for 3 h. The resulting yellow
paste is cooled to 0°C and dissolved in CDCl₃. Upon evaporation of solvent, the
residue is washed with ether and dissolved in hot hexane. Upon cooling of the solvent,
crystals grew over a week period. 3.21 mp 153-156°C (0.53 g, 82.5%). ¹H NMR
(CDCl₃) δ 6.05 (t, 2H), 3.53 (s, 3H), 3.51 (s, 3H), 3.21 (s, 3H), 3.10 (s, 3H), 2.67
(t, 2H), 2.65-2.53 (m, 4H), 2.48-2.30 (m, 2H), 2.08-1.88 (m, 2H), 1.83-1.62 (m,
2H), 0.98-0.77 (m, 2H); ¹³C (CDCl₃) δ 132.48, 128.58, 117.76, 111.22, 79.35,
52.61, 52.29, 52.05, 51.71, 51.50, 49.76, 42.60, 26.80, 22.65. HRMS:
C₂₂H₂₈Cl₄O₄ Calcd. 496.0741, Obsd. 496.0741; C₂₂H₂₈Cl₃Cl₂O₄ Calcd.
498.0712, Obsd. 498.0712; C₂₂H₂₈Cl₂Cl₂O₄ Calcd. 500.0674, Obsd. 500.0689.
FT-IR: 2950.7, 2932.1, 2862.8, 2830.6, 2245.6, 1753.1, 1605.3, 1471.6, 1463.6,
1340.5, 1302.1, 1284.7, 1269.5, 1199.1, 1105.2, 1067.1, 992.8, 912.8 cm⁻¹.
3.4.23 Synthesis of *endo-endo-anti*-17,17-diethoxy-6,7,8,9,18,18-hexachloropentacyclo[12.2.1.16,9,02,13,05,10]octadeca-7,15-diene (3.24).

This compound was formed by recrystallizing 3.20 in hot absolute ethanol. 3.22 mp 177-180°C. $^1$H NMR (CDCl$_3$) $\delta$ 6.04 (t, 2H), 3.48 (q, 2H), 3.33 (q, 2H), 2.87-2.74 (m, 4H), 2.68 (t, 2H), 2.49-2.32 (m, 2H), 2.15-1.97 (m, 2H), 1.86-1.66 (m, 2H), 1.22 (t, 3H), 1.10 (t, 3H), 1.06-0.78 (m, 2H); $^{13}$C (CDCl$_3$) $\delta$ 132.43, 130.62, 117.10, 112.70, 82.90, 59.72, 57.66, 52.86, 51.75, 42.53, 26.86, 23.49, 15.59, 15.26. HRMS: C$_{22}$H$_{26}$Cl$_6$O$_2$ Calcd. 532.0066, Obsd. 532.0061; C$_{22}$H$_{26}$Cl$_5$O$_2$ Calcd. 534.0037, Obsd. 534.0032. FT-IR: 2970.5, 2952.0, 2931.5, 2906.1, 2866.1, 2360.6, 2239.3, 1795.9, 1775.3, 1604.7, 1471.7, 1442.6, 1280.3, 1263.8, 1165.8, 1091.9, 1065.3, 1013.9, 992.3, 910.1 cm$^{-1}$.

3.4.24 Synthesis of *endo-endo-anti*-17,17,18,18-tetramethoxy pentacyclo[12.2.1.16,9,02,13,05,10]octadeca-7,15-diene (3.32)
This compound was prepared by modification of a method of Gassman & Marshall. A mixture of sodium metal (24 g, 1 mol) in tetrahydrofuran (120 mL) and \( t \)-butanol (25 mL) is refluxed with mechanical stirring under argon. A solution of 3.9 (20 g, 31 mmol) in tetrahydrofuran (80 mL) is slowly added over a period of 1.5 h. The resulting mixture is refluxed for 36 h, cooled to r.t. and filtered through a wire screen. The resulting dark filtrate is mixed with ice and ether (300 mL). The organic phase is washed with brine, dried over magnesium sulfate and concentrated under reduced pressure to afford a yellow solid (4.7 g, 42%). A small sample was recrystallized from slow cooling of xylenes. 3.32 mp 239-242°C. \(^1\)H NMR (CDCl\(_3\)) \( \delta \) 6.04 (t, 4H), 3.19 (s, 6H), 3.09 (s, 6H), 2.64 (broad s, 4H), 2.32 (d, 4H), 1.58 (d, 4H), 0.95 (t, 4H); \(^{13}\)C (CDCl\(_3\)) \( \delta \) 132.4, 117.8, 52.2, 51.6, 49.7, 43.0, 27.6; HR-MS, m/z (M\(^+\)) C\(_{22}\)H\(_{32}\)O\(_4\) Calcd. 360.2310; Obsd. 360.2296; \(^{13}\)CC\(_{21}\)H\(_{32}\)O\(_4\) Calcd. 361.2328; Obsd. 361.2337; C\(_{21}\)H\(_{29}\)O\(_4\) Calcd. 345.2051; Obsd. 345.2062; C\(_{21}\)H\(_{29}\)O\(_3\) Calcd. 329.2113; Obsd. 329.2117; C\(_{20}\)H\(_{25}\)O\(_3\) Calcd. 313.1796; Obsd. 313.1808; C\(_9\)H\(_{11}\)O\(_2\) Calcd. 151.0739; Obsd. 151.0763; C\(_7\)H\(_{11}\)O\(_2\) Calcd. 127.0775; Obsd. 127.0757; C\(_8\)H\(_9\) Calcd. 105.0722; Obsd. 105.0702; C\(_7\)H\(_7\) Calcd. 91.0564; Obsd. 91.0546; FTIR: 2972.1, 2933.3, 2924.7, 2861.4, 2826.7, 1469.8, 1295.8, 1287.9, 1102.2, 1057.8, 728.9 cm\(^{-1}\).

3.4.25 Synthesis of \textit{endo-endo-anti-17,18-dioxopentacyclo[12.2.1.1\textsuperscript{6}.9.0\textsuperscript{2}.13.0\textsuperscript{5}.10]octadeca-7,15-diene} (3.33).

This compound was prepared by modification of a method of Grimme &
A solution of water (15 mL) in glacial acetic acid (60 mL) is warmed to 50-60°C. 3.32 is slowly added (2.5 g, 6.9 mmol). The resulting solution is allowed to stir at that temperature for 2 h, cooled and filtered affording a yellowish powder (1.6 g, 87%). A small sample was recrystallized from slow cooling of ethanol. 3.33 mp 224-226°C. $^1$H NMR (CDCl$_3$) $\delta$ 6.43 (t, 4H), 2.78 (t, 4H), 2.42 (d, 4H), 1.71 (d, 4H), 1.10 (t, 4H); $^{13}$C (CDCl$_3$) $\delta$ 205.3, 131.4, 54.8, 41.2, 26.4; HR-MS, (M$^+$) m/z; C$_{17}$H$_{20}$O$_3$ (M$^+$ - CO) Calcd. 240.1515; Obsd. 240.1514; C$_{16}$H$_{20}$O$_2$ (M$^+$ - 2CO) Calcd. 212.1571; Obsd. 212.1563; C$_{15}$CH$_{20}$ Calcd. 213.1504; Obsd. 213.1600; C$_{15}$H$_{17}$ Calcd. 197.1351, Obsd. 197.1325; C$_{14}$CH$_{17}$ Calcd. 198.1358, Obsd. 198.1365; C$_{14}$H$_{15}$ Calcd. 183.1183, Obsd. 183.1171; C$_{11}$H$_{11}$ Calcd. 143.0858, Obsd. 143.0861; C$_{10}$H$_{9}$ Calcd. 129.0727, Obsd. 129.0701. FT-IR: 2986.6, 2934.9, 1787, 1467.9, 1330, 1210, 1131.3 cm$^{-1}$.

\[ \text{3.33} \xrightarrow{\text{NH}_2\text{NH}_2, \text{KOH}} \text{3.34} \]

3.4.26 Synthesis of endo-endo-anti-pentacyclo

[12.2.1.1$^6,9$.0$^2,13$.0$^5,10$]octadeca-7,15-diene (3.34)

This compound was prepared by modification of a method by Todd. A mixture of 3.33 (1.3 g, 4.9 mmol), hydrazine-monohydrate (0.6 mL, 12 mmol), and potassium hydroxide (1.6 g, 29 mmol) in diethylene glycol (15 mL) is slowly brought to reflux and allowed to stir for 1 h (reaction mixture temp. 200°C). The resulting mixture of solids was extracted with ether, washed with brine, with water, dried over magnesium sulfate, and filtered affording a pale yellowish powder (0.73 g, 62%). A
small sample was recrystallized from slow cooling of ethanol and sublimed at 80°C (@ high vacuum). 3.34 mp 124-127°C. \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 6.01 (t, 4H), 2.58 (t, 4H), 2.07 (d, 4H), 1.61 (d, 4H), 1.25 (d, 2H), 1.23 (d, 2H), 0.82 (t, 4H); \(^{13}\)C (CDCl\(_3\)) \(\delta\) 135.0, 50.1, 49.3, 45.4, 29.0; HR-MS, m/z (M\(^+\)) C\(_{18}\)H\(_{24}\) Calcd. 240.1898, Obsd. 240.1871; C\(_{17}\)\(^{13}\)CH\(_{24}\) Calcd. 241.1938, Obsd. 241.1903; C\(_{13}\)H\(_{18}\) Calcd. 174.1412, Obsd. 174.1408; C\(_{10}\)H\(_{12}\) Calcd. 132.0948, Obsd. 132.0938; C\(_{8}\)H\(_{11}\) Calcd. 107.0893, Obsd. 107.0857. FT-IR: 2959.6, 2909.5, 2884.4, 2855.7, 2360.1, 1465.3, 1337.9, 1202.5, 1100.4, 1077 cm\(^{-1}\).

3.4.27 Synthesis of \textit{endo-13-oxatricyclo[8.2.1.0\(_2\)2.9]trideca-5,11-diene} (3.29)

This compound was prepared by the method of Eaton \textit{et al.} An ether solution (8 mL) of 3.14 (3 g, 13 mmol) is allowed to stir at room temperature with a 10% mol. sulfuric acid solution (31 mL) for 24 h. The organic layer is separated and the aqueous phase extracted with ether. The combined organic extracts are washed with a 10% aqueous sodium carbonate solution, brine, water, then dried over magnesium sulfate, filtered and concentrated under reduced pressure affording a white powder which is recrystallized from petroleum ether to fine needles followed by another recrystallization in ethanol. mp. 65-67°C 3.29 (0.95 g, 39.5%). \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 6.46 (t, 2H), 5.76 (t, 2H), 2.87-2.81 (m, 2H), 2.52-2.44 (m, 2H), 2.38-2.19 (m, 2H), 2.10-1.92 (m, 2H), 1.91-1.72 (m, 2H), 1.70-1.53 (m, 2H).
3.4.28 Synthesis of *endo*-tricyclo[8.2.1.0²,⁹]trideca-5,11-diene (3.30)

This compound was prepared by the method of Lap and Paddon-Row. An ethanol solution (160 mL) of 3.13 (11 g, 29 mmol) is allowed to gentle reflux under vigorous stirring. Sodium metal (25 g, 1.1 mol) is slowly added over a 3 h period. Upon addition of sodium, the resulting suspension is allowed to reflux overnight. The cooled mixture is treated with ice. The resulting mixture is extracted with petroleum ether, dried over sodium sulfate, filtered and concentrated under reduced pressure affording a pale yellowish liquid which is purified by distillation @ high vacuum affording a colorless liquid, bp. 90-95°C. NMR (CDCl₃) δ 6.08 (t, 2H), 5.73 (t, 2H), 2.64 (t, 2H), 2.36-2.28 (m, 2H), 2.10-1.90 (m, 2H), 1.84-1.69 (m, 2H), 1.45-1.26 (m, 2H), 1.35 (d, 2H), 0.92-0.76 (m, 2H); ¹³C (CDCl₃) δ 135.8, 132.1, 50.5, 50.0, 44.7, 31.4, 26.2; HR-MS, C₁₃H₁₈ Calcd. 174.1407, Obsd. 174.1418; C₁₂¹³CH₁₈ Calcd. 175.1438, Obsd. 175.1459; C₁₀H₁₃ Calcd. 133.1017, Obsd. 133.1022; C₁₀H₁₁ Calcd. 131.0868, Obsd. 131.0816; C₉H₁₁ Calcd. 119.0866, Obsd. 119.0825; C₇H₇ Calcd. 91.0545, Obsd. 91.0573; FTIR: 3059.2, 3016.5, 2955, 2932.6, 2863.5, 1652.8, 1475.7, 1463, 1437.1, 1339.4, 1253.3, 1165.7 cm⁻¹.
3.4.29 Synthesis of endo-tricyclo[8.2.1.02,9]trideca-5-ene (3.31)

This compound was prepared by the method of Brown & Ahuja\textsuperscript{188}

Preparation of a 1M sodium borohydride solution in ethanol: An absolute-ethanol solution (95 mL) of sodium borohydride (4 g) is vigorously stirred with a 2N sodium hydroxide solution (5 mL) for 30 min and filtered. This solution is best prepared freshly the day of use for maximum catalyst reproducibility. A 95% ethanol solution (49 mL) of nickel acetate tetrahydrate (1.24 g, 5 mmol) is vigorous stirred under argon atmosphere at room temperature. 1M sodium borohydride solution in ethanol (5 mL) is injected over 15 sec period. When gas evolution from the mixture ceases, the P2-nickel catalyst is ready for use. 3.30 (1.0 g, 5.7 mmol) is slowly injected and the resulting mixture is allowed to stir for 25 min. Activated carbon is added to the resulting suspension, followed by filtration through a thin pad of carbon on a buchner funnel. The filter pad is washed with ethanol and acetone. The resulting solution is concentrated under reduced pressure affording a colorless oily liquid. One third of this liquid is passed through a silica gel preparative plate using hexane as eluent affording a colorless liquid. 3.31 \textsuperscript{1}H NMR (CDCl\textsubscript{3}) \( \delta \) 5.75 (t, 2H), 2.39-2.21 (m, 2H), 2.08-1.91 (m, 4H), 1.86-1.53 (m, 4H), 1.51-1.32 (m, 4H), 1.32-1.18 (m, 4H); \textsuperscript{13}C (CDCl\textsubscript{3}) \( \delta \) 131.8, 44.2, 42.7, 40.6, 28.6, 26.1, 22.2; HRMS: C\textsubscript{13}H\textsubscript{20} Calcd. 176.1577, Obsd. 176.1562, C\textsubscript{13}H\textsubscript{20} Calcd. 177.1592, Obsd. 177.1600, C\textsubscript{11}H\textsubscript{17} Calcd. 161.1329, Obsd. 161.1331, C\textsubscript{11}H\textsubscript{16} Calcd. 148.1294, Obsd. 148.1245, C\textsubscript{11}H\textsubscript{16} Calcd. 149.1309, Obsd. 149.1281, C\textsubscript{10}H\textsubscript{13} Calcd. 133.1005, Obsd. 133.1019; FT-IR: 3016.4, 2938.5, 2874.6, 2841.7, 2360.9, 2342.7, 1476.8, 1463.4 cm\textsuperscript{-1}. 

3.4.30 Synthesis of endo-endo-1,5,6,7,8,14,15,16,17,17,18,18-
dodecachlorohexacyclo[12.2.1.15,8,02,13,03,12,04,9]octadeca-
6,10,15-triene (3.37)

This compound was prepared by modification of a method of Akhtar et al.91 A neat solution of cyclooctatetraene (0.5 g, 4.6 mmol) with hexachlorocyclopentadiene (13.6 g, 49.9 mmol) is slowly heated (oil bath) under continuous stirring and argon atmosphere until the oil bath reaches 235°C, then the resulting dark oily material is cooled down to room temperature and allow to sit in the freezer overnight, then passed through a silica-gel column using hexane as eluent. Upon concentration of the 4th 250 ml fraction, a white solid deposited in the flask which is recrystallized from ethanol. mp 172-175°C (1.1 g, 37%). 1H NMR (CDCl3) δ 5.90 (t, 2H), 3.40 (d, 1H), 3.04 (dd, 1H), 2.84 (dd, 2H), 2.45 (dd, 1H), 1.52 (dd, 1H); 13C (CDCl3) δ 132.80, 130.98, 120.85, 82.62, 81.70, 51.67, 51.37, 47.12, 43.39, 29.19, 27.37. HRMS: C_{18}H_{8}^{35}Cl_{10}^{37}Cl_{2} Calcd. 647.6828, Obsd. 647.6830; C_{18}H_{8}^{35}Cl_{9}^{37}Cl_{3} Calcd. 649.6802, Obsd. 649.6794; FT-IR: 3029.0, 2970.6, 2935.1, 2921.0, 2359.9, 2342.4, 1603.2, 1270.0, 1262.4, 1184.6, 1170.1, 1080.6, 1060.1, 1025.0, 1005.7 cm⁻¹.
3.4.31 Synthesis of endo-endo-endo-1,8,9,10,11,18,19,20,21,21,23,23-Dodecachloro-22-oxoheptacyclo[16.2.1.1^3,16.1^8,11.0^2,17.0^4,15.0^7,12.]trieicosa-9,19-diene (T)

This compound was prepared by modification of a method of Akhtar et al. A neat solution of 3.29 (0.37 g, 20 mmol) with hexachlorocyclopentadiene (1.61 g, 59 mmol) is slowly heated (oil bath) under continuous stirring and argon atmosphere at 133-140°C for 3 h. Hexane is added to the cooled resulting paste precipitating a yellowish powder which is recrystallized from ethanol. Tmp >315°C (dec.). \( ^1H \) NMR (CDCl\(_3\)) \( \delta \) 3.06 (s, 2H), 2.98 (dd, 2H), 2.37 (dd, 2H), 2.20 (t, 2H), 2.14 (dd, 2H), 1.90 (dd, 2H), 1.60-1.39 (m, 2H), 1.07-0.87 (m, 2H); \( ^1^3C \) (CDCl\(_3\)) \( \delta \) 204.83, 133.36, 130.63, 102.66, 101.99, 82.66, 80.50, 51.29, 46.85, 46.30, 37.28, 25.04, 22.89. HRMS, C\(_{23}\)H\(_{14}\)O\(_{35}\)Cl\(_8\)\(_{37}\)Cl\(_4\) Calcd. 733.7179, Obsd. 733.7216; FT-IR: 3020.4, 2980.7, 2952.5, 2937.7, 2907.5, 2867.5, 2360.1, 2341.6, 1768.8, 1603.4, 1473.8, 1266.8, 1217.2, 1169.9, 1076.9, 1067.1, 1033.2 cm\(^{-1}\).
3.4.32 General NMR methodology

List of reactants with abbreviations:

- COD
- Monoadduct
- Reduced Monoadduct
- HCCP
- DMTCCP
- DPIBF
- TCCP

Several trials (at least 3) on each of the following individual reactions were performed under the below described procedure. The objective of these experiments is to monitor the stereoisomeric ratio of their corresponding products by NMR spectroscopy.

a) 1 eq. COD + 4 eq. \{HCCP, DMTCCP, DPIBF, TCCP\}

b) 1 eq. Monoadduct \((X=\text{OCH}_3)\) + 3 eq. \{HCCP, DMTCCP, TCCP\}
c) 1 eq. Monoadduct (X=Cl) + 3 eq. {HCCP, DMTCCP, TCCP}
d) 1 eq. Reduced monoadduct (X=OCH₃) + 3 eq. {HCCP, DMTCCP}
e) 1 eq. Reduced monoadduct (X=O) + 3 eq. {HCCP, DMTCCP}
f) 1 eq. Reduced monoadduct (X=O) + 1 eq. {HCCP, DMTCCP}
g) 1 eq. Reduced monoadduct (X=H) + 3 eq. {HCCP, DMTCCP}
h) 1 eq. Reduced monoadduct (X=H) + 1 eq. {HCCP, DMTCCP}
i) 1 eq. 3.31 + 3 eq. {HCCP, DMTCCP}

A neat solution of the dienophile (0.01 - 0.1 mmol) with the electron deficient diene (0.03 - 0.3 mmol) is heated at 133-140°C (oil-bath) for 3 h in a septum-sealed ampule under argon atmosphere and continuous (magnetic) stirring. Upon cooling, the resulting mixture is completely dissolved in CDCl₃, from which an aliquot is taken for its NMR analysis.
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José Gabriel García was born on March 24, 1959 in Ciudad de México, MEXICO. He received his B.S. degree in Chemistry from the Universidad Iberoamericana in 1983, he received his M.S. degree in Chemistry from Louisiana State University in 1986, and continued his education with Dr. Mark L. McLaughlin at Louisiana State University from 1987 to the present. He is currently a candidate for the degree of Doctor of Philosophy in the department of Chemistry.
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Candidate: Jose Gabriel Garcia

Major Field: Chemistry


Approved:

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Major Professor and Chairman

[Signature]
Dean of the Graduate School

EXAMINING COMMITTEE:

[Signature]

Date of Examination:

November 30, 1990