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Approaches to a generalized synthesis for hexaphenylbutadiene

Karena Kaye Linkenhoger Robinson

APPROACHES TO A GENERALIZED SYNTHESIS FOR HEXAPHENYLBUTADIENE

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Karena Kaye Linkenhoger Robinson

Marshall University

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Gary O. Anderson
Advisor, Department of Chemistry

Member, Department of Chemistry

Robert J. Mayer
Member, Department of Chemistry

Ronald J. Deutsch
Dean, Graduate College

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TO MY PARENTS FOR PREPARING ME
FOR LIFE'S CHALLENGES
AND TO MY HUSBAND, ERIC,
FOR HIS PATIENCE AND SUPPORT

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ABSTRACT

This study was concerned with the attempted development of a generalized synthesis of hexaphenylbutadiene. Three methods were attempted: Michael Addition of cyanide to α-phenylcinnamate followed by organolithium or Grignard addition; reaction of benzil with two moles of the Wittig reagent prepared from bromodiphenylmethane; reaction of two moles of benzophenone with the bisphosphorane prepared from 1,2-dibromo-1,2-diphenylethane.

INTRODUCTION

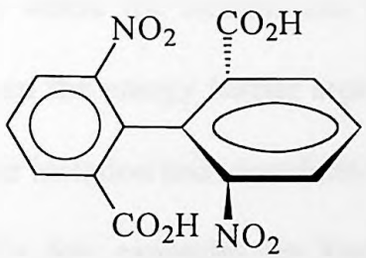
Stereochemistry is a subdicipline of organic chemistry devoted to the study of the three dimensional spatial configurations of molecules.[1] One aspect of stereochemistry deals with stereoisomers - compounds that differ only in the spatial configuration of substituent groups within a molecule (same atomic bonding order) and that are likely to have very similar physical and chemical properties. Several different classes of stereoisomers can be distinguished.

Two of these classes are conformational isomers and configurational isomers. Conformational isomers, or conformers, can be interconverted by rotation about single bonds. Configurational isomers differ from each other only in the arrangement of their atoms in space and cannot be converted from one into another by rotations about single bonds within the molecules.

Configurational isomers are classified as either enantiomers or diastereomers. Enantiomers are stereoisomers that lack a plane of symmetry and their mirror images are nonsuperimposable. Many, but not all, enantiomers contain at least one chiral center - a tetrahedral atom bearing four different substituents. Except for their ability to rotate the plane of polarized light to equal extents but in opposite directions, enantiomers have identical physical and chemical properties unless they are interacting with another chiral molecule. If only one of these enantiomers is present in a solution, the compound rotates the plane of polarized light to either the right or the left as the it passes through the solution and the molecule is said to be optically active.[2] The presence of a chiral center is

one of the most common situations which leads to molecular dissymmetry. However, it is possible to have a chiral molecule that does not contain a chiral center.

The term atropisomerism was coined by Kuhn in 1933 to describe stereoisomers which are chiral solely as a result of hindered rotation about a single bond.[3] Atropisomers are configurationally stable at room temperature. An energy barrier of 16-20 kcal/mol is considered sufficient for isolation of the isomers at room temperature. The first resolution of an atropisomeric compound, 2,2'-dinitro-6,6'-diphenic acid (**1**), was reported by



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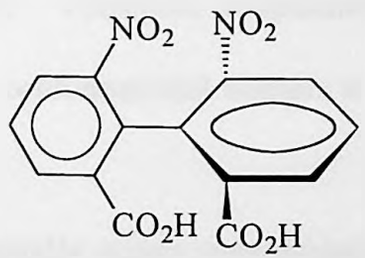
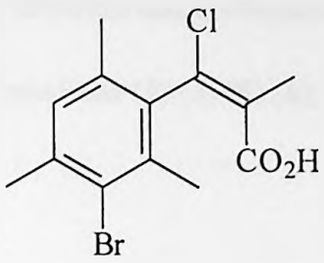


(-)-1

Christie and Kenner in 1922.[4] They found that the large substituents in the ortho positions forced the rings into a non-coplanar conformation and prevented free rotation about the central bond.

Although atropisomerism was originally used to describe biphenyls with bulky substituents, Adams[5] showed that restricted rotation was not limited to two ring systems by resolving β-chloro-β-(2,4,6-trimethyl-3-bromophenyl)-α-methylacrylic acid (**2**). This



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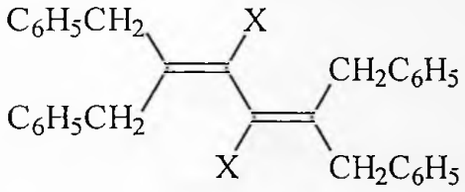
compound contains a highly substituted double bond and an ortho substituted aromatic ring which combine to prevent free rotation. This led to a more generalized definition of atropisomerism, namely, any kind of stereoisomerism due to the restricted rotation about single bonds where the isomers can be isolated.[6] Therefore, atropisomerism will be observed when the energy barrier separating the conformational isomers is high enough to permit their isolation and identification.[7]

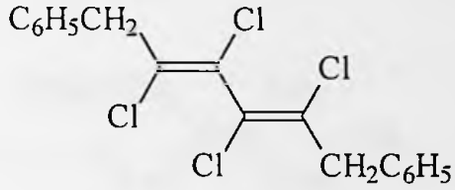
Only a few examples are known of optically active stereoisomers of alkenes bearing no chiral centers.[8-12] In principle both the cis and the trans form of olefins should be capable of existence as stable optically active stereoisomers, provided bulky substituents cause a permanent out-of-plane distortion of the double bond. Substituted 1,3-butadienes with bulky substituents in the 2 and 3 positions that restrict rotation would be expected to prefer non-planer (skew) conformations and can conceivably be chiral.[13] In these types of compounds chirality would be caused, not by an asymmetric carbon atom, but by a plane or axis of symmetry.

Hexasubstituted butadienes should meet the requirements for chirality of butadienes. Previous studies of 1,3-butadienes prove that highly substituted butadienes

are chiral. For instance, in 1972 Köbrich and co-workers[13] demonstrated the chirality of the following derivatives of 1,3-butadiene (**3**) (**4**) (**5**) (**6**):



3, X = Br
4, X = I
5, X = Cl



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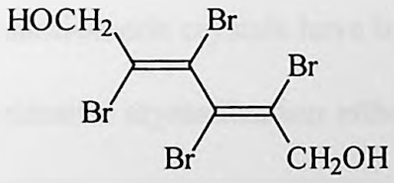
In a separate study, Rösner and Köbrich[14] reported the partial resolution of 2,3,4,5-tetrabromo-2,4-hexadiene-1,6-diol (**7**) and 2,2'-[2,3,4,5-tetrabromo-2,4-hexadienylene bis(oxycarbonyl)]dibenzoic acid (**8**).



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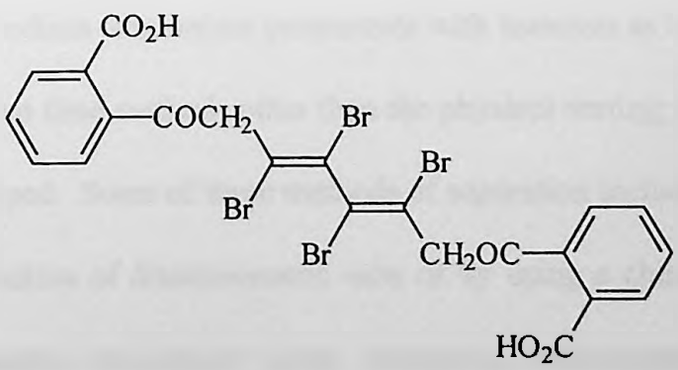

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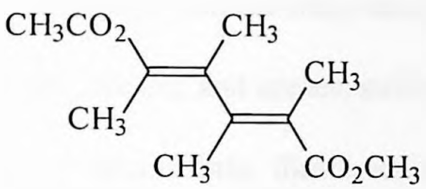
Additionally, Becher and Mannschreck[15] in 1983 successfully synthesized the diastereoisomers of dimethyl-2,3,4,5-tetramethyl-2,4-hexadienedioate (**9**) and (*E,Z*)-1,6-dimethoxy-2,3,4,5-tetramethyl-2,4-hexadiene (**10**).



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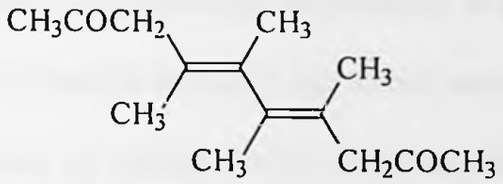

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These results show that, in general, hexasubstituted butadienes can be chiral. However, the chirality of simple 1,3-butadienes with bulky substituents at the 2 and 3 positions and no functional groups has never been demonstrated.

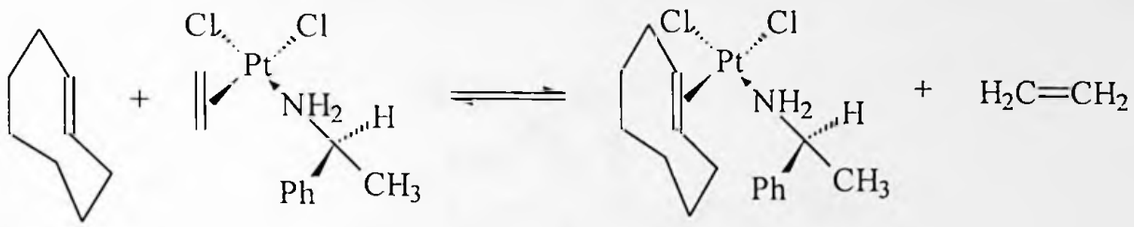
A key aspect of the study of enantiomers focuses on the techniques for separation. The first reference to the isolation of enantiomers was noted in 1848 when Louis Pasteur separated the two crystalline forms of sodium ammonium paratartrate with tweezers as he looked through a microscope. Since that time methods other than the physical sorting of enantiomeric crystals have been developed. Some of these methods of separation include selective crystallization either by formation of diastereomeric salts or by using a chiral solvent, kinetic techniques (asymmetric destruction using enzymes), calorimetric methods, isotope labeling, and NMR spectroscopy.

The largest number of recorded resolutions has been accomplished by conversion of enantiomers to a mixture of diastereomers. Diastereomers containing a functional group are formed through chemical transformation by reaction with an enantiomerically pure (homochiral) derivatizing agent. For example, amphetamine is resolved by the acid-base reaction with tartaric acid to give two ammonium salts, one from each of the enantiomers. On the other hand, diastereomers devoid of conventional functionality (e.g. chiral alkenes, and arenes, sulfoxides, and phosphines) can be formed in one of two ways: incorporation into diastereomeric metal complexes or reaction with chiral π-acids (formation of transient diastereomer association complexes).

One method of forming diastereomers from enantiomers without functional groups is by incorporation into metal complexes. For example, Cope et al.[16] first described the resolution of *trans*-cyclooctene (**11**) by incorporation of the alkene enantiomers into

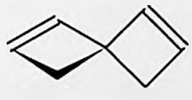
11

diastereomeric trans platinum(0) square planar complexes (**12**) that are separable by low-temperature crystallization.



11 **12**

In 1974, Wynberg et al.[17] also used this technique to resolve the compound, spiro[3.3]hepta-1,5-diene (**13**). These authors utilized the principle of attaching both



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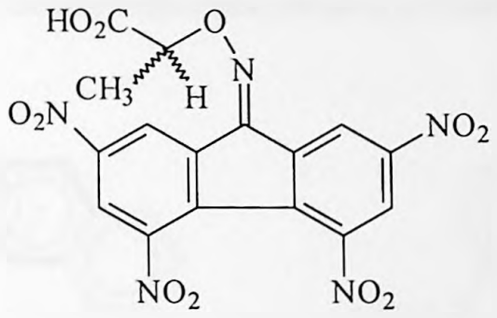
racemic spirocycle and the optically active amine to the square planar platinum (II) to form a pair of diastereomers separable by fractional crystallization.

The second method for forming diastereomers from enantiomers without functional groups is by forming diastereomeric π- (or charge transfer) complexes. Chiral aromatic hydrocarbons have been resolved with α-(2,4,5,7-tetranitro-9-

fluorylideneaminoöxy) propionic acid, or TAPA (**14**), using this technique. For example,



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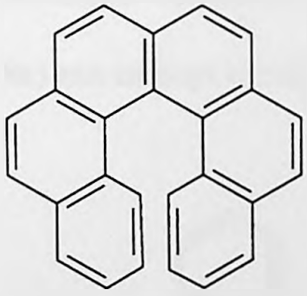
in 1955 Newman et al.[18] resolved the enantiomers of hexahelicene (**15**) by forming



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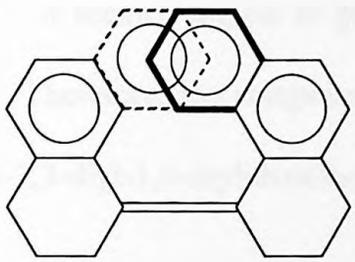
π-complexes with TAPA and allowing one of the complexes to crystallize out of solution. Gil-Av et al.[19] then separated ten helicenes, including hexahelicene, by high performance

liquid chromatography (HPLC) using short slurry-packed silica gel columns coated *in situ* with TAPA. In a separate study, Feringa and Wynberg[20] resolved the cis- (**16**) and trans-4,4'-Bi-1,1',2,2',3,3'-hexahydrophenanthrylidene (**17**) using TAPA.



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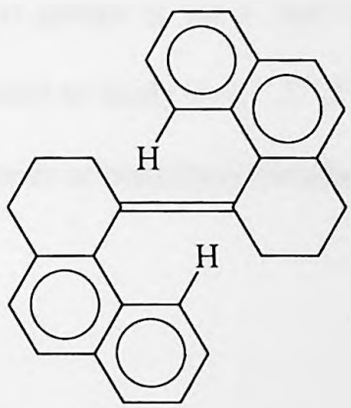

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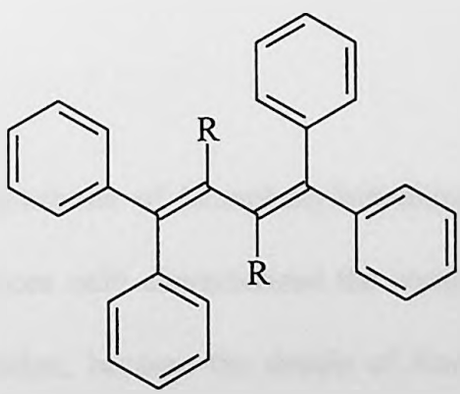
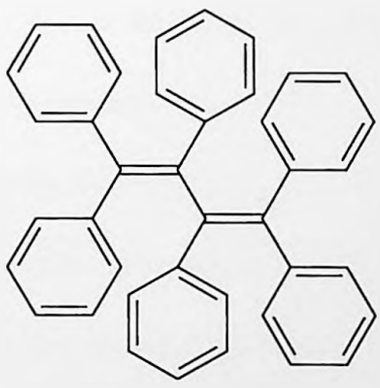
With these findings in mind, the purpose of this investigation was to develop a generalized synthesis for highly substituted butadienes that contain bulky substituents in the 2 and 3 positions (**18a, 18b, 18c**) and attempt to resolve the enantiomers. This would



18a, R = isopropyl
18b, R = t-butyl
18c, R = phenyl

allow future investigators to study the rotational barriers and optical stabilities of this series of compounds. Based on the finding of Hesse and Hagel[21] that separation of enantiomers is more effective if one of the substituents is aromatic and considering the successful resolution of aromatic compounds by Mannschreck and co-workers,[22, 23] it seemed logical to place phenyl groups at the 1- and 4- positions of 1,3-butadiene. Therefore, the compound we elected to study is 1,1',1'',1''',1'''',1'''''-(1,3-butadiene-2,3-diyl-1,4-diylidene)hexakisbenzene or hexaphenylbutadiene (**19**).



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References to the synthesis of hexaphenylbutadiene exist in the literature.[24-26] Unfortunately, these references only characterized the compound by melting point and elemental analysis. In addition, because the details of Koelsch's experiments were so vague, attempts to reproduce his original synthesis[24] yielded only 6.8% of the crude

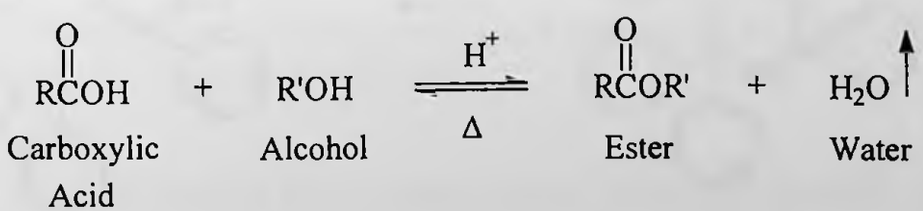
product.[27] Further attempts to synthesize hexaphenylbutadiene via 1,4-reductive elimination using titanium (0) and oxidative coupling using copper (I) iodide were unsuccessful as well.[27]

RESULTS AND DISCUSSION

A. The first method used to attempt the synthesis of hexaphenylbutadiene involved a multi-step synthetic route starting with α-phenylcinnamic acid. The plan was to methylate the acid to make the ester which can then undergo the Michael addition with cyanide to give the cyano derivative. Through hydrolysis we would obtain diphenylsuccinic acid which would then react with an organolithium or Grignard reagent to form hexaphenylbutadiene. This approach is shown in Scheme 1.

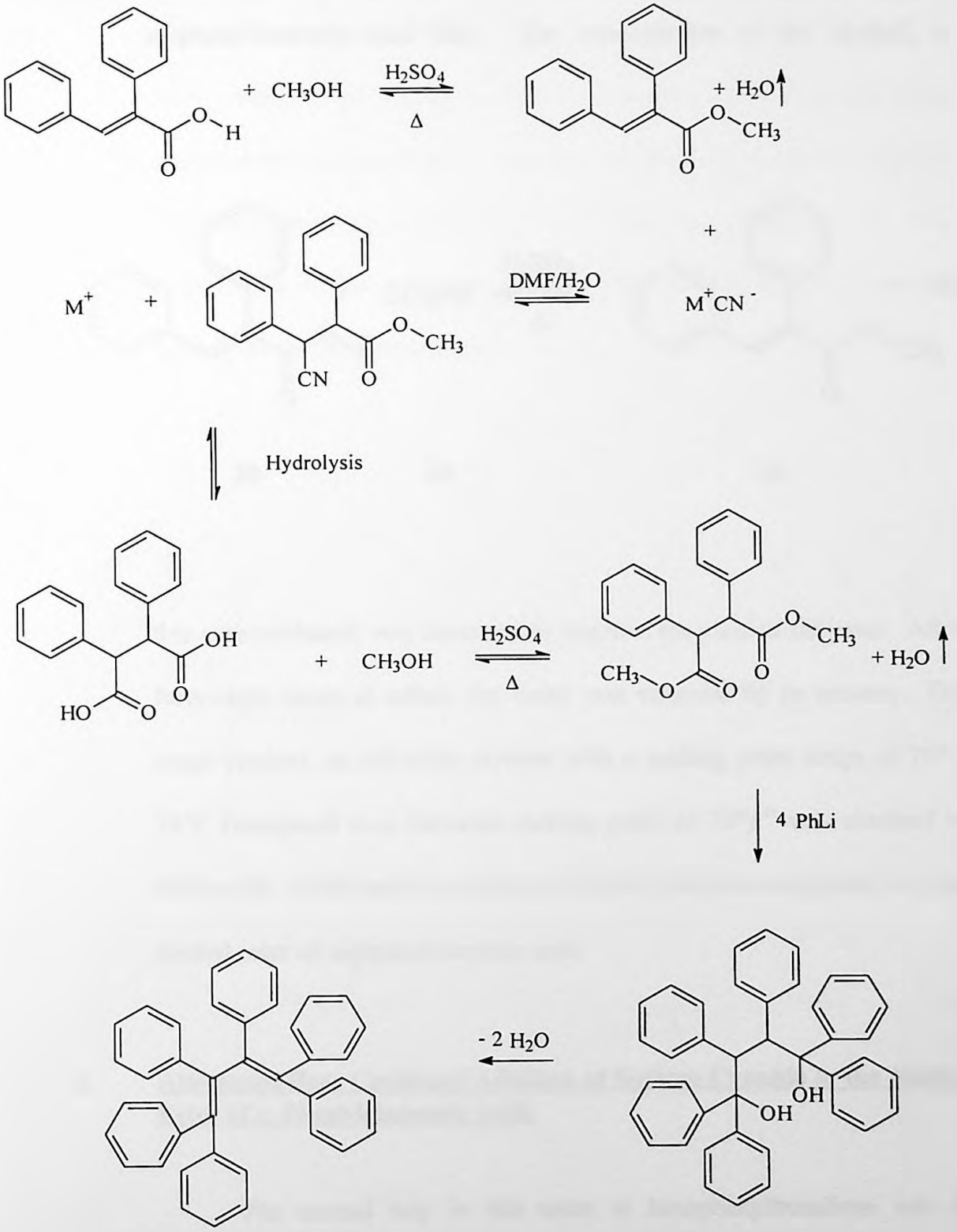
1. Synthesis of Methyl Ester of α-Phenylcinnamic Acid.

The first step in this synthetic approach was to make the methyl ester of α–phenylcinnamic acid. The most common route for making esters is to react the corresponding carboxylic acid with an alcohol in the presence of a strong acid which gives the desired ester (Scheme 2). Because this reaction is reversible, it usually is not done stochiometrically. The yield of the ester can be increased either by removing one of the products of the reaction as it is formed or by increasing the concentration of one of the reactants. In some particularly tough cases, both measures can be taken.

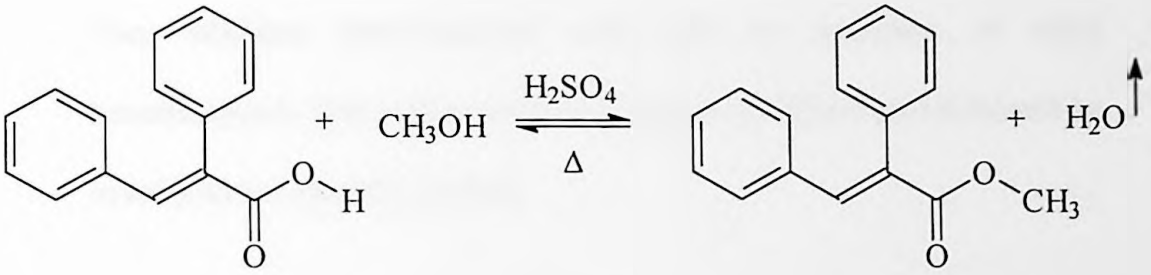


Scheme 2

Scheme 1



Therefore, α–Phenylcinnamic acid (**20**) was reacted with methanol (**21**) in the presence of sulfuric acid to obtain the methyl ester of α–phenylcinnamic acid (**22**). The concentration of the alcohol, in



20 **21** **22**

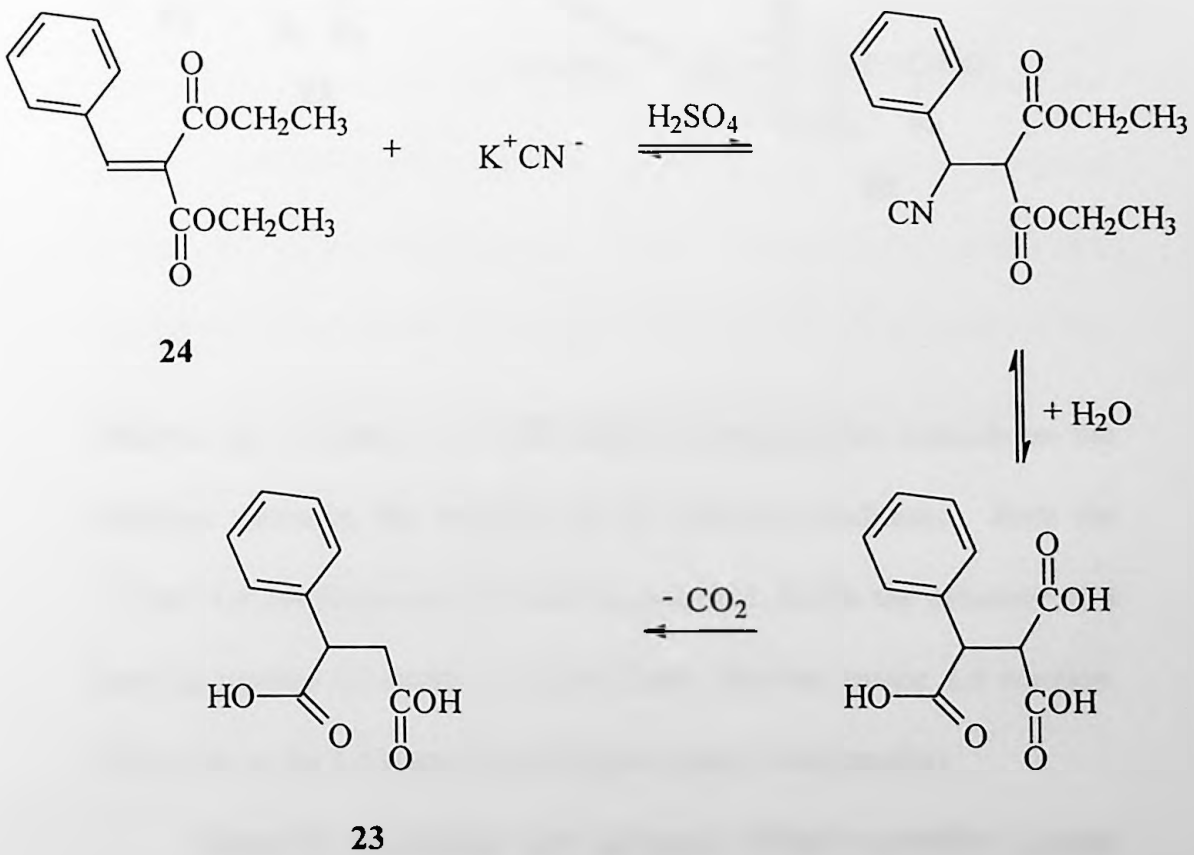
this case methanol, was increased to improve the yield of the ester. After forty-eight hours at reflux, the water was removed by *in vacuuo*. The crude product, an off-white powder with a melting point range of 70° - 74°C (compared to a literature melting point of 75°),[28] was obtained in 83% yield. NMR and IR analyses confirmed that the compound was the methyl ester of α-phenylcinnamic acid.

2. Attempted Base Catalyzed Addition of Sodium Cyanide to the Methyl Ester of α-Phenylcinnamic Acid.

The second step in this route to hexaphenylbutadiene was to synthesize the cyano derivative of the methyl ester of α-phenylcinnamic

acid by Michael addition of cyanide. Hydrogen cyanide adds to α,β–unsaturated compounds activated by groups such as nitro,[29-31] sulfone,[29] and carbonyl.[32]

Addition of hydrogen cyanide to a carbon-carbon double bond activated by a carbonyl group was first observed by Bredt and Kallen.[32] They obtained phenylsuccinic acid (**23**) by treatment of ethyl benzalmalonate (**24**) with potassium cyanide and sulfuric acid followed by hydrolysis and decarboxylation.



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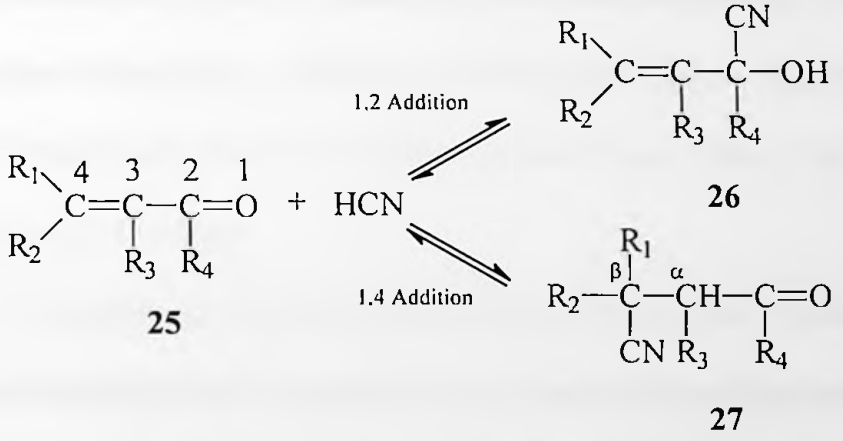
23

The addition of hydrogen cyanide to a conjugated carbonyl system occurs in the presence of an appropriate catalyst through a process called hydrocyanation.[33] The addition to an α,β–unsaturated carbonyl compound (**25**) gives a 1,2 adduct, α–cyanohydrin (**26**), and a 1,4 adduct, β -cyano ketone (**27**).



Whether the 1,2 (**26**) or 1,4 (**27**) addition predominates depends on the substrate structure, the reagent, and the reaction conditions. Both the 1,2 and 1,4 additions are reversible in principle, but in the presence of a base the reverse 1,2 addition is much faster than the reverse 1,4 reaction. This leads to the 1,4 adduct as the major (usually sole) product.

However, the ketone also undergoes further reversible cyanide addition to give β-cyano ketone cyanohydrin. Because the reversible 1,2

addition is faster than the reversible 1,4 addition, and the reverse 1,4 addition is much slower than the forward one, the latter step is the rate determining step. The cyanohydrin is unstable in basic medium; thus, the final product is the β-cyano ketone (**27**).

In addition, at higher temperatures, both reverse reactions are more favorable than the forward reactions.[34] Therefore, hydrocyanation of an α,β-ethylenic ketone with hydrogen cyanide in the presence of a basic catalyst selectively gives 1,2 adduct at lower temperatures and 1,4 adduct at higher temperatures. Reaction involving an alkali or alkaline-earth metal cyanide affords only 1,4 adduct in most cases owing to the highly basic reaction medium.

Considering these discoveries, along with the work of Kurtz[29] and Lapworth and McRae[35] who synthesized α-phenylcinnamonitrile using this method, the desired reaction seemed feasible. Therefore, the methyl ester of α–phenylcinnamic acid obtained from the reaction described above was added to 20 mL DMF. Sodium cyanide, dissolved in water in the presence of ammonium chloride, was added. The reaction mixture was stirred at room temperature for forty-eight hours while undergoing analysis periodically via TLC. Because the TLC results were inconclusive, the mixture was stirred at room temperature for an additional twenty-four hours.

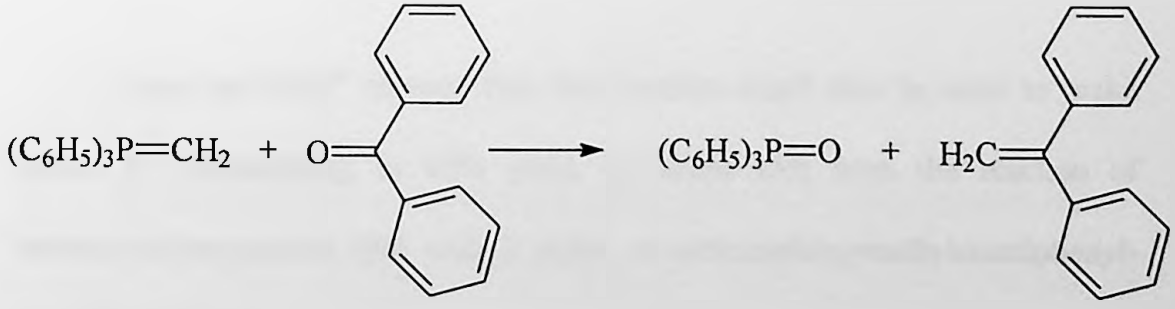
The mixture was then extracted three times with diethyl ether. The

three ether extracts were combined and then washed with 20 mL water. The ether was removed using a rotary evaporator at 60° C and 5 mmHg. The resulting material, an off-white solid with a melting point of 71-73° C, was found to be the starting material.

The above experiment was then repeated using an internal GC standard, bromotriphenylethylene, and was analyzed via GC to monitor the reaction. After stirring at room temperature for forty-eight hours, none of the starting materials had been consumed. The reaction was considered unsuccessful so this method was abandoned and other methods were considered.

B. Attempted Synthesis of Hexaphenylbutadiene by the Wittig Reaction using Bromodiphenylmethane and Triphenylphosphine.

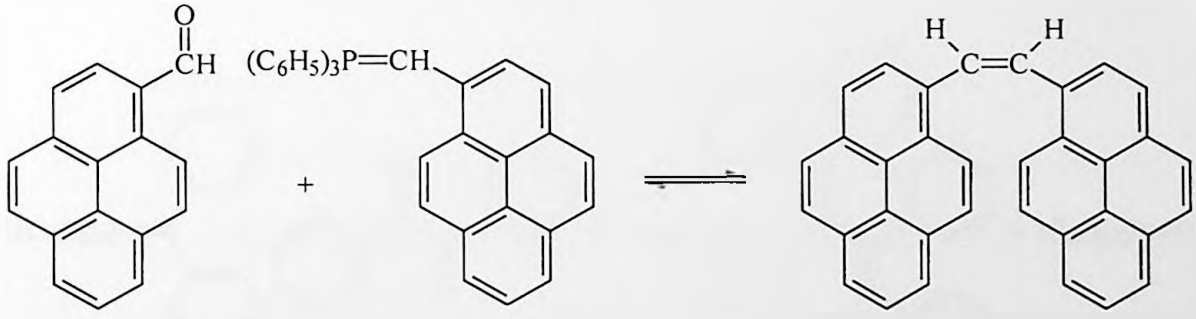
In 1953 Wittig and Geissler[36] found that reaction of methylenetriphenylphosphorane (**28**) with benzophenone (**29**) gave triphenylphosphine oxide (**30**) and 1,1-diphenylethylene (**31**) in almost quantitative yield. This discovery led in



28 **29** **30** **31**

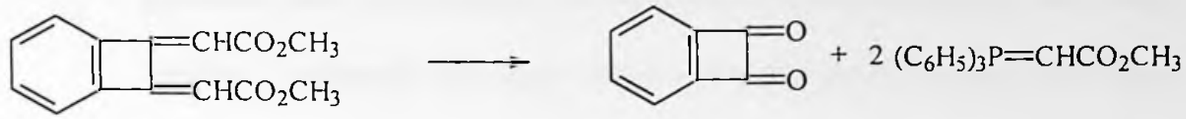
the following years to the development of a new method for the synthesis of olefins which, under the name Wittig reaction, soon attained major importance in preparative organic chemistry.

The preparation of symmetrical 1,2-diarylethylenes containing large aromatic groups has also been reported by this method. For example, in 1960 Geerts and Martin[37] used 1-pyrenecarboxaldehyde (**32**) and triphenylpyrenyl-methylenephosphorane (**33**) to synthesize 1,2-bis-(3-pyrenyl)ethylene **(34)** in 91% yield.



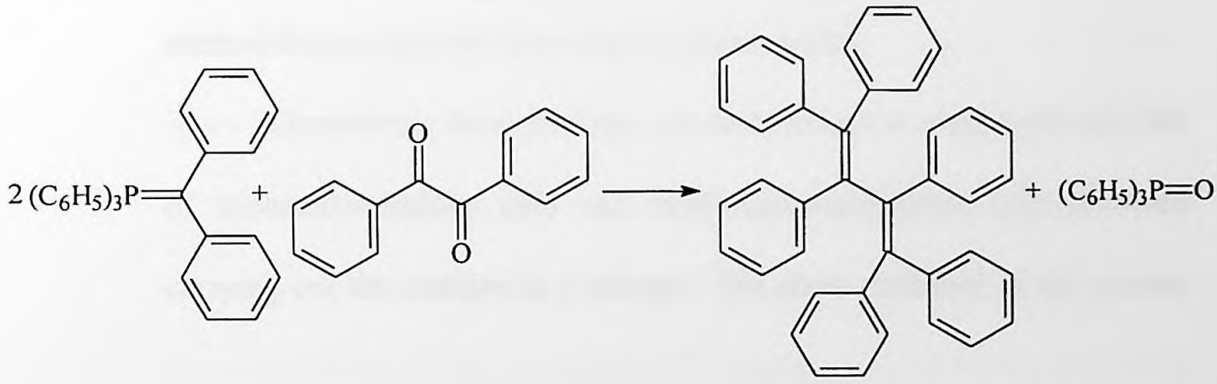
32 **33** **34**

Cava and Pohl[38] showed that this reaction could also be used to make dienes by synthesizing, in 85% yield, the diene **(35)** from the reaction of benzocyclobutenedione **(36)** with 2 moles of carbomethoxymethylenetriphenyl-phosphorane **(37)**.



35 **36** **37**

Based on these results, the synthesis of hexaphenylbutadiene (**19**) via the Wittig reaction of 2 moles of bromodiphenylmethanetriphenylphosphorane (**38**) and benzil (**39**) seemed feasible.



38 **39** **19** **30**

1. <u>Synthesis of Salt of Bromodiphenylmethane and Triphenylphosphine.</u>

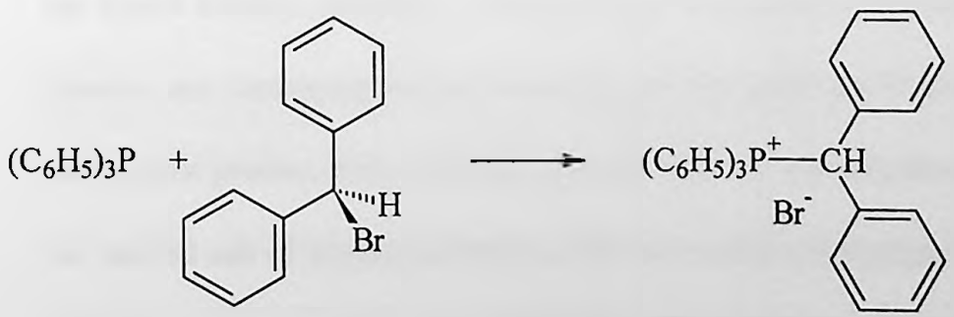
The first step in this approach required forming the salt of bromodiphenylmethane and triphenylphosphine. Triphenylalkylphos-

phonium salts are generally prepared from triphenylphosphine and alkyl halides. Although the alkyl iodides are the most reactive, the alkyl bromides are used most frequently because they are often more readily accessible. In general, three methods may be used for this reaction:[39]

1. Liquid halides may be made to react with triphenylphosphine without the use of a solvent.
2. The reaction of solid halides with triphenylphosphine may be carried out in the melt.
3. Equimolar quantities of triphenylphosphine and an alkyl halide are allowed to react in a suitable solvent.

The first two modes of preparation are customarily used only if the third method fails to give the desired phosphonium salts.

Considering these findings, our first attempt at making the salt (**40**) of triphenylphosphine (**41**) and bromodiphenylmethane (**42**) involved carrying out the reaction in a solvent. We chose methanol as the solvent



41 **42** **40**

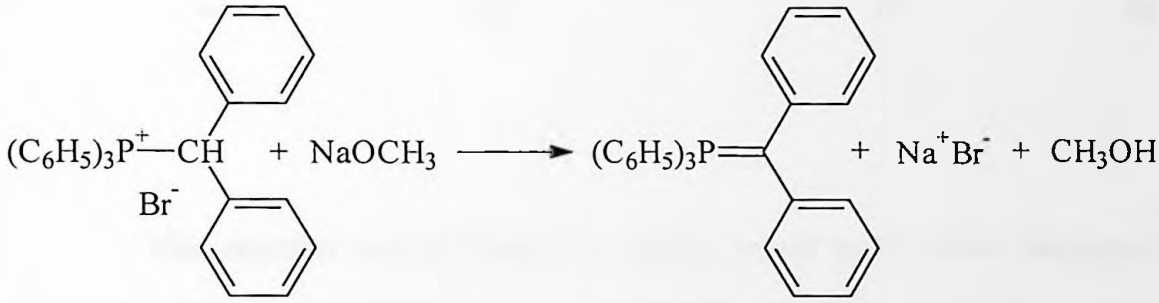
and used bromotriphenylethylene as an internal GC standard. The reaction mixture was heated to reflux while being analyzed via GC periodically to monitor the reaction. After twenty-four hours the GC results indicated that none of the reactants had been consumed so the reaction was considered unsuccessful.

We decided to try to make the salt using one of the other two techniques. In 1955, Horner and Lingnau[40] prepared the phosphonium salt from triphenylphosphine and bromodiphenylmethane in 50% yield using the melt technique. Further support for doing the reaction in the melt was that both of the starting materials are solid. Because this approach seemed to be the most reasonable next step, we decided to make the salt via this approach.

Bromodiphenylmethane and triphenylphosphine were weighed into a beaker. The beaker was heated allowing both solids to melt. After several minutes a solid started precipitating out of solution and eventually the liquid mixture solidified. Diethyl ether was added to the beaker to dissolve any remaining starting materials and the solid was filtered. The pale yellow product with a melting point of >300° C, was considered to be the desired salt of triphenylphosphine and bromodiphenylmethane.[40] The procedure was repeated for reproducibility and to obtain more product.

2. **Synthesis of Ylide of Bromodiphenylmethane and Triphenylphosphine.**

The next step in this procedure was to make the ylide (**43**) from the salt (**40**) of triphenylphosphine and bromodiphenylmethane. The salt

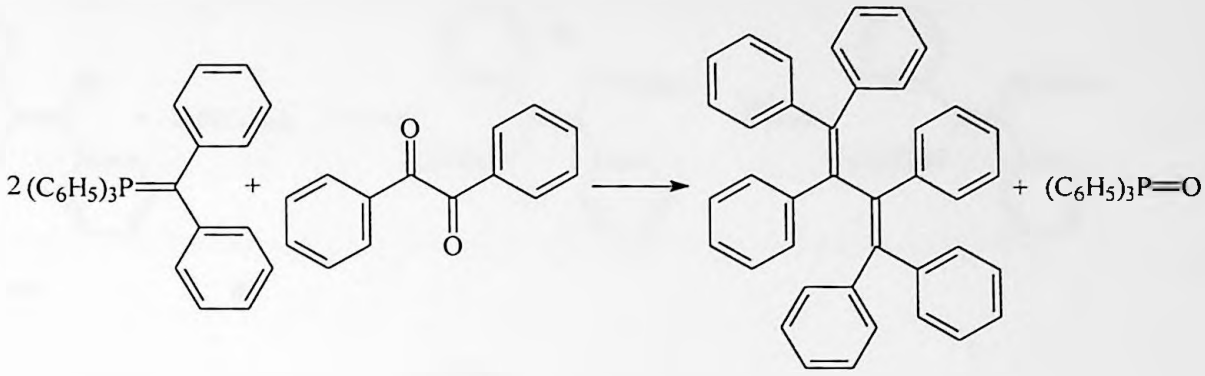


40 **43**

obtained by the reaction described above was dissolved in methanol. Sodium methoxide was added and a color change occurred. The reaction was assumed to have taken place and the product was not isolated.

3. **Attempted Synthesis of Hexaphenylbutadiene from Ylide of Bromodiphenylmethane and Triphenylphosphine.**

The final step in this approach involved reacting 2 moles of the ylide (**43**) with 1 mole of benzil (**39**) to get 1 mole of the final product, hexaphenylbutadiene (**19**), and 2 moles of triphenylphosphine oxide (**30**).

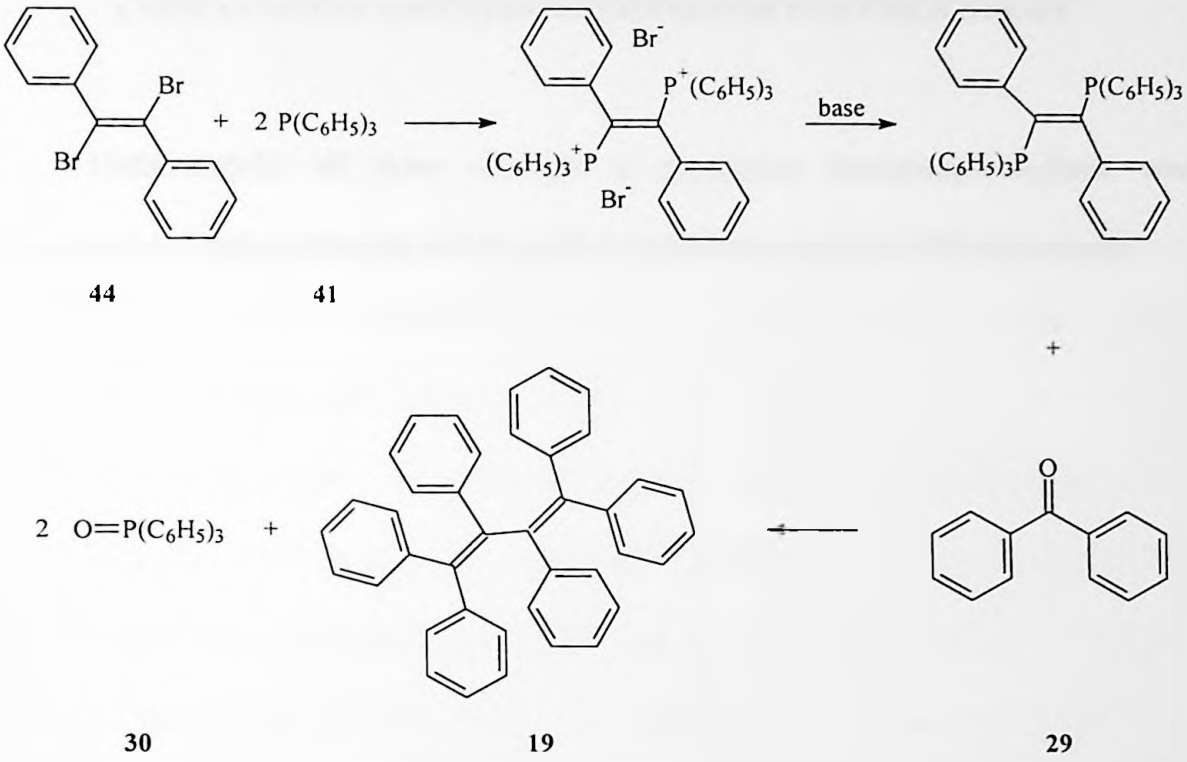


43 **39** **19** **30**

This reaction was attempted by adding benzil and a small amount of bromotriphenylethylene as an internal GC standard. The mixture was heated to reflux for forty-eight hours while being analyzed periodically by GC. After forty-eight hours all of the starting materials remained. The reaction was repeated and the results confirmed that none of the starting materials had been consumed. Therefore, the reaction was considered to be unsuccessful and another approach was then considered.

C. Attempted Synthesis of Hexaphenylbutadiene by the Wittig Reaction using 1,2-Dibromo-1,2-diphenylethane and Triphenylphosphine.

Our next approach to synthesize hexaphenylbutadiene (**19**) was similar to the previous attempt. We elected to try the Wittig reaction again, but using 1,2-dibromo-1,2-diphenylethane (**44**) and benzophenone (**29**).



1. **<u>Attempted Synthesis of Salt of using 1,2-Dibromo-1,2-diphenylethane and Triphenylphosphine.</u>**

Considering the melting point of 1,2-dibromo-1,2-diphenylethane (238° C with decomposition),[41] we chose to attempt this reaction using the solvent technique. Therefore, the two starting materials were dissolved in toluene. Bromotriphenylethylene was used as an internal GC standard. The mixture was heated to reflux for six hours. The results of the GC analyses indicated that none of the starting materials had been consumed. The reaction was repeated and the results were the same. Therefore, this approach to obtaining hexaphenylbutadiene was abandoned.

CONCLUSIONS AND SUGGESTIONS FOR FURTHER STUDY

Unfortunately, all three attempts to synthesize hexaphenylbutadiene were unsuccessful. Further attempts will be made to attempt to synthesize this compound.

EXPERIMENTAL

A. Analytical Methods

All melting points were determined on a calibrated Uni-Melt Thomas Hoover Capillary Melting Point apparatus in unsealed 1.5-1.8 x 90 mm capillary tubes. Melting points are uncorrected.

The proton nuclear magnetic resonance spectra were obtained on a Varian XL-200 NMR spectrometer operating at 200 MHz or a Varian Gemini 300 spectrometer operating at 300 MHz. Spectra were collected using chloroform-d as the solvent. Spectral features are reported in δ units relative to TMS as an internal GC standard. The carbon-13 nuclear magnetic resonance spectrum was obtained on a Varian Gemini 300 NMR spectrometer operating at 75 MHz. The data were collected on the Gemini and then processed on a Sun 4/110 workstation. The spectra were collected using chloroform-d as the solvent and the internal reference. Spectral features are reported in δ units.

Infrared spectra were obtained on a Mattson Cygnus 100 Fourier Transform Infrared Spectrometer and data were processed using WinFIRST v1.1 software or on a Nicolet 20DXB Fourier Transform Infrared Spectrometer. Absorbance spectra were obtained using potassium bromide pellets or sodium chloride plates. Spectral features are reported in reciprocal centimeters (cm^{-1}).

Gas Chromatography was performed using a Hewlett Packard 5890 Series II Gas Chromatograph equipped with a HP7673 GC/SFC injector and

autosampler. Data were processed using PE Nelson Turbochrom Navigator v.4.1. Samples were analyzed using a 12 m x 20 mm x 0.3 μm Supelco SPB-1 column.

B. Materials

α-Phenylcinnamic Acid (Aldrich)

Methanol (Aldrich)

Sulfuric Acid (Aldrich)

Sodium Carbonate (Aldrich)

Diethyl Ether (Aldrich)

Sodium Sulfate (Aldrich)

Potassium Cyanide (Aldrich)

Ammonium Chloride (Aldrich)

Dimethyl Formamide (Aldrich)

Bromodiphenylmethane (Aldrich)

Triphenylphosphine (Aldrich)

Sodium Methoxide (25% by wt.) in Methanol (Aldrich)

Benzil (Aldrich)

1,2-Dibromo-1,2-diphenylethane (Aldrich)

Toluene (Aldrich)

Benzophenone (Aldrich)

Bromotriphenylethene (Aldrich)

1,5-Diazabicyclo[4.3.0]non-5-ene (Aldrich)

C. Chromatographic Techniques.

1. Thin-layer Chromatography.

Thin-layer chromatography was performed by conventional analytical methods. All samples were dissolved in the developing solvents and spotted on the plates (Whatman, silica gel 60 Å, MK6F, Fluorescent at 254 nm) via open-ended capillary tubes. The developing solvents used were 10% ethyl acetate/hexane and chloroform. Colorless compounds were detected by irradiation with ultraviolet light at 254 nm or with iodine.

2. Gas Chromatography.

All GC analyses were performed using a 12 m x 20 mm x 0.3 μm Supelco SPB-1 column. The temperature program started at 100°C and increased 10°/minute to the maximum temperature of 300°C. Both the injector and the detector (FID) were 280°C. A sample size of 1 μL was injected onto the column.

D. Attempted Michael Addition of Cyanide to a-Phenylcinnamate Followed by Organolithium or Gringnard Addition.

1. Synthesis of Methyl Ester of α-Phenylcinnamic Acid.

α-Phenylcinnamic acid (6.6 g, 0.02 mol) and methanol (200 g, 6 mol) were added to a 250 mL, three-necked round-bottom flask equipped with a thermometer and a condenser. The reaction was conducted under a

nitrogen atmosphere. Several drops of sulfuric acid were added. The reaction mixture was heated to reflux for seventy-two hours while being analyzed via thin-layer chromotography periodically to determine if the reaction was occurring. After seventy-hours at reflux, a minimal amount of starting material was present so the reaction was assumed complete.

The reaction mixture was then transferred to a separatory funnel and 600 mL water was added. The mixture was washed three times with 50 mL of diethyl ether. The three ether layers were combined and washed with 25 mL of water. The ether layer was extracted with 25 mL of 5% aqueous sodium carbonate and then dried using sodium sulfate. The sodium sulfate was filtered and the remaining mixture was stripped at 5 mmHg and 60°C using a rotary evaporator yielding an off-white powder(5.8 g, 83%), the methyl ester of α-phenylcinnamic acid (mp 71-73°, lit.[28] mp 75°C).

2. Attempted Base-Catalyzed Addition of Sodium Cyanide to the Methyl Ester of α-Phenylcinnamic Acid.

a. Experiment 1.

The methyl ester of α-phenylcinnamic acid obtained from the reaction above (0.95 g, 0.004 mol) was added to a 100 mL Erlenmeyer flask containing 20 mL of DMF. Sodium cyanide (0.98 g, 0.02 mol) was added to a separate 100 mL Erlenmeyer

flask containing ammonium chloride (0.5 g, 0.01 mol) and water (10 mL; 0.5 mol). The water solution was added to the THF solution and the reaction mixture was stirred at room temperature for 48 hours while being analyzed periodically by thin-layer chromotography to determine if the reaction had occurred. Although the thin-layer chromotography results were unclear after 48 hours, the procedure was continued.

Water (100 mL; 5.5 mol) was then added and the mixture was extracted three times with diethyl ether (35 mL; 0.47 mol). The three ether extracts were combined, washed with 10 mL of water, and dried with sodium sulfate. The sodium sulfate was filtered and the ether was evaporated using a rotary evaporator at 5 mmHg and 60°C. The resulting compound, an off-white solid with a melting point of 71-73°C, was the starting material methyl α-phenylcinnamate.

b. <u>Experiment 2.</u>

The reaction above was then repeated to confirm the results. The methyl ester of α-phenylcinnamic acid obtained from the reaction described in Section 1 above (0.95 g, 0.004 mol), was added to a 100 mL Erlenmeyer flask containing 20 mL of DMF. Sodium cyanide (0.98 g, 0.02 mol) was added to a separate 100 mL

Erlenmeyer flask containing ammonium chloride (0.5 g, 0.01 mol) and water (10 mL; 0.5 mol). The water solution was added to the THF solution and several drops of bromotriphenylethylene was added as an internal GC standard. The reaction mixture was stirred at room temperature for 48 hours while being analyzed periodically by gas chromotography to determine if the reaction had occurred. After 48 hours, GC results confirm that none of the reactants had been consumed so the reaction was aborted.

E. Attempted Synthesis of Hexaphenylbutadiene by the Wittig Reaction using Bromodiphenylmethane and Triphenylphosphine.

1. Synthesis of Salt of Bromodiphenylmethane and Triphenylphosphine.

a. Experiment 1.

Bromodiphenylmethane (2.5 g, 0.01 mol) and triphenylphosphine (2.6 g, 0.01 mol) were dissolved in 100 mL of methanol. Several drops of bromotriphenylethylene were added as an internal GC standard and the reaction mixture was stirred at room temperature for 24 hours. The solution was analyzed via GC and the results indicated that none of the reactants had been consumed. Therefore the reaction was assumed to be unsuccessful.

b. Experiment 2.

Bromodiphenylmethane (2.5 g, 0.01 mol) and triphenyl-

phosphine (2.6 g, 0.01 mol) were weighed in a 50 mL beaker. The beaker was heated until both solids melted. After several minutes a white solid started falling out of solution and then the solution eventually became solid again. Diethyl ether (50mL) was added and the solution was filtered. The pale yellow product with a melting point of >300°C, the salt of bromodiphenylmethane and triphenylphosphine (2.5 g, 49%), was collected.[40] The procedure was repeated for reproducability and when more product was needed.

2. **Synthesis of Ylide of Bromodiphenylmethane and Triphenylphosphine.**

The salt of bromodiphenylmethane and triphenylphosphine (2.0 g; 0.004 mol), obtained by the method describe above, was dissolved in 100 mL of methanol. Sodium methoxide, 25% by weight in methanol, was added (0.16 g; 0.004 mol). The reaction was assumed to have occurred and the product was not isolated.

3. **Attempted Synthesis of Hexaphenylbutadiene from Ylide of Bromodiphenylmethane and Triphenylphosphine.**

To the reaction mixture obtained by the method described above, benzil (0.4 g; 0.002 mol) was added. A small amount of bromotriphenylethylene was added as an internal GC standard. The mixture was heated to

reflux for 48 hours while being analyzed periodically via GC. After 48 hours, results indicated that none of the reactants were consumed so the reaction was assumed to be unsuccessful. The procedure was repeated several times and the results confirmed that the reaction had not occurred.

F. Attempted Synthesis of Hexaphenylbutadiene by the Wittig Reaction using 1,2-Dibromo-1,2-diphenylethane and Triphenylphosphine.

1. Synthesis of Salt using 1,2-Dibromo-1,2-diphenylethane and Triphenylphosphine.

1,2-dibromo-1,2-diphenylethane (3.4 g; 0.01 mol) and triphenylphosphine (5.5 g; 0.02 mol) were added to 100 mL of toluene in a 250 mL round-bottom flask equipped with a mechanical stirrer and a thermometer and under a nitrogen atmosphere. A few drops of bromotriphenylethylene were added as an internal GC standard. The mixture was heated to reflux while stirring for 6 hours. The solution was analyzed via GC at the beginning of the reaction and after 2, 4 and 6 hours of refluxing. The results of the GC indicated that none of the reactants had been consumed so the reaction was assumed to be unsuccessful. The procedure was repeated several times and the results confirm that the reaction did not occur.

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VITA

The author was born on March 25, 1969, in Charleston, West Virginia. She graduated from St. Albans High School in June, 1987.

She began her undergraduate studies at Marshall University in August, 1987. In January, 1990, she accepted a student intern position as an Information Technician with the ThermoPhysical Properties Skill Center at the Union Carbide Technical Center in South Charleston, West Virginia. She received her Bachelor of Science Degree in Chemistry from Marshall University in July, 1992. In August, 1992, she was hired full-time as an Analytical Laboratory Technician with the Urethane Additives Research and Development Group (now the UA Division/OrganoSilicones Group of Witco Corporation).

She began her graduate studies at Marshall University in January, 1994. In August, 1994, she was promoted to the position of Research Chemist responsible for new product development. She received her Master of Science Degree in Organic Chemistry from Marshall University in December, 1998.