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Title: THE SYNTHESIS AND ELECTROCYCLIZATION OF SOME LINEAR AND CROSS-CONJUGATED HEXATRIENES.

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As part of the continuing investigation of the thermal cis-1, 3, 5-hexatriene to 1,3-cyclohexadiene rearrangement, four new trienes and a cross-conjugated pentaene have been prepared and their thermal reactions studied. A new route to the synthesis of highly substituted trienes has been developed. The synthesis of three of these polyenes was described using the hydrogenation of enynenes to generate the polyene system. A recently reported coupling reaction was extended to the coupling of enynes and vinyl halides and gives enynenes in high yield.

The electrocyclization of all of the polyenes was described. Electrocyclization of trans, cis, trans-1-phenyl-1,3,5-heptatriene 74 ($k = 2.1 \times 10^{-4}$ sec^{-1} at 134.4°C, $\Delta H^{\ddagger} = -29.0$ kcal/mole, $\Delta S^{\ddagger} = -6.8$ cal deg^{-1} $mole^{-1}$ gave cis-5-phenyl-6-methyl-1,3-cyclohexadiene and the trans isomer in a ratio = 550:1. Trans, cis, cis-1-phenyl-1,3,5-heptatriene 77 was shown to cyclize about 200 times slower than 74. Electrocyclization of ethyl 3-(trans-2-styrylcyclohexen-1-yl)-trans-propenoate 108 and ethyl 3-[trans-2-(4'-methoxystyrl)cyclohexen-1-yl]-trans-propenoate 116 (for both $k = 4.00 \times 10^{-4}$ sec^{-1} at 410.9°K, $\Delta H^{\ddagger}$

= 28.9 kcal/mole, $\Delta S^{\neq}$ = -9.0 cal deg^{-1} $mole^{-1}$ gave <u>cis</u> substituted 1,2,3,4,6,7-hexahydronapthalenes. Finally the thermolysis of 3-ethylidene-1,5-(dicyclohexen-1-yl)-1,4-pentadiene gave a tetracyclic molecule.

The Synthesis and Electrocyclization of some Linear and Cross-conjugated Hexatrienes

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To B. W.

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A special note of thanks is due to my special wife Jan, for her love, support, encouragement, sacrifice and patience during the past four years.

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THE SYNTHESIS AND ELECTROCYCLIZATION OF SOME LINEAR AND CROSS-CONJUGATED HEXATRIENES

INTRODUCTION

Woodward and Hoffmann's initial paper[4] on the conservation of orbital symmetry theory evoked a flood of publications predominantly concerned with testing the stereochemical predictions of the theory. Verification proved virtually universal. More recently interest has turned to three different areas relevant to the theory. First--and most frustrating experimentally--has been the question of the extent of stereoselectivity, or in other words the difference in activation free energy between the symmetry allowed and symmetry forbidden routes. Studies have provided at least lower bounds to this energy difference for both four electron[19, 20, 27] and eight electron[30, 31, 32] electrocyclic reactions, but in no case was the mechanism of formation of the "forbidden" product ascertained. Also two very different values were obtained for the eight electron case. No such study of a six electron electrocyclization has been made. A study of the six electron case would be very valuable since it might help to delineate the route to the "forbidden" products, and it might also suggest which of the two eight electron values was more reasonable. An experimental study of the six electron electrocyclic reaction will be described in this thesis.

Second: substituents should be expected to play an important role relative to predictions of the symmetry conservative theory.

Epiotis has recently published a number of predictions of the influence of substituents on the rates and the stereochemistry of electrocyclic (and other pericyclic) reactions.[11-15] A test of Epiotis' predictions will be described in this work. Third: the stereochemical predictability of pericyclic reactions has made them of considerable value in synthesis, but six electron electrocyclic reactions have seen limited service in this regard. The main limitation has generally centered around the difficulties of preparing trienes with proper configurations. Properly oriented cross-conjugated systems will permit formation of more than one ring at a time, materially increasing the synthetic value of this electrocyclic reaction. Some schemes for the synthesis of such cross-conjugated polyenes have been evaluated during this research, and a novel electrocyclic process leading to a tetracyclic molecule will be presented.

HISTORICAL

Introduction

The summary of the literature pertinent to this work has been divided into four parts. The first section covers briefly the thermal reactions of cis-1, 3, 5-hexatrienes, and it is followed by a review of the theory related to the pathways leading to forbidden products. Only those triene systems directly related to this work will be discussed in the first section. For more complete reviews of the electrocyclization to cis-1, 3, 5-hexatrienes we refer the reader to the doctoral theses of J. L. Platt,[1] C. E. Delphey,[2] and M. F. Cleary.[3]

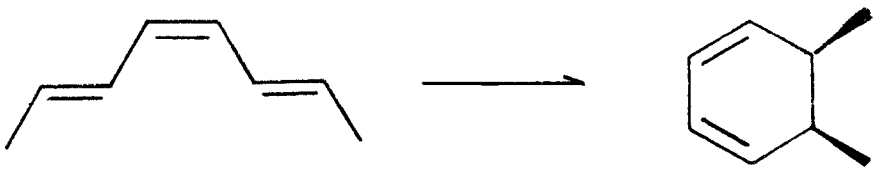
The third section explores, again briefly, synthetic routes leading to cis-1, 3, 5-hexatrienes, a problem of no small magnitude facing workers in this area.

The final section highlights certain aspects of the chemistry developed in this work. Catalytic coupling as a means for the production of polyenes of definite stereochemistry will be explored. A thorough review of the literature of this subject will be presented.

Thermal Reactions of 1, 3, 5-Hexatrienes

The advent of conservation of molecular orbital symmetry theory in 1965[4] sparked more than a decade of research seeking

to illuminate the theory and provide experimental tests of its predictions. The theory correctly predicts that cis-hexatrienes should undergo a disrotatory ring closure. The disrotatory route for the six electron gericyclic reaction has been amply demonstrated experimentally.[5-6]



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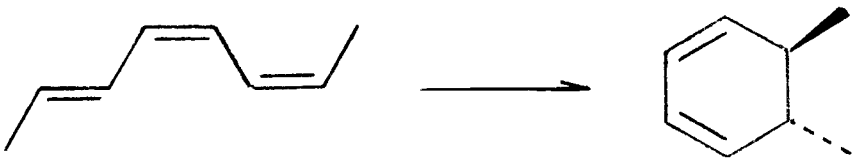


3 4

Thus, for example, trans, cis, trans-octatriene 1 gave only cis-dimethylcyclohexadiene[5] while trans, cis, cis-octatriene 3 gave only trans-dimethylcyclohexadiene.

Rates and activation parameters have been determined for the electrocyclization of a large number of cis-hexatrienes (see ref. 1).

Trans substituents on the terminal carbons of the triene have little or no effect on the rate of cyclization, regardless of their nature.

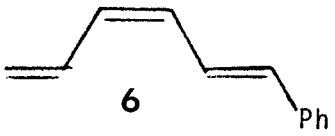
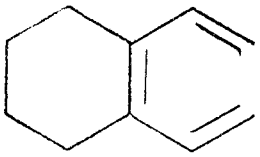
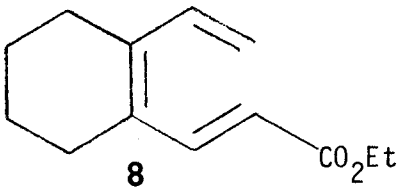
Compound	T (^{o}C)	Rate (sec^{-1})
 **5**	125	3.0×10^{-5}
 **6**	125	3.0×10^{-5}
 **7**	126.5	3.7×10^{-5}
 **8**	125	3.7×10^{-5}

Table 1. Relative Rates of Triene Electrocyclizations

The early work of Lewis and Steiner[9] provided rate data and activation parameters for the parent compound, cis-1, 3, 5-hexatriene 5. Marvell and coworkers[10] showed that a trans-phenyl group in the

terminal position did not alter the rate of electrocyclization by studying the thermal isomerization of 6. Marvell and coworkers also provided rate information for another parent compound, 1, 2-divinylcyclohexene 7. Comparison of the ring closures of 7 and 8, by Marvell and Cleary[3] demonstrated that a strong electron withdrawing group in a terminal position also has negligible effect on the rate of the reaction.

Theory

In 1972 and 1973, Epiotis in a series of papers[11-15] suggested that certain types of substituents at the terminal positions in pericyclic reactions could have an effect on both the rate and the stereochemical results of the reaction.

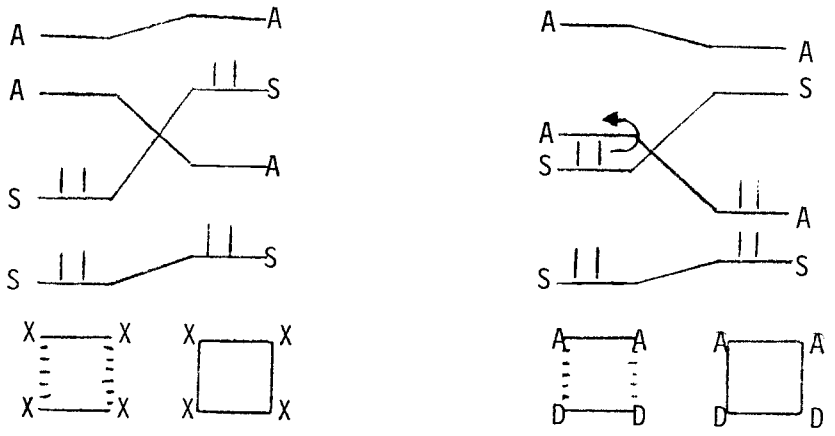
Looking first at the cycloaddition reaction, Epiotis showed qualitatively that the S + S transition state would be stabilized with respect to the thermally "allowed"[4] S + A transition state if one of the cycloaddends behaved as a donor molecule while the other acted as an acceptor molecule. A reversal of stereochemical results might be expected if substitution produced sufficient polarity differential.

Epiotis also reported in the same papers[11, 12] that rate enhancement could be expected for the polar (acceptor-donor) 4 + 2 cycloaddition, due to energy level proximity and more favorable

overlap effects.

In his later papers,[13-15] Epiotis used configuration interactions instead of resonance formulations of the transition state. In the case of the 4 + 2 cycloaddition he suggested that the HOMO of the donor molecule and the LUMO of the acceptor molecule can be of similar energy. In the transition state these orbitals can interact in a stabilizing manner, enhancing the rate.

In the case of the 2 + 2 cycloaddition reversal of the stereochemistry might be expected. Referring to Figure 1 below, a



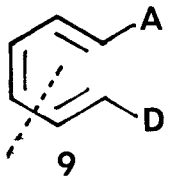
2s + 2s Cycloaddition

Figure 1. The Effect of Donor-Acceptor Substitution on the Energy Levels of the HOMO and LUMO during 2+2 Cycloadditions

schematic diagram of the disallowed 2s + 2s cycloaddition shows that when the HOMO of the donor molecule and the LUMO of the

acceptor molecule are relatively close in energy, promotion of 2 electrons from the HOMO to the LUMO would lead to ground state products of reversed stereochemistry via an allowed concerted pathway.

Epiotis extended his calculations to electrocyclic reactions as well.[14, 15] Push-pull substitution on opposite ends of the molecule should have the same effect. He treated the electrocyclization in a manner analogous to the Diels-Alder reaction by considering the two ends of the molecule as separate entities. With hexatrienes the calculations assumed that the transition state was planar, but



9

Marvell[16] has calculated that the transition state geometry is not planar. Epiotis concluded from his calculations that the rate of electrocyclization should be increased by push-pull substitution and that in cases of extreme substitution reversal of stereochemistry might be observed.

Conservation of orbital symmetry theory[4] classifies pericyclic reactions into symmetry allowed, symmetry forbidden or symmetry independent. Epiotis essentially proposed that pericyclic reactions

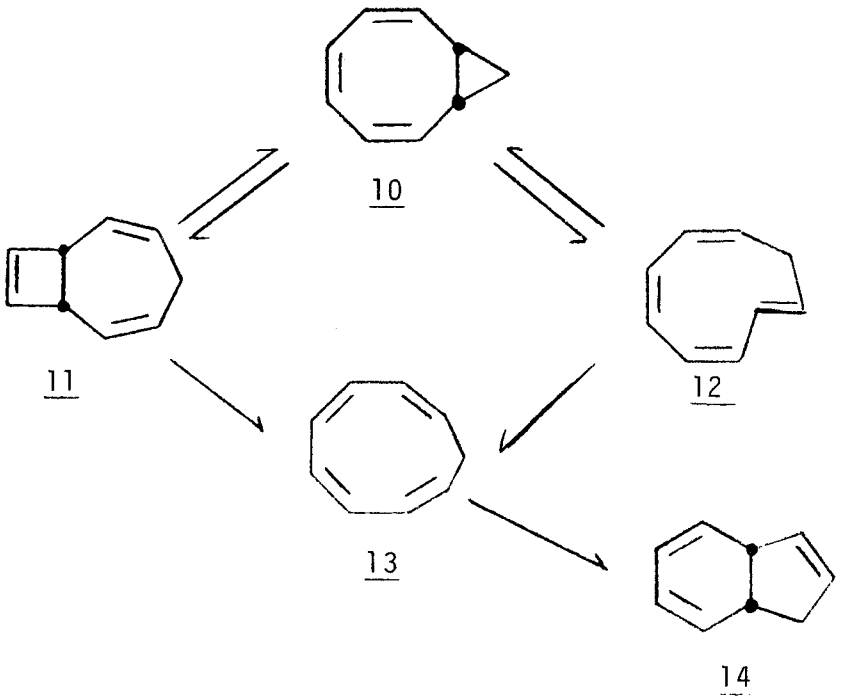
could give forbidden products because proper substitution might bring the activation energy of a forbidden path as low as or lower than that of the allowed route. Others have looked at the possibility of products arising from the symmetry forbidden and symmetry independent pathways.

In 1970 Woodward and Hoffman made the statement, "orbital symmetry is conserved in concerted reactions."[17] They apparently assumed that disallowed products arising from reactions in which orbital symmetry was not conserved would derive from diradical or ionic intermediates.[18]

Baldwin and coworkers noted that geometrical restraints make some allowed reactions energetically prohibitive.[19] In such cases some molecules may convert to symmetry forbidden products by one step processes, since this route could be energetically advantageous to alternatives involving singlet diradical intermediates. Baldwin suggested that configuration interaction might provide the stabilization necessary to make the concerted forbidden pathway favored over the singlet diradical route. Introducing configuration interaction between the HOMO and LUMO of cyclobutene during its thermally forbidden ring opening ($\sigma_{2s}+\pi_{2s}$) reduces the energy difference between the allowed and forbidden concerted reaction from 49 kcal/mole to 13.6 kcal/mole.[20] This essentially amounts to the same approach as Epiotis' configuration interaction

treatment, but with a less drastic conclusion.

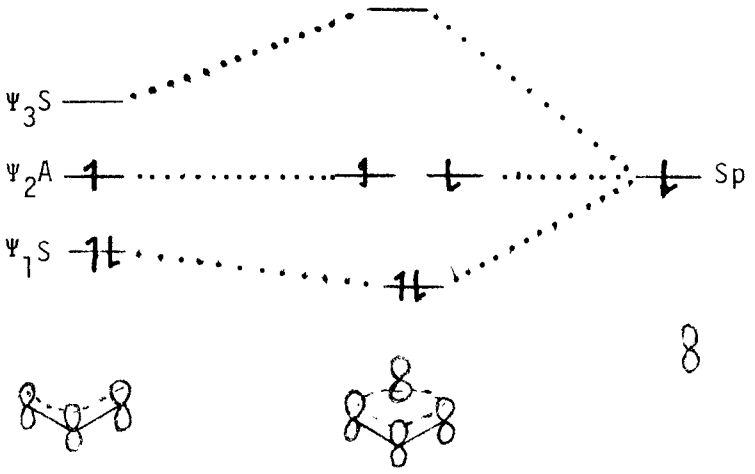
Simple molecular orbital analysis of the facile thermal isomerization of cis-bicyclo[6.1.0]nona-2, 4, 6-triene to cis-3a, 7a-dihydroindene showed that a state conservative and concerted isomerization 11→13 is an excellent possibility even though thermally forbidden. The alternative, 12→13, also forbidden is unlikely



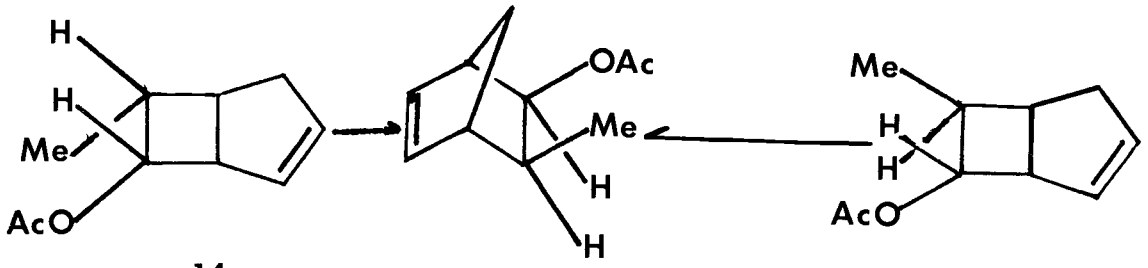
since the transition state energy is estimated to be 2.5 times higher than for the configuration interaction stabilized route 11→13.

Berson approached the question of concerted forbidden reactions from another direction.[21] He considered the 1, 3-sigmatropic shift, during which the migrating center must invert in order for

reaction to be allowed. He suggested that subjacent orbital control of the transition state geometry could become important if steric factors became unfavorable for Woodward-Hoffman control. His calculations show that the stabilization energy provided by subjacent orbital interaction lowers the energy requirement of the forbidden process below that of the diradical route. In most geometries there is a stabilizing interaction of the migrating p-orbital with the bonding orbital of the allyl system. Two of the four electrons can thus be accommodated in a more stable orbital than in the fragmented (diradical) case.[22]

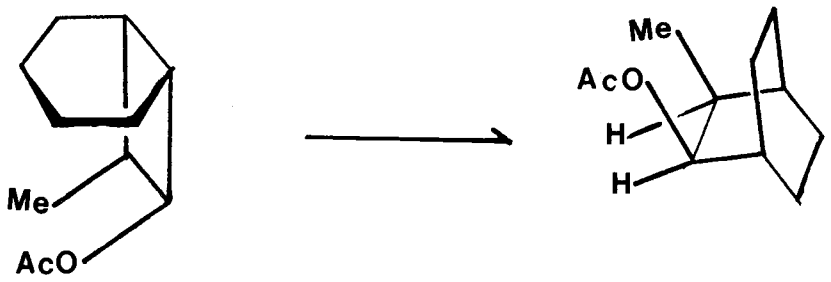


Berson and coworkers have provided support for the concept of concerted yet forbidden reactions. The 1, 3-sigmatropic rearrangement of endo-7-methyl-6-acetoxybicyclo[3.2.0] hept-2-ene 14 occurs with retention at the migrating center.[23] The ratio of the allowed to forbidden product was 1:54. This is in contrast to the



14 16 15

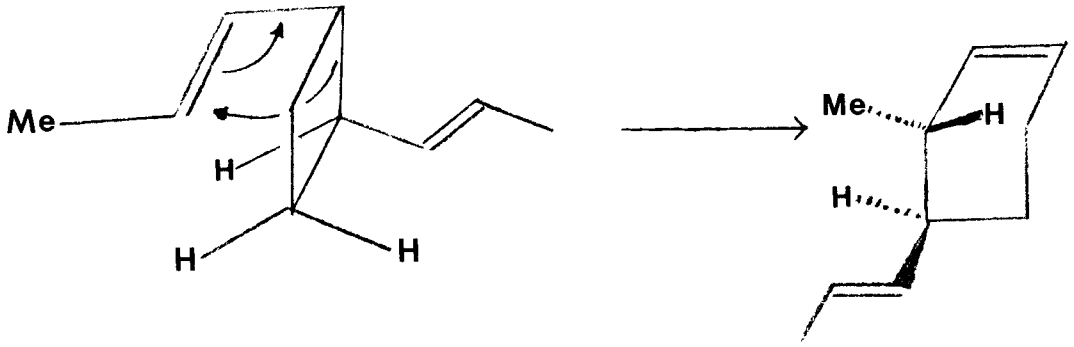
exo-methyl heptene 15 which also gives 16, proceeding by the allowed route with complete inversion at the migrating center. The heptene 15 reacts under Woodward-Hoffman control while 14 can not because the endo methyl group makes that pathway sterically difficult. The 54:1 ratio of forbidden to allowed product makes it unlikely that 14 is rearranging via a diradical which should give a more random product distribution. In a similar manner endo-7-acetoxy-8-methylbicyclo[4.2.0]oct-2-ene 17



17 18

underwent rearrangement to give predominantly 18.[24] Also,

trans-1, 2-di(trans-propen-1-yl)cyclobutene 19 rearranged to give



19 20

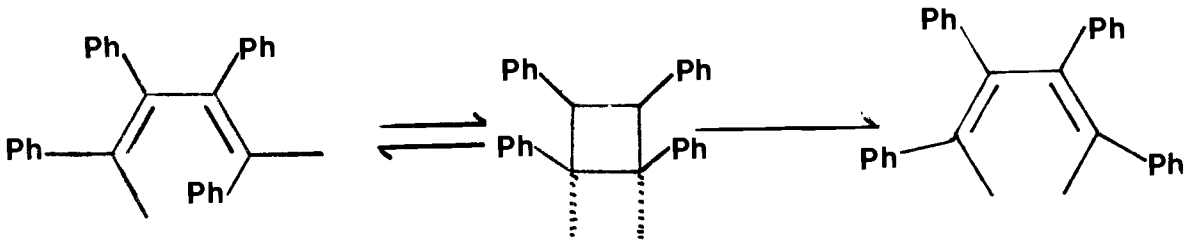
20 (96.1 %).[25]

These examples, and others[23, 24, 25] with highly stereoselective, "forbidden" results imply that the products are being produced by a concerted pathway and not via a symmetry independent diradical.

Other than the few cases where geometric restrictions favor the disallowed over the symmetry allowed pathway, reactions proceed under orbital symmetry control. This has permitted the generation of a large body of detailed information about the allowed process. The independent or forbidden pathways have been somewhat inaccessible experimentally since no measurable disallowed product is formed in most pericyclic reactions. Workers have made several attempts to determine the energy requirements of the forbidden pathway, usually establishing only minimum values for the difference

between the orbital symmetry allowed pathway and some, usually unknown, disallowed pathway.

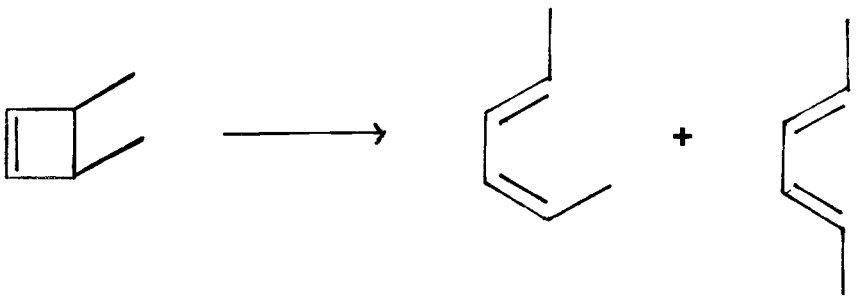
Freedman and Doorakian[26] studied the reversible cyclobutene to butadiene interconversion using cis, trans-1, 4 dimethyl-1, 2, 3, 4-tetraphenyl-1, 3-butadiene 21. After a time which allowed



21 22 23

more than one million ring openings to occur they were unable to detect any of the cis butadiene 23. They concluded that ΔE_a - (allowed-disallowed) was at least 7.1 kcal/mole.

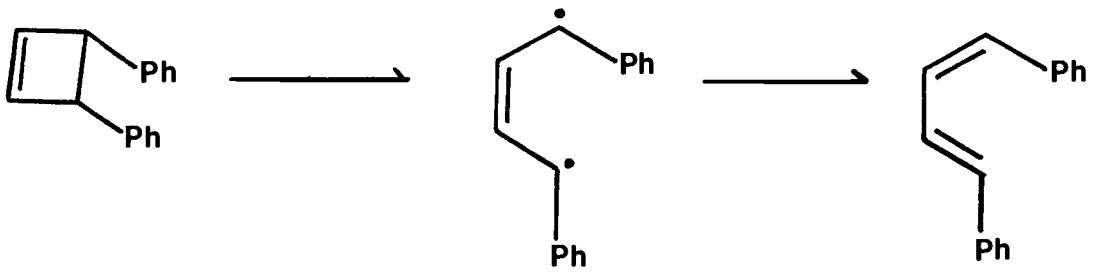
Brauman and Archie[27] provided an estimated ΔE_a(allowed-disallowed) of 15 kcal/mole from their investigation of the ring opening of cis-3, 4-dimethylcyclobutene 24. The cyclobutene 24 opens at 280°C to give 0.005% of trans, trans-2, 4-hexadiene 25. This corresponds to $\Delta\Delta G^{\ddagger}$ = 10.7 kcal/mole. The allowed reaction requires that one of the methyl groups move in while the disallowed pathway does not. Consequently, Brauman and Archie concluded



24 25 26

that ΔE_a(allowed-disallowed) was best estimated to be 15 kcal/mole due to the steric strain added to the energy of the transition state leading to the allowed product. The diradical pathway had also been estimated to be about 15 kcal/mole higher in energy than the allowed pathway so the authors were unable to determine the mechanism of the formation of the disallowed product.

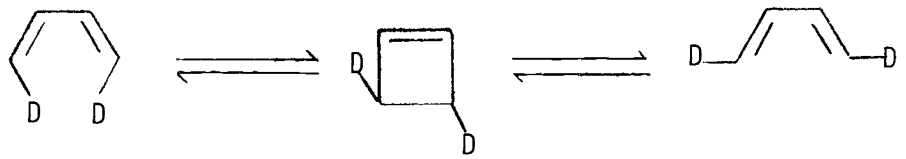
Brauman and Archie also examined the opening of cis-3, 4-diphenylcyclobutene 27.[28] Substitution of phenyl groups at positions 3 and 4 on the cyclobutene ring was expected to stabilize a diradical intermediate 28 enough to make it more stable than the allowed transition state. However the phenyl groups also stabilize the concerted transition state and none of the disallowed product was formed.



27 28 29

>99%

Brauman and Stephenson studied the isomerization of trans, cis -1, 4-dideutero-1, 3-butadiene 33.[29] This isomerization



30 31 32

33

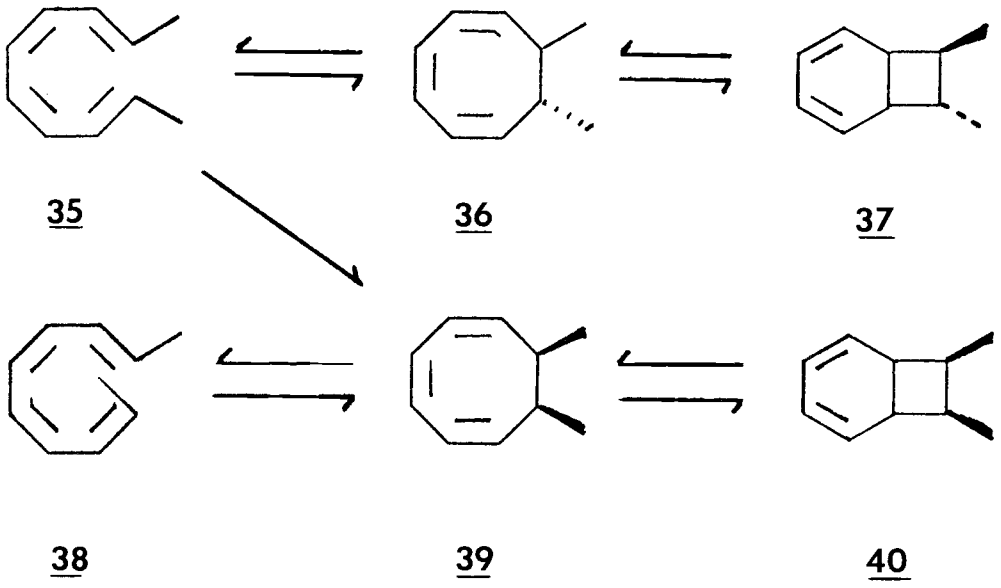
30 + 32

$$k(30 \longrightarrow 32) \simeq 10k(33 \longrightarrow 30 + 32)$$

had been presumed to proceed through the diradical. The kinetics of

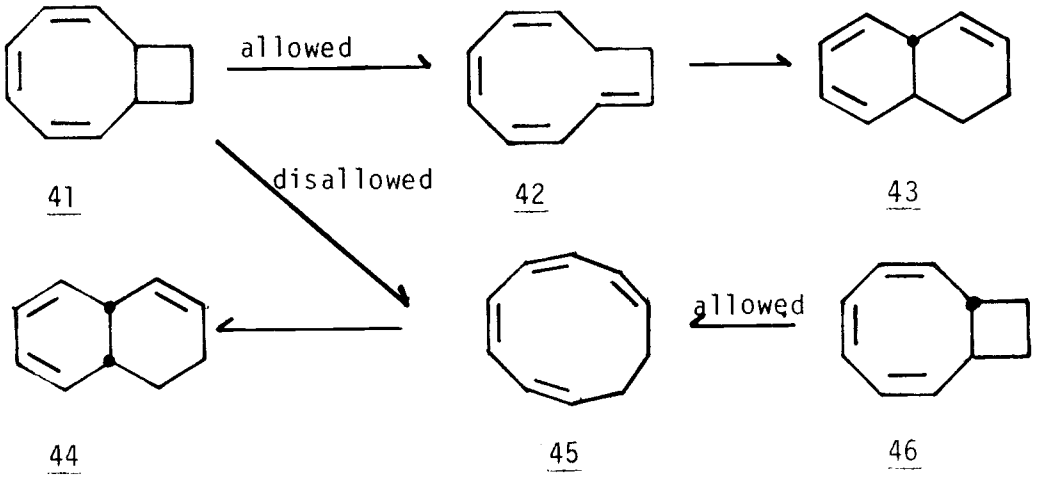
the isomerization, though complicated, allowed the authors to calculate ΔE_a(diradical-cyclobutene) which was found to be at least 8 kcal/mole.

Huisgen and Dahmen investigated the electrocyclic ring closure of trans, cis, cis, trans-2, 4, 6, 8-decatetraene 35.[30] Because the ring closure is a readily reversible process, they were able to run the cyclization long enough to see a small amount of the disallowed product 40, formally arising from a disrotatory closure



of the tetraene. The difference in free energies of activation between the allowed and disallowed pathways was estimated to be 11.1 kcal/mole.

Staley and Henry undertook a study of the thermal rearrangements of cis-bicyclo[6.2.0]-2, 4, 6-decatriene 41.[31] From the



product ratio 43:44 they found the difference in free energies of activation for the allowed vs. disallowed pathway to be 4 kcal/mole. The activation energy for the process was determined to be 32.2 ± 0.2 kcal/mole. The activation energy for the conversion of trans-bicyclo[6.2.0]-2, 4, 6-decatriene to 44 was found to be 15 kcal/mole.[32] Staley and Henry estimated that the intrinsic energy difference between the allowed and disallowed processes was about 17 kcal/mole, the difference in enthalpies of activation. Since only a small amount of disallowed product was formed ($\Delta\Delta G^{\ddagger}$ = 4.0 kcal/mole), the authors concluded that ΔE_a(allowed-disallowed) could be 18-20 kcal/mole, a much larger value than that obtained by Huisgen and Dahmen.[30] Staley and Henry pointed out that the disallowed

product formation in Huisgen and Dahmen's study could have arisen from a series of allowed hydrogen shifts.[31]

One would like to include at this point a discussion of ΔE_a (allowed-dis) for the six electron systems. Unfortunately no such studies have been reported, leaving a void in the theory.

A summation of what has been discussed can best be made graphically. Using the data of Benson[33] the heats of formation of the various starting materials for the 4, 6, and 8π electron electrocyclic reactions have been calculated.[34] Using measured enthalpies of activation for the three allowed reactions, 12 kcal/mole for the stabilization energy of the allyl radical[35, 36] and 22 kcal/mole stabilization energy for the pentadienyl radical,[33, 37] allows the placement of ΔH_f^o for the allowed and diradical processes on the same scale.[34]

From the data in figure 2 the following conclusions can be drawn:

ΔE_a (allowed-disallowed) = 13.6 -15 kcal/mole for 4 electrons.

ΔE_a (allowed-disallowed) = 11-12 or 18-20 kcal/mole for 8 electrons.

ΔE_a (allowed-diradical) = 10.6 kcal/mole for 4π electrons.

ΔE_a (allowed-diradical) = 13.0 kcal/mole for 6π electrons.

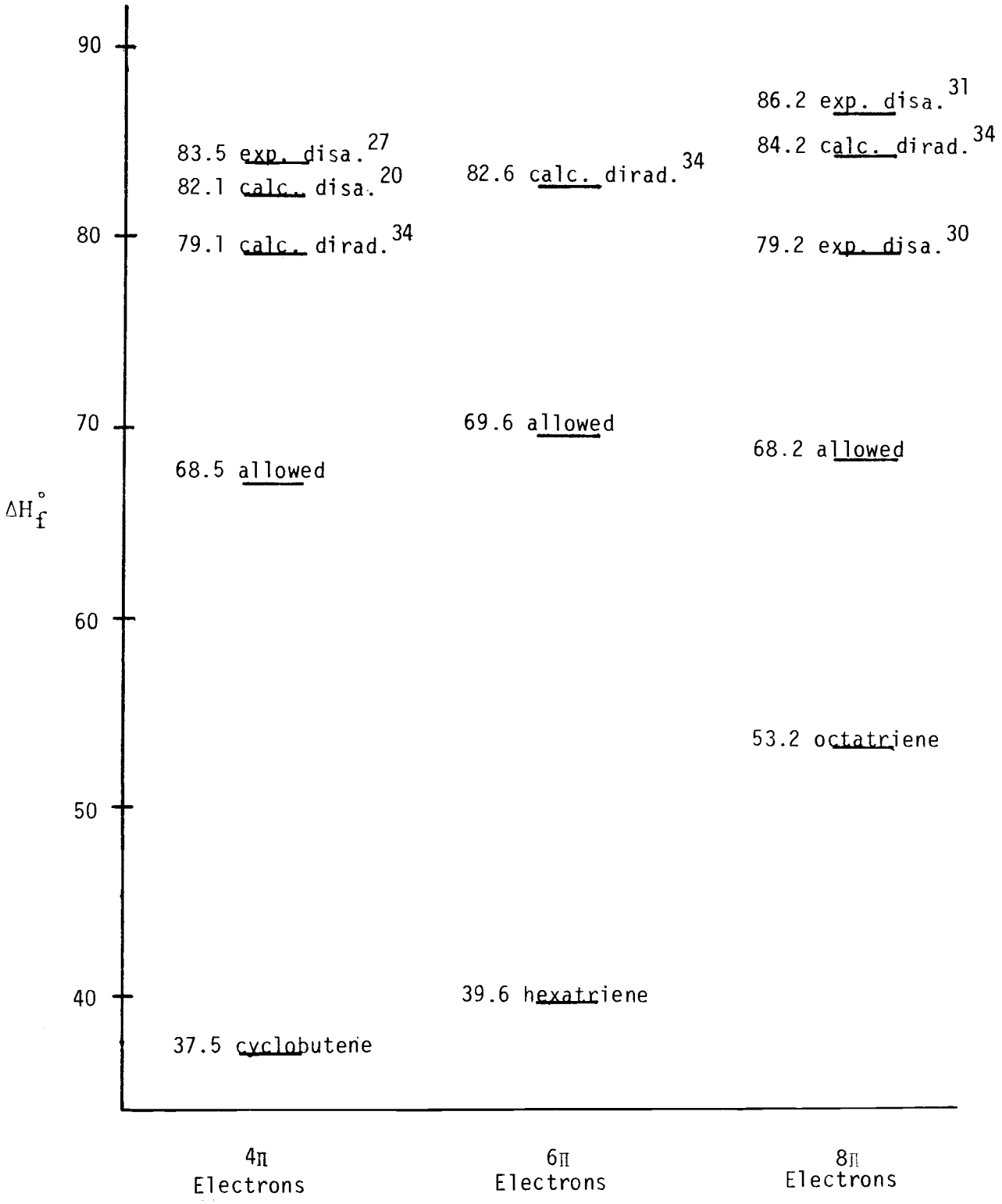


Figure 2. Some Calculated Enthalpies for Electrocyclic Reactions

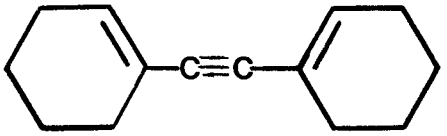
ΔE_a (allowed-diradical) = 16.0 kcal/mole for 8π electrons.

Synthetic Routes to Cis-1, 3, 5-Hexatrienes

Syntheses of cis-1, 3, 5-hexatrienes are dominated by two necessary structural requirements if the trienes are to be of use in obtaining information about electrocyclic reactions. The trienes must have a cis-center bond and the stereochemistry of terminal substituents must be defined. Both requirements can present severe difficulties, especially if mixtures of several trienes prove to be inseparable.

An obvious route to trienes of known configuration would be to define the stereochemistry at the terminal positions prior to generation of the cis center bond, i.e. by preparing an en-yn-ene of high purity. The last step could be then to reduce triple bond unambiguously to an ene of cis configuration. Unfortunately, reductions of en-yn-enes do not give clean results.

Marvell and Pippin prepared 1, 2-dicyclohexenylacetylene and attempted to semihydrogenate the acetylene. Semihydrogenation gave a complex mixture containing less than 50% of the desired cis triene.[38] Schlatmann and Havinga reported similar results for the semi-hydrogenation of 48.[39]



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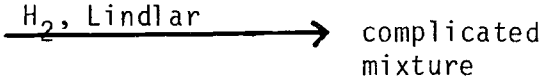
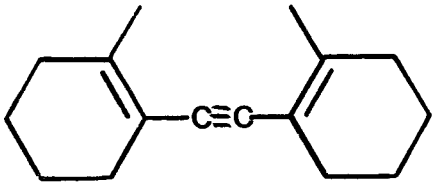
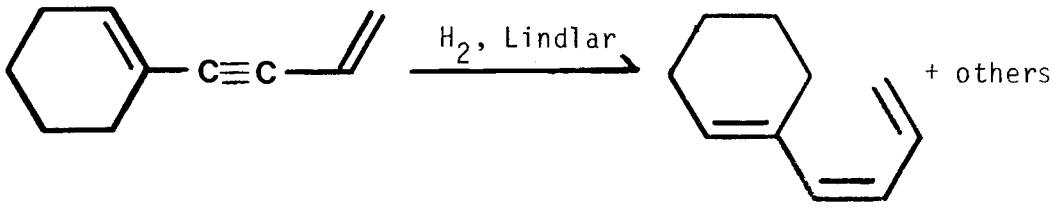




48

Marvell and Tashiro investigated the semi-hydrogenation of a variety of 1, 5-dien-3-ynes and found that complex mixtures were generally obtained.[40] The semi-hydrogenation of 1-cyclohexenyl-3-buten-1-yne 49 gave ten products with the desired product cis-1-cyclohexenyl-1, 3-butadiene 50 making up just 47% of the mixture.



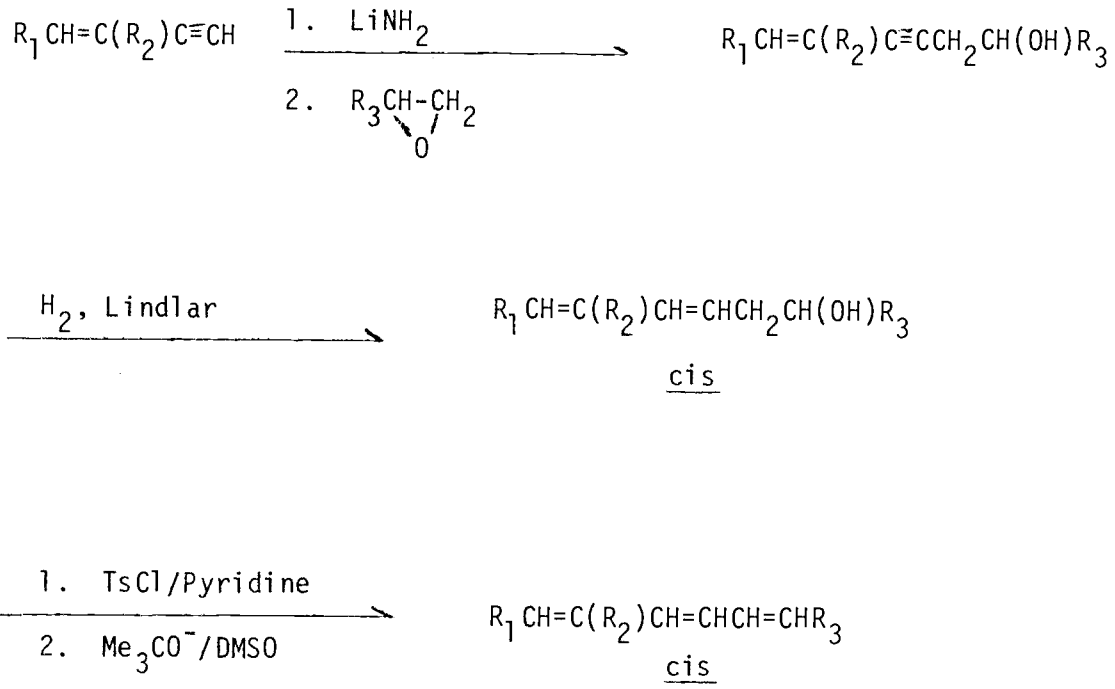
47%

49

50

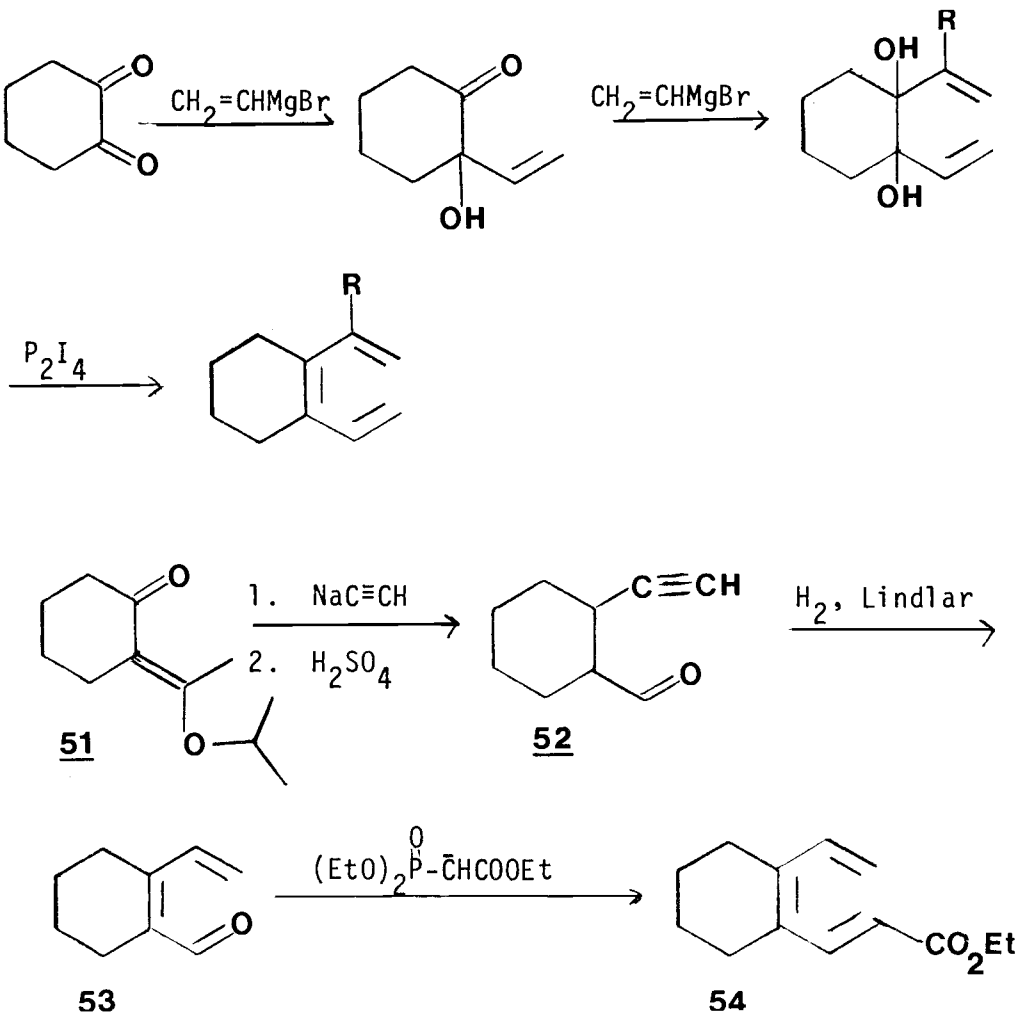
In the same paper it was also reported that en-ynes do reduce cleanly and with high stereoselectivity.

The general synthetic scheme developed by Marvell and coworkers[41] and based on the clean semi-hydrogenation of en-ynes is presented in figure 3.



Marvell and coworkers also developed synthetic procedures taking advantage of the cis geometry required of a cyclohexene double bond,[3, 41] following a scheme developed by Schiess.[42, 43]

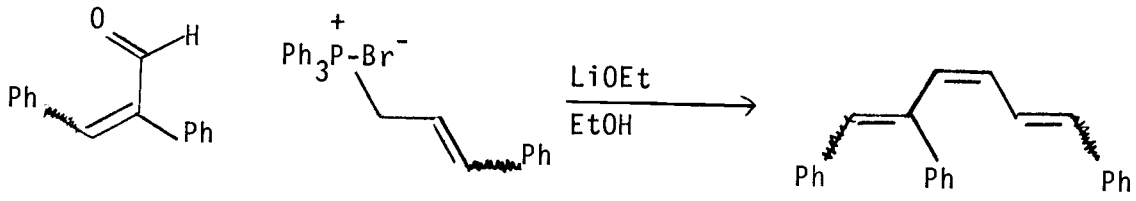
The use of a Wadsworth-Emmons Wittig reagent[44] in the latter sequence generates the trans ester 54 with a high degree of stereoselectivity.



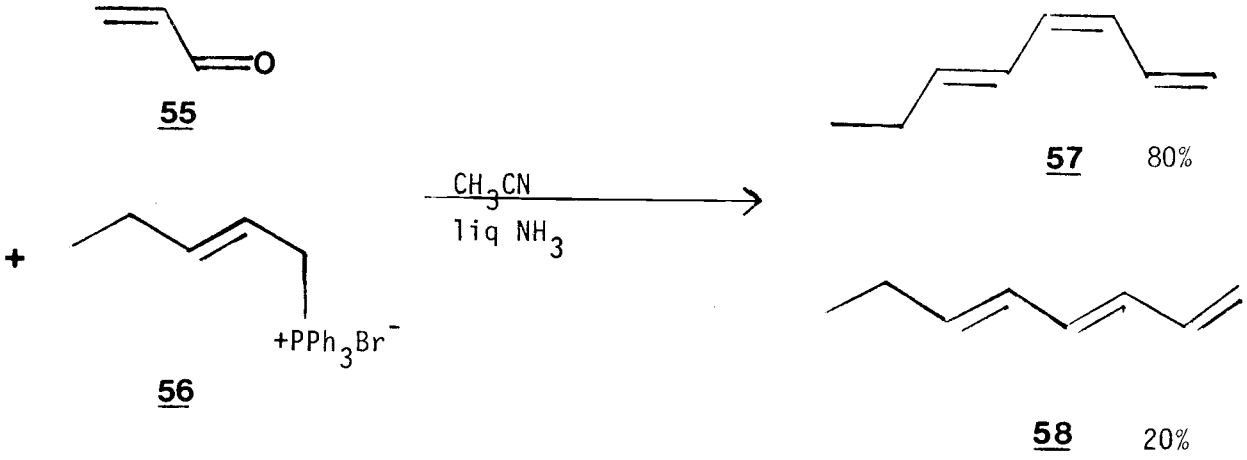
Spangler generated the center double bond in the final step of his sequence by elimination. A brief review of his work, and a list of references is presented in reference 3. The major problem with his route is the production of large amounts of the trans isomer in many cases.

The Wittig reaction has been used with limited success by several workers to generate conjugated cis-double bonds. This procedure is again limited in scope because most resonance stabilized ylids react with aldehydes to give trans olefins.[45]

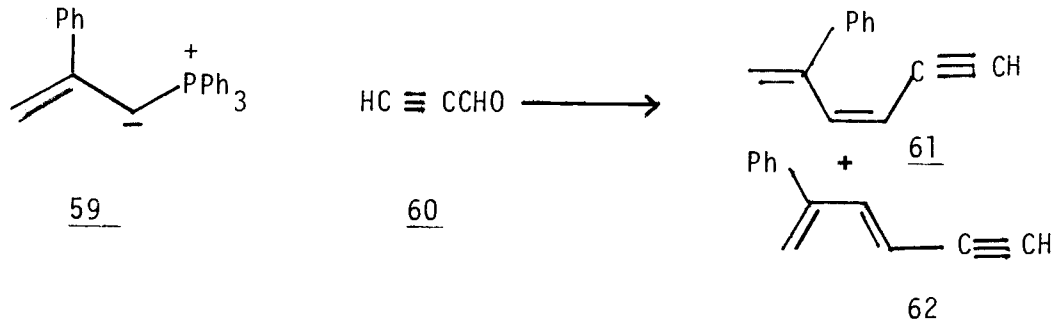
Padwa used a Wittig reaction the preparation of 1, 2, 6-triphenyl-1, 3, 5-hexatrienes giving a center double bond with cis geometry.



Jaenicke and Seferiadis[48] reported the selective preparation of the cis-hexatriene 57 by dissolving the aldehyde 55 and the alkyltriphenylphosphonium bromide 56 in acetonitrile and adding

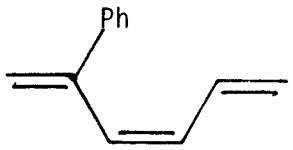


the resulting solution to liquid ammonia. Finally, Moy and Marvell[49] used a Wittig reaction to generate 61 and 62 in a ratio

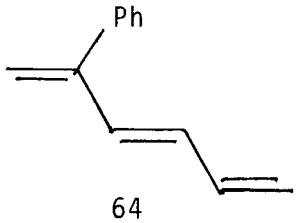


59 60 61 62

of 30:70. The mixture of 61 and 62 was then semi-hydrogenated cleanly to give 63 and 64.



63



64

This gives a total of five routes leading to cis-1, 3, 5-hexatrienes, each with its own limitations and difficulties. The semi-hydrogenations of en-yn-ols does not allow substitution on the 3 or 4 position and will usually give a mixture of cis and trans isomers at the terminal position in the elimination step. The cyclohexene systems allow well defined stereochemistry at the terminal positions but again do not allow substitution on the 3 or 4 positions.

Elimination of a 3-ol in the last step permits definition of the stereochemistry about the terminal positions and substitution at positions 3 and 4 but suffers because the elimination is not often stereospecific.

Wittig reactions in general give trienes directly which can be substituted at all positions but again often give products which are mainly trans about the center bond. Wittig reactions also can give rearranged products.[3, 49, 50, 51] The synthesis of a 1, 3-dien-5-yne via a Wittig reaction enables one to substitute the triene at 5 of 6 positions but does give mixtures at the center bond. However, GLC resolution of the product mixture is accomplished readily since the dien-ynes don't undergo valence isomerization at normal GLC operating temperatures. In addition the dien-yne route stops the direct formation of cyclohexadienes which has been a problem in some syntheses.[3, 49, 50, 51]

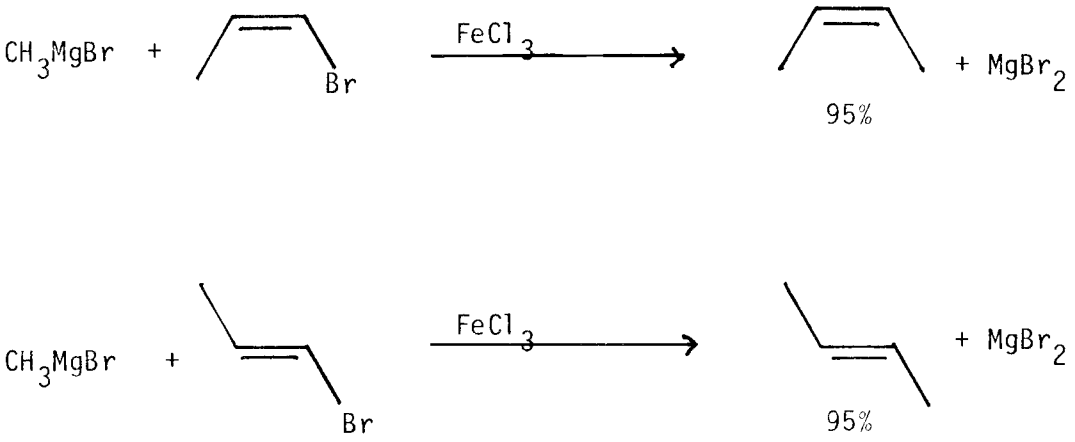
Catalytic Coupling Leading to Stereochemically Well Defined Polyenes

The past few years have seen a number of direct synthetic routes to conjugated polyenes developed. Although the foundation for much of the current work may have been laid some years ago, virtually all major advances in this area have been made in the past two and one half years. This review will, accordingly, present

material of relevance reported from 1975 through April 1978. Procedures not leading directly to "polyenes" have been excluded, as have dimerizations, which are useful only to synthesize symmetrical molecules. This review is further restricted to the syntheses of polyenes containing only two units of conjugation, though not by choice. Examples of syntheses of higher order unsymmetrical polyenes have not appeared.

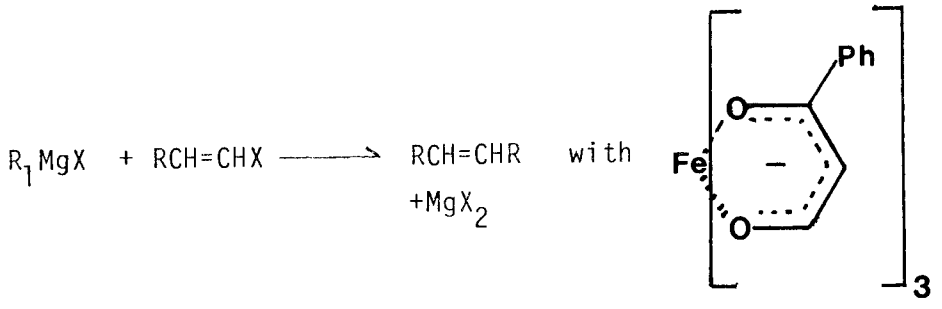
Current work on the syntheses of stereochemically well defined polyenes can be divided into two parts, the syntheses of dienes directly and syntheses of enynes, which can be easily converted into dienes. Routes leading to dienes have involved coupling of metalated olefins with vinyl halides, the direct reaction of vinyl halides and olefins, and the reaction of an alkyne with an olefin. Enynes are produced from the reaction of acetylides or acetylenes and vinyl halides.

In order for a reaction sequence to lead to stereochemically well defined products it is usually necessary to know the geometric structures of the starting materials as well as the stereochemistry of the transformation taking place. Kochi and Tamura showed that iron(III) promoted coupling of alkyl Grignard reagents and vinyl halides with complete retention at the reacting carbon.[52] They reported that methylmagnesium bromide reacted with cis and trans 2-bromopropenes to give only the corresponding cis and trans



2-butenes.

Kochi and Newman[53] determined the activity of many iron(III) complexes and found that the most active catalysts were β-diketonate complexes of iron(III). Using tris(methidobenzoyl)iron(III) they were able to obtain moderate yields of coupled products. Although



R_1	RX	Product	% Yield
Et	$BrCH=CHCH_3$	$EtCH=CHCH_3$	58
Et	BrCH=CHPh	EtCH=CHPh	60
i-Pr	$BrCH=CHCH_3$	$(CH_3)_2CHCH=CHCH_3$	60
Ph	BrCH=CHPh	PhCH=CHPh	32

they did not report the use of vinyl Grignard reagents, the limited success of phenylmagnesium bromide suggests that iron(III) might serve as a catalyst for the production of dienes.

Vinyl, as well as aryl and alkyl Grignard reagents were successfully coupled to vinyl or aryl halides by Kumada and co-workers.[54] They employed several nickel catalysts, the most active being nickel complexed by the bidentate phosphine ligands 66, 67, and 68. Unidentate phosphine ligands formed nickel

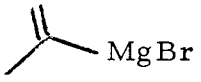
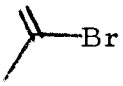
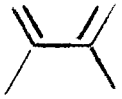
$$RMgX + R'X \xrightarrow[\text{Ether}]{NiL_2Cl_2(0.1\text{-}1.0\ \text{mol}\%)} R\text{-}R' + MgX_2$$

$L = Ph_2P(CH_2)_3PPh_2$ or $Ph_2P(CH_2)_2PPh_2$ or $Me_2P(CH_2)_2PMe_2$

66 67 68

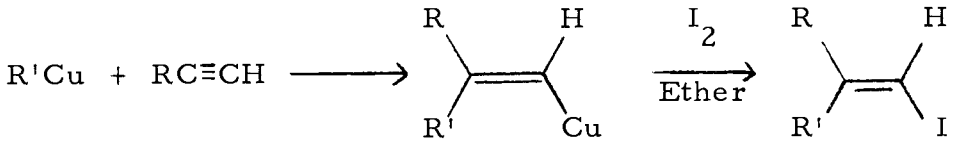
complexes that were inactive. The procedure generates dienes and arylenes in excellent yields. The interesting double coupling reaction of 1, 2-dichloroethylene introduces two groups cis to one another, regardless of the stereochemistry of the starting

dichloride, and as such represents a new route to cis double bonds.

RMgX	R'X	Product	% Yield	L
PhMgBr	CH_2=CHCl	PhCH=CH_2	87	66
CH_3CH=CHMgCl	PhBr	PhCH=CHCH_3	84	67
PhMgBr	CH_2=CCl_2	CH_2=CPh_2	82	66
PhMgBr	Z-ClCH=CHCl	PhCH=CHPh	91(90Z)	66
PhMgBr	E-ClCH=CHCl	PhCH=CHPh	100(80Z)	67
			79	67

Differences in the reactivity of vinyl chlorides and vinyl bromides suggest that non-symmetrical double coupling might be possible. These examples of double coupling are the only ones that the author has found in the literature.

Normant and coworkers[55] developed an easy route to vinyl

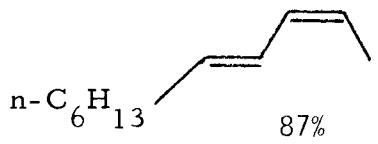


halides which provided some of the halides used in these coupling procedures.

Dang and Linstrumelle have added a third example of vinyl halide-Grignard reagent coupling.[56] Tetrakis (tri-phenylphosphine)-palladium(0) 68 catalyzed the coupling, giving products with greater

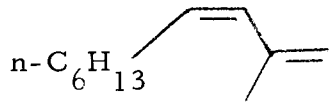
than 97% isomeric purity.

$$E\text{-}C_6H_{13}\text{-}CH{=}CHI + Z\text{-}CH_3CH{=}CHMgBr \xrightarrow{Pd(PPh_3)_4}$$



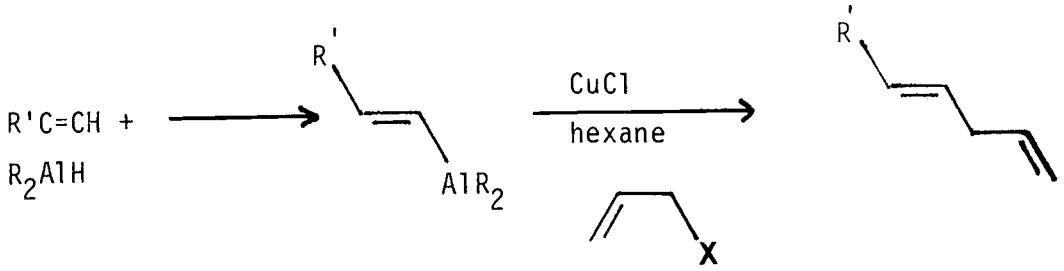
87%

$$Z\text{-}C_6H_{13}\text{-}CH{=}CHI + CH_2{=}C(CH_3)MgBr \longrightarrow$$



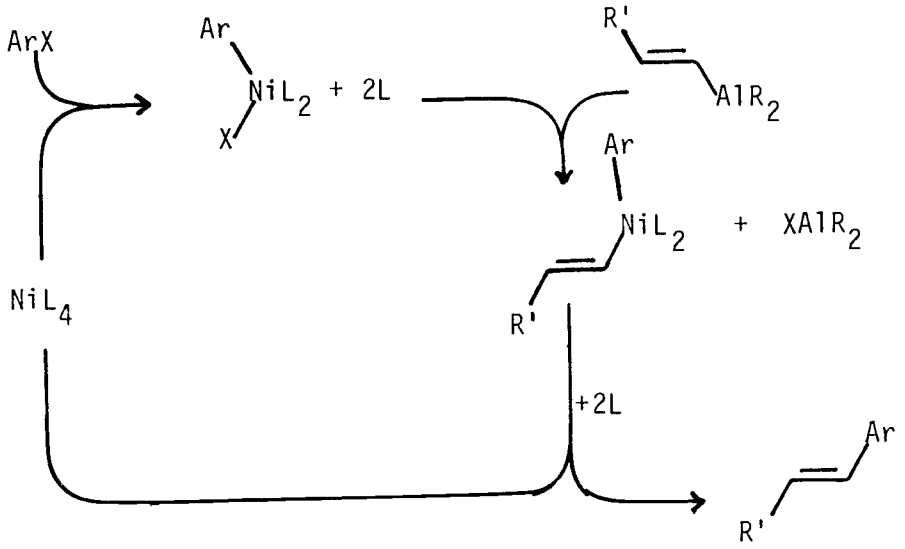
84%

The cis addition of dialkylaluminumhydrides to triple bonds yields almost exclusively trans vinyl alanes. Zweifel and Miller determined in 1970 that cuprous chloride in tetrahydrofuran initiates the dimerization of vinyl alanes.[57] More recently, Zweifel and Lynd[58] reported that cuprous chloride in hexane catalyzed the coupling of vinyl alanes and allylic halides in 60-70% yields. The relatively cheap catalyst was not extremely active as 25 mol% was required for satisfactory results. Products were formed with an



isomeric purity of more than 99%.

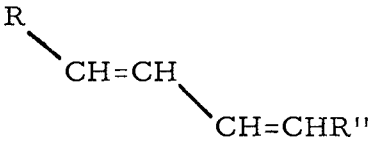
Negishi and Baba have also investigated vinyl alane/halide coupling.[59] They prepared arylenes in good yields from aryl halides and vinyl alanes. The catalyst, tetrakis(triphenylphosphine)-nickel(0) 69 is prepared in situ prior to use. Negishi proposed the



catalytic cycle above to explain the formation of products. Other nickel(0) complexes proved to be unsatisfactory.

Negishi and Baba expanded their original work to include coupling of vinyl alanes to vinyl halides,[60] using either 69 or a catalyst generated in situ from bis(triphenylphosphine)palladium(II) chloride 70 and two equivalents of diisobutylaluminum hydride. Both 69 and 70 work well but 70 gives products of higher isomeric purity (+99%) than 69 (90-95%). It should be possible to extend this work to

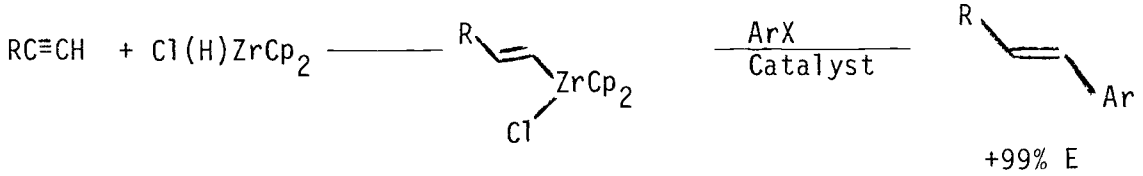
$$RC{\equiv}CH + HAlR'_2 \longrightarrow RCH{=}CHAlR'_2 \xrightarrow[\underline{69} \text{ or } \underline{70}]{R''CH{=}CHX}$$



R	R''	X	Catalyst	Yield
n-pentyl	n-butyl	trans-I	70 (Pd)	74%
n-pentyl	n-butyl	trans-I	69 (Ni)	70%
n-pentyl	n-butyl	cis-I	70	55%
n-pentyl	n-butyl	cis-I	69	55%
n-butyl		E-Br	70	75%

longer chain polyenes by coupling to cis-dienylhalides.

In an analogous fashion, Negishi and Van Horn[61] have prepared alkenylzirconium derivatives from acetylenes which can then be coupled to aryl or vinyl halides, again using 69 or 70 catalytically. As in the preparation of the vinyl alanes, the addition of hydridobis-(cyclopentadienyl)zirconium(IV) chloride 71 gives nearly exclusively the E alkenyl zirconium derivative.

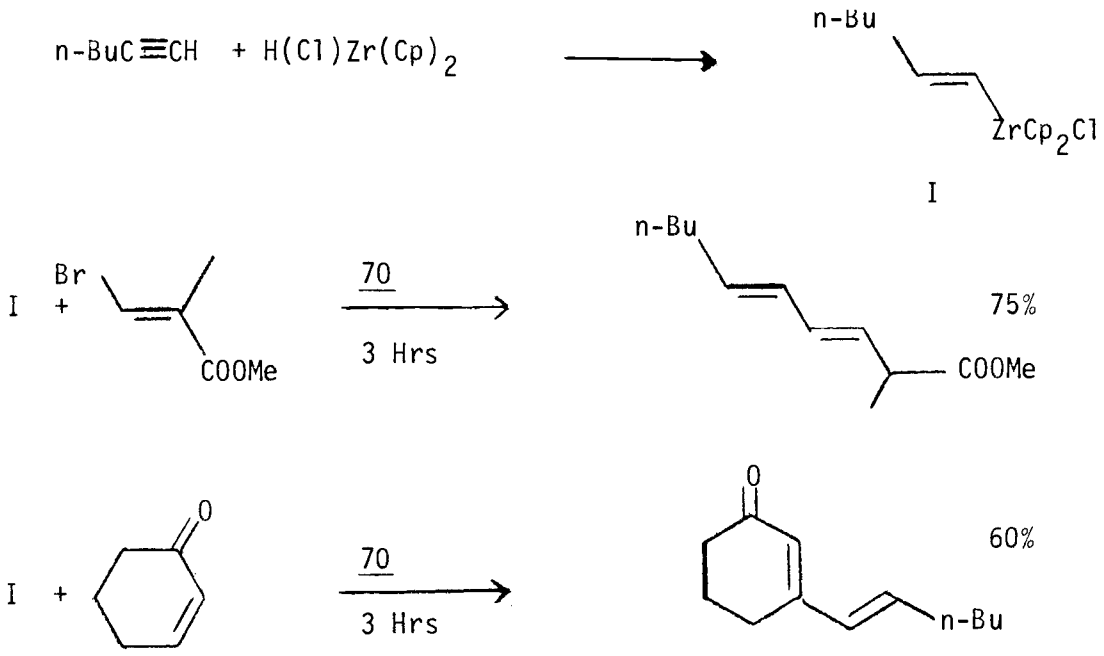


The coupling reaction proceeds with yields comparable to those

Acetylene	Coupled to	Yield
1-heptyne	PhI	96%
1-heptyne	Napthylbromide	70%
ß-ethoxyethyne	PhI	99%

obtained with vinyl alanes.

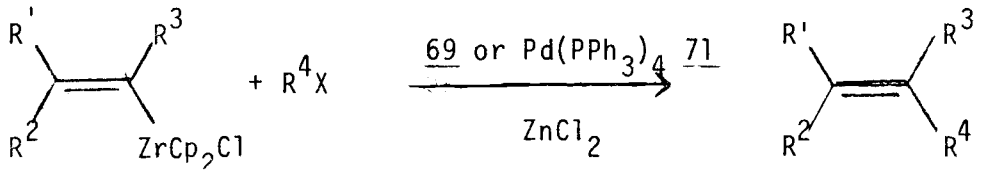
Negishi and coworkers[62] pointed out an important value of the alkenylzirconium coupling reagent, that is they do not react



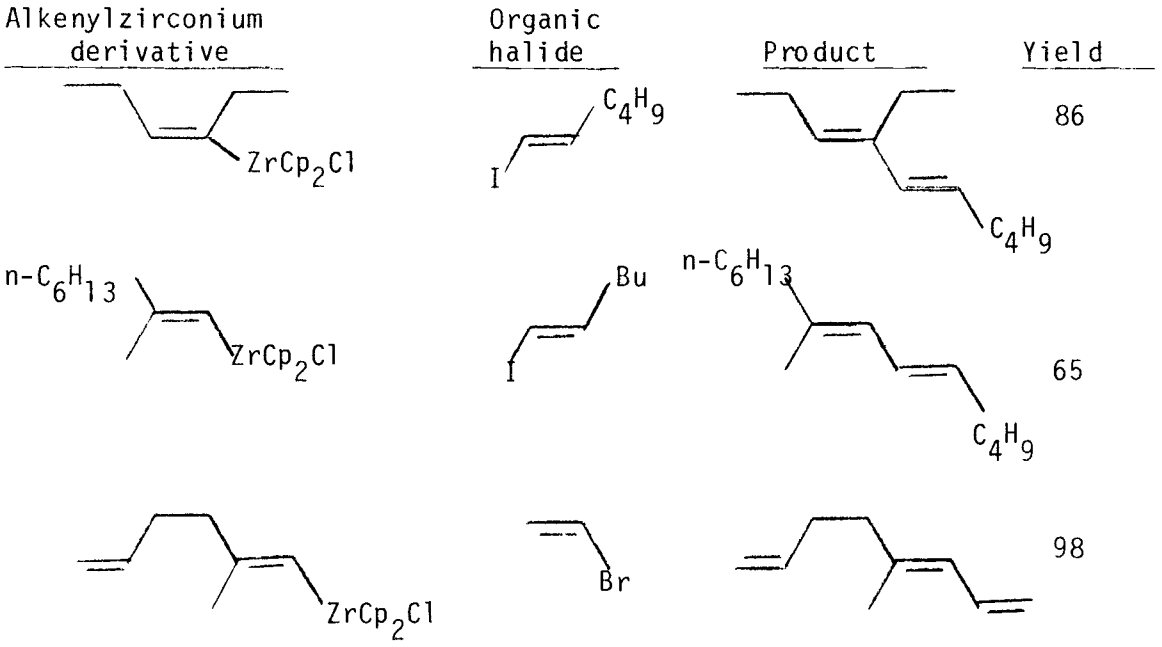
with carbonyl or oxygen functional groups. Consequently, more

complex systems can be prepared. The reaction shows considerable selectivity between vinyl (aryl) chlorides and vinyl (aryl) bromides. The reaction also worked well using 3-tetrahydropyranyl-1-propyne as the starting acetylene, giving coupling yields ranging from 60-75% at room temperature.

In their first paper on the use of alkenylzirconium derivatives, Negishi and coworkers found that non-terminal alkenylzirconium derivatives couple at a rate slow enough to allow dimerization of the vinyl halides to compete.[61] Recently, they have reported[63] that

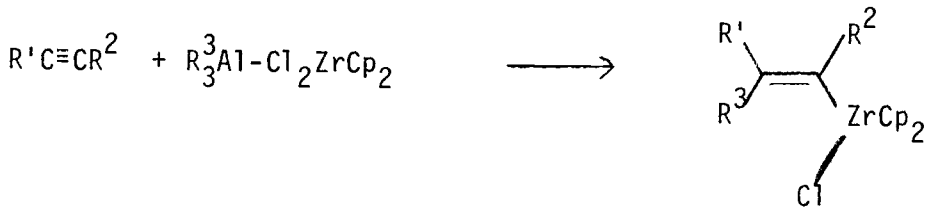


the addition of small amounts of zinc chloride as a cocatalyst greatly enhanced the rate of the coupling reaction. Moderate yields of highly substituted dienes were obtained.

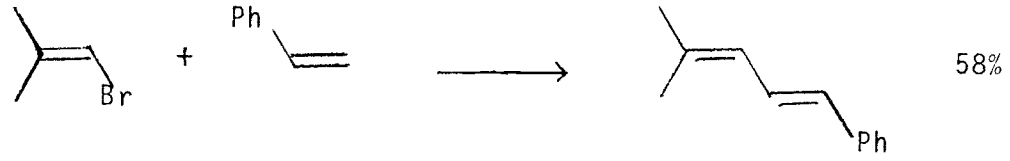


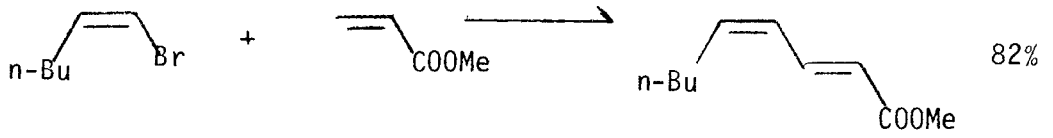
The function of the zinc chloride has not yet been fully established. In the transmetalation step where steric demands are severe the substitution of the sterically undemanding zinc chloride for the zirconium derivative followed by transmetalation with the catalyst could enhance the rate dramatically.

The importance of this route to highly substituted dienes should be emphasized because of the ready availability of highly substituted alkenylzirconium derivatives. In a publication accompanying this report, Negishi and Van Horn reported the carbometalation of alkynes in high, stereospecific yields.[64] The procedure is presented below.



A process which does not need metalated alkenyl derivatives was devised by Heck and coworkers.[65, 66] The scope of this reaction, which couples olefins and vinyl halides, was investigated recently.[67] Moderate yields of dienes were obtained using bis-(triphenylphosphine)palladium diacetate 72 and trialkyl amines

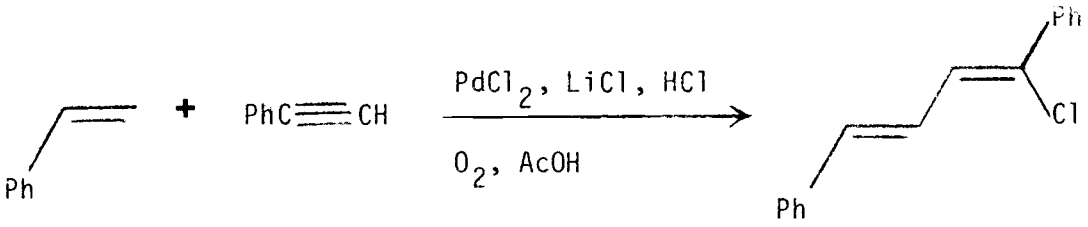




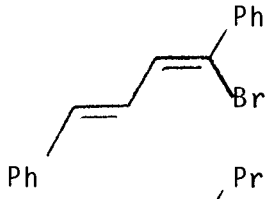
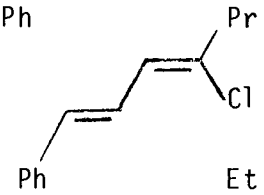
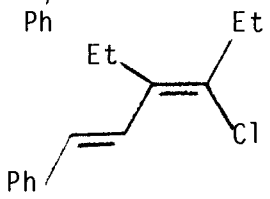
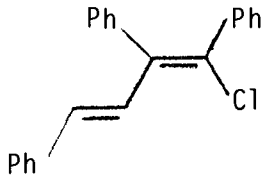
at 100-150°C.

Perhaps the most useful coupling reaction developed in recent

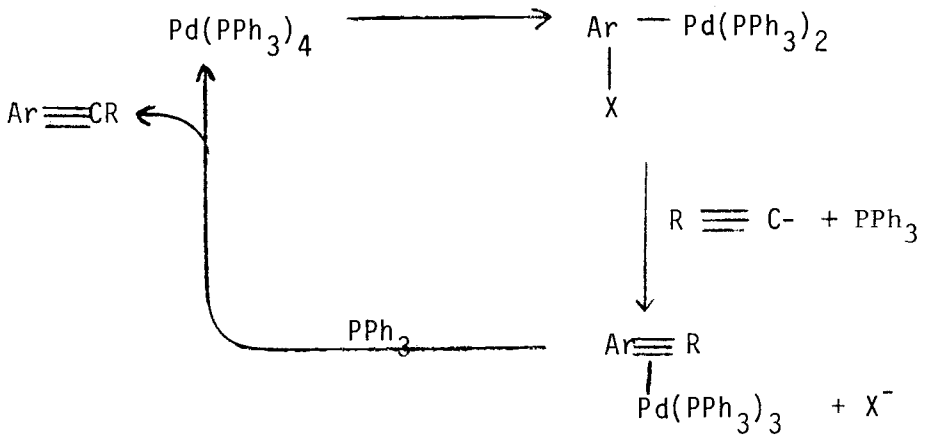
times was reported by Kaneda and coworkers.[68] Their procedure couples acetylenes and olefins and yields very valuable (E, Z)-1-alkyl-4-halogeno-1, 3-dienes. The starting materials are cheap while the products are not so readily attainable Z-halogenodienes, which can be used in the coupling reactions already presented. The reaction of phenylacetylene and styrene below is representative.



The use of palladium bromide and lithium bromide gives bromodienes. Other acetylenes give moderate yields of codimers as well. Applications of this codimerization to other olefins are reported to be in progress.

Acetylene	Codimer with Styrene	Yield
PhC≡CH		73
n-PrC≡CH		60
EtC≡CH		66
PhC≡CH		26

Routes to the important enynes were reported by three groups simultaneously. Cassar reported that vinyl or aryl halides could be coupled to acetylides using tetrakis(triphenylphosphine)palladium-(0) 73.[69] Cassar proposed the scheme below to explain the formation of products.



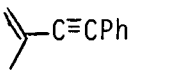
This procedure leads to moderate to excellent yields of enynes and arylynes as indicated below.

Halide	Acetylene	Yield %
PhI	PhC≡CH	95
PhI	n-PrC≡CH	97
PhI	$HOCH_2C{\equiv}CH$	50
CH_2=CHBr	PhC≡CH	52
PhCH=CHBr	PhC≡CH	89

PhI + HC≡CH ——— PhC≡CH + PhC≡CPh

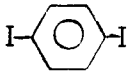
50% 50%

In a similar process, Dieck and Heck[70] prepared enynes by coupling vinyl halides and acetylenes, and arylenynes by coupling enynes with aryl iodides. The latter is the closest example of the coupling of terminal enynes to extend conjugation to be found in the literature. Dieck and Heck used a catalyst similar to 70 but prepared instead from palladium(II) acetate in situ with triphenylphosphine and trialkylamines. Moderate yields of enynes or arylynes are obtained.

Halide	Acetylene	Product	Yield %
PhI	$HC{\equiv}CC_4H_9$	$PhC{\equiv}C\text{-}C_4H_9$	62
E- PhCH=CHBr	$PhC{\equiv}CH$	E- $PhCH{=}CH\text{-}C{\equiv}CPh$	70
Z- PhCH=CHBr	$PhC{\equiv}CH$	Z- $PhCH{=}CH\text{-}C{\equiv}CPh$	67
ArI	$HC{\equiv}C\text{-}C(CH_3){=}CH_2$	$PhC{\equiv}C\text{-}C(CH_3){=}CH_2$	71
$CH_3C(Br){=}CH_2$	$PhC{\equiv}CH$		88

The procedure developed by Sonagashira and coworkers gives the best yields of enynes and arylynes under exceedingly mild conditions.[71] A mixture of the alkyne and vinyl or aryl halide in

diethylamine couple smoothly at room temperature in the presence of bis(triphenylphosphine)palladium chloride and cuprous iodide. Yields are excellent as the table below will show. The procedure is compatible with the presence of hydroxyl in the molecule, which in turn could be used to extend conjugation. As will be seen in our work, this procedure is also capable of being extended to the coupling of enynes with vinyl halides to form dienynes.

Acetylene	Halide	Product	Yield
$HC{\equiv}CH$	PhI	$PhC{\equiv}CPh$	85
$PhC{\equiv}CH$	PhI	$PhC{\equiv}CPh$	90
$HC{\equiv}CCH_2OH$	PhI	$PhC{\equiv}CCH_2OH$	80
$PhC{\equiv}CH$			98
$PhC{\equiv}CH$	$CH_2{=}CHBr$	$PhC{\equiv}C\text{-}CH{=}CH_2$	91
$HOCH_2C{\equiv}CH$	$CH_2{=}CHBr$	$HOCH_2C{\equiv}CCH{=}CH_2$	40
$HC{\equiv}CH$	$PhCH{=}CHBr$	$PhCH{=}CHC{\equiv}CCH{=}CHPh$	95
$PhC{\equiv}CH$	$PhCH{=}CHBr$	$PhC{\equiv}CCH{=}CHPh$	90
$HOCH_2C{\equiv}CH$	$PhCH{=}CHBr$	$HOCH_2C{\equiv}CCH{=}CHPh$	70

Complete stereochemistry about the double bond is preserved.

DISCUSSION

Introduction

Three separate but related topics were studied in the course of this work. For organizational purposes these studies will be presented in three sections:

I. The synthesis and thermolysis of 1-phenylheptatrienes.

II. The synthesis and thermolysis of 1-aryl-6-carbethoxy-hexatrienes.

III. The synthesis and thermolysis of a cis,cis-cross-conjugated pentaene.

I. The synthesis and thermolysis of 1-phenylheptatrienes.

Introduction

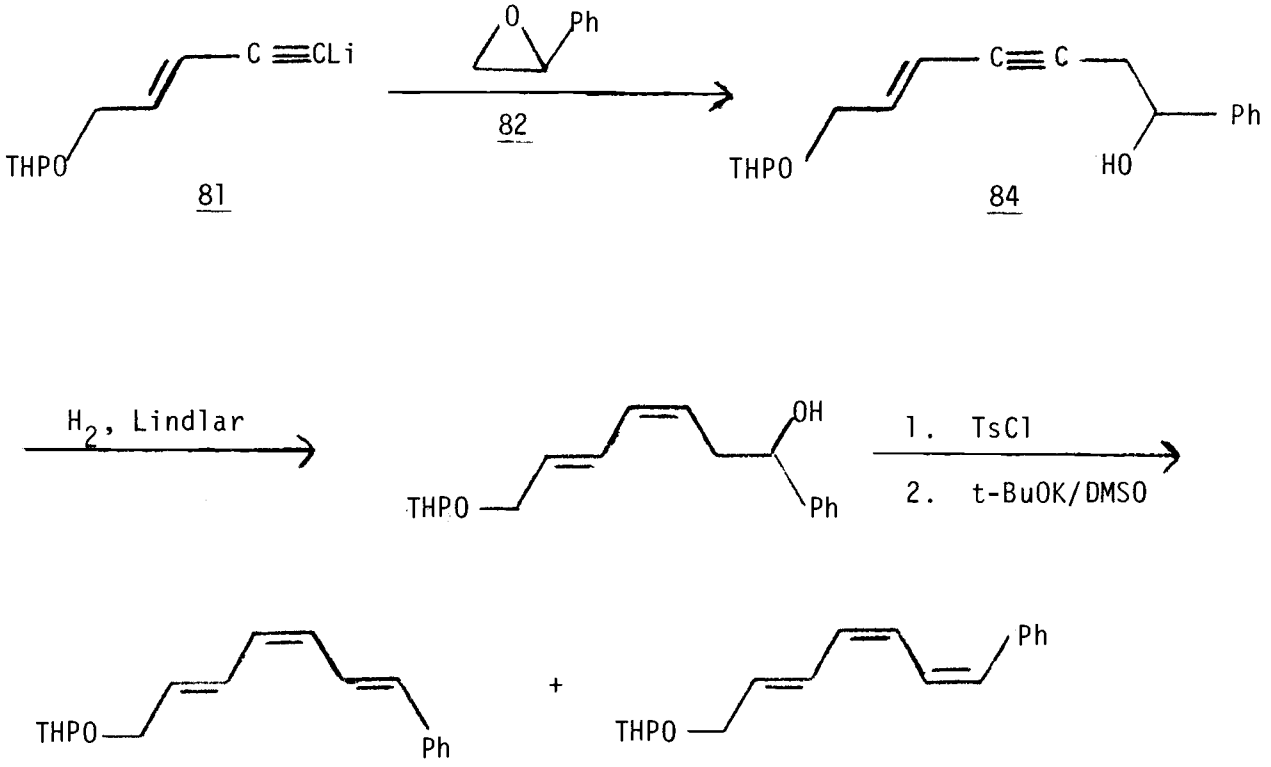
Most previous studies of the energy differential between the allowed and forbidden pathways have exploited the ability to block the allowed process in a conrotatory reaction, or the reversibility of the allowed reaction in special cases. Neither is particularly useful with the disrotatory six electron electrocyclization. In order to obtain some estimate of this energy differential we opted to attempt to increase the rate of a diradical reaction sufficiently to permit it to compete with the allowed reaction. For this method to be successful the diradical process must be accelerated to a far greater extent than the allowed reaction. Some experimental means of identifying the product from the diradical reaction must be also be developed. Care must be taken to eliminate alternative sources of the diradical product. These

requirements are not easily satisfied.

Because it had been previously established that a terminal phenyl group does not accelerate the allowed reaction,[1] but might be expected to stabilize a radical route by as much as 12.5 kcal/mole, it was decided to study the thermal isomerization of a terminally substituted 1-phenylheptatriene. Identification of the diradical product could be accomplished by detection of the "wrong" stereochemical product. The most likely source of the "wrong" product would be the reactant with one terminal configuration reversed. If a trans, cis, trans reactant were being used it had previously been shown that the trans, cis, cis contaminant reacts several orders of magnitude slower. Thus, trans, cis, trans-1-phenylheptatriene appeared to satisfy the requirements for the proposed study and we proceeded to prepare it.

Synthetic considerations

The most desirable synthesis would permit complete control of the stereochemistry at all three double bonds. Since this does not appear to be possible by way of any route previously reported, a separation method capable of producing the desired triene in high purity must be available. Precedence for separation had been set using the previously reported procedures. Initially we chose to use the route developed by Marvell and Tashiro which involves generation of a configurationally uniform enyne, conversion to an enynol, semi-hydrogenation and separation of a pure dienol and finally elimination to a triene.[40] The overall procedure is illustrated in scheme 1. The ultimate step does not give a stereochemically pure triene, but generates two stereoisomers in about a 4:1 ratio. Thus, separation of the final product mixture into pure



Scheme 1. Approach to 7-Phenyl-2,4,6-heptatrien-1-ol

stereoisomers is an obvious necessity. Our plans were based on the results of Platt who prepared trans, cis-1-phenylhexatriene by such a route and reported that trans, cis and cis, cis-trienes could be separated by glc. His work also showed the extreme sensitivity of these trienes to polymerization by oxygen. Since it had also been established that a pentenyne generated by elimination gives predominantly the cis-enyne, we chose to prepare 7-phenyl-trans,cis,trans-2,4,6-heptatrien-1-ol. In this case the formation of trans-2-penten-3-yn-1-ol is favored in the elimination.

Approach to trans,cis,trans-7-phenyl-2,4,6-Heptatrien-1-ol (78)

Following the general scheme of Marvell and Tashiro[40] the route to 78 above was devised.[34] A modification of the procedure of Heilbron and

and coworkers[74] was used to prepare trans-2-penten-4-yn-1-ol 80 free from contamination with the cis isomer.

Epichlorohydrin 79 was converted to 80 in 60-70% yield. A small portion of the alcohol was distilled, and the pure product had physical properties which matched those reported for trans-2-penten-4-yn-1-ol.[74] The nmr spectrum allows unambiguous assignment of trans stereochemistry to the product. It shows signals at δ6.31 and 5.68 with a coupling constant of 15 Hz. The cis isomer, which can be isolated if the procedure of Heilbron and coworkers[74] is used, has bands at δ6.04 and 5.43 with J=12 Hz. Our modification was the addition of a cosolvent, ether, which was done in an attempt of decrease the amount of polymer formed. The yield was increased from 25% to 60-70%, but the increased isomeric purity of the product 80 was an unexpected stroke of luck. It is possible that the sodium acetylide is complexed with the ether increasing its steric bulk and favoring the transition state for formation of trans isomer.

The crude alcohol 80 was converted to its tetrahydropyranyl ether which was isolated by distillation in 85% yield. The structure was 81 assigned from the nmr spectrum which shows bands at δ6.23 and 5.62 (J=15 Hz, vinyl protons), δ4.59, 3.9-3.2 and 1.8-1.2 (tetrahydropyranyl ring) and a weakly coupled signal at δ2.79 (acetylenic proton).

Reaction of 81 with ethylmagnesium bromide was expected to give an alkynyl Grignard reagent. Indeed, evolution of ethane was observed but addition of styrene oxide 82 gave a residue which contained neither the expected alcohol 84 nor the starting alkyne 81. Addition of phenylacetaldehyde 83 also gave a residue from which none of the expected alcohol 85 could be isolated.

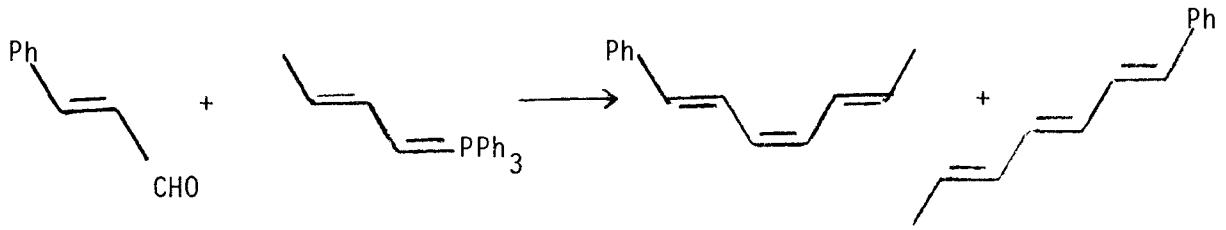
The lithium anion of 81 was prepared via methyllithium and allowed to react with 83. Again neither product 85 nor starting alkyne was isolated. Consequently, this route to 78 was abandoned.

Destruction of the Grignard and lithium reagents was assumed to occur by reaction with the relatively acidic alpha hydrogen of the pyran.

Wittig approach to trans, cis, trans-1-phenyl-1,3,5-heptatriene (74)

The failure of the initial route led us to attempt to adapt the procedure of Jaenicke and Seferiadis which uses a Wittig reaction to generate the central cis double bond.[48] This has the advantage of leaving the terminal double bond of predetermined stereochemistry, but the disadvantage of producing more trans than cis configuration at the central bond.

Thus, 2-buten-1-ylidenetriphenylphosphorane 86 was allowed to react with cinnamaldehyde 87. The crude product was isolated in about 40%



86 87 74 88

yield, and a pure sample, mp 68-70°C, was obtained from glc. The nmr spectrum indicates the presence of triene, since it involves a multiplet (5H) at δ7.4-7.1 (aromatic ring), a very complex multiplet (6H) between δ 7.0-5.4 (olefinic protons) and a doublet (3H) at δ1.79, J=6 Hz (methyl group). Neither the crude product nor the glc purified product underwent any thermal isomerization, and the product was assumed to be

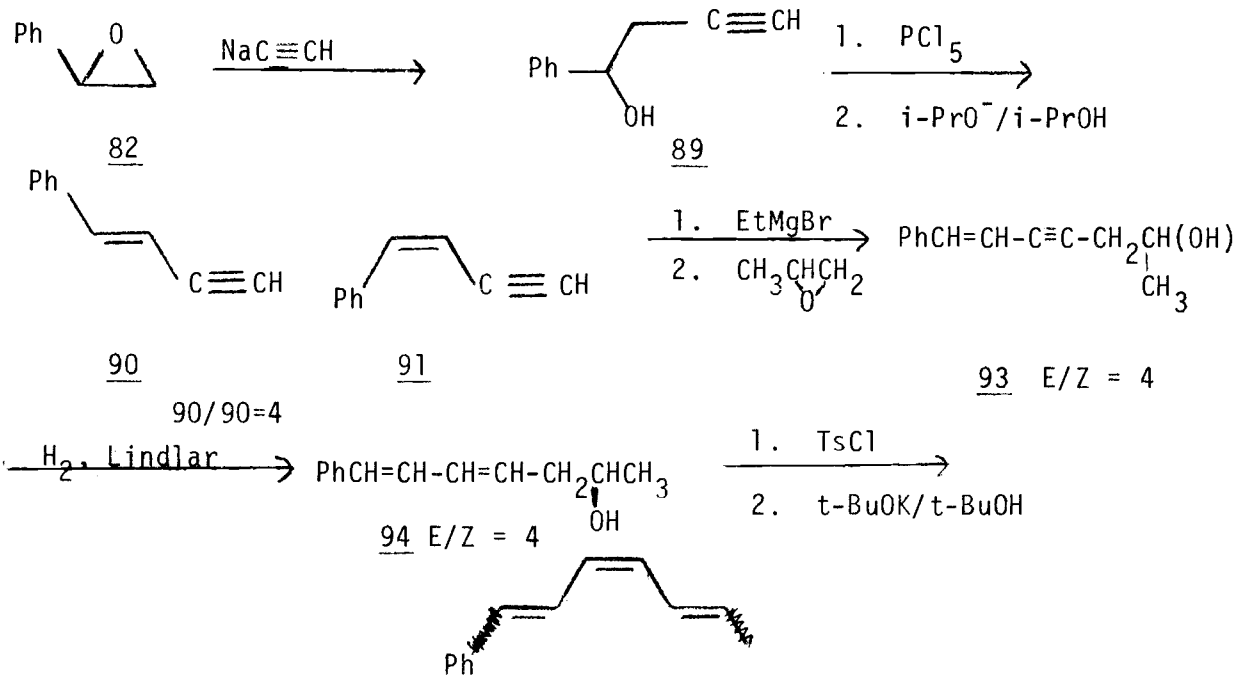
the all trans isomer 88.

Approach to trans, cis, trans-1-phenyl-1,3,5-heptatriene (74) from 1-phenyl-1-buten-3-yne

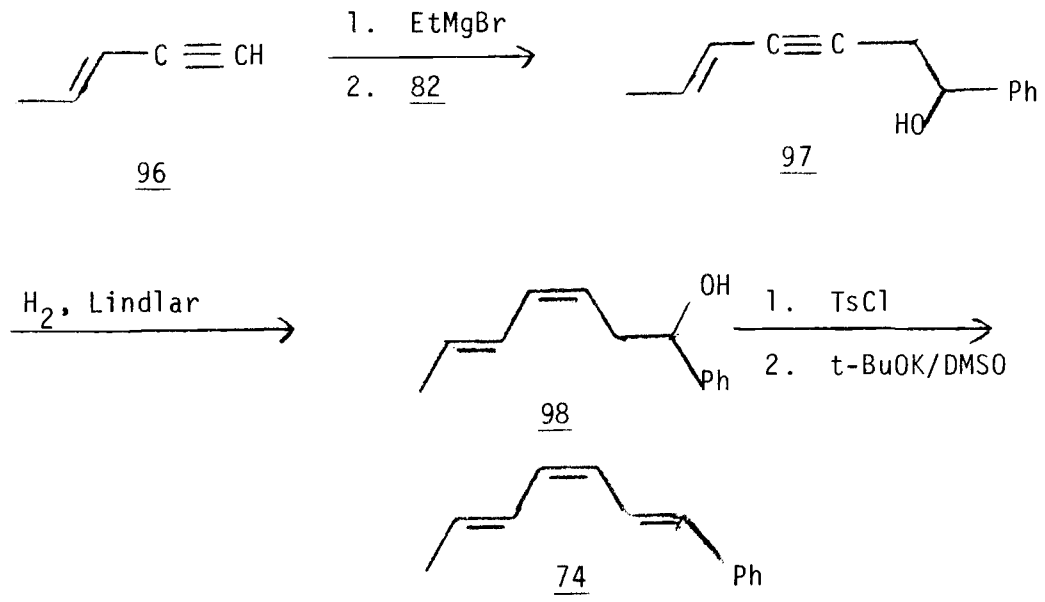
Failure of the Wittig approach returned our thoughts to variations on the original theme. Since it seemed reasonable that the presence of the tetrahydropyranyl group was responsible for the initial failure, we investigated two related routes based on the Marvell-Tashiro[40] procedure. These are illustrated in schemes 2 and 3. The 1-phenyl-1-buten-3-ynes 90 and 91 were prepared without incident as shown, but attempts to separate the pure isomers were disastrous. Fractional distillation led to polymerization and in one case to a near explosion. Thus further work on this route was carried out using the mixture of isomers.

The mixture of isomers was converted to a mixture of Grignard reagents and allowed to react with 82 giving 93, a mixture of E and Z isomers, which could be identified by spectral characteristics. The nmr spectrum shows doublets at δ6.80 and 6.40 (J=16 and 12 Hz), E and Z isomers (vinyl protons). The remaining nmr spectral data is in accord with a mixture of E and Z isomers of 93 and glc analysis showed two peaks (4:1 ratio).

The mixture was semi-hydrogenated over the Lindlar catalyst[76] giving a mixture of Z,E and Z,Z- 94, for which glc analysis showed two peaks (4:1 ratio). The major product was isolated by preparative glc and its nmr spectrum found to be consistent with Z, E-94. A multiplet from δ7.2-6.1 represents three vinyl protons while a doublet in the vinyl region, δ5.51, (J=11 Hz) supports the assignment of cis stereochemistry for the center bond.



Scheme 2. Approach to t,c,t-1-phenyl-1,3,5-heptatriene from phenylbutenyne



Scheme 3. Approach to t,c,t-1-phenyl-1,3,5-heptatriene from pentenyne

The alcohol 94 was converted to the tosylate 95. Evidence for the formation of the tosylate includes the absence of the OH band in the infrared spectrum and the appearance of typical sulfonate ester bands at 1380, 1190, and 1180 cm^{-1}.[77]

Compound 95 was treated with potassium t-butoxide both in the presence and absence of light. Oxygen was carefully excluded from contact with the products. Nonetheless, none of the desired product 74 was ever isolated by gas chromatography. In fact, only the all trans isomer 88, identified by its melting point, its nmr spectrum and its inability to undergo cyclization thermally, was obtained. Products were obtained in small amounts which may have been cyclized products. These products were identified only by their uv absorptions and consequently any structural assignment would be questionable.

Since the all trans isomer 88 was the only triene isolated, it is conceivable that 88 is the direct product of the elimination of 95. It is certainly the most stable of all of the expected products as the work of Zechmeister[78] indicates. But, Marvell and coworkers[1,40,41] have prepared several trienes by elimination in the final step and never observed isomerization of the other double bonds in the molecule. Thus, it is probable that 74 was obtained, along with a mixture of cis-1 and cis-5 isomers.

The intent of this work was to determine the amount of disallowed product formed in the electrocyclization of 74. To begin with a mixture of trienes would not solve the problem. We chose to try to isolate 74 and obtained only 88. We can only conclude that if 74 was actually formed, it was either cyclized or isomerized during separation. Later in this work it was established that 74 is in fact, unstable to glc separation.

While Platt[1] reported that 1-phenyl-1,3,5-hexatrienes were separable by glc, he did not adequately establish that the trienes he observed had not undergone cis/trans isomerization. His kinetic and product studies were done with material which had not been glc purified. Thus, while it appeared that precedence for glc separation of trienes had been set, it may well have been a mirage.

Approach to trans, cis trans-1-phenyl-1,3,5-heptatriene from trans-3-penten-1-yne (96)

The elimination of 1-phenyl-3-butyn-1-ol 89 gave a mixture of enynes containing about 10-20% of the cis isomer. It seemed probable that the elimination of 1-phenyl-cis,trans-3,5-heptadien-1-ol 98 would give nearly pure 74. Because cis and trans-3-penten-1-yne had been separated by fractional distillation[41] it was thought that 98 could be prepared with high purity, allowing the synthesis of nearly pure 74. Thus we proceeded via Scheme 3 to attempt to prepare 74.

The Grignard reagent of 96 was prepared and allowed to react with styrene oxide 82, giving the enynol 97 which was fully characterized by its nmr spectrum: singlet δ7.30 (5H, phenyl), 6.12 and 5.52 with J_{AB}=16 Hz (trans double bond), and doublet, J= 7Hz (methyl).

The alcohol 97 was hydrogenated over the Lindlar catalyst with somewhat less selectivity than is normally experienced. About 50% of the mixture was the desired dienol, 98 , with the remainder of the products the result of under and overhydrogenation. Relatively pure 98 was isolated by repeated distillations in 17% yield. The assignment of cis-3-trans-5 stereochemistry was supported by the nmr spectrum where the signal for one

vinyl proton was isolated from the other three permitting its coupling constant of 11 Hz to be obtained. The dienol 98 was converted to its tosylate (99) using a standard procedure.

Elimination was carried out in dimethylsulfoxide and the product was expected to consist of mainly 74 plus cis, cis, trans-1-phenyl-1,3,5-heptatriene (100) in much smaller amount. Isolation of 74 was attempted by preparative glc. One product which had a retention time corresponding to that of a triene was collected and was found not to undergo thermal isomerization. It was consequently assumed to be either all trans 88 or 100. Later work showed that these glc conditions were sufficient to cause 74 to cyclize as well as to isomerize. The major product indicated by glc analysis was not a triene but had a retention time characteristic of the cyclohexadienes.

Since we were unable to isolate a pure sample of 74 from this reaction, it was not pursued further. However we cannot state that this scheme did not produce the desired triene 74, only that were unable to isolate it.

Synthesis of trans, cis, cis-1-phenyl-1,3,5-heptatriene (77)

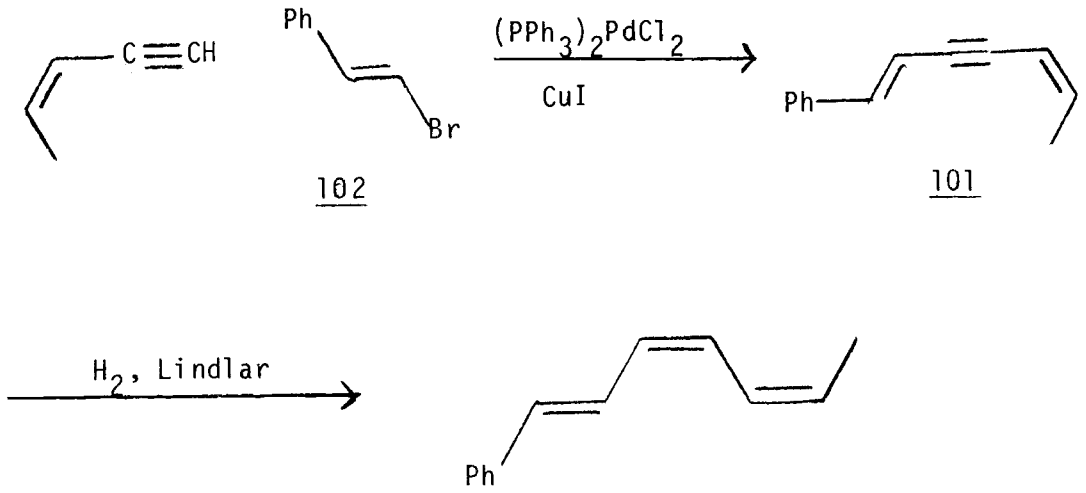
There seemed to us little reason to assume that the Marvell-Tashiro scheme was failing to give any of the desired triene. Thus the true problem was the separation of the triene from the reaction mixture. In view of the difficulties we had experienced with trying to use gas chromatography, column chromatography and preparative layer chromatography, it appeared to us that any preparative route which generated isomeric mixtures at a terminal bond in the final step was untenable. Unlike

the terminal bonds, whose configurational uniformity is a necessary consequence of the use of a stereochemical probe, the central bond need not be configurationally uniform. It is solely necessary that a reasonable proportion of the mixture have the proper cis configuration, since only that isomer can undergo the electrocyclic ring closure at temperatures below 200°C.

This analysis turned our thoughts once again to routes which generate the central double bond in a final step. The simplest of these is semi-hydrogenation of a dienyne, but it is known that this is not a clean reaction. Careful analysis of the hydrogenation in a number of examples has shown that the product consists of the desired cis-triene (ca. 50%), some trans-triene, overhydrogenated products (dienes) and unreacted starting material. In no case was any stereomutation of a terminal bond found. If this proved accurate then the product of semi-hydrogenation would contain only one compound which could isomerize thermally to a cyclohexadiene. Hydrogenation of the thermolysis mixture over Adam's catalyst would reduce the mixture to cyclohexanes and 1-phenylheptane which are separated easily.

The synthesis of 77 was accomplished in the following manner: Trans-β-bromostyrene 102 was prepared by the procedure of Biltz.[79] The mixture of cis and trans-β-bromostyrenes was purified by the method of Dolly, Wilkens and Frey.[80] After purification, 102 was obtained free from contamination with the cis isomer in an overall yield of 35%. The assigned structure and the purity of the product are indicated by the nmr spectrum which has a partially obscured doublet, J=15 Hz (trans olefin) at δ7.10 (the β-vinyl proton) and a doublet, J=15 Hz (trans

olefin) at δ 6.64 (α-vinyl proton).



102 101

77

85%

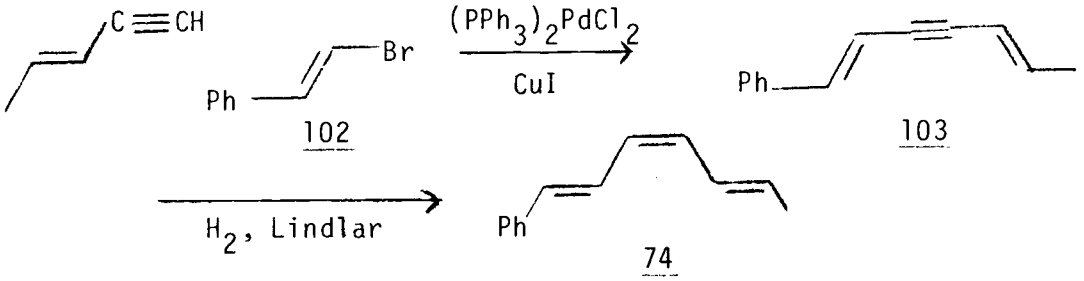
A modification of the procedure of Sonagashira, et. al.,[71] was used to prepare the alkyne 101. A solution of cis-3-penten-1-yne and 102 in diethylamine was treated with bis(triphenylphosphine)dichloropalladium (II) and cuprous iodide affording 101 in a yield of 89%. The structure can be assigned completely from the nmr spectrum alone. This consists of a doublet at δ6.90, J=16 Hz (trans-PhCH=CH), a doublet of doublets at 6.18, J=16, 1 Hz(trans-PhCH=CH-), a similar multiplet of doublets at 5.69, J=10, 1 Hz (cis-CH=CHCH$_3$), a doublet of quartets at 6.00, J=10, 6 Hz (cis-CH=CHCH$_3$), and a doublet of doublets with J=1, 6 Hz at 1.89 (the methyl group). The ir spectrum shows the expected C≡C stretching band at 2355 cm^{-1}, the trans double bond band at 945 cm^{-1}, and the cis-double bond band at 680 cm^{-1}. The uv spectrum is consistent with a system of extended conjugation (uv_{max}= 311 nm, ε=30,000).

A solution of 101 was semi-hydrogenated over the Lindlar catalyst[76] in the presence of quinoline giving only one major (85%) and four minor

products (15%). The major product was isolated by preparative glc and its spectral characteristics were consistent with those expected of 77. The triene 77 could be isolated by glc because it does not undergo cyclization as readily as 74, and it was the only expected product. Because of the second point, glc conditions could be changed to allow contact time to be decreased considerably, decreasing the possibility of isomerization in the column. The nmr shows multiplets at δ7.4-7.0 and 7.0-5.3 with relative areas 5:6 for the phenyl and olefinic protons. The terminal methyl group gives rise to a doublet of doublets (J=7, 1 Hz) at 1.90. The uv spectrum (uv_{max}=318, ε=43,500) is reasonable for a triene conjugated to a terminal phenyl group.

Synthesis of trans,cis,trans-1-phenyl-1,3,5-heptatriene (74)

Via an analogous procedure, trans, trans-1-phenyl-1,5-heptadien-3-yne 103 was prepared form 102 and trans-3-penten-1-yne in the presence of bis(triphenylphosphine)dichloropalladium (II) and cuprous iodide in an overall yield of 83%. The alkyne was semi-hydrogenated over the Lindlar



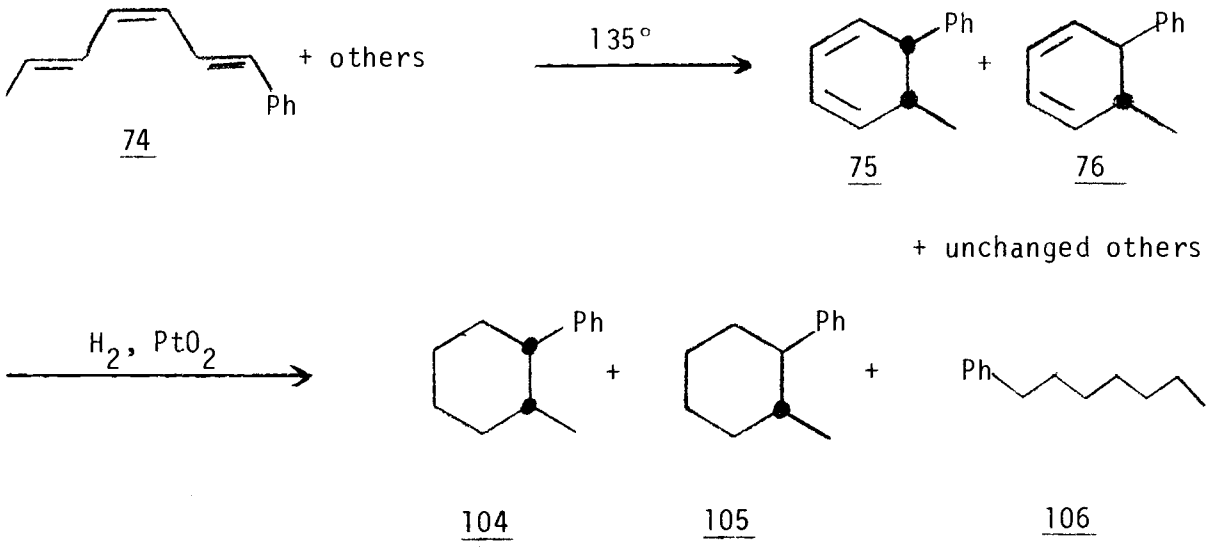
catalyst[76] giving the triene 74 (81%) and several minor products (19%). The spectral characteristics of 103 were completely in accord with the assigned structure. The nmr spectrum exhibited one AB pattern at δ6.96,

6.21 (J_{AB}=16 Hz) and a second AB pattern at 6,12, 5.61 (J_{AB}=16 Hz) and the terminal methyl group produced a doublet (J=7 Hz) at δ1.85. The uv spectrum of the alkyne (uv_{max}=311 and ϵ=37,000) and its ir spectrum, 2275 cm^{-1}(triple bond) and 945 cm^{-1} (trans double bond) were as expected.

The triene 74, on the other hand shows a very complex nmr spectrum and only the relative areas for phenyl, olefinic and methyl protons could be obtained. The uv spectrum (uv_{max}= 317 nm and ϵ=40,500) is consistent with the structure of a conjugated triene having a terminal phenyl group. In addition the uv spectrum shows shoulders at 304 and 327 nm giving it the three-fingered character normal for a trans,cis,trans triene.[41,78] The uv spectrum for 77 does not show this fine structure.

Thermolysis of trans,cis,trans-1-phenyl-1,3,5-heptatriene (74)

A dilute solution of 74 in spectral grade cyclohexane was placed in a clean pyrex tube, degassed thoroughly by the freeze-thaw method, and heated to 135° for three hours. Because of the presence of several compounds (from the semi-hydrogenation of 101) with glc retention times similar to the expected thermolysis products 75 and 76, no attempt was



74 75 76

104 105 106

made to isolate the cyclohexadienes. The thermolysis mixture was immediately hydrogenated over platinum oxide giving a mixture of 1-phenylheptane 106 and cis-5-phenyl-6-methylcyclohexane 104 in a ratio of 1:4. Both 106 and 104 were isolated by preparative glc and identified, 106 by its nmr spectrum and 104 by its nmr spectrum and by comparison with an authentic sample.

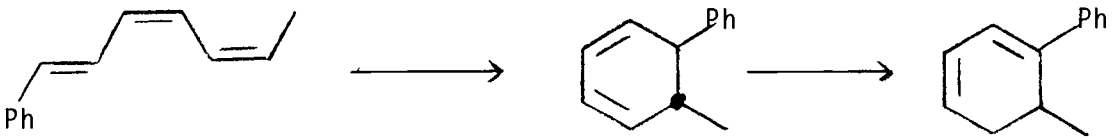
Along with the peaks due to these compounds there appears a very small peak with the same retention time as trans-5-phenyl-6-methyl-cyclohexane (105). Too little material was present to permit isolation of the product responsible for this peak, and the peak overlaps slighlty with the peak for 1-phenylheptane, thus precluding our obtaining mass spectral information. Careful and repeated integration gave the ratio of 104/105 as 550:1. We assume, though with obvious reservation, that the small peak is due to 105, and further discussion is based on that assumption. This assumption is not unreasonable since any error can only reduce the amount of 105 actually present altering our conclusions in one direction only.

The nmr spectrum of 104 is most interesting because the multiplet at δ2.79 appears as a clean doublet of triplets. We would have expected this to be the X portion of an AB_2X type of pattern[81] (assuming the two adjacent equatorial protons to be accidently equivalent, and ignoring the additional methylenes of the ring) since the principal conformation of 104 should have an equatorial phenyl. However, the doublet of triplets, apparent J's = 11, 4 Hz, appears to be better attributed to an AM_2X system. Both of the isomers were prepared by the procedure of Pines[82] who assigned cis and trans structures on the basis of the ratio of the two

products formed during reduction of a mixture of 1-phenyl-2-methylcyclohexene and 1-phenyl-6-methylcyclohexene (note that there is an ambiguity in their paper since the structure shown for their cis isomer is actually trans). Later work by Descotes, et al. provided an assignment based principally on the ratio of isomers formed during reduction of 1-phenyl-2-methylcyclohexene and their nmr spectrum[83] for the cis isomer matches ours.

Kinetic results of the thermolysis of 1-phenyl-1,3,5-heptatrienes

Solutions of 74 (2×10^{-3}M and 77 (0.2M) in spectral grade cyclohexane were prepared. The rate of disappearance of 74 was monitored by ultraviolet spectroscopy, but with 77 the rate of disappearance had to be measured by glc using acenapthalene as an internal standard. At the higher temperatures required for cyclization of 77 a 1,5-hydrogen shift also occurred giving a secondary product which interfered with the ultraviolet measurements. We assume this interfering product is 107



77 76 107

which would give a band at 307 nm,[49] though we did not isolate and identify it. The presence of a transient intermediate, 76, was noted during the glc studies.

First-order rate constants were determined at several temperatures for both trienes. From plots of ln k versus 1/T the activation

parameters $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ were calculated[86] for the electrocyclization of 74. From the same plot it was possible to estimate the rate of cyclization of 74 at higher temperatures for direct comparison with 77.

(a) trans, cis, trans-1-phenyl-1,3,5-heptatriene 74

$$E_a = 29.0 \pm 0.5 \text{ kcal/mol}$$

$$\Delta H^{\ddagger} = 28.2 \pm 0.5 \text{ kcal/mole}$$

$$\Delta S^{\ddagger} = -6.8 \pm 0.1 \text{ cal/mole } ^{o}K$$

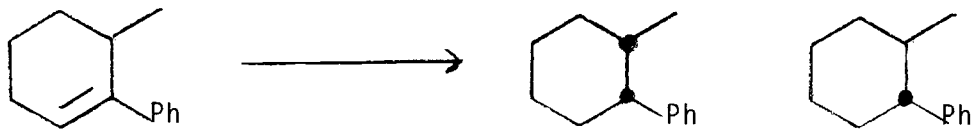
(b) trans, cis, cis-1-phenyl-1,3,5-heptatriene 77

$$k_{74}/k_{77} = 200$$

Conclusions

The most important consideration to be made here is the formation of the product with the forbidden stereochemistry. Tacitly we assume that the minor peak in the glc trace of the hydrogenated product results purely from trans-2-methyl-1-phenylcyclohexane. First we shall consider the possible sources of this product. One possible source is during hydrogenation of the electrocyclization product, a process which would necessarily involve double bond migration followed by hydrogenation. This process is normally minimized by the use of a platinum catalyst.[84] However, it is not possoble a priori to dismiss this route initially since only a very small amount is involved. We assume that the degree to which this may occur is likely to be irreproducible, since heterogeneous catalysts are notoriously variable. Thus the isolation of the same amount from two fully independent runs argues against such a source of this material.

More difficult to eliminate is the 1, 5-hydrogen shift route. We have found that hydrogenation of a sample rich in 1-phenyl-6-methyl-



cyclohexene gave a 9:1 mixture of cis:trans product. Thus if a similar result holds for 107, it would require 1.6% of 107 to account for the peak attributed to 105 or in other words the hydrogen shift would have to be at least 1/70 times as fast as the allowed electrocyclization[85] to produce this result.

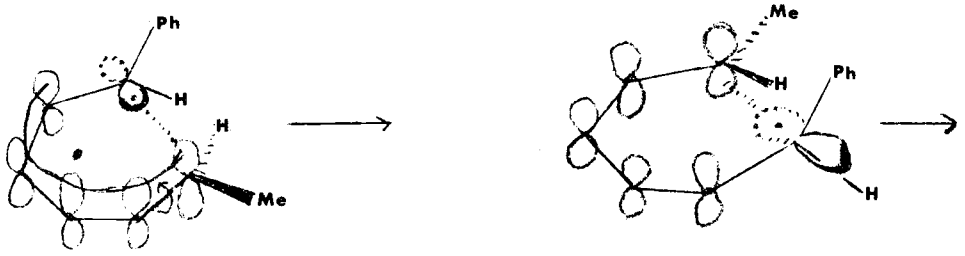
No direct measure of this hydrogen shift rate has been made. However, in the kinetic study of 77 it was observed that an intermediate, presumably 76, was formed and disappeared again. Thus assuming a consecutive set of first order reactions, the ratio k_2/k_1, which would

$$77 \xrightarrow{k_1} 76 \xrightarrow{k_2} 107$$

approximate the rate of formation and disappearance of 76 can be estimated at about one. Since the ratio of rates of electrocyclization of 74 / 77 was 200, we can conclude that the electrocyclization of 74 is 200 times faster than the hydrogen shift. Given that the ratio of cis/trans products in the hydrogenation is reasonable, this suggests that about two-thirds of the 105 was not formed by this route.

A further route to formation of 105 would be via the allowed cyclization of 77, if this were present in the semi-hydrogenation mixture from 103. Since 77 reacts 200 times slower than 74, it would require 15% of 77 to account for the amount of 105 found.[86] The precursor of 74, trans, trans-1-phenyl-1,5-heptadien-3-yne (103) was greater than 99% pure, and inversion of terminal double bonds to such an extent can clearly be dismissed. Furthermore, the presence of such an amount of almost inert material in the reactant would have been obvious from the kinetic studies.

Finally, the 105 could have been derived from 76 via either a forbidden concerted or a symmetry independent diradical path. The symmetry forbidden concerted route must lead exclusively to 76. Conversely the diradical path will give neither pure 76 nor a stereo-random result. The only planar conformation of the diradical intermediate with the terminal atoms in bonding proximity does not allow the orbitals at these carbons to overlap in a bonding fashion. One reasonable solution is for the pentadienyl radical to adopt a helical rather than planar conformation so that a rotation about the C_1 - C_2 bond would permit adequate orbital overlap and initiation of sigma bond formation.



Two diasteriomeric conformations are possible leading to diasteriomeric transition states and different products. Of the two possible helical conformations, the first leading to the cis cyclohexadiene 104 is favored. Thus the symmetry independent pathway leads to the same product as the concerted allowed pathway.

The arguments presented above show very clearly that the amount of 76 obtained form the electrocyclization of 74 does not exceed 0.1% and may indeed be considerably less. At present there is no evidence to suggest whether this tiny amount is derived from the forbidden concerted or the diradical route. Since the phenyl group must enhance the configuration interaction influence[11-15,19,21] and thus the rate of the forbidden concerted cyclization, whereas the phenyl has little effect on the rate of the allowed cyclization,[1] the forbidden concerted route could indeed be a viable pathway. Unfortunately, there is at present no way to obtain experimental evidence for the rate increase in the forbidden concerted reaction, so further consideration of that possibility will not be useful here.

If, on the other hand, 76 was formed by the diradical route, some interesting estimates of the difference in free energy of activation between the allowed and the symmetry independent routes, $\Delta\Delta G^{\ddagger}$, can be made. The direct $\Delta\Delta G^{\ddagger}$ in the present case is equal to or greater than 5.5 kcal/mole depending on the actual amount produced by that route. A phenyl group stabilizes a free radical by 12.5 kcal/mole, and thus if the diradical route gave solely the disallowed stereochemistry, the $\Delta\Delta G^{\ddagger}$ would be at least 18.0 kcal/mole. Should the diradical route lead to 10% of 76 and 90% of the allowed product, the $\Delta\Delta G^{\ddagger}$ would be reduced to

about 16 kcal/mole, and if only 1% of 76 were formed from the diradical during closure, $\Delta\Delta G^{\ddagger}$ would be about 14 kcal/mole.

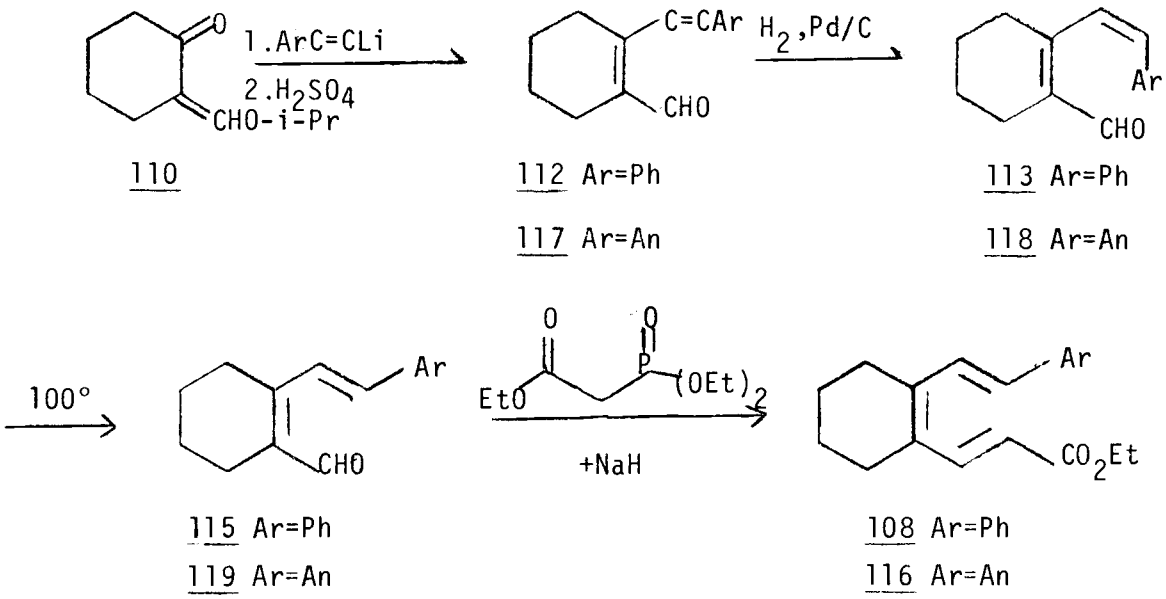
The final conclusions which we can deduce from our data are: 1. if 76 results from a forbidden concerted route, then we can state only that for the unsubstituted six electron electrocyclization of a triene, $\Delta\Delta G^{\ddagger}$ (forbidden-allowed) = 5.5 kcal/mole, and 2. if 76 results from a diradical route, then $\Delta\Delta G^{\ddagger}$ (disallowed - allowed) is probably as large as 14-15 kcal/mole, and the forbidden path would then have a higher $\Delta\Delta G^{\ddagger}$ than the diradical path. It is of some interest to note here that if indeed some of the 76 observed did come from a diradical, then a study of cis, cis, trans-1-phenyl-1,3,5-heptatriene will prove important. In this case the allowed reaction will be at least 200-500 times slower than for 74[1] while the radical route should occur at the same rate as before and in this case it will produce predominantly the cis disallowed product from the diradical intermediate instead of the allowed product!

The Influence of Push-Pull Substitution on Triene Electrocyclization

Introduction

Epiotis, in a series of papers[11-15] suggested that substituents should be expected to play an important role relative to the predictions

derived from the conservation of molecular orbital symmetry theory advanced by Woodward and Hoffman.[4] He essentially proposed that terminal push-pull substitution could be expected to enhance the rate and possibly alter the stereochemical outcome of electrocyclic and other pericyclic reactions. He suggested that extreme substitution could give rise to "forbidden" products through an orbital symmetry allowed pathway. To test the predictions of Epiotis we prepared two aryl-carbethoxy trienes. The procedure developed by Schiess and coworkers[42,43] was followed.



110

112 Ar=Ph

117 Ar=An

113 Ar=Ph

118 Ar=An

115 Ar=Ph

119 Ar=An

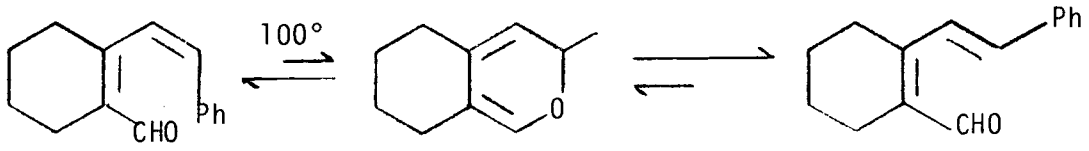
108 Ar=Ph

116 Ar=An

Synthesis of ethyl 3-(trans-2-styrylcyclohexen-1-yl)-trans-propenoate (108)

Following the procedure of Schiess and coworkers[42] the lithium anion of phenylacetylene 109 was mixed with 2-isopropoxymethylenecyclohexanone 110 giving 1-phenylethynyl-2-isopropoxymethylenecyclohexanol 111, which was reacted with sulfuric acid to give 2-phenylethynylcyclohexen-1-carboxaldehyde 112. The spectral properties of 112 matched those obtained

by Schiess.[42] A solution of 112 was semi-hydrogenated over palladium on carbon to give 2-(cis-β-styryl)cyclohexen-1-carboxaldehyde 113 which was converted to the trans isomer 115 via the intermediate pyran 114. The



113 114 115

crystalline aldehyde 115, mp. 78.5-80.5°C was converted to the title compound 108 by the procedure of Wadsworth and Emmons.[44] The anion of triethylphosphonoacetate was added to 115 and the solution was heated. After purification by column chromatography ethyl 3-(trans-2-styrylcyclohexen-1-yl)-trans-propenoate 108 was obtained in 89% yield. The spectral characteristics of 108 were completely in accord with the assigned structure. The nmr spectrum exhibits one AB pattern at δ8.07 and 7.48, J=15 Hz (trans olefin) and a second AB pattern at δ6.61 and 5.81, J=15 Hz (trans olefin) as well as bands for the ethoxy group (q- 2H, at δ4.18 and t, 3H, at 1.16, J=7 Hz), and multiplets from 2.5-1.2 with peak areas corresponding to the correct number of cyclohexenyl protons. The ir spectrum, 1690 (conjugated ester), and 960 cm^{-1} (trans-double bond) and the uv spectrum (uv_{max}= 343 nm, ε = 54,000) are consistent with the assigned structure.

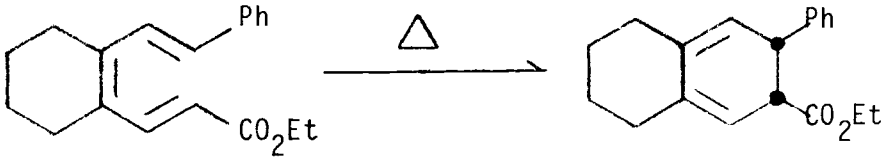
The synthesis of ethyl 3-[trans-2-(4'-methoxystyryl)cyclohexen-1-yl]-trans-propenoate (116)

Beginning with p-methoxyphenylacetylene, 116 was prepared in a manner exactly analagous to the preparation of 108. The spectral properties of

all intermediate structures were consistent with the chemically expected structures. The structure of the title compound can be assigned solely on the basis of its nmr spectrum which shows one AB pattern centered at δ7.36 and 6.81 (J=10 Hz), 4H,(phenyl protons),a second AB pattern at δ8.10 and 5.84 (J=16 Hz), 2H, (trans olefin), and a third AB pattern at δ7.38 and 6.60 (J=16 Hz), 2H, (trans olefin). The ethoxy group (δ4.13, q, 2H, J=7 Hz and 1.33, t, 3H, J=7 Hz) and the methoxy group (s, 3H at δ3.80) add support to the structure assignment. The ir spectrum shows a band at 1705 cm^{-1} (conjugated ester) while the uv spectrum (uv_{max}= 356, ε = 53,000) showed a shift from 108 to longer wavelength due to an effective lengthening of conjugation due to the p-methoxy substitution.

Thermolysis of ethyl 3-(trans-2-styrylcyclohexen-1-yl)-trans-propenoate (108)

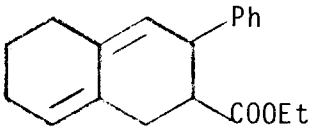
A dilute solution of 108 was placed in a clean pyrex tube, degassed and heated to 115°C for 24 hours. The cyclized product was isolated and analyzed spectrally. The spectral data supports the assigned structure for the thermolysis product 120. A broad multiplet characterizes the two new allylic protons and the two vinyl protons appear as a broad singlet at 5.81. The uv spectrum suggests that the product is indeed a homoannular diene



108 120

(uv_{max}= 260 nm, ε =3000) while the ir spectrum (1740 cm^{-1}, non-conjugated ester) supports this analysis.

Further heating of a solution of 120 led to a compound with a uv maximum at 243 nm and a much larger extinction coefficient. The vinyl protons also separated into two broad multiplets. The new product which was not characterized further is presumed to be 121 or 122. Heteroannular



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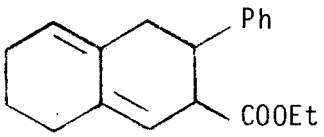
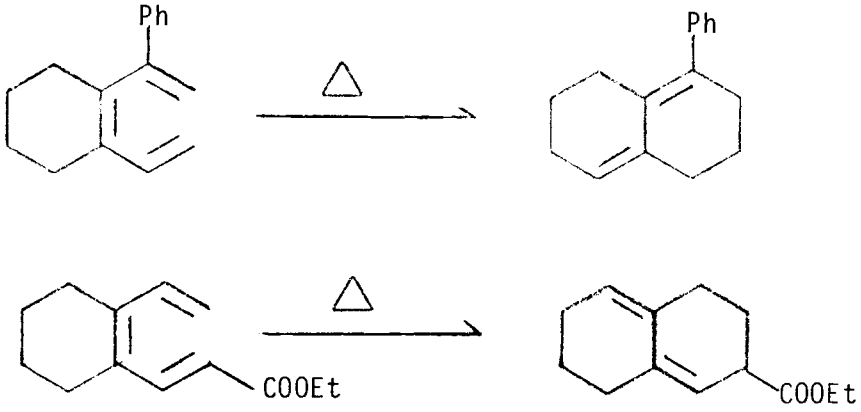
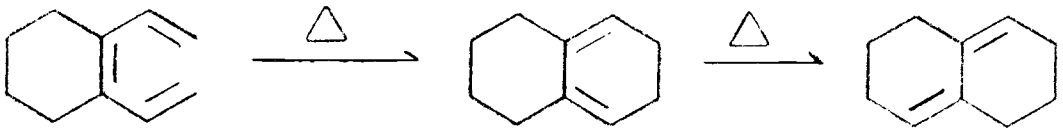


122

dienes of this type have been observed previously by Delphey[4] and Cleary.[3]



Delphey also reported that 127 gave the homoannular diene 128 when heated to 125°C but gave 129 when heated to 150°C for the same time period.



127 128 129

Thus the product expected from the thermolysis of 108 might well have been 121 or 122. These can be eliminated on the following basis: First - the nmr spectra for both 121 and 122 should show the presence of 7 allylic protons instead of 6 and these 7 protons would be in two groups of 6 and 1. Second - the uv spectrum is consistent with that of a homoannular diene (small extinction coefficient and absorption at 260 as predicted). For 129, uv_{max} was reported[4] at 242 nm (ε= 17,000). The dienes 121 and 122 would be expected to give similar spectra. Finally, further heating of the initial thermolysis product gave a new product consistent with 121 or 122 as Delphey noted with 127. Within the limits of detection by nmr, 108 gave only a single product 120, presumed to be the cis isomer.

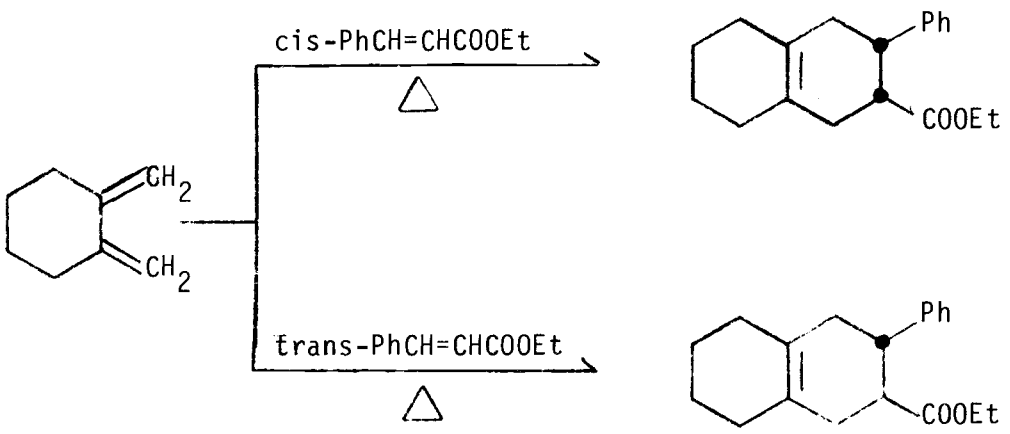
We hoped to determine the stereochemical result of the thermolysis with a high degree of accuracy. We planned two approaches. The 1,4-hydrogenation of 120 to give 130 would allow direct correlation to both

120 130

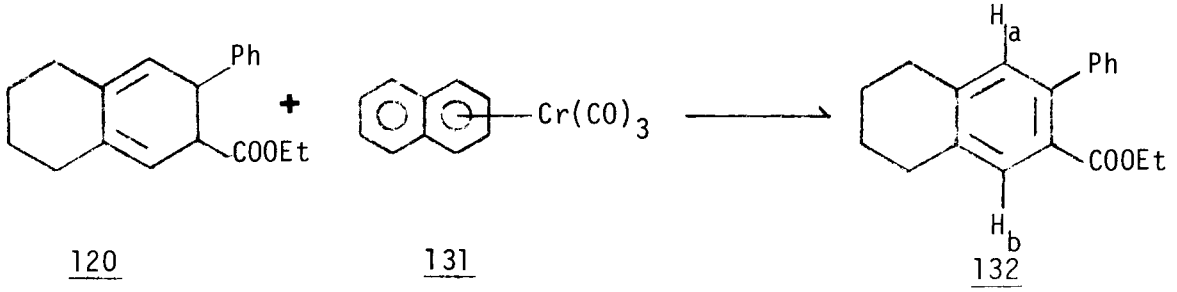
cis and trans 130 which could easily be prepared by an independent synthesis.

Attempts to semi-hydrogenate 120 failed. Platinum oxide and hydrogen gave a complex mixture of products.

Cais[83] had reported that the most active of known homogeneous 1,4-hydrogenation catalysts was napthalene chromiumtricarbonyl 131.



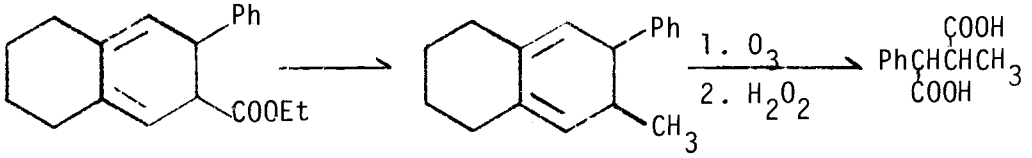
In the presence of 2000 psi hydrogen and 131,[88] 120 dehydrogenated giving 132 which was characterized by its molecular ion (MW = 280) and



120 131 132

its nmr spectrum which shows four benzylic protons, five aromatic protons as a multiplet at δ7.14 and two new aromatic singlets at δ 7.50 (H_b) and 7.0 (H_a).

The second approach we planned involved the conversion of the



120

carbethoxy group into a methyl group followed by ozonolysis to the

known and well characterized succinic acids 133 and 134. This approach also failed. During the conversion of the carbethoxy group to a methyl group the homoannular diene rearranged. Later it was found that elution of 120 through either an acidic or basic column converted 120 into a heteroannular diene (probably 121 or 122).

Thermolysis of ethyl 3-[trans-2-(4'-methoxystyryl)cyclohexen-yl]-trans-propenoate (116)

A solution of 116 in cyclohexane was degassed and heated in a sealed pyrex tube. The contents of the bomb were concentrated giving 6-carbethoxy-7-(4'-methoxyphenyl)-1,2,3,4,6,7-hexahydronapthalene 135, which was identified by its spectral properties. The nmr spectrum shows an AB quartet, 4H, at δ7.02 and 6.66 (phenyl), a broad singlet at δ5.67, 2H, vinyl protons, and a broad singlet at δ3.83, 2H, (new allylic protons). The ir absorption band at 1740 cm^{-1} is characteristic for non-conjugated esters while the uv spectrum (uv_{max} = 276 nm, ε = 2000) supports the assignment of 135 as a homoannular diene. To the limits of nmr detection the thermolysis product appeared to consist of just one compound, presumed to be the cis isomer.

Kinetic results of the thermolysis of aryl-carbethoxytrienes

The rates of electrocylization of 108 and 116 were determined by following the disappearance of the starting material by ultraviolet spectroscopy. Solutions of both trienes (ca. 2 X 10^{-3}M) were placed in clean Pyrex tubes, degassed and heated. A plot of log A/A_0 versus time gave as expected a straight line indicating first order kinetics.

From a plot of ln K versus 1/T the following activation parameters were obtained.[86]

(a) Ethyl 3-(2-trans-styrylcyclohexen-1-yl)-trans-propenoate 108

$\Delta H^{\ddagger}$ = 27.0 ± 0.1 kcal/mole

$\Delta S^{\ddagger}$ = -9.0 ± 0.1 e.u.

(b) Ethyl 3-[2-trans-(4'-methoxystyryl)cyclohexen-1-yl]-trans propenoate 116

$\Delta H^{\ddagger}$ = 27.0 ± 0.1 kcal/mole

$\Delta S^{\ddagger}$ = -9.0 ± 0.1 e.u.

Conclusions

The influence of push-pull substituents in the rate of electrocyclization was found to be negligible with 108 and 116, even though, as indicated by the uv maxima shift from 343 to 356 nm, 116 is certainly reducing the HOMO-LUMO energy difference for the triene system.

Comparison of the rates of 1,2-divinylcyclohexene and of 108 shows that the push-pull effect of the phenyl and carbethoxy groups on rate is quite modest, a factor of four, or a change of $\Delta G^{\ddagger}$ of about one kcal/mole. It might be argued however that the electronic push-pull effect was very much larger than this measured result, and that its effect was greatly reduced by a steric effect acting in opposition. That this is not the case is shown by the equal rates observed for 108 and 116. Were the push-pull effect of considerable magnitude, it should be further increased by the electron-donating methoxyl and no additional steric effect would be present. Thus we are led to the inevitable conclusion that the push-pull influence on rate is relatively ineffective in the

six electron electrocyclization.

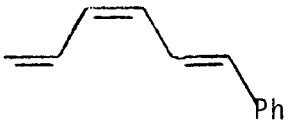
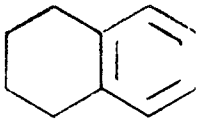
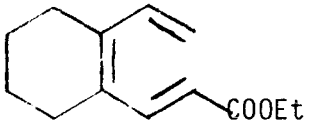
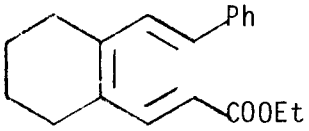
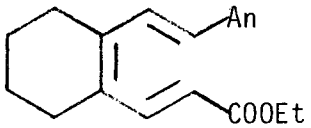
Compound	T(°C)	k (sec^{-1} X 10^5)	Ref.
	125	3.0	9
	125	3.0	10
	126.5	3.7	10
	125	3.7	3
	125	14	this work
	125	14	this work

Table 2. Rates of Electrocyclization of Trienes

The question of the effect of push-pull substitution on the stereochemical outcome of an electrocyclization has not really been answered here. Since we would be unable to detect less than about 5% of trans 120 in cis 120 by nmr, a small but significant incursion of the forbidden concerted reaction would not have been noticed. It is certain that

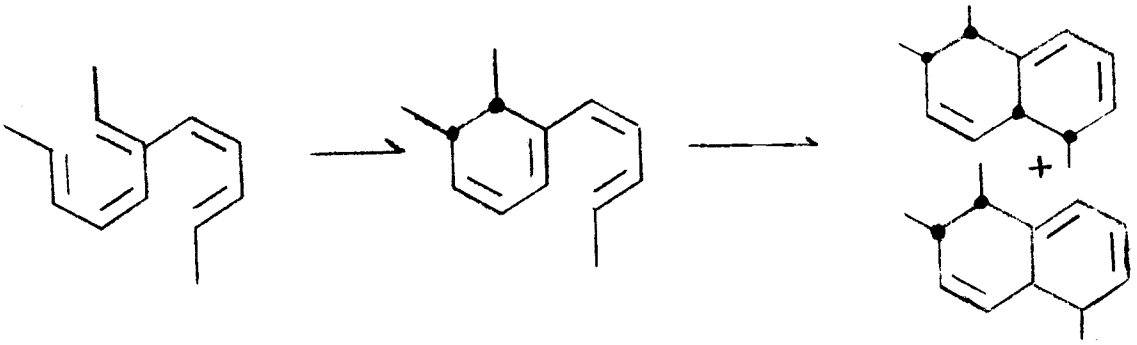
no extreme effect (leading to much more than 5% of trans 120) did occur, but whether a more modest effect was present must remain unanswered for the present.

The Synthesis and Thermolysis of a Cross-conjugated Penatene

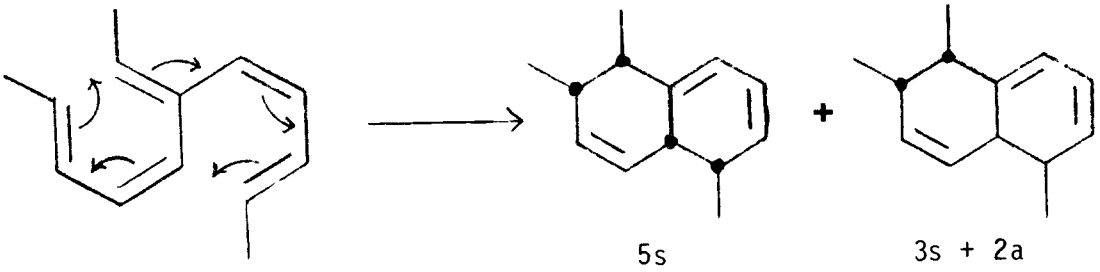
Introduction

The stereochemical predictability of pericyclic reactions has made them of considerable value in synthesis. Properly oriented cross-conjugated systems will permit the formation of more than one ring at a time in what Marvell has termed a polypericyclic reaction,[34] materially increasing the synthetic value of the six electron electrocyclization. We have prepared a cis, cis-cross-conjugated pentaene to investigate both the synthetic potential and interesting theoretical aspects of the double ring closure of such systems.

A cross-conjugated pentaene might be expected to cyclize thermally in two possible ways; by two consecutive 6 electron cyclizations or by a single concerted 10 electron double cyclization. Both 6 electron electrocyclizations must proceed thermally in a disrotatory manner. The 10 electron concerted double cyclization might also proceed with

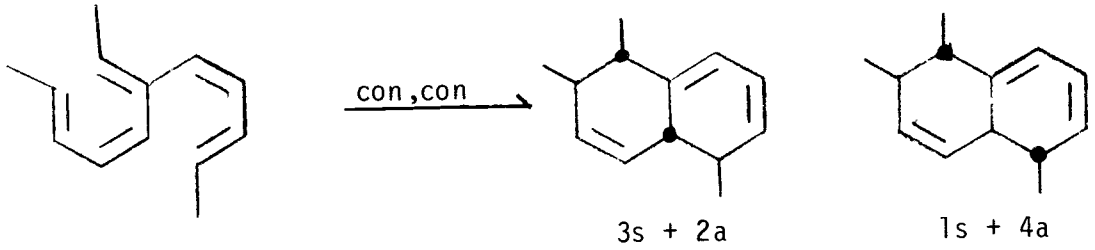


disrotatory cyclizations at both newly formed bonds, in a 5s allowed

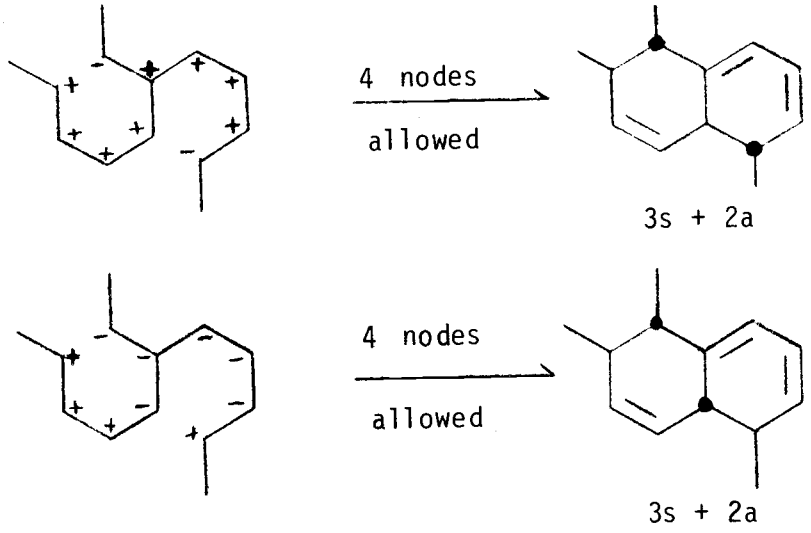


process giving the first product or in a 3s + 2a allowed process giving the second product.

With a 10 electron concerted cyclization, however, there also exist two routes leading to allowed conrotatory-conrotatory ring closure.

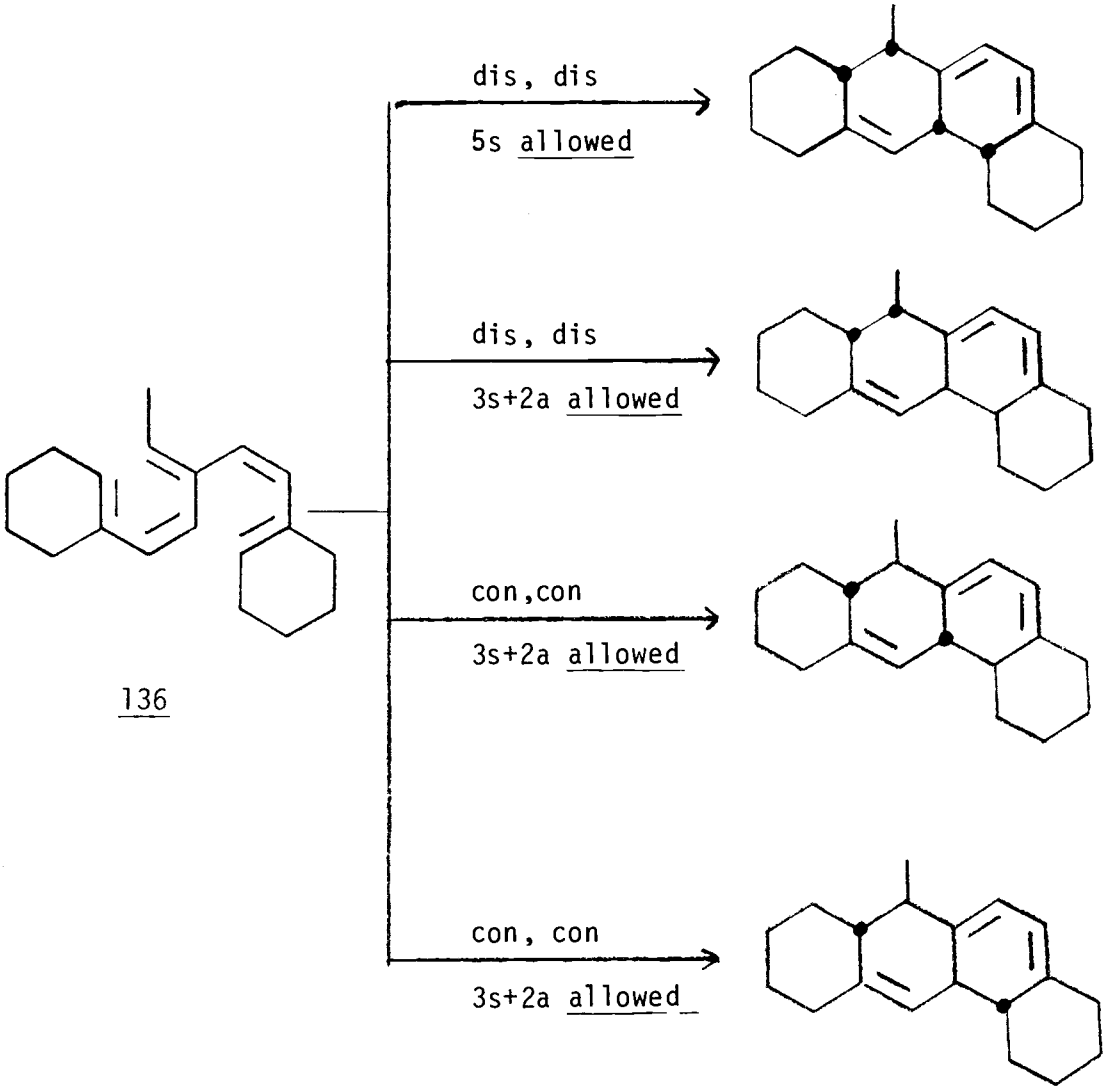


The formation of two products can be explained by observation of the two possible routes to con - con cyclization. Thus, even though one does



not normally consider the conrotatory formation of a six membered ring, the simultaneous formation of two six membered rings can occur in a conrotatory - conrotatory allowed process.

To facilitiate the synthesis of a cis, cis-cross-conjugated pentaene we prepared a more highly substituted compound to lessen the tendency of the pentaene to polymerize. The pentaene prepared, 3-ethylidene-(1,5-dicyclohexen-1-yl)-1,4-pentadiene (136), can also cyclize

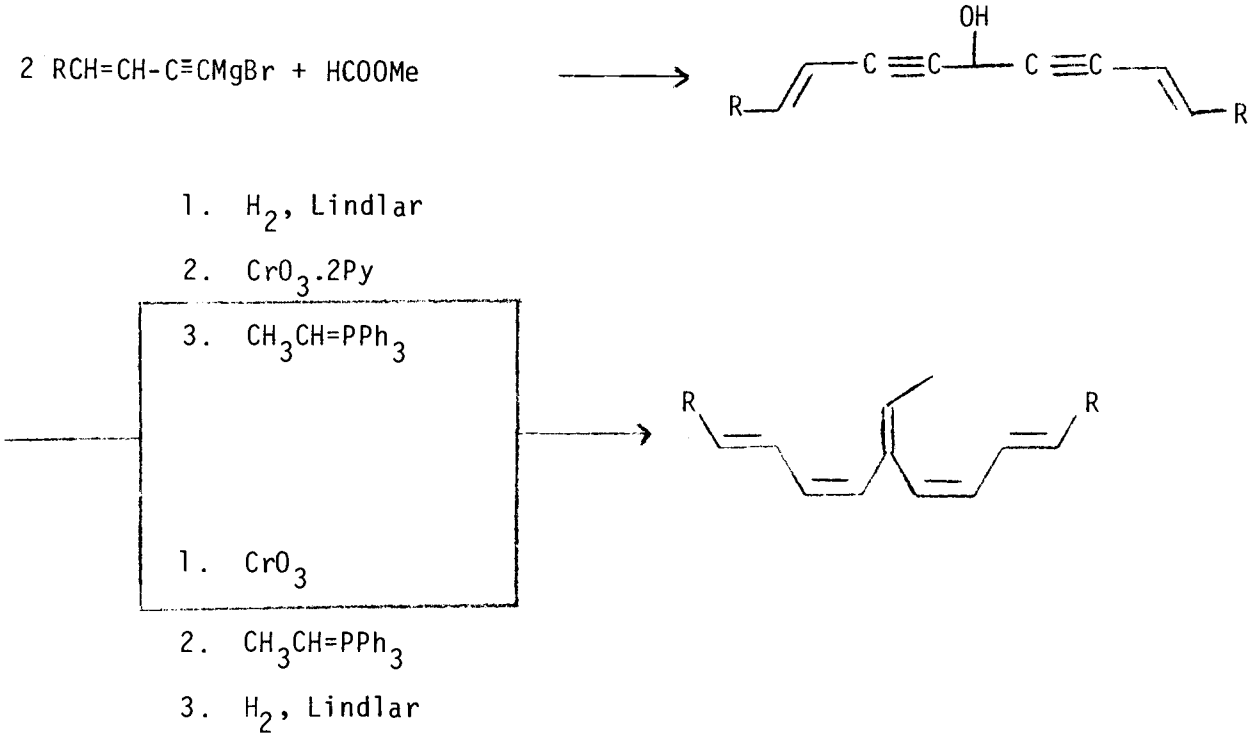


136

to give two products by consecutive six electron electrocyclizations (both dis,dis) or all four products by simultaneous ten electron cyclization.

Approach to 3-ethylidene-(1,5-dicylcohexen-1-yl)-1,4-pentadiene (136)

A procedure suitable to the production of symmetrical cross-conjugated pentaenes was devised.[34]

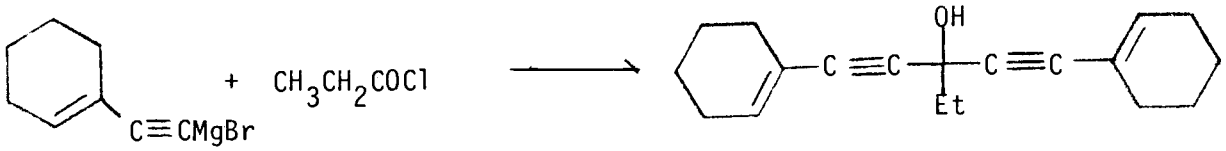


From 1-ethynylcyclohexanol, 1-ethynylcyclohexene (137) was prepared by the method of Jones and coworkers.[89] The Grignard reagent of 137 was allowed to react with methyl formate giving 1,5-(dicyclohexen-1-yl)-1,4-pentadiyn-3-ol 138 in 37% yield. The alcohol was characterized by its nmr spectrum which showed a broad multiplet at δ 6.11 (2H, vinyl protons), a singlet at δ5.18 (1H, CHOH), and multiplets for the cyclohexenyl protons.

The alcohol 137 was converted to 1,5-(dicyclohexen-1-yl)1,4-pentadiyn-3-one 139 with Jones' reagent[90] and used immediately. The ketone 139 was mixed with triphenylethylidenephosphorane, giving

1,5-(dicyclohexen-1-yl)-3-ethylidene-1,4-pentadiyne 140. The cyclohexyl protons were characterized by multiplets, two vinyl protons appear at δ6.05 while the third, the ethylidene vinyl proton appears as a quartet, J=7 Hz at δ6.14, and the methyl protons appear as a doublet, J=7 Hz, supporting the structure assigned.

Compound 140 was also prepared by reaction of 1,5-(dicyclohexen-1-yl)-3-ethyl-1,4-pentadiyn-3-ol 141 (from the Grignard reagent of 137

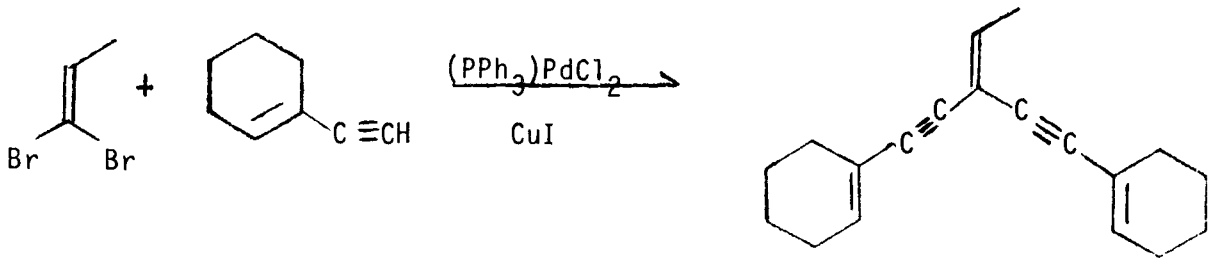


and propanoyl chloride) with phosphorus oxychloride in 54% yield.

The diyne, 140, prepared by either route did not react with hydrogen in the presence of the Lindlar catalyst,[76] possibly because of trace amounts of a poison which deactivated the catalyst.

Synthesis of 3-ethylidene-(1,5-dicyclohexen-1-yl)-1,4-pentadiene (136)

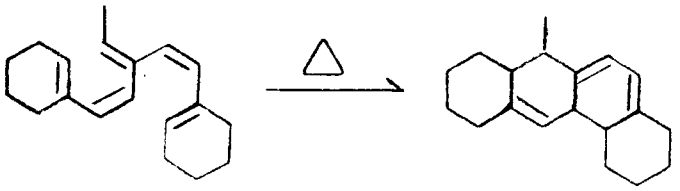
The synthesis of 136 was accomplished by hydrogenation of the diyne 140 which had been prepared by an extension of the procedure developed by Sonagashira and coworkers.[71] The dibromide, 1,1-dibromopropene 142[91] was coupled with two equivalents of 137 with bis(triphenylphosphine)-dichloropalladium (II) and cuprous iodide in diethylamine. The coupling proceeded rapidly to completion. At no time did a noticeable concentration of a monocoupled intermediate build up. After purification 140 was obtained in 52% yield. The nmr spectrum matched those obtained above.



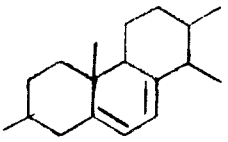
In contrast to earlier preparations, The product obtained form the double coupling reaction readily took up hydrogen over the Lindlar catalyst until 1.2 equivalents had been absorbed. The main product was isolated in 57% yield and characterized by its spectral properties. The nmr spectrum shows bands from seven vinyl protons (δ6.1 - 5.3), a three proton doublet (1.68, J=7 Hz, methyl) and multiplets for the cyclohexenyl protons. The uv spectrum (uv_{max}= 240 nm. ε= 19,500) was uncharacteristic of trienes but can be explained by out-of-plane rotation of the bulky cyclohexenyl groups.

Thermolysis of 3-ethylidene-(1,5-dicyclohexen-1-yl)-1,4-pentadiene (136)

A solution of 136 in cyclohexane was degassed and heated to 125°C for 20 hours. The thermolysis product has spectral characteristics which support its assignment as a tetracyclic ring system, perhaps the expected product 143. The nmr spectrum shows three vinyl protons (δ 5.8-5.4) calibrated against the three proton methyl group doublet (δ 1.09, J=7Hz). The mass spectrum shows a molecular ion at 254. The product, when completely hydrogenated shows a molecular ion at 260. Finally, the uv spectrum (uv_{max}= 283, ε=14,000) is consistent with homoannular dienes of similar structure.



136 143



ergosterol (uv_{max}=282)

Conclusions

It is virtually certain that 136 underwent a double cyclization. The structure of the thermolysis product is, however, tentative. The complexity of the spectra does not allow definitive structural assignment. The exact ring structure is not known but could be determined by dehydrogenation. Stereochemical information will probably have to be obtained by an X-ray crystal study.

The development of the double coupling reaction has allowed entry into the complex cross-conjugated pentaene system in just a single, high yield step. In just three steps we have prepared a tetracyclic ring system in excellent yield starting with simple, relatively cheap starting materials. Since it has been shown that bromo-olefins couple faster than chloro-olefins[71] it is quite possible that monocoupling of a 1,1-dihaloalkene will be feasible. If so, the synthetic value of this procedure will be greatly increased. Because non-symmetrical pentaenes would become readily available it might prove possible to prepare much more valuable ring systems in an equally sucessful procedure; the possibilities are virtually unbounded!

EXPERIMENTAL

Part I. Phenylheptatrienes

Trans-2-penten-4-yn-1-ol (80)

A modification of the procedure of Haynes, Heilbron, Jones and Sondheimer[74] was used to prepare trans-2-penten-4-yn-ol, free from the cis isomer.

Sodium acetylide (2, 5 mole) was prepared by adding sodium (57.5 g) to a solution of acetylene in liquid ammonia.

Dry ether (500 ml) was added to the acetylide solution followed by addition of 92.5 g 1-chloro-2, 3-epoxypropane (1 mole) in 420 ml dry ether over 30 minutes.

After the solution had been stirred for 9 hrs, 135 g of ammonium chloride was added. The ammonia was allowed to evaporate. The resulting suspension was filtered. The solid was dissolved in 500 ml water and the solution was filtered to remove a small amount of tar. The aqueous and organic layers were combined, shaken and separated. The aqueous layer was extracted with ether. The ether solutions were combined, dried ($MgSO_4$), and concentrated by evaporation, leaving 90g of crude alcohol 80 containing 35% ether by glc. Yield of the alcohol was approximately 60-70%.

A small portion of the crude alcohol was distilled, giving a

clear liquid which colored on exposure to air: bp 72-73° (18mm) (lit.[74] 90°C- 50mm), nmr (CCl_4) δ 6.31 (d of t, 1H, J=15, 5 Hz, =CH-CH_2O-H), 5.68 (d of m, 1H, J=15 Hz, 2 Hz, C≡C-CH=C-), 4.51 (s, 1H, -OH), 4.17 (d of d, 2H, J=5 Hz, 2 Hz, -CH_2-), 2.98 (d, 1H, J=2 Hz, HC≡C-).

Trans-1-tetrahydropyranoxy-2-penten-4-yne (81)

The crude alcohol 80 was added to 120 ml of distilled dihydropyran. A few crystals of para-toluenesulfonic acid were added which initiated a vigorously exothermic reaction. After the solution had been stirred for 15 min, 5g of potassium carbonate was added. The mixture was stirred for 30 min and then filtered.

The filtrate was flash distilled (pot 200°C, 30 mm), and the distillate was redistilled, yielding 73g of clear liquid: bp 69-73° (2mm), 85% THP derivative II (37% based on 1-chloro-2, 3-epoxypropane). The liquid was fractionally distilled on a Podbeilniak column before use: nmr (CCl_4), δ 6.23 (d of t, 1H, J=15.5 Hz, 5 Hz, C=CH-C-O), 5.61 (d of m, 1H, J=15.5, 2 Hz, C≡C-CH=C-), 4.59 (s, broad, 1H, O-CH-O-), 4.08 (two overlapping d of d, J=5, 2 Hz, -C=C-CH_2-O), 3.9-3.2 (m, 2H, O-CH_2-CH_2-), 2.79 (d, 1H, J=2, C≡CH), 1.8-1.2 (m, 6H, pyran protons).

Trans-7-tetrahydropyranoxy-1-phenylhept-5-en-3-yn-1-ol (84) and -2-ol (85)

All attempts to prepare 84 or 85 were unsuccessful. The following procedure was typical of those used: The Grignard reagent of 4.50g of 81 (0.027 mol) was prepared by refluxing 81 in a solution of ethylmagnesium bromide (0.033 mol) in tetrahydrofuran under a nitrogen atmosphere. The evolution of one equivalent of ethane was noted. To the solution of Grignard reagent was added a solution of phenylacetaldehyde in ether (0.033 mol) (or styrene oxide in ether (0.033 mol) in another procedure). The solution was stirred for 4 hrs. A saturated solution of aqueous ammonium chloride (100 ml) was added and the layers were separated. The organic layer was combined with ether extracts from the aqueous layer, dried ($MgSO_4$), and concentrated to a thick oil from which no distillable products could be isolated.

Trans, trans, trans-1-phenyl-1, 3, 5-heptatriene (88)

To 200 ml of dry ether were added under nitrogen 16.0g of 2-butenyltriphenylphosphonium chloride (0.045 mol), (from triphenylphosphine and 1-chloro-2-butene in refluxing benzene) and 23 ml of butyllithium solution (2.0M in hexane). The deep red ylid formed immediately. After a few minutes, 8.5g of cinnamaldehyde (0.064 mol) was added, and the solution was stirred for 1 hr. Ice water

(100 ml) was added, the layers were separated, and the aqueous layer was extracted with ether. The ether solutions were combined, washed twice with water, dried ($MgSO_4$) and concentrated by evaporation. Ice-cold pentane (100 ml) was added to the residue, and the precipitated triphenylphosphine oxide was removed by filtration. The filtrate was concentrated and glc analysis of the solution indicated that 40% of the theoretical yield of the triene 88 was obtained.

The only major peak was collected after separation by glc (2% SE-30 on Chromsorb G 45/60, 8 ft by 1/4 in, 135°C, 100 ml/min) giving a white solid with a retention time of 23-26 min, mp 71-72°C, nmr(CCl_4), δ7.4-7.1 (m, 5H, phenyl protons), 7.0-5.4 (m, 6H, vinyl protons), 1.79 (d, 3H, J=6Hz, $C=C-CH_3$).

The triene 89 was also prepared by the method of Jaenicke and Seferiadis[46] in lower yield from 15.7g of 2-butenyltriphenylphosphonium chloride and 7.6g of cinnamaldehyde dissolved in acetonitrile. The acetonitrile solution was added to liquid ammonia at -78°C and stirred at -36°C for 3 hrs. After the ammonia had evaporated, the polymeric residue was extracted with ice-cold pentane. The pentane solution was filtered, concentrated and analyzed, giving a product with physical properties identical to those of 88 above.

1-Phenyl-3 butyn-1-ol (89)

This alcohol was prepared according to the method of Marvell

and Platt,[1] and Jacobs.[75] Sodium acetylide (1.74 mol) was prepared from sodium and acetylene in 1 liter of liquid ammonia. A solution of styrene oxide 82 (1 mol) in 100 ml ether was added over 30 min to the ammonia solution. The solution was stirred for 3 hrs before ammonium chloride (94g) was added. After the ammonia had evaporated, water (500 ml) was added and the solution filtered. The layers were separated and the aqueous layer extracted twice with ether. The ether solutions were combined, dried ($CaSO_4$), and concentrated. The concentrate was distilled, yielding 61.3g of clear liquid: bp 78-81°C (0.5-0.7mm). Styrene oxide (55g) was also recovered. Based on the amount of styrene oxide actually used, the yield was 74.5%. The compound had: nmr(CCl_4), δ 7.26 (s, 5H, phenyl protons), 4.62 (d of d, 1H, J=7, 3 Hz, -C<u>H</u>OH), 3.38 (s, broad, 1H, -OH), 2.05 (d of d, 2H, J=7, 2.5 Hz, C<u>H</u>$_2$C=C), 1.78 (d 1H, J=2.5 Hz, C≡C<u>H</u>). The nmr spectrum matched the spectrum obtained by Platt.[1]

E-1-Phenyl-1-buten-3-yne (90) and z-1-phenyl-1-buten-3-yne (91)

These compounds were prepared according to the method of Platt.[1] To a flask cooled to 0°C were added 92.5g of phosphorous pentachloride (0.445 mol) followed by dropwise addition of 58.10g of 4 (0.498 mol). The temperature was not allowed to exceed 25°C during the addition. The solution was then heated to 90°C for

30 min, cooled, and poured over 500 ml of ice water. The organic product was taken up in ether, and the ether was evaporated, leaving 49.0g of crude 1-phenyl-1-chloro-3-butyne (76%). IR analysis showed no OH. (The crude chloride was not purified further).

Under a nitrogen atmosphere, 445 ml of 1.35N potassium hydroxide in dry isopropanol was added to the crude chloride at 0°C. The mixture was heated to reflux for 4 hrs, then cooled. Ether (75 ml) and pentane (75 ml) were added to the mixture, followed by 1 l of water. The aqueous layer was extracted with pentane. The ether and pentane solutions were combined, washed with saturated aqueous sodium chloride, and dried ($CaSO_4$). The solvent was evaporated and the residue was distilled yielding 26.8g of a mixture of 91 and 92: bp 34-36°C (0.18 mm), E:Z = 78:22, nmr (mixture of E and Z isomers in CCl_4), δ 7.23 (s, 5H, phenyl protons), 6.96 (d, 1H, J=17 Hz, E-PhCH=C-), 6.61 (d, 1H, J=12 Hz, Z-PhCH=C-), 5.98 (d of d, 1H, J=17, 3 Hz, E-C=CH-C=C-), 5.97 (d of d, 1H, J=12, 3 Hz, Z-C=CH-C=C), 3.20 (d, 1H, J=3 Hz, Z-C≡CH), 2.88 (d, 1H, J=3 Hz, E-C≡CH).

7-Phenylhept-6-en-4-yn-2-ol (93)

The procedure developed by Platt and Marvell was followed.[1] In a dry flask which had been flushed with nitrogen, ethylmagnesium bromide was prepared from 7.30g of magnesium turnings (0.30 gram

atoms) and 30.5g of bromoethane (0.28 mol) in 400 ml of dry ether. A solution containing 25.11g of 90 and 91 in 100 ml of ether was added to the Grignard solution. The solution was heated to reflux until ethane evolution ceased (2.5 hrs). The flask was cooled to 2°C, propylene oxide 92 (0.38 mol) was added and the solution was stirred at 5-6°C for 6 hrs. The solution was neutralized with dilute hydrochloric acid. The layers were separated and the aqueous phase was extracted with pentane until the extract was clear. The pentane and ether solutions were combined, washed once with dilute sodium bicarbonate, dried, concentrated by evaporation and distilled, giving 18.55g of 93, a clear liquid (50%): bp 117-118°C (0.13mm), nmr (CCl_4), δ 7.17 (s, 5H, phenyl protons), 6.80 (d, 1H, J=16 Hz, E-PhCH=C-), 6.43 (d, 1H, J=12 Hz, Z-PhCH=C-) 6.00 (t of d, 1H, J=2, 16 Hz, E-PhC=CH), 5.77 (t of d, 1H, J=2, 12 Hz, Z-PhC=CH-), 4.00 (s, 1H, -OH), 3.98 (sextet, 1H, J=6 Hz, $CH_2CH(OH)CH_3$), 2.50 (d of d, 2H, J=2, 6 Hz, C=C-CH_2), 1.27 (d, 3H, J=6 Hz, CH_3-). Glc analysis (2% SE-30 on Chromsorb G 45/60, 1/4 in by 3M, 195°C, 85 ml/min) gave two peaks in a ratio of 78:22 with retention times of 7 and 4 min respectively.

7-phenyl-4, 6-heptadien-2-ol (94)

An atmospheric pressure hydrogenation of 93 (15g) was carried out using 1.5g of Lindlar catalyst[76] and 15 μl of quinoline. After 30%

of the theoretical uptake of hydrogen, the hydrogenation slowed considerably. An additional amount of catalyst (1.0g) was added and the hydrogenation proceeded rapidly to one equivalent uptake. The suspension was filtered under nitrogen and refrigerated. The product was not purified further. A small amount of the solution was concentrated. Glc analysis (20% SE-30 on Chromsorb G 45/60, 1/4 in by 6 ft, 160°, 75 ml/min) showed 2.5% of overhydrogenated products (10 min), 7.5% of starting material (23:20 min), 15% of cis, cis-7-phenyl-4, 6-dien-2-ol (17:20 min) and 74% of 94 (21:40 min). The major product was isolated by preparative glc on the same column: nmr (CCl_4), δ 7.28 (m, 5H, phenyl protons), 7.2-6.1 (m, 3H, PhCH=CH-CH=C-), 5.51 (t of d, 1H, J=8, 11 Hz, cis-CH=CH-CH_2-), 3.83 (sextet, 1H, J=6 Hz, CH_2CO-), 1.09 (d, 3H, J=6 Hz, -CH_3).

7-Phenyl-4, 6-heptadien-2-tosylate (95)

Crude 94 (21.8g - 11.6 mmol) was dissolved in 5 ml of pyridine and added to 2.43g of p-toluenesulfonyl chloride in nitrogen. Water (10 ml) was then added and the layers were separated. The aqueous layer was extracted with ether. The ether solutions and the organic layers were combined, washed with water, dilute phosphoric acid, dilute sodium bicarbonate, and again with water and dried (Na_2CO_3). The solution was concentrated by evaporation to 3.54g (93.6%) of 95. The tosylate was not purified further, and

spectrally it showed: ir (neat) no alcohol, 1380, 1190, 1180 - normal tosylate bands; nmr (CCl_4) δ 7.71 (d, 2H, J=8 Hz, ortho protons on tosylate ring), 7.24-7.1 (m, 7H, remaining phenyl protons), 6.9-6.0 (m, 3H, PhCH=CH-CH=C-), 5.31 (d of t, 1H J=11, 8 Hz, C=CH-CH_2), 4.62 (sextet, 1H J=6 Hz, $CH_2CH(OTs)CH_3$), 2.50 (d of d, 2H, J=5, 6 Hz, -CH_2CO-) 2.34 (s, 3H, Para-CH_3), 1.25 (d, 3H J=6 Hz, -CH_3).

Elimination of 7-phenyl-cis-4, 6-heptadien-2-tosylate (95)

All attempts to cause the elimination of 95 led to a mixture of products from which we were unable to isolate any of the desired triene 74. A typical procedure is presented below.

Under nitrogen, potassium t-butoxide (8.33 mmol) was dissolved in 10 ml of dimethylsulfoxide (distilled from CaH_2). A solution of 2.86g of 95 (8.77 mmol) in 10 ml of dimethylsulfoxide was added at room temperature. The solution was stirred 2 min and poured into 100 ml of water. The products were taken up in pentane which was then washed with water and concentrated. The concentrate was cooled to -78°C giving 0.30g of white crystals (20%): mp 62-66°C, nmr(CCl_4) δ 7.24 (m, 5H, phenyl), 6.9-5.4 (m, 6H, vinyl protons) 1.78 (d, 3H, J=6 Hz, CH_3C=).

The crystals were dissolved in cyclohexane and placed in a tube and degassed. The tube was sealed and heated to 150°C for

24 hrs. Analysis of the tube contents indicated that the starting material was unchanged.

In other similar procedures the major product of the elimination was collected by preparative glc, sealed in a tube and heated as above, again undergoing no change.

Trans-1-phenyl-5-hepten-3-yn-1-ol (97)

A solution of 7.50g of trans-3-penten-1-yne 96 (0.113 mol) in 100 ml of ether was added to a solution of ethylmagnesium bromide (0.125 mol) in ether and stirred for 9 hrs at room temperature. Styrene oxide 82 (0.137 mol) was added and the suspension heated to reflux for 22 hrs. Water and hydrochloric acid (0.12 mol) were added, the layers were separated and the ether layer was washed with dilute sodium bicarbonate solution and dried ($MgSO_4$). Additional product was extracted from the aqueous layer with ether which was then washed and dried as above and combined with the ether layer. The combined ether solutions were concentrated and the concentrate distilled twice yielding 43.6g of yellowish oil (21%); bp 110-113°C (0.005mm), nmr(CCl_4), δ 7.30 (m, 5H, phenyl protons), 6.12 (d of q, 1H, J=16, 6 Hz, $CH_3\underline{CH}$=CH), 5.52 (m of d, 1H, J=2, 16 Hz, C≡C-$\underline{CH}$=CH), 3.7 (m, 3H, $\underline{CH}(OH)\underline{CH_2}$), 2.08 (s, 1H, $\underline{OH}$), 1.82 (d of d, 3H, J=6, 2, Hz, CH_3CH=C).

1-phenyl-cis, trans-3, 5-heptadien-1-ol (98)

A sample of 96 (4.36g) was semi-hydroganated over the Lindlar catalyst[76] giving a mixture of overhydrogenated and underhydrogenated products from which 0.74g of 98 was obtained after several distillations (17%). The dienol was used immediately without further purification. Glc analysis showed only a single product.

1-phenyl-cis, trans-3, 5-heptadien-1-tosylate (99)

In 5 ml of pyridine 98 (0.74g) was dissolved. After the solution had been cooled to 0°C, 0.82g of p-toluenesulfonyl chloride (4.33 mmol) was added to the solution which was then stirred at 10-15°C for 35 hrs. Water (10 ml) was added and the product was taken up in ether. The ether was washed with water, dilute acid, dilute sodium bicarbonate solution, water again; dried ($MgSO_4$) and concentrated to 1.20g (93%): ir ($\tilde{\gamma}$), 1180, 1190, 1380. The crude tosylate was used immediately without further characterization.

Elimination of 1-phenyl-cis, trans-3, 5-heptadien-1-tosylate (99)

A solution of 99 (1.20g) in 15 ml of dry dimethylsulfoxide was added to a solution of potassium t-butoxide (0.45g) in dimethylsulfoxide at 0°C and stirred for 5 min. The combined solution was poured

into 100 ml of water. The products were taken up in ether which was then washed with water, dried ($MgSO_4$) and concentrated. major triene product (23%) was isolated by preparative glc (20% SE-30 on Chromsorb G 45/60, 150°C, 80 ml/min, 7:00 min) and had: uv_{max} = 318. The major triene product did not undergo ring closure when heated to 150°C for 10 hrs. Other products at 2:00 min (53%) and 2.30 min (22%) may have been cyclohexadienes but were not isolated.

Trans-β-bromostyrene (102)

The vinyl halide 102 was prepared by the procedure of Blitz,[79] giving a mixture of cis and trans isomers. The mixture was purified by the method of Dolly, Wilkins and Frey.[80] The cis product was converted to phenylacetylene by heating the mixture of isomers with 0.4M sodium isopropoxide (in isopropanol) for 2 hrs. The isolated olefin 102 was obtained completely free of the cis isomer with an overall yield of 35%, nmr (CCl_4) δ 7.26 (s, 5H, phenyl protons), 7.10 (d, partially obscured, 1H, J=15 Hz, trans PhCH=CHBr), 6.64 (d, 1H, J=15 Hz, trans PhCH=CHBr).

Trans, cis-1-phenyl-1, 5-heptadien-3-yne (101)

Phenylacetylene 102 was prepared in moderate yield (62%)

from 1, 2-dibromophenylethane by the action of strong base.

A modification of the procedure of Sonagashira et al.,[71] was used to prepare the alkyne 101. An ether solution (2.5g) containing 1.2g of cis-3-penten-1-yne (18.2 mmol) was mixed with 2.75g of 102 (15 mmol), diethyl amine (30 ml), 0.040g of bis(triphenylphosphine)-dichloropalladium (II) (0.057 mmol) and 0.0217g of cuprous iodide (0.114 mmol). The solution was stirred under nitrogen for 10 hrs. Water (20 ml) was added and the solution was extracted with petroleum ether. The extract was washed with dilute acid, saturated aqueous sodium bicarbonate, water, dried ($MgSO_4$) and concentrated. The concentrate was eluted from a short alumina column with petroleum ether. The eluent was concentrated to 2.25g of 101 (89%), nmr (CCl_4) δ 7.3 (m, 5H, phenyl protons), 6.90 (d, 1H J=16 Hz, Ph<u>CH</u>=CH-), 6.18 (d of d, 1H, J=16, 2 Hz, PhCH=<u>CH</u>-C≡C-), 6.00 (d of q, 1H J=10, 6 Hz, CH=<u>CH</u>-CH_3), 5.64 (m of d, 1H J=10, 1 Hz, -C=C-<u>CH</u>=CHCH_3), 1.96 (d of d, 3H, J=6, 1 Hz, <u>CH_3</u>CH=CH-); ir (neat) $\tilde{\nu}$ 2355 (C≡C), 945 (trans double bond), 680 (cis double bond), 740 and 705 (monosubstituted phenyl); uv_{max}(cyclohexane), 311 (30,000) 229 (12, 000), 223 (13, 000). Calculated for $C_{13}H_{12}$: C(92.81) H (7.19). Found: C(92.71) H(7.19).

<u>Trans, cis, cis-1-phenyl-1, 3, 5-heptatriene (77)</u>

A suspension of 0.4g of Lindlar catalyst,[76] 4 µl of quinoline and

15 ml of cyclohexane was stirred briefly under hydrogen and 2.11g of 101 in 10 ml of cyclohexane was added. Hydrogen uptake was monitored until 1.15 equivalents of hydrogen had been absorbed. Glc analysis (9% SE-30 on Chromsorb W 45/60, 1/4 in by 8 ft, 165°, 80 ml/min) of the product mixture showed the presence of one major product with a retention time of 10 min (85%) and four minor products with retention times ranging from 2-6 min (15%). The major product had: nmr(CCl_4) δ 7.4-7.0 (m, 5H, phenyl protons) 7.0-5.3 (m, 6H, vinyl protons) 1.90 (d of d, 3H, J=7, 1 Hz, $CH_3CH=CH$); ir(CCl_4), $\tilde{\nu}(cm^{-1})$ = 2940, 1420, 1240; uv_{max}(cyclohexane) = 318(43, 500).

Trans, trans-1-phenyl-1, 5-heptadien-3-yne (103)

The procedure of Sonagashira et al.,[71] was employed to synthesize 103. To a solution of 2.88g of 102 (15.7 mmol), 1.32g of trans-3-penten-1-yne (20.0 mmol) and 50 ml of diethylamine, were added 0.50g of bis(triphenylphosphine)dichloropalladium(II) (0.073 mmol) and 0.028g of cuprous iodide (0.153 mmol). The solution was stirred under a nitrogen atmosphere for 5.7 hrs.

Water (20 ml) was added to the solution which was extracted with petroleum ether. The extracts were washed with dilute acid, water and saturated aqueous sodium bicarbonate, dried ($MgSO_4$) and

concentrated to an oil. The oil was eluted from a short column of alumina with petroleum ether. The eluate was concentrated to 2.20g of light yellow oil (83%). The concentrate 103 was dissolved in cyclohexane, and this solution was degassed thoroughly and stored at -20°C. An analytical sample was prepared by distilling a small amount of 103 twice, nmr (CCl_4), δ7.2-7.4 (m, 5H, phenyl protons), 6.96 (d, 1H, J=16 Hz, PhCH=C-), 6.21 (d of d, 1H, J=16, 2 Hz, PhCH=CH-), 6.12 (q of d, partially obscured, 1H, J=16, 7 Hz, CH=CH-CH_3), 5.61 (m of d, 1H, J=16, 2 Hz, CH=CHCH$_3$), 1.85 (d of d, 3H, J=7, 2 Hz, CH_3CH=CH); uv_{max}(cyclohexane), 311 (37, 000), 338, 305 (inflections), 231 (13, 000), 224 (14, 000); ir (CCl_4), ν 2275 (C≡C), 945 (trans double bond). Calculated for $C_{13}H_{12}$: C(92.81) H(7.19). Found: C(92.66) H(7.12).

Trans, cis, trans-1-phenyl-1, 3, 5-heptatriene (74)

A suspension of 0.4g of Lindlar catalyst,[76] 5 µl of quinoline and 10 ml of cyclohexane was prehydrogenated, and 1.10g of 14 (6.55 mmol) in 20 ml of cyclohexane was added to the suspension. Hydrogen uptake at atmospheric pressure was monitored until 1.1 equivalents of hydrogen had been absorbed. The suspension was filtered and the filtrate thoroughly degassed by the freeze-thaw method. Glc analysis (9% SE-30 on Chromsorb W 45/60, 1/4 in by 8 ft, 165°,

85 ml/min) of the filtrate showed the presence of 15 (81%) with a retention time of 10 min, and cyclized or overhydrogenated products (19%) with retention times ranging from 2-6 min. A pure sample of 74 was obtained by preparative glc, nmr(CCl_4)δ7.5-7.05 (m, 5H, phenyl protons) 7.05-5.5 (m, 6H, vinyl protons) 1.88 (d of d, 3H J=7, 1 Hz, $\underline{CH_3}CH=C$); ir (CCl_4): $\tilde{\nu}$-(cm^{-1}) = 1460, 1430, 960 (trans double bond); uv_{max}(cyclohexane) = 317 (40, 500), 304 (35, 600), 327 (28, 800).

5-Phenyl-6-methyl-1, 3-cyclohexadiene (75) and (76)

A solution of 74, 4% in cyclohexane was placed in a pyrex tube which had been washed with conc. ammonium hydroxide and boiling distilled water. The solution was degassed by the freeze-thaw mehtod and the tube sealed. The sealed tube was placed in an oil bath and heated to 135°C for 3 hrs. The contents of the tube were immediately reduced with hydrogen and platinum oxide.

Cis-5-phenyl-6-methylcyclohexane (104), trans-5-phenyl-6-methylcyclohexane (105) and 1-phenylheptane (106)

The solution of the dienes 75 and 76 was hydrogenated at atmospheric pressure over platinum oxide. Glc analysis (15% Carbowax 20M on Firebrick, 1/8 in by 14 ft, 165°C, 29 ml/min) showed the presence of 1-phenylheptane 106 at 10:00 min (20%), 104 at 15:30 min

and 105 at 11:40 min. The ratio of 104 to 105 was found to be 550:1. Identification of 105 was based on the glc retention time, established by an independent synthesis of both 105 and 104. The major product 104 was isolated by glc, nmr (CCl_4) δ7.3-7.0 (m, 5H, phenyl protons), 2.79 (d of t, 1H, J=11, 4 Hz, PhCH(CH)CH_2-), 2.2-1.2 (m, 9H), 0.66 (d, 3H, J=7 Hz, CH_3CH-). Identification of 106 was made by comparison of its nmr spectrum with its known spectrum.

2-Methylcyclohexanone (144)

The title compound 144 was prepared in 58% yield from 2-methylcyclohexanol using Jones reagent[90] by the method of Warhoff, Martin and Johnson.[92]

1-Phenyl-2-methylcyclohexanol (145)

The alcohol 145 was prepared according to the method of Pines, Sih and Lewicki.[82] Phenylmagnesium bromide (0.10 mol) was prepared from 15.7g of bromobenzene (0.10 mol) and 2.88g of magnesium turnings (0.12 gram atoms) in 100 ml of dry ether. A solution of 0.058 mol of 144 in ether was added to the Grignard reagent over 10 min. The solution was refluxed gently overnight, then neutralized with dilute hydrochloric acid. The layers were separated. The aqueous layer was extracted with ether. The

extracts were combined with the original ether layer and were washed with water, saturated aqueous sodium bicarbonate and saturated salt water. The solution was concentrated to 10.6g of a yellowish liquid (85%). The crude product 19 was not purified further, nmr (CCl_4), δ 7.5-7.0 (m, 5H, phenyl protons) 2.3-2.0 (s, broad, 1H, OH), 2.0-1.0 (m, 9H, ring protons), 0.55 (d, 3H, J=6 Hz, CH_3-).

1-Phenyl-2-methylcyclohexene (146) and 2-phenyl-3-methylcyclohexene (147)

The mixture of alkenes was prepared by the procedure of Pines, Sih and Lewicki.[82] The crude alcohol 145 was mixed with 0.5g of potassium bisulfate and water (25 ml). The mixture was refluxed for 12 hrs. A few crystals of para-toluenesulfonic acid were then added and the solution refluxed one more hour. Saturated aqueous sodium bicarbonate (100 ml) was added and the products were taken up with ether. The ether extract was washed, dried ($CaCl_2$) and concentrated. The concentrate was distilled, giving a mixture of 146 and 147. The yellowish oil (6.5g, 76%) was analyzed by glc (15% Carbowax 20M on Chromsorb G 45/60, 1/4 in by 6 ft, 150°C, 75 ml/min) and found to contain 85% 147 (5:30 min) and 15% 146 (3:30 min). The mixture had: nmr(CCl_4), δ 7.3 (s, 5H, phenyl protons) 5.76 (t, 1H, J=4 Hz, CH_2CH=C-), 2.9-1.2 (m, 7H, ring protons), 0.87 (d, 3H J=7 Hz, CH_3CH-).

Cis-1-phenyl-2-methylcyclohexane (104) and trans-1-phenyl-2-methylcyclohexane (105)

Method A:

A 987 mg sample of the alkenes 146 and 147 was stirred over 200 mg of W-4 Raney nickle catalyst under one atmosphere of hydrogen in ethanol for two hours. A 30 mg quantity of platinum oxide was then added. The hydrogenation continued for 4-5 hrs. until 1.08 equivalents of hydrogen had been added. Glc analysis (15% Carbowax 20M on Chromsorb G 45/60, 1/4 in by 6 ft, 150°C, 75 ml/min) of the mixture showed the final composition to be 104 (80%) at 4:30 min, 105 (9%) at 2:30 min, and 146 (11%) at 3:30 min.

Method B:

A 565 mg quantity of 146 and 147 was reduced by ytterbium in liquid ammonia over 30 minutes without the presence of a proton source.[93] Water was added, the ammonia evaporated and the water extracted with ether. The extract was dried ($MgSO_4$) and concentrated to 490 mg of oil. The composition of the oil was found to be 104 (91%), 105 (3%), and 146 (6%) giving an overall yield of reduced alkenes of 81%. The major product was purified by preparative glc, nmr(CCl_4) δ 7.3-7.0 (m, 5H phenyl protons), 2.79 (d of t, 1H J=11, 4 Hz, Ph$\underline{CH}$(CH)CH_2-), 2.2-1.2 (m, 9H), 0.66 (5, 3H J=7 Hz, CH_3CH-).

Method C:

In a similar fashion 145 and 146 were reduced in the presence of t-butanol by ytterbium in liquid ammonia.[93] Product composition was 104 (63%), 105 (31%), and 146 (6%).

Part II. Aryl-carbethoxytrienes

2-Hydroxymethylenecyclohexanone (148)

This compound was prepared by the method of Cleary.[3] To a solution of cyclohexanone (1.0 mol), methyl formate (1.5 mol) and dry ether (1 l), sodium shot (1.0 gram atom) was added. The reaction was initiated by the addition of 10 ml of methanol. Hydrogen evolution began immediately while the solution thickened and turned brown. After the solution had been stirred one hour, dry ether (500 ml) was added.

The solution was stirred an additional hour and then poured onto 300g of ice. The layers were separated, and the ether portion was washed with water. The water washes were extracted with ether.

The aqueous layer was acidified with cold hydrochloric acid and then extracted with ether. The ether extracts were combined with the ether portions above and washed with saturated aqueous ammonium chloride, dried (anh. Na_2SO_4) and concentrated to give

126g of crude alcohol 148 (100%).

2-Isopropoxymethylenecyclohexanone (110)

The procedure of Cleary[3] was followed to prepare this compound. The crude alcohol 148 (1.0 mol), isopropyl bromide (1.2 mol) and anhydrous potassium carbonate (0.58 equivalents) were dissolved in dimethylsulfoxide (400 ml) and stirred at room temperature overnight. The mixture was heated to reflux for 10 hrs until carbon dioxide and hydrogen evolution had ceased.

The layers were separated. The lower layer was extracted with ether, which was combined with the upper layer and washed with water, dried ($MgSO_4$), and concentrated to an oil.

The oil was distilled yielding 98.9g of a mixture of O-alkylated products, 80-84° (0.2mm) (57%). Analysis by gas chromatography (5% FFAP on Chromsorb W 80/100, 1/8 in by 6 ft, 150°C, 40 ml/min) showed by comparison with authentic samples[87] the presence of 2-isopropoxy-3, 4, 5, 6-tetrahydrobenzaldehyde 149 (19%), 110 (78%), and 148 (2%).

The products were separated by spinning band distillation, giving 58g of 110 of 95% purity.

2-Phenylethynylcyclohexen-1-carboxaldehyde (112)

The procedure developed by Schiess, Seeger and Suter was followed.[42] A solution of 83 ml of 1.8M methyllithium (0.15 mol) in 85 ml of dry ether was cooled to 0°C and 15.0g of 109 (0.147 mol) was added. The solution was stirred 6 hrs at room temperature and then cooled to -50°C. A solution of 25.0g of 110 (0.145 mol) in 40 ml of ether was then added over 10 min. After the addition had been completed the solution was allowed to warm to 0°C over 25 min. Ice-cold, 10% acetic acid (150 ml) was added. The layers were separated. The aqueous layer was extracted with ether and the ethereal solutions were combined, concentrated and dissolved in 250 ml of isopropanol. Sulfuric acid (100 ml of 1N) was added and the solution stirred for 3 hrs. The organic materials were taken up in ether, which was washed with water and saturated aqueous sodium bicarbonate, and finally concentrated. The concentrate was distilled (Kugel ruhr) giving 15.0g of a dark red oil, bp. 100-110°C (0.001mm (0.001mm). The red oil was redistilled giving 13.82g of orange oil (45%), bp 100-110°C (0.001mm); nmr (CCl_4), δ10.25 (s, 1H, CHO), 7.5-7.0 (m, 5H, phenyl protons), 2.6-2.0 (m, 4H), 1.9-1.3 (m, 4H).

2-(Cis-β-styryl)cyclohexen-1-carboxaldehyde (113)

The method of Schiess, Seeger and Suter was used.[42] One

gram of 10% palladium on carbon was suspended in 20 ml of methylcyclohexane and hydrogenated at atmospheric pressure. A solution of 6.0g of 112 (28.6 mmol) in 10 ml of methylcyclohexane was added and hydrogenated until 1.05 equivalents of hydrogen had been taken up. The nmr spectrum of a small amount of concentrated product indicated that about 20% of the alkyne 112 had not reacted.

2-(Trans-β-styryl)cyclohexen-1-carboxaldehyde (115)

The procedure developed by Schiess and Chia[43] and Schiess, Seeger, and Suter[42] was used. The solution of 113 above (containing 20% 112) was refluxed for 7.5 hrs. A small amount of ether was then added and the solution cooled to -78°C. The aldehyde 115 crystallized. The crystals were recrystallized from hot cyclohexane to give 2.05g of light yellow crystals, mp. 78.5-80.5° (lit.[42] 76-80°), (33% from 26). An additional 0.47g of product was recovered from the mother liquor by column chromatography on silica gel (42%). The compound had: nmr(CCl_4) δ 10.30 (s, 1H, CHO), 7.65 (d, 1H, J=17 Hz, PhCH=CH), 7.1 (m, 5H, phenyl protons), 6.70 (d, 1H, J=17 Hz, PhCH=CH), 2.6-2.1 (m, 4H, allylic CH_2), 1.8-1.5 (m, 4H, cyclohexyl protons).

Ethyl 3-(trans-2-stytylcyclohexen-1-yl)-trans-propenoate (108)

The title compound was prepared using the procedure of

Wadsworth and Emmons.[44] A 57% dispersion of sodium hydride in mineral oil (0.365g) was washed with dry benzene several times to give 0.208g of sodium hydride (8.67 mmol). The sodium hydride was suspended in 8 ml of benzene and 2.17g of triethylphosphonoacetate (9.59 mmol) was added to it. The resulting slurry was cooled with a cold water bath and 0.95g of 28 (4.48 mmol) in 3 ml of benzene added to the slurry. The resulting solution was heated to 70°C for ten minutes, cooled to room temperature and chromatographed on a short column of silica gel using ether as the eluant. The eluate was concentrated and the concentrate was rechromatographed using ether/pentane (10/90). Concentration of the ether/pentane solution gave 1.36g of yellow oil. The oil was dissolved in 10 ml of cyclohexane and refrigerated overnight. The desired product crystallized, giving 1.16g of white crystals (89%), mp. 46-48°C: nmr(CCl_4), δ 8.07 (d, 1H, J=15 Hz), 7.48 (d, partially obscured, 1H, J=15), 7.5-7.1 (m, 5, phenyl protons), 6.61 (d, 1, J=15) 5.81 (d, J=15 Hz), 4.18 (q, 2H, J=7 Hz, $-O\underline{CH_2}CH_3$), 2.6-2.1 (m, 4H), 1.9-1.5 (m, 4H), 1.16 (t, 3H, J=7 Hz, $-OCH_2\underline{CH_3}$); uv_{max} (cyclohexane), 343 (54, 000) 258 (32, 000); ir(CCl_4): $\tilde{\nu}$ = 1690(COOEt), 960 (trans double bond).

6-Carbethoxy-7-phenyl-1, 2, 3, 4, 6, 7-hexahydronapthalene (120)

A 5% solution of the triene 108 in methylcyclohexane was placed

in a pyrex tube that had been cleansed with concentrated ammonium hydroxide and boiling distilled water. The solution was degassed by the freeze-thaw method under nitrogen and the tube was sealed under high vacuum. The sealed tube was heated to 115°C for 24 hrs. The cyclized product 120 was isolated and was analyzed by nmr and uv spectroscopy, nmr (CCl_4), δ 7.10 (s, 5H, phenyl protons), 5.61 (m, broad, 2H, vinyl CH), 3.86 (q, 2H, J=7 Hz, $-O\underline{CH_2}CH_3$), 3.70 (m, broad, 2H, Allylic CH), 2.5-2.1 (m, 4H, allylic $\underline{CH_2}$), 1.9-1.4 (m, 4H, Sat'd CH_2), 0.98 (t, 3H, J=7 Hz, $-OCH_2\underline{CH_3}$); uv_{max}(cyclohexane), 260 (3400), shldr -273 (3000).

6-Carbethoxy-7-phenyl-1, 2, 3, 4-tetrahydronapthalene (132)

A solution of 120 (0.67 mmol) in 2 1/2 ml of acetone was mixed with napthalenechromium tricarbonyl (0.028 mmol) and placed in a Parr hydrogenation apparatus. The apparatus was pressurized with hydrogen (2000 psi) and the solution shaken for 24 hrs. The solution was chromatographed with silica gel and the eluate was concentrated to an oil, nmr (CCl_4)δ7.50 (s, 1H, aromatic) 7.14 (m, 5H, phenyl protons), 7.0 (s, 1H, aromatic), 4.00 (q, 2H, J=7 Hz, $\underline{CH_2}CH_3$), 3.00-2.75 (m, 4H, benzylic protons), 2.0-1.8 (m, 4H, cyclohexyl protons), 0.95 (t, 3H, J=7 Hz, $-CH_2\underline{CH_3}$): mass spectrum (molecular ion = 280).

2-(p-Anisylethynyl)cyclohexen-1-carboxaldehyde (117)

The aldehyde 117 was prepared according to the method of Schiess, Suter and Seeger.[42] A solution of 14.0g of p-methoxyphenylacetylene (0.106 mol) in 25 ml of ether was added to 60 ml of 1.8M methyllithium in ether at 0°C. The solution was stirred two hours at 0°C, cooled to -40°C, and mixed with 17.8g of 110 (0.100 mol) dissolved in ether. The resulting solution was then stirred 15 minutes at -50°C before being allowed to warm to 0° over 15 minutes. Ice-cold 5% acetic acid (210 ml) was added.

The organic and aqueous layers were separated. The aqueous portion was extracted with ether. All ethereal solutions were combined, washed with water, and concentrated by evaporation. The residue was dissolved in 250 ml of isopropanol. To this solution was added 150 ml of 1M sulfuric acid and this solution was stirred for 3.5 hrs.

Water (300 ml) was added, the solution extracted repeatedly with ether. The ether solution was washed with 1N sodium hydroxide and saturated aqueous sodium chloride, dried ($MgSO_4$ and $CaCl_2$), concentrated by evaporation and the residue was distilled three times (Kugelruhr) leaving 5.2g of the crude aldehyde 117 (22%). A 5.88g quantity of p-methoxyphenylacetylene was recovered. Purified by bulb to bulb distillation, 117 gave the following spectral

data: nmr(CCl_4), δ 10.19 (s, 1H, CHO), 7.31 (d, 2H, J=10 Hz, phenyl protons), 6.84 (d, 2H, J=10 Hz, phenyl protons), 3.77 (s, 3H, $-OCH_3$), 2.6-2.0 (m, 4H, allylic protons), 1.9-1.4 (m, 4H, non-allylic ring protons); ir (CCl_4) $\tilde{\nu}$ (cm^{-1}) 2285 (C≡C), 1675 (CHO); uv_{max}(cyclohexane), 320 (24, 000), 259 (16, 000) 247 (22, 000). Calculated for C, 4.0 (79.31, 1.49, 13.21). Found (79.32, 7.50).

Trans-2-(p-methoxystyryl)-3, 4, 5, 6-tetrahydrobenzaldehyde (119)

This compound was prepared using the method of Schiess and Chia.[43] About 5.0g of crude alkyne 31 was dissolved in 30 ml of cyclohexane and hydrogenated at atmospheric pressure over 1.0g of 10% palladium on charcoal until 1.05 equivalents had been used. An NMR spectrum showed that more than 90% of the alkyne had been hydrogenated by comparison of the aldehyde proton signals. The aldehyde 118 [cis-2-(p-methoxystyryl)-3, 4, 5, 6-tetrahydrobenzaldehyde] was isolated by concentration.

The concentrate was dissolved in 50 ml of methylcyclohexane and refluxed for 6.5 hrs. The solution was concentrated to a red oil. The oil was purified by column chromatography (silica gel) with ether as the eluent. The eluate was concentrated and the residual material was dissolved in 2 ml of ether and 8 ml of methylcyclohexane. Refrigeration of the solution gave 1.84g of orange crystals 119 (37%

from 117). The crystals were recrystallized twice from ether/petroleum ether (20/80) giving 1.40g of light orange crystals, mp. 57-58°C; nmr(CCl_4) δ 10.52 (s, 1H, CHO), 7.62 (d, 1H, J=16 Hz, trans ArCH=CH) 7.36 and 6.75 (AB quartet, 4H, J=10 phenyl protons) 6.68 (d, 1H, J=16 Hz, trans ArCH=CH), 3.79 (s, 3H, $-OCH_3$), 2.6-2.2 (m, 4H, allylic protons), 1.9-1.5 (m, 4H, non-allylic protons); ir(CCl_4) $\tilde{\nu}$, 1695(CHO); uv_{max}(cyclohexane), 336 (20,000), 256 (11,000). Calculated for $C_{16}H_{18}O_2$: C(79.31) H(7.49). Found: C(79.32) H(7.50).

Ethyl 3-[trans-2-(4'-methoxystyryl)cyclohexen-1-yl]-trans-propenoate (116)

The ester 116 was prepared by the method of Wadsworth and Emmons.[44] A 57% sodium hydride dispersion in mineral oil was washed in benzene to give 0.229g of sodium hydride (9.58 mmol). The sodium hydride was suspended in benzene under nitrogen and 2.38g of triethylphosphonoacetate (10.54 mmol) was added to it. The resulting slurry was then cooled with a water bath.

A solution of 1.16g of 116 (4.79 mmol) in 3 ml of benzene was added to the above solution and the mixture was heated to 70° for 10 min. The reaction mixture was filtered through a column of silica gel and the product eluted with ether/petroleum ether (15/85). The eluate was concentrated, dissolved in 10 ml of methylcyclohexane

and cooled to -20°C, giving light yellow crystals, 1.27g (85%), mp. 66-67°C; nmr (CCl_4) δ8.10 (d, 1H, J=16 Hz, CH=CH-COOEt), 7.38 (d, partially obscured, 1H, J=16 Hz, CH=CH-COOEt), 7.36 and 6.81 (AB quartet, 4H, phenyl protons), 6.60 (d, 1H, J=16 Hz, PhCH=CH), 5.84 (d, 1H, J=16 Hz, CH=CHCOOOEt), 4.13 (q, 2H J=7 Hz, $-O\underline{CH_2}CH_3$), 3.80 (s, 3H, $-O\underline{CH_3}$), 2.6-2.2 (m, 4H, allylic ring protons), 1.9-1.6 (m, 4H, other ring protons), 1.33 (t, 3H, J=7 Hz, $-OCH_2\underline{CH_3}$); uv_{max}(cyclohexane) =356 (33, 000); ir(CCl_4) $\tilde{\nu}$ = 1705 (COOEt). Calculated for $C_{20}H_{24}O_3$: C(76.92) H(7.69). Found: C(77.05) H (7.85).

6-Carbethoxy-7-(4'-methoxyphenyl)-1, 2, 3, 4, 6, 7-hexahydro-napthalene (135)

A 4% solution of 116 in cyclohexane was placed in a pyrex tube which had been cleansed with concentrated ammonium hydroxide and boiling distilled water. After the solvent was degassed by the freeze-thaw method, the tube was sealed. The sealed tube was heated to 115°C for 24 hrs. The contents of the tube were concentrated giving 135, nmr(CCl_4) δ 7.02 (d, 2H J=9 Hz, phenyl protons), 6.66 (d, 2H J=9 Hz, phenyl protons), 5.60 (s, broad, 2H, vinyl protons), 3.93 (q, 2H, J=7 Hz, $-O\underline{CH_2}CH_3$), 3.67 (s, broad, 2H), 2.6-2.0 (m, 4H), 1.08 (t, 3H, J=7 Hz, $-OCH_2\underline{CH_3}$); ir(CCl_4) $\tilde{\nu}$ = 1740 (COOEt); uv_{max} (cyclohexane) = 276 (2000), 283 (1700).

Part III. Cross-conjugated Pentaenes

Cis, cis-2, 9-undecadien-4, 7-diyn-6-ol (150)

In a dry flask under a nitrogen atmosphere, ethylmagnesium bromide was prepared from 2.200g of magnesium (0.090 gram atoms) and 13g of bromethane (0.119 mol) in 50 ml of ether. Cis-3-penten-1-yne (0.086 mol) was diluted with 25 ml of ether and added to the flask. The solution was refluxed for 4 hrs under nitrogen. Methyl formate (0.045 mol) in 10 ml of ether was added. After the solution had been stirred for 23 min, 20 ml water and 45 ml of 2N hydrochloric acid were added. The aqueous layer was extracted with ether, the ether solutions combined, dried and concentrated.

A small amount of pure 150 was obtained from the concentrated solution by preparative glc, (2% SE-30 on Chromsorb G 45/60, 1/4 in by 8 ft, 110°C, 80 ml/min) which had a retention time of 4:40 min. The clear liquid had: nmr (CCl_4) δ 6.02 (d of q, 2H J=11, 6 Hz, $CH_3\underline{CH}$=C) 5.55 (m of d, 2H, J=11, 2 Hz, C=$\underline{CH}$-C=C-) 5.33 (s, broad, 1H, -$\underline{CH}$OH) 2.10 (s, 1H, -$\underline{OH}$) 1.93 (d of d, 6H J=6, 2 Hz, $\underline{CH_3}$). By glc estimate the yield of alcohol was 2.7g (20%).

Cis, cis-2, 9-undecadien-4, 7-diyn-6-one (151)

A suspension of 6.1g of pyridinium chlorochromate[94] in 50 ml of methylene chloride was added to the crude alcohol (36) which

had been diluted with 30 ml of methylene chloride. After the resulting suspension had been stirred for 2 hrs, 100 ml of pentane was added and the brown suspension was filtered through Florisil. The filtrate was refiltered to remove Floricil and was concentrated to 20 ml. Preparative glc (5% OV-17 on Chromsorb G 45/60, 1/4 in by 5 ft, 140°C, 85 ml/min) yielded a clear liquid from two overlapping peaks at 15 min and 18 min, nmr (CCl_4), signals from the alcohol 150 plus δ 6.37 (d of q, 2H, J=11, 6 Hz, $CH_3\underline{CH}$=C) 5.66 (m of d, 2H, J=11, 2 Hz, C=$\underline{CH}$-C=C-) 2.03 (d of d, 6H J=6, 2 Hz, $\underline{CH_3}$C=C-). Peak area comparison showed approximately 50% conversion to the ketone 151.

6-Ethylidene-cis, cis-2, 9-undecadien-4, 7-diyne (152)

Ethyltriphenylphosphonium bromide (0.020 mol) was suspended in 100 ml of dry ether and converted to the ethylidene phosphorane with 11.1 ml of butyllithium solution (1.8M in hexane). The ketone solution 151 was added to the deep red ylid at 0°C and the solution was stirred at that temperature for 2 hrs. Ice water (200 ml) was added, the layers were separated, and the aqueous layer was extracted with pentane. The ether and pentane solutions were combined, dried ($CaSO_4$), and concentrated. Ice-cold pentane was added and the suspension was filtered to remove triphenylphosphine oxide.

The filtrate rapidly darkened. Glc analysis (5% OV-17 on Chromsorb G 45/60, 1/4 in by 5 ft, 140°C, 85 ml/min) of the filtrate showed the alcohol 36 at 18:00 min, the ketone 37 at 15:00 min, and product peaks (8 and 10 min). This is the only evidence for the formation of the expected compound 152, since the mixture was quite unstable.

1, 5-(Dicyclohexen-1-yl)-1, 4-pentadiyn-3-ol (138)

From 1-ethynylcyclohexanol, 1-ethynlcyclohexene 137 was prepared in 77% yield by the procedure of Hamlet, Henbest and Jones.[89]

In dry ether (100 ml) under a nitrogen atmosphere, ethyl magnesium bromide (0.041 mol) was prepared from 1.004g of magnesium and 5.4g of bromoethane. To this, 10.0g of 137 (0.094 mol) was added, and the solution was refluxed for 6 hrs. Methyl formate (0.0416 mol) was diluted with 60 ml of ether and was added and the solution was stirred for 1 hr before 2.25g of ammonium chloride in 100 ml of water was added. The layers were separated and the aqueous lyaer was extracted with ether. The ethereal solutions were combined, dried ($NaHCO_3$ and $MgSO_4$) and concentrated to a yellow oil. The oil was crystallized from cold pentane giving 1.83g of light yellow needles (37%); nmr(CCl_4) δ 6.11 (m, 2H, vinyl protons) 5.18 (s, 1H, C=CCHOH) 2.15 (m, 9H, allylic cyclohexene protons and OH) 1.64 (m, 8H, other cyclohexene protons). Two

more recrystallizations form hot pentane gave white crystals: mp 61.8-62.5°C.

1,5-(Dicyclohexen-1-yl)-1,4-pentadiyn-3-one (139)

A flask containing 0.789g of 138 and 15 ml of acetone was cooled to 0°C. To this solution 1.2M Jones reagent[94] was added until a definite orange-green color remained. Water (1 ml) was added and the solution was saturated with sodium chloride. The layers were separated, and the green Cr(IV) layer was extracted with ether. The ethereal solutions were combined with the acetone solution, dried ($MgSO_4$) and concentrated by evaporation. The concentrate was dissolved in dry ether and used immediately in the next step.

1,5-(Dicyclohexen-1-yl)-3-ethyl-1,4-pentadiyn-3-ol (141)

To 100 ml of dry ether were added 4.00g of 137 (0.0377 mol) and 18.8 ml of 2.0M butyllithium in hexane. After the solution had been refluxed for 2.3 hrs, 1.67g of freshly distilled propanoyl chloride (0.018 mol) in 50 ml ether was added to it. The mixture was then sitrred for 20 hrs, at room temperature. Ammonium chloride (2.1g) in 25 ml of water was added, the layers were separated, and the aqueous layer was extracted with ether. The ether solutions were combined, washed once with 30 ml of 1N sodium

hydroxide, dried ($MgSO_4$) and concentrated to an orange oil. The oil was dissolved in 50 ml of pentane for storage.

A 25 ml portion of the pentane solution was concentrated by evaporation, and purified by passage through a silica gel column (Silica Gel Woelhm, Act. 1) with ether/pentane (10/90). Fractions with the same composition by TLC were combined and the solvent was removed, leaving 1.36g of a clear oil 141 (54%), nmr (CCl_4) δ 6.06 (m, 2H, vinyl protons), 2.94 (s, 1H, -OH), 2.18 (m, 8H, allylic cyclohexene protons), 1.72 (q, partially obscured, 2H J=7 Hz, $-CH_2CH_3$), 1.44 (m, 8H, J=2 Hz, other cyclohexene protons), 1.12 (t, 3H J=7 Hz, $-CH_2CH_3$).

1,5-(Dicyclohexen-1-yl)-3-ethylidene-1,4-pentadiyne (140)

Ethyltriphenylphosphonium bromide in ether was converted to triphenylethylidinephosphorane with 3.2 ml of 1.6M butyllithium in hexane under nitrogen. This solution was cooled to 0°C and the solution of 139 was added to it. After the combined solution had been stirred for 3 hrs at 0°C, ice water was added. The layers were separated and the aqueous phase was extracted with cold pentane. The pentane and ether solutions were combined, dried ($MgSO_4$) and concentrated by evaporation. Cold pentane (0°C) was added to the residue and the suspension was filtered. The filtrate was concentrated and the concentrate was purified by column chromatography using

Silica Gel Woelhm, Act. 1 and ether-pentane (10:90) as eluent. The first fractions were concentrated to a clear oil, 0.267g, nmr (CCl_4) δ 6.14 (q, 1H J=8 Hz, $CH_3\underline{CH}$=C-), overlapping 6.05 (m, 2H, cyclohexene vinyl protons), 2.13 (m, 8H, allylic cyclohexene protons), 1.74 (m, 8H, other cyclohexene protons), 1.90 (d, 3H J=8 Hz, $\underline{CH_3}$-).

Compound 140 was also prepared from 141. Under a nitrogen atmosphere, a solution of 1.36g of 141 (0.005 mol) in 15 ml of pyridine was added to 0.614g of phosphorus oxychloride (0.004 mol) in 5 ml of pyridine. The solution was heated to 80-90°C for 1 hr, then poured over 50g ice. The water solution was extracted with pentane. The pentane solution was washed with dilute hydrochloric acid and water, dried ($MgSO_4$ and $NaHCO_3$) and concentrated. The residue was purified as above yielding 0.45g of 140 (35%) which had an nmr spectrum identical to that above in the procedure from 41.

1, 1-Dibromopropene (142)

The dibromide 142 was prepared by the method of Bachman[91] in an overall yield of 34%. Trans-crotonic acid was brominated and the resulting dibromide heated in a 10% aqueous solution of sodium carbonate. The isolated products, 2-bromobutenoic acid and 1-bromopropene were brominated giving tribromides. The tribromides were heated in aqueous sodium carbonate giving the dibromide 142,

bp. 73-75°C (110 nm), nmr(CCl_4) δ 6.37 (q, 1H, J=7 Hz, $CH_3\underline{CH}$-), 1.66 (d, 3H, J=7 Hz, $\underline{CH_3}CH$-).

3-Ethylidene-(1, 5-dicyclohexen-1-yl)-1, 4-pentadiyne (140)

The procedure developed by Sonagashira et al.[71] was followed. A 4.03g quantity of 142 (20.2 mmol) and 4.28g of 137 (40.4 mmol) were added to 40 ml of diethylamine containing 0.113g of bis(triphenylphosphine)palladium(II) chloride (0.162 mmol) and 0.062g of cuprous iodide (0.324 mmol). The solution was stirred for 5 hrs.

Water (35 ml) was added and the product was taken up in petroleum ether. The petroleum ether solution was washed with water, dried ($CaCl_2$) and concentrated to an oil. The oil was purified by column chromatography (Silica Gel Woelhm) with petroleum ether as eluent giving 2.9g of pure 140 (52%), nmr(CCl_4) δ 6.14 q, 1H, J=8 Hz, $CH_3\underline{CH}$=C-), overlapping 6.05 (m, 2H, cyclohexene vinyl protons), 2.13 (m, 8H, allylic protons), 1.74 (m, 8H, cyclohexane protons), 1.90 (d, 3H, J=8 Hz, CH_3-).

3-Ethylidene-(1, 5-dicyclohexen-1-yl)-1, 4-pentadiene (136)

A 2.1g sample of 140 was hydrogenated over 0.6g of Lindlar catalyst[76] in the presence of 8 μl of quinoline until 1.2 equivalents had been absorbed. The main product was isolated by column

chromatography, first through alumina and then through silica gel with petroleum ether as eluent. The product, 1.2g, was an oil, nmr (CCl_4) δ 6.1-5.3 (m, 7H, vinyl protons), 2.4-1.9 (m, 8H, allylic cyclohexenyl protons), 1.68 (d, partially obscured, 3H, J=6 Hz, $\underline{CH_3}CH=C-$), 1.7-1.5 (m, 8H, non-allylic cyclohexenyl protons); uv_{max}(cyclohexane)= 240 (19, 500).

Thermolysis of 3-ethylidene-(1, 5-dicyclohexen-1-yl)-1, 4-pentadiene (136)

A solution of 136 was placed in a clean pyrex tube and degassed by the freeze-thaw method. The tube was sealed and heated to 125°C for 20 hrs. The product was isolated by preparative thick layer chromatography, nmr (CCl_4) δ 5.8-5.4 (m, 3H, vinyl protons), 2, 8-1.2 (m, 16H), 1.09 (d, 3H, J=7 Hz, $\underline{CH_3}CH-$); uv_{max}(cyclohexane) = 283 (ε = 14, 000); mass spectrum, molecular ion 254. The product was hydrogenated over platinum oxide, mass spectrum, molecular ion 260.

Kinetic Studies

All Pyrex tubes used in the kinetic studies were cleansed in concentrated ammonium hydroxide, rinsed with boiling distilled water and dried at 110°C. Before use the tubes were cooled to room temperature under nitrogen. A stock solution of the triene

to be studied was prepared, 0.002M (74, 108 and 116) or 0.01M (77), and an aliquot of these solutions (100μl) placed in the tubes and degassed. The tubes were then sealed and placed in a thermostatted oil bath for the desired length of time.

The contents of the sealed tubes were analyzed by uv (74, 108 and 116) or gas chromatography (77 - Varian 204-B, hydrogen-flame detector, 3% XF-1150 on Chromsorb W 80/100 mesh, oven temperature 130°C, helium flow 25 ml/min). With 77, the stock solution also contained acenapthalene (0.005M). Peak areas were expressed as ratios relative to acenapthalene. The data observed are presented in figures 3-11. A refers to absorbence while C refers to concentration.

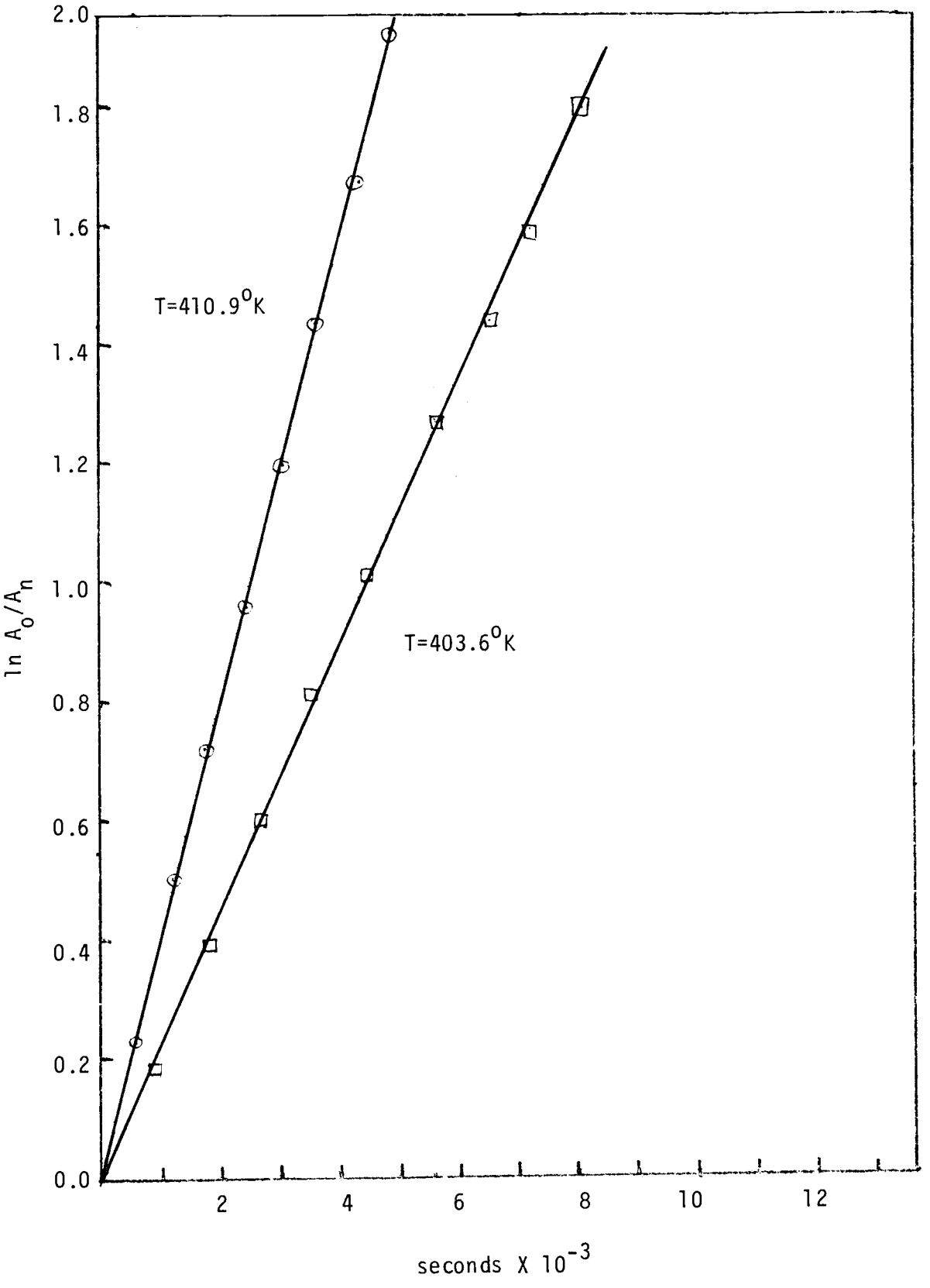


Figure 3. Plot of the logarithm of A_o/A vs time (sec) for the electrocyclization of 116.

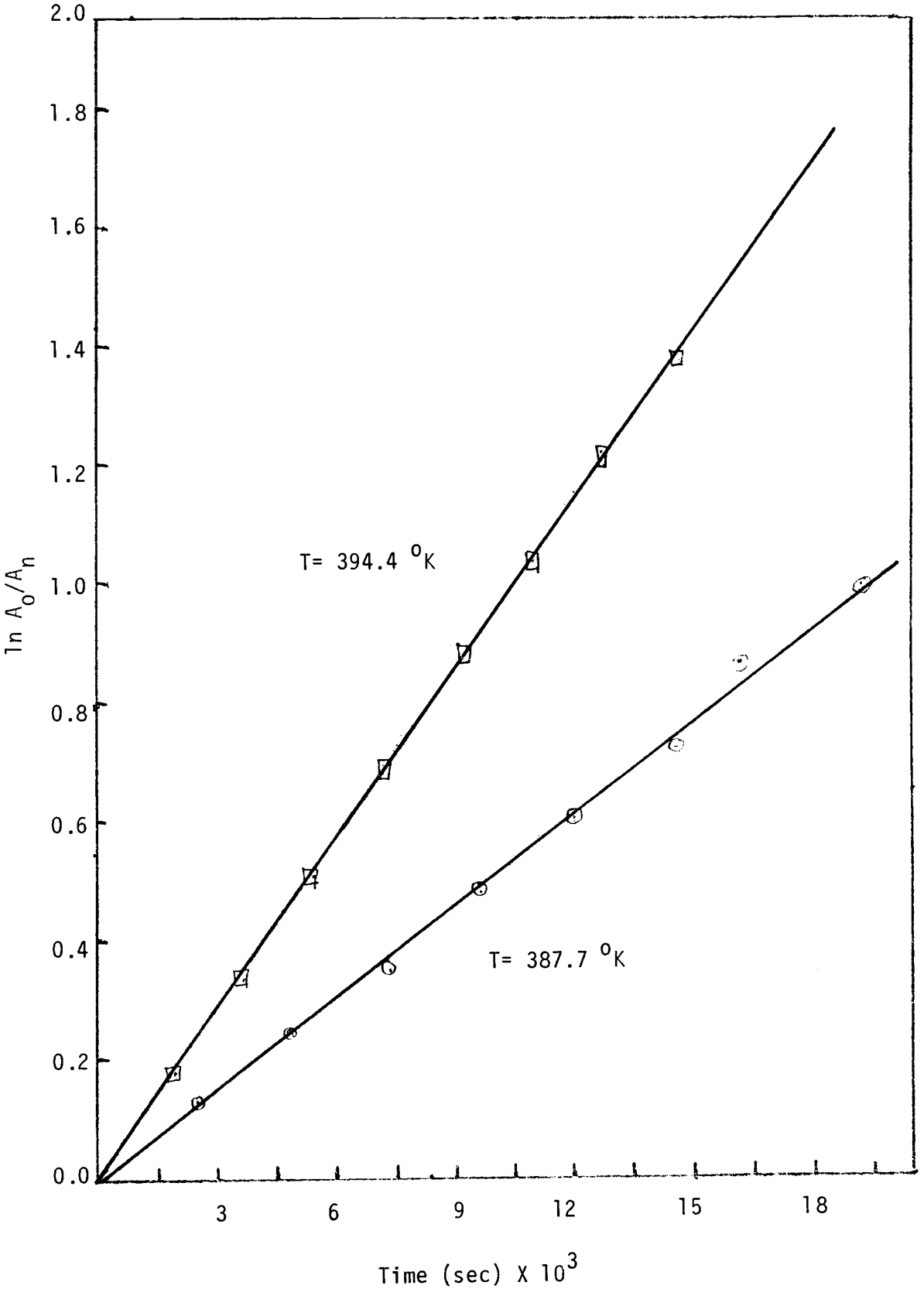


Figure 4. Logarithm of A_o/A_n versus time (sec) for the electrocyclization of 116

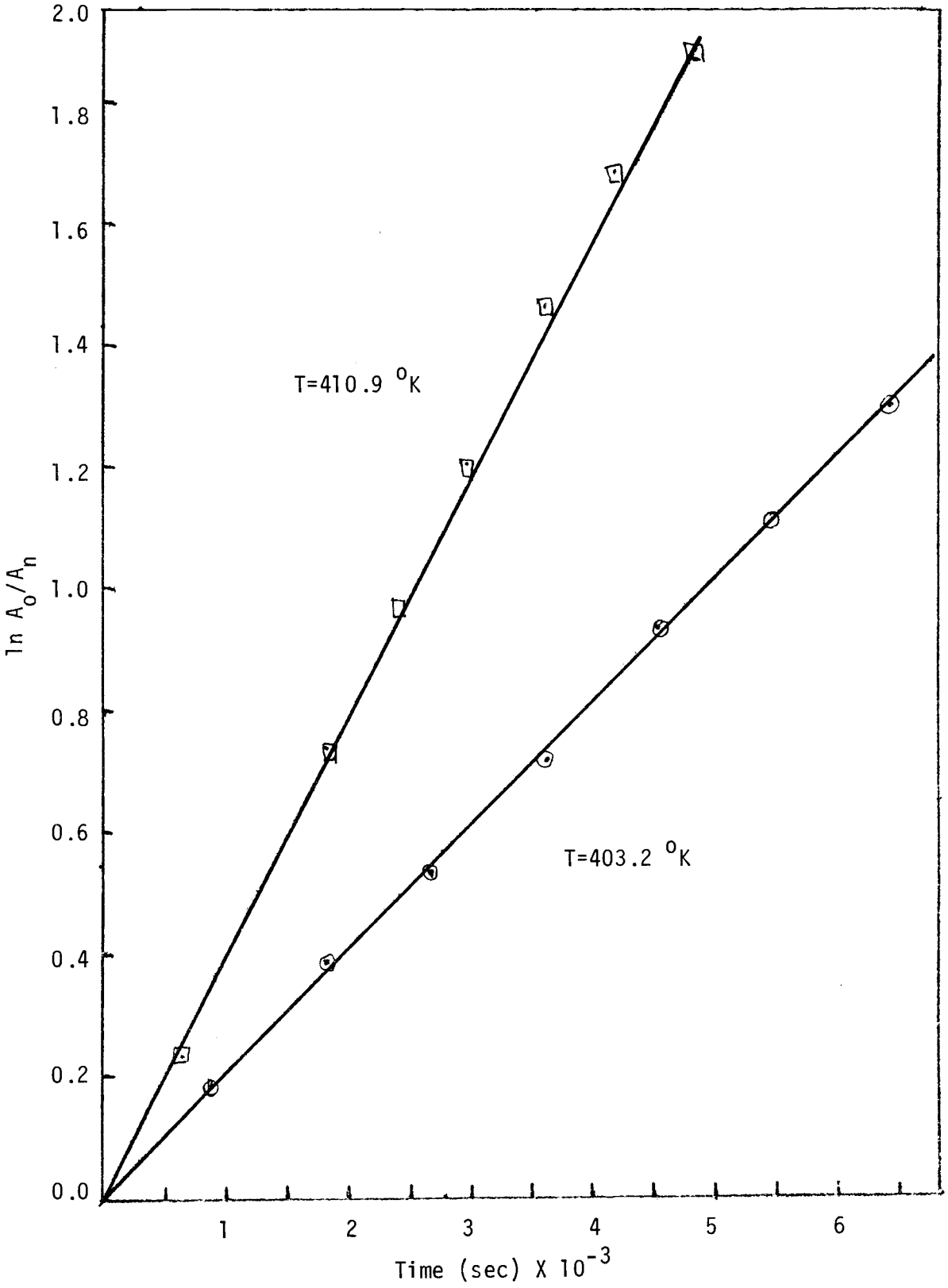


Figure 5. Plot of logarithm of A_o/A_n vs time (sec) for the electrocyclization of 108

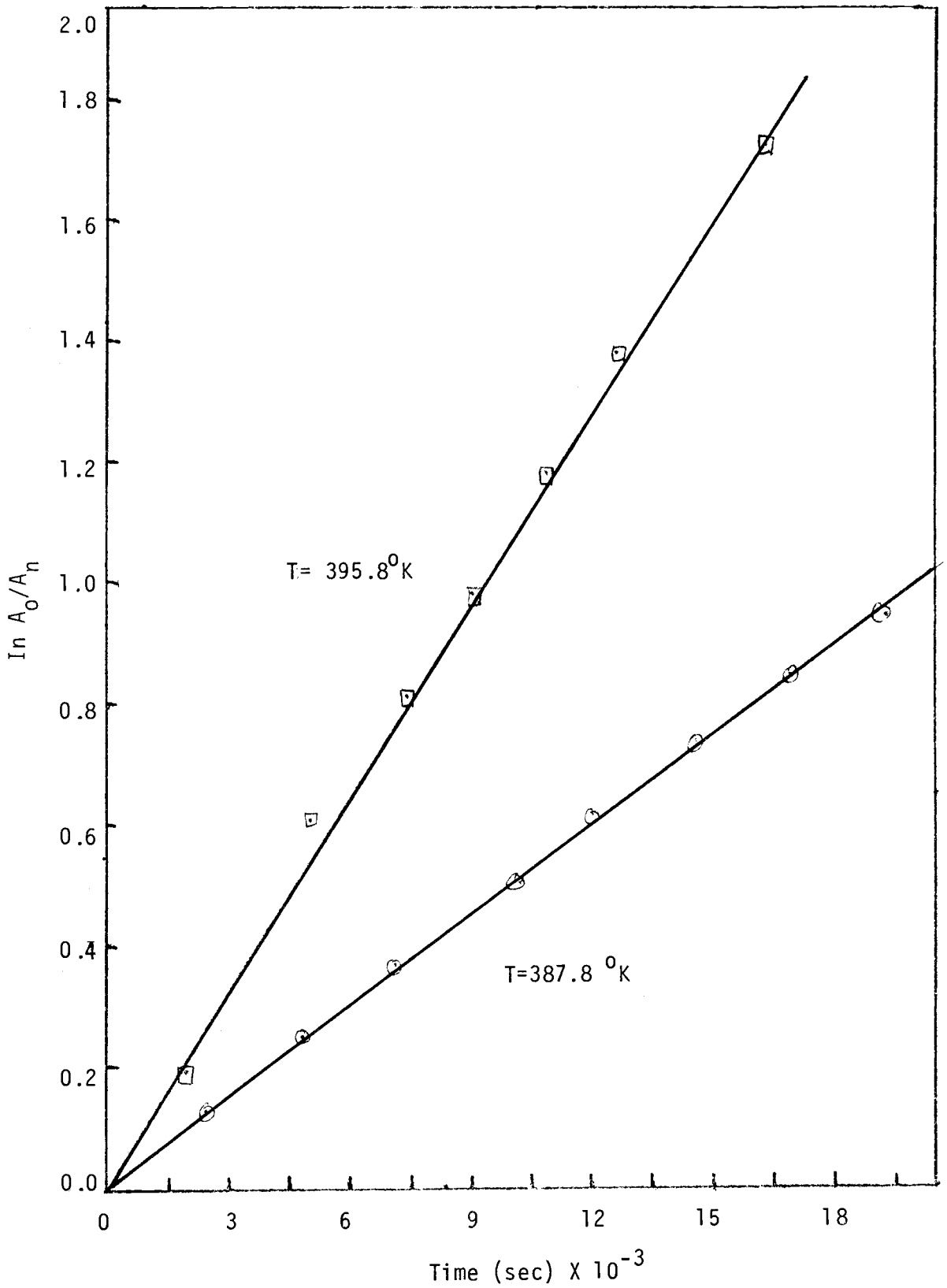


Figure 6. Plot of logarithm of A_o/A_n vs time (sec) for the electrocyclization of 108.

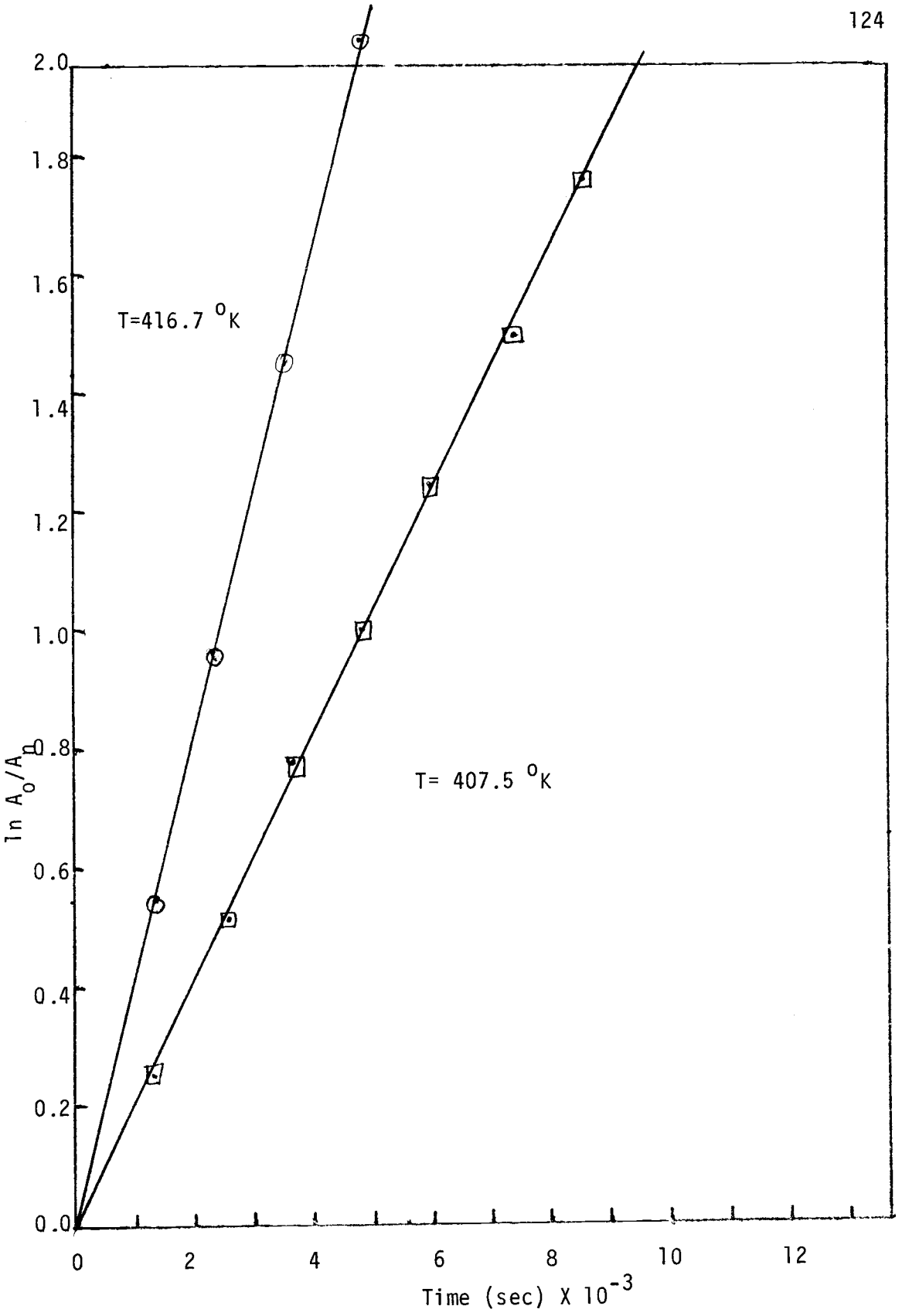


Figure 7. Plot of the logarithm of A_o/A_n vs time (sec) for the electrocyclization of 74.

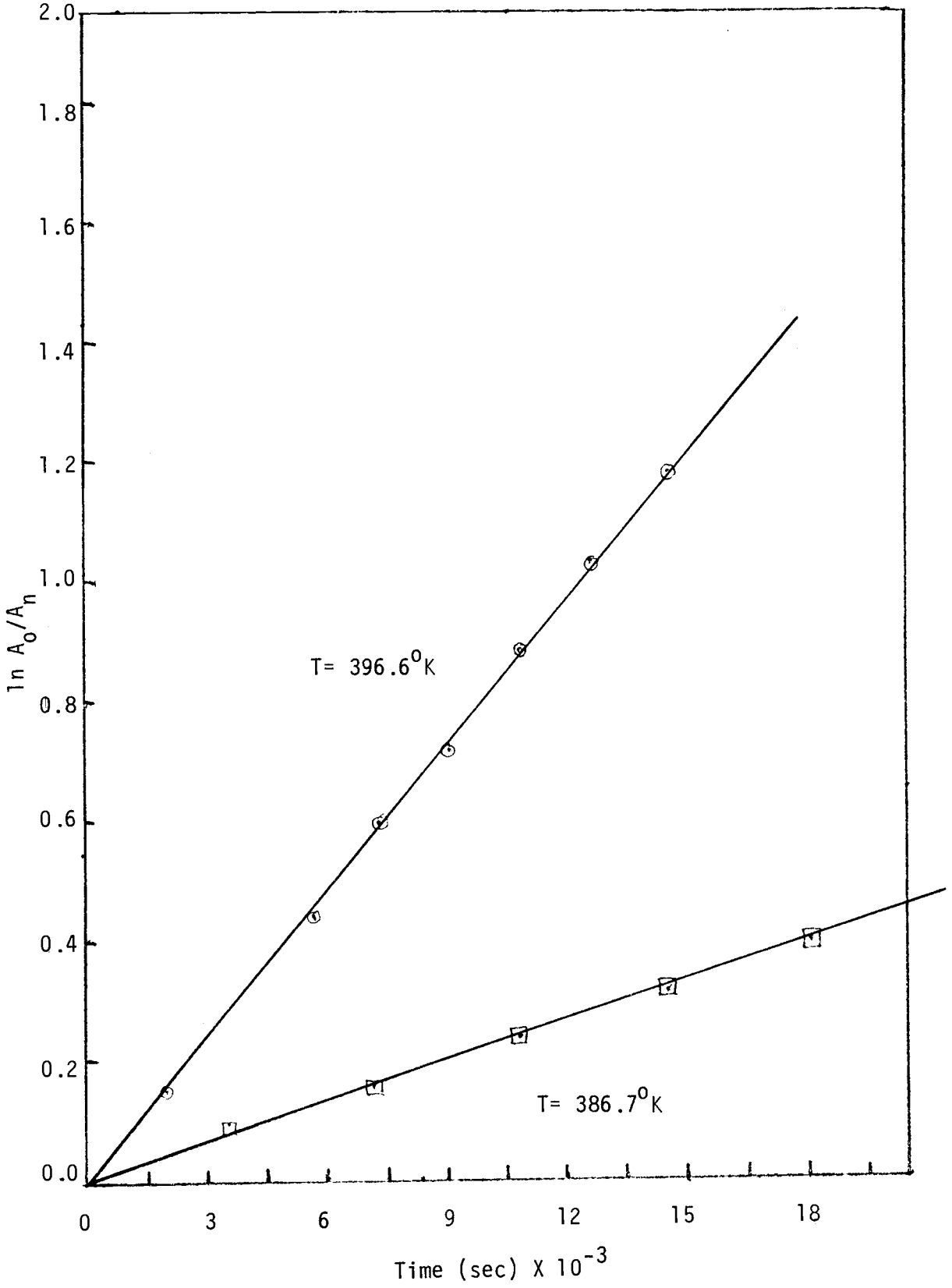


Figure 8. Plot of logarithm of A_o/A_n vs time (sec) for the electrocyclization of 74

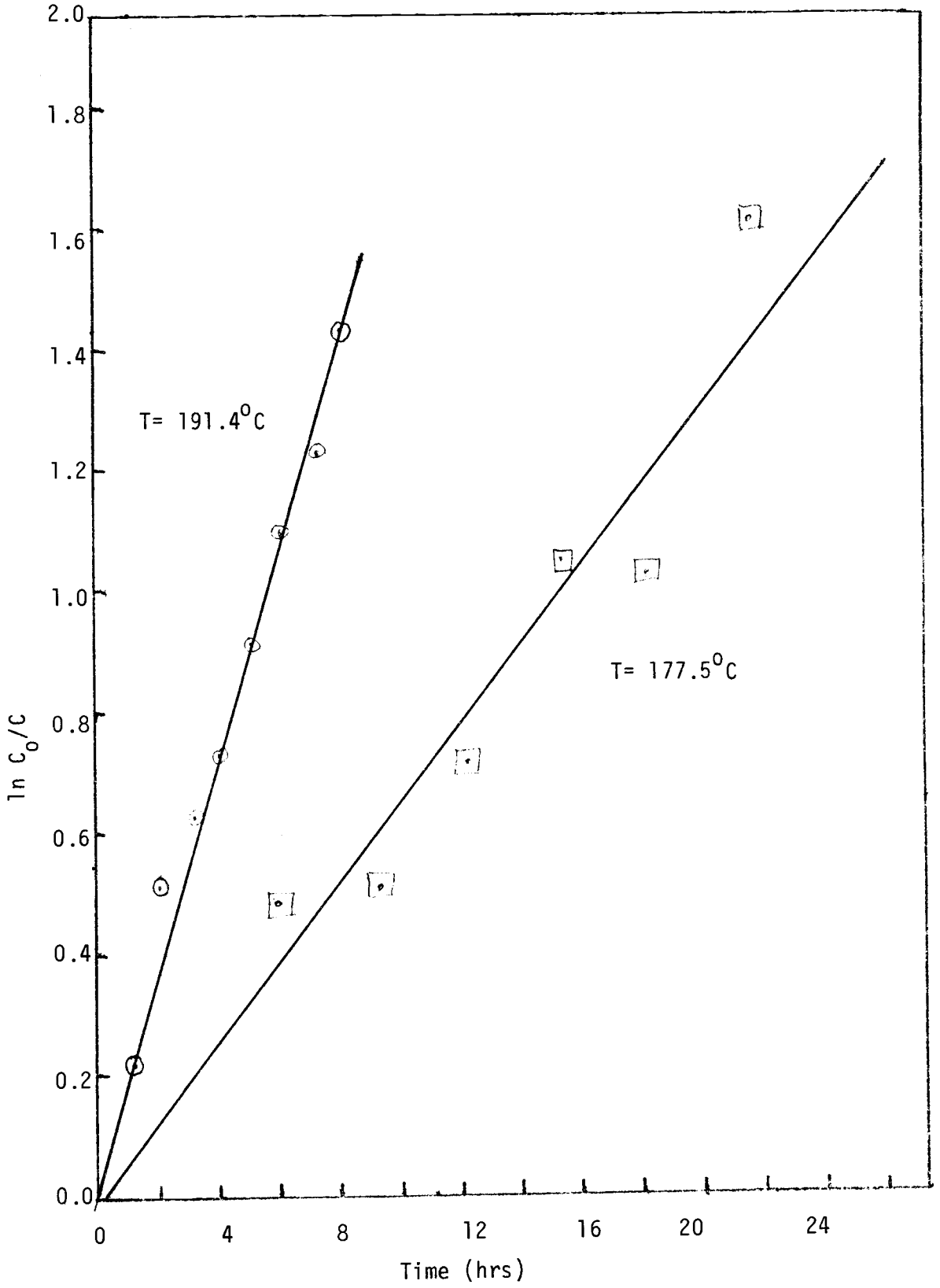


Figure 9. Plot of logarithm of C_o/C vs time (hrs) for the electrocyclization of 77

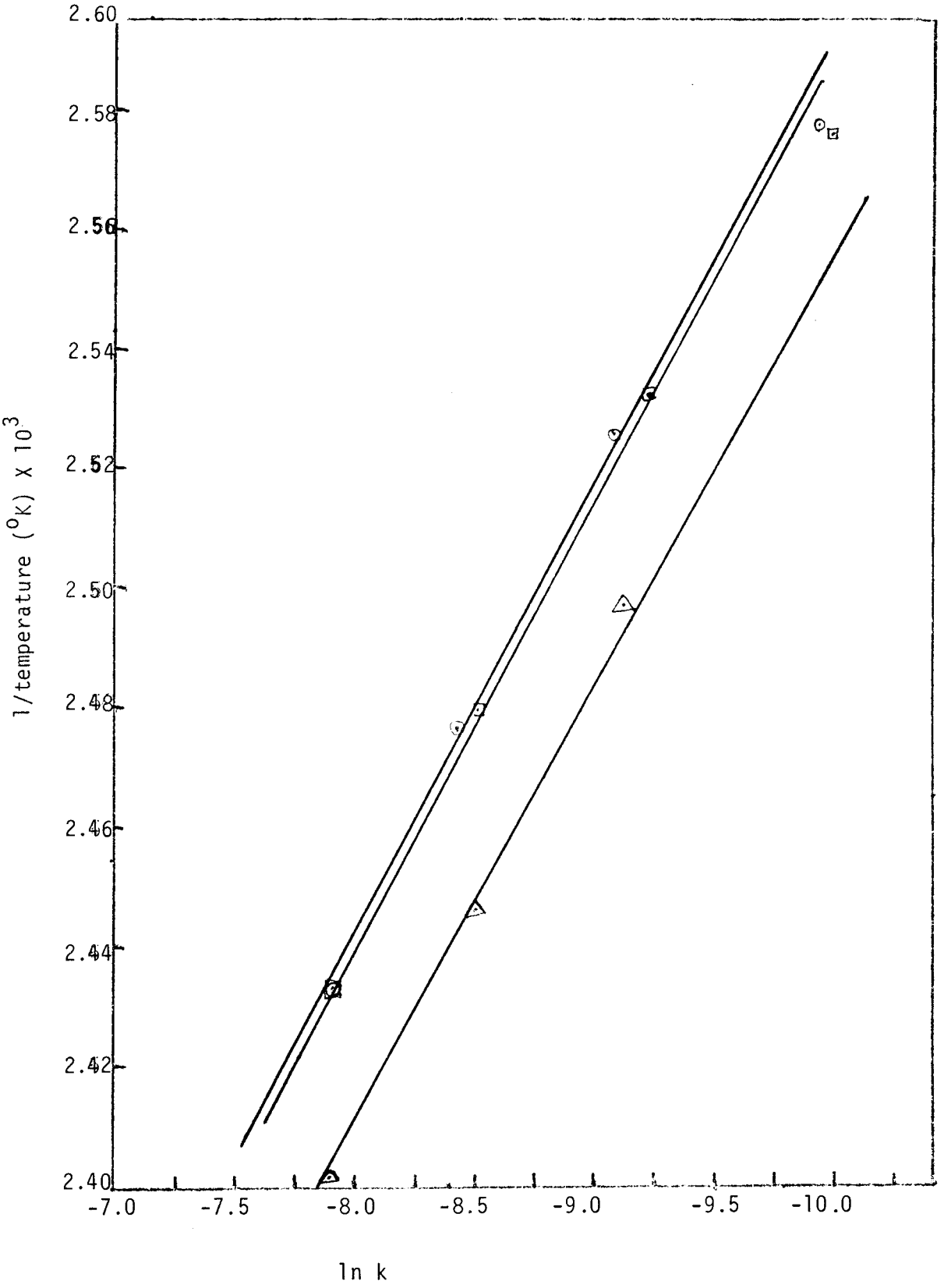


Figure 10. Plot 1/temperature vs logarithm of the rate constant for 74 (Δ), 108 (O), and 116 (□).

BIBLIOGRAPHY

1. J. L. Platt, Ph.D. Thesis, Oregon State University, Corvallis, Oregon (1970).

2. C. E. Delphey, Ph.D. Thesis, Oregon State University, Corvallis, Oregon (1976).

3. M. F. Cleary, Ph.D. Thesis, Oregon State University, Corvallis, Oregon (1975).

4. R. B. Woodward and R. Hoffman, Angew. Chem., Int. Ed. Eng., 8, 781 (1969).

5. E. N. Marvell, G. Caple, B. Schatz and W. Pippin, Tetrahedron, 29, 3781 (1973).

6. E. N. Marvell, G. Caple and B. Schatz, Tetrahedron Lett., 1965, 385.

7. E. Vogel, W. Grimme and E. Dinne, Tetrahedron Lett., 1965, 391.

8. D. S. Glass, J. W. H. Wattney and S. Winstein, Tetrahedron Lett., 1965, 377.

9. K. E. Lewis and H. Steiner, J. Chem. Soc., 1964, 3080.

10. E. N. Marvell, G. Caple, C. Delphey, J. Platt, N. Polstron and J. Tashiro, Tetrahedron, 29, 3797 (1973).

11. N. D. Epiotis, J. Amer. Chem. Soc., 94 1935 (1972).

12. N. D. Epiotis, ibid, 94, 1935 (1972).

13. N. D. Epiotis, ibid, 95, 1191 (1973).

14. N. D. Epiotis, ibid, 95, 1200 (1973).

15. N. D. Epiotis, ibid. 95, 1214 (1973).

16. E. N. Marvell, Tetrahedron, 29, 3790 (1973).

17. R. B. Woodward and R. Hoffman, "The Conservation of Orbital Symmetry," Academic Press, New York, N.Y., 1970, p. 1.

18. Ibid, p. 173.

19. J. E. Baldwin, A. H. Andrist, and R. K. Pinschmidt, Jr., Accts. Chem. Res., 5, 402 (1972).

20. K. Hsu, R. J. Buenker, and S. Peyerimhoff, J. Amer. Chem. Soc., 93, 2117 (1971).

21. J. A. Berson, Accts, Chem. Res., 5, 406 (1972).

22. J. A. Berson and L. Salem, J. Amer. Chem. Soc., 94, 8917 (1972).

23. J. A. Berson and G. L. Nelson, ibid, 92, 1096 (1970).

24. J. A. Berson and R. W. Holder, ibid, 95, 2037 (1973).

25. J. A. Berson and P. B. Dervan, ibid, 95, 269 (1973).

26. H. H. Freedman and G. A. Doorakian, ibid, 90 5310 and 6896 (1972).

27. J. I. Brauman and W. C. Archie, ibid, 94, 4262 (1972).

28. J. I. Brauman and W. C. Archie, Tetrahedron, 27, 1275 (1971).

29. L. M. Stephenson and J. I. Brauman, Accts. Chem. Res., 7, 65 (1974).

30. A. Dahmen and R. Huisgen, Tetrahedron Lett., 1969, 1465.

31. S. W. Staley and T. J. Henry, J. Amer. Chem. Soc., 93, 1292 (1971).

32. S. W. Staley and T. J. Henry, ibid, 92, 7612 (1970).

33. S. W. Benson, "Thermochemical Kinetics," John Wiley and Sons, Inc., New York, N. Y., 1968, p. 74.

34. E. N. Marvell, personal communication.

35. W. von E. Doering and G. H. Beasley, Tetrahedron, 29, 223; (1973).

36. W. R. Roth, G. Ruf and P. W. Ford, Chem. Ber.,107, 48 (1974).

37. D. G. L. James and R. D. Stuart, Trans. Faraday Soc., 64, 2752 (1968).

38. W. H. Pippin, Master's Thesis, Oregon State University, Corvallis, Oregon (1961).

39. J. L. M. A. Schlatmann and E. Havinga, Rec. Trav. Chim., 80, 1101 (1961).

40. E. N. Marvell and J. Tashiro, J. Org. Chem., 30, 3991 (1965).

41. E. N. Marvell, G. Caple, C. Delphey, J. Platt, N. Polstron and J. Tashiro, Tetrahedron, 29, 3797 (1973).

42. P. Schiess, R. Seeger, and Chr. Suter, Helv. Chim. Acta, 53, 1713 (1970).

43. P. Schiess and H. L. Chia, Helv. Chim. Acta, 53, 485 (1970).

44. W. S. Wadsworth and W. D. Emmons, J. Amer. Chem. Soc., 83, 1733 (1961).

45. M. Schlosser in "Topics in Stereochemistry, Vol. V," E. Eliel and N. Allinger, Ed., John Wiley and Sons, Inc., New York, N. Y. (1970), p. 1.

46. A. Padwa and S. Clough, J. Amer. Chem. Soc., 92, 5803 (1970).

47. A. Padwa, L. Brodsky and S. Clough, ibid, 94, 6767 (1972).

48. L. Jaenicke and K. Seferiadis, Chem. Ber., 108, 225 (1975).

49. G. G. Moy, Ph.D. Thesis, Oregon State University, Corvallis, Oregon, 1977.

50. G. Buchi and H. Wuest, Helv. Chim. Acta, 54, 1767 (1971).

51. W. G. Dauben and J. Ipakschi, J. Amer. Chem. Soc., 95, 5080 (1973).

52. J. Kochi and M. Tamura, ibid, 93, 1487 (1971).

53. J. M. Newman and J. K. Kochi, J. Org. Chem., 40, 599 (1975).

54. K. Tamao, K. Sumitani, Y. Kiso, M. Zembayashi, A. Fujioka, S. Kodama, I. Nakajima, A. Minato and M. Kumada, Bull. Chem. Soc. Jpn., 49, 1958 (1976).

55. J. F. Normant, G. Cahiez and C. Chuit, J. Organomet. Chem., 77, 269 (1974).

56. H. P. Dang and G. Linstrumelle, Tetrahedron Lett., 1978, 191.

57. G. Zweifel and R. L. Miller, J. Amer. Chem. Soc., 92, 6678 (1970).

58. G. Zweifel and R. A. Lynd, Synthesis, 1974, 658.

59. E. Negishi and S. Baba, Chem. Commun., 1976, 596.

60. E. Negishi and S. Baba, J. Amer. Chem, Soc., 98, 6729 (1976).

61. E. Negishi and D. Van Horn, ibid, 99, 3168 (1977).

62. E. Negishi, D. E. Van Horn, N. Okukado, and W. L. Klima, Tetrahedron Lett., 1978, 1027.

63. E. Negishi, N. Okukado, A. O. King, D. E. Van Horn, and B. I. Spiegel, J. Amer. Chem. Soc., 100, 2254 (1978).

64. E. Negishi and D. E. Van Horn, ibid, 100 2251 (1978).

65. R. F. Heck and J. P. Nalley, J. Org. Chem., 37, 2320 (1972).

66. H. A. Dieck and R. F. Heck, J. Amer. Chem. Soc., 96, 1133 (1974).

67. H. A. Dieck and R. F. Heck, J. Org. Chem., 40, 1083 (1975).

68. K. Kaneda, T. Uchiyama, H. Koyayashi, Y. Fujiwara, T. Imanaka, and S. Teranishi, Tetrahedron Lett., 1977, 2005.

69. L. Cassar, J. Organomet. Chem., 93, 253 (1975).

70. H. A. Dieck and R. F. Heck, ibid, 93, 259 (1975).

71. K. Sonagashira, Y. Tohda and N. Hagihara, Tetrahedron Lett. 1975, 4467.

72. K. W. Egger, D. M. Golden and S. W. Benson, J. Amer. Chem. Soc., 86, 5420 (1964).

73. J. T. Tashiro, Ph.D. Thesis, Oregon State University, Corvallis, Oregon, (1965).

74. L. J. Haynes, Sir Ian Heilbron, E. R. H. Jones, and F. Sondheimer, J. Chem. Soc., 1947, 1583.

75. T. L. Jacobs, "The Synthesis of Acetylenes," in: Organic Reactions, ed. by R. Adams, Vol. 5, New York, N. Y., Wiley, 1949, p. 2-78.

76. H. Lindlar, Organic Synthesis, 46, 89 (1966).

77. L. J. Bellamy, "The infrared spectra of complex molecules," p. 364 New York, N. Y., Wlley, 1958, 425 p.

78. L. Zechmeister, "Cis-Trans Isomeric Carotenoids, Vitamin A and Arylpolyenes," Academic Press Inc., New York, N. Y., 1962, pp. 169-75.

79. H. Biltz, Justus Liebig's Ann. Chem., 296, 293 (1897).

80. L. J. Dolly, C. Wilkins and T. G. Frey, J. Org. Chem., 31, 1114 (1966).

81. R. J. Abraham, J. W. Ronaldson, E. O. Bishop and R. E. Richards, J. Mol. Physics, 3, 485 (1960).

82. H. C. Pines, N. C. Sih and E. Lewicki, J. Org. Chem., 30, 1457 (1975).

83. G. Descotes, P. Legrand-Berlebach, and J. Sabadie, Bull. Soc. Chim. Fr., 4(2) 1517 (1973).

84. R. L. Augustine, "Catalytic Hydrogenation," Marcel Dekker, Inc., New York, N. Y., 1965, p. 60.

85. A. A. Frost and R. G. Pearson, "Kinetics and Mechanism", John Wiley and Son, Inc., New York, N.Y., 1953, pp. 153-156.

86. K. J. Laidler, "Chemical Kinetics", McGraw-Hill, Inc. San Francisco, Calif., 1965, pp. 88-90.

87. M. Cais, D. Fraenkel, and K. Weidenbaum, Coordination Chemistry Reviews, 16, 27 (1975).

88. E. O. Fischer, K. Ofele, H. Essler, W. Fronlich, J. P. Mortenson and N. Semmlinger, Chem. Ber., 91, 2763 (1958).

89. J. C. Hamlet, H. B. Henbest and E. R. H. Jones, J. Chem. Soc., 1951, 2652.

90. L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," John Wiley and Son, Inc., New York, N. Y., 1967, p. 142.

91. G. B. Bachman, J. Amer. Chem. Soc., 55, 4279 (1933).

92. E. W. Warhoff, D. G. Martin and W. S. Johnson, Org. Syn. Coll. Vol. 4, 1963, 162.

93. This work done by Dr. G. L. Larson, Oregon State University, Corvallis, Oregon (1978).

94. E. J. Corey and J. W. Suggs, Tetrahedron Lett., 1975, 2647.