1968

Studies in stereochemistry

Donald Charles Best
Iowa State University

STUDIES IN STEREOCHEMISTRY

by

Donald Charles Best

A Dissertation Submitted to the
Graduate Faculty in Partial Fulfillment
of the Requirements for the Degree of
DOCTOR OF PHILOSOPHY

Major Subject: Organic Chemistry

Approved:

Signature was redacted for privacy.

In Charge of Major Work

Signature was redacted for privacy.

Head of Major Department

Signature was redacted for privacy.

Dean of Graduate College

Iowa State University
of Science and Technology
Ames, Iowa

1968

TABLE OF CONTENTS

PART I: CONFORMATIONAL PREFERENCES OF ACYCLIC DIASTEREOMERS

HISTORICAL

The subject of conformational analysis was introduced about seventy-five years ago by Sachse (49). However, conformational analysis experienced a slow development until the appearance of a pioneering paper by Barton in 1950 (5). Since 1950, the literature dealing with conformational analysis has proliferated. However, most of the literature dealing with conformational analysis was concerned with cyclic compounds. At the time this work was initiated, a relatively small amount of information had accumulated concerning the conformational preferences of acyclic compounds.

Although many techniques are available for conformational studies, (31) the advent of nuclear magnetic resonance spectroscopy has greatly facilitated the conformational analysis of organic molecules.

The Karplus relationship (37) which relates the magnitude of the coupling constant between vicinal protons to the magnitude of the dihedral angle between the coupled protons has frequently been used to determine the average conformation of a molecule.

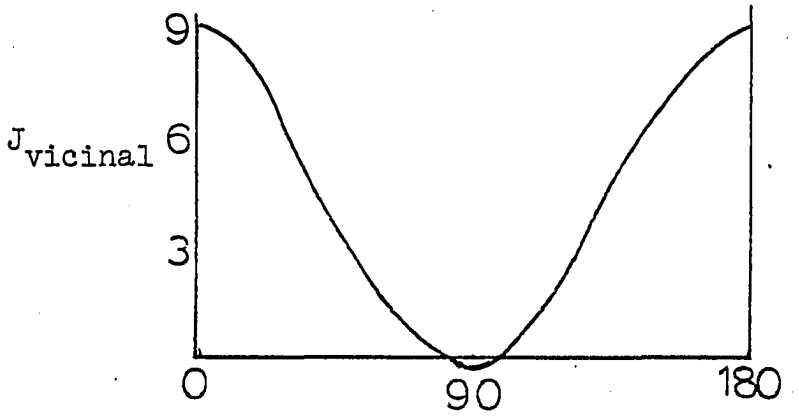
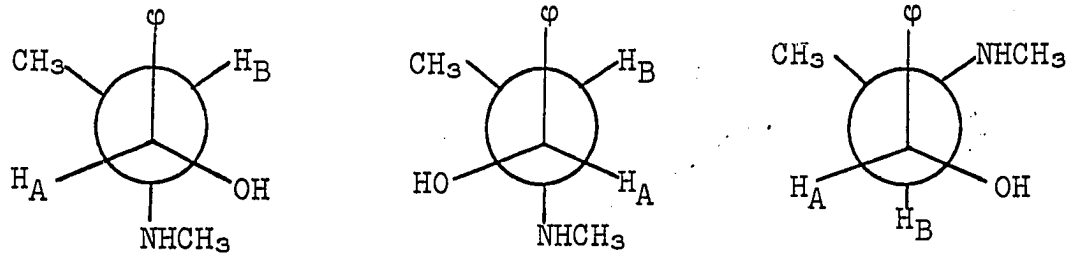


Figure 1
Karplus relationship.

Hyne (35) has studied the conformational preferences of the ephedrines using NMR techniques. He concluded from the magnitudes of the observed coupling constants that (+) ephedrine exists predominantly in conformer I while both conformers II and III are important for (-) ephedrine.

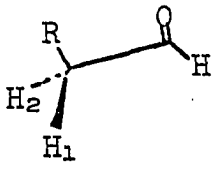


I $J_{AB} = 8.2$ II III $J_{AB} = 4.0$

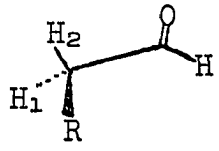
Figure 2
Conformational preferences of
the ephedrines.

Similar studies on the conformations of meso and dl 2,3-dibromobutane have been reported by Anet (2) and Bothner-By (14). Anet suggested that the difference between the coupling constants of the methine protons in meso and dl 2,3-dibromobutane (meso J = 7.85 cps and dl J = 3.15 cps) reflects the difference in the relative populations of rotomers with trans and gauche vicinal protons.

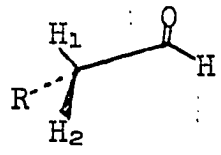
The NMR technique has also been applied to the determination of the favored conformations of some substituted aldehydes and alkenes. Karabatsos' study of mono and disubstituted acetaldehydes has shown that conformation IV predominates when R is methyl, ethyl, n-propyl, n-amyl or isopropyl; however, when R is t-butyl conformations V and VI predominate (36). Conformations VII and VIII were found



IV



V

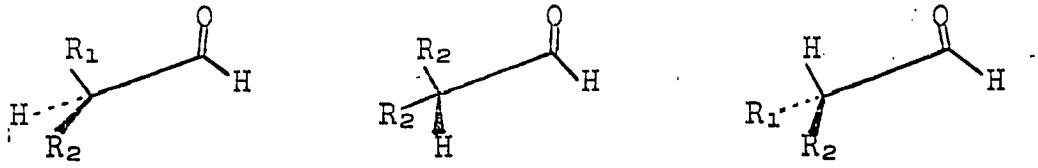


VI

Figure 3
Conformations of monosubstituted acetaldehydes.

to predominate when R_1 and R_2 were methyl; however, conformation IX was dominant when both R_1 and R_2 were ethyl or t-butyl. Karabatsos has suggested that the steric interactions

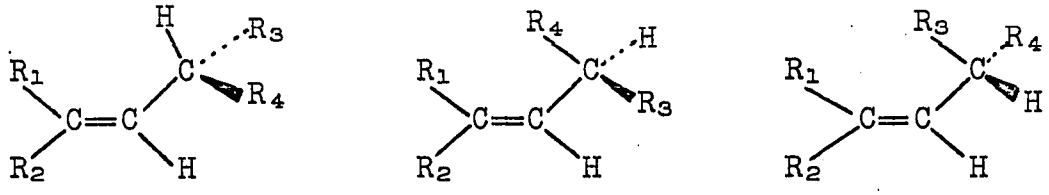
which exist between the carbonyl oxygen and the methyl protons on the t-butyl group destabilize conformations IV, VII and VIII relative to V, VI and IX.



VII VIII IX

Figure 4
Conformational preferences
of disubstituted aldehydes.

Bothner-By (13) has studied the conformational preferences of some substituted ethylenes. His studies show that when R_1, R_2 and R_3 are hydrogen and R_4 is methyl the three possible conformations



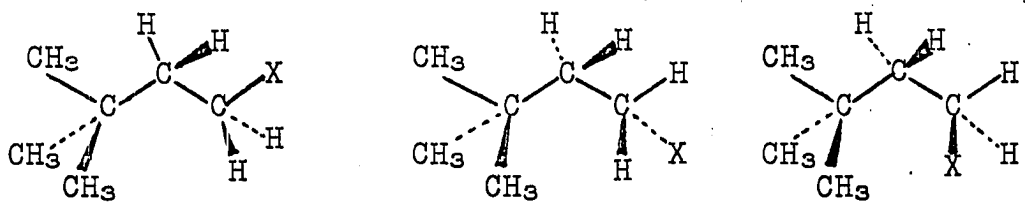
X XI XII

Figure 5
Conformations of alkyl-substituted ethylenes.

X, XI, and XII are essentially equally populated. When R_4 is t-butyl and R_1, R_2 and R_3 are hydrogen conformations X and XII are populated in slight preference to conformation XI. A strong preference for conformation X was observed when R_3

and R_4 were t-butyl and R_1 and R_2 were hydrogen. When R_1 and R_2 are methyl and R_3 and R_4 are t-butyl the compound exists almost exclusively in conformation X.

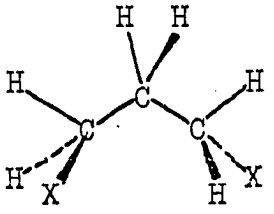
Whitesides (63) has presented an extensive NMR study of the conformational preferences of the 1-substituted derivatives of 3,3-dimethylbutane. Conformation XIII was favored in all cases and further it was noted that the predominance of conformation XIII increased with increasing steric bulk of the substituent group X. Whitesides suggested that the 1,3-steric interactions which exist in conformations XIV and XV are responsible for the predominance of rotamer XIII.



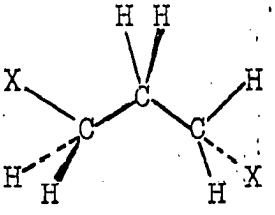
XIII XIV XV

Figure 6
Conformations of 1-substituted 3,3-dimethylbutanes.

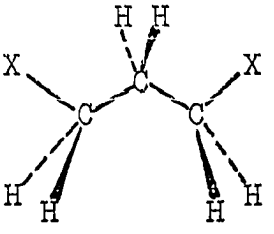
Infrared studies (42) have shown that in the solid state 1,3-dichloropropane; 1,3-dibromopropane and 1-bromo-3-chloropropane exist in conformation XVI. In the liquid phase conformations XVI, XVII and XVIII are populated; however, conformation XIX is absent. The lack of rotomer XIX was attributed to the 1,3-interactions which exist in this conformation.



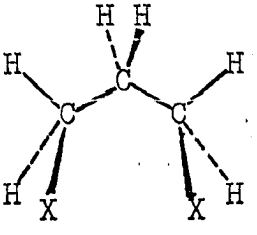
XVI



XVII



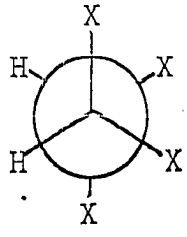
XVIII



XIX

Figure 7. Conformations of the 1,3-dihalopropanes.

Although the favored conformations of organic molecules are often predicted on the basis of steric considerations alone, this practice has frequently led to erroneous results (33). For example, the preferred conformation (Figure 8) of tetrabromo and tetrachloroethane XX have been deduced from infra-red studies (50).



XX

Figure 8
Preferred conformations of tetrachloro and tetrabromoethane in the liquid phase.

Obviously, conformation XX would not have been predicted from either steric or electronic considerations.

The effect of conformation on the reactivity of organic compounds is well documented (30). It has become apparent that a knowledge of the conformation of a molecule is essential to the understanding of its modes of reaction.

The first part of this dissertation is concerned with the determination of the preferred conformations of several sets of diastereomers.

RESULTS AND DISCUSSION

The effect of varying the bulk of a substituent on the preferred conformation of a pair of diastereomers was first investigated. The erythro (I) and threo (II) isomers of the 1,2-diphenyl-1-propyl system were chosen for study. The compounds studied were the alcohols, chlorides, bromides, iodides, acetates, and p-nitrobenzoates (26).

I II

Figure 9
Erythro and threo isomers of the
1,2-diphenyl-1-propyl system.

The vicinal coupling constants within each series of diastereomers were measured and are listed in Table 1. Although the magnitude of the vicinal coupling constant is most sensitive to changes in the dihedral angle between the coupled protons, it is also somewhat sensitive to the hybridization and the electro-negativity of groups bonded to the vicinal carbons (38). If the variation in J_{AX} observed was simply due to changes in the electronegativity of the groups, one would expect the magnitude of change in J_{AX} to be

Table 1. Coupling constants for the diastereomers of the 1,2-diphenyl-1-propyl system

Diastereomer	X	J_{AX} cps[a]
Erythro	OH	8.4
Threo	OH	6.0
Erythro	CL	8.7
Threo	CL	8.4
Erythro	Br	9.7
Threo	Br	9.5
Erythro	I	10.5
Threo	I	10.1
Erythro	PNB	8.1
Threo	PNB	7.4
Erythro	OAc	8.7
Threo	OAc	7.8

[a]Coupling constants taken from expanded spectra recorded using 100 cps sweepwidth.

the same for both the <u>erythro</u> and <u>threo</u> isomers. This is obviously not the case, and the observed variation of the vicinal coupling constant is best attributed to a change in the average conformation.

The observed vicinal coupling constant is a weighted mean derived from the populations of the two <u>gauche</u> rotomers (J_{AX} = 1-3 cps) and the <u>trans</u> rotomer (J_{AX} = 11-13 cps). The vicinal coupling constants listed in Table 1 show a fairly

steady increase with increasing bulk of the substituent X. It is also apparent that the erythro isomer consistently exhibits a higher coupling constant than the threo isomer.

For the erythro diastereomers conformation E_1 with trans protons is more highly populated than conformations E_2 or E_3 (Figure 10). Both conformations E_2 and E_3 involve three gauche interactions, whereas rotomer E_1 has only two. For the threo series, rotomer T_1 with trans protons becomes more highly populated as the bulk of X increases. It should be noted that rotomers T_2 and T_3 involve three gauche interactions while rotomer T_1 involves only two. However, the gauche interaction which exists in rotomer T_1 is between the two bulky phenyl groups. Thus, the energy difference between rotomers T_1 and T_2 may not be appreciable with small x groups.

As the bulk of X increases the gauche interaction between phenyl and X in rotomer T_2 becomes appreciable and conformation T_1 is favored.

The effect of substituting an isopropyl group for the 1-phenyl group of the 1,2-diphenyl-1-propyl system was also investigated. The alcohols and acetates of the 2-phenyl-4-methyl-3-pentyl system were studied (54).

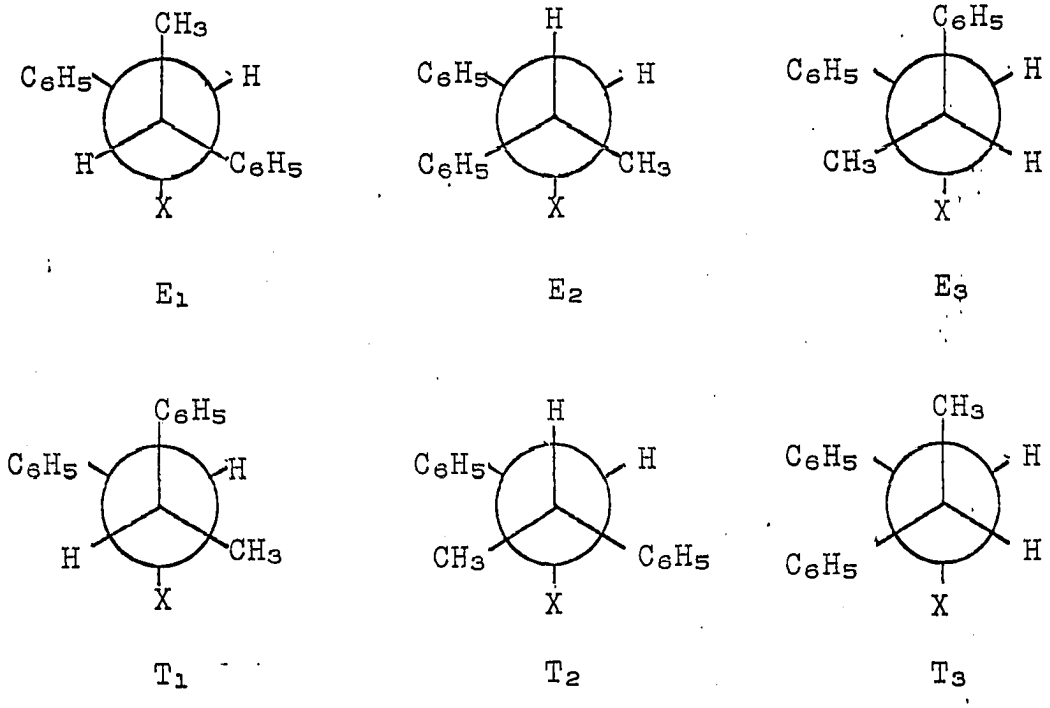
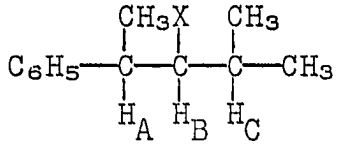


Figure 10
Conformations of the erythro and threo
1,2-diphenyl-1-propyl system.

The addition of 2-phenyl-propionaldehyde to 2-propyl magnesium bromide gave a mixture containing 80% threo (III) and 20% erythro (III) 2-phenyl-4-methyl-3-pentanol. The major product was assigned the threo configuration by application of Cram's rule (22). The alcohol was purified by vapor phase chromatography and its spectrum was recorded. The erythro alcohol was obtained by reduction of 2-phenyl-4-methyl-3-pentanone with lithium aluminum hydride and was purified by vapor phase chromatography. Both the erythro

and threo acetates were prepared by reaction of the corresponding alcohol with acetyl chloride. The acetates were purified by vapor phase chromatography and their NMR spectra were recorded.

The coupling constants of the alcohols and acetates are listed in Table 2.



III

Figure 11
The 2-phenyl-4-methyl-3-pentyl system.

Table 2. Coupling constants of the alcohols and acetates of erythro and threo 2-phenyl-4-methyl-3-pentyl system

Diastereomer[a]	X	J_{AB}[b]	J_{BC}[b]
Erythro	OH	7.35	4.2
Threo	OH	6.6	4.8
Erythro	OAc	7.0	5.8
Threo	OAc	9.4	3.4

[a] NMR data obtained in carbon-tetrachloride.

[b] Coupling constants were taken from spectra recorded using a 100 cps sweepwidth.

A direct comparison of the vicinal coupling constants of the 2-phenyl-4-methyl-3-pentyl system with those of the 1,2-diphenyl-1-propyl system cannot properly be made without some allowance for the electronegativity difference between the phenyl and isopropyl groups. Since the magnitudes of vicinal couplings vary inversely with the electronegativity of groups (38) bonded to the vicinal carbons, the values observed for the 1,2-diphenyl-1-propyl system should be slightly smaller than those observed for the 2-phenyl-4-methyl-3-propyl system. Since the effect of electronegativity on the vicinal coupling constants is small, it appears more reasonable to assume that the differences in couplings between the two systems is due to differences in their conformational preferences.

Comparison of the magnitudes of J_{AB} observed for <u>erythro</u> 1,2-diphenyl-1-propanol (J_{AB} = 8.4) and <u>erythro</u> 2-phenyl-4-methyl-3-propanol (J_{AB} = 7.35) indicates that conformation E_1 is less populated for the latter compound. This is somewhat

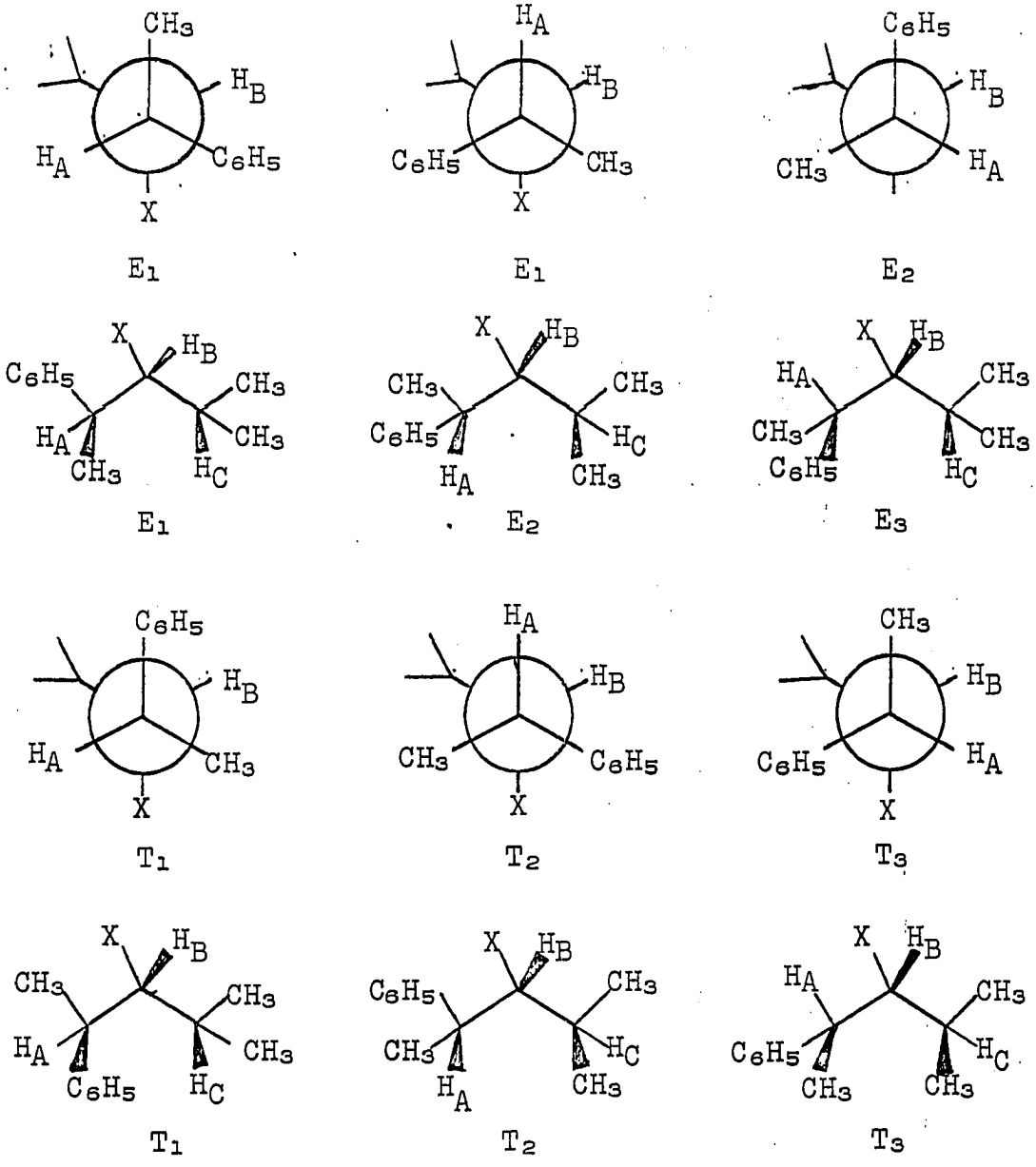


Figure 12
Conformations of erythro and threo isomers of the 2-phenyl-4-methyl-3-propyl system.

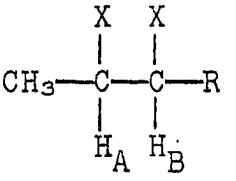
surprising since the i-propyl group is almost certainly bulkier than the phenyl group. Further it is noted that upon increasing the bulk of X conformation E_2 is favored over conformation E_1 in contrast to the results noted for the erythro 1,2-diphenyl-1-propyl system.

The results for the threo isomers of the 2-phenyl-4-methyl-3-pentyl system are similar to those obtained upon increasing the bulk of X in the 1,2-diphenyl-1-propyl system. Conformation T_1 is populated at the expense of T_2 as the bulk of X increases.

The variation of J_{BC} with X is consistent with the above interpretation. Thus, for the erythro isomer J_{BC} increases with an increase in the bulk of X as it should if rotomer E_2 is populated at the expense of E_1. For the threo isomers since rotomer T_1 is favored over T_2 with an increase in the bulk of X, J_{BC} should decrease from alcohol to acetate and indeed it does.

Conformations E_3 and T_3 involve a large 1,3 steric interaction and are not expected to be significantly populated.

The next series of diastereomers to be investigated were the 2,3-dihalo-3-substituted propanes IV. These compounds were prepared by bromination and/or chlorination of the corresponding cis and trans alkenes.



IV

Figure 13
The 2,3-dihalo-3-substituted propane system.

Spectral data for the case R is methyl were found in the literature (2) (13) and are reproduced in Table 3. For the cases R = isopropyl and t-butyl both the dichlorides and dibromides were examined. Spectral data for the compounds in which R is phenyl were kindly provided by G. M. Underwood (57).

As the data in Table 3 indicate the type of halogen substituent does not appear to greatly affect the vicinal coupling constants. The variation of the coupling constants J_{AB} is best discussed in terms of the three rotomers shown in Figure 14.

Table 3. Coupling constants and dipole moments for the 2,3-dihalo-3-substituted propanes

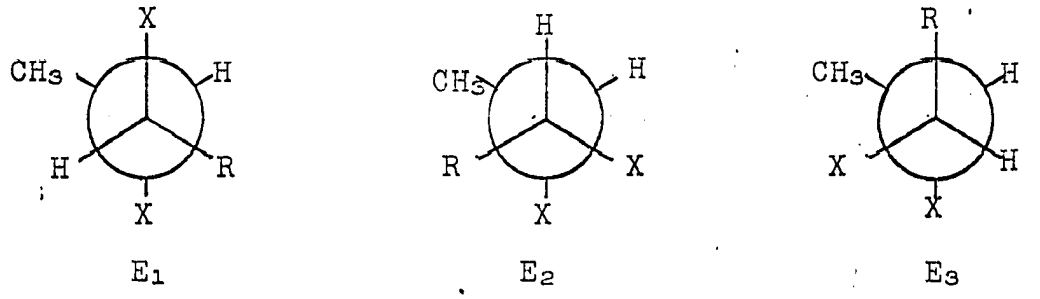
Diastereomer	R	X	J_{AB}[a] cps	Dipole moment Debye[b]
Erythro	CH_3	CL	7.4	1.75[c]
Threo	CH_3	CL	3.45	1.63[c]
Erythro	CH_3	Br	8.81	--
Threo	CH_3	Br	3.11	--
Erythro	C_6H_5	Br	10.0	--
Threo	C_6H_5	Br	5.2	--
Erythro	$(CH_3)_2CH$	CL	9.2	0.95
Threo	$(CH_3)_2CH$	CL	3.7	2.40
Erythro	$(CH_3)_2CH$	Br	10.6	0.85
Threo	$(CH_3)_2CH$	Br	3.5	2.21
Erythro	$(CH_3)_3C$	CL	2.36	2.43
Threo	$(CH_3)_3C$	CL	1.40	2.51
Erythro	$(CH_3)_3C$	Br	2.02	2.66
Threo	$(CH_3)_3C$	Br	1.60	2.50

[a]Approximate conc. 140 mg/ml in CCl_4.

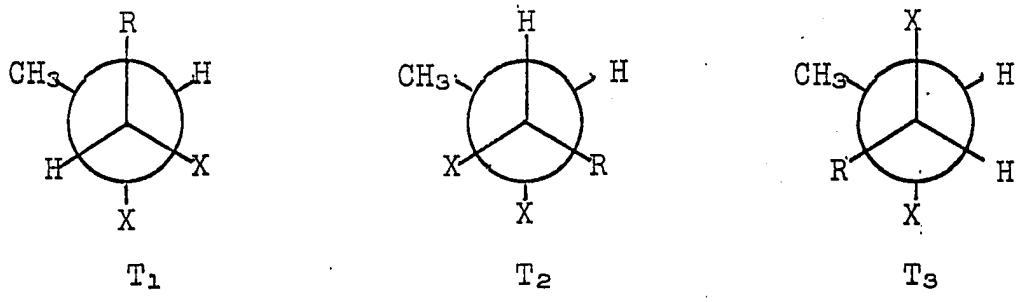
[b]Cyclohexane was used as solvent, $\pm$ 0.05 D.

[c]Dipole moments taken from reference (41).

As the size of the R group is increased from methyl to phenyl to isopropyl for the <u>erythro</u> dibromides,



Erythro Series



Threo Series

Figure 14
Conformations of the 2,3-dihalo-3-substituted propanes.

The coupling constant J_{AB} is seen to increase from 8.81 (R = Methyl) to 10.6 (R = isopropyl). This trend indicates that rotomer E_1 is being populated at the expense of E_2 and E_3. However, when R is <u>t</u>-butyl a discontinuity in the trend occurs. A near minimum coupling constant is observed and conformation E_1 is no longer favored.

In contrast to the erythro series as the bulk of R is increased from methyl to isopropyl in the threo series the data show no obvious trend. However, the combination of dipole moment and NMR data allow an exact identification of the dominant rotomers. For the threo isopropyl and t-butyl dihalides a large dipole moment and a small vicinal coupling constant are observed. Thus, the dominant rotomer must possess gauche protons and gauche halogens. Only rotomer T_2 satisfies these conditions. Similar reasoning leads to the conclusion that conformation E_1 is dominant for the erythro isopropyl dihalides; however, the data do not permit the exact identification of the conformation of the erythro t-butyl dihalides. Both conformations E_2 and E_3 are consistent with the data.

To summarize, for the erythro dihalides conformation E_1 is dominant with the exception of the t-butyl compounds. For the threo dihalides, conformation T_2 is dominant when R is i-propyl or t-butyl and conformation T_3 is dominant when R is methyl. The data for the threo phenyl compound is not definitive; however, conformation T_1 must be significantly populated since a value of 5.2 cps for J_{AB} requires substantial population of a rotomer with trans protons.

The increased population of rotomer T_1 observed upon increasing the bulk of R from methyl to phenyl is easily understood. Apparently the dipole-dipole repulsion between the two bromine atoms in threo 2,3-dibromobutane (R = methyl) is

the dominant factor in determining the conformation. Thus, rotomer T_3 is heavily populated even though this rotomer possesses three gauche interactions. However, when R is phenyl two of the three gauche interactions in rotomer T_3 are increased resulting in a substantial decrease in the energy difference between rotomers T_1 and T_3.

Since the isopropyl and phenyl groups are both large, it was expected that the effect of replacing R with either the phenyl or isopropyl group on the conformational preferences of these diastereomers would be similar. The coupling constants, J_{AB}, obtained for the erythro dibromides when R is phenyl or isopropyl are quite similar. However, the values of J_{AB} obtained for the threo phenyl and isopropyl dibromides (5.2 cps and 3.5 cps respectively) are substantially different, suggesting that conformation T_1 is not as important when R is isopropyl as when R is phenyl. This result indicates that yet another factor other than 1,2-gauche interactions and dipole-dipole interactions is important in determining the preferred conformation of the isopropyl compounds.

The values of J_{BC} (Figure 15) for the erythro and threo isopropyl dibromides were 2.7 cps and 7.6 cps, respectively indicating that rotation about the C_2-C_3 bond is also somewhat restricted. The combination of coupling constant data and dipole-moment data show that the best overall conformation of

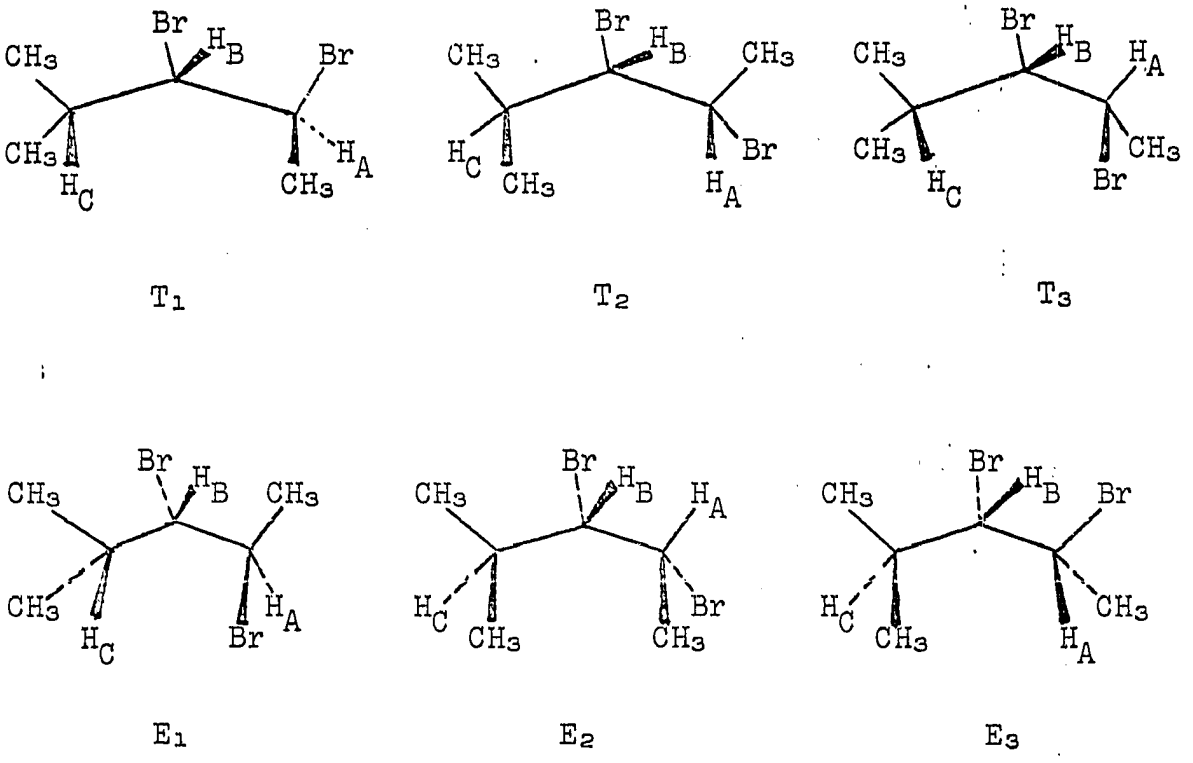


Figure 15
Conformations of threo and erythro
4-methyl-2,3-dibromopentanes.

the threo isopropyl compound is T_2 (Figure 15). It can be seen from an examination of conformation T_3 that a methyl-methyl 1,3 steric interaction would necessarily be present in the threo compound if bromines are placed trans. Such an interaction is extremely unfavorable and conformation T_3 is thus not important. However, it is difficult to understand why conformation T_1 is not significantly populated.

Although the threo t-butyl dibromides and dichlorides are known to exist almost exclusively in conformation T_2 (Figure 16), the data does not allow positive identification

of the favored rotomer of the erythro t-butyl dihalides. Either conformation E_2 or E_3 will satisfy the data; however, it is noted that conformation E_3 involves two unfavorable 1,3 steric interactions and thus conformation E_2 is believed to represent the favored conformation of the erythro t-butyl dihalides.

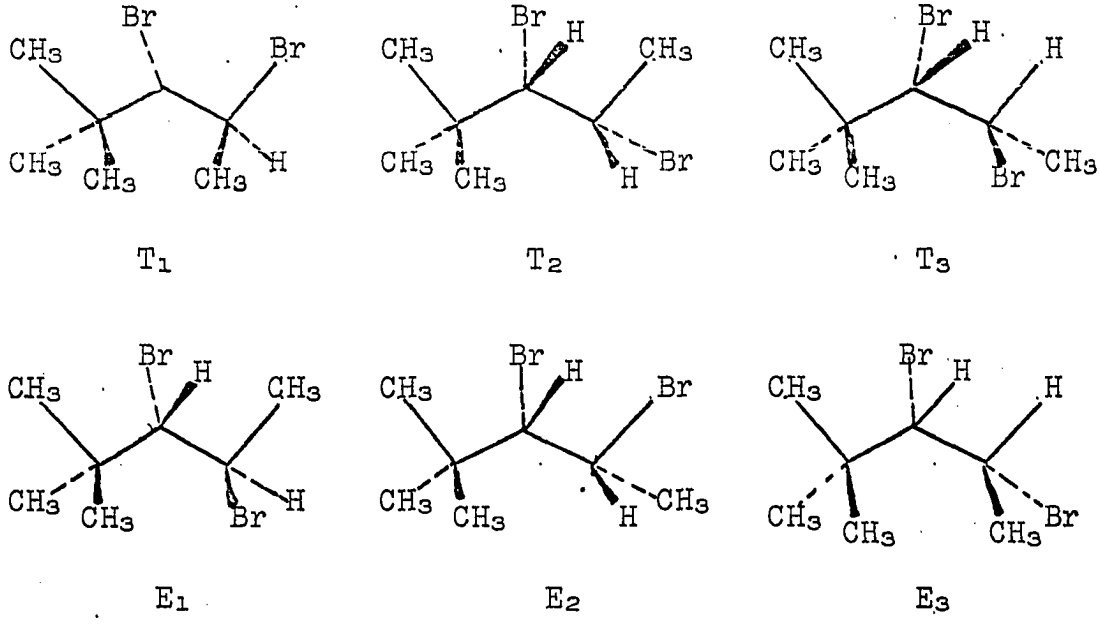


Figure 16
Conformations of threo and erythro
4,4-dimethyl-2,3-dibromopentane.

A reasonable explanation for the lack of conformations T_3 and E_3 may be the large 1,3-steric interactions, which would exist in these rotomers; however, the absence of conformations T_1 and E_1 is baffling.

Angle deformation does not seem to be the reason for the stability of rotomers T_2 and E_2. The C^{13}-H coupling constant

was determined from a neat sample of the erthryo dibromide. This value (152 cps) is very similar to that of bromomethane (150 cps), showing that interorbital angles are probably similar in the two compounds.

The temperature dependence of J_{AB} of the erythro dibromide is quite normal. At 130° J_{AB} increased to 2.3 cps from 2.0 cps showing that rotomer E_1 probably increases in importance.

The possibility that the interaction between bromines is attractive seems unlikely since rotomer T_1 should also be appreciably populated on this basis.

In view of the above findings it appeared desirable to examine the conformational preferences of additional molecules containing the t-butyl group. To this end the dibromides of cis and trans 1-phenyl-3,3-dimethyl-1-butene and the dichlorides of cis and trans di-t-butyl ethylene were prepared.

A mixture containing 75% cis and 25% trans 1-phenyl-3,3-dimethyl-1-butene was prepared by the Wittig reaction of pivalaldehyde with benzyltriphenylphosphonium chloride in DMSO using lithium ethoxide as the base (Chart 1). The pure alkenes were obtained by preparative scale gas phase chromatography. The alkenes were then brominated in carbon tetrachloride and spectral data were obtained on the crude reaction mixtures. The brominations were quite clean and no rearrangement products could be detected.

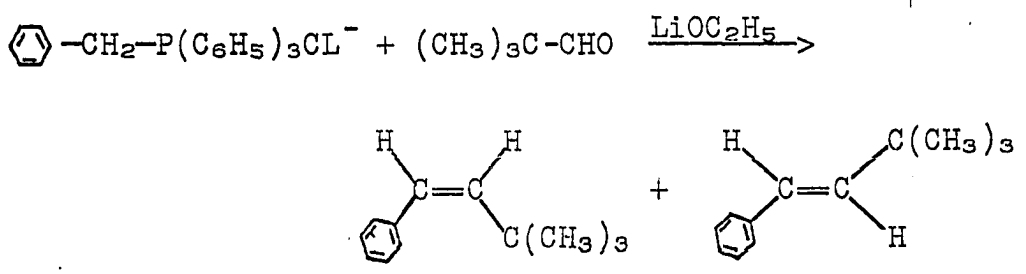


Chart 1
Synthesis of cis and trans
1-phenyl-3,3-dimethyl-1-butene.

The dichlorides of cis and trans di-t-butyl ethylene were prepared and purified by the method of Fahey (33). Since NMR data for the erythro and threo dichlorides were reported by Fahey, only the dipole moments of these compounds were measured.

The synthesis of the cis and trans di-t-butyl ethylene is outlined in Chart 2. The reaction sequence is that of Newman and Puterbaugh (47) but with one modification. The elimination of pinacolone dichloride to t-butyl acetylene involved treatment of the dichloride with potassium hydroxide in an ethanol-mineral oil mixture at elevated temperatures. It was found that this procedure required five to six days at elevated temperatures to obtain a reasonable yield of the acetylene. Further no acetylene was produced until the pot temperature was sufficient to melt the potassium hydroxide

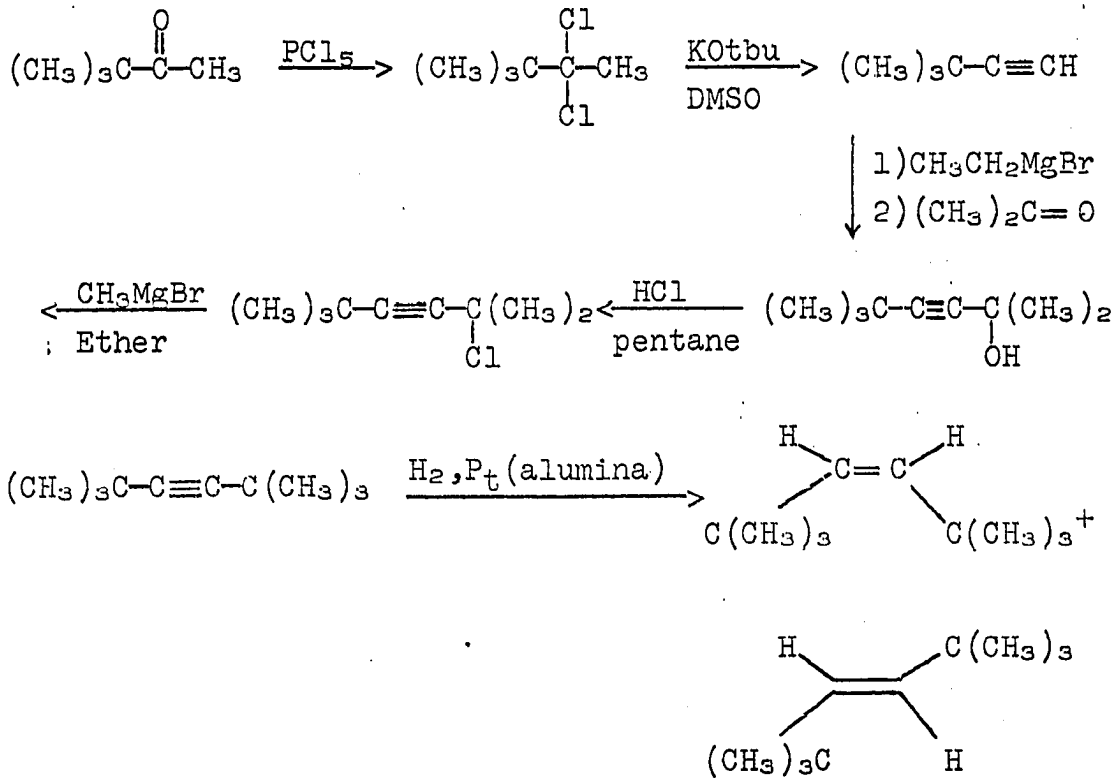


Chart 2
Preparation of cis and trans di-t-butylethylene.

and then the initial evolution of the acetylene from the reaction mixture was nearly uncontrollable.

It was found that the use of potassium t-butoxide in dimethylsulfoxide greatly facilitated the elimination of of pinacalone dichloride to t-butyl acetylene. The evolution of t-butyl acetylene begins at a pot temperature of approximately 60° and can be controlled easily at pot temperatures of 80-100°. Using this procedure t-butyl acetylene may be prepared in 85-90% yields in a period of six to eight hours.

One other step in the synthetic sequence is also quite crucial. The use of methyl magnesium iodide rather than methyl magnesium bromide for the conversion of 2-chloro-2,5,5-trimethyl-3-hexyne to di-t-butyl acetylene results in the formation of 2,2,5,5,6,6,9,9-octamethyldeca-3,7-diyne as the only product isolable in good yield.

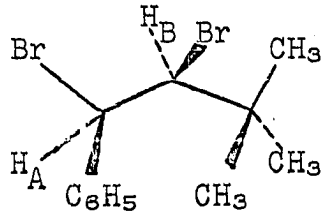
Table 4. Coupling constants and dipole moments of the erythro and threo isomers of 1-phenyl-1,2-dibromo-3,3-dimethylbutane (V); 1,2-diphenyl-3,3-dimethyl-1-cyanobutane (VI); and 2,2,5,5-tetramethyl-3,4-dichlorohexane (VII)

	Compound	Diastereomer	J_{AB}	Dipole-moment Debye[a]
V	C_6H_5-CH(Br)-CH(Br)-$C(CH_3)_3$	Erythro	4.3	---
V	"	Threo	3.3	---
VI	$(CH_3)_3C$-CH(C_6H_5CN)—CH-C_6H_5	Erythro[b]	3.9	---
VI	"	Threo[b]	10.0	---
VII	$(CH_3)_3C$-CH(CL)-CH(CL)-$C(CH_3)_3$	Erythro	5.2	1.9
VII	"	Threo	0.8	2.77

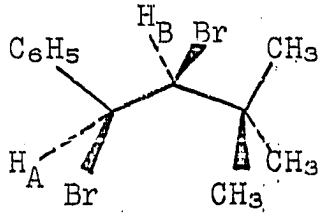
[a]Cyclohexane was used as the solvent for dipole moment measurements.

[b]Data kindly provided by Dr. C. A. Kingsbury.

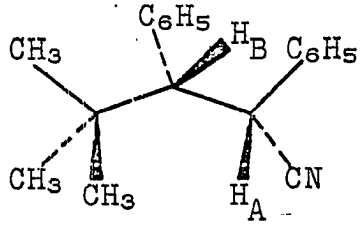
Spectral data for the <u>erythro</u> and <u>threo</u> isomers of 1-phenyl-1,2-dibromo-3,3-dimethylbutane (V); 1,2-diphenyl-3,3-dimethyl-1-cyanobutane (VI); and 2,2,5,5-tetramethyl-3,4-dichlorohexane (VII) are given in Table 4. Flying wedge formulas for the favored conformation of each of these diastereomers is shown in Figure 17.



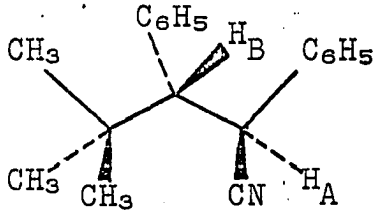
Erythro V



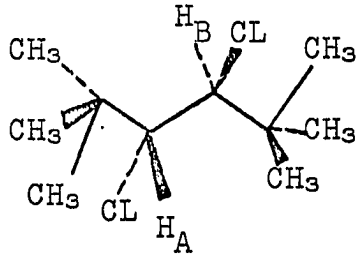
Threo V



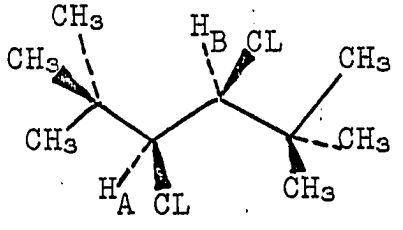
Erythro VI



Threo VI



Erythro VII



Threo VII

Figure 17
Preferred conformations of
diastereomers V, VI, and VII.

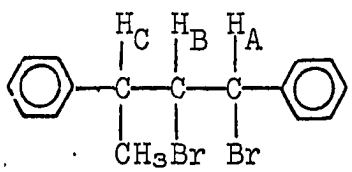
The NMR data indicate that these compounds with the exception of erythro VII exhibit rather strong conformational preferences.

The favored conformations of the threo diastereomers is the one in which the two bulkiest groups are trans. However, of the erythro diastereomers only erythro VI is found to exist almost exclusively in a conformation with bulky groups trans. Erythro V exists in a conformation which possess three large gauche interactions and it is difficult to understand why the conformation which may be obtained by a 60° counter clock-wise rotation about the C_2-C_3 bond (Figure 17) is not favored.

Although the conformation shown in Figure 17 for erythro VII is substantially populated, as the dipole moment data indicate another rotomer which possesses gauche t-butyl groups and gauche chlorines is also highly populated.

An explanation for the observed conformational preferences of erythro V and VII is not obvious, and must involve factors other than those based upon steric considerations.

The conformational preferences of the four diastereomers of 1,2-dibromo-1,3-diphenylbutane VIII were next investigated.



VIII

Figure 18
1,2-dibromo-1,3-diphenylbutane.

These dibromides were prepared by bromination of cis and trans 1,3-diphenyl-1-butene. These olefins were obtained by the Wittig reaction of benzyltriphenylphosphonium chloride with 2-phenyl-propionaldehyde in absolute ethanol using lithium ethoxide as the base.

The crude cis and trans 1,3-diphenyl-1-butenes were separated by spinning band distillation. Unfortunately, the addition of bromine to either cis or trans 1,3-diphenyl-1-butene yielded mixtures of the four possible diastereomeric dibromides (IX, X, XI, XII, Chart 3). Data for the yield of each of the dibromides were obtained by integration of expanded spectra of the crude bromination mixtures. These data are given in Table 5.

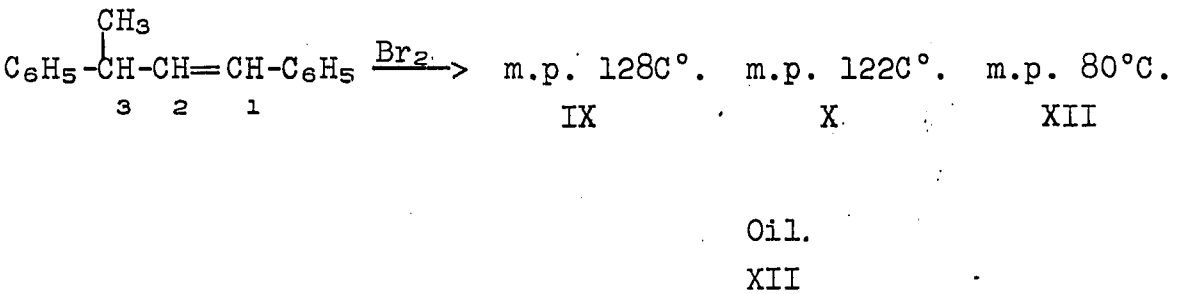


Chart 3
Bromination of 1,3-diphenyl-1-butene.

Three of the four diastereomers were obtained crystalline in agreement with Stoermer and Kootz (53) and will be identified by melting point for the present. The fourth diastereomer, (XII), was an oil, somewhat impure by a mixture with IX and X, which defied all attempted means

of purification. Fortunately, the resonance absorptions of the oil, XII, were fairly well separated from its impurities, IX and X, and the coupling constants and chemical shifts could be accurately determined. These data for XII as well as similar data for IX, X, and XI are listed in Table 6.

Table 5. Relative yields of diastereomers IX-XII from bromination of cis and trans 1,2-dibromo-1,3-diphenylbutane

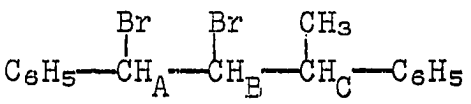
Alkene	Diastereomeric Yield[a]			
	IX	X	XI	XII
cis[b]	17%	41%	25%	17%
trans[c]	40%	39%	17%	5%

[a] ± 4%.

[b] Brominated in carbon tetrachloride solution at 0°, protected from light.

[c] Brominated in carbon disulfide solution at 0°C in diffuse light.

Table 6. NMR coupling constants, chemical shifts and dipole moments for diastereomers IX-XII



Diastereomer	Assignment[a]	m.p.	J_{AB}	J_{BC}	Chemical Shift[b] H_A	H_B	H_C	Dipole moment[c] Debye
IX	EE	128	11.7	2.1	4.60	4.80	4.00	1.30
X	ET	122	11.0	2.8	5.17	4.68	3.90	1.20
XI	TE	80	4.2	8.2	4.90	4.30	3.15	2.55
XII	TT	oil	6.2	6.2	5.15	4.50	3.20	--

[a] Justification for these assignments of configuration is given in the discussion.

[b] Approximately 10-15% solutions in CCl_4 using tetramethylsilane as an internal standard taken as 0 p.p.m. Spectra were recorded on a Varian A-60 spectrometer.

[c] These data are considered good $\pm$ 0.20.

Theoretically two of the diastereomeric dibromides can be visualized as arising by trans addition of bromine to the trans alkene and two by trans addition of bromine to the cis alkene. Thus, if a stereospecifically trans elimination of bromine from each of the four diastereomers was carried out only two of the dibromides would give rise to trans 1,3-diphenyl-1-butene. The two dibromides which give rise to trans alkene would possess the erythro configuration at C-1,2 and the other two dibromides would be threo at C-1,2.

The iodide catalyzed debromination (66) in methanol proved to be stereoselective rather than stereospecific. All four diastereomers yielded trans 1,3-diphenyl-1-butene as the major product. The elimination data are recorded in Table 7.

Table 7. Percent trans 1,3-diphenyl-1-butene obtained from reaction of dibromides IX-XII with potassium iodide in methanol

	Diastereomer			
	IX	X	XI	XII
% trans	100	100	87	67[a]

[a]Corrected for contribution of impurities IX and X.

Although the elimination reaction was stereoselective, it is noteworthy that only dibromides XI and XII gave rise to cis 1,3-diphenyl-1-butene. Since control experiments proved that no cis to trans isomerization of the olefins occurred under the reaction conditions, diastereomers XI and XII are thought to possess the threo configuration at C-1,2. If dibromides XI and XII are threo at C-1,2 then dibromides IX and X are erythro at these centers. These assignments are supported by the NMR and dipole-moment data.

It is apparent from the coupling constant data in Table 6 that diastereomers IX and X are characterized by strong

conformational preferences involving predominantly trans A and B protons and gauche B and C protons.

The dipole moment data for dibromide XI are fairly close to other examples thought to contain gauche bromines (39). The somewhat lower values observed for diastereomers IX and X are taken to indicate trans bromines with the resultant moment being due primarily to the phenyl groups. The assignment of the configuration for diastereomers IX and X at carbons 1 and 2 may now be made (Figure 19).

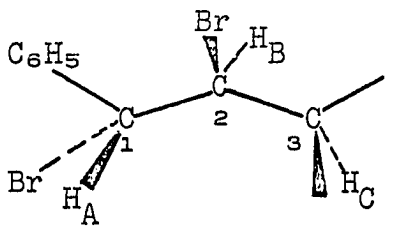


Figure 19
Partial configuration of diastereomers IX and X.

trans Bromines and trans protons A and B define the erythro configuration at C-1,2. Compounds IX and X then differ in configuration at C-3. If dibromides IX and X are erythro at carbons 1 and 2 then dibromides XI and XII must be threo.

As was stated above the dipole moment of dibromide XI is consistent with the presence of gauche bromines at C-1, 2. The observed values of J_{AB} and J_{BC} suggest that protons A and B are gauche while protons B and C bear a trans relationship. These observations support the assignment of the threo configuration at carbons 1 and 2 for dibromide XI.

The configuration of dibromides IX and X at C-2 and C-3 may be tentatively assigned on the basis of the chemical shift of proton H_A. In one diastereomer, models show that H_A is opposite the face of a phenyl group at C-3. In the other diastereomer proton H_A is opposed to a methyl group at C-3 (Figure 20).

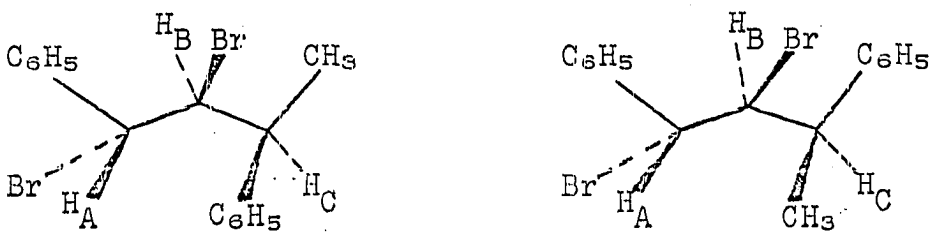


Figure 20
Conformations of diastereomers IX and X.

The former diastereomer should exhibit H_A far upfield compared to the latter diastereomer. Since dibromide IV exhibits the upfield proton (Table 6), it is thought to have the erythro configuration at C-2, 3. Therefore, the configuration of diastereomer IX is erythro at C-1, 2 and erythro at C-2, 3 while the configuration of X is erythro at C-1, 2 and threo at C-2, 3.

The assignment of the configuration at C-2, 3 for diastereomers XI and XII is much less secure. However, if one accepts that 1,3-steric interactions are important in determining the favored conformation of molecules, then the only possible conformations of dibromides XI and XII are TE_1, TE_2, TT, and TT_2 (Figure 21).

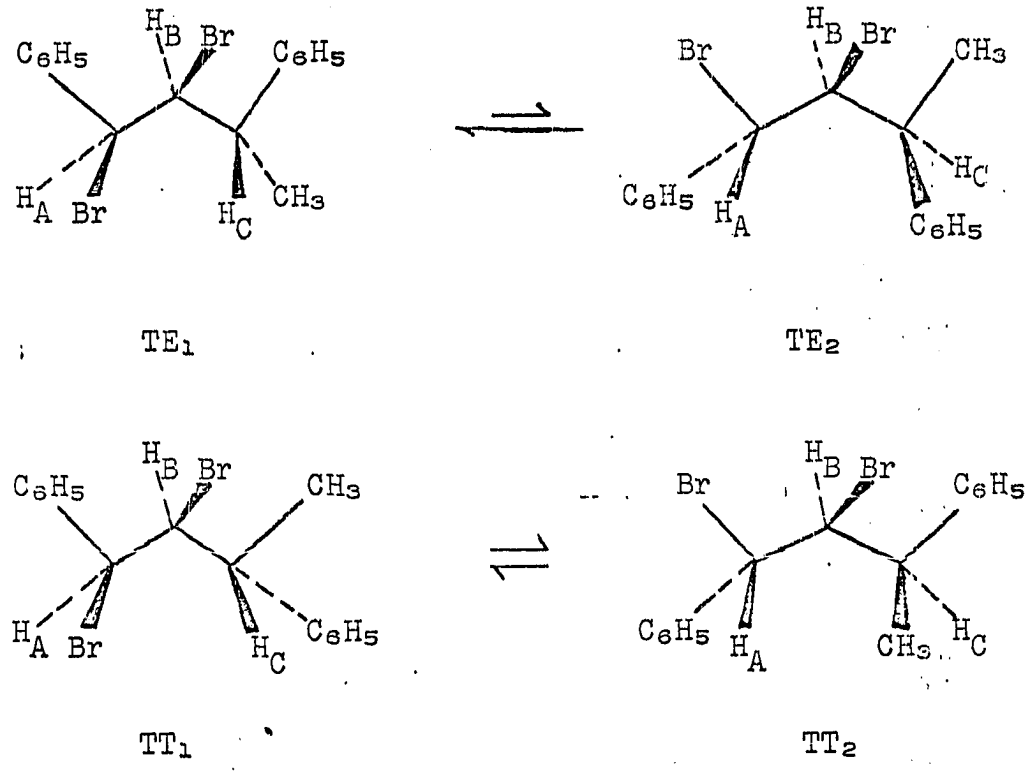


Figure 21
Conformations of diastereomers XI and XII.

Examination of Stuart-Breigleb models of the threo-erythro diastereomer shows that conformation TE_1 is more stable than TE_2 owing to the steric interference of the phenyls at C-1 and C-3 in the latter conformation. For the threo-threo diastereomer, the models indicate that conformations TT_1 and TT_2 are of approximately equal energy with respect to 1,3-steric interactions. Thus it would appear that the threo-erythro diastereomer will be more conformationally pure than the threo-threo diastereomer.

The NMR data in Table 6 shows that diastereomer XI exists to a slight predominance in a conformation in which protons A and B are gauche while protons B and C are trans. Further diastereomer XII exhibits average J values suggesting nearly equal population of two conformations one with J_{AB} large and J_{BC} small and the other with J_{AB} small and J_{BC} large. The latter situation is identical to that expected for the threo-threo diastereomer. Thus, dibromide XI is assigned the threo-erythro configuration and dibromide XII the threo-threo configuration.

The assignment of the configurations of dibromides XI and XII is based upon the assumption that the favored conformations of these dibromides are those in which 1,3-steric interactions are minimized. The validity of this assumption is supported by the known conformations of the 1,3-dihalopropanes (51); α-substituted acetaldehydes (36); 1-substituted 3,3-dimethylbutanes (63); cis 1,3-disubstituted cyclohexanones (1); 2,4-pentanedithiols (45); 2,4-dichloropentanes (51); and 1-substituted-1,2-dibromoethanes (18).

In each of the above studies, the favored conformations were found to be those in which 1,3-steric interactions were minimized.

It is interesting to inquire which of the two steric interactions, 1,2 gauche or 1,3 eclipsing is the dominant factor in determining the favored conformation of these

molecules. It is noted that in both the erythro-erythro and erythro-threo diastereomers the bromines may assume a trans relationship without the advent of appreciable 1,3-eclipsing interactions. This is not the case for the remaining two diastereomers. Any conformation which may be written for either the threo-erythro or threo-threo diastereomers which involves trans bromines must of necessity involve the eclipsing in a 1,3-fashion of groups larger than hydrogen. The dipole moment data for dibromide XI clearly excludes the presence of trans bromines. Thus, the 1,3-eclipsing effects seem to be the dominant factor in determining the favored conformation of these diastereomers.

As mentioned earlier the bromination of either cis or trans 1,3-diphenyl-1-butene produced all four diastereomers IX-XII in unequal yields (Table 5).

Initial attack of the brominating species very likely occurs at C-2, and the resulting benzylic ion is assumed to be an open ion (46). The initial mode of attack determines the stereochemistry at C-2,3. The situation is most clear for the cis 1,3-diphenyl-1-butene. This olefin exists almost exclusively in a conformation with the methine proton eclipsed with the double bond as is shown by the large methine-vinyl proton J value (11 cps).

The less sterically hindered trans alkene may accommodate other groups eclipsed with the double bond (10).

The stereochemistry of attack on the cis alkene is illustrated in Chart 4.

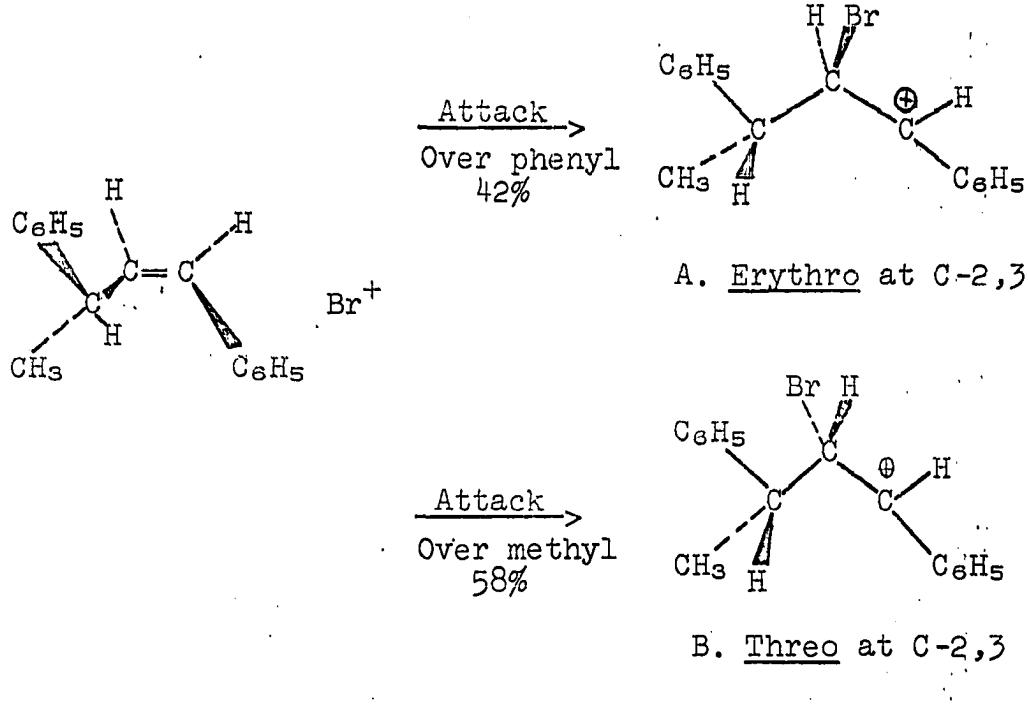


Chart 4
Model for bromination of cis 1,3-diphenyl-1-butene.

As shown, attack of the brominating species over phenyl gives the erythro ion A in 42% yield (sum of IX and XI), whereas the somewhat preferred attack over methyl gives the threo ion B in 58% yield (sum of X and XII). Although the difference in yields is not large, it is consistent with this model.

Initial attack on the trans alkene (Chart V) yields the threo ion C in 44% yield (sum of X and XII) and the erythro ion D in 56% yield (sum of IX and XI). Predominant attack over hydrogen on a conformation with methyl eclipsed with the

double bond seems attractive.

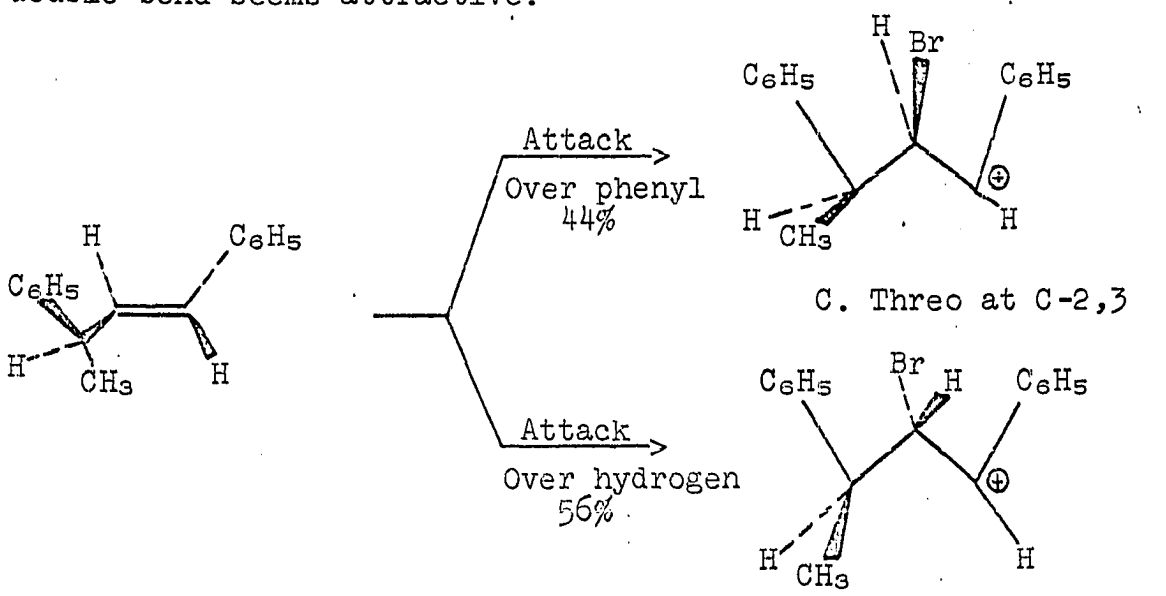


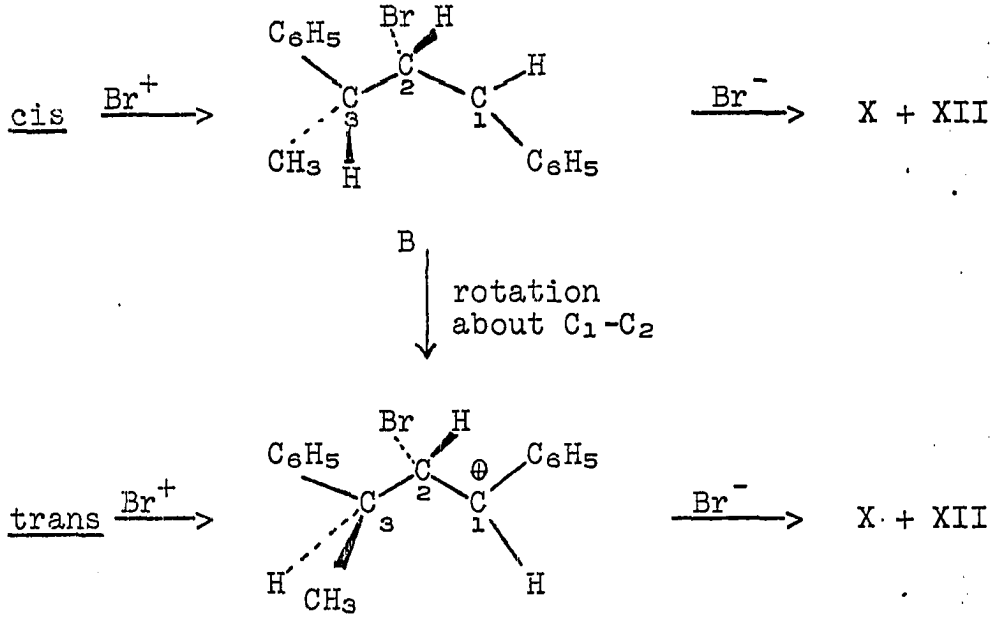
Chart 5
Model for bromination of trans 1,3-diphenyl-1-butene.

Completion of the reaction sequence involves attack by bromide ion at C-1 on the ions A-D after varying amounts of rotation have occurred. The stereochemistry at C-1,2 is determined in this reaction.

The intermediate ions of threo configuration at C-2,3 (B and C) will be considered first. The yield of product, X, of erythro configuration at C-1,2 derived from ions B and C is larger than that of the threo configuration (XII). Furthermore, the yields are similar beginning with ether the cis olefin (71% X, 29% XII) or the trans olefin (89% X, 11% XII).

It seems likely that a common intermediate exists in the bromination of either the cis or trans olefin. The highly hindered ion B formed initially from the cis olefin probably rotates to the sterically less crowded ion C before attack by bromide ion occurs. Although some capture of ion B probably occurs so that the yields of products X and XII are not quite the same from the cis and trans alkenes.

The predominant mode of attack by bromide ion on C occurs from the opposite side of the molecule from the bromine at C-2, to yield the erythro isomer X. Whether or not there is some bridging by the bromine at C-2 is not known; however, some bridging seems likely. The sequence is summarized in Chart 6.



C Threo at C-2,3

Chart 6

Model for bromination of cis and trans 1,3-diphenyl-1-butene.

Ions A and D possess the erythro configuration at C-2,3 and it appears that ion A does not rotate to ion D appreciably before attack by bromide ion occurs at C-1 (Chart 7). The product of threo configuration at C-1,2, XI, predominates (60% XI, 40% IX) when the cis olefin is the starting material, whereas the erythro product, IX, predominates (70% IX, 30% XI) when the trans olefin is the precursor.

Beginning with the trans alkene, initial attack of the brominating species yields the sterically unhindered ion D (Chart 7). Again the bromine at C-2 may form the bridged species in part. The predominant product arises from attack by bromide ion on ion D. This attack occurs preferentially from the side of ion D remote from the bromine at C-2 to yield IX.

Beginning with the cis alkene ion A is formed which shows severe steric crowding. However, rotation from ion A to ion D apparently does not occur readily. This is no doubt partially due to the fact that ion A cannot rotate into ion D without the breaking of overlap between the p orbital at C-1 and the aromatic group.

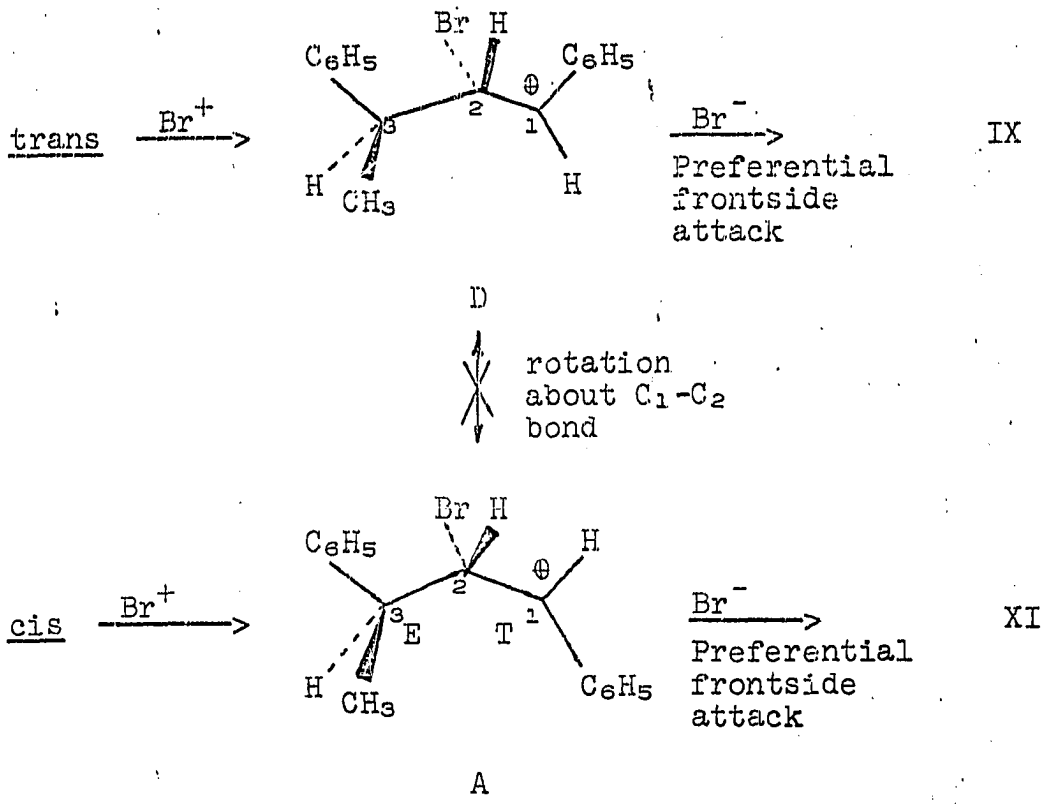


Chart 7
Model for bromination of cis and trans 1,3-diphenyl-1-butene.

The rates of the iodide catalyzed elimination of bromine from the erythro and threo isomers of 4-methyl-2,3-dibromopentane and 4,4-dimethyl-2,3-dibromopentane were next investigated.

The iodide catalyzed elimination of bromine from vicinal dibromides is a well known reaction. Kinetic studies on the reaction have been reported by several groups of workers (58)(59)(60)(29)(34). The reaction follows overall second order kinetics, first order in iodide ion and first order in dibromide. Two mechanisms have been established for the reaction. Mechanism A (Chart 8) involves nucleophilic attack by iodide ion on bromine and results in an overall trans elimination of bromine. Mechanism B involves a rate determining SN2 reaction by iodide ion on the dibromide followed by elimination. Mechanism B thus involves an overall cis elimination

The latter mechanism has been established as the major pathway of elimination for 1,2-dibromo-1,2-dideuterioethane, 1,2-dibromopropane and 1,2-dibromobutane (3).

Mechanism A has been established as the predominant pathway of elimination for the erythro and threo isomers of 2,3-dibromobutane; 2,3-dibromopentane; 3,4-dibromohexane; 4,5-dibromooctanes and the dibromides of fumeric and maleic acids (67).

The rates of the iodide catalyzed elimination of bromine from the erythro and threo isomers of 4-methyl-2,3-dibromopentane and 4,4-dimethyl-2,3-dibromopentane were next investigated.

The iodide catalyzed elimination of bromine from vicinal dibromides is a well known reaction. Kinetic studies on the reaction have been reported by several groups of workers (58)(59)(60)(29)(34). The reaction follows overall second order kinetics, first order in iodide ion and first order in dibromide. Two mechanisms have been established for the reaction. Mechanism A (Chart 8) invclves nucleophilic attack by iodide ion on bromine and results in an overall trans elimination of bromine. Mechanism B involves a rate determining SN2 reaction by iodide ion on the dibromide followed by elimination. Mechanism B thus involves an overall cis elimination

The latter mechanism has been established as the major pathway of elimination for 1,2-dibromo-1,2-dideuterioethane, 1,2-dibromopropane and 1,2-dibromobutane (3).

Mechanism A has been established as the predominant pathway of elimination for the erythro and threo isomers of 2,3-dibromobutane; 2,3-dibromopentane; 3,4-dibromohexane; 4,5-dibromooctanes and the dibromides of fumeric and maleic acids (67).

8). The eliminations were followed by titration of the iodine produced in the reaction (Chart 9) with sodium thiosulfate. Rate constants were calculated using the rate

$$R\text{—}CH\text{—}CH\text{—}R' + I^- \longrightarrow R\text{—}CH{=}CH\text{—}R' + IBr + Br^-$$

$$IBr + I^- \longrightarrow I_2 + Br^-$$

Chart 9. Iodide catalyzed elimination reaction.

equation of Dillon, Lucas and Young (29) in which t is the

$$kt = \frac{2,303}{a-b} \operatorname{Log}_{10}\left[\frac{1 - \frac{2b\phi}{a}}{(1-\phi)}\right]$$

time in seconds, ϕ is the fraction of total dibromide which has reacted at time t, and a and b are the initial concentrations of potassium iodide and dibromide respectively in moles per liter at 20°C.

Table 8. Second order rates for the iodide catalyzed elimination of bromine from the erythro and threo isomers of 4-methyl and 4,4-dimethyl 2,3-dibromopentane

Compound	Diastereomer	Temp. °C	k_2[a,b] l.mole^{-1} sec^{-1}
$CH_3-\underset{Br}{\underset{\mid}{C}}H-\underset{Br}{\underset{\mid}{C}}H-CH(CH_3)_2$	erythro	60	7.8×10^{-6}
$CH_3-\underset{Br}{\underset{\mid}{C}}H-\underset{Br}{\underset{\mid}{C}}H-CH(CH_3)_2$	threo	60	1.89×10^{-6}
$CH_3-\underset{Br}{\underset{\mid}{C}}H-\underset{Br}{\underset{\mid}{C}}H-C(CH_3)_3$	erythro	60	3.89×10^{-5}
$CH_3-\underset{Br}{\underset{\mid}{C}}H-\underset{Br}{\underset{\mid}{C}}H-C(CH_3)_3$	threo	60	2.53×10^{-6}

[a]Average of two runs.

[b]The rates of elimination have been increased by 4.8% to correct for solvent expansion.

Plots of log $\frac{(1 - \frac{2b\emptyset}{a})}{(1-\emptyset)}$ vs. time were found to exhibit some curvature due to the fact that some of the iodine produced in the reaction is being consumed by a side reaction. This same problem was encountered by Dillon, Young and Lucas (29).

The rates of elimination of erythro diastereomers were found to be faster than the corresponding dibromides with the threo configuration. This trend was also observed by Young (69) and Winstein (67) in studies of the rates of elimination of the erythro and threo isomers of 2,3-dibromobutane; 3,4-dibromopentane; 3,4-dibromohexane; and 4,5-dibromooctane (Table 9). An erythro to threo rate ratio of approximately two is observed for the pairs of diastereomers.

Table 9. Rates of iodide catalyzed elimination of some *erythro* and *threo* dibromides

Dibromide	Diastereomer	k_2[c] $l.mole^{-1}\ sec^{-1}$
$CH_3\underset{Br}{\underset{\vert}{C}}H\underset{Br}{\underset{\vert}{C}}H-CH_3$	erythro[a]	2.5×10^{-6}
$CH_3\underset{Br}{\underset{\vert}{C}}H\underset{Br}{\underset{\vert}{C}}H-CH_3$	threo[a]	1.3×10^{-6}
$CH_3\underset{Br}{\underset{\vert}{C}}H-\underset{Br}{\underset{\vert}{C}}H-CH_2CH_3$	erythro[b]	2.66×10^{-6}
$CH_3\underset{Br}{\underset{\vert}{C}}H-\underset{Br}{\underset{\vert}{C}}H-CH_2CH_3$	threo[b]	1.57×10^{-6}
$CH_3CH_2\underset{Br}{\underset{\vert}{C}}H-\underset{Br}{\underset{\vert}{C}}H-CH_2CH_3$	erythro[b]	3.99×10^{-6}
$CH_3CH_2\underset{Br}{\underset{\vert}{C}}H-\underset{Br}{\underset{\vert}{C}}H-CH_2CH_3$	threo[b]	1.41×10^{-6}
$CH_3(CH_2)_2\underset{Br}{\underset{\vert}{C}}H-\underset{Br}{\underset{\vert}{C}}H(CH_2)_2CH_3$	erythro[b]	3.76×10^{-6}
$CH_3(CH_2)_2\underset{Br}{\underset{\vert}{C}}H-\underset{Br}{\underset{\vert}{C}}H(CH_2)_2CH_3$	threo[b]	3.05×10^{-6}

[a]Data from reference (66).

[b]Data from reference (67).

[c]Rates increased by 4.8% to correct for solvent expansion.

An *erythro* to *threo* rate ratio of approximately four is observed for the 4-methyl-2,3-dibromopentanes while an *erythro* to *threo* ratio of c.a. ten is observed for the 4,4-dimethyl-2,3-dibromopentanes. The slightly enhanced rate of the *erythro* 4,4-

dimethyl-2,3-dibromopentane is most reasonably attributed to steric acceleration of elimination.

The rates of elimination of the 4-methyl and 4,4-dimethyl-2,3-dibromopentanes corroborate the Curtin-Hammett principle (30).

EXPERIMENTAL

Instruments and Methods

All temperatures reported in this dissertation are in centigrade degrees. All melting points (m.p.) and boiling points (b.p.) are uncorrected and pressures are given in millimeters (mm.) of mercury unless otherwise stated.

All nuclear magnetic resonance (nmr) spectra were recorded on either a Varian Associates HR-60 or A-60 spectrometer. Tetramethylsilane was used exclusively as an internal standard. The chemical shifts are reported in parts per million (p.p.m.), (δ) units.

Infrared spectra (IR) were recorded on either a Perkin-Elmer model 21 or Infra-Cord spectrometer. All absorptions are given in reciprocal centimeters ($cm.^{-1}$).

All carbon-hydrogen analyses were performed by Galbraith Laboratories, Inc.

All vapor phase chromatography measurements were made on an Aerograph Model A-90-P instrument.

Preparation of Materials

Threo 2-phenyl-4-methyl-3-pentanol

Threo 2-phenyl-4-methyl-3-pentanol was prepared by the addition of 2-propyl magnesium bromide to 2-phenylpropionaldehyde according to the procedure described by J. Sicher (54).

A solution of 2-phenylpropionaldehyde (16.75 gm., 0.125

mole) in one hundred ml. of anhydrous ether was added dropwise to the Grignard reagent prepared from magnesium (4.0 gm., 0.166 moles) and 2-bromopropane (20.42 gm., 0.166 mole). After the addition was complete, the reaction mixture was stirred for an additional two hours at gentle reflux. The reaction mixture was allowed to cool to room temperature and then poured over ice covered with a thin layer of ammonium chloride. After the ice had melted, the reaction mixture was acidified with cold dilute hydrochloric acid and extracted with ether. The organic material was washed with water dried over anhydrous magnesium sulfate, filtered and concentrated by rotary evaporation. The threo alcohol was purified by preparative scale vapor-phase chromatography (5 ft. x 0.75 inch column of 20% LAC-446 on HMDS treated chromosorb at 175°).

Threo 2-phenyl-4-methyl-3-pentanol, oil. Nmr: CCl_4; 0.85 (doublet), 0.88 (doublet, 1.47 (multiplet), 1.76 (singlet), 2.77 (quintet 7 cps spacing), 3.26 (doublet 6.6 cps spacing), 3.35 (doublet 6.6 cps spacing), 7.12 (singlet).

2-Phenyl-4-methyl-3-pentanone

The 2-phenyl-4-methyl-3-pentanone was prepared by oxidation of crude threo 2-phenyl-4-methyl-3-pentanol with Jones reagent (15).

Jones reagent was added dropwise to a rapidly stirring solution of threo 2-phenyl-4-methyl-3-pentanol (5.0 gm.) in acetone (50 ml.). The oxidation was conducted at zero degrees

and sufficient Jones reagent was added until the red color of the reagent persisted in the reaction mixture. The reaction mixture was poured into a separatory funnel and sufficient water was added to dissolve all the chromium salts. The aqueous solution was extracted with ether. The organic material was washed with water, dried over anhydrous magnesium sulfate, filtered, and concentrated by rotary evaporation. The remaining oil was dissolved in carbon-tetrachloride and again concentrated by rotary evaporation. The oil was taken up in a small volume of fresh carbon-tetrachloride and an nmr of the crude ketone was recorded.

2-Phenyl-4-methyl-3-pentanone Nmr: CCl_4; 0.85 (doublet), 1.02 (doublet), 1.32 (doublet 7 cps spacing), 2.60 (quintet), 3.83 (quartet), 7.14 (singlet).

Erythro-2-phenyl-4-methyl-3-pentanol

Erythro-2-phenyl-4-methyl-3-pentanol was prepared by the reduction of 2-phenyl-4-methyl-3-pentanone with lithium aluminum tri-t-butoxyhydride.

The 2-phenyl-4-methyl-3-pentanone (0.012 mole) was dissolved in 50 ml. of anhydrous tetrahydrofuran (THF) and added dropwise to a rapidly stirring suspension of lithium aluminum tri-t-butoxyhydride (4.55 gm., 0.018 mole) in 50 ml. of anhydrous THF. The reaction mixture was gently refluxed for four hours and then cooled to zero degrees. A saturated solution of potassium carbonate was added dropwise to decompose

excess hydride. The reaction mixture was poured over ice covered with a thin layer of ammonium chloride and acidified with cold dilute hydrochloric acid solution. The reaction mixture was then extracted with ether. The organic material was washed with water, dried over anhydrous magnesium sulfate, filtered and concentrated by rotary evaporation. The erythro alcohol was purified by preparative scale vapor phase chromatography (5 ft. x 0.75 in. column of 20% LAC-446 on HMDS treated chromosorb w at 175C°).

Erythro 2-phenyl-4-methyl-3-pentanol, oil Nmr: CCl_4; 0.87 (doublet), 0.98 (doublet), 1.20 (doublet), 1.32 (singlet), 1.67 (multiplet), 2.75 (quintet), 3.27 (doublet 7.35 cps spacing), 3.33 (doublet 7.35 cps spacing), 7.15 (singlet).

Acetates of erythro and threo 2-phenyl-4-methyl-3-pentanol

One gram of the diastereomerically pure alcohol was dissolved in anhydrous ether and pyridine (4 ml.) was added. The reaction mixture was cooled to zero degrees and a solution of acetyl chloride (0.5 ml.) dissolved in anhydrous ether (20 ml.) was added dropwise to the rapidly stirring mixture. The reaction was maintained at zero degrees for three hours and then stirred for an additional three hours at room temperature and then poured over ice and extracted with ether. The organic material was separated and washed twice with a cold ten percent sulfuric acid solution then twice with water and finally dried over anhydrous magnesium

sulfate. After filtering, the organic material was concentrated by rotary evaporation. The resulting acetates were purified by preparatory scale vapor phase chromatography (5 ft. x 0.75 in. column 20% QF-1 on HMDS treated Chromosorb W at 170C°).

Acetate of threo 2-phenyl-4-methyl-3-pentanol, oil

Nmr: CCl_4; 1.30 (doublet), 1.32 (doublet), 1.17 (doublet), 1.98 (singlet), 2.80 (quartet), 2.96 (quartet), 4.95 (doublet 9.4 cps spacing), 5.02 (doublet 9.4 cps spacing), 7.15 (singlet).

Acetate of erythro 2-phenyl-4-methyl-3-pentanol Nmr: CCl_4; 1.87 (doublet), 1.20 (doublet), 1.77 (singlet), 2.93 (quintet), 4.85 (doublet 7.0 cps spacing), 4.95 (doublet 7.0 cps spacing), 7.12 (singlet).

1,2-Diphenylpropane

The alkane was prepared from 2-phenylpropylphenone using the Huang-Minlon modification of the Wolff-Kishner reduction.

In a 250 ml. round bottom flask were placed 2-phenylpropylphenone (8.0 gm., 0.038 mole), 100 ml. of diethyleneglycol, hydrazine hydrate (3.8 gm., 0.076 mole) and potassium hydroxide (6.5 gm.). The mixture was refluxed for one hour and then the water and excess hydrazine was distilled from the solution. The pot temperature was then raised to 190C° and maintained for five hours. The reaction mixture was allowed to cool to room temperature and then poured over ice

and acidified with dilute hydrochloric acid. Ether was added and the organic phase was separated, washed four times with water, dried over anhydrous magnesium sulfate and concentrated by rotary evaporation. The resulting oil was passed through alumina (25 gm. activity grade 1) using Skellysolve "B" as the eluent. After concentration, the resulting oil was vacuum distilled. The fraction distilling between 88-91C° at 0.25 mm. was collected yielding 2.03 gm. 26.8% of the desired alkane.

1,2-Diphenylpropane, b.p. 90C° (0.25 mm.) Lit. 166-67 C° (28 mm.) (6). Nmr: CCl_4; 1.17 (doublet), 2.53-3.15 (multiplet, 6.9-7.33 (multiplet), 7.05 (singlet).

1-(p-methoxyphenyl)-2-phenylpropane

The 1-(p-methoxyphenyl)-2-phenylpropane was prepared by Wolff-Kishner reduction of p-methoxyphenyl-2-phenylethyl ketone. The experimental procedure was identified to that described for the preparation of 1,2-diphenylpropane.

1-(p-methoxyphenyl)-2-phenylpropane b.p. 117-120C° (0.1 mm). Nmr: CCl_4; 1.19 (doublet), 2.75 (center of multiplet), 3.58 (singlet), 6.6 (doublet of A_2B_2 pattern 9 cps spacing), 6.85(doublet of A_2B_2 pattern 9 cps spacing), 7.06 (singlet).

Reaction of 1-(p-methoxyphenyl)-propane and 1,2-diphenyl-propane with N-bromosuccinimide

The appropriate hydrocarbon (2.0 gms.) and dibenzoyl

peroxide (100 mg.) was dissolved in carbon tetrachloride (20 ml.). The reaction mixture was stirred magnetically and maintained at gentle reflux for four hours and then cooled to zero degrees and filtered to remove the succinimide. The filtrate was washed with water, dried over anhydrous magnesium sulfate, filtered, and then concentrated to a volume of about five ml. by rotary evaporation. An nmr spectrum of the concentrated carbon tetrachloride solution was recorded. The products observed were erythro and threo 1,2-diphenyl-1-bromopropane; 1,2-diphenyl-2-bromopropane; 1,2-dibromo-1,2-diphenylpropane; and a trace of 1,2-diphenylpropene. These products were identified by comparison of the nmr spectrum of the crude reaction mixture with nmr spectra of authentic samples of the suspected products.

The major products observed from the reaction of both hydrocarbons with N-bromosuccinimide were the erythro and threo 1,2-diphenyl-1-bromo propanes and 1,2-diphenyl-2-bromopropanes. The product distribution of the monobromination products derived from 1,2-diphenylpropane and 1-(p-methoxyphenyl)-2-phenylpropane is recorded in Table 14.

Table 14. Distribution of monobromination products obtained upon bromination of 1,2-diphenylpropane and 1-(p-methoxyphenyl)-2-phenylpropane

Hydrocarbon	%Tertiary bromide	%Secondary bromide	%erythro	%threo
$C_6H_5-\underset{\displaystyle CH_3}{\underset{\vert}{CH}}-CH_2C_6H_5$	49	51	41	59
$C_6H_5-\underset{\displaystyle CH_3}{\underset{\vert}{CH}}CH_2-C_6H_4-OCH_3$	17	83	53	47

1,2-Diphenyl-2-propanol

The alcohol was prepared by reaction of acetophenone with benzyl magnesium chloride.

Acetophenone (0.2 mole) dissolved in anhydrous ether (100 ml.) was added dropwise to the Grignard reagent prepared from benzylchloride (0.2 mole) and magnesium (4.8 gm. 0.2 mole) in anhydrous ether (500 ml.). The reaction mixture was stirred for two hours at room temperature after the addition was complete and then poured over ice covered with a layer of ammonium chloride. The pH of the reaction mixture was adjusted to approximately 7.5 by the addition of cold dilute hydrochloric acid. The ether layer was separated and washed with water, dried over anhydrous magnesium sulfate, filtered, and concentrated by rotary evaporation. The resulting oil was vacuum distilled. The fraction distilling between 122-24C°

(0.2 mm) was collected and crystallized upon standing. The alcohol was further purified by recrystallization from pentane.

1,2-Diphenyl-2-propanol b.p. 122-124C° (0.2mm); m.p. 48-9 C°, lit. 50-51C° (7); Nmr: CCl_4; 1.43 (singlet), 1.78 (singlet), 2.82 (doublet of AB pattern, 12 cps spacing), 3.08 (doublet of AB pattern, 12 cps spacing), 6.77-7.47 (multiplet).

1,2-Diphenyl-2-propylbromide

The bromide was prepared by reaction of 1,2-diphenyl-2-propanol with anhydrous hydrogen bromide in pentane.

Anhydrous hydrogen bromide was bubbled into a rapidly stirring solution of 1,2-diphenyl-2-propanol (2.0 gms.) in olefin free pentane (150 ml.) at zero degrees. The reaction was stirred at zero degrees for two hours and then the reaction mixture was poured into ice water. The pentane layer was separated, washed with water, dried over anhydrous magnesium sulfate, filtered, and concentrated by rotary evaporation. The resulting oil was taken up in carbon-tetrachloride and again the solvent was removed by rotary evaporation. The oil was then taken up five ml. of fresh carbon-tetrachloride and an nmr spectrum of a portion of the solution was recorded.

1,2-Diphenyl-2-propylbromide, oil Oil gave instantaneous precipitate with ethanolic silver nitrate. Nmr: CCl_4: 1.98 (doublet, 3.52 (singlet), 6.65-7.52 (multiplet.

2,3-Dihalo-4-4-methylpentanes and 2,3-dihalo-4,4-dimethyl-pentanes

The dichlorides and dibromides were prepared by addition of the appropriate halogen to cis and trans 4-methyl-2-pentene and 4,4-dimethyl-2-pentene. These alkenes were obtained from Columbia Organic Chemical Company. The basic procedure was a modification of that of Lucas, Simpson, and Carter (40).

The apparatus consisted of a 250 ml, three-necked flask fitted with an addition funnel, a mercury-sealed stirrer, and a glass tube leading to a gas trap which contained sodium thiosulfate solution. The reaction flask was protected from light.

A solution of trans-4-methyl-2-pentene (10.0 gm., 0.119 mole) dissolved in pentane (50 ml.) was placed in the reaction flask.

To this solution, cooled to -50°C and under nitrogen, a solution of bromine (18.2 gm., 0.115 mole) in pentane (75 ml.) was added dropwise with stirring. After the bromine color had disappeared, the reaction mixture was poured over ice. The organic material was separated and washed with cold, dilute sodium thiosulfate solution and then three times with water. After drying over anhydrous magnesium sulfate, the organic material was filtered and the pentane was evaporated yielding an oil. The crude dibromide was vacuum distilled and the fraction distilling from 49C° to 52C° (1.9 mm.), 20.7 gm., was used for spectral purposes.

The chlorinations were similar to the brominations except that a gas inlet tube was used. Chlorine was introduced periodically until the yellow color persisted for twenty minutes.

Erythro 2,3-dibromo-4-methylpentane b.p. 49-52°C (1.9 mm.). Nmr: CCl_4; 0.93 (doublet 7 cps spacing), 1.05 (doublet 7 cps spacing), 1.92 (doublet 7 cps spacing), 2.42 (multiplet), 4.05 (doublet doublet), 4.38 (multiplet).

Threo-2,3-dibromo-4-methylpentane b.p. 47-49°C (1.1 mm.). Nmr: CCl_4; 1.06 (doublet), 1.13 (doublet), 1.77 (doublet), 2.08 (multiplet), 3.74 (double doublet), 4.3 (double quartet).

Erythro-2,3-dichloro-4-methylpentane b.p. 23°C (0.7 mm.). Nmr CCl_4; 0.95 (doublet), 1.05 (doublet), 1.67 (doublet, 2.50 (multiplet), 3.78 (double doublet), 4.16 (double quartet).

Threo 2,3-dichloro-4-methylpentane b.p. 37°C (1.7 mm.). Nmr: CCl_4; 1.04 (doublet), 1.09 (doublet), 1.60 (doublet), 2.16 (multiplet), 3.64 (double doublet), 4.32 (double quartet).

Erythro 2,3-dibromo-4,4-dimethylpentane b.p. 66°C (1.2 mm.). Nmr: CCl_4; 1.13 (singlet), 1.79 (doublet), 4.32 (doublet), 4.52 (double quartet).

Threo 2,3-dibromo-4,4-dimethylpentane b.p. 66-7°C (1.3 mm.). Nmr: CCl_4; 1.16 (singlet), 1.80 (doublet), 3.90

(doublet), 4.46 (double quartet).

Erythro 2,3-dichloro-4,4-dimethylpentane b.p. 40°C (1.6 mm.). Nmr: CCl_4; 1.10 (singlet), 1.61 (doublet), 4.11 (doublet, 4.5 (double quartet).

Threo 2,3-dichloro-4,4-dimethylpentane b.p. 53°C (2.5 mm.). Nmr: CCl_4, 1.13 (singlet), 1.62 (doublet), 3.73 (doublet), 4.47 (double quartet).

Dipole Moment Measurements

The basic technique was that described by Weissburger (62). Dielectric constants were measured with a transistorized heterodyne beat apparatus which was built by R. W. King and J. G. Verkade and will be described in a future publication by these authors. Dipole moments were calculated from the dielectric constants by utilizing the following relations (56) where μ = dipole moment in Debye units (D),

$$\mu = \frac{(9kTP_t)0.5}{4N\pi}$$

$$P_t = \frac{3(MW)}{d(\epsilon t2)^2} \left[\frac{\partial \epsilon}{\partial X} - 2\, N\infty \frac{\partial N}{\partial X}\right]$$

P_t = total molar polarizability, d = density of solvent, ϵ = observed dielectric constant, $\frac{\partial \epsilon}{X}$ = slope of plot of ϵ vs. mole fraction, MW = molecular weight of solvent, k = Boltzmann's constant, T = temperature in degrees Kelvin, N = Avogadro's number.

The slope of the straight line obtained by plotting the observed dielectric constant vs. mole fraction of solute. A least-squares analysis by computer techniques was applied to each set of data. Since $\partial N/\partial \chi$ is very small, the quantity of $2 N \infty \partial N/\partial \chi$ makes a negligible contribution to P_t and was therefore neglected.

Table 15. Dipole moments at 20°C in cyclohexane

Compound	μ (Debye)
Erythro 4-methyl-2,3-dibromopentane	0.82
Threo 4-methyl-2,3-dibromopentane	2.28
Erythro 4-methyl-2,3-dichloropentane	0.95
Threo 4-methyl-2,3-dichloropentane	2.41
Erythro 4,4-dimethyl-2,3-dibromopentane	2.66
Threo 4,4-dimethyl-2,3-dibromopentane	2.50
Erythro 4,4-dimethyl-2,3-dichloropentane	2.43
Threo 4,4-dimethyl-2,3-dichloropentane	2.51
Erythro 2,2,5,5-tetramethyl-3,4-dichlorohexane	1.98
Threo 2,2,5,5-tetramethyl-3,4-dichlorohexane	2.77
1,3-Diphenyl-1,2-dibromobutane (m.p. 129)	1.30
1,3-Diphenyl-1,2-dibromobutane (m.p. 122)	1.20
1,3-Diphenyl-1,2-dibromobutane (m.p. 78-80)	2.55

Triphenylbenzylphosphonium chloride

Triphenyl phosphine (100 gm., 0.382 mole) was placed in a one liter three-necked round bottom flask. A solution of benzyl chloride (48.5 gm., 0.382 mole) in xylene (300 ml.) was added and the mixture was stirred at reflux temperature overnight. The white salt was collected by filtration, washed with pentane and dried in a vacuum oven at 60°C for five hours; yield, 128 gm. (86.5%).

1-Phenyl-3,3-dimethyl-1-butenes

These alkenes were prepared by the Wittig reaction of 2,2-dimethylpropionaldehyde (pivaldehyde) with triphenylbenzylphosphonium chloride.

The apparatus consisted of a one liter three-necked flask fitted with a mechanical blade stirrer, nitrogen inlet, pressure compensating addition funnel, and a condenser.

Triphenylphosphonium chloride (19.4 gm., 0.05 mole) was placed in the flask and a solution of pivaldehyde (4.3 gm., 0.05 mole) in one-hundred ml. of anhydrous dimethylsulfoxide (DMSO) was added. After the system was purged with nitrogen, one-hundred ml. of an 0.5 N lithium ethoxide solution was added to the rapidly stirring solution. The temperature was maintained at 80°C throughout the entire reaction. After the addition of base was complete, the reaction was stirred for an additional six hours and then allowed to cool to room temperature. The reaction mixture was poured over ice, acidified and extracted with ether. The organic material was

washed five times with water (200 ml. portions), dried over anhydrous magnesium sulfate, filtered and concentrated by rotary evaporation. The remaining oil was cooled and the insoluble triphenylphosphine oxide was removed by filtration. Further purification of the olefins was accomplished by preparative scale vapor phase chromatography (8 ft. x 0.75 inch column of 20% QF-1 on HMDS treated Chromosorb W at 175°C). The mixture consisted of 75% cis and 25% trans 3,3-dimethyl-1-phenyl-1-butene.

trans-3,3-Dimethyl-1-phenyl-1-butene, oil Nmr: 1.08 (singlet), 6.03 (doublet 16.2 cps spacing), 6.30 (doublet 16.2 cps spacing), 7.01-7.38 (multiplet). Analysis: Calc. for $C_{12}H_{16}$; C, 89.93; H, 10.07. Found: C, 89.83; H, 10.08.

cis-3,3-Dimethyl-1-phenyl-1-butene, oil Nmr: CCl_4; 0.95 (singlet), 5.52 (doublet 12.7 cps spacing), 6.36 (doublet 12.7 cps spacing), 7.11 (singlet). Analysis: Calc. for $C_{12}H_{16}$: C, 89.93; H, 10.07. Found: C, 89.86; H, 10.02.

Erythro and threo 1-phenyl-1,2-dibromo-3,3-dimethylbutane

The dibromides were prepared by addition of bromine to the appropriate olefin in carbon-tetrachloride.

Trans 1-phenyl-3,3-dimethyl-1-butene (1.0 gm.) was dissolved in carbon-tetrachloride (25 ml.) and placed in a 125 ml. Erlenmeyer flask. The flask was wrapped with aluminum foil to exclude light. A magnetic stirring bar was placed in the flask and the flask was cooled to 0°C. A solution of bromine in carbon-tetrachloride was added dropwise to the

rapidly stirring mixture until a faint red color persisted. The reaction mixture was poured over ice. The organic material was separated and washed with a cold dilute sodium bisulfite solution, water, and then dried over anhydrous magnesium sulfate. After filtration, the organic material was concentrated by rotary evaporation to a volume of approximately three ml. An nmr spectrum was recorded on a portion of the above solution and the presence of two diastereomeric dibromides was easily discernable. The reaction mixture consisted of eighty-five percent erythro and fifteen percent threo 1-phenyl-1,2-dibromo-3,3-dimethylbutane.

The bromination of the cis 1-phenyl-3,3-dimethyl-1-butene gave seventy percent erythro and thirty percent threo 1-phenyl-1,2-dibromo-3,3-dimethyl butane.

Erythro 1-phenyl-1,2-dibromo-3,3-dimethylbutane, oil

Mass spectrum: Molecular ion triplet; 318, 320, 322 base peak corresponded to loss of a bromine atom. Nmr: CCl_4; 0.98 (singlet), 4.46 (doublet 4.2 cps spacing), 5.40 (doublet 4.2 cps spacing), 7.1-7.21 (multiplet), 7.48-7.67 (multiplet).

Threo 1-phenyl-1,2-dibromo-3,3-dimethylbutane, oil

Nmr: CCl_4; 1.17 (singlet), 3.93 (doublet 2.1 cps spacing), 5.41 (doublet 2.1 cps spacing), 7.10-7.35 (multiplet), 7.50-7.68 (multiplet).

Pinacolone dichloride

Pinacolone dichloride was prepared from pinacolone and

phosphorous pentachloride according to the procedure described by Bartlett and Rosen (4). Pinacolone was purchased from Aldrich Chemical Company.

The apparatus consisted of a three liter three-necked round bottom flask fitted with a mechanical blade stirrer, condenser, and a pressure compensating addition funnel.

Pinacolone (120 gm., 1.2 mole) was added dropwise with constant stirring to phosphorous pentachloride (225 gm., 1.2 mole). After the addition of pinacolone was complete (three hours), the reaction was stirred for an additional twenty-four hours. The temperature was maintained below ten degrees throughout the entire reaction. Water was carefully added to the reaction mixture to decompose the phosphorous oxychloride formed in the reaction. After all the phosphorous oxychloride was decomposed, the reaction mixture was poured over ice and extracted with ether. The etheral extract was washed with water, dried over anhydrous magnesium sulfate, and concentrated distillation of the ether. The remaining dark brown oil was cooled and the crystalline pinacolone dichloride (53 gm.) collected by filtration. The filtrate was distilled yielding 3,3-dimethyl-2-chloro-1-butene (61.4 gm.).

Pinacolone dichloride m.p. 148-50, lit. m.p. 151-152°C (4).

3,3-Dimethyl-2-chloro-1-butene b.p. 95-99°C, lit. b.p. 97-99°C (4).

3,3-Dimethyl-1-butyne

The 3,3-dimethyl-1-butyne (t-butyl acetylene) was prepared by reaction of pinacolone dichloride and 3,3-dimethyl-2-chloro-1-butene with potassium t-butoxide in dimethyl sulfoxide (DMSO).

The apparatus consisted of a two liter three-necked round bottom flask fitted with a West condenser and a thermometer. A distilling adapter fitted with a thermometer was attached to the top of the West condenser and the adapter was connected to the sidearm of a Friedrich condenser. A vacuum adapter connected to a round bottom flask immersed in an ice bath was attached to the Friedrich condenser.

A solution of pinacolone dichloride (53 gm., 0.344 mole) and 3,3-dimethyl-2-chloro-1-butene (61.4 gm., 0.52 mole) in five-hundred ml. of anhydrous dimethylsulfoxide was placed in the reaction flask. Potassium t-butoxide (225 gm., 0.86 mole) was added. A magnetic stirring bar was placed in the flask and the pot temperature was raised to eighty degrees and maintained for three hours. The flow of water through the West condenser was interrupted periodically and distillate was collected until the still-head temperature reached forty-five degrees. The condensate was redistilled through a twenty cm. glass helices packed column and the fraction distilling between 35-9°C was collected yielding 66.5 gm. (81%) t-butyl acetylene.

t-Butyl acetylene b.p. 35-9°C, lit. (47), Nmr: CCl_4; 1.20 (singlet), 1.88 (singlet).

2,5,5-Trimethyl-3-hexyne-2-ol

The 2,5,5-trimethyl-3-hexyne-2-ol was prepared by reaction of acetone with t-butyl acetylide magnesium bromide.

t-Butyl acetylene (66.5 gm., 0.81 mole) dissolved in anhydrous ether (150 ml.) was added dropwise to the Grignard reagent prepared from ethyl bromide (88.5 gm., 0.81 mole) and magnesium (19.45 gm., 0.81 mole). The reaction was gently refluxed for thirty minutes after the addition was complete and then allowed to stand for twenty-four hours. The Grignard was cooled to zero degrees and acetone (47 gm., 0.81 mole) dissolved in anhydrous ether (100 ml.) was added dropwise with constant stirring. After the addition was complete, the reaction mixture was stirred for two hours at gentle reflux and then cooled to room temperature. The contents of the flask were poured over ice and acidified with cold dilute hydrochloric acid solution. The organic material was separated, washed with water, dried over anhydrous magnesium sulfate, filtered, and distilled at aspirator pressure. The fraction distilling between 64-6C° was collected and solidified upon standing, (yield 78.5 gm., 85.5%).

2,5,5-Trimethyl-3-hexyne-2-ol b.p. 64-6°C (aspirator, Nmr: CCl_4; 1.15 (singlet), 1.40 (singlet, 3.60 (singlet).

2,5,5-Trimethyl-2-chloro-3-hexyne

The 2,5,5-trimethyl-2-chloro-3-hexyne was prepared by reaction of 2,5,5-trimethyl-3-hexyne-2-ol with anhydrous hydrogen chloride.

Anhydrous hydrogen chloride was slowly passed through a rapidly stirring solution of 2,5,5-trimethyl-3-hexyne-2-ol (78.5 gm., 0.69 mole) in pentane (250 ml.) at zero degrees for two hours. The reaction mixture was then poured over ice and the pentane solution was separated, washed with water, dried over anhydrous magnesium sulfate; filtered and concentrated by rotary evaporation. The resulting oil was distilled under vacuum to give one-hundred and five grams (96%) of the chloride.

2,5,5-Trimethyl-2-chloro-3-hexyne b.p. 135-140°C., lit. 138-140°C (760 mm.) (47). Nmr: CCl_4; 1.20 (singlet), 1.78 (singlet).

2,2,5,5-Tetramethyl-3-hexyne

The 2,2,5,5-tetramethyl-3-hexyne (di-t-butyl ethylene) was prepared by the reaction of 2,5,5-trimethyl-2-chloro-3-hexyne with methyl magnesium bromide according to the procedure of Puterbaugh and Newman (47).

A solution of 2,5,5-trimethyl-2-chloro-3-hexyne (105 gm., 0.665 mole) in anhydrous ether (200 ml.) was added dropwise to the Grignard prepared from methyl bromide and magnesium (16 gm., 0.665 mole). The temperature was maintained at zero

degrees while the addition of the chloride. After the addition was complete, the reaction was stirred at room temperature for an additional four hours and then poured over ice. The mixture was acidified with cold dilute hydrochloric acid and the organic material was separated, washed with water, dried over anhydrous magnesium sulfate, filtered and distilled. The fraction boiling between 115-117°C was collected giving 64 gm. (69%) di-t-butylacetylene.

2,2,5,5-Tetramethyl-3-hexyne b.p. 115-117°C (760 mm.), lit. 116-118°C (47). Nmr: CCl_4; 1.16 (singlet).

Cis and trans 2,2,5,5-tetramethyl-3-hexene

The olefins were prepared by reduction of 2,2,5,5-tetramethyl-3-hexyne according to the procedure developed by Puterbaugh and Newman (47).

A hydrogenation flask was charged with twenty grams of 2,2,5,5-tetramethyl-3-hexyne in absolute ethanol (50 ml.) and one gram of platinum (5%) on alumina. After the theoretical amount of hydrogen was consumed (one hour), the catalyst was removed by filtration and the filtrate was poured into water and extracted with ether. The etheral extracts were combined, washed with water, dried over anhydrous magnesium sulfate, filtered, and concentrated by distillation of the ether.

The cis alkene was obtained by preparative scale vapor phase chromatography of the crude mixture of alkenes (8 ft. x 3.8 inch column of 20% QF, on HMDS treated Chromosorb W).

The trans alkene was obtained by irradiation of the crude mixture of cis and trans olefins in the presence of a trace of iodine according to the procedure described by Fahey (33).

The apparatus consisted of a 250-ml. single-necked round bottom flask, a Friedrich condenser and a General Electric sun lamp. Ten grams of the crude cis alkene together with a crystal of iodine was placed in the flask and irradiated for two hours. After cooling to room temperature, the reaction mixture was poured over ice and extracted with ether. The etheral extract was washed with a dilute sodium thiosulfate solution, and then with water. After drying over anhydrous magnesium sulfate, the etheral solution was concentrated by distillation of the ether.

The trans alkene was purified by preparative scale vapor phase chromatography (8 ft. x 3/8 inch column of 20% QF, on HMDS treated Chromosorb W).

Cis 2,2,5,5-tetramethyl-3-hexene IR: CCl_4; 910, 946, 1200, 1362, 1380, 1463, 1480, 1627, 2940.

Trans 2,2,5,5-tetramethyl-3-hexene IR: CCl_4; 926, 941, 973, 1261, 1361, 1390, 1470, 1655, 2950.

meso and dl-3,4-Dichloro-2,2,5,5-tetramethylhexane

The dichlorides were prepared by chlorination of cis and trans 2,2,5,5-tetramethyl-3-hexenes. The chlorination procedure was similar to the procedure described by Fahey (33).

A 4:1 mixture of air and chlorine was passed into a solution of six grams of the appropriate 2,2,5,5-tetramethyl-3-hexene in carbon-tetrachloride (100 ml.) with stirring at zero degrees until a faint yellow color persisted in the reaction mixture. The reaction mixture was poured over ice and the organic material was separated and washed twice with a cold dilute sodium bisulfite solution, twice with water and then dried over anhydrous magnesium sulfate. After filtration, the carbon-tetrachloride was removed by distillation and the dichlorides were purified by preparative scale vapor phase chromatography (8 ft. x 3/4 inch column of 20% QF-1 on HMDS treated Chromasorb W).

1,3-Diphenyl-1-butenes

The 1,3-diphenyl-1-butenes were prepared by reaction of triphenylbenzylphosphonium chloride with 2-phenylpropionaldehyde.

To a solution of 26.8 g. (0.2 mole) of hydratropaldehyde (Aldrich Chemical Co., Inc.) and 77.6 g. (0.2 mole) of triphenylbenzylphosphonium chloride in 500 ml. of commercial absolute ethanol was added dropwise, under nitrogen, 1 liter at 0.2 M lithium ethoxide. After the addition was complete, the reaction was stirred for an additional 24 hours at room temperature. Sufficient water was added to give a 60% ethanol solution and the entire mixture was poured into a large separatory funnel. The dark brown oil which separated was collected and washed two times with 50 ml. portions of

60% ethanol and then dried over molecular sieve (Linde 4A). The crude mixture of cis and trans olefins was separated by distillation through an 18 inch spinning band column at reduced pressure (c.a., 2 mm.). Twenty-four 2 ml. fractions were collected and analyzed by vapor phase chromatography using a 1/4" x 8' QF-1, column (5% QF-1, on 60-80 mesh HMDS treated Chromosorb W). At a column temperature of 195°C using a 65 cc/min. helium flow. The retention times of cis and trans were 3 min. and 4.5 min., respectively. Fractions 2-10 b.p. (2 mm.) 109-112°C. were cis alkene of 99% purity, fractions 11-14 were a mixture of cis and trans alkene of 99% purity. The nmr spectral data for the olefins are identical with those reported by Cram (24

Bromination of cis 1,3-diphenyl-1-butene A solution of 10 g. (0.027 moles) of the olefin in 50 cc. of carbon tetrachloride was cooled to zero degrees. The reaction flask was wrapped in aluminum foil and a solution of 4.4 g. (0.0275 moles) of bromine in 20 ml. of CCl_4 was added dropwise. After the addition was complete (30 min.), the reaction mixture was stirred for an additional 60 min. and then poured over ice and extracted with CCl_4. The CCl_4 layer was washed with dilute sodium bisulfite, water and then dried over anhydrous magnesium sulfate. A small amount of the carbon tetrachloride solution was concentrated by rotary evaporation at room temperature. The resulting residue was dissolved in $CDCl_3$ and an nmr spectrum was recorded. The portion of the

spectrum from 220 cps to 320 cps was again recorded using a 100 cps sweep width. Integration over this expansion allowed calculation of yield of each diastereomer.

The carbon tetrachloride was removed from the major portion of the crude product by rotary evaporation and the residue crystallized upon standing. The crystals (crop A) were collected and the residual oil was allowed to stand. After several days the oil crystallized in large plates, m.p. 61-67°C. The crystals were taken up in fresh CCl_4 and pentane was added. The first crystals to separate were filtered off and the mother liquor was cooled yielding a dibromide m.p. 78-80°C.

A second dibromide m.p. 122-123° was obtained by dissolving crop A in a suitable volume of solvent prepared by mixing 100 ml. of ethanol with 50 ml. of ethyl acetate and 25 ml. of water. After four recrystallizations from this solvent the pure dibromide was obtained.

Bromination of trans 1,3-diphenyl-1-butene A solution of 4.4 g. of bromine in 25 ml. of CS_2 was added dropwise to a solution of 10 grams (0.027 moles) of the olefin in 50 ml. of carbon disulfide. The reaction mixture was stirred at 0°C. for 2 hours and then allowed to warm to room temperature. The carbon disulfide was removed by rotary evaporation at room temperature and the residue was dissolved in carbon tetrachloride and again stripped of solvent. The crude product was taken up in fresh carbon tetrachloride and washed with sodium

bisulfite, water, and then dried over magnesium sulfate. A small portion of the carbon tetrachloride solution was concentrated and the residue was dissolved in deuterochloroform and an nmr spectrum was recorded. The portion of the spectrum from 220 cps to 320 cps was again recorded using a 100 cps sweep width. Integration over this expansion allowed calculation of yield of each diastereomer.

After removal of the solvent from the bulk of the product, the residue was dissolved in a large excess of ethanol and allowed to stand at room temperature. Long needles of a third dibromide m.p. 128-129°C. (lit. 128-129°C.) separated after several hours.

The fourth dibromide was not obtained free from diastereomeric impurities, however a mixture of the fourth dibromide and dibromides m.p. 122 and m.p. 128-129 was obtained by repeated fractional recrystallization. This mixture contained 34% dibromide, 28% dibromide m.p. 122° and 38% dibromide m.p. 129° via nmr integration.

cis 1,3-Diphenyl-1-butene b.p. 109-112°C (2 mm.) Nmr: CCl_4; 1.33 (doublet), 3.96 (double quartet), 5.71 (double-doublet), 6.4 (doublet), 7.25 (singlet).

trans 1,3-Diphenyl-1-butene b.p. 123-126°. Nmr: CCl_4; 1.36 (doublet), 3.5 (unresolved quartet of triplets), 6.25-6.35 (closely spaced unsymmetrical pair of doublets), 7.16 (singlet).

Erythro-erythro 1,3-diphenyl-1,2-dibromobutane m.p. 128-129°, lit. m.p. 128-129° (53). Nmr: $CDCl_3$; 1.52 (doublet), 4.00 (doublet quartet), 4.60 (doublet), 4.80 (double doublet), 7.21 (singlet), 7.26-7.67 (multiplet).

Erythro-threo 1,3-diphenyl-1,2-dibromobutane m.p. 121-122°, lit. m.p. 122°C (53). Nmr: $CDCl_3$; 1.44 (doublet), 3.90 (double quartet), 4.68 (double doublet), 5.17 (doublet), 7.30 (singlet).

Threo-erythro 1,3-diphenyl-1,2-dibromobutane m.p. 78-80°, lit. m.p. 78-80° (53). Nmr: $CDCl_3$; 1.39 (doublet), 3.15 (double quartet), 4.30 (double doublet), 4.90 (doublet), 7.26 (singlet).

Threo-threo-1,3-diphenyl-1,2-dibromobutane, oil Nmr: $CDCl_3$; 1.43 (doublet), 3.20 (double quartet), 4.50 (double doublet), 5.15 (doublet), 7.31 (singlet).

Elimination of the diastereomers of 1,2-dibromo-1,3-diphenylbutane with potassium iodide in methanol

A solution of potassium iodide (1 gm.) in 50 ml. of commercial absolute methanol was prepared and 5 ml. of this solution was pipeted into a test tube containing 0.10 g. of the appropriate dibromide. The tubes were sealed and placed in a bath at 60°C. for 85 hours. The tubes were cooled to room temperature, broken and poured over ice. Sufficient dilute sodium thiosulfate was added to reduce the iodine to iodide and the solution was extracted three times with small

portions of ether. The combined etheral extracts were washed four times with water and then dried over anhydrous magnesium sulfate. After filtration, the etheral solutions were analyzed by vapor phase chromatography (8 ft. x 0.25 inch column of 20% QF-1 on HMDS treated Chromosorb W at 175C°). The diastereomers melting at 129°C and 122°C gave on elimination 100% trans 1,3-diphenyl-1-butene. The diastereomer melting at 80°C produced a mixture containing 13% cis and 87% trans while the fourth diastereomer gave 33% cis and 67% trans 1,3-diphenyl-1-butene.

Control experiment on possible cis to trans isomerization of 1,3-diphenyl-1-butenes

A solution containing 0.5 gm. of iodine, 0.5 gm. of potassium iodide and 1.0 gm. of cis 1,3-diphenyl-1-butene in 5 ml. of commercial absolute methanol was prepared and sealed in a test tube. The test tube was placed in a bath at 60°C for 250 hours. After cooling to room temperature, the tube was broken and the contents poured over ice. Sufficient dilute sodium thiosulfate was added reduce the iodine to iodide and the solution was extracted three times with small portions of ether. The combined etheral extracts were washed with water, dried over anhydrous magnesium sulfate, and filtered. The etheral solution was concentrated by distillation of the ether and the residue (0.98 gm.) was analyzed by vapor phase chromatography. No trans 1,3-diphenyl-1-butene could be detected.

Methanol

Anhydrous methanol was prepared by the method of Wiberg (64). The center cut of the distillation of methanol from magnesium methylate was taken and sufficient redistilled water was added to produce 99% methanol.

Potassium iodide

Baker's analytical reagent grade potassium iodide was powdered, dried in a vacuum oven at 100°C. and then stored in a dessicator until used.

Sodium thiosulfate

Two liters of approximately 0.01 molar sodium thiosulfate solution was prepared by dissolving the appropriate quantity of Baker's analytical reagent grade sodium thiosulfate in redistilled water. The solution was allowed to stand for several days, and then standardized by titration of accurately weighed portions of resublimed Baker's analytical reagent grade iodine to the starch end point.

Kinetic data

Approximately 3×10^{-1} M solutions of potassium iodide in 45 ml. of methanol were prepared in a 50 ml. volumetric flask. The volumetric flask was placed in a constant temperature bath at 20°C and the solutions were allowed to equilibrate. Approximately 5 mmoles of the appropriate dibromide was added to the flask and then methanol was added to bring the total volume to 50 ml. at 20°C. The solutions were thoroughly mixed and then nine 5 ml. aliquots were taken and placed in

test tubes. The tubes were sealed and placed in a constant temperature bath at 60.0°C. The time of immersion was taken as "zero time". At appropriate times the tubes were removed and immersed in an ice bath and cooled to zero degrees. After cooling, the tubes were broken and the contents were carefully rinsed into a 125 ml. Erlenmeyer flask containing 20 ml. of a saturated potassium iodide solution. The iodine produced in the elimination reaction was then titrated with a standard sodium thiosulfate solution to the starch end point. The second order rate constants were determined by applying the integrated second order rate equation.

$$kt = \frac{2.303}{a-2b} \operatorname{Log}_{10} \left[\frac{(1 - \frac{2b\phi}{a}}{(1 - \phi)} \right]$$

t = time in seconds

a = initial concentration of potassium iodide in moles/liter at 20°C

b = initial concentration of dibromide in moles/liter at 20°C

ϕ = fraction of total dibromide which has reacted at time t

$$\phi = \frac{b-bt}{b}$$

where $b_t = bo - [\text{ml. } Na_2S_2O_3 \times MNa_2S_2O_3]$

Table 10. Second-order rate constant for the elimination of erythro 4-methyl-2,3-dibromopentane with potassium iodide in methanol at 60°C

Time min.	Titre[a] ml.	b_t mole/l.	Ø	$\frac{2.303}{a-2b}$ Log $\frac{(1-\frac{2b\text{Ø}}{a})}{(1-\text{Ø})}$	$K_2 \times 10^6$ l. mole^{-1} sec.$^{-1}$
300	0.67	0.01795	0.0367	0.1384	4.62
696	1.52	0.01708	0.0834	0.3224	4.64
1000	2.16	0.01643	0.122	0.4711	4.71
1950	3.89	0.01464	0.214	0.9061	4.64
2330	4.53	0.01400	0.248	1.0764	4.62
3575	6.385	0.01211	0.351	1.6362	4.57
3925	6.74	0.01175	0.370	1.7633	4.49[d]
5390	8.47	0.00998	0.465	2.3948	4.44[d]
8245	11.00	0.00739	0.604	3.5939	4.36[d]

[a]Ml. of 0.0126 M $Na_2S_2O_3$ required to titrate 5 ml. aliquot of reaction mixture.

[b]Initial concentration of potassium iodide, a = 0.270 mole/liter.

[c]Initial concentration of dibromide, b = 0.01864 mole/liter.

[d]Not included in average rate constant.

Table 11. Second-order rate constant for the elimination of erythro 4,4-dimethyl-2,3-dibromopentane with potassium iodide in methanol at 60°C

Time min.	Titre[a] ml.	[b]t mole/l.	Ø	$\frac{2.303}{a-2b}$ Log $\frac{(1-\frac{2b\emptyset}{a})}{(1-\emptyset)}$	$K_2 \times 10^5$ l. mole^{-1} sec.$^{-1}$
124	0.534	0.00764	0.0669	0.2653	3.56
295	1.220	0.00694	0.1528	0.6460	3.65
474	1.865	0.00628	0.2336	1.0325	3.64
619	2.270	0.00586	0.2843	1.3002	3.50
809	2.865	0.00525	0.3587	1.7323	3.56
1774	5.81	0.00223	0.7276	5.1464	2.90[d]
2954	6.22	0.00181	0.7788	5.9870	2.03[d]

$K_2 = 3.56 \pm 0.06 \times 10^{-5}$ l. mole^{-1} sec.$^{-1}$

[a]Ml. of 0.01026 M $Na_2S_2O_3$ required to titrate 5 ml. aliquot of reaction mixture.

[b]Initial concentration of potassium iodide, a = 0.2841 mole/liter.

[c]Initial concentration of dibromide, b = 0.00819 mole/liter.

[d]Not included in average rate constant.

Table 12. Second-order rate constant for the elimination of <u>threo</u> 4-methyl-2,3-dibromopentane with potassium iodide in methanol at 60°C

Time min.	Titre[a] ml.	b_t mole/l.	ϕ	$\frac{2.303}{a-2b}$ Log $\frac{(1-\frac{2b\phi}{a})}{(1-\phi)}$	$K_2 \times 10^6$ l. mole^{-1} sec.$^{-1}$
399	0.140	0.01340	0.01063	0.04286	1.79
684	0.220	0.01332	0.01668	0.06419	1.57[d]
1500	0.540	0.01299	0.04089	0.16074	1.78
2904	1.050	0.01247	0.07958	0.32367	1.83
3489	1.225	0.01229	0.0927	0.37527	1.79
4259	1.480	0.01203	0.1121	0.46139	1.77
4959	1.635	0.01186	0.1239	0.51517	1.70

$K_2 = 1.78 \pm .04 \times 10^{-6}$ l. mole^{-1} sec.$^{-1}$

[a]Ml. of 0.01026 M $Na_2S_2O_3$ required to titrate 5 ml. aliquot of reaction mixture.

[b]Initial concentration of potassium iodide, b = 0.2592 mole/liter.

[c]Initial concentration of dibromide, b = 0.01355 mole/liter.

[d]Not included in average rate constant.

Table 13. Second-order rate constant for the elimination of threo 4,4-dimethyl-2,3-dibromopentane in methanol at 60°C.

Time min.	Titre ml.	b_t mole/l.	ϕ	$\frac{2.303}{a-2b}$ Log $\frac{(1-\frac{2b\phi}{a})}{(1-\phi)}$	$K_2 \times 10^6$ l. mole^{-1} sec.$^{-1}$
329	0.132	0.00824	0.0162	0.05912	2.48
603	0.250	0.00812	0.0306	0.11017	2.57
1298	0.540	0.00792	0.0542	0.19245	1.48[d]
1918	0.760	0.00795	0.0932	0.34500	2.57
2738	0.980	0.00736	0.1202	0.45208	2.37
3248	1.240	0.00710	0.1519	0.58181	2.55
5723	1.62	0.00671	0.1985	0.78045	1.37[d]

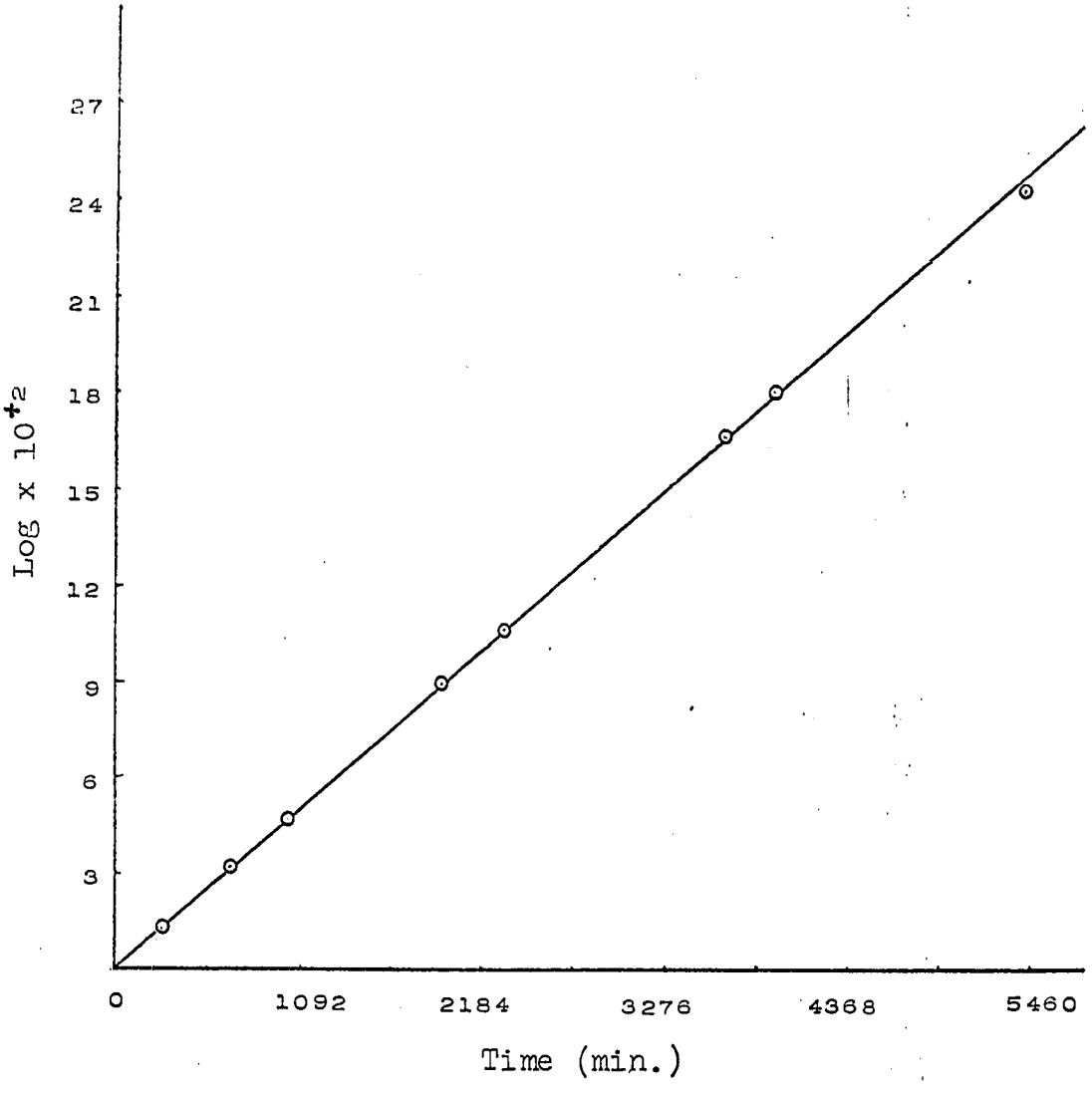
$K_2 = 2.51 \pm 0.08 \times 10^{-6}$ l. mole^{-1} sec.$^{-1}$

[a] Ml. of 0.01026 M $Na_2S_2O_3$ required to titrate 5 ml. aliquot of reaction mixture.

[b] Initial concentration of potassium iodide, a = 0.2851 mole/liter.

[c] Initial concentration of dibromide, b = 0.00837 mole/liter.

[d] Not included in average rate constant.


27
24
21
18
15
12
9
6
3
Log x 10^{+2}
0
1092
2184
3276
4368
5460
Time (min.)

PART II: SUBSTITUENT EFFECTS ON SUSPECTED PHENONIUM ION INTERMEDIATES

HISTORICAL

Carbonium ions have long been recognized as an important class of reactive intermediates in certain types of organic reactions.

During the past few decades reactions involving carbonium ion intermediates have been subjected to careful study in an attempt to better understand the nature of these species.

In 1937, Roberts and Kimball postulated the existence of a bridged carbonium ion to account for the observation that polar addition of bromine to a double bond produces exclusively the "trans" product (48).

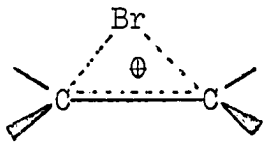


Figure 1. Proposed bridged carbonium ion.

Kinetic evidence for the existence of bridged halogenonium ions was reported by Winstein in 1948 (65). The rates of acetolysis of the cis and trans 2-bromo and 2-iodocyclohexyl-brosylates were studied and the trans isomers were found to undergo acetolysis at greatly enhanced rates compared to the cis isomers.

Since similar rates of acetolysis for the cis and trans 2-substituted cyclohexyl brosylates would be expected in the absence of participation by neighboring halogen, these rate studies indicate the intermediacy of bridged halogenonium ions.

During the last thirty years many other types of bridged carbonium ions have been proposed. Excellent reviews (19) (8) (55) (17) (23) have appeared in which the evidence for and against the intermediacy of many of the proposed bridged ions is presented.

One of the types of bridged ions whose existence as a discrete intermediate has been extensively debated is the phenonium ion.

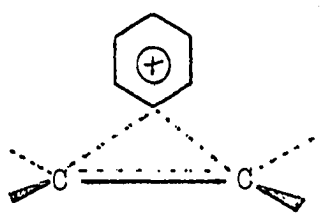


Figure 2. Phenonium ion

Experimental evidence for the existence of a phenonium ion was first reported by Cram in 1949 (22). The optically pure diastereomers of 3-phenyl-2-butyl p-toluenesulfonate were solvolyzed in both acetic and formic acids. The ester products were converted to alcohols by reduction with lithium aluminum hydride and the alcohol mixtures were separated and

analyzed. The results are given in Table 1. Solvolysis of the optically pure threo tosylate gives racemic threo acetate or formate as the major product, whereas the optically pure erythro tosylate gives rise to essentially optically pure erythro acetate or formate. The overall stereochemical result is thus one of retention. Since net inversion is the usual result in the acetolysis of simple secondary tosylates (55). The presence of a phenyl group β to the tosylate leaving group markedly affects the stereochemistry of the reaction. Cram proposed the formation of the phenonium ion intermediates I and II (Chart 1) to explain the stereochemical

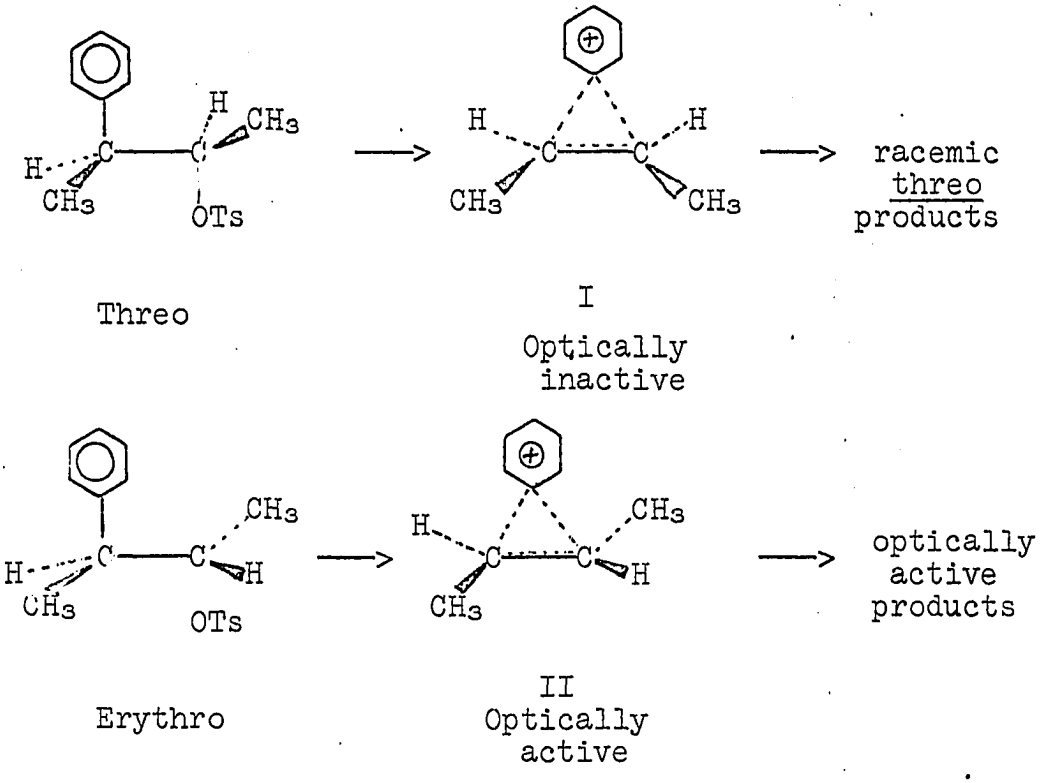


Chart 1. Proposed phenonium ion intermediates.

Table 1. Acetolysis and formolysis of the optically pure diastereomers of 3-phenyl-2-butyl p-toluenesulfonate[a]

Diastereomer	Conditions	Yield of alcohols	Product Composition
L-threo	acetolysis at 75°C	53%	95% racemic threo 0.6% L-threo 4% erythro
L-threo	formolysis at 25°C	70%	>99% racemic threo <0.02% L-threo <0.01% erythro
D-erythro	acetolysis at 75°C	68%	94% D-erythro 5% D-threo
D-erythro	formolysis at 25°C	71%	>99% D-erythro <0.5% D-threo

[a]Data from reference (22).

course of these solvolyses.

This mechanistic scheme involving phenonium ion intermediates was recently questioned by H. C. Brown (17). Brown has suggested the stereochemical outcome of the solvolyses of the 3-phenyl-2-butyl tosylates could be explained by a dynamic pair of rapidly equilibrating classical open ions rather than by a phenonium ion intermediate. In this scheme, the phenonium ion would represent the transition state between the two rapidly equilibrating classical ions. Brown states that the

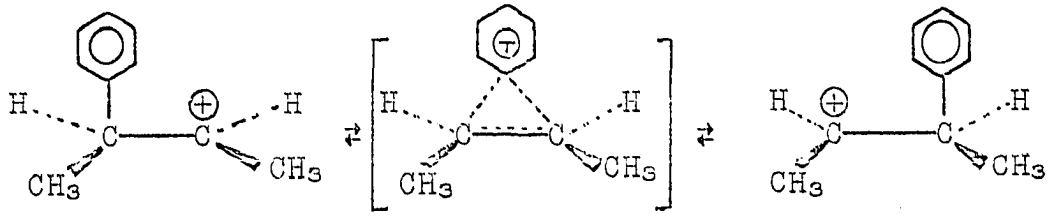


Figure 3. Proposed pair of rapidly equilibrating ions.

stereochemistry of substitution on rapidly equilibrating cations and ion pairs may well be one of retention.

Brown argues that if phenyl participation is important in the solvolysis of β-phenylethyl compounds, one would expect that the rate of solvolysis of β-phenylethyl tosylate should be significantly faster than that of ethyl tosylate. However, kinetic data on the rates of solvolysis of β-phenylethyl tosylate in ethanol, acetic acid and formic acid do not indicate appreciable phenyl participation (65).

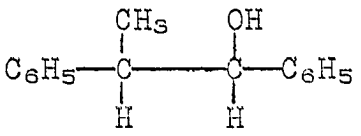
Cram has refuted the kinetic argument stating that rate comparisons reflect only differences in activation energies, and therefore provide no information about structure after the rate-determining transition state is reached (23).

Recently Olah has reported the observation by nmr of both rapidly equilibrating carbonium ions (43) and phenonium ions (44). Although these observations definitely establish the existence of both types of carbonium species, Olah emphasizes that these results do not prove that these species exist in solvolysis reactions.

Strong evidence for the existence of a dynamic pair of rapidly equilibrating classical cations in the 1,2,2,-triphenylethyl system under solvolysis conditions was reported in a series of papers by Collins and Bonner (9, 10, 11, 20, 21).

Thus, the question as to the intermediacy of phenonium ions or rapidly equilibrating classical cations in symmetric β-phenylethyl systems remains open for debate.

Cram and Elhafez have reported the results of a study of the reactions of the diastereomers of 1,2-diphenyl-1-propanol (III) with various halogenating agents (27).



III

Figure 4. 1,2-diphenyl-1-propanol.

The stereochemistry of the halides obtained by reaction of racemic and optically active <u>erythro</u> and <u>threo</u> 1,2-diphenyl-1-propanol with thionyl chloride, phosphorous tribromide, phosphorous pentachloride, and hydrobromic acid-sulfuric acid mixtures are given in Table 2.

Table 2. Reaction of the diastereomeric 1,2-diphenyl-propanols with various halogenating agents[a]

	Configuration starting ROH	Reagent	Molar Ratio reagent to ROH	Product Ratio Threo to Erythro
1	DL-erythro	$SOCl_2$	2:1	2.6:1
2	L -erythro	$SOCl_2$	29:1	1.5:1
3	DL-threo	$SOCl_2$	2:1	4.3:1
4	DL-threo	$SOCl_2$	8:1	only threo
5	L -threo	$SOCl_2$	10:1	only threo
6	DL-erythro	PCl_5	2.4:1	4.3:1
7	DL-threo	PCl_5	2.4:1	5.4:1
8	DL-erythro	PBr_3	3:1	3:1
9	L -erythro	PBr_3	3:1	2.8:1
10	DL-threo	PBr_3	3:1	5:1
11	L -threo	PBr_3	3:1	5.8:1
12	DL-erythro	$HBr-H_2SO_4$	---	1.2:1
13	DL-threo	$HBr-H_2SO_4$	---	8:1

[a]Data taken from reference (27).

As the data in Table 2 show these conversions are stereoselective. The degree of stereoselectivity is seen to be dependent upon the reagent used and the molar ratio of reagent to alcohol. Cram proposed that these reactions proceeded by a pathway involving both classical open ion and phenonium ion intermediates (Chart 2).

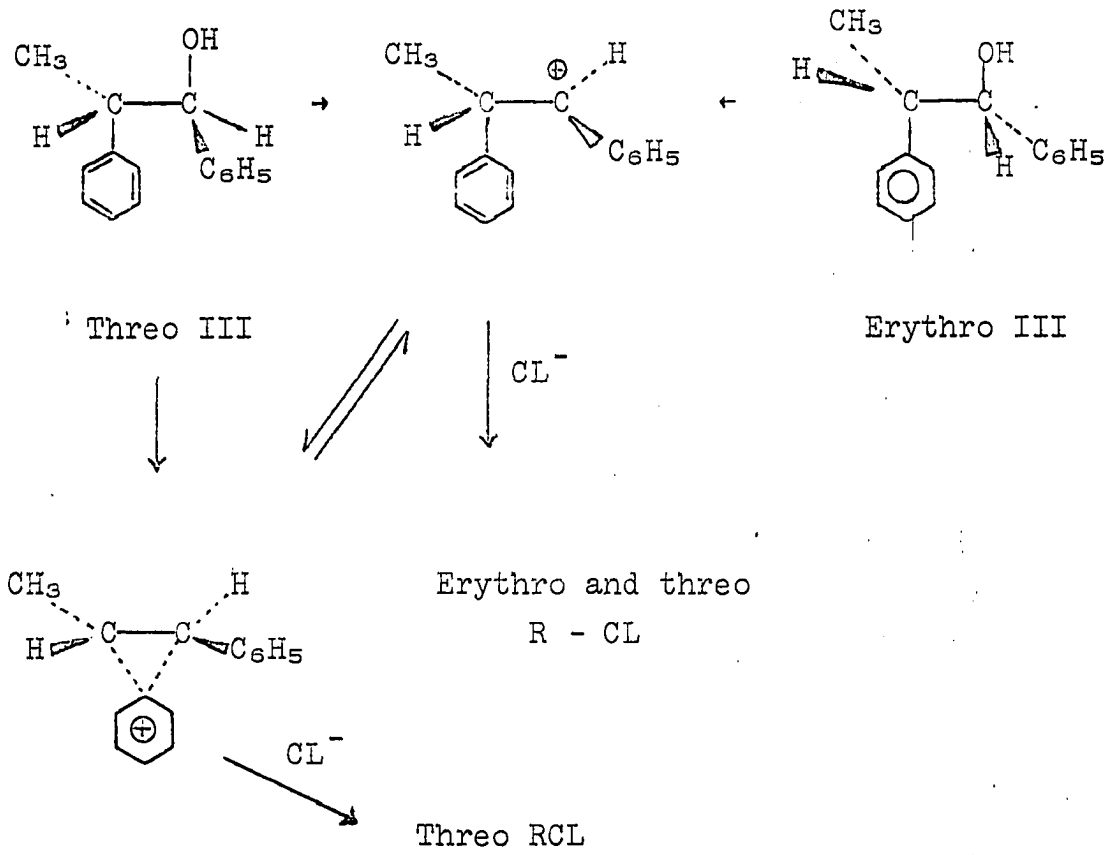
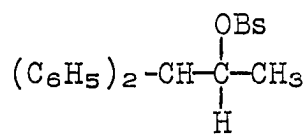


Chart 2. Proposed mechanistic scheme.

In another paper, Cram and Elhafez reported the stereochemical results of the acetolysis of optically active 1,1-diphenyl-2-propyl brosylate, IV (28).



IV

Figure 5. 1,1-diphenyl-2-propylbrosylate.

Acetolysis of the optically active brosylate, IV, at 25°C gave rise to virtually optically pure erythro and threo 1,2-diphenyl-1-propylacetate accompanied by minor amounts of racemic 1,1-diphenyl-2-propylacetate. Further, it was shown that acetolysis of optically pure L-1,1-diphenyl-2-propyl-brosylate and optically pure D-threo-1,2-diphenyl-1-propyl-brosylate produce the same ratio of threo to erythro 1,2-diphenyl-1-propylacetates. This latter observation strongly suggests the intervention of a common intermediate in the acetolysis of the two brosylates. Cram proposed the mechanistic scheme outlined in Chart 3.

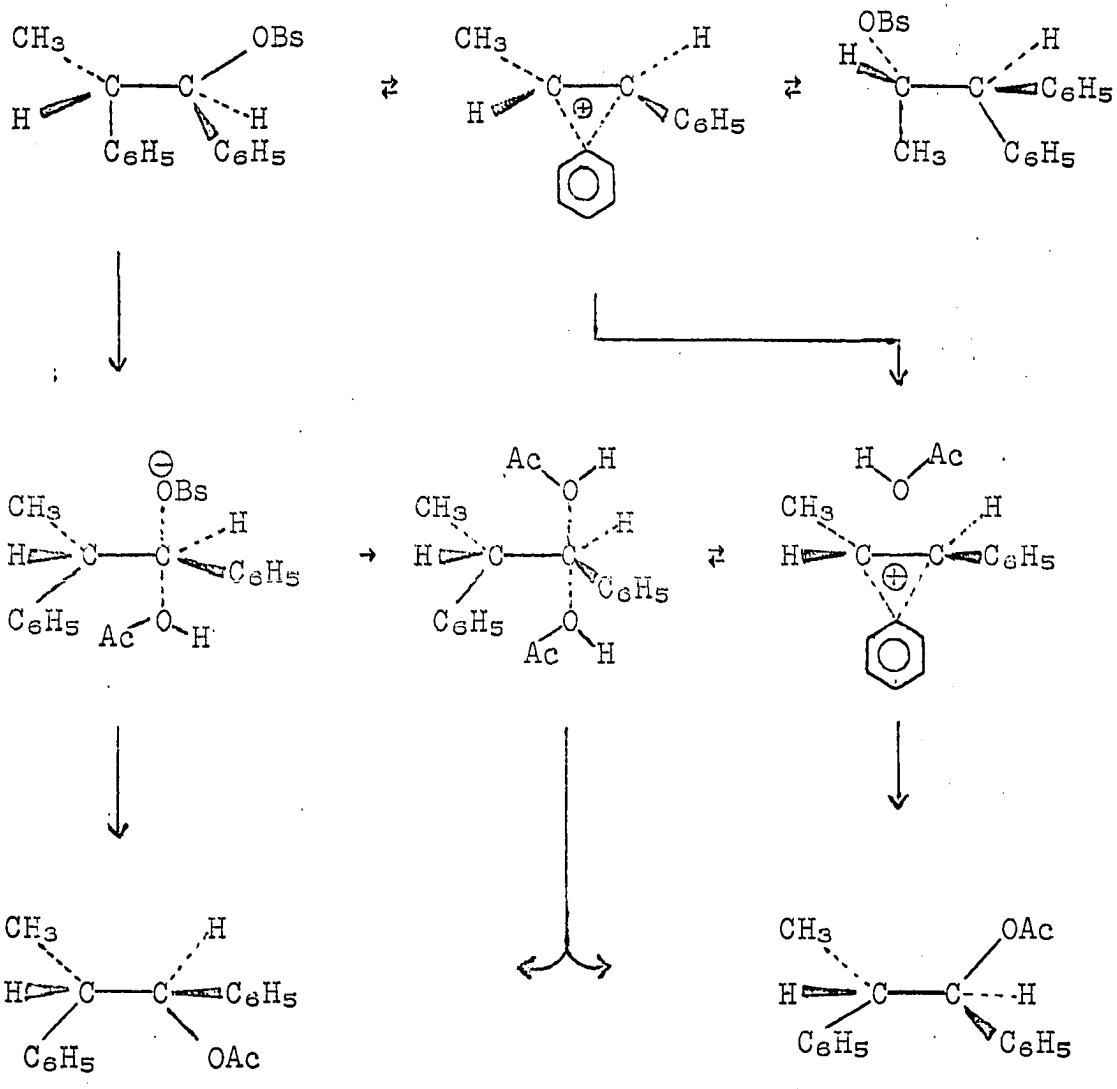
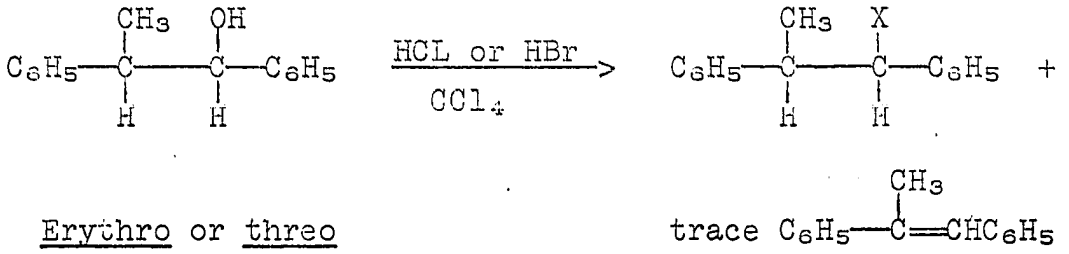


Chart 3. Proposed mechanistic scheme.

The second part of this dissertation is concerned with the substituent effect on the stereochemistry of the products derived by reaction of the diastereomers of various <u>para</u> substituted 1,2-diphenyl-1-propanols with hydrochloric and hydrobromic acids.

RESULTS AND DISCUSSION

The reaction of *erythro* and *threo* 1,2-diphenyl-1-propanol with hydrochloric or hydrobromic acid in carbon tetrachloride is stereoselective. Thus, both the *erythro* and *threo* alcohols give rise to a predominance of the *threo* chloride or bromide as the major product (Chart 4).



Erythro or *threo*

Threo and *erythro*

Chart 4. Reaction of diastereomeric 1,2-diphenyl-1-propanols with hydrochloric or hydrobromic acids.

Therefore, the reaction proceeds with net retention if the *threo* alcohol is the starting material and with net inversion if the *erythro* alcohol is the starting material.

Only a small amount (*ca.* 1-5%) of 1,3-diphenyl-1-propene is formed in these reactions. Control experiments showed that the halide products do not arise by addition of hydrogen halide to 1,3-diphenyl-1-propene.

The stereochemistry of the halide products is easily determined by nmr. The chemical shift of the methyl group in the threo halides consistently falls approximately 0.5 p.p.m. downfield from the methyl group of the corresponding erythro halides. Integration over the methyl region of a mixture of the two diastereomers allows computation of the erythro to threo ratio of the mixture.

In a typical run, one-hundred milligrams of the appropriate alcohol dissolved in twenty ml. of carbon-tetrachloride was placed in a 125 ml. Erlenmeyer flask and cooled to zero degrees centigrade. A magnetic stirring bar was placed in the flask and then 10 ml. of concentrated hydrochloric acid was pipetted into the rapidly stirring mixture. After suitable reaction time, the reaction mixture was poured over ice and extracted with carbon-tetrachloride. The organic layer was separated, dried, and concentrated to a volume of approximately two ml. An nmr spectrum of a portion of this solution was recorded; the erythro to threo ratio of the products being determined from integration over the methyl region.

If a phenonium ion is an intermediate in these reactions as Cram has postulated (27), then the stereochemistry of the halides produced in these reactions should be sensitive to para substituents in the phenyl rings (Figure 6).

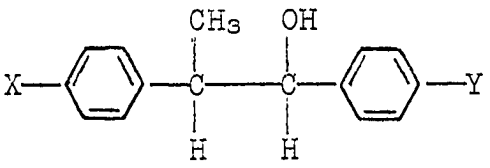


Figure 6. p-Substituted 1,2-diphenyl 1-propanols.

The effect of various substituents X and Y on the stereochemistry of the reaction should be predictable from a consideration of the resonance effect of the substituent. Thus, if X is electron donating the reaction should exhibit greater stereoselectivity than if X is electron withdrawing. Similarly if Y is electron donating the stereoselectivity of the reaction should decrease.

If a classical open ion (Figure 7) was the sole intermediate in the reaction, the stereochemistry of the products would not be expected to be sensitive to substituent effects and further an open ion intermediate should give rise to a

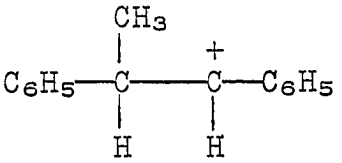


Figure 7. Classical open ion.

predominance of the thermodynamic product.

The intermediacy of a species involving rapid equilibration of the 2-phenyl group seems unlikely since such an intermediate would require equilibration of two ions of greatly different energies (Figure 8). Further, in both

Figure 8. Rapidly equilibrating classical cations.

this study and those reported by Cram (27) (28) no products arising from the 1,1-diphenyl-2-propyl cation could be detected in the reaction mixtures.

Only one other possibility for a rapidly equilibrating intermediate exists (Figure 9). This intermediate involves a rapidly equilibrating methyl group, and was excluded by a deuterium labelling experiment.

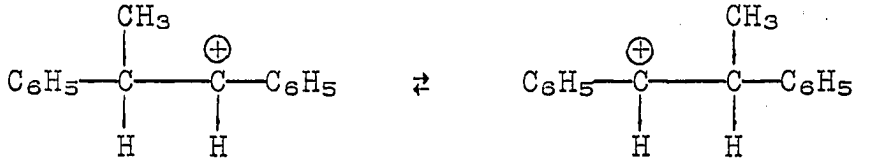
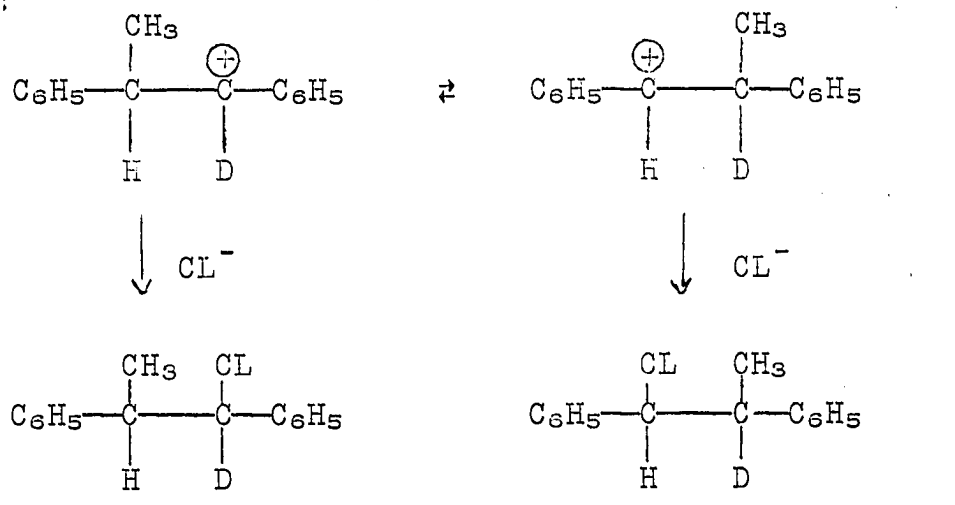


Figure 9. Rapidly equilibrating methyl group.

Erythro 1,2-diphenyl-1-propanol-1-d was prepared and treated with hydrochloric acid under the normal reaction conditions. If an intermediate involving rapid methyl equilibration was important, four easily distinguishable chlorides would be obtained (Chart 5). The nmr spectrum of a mixture



A
Erythro and threo methyl group a doublet

B
Erythro and threo methyl group a singlet

Chart 5. Products from rapidly equilibrating cations.

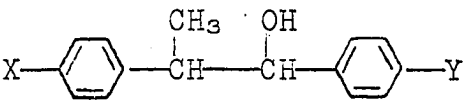
of chlorides A and B would show a doublet for the methyl group of A and a singlet for the methyl group of B. Since the nmr of the chloride products obtained from erythro 1,2-diphenyl-1-propanol-1-d showed only doublet methyl groups, an intermediate involving a rapidly equilibrating methyl group can be excluded.

Equilibration of the erythro and threo 1,2-diphenyl-1-propanols was accomplished by gently refluxing a mixture of the appropriate alcohol, aluminum isopropoxide, and acetone in isopropanol for three hundred hours (32). The mixture thus obtained consists of 54% erythro and 46% threo 1,2-diphenyl-1-propanol.

Cram has equilibrated the erythro and threo 1,2-diphenyl-1-propyl formates and found that the equilibrium mixture consists of 55% erythro and 45% threo. Thus, the erythro isomers are more stable than the threo, although the difference is not large.

The diastereomerically pure threo 1,2-diphenyl-1-propanols listed in Table 3 were obtained by hydrolysis of the corresponding p-nitrobenzoates. The erythro alcohols were in most cases crystalline and conversion to the p-nitrobenzoate for purification was not necessary.

Table 3. Substituted erythro and threo 1,2-diphenyl-1-propanols



Diastereomer	X	Y
Erythro	H	H
Erythro	p-NO_2	H
Erythro	p-CH_3O	H
Erythro	H	CH_3O
Erythro	o-CH_3O	H
Threo	H	H
Threo	p-CH_3O	H
Threo	p-CL	H
Threo	o-CH_3O	H
Threo	H	CH_3O

Table 4 shows the stereochemistry of the products as X and Y are varied.

Table 4. Stereochemistry of reaction products from substituted 1,2-diphenyl-1-propanols with concentrated HCL at 0°C

ROH			RCL		Rx. time	
Diastereomer	X	Y	%Erythro	%Threo	(hr.)	Comments
Erythro	p-CH_3O	H	26%	74%	6.8	rx complete
Erythro	o-CH_3O	H	29%	71%	8.25	rx complete
Erythro	H	H	33%	66%	6.5	rx complete
Erythro	p-NO_2	H	60%	40%	9.1	rx complete
Erythro	H	p-CH_3O	60%	40%	1.75	rx complete
Threo	o-CH_3O	H	2%	98%	1	rx complete
Threo	p-CH_3O	H	11%	89%	6	rx complete
Threo	H	H	20%	80%	1.5	rx complete
Threo[a]	p-CL	H	37%	62%	12	ca. 60% reaction
Threo	H	p-CH_3O	46%	54%	0.2	rx complete

[a]At 25°C rather than 0°C.

The data clearly show that substituents in the aromatic rings have a profound effect on the stereochemistry of the reaction.

Any proposed mechanism must account for the following observations: (a) the stereochemistry of the reaction is dependent upon the nature of the substituents X and Y; (b) no rearranged products are observed; (c) intermediates involving rapidly equilibrating intermediates are not important; (d) the reaction proceeds with net inversion if erythro alcohol is the starting material and net retention if threo

alcohol is the starting material.

The fact that no rearranged products are observed excludes a symmetrically bridged intermediate since such an intermediate should give rise to products from attack by nucleophile at both carbons 1 and 2. The intermediacy of a π-bridged species (17) would account for the observed stereoselectivity of the reaction and for the lack of rearrangement products. The proposed mechanism is outlined in Chart 6.

Although the <u>trans</u> π-bridged intermediate was proposed, the unsymmetrical σ-bonded bridged ion (Figure 10) originally proposed by Cram (27) cannot be excluded.

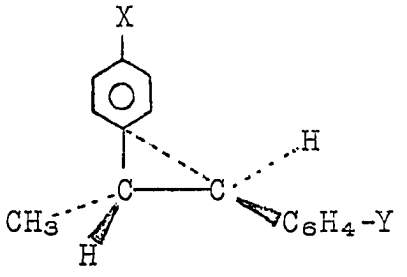
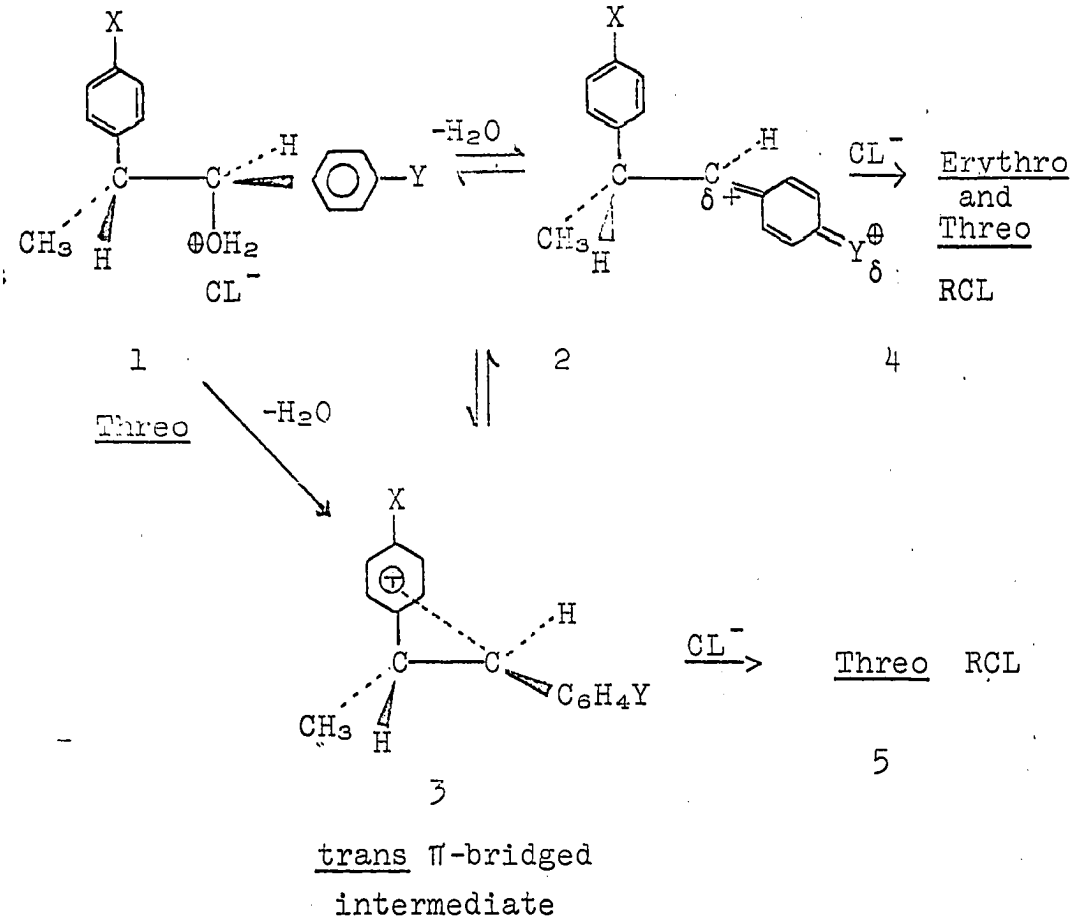


Figure 10. σ-Bonded phenonium ion.



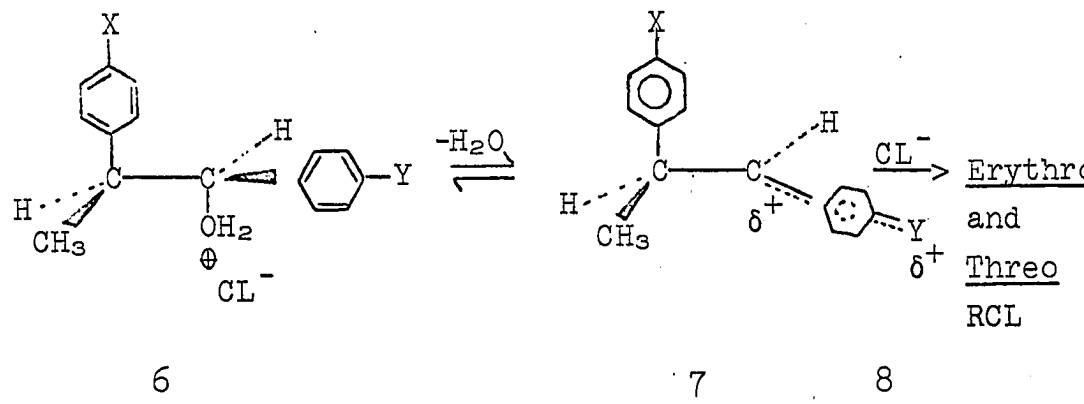


Chart 6. Proposed mechanism.

In terms of the mechanistic scheme outlined in Chart 7, an explanation of the results similar to that of Cram (27) can be given. Beginning with threo alcohol, with a strongly electron donating substituent X = p-CH_3O predominantly threo chloride is obtained via pathway 1 → 2 → 3 → 5. However, path 1 → 3 → 5 cannot be excluded. With poorer electron donating groups, X, pathway 1 → 2 → 4 becomes favored. With Y = p-CH_3O and X = H pathway 1 → 2 → 4 is thought to be the only important route of reaction.

Beginning with erythro alcohol the trans π-bridged intermediate, 3, cannot be formed directly and pathway 6 → 7 → 3 → 5 may be important. The open ion 7 must be formed initially and then undergo internal rotation before 3 is formed. It is noteworthy that the stereoselectivity is lower for the erythro series of compounds. Thus, capture of the open ion (path 6 → 7 → 8) must compete favorably with internal rotation. The latter pathway increases in importance as X becomes poorly electron donating or as Y becomes strongly electron donating.

Another pathway is thought to be important for the threo ortho substituted alcohol. An intermediate involving methoxyl participation seems attractive (Figure 11).

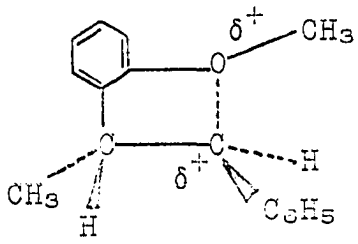


Figure 11. Proposed intermediate.

The possibility of such an intermediate is suggested by the fact that the threo alcohol X = o-CH_3O shows a higher degree of stereoselectivity than the threo alcohol X = p-CH_3O.

The stereochemical outcome of the reactions of 1,2-diphenylpropane and 1-(p-methoxyphenyl)-2-phenylpropane with N-bromosuccinimide in the presence of dibenzoylperoxide was next investigated (Chart 7).

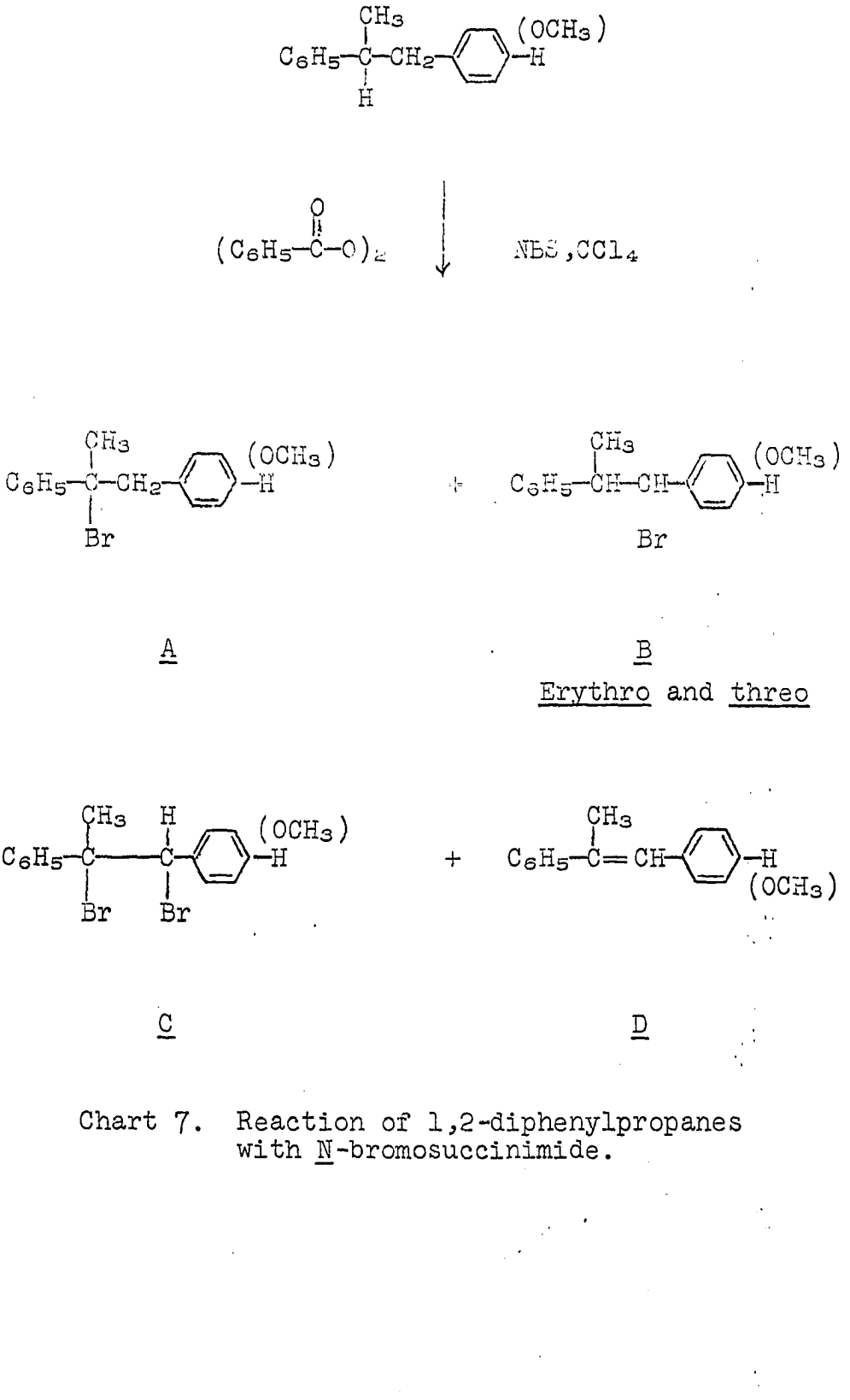


Chart 7. Reaction of 1,2-diphenylpropanes with N-bromosuccinimide.

The reaction products were identified by nmr and the yield of each product was determined by integration of spectra of the crude product mixtures. This method of analysis circumvents fractionation of the diastereomeric products. The yields of the monobromination products obtained are given in Table 5. Small amounts of 1,2-diphenyl-1,2-dibromopropane and 1,2-diphenyl-1-propene were also formed.

Table 5. Yields of monobromination products obtained from reaction of 1,2-diphenylpropane and 1(p-methoxyphenyl)-2-phenylpropane with N-bromosuccinimide

Alkane	1,2-diphenyl-1-bromopropane		-Total of- 1,2-diphenyl-1-bromopropane	1,2-diphenyl-2-bromopropane
	%Erythro	%Threo	%	%
$C_6H_5\underset{\displaystyle CH_3}{\underset{\vert}{C}}H-CH_2-C_6H_5$	41%	59%	51%	49%
$C_6H_5-\underset{\displaystyle CH_3}{\underset{\vert}{C}}H-CH_2-C_6H_4-OCH_3$	53%	47%	83%	14%

These reactions were carried out in an attempt to determine the stereochemical fate of the intermediate radical. It was thought that radical Figure 12 formed by hydrogen abstraction would be a planar species and that the erythro to threo ratio of the bromides obtained from this intermediate

would serve as a model for the open ions derived from the 1,2-diphenyl-1-propanols. However, the stereochemical outcome of these reactions also seems to be substituent dependent. Mechanistic implications must await further research.

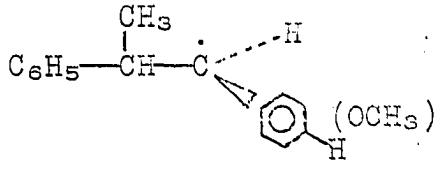


Figure 12. 1,2-Diphenyl-1-propyl radical.

EXPERIMENTAL

Instruments and Methods

All temperatures reported in this dissertation are in centigrade degrees. All melting points (m.p.) and boiling points (b.p.) are uncorrected and pressures are given in millimeters (mm.) of mercury unless otherwise stated.

All nuclear magnetic resonance (nmr) spectra were recorded on either a Varian Associates HR-60 or A-60 spectrometer. Tetramethylsilane was used exclusively as an internal standard. The chemical shifts are reported in parts per million (p.p.m.), (δ) units.

Infrared spectra (IR) were recorded on either a Perkin-Elmer model 21 or Infra-Cord spectrometer. All absorptions are given in reciprocal centimeters ($cm.^{-1}$).

All carbon-hydrogen analyses were performed by Galbraith Laboratories, Inc.

All vapor phase chromatography measurements were made on an Aerograph Model A-90-P instrument.

EXPERIMENTAL

Preparation of Materials

Threo 1,2-diphenyl-1-propanols

The threo 1,2-diphenyl-1-propanols were prepared by the addition of the appropriately substituted 2-phenylpropionaldehyde to phenyl magnesium bromide. The preparation of threo 1,2-diphenyl-1-propanol exemplifies the method of preparation. Magnesium turnings (24 gm., 1.0 mole) were added to a 2 l three-necked round bottom flask with 200 ml. of anhydrous ether. The flask was fitted with a condenser, mechanical stirrer, and an addition funnel. Bromobenzene (157 gm., 1 mole) in 500 ml. anhydrous ether was added, with stirring at a rate sufficient to maintain gentle reflux. After the addition of bromobenzene was complete, the reaction mixture was stirred for an additional hour at room temperature. Hydratropaldehyde (62.5 gm., 1 mole) in 250 ml. of anhydrous ether was added at such a rate as to maintain gentle reflux. The reaction mixture was stirred for an additional two hours at room temperature after the addition of hydratropaldehyde was completed. The reaction mixture was poured over ice and ammonium chloride in a four liter beaker, and sufficient 10% hydrochloric acid was added to acidify the reaction mixture. The two phases were separated and the aqueous phase was extracted with ether. The combined organic material was washed with distilled water,

dried over anhydrous magnesium sulfate, then filtered and concentrated by rotary evaporation. The crude alcohol 172 g (81%) was distilled at reduced pressure using a 10 cm. Vigreax column. The alcohol thus obtained consists of 80% threo and 20% erythro 1,2-diphenyl-1-propanol.

Threo 1,2-diphenyl-1-propanol b.p., 154-156°C (1.7 mm.), m.p. of paranitrobenzoate (PNB) 143-144°C, lit., m.p. 143-144°C (26).

IR: 3630, 3500, 3030, 2960, 2870, 1505, 1495, 1455, 765, 697. Between salt plates.

Nmr: $CDCl_3$; 1.22 (doublet 7 cps spacing), 1.82 (singlet), 2.95 (quintet), 4.6 (doublet 6 cps spacing), 7.15 (singlet).

Threo 1-phenyl-2-(p-chlorophenyl)-1-propanol b.p., 148-150°C (0.7 mm.), yield 57.5%, m.p. of PNB, 111-112°C. Nmr: CCl_4; 1.18 (doublet 7 cps spacing), 2.35 (singlet), 2.87 (multiplet), 4.75 (doublet 6.0 cps spacing), 7.05 (multiplet).

Threo 1-phenyl-2-(p-methoxyphenyl)-1-propanol b.p. 150°C (0.1 mm.), 86% yield, m.p. of PNB, 92.8-93.8°C. Nmr: CCl_4; 1.17 (doublet 7 cps spacing), 2.45 (singlet), 2.87 (multiplet), 3.54 (singlet), 4.48 (doublet 6.0 cps spacing), 6.8 (multiplet).

Threo 1-(p-methoxyphenyl)-2-phenyl-1-propanol b.p. 151-152°C (0.2 mm.), yield 47%. Nmr: CCl_4; 1.0 (doublet 7 cps spacing), 2.55 (singlet), 2.88 (quintet), 3.53 (singlet),

4.5 (doublet 7.0 cps spacing), 7.86 (AB pattern), 7.08 (singlet).

Threo 1-phenyl-2-(o-methoxyphenyl)-1-propanol b.p. 140-144°C (0.05 mm.), m.p. of PNB, 99.5-100.5°C. Nmr: CCl_4; 1.11 (doublet 7 cps spacing), 2.65 (singlet), 3.50 (singlet), 4.66 (doublet 5.0 cps spacing), 6.5-7.2 (multiplet), 7.06 (singlet).

Pure threo 1,2-diphenyl-1-propanols

The various threo 1,2-diphenyl-1-propanols free from diastereomeric impurities were obtained by hydrolysis of the corresponding diastereomerically pure paranitrobenzoates.

Three grams of the appropriate p-nitrobenzoate was dissolved in 50 ml. of a solution which was prepared by dissolving potassium hydroxide (8 gm.) in a mixture of ethanol (100 ml.), dimethylsulfoxide (50 ml.), and water (50 ml.). This solution was warmed on a steam bath for twenty minutes and then poured over ice. The alcohol was extracted into ether and the etheral extract was washed five times with 100 ml. portions of water, dried over anhydrous magnesium sulfate, and concentrated by rotary evaporation. The resulting alcohols were then passed through a column of florisil. The alcohols thus obtained were clear, colorless oils which appeared to be diastereomerically pure by nmr.

Erythro 1,2-diphenyl-1-propanols

The erythro 1,2-diphenyl-1-propanols were prepared by

reduction of the appropriately substituted 2-phenylpropylphenone. Lithium aluminum hydride was used as the reducing agent in all cases with but one exception. Lithium aluminum tri-t-butoxy hydride (16) was used to reduce 2-(p-nitrophenyl)-propylphenone.

The reduction of 2-phenylpropylphenone to erythro 1,2-diphenyl-1-propanol exemplifies the experimental procedure followed.

A solution of 2-phenylpropylphenone (87 gm., 0.42 mole) in 250 ml. of anhydrous ether was added dropwise to a constantly stirring suspension of lithium aluminum hydride (5 gm., 0.14 mole). The reaction flask was fitted with a condenser, mechanical stirrer, and an addition funnel. A positive pressure of nitrogen was maintained throughout the reaction. After the addition was completed the reaction mixture was stirred for an additional four hours at room temperature. The reaction mixture was cooled to zero degrees and the excess hydride was decomposed by the dropwise addition of a saturated potassium carbonate solution. The contents of the reaction flask were poured over ice and carefully acidified with 10% hydrochloric acid. The two phases were separated and the aqueous phase was extracted with ether. The combined organic material was dried over anhydrous magnesium sulfate, then filtered, and concentrated by rotary evaporation. The resulting oil was distilled at reduced pressure to yield

65 gm. 74% of crude erythro 1,2-diphenyl-1-propanol. The erythro alcohol crystallized upon cooling and was recrystallized from pentane.

Erythro 1,2-diphenyl-1-propanol b.p. 118-123°C (1.5 mm.), m.p. 52-53°C, lit., m.p. 51-52°C (26). Nmr: CCl_4; 1.06 (doublet spacing 7 cps), 1.60 (singlet), 2.95 (quintet), 4.5 (doublet 8.4 cps), 7.12 (singlet).

Erythro 1,2-diphenyl-1-propanol-1-D

Erythro 1,2-diphenyl-1-propanol-1-D was prepared by reduction of 2-phenylpropylphenone with lithium aluminum deuteride. The reduction was conducted under the same conditions as described for the preparation of erythro 1,2-diphenyl-1-propanol. A solution of 2-phenylpropylphenone (5.0 gm., 0.024 mole) in anhydrous ether was added dropwise to a rapidly stirring suspension of lithium aluminum deuteride (0.25 gm., 0.006 mole) in 25 ml. of anydrous ether. After the addition was completed the reaction mixture was stirred at room temperature for two hours. The reaction mixture was cooled to zero degrees and 5 ml. of a saturated potassium carbonate solution was added dropwise to destroy excess hydride. The contents of the reaction flask were poured over ice and the organic phase was collected. The aqueous phase was extracted with ether and the combined organic material was dried over anhydrous magnesium sulfate. After filtration, the alcohol was concentrated by rotary evaporation. The alcohol

was recrystallized from pentane to yield 3.0 gm. of erythro alcohol.

Erythro 1,2-diphenyl-1-propanol-1-D m.p. 51-52°. Nmr: $CDCl_3$; 1.05 (broadened doublet 7 cps spacing), 1.82 (singlet), 3.0 (quartet with further splitting), 7.28 (two. sharp nearly over-lapping singlets).

Erythro 1-phenyl-2-(p-chlorophenyl)-1-propanol m.p. 87-88°C, yield 60%. Nmr; $CDCl_3$; 1.06 (doublet 7 cps spacing), 1.93 (singlet), 3.0 quintet), 4.61 (doublet 8.2 cps spacing), 7.28 (singlet), 7.05-7.38 (A_2B_2 pattern).

ANALYSIS: Calc. for $C_{15}H_{15}OCl$: C, 73.02; H, 6.13. Found: C, 73.12; H, 6.07.

Erythro 1-phenyl-2-(p-methoxyphenyl)-1-propanol m.p. 86-87°C, yield 60.6%. Nmr: $CDCl_3$; 1.05 (doublet 7 cps spacing), 1.95 (singlet), 2.96 (quintet), 4.58 (doublet 8.4 cps spacing), 7.04 (A_2B_2 pattern), 7.3 (singlet).

ANALYSIS: Calc. for $C_{16}H_{18}O_2$: C, 79.12; H, 7.50. Found: C, 79.34; H, 7.60.

Erythro-1-(p-methoxyphenyl)-2-phenyl-1-propanol m.p. 89.2-90°C, yield 61%. Nmr: $CDCl_3$; 1.03 (doublet 7 cps spacing), 1.84 (broad singlet), 3.0 (quintet), 3.77 (singlet), 4.6 (doublet 8.8 cps spacing), 7.04 (H_2B_2 pattern), 7.26 (singlet).

ANALYSIS: Calc. for $C_{16}H_{18}O_2$: C, 79.12; H. 7.50. Found: C, 78.98; H, 7.36.

Erythro 1-phenyl-2-(o-methoxyphenyl)-1-propanol, oil

PNB, oil, 3,5-dinitrobenzoate, oil. Nmr: CCl_4; 0.98 (doublet 7 cps spacing), 2.3 (broad singlet), 3.51 (quintet), 3.58 (singlet), 4.6 (doublet 7.7 cps spacing), 6.55-7.23 (multiplet), 7.22 (singlet).

Erythro 1-phenyl-2-(p-nitrophenyl)-1-propanol

Erythro 1-phenyl-2-(p-nitrophenyl)-1-propanol was prepared by the reduction of 2-(p-nitrophenyl)-1-propylphenone with lithium aluminum tri-t-butoxy hydride. A solution of 2-(p-nitrophenyl)-1-propylphenone (9.45 gm., 0.037 mole) in 40 ml. of anhydrous tetrahydrofuran (THF) was added dropwise to a rapidly stirring suspension of lithium aluminum tri-t-butoxy hydride (10.0 gm., 0.039 mole) in 40 ml. of THF. The reaction was conducted in a nitrogen atmosphere in a 1 l. three-necked round bottom flask fitted with a mechanical stirrer, addition funnel, and a condenser. After the addition was complete the reaction mixture was gently refluxed for four hours and then cooled to room temperature. A saturated solution (10 ml.) of potassium carbonate was added dropwise to destroy excess hydride. The contents of the flask were poured over ice and the organic phase was collected. The aqueous phase was extracted with ether and the combined organic material was washed three times with distilled water then dried over anhydrous magnesium sulfate. After filtering, the crude alcohol was concentrated by rotary evaporation. The

resulting oil was chromatographed on silica gel (60 gm.). The alcohol was eluted with benzene and after concentration of the combined benzene fractions the alcohol was obtained as a faint yellow crystalline solid.

Erythro 2-phenyl-1-(p-nitrophenyl)-1-propanol m.p. 102.8-103.8°C. Nmr: $CDCl_3$; 1.16 (doublet 7 cps spacing), 1.88 (singlet), 3.16 (quintet), 4.74 (doublet 7.76 cps spacing), 7.28 (singlet), 7.36 and 8.13 (doublets of A_2B_2 pattern).

ANALYSIS: Calc. for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.87. Found: C, 70.00; H, 5.84.

Paranitrobenzoates of 1,2-diphenyl-1-propanols

The paranitrobenzoates of the 1,2-diphenyl-1-propanols were prepared by the pyridine method (52).

The appropriate alcohol (3 to 5 gm.) was dissolved in anhydrous pyridine (10 to 20 ml.) and placed in a 125 ml. Erlenmeyer flask. A magnetic stirrer was placed in the flask and then p-nitrobenzoylchloride (approximately 5% molar excess) was added to the rapidly stirring solution.

The reaction mixture was heated on a steam bath for approximately 15 minutes and then stirred while cooling to room temperature. The reaction mixture was poured into a separatory funnel containing 50 ml. of a cold 10% sulfuric acid solution and 100 ml. of ether. The etheral solution was washed a second time with 50 ml. of 10% sulfuric acid

solution, then twice with 50 ml. of a 10% sodium hydroxide solution and finally twice with 50 ml. portions of distilled water. The organic material was dried over anhydrous magnesium sulfate, then filtered and concentrated by rotary evaporation. The resulting p-nitrobenzoates were recrystallized from an appropriate solvent.

p-Nitrobenzoate of erythro 1,2-diphenyl-1-propanol m.p. 103-104°C, recrystallized from chloroform-pentane, lit., m.p. 106-107°C (26). Nmr: $CDCl_3$; 1.22 (doublet), 3.45 (quintet), 6.09 (doublet 8.9 cps spacing), 7.26 (singlet), 7.38 (singlet), 7.90-8.3 (A_2B_2 pattern).

p-Nitrobenzoate of threo-1,2-diphenyl-1-propanol m.p. 143-144°C, recrystallized from ethylacetate, lit., m.p. 143-144°C (26). Nmr: $CDCl_3$; 1.46 (doublet), 3.45 (quintet), 6.15 (doublet 7.5 cps spacing), 7.16 (broad singlet), 7.2 (singlet), 8.27 (singlet).

p-Nitrobenzoate of threo 1-phenyl-2-(p-chlorophenyl)-1-propanol m.p. 111.6-111.8°C recrystallized from CCl_4-pentane. IR: 1710, 1605, 1527, 1495, 1345, 1275, 1100, 720, 692, KBr. Nmr: CCl_4; 1.41 (doublet 7 cps spacing), 3.4 (quintet), 6.06 (doublet 7.6 cps spacing), 6.87-7.32 (multiplet), 8.2 (singlet).

ANALYSIS: Calc. for $C_{22}H_{18}O_4NCL$: C, 66.75; H, 4.59. Found: C, 66.53; H, 4.52.

p-Nitrobenzoate of threo 1-phenyl-2-(p-methoxyphenyl)-1-propanol m.p. 92.8-93.8°C, recrystallized from chloroform-pentane. IR: 1720, 1610, 1530, 1518, 1348, 1272, 1242, 1100, 757, 715, 698, (KBr). Nmr: $CDCl_3$; 1.42 (doublet 7 cps spacing), 3.42 (quintet), 3.75 (singlet), 6.01 (doublet 7.50 cps spacing), 6.67-7.10 (A_2B_2 pattern), 7.22 (singlet), 8.27 (singlet).

ANALYSIS: Calc. for $C_{23}H_{21}O_5N$: C, 70.57; H, 5.42. Found: C, 70.50; H, 5.57.

p-Nitrobenzoate of threo 1-phenyl-2-(o-methoxyphenyl)-1-propanol m.p. 99.5-100.5°C, recrystallized from ethanol-water. Nmr: $CDCl_3$; 1.35 (doublet 7 cps spacing), 3.67 (singlet), 3.90 (quintet), 6.25 (doublet 7.0 cps spacing), 6.60-7.20 (ABCD pattern), 7.20 (singlet), 8.18 (singlet).

ANALYSIS: Calc. for $C_{23}H_{21}O_5N$: C, 70.57; H, 5.42. Found: C, 70.26; H, 5.54.

Substituted 2-phenylpropylphenones

The substituted 2-phenylpropylphenones were prepared by oxidation of the appropriate threo 1,2-diphenyl-1-propanol with Jones Reagent (15). The preparationof 2-(p-methoxyphenyl)propylphenone exemplifies the oxidation procedure.

Threo 1-phenyl-2-(p-methoxyphenyl)-1-propanol (4.0 gm., 0.0165 mole) was dissolved in acetone (50 ml.) and placed in an Erlenmeyer flask. The flask was placed in an ice bath and cooled to zero degrees centigrade. Jones reagent* was added

*Jones reagent was prepared by dissolving 13.50 gm. of

chromium trioxide in 25 ml. of water. Concentrated sulfuric acid (11.0 ml.) is then slowly added and the total volume of the solution is brought up to 50 ml. by the addition of water.

dropwise to the rapidly stirring mixture until the red color of unreduced reagent persisted for fifteen minutes. The reaction mixture was stirred for an additional 30 minutes and then poured into a separatory funnel. Distilled water (500 ml.) was added and the reaction mixture was extracted with ether. The organic phase was separated and washed twice with 100 ml. portions of distilled water and then dried over anhydrous magnesium sulfate. After filtration, the ether was removed by rotary evaporation. The crude ketone (oil) was chromatographed on silica gel (30 gm.). The ketone was eluted with Skelly solve "B". The fractions eluted with Skelly solve "B" were combined and the solvent was removed by rotary evaporation to yield 3.66 gm. (92.5%) of the ketone.

2-(p-Methoxyphenyl)propylphenone Nmr: $CDCl_3$; 1.43 (double 7 cps spacing), 3.55 (singlet), 4.55 (center of quartet 7 cps spacing), 6.7 (doublet of A_2B_2 pattern), 7.13 (doublet of A_2B_2 pattern), 7.28 (multiplet), 7.9 (multiplet).

2-(p-Chlorophenyl)-propylphenone, oil Yield 92%. Nmr: CCl_4; 1.42 (doublet), 4.54 (quartet), 7.12 (singlet), 7.25 (multiplet), 7.83 (multiplet).

2-(o-Methoxyphenyl)-propylphenone, oil Yield 98%. Nmr: CCl_4; 1.40 (doublet), 3.70 (singlet), 5.0 (quartet), 7.0 (center of multiplet), 7.88 (center of multiplet).

p-Methoxyphenyl-2-phenylethyl ketone, oil Yield 89%. Nmr: CCl_4; 1.44 (doublet), 3.65 (singlet), 4.52 (center of quartet), 6.70 (center of A_2B_2 doublet), 7.16 (singlet), 7.82 (center of A_2B_2 doublet).

Erythro and threo 1,2-diphenyl-1-propylhalides

Erythro and threo 1,2-diphenyl-1-propylhalides were prepared by the reaction of concentrated hydrochloric acid with threo 1,2-diphenyl-1-propanol in carbon tetrachloride.

Threo 1,2-diphenyl-1-propanol (10 gm., 0.047 moles) was dissolved in 20 ml. of carbon tetrachloride and placed in a 250 ml. Erlenmeyer flask. The reaction mixture was cooled to zero degrees and 50 ml. of the appropriate concentrated hydrohalic acid was pipeted into the rapidly stirring mixture. The reaction was stirred for four hours at zero degrees and then allowed to come to room temperature. The reaction mixture was poured over an ice and water mixture. The organic phase was separated and the aqueous phase was extracted with carbon tetrachloride. The combined organic material was washed with distilled water, dried over anhydrous magnesium sulfate, then filtered and concentrated by rotary evaporation. The crude mixtures of erythro and threo halides consisted of 75-80% of the threo isomer and 20-25% of the erythro diastereomer. The

crude halides were taken up in ethanol. The erythro halides are not soluble in ethanol and were collected by filtration. The threo halides were obtained by concentrating the filtrate and cooling to induce crystallization.

Erythro 1,2-diphenyl-1-propylchloride m.p. 138-139°C, lit., m.p. 138-139°C (26). Nmr: $CDCl_3$; 1.14 (doublet 7 cps spacing), 3.37 (double quartet), 5.07 (doublet 8.73 cps spacing), 7.28 (singlet), 7.33 (singlet).

Threo 1,2-diphenyl-1-propylchloride m.p. 52-53°C, lit., m.p. 52-53°C. (26). Nmr: $CDCl_3$; 1.52 (doublet 7 cps spacing), 3.34 (double quartet), 4.97 (doublet 8.40 cps spacing), 7.10 (singlet), 7.18 (singlet).

Erythro 1,2-diphenyl-1-propylbromide m.p. 157-159°C, lit., m.p. 159-160°C. (26). Nmr: $CDCl_3$; 1.14 (doublet 7 cps spacing), 3.49 (double quartet), 5.07 (doublet 9.66 cps spacing), 7.30 (singlet), 7.35 (singlet).

Threo 1,2-diphenyl-1-propylbromide m.p. 57-59°C, lit., m.p. 60-61°C (26). Nmr: $CDCl_3$; 1.60 (doublet 7 cps spacing), 3.43 (doublet quartet), 5.06 (doublet 9.53 cps spacing), 7.02 (singlet), 7.11 (singlet).

Erythro 1,2-diphenyl-1-propyliodide m.p. 123-125°C., lit., m.p. 124-125°C. (26). Nmr: $CDCl_3$; 1.13 (doublet 7 cps spacing), 3.53 (double quartet), 5.20 (doublet 10.50 cps spacing), 7.30 (singlet).

Threo 1,2-diphenyl-1-propyliodide m.p. 130-131°C., lit., m.p. 130-131°C. (26). Nmr: $CDCl_3$; 1.61 (doublet), 3.53 (double quartet), 5.25 (doublet, 10.58 cps spacing), 7.5 (broad singlet).

Acetates of erythro and threo 1,2-diphenyl-1-propanol

The acetates of erythro and threo 1,2-diphenyl-1-propanol were prepared by reaction of the appropriate alcohol with acetyl chloride.

Erythro 1,2-diphenyl-1-propanol (3 gm.) was dissolved in 50 ml. of anhydrous ether containing 10 gm. of anhydrous pyridine and placed in a 250 ml. three-necked round bottom flask. The flask was fitted with an automatic stirrer, reflux condenser and an addition funnel. The alcohol-ether-pyridine mixture was cooled by means of an ice bath to zero degrees and a solution of acetyl-chloride (2 gm.) in 50 ml. of anhydrous ether was added dropwise to the rapidly stirring mixture. After the addition was complete, the ice bath was removed and the reaction mixture was stirred for one hour at room temperature and then for one hour at gentle reflux. The reaction mixture was poured over ice and water was added. The organic phase was washed three times with 50 ml. portions of cold dilute (10%) sulfuric acid, twice with 50 ml. portions of a 5% sodium bicarbonate solution, and then twice with 50 ml. portions of distilled water. The organic material was

dried over anhydrous magnesium sulfate, then filtered and concentrated by rotary evaporation. The erythro acetate was recrystallized from heptane.

Erythro 1,2-diphenyl-1-propylacetate m.p. 107-108°C. Nmr: $CDCl_3$; 1.12 (doublet 7 cps spacing), 1.81 (singlet), 3.24 (double quartet), 5.89 (doublet 8.65 cps spacing), 7.25 (singlet), 7.30 (singlet).

Threo 1,2-diphenyl-1-propylacetate, oil Nmr: $CDCl_3$; 1.33 (double 7 cps spacing), 2.0 (singlet), 3.22 (quintet), 5.90 (doublet 7.80 cps spacing), 7.12 (singlet).

Erythro 1,2-diphenyl-1-propyltosylate

Erythro 1,2-diphenyl-1-propanol (7 gm., 0.033 moles) was placed in a 250 ml. Erlenmeyer flask and pyridine (70 ml.) was added. This mixture was cooled to zero degrees centigrade and p-toluenesulfonic acid (5.8 gm., 0.036 mole) was added over a period of 15 minutes. The flask was stoppered and placed in a freezer and allowed to stand. Pyridine hydrochloride began to crystallize from the reaction mixture after two days. After six days, the reaction mixture was taken from the freezer and poured over ice. The tosylate separated and was collected by vacuum filtration. The crude tosylate was dissolved in a chloroform-pentane (1:4) mixture and the organic material was washed once with 25 ml. of ice cold 0.5 N sulfuric acid, twice with 25 ml. portions of 5% sodium bicarbonate, once with water

and then dried over anhydrous magnesium sulfate. After filtration, the solvent was concentrated and allowed to stand. The tosylate was collected by filtration and a second crop was obtained by concentration of the mother liquors.

Erythro 1,2-diphenyl-1-propyltosylate m.p. 90-90.5°C., lit., 84-85°C. (26), yield 5.6 gm., 48%. Nmr: $CDCl_3$; 1.08 (doublet 7 cps spacing), 2.32 (singlet), 3.25 (quintet), 5.49 (doublet 7.95 cps spacing), 7.03 (doublet of A_2B_2 pattern), 7.18 (multiplet), 7.37 (doublet of A_2B_2 pattern).

Reaction of the diastereomeric 1,2-diphenyl-1-propanols with hydrobromic and hydrochloric acids in carbon tetrachloride

The reaction of erythro 1,2-diphenyl-1-propanol with concentrated hydrochloric acid in carbon tetrachloride exemplifies the experimental procedure.

Erythro 1,2-diphenyl-1-propanol (100 mg.) was placed in 125 ml. Erlenmeyer flask and 20 ml. of carbon tetrachloride was pipeted into the flask. The flask was fitted with a condenser and a drying tube. A small magnetic stirrer was placed in the flask and the alcohol was stirred into solution. An ice bath was placed around the Erlenmeyer and the reaction mixture was cooled to zero degrees. Concentrated hydrochloric acid was cooled to zero degrees and 10 ml. was pipeted into the rapidly stirring mixture. The reaction was stirred at zero degrees for eight hours and then poured over ice in a

separatory funnel. Water was added and the organic phase was separated. The aqueous phase was extracted with two 25 ml. portions of carbon tetrachloride. The combined organic material was washed three times with distilled water, dried over anhydrous magnesium sulfate, filtered, and then concentrated by rotary evaporation at room temperature. The residue was taken up in deuteriochloroform (1-2 ml.) and filtered through sintered glass directly into an nmr tube. The erythro to threo ratio of the product chlorides was determined by integration over the methyl region. The methyl absorption of the threo derivatives occurs at c.a. 1.5 and that of the erythro diastereomer occurs at c.a. 1.2 δ.

Erythro 1-phenyl-2-(p-methoxyphenyl)-1-propylbromide m.p. 132-133°C. Nmr: $CDCl_3$; 1.13 (doublet), 3.43 (double quartet), 3.78 (singlet), 5.00 (doublet 9.2 cps spacing), 6.84 (doublet of A_2B_2 9 cps spacing), 7.15 (doublet of A_2B_2), 7.30 (singlet).

ANALYSIS: Calc. for $C_{16}H_{17}OBr$: C, 62.96; H, 5.61. Found: C, 62.83; H, 5.49.

Erythro 2-(p-chlorophenyl)-1-propylchloride Nmr: $CDCl_3$; 1.10 (doublet), 3.30 (quintet), 4.87 (doublet 8.4 cps spacing), 6.87 (doublet of A_2B_2), 7.12 (doublet of A_2B_2), 7.12 (singlet).

Threo 2-(p-methoxyphenyl)-1-propylbromide, oil Nmr: CCl_4; 1.51 (doublet 7 cps spacing), 3.3 (double quartet), 3.45 (singlet), 4.95 (doublet 9.2 cps spacing), 6.52 (doublet

of A_2B_2, 9 cps spacing), 6.82 (doublet of A_2B_2, 9 cps spacing), 6.84-7.30 (multiplet).

Mass spectrum: gave molecular ion 304, 306; base peak 135.

Threo 2-(p-chlorophenyl)-1-propylchloride, oil Nmr: $CDCl_3$; 1.45 (doublet), 3.30 (quintet), 4.87 (doublet 8.3 cps spacing), 6.9 (doublet of A_2B_2), 7.12 (doublet of A_2B_2), 7.12 (singlet).

Erythro 2-(p-nitrophenyl)-1-propylbromide m.p. 139-140°C. Nmr: $CDCl_3$; 1.16 (doublet 7 cps spacing), 3.62 (double quartet), 5.03 (doublet 9.7 cps spacing), 7.35 (singlet), 7.40 (doublet of A_2B_2, 8 cps spacing), 8.20 (doublet of A_2B_2, 8 cps spacing).

ANALYSIS: Calc. for $C_{15}H_{14}D_2NBr$: C, 56.45; H, 4.11. Found: C, 56.30; H, 4.11.

Erythro 2-(p-chlorophenyl)-1-propylbromide m.p. 115-116°C. Nmr: $CDCl_3$; 1.10 (doublet), 3.45 (double quartet), 4.98 (doublet 9.6 cps spacing), 7.20 (doublet of A_2B_2, 9 cps spacing), 7.30 (doublet of A_2B_2, 9 cps spacing), 7.30 (singlet).

ANALYSIS: Calc. for $C_{15}H_{14}CLBr$: C, 58.18; H, 4.56. Found: C, 58.18; H, 4.41.

Threo 1-phenyl-2-(p-nitrophenyl)-1-propylchloride Nmr: CCl_4; 1.51 (doublet), 3.43 (quintet), 4.90 (doublet), 7.13 (singlet), 7.14 (doublet of A_2B_2), 7.98 (doublet of A_2B_2, 9 cps spacing).

Threo 1-phenyl-2-(p-nitrophenyl)-1-propylbromide Nmr: $CDCl_3$; 1.60 (doublet), 3.58 (double quartet), 5.08 (doublet 9 cps spacing), 7.15 (singlet), 7.17 (doublet of A_2B_2), 8.0 (doublet of A_2B_2).

Threo 1-phenyl-2-(o-methoxyphenyl)-1-propylbromide m.p. 86-87°C. Nmr: $CDCl_3$; 1.52 (doublet 7 cps spacing), 3.66 (singlet), 3.83 (double quartet), 5.33 (doublet 8.60 cps spacing), 6.5-7.42 (multiplet).

ANALYSIS: Calc. for $C_{16}H_{17}OBr$: C, 62.91; H, 5.61. Found: C, 62.76; H, 5.70.

Erythro 1-phenyl-2-(o-methoxyphenyl)-1-propylchloride Nmr: $CDCl_3$; 1.10 (doublet 7 cps spacing), 3.66 (singlet), 3.76 (quintet), 5.19 (doublet 7.6), 6.5-7.4 (multiplet).

Threo 1-phenyl-2-(o-methoxyphenyl)-1-propylchloride Nmr: $CDCl_3$; 1.41 (doublet), 3.60 (singlet), 3.75 (quintet), 5.19 (doublet 7.4 cps spacing), 6.5-7.4 (multiplet).

Erythro 1-(p-methoxyphenyl)-2-phenyl-1-propyl bromide m.p. 106°C decomposition. Nmr: $CDCl_3$, 1.13 (doublet), 3.46 (double quartet), 3.76 (singlet), 5.06 (doublet), 6.64 (doublet of A_2B_2), 7.28 (doublet of A_2B_2), 7.28 (singlet).

Threo 1-(p-methoxyphenyl)-2-phenyl-1-propylbromide m.p. 106°C decomposition. Nmr: $CDCl_3$, 1.57 (doublet), 3.46 (double quartet), 3.65 (singlet), 5.09 (doublet), 6.65 (doublet of A_2B_2), 7.12 (doublet of A_2B_2), 7.06 (singlet).

ANALYSIS: Calc. for $C_{16}H_{17}OBr$: C, 62.96; H, 5.61. Found: C, 62.76; H, 5.70.

Erythro 2-(p-methoxyphenyl)-1-phenyl-1-propylchloride

Nmr: $CDCl_3$; 1.12 (doublet), 3.27 (quintet), 3.72 (singlet), 4.90 (doublet 8.4 cps spacing), 6.62 (doublet of A_2B_2 9 cps spacing), 7.92 (doublet of A_2B_2 9 cps spacing), 7.23 (singlet).

Threo 1-phenyl-2-(p-methoxyphenyl)-1-propylchloride, oil

Nmr: $CDCl_3$; 1.44 (doublet), 3.23 (quintet), 3.60 (singlet), 4.83 (doublet 8.3 cps spacing), 6.56 (doublet of A_2B_2), 6.85 (doublet of A_2B_2), 7.06 (singlet).

Erythro 1-phenyl-2-(p-nitrophenyl)-1-propylchloride

Nmr: CCl_4; 1.20 (doublet 7 cps spacing), 3.45 (quintet), 4.90 (doublet), 7.25 (singlet), 7.28 (doublet of A_2B_2), 8.10 (doublet of A_2B_2).

Threo 1-(p-methoxyphenyl)-2-phenyl-1-propylchloride

Nmr: CCl_4; 1.48 (doublet), 3.28 (quintet), 3.52 (singlet), 4.87 (doublet), 6.58 (doublet of A_2B_2), 7.11 (doublet of A_2B_2), 7.14 (singlet).

Erythro 1-(p-methoxyphenyl)-2-phenyl-1-propylchloride

Nmr: CCl_4; 1.12 (doublet), 3.28 (quintet), 3.62 (singlet), 4.88 (doublet), 6.72 (doublet of A_2B_2), 7.0 (doublet of A_2B_2), 7.0 (singlet).

Threo 1-phenyl-2-(p-chlorophenyl)-1-propylbromide

Nmr: CCl_4; 1.47 (doublet), 3.30 (double quartet), 4.88 (doublet), 6.79 (doublet of A_2B_2), 7.01 (doublet of A_2B_2, 7.04 (singlet).

2-(p-Methoxyphenyl)propionaldehyde

The 2-(p-methoxyphenyl)propionaldehyde (p-methoxyhydratropaldehyde) was prepared by the acid catalyzed rearrangement of 1-(p-methoxyphenyl)-1,2-dibromopropane (anethole dibromide).

Anethole (148 gm., 1 mole) was placed in a three liter three-necked flask and pentane (500 ml.) was added. The flask was fitted with a reflux condenser, addition funnel and a mechanical stirrer. The anethole-pentane solution was cooled to -20°C and then a solution of bromine (1 mole) in pentane (150 ml.) was added dropwise with constant stirring. The anethole dibromide crystallized from the pentane solution and was collected by filtration yielding 260 gms., 84%.

Anethole dibromide (148 gms., 0.48 mole) was placed in a two liter single necked round bottom flask and ethanol (200 ml.) was added followed by six hundred ml. of fifteen percent sulfuric acid. A magnetic stirring bar was placed in the flask and then the flask was fitted with a reflux condenser. The mixture was stirred and maintained at gentle reflux for ten hours. After cooling to room temperature, the reaction mixture was poured over ice and extracted with ether. The ether layer was washed three times with distilled water, dried over anhydrous magnesium sulfate, and then concentrated on the rotary evaporator. The resulting oil was vacuum distilled and the fraction distilling between 88-90°C at 0.2 mm. was collected giving 52 gm., 65% yield of p-methoxyhydratrop-

aldehyde.

2-(p-Methoxyphenyl)propionaldehyde(p-methoxyhydratropaldehyde) b.p. 90°C., 0.2 mm., lit., 100°C., 2 mm. (68). Nmr: $CDCl_3$; 1.34 (doublet), 3.52 (quartet each peak further split into a doublet), 6.85 (doublet).

1-(o-Methoxyphenyl)-1-propene

The 1-(o-methoxyphenyl)-1-propene was prepared from 1-(o-methoxyphenyl)-1-propanol by acid catalyzed dehydration.

One mole of o-methoxybenzaldehyde in five hundred ml. of anhydrous ether was added dropwise to a rapidly stirring solution of ethyl magnesium bromide (1 mole) in anhydrous ether (1500 ml.). After the addition was complete, the reaction mixture was stirred at reflux for an additional two hours and then allowed to cool to room temperature. The reaction mixture was poured over ice and acidified with a fifteen percent hydrochloric acid solution. The organic phase was separated and washed three times with distilled water (100 ml. portions), dried over anhydrous magnesium sulfate, filtered and concentrated by rotary evaporation. The alcohol (an oil) was taken up in benzene (150 ml.) and placed in a single necked round bottom flask (500 ml.). P-toluene sulfonic acid (1/2 gram) was added and the mixture was gently refluxed for sixteen hours and then allowed to cool to room temperature. The reaction mixture was poured over ice and the organic phase was separated, dried over anhydrous magnesium sulfate, filtered

and vacuum distilled. The fraction distilling between 52°C and 56°C at 0.05 mm. was collected. An nmr of this material showed the presence of both the cis and trans olefins, yield 60 gm., 40%.

1-(o-Methoxyphenyl)-1-propene b.p. 52-56°C, (0.05 mm.). Nmr: CCl_4; 1.51 (doublet 6 cps spacing), 1.53 (doublet 6 cps spacing), 3.65 (singlet), 5.92 (quartet), 6.27 (quartet), 6.53 (singlet exhibiting further splitting), 6.71 (singlet exhibiting further splitting), 6.7-7.37 (multiplet).

1-(o-Methoxyphenyl)-1,2-dibromopropane

The 1-(o-methoxyphenyl)-1,2-dibromopropane was prepared by the addition of bromine to 1-(o-methoxyphenyl)-1-propene using the same procedure as described for the preparation of 1-(p-methoxyphenyl)-1,2-dibrompropane. The dibromide (an oil) was obtained after removal of the pentane by rotary evaporation and was used without further purification. Yield 121 gms., 88%.

2-(o-Methoxyphenyl)-propionaldehyde

The 2-(o-methoxyphenyl)propionaldehyde (o-methoxyhydratropaldehyde) was prepared by the acid catalyzed rearrangement of 1-(o-methoxyphenyl)-1,2-dibromopropane.

1-(o-Methoxyphenyl)-1,2-dibromopropane (121 gm., 0.39 mole) was placed in a one liter round bottom flask and ethanol (100 ml.) was added. A magnetic stirring bar was placed in the flask and five-hundred ml. of fifteen percent sulfuric

acid was added. The reaction mixture was gently refluxed for ten hours. After cooling to room temperature, the reaction mixture was poured over ice and extracted with ether. The organic layer was washed with distilled water, dried over anhydrous magnesium sulfate, filtered and concentrated by rotary evaporation. The resulting oil was vacuum distilled yielding 45.7 gms., 71% 2-(o-methoxyphenyl)propionaldehyde.

2-(o-Methoxyphenyl)propionaldehyde b.p. 92°C., (0.2 mm.). Nmr: CCl_4; 1.3 (doublet), 3.75 (singlet), 3.76 (quartet), 6.96 (multiplet), 9.55 (doublet 0.6 cps spacing).

2-(p-Chlorophenyl)propionaldehyde

The 2-(p-chlorophenyl)propionaldehyde was prepared by the Darzens glycidic ester condensation (61).

Ethylchloroacetate (0.5 mole), p-chloroacetophenone (0.5 mole), and 100 ml. of benzene were placed in a two liter three necked round bottom flask. The flask was fitted with a reflux condenser and a mechanical stirrer. Potassium t-butoxide (0.5 mole) was added in small portions over a two hour period and the reaction mixture was stirred for an additional twenty-four hours. The reaction mixture was poured over ice and extracted with benzene. The organic material was dried over anhydrous magnesium sulfate, filtered and vacuum distilled. The fractions distilling between 115-122°C. at 0.75 mm. were collected. The glycidic ester thus obtained was placed in a one liter round bottom flask and sodium

ethoxide in ethanol (5.8 gms. sodium in one hundred ml. ethanol) was added. The reaction mixture was stirred for two hours and then the flask was surrounded by an ice bath. Eight ml. of water was added dropwise to the reaction mixture and the sodium salt of the glycidic ester separated from the reaction mixture. The salt was placed in an Erlenmeyer flask (500 ml.) and was decomposed by treatment with a hydrochloric acid solution (28 ml. concentrated hydrochloric acid in 150 ml. water). After the initial evolution of carbon dioxide subsided, the reaction mixture was heated on a steam bath for two hours and then allowed to cool to room temperature. The reaction mixture was poured over ice and extracted with ether. The organic material was washed with water, dried over anhydrous magnesium sulfate, filtered and concentrated by rotary evaporation. The resulting oil was vacuum distilled and the fraction distilling between 78-80°C. at 0.8 mm. was collected yielding the aldehyde (12.72 gm.).

2-(p-Chlorophenyl)propionaldehyde b.p. 78-80°C., (0.8 mm.). Nmr: CCl_4; 1.37 (doublet 7 cps spacing), 3.55 (quartet with each peak further split into a doublet), 7.2 (center of A_2B_2 pattern), 9.57 (doublet 1 cps spacing).

LITERATURE CITED

1. Allinger, N. L., Allinger, J., Chow, L. W., and Wang, G. L., J. Org. Chem., 32, 522 (1967).

2. Anet, F. A. L., J. Am. Chem. Soc., 84, 747 (1962).

3. Banthorpe, D. V., "Elimination Reactions", in E. D. Hughes, "Mechanisms in Organic Chemistry", Vol. 2, 140-141, Elsevier, New York, N.Y., 1963.

4. Bartlett, P. D. and Rosen, J. L., J. Am. Chem. Soc., 64, 543 (1942).

5. Barton, D. H. R., Experienta, 6, 316 (1950).

6. Beilstein's Handbuch der Organischen Chemie, Vol. 5, Suppl. 1, Deutschen Chemischen Gesellschaft, Berlin, Germany, 1930.

7. Beilstein's Handbuch der Organischen Chemie, Vol. 6, Suppl. 1, Deutschen Chemischen Gesellschaft, Berlin, Germany, 1931.

8. Bethell, D. and Gold, V., Quart. Revs. (London), 12, 173 (1958).

9. Bonner, W. A. and Collins, C. J., J. Am. Chem. Soc., 75, 5372 (1953).

10. Bonner, W. A. and Collins, C. J., J. Am. Chem. Soc., 77, 99 (1955).

11. Bonner, W. A. and Collins, C. J., J. Am. Chem. Soc., 78, 5587 (1956).

12. Bothner-By, A. A., Naar-Colin, C., and Gunther, H., J. Am. Chem. Soc., 84, 2742 (1962).

13. Bothner-By, A. A., Naar-Colin, C., and Gunther, H., J. Am. Chem. Soc., 84, 2748 (1962).

14. Bothner-By, A. A. and Naar-Colin, C., J. Am. Chem. Soc., 84, 743 (1962).

15. Bowers, A., Halsall, T. G., Jones, E. R. H. and Lemin, A. J., J. Chem. Soc., 2548 (1953).

16. Brown, H. C. and McFarlin, R. F., J. Am. Chem. Soc., 80, 5372 (1958).

17. Brown, H. C., Morgan, K. J., and Choupek, F. J., J. Am. Chem. Soc., 87, 2137 (1965).

18. Buza, M. and Snyder, E. I., J. Am. Chem. Soc., 88, 1161 (1966).

19. Capon, B., Quart. Revs. (London), 18, 45 (1964).

20. Collins, C. J. and Bonner, W. H., J. Am. Chem. Soc., 77, 92 (1955).

21. Collins, C. J. and Bonner, W. H., and Lester, C. T., J. Am. Chem. Soc., 81, 466 (1959).

22. Cram, D. J., J. Am. Chem. Soc., 71, 3863 (1949).

23. Cram, D. J., J. Am. Chem. Soc., 86, 3767 (1964).

24. Cram, D. J. and Ela, S. W., J. Am. Chem. Soc., 88, 5777 (1966).

25. Cram, D. J. and Elhafez, F. A. Abd., J. Am. Chem. Soc., 74, 5828 (1952).

26. Cram, D. J. and Elhafez, F. A. Abd., J. Am. Chem. Soc., 74, 5852 (1952).

27. Cram, D. J. and Elhafez, F. A. Abd., J. Am. Chem. Soc., 75, 339 (1953).

28. Cram, D. J. and Elhafez, F. A. Abd., J. Am. Chem. Soc., 76, 30 (1954).

29. Dillon, R. T., Young, W. G., and Lucas, H. J., J. Am. Chem. Soc., 52, 1953 (1930).

30. Eliel, E. L., "Stereochemistry of Carbon Compounds", McGraw-Hill Book Co., Inc., New York, N.Y., 1962.

31. Eliel, E. L., Allinger, N. L., Angyal, J. S., and Morrison, G. A., "Conformational Analysis", Interscience Publishers, Inc., N.Y., 1966.

32. Eliel, E. L. and Ro, R. S., J. Am. Chem. Soc., 79, 5992 (1957).

33. Fahey, R. C., J. Am. Chem. Soc., 88, 4681 (1966).

34. Hine, J. and Brader, W. H., Jr., J. Am. Chem. Soc., 77, 361 (1955).

35. Hyne, J. B., Can. J. Chem., 39, 2536 (1961).

36. Karabatsos, G. J. and Hsi, N., J. Am. Chem. Soc., 87, 2864 (1965).

37. Karplus, M., J. Chem. Phys., 30, 11 (1959).

38. Karplus, M., J. Am. Chem. Soc., 85, 2870 (1963).

39. Kingsbury, C. A. and Best, D. S., J. Org. Chem., 32, 6 (1967).

40. Lucas, H., Simpson, M., and Carter, I., J. Am. Chem. Soc., 47, 1465 (1925).

41. McClellan, A. L., "Tables of Experimental Dipole Moments", W. H. Freeman and Co., San Francisco, Calif., 1963.

42. Millen, D. J., Progress in Stereochemistry, 3, 139 (1962).

43. Olah, G. A., Namanworth, E., and Comisaro, M. B., J. Am. Chem. Soc., 89, 711 (1967).

44. Olah, G. A., Pittman, C. U., Jr., Namanworth, E., and Comisarow, M. B., J. Am. Chem. Soc., 88, 5571 (1966).

45. Overberger, C. G. and Kurtz, T., J. Org. Chem., 31, 288 (1966).

46. Poutsma, M. L., J. Am. Chem. Soc., 87, 4285 (1965).

47. Puterbaugh, W. H. and Newman, M. S., J. Am. Chem. Soc., 81, 1611 (1959).

48. Roberts, I. and Kimball, G. E., J. Am. Chem. Soc., 59, 947 (1937).

49. Sachse, H., Chem. Ber., 23, 1363 (1890).

50. Sheppard, N., Advan. Spectr., 1, 295 (1959).

51. Shimanonchi, T. and Tasumi, M., Stectrochimica Acta, 17, 755 (1961).

52. Shriner, R. L., Fuson, R. C. and Curtin, D. Y., "The Systematic Identification of Organic Compounds", 5th Ed., John Wiley and Sons, Inc., New York, N.Y. 1964.

53. Stoermer, R. and Kootz, B., Chem. Ber., 58, 2613 (1938).

54. Sicher, J., Cherest, M., Gault, Y., and Felkins, H., Collection Czech. Chem., Commun., 28, 72 (1963).

55. Streitweiser, A., Jr., "Solvolytic Displacement Reactions", McGraw-Hill Book Co., Inc., New York, N.Y. 1962.

56. Thompson, H. B., J. Chem. Edu., 43, 66 (1966).

57. Underwood, G. M., Molecular Intercourse, to appear as an unpublished Ph. D. Thesis, Library, University of Nebraska, Lincoln, Nebraska, 1970.

58. Van-Duin, C. F., Rec. Trans. Chem., 43, 341 (1924).

59. Van-Duin, C. F., Rec. Trans. Chem., 45, 345 (1926).

60. Van-Duin, C. F., Rec. Trans. Chem., 47, 715 (1928).

61. Vogel, A. I., "Practical Organic Chemistry", 3rd Ed., Longmans Green and Co., Ltd., London, 1956.

62. Weissburger, A., "Technique of Organic Chemistry", Vol. 1, 3rd Ed., Interscience Publishers, Inc., New York, N.Y., 1960.

63. Whitesides, G. M., Sevenair, J. P., and Goetz, R. W., J. Am. Chem. Soc., 89, 1135 (1967).

64. Wiberg, K. B., "Laboratory Technique in Organic Chemistry", McGraw-Hill Book Co., Inc., New York, N.Y. 1960.

65. Winstein, S., Grunwald, E., and Ingraham, L. L., J. Am. Chem. Soc., 70, 821 (1948).

66. Winstein, S., Lindergren, C. R., Marshall, H., and Ingraham, L. L., J. Am. Chem. Soc., 75, 147 (1953).

67. Winstein, S., Pressman, D., and Young, W. G., J. Am. Chem. Soc., 61, 1645 (1939).

68. Yoshida, N., Omoto, M., and Inoi, T., Yakugaku Zasshi, 78, 183 (1958).

69. Young, W. G., Pressman, D., and Corryell, C. D., J. Am. Chem. Soc., 61, 1640 (1939).

ACKNOWLEDGEMENTS

The author wishes to thank Dr. C. A. Kingsbury for his suggestions and guidance throughout the course of this work and his various lab partners while at Iowa State who helped make the completion of this work a more enjoyable experience.

The author wishes to thank Shell Companies Foundation, Inc., for financial assistance which helped support part of this work.

He also wishes to thank his parents for encouragement and financial assistance and especially his loving wife whose many sacrifices made completion of this work possible.