THE STEREOCHEMISTRY AND MECHANISM OF THE ADDITION OF HYDROGEN CHLORIDE TO 4-TERT-BUTYL-1-PHENYLCYCLOHEXENE AND DERIVATIVES

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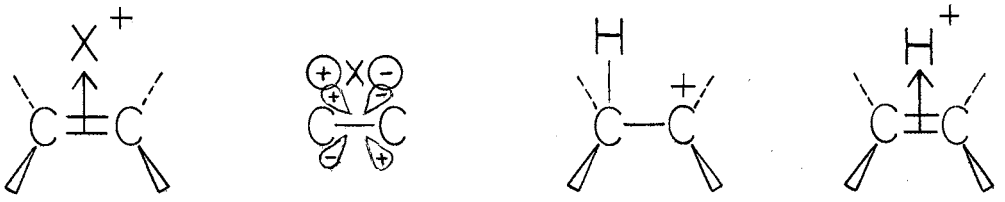
CHAPTER I

HISTORICAL

The mechanisms and stereochemistry of electrophilic additions to alkenes have been studied for many years, but with the use of modern instrumentation, many previous assumptions and even conclusions have been proved incorrect. The first prediction of stereospecific trans addition occurred in 1912.[29] The belief that all additions proceed with a trans mode of addition has been accepted as fact until the last seven years.[16] Electrophilic addition has long been characterized as involving a reagent XY attacking an unsaturated species via a transition state incorporating a net positive charge or carbonium ion. It is commonly accepted that the intermediates may not be simple carbonium ions since stereospecific additions are obtained from certain reactions.

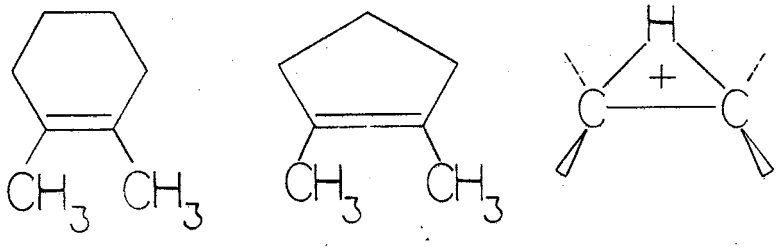
The stereochemistry of electrophilic addition is known to depend on several factors including the reaction conditions, the structure of the alkene, and the nature of the attacking species. Dewar explained the early stereospecific trans additions by postulating the intermediate to be a π-complex taking one of several forms.[14] For example, the π-complex $\underset{\sim}{1}$ might be a complex in which the filled π-orbital of the alkene is used to form a dative (coordinate covalent) bond by interaction with the empty valence orbital of the acceptor X^+. If the acceptor X^+ has unshared p or d electrons or π electrons, these can be used to form a reverse dative bond to the olefin by interaction with



1 2 3 4

the empty antibonding π-molecular orbital 2. The question of whether a π-complex 4 or a classical carbonium ion 3 is the more stable will have to be decided on conclusive proof of the stereospecificity of the reaction of an acid, e.g., HBr to an alkene. Trans addition would indicate that the classical carbonium ion 3 is less stable than the π-complex 4.

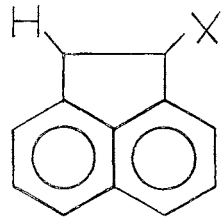
The classical work by Hammond, Nevitt, and Collins, in which they demonstrated stereospecific trans addition of HBr to 1,2-dimethylcyclohexene (5) and of HCl to 1,2-dimethylcyclopentene (6), has been used to argue for a π-complex or an onium bridge intermediate 7.[35,36]



5 6 7

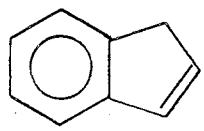
Stereospecific cis addition, however, has been demonstrated by Dewar for the addition of both DCl and DBr to acenaphthylene (8) using cis and trans coupling constants for the protons originally attached to

the vinyl group. This was supported by the almost quantitative elimination of HBr after the addition, leaving deuterium fully incorporated in 8a.[16]



8 X = H

8a X = D



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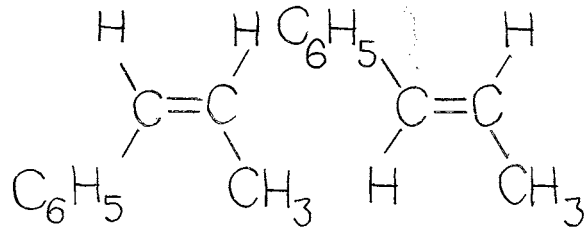
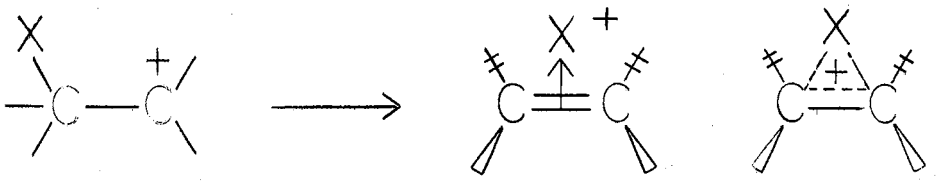


10 11

Temperature variations from -78 to 25° caused no significant change in the products. The addition of DBr to indene (9) (studied via the NMR coupling constants) and to cis- and trans-1-phenylpropene (10 and 11), studied by quantitative elimination to yield either DBr from the DBr adduct formed from 10 or HBr from the DBr adduct formed from 11, was shown conclusively to be of the cis type.[17,18] These results proved conclusively that additions of hydrogen halides to these four compounds could not proceed through π-complexes or free carbonium ions as intermediates because the former would yield exclusively trans adducts while the latter would yield mixtures of equal amounts of the cis and trans adducts. Dewar's tentative assumption was that the normal course of addition of hydrogen halides to alkenes is a polar electrophilic process involving classical carbonium ions as intermediates and leads mostly, but not exclusively, to cis adducts unless steric factors interfere.[15] The question is then why some electrophilic additions to alkenes take place via π-complexes, while others involve carbonium ions as intermediates. A qualitative explanation is based

on the heat of isomerization (ΔH) for 12 and 13. The whole positive



12 13 13a

charge resides on the carbon in 12, while in 13 a part, δq, of it resides on X. If E_{C-C}, $E_{C=C}$, E_{C-X} are the bond energies (B.E.) of the C-C, C=C, and C-X bonds, respectively, E_{π} is that of the dative bond in (13), and I_C and I_X are the ionization potentials of carbon and X, respectively, then:

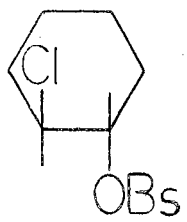
$$\Delta H = E_{C=C} + E_{\pi} - E_{C-C} - E_{C-X} + \delta q(I_C - I_X)$$

$$\Delta H = C + E_{\pi} - E_{C-C} - E_{C-X} - \delta q \cdot I_X$$

where C is a constant for attack on a given alkene by different reagents X. This equation shows that the complex structure will be all the more favored the weaker the C-X bond and the less electronegative X, because the dative bond will be relatively weak and variations in its small bond energy are likely to be relatively unimportant. Two other contributing factors to consider are; (1) the possibility of back coordination from unshared p or d electrons on X as in 2 which would stabilize the π-complex; (2) the carbonium ion will be selectively stabilized by -E or $\pm$E substituents.

Until the work of Olah was published, evidence of free carbonium ions or π-complexes was plentiful but not concrete. He has successfully

obtained proof of the existence of discrete carbonium ions in antimony pentafluoride-fluorosulfonic acid-sulfur dioxide solutions [e.g., $(C_6H_5)_2\overset{+}{C}H$, $(CH_3)_3C^{+}$, $CH_3\overset{+}{C}HCH_2CH_3$] from their NMR spectra.[54,55] Halogen participation has been postulated as occurring through bridging, as witnessed by enhancement in rate of certain solvolysis reactions in conjunction with retention of configuration in the solvolysis products.[4]



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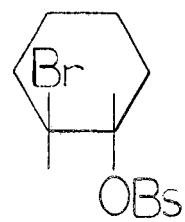

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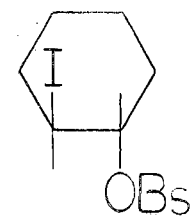
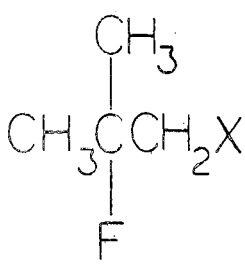


2,700,000

Rate Enhancement; trans/cis

The conclusive proof for halonium ion participation and formation has again been provided by Olah.[56] That Br and I will form bridged halonium ions 15, starting with 14, and under the proper conditions, was again determined from NMR data. It was found, however, that the chloro



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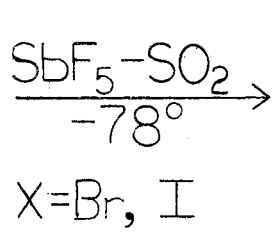

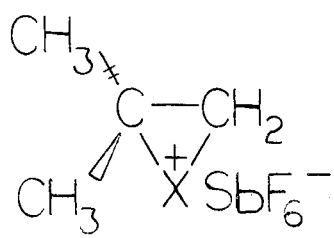

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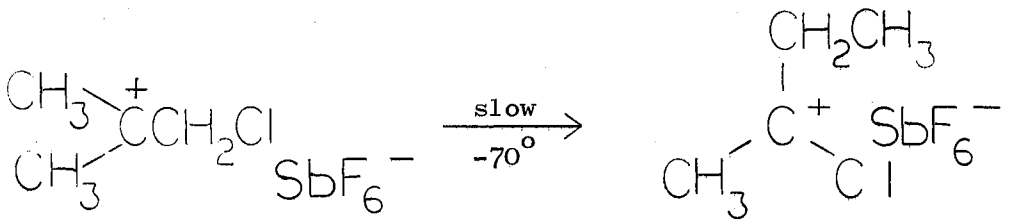
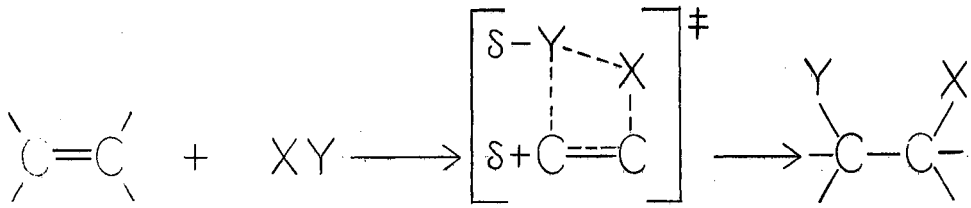
derivative formed only classical carbonium ions 16 and 17.[56]



16 17

From comparing these experimental results with Dewar's qualitative explanation, a correlation is apparent. The carbon-chlorine bond (81 kcal/mole) is appreciably stronger than the carbon-bromine (68 kcal/mole) or carbon-iodine (51 kcal/mole) bond.[9] Also, the ionization potentials (I.P.) of Cl, Br, and I are respectively 13.01, 11.84, and 10.44 e.v., again assigning Cl the largest value.[34] These data applied to Dewar's equation would have helped to predict that 16 should exist as a classical carbonium ion and 14 and 15 would favor the π-complex or halonium ion. The assumption is made that Dewar's equation would apply equally to a π-complex or bridged species. Using these same criteria one must conclude that the hydrogen atom (C-H B.E., 98.7 kcal/mole; I.P., 13.60 e.v.) in HBr and HCl, like chlorine in Cl_2, would be very reluctant to form a π-complex or bridged species in preference to a classical carbonium ion.[9,34]

Now that the types of intermediates which can form have been considered, the pathways of their formation should be elucidated. The simplest mechanism which can be written for the addition of XY to an alkene is a molecular addition proceeding via a cyclic transition state and giving exclusively cis addition.[22] Both bonds are formed in the slow step. Although this mechanism is probably involved in most



cis

nonradical gas phase reactions, no kinetic data could be found to indicate that this mechanism is active for solutions.

Probably the most important mechanism for electrophilic addition in the liquid phase is stepwise addition via an onium-ion intermediate, where the

$$E + XY \xrightarrow{slow} EX^+ + Y^- \xrightarrow{fast} EXY$$

Ad_E2 mechanism

rate-limiting reaction of an olefin E with XY gives a cationic intermediate which rapidly collapses to products. Mechanisms of this type have been classified by Ingold to be Ad_E2 (addition, electrophilic, bimolecular).[40] The mechanism can lead to either cis or trans adducts depending on the structure of the intermediate EX^+. If the cation has an open structure 12, a mixture of cis and trans adducts is generally expected. However, ion-pairing phenomena can cause preferential formation of cis adduct,[6] while electronic, steric, or conformational effects can cause attack at one or the other side of 12.[17] Also, the intermediate could have the bridged or onium ion structure 13a. The bridged ion (or π-complex), as in nucleophilic displacement reactions,

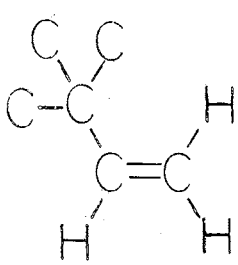
is presumed to be opened stereospecifically to trans adduct. Since the bridged intermediate has never been proven to exist as a discrete entity for HX (X = F, Cl, Br, I) addition to alkenes, the kinetics or mechanism will not be dealt with extensively.

The addition of HCl to isobutylene in heptane was investigated by Mayo and Katz to determine the kinetic rate equation if possible.[48] Kinetic terms of the type shown below were tentatively given in which

$$-\frac{d[\text{olefin}]}{dt} = k[\text{olefin}][HCl]^3 + k'[\text{olefin}][HCl][\text{catalyst}]$$

part of the reaction is seen to be first order in both HCl and isobutylene, which supports the Ad_E2 mechanism.

By studying the kinetics of the hydrochlorination of tert-butylethylene (18) and styrene (25) in acetic acid, Fahey and McPherson were able to show the reaction to be first order in both alkene 18 and HCl at low acid (< 0.1M) concentration.[23] The reaction yielded products 19, 20, and 21, which were used to monitor the rate of



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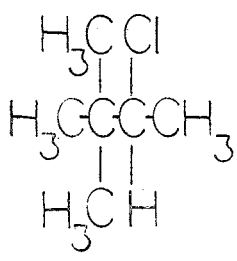

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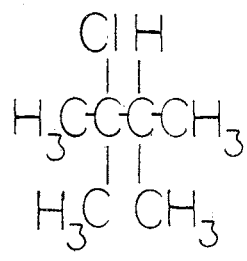

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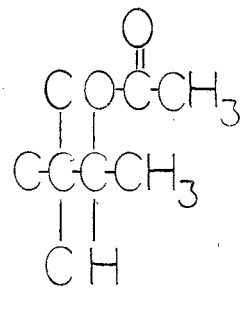
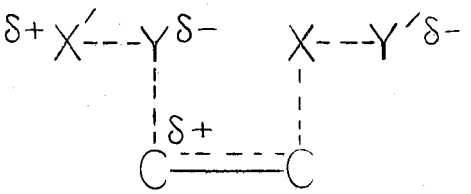


21

reaction. Hydrochlorination of styrene (25) yielded the same kinetic results. His conclusion drawn from the evidence obtained was that formation of a solvated carbonium-chloride ion-pair must be the

rate-limiting step. This is consistent with the fact that a small positive isotope effect ($k_H/k_D = 1.15 \pm 0.07$) occurred when DCl was used and that styrene (25), capable of forming a resonance-stabilized benzylic cation, reacts at about 300 times the rate of 18.

Finally, a mechanism, which has considerable kinetic backing, postulates that C-X and C-Y bonds are both formed in the transition state, but X^+ and Y^- are derived from separate molecular species. The transition states as shown for 22 and 23 can lead to cis or trans



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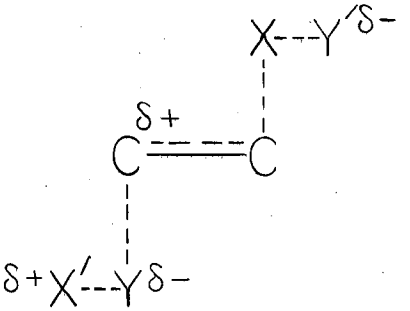


23

addition, respectively, and are denoted as Ad_E3 (addition, electrophilic, termolecular). Pocker has demonstrated that for a series of aliphatic and aromatic compounds the rate is proportional to [compound][HCl]^{2}.[59,60] The addition of HCl to isobutylene (24), styrene (25), 2-methyl-1-butene (26), 2-methyl-2-butene (27) and isoprene (28) in nitromethane was studied by following the disappearance of acid, of chloride ions, and of the olefin. The reaction was examined over a 5-fold concentration range and, under kinetic control, the addition of DCl to 25 is ca. 28 times as fast as the incorporation of D into 25 to give 29. DCl addition to 1-phenylpropene (30) gave ca. 65% cis adduct. These observations are explained in terms of a rate-determining proton transfer to alkene to produce a carbonium ion

$C_6H_5CH=CHD$ (29)

$C_6H_5CH=CHCH_3$ (30)

and a "hydrogen bichloride anion" as partners of a tight ion-pair, followed by a rapid transfer of Cl^- from HCl_2^- to the carbonium ion.

The three mechanisms discussed represent limiting cases and other factors as mentioned before may play an important role in any given reaction. Many electrophilic reagents such as HCl form molecular complexes with olefins and such complexes are probably formed reversibly under the conditions of many electrophilic additions.[5] In weakly dissociating solvents, ion-pairs are likely to be important in Ad_E2 additions, which may complicate the description of any given electrophilic addition.

Knowledge of the stereochemical course of a given electrophilic addition is not sufficient to specify the mechanism. The reaction rate as a function of structure is needed to prove the addition electrophilic and to characterize the structure of the transition state. Especially important are data on the formation of structurally rearranged products, since this provides the best evidence for a discrete cationic intermediate.[22]

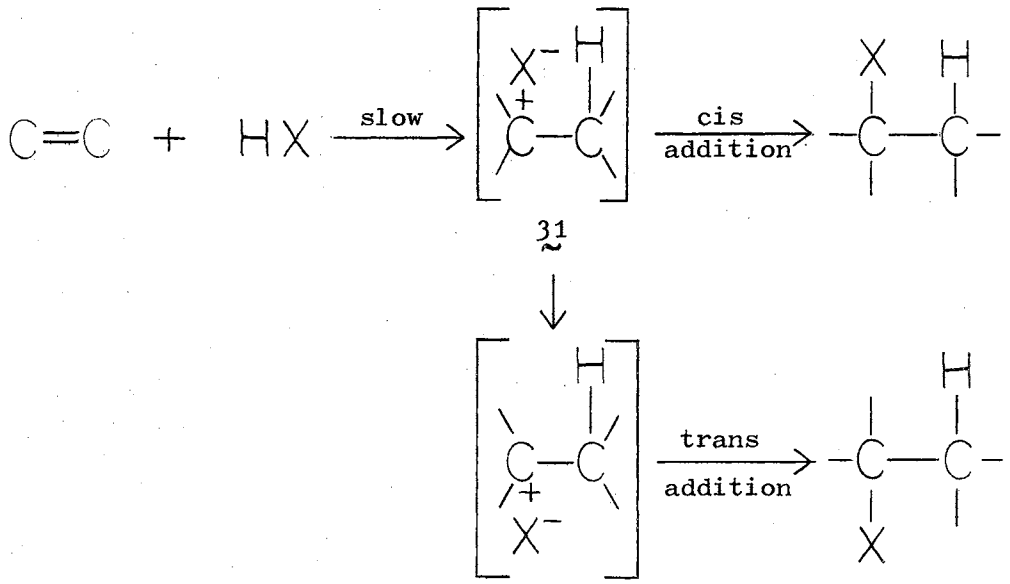
All four hydrogen halides, HF, HCl, HBr, and HI, will add to olefinic substances. The addition of HF to simple olefins is relatively easy and usually gives Markovnikov products, but the isolation of the adducts is sometimes made difficult by the instability of the monofluoroalkanes, particularly in the presence of acids or water, so

that yields are reduced by decomposition or polymerization.[46] Of the four hydrogen halides, HF has received the least study.[13] HI also undergoes Markovnikov addition to alkenes, but again has not received as extensive study as have HCl and HBr. The kinetic form for the addition of HI to cyclohexene in acetic acid is

$$-\frac{d[HI]}{dt} = k[\text{olefin}][HI]^2$$

corresponding to the Ad_E3 mechanism.[64] Also, 1,2-dimethylcyclohexene is much more reactive and allyl chloride is much less reactive than cyclohexene; this is consistent with initiation of the reaction by an electrophilic proton (or HX).

By far, the most attention has been given to the electrophilic additions of HBr and HCl. The stereochemistry of the products and the mechanisms postulated from the stereochemistry and kinetic data from the reactions are as much a function of the olefins and reaction conditions as of the acids themselves. The importance of the nature and structure of the alkene in determining the stereochemistry of the addition of HX is readily apparent from inspection of Tables I, II, and III. Table I shows conclusively that arenes add HBr and HCl with predominate cis stereochemistry, but the reaction tends to be more non-stereospecific in more polar solvents. This observation is consistent with an Ad_E2 type mechanism involving rate-limiting formation of a carbonium-halide ion-pair $\underset{\sim}{31}$ which collapses to cis adduct or rearranges to ion pair $\underset{\sim}{32}$ which then collapses to trans adduct.[15] In aprotic solvents the halide ion formed in the slow step is probably solvated by one or more molecules of hydrogen halide. The situation is reversed for cyclic alkenes as is seen in Table II. Except for the anomalous



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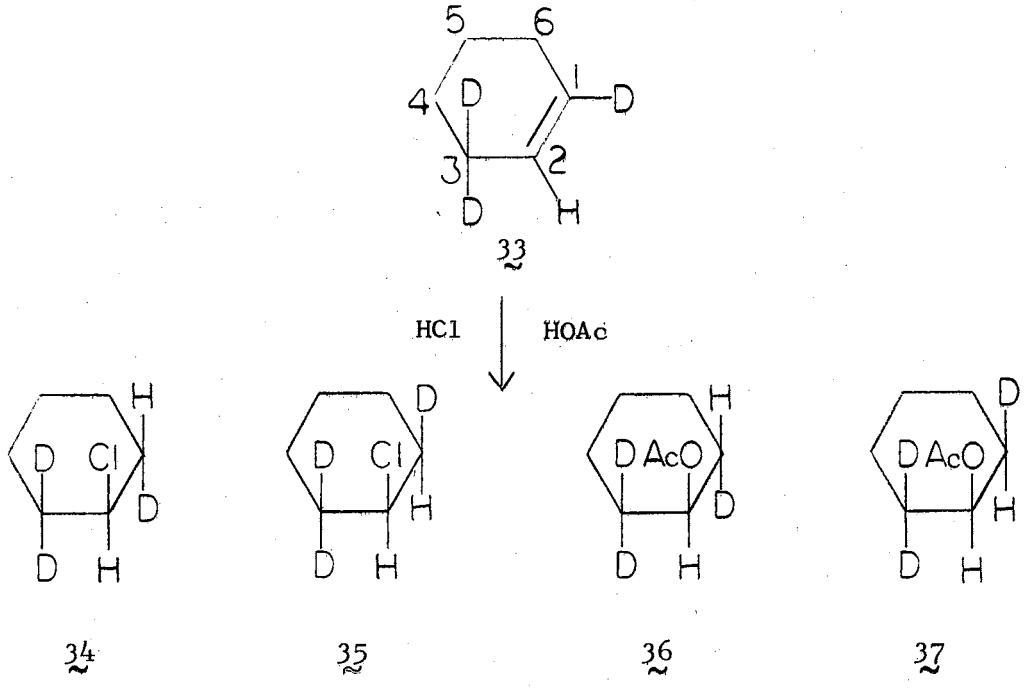
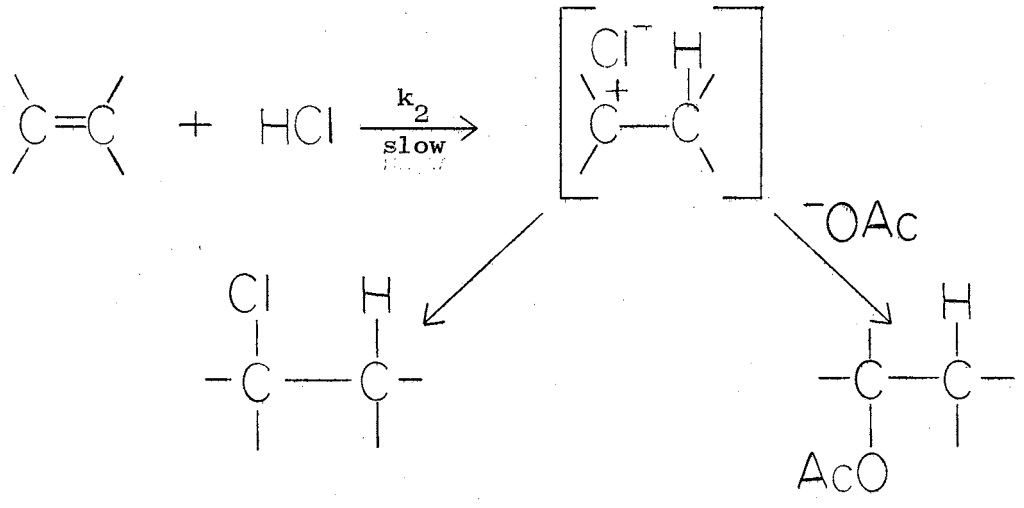
results of reference 65, the trans mode of addition predominates. The reported cis addition of DBr to cyclohexene should be questioned in view of the more recent work of Fahey.[27] The results, obtained by allowing HCl addition to cyclohexene-1,3,3,d_3 (33) in acetic acid at 25 and 80° indicated competing bimolecular and termolecular mechanisms.[24] The major product in all cases was the HOAc trans adduct 37. No explanation was advanced explaining the absence of product obtained from initial attack at position 2. The HCl trans adduct (35) was always observed in greater yield than the cis adduct (34), but the cis/trans ratio increased at the higher temperature. Increased HCl concentration increased the trans-chloride (35) at the expense of the trans-acetate (37). The presence of water or tetramethylammonium chloride enhanced the reaction rate by accelerating formation of the

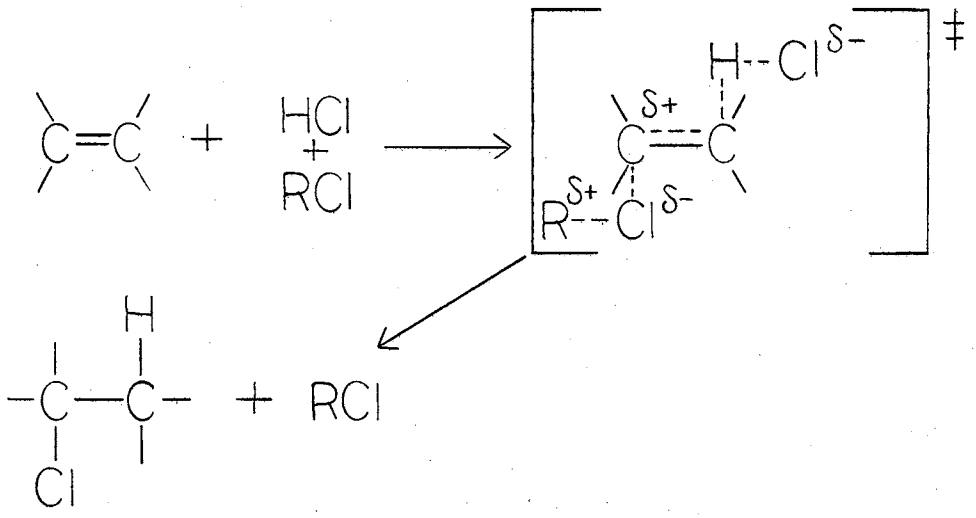


33 34 35 36 37

trans-chloride (35). These observations are indicative of the two competing reactions. One involves a bimolecular reaction between HCl and cyclohexene to form a carbonium-chloride pair which collapses largely to cis-hydrochloride or yields trans-acetate. The other



termolecular reaction involves nucleophilic attack by R^+Cl^- ($R^+ = H^+$ or Me_4N^+) in the rate-determining step. The trans-acetate is probably formed primarily by an analogous termolecular process. Addition of HBr



to 33 under similar conditions gave 87% of the trans-hydrogen bromide adduct at 15° and 71% of the trans-hydrogen bromide adduct at 60°. In view of the results with HCl, it seems probable that HBr adds in a trans manner to cyclohexene primarily via an Ad_E3 mechanism. Since HBr is a stronger acid than HCl, both Ad_E2 or Ad_E3 addition should be favored, but since HBr is a better nucleophile than HCl, the Ad_E3 mechanism would be specifically favored.[22]

A unified mechanistic picture based on available evidence has been advanced by Dolbier as shown in Figure 1.[19] He concludes that the occurrence of cis or trans addition depends on the relative stabilities of the onium ion and the open carbonium ion. Trans products are favored when the onium ion is more stable, whereas the open carbonium ion favors cis addition. The nature of the adding species and the structure of the alkene determine the relative stabilities of the two intermediates. Table III shows the relative capabilities of some

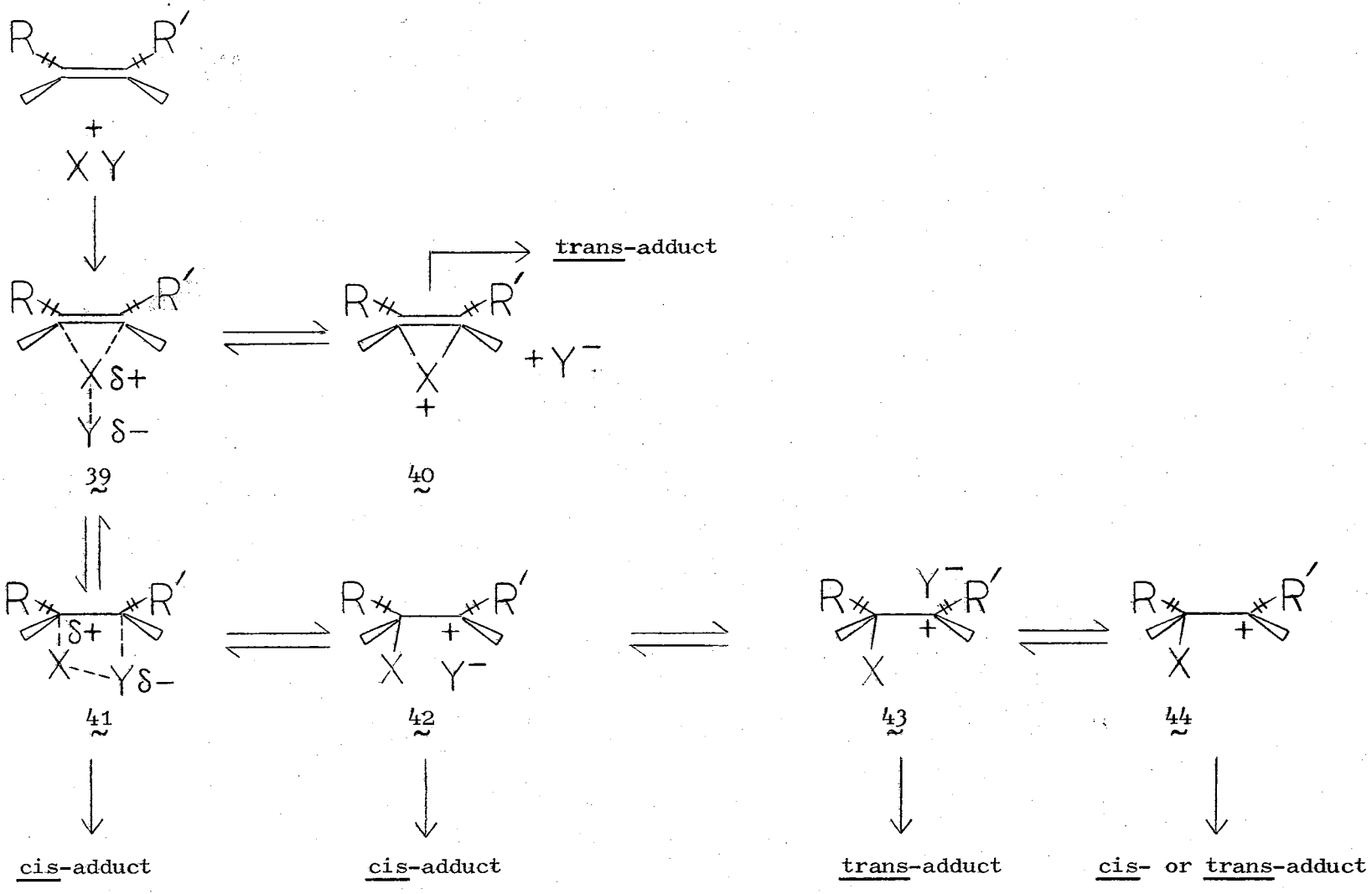


Figure 1. A Unified Mechanistic Picture for the Electrophilic Addition to Alkenes

diverse electrophilic reagents to form onium ions (if trans addition can be used as a measure of relative onium ion stability). The ability of X to form stable onium ions increases in the order: H < F < Cl < Br < I, S. Thus, the larger and more electropositive atoms form the most stable onium species.

The structure of the alkene appears to be unimportant where extremely stable onium ions can form, such as iodonium and episulfonium ions. This is evidenced by the fact that only trans addition has always been observed, regardless of the alkene structure. For onium ions less stable than bromonium, however, the structure can be the major factor in determining the stereochemical outcome of the reaction. Table IV shows the importance of the alkene structure in determining the stereochemistry of chlorine addition. Johnson and Trachtenberg have shown that the stereochemistry of the addition of chlorine to various substituted cinnamates became more random as the stability of the open carbonium ion became greater (Table V).[42] Thus, in such cases one has apparently reached the other end of the spectrum from the onium ion to give the totally open carbonium ion.

The solvent may influence the stereochemistry in that the cis adduct will be more favored as the solvent becomes more polar. The chlorination of 1-cyclohexyl-2-phenylethene (44) gives 53% erythro (trans adduct) 45 and 34% threo (cis adduct) 46 in CS_2, but only 26% of 45 and 46% of 46 in $CCl_3COOC_2H_5$.[38]

In systems where the onium ion is more stable, when X = I or ArS, the initially formed π-complex, 39, will collapse primarily to 40, which leads to predominant trans product. As the carbonium ion becomes more stable, when X = H, Cl, or F and R and/or R' are phenyl, 40 will

be less important and species 41 and/or 42 will be formed, leading to cis stereochemistry. As the carbonium ion becomes yet more stable and thus more long-lived, as when X = Cl, R' = p-anisyl, and R = CO_2CH_3, the reaction may proceed through intermediates 43 and 44 to give rise to a nonstereospecific, thermodynamically controlled product mixture.

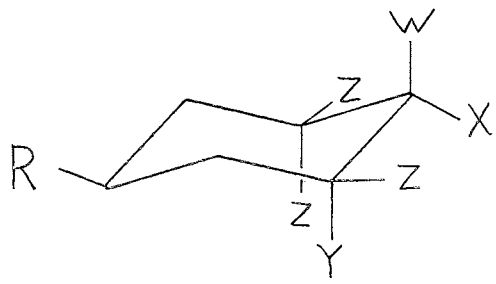
Only one study has been published on the stereochemistry of the addition of a hydrogen halide (HBr) to a simple aliphatic alkene. It was found that the addition of DBr to cis- and trans-2-butene gave in 85% yield the product of trans addition when conducted in acetic acid -O-d.[58] The determination of the stereochemistry of the products was made by NMR and elimination of acetic acid from the acetate derivative formed from the bromide. The kinetics of the reaction were not studied and the importance of the various mechanisms of addition will have to be evaluated by future work on such a system.

CHAPTER II

RESULTS AND DISCUSSION

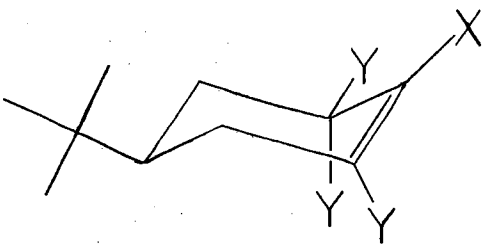
The research was undertaken to determine the stereochemistry and elucidate the mechanism of the electrophilic addition of hydrogen chloride to 4-tert-butyl-1-phenylcyclohexene (45) and some of its derivatives. Most of the additions were carried out at -70° with a few conducted at -30°. It was found during preliminary experiments that water could have a dramatic effect on the additions so all the results reported here were obtained with scrupulous care to exclude all traces of moisture. This study is primarily devoted to the stereochemistry of the aforementioned additions. However, during the course of the experiments, an attempt was made to obtain semiquantitative kinetic data to allow the relative merits of various mechanisms to be evaluated.

It was found that two products could be isolated and characterized from the electrophilic addition (in n-pentane at -70°) of HCl to 4-tert-butyl-1-phenylcyclohexene (45). The presence of the phenyl group in the alkene 45 should facilitate Markovnikov addition of the HCl, minimizing the possibility that the two products could be the result of Markovnikov and anti-Markovnikov addition. Moreover, the tert-butyl group, known for its ability to "lock" the cyclohexane ring into a single conformation, allows the possible formation of geometrical isomers 46 and 47.[70]

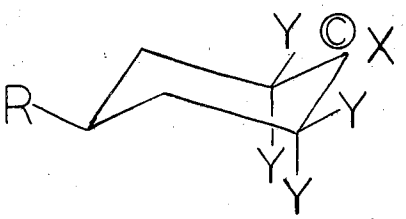


Cmpd.	W	Y	Y	Z	R
46	C_6H_5	Cl	H	H	$(CH_3)_3C$
47	Cl	C_6H_5	H	H	$(CH_3)_3C$
48a	C_6H_5	Cl	H	H	H
48b	Cl	C_6H_5	H	H	H
50	C_6H_5	Cl	D	D	$(CH_3)_3C$
51	C_6H_5	Cl	H	D	$(CH_3)_3C$
52	C_6H_5	OH	H	H	$(CH_3)_3C$
53	OH	C_6H_5	H	H	$(CH_3)_3C$
54	C_6H_5	H	H	H	$(CH_3)_3C$
55	H	C_6H_5	H	H	$(CH_3)_3C$
56	H	C_6H_5	H	H	H
63	CH_3	OR	H	H	$(CH_3)_2CH$
64	OR	CH_3	H	H	$(CH_3)_2CH$
67	OH	p-XC_6H_4	H	H	$(CH_3)_3C$
70	p-$CH_3OC_6H_4$	OH	H	H	$(CH_3)_3C$
71	OH	p-$CH_3OC_6H_4$	H	H	$(CH_3)_3C$
72	p-$CH_3OC_6H_4$	Cl	H	H	$(CH_3)_3C$
73	OH	p-$CH_3OC_6H_4$	H	H	$(CH_3)_3C$
83	C_6H_5	OH	D	D	$(CH_3)_3C$
84	OH	C_6H_5	D	D	$(CH_3)_3C$

Figure 2. Compounds Frequently Mentioned in the Discussion

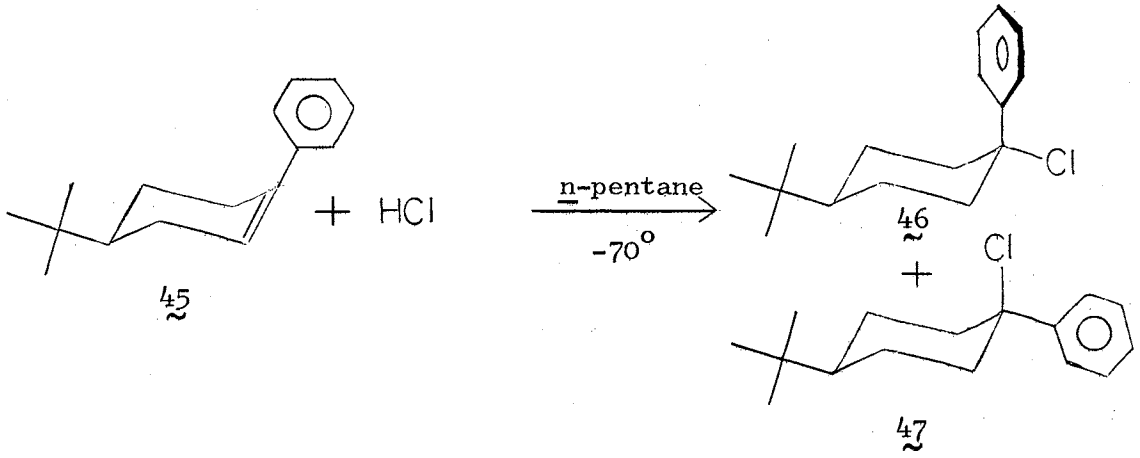


Cmpd.	X	Y
45	C_6H_5	H
49	C_6H_5	D
74	p-$CH_3OC_6H_4$	H



Cmpd.	X	Y	R	C(+ or O)
59	C_6H_5	H	$(CH_3)_3C$	+
60	=O	H	$(CH_3)_3C$	O
75	p-$CH_3OC_6H_4$	H	$(CH_3)_3C$	+
80	C_6H_5	H	$(CH_3)_3C$	+
85	=O	H	$(CH_3)_2H$	O
86	=O	D	$(CH_3)_3C$	O

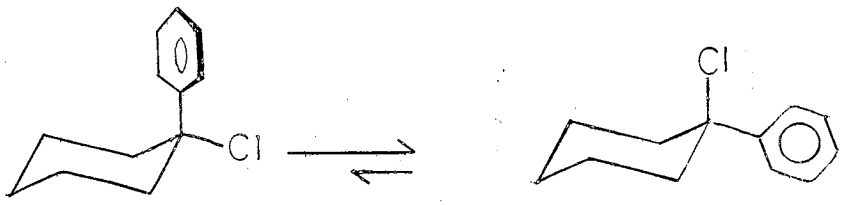
Figure 3. Compounds Frequently Mentioned in the Discussion



45 46 47

The evidence for the existence of the geometrical isomers is as follows. It is well documented that functional groups give different stretching frequencies in their IR and Raman spectra indicative of their axial or equatorial bonding to the cyclohexane system. The C-Cl bond is unique since in most cases it is both Raman- and IR-active owing to the fact that it is polarized during the stretching mode and experiences a net dipole moment change.[69] From the empirical analysis of different chlorocyclohexane systems, it has been determined that axial C-Cl bonds exhibit stretching frequencies between 646 and 730 cm^{-1} while equatorial C-Cl bond stretches are located at 736 to 856 cm^{-1}.[20] The consistently higher energy of the equatorial carbon-X (X = OH, OMe, Cl, Br, D) bonds has been interpreted to arise from ring expansion caused from the movement of the carbon atom.[7] The axial C-X stretch will have a smaller restoring force since the stretch is perpendicular to the plane of the ring. The greater restoring force of the equatorial C-X stretch is evidenced by the higher frequency observed both in the IR and Raman spectra. After the HCl addition reaction to alkene 45 had proceeded for 15 min., cis-4-tert-butyl-1-chloro-1-phenylcyclohexane (46) could be detected as the major product. Trans-4-tert-butyl-1-chloro-1-

phenylcyclohexane (47) could be isolated as the major product after 30 min. reaction time (Table VI). The cis-chloride 46, when dissolved in n-heptane, exhibited a Raman maximum at 685 $cm.^{-1}$ (Plate I) while a KBr pellet of the material gave an IR maximum at 686 $cm.^{-1}$ (Plate IV). The trans-chloride 47 in n-heptane gave a maximum at 647 $cm.^{-1}$ (Plate II) in the Raman spectra and at 641 $cm.^{-1}$ (Plate V) in the IR spectra as a KBr pellet. Although these frequencies are somewhat lower than those of most other chlorocyclohexanes, their relative order, with the cis-chloride 46 having the higher frequency, is probably correct for assignment of the configuration. The lower frequencies for the two chlorides 46 and 47 are explicable in terms of the Raman spectra of chloromethane and α-chlorotoluene. A C-Cl maximum is observed in the spectrum for chloromethane at 712 $cm.^{-1}$ while for the α-chlorotoluene, is observed at 679 $cm.^{-1}$.[44] The phenyl group is seen to decrease the frequency by 33 $cm.^{-1}$. The two frequencies, 732 and 686 $cm.^{-1}$, for chlorocyclohexane have been assigned to the equatorial and axial C-Cl stretch, respectively.[44] Subtracting the contribution of the phenyl group from the chlorocyclohexane values would give the approximate absorption maxima expected for 1-chloro-1-phenylcyclohexane (48). The calculated frequencies for 48a would then



48a 48b

be 699 $cm.^{-1}$ and 653 $cm.^{-1}$ for 48b. This is in fair agreement with the experimental values of 686 and 642 $cm.^{-1}$ for 48.[44] These calculated

values are also near to the frequencies, 685 and 647 cm^{-1}, found respectively for 46 and 47. The IR C-Cl maxima occur at 686 cm^{-1} (for cis- 46) and 641 cm^{-1} (for trans-47) as seen in Plates IV and V.

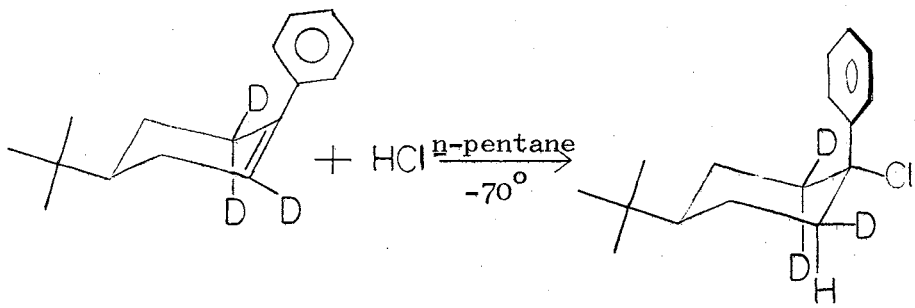
The NMR spectrum could be used to monitor the addition of HCl to alkene 45, allowing determination of the relative amounts of the alkene 45 and chlorides 46 and 47 in the reaction mixture at various times. At 50 Hz sweep, the tert-butyl proton peaks associated with the cis-chloride 46 (δ 0.74, Plate XIII) and trans-chloride 47 (δ 0.92, Plate XIV) are cleanly separated and can be integrated using a polar planimeter to determine the relative amounts (Table VII, Plate XV). The tert-butyl and vinyl proton peaks for alkene 45 are found at δ 0.89 and 6.10 (Plate XVI), respectively, so that completeness of the reaction can be determined by their absence.

The addition of HCl to 4-tert-butyl-1-phenylcylohexene (45) is the first reported reaction of this type for which isolation and characterization of epimeric products has been achieved. No other report of the isolation of epimers formed from the addition of HCl to a cyclohexene could be found in the literature.

Previous evidence indicated that the cis-chloride 46 was the initially formed product and the trans-chloride 47 was the thermodynamically more stable product formed by isomerization.[33] Gibbs found that the cis-chloride 46, when heated to its melting point, gave as products the trans-chloride 47 and alkene 45.[33] Also, the trans-chloride 47 exhibited no rearrangement when subjected to the reaction conditions. To test this hypothesis further, we subjected an equimolar mixture of the cis- and trans-chlorides 46 and 47 to the identical conditions of the addition reaction (Plate XV). After 45 min., NMR

analysis of the tert-butyl protons indicated the mixture to contain 86% of the trans-chloride 47 and only 14% of the cis-chloride 46. The absence of any alkene formation was indicated by the lack of any proton absorptions at δ 0.89 (tert-butyl protons) or 6.10 (vinyl proton). From this experimental evidence, trans-4-tert-butyl-1-chloro-1-phenylcyclohexane (47) is the thermodynamically more stable epimer. All monitored additions of HCl to alkene 45 indicated that the cis-chloride 46 is indeed the initially formed product (Table VI), with isomerization to the trans-chloride 47 occurring as the reaction time is increased.

The stereochemistry of the initial product (cis-chloride 46) formed from the addition of HCl to the alkene 45 was deduced by using the 4-tert-butyl-1-phenyl-2,6,6-trideuteriocyclohexene (49) analog. Two deshielded doublets corresponding to two protons each are distinguishable at δ 2.30 (2,6-ax. protons) and 2.95 (2,6-eq. protons) in the NMR spectrum of the cis-chloride 46 (Plate XIII). These doublets are not present in the NMR spectrum of cis-4-tert-butyl-1-chloro-1-phenyl-2,2,6,6-tetrodeuteriocyclohexane (50) as evidenced in Plate XVII. The initial reaction product was isolated from the HCl addition to the deuterioalkene 49 to give cis-4-tert-butyl-1-chloro-1-phenyl-2-eq.-6,6-trideuteriocyclohexane (51) after 15 min. reaction time. The NMR spectrum showed the presence of only one deshielded doublet integrating for one proton at δ 2.25 and indicating axial substitution of the proton (Plate XVIII). The stereochemistry of 51 is most consistent with a mechanism involving cis addition of the HCl to the cyclohexene ring.



49 50

The epimeric chlorides 46 and 47 were also synthesized and isolated via a separate route. When cis-4-tert-butyl-1-phenylcyclohexanol (52), suspended in n-pentane at -70°, was allowed to react with HCl, the cis-chloride 46 of the same configuration as the cis-alcohol 52 was obtained as the major product. Retention of configuration was also observed in the product of the reaction of HCl with trans-4-tert-butyl-1-phenylcyclohexanol (53) to give trans-chloride 47 (Table VIII and Figure 4). This is the first reported example of the reaction of cyclohexyl epimeric alcohols with HCl to give the corresponding chlorides with retention of configuration.

It is necessary to establish the actual configurations of the alkenes, alcohols, and chlorides mentioned thus far because the stereochemical assignments and the mechanisms discussed are based on these configurations. The stereochemistry of the alcohols 52 and 53 has been assigned by Garbisch and Patterson.[31] The pure alcohols were isolated by column chromatography in order to obtain their NMR spectra. The alcohol eluted first from the column was considered to be the trans-alcohol 53 and that eluted last to be the cis-alcohol 52 because the equatorial hydroxyl proton in 52 should have a greater interaction

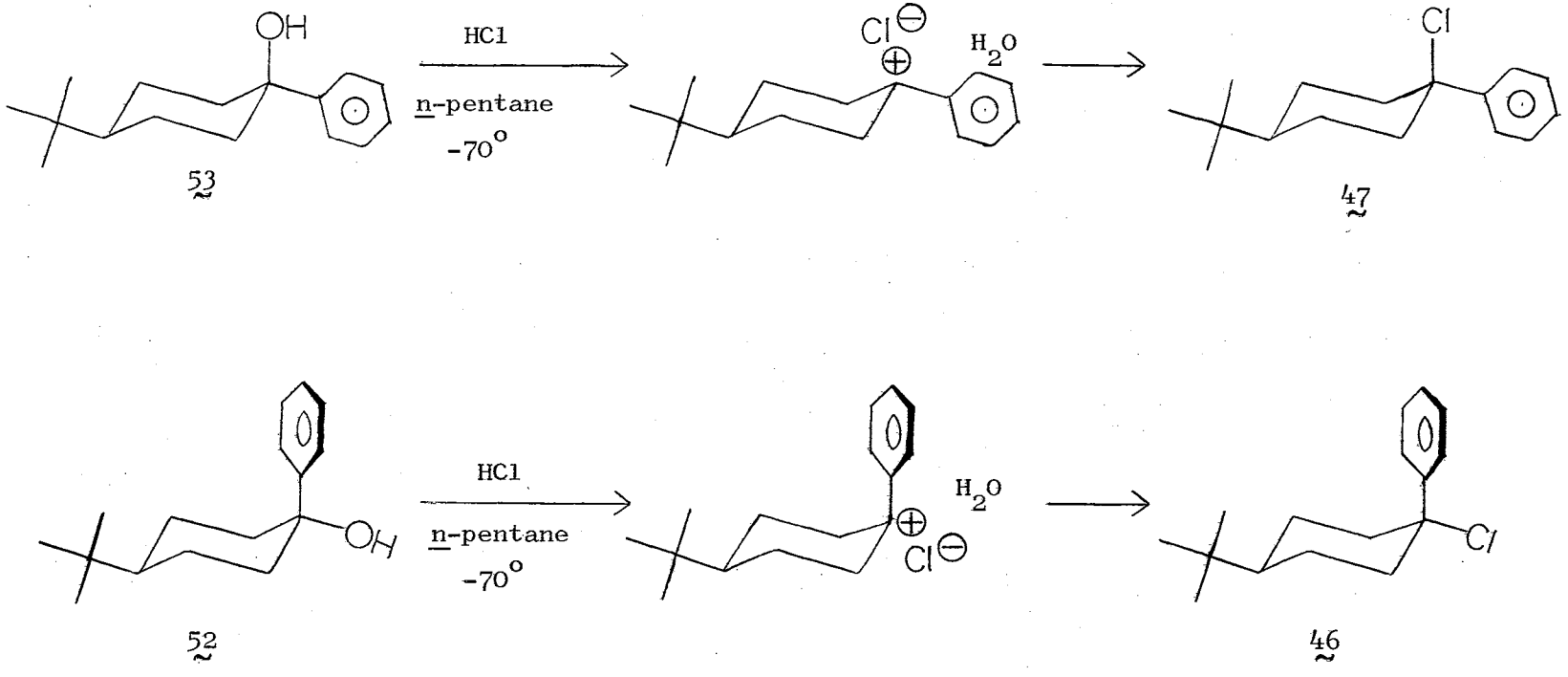
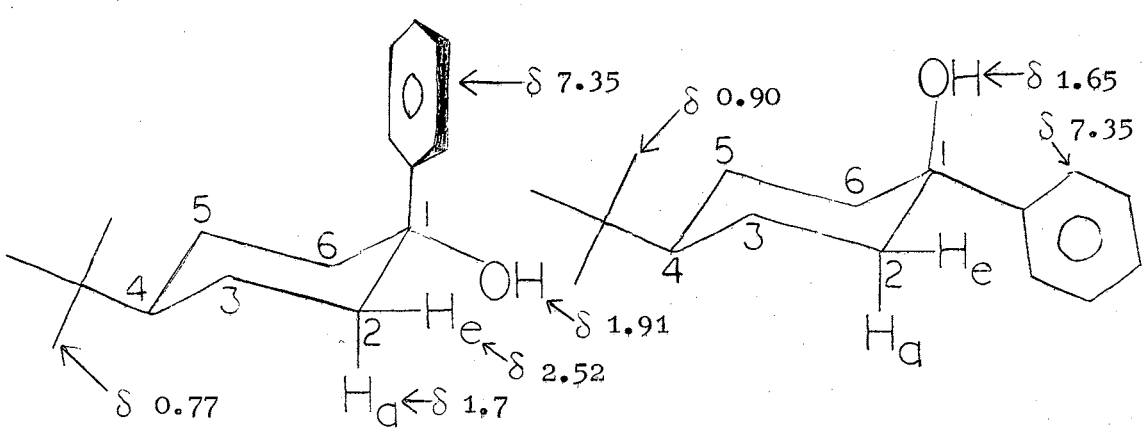


Figure 4. Retention of Configuration for the Reaction of HCl with cis- and trans-4-tert-Butyl-1-phenylcyclohexanols (52 and 53) Through Ion-Pair Intermediates

with the silica gel column. The hydroxyl proton for 52 was observed at δ 1.91 compared to 1.65 for 53; the difference was attributed to more hydrogen bonding in 52. A deshielded doublet was observed for 52 at δ 2.52 which appeared as the low-field half of a AB spectrum. The doublet disappeared in the NMR spectrum of the 2,2,6,6-tetradeuterio derivative showing that the absorption derived from the 2,6-protons and that the high-field part of the AB spectrum was centered at δ 1.7. It has been demonstrated for most cyclohexane systems that equatorial protons are deshielded relative to axial protons on the same carbon.[45] The doublet at δ 2.52 therefore was considered to arise from the 2,6-equatorial protons, while the doublet at δ 1.7 was assigned to the 2,6-axial protons. The chemical shift difference (0.82 Hz) between $H_{2,6e}$ and $H_{2,6a}$ is made somewhat larger than usual by the essential confinement of the phenyl group of 52 in the conformation shown in 52.

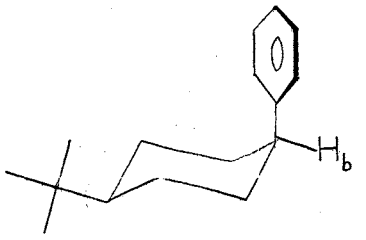


52 53

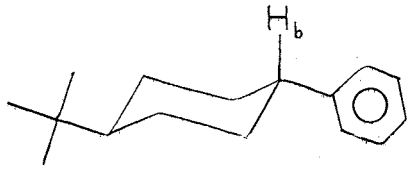
In this conformation, both the equatorial and axial protons will be deshielded by the diamagnetic field of the benzene ring, but the 2,6-equatorial protons are influenced to a greater extent because of their proximity to the phenyl ring.

Conditions which allow conversion of the alcohols 52 and 53 to

cis-4-tert-butyl-1-phenylcyclohexane (54) and trans-4-tert-butyl-1-phenylcyclohexane (55), respectively, with > 90% retention of configuration were employed.[31] The benzylic proton absorption (H_b) is found

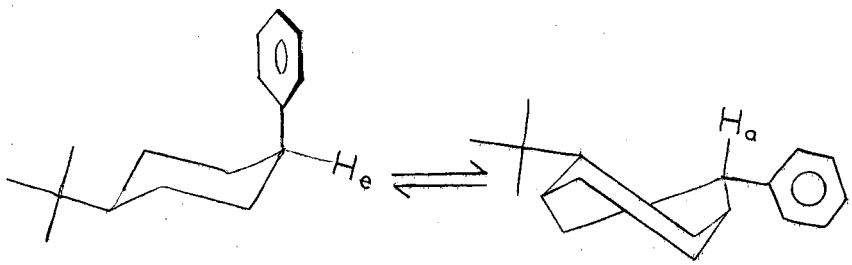


54



55

at δ 2.98 for 54 and 2.37 for 55, both peaks being broad singlets. In the NMR spectrum of a fixed 1,4-disubstituted cyclohexane molecule, it is possible to distinguish different kinds of proton environments by the chemical shift of the proton.[28] The tertiary protons have a lower magnetic shielding, and thus generally appear at a lower field than ring protons. Also it is usually observed that tertiary equatorial protons absorb at a lower field than the tertiary axial protons. Phenylcyclohexane (56) exhibits a benzylic proton absorption at δ 2.38, almost coinciding with that of 55, indicating that the phenyl group is in the equatorial position for both molecules. Occurrence of absorption for the benzylic proton for 54 at lower field than in 55 or 56 confirms that the phenyl has an axial configuration in 54. It was found, however, that the absorption for the benzylic proton in 54 was converted from a broad singlet at 25° to a quintet at 150° with the same chemical shift. Garbisch ascribed this to an equilibrium between chair and twist-boat conformations for the molecule.[46] If, however, 54a existed to an appreciable extent (≈ 20%) as he suggests, the



54 54a

benzylic proton absorption would broaden so as to average the chemical shifts that would be expected for equatorial and axial benzylic protons present in the compounds at equilibrium. This broadening was not noted.

A rough calculation of the free energy ΔG° of the reaction 54→54a is possible. It has been shown experimentally that the chair form of cyclohexane is more stable than the twist conformation by 5.5 kcal/mole.[43] From this figure and the conformational energy differences for substituent groups found below, the relative stabilities of 54 and 54a can be approximated.

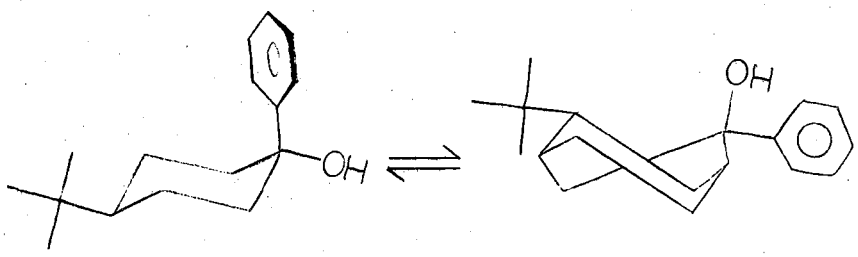
Group	$-\Delta G^\circ_x$, kcal/mole
OH	0.7
Cl	0.4
C_6H_5	3.1
$(CH_3)_3C$	~ 5

Conformational Free Energy Differences for Substituent Groups[50]

In going from 54 to 54a, the phenyl contribution would be -3.1 kcal/mole; adding this to the 5.5 kcal/mole ring factor gives ΔG° = 2.4 kcal/mole. Relating ΔG° to the equilibrium constant K by use

of the equation $\Delta G = -RT\ln k$ gives $K = 0.02$ at 25°, i.e., 2% of the molecules exist in the twist conformation. At 150°, 5.68% of the molecules would exist in the twist conformation. I think it is rather unlikely that 20% of the twist form exists in the equilibrium mixture as supposed by Garbisch.

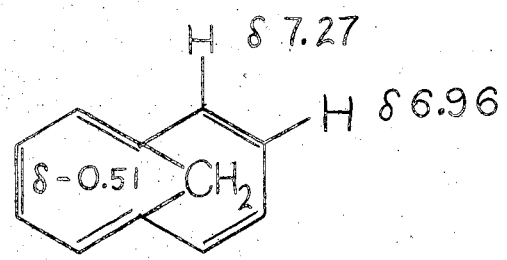
The extension of these conformational arguments to the cis- and trans-alcohols 52 and 53 is then obvious if conversion of the alcohols 52 and 53 to the hydrocarbons 54 and 55 with retention of configuration is accepted. The equilibrium 52 ⇌ 52a would be even more unfavorable to existence of 52a than that of the hydrocarbon 54 ⇌ 54a owing to the added contribution of the change of the OH group from an equatorial to an axial position, $\Delta G = 5.5 - 3.1 + 0.7 = 3.1$ kcal/mole at 25°. Also,



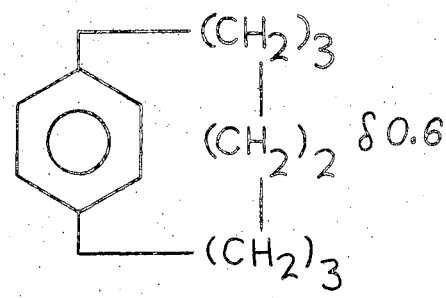
52 52a

we have observed experimentally that the tert-butyl protons in cis-alcohol 52 are more shielded by ~ δ 0.13 than the tert-butyl protons of the trans-alcohol 53 indicating an axial position for the phenyl group (Table IX). Inspection of molecular models (Courtauld) indicate that the tert-butyl protons for 52 approach within 1.25 Å of the face of the phenyl group and that a line perpendicular to the face of the phenyl group and passing through its center intersects the cylinder of revolution defined by the rotating tert-butyl protons.

It has long been known that aromatic compounds are characterized by abnormally high diamagnetism in the direction perpendicular to the plane of the ring and the effect is readily apparent even at 5Å.[41] This diamagnetism is exhibited by interatomic or intramolecular diamagnetic shielding. A number of examples illustrate that the central region above and below the plane of the aromatic ring system is strongly shielded. The methylene-bridged annulene 57 is seen to have its methylene protons strongly shielded.[68] Another illustration is provided by 1,4-decamethylenebenzene (58).[41] If the tert-butyl protons in 52 were not being shielded, one would expect them to have the same chemical shift as those for the trans-alcohol 53 since they would have comparable environments.

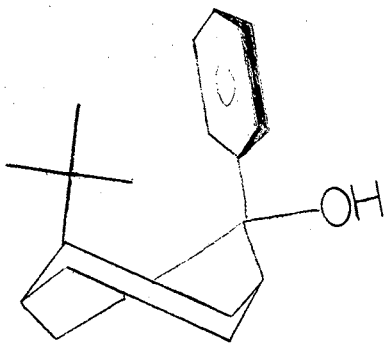


57



58

We examined the possibility that the cis-alcohol 52 could exist in a twist conformation (52b) having both the tert-butyl and phenyl groups pseudo axial. This conformation would also place the tert-butyl protons in a line directly perpendicular to the face of the phenyl group, again demonstrated by molecular models. This thought was prompted initially by the retention of configuration observed in the reaction of HCl with the cis- and trans-alcohols 52 and 53 as mentioned earlier. The proposition was considered that at the low temperature of the reaction, two stable carbonium ion intermediates were formed which



52b

then collapsed to epimer products 46 and 47 (Figure 5). Neglecting the phenyl groups, which would have little conformational preference, in the two intermediates 52c and 59, 59 would be conformationally preferred by ~ 10 kcal/mole (~ 5 for axial tert-butyl and ~ 5 kcal/mole for twist form). Also, it was found that the reaction conducted at -30° resulted in essentially the same product ratio (Table VIII).

The product composition of the reaction precludes the usual S_N1 and S_N2 mechanisms used to describe the reaction of HCl with an alcohol. Since the alcohols in this case are benzylic and tertiary, the S_N2 mechanism would be less likely than S_N1. Indeed, an S_N2 mechansim would have predicted inversion at the epimeric center, which is certainly not the case. The most commonly mentioned mechanism for the conversion of tertiary alcohols to their respective chlorides is, of course, S_N1. Assuming no steric effects and if both alcohols yield the same carbonium ion intermediate 59, one naively might expect the S_N1 mechanism would result in equimolar amounts of chlorides 46 and 47. However, steric interactions of the chloride ion 59 with the 3,5-axial hydrogens during the approach would, as expected, cause preferential attack to give predominately the cis-chloride 46. The intermediate 59

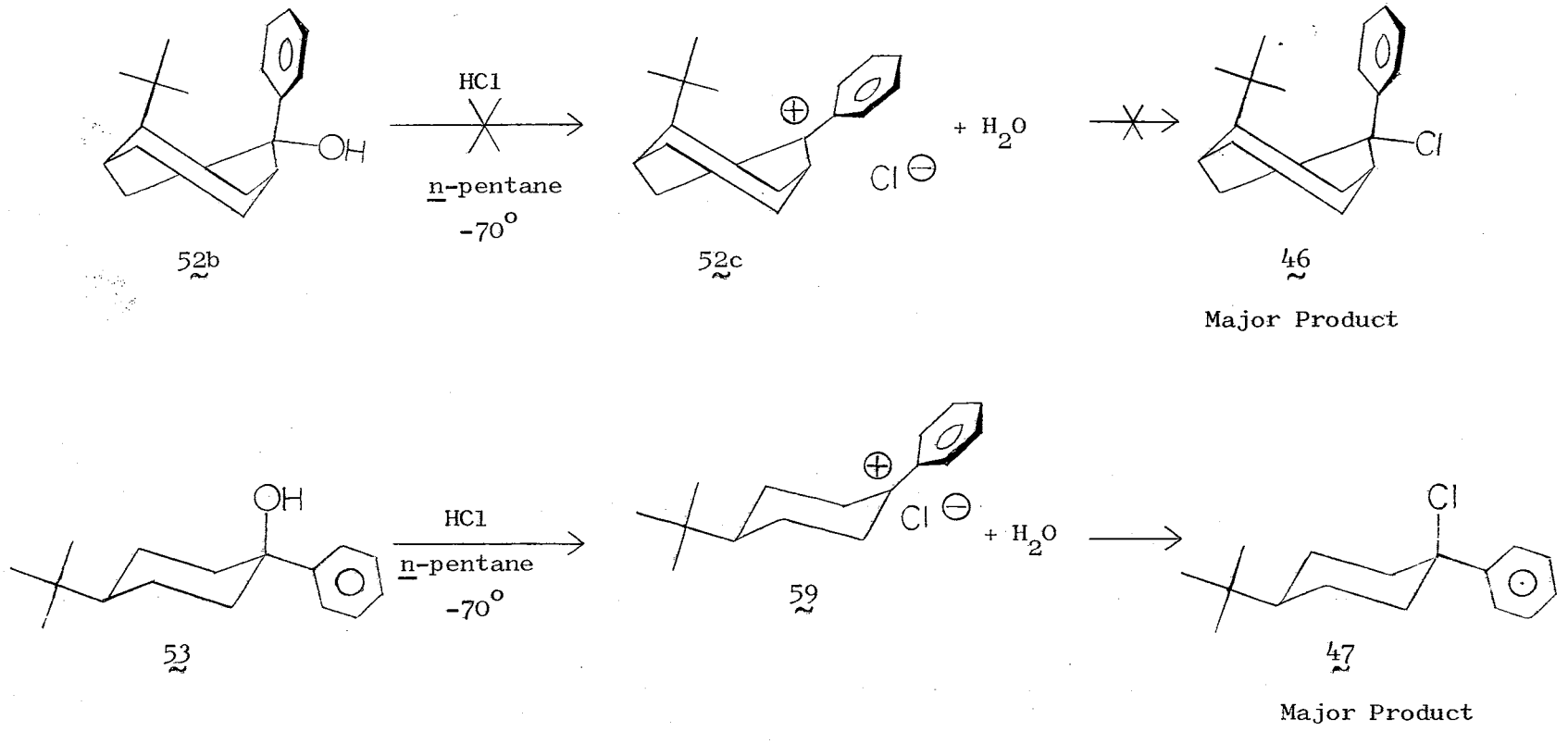
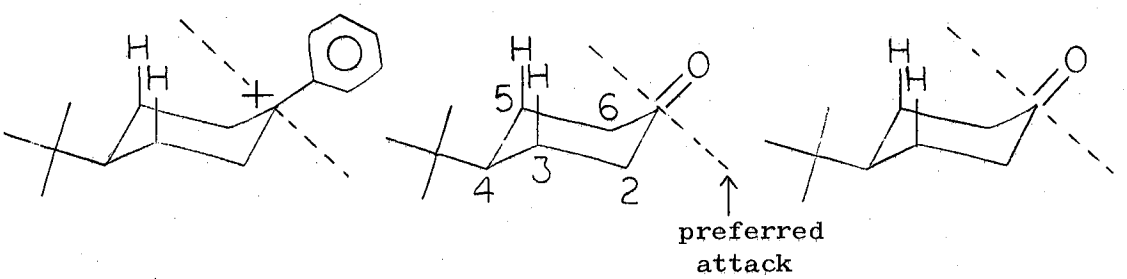


Figure 5. Reaction of HCl with cis- and trans-4-tert-Butyl-1-phenylcyclohexanol (52b and 53) Through Conformationally Different Intermediates

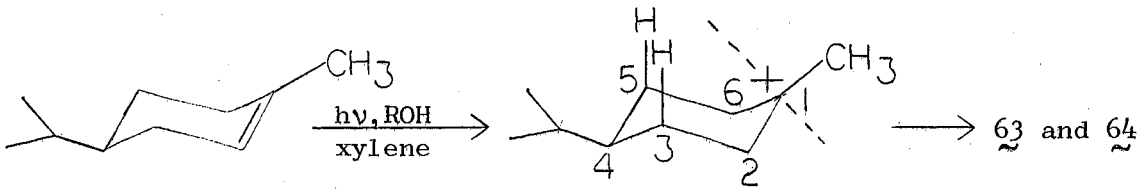
should have essentially the same stereochemistry as 4-substituted cyclohexanones, e.g., 60, as both 1-carbons are sp^2-hybridized. The preference of attack in the cyclohexanone systems should also apply then to 59. It has been found that CH_3MgI attacks 4-tert-butylcyclohexanone (60) preferably from the underside to give the trans alcohol



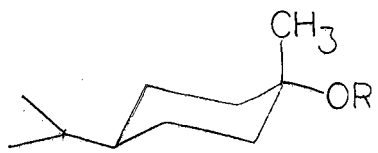
59 60 85

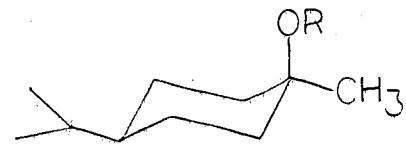
(55%).[50] Methyllithium attack of ketone 85 produced the trans alcohol in 60% yield.[47] Marshal found that photosensitized ionic additions to 1-menthane 61 proceeded through a cationic intermediate 62, which in turn underwent preferential attack to give the cis-ethers 63 in greater yield than the trans-ethers 64. Again, this difference results from steric hindrance by the 3,5-axial hydrogens.[47] The cis-chloride 46 is not the major product from the reaction of the trans-alcohol 53, indicating that there is no free carbonium ion intermediate that undergoes preferential stereochemical attack.

A reasonable explanation for the retention of configuration is the formation of tight ion-pairs that collapse to product before backside attack can occur (Figure 4). Retention of configuration in the reaction of HBr with both erythro- and threo-2-deuterio-1,2-diphenylethanol (65 and 66) has been reported.[12] The initial bromides underwent elimination to yield the alkenes expected if the alcohols were converted to



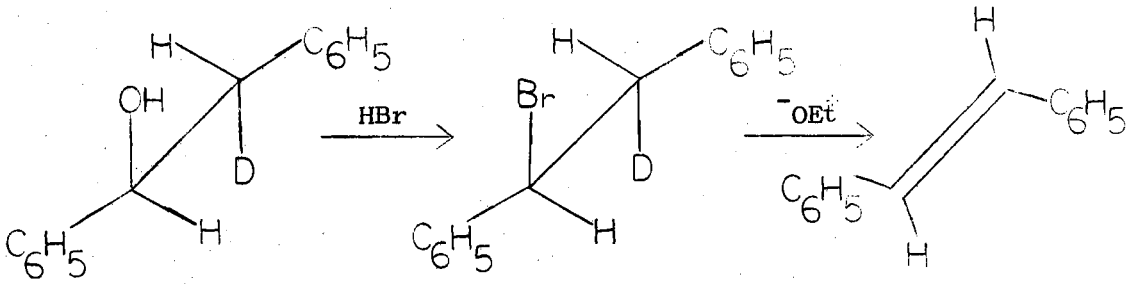
61 62



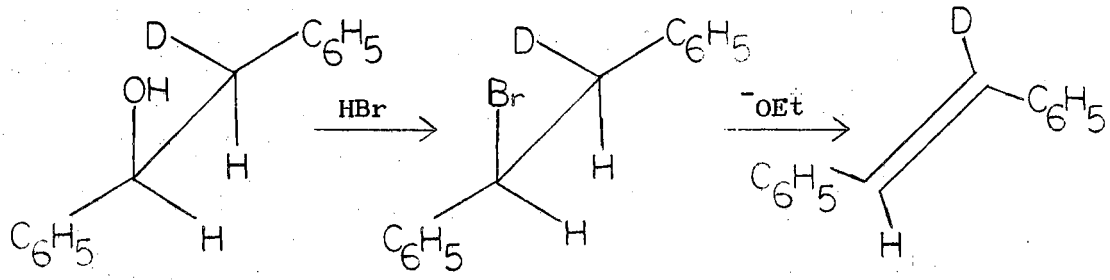


63 64

R	63/64
H	1.3
CH_3	1.5
C_2H_5	1.3
$(CH_3)_2CH$	1.7

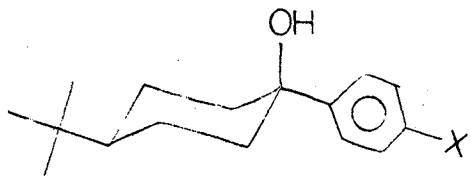


erytho - 65 87%



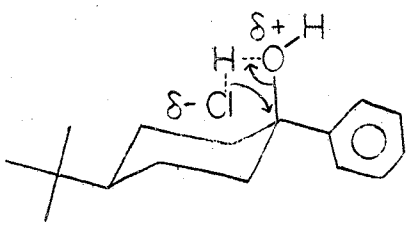
threo - 66 89%

the bromides with retention of configuration. The reaction of thionyl chloride with alcohol 65 was also found to proceed with 90% retention of configuration using the same method of determination.[12] Experimental evidence has been presented that the S_Ni reaction, commonly accepted for the reaction of thionylchloride with alcohols, proceeds through discrete ion-pair intermediates.[10] The reaction of HCl with cis- and trans-alcohols 52 and 53 could be an example of the S_Ni reaction involving discrete ion-pair intermediates. The validity of this assumption could be tested by rate analysis for the reaction of the alcohols 67. The Hammett ρ value for the reaction could be obtained and a choice could be made if there was a significant positive charge developing in the intermediate or if the reaction proceeded through concomitant bond-breaking and bond-making such as in 68 and 69.

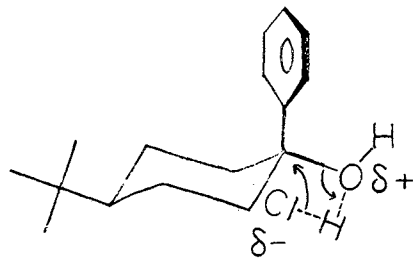


67

X = NO_2, CH_3, Br, CH_3O



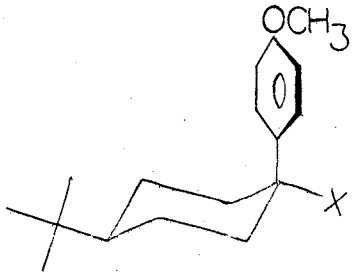
68



69

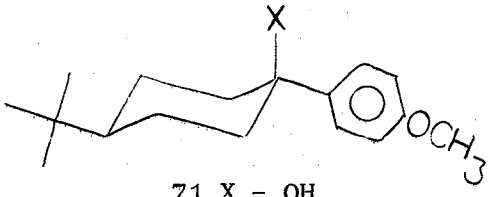
In order to determine the effect of an electron-releasing substituent attached to the phenyl ring of the alcohols 52 and 53, cis- and trans-4-tert-butyl-1-(p-methoxyphenyl)cyclohexanols (70 and 71) were synthesized and isolated (for the first time). The characteristic NMR absorptions for the two compounds were not too different from those for the corresponding alcohols 52 and 53 with the exception of the phenyl and methoxyl proton absorptions (Table IX, Plates XIX and XX). Unlike the reaction of HCl with alcohols 52 and 53, that of the methoxy alcohols 70 and 71 evidently proceeds through a common intermediate at -70°.

Table VIII shows that the ratio of cis-4-tert-butyl-1-chloro-1-(p-methoxyphenyl)cyclohexane (72) to trans-4-tert-butyl-1-chloro-1-(p-methoxyphenyl)cyclohexane (73) was approximately 1:7 when formed



70 X = OH

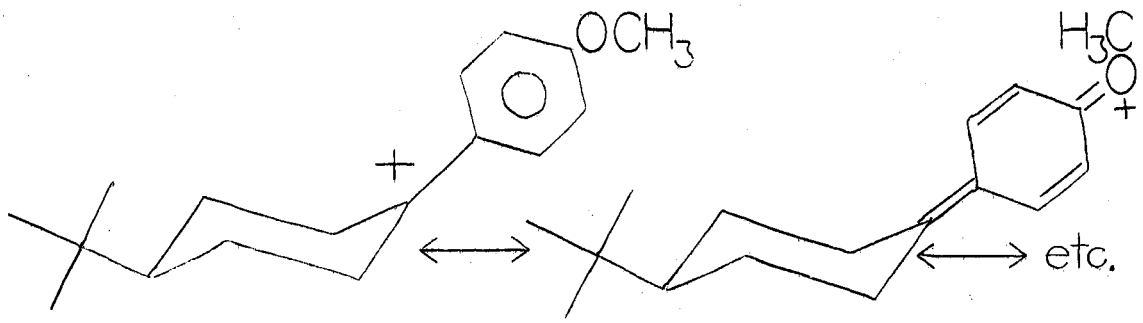
72 X = Cl



71 X = OH

73 X = Cl

from either alcohol 70 or 71 for the same reaction time. Within 15 min. the reaction reached an equilibrium between the cis- and trans-chlorides 72 and 73 and 4-tert-butyl-1-(p-methoxyphenyl)cyclohexene (74). The analyses of the products was performed by peak height measurement of the respective tert-butyl protons in the NMR spectra. After 15 min. when equilibrium was reached, there was little change in the product ratios while the HCl addition to the system remained constant. The trans-chloride 71 : alkene 74 ratio increased with increased HCl flow to a small extent. The alkene 74 was synthesized independently to confirm the identity of its NMR peaks (Table IX). Because of their extreme instability, the chlorides 72 and 73 could not be isolated and characterized. A conclusion cannot be drawn for the mechanism of addition since the position of the equilibrium is governed by thermodynamic stabilities of the products. These results would allow the assumption of a free carbonium ion intermediate 75 which would be greatly stabilized relative to 59. This type of stabilized

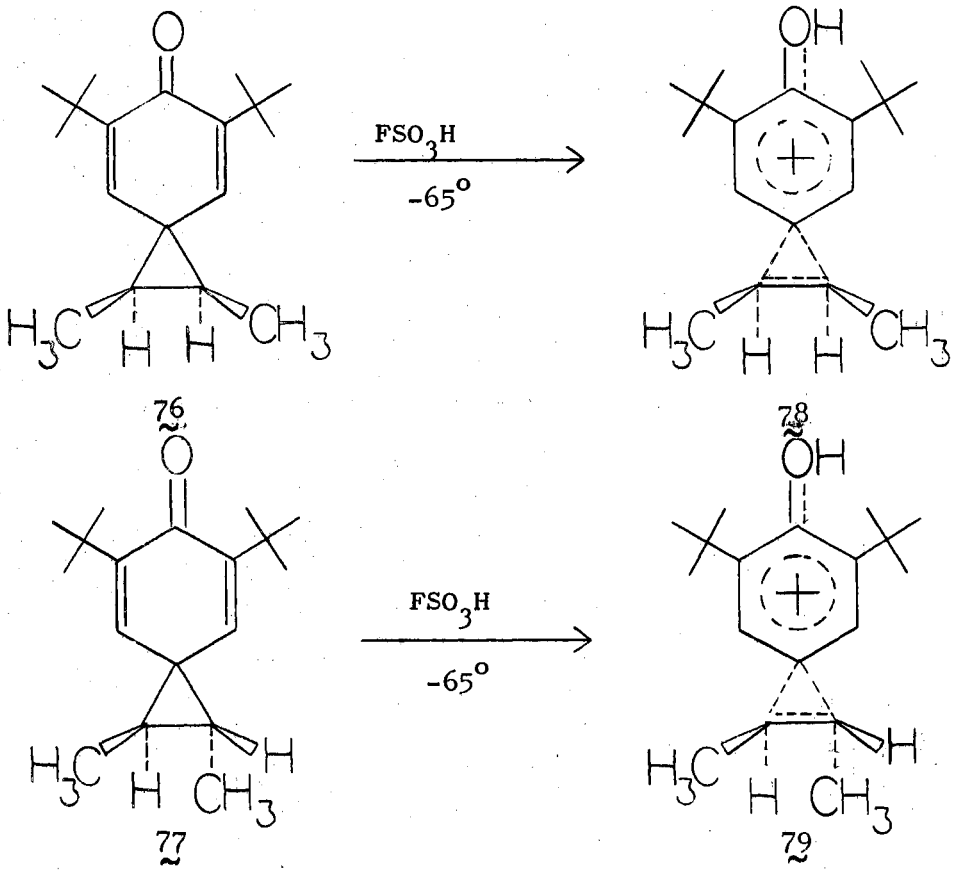


75

intermediate 75 will give rise to a less stereospecific, thermodynamically-controlled product mixture.[19]

One further study was undertaken to elucidate the nature of the intermediate by dissolving the cis- and trans-alcohols 52 and 53 separately and together in SbF_5-FSO_3H-SO_2 (Olah's solvent) solutions at -70° and examining the resultant NMR spectra. As noted in Chapter I, tertiary alcohols ionize in this solution to the most stable carbonium ion without undergoing the degradation usual in oleum solvents.[54,55] If both alcohols 52 and 53 ionized to the same carbonium ion, e.g., 59, only one type of NMR spectrum should be observed regardless of which alcohol was used. As noted before, the tert-butyl proton absorptions are the most discernible in the spectra of the alcohols and are fairly sensitive to their environment, as demonstrated by their chemical shift difference in the two alcohols 52 and 53. The appearance of two absorptions in the tert-butyl proton region might indicate the existence of two stable conformations of the carbonium ion such as 52c and 59. The tremendous solvating power of the solvent could perhaps stabilize the highly energetically unfavored 52c.

Direct NMR observation of stereochemically distinct ions has been reported.[6] Protonation of cis-1,2,-dimethyl-5,7-di-tert-butylspiro [2.5] octa-4,7-dien-6-one (76) with FSO_3H at -65° and the trans isomer 77 gave distinguishable NMR spectra attributed to the "ethylene-phenonium" cations 78 and 79, respectively. The distinct ions were

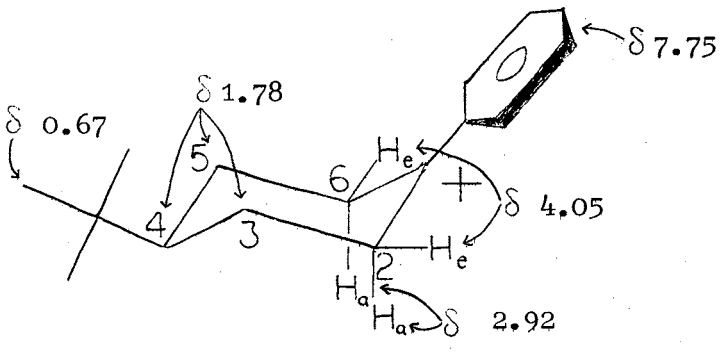


76 77 78 79

stable up to -40°, at which time both were converted to the same tertiary carbonium ion.

When cis-4-tert-butyl-1-phenylcyclohexanol 52 was submitted to the ionizing conditions of Olah's solvent at -70° and the NMR spectrum of the resulting cation taken at -66°, the spectrum was fairly simple and resembled that of the cis-alcohol 52 (Plates XXI and XXIII). Resonances were observed at δ 0.67 singlet, 0.88 singlet, 1.78 singlet, 2.92 broad doublet, 4.05 doublet, and 7.75 triplet. These types of absorptions

can be accounted for by examination of 80. For maximum delocalization



80

of the positive charge, the phenyl group would expectedly lie in the plane defined by carbons 1,2 and 6. The protons attached to C_2 and C_6 will be deshielded most by the inductive effect of the positive charge on C_1. This effect will be magnified for the 2,6-equatorial protons since they fall directly into the anisotropic deshielding area of the phenyl ring so that the δ 4.05 doublet is assigned to these protons. The 2,6-axial protons are influenced by the phenyl ring and occur as a broad doublet centered at δ 2.92. The remainder of the ring protons are found at δ 1.78 as a broad singlet. The tert-butyl protons absorb at δ 0.67 as a singlet and the phenyl protons absorb as a triplet at δ 7.75. The singlet at δ 0.88 might arise from slight degradation of the molecule in the acid as it was only observed in this one experiment and was temperature independent. The singlet at δ 1.00 is a TMS spinning sideband. All δ-values are with reference to external TMS. Spectra were also taken at -80° and -54° with no significant change observed in the absorptions (Table XI).

The spectrum of trans-4-tert-butyl-1-phenylcyclohexanol (53) at -70° was almost identical with that of the cis-alcohol 52 with the exception of a strong singlet at δ 0.95 (Plate XXIV). The other

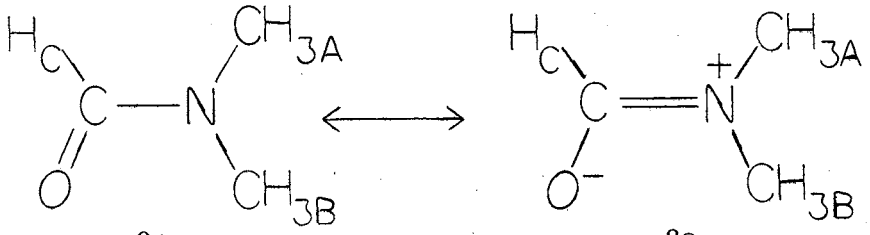
absorptions are assigned in the same order as given for the cis-alcohol 52: δ 4.07, 2.96, 1.83, 0.70, 7.78. Spectra were then recorded at -60°, -72°, -85°, and -77° with the singlet at δ 0.95 not being evident at these temperatures (Table X).

Finally, an equimolar mixture of the alcohols 52 and 53 was subjected to the ionizing conditions at -70° to give a spectrum (taken at -79°) comparable to that obtained for the trans-alcohol 53 (Plate XXV). When the spectrum was recorded at -50.5° the peak at δ 0.85 (corresponding with that at δ 0.95 for the trans-alcohol 53) disappeared (Table XII).

The only conclusion which can be drawn is that both the cis- and trans-alcohols 52 and 53 can react with Olah's solvent to give the same carbonium ion which is probably represented by 80. The trans-alcohol 53 may react to give a different carbonium ion which exists at low temperatures (< -70°) but changes to 80 as the temperature is raised.

We were fortunate to have the alcohols 52 and 53 analyzed for the nuclear Overhauser effect by one of Dr. Berlin's former associates, Dr. Mandava.[1,3] Besides the assignment of conformations using the chemical shifts and coupling constants of nuclear magnetic resonance, additional valuable information can sometimes be obtained by a consideration of the intramolecular spin-lattice relaxation paths for the various paths in a molecule. With most organic compounds, the main relaxation mechanism is direct dipole-dipole interaction between molecules. If care is taken to avoid nuclei with high magnetic moments such as fluorine and oxygen, the relaxation will take place intramolecularly between atoms. The condition must be satisfied that the nuclei are in close proximity so that relaxation between them can occur.

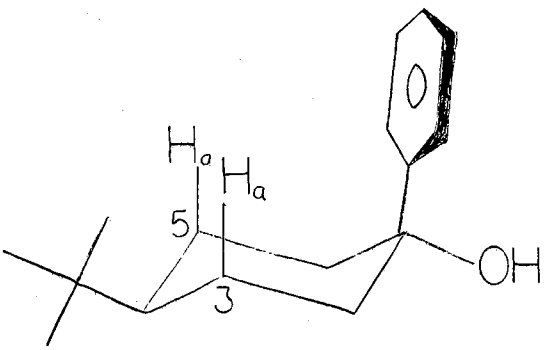
If one of these nuclei is irradiated while the NMR absorption of the second one is recorded, the absorption of the second nucleus may exhibit a positive or negative enhancement of intensity.[2] This enhancement is called the nuclear Overhauser effect (nOe). A good example of this effect is exhibited by dimethylformamide (81). Because of significant



81 82

contribution from resonance form 82, there is restriction of rotation of the C-N bond, placing the methyl groups in different chemical environments. This results in the methyl groups having different chemical shifts at δ 2.79 and 2.94. Irradiation of CH_{3A} while recording the H_c absorption increased the H_c intensity 28% at 31°.[63] Only a 3% enhancement is observed for the same procedure using CH_{3B} indicating that CH_{3A} spends more time in close proximity to H than does CH_{3B}. At 90° each methyl group caused a 28% increase in intensity for H. The thermal energy is now able to overcome the hindered bond rotation so that the methyl groups spend equal time near the H.

Negative nuclear Overhauser effects can occur when an intervening proton is situated between the irradiated and the observed nuclei.[2] As a check on the proximity of the phenyl and tert-butyl groups in cis-4-tert-butyl-1-phenylcyclohexanol (52), the molecule was observed for any nOe. Molecular models indicate a closest approach of 1.25Å for the tert-butyl and phenyl protons. Also, $3H_a$ and $5H_a$ are situated directly



52

between the phenyl and the tert-butyl groups. While observing the tert-butyl protons, the phenyl protons were irradiated and an 11.5% negative nOe was noted for the average of three scans. Irradiation of the tert-butyl protons while scanning the phenyl protons gave a 6.6% negative nOe average for three runs. This data combined with that given earlier is compelling evidence for the configuration of 52 as shown.

Trans-4-tert-butyl-1-phenylcyclohexanol (53) did not show any nOe for the tert-butyl and phenyl protons, as would be expected.

An estimation of the relative stabilities of the two alcohols 52 and 53 was made by heating an equimolar mixture at 150° for 24 hrs. in vacuo. The resulting red liquid was vacuum distilled to give alkene 45. The syrupy residue was washed with hexane, and filtered to give the trans-alcohol 53 with no trace of the cis-alcohol 52.

The configurations of the alcohols 52 and 53 having been established, the credibility of the assigned configurations of the chlorides 46 and 47 can be strengthened by analogy, along with the previously mentioned Raman and IR data. Comparison of the NMR tert-butyl proton absorptions in Tables VII and IX, for the corresponding alcohols and

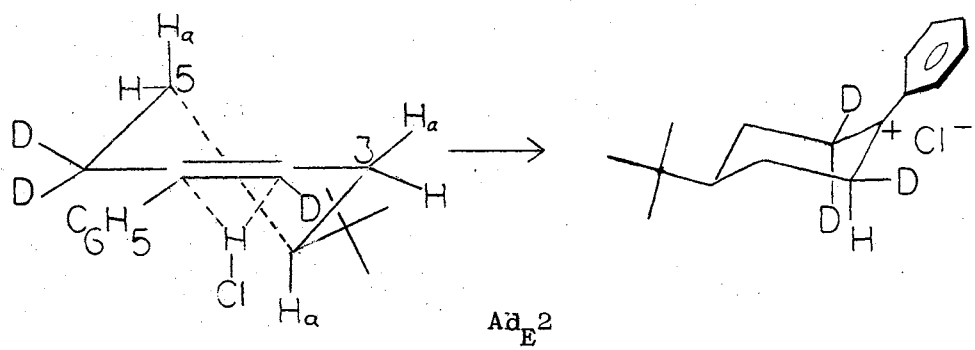
chlorides, indicate that the same shielding effects for the cis molecules must be operative. The relatively shielded nature of the tert-butyl protons in 46 would argue against a twist form which would dispose both the tert-butyl and phenyl groups to pseudo equatorial positions. The twist form would also require the chlorine in a pseudo axial position, which is discounted by the equatorial Raman and IR absorptions observed for an active C-Cl bond.

The mechanism of the addition of HCl to 4-tert-butyl-1-phenylcyclohexene (45) cannot be proven conclusively in the absence of kinetic data. However, the stereochemistry observed for the reaction definitely rules out several possible mechanisms, while at the same time denoting the ones which are most likely.

An equimolar mixture of cis- and trans-4-tert-butyl-1-phenyl-2,2,6,6-tetradeuteriocyclohexanols (83 and 84) was dehydrated to give the trideuterioalkene 49. Addition of HCl to this alkene and isolation of the initially formed product 51 proved that cis addition to the alkene occurs. It was never possible to observe the cis-chloride 46 as the only product present in the reaction mixture even after only 5 min. reaction time. This may be a consequence of very rapid isomerization to the trans-chloride 47 while the solution is brought to room temperature in order to record the NMR spectra, or it may indicate addition by a different mechanism which is much slower than cis addition. At -70^{o} the isomerization of cis-46 to trans-47 is fairly slow.

The following mechanisms can be ruled out as the major contributors to cis addition: any process involving the initial formation of a π-complex, Ad_E3 mechanisms involving backside attack, and a mechanism giving rise to a free carbonium ion.

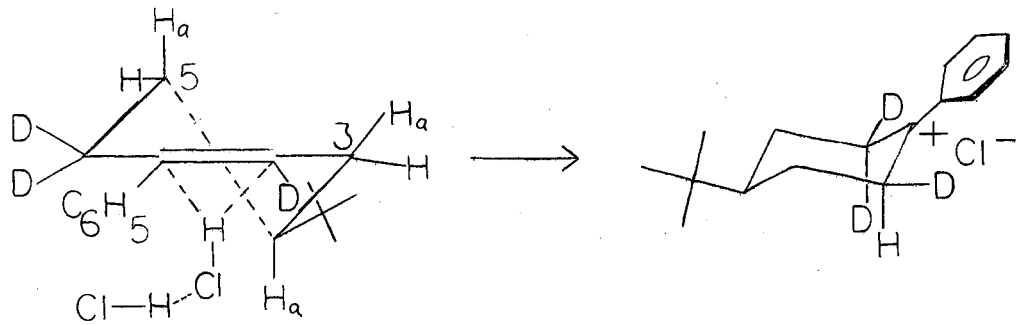
Three types of mechanisms would explain cis addition to a cyclohexene system. The simplest would be a 4-center molecular cis addition in which both bonds perhaps not in a synchronous fashion are formed in the slow step. It has been found, however, that solvent polarities will effect the proportion of cis addition.[16] A molecular cis addition would not be expected to exhibit such a change. A second possibility is the Ad_E2 in which the addition is stepwise via a carbonium ion involved in a tight ion-pair. Collapse of the tight ion-pair before rearrangement would lead to cis addition. Molecular models show that



Ad_E2

the pseudo 3-axial and the 5-axial hydrogens will probably cause shielding of that side of the double bond from attack, favoring attack on the opposite side of the ring. Collapse of the ion-pair would then give cis addition. The third possibility concerns the Ad_E3 mechanism. This process allows stabilization of the initially formed ion pair by another molecule of HCl. Without kinetic data a decision cannot be reached on which step-wise description is correct.

It is known, however, that HCl becomes more soluble in the reaction solvent, pentane, at lower temperatures.[5] The addition of HCl to alkene 45 will not take place at -30°, as evidenced by the absence



Ad_E3

of chlorides 46 or 47 as products and complete recovery of the alkene 45.

This consideration would speak for the Ad_E3 mechanism since at lower temperatures more HCl would be available to stabilize the ion-pair. The addition of HCl to 4-tert-butyl-1-(p-methoxyphenyl)-cyclohexene (74) formed the same equilibrium mixture as described before for the methoxy alcohols 70 and 71. Again, this equilibrium mixture would result from the free cation 75. The equilibrium mixture contained 53% trans-chloride 73, 40.3% alkene 74, and 6.7% cis-chloride 72.

The stereochemistry and product formation obtained from the two alkenes 45 and 74 are what would be predicted by Dolbier in his "unified mechanistic picture" (Figure 1).[19] When R' is phenyl, 40 will be less important and species 41 and/or 42 will be formed, leading to cis stereochemistry. As the carbonium ion becomes yet more stable and thus more long-lived (R' = p-anisyl), the reaction could proceed through intermediates 43 and 44 to give rise to a nonstereospecific, thermodynamically controlled product mixture.

TABLE I

STEREOCHEMISTRY OF ADDITION OF DBr AND DCl TO ALKENYLARENES

Compound	Acid	Solvent	% cis Addition	% trans Addition	Source
Acenaphthylene	DBr	CH_2Cl_2	90	10	17
	DBr	DOAc	75	25	17
	DCl	CH_2Cl_2	85	15	17
Indene	DBr	CH_2Cl_2	80	20	16
cis-1-Phenylpropene	DBr	CH_2Cl_2	85	15	18
	DCl	CH_3NO_2	~ 65	~ 35	60
trans-1-Phenylpropene	DBr	CH_2Cl_2	85	15	18
	DCl	CH_3NO_2	~ 65	~ 35	60

TABLE II

STEREOCHEMISTRY OF ELECTROPHILIC ADDITIONS TO CYCLIC ALKENES

Alkene	Environment	Addend	% trans	% cis	Ref.
1,2-Dimethylcyclohexene	HNO_3, H_2O, 25°	H_2O	~ 50	~ 50	8
	HBr, HOAc, 25°	HBr	100	0	36
	HBr, Pentane, 25°	HBr	100	0	36
1,2-Dimethylcyclopentene	HCl, Pentane, 25°	HCl	> 92	< 8	35
Cyclohexene	DBr, HOAc, 10°	DBr	76	24	65
	DBr, HOAc, 60°	DBr	24	76	65
Cyclohexene-$\underline{1},\underline{3},\underline{3}$-$d_3$	HBr, HOAc, 15°	HBr	$\geq$ 87	$\leq$ 4	27
		HOAc	$\geq$ 8	$\leq$ 1	
	HBr, HOAc, 60°	HBr	$\geq$ 71	$\leq$ 5	27
		HOAc	$\geq$ 22	$\leq$ 2	

TABLE III

DEPENDENCE OF THE STEREOCHEMISTRY OF ADDITION ON THE NATURE OF THE ADDING SPECIES

Adding Species	Environment	Alkene	% trans Addition	Ref.
DBr	CH_2Cl_2,0°	1-Phenylpropene	12	18
F_2	CCl_3F,-126°	1-Phenylpropene	22[a], 27[b]	53
Cl_2	CH_2Cl_2,0°	1-Phenylpropene	25[a], 33[b]	26
Br_2	CCl_4,2-5°	1-Phenylpropene	83[a], 88[b]	25
INCO	Et_2O,25°	β-deuteriostyrene	100	37
ArSCl	CCl_4,25°	1-Phenylpropene	100	25

[a]From cis alkene.

[b]From trans alkene.

TABLE IV

DEPENDENCE OF THE STEREOCHEMISTRY OF CHLORINE ADDITION ON THE STRUCTURE OF THE ALKENE

Alkene	Environment	% trans product	Ref.
cis-2-Butene	neat, -9°	100	61
cis-2-Butene	HOAc, 25°	100	26
Stilbene	$CHCl_3$, 0°	42	11
cis-1-Phenylpropene	CH_2Cl_2, 0°	25	26
cis-1-Phenylpropene	HOAc, 25°	22	26

TABLE V

DICHLORIDE PRODUCTS FROM ADDITION OF CHLORINE TO METHYL CINNAMATES IN HOAc AT $20^{\circ}C$

p-Subst.	Cinnamic isomer used	% yields[a] threo adduct	erythro adduct
NO_2	trans	13	trace
CF_3	trans	16	trace
Cl	trans	39	15
Cl	cis	11	52
H	trans	40	12
H	cis	11	43
Me	trans	49	28
MeO	trans	23	77
MeO	cis	5	90

[a]Other product due to the trans addition of acetate ion to the intermediate chloronium ion.

TABLE VI

MONITORED ADDITION OF HCl TO 4-TERT-BUTYL-1-PHENYLCYCLOHEXENE (45)[a]

Reaction Time, min.	Product Analysis, %								
	Reaction 1[b]			Reaction 2[c]			Reaction 3[d]		
	45	46	47	45	46	47	45	46	47
5							9.2	69.4	21.4
15	30.9	48.6	20.5				0.0	79.1	20.9
20				0.0	77.9	22.1			
30	0.0	52.0	48.0						
45	0.0	32.3	67.7	0.0	69.2	30.8	0.0	71.8	28.2
100				0.0	53.5	46.5		66.5	33.5

[a] In n-pentane solution at -70°.

[b] 0.0013 mole alkene/100 ml n-pentane.

[c] 0.0056 mole alkene/100 ml n-pentane.

[d] 0.0037 mole alkene/100 ml n-pentane.

TABLE VII

CHARACTERISTIC NMR PROTON ABSORPTIONS FOR 4-TERT-BUTYL-1-CHLORO-1-PHENYLCYCLOHEXANES AND 4-TERT-BUTYL-1-PHENYLCYCLOHEXENES[a]

Compound	tert-butyl	2,6-ax	2,6-eq.	Vinyl	Phenyl
46	0.74s[b]	2.30d	2.95d		7.35m
47	0.92s	ni[c]	2.42d		7.35m
50	0.72s				7.42m
51	0.73s	2.20d			7.40m
45	0.89s	ni	ni	6.10bs	7.25m
49	0.89s				7.25m

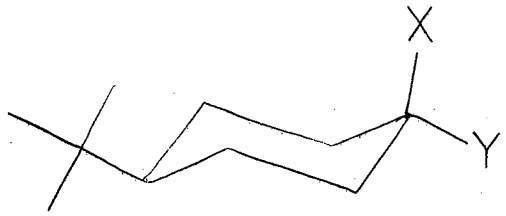
[a] δ-values for protons from internal TMS.

[b] s-singlet, d-doublet, m-multiplet, b-broad.

[c] Not identifiable, buried under ring protons.

TABLE VIII

PRODUCTS OF THE REACTION OF HCl WITH 4-TERT-BUTYL-1-SUBSTITUTED CYCLOHEXANOLS[a]



52 X = C_6H_5, Y = OH

53 X = OH, Y = C_6H_5

70 X = p-$CH_3OC_6H_4$, Y = OH

71 X = OH, Y = p-$CH_3OC_6H_4$

Reactant	Temp., °C.	Product Analysis, %				
		46	47	74	72	73
52	-70	78.6	21.4			
53	-70	28.2	71.8			
52	-30	78.6	21.4			
53	-30	19.4	80.6			
70	-70			38.1[b]	7.1	54.8
71	-70			41.5[b]	7.1	51.4

[a] In n-pentane, reaction time 45 min.

[b] Determined by tert-butyl proton peak heights.

TABLE IX

CHARACTERISTIC NMR PROTON ABSORPTIONS FOR 4-TERT-BUTYL-1-PHENYL- AND 4-TERT-BUTYL-1-(p-METHOXYPHENYL)CYCLOHEXYL DERIVATIVES[a]

Compound	tert-butyl	hydroxyl	2,6-ax.	2,6-eq.	methyl	vinyl	phenyl
52	0.77s[b]	1.87s	1.60d	2.52d			7.35m
83	0.77s	1.82s					7.42m
53	0.90s	1.83s	ni[c]	ni			7.35m
84	0.90s	1.92s					7.30m
70	0.77s	1.75s	ni	2.50d	3.79s		7.13q
71	0.90s	1.60s	ni	ni	3.78s		7.13q
74	0.89s		ni	ni	3.74s	6.00bs	7.02q

[a] δ-values of protons from internal TMS.

[b] s-singlet, d-doublet, q-quartet, m-multiplet, b-broad.

[c] Not identifiable, buried under ring protons.

TABLE X

NMR ABSORPTIONS FOR TRANS-4-TERT-BUTYL-1-PHENYLCYCLOHEXANOL (53) DISSOLVED IN OLAH'S SOLVENT

Protons[a]	Temp., °C.			
	-85	-77	-70	-60
tert-Butyl	49s	52s	42s	41s
Ring	111bs	111bs	110bs	106bs
2,6-Axial	181bd	189bd	178bd	176bd
2,6-Equatorial	233d	256d	244d	243d
Phenyl	472t	583t	467t	462t

[a]Hz downfield from external TMS.

TABLE XI

NMR ABSORPTIONS FOR CIS-4-TERT-BUTYL-1-PHENYLCYCLOHEXANOL (52) DISSOLVED IN OLAH'S SOLVENT

Protons[a]	Temp., °C.		
	-80	-66	-54
tert-Butyl	40s	41s	43s
	52s	53s	55s
Ring	107bs	106bs	104bs
2,6-Axial	176bd	178bd	177bd
2,6-Equatorial	242d	242d	242d
Phenyl	467t	465t	466t

[a]Hz downfield from external TMS.

TABLE XII

NMR ABSORPTIONS OF CIS- AND TRANS-4-TERT-BUTYL-1-PHENYLCYCLOHEXANOLS (52 AND 53) DISSOLVED IN OLAH'S SOLVENT

Protons[a]	Temp., °C.	
	-79	-50.5
tert-Butyl	40s	32s
	51[b]	
Ring	105bs	100bs
	172bs	166bs
2,6-Axial	177bd	175bd
2,6-Equatorial	242d	235d
Phenyl	464t	457t

[a] Hz downfield from external TMS.

[b] May be tert-butyl absorption from different carbonium ion.

CHAPTER III

EXPERIMENTAL[a-i]

Preparation and Isolation of cis- and trans-4-tert-Butyl-1-phenylcyclohexanols (52 and 53). The alcohols were prepared by the method of Garbisch and Patterson but with sufficient modifications that the whole procedure will be described.[31] The reaction was conducted under N_2 dried with three drying towers (one containing conc. H_2SO_4 and two 3-Å Linde molecular sieve). The reaction vessel was heated to 130° with a heat gun while being flushed with N_2. All liquid reagents were dried at least 24 hr. (3-Å molecular sieve).

A 500-ml., Morton flask was equipped with an addition funnel, N_2 inlet, mechanical stirrer, and a Friedrich condenser with $CaCl_2$ drying tube. Magnesium turnings (8.47 g., 0.349 g.-atom) were added to the flask and heated with a heat gun for 5 min. After 20 ml. of ether was added to the flask, three 1-ml. portions of bromobenzene were added over a 5-min. period with vigorous stirring. When the solution had acquired a dark brown color while boiling, the remainder of a total of 52.19 g. (0.333 mole) of bromobenzene in 100 ml. of ether was added at a rate to maintain steady reflux. After complete addition, the solution was boiled for 1.5 hr. and then diluted to 250 ml. with additional ether.

While being stirred, the solution of phenylmagnesium bromide, containing some unreacted magnesium, was treated dropwise with 50 g.

(0.317 mole) of 4-tert-butylcyclohexanone (60) [International Flavors and Fragrances Inc., m.p. 48-49° (lit.,[39] m.p. 47.8-48.7°)] dissolved in 100 ml. of ether. Addition, while maintaining vigorous reflux, required 30 min. Reflux was then maintained overnight, although 2 hr. is sufficient time.

The yellowish-gray suspension contained in the flask was poured into 300 ml. of an ice-water mixture and 300 ml. of 3N HCl was slowly added, followed by 600 ml. of ether. The solid was dissolved with stirring and the organic phase was separated, dried ($MgSO_4$), and concentrated under aspirator pressure. The light yellow solid remaining was pulverized and vacuum dried at 45° for 1 hr. The 65 g. (88.3% yield) of material was shown by NMR to contain approximately equal amounts of alcohols 52 and 53. Infrared analysis and gas-liquid chromatography indicated the presence of small amounts of ketone 60.

Ninety grams of the isomeric alcohols 52 and 53 were recrystallized four times, twice from 95% ethanol at room temperature and twice from n-pentane at -15°. A white, flaky crystalline material (15.5 g.) was isolated and found to be cis-4-tert-butyl-1-phenylcyclohexanol (52) m.p. 155-156° (lit.,[31] m.p. 158-159°). GLC analyses indicated 52 to be of purity greater than 99%. NMR absorptions are found in Table IX and Plate XXI. The IR absorptions are seen in Plate VI. Attempts to isolate the trans alcohol 53 from the mother liquors were unsuccessful.

Both the cis-52 and trans-53 alcohols could be isolated pure by column chromatography using the method of Meakins.[50] Equimolar quantities of alcohols 52 and 53 (5.0 g) dissolved in 150 ml. of Skelly B were introduced onto a 3 x 28 cm. column packed with alumina

(Merck neutral) in hexane and 40-ml. fractions were collected. Successive elution with Skelly B (1 l.) followed by 5% (4 l.), 10% (2.5 l.), and 90% (2 l.) of ether-Skelly B solutions gave 1.8 g. of trans-4-tert-butyl-1-phenylcyclohexanol (53) etuted with the 5-10% solutions. Recrystallization (n-pentane, -15°) gave 1.7 g. of 53, m.p. 115-116° (lit.,[31], 117-118°). GLC analysis showed no impurities. The NMR absorptions are given in Table IX and Plate XXII. IR absorptions are shown in Plate VII.

The cis-alcohol 52 was eluted with the 90% ether-hexane solution and recrystallization (n-pentane, -15°) gave 0.7 g., m.p. 155°. GLC analysis showed no impurities and NMR and IR data were as given previously.

Preparation of 4-tert-Butyl-1-phenylcyclohexene (45). The isomeric alcohols 52 and 53 were dehydrated with a mixture of 5 ml. of concentrated H_2SO_4 and 20 ml. of glacial acetic acid as described by Garbisch with slight modifications. The crude alcohols 52 and 53 (25 g., 0.108 mole) were stirred magnetically with a freshly prepared mixture of the acids for 30 min. The alcohols dissolved and gave a dark-red, viscous solution, which was added to a mixture of ether-water (100 ml.: 200 ml.). The organic layer was washed with 100 ml. of water and 100 ml. of a 10% solution of K_2CO_3, and then dried ($MgSO_4$) for 30 min. The ether solvent was removed under reduced pressure, leaving 25 ml. of a red viscous oil which was vacuum distilled to give alkene 45.

The following fractions were collected using a long-path distillation head: 1) b.p. 50-105°/0.15 mm., 1 ml.; 2) b.p. 105-107°/0.20 mm., 11.7 g. (50.6% yield), of 4-tert-butyl-1-phenylcyclohexene (45) η_D^{25} 1.5401 [lit.,[30] b.p. 106-107°/0.4 mm., η_D^{20} 1.5437].

GLC analyses showed the second fraction to have only one component. Typical IR absorptions for a trisubstituted alkene are found at 1640 (C=C) and 835 $cm.^{-1}$ in Plate VIII. The NMR absorptions are seen in Plate XVI and Table VII.

A second and superior method of dehydrating the alcohols 52 and 53 to alkene 45 was found. A 100-ml., round-bottom flask was fitted with condenser and magnetic stirring bar. To the flask was added 14.3 g. (0.062 mole) of the alcohols 52 and 53 and 3 ml. of dimethyl sulfoxide.[66] The mixture was boiled at 200° for 3 hr. using an oil bath. The red viscous oil obtained was vacuum distilled using a long-path vacuum-insulated distillation head. The first cut (31-105°/0.05mm) was discarded; the second contained 11.37 g. (86.4% yield) of 4-tert-butyl-1-phenylcyclohexene (45) b.p. 106-110°/0.05mm., η_D^{25} 1.5401. The IR and NMR spectra were identical to those obtained from the product from sulfuric-acetic acid dehydration. The advantage of this procedure is the simpler isolation method as well as the higher yield.

Preparation of cis-4-tert-Butyl-1-chloro-1-phenylcyclohexane (46). A 250-ml., 4-neck, round-bottom flask was equipped as shown in Figure 6. This apparatus was used on all low-temperature additions of hydrogen chloride. The 60-ml. addition funnel, half filled with 3-Å molecular sieve, supported the Dewar condenser. Also assembled in the apparatus were a low-temperature thermometer, a 4.5-mm. I.D. glass inlet tube 175 mm. long, a 4-mm. I.D. J-shaped glass outlet tube fitted with stopcock and a 3-neck 15-ml. flask with septum, a magnetic stirrer, and necessary Teflon inserts, glass and Tygon tubing.

The glass apparatus was dried for 1 hr. at 130° and then assembled and flushed with dry N_2 for 1 hr. The 250-ml. flask was heated with a

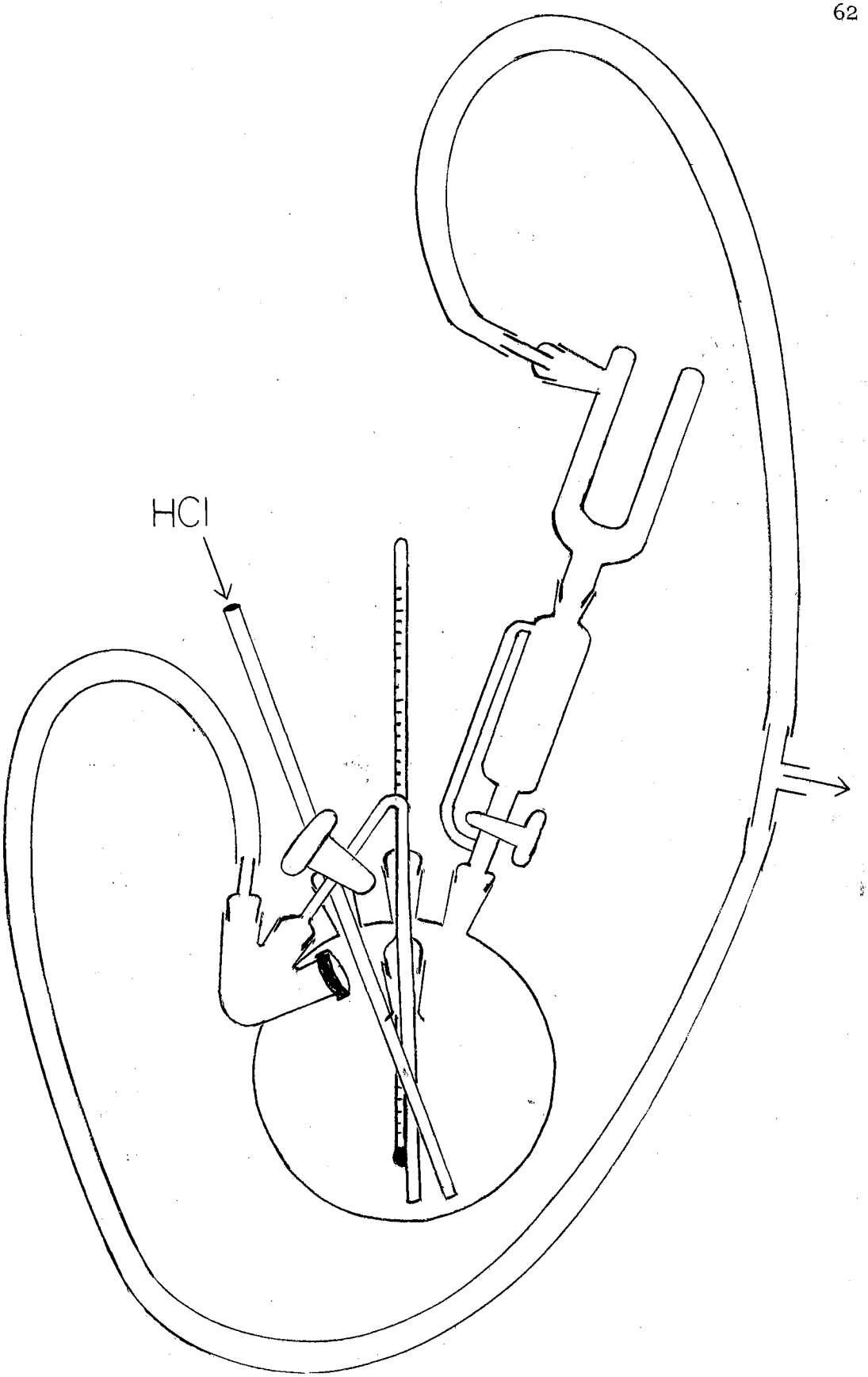


Figure 6. Low Temperature Apparatus

heat gun to insure anhydrous conditions. Dry ice was added to the Dewar condenser and 100 ml. of n-pentane (dried over 3-Å molecular sieve) was added through the top joint in that condenser to the addition funnel. The n-pentane was then allowed to flow slowly into the reaction flask. The thermometer holder was removed, 2.0 g. (0.0086 mole) of cis-4-tert-butyl-1-phenylcyclohexanol (52) added, and the thermometer holder quickly replaced. A polystyrene beaker containing dry ice-ethanol, supported by a magnetic stirring plate and lab jack, was raised so as to immerse the reaction flask. After the temperature of the solution had been lowered to -70°, the nitrogen was shut off and hydrogen chloride which first passed through a 3-Å molecular sieve trap was allowed to bubble through the solution. At various time intervals the outlet from the Dewar condenser was clamped shut, and the stopcock leading to the 15-ml. flask was opened, forcing a portion of the solution into the 15-ml. flask. The clamp was then opened and the stopcock shut allowing any solution remaining in the tube to return to the reaction flask. Aliquots (2 ml.) were extracted from the 15-ml. flask through the septum with a 5-ml. syringe and placed in a 10-ml. Erlenmeyer flask. The n-pentane was removed at aspirator pressure and the crystalling material remaining was dissolved in chloroform-d and placed in an NMR tube to determine the species present for the particular reaction time. The reaction was monitored in this way.

The relative amounts of the cis- and trans-4-tert-butyl-1-chloro-1-phenylcyclohexanes (46 and 47) were determined from the NMR spectra by the area under the tert-butyl proton absorptions. Total product isolated after 45 min. weighed 1.9 g. (88% yield) and contained 78.6% cis-chloride 46 and 21.4% trans-chloride 47 (Table VIII). After two

recrystallizations (n-pentane, -15°), 1.2 g.(55.6% yield) of cis-4-tert-butyl-1-chloro-1-phenylcyclohexane 46, m.p. 89.5-91°, was isolated.

The equatorial chloride was identified by the maximum in the Raman spectrum (Plate I) at 685 $cm.^{-1}$ and that in the IR spectrum (Plate IV) at 686 $cm.^{-1}$.[7,20,69] The NMR absorptions are given in Plate XIII and Table VII.

Anal. Calcd. for $C_{16}H_{23}Cl$: C, 76.60; H, 9.26; Cl, 14.14.
Found: C, 76.36; H, 9.14; Cl, 13.80.

Preparation of trans-4-tert-Butyl-1-chloro-1-phenylcyclohexane (47). Hydrogen chloride was bubbled through 100 ml. of n-pentane containing 1.0 g. (0.0047 mole) of trans-4-tert-butyl-1-phenylcyclohexanol (53) at -70°. After 45 min., the flow of HCl was stopped and the n-pentane was removed under reduced pressure leaving 1.0 g. (92.6% yield) of white flakes.

Inspection of the NMR spectrum gave no evidence of hydroxyl absorptions at ≈ δ 1.8 to 2.0 (as in alcohols 52 and 53) and thus indicated the reaction to be complete. Upon integration (polar planimeter) of the peak area for the protons of the tert-butyl group, it was determined that the mixture contained 71.8% trans-chloride 47 and 28.2% cis-chloride 46 (Table VIII). The mixture of chlorides 47 and 46 was recrystallized twice (absolute ethanol, -15°) to give 0.48 g. (40.7% yield) of trans-4-tert-butyl-1-chloro-1-phenylcyclohexane (47), m.p. 60-62°. A maximum at 647 $cm.^{-1}$ was observed in the Raman spectrum (Plate II); one at 640 $cm.^{-1}$ in the IR spectrum (Plate V) was assigned to the axial carbon-chlorine stretch.[7,20,69]

Anal. Calcd. for $C_{16}H_{23}Cl$: C, 76.60; H, 9.26; Cl, 14.14.
Found: C, 76.56; H, 9.17; Cl, 14.02.

Reaction of Hydrogen Chloride with cis-4-tert-Butyl-1-phenylcyclohexanol (52) at -30°. Hydrogen chloride was bubbled through a suspension of 0.4 g. (0.0017 mole) of cis-4-tert-butyl-1-phenylcyclohexanol (52) and 100 ml. of n-pentane. The temperature was maintained at -30° by partial immersion of the reaction flask in a dry ice -95% ethanol bath. The HCl was discontinued after 45 min. and the n-pentane removed under aspirator pressure. The white residue remaining was immediately dissolved in $CDCl_3$ and the NMR spectrum taken to determine the relative amounts of the product chlorides 46 and 47. The alcohol 52 had completely reacted as evidenced by the complete absence of any hydroxyl proton absorptions at δ 1.87 in the NMR spectrum. Integration of the tert-butyl protons at δ 0.74 and δ 0.92 indicated the product composition to be: cis-4-tert-butyl-1-chloro-1-phenylcyclohexane (46) 78.6%, trans-4-tert-butyl-1-chloro-1-phenylcyclohexane (47) 21.4% (Table VIII).

Reaction of Hydrogen Chloride with trans-4-tert-Butyl-1-phenylcyclohexanol (53) at -30°. Hydrogen chloride was bubbled through a suspension of trans-4-tert-butyl-1-chloro-1-phenylcyclohexanol (53) (0.5 g., 0.0022 mole) and 100 ml. of n-pentane. The temperature was maintained at -30° throughout the reaction. After discontinuing the HCl after 45 min. and removing the n-pentane in vacuo, the white residue was dissolved in $CDCl_3$ to obtain the NMR spectrum. The absence of any alcohol (53) remaining was proven by the absence of hydroxyl proton at δ 1.83. Analysis of the areas of the tert-butyl protons demonstrated that trans-4-tert-butyl-1-chloro-1-phenylcyclohexane (47) (80.6% at δ 0.92) to be the major product. The minor product (19.4%) was cis-4-tert-butyl-1-chloro-1-phenylcyclohexane (46) (δ 0.74).

See Table VIII.

Isolation of cis-4-tert-Butyl-1-chloro-1-phenylcyclohexane (46) After the Addition of Hydrogen Chloride to 4-tert-Butyl-1-phenylcyclohexene (45). Hydrogen chloride was bubbled through a n-pentane solution containing 5.5 g. (0.0219 mole) of alkene 45 at -70°. Aliquots (2 ml.) were taken at 5, 20, 45, and 100 min. and the relative amounts of cis- and trans-chlorides 46 and 47 were determined as usual. After 20 min., the addition was complete to give 77.9% of the cis-chloride 46 and 22.1% of the trans-chloride 47. The n-pentane was removed in vacuo after 100 min. and the chloride mixture was recrystallized twice (n-pentane, -15°) to give 0.5 g. (7.6% yield) of cis-4-tert-butyl-1-chloro-1-phenylcyclohexane (46), m.p. 90-91°. The NMR and IR absorptions were as given previously (Table VII, Plates XIII and IV).

Isolation of trans-4-tert-Butyl-1-chloro-1-phenylcyclohexane (47) After the Addition of Hydrogen Chloride to 4-tert-Butyl-1-phenylcyclohexene (45). Hydrogen chloride was bubbled through a n-pentane solution containing 1.75 g. (0.0818 mole) of alkene 45 at -70°. Aliquots were taken at 15 and 60 min. and the relative amounts of cis-46 and trans-47 chlorides were determined as usual. The addition was complete after 15 min. to give 61.7% of the cis-chloride 46 and 38.3% of the trans-chloride 47. After 60 min., much of the cis-chloride 46 had isomerized to give 80.1% trans-chloride 47 and 19.9% cis-chloride 46. The n-pentane was removed in vacuo after 90 min. and the chloride mixture recrystallized once (100% ethanol, -70°), filtered, and vacuum dried at 25° for 30 min. This procedure gave 0.9 g. (44% yield) of trans-4-tert-butyl-1-chloro-1-phenylcyclohexane (47). A vacuum-sealed capillary tube was used to obtain a m.p. of 64.5-65.5°. The NMR and IR

spectra were as given previously (Table VII, Plates XIV and V).

Attempted Addition of Hydrogen Chloride to 4-tert-Butyl-1-phenylcyclohexene (45). By partial immersion of the reaction flask, containing 4-tert-butyl-1-phenylcyclohexene 45 (0.5 g., 0.0023 mole) and 100 ml. of n-pentane, in a cold bath, a temperature of -30° was maintained. HCl was admitted to the solution for 45 min. and the reaction progress monitored at 15, 30, and 45 min. using NMR analysis. A tert-butyl proton absorption corresponding to cis-chloride (46) at δ 0.74 or one at δ 0.92 for the trans-chloride (47) was not found at any of the times mentioned. Each spectra yielded absorptions of only the alkene 45 with the characteristic protons absorptions at δ 0.89 (tert-butyl), δ 6.10 (vinyl), and δ 7.25 (phenyl).

Preparation of cis- and trans-4-tert-Butyl-1-phenyl-2,2,6,6-tetradeuteriocyclohexanol (83 and 84). The method of Garbisch was followed in synthesizing 4-tert-butyl-2,2,6,6-tetradeuteriocyclohexanone (86).[31] A 200-ml. 3-neck flask was equipped with N_2 inlet, magnetic stirring bar, thermometer, water condensor, and a Drierite tube. The system was flushed for 30 min. with nitrogen while a heat gun was used to dry the flask. After cooling, 10 g. (0.065 mole) of 4-tert-butylcyclohexanone (60), 90 g. (4.5 mole) of deuterium oxide, and 1.50 g. (0.014 mole) of anhyd. Na_2CO_3 were added to the flask and the mixture was boiled 340 min. It was then heated at 99° until practically all of the liquid had distilled. The distillate was extracted with two 20-ml. portions of pentane and dried (Na_2SO_4) for 1 hr. The pentane was removed in vacuo leaving behind 9.8 g. (95.2% yield) of white residue assumed to be the 4-tert-butyl-2,2,6,6-tetradeuteriocyclohexanone (86). This ketone was then used in the Grignard reaction

as described previously to synthesize alcohols 83 and 84. To 1.575 g. (0.065 g.-atom) of magnesium was added 10.15 g. (0.065 mole) of bromobenzene to give phenylmagnesium bromide after 3 hr. To this Grignard solution was added 9.8 g. (0.062 mole) of ketone 86. After ether extraction and drying ($MgSO_4$), 14.7 g. (100% yield) of crude cis- 83 and trans- 84 deuterio alcohols were recovered. Column chromatography (alumina) as described previously for the separation of alcohols 52 and 53 was utilized to separate the deuterio alcohols 83 and 84.

Starting with 3.15 g. of the mixture of 83 and 84, 1 g. of trans-4-tert-butyl-1-phenyl-2,2,6,6-tetradeuteriocyclohexanol (84) was recovered after recrystallization (95% ethanol) m.p. 115-116°. The NMR absorptions (Table IX and Plate XXVII) indicate the replacement of the 2,6-hydrogens at δ 1.75 by deuterium atoms. The mass spectrum gave the parent peak m/e 236 with no peaks at m/e 232, 233, 234, or 235, indicating complete replacement at the 2,6 positions with deuterium. Also isolated in the chromatography was 1 g. of cis-4-tert-butyl-1-phenyl-2,2,6,6-tetradeuteriocyclohexanol 83 after recrystallization (pentane), m.p. 155.5-156°. The NMR absorptions (Table IX and Plate XXVI) indicate the absence of hydrogens at the 2,6 positions (no peaks at δ 1.60 and 2.52) and the mass spectrum confirms this with m/e 236 as the parent peak and none at m/e 232, 233, 234, or 235.

Preparation of 4-tert-Butyl-1-phenyl-2,6,6-trideuteriocyclohexene (49). A mixture of cis- and trans-4-tert-butyl-1-phenyl-2,2,6,6-tetradeuteriocyclohexanols (83 and 84) (3.1 g., 0.013 mole) was placed in a 50-ml., round-bottom flask fitted with a condenser and magnetic stirring bar. The alcohols 83 and 84 were then heated at 210° for 2 hr. The dark red oil that formed was vacuum distilled, giving 1.3 g. at

100°/0.075 mm. Impurities were shown present by GLC; these were removed by chromatographing the liquid on a 2 by 25 cm. column (neutral alumina) using Skelly B as the solvent.

The Skelly B was evaporated under reduced pressure from the eluate leaving 1.0 g. (35.1% yield) of 4-tert-butyl-1-phenyl-2,6,6-trideuteriocyclohexene (49). The alkene 49 was 100% pure by GLC and the NMR analysis (Plate XXVIII and Table VII) which did not show the presence of any vinylic hydrogen (≈ δ 6.10). The IR spectrum is found in Plate XII. The mass spectrum gave the parent peak m/e 217 with no m/e 214, 215, or 216.

Preparation of cis-4-tert-Butyl-1-chloro-1-phenyl-2,2,6,6-tetradeuteriocyclohexane (50). Cis-4-tert-butyl-1-phenyl-2,2,6,6-tetradeuteriocyclohexanol (83) (0.15 g., 0.00064 mole) was added to 65 ml. of n-pentane and the solution was cooled to -70°. Hydrogen chloride gas was then caused to bubble through the solution for 15 min. The n-pentane was then removed in vacuo and the white residue was recrystallized twice (n-pentane, -70°) to obtain 0.07 g. (42.4% yield) of cis-4-tert-butyl-1-chloro-1-phenyl-2,2,6,6-tetradeuteriocyclohexane (50), m.p. 90-91°. The NMR absorptions (Plate XVII and Table VII) confirm its identity with no evidence of 2,6-hydrogens (~ δ 1.60 and 2.52) in the spectrum. The mass spectrum gave the parent peak at m/e 254 with none at m/e 250, 251, 252, or 253. The relative intensity of the p+2 chlorine isotope peak was 34% of the parent peak.

Addition of Hydrogen Chloride to 4-tert-Butyl-1-phenyl-2,6,6-trideuteriocyclohexene (49). The alkene 49 (1.0 g., 0.005 mole) was added to 100 ml. of n-pentane and the temperature was lowered to -70°. After hydrogen chloride was bubbled through the solution for 15 min.,

the system was flushed with dry N_2 while the solution was raised to room temperature. The n-pentane was removed under reduced pressure and after two recrystallizations (n-pentane, -70°), 0.3 g. (24.8% yield) of cis-4-tert-butyl-1-chloro-1-phenyl-2-eq.-6,6-trideuteriocyclohexane (51), m.p. 90-91°, was isolated. Integration of the NMR spectrum (Plate XVIII and Table VII) showed one proton in the 2-axial position (δ 1.60) and none in the 2- or 6-equatorial positions. Mass spectral analyses gave the parent peak at m/e 253 with no peaks at m/e 250, 251, or 252. The p+2 chlorine isotope peak had an intensity 35% of the m/e 253, as expected.

Addition of Deuterium Chloride to 4-tert-Butyl-1-phenylcyclohexene (45). DCl was bubbled through a solution of 4-tert-Butyl-1-phenylcyclohexene (45) (3.85 g., 0.018 mole) and n-pentane (100 ml.) at -70°. After 15 min., the DCl gas was discontinued and the n-pentane removed with aspirator vacuum. After two recrystallizations (n-pentane, -70°), 0.1 g. (2.16% yield) of cis-4-tert-butyl-1-chloro-1-phenylcyclohexane (46) was isolated. The NMR absorptions for the cis-chloride obtained were the same as shown in Table VII for cis-chloride 46, with no apparent decrease at the 2,6-axial position (2.30 δ) or at the 2,6-equatorial position (2.95 δ). This indicates that scrambling occurred or the DCl purity (> 99.5% by specifications) was not as specified.

Preparation of cis- and trans-4-tert-Butyl-1-(p-methoxyphenyl)-cyclohexanols (70 and 71). The alcohols 70 and 71 were synthesized via the Grignard reaction described previously. To a dry 100-ml., 3-neck flask was added 1.3 g. (0.054 g.-atom) magnesium and 10 g. (0.053 mole) of p-bromoanisole in 20 ml. of ether. Iodine was needed to initiate

the reaction. 4-tert-Butylcyclohexanone (60) (8.24 g., 0.054 mole) was then added to complete the reaction.

The Grignard reaction mixture was decomposed with water (pH=7) as acid conditions tend to cause dehydration of the alcohols 70 and 71 to 4-tert-butyl-1-(p-methoxyphenyl)cyclohexene (74). The resultant sludge was extracted twice with a 1:9 benzene-ether solution (100 ml. total). The mixture of the alcohols 70 and 71 was then isolated by removal of the solvent. The reactive amounts of the alcohols 70 and 71 could not be determined by GLC as they both underwent dehydration to give the alkene 74 on the column. Integration (polar planimeter) of the respective tert-butyl group protons in the NMR spectrum gave 63.5% trans-alcohol 71 and 36.5% cis-alcohol 70.

The mixture was recrystallized (n-pentane, -70°) twice and dried at 50° under vacuum for 2 hr. to give 1.5 g. (10.7% yield) of cis-4-tert-butyl-1-(p-methoxyphenyl)cyclohexanol (70), m.p. 126-127°. The NMR spectrum (Plate XIX and Table IX) showed the absense of any trans-alcohol 71 or alkene 74. The IR spectrum is shown in Plate IX.

Anal. Calcd. for $C_{17}H_{26}O_2$: C, 77.80; H, 9.99.

Found: C, 77.82; H, 9.99.

The mother liquors from the n-pentane recrystallizations were concentrated in vacuo to give a yellowish solid. The solid was dissolved in Skelly B and chromatographed on a 3 by 24 cm. column (neutral alumina). Successive elutions with Skelly B and 5, 10, 30, 60, and 90% ether-Skelly B solutions gave the alkene 74 (eluted with Skelly B), 0.9 g. (6.43% yield) of trans-alcohol 71 (eluted with 5% solution), and a small amount of cis-alcohol 70 (eluted with 90% solution). After recrystallization (n-pentane, -70°) and drying at 50°

under vacuum for 2 hr., trans-4-tert-butyl-1-(p-methoxyphenyl)cyclohexanol (71), m.p. 105-107°, was obtained.

The NMR spectrum (Plate XX and Table IX) showed the absence of any cis-alcohol 70 or alkene 74. The IR spectrum is seen in Plate X.

Anal. Calcd. for $C_{17}H_{26}O_2$: C, 77.80; H, 9.99.

Found: C, 78.18; H, 9.74.

It was found that both alcohols 70 and 71 are hygroscopic and have a propensity to eliminate within 2 to 3 hr. if left in the atmosphere.

Preparation of 4-tert-Butyl-1-(p-methoxyphenyl)cyclohexene (74). An equimolar mixture (5.0 g., 0.019 mole) of cis- and trans-alcohols 70 and 71 was dehydrated using a fresh mixture of 5 ml. conc. H_2SO_4 and 20 ml. glacial acetic acid as described previously. After extraction of the alkene 74 with n-pentane, drying ($MgSO_4$), and recrystallization (n-hexane), 3.8 g. (82.6%) of 4-tert-butyl-1-(p-methoxyphenyl)-cyclohexene (74), m.p. 77.5-78°, was recovered.

The NMR spectrum (Plate XXIX and Table IX) showed the absence of any hydroxyl group absorptions (δ 1.60 or 1.75) and the IR spectrum is seen in Plate XI.

Anal. Calcd. for $C_{17}H_{24}O$: C, 83.55; H, 9.90.

Found: C, 83.64; H, 9.90.

Addition of Hydrogen Chloride to 4-tert-Butyl-1-(p-methoxyphenyl)-cyclohexene (74), cis-4-tert-Butyl-1-(p-methoxyphenyl)cyclohexanol (70), and trans-4-tert-Butyl-1-(p-methoxyphenyl)cyclohexanol (71). The addition of hydrogen chloride to 0.5 g. (0.002 mole) of alkene 74 in 100 ml. of n-pentane or 0.2 g. (0.00076 mole) of cis-alcohol 70 in 100 ml. of n-pentane, or 0.1 g. (0.00038 mole) of trans-alcohol 71 in 75 ml. of n-pentane was conducted at -70° and in an identical manner.

Aliquots were taken in all cases at 5, 15, 30, 45, and 60 min. to determine the relative concentrations of the species present via NMR. The reaction reached equilibrium within 15 min. starting from each of the reactants. The final equilibrium mixture starting from either 70, 71, or 74 was approximately the same: cis-4-tert-butyl-1-chloro-1-(p-methoxyphenyl)cyclohexane (72) 7%; trans-4-tert-butyl-1-chloro-1-(p-methoxyphenyl)cyclohexane (73) 52%; and 4-tert-butyl-1-(p-methoxyphenyl)cyclohexene (74) 41% as determined by peak heights of the tert-butyl proton absorptions in the NMR spectrum.[16]

Reaction of trans-4-tert-Butyl-1-phenylcyclohexanol (53) with FSO_3H-SbF_5-SO_2 at Low Temperatures. All operations were carried out under atmospheric laboratory conditions.

Technical fluorosulfonic acid (City Chemical Corporation, N.Y., N.Y., b.p. 160°/760 mm.) is hygroscopic and reacts with water vapor to give hydrofluoric acid and sulfuric acid, so that all operations should be performed in a well ventilated hood. Mellor should be consulted before any laboratory work is attempted.[51] After drying an all-quartz distillation apparatus equipped with Drierite outlet tube, the apparatus was assembled and flushed with N_2. Approximately 20 ml. of crude FSO_3H was pipetted into the distillation flask and the N_2 was allowed to sweep the fumes from the system. The N_2 inlet was then closed and the acid was distilled using a flame to obtain approximately 10 to 15 ml. of pure fluorosulfonic acid. The receiving flask was removed and the flask mouth quickly covered with aluminum foil. A pipette was then inserted through the aluminum foil and the FSO_3H was pipetted into a quartz test tube which had been dried and flushed with N_2. Aluminum foil was used to cover the test tube allowing storage of

the FSO_3H for up to one month without appreciable contamination with water.

Anhydrous technical antimony pentafluoride (Research Organic/Inorganic Chemical Co., Sun Valley, Calif., b.p. 149.5°/760 mm.) is hygroscopic and fumes badly in the air, so that a well ventilated hood is necessary. References should be consulted before any work is attempted.[49,52] The quartz distillation apparatus was assembled as with FSO_3H and approximately 10 ml. of crude SbF_5 was poured into the distillation flask. After closing the N_2 inlet, the material was distilled to obtain approximately 5 to 7 ml. of antimony pentafluoride. Because of its very high viscosity, there was still liquid flowing from the condenser 15 min. after the flame was removed. The flow appeared as a very fine thread of the crystal clear liquid hanging from the condenser into the receiving flask. The receiving flask was removed and the opening immediately covered with aluminum foil. The SbF_5 could be stored for up to two weeks in the receiving flask.

Sulfur dioxide was obtained in lecture bottles and was condensed to liquid. After drying at 130°, a 10-ml. 2-neck standard-taper flask, small Dewar condenser, Drierite tube, and inlet adapter were assembled and flushed with N_2 for 15 min. The lecture bottle was connected to the system and a Dewar flask containing dry ice-acetone was used to cool the 10-ml. flask. Dry ice-acetone was added to the Dewar condenser also and the SO_2 lecture bottle valve opened to condense approximately 2 drops/sec. of liquid SO_2 for a total of 8 ml. The liquid was poured into a pre-cooled test tube, covered with aluminum foil and stored in a styrofoam beaker containing dry ice-ethanol. All operations should be performed in a well ventilated hood.

Using a small-bore 1-ml. pipette for the FSO_3H and a large-bore pipette for SbF_5, 0.574 ml. (1 g., 0.01 mole) of FSO_3H and 0.727 ml. (2.17 g., 0.01 mole) of SbF_5 were mixed in a quartz test tube with vigorous shaking.[57] The quartz test tube, containing the acid solution, was cooled to allow addition of 1.5 ml. of liquid SO_2 with vigorous shaking. The solution was then cooled to -70° by immersion in dry ice-ethanol.

To a dry quartz test tube containing a seed size magnetic stirring bar was added 0.3 g. (0.00129 mole) of trans-4-tert-butyl-1-phenylcyclohexanol (53). After cooling, 1.5 ml. of SO_2 was pipetted into the test tube, forming a suspension with the alcohol 53. The test tube was cooled to -70° with stirring.

The total acid solution (2.8 ml.) was pipetted into the SO_2-suspended alcohol 53 in three equal portions with vigorous shaking and stirring between addition. A dark red solution formed immediately with some brownish material floating on top of the solution. A sealed capillary tube containing carbon tetrachloride and tetramethylsilane was placed in a flared-mouth NMR tube. The NMR tube was of the type used with spherical ampules for small-volume samples. After cooling the NMR tube to -70°, a portion of the red solution was pipetted into it using a Pasteur pipette. A Teflon insert was then placed in the NMR tube to center the capillary tube and the NMR tube was capped. Any leftover solutions could be disposed of by carefully pouring into 95% ethanol in a well ventilated hood.

The NMR variable temperature probe was lowered initially to -80° following the procedure given in the instruction manual.[67] The instrument must be turned at each new temperature by adjustment of the Phase

Detector to control line slope and the Y-Course and Y-Gradient for amplitude. The methanol spectrum was used with the instrument in Operate mode. Ringing should be evident and a displacement of 190 divisions of the doublet for the following settings; Amplitude - 0.12, Filter Bandwidth - 4, and R. F. Field - 0.005, indicates adequate tuning.

The Temperature Control Dial is not accurate, necessitating temperature calibrations using the displacement of the quartet and doublet from each other in the spectrum of methanol. The probe temperature was adjusted to -70° and the methanol NMR tube removed, quickly replacing the plastic probe cap. The Teflon holder was removed from the methanol NMR tube and placed on the NMR tube containing the alcohol 53 - acid solution. While the NMR tube was kept in the cold bath, the Teflon holder was dried with a Chem-Wipe and the plastic probe cap removed; then the NMR tube was removed from the cold bath, quickly wiped dry, placed in the probe before any frost could form, and closed with the plastic probe cap. Adjustments of the spinner control and the metal screw in the plastic probe cap were made to allow the NMR tube to spin properly. The NMR tube was allowed to equilibrate for 20 min. before the spectrum was taken. After the spectrum was taken, the NMR tube was removed quickly from the probe, the probe cap replaced, and the NMR tube replaced in the cold bath. The methanol tube was then reinserted in the probe and the probe adjusted to a new temperature to repeat the process. The spectra were taken, in order, at -70° (Plate XXIV), -60°, -70°, -85°, and -77°. The absorptions are tabulated in Table X. Two peaks were discernable in the tert-butyl proton region (δ 0.70 and 0.95) at -70° but one disappeared when the

temperature was raised to -60, and did not reappear at the lower temperatures.

The probe was allowed to return to room temperature following the instruction manual.[67]

Reaction of cis-4-tert-Butyl-1-phenylcyclohexanol (52) with FSO_3H-SbF_5-SO_2 at Low Temperatures. The reaction was carried out exactly as described previously. The acid solution was added to 0.3 g. (0.00129 mole) of the cis-alcohol 52 suspended in SO_2 at -70°. The NMR spectra were recorded, in order, at -80° (Plate XXIII), -66, and -54°. The NMR absorptions for the three temperatures are recorded in Table XI. There was no significant change in the spectra as the temperature was varied.

Reaction of cis- and trans-4-tert-Butyl-1-phenylcyclohexanol (52 and 53) with FSO_3H-SbF_5-SO_2 at Low Temperatures. The reaction was carried out as described previously. The acid solution was added to a equimolar mixture (0.14 g., 0.0006 mole each) of the cis-52 and trans-53 alcohols suspended in SO_2 at -70°. The NMR spectra were recorded at -79° (Plate XXV) and -50.5°. Two absorptions (δ 0.7 and 0.9) were evident in the tert-butyl proton region of the NMR spectra at the lower temperature while the high field absorption disappeared at the higher temperature. The NMR absorptions are recorded in Table XII.

FOOTNOTES

[a]Elemental microanalyses were determined by Galbraith Laboratories, Knoxville, Tennessee, and Midwest Microlab, Inc., Indianapolis, Indiana.

[b]Gas-liquid chromatographic analyses were performed with a Varian-Aerograph 1720 instrument equipped with a dual-differential thermal conductivity bridge. The column packing used was 5% SE-30 on 100/120, A-W, DMCS-treated Chromosorb G (6 ft. by ¼ in.).

[c]The infrared spectra were taken with a Beckman IR-5A spectrophotometer as films on sodium chloride or as potassium bromide pellets.

[d]Molecular weight determinations were made on a prototype of the LKB-9000 combination gas chromatograph-mass spectrometer.

[e]Melting points were obtained on a Thomas-Hoover Capillary Melting Point Apparatus and are uncorrected.

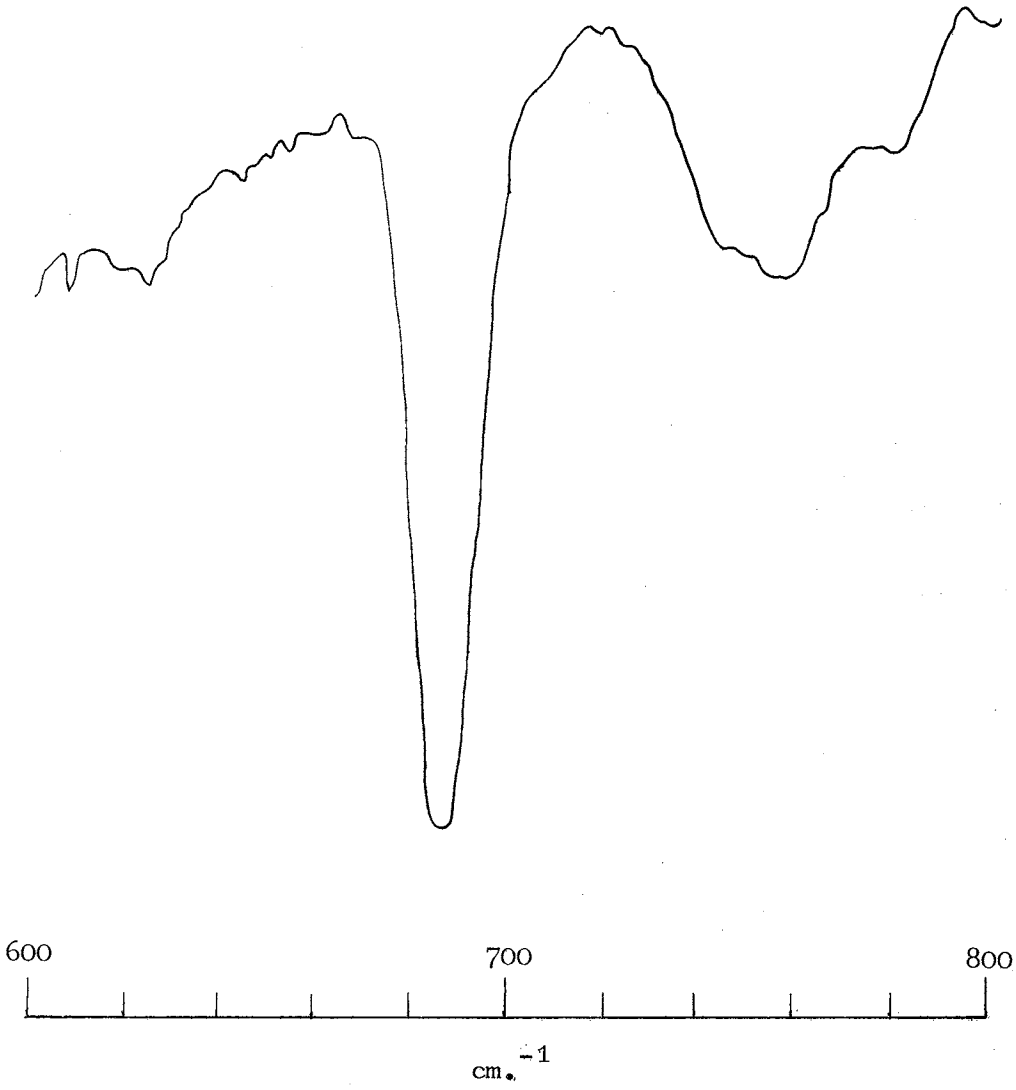
[f]Proton magnetic resonance spectra were taken on a Varian A-60 high resolution spectrometer equipped with a V-4341/V-6057 Variable Temperature Accessory. Tetramethylsilane was used as internal or external standard. Chloroform-d was used as the solvent to obtain approximately 10% solutions unless otherwise specified.

[g]Nuclear Overhauser effects were determined with a Varian HA-100 MHz high resolution nuclear magnetic resonance spectrometer equipped with a V-3521A integrator/decoupler operating in frequency sweep mode. Tetramethylsilane was used as the internal frequency lock.

[h]Integration of proton magnetic resonance spectra to determine relative amounts of isomers was performed with a Keuffel and Esser compensating polar planimeter.

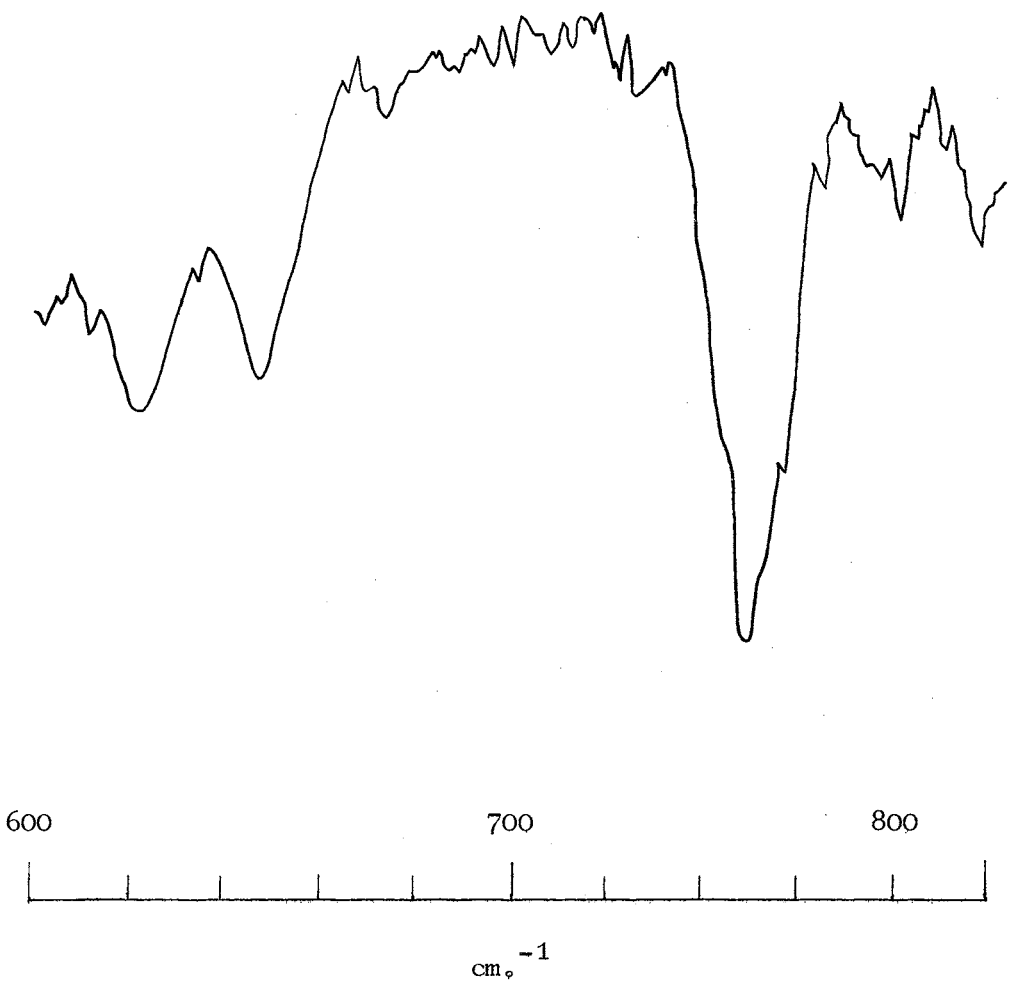
[i]Raman spectra were recorded with a helium-neon laser Raman spectrophotometer with a Jarrell-Ash double monochromator. Samples were measured as 10% solutions in n-heptane.

Plate I



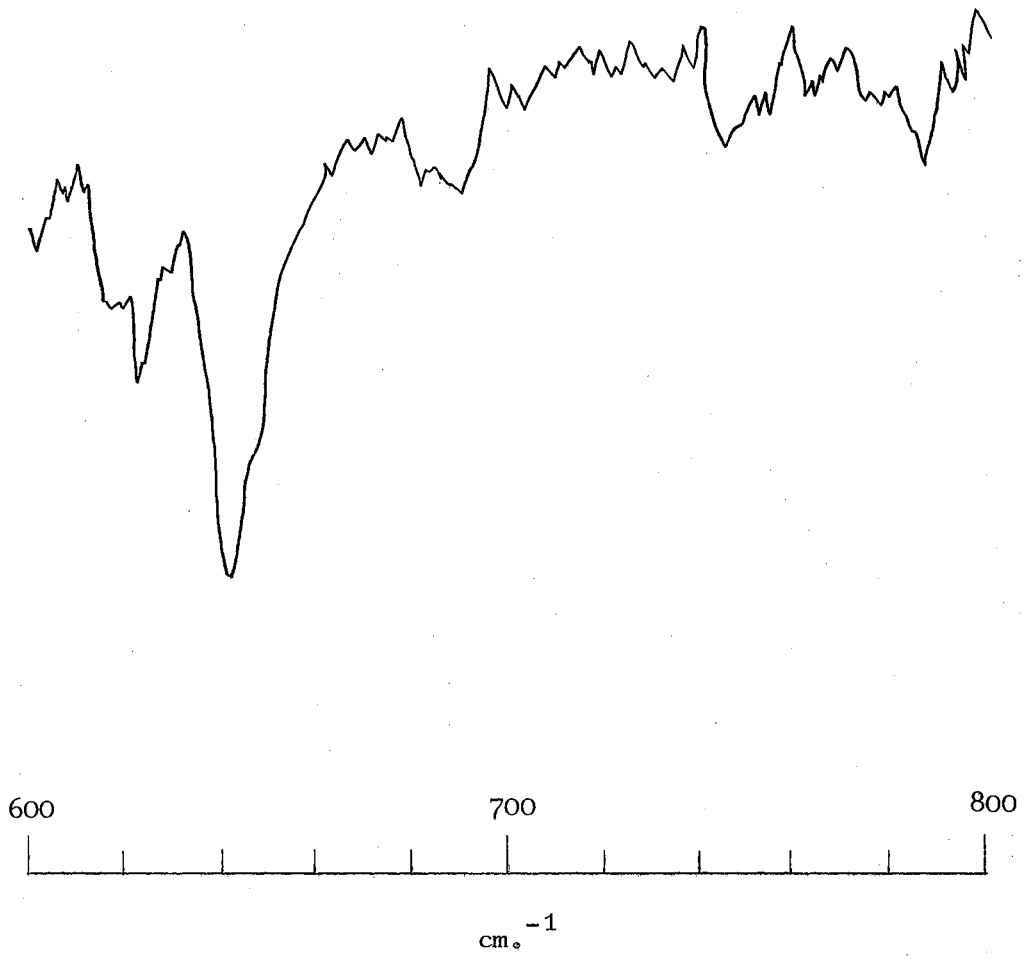
cis-4-tert-Butyl-1-chloro-1-phenylcyclohexane (46), Solution in n-Heptane

Plate II



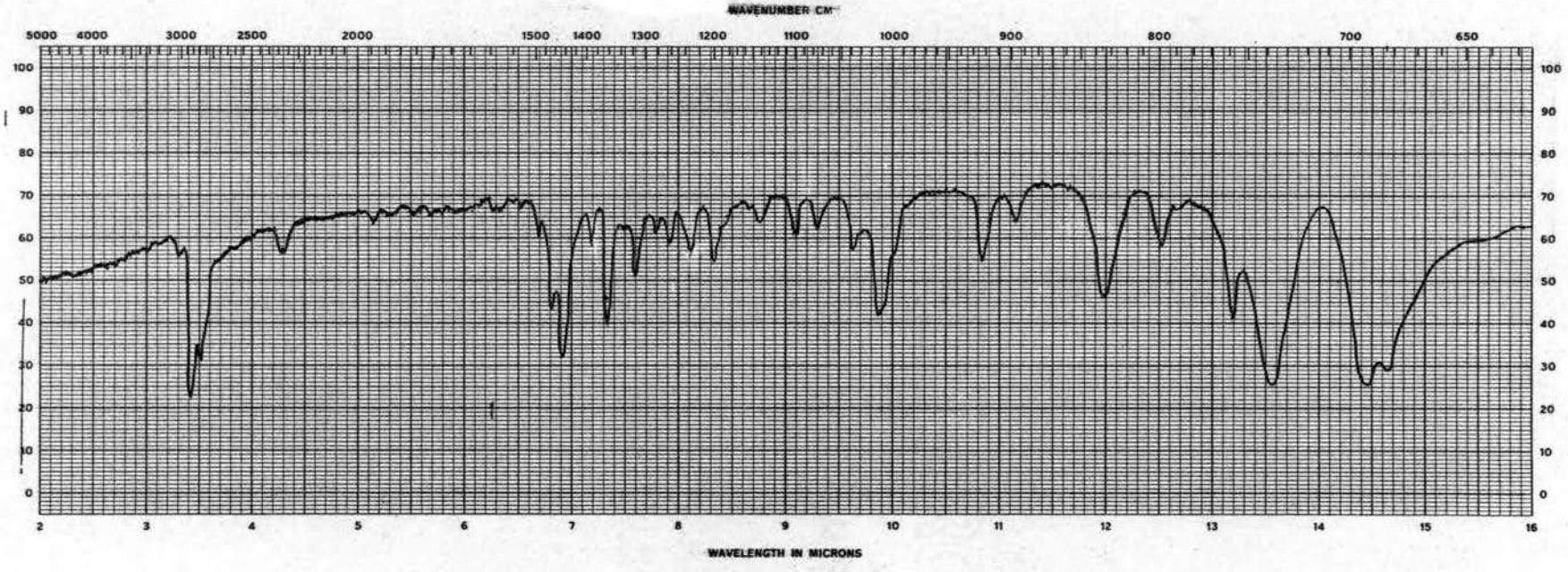
trans-4-tert-Butyl-1-chloro-1-phenylcyclohexane (47), Solution in n-Heptane

Plate III



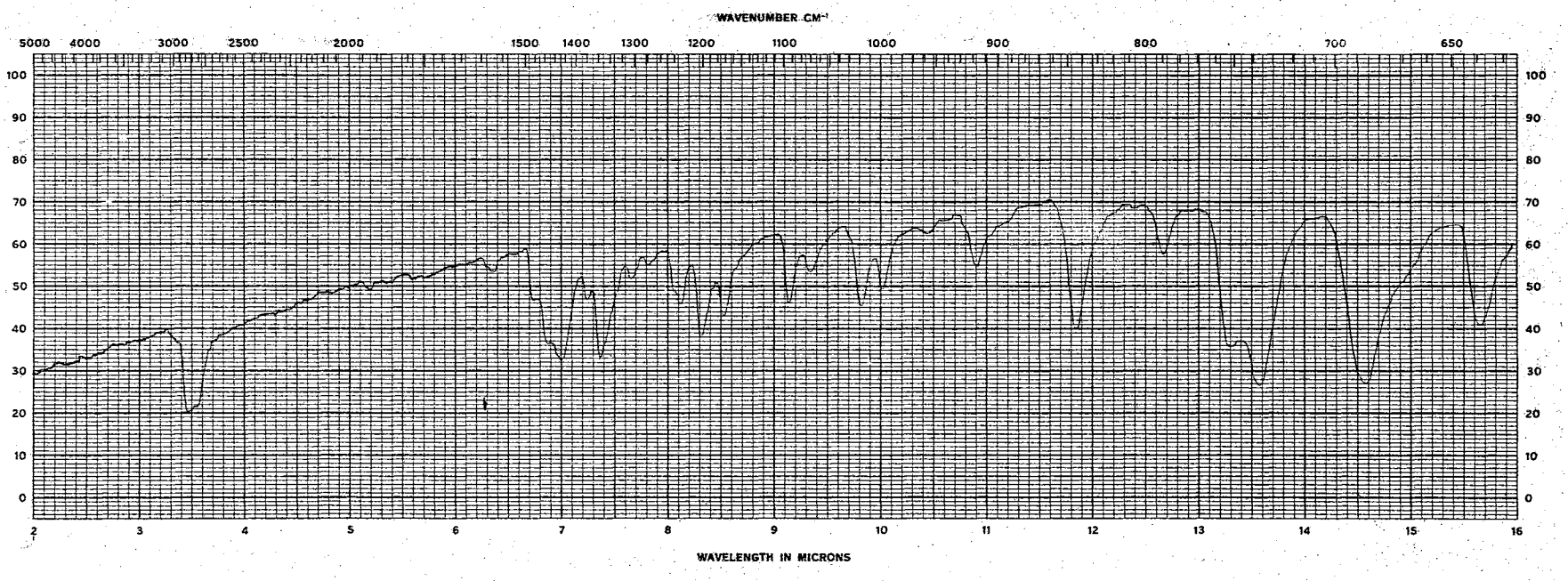
1-Chloro-1-phenylcyclohexane (48), Neat Liquid

Plate IV



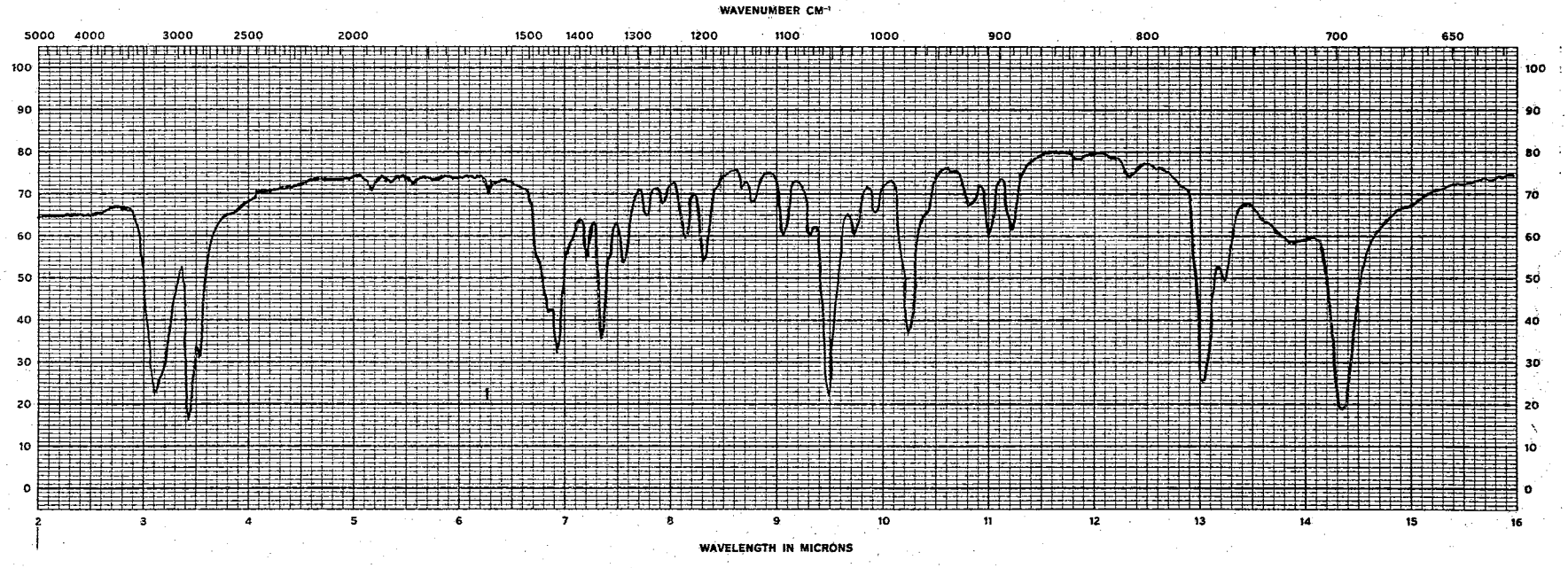
cis-4-tert-Butyl-1-chloro-1-phenylcyclohexane (46), KBr Pellet

Plate V



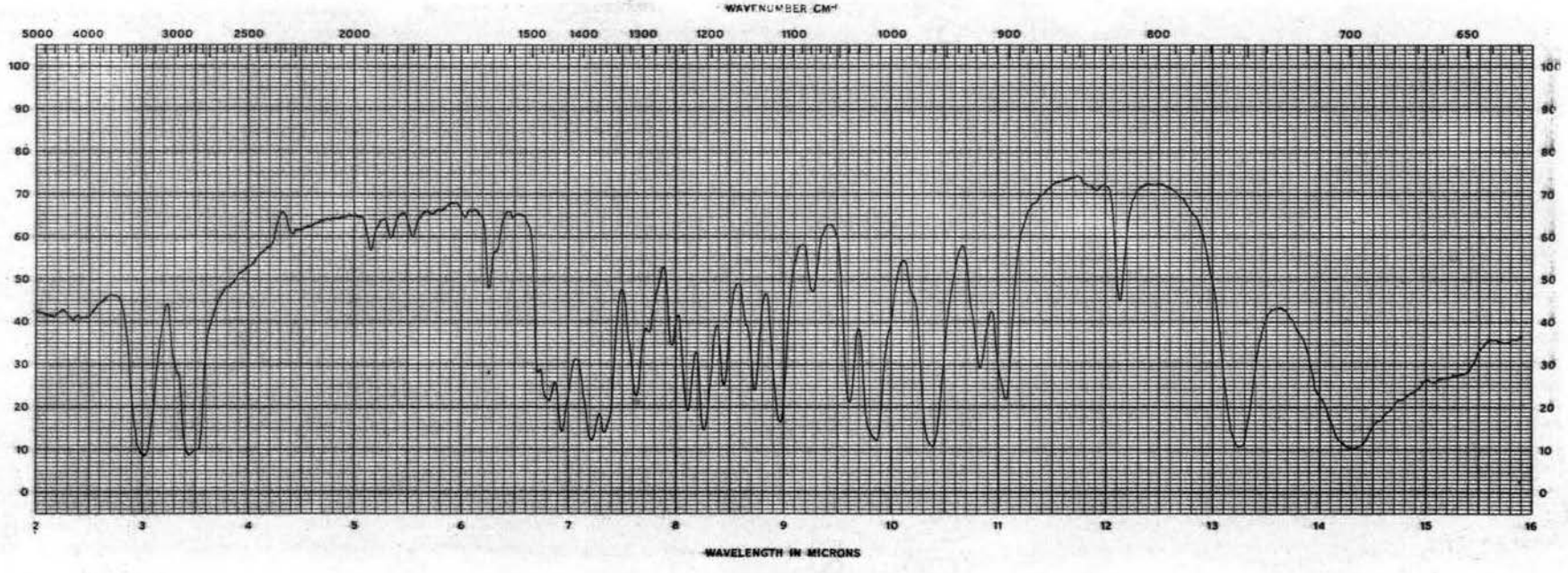
trans-4-tert-Butyl-1-chloro-1-phenylcyclohexane (47), KBr Pellet

Plate VI



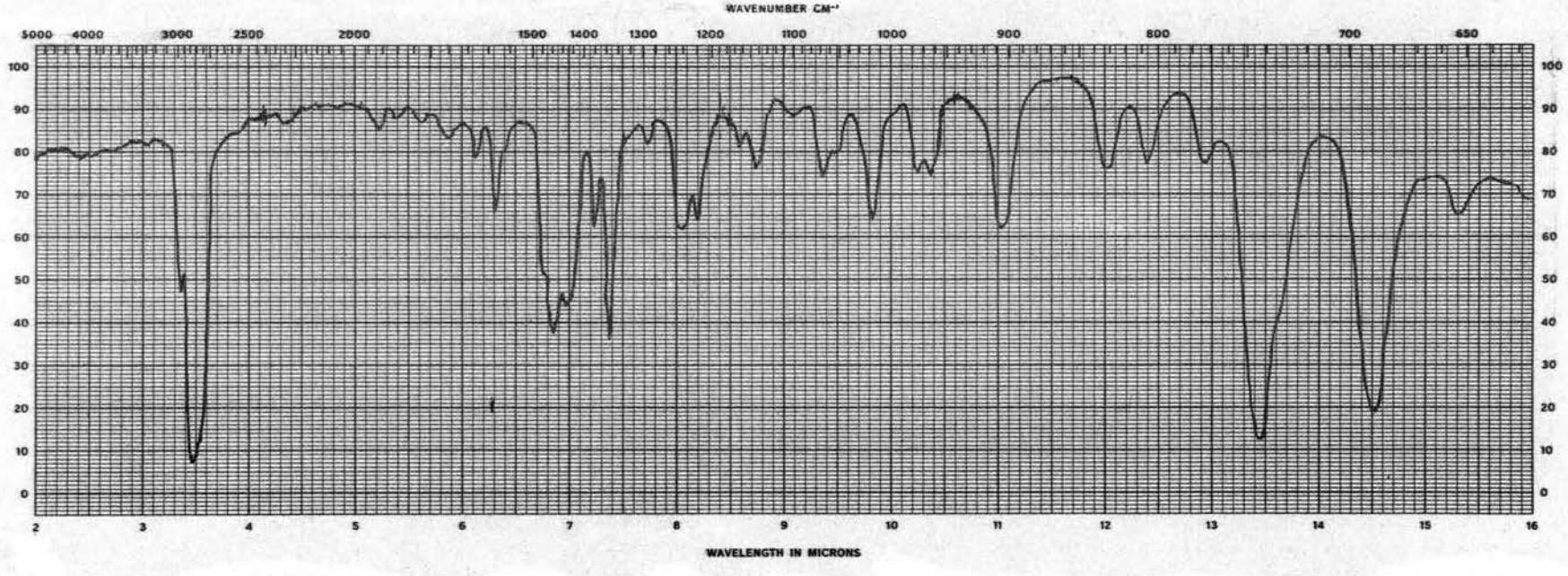
cis-4-tert-Butyl-1-phenylcyclohexanol (52), KBr Pellet

Plate VII



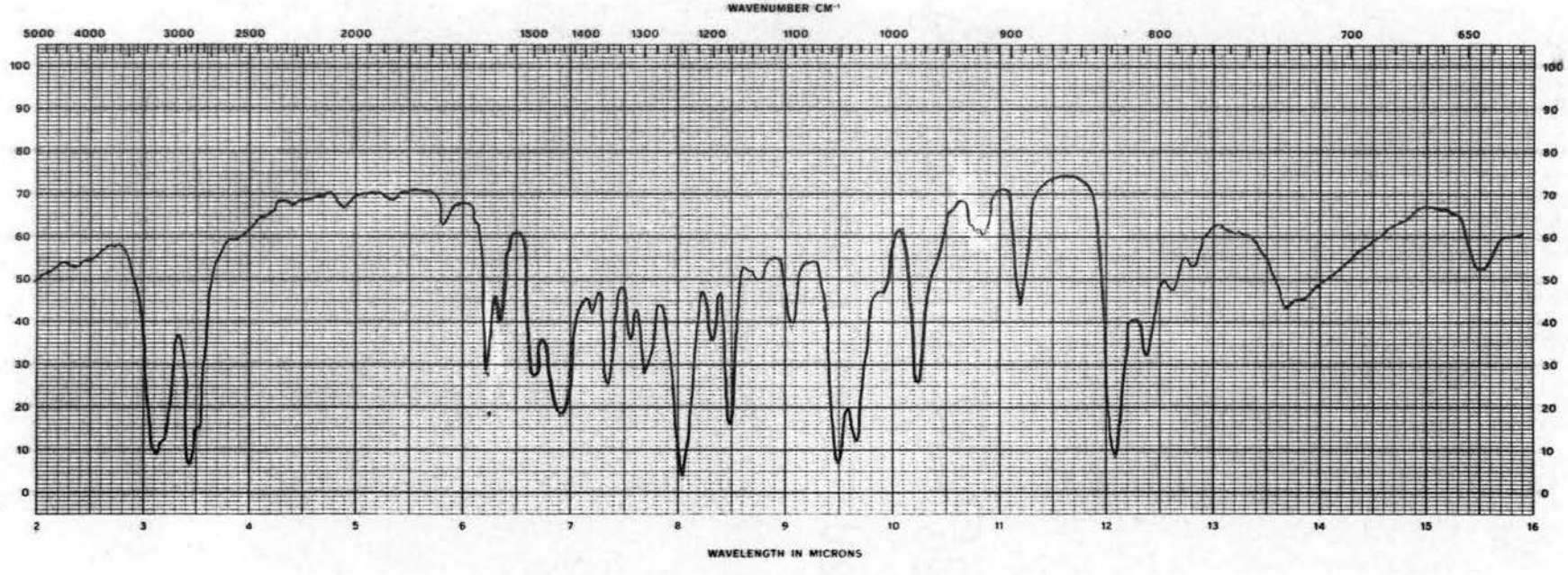
trans-4-tert-Butyl-1-phenylcyclohexanol (53), KBr Pellet

Plate VIII



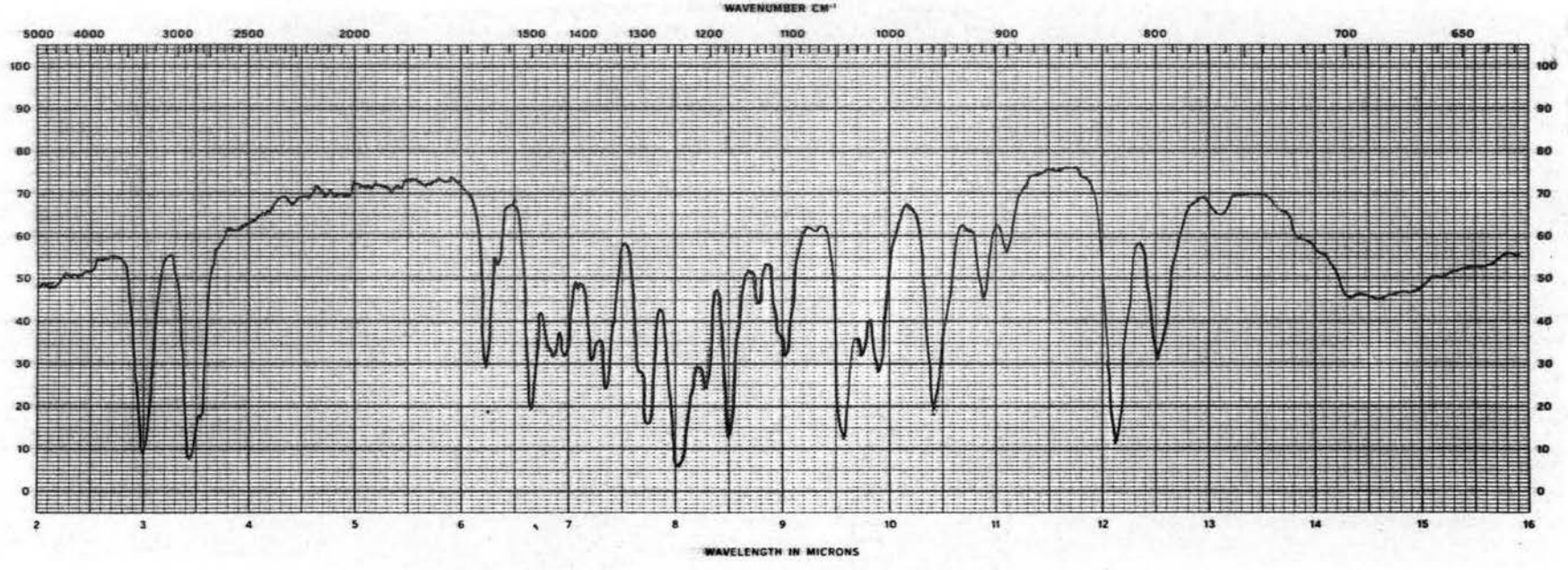
4-tert-Butyl-1-phenylcyclohexene (45), Film on NaCl Plates

Plate IX



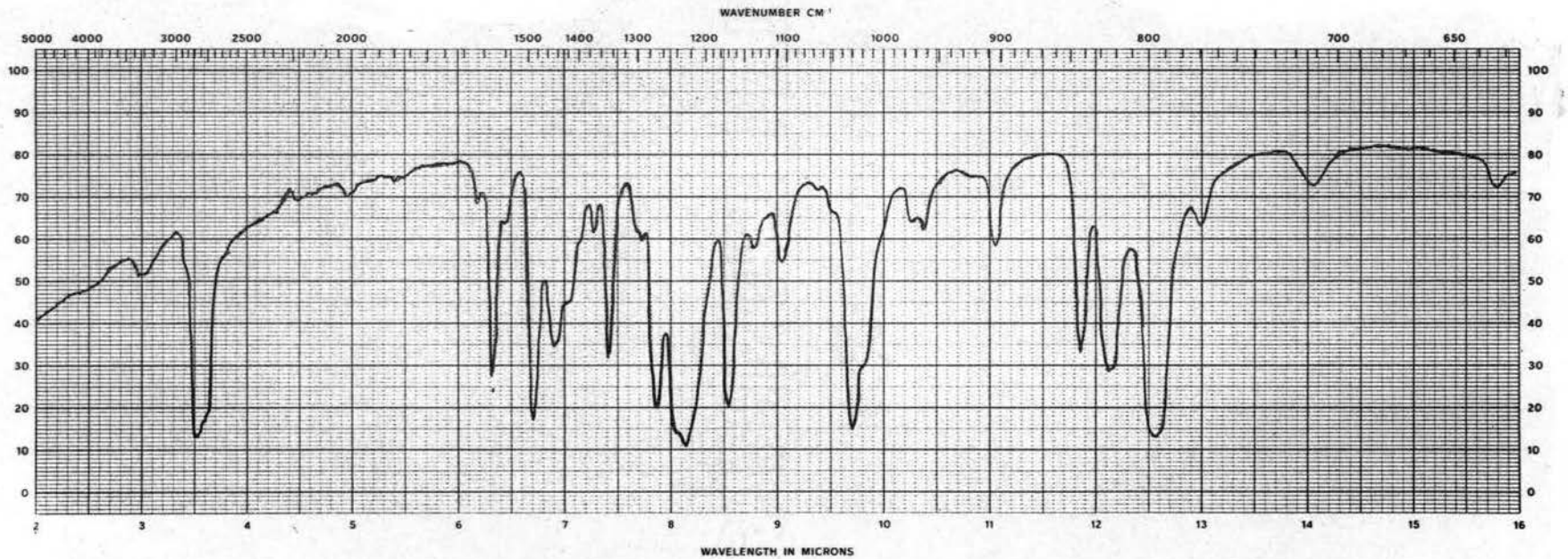
cis-4-tert-Butyl-1-(p-methoxyphenyl)cyclohexanol (70), KBr Pellet

Plate X



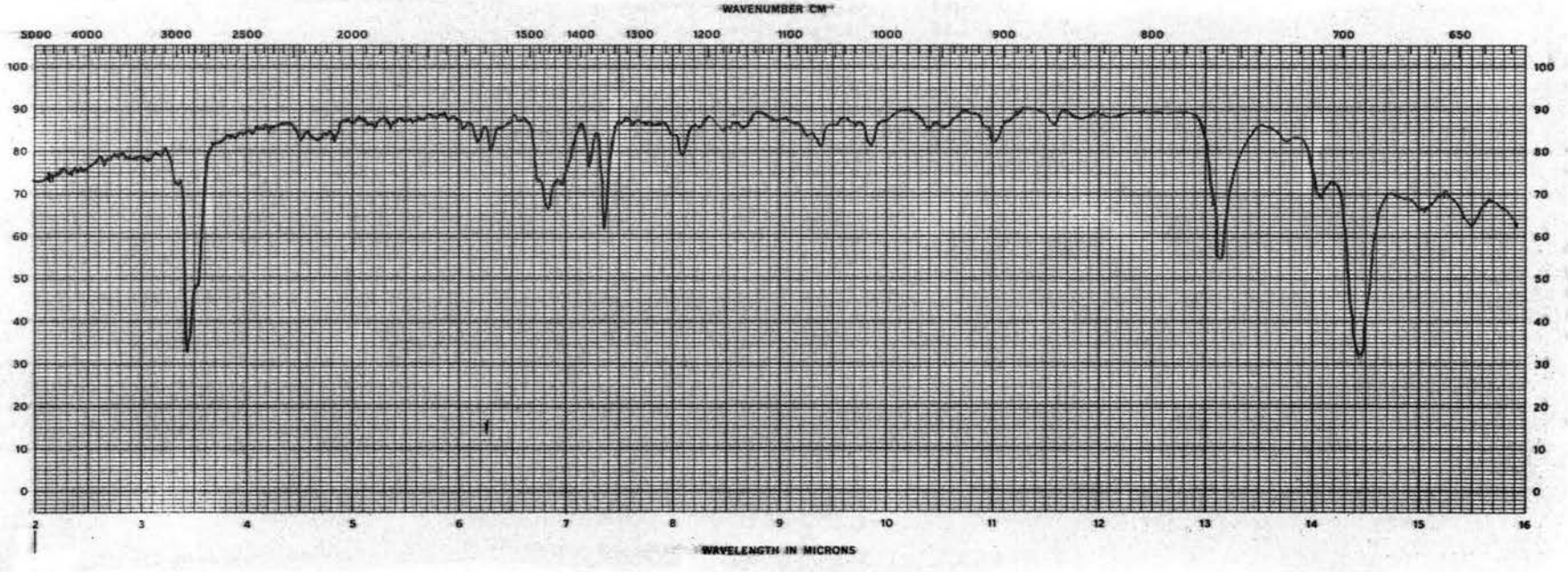
trans-4-tert-Butyl-1-(p-methoxyphenyl)cyclohexanol (71), KBr Pellet

Plate XI



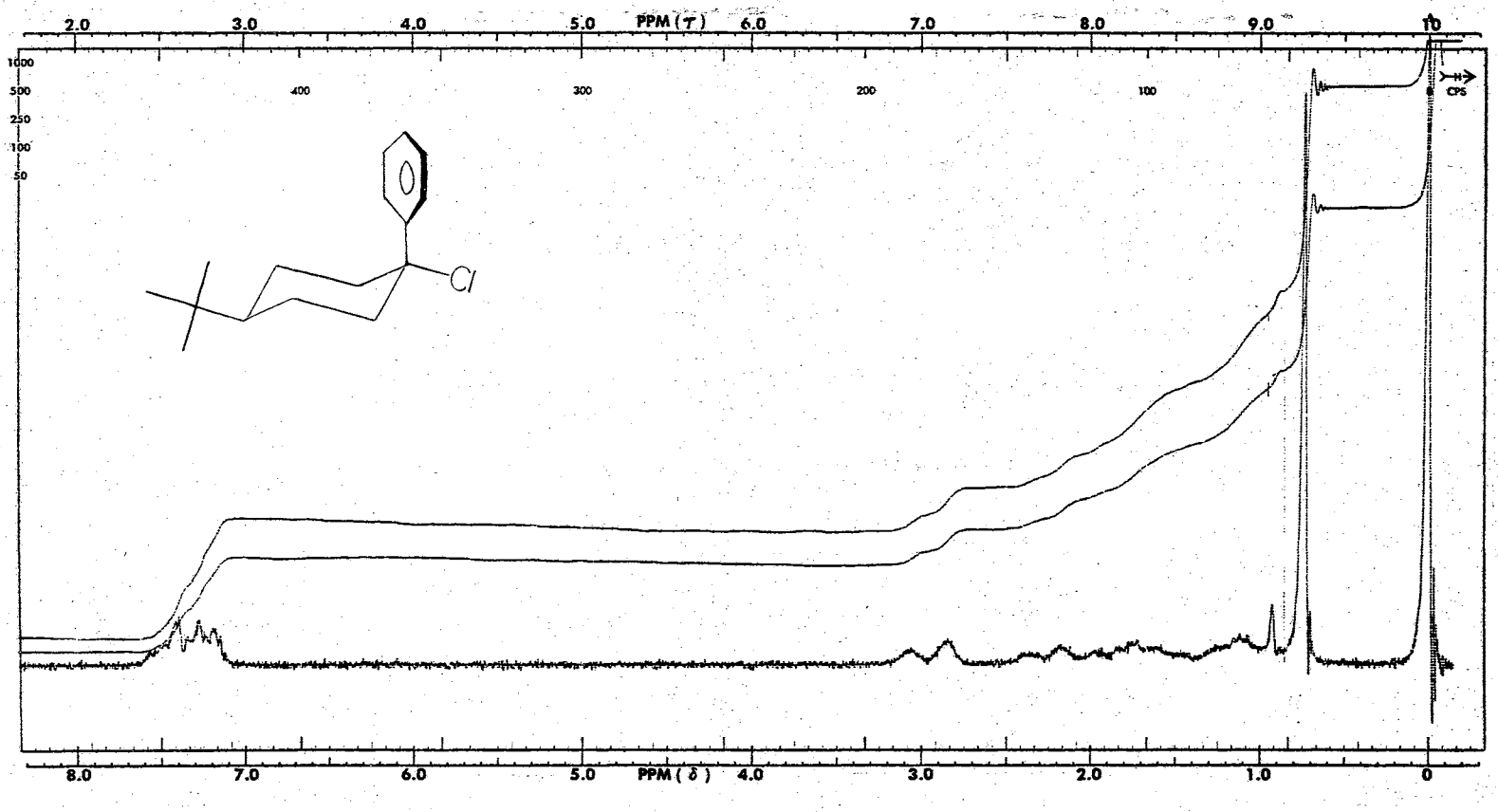
4-tert-Butyl-1-(p-methoxyphenyl)cyclohexene (74), KBr Pellet

Plate XII



4-tert-Butyl-1-phenyl-2,6,6-trideuteriocyclohexene (49), Film on NaCl Plates

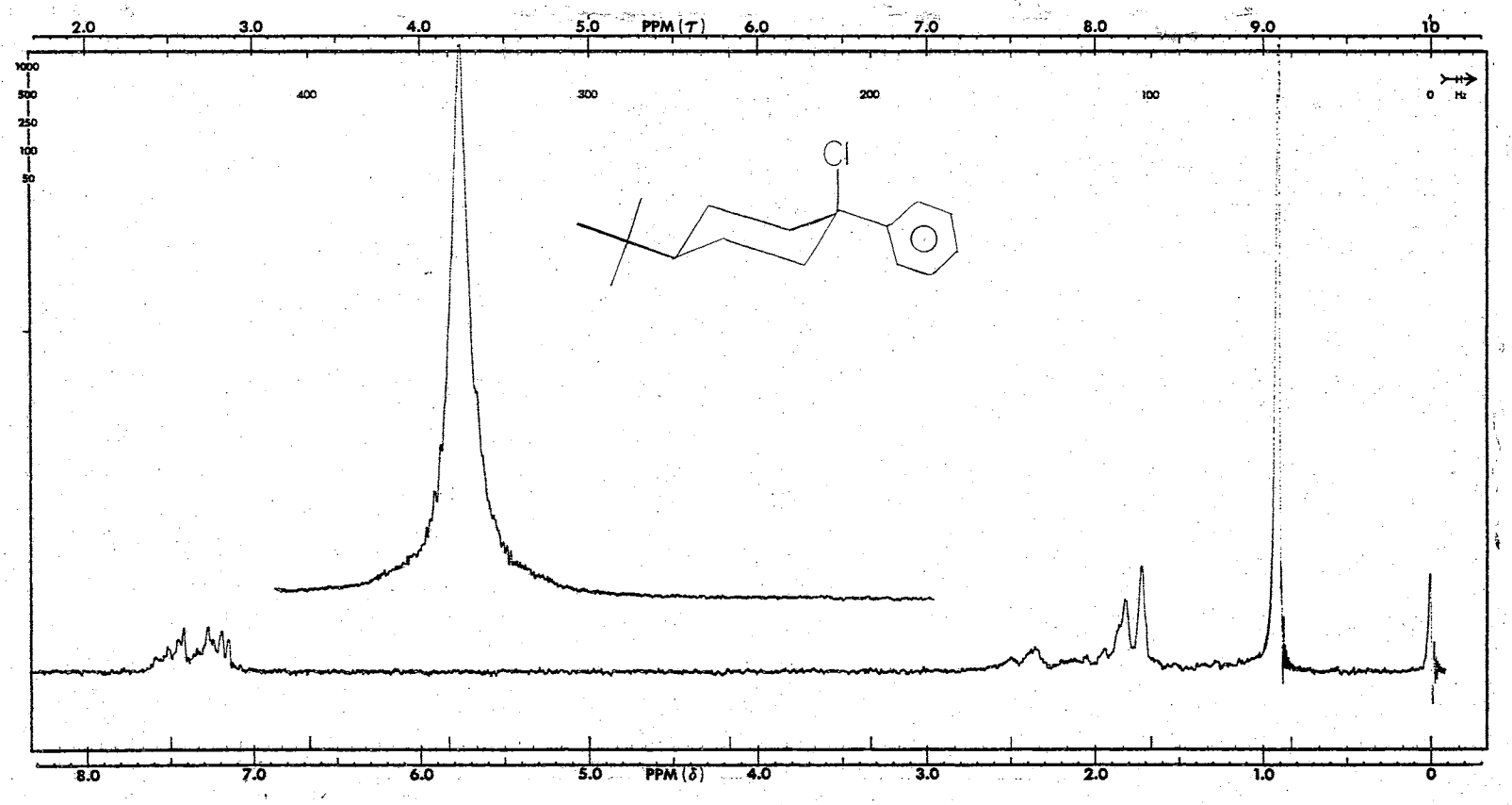
Plate XIII



cis-4-tert-Butyl-1-chloro-1-phenylcyclohexane (46)

Solvent	CCl_4	R.F.	0.05 mG	S.W.	500 Hz	S.A.	8
F.B.	4.0 Hz	S.T.	250 sec	S.O.	0.0 Hz	I.A.	40,50

Plate XIV

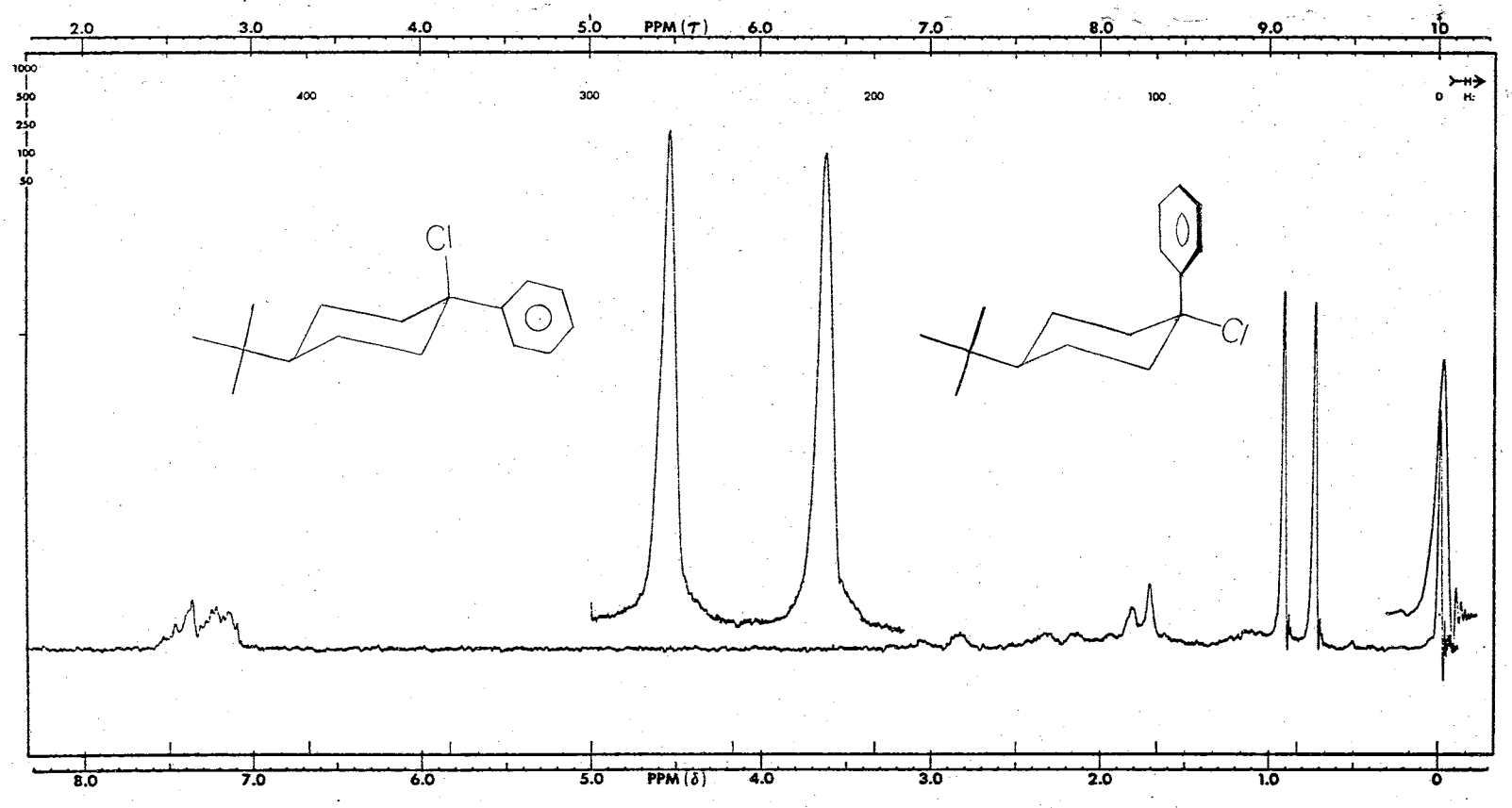


trans-4-tert-Butyl-1-chloro-1-phenylcyclohexane (47)

Solvent . . . . $CDCl_3$ R.F. . . . . 0.04 mG S.W. . . . 500,50 Hz S.A. 6.3,4

F.B. . . . . 2.0 Hz S.T. . . . . 250 sec S.O. . . . . 0,30 Hz I.A. . . . . off

Plate XV

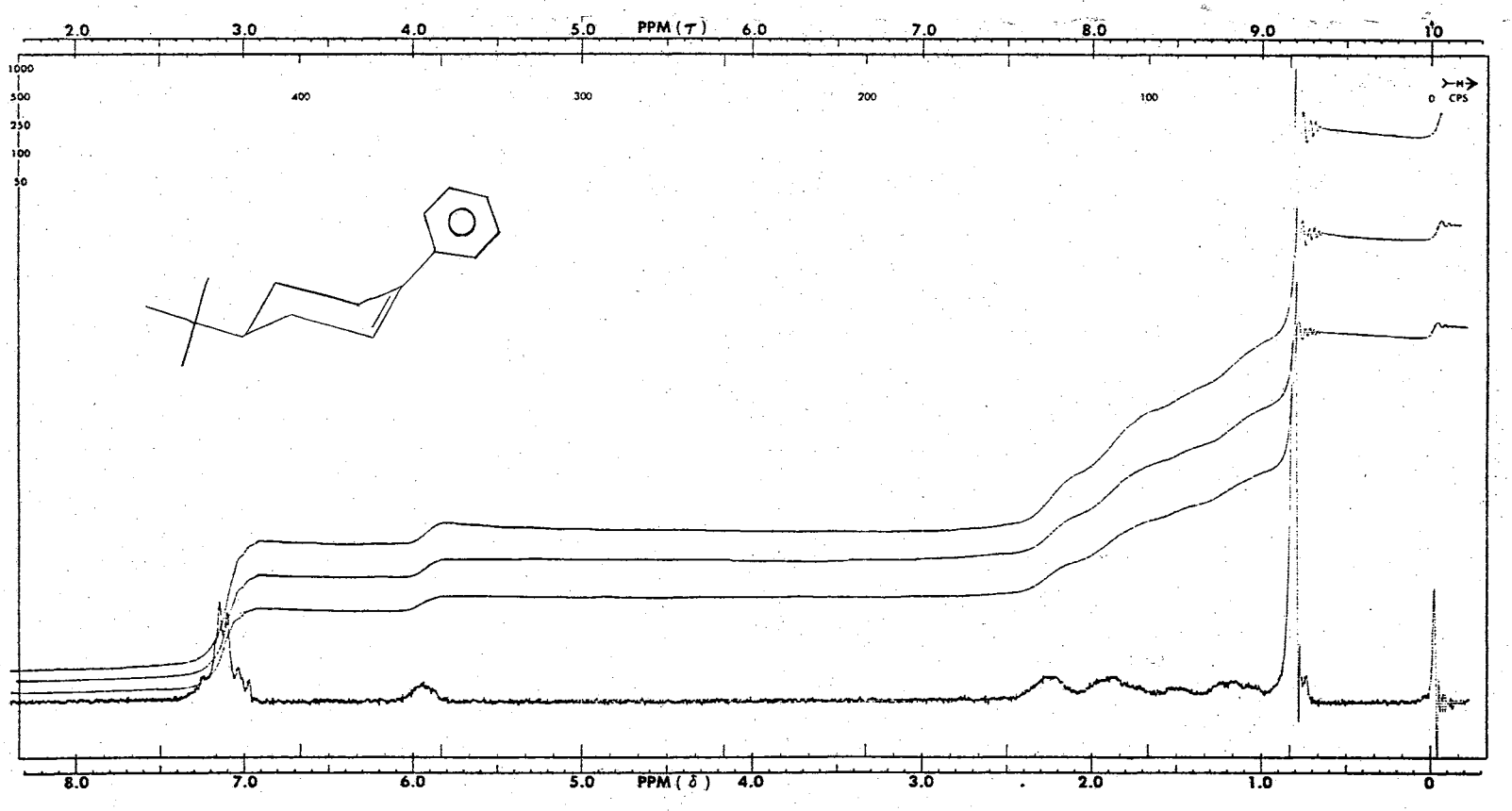


cis- and trans-4-tert-Butyl-1-chloro-1-phenylcyclohexane (46 and 47)

Solvent . . . . CCl_4 R.F. . . . . 0.05 mG S.W. . . . 500, 100 Hz S.A. 10, 12

F.B. . . . . 1.0 Hz S.T. . . . . 250 sec S.O. . . . . 0.0 Hz I.A. . . . . off

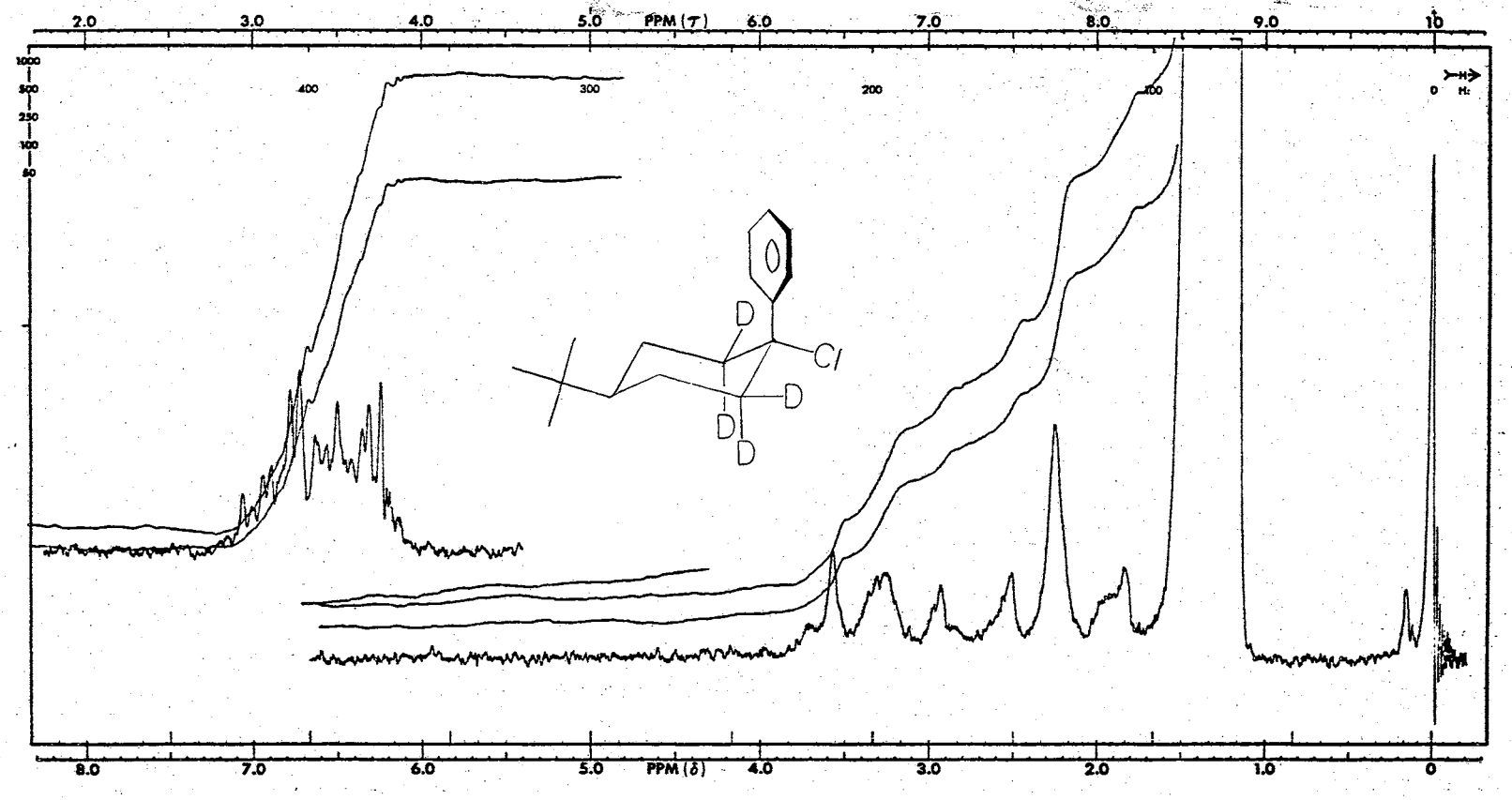
Plate XVI



4-tert-Butyl-1-phenylcyclohexene (45)

Solvent	Neat	R.F.	0.01 mG	S.W.	500 Hz	S.A.	10,12
F.B.	4.0 Hz	S.T.	250 sec	S.O.	0.0 Hz	I.A.	32,40,50

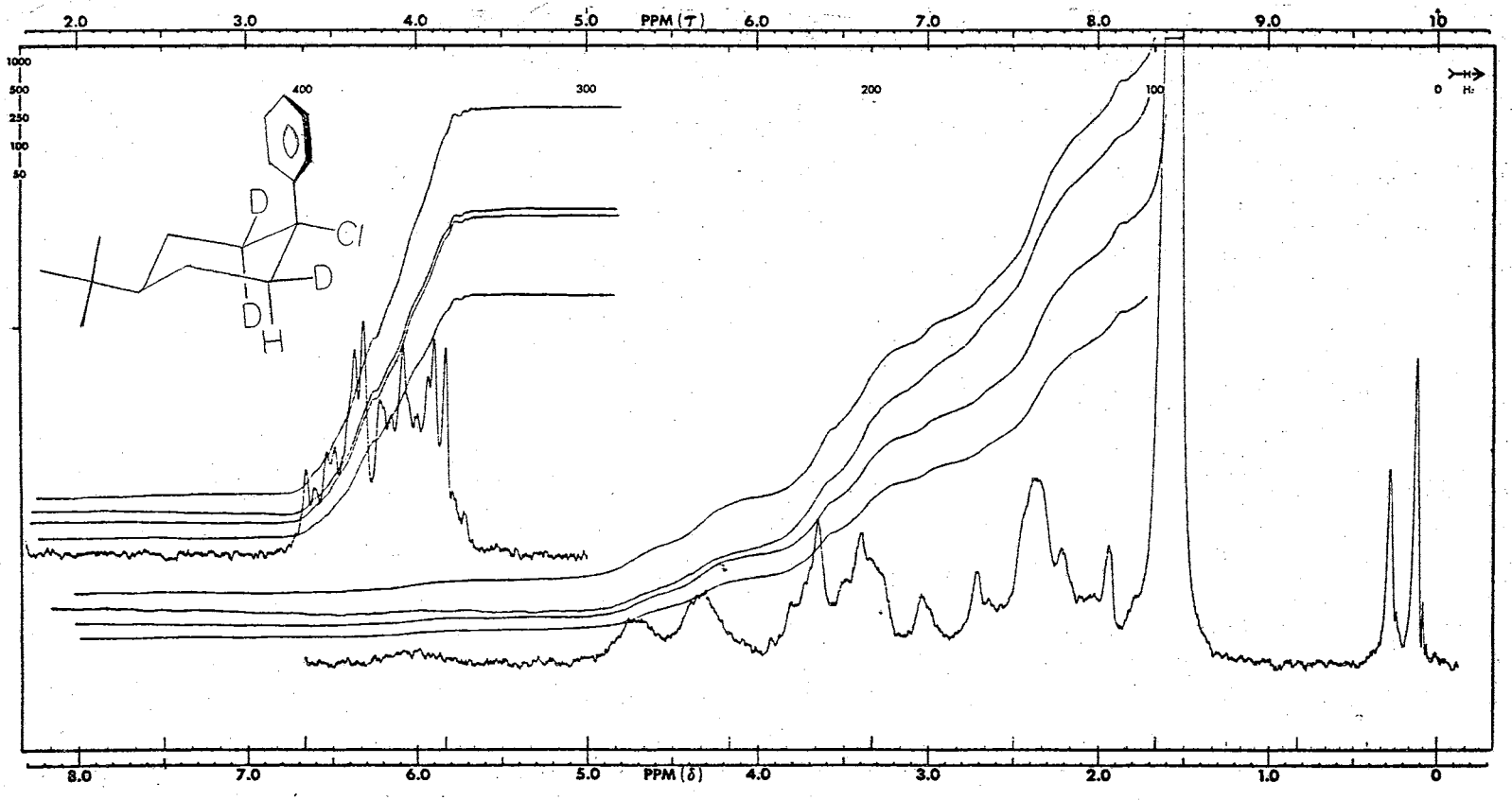
Plate XVII



cis-4-tert-Butyl-1-chloro-1-phenyl-2,2,6,6-tetradeuteriocyclohexane (50)

Solvent	$CDCl_3$	R.F.	0.1 mG	S.W.	250 Hz	S.A.	63
F.B.	0.4 Hz	S.T. . . .	250 sec	S.O.	0,240	I.A.	16,20

Plate XVIII

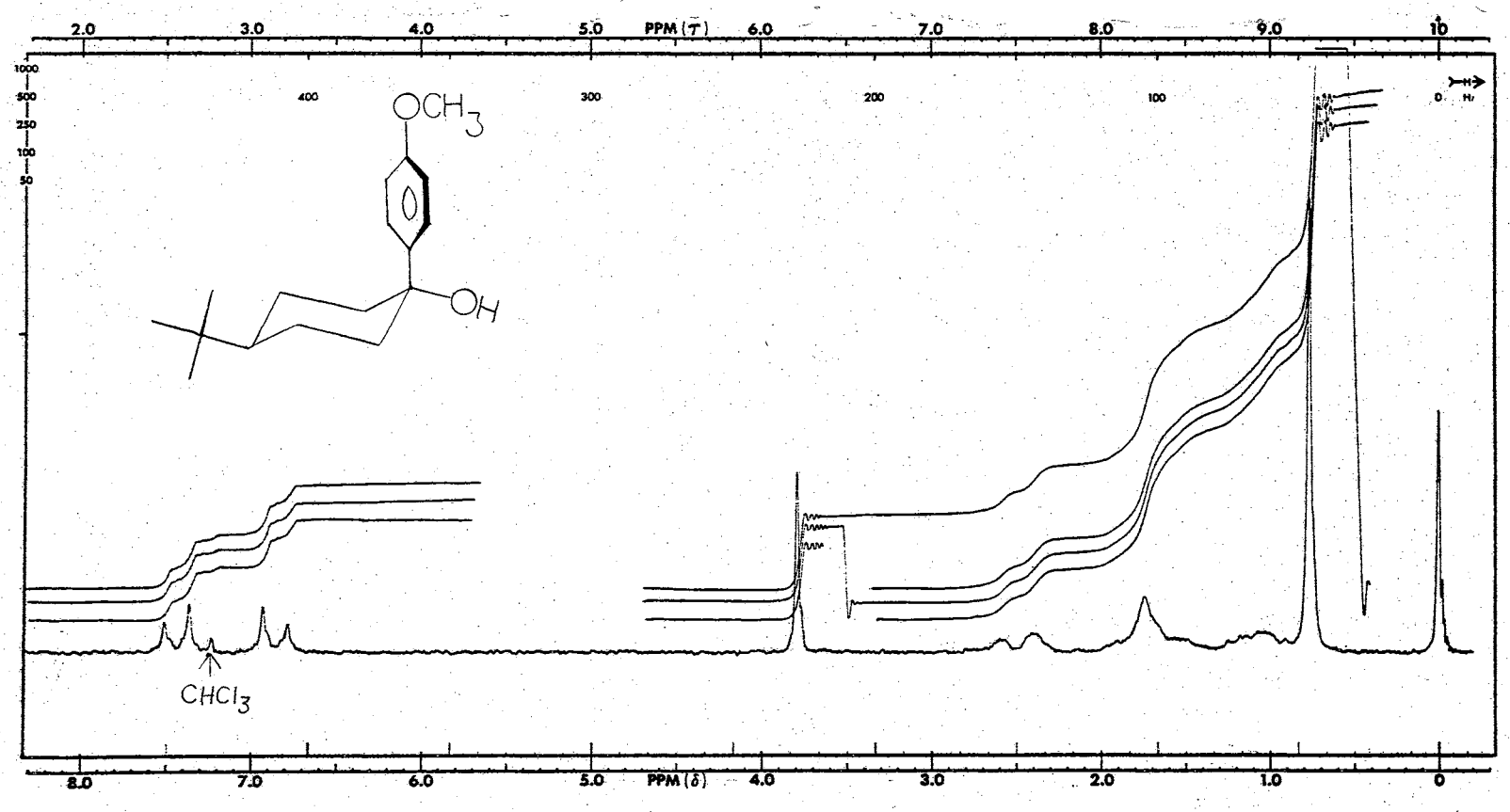


cis-4-tert-Butyl-1-chloro-1-phenyl-2-eq.-6,6-trideuteriocyclohexane (51)

Solvent . . . . $CDCl_3$ R.F. . . . . 0.1 mG S.W. . . . . 250 Hz S.A. 50

F.B. . . . . 0.4 Hz S.T. . . . 250 sec S.O. . . . . 0,255 Hz I.A. . 10,12.5,16

Plate XIX

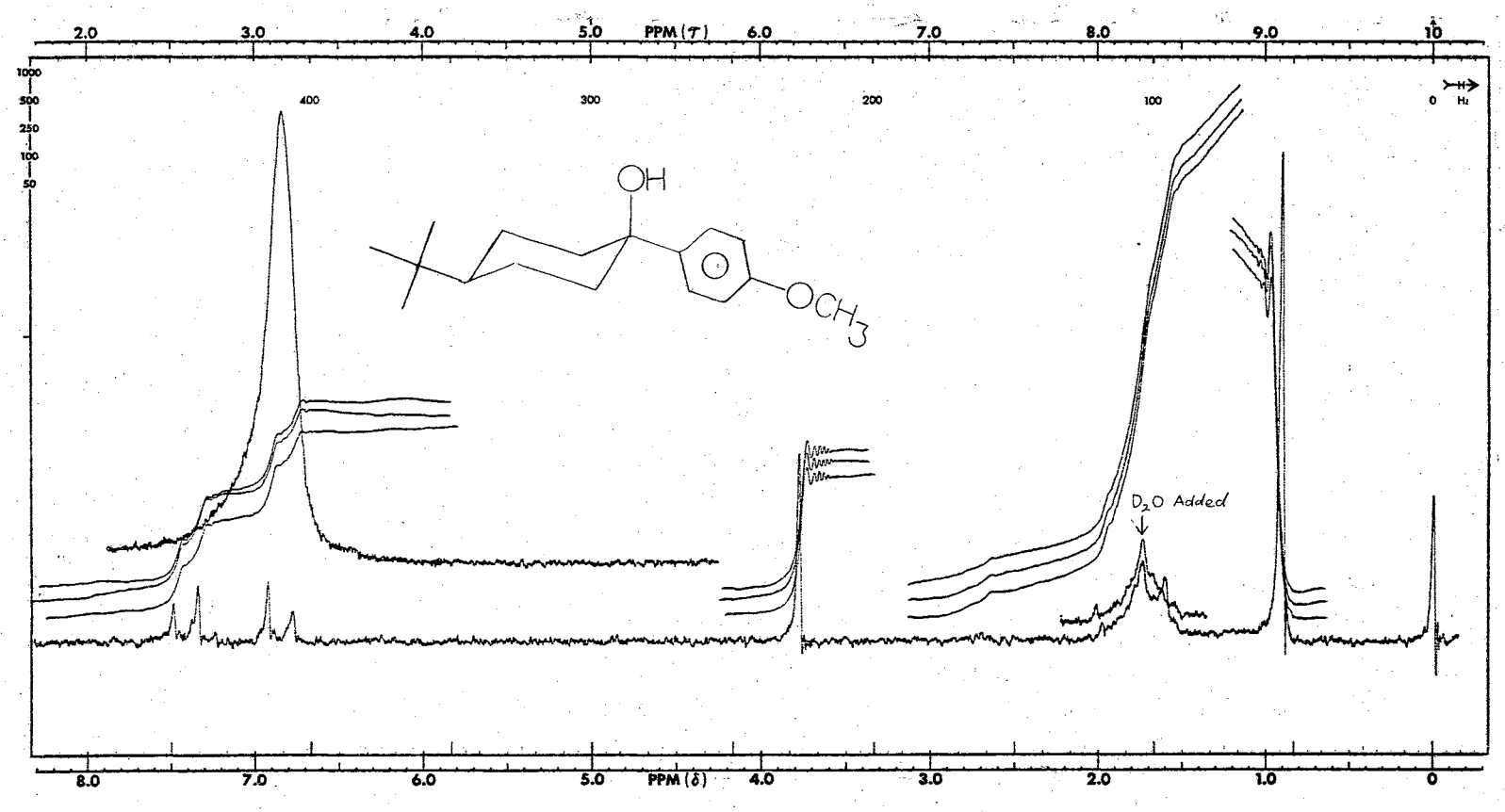


cis-4-tert-Butyl-1-(p-methoxyphenyl)cyclohexanol (70)

Solvent . . . . $CDCl_3$ R.F. . . . . 0.04 mG S.W. . . . . 500 Hz S.A. 5

F.B. . . . . 1.0 Hz S.T. . . . . 250 sec S.O. . . . . 0.0 Hz I.A. 80

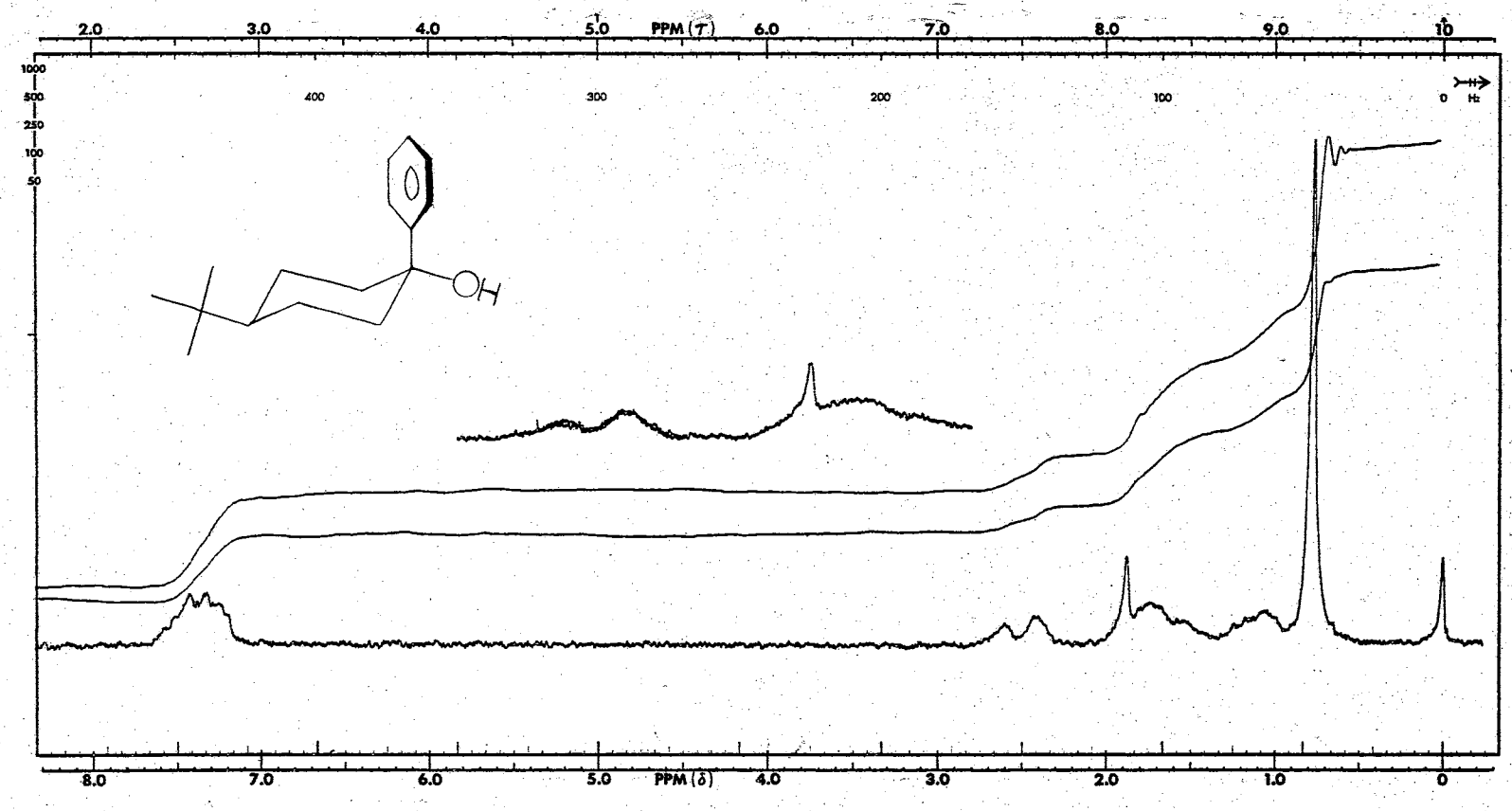
Plate XX



trans-4-tert-Butyl-1-(p-methoxyphenyl)cyclohexanol (70)

Solvent	$CDCl_3$	R.F.	0.04 mG	S.W.	500,50 Hz	S.A.	12,10,12
F.B.	1.0 Hz	S.T.	250 sec	S.O.	0.0 Hz	I.A.	80

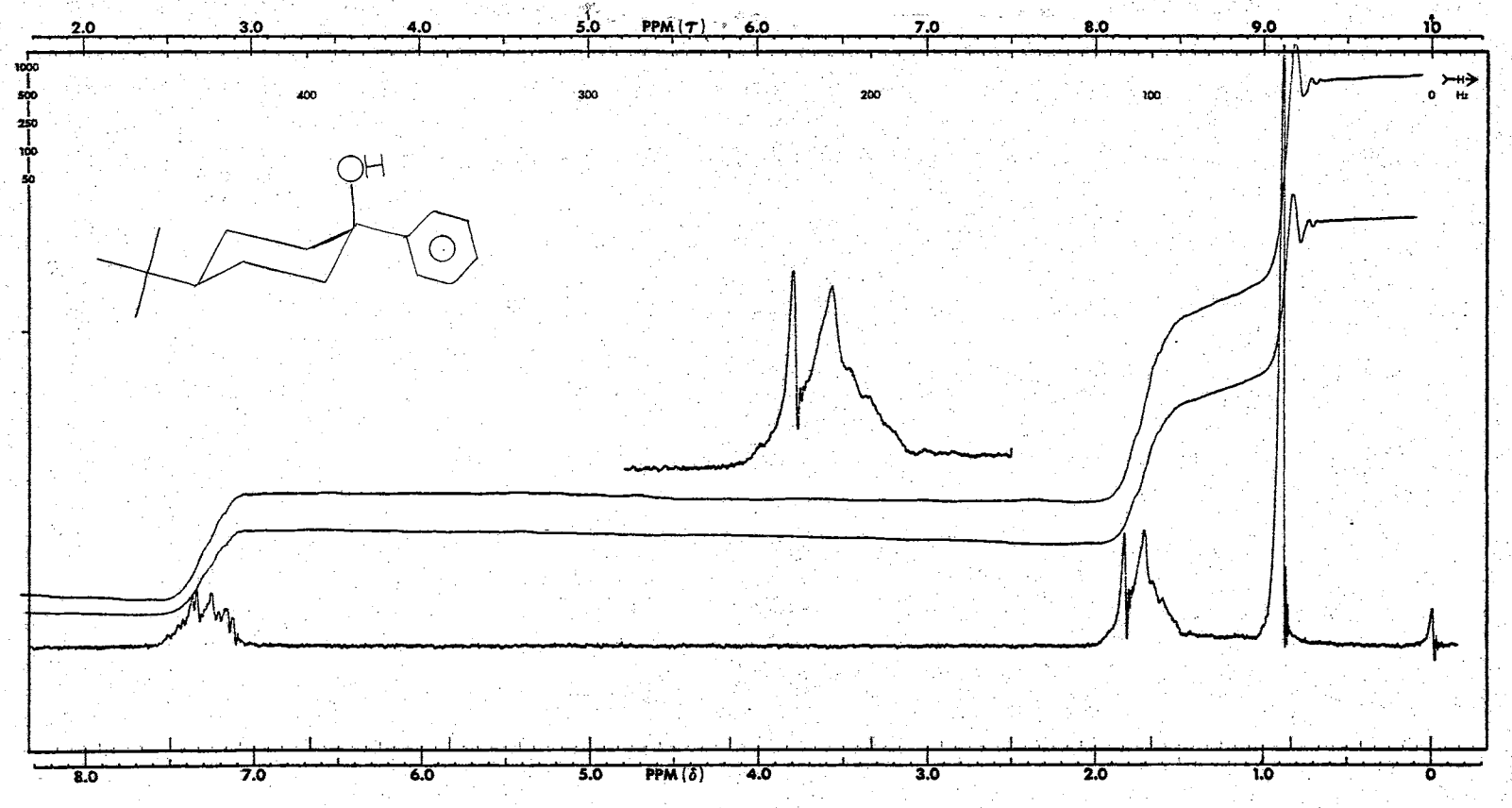
Plate XXI



cis-4-tert-Butyl-1-phenylcyclohexanol (52)

Solvent . . . . $CDCl_3$	R.F. . . . . 0.055 mG	S.W. . . . . 500,250 Hz	S.A. 16
F.B. . . . . 1.0 Hz	S.T. . . . . 250 sec	S.O. . . . . 0.0 Hz	I.A. . . . 40,50

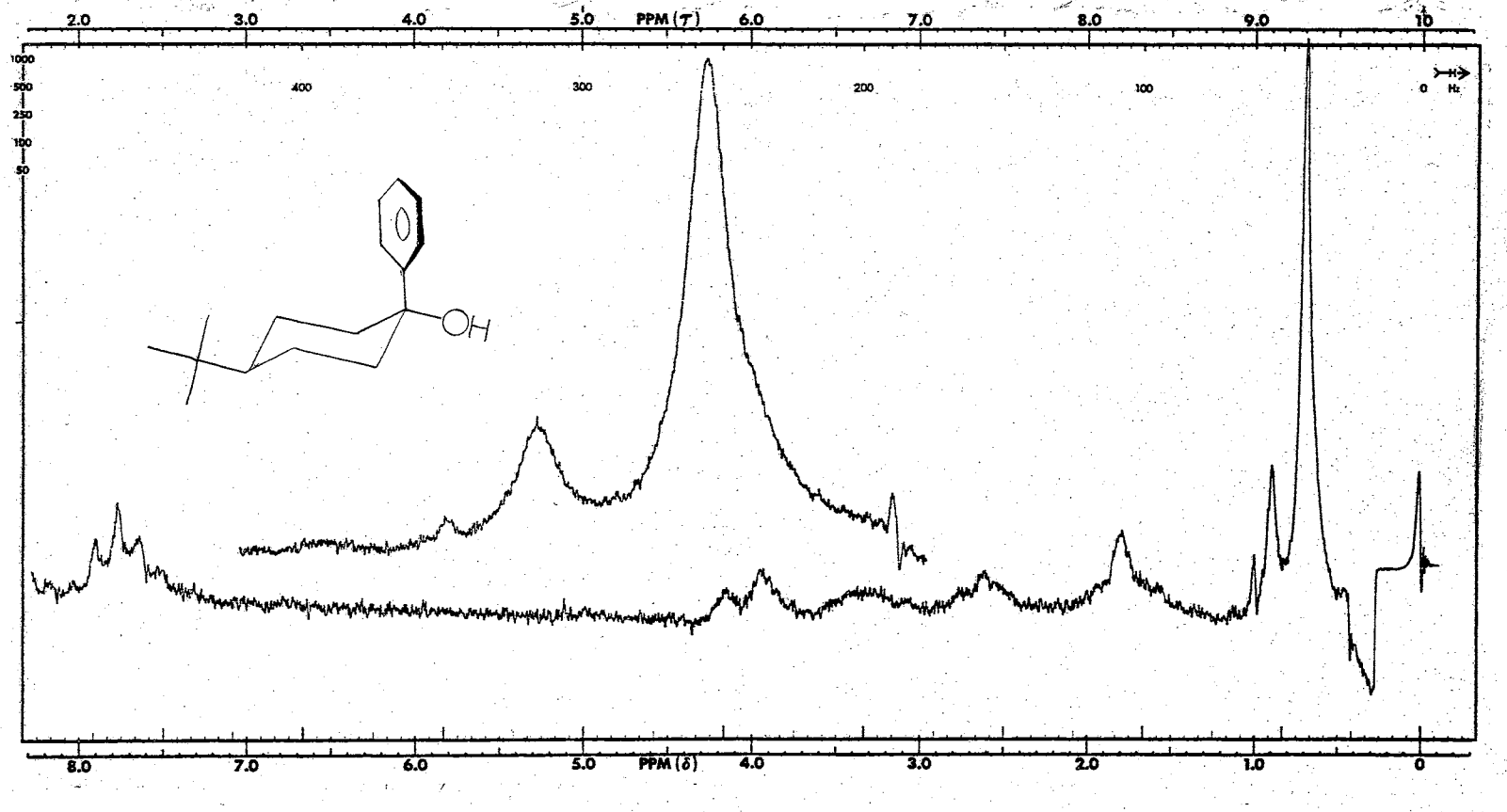
Plate XXII



trans-4-tert-Butyl-1-phenylcyclohexanol (53)

Solvent . . . . $CDCl_3$	R.F. . . . . 0.05 mG	S.W. . . . . 500,250 Hz	S.A. 5,8
F.B. . . 2.0,1.0 Hz	S.T. . . . . 250 sec	S.O. . . . . 0.0 Hz	I.A. . . . 63,80

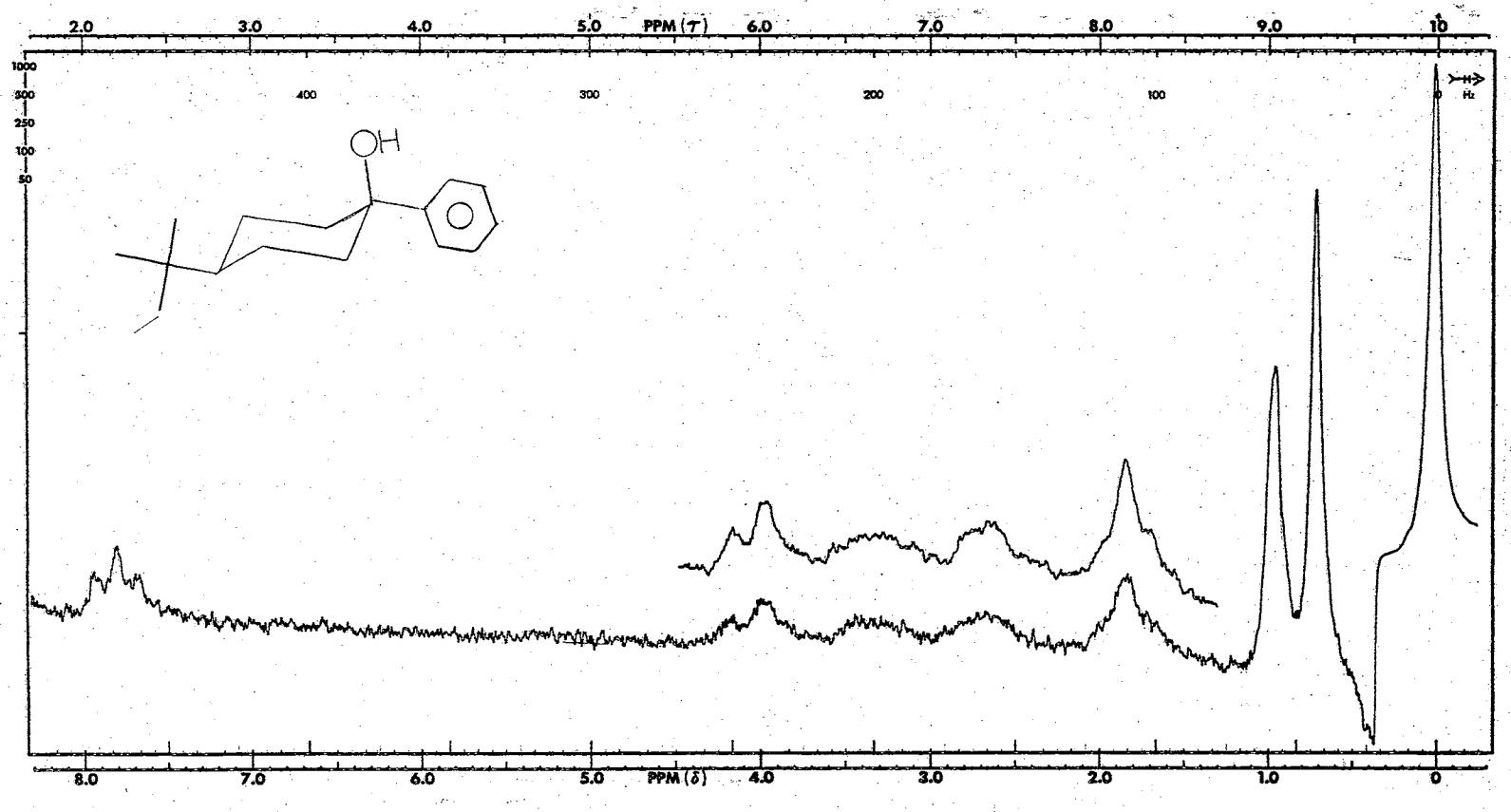
Plate XXIII



cis-4-tert-Butyl-1-phenylcyclohexanol (52) in Olah's Solvent

Solvent	Olah's	F.B.	2.0 Hz	S.T.	250 sec	S.O.	0.0 Hz
Temp.	-66°	R.F. . . .	0.04 mG	S.W. . . .	500,100 Hz	S.A.	20,16

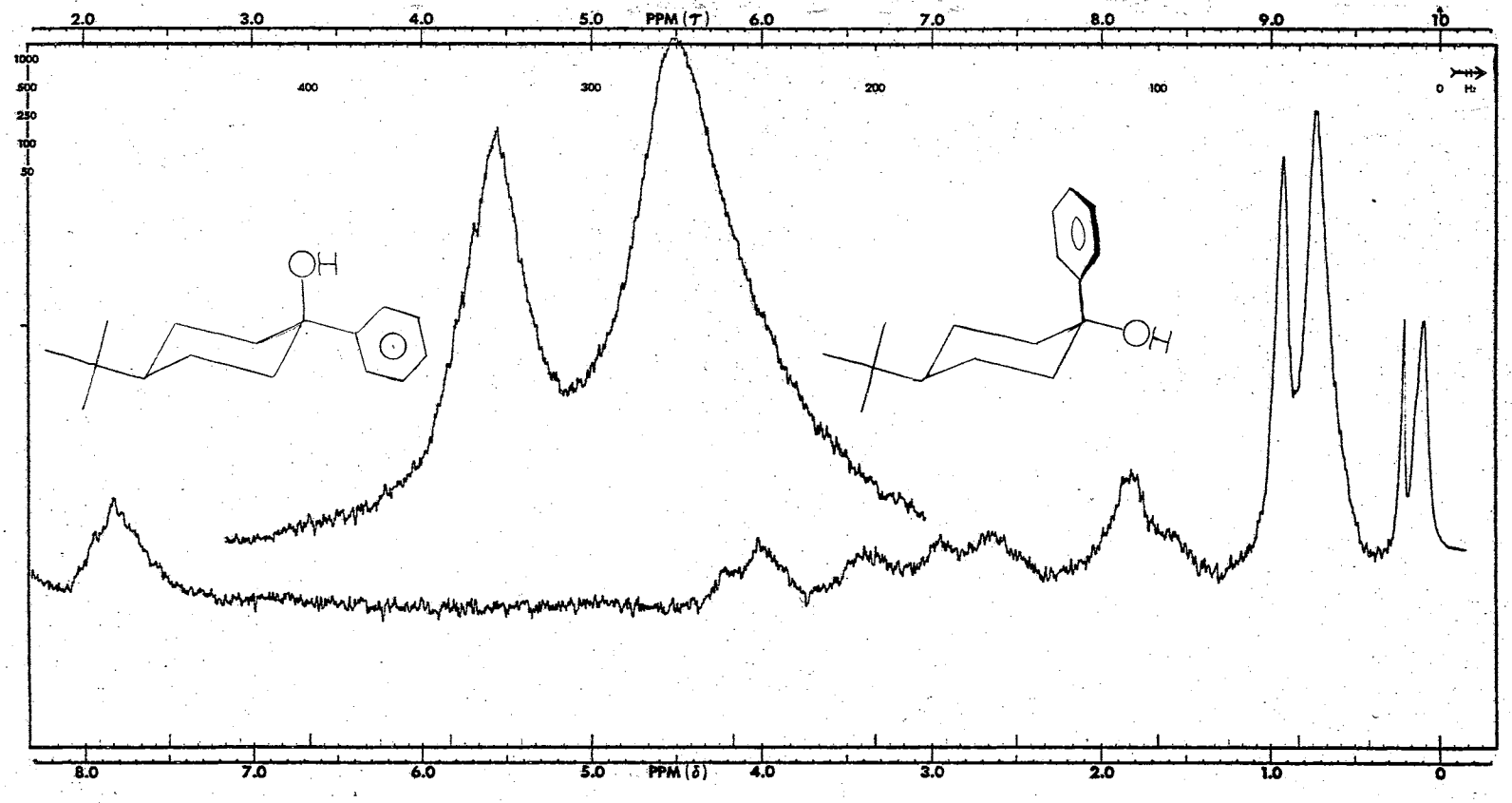
Plate XXIV



trans-4-tert-Butyl-1-phenylcyclohexanol (53) in Olah's Solvent

Solvent	Olah's	F.B.	1.0,0.4 Hz	S.T.	250 sec	S.O.	0.0 Hz
Temp.	-70^{o}	R.F. . . .	0.05,0.055 mG	S.W.	500 Hz	S.A.	40,63

Plate XXV

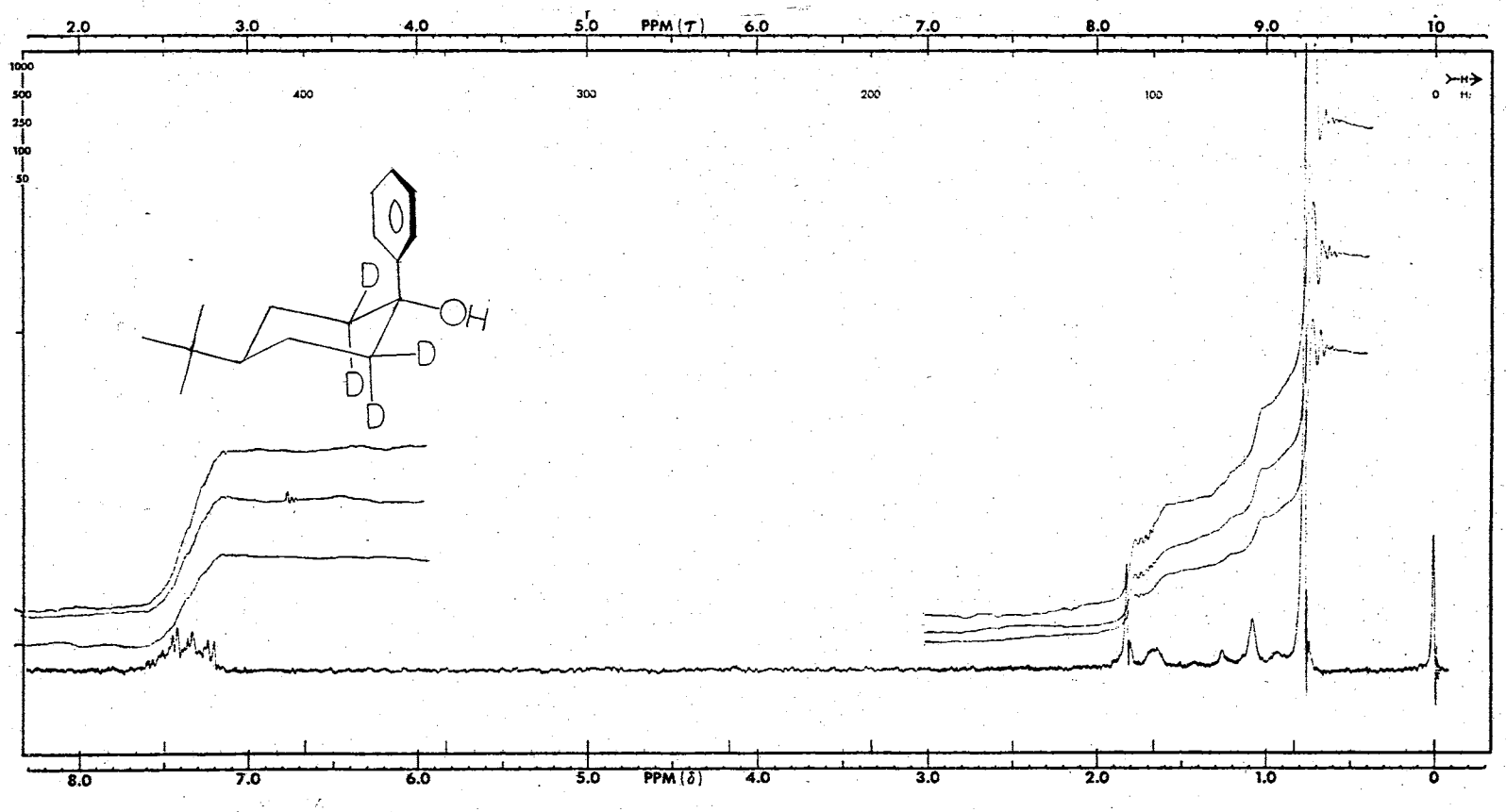


cis- and trans-4-tert-Butyl-1-phenylcyclohexanol (52 and 53) in Olah's Solvent

Solvent . . . . Olah's F.B. . . . . 1.0 Hz S.T. . . . . 250 sec S.O. . . . . 0.0 Hz

Temp. . . . . -79° R.F. . . . 0.04 mG S.W. . . . 500,100 Hz S.A. 20

Plate XXVI

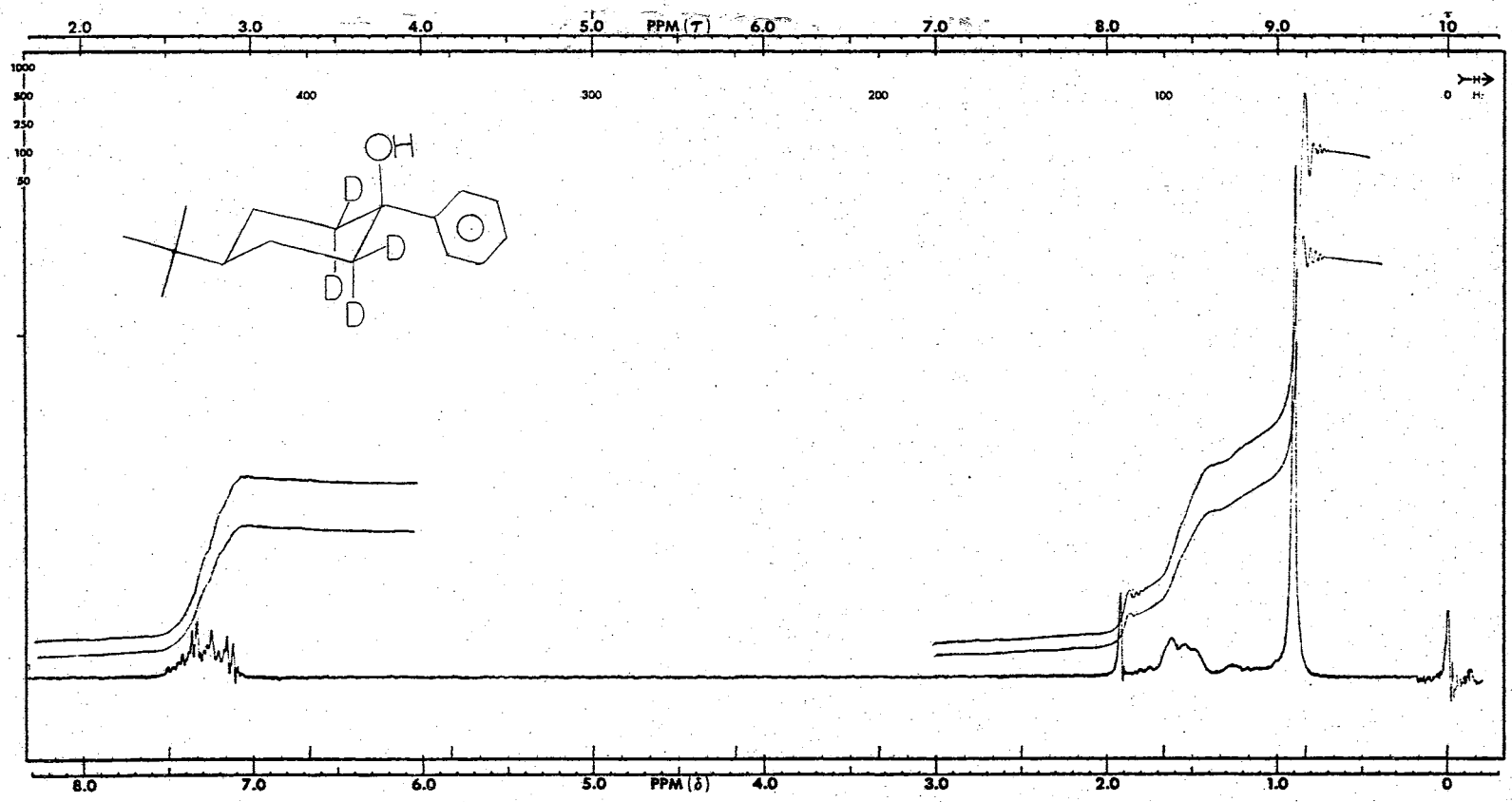


cis-4-tert-Butyl-1-phenyl-2,2,6,6-tetradeuteriocyclohexanol (83)

Solvent . . . . $CDCl_3$ R.F. . . . . 0.05 mG S.W. . . . . 500 Hz S.A. 10

F.B. . . . . 1.0 Hz S.T. . . . . 250 Hz S.O. . . . . 0.0 Hz I.A. . . 50,63,80

Plate XXVII

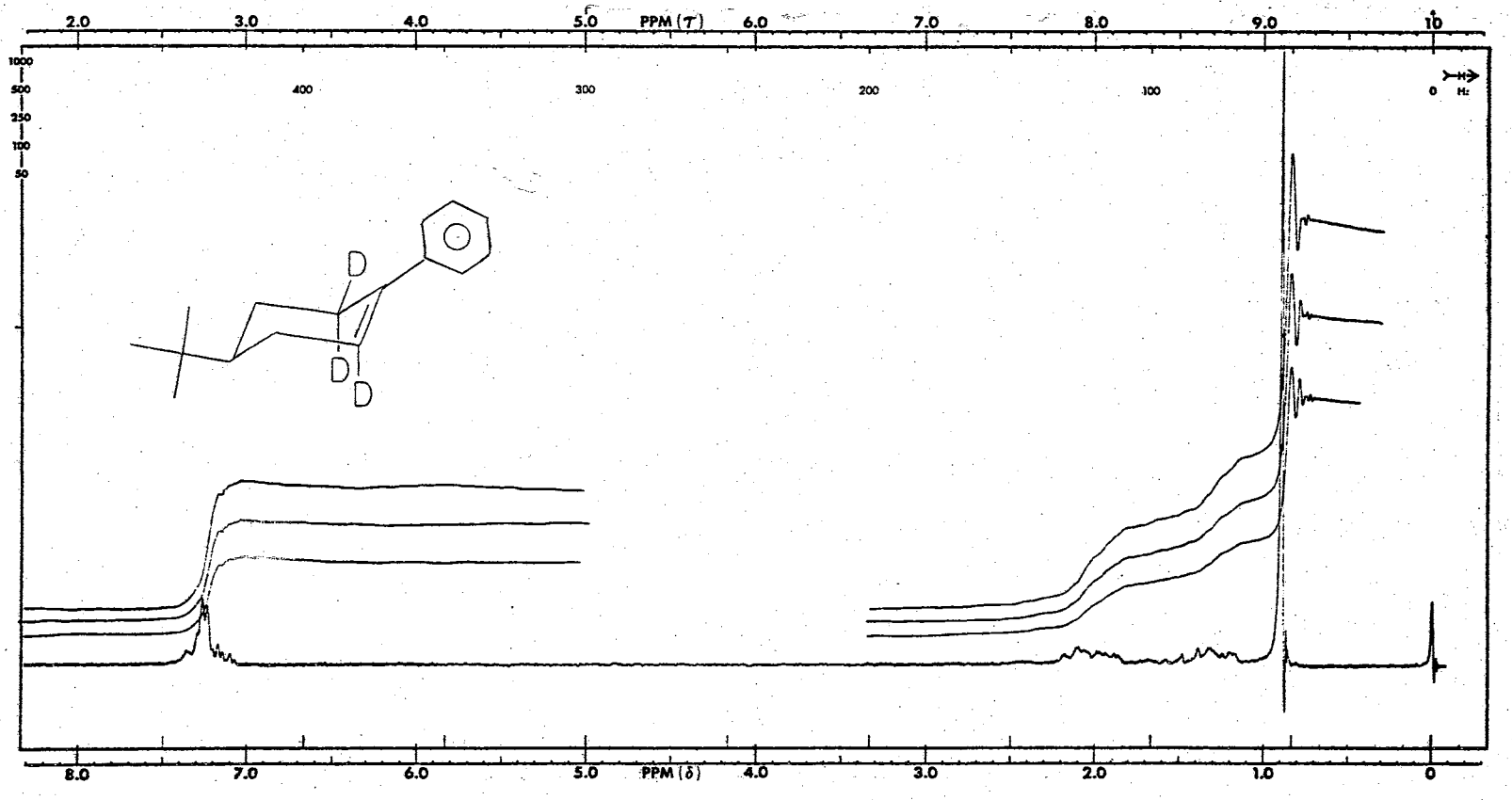


trans-4-tert-Butyl-1-phenyl-2,2,6,6-tetradeuteriocyclohexanol (84)

Solvent . . . . $CDCl_3$ R.F. . . . . 0.05 mG S.W. . . . . 500 Hz S.A. 3.2

F.B. . . . . 2.0 Hz S.T. . . . . 250 sec S.O. . . . . 0.0 Hz I.A. 20,35

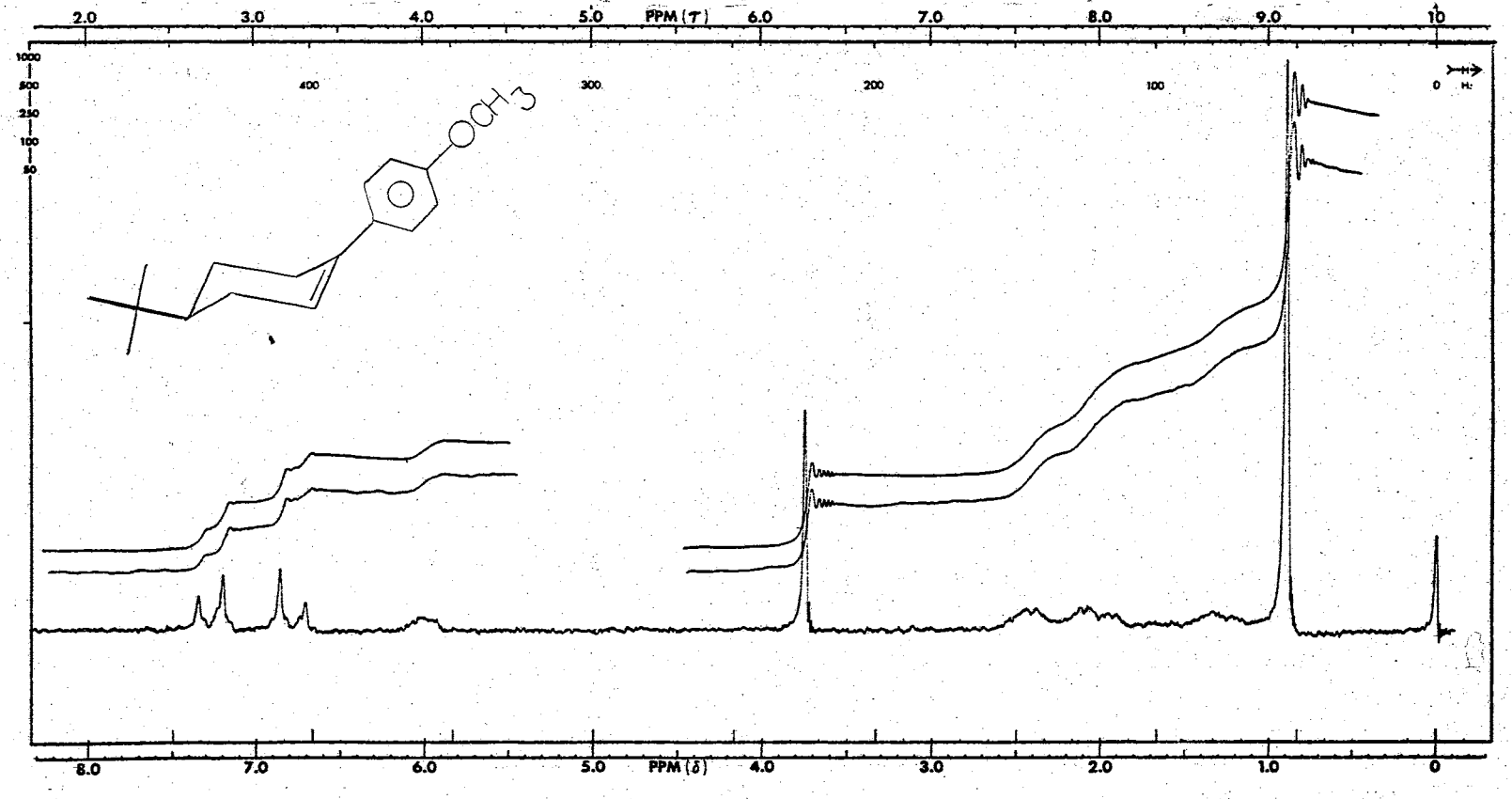
Plate XXVIII



4-tert-Butyl-1-phenyl-2,6,6-trideuteriocyclohexene (49)

Solvent . . . . $CDCl_3$	R.F. . . . . 0.05 mG	S.W. . . . . 500 Hz	S.A. 4
F.B. . . . . 2.0 Hz	S.T. . . . . 250 sec	S.O. . . . . 0.0 Hz	I.A. . . . 50,63,80

Plate XXIX



4-tert-Butyl-1-(p-methoxyphenyl)cyclohexene (74)

Solvent . . . . $CDCl_3$	R.F. . . . . 0.05 mG	S.W. . . . . 500 Hz	S.A. 10
F.B. . . . . 1.0 Hz	S.T. . . . . 250 sec	S.O. . . . . 0.0 Hz	I.A. . . . 50,63

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VITA

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Thesis: THE STEREOCHEMISTRY AND MECHANISM OF THE ADDITION OF HYDROGEN CHLORIDE TO 4-TERT-BUTYL-1-PHENYLCYCLOHEXENE AND DERIVATIVES

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