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I hereby recommend that the thesis prepared under my supervision by Harry Moers Leyland

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ELIMINATION OF HYDROGEN CHLORIDE FROM CIS-2-CHLOROCYCLOHEXYL PHENYL KETONE

A dissertation submitted to the

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HISTORICAL

I. INTRODUCTION

Friedel's and Crafts' historic discovery of the catalytic action of aluminum chloride in organic reactions[1] opened the way to many new synthetic procedures. In 1877 these authors investigated the action of metallic aluminum on amyl chloride as a possible modification of the Wurtz reaction. Subsequent investigations by these men established the fact that aluminum chloride, rather than metallic aluminum, was the activating agent. Rapid and prolific publications followed demonstrating the use of aluminum chloride as a catalytic agent in the alkylation and acylation of aromatic nuclei. They noted, in addition, the use of this catalyst in the cracking of aliphatic hydrocarbons and in the polymerization of unsaturated hydrocarbons.

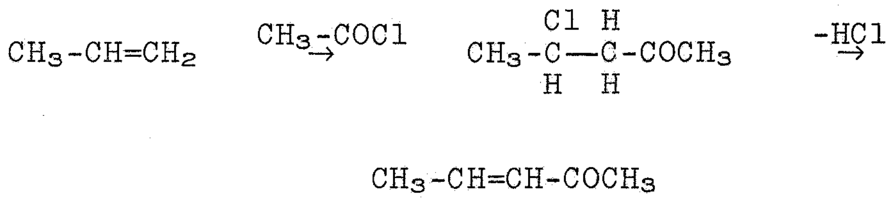
The aforementioned uses of aluminum chloride are universally recognized, although still another use has remained relatively obscure. Around the turn of the twentieth century, it was found that acyl halides could be condensed

[1] C. Friedel and J.M. Crafts, Bull. soc. chim. Paris, 27, 530 (1877).

with olefinic hydrocarbons in the presence of aluminum chloride.[2] Apparently the lack of reproducible results due to variation in products and resultant low yields, has retarded the growth of this field. It is with this phase of the Friedel-Crafts reaction that this historical review is concerned.

II. REACTION OF OLEFINS WITH ACYL HALIDES

In 1892 Kondakoff[2] reported the condensation of trimethylene and acetyl chloride in the presence of zinc chloride to yield 2,3-dimethyl-2-penten-4-one. This work was extended to include the action of acetyl chloride on propylene and isobutylene to yield the 2-chloroketones and



$$\mathrm{CH_3\text{-}CH{=}CH_2} \xrightarrow{\mathrm{CH_3\text{-}COCl}} \mathrm{CH_3\text{-}}\overset{\mathrm{Cl}}{\underset{\mathrm{H}}{\mathrm{C}}}\text{—}\overset{\mathrm{H}}{\underset{\mathrm{H}}{\mathrm{C}}}\mathrm{\text{-}COCH_3} \xrightarrow{\mathrm{-HCl}} \mathrm{CH_3\text{-}CH{=}CH\text{-}COCH_3}$$

then dehydrohalogenation to give the corresponding α,β-unsaturated ketones. Krapivin[3] utilized the stronger Friedel-Crafts catalysts, aluminum chloride and bromide,

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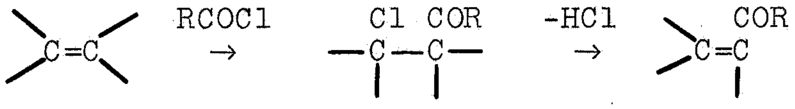
[2] J. Kondakoff, Bull. soc. chim. France, 7, 576 (1892).

[3] S. Krapivin, Bull. soc. imp. Nat. Moscow, 1 (1908) C.A. 5, 1281 (1911).

to effect the condensation of the acyl halide and the olefin. The reaction mixture was maintained at 0° to minimize side reactions and carbon disulfide used as a solvent in all the condensations except those of ethylene and propylene where hexane was used. Trimethylethylene and acetyl chloride gave a product identified as 2,3-dimethyl-2-penten-4-one and under analogous conditions 2-hexene, 3-heptene and 1-octene gave unsaturated ketones. The scope of the reaction was extended to include aryl halides by Norris and Couch[4] who demonstrated that benzoyl chloride combined with ethylene to yield phenyl vinyl ketone.

One can surmise that the acylation of olefins proceeds through an intermediate formation of a β-chloroketone which then gives rise to the unsaturated ketone by elimination of hydrogen chloride.[5] Krapivin[3] reported



isolation of β-chloroketones and Wieland and Bettag obtained a 16.3 o/o yield of 4-chloro-3,4-dimethylpentan-2-one

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[4] J.F. Norris and H.B. Couch, J. Am. Chem. Soc., 42, 2239 (1920).

[5] C.A. Thomas, "Anhydrous Aluminum Chloride in Organic Chemistry", Rheinhold Publishing Corp., New York, N.Y., 1947, pp. 752-760.

by acetylation of trimethylethylene with acetyl chloride at -18°. They reported that this ketone is unstable and easily loses hydrogen chloride. Catch, Elliot, Hey and Jones[6] recently reported the preparation of a variety of chloroketones by using aluminum chloride as the condensing agent and excess acyl halide as the solvent. Yields varying from 30 to 90 o/o were obtained by the addition of ethylene, acetylene, vinyl chloride and di- and trichloroethylene to the aluminum chloride-acyl chloride complex dissolved in excess acyl halide. These authors report that 2-chloroethyl ketones are reasonably stable; chloromethyl 2,2-dichloroethyl ketone did not decompose appreciably when stored at 0°, but at room temperature the material decomposed with the evolution of hydrogen chloride.

The manufacture of β -chloroketones has been patented. Schoeller and Zollner[7] reported that fair yields of β-haloketones were obtained by introducing the olefin and acid catalyst to the acyl halide with cooling and vigorous stirring. They used as solvents or diluents excess acid halide, chloroform, hexane, nitrobenzene or

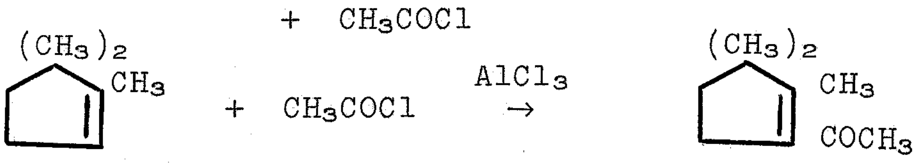
[6] J.R. Catch, D.F. Elliot, D.H. Hey and E.R. Jones, J. Chem. Soc., 278 (1948).

[7] W. Schoeller and C. Zollner, U.S.P. 1,737,203 (1929).

carbon disulfide. Acyl chlorides or bromides were used as the acylating agents and aluminum chloride, aluminum bromide or ferric chloride as the catalysts. Frolich and Wiezevich[8] performed the acylations at pressures of 20-200 atmospheres and temperatures of 100-300°. The patent covers the use of acetic, propionic, butyric acid halides (chlorides, bromides and iodides) as acylating agents. Ethylene, propylene, butylene and amylene were used as the olefins and non alkaline condensing agents such as charcoal, pumice, hydrogen chloride, bismuth chloride, cupric chloride, and aluminum chloride were used as catalysts.

III. REACTIONS OF ALICYCLIC OLEFINS WITH ACYL HALIDES

While studying the structure of *iso*-lauronolic acid, Blanc[9] observed that when 1,1,2-trimethyl-2-cyclopentene was dissolved in carbon disulfide and treated with acetyl chloride and aluminum chloride the corresponding unsaturated ketone was obtained. This structure was

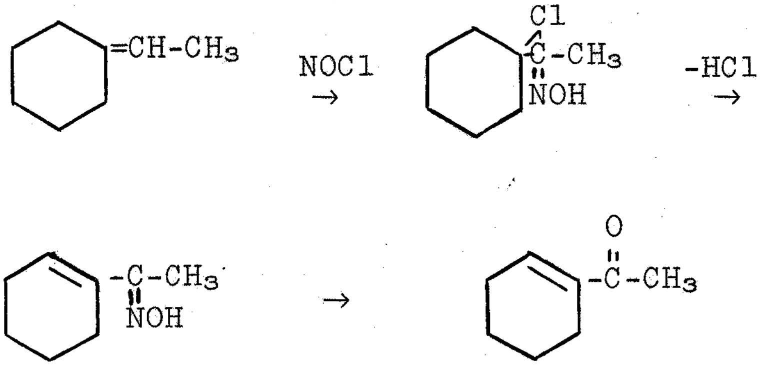


[8] K. Frolich and R.J. Wiezevich, U.S.P. 2,006,198 (1936).

[9] G. Blanc, Bull. soc. chim., 19, 699 (1898).

established by degradation studies and an independent synthesis.

Darzens[10] found that treatment of cyclohexene at 0° with acetyl chloride and aluminum chloride produced the intermediate β-chloroketone which was dehydrohalogenated by refluxing with N,N-dimethylaniline. The product was identified by comparing it with 1-acetylcyclohexene synthesized by Wallach's procedure.[11] In a



succeeding paper Darzens and Rost[12] established the acylation of cyclohexene as a general synthetic procedure as they prepared several additional cyclohexenyl ketones. Wieland and Bettag[13] indicated that working at lower temperatures

[10] G. Darzens, Compt. rend., 150, 707 (1910).

[11] O. Wallach, Ann., 560, 26 (1908).

[12] G. Darzens and H. Rost, Compt. rend., 151, 758 (1910).

[13] H. Wieland and L. Bettag, Ber., 55, 2246 (1922).

was conducive to the formation of the β-chloroketone. Running the reactions at -18° they were able to obtain β-chlorocyclohexyl phenyl ketone and β-chlorocyclohexyl methyl ketone comtaminated with their respective unsaturated ketones. The unsaturated ketone was removed from the phenyl derivative by oxidation with permanganate and the methyl ketone was purified through the semicarbazone. Dehydrohalogenation of these chloroketones by warming with aluminum chloride was incomplete.

In recent years several authors have used, with modifications, Wieland's[13] and Darzens'[12] procedures for the preparation of the chloroketones and then effected dehydrohalogenation by various means. Christ and Fuson[14] acetylated cyclohexene with acetyl chloride as described by Darzens and completed dehydrohalogenation of the resulting oil by distilling it from sodium carbonate. In preparing 1-cyclohexenyl phenyl ketone, they duplicated Wieland and Bettag's procedure for acylation and dehydrohalogenated the product by refluxing it with ethanolic potassium hydroxide. Nightingale *et. al.*[15] reported, however, that distilling crude 1-cyclohexenyl methyl ketone

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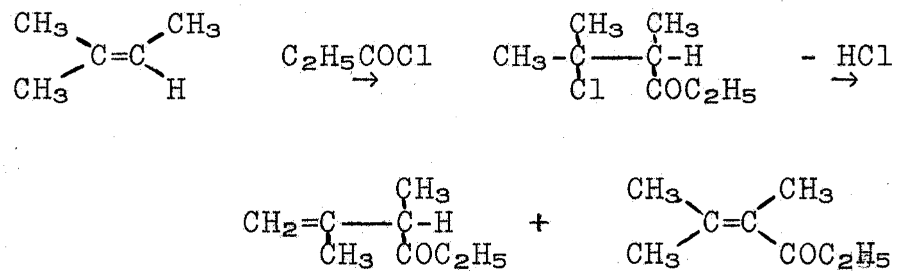
[14] R.E. Christ and R.C. Fuson, J. Am. Chem. Soc., 59, 893 (1937).

[15] D. Nightingale, E. Milberger and A. Tomisek, J. Org. Chem., 13, 357 (1948).

from sodium carbonate did not effect complete dehydrohalogenation whereas refluxing with N,N-dimethylaniline did. Royals and Hendry[16] were unable to induce complete dehydrohalogenation with either sodium carbonate or N,N-dimethylaniline.

IV. ISOMERISM IN ACYLATION

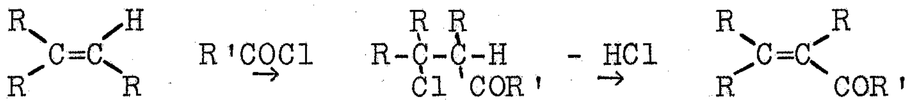
Colonge and Mostavi[17] found that acylation of trimethylethylene with propionyl chloride, using stannic chloride as the catalyst, resulted in an impure chloroketone which when dehydrohalogenated with N,N-dimethylaniline produced two products. The isomeric unsaturated ketones were separated and purified as the semicarbazones and then the free ketones were regenerated with oxalic acid. The structures of these ketones were established by



[16] E. Royals and C. Hendry, <u>ibid</u>., <u>15</u>, 1147 (1950).

[17] J. Colonge and K. Mostafavi, Bull. soc. chim. France, <u>6</u>, 335 (1939).

by reduction of both isomers to the same known saturated ketone and by ozonolysis studies. The presence of an α-methyl group apparently favors the formation of the β, γ-unsaturated ketone because these authors were able to isolate only one isomer from the corresponding acylation product of 2-methylpropene. They also established that with unsymmetrical olefins the chlorine atom becomes attached to the more highly substituted carbon and the acyl radical to the other carbon atom of the double bond.



This was shown by comparing the unsaturated ketones and their crystalline derivatives with known compounds; the reduced ketones were compared with known compounds and degradation studies were made. These results are in agreement with those predicted from electronic considerations. Colonge and Duroux[18] were unsuccessful in an attempt to show the presence of isomeric olefins in the acylation of 1-methylcyclohexene with propionyl chloride and stannic chloride. Royals and Hendry[16] were unable to reproduce the yields of these authors using catalytic quantities of stannic chloride as reported by Colonge and

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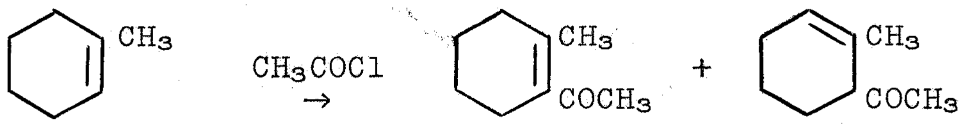
[18] J. Colonge and E. Duroux, *ibid.*, *7*, 459 (1940).

Duroux[18] and found it necessary to use larger amounts of stannic chloride.

Braude *et*. *al*.[19] condensed 1-methyl cyclohexene with acetyl chloride as reported by Ruzicka, Koolhaus and Wind.[20] After distillation, the crude unsaturated ketone was treated with semicarbazide acetate to yield two isomeric unsaturated ketones. Ruzicka *et*. *al*. had postulated that the higher melting substance was a pyrazoline, but ultra-violet absorption data[19,21] for the semicarbazones and the free ketones showed the existance of an α,β-unsaturated ketone and the isomeric β,γ-unsaturated ketone. Deno and Chafetz[22] found that treating



1-methylcyclohexene with acetic anhydride and zinc chloride produced a 70 o/o yield of pure 1-methyl-6-acetylcyclohexene.

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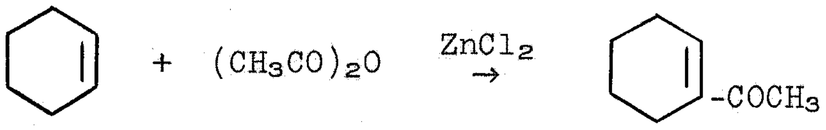
[19] E.A. Braude, E.R. Jones, H. Koch, R. Richardson, F. Sondheimer and J. Toogood, J. Chem. Soc., 1890 (1949).

[20] L. Ruzicka, D. Koolhaus, and A. Wind, Helv. Chim. Acta., 14, 1151 (1931).

[21] R.B. Turner and D. Voitle, J. Am. Chem. Soc., 73, 1403 (1951).

[22] N. Deno and H. Chafetz, *ibid*., 74, 3940 (1952).

They based the purity of the compound upon the following evidence: 1. Negative halogen test 2. Refractive index 3. Melting point of the semicarbazone and 4. Ultra-violet absorption at 248 mμ(ε 277) which indicated that little if any conjugated ketone was present. In contrast to this, Royals and Hendry[16] report that the acetylation of cyclohexene with acetic anhydride and zinc chloride produced 1-acetylcyclohexene. Their proof of structure was



limited to comparing physical constants of the free ketone and its solid derivatives with those reported for the conjugated ketone in the literature. No ultra-violet absorption data were given.

V. HALOGEN MIGRATION

Nenitzescu and Gavat[23] have shown that a migration of the halogen atom can occur in these aluminum chloride catalyzed reactions. Cyclohexene was treated with acetyl chloride as described by Darzens, but, rather than dehydrohalogenating the resulting product, these authors refluxed it with benzene. They isolated from this 4-phenylcyclohexyl

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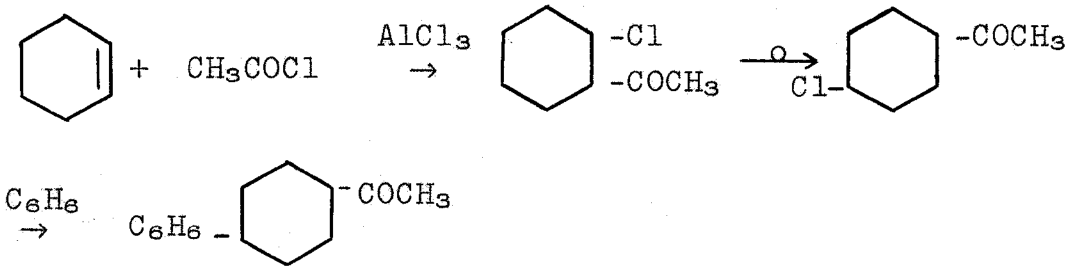
[23] C. Nenitzescu and J. Gavat, Ber., 70, 1883 (1937).

methyl ketone. This was confirmed by Johnson and Offenhauer,[24] and then at a later date Johnson and Gutsche[25] succeeded in isolating the 2-phenylcyclohexyl methyl ketone from the reaction mixture. The presence of the 4-phenylcyclohexyl methyl ketone was explained as resulting from the migration of the chlorine atom from the 2-position to the 4-position and then a subsequent condensation with



benzene. In support of this postulate Farkas and Stevens[26] isolated and identified 4-chlorocyclohexyl phenyl ketone from the reaction of benzoyl chloride with cyclohexene. In addition, they were able to demonstrate that 2-chlorocyclohexyl phenyl ketone could be isomerized to the 4-chloroketone by the action of aluminum chloride.

Additional halogen migrations were demonstrated

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[24] W.S. Johnson and D. Offenhauer, J. Am. Chem. Soc., <u>67</u>, 1045 (1945).

[25] C. Gutsche and W. S. Johnson, <u>ibid</u>., <u>68</u>, 2239 (1946).

[26] C. Farkas and C. Stevens, unpublished work; Dissertation (Ph. D), Wayne University (1952).

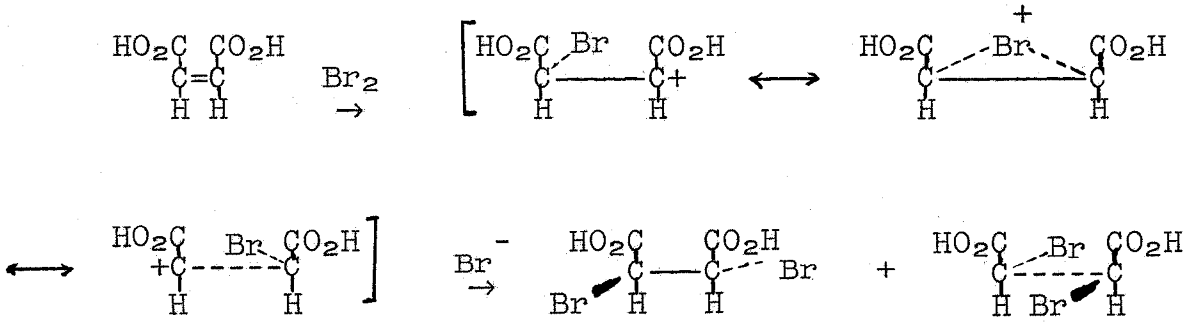
by Nenitzescu and Gavat.[23] They showed that the cyclopentene acetylation product on refluxing with benzene yielded 3-phenylcyclopentyl methyl ketone. The acetylation of 1-butene followed by refluxing with benzene produces a rearranged phenyl substituted ketone, but benzene condensation with the acetylated product from propene results in the 2-phenyl substituted ketone. Apparently the chlorine atom can migrate from one methylene group to another, but not to a methyl group.

DISCUSSION OF RESULTS

I. MECHANISMS

A. Ionic Additions

"It has long been recognized that addition to olefinic linkages by ionic mechanisms, in the absence of complicating factors, proceeds in the trans sense[27]." The most notable of those studied is the addition of bromine to fumaric and maleic acids. In this instance fumaric acid yields meso-dibromosuccinic acid and maleic acid affords racemic dibromosuccinic acid. This specificity has been explained by postulating a two step process with the occurrence of an intermediate bromonium ion which maintains the configuration of the molecule during the backside attack of the bromide ion.



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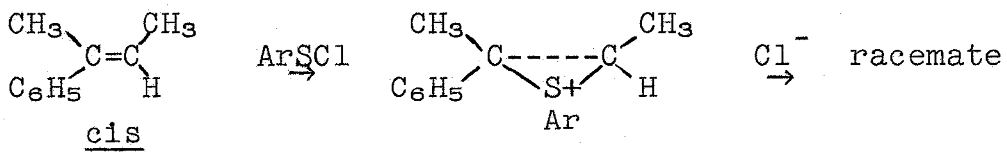
[27] D.H.R. Barton, J. Chem. Soc., 2174 (1949).

As indicated by Ingold,[28] the stabilization of the carbonium ion configuration need not be of a covalent nature, but may exist in the form of electrostatic forces.

Another example of an ionic addition producing a trans product is the addition of 2,4-dinitrobenzensulfenyl chloride to an olefinic linkage. Kharasch and Beuss[29] have demonstrated that it adds according to Markownikoff's rule and suggested that it proceeds through an intermediate sulfonium ion. Cram[30] supported this supposition by demonstrating that stereospecific trans addition occurs.



It is generally postulated that the Friedel-Crafts acylation of olefins is ionic in nature, proceeding via the initial attack of an intermediate oxocarbonium ion and a subsequent attack by the chloride ion.[31]

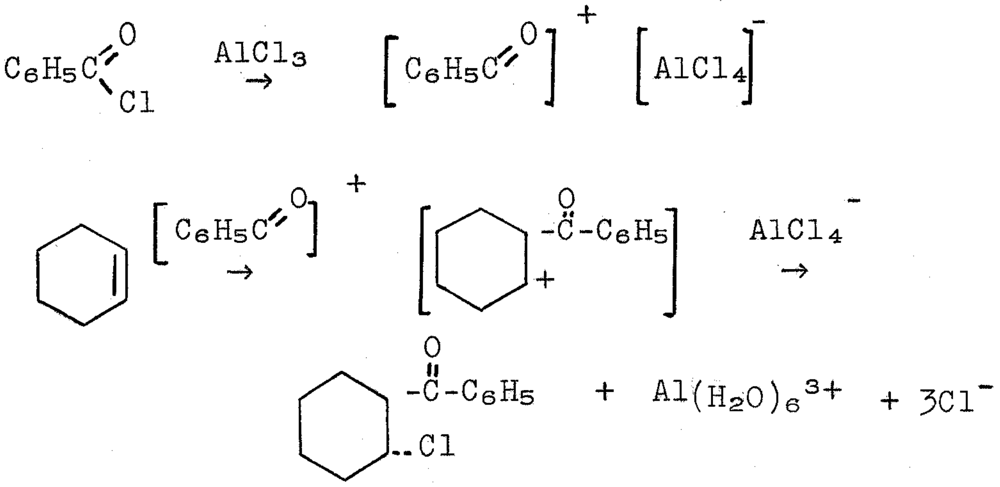
[28] C.K. Ingold, "Structure and Mechanism in Organic Chemistry", Cornell University Press, Ithaca, N.Y., 1953, pp. 646-670.

[29] N. Kharasch and C.M. Beuss, J. Am. Chem. Soc., 71, 2724 (1949).

[30] D.J. Cram, ibid., 71, 3883 (1949).

[31] W. Dilthey, Ber., 71, 1350 (1938).

Considering the fact that the acylation is an ionic addition, the *trans* chloroketone should result.



B. Ionic Eliminations

Compilation of elimination reactions appearing in the literature indicated that the reactions had a preferential steric course. Michael[32] found that chlorofumaric acid is converted, with alkali, to acetylene dicarboxylic acid 50 times faster than is chloromaleic acid. Chavanne[33] reported that *cis*-dichloroethylene reacts 20 times faster with base to form chloroacetylene than does *trans*-dichloroethylene. In addition, Lucas *et*. *al*.[34]

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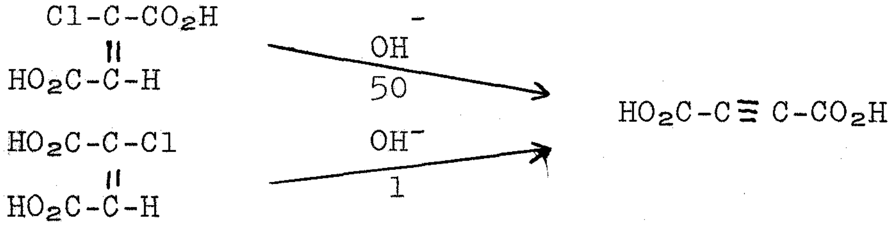
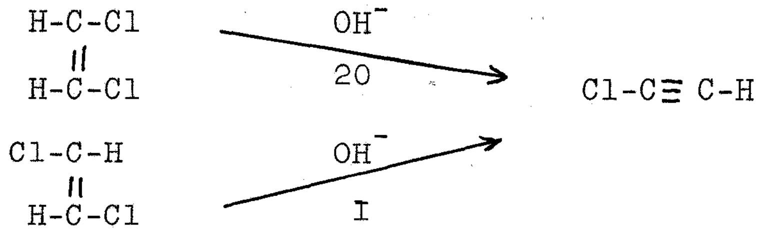
[32] A. Michael, J. prakt. Chem., **52**, 308 (1895).

[33] G. Chavanne, Bull. Soc. chem. Belges, **26**, 287 (1912).

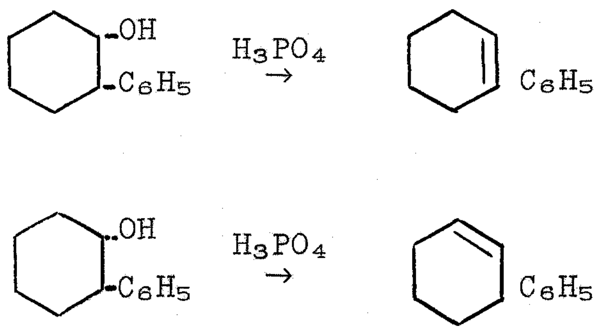
[34] H.J. Lucas, T.P. Simpson, and J.M. Carter, J. Am. Chem. Soc., **47**, 1462 (1925).





reported that the rate of trans elimination of hydrogen bromide from 2-bromopentane is about six times faster than the cis elimination.

This stereospecificity was extended to alicyclic compounds by Price and Karabinos[35] who studied the elimination of water from 2-phenylcyclohexanols with phosphoric acid. The cis-2-phenylcyclohexanol yielded 1-phenylcyclohexene while the trans compound afforded 3-phenylcyclohexene.



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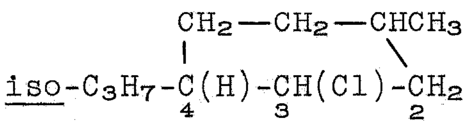
[35] C. Price and J. Karabinos, ibid., 62, 1159 (1940).

These studies definitely indicate a preference for a trans elimination of the atoms involved. Considerable work pertaining to the stereochemistry of elimination reactions has appeared in recent years. Cristol[36] conducted a series of kinetic studies on the alkaline removal of hydrogen chloride from the various isomeric hexachlorobenzenes. He found that β-hexachlorobenzene, the isomer in which all the adjacent chlorine atoms are trans to each other, was inert to the action of alkali under conditions which eliminated hydrogen chloride from the other isomers. This is certainly strong support for preferential trans elimination since in the β-isomer there is no adjacent hydrogen in a trans position to a chlorine atom and as a result the elimination is retarded.

Elimination studies utilizing menthyl and neo-menthyl chlorides[28] have further substantiated preferential trans elimination. Neo-menthyl chloride (trans-4-hydrogen and chlorine) on treatment with alcoholic ethoxide yields 75 o/o 3-menthene and 25 o/o 2-menthene although menthyl chloride (cis-4-hydrogen and chlorine) gives 100 o/o 2-menthene.



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[36] S.J. Cristol, J. Am. Chem. Soc., 69, 338 (1947).

More recently Cram and Elhafez[37] studied the reactions of different bases with the isomeric 1,2-diphenyl-1-propyl halides. They found the *erythro*-chloride to be more resistant to the action of base than the *threo* isomer. Using *d*,*l* potassium 2-octylate as the base, they were unable to form *cis*-α-methyl-stilbene from the *erythro* chloride whereas under identical experimental conditions the *threo*-halide afforded a 92 o/o yield of *trans*-α-methyl-stilbene. This difference in reactivity was attributed to differences in resonance stabilization of the transition state; the *threo* isomer having fewer steric repulsions and as a result a more stable transition state.

The first indication of preferential *cis* ionic elimination of hydrogen chloride was reported in 1952 by Cristol and Hause[38] who found that *trans*-11, 12-dichloro-9,10-dihydro-9,10-ethanoanthracene (hydrogen and chlorine atoms *cis*) reacts 8 times faster than does the *cis* compound with base. They explain this by the fact that the entropy term in the rate expression favors the *cis* elimination

[37] D.J. Cram and F.A.A. Elhafez, J. Am. Chem. Soc., 74, 5851 (1952).

[38] S.J. Cristol and N. Hause, J. Am. Chem. Soc., 74, 2193 (1952).

although the energy of activation for the *trans* compound is lower. Also, although the *trans* compound fulfills the steric requirement of *trans* substituents it does not fulfill the requirement of having the reaction centers lying in the same plane.

In 1953 Cristol and Norris[39] reported their studies concerning second order eliminations of hydrogen bromide from *cis* and *trans*-*p*-nitro-β-bromostyrene and the analog without the nitro group. They found that the *cis* isomers reacted much faster and that the energy of activation of the *cis* compounds were lower. The results were interpreted in terms of a concerted process for the *trans* elimination and a multistage carbanion intermediate mechanism for the *cis* elimination.

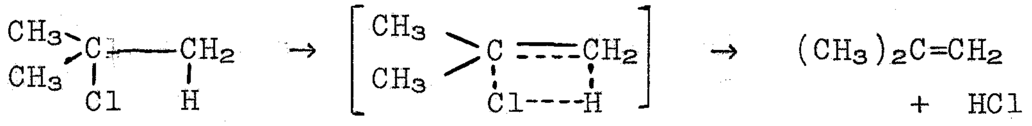
C. Pyrolytic Eliminations

The foregoing has been concerned with heterolytic or ionic eliminations. In the case of homolytic eliminations the results appear to be quite different. In this instance, all evidence appears to favor a preferential *cis* elimination in comparison to the *trans* elimination

[39] S.J. Cristol and W.P. Norris, presented at the A.C.S. Meeting, Los Angeles, Calif., March, 1953.

occurring with base. Huckel *et. al.*[40] conducted stereochemical studies on the pyrolytic decomposition of menthyl and *neo*-menthyl methyl xanthates. They found that menthyl methyl xanthate (*cis*-4-hydrogen and xanthate) yielded on heating 70 o/o 3-menthene and 30 o/o 2-menthene whereas *neo*-menthyl methyl xanthate afforded a 20 o/o yield of 3-menthene and 80 o/o 2-menthene.

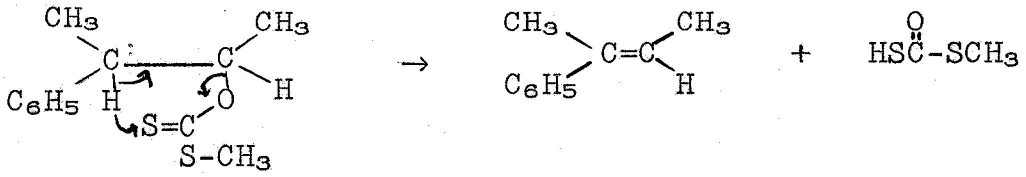
Barton *et. al.*[27] considered homolytic eliminations as proceeding through a cyclic intermediate which would necessitate a *cis* relationship of the elements being removed. Thus, in thermal elimination of hydrogen chloride from alkyl halides a *syn* relationship between the hydrogen and chlorine atom would facilitate their removal.



$$(CH_3)_2C(Cl)-CH_2H \rightarrow \left[(CH_3)_2C \cdots CH_2 \; ; \; Cl \cdots H \right] \rightarrow (CH_3)_2C{=}CH_2 + HCl$$

Several similar explanations have been advanced for the Chugaev reaction; the most generally accepted one being that proposed by Cram.[30] The mechanism as set forth by this author entails a concerted process in which the decomposition of thiomethyl carbonate is considered to be a second and independent reaction.

[40] W. Huckel, W. Tappe and G. Legutke, Ann., 543, 191 (1940).



Alexander and Mudrak[41] extended these pyrolytic examinations of esters to compounds in which there was no longer a second hydrogen available for elimination. They studied the relative stabilities of the acetates and xanthates of 2-methyl-1-tetrol in which the 2-hydrogen is the only one available for removal. The <u>cis</u>-2-methyl-1-tetrol methyl xanthate was stable at 98-100° whereas the <u>trans</u> isomer was rapidly decomposed. The difference was not quite so striking with the acetates, but the <u>cis</u> compound was much more stable to heat than was the <u>trans</u> isomer. In the pyrolysis of the acetates, the <u>cis</u> compound yielded, unexpectedly, 2-methylnaphthalene although the <u>trans</u> isomer gave the anticipated 2-methyl-3,4-dihydronaphthalene.

D. Application to Friedel-Crafts Acylation Products

Application of the preceeding information to the Friedel-Crafts acylation of cyclohexene leads to some interesting conclusions. First, considering the

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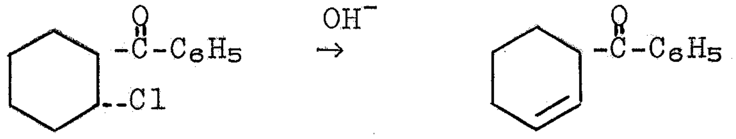
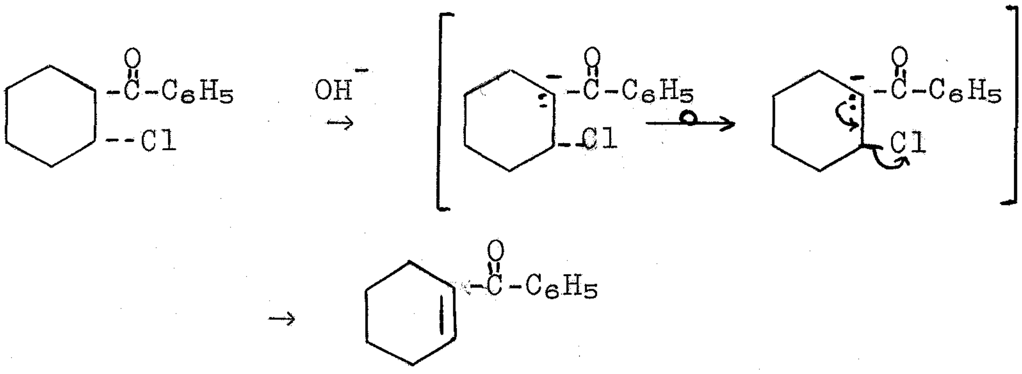
[41] E.R. Alexander and A. Mudrak, J. Am. Chem. Soc., <u>72</u>, 3194 (1950).

acylation process as an ionic addition the resultant chloroketone should be of a trans configuration. Second, elimination of hydrogen chloride could possibly occur via either a thermal or an ionic mechanism. Assuming a trans configuration of the chloroketone, a heterolytic removal of hydrogen chloride should proceed through a trans mechanism producing the β,γ-unsaturated ketone.

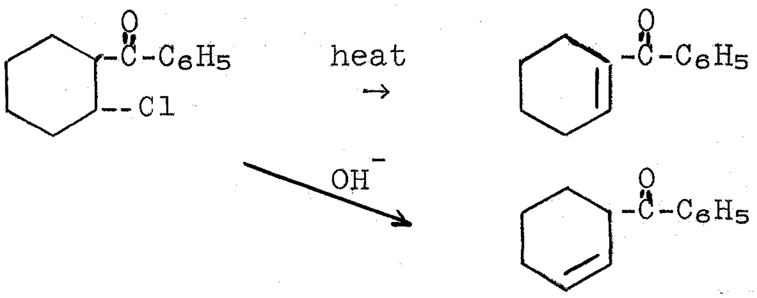


Two things could possibly influence the nature of the final product. An equilibration of β, γ-unsaturated ketone with the α,β isomer has been shown to occur in the presence of base.[42] This is thought to arise from the equilibrium existing between the carbanions which are formed under basic influences. Another possible action of the base could be the removal of the active α-hydrogen, resulting in the formation of the carbanion which could then rearrange to provide a structure favorable for the elimination of the chloride ion. Thermal elimination of hydrogen chloride from trans-2-chlorocyclohexyl phenyl ketone should result in the formation of 1-cyclohexenyl

[42] H. Gilman, "Organic Chemistry", John Wiley and Sons, New York, N.Y., 1943, pp. 1041-1043.



phenyl ketone, in accord with previous homolytic eliminations. Thus, barring rearrangement in the heterolytic elimination, the eliminations should proceed in the following manner:



II. ATTEMPTED PREPARATION OF ~~trans~~-2-CHLOROKETONES

A. Attempted Preparation of trans-2-Chlorocyclohexyl Phenyl Ketone

All previous workers reported the formation of the α,β-unsaturated ketone with very scanty evidence as to its identity. This work was directed at obtaining a pure 2-chloroketone and then studying the nature of the olefins produced by homolytic and heterolytic eliminations. In 1922 Wieland and Bettag[13] reported the preparation of 2-chlorocyclohexyl phenyl ketone contaminated with the corresponding α, β-unsaturated ketone. They oxidized the contaminating unsaturated ketone with an ice cold acetone solution of potassium permanganate and then the oxidized material was removed by extraction with sodium bicarbonate solution. Distillation of the resulting product, yielded according to them, the desired 2-chlorocyclohexyl phenyl ketone boiling at 120-122°/1 mm. (13 o/o yield). Analysis of the product agreed with that calculated for a chlorocyclohexyl phenyl ketone.

Since Wieland and Bettag had reported the preparation of pure 2-chlorocyclohexyl phenyl ketone, an attempt was made to reproduce their results. All oxidation attempts, however, resulted in a chloroketone which still contained varying quantities of unsaturated material as evidenced by positive tests with potassium permanganate and bromine solutions and an elemental analysis which indicated the presence of olefinic material. Attempts were made to remove the unsaturated ketone as the semicarbazone, but were unsuccessful. Two apparently isomeric semicarbazones, as indicated by analysis, were isolated and purified by fractional crystallization and chromatography with one melting at 201-202° and the other at 185-187°. Ultra violet absorption data on these were the same and infra red data shows them to be diamorphic forms of the same compound.

Fractional distillation of the oil resulting from the Friedel-Crafts acylation, without oxidation with permanganate, afforded several cuts. Crystals formed, on refrigeration, in the lower boiling and higher boiling fractions. The lower boiling material gave crystals which melted at 31-32° after recrystallization and the higher boiling fraction yielded crystals which melted at 113-114° after recrystallization. Both solids were obtained in less than 5 o/o yields, with the 113-114° material failing to appear in many runs. The material melting at 31-32° gave qualitative tests for an unsaturated ketone and formed a semicarbazone which was shown by elemental analysis to be the semicarbazone of cyclohexenyl phenyl ketone. The crystalline material melting at 113-114° gave qualitative tests expected for a chlorocyclohexyl phenyl ketone and a confirming elemental analysis.

B. Attempted Preparation of trans-2-Chlorocyclohexyl 2-Naphthyl Ketone

The inconsistant crystallization and extremely low yields of the chlorocyclohexyl phenyl ketone were attributed to the presence of impurities which prevented crystallization from the oil. In the hope of circumventing this difficulty an attempt was made to prepare the corresponding naphthalene analog by acylating cyclohexene with β -naphthoyl chloride and aluminum chloride in nitroethane. The only crystalline material obtained from an acylation conducted at -18° was β-naphthoic acid. If the reacting temperature was maintained at -10 to -5° a crystalline product was obtained which melted at 143.8-144.5°. This substance has an empirical formula of $C_{17}H_{18}O_2$ and since it gave negative tests for halogen and unsaturation it was investigated no further.

III. PREPARATION OF cis-2-CHLOROCYCLOHEXYL PHENYL KETONE

Addition of anhydrous hydrogen chloride to an ether solution of the oil resulting from the Friedel-Crafts acylation of cyclohexene with benzoyl chloride produced a crystalline chloroketone melting at 101-101.5° in yields varying from 10 to 50 o/o. In an attempt to increase the percentage of the α,β-unsaturated ketone in the oil and thus increase the yield of chloroketone an acylation was performed and the product dehydrohalogenated with alcoholic potassium hydroxide as directed by Christ and Fuson.[14] Hydrogen chloride addition to the resulting oil in ether produced a 66 o/o yield of chloroketone. In addition the crude oil was dehydrohalogenated with N,N-dimethylaniline as directed by Nightingale et. al.[15] to give an oil with a negative Beilstein test. The addition of hydrogen chloride to an ether solution of this oil produced the same chloroketone in a 24 o/o yield.

In an attempt to modify the Christ and Fuson procedure, 0.5 moles of distilled oil was refluxed with alcoholic potassium hydroxide solution. The difference being that in this instance the oil was distilled and the benzoyl chloride removed prior to treatment with base, whereas, in the original procedure the crude Friedel-Crafts reaction product was treated with base immediately after removal of the carbon disulfide solvent. A considerable quantity of resinification occurred and only 6 g. of distillable material was obtained. This material yielded no chloroketone when treated with hydrogen chloride; no semicarbazone when treated with semicarbazide hydrochloride and sodium acetate; no unsaturation test with potassium permanganate and bromine solution. After standing for several weeks in the refrigerator, crystals formed and filtration yielded 60 mg. of material which melted at 82-83° after recrystallization. The molecular formula was calculated to be $C_{13}H_{14}O$ from a carbon hydrogen analysis and a molecular weight determination.

IV. IDENTIFICATION OF cis-2-CHLOROCYCLOHEXYL PHENYL KETONE AND 4-CHLOROCYCLOHEXYL PHENYL KETONE

A. Physical Properties

The question arose as to the stereochemical identity of the two chloroketones, A-obtained inconsistently and in small quantities from the Friedel-Crafts acylation (m.p. 113-114°) and B-obtained by the addition of hydrogen chloride to the impure oil resulting from the acylation (m.p. 101-101.5°). The major difference existing between the two compounds was the ease with which B decomposed with heat (120°) whereas compound A was apparently stable to 190-200°.

The compounds apparently were isomeric as indicated by the similarity of their infra red curves. Dipole moment studies were initiated with the hope that the two compounds could be differentiated in this manner.

The extrapolation method of Everard, Sutton and Hill[43] was used in which it is assumed that for sufficiently dilute solutions, the dielectric constant and specific volume vary linearly with concentration and that the molecular refractivity of the solute may be expressed in terms of the refractive index gradient. Expressing concentration in weight fractions this may be expressed as follows:

$$\epsilon_{1,2} = \epsilon_1 + \alpha w_2$$

$$v_{1,2} = v_1 + \beta w_2$$

$$n_{1,2} = n_1 + \gamma w_2$$

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[43] K.B. Everard, L.E. Sutton and R.A. Hill, Trans. Faraday Soc., 46, 417 (1950).

Application of this to the Debye equation in which it is assumed that at infinite dilution the polar molecules in a solution of non-polar solvent will behave essentially as a gas, affords the following equation:

$$\mu_2^2 = \frac{9\ KT}{4\pi N} M_2 \left\{ \left[\frac{\epsilon_1 - 1}{\epsilon_1 + 2} (v_1 + \beta) + \frac{3\alpha v_1}{(\epsilon_1 + 2)^2} \right| - \left[\frac{n_1^2 - 1}{n_1 + 2} (v_1 + \beta) + \frac{6 n_1 \gamma v_1}{(n_1 + 2)^2} \right] \right\}$$

Subscripts: $_1$ = non polar solvent

$_2$ = polar solute

ϵ = dielectric constant

M = molecular weight

N = Avogadro's Number

μ = permanent dipole

T = absolute temperature

v = specific volume

n = refractive index

K = Boltzman constant

α = Limiting dielectric constant gradient

β = specific volume gradient

γ = refractive index gradient

For benzene as the solvent at 30°:

$\epsilon_1 = 2.263$ $\quad$ $n_1 = 1.4949$

$v_1 = 1.1517$

$$\mu_2^2 = M_2(0.00948\,\alpha + 0.000234\,\beta - 0.0278\,\gamma)\,10^{-36}\ \text{e.s.u.}$$

The dielectric constant, specific volume, and refractive index values at various concentrations were plotted against the weight fractions to give α, β and γ as the slopes of the respective curves. From these determinations the following dipole moments were assigned to the chloroketones:

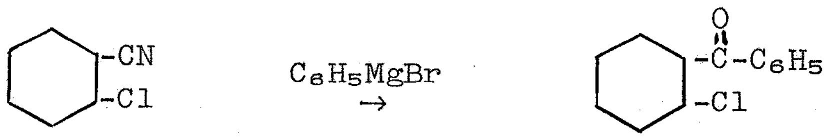
A - 3.95 D

B - 3.08 D

Dr. Gerard Kraus* attempted to correlate these values with structural assignments. He said, however, that the complexities of the molecules necessitated so many assumptions that they invalidated the results.

B. Stereospecific Synthesis of cis-2-Chlorocyclohexyl Phenyl Ketone

At this point an independent stereospecific synthesis was undertaken. The reaction of phenylmagnesium bromide with 2-cyano-1-chlorocyclohexane was considered the most profitable attack.



Van Coillie[44] had reported the separation of the cis and

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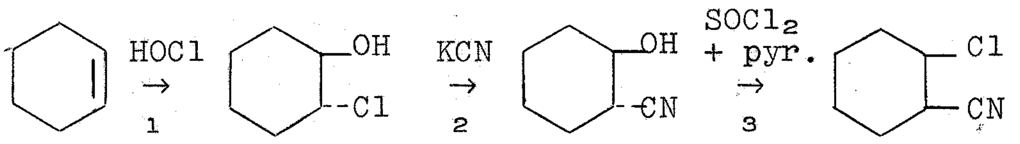
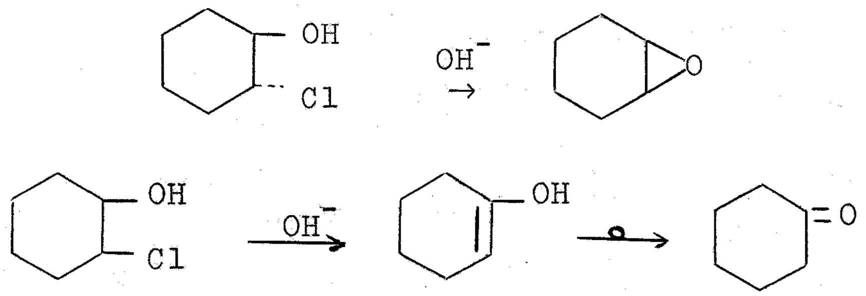
[44] R. Van Coillie, Bull. soc. chim. Belg., 42, 419 (1933).

* Dr. Gerard Kraus, Applied Science, University of Cincinnati.

trans isomers of 2-cyano-1-chlorocyclohexane, but no yields were reported. His only criteria for the structural configurations assigned were the calculated and experimental values of molecular refractivities. Since this element of doubt existed as to the relative stereochemical configurations, a synthesis was devised in which reactions used were of a known stereochemical nature.



The stereochemistry of reaction 1 was established by Bartlett[45] when he demonstrated that cis and trans-2-chlorocyclohexanol reacted differently under the influence of base. The isomer obtained by the addition of hypochlorous acid to cyclohexene produced the epoxide on treatment with base, whereas the other isomer yielded cyclohexanone. These facts could only be accounted for by assuming the following:



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[45] P.D. Bartlett, J. Am. Chem. Soc., 57, 224 (1935).

Reaction 2 has been performed by Mousseron et. al.[46] who explained the retention of configuration arising as an intermediate epoxide formation. In support of this, he found cis-2-chlorocyclohexanol to be inert under the experimental conditions used. This could be explained equally well by assuming a neighboring group effect.

Reaction 3 involving the substitution of a chlorine atom for a hydroxyl group through the use of thionyl chloride and pyridine results in almost complete if not complete inversion.[47,48,49] At times these results are altered slightly, to produce some retention, by the possibility of a neighboring group effect. However, in this instance the adjacent cyanide group is incapable of participating as a neighboring group.

Treatment of trans-2-cyanocyclohexanol with thionyl chloride and pyridine resulted in the formation of a 60 o/o yield of cis-2-cyano-1-chlorocyclohexane with

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[46] M. Mousseron, J. Jullien and F. Winternitz, Bull. soc. chim. France, 5 15, 878 (1948).

[47] H.J. Lucas and C. Gould, J. Am. Chem. Soc., 63, 2541 (1941).

[48] B. Carroll, D.G. Kubler, H.W. Davis and A.M. Whaley, ibid., 73, 5382 (1951).

[49] H.C. Stevens and O. Grummitt, ibid., 74, 4876 (1952).

physical constants in agreement with those reported by Van Coillie for the *cis* compound. This appears therefore to be a synthetic confirmation of the structural configurations assigned by this worker.

Since thionyl chloride alone has on several occasions[47,48,49,50] caused substitution with retention of configuration, its action on the *trans*-cyanohydrin was tried in the hope that it could possibly give rise to the *trans*-2-cyano-1-chlorocyclohexane. Such treatment, however, resulted in the production of a 24 o/o yield of *cis*-chloronitrile and considerable amount of unsaturated nitrile. This was not unexpected,in as much as all reactions reported in the literature leading to retention of configuration involved compounds which had one of two things: either the hydroxyl group was attached to a carbon which had a phenyl group on it which could result in increased stabilization of the intermediate carbonium ion, or a halogen was on the β-carbon atom which could participate in retention as a neighboring group.

The treatment of *cis*-2-cyano-1-chlorocyclohexane with an equivalent amount of phenylmagnesium bromide at 0° resulted in the formation of the *cis*-2-chlorocyclohexyl

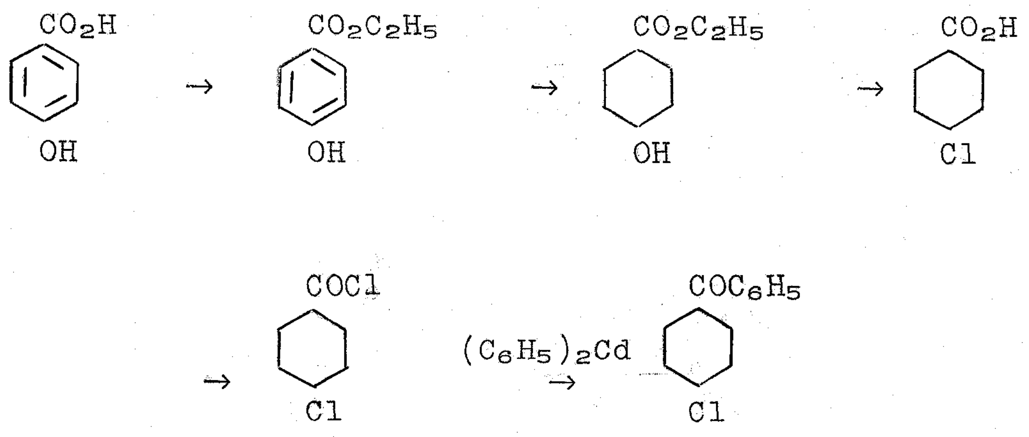
[50] J. Kenyon, H. Phillips and F. Taylor, J. Chem. Soc., 382 (1951).

phenyl ketone (15 o/o yield based on chloronitrile used). A mixed melting point of this chloroketone and the one obtained by the addition of hydrogen chloride to the α,β unsaturated ketone showed no depression. A lowering of melting point was observed when this was mixed with the isomeric ketone melting at 113-114°.

C. 4-Chlorocyclohexyl Phenyl Ketone

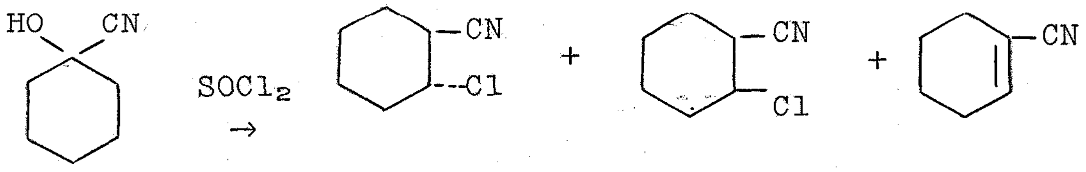
These findings indicated that the chloroketone melting at 113-114° was some isomer other than the *trans*-2-chlorocyclohexyl phenyl ketone. This was surmised because the *trans*-2-chloroketone has the active α-hydrogen and chlorine atom in a *cis* relationship and as a result should be more susceptible to thermal elimination of hydrogen chloride than the *cis*-2-chloroketone where the α-hydrogen and chlorine atoms are in a *trans* configuration. The *cis* compound, as mentioned above, loses hydrogen chloride when heated to 120°, whereas, the other isomer is apparently stable to 190-200°.

Farkas and Stevens[26] have shown the chloroketone melting at 113-114° (isolated by them in a 3.5 o/o yield from the reaction of cyclohexene, benzoyl chloride and aluminum chloride) to be 4-chlorocyclohexyl phenyl ketone by an independent synthesis.



V. ATTEMPTED PREPARATION OF trans-2-CYANO-1-CHLOROCYCLOHEXANE

Several attempts were made to prepare the trans-2-cyano-1-chlorocyclohexane and thus the trans-2-chloroketone, but all were unsuccessful. The first attempt was made with the method reported by Van Coillie.[44] This reaction is by its very nature unusual and the yields and procedure reported by this author were obscure. He reported that treatment of cyclohexanone cyanohydrin with thionyl chloride results in the formation of cis and trans-2-cyano-1-chlorocyclohexane along with an appreciable quantity of the unsaturated nitrile. Repetition of his experimental



procedure as closely as possible and distillation through a 60 cm. glass helices-filled column gave no material distilling at the temperature reported for the _trans_-chloronitrile.

Lucas _et_. _al_.[47] have shown in their work on halogen substitution with thionyl chloride that a neighboring chlorine atom can effect retention of structure by holding the intermediate carbonium ion in position. With this in mind an attempt was made to convert _trans_-1,2-dichlorocyclohexane with potassium cyanide into _trans_-2-cyano-1-chlorocyclohexane in a manner similar to that used in the preparation of the _trans_-1,2-chlorohydrin.

Refluxing the _trans_-dichloride with one equivalent of alcoholic potassium cyanide for three hours gave no evidence of the formation of the nitrile. Repetition of the attempt with a 100 o/o excess of alcoholic potassium cyanide and refluxing for three days gave no 2-cyano-1-chlorocyclohexane. An attempt was then made to effect the substitution with cuprous cyanide in refluxing _trans_-dichloride (190-200°) with no success.

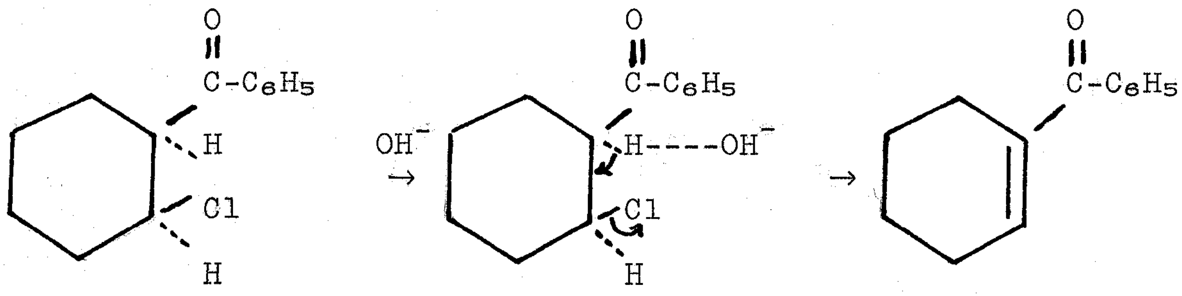
VI: ELIMINATION OF HYDROGEN CHLORIDE FROM _cis_-2-CHLOROCYCLOHEXYL PHENYL KETONE

At this point, elimination studies were undertaken on the available _cis_-2-chlorocyclohexyl phenyl ketone.

In the process of this investigation, it was found that this isomer on heating yielded an apparently pure unsaturated ketone (n_D^{25} 1.5653) which easily crystallized on refrigeration. As a matter of fact, pure olefin can be obtained in much larger amounts and much more easily by this method than by fractional distillation of the oils from the Friedel-Crafts acylations. Treatment of an alcoholic solution of the cis-chloroketone at room temperature with an equivalent amount of potassium hydroxide afforded the same olefin (n_D^{25} 1.5652) on distillation which easily crystallized when refrigerated. This olefin has the same melting point (31-32°) as the material obtained from the thermal elimination and forms a semicarbazone which shows no depression in melting point when mixed with the semicarbazone from the olefin derived from pyrolytic elimination.

A. Ionic Elimination of Hydrogen Chloride

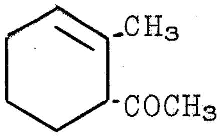
The ionic elimination of hydrogen chloride from the 2-chloroketone with alcoholic potassium hydroxide afforded the trans elimination product as expected from previous studies on heterolytic eliminations of hydrogen chloride. This elimination was effected by the addition of an equivalent amount of solid potassium hydroxide to an alcoholic solution of 2-chlorocyclohexyl phenyl ketone. As the base dissolved, potassium chloride precipitated and at no time did the base appear to be in excess as evidenced by the absence of the red color which base produces in the presence of 1-cyclohexenyl phenyl ketone. In view of what is known of ionic eliminations, the following can be postulated as the mechanism involved in this elimination:



B. Thermal Elimination of Hydrogen Chloride

Thermal elimination of the hydrogen chloride from cis-2-chlorocyclohexyl phenyl ketone produces 1-cyclohexenyl phenyl ketone which is contrary to previous stereochemical reports on homolytic eliminations. This is not surprising, however, since this is apparently the first elimination studied stereochemically, using a compound which contains an active α-hydrogen adjacent to the halogen atom. The possibility of the γ-hydrogen being removed and then the β,γ-unsaturated ketone rearranging to the α,β-unsaturated ketone appears to be remote for several reasons.

(1) Deno and Chafetz[22] report distillation of 1-methyl-6-acetylcyclohexene to give a pure β,γ-unsaturated ketone, which indicates the stability of the ketone to distillation.



(2) There is no reason to expect the γ-hydrogen to be removed with the chlorine atom at such a low temperature (120°) since there is no apparent activation of this position. The 4-chlorocyclohexyl phenyl ketone is stable to 190-200° and the γ-hydrogen must be eliminated with the chlorine atom in this instance since elimination in either direction would involve a γ-hydrogen.

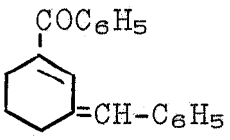
(3) Even if the β,γ-unsaturated ketone were formed and then rearranged with heat, it is doubtful that the rearrangement would occur to such an extent as to give α,β-unsaturated ketone of the purity indicated by its high index of refraction and ease of crystallization.

C. Identification of 1-Cyclohexenyl Phenyl Ketone

The olefin obtained from the above eliminations was established as the 1-cyclohexenyl phenyl ketone on the basis of the following:

(1) Infra red and ultraviolet data are in agreement with the assignment. Infra red data show that the carbonyl band is displaced to 6.12μ and a phenyl band is missing, but Dr. W. A. Patterson of Baird Laboratories agreed that these do not throw out the assigned structure. Ultra-violet data show that the λ_{max} is 245 mμ which corresponds with increased conjugation as it is a shift to the right from the λ_{max} of acetophenone which is 241 mμ. Dr. M. Orchin*agrees that this curve is reasonable for the 1-cyclohexenyl phenyl ketone.

(2) Christ's and Fuson's[14] work indicates the presence of this material as evidenced by the condensation product obtained with benzaldehyde. Their olefin can be purified by careful distillation to give crystalline olefin melting at 31-32° and forms the same semicarbazone as that obtained from other procedures.



(3) Farkas and Stevens[26] compared the olefins obtained by heating 2-chlorocyclohexyl phenyl ketone

* Dr. M. Orchin - Applied Science, University of Cincinnati.

(prepared by adding hydrogen chloride to an acetic acid solution of the olefin obtained by Christ's and Fuson's procedure) and 1-chlorocyclohexyl phenyl ketone and found them to be identical.

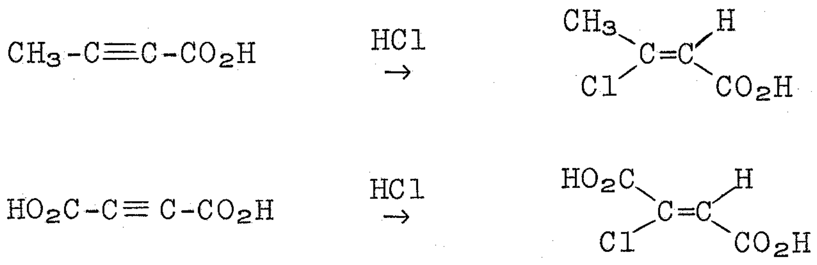
(4) Addition of hydrogen chloride to the olefin produced 2-chlorocyclohexyl phenyl ketone in 87 o/o yield.

D. Reaction of 1-Cyclohexenyl Phenyl Ketone with Base

Treatment of 1-cyclohexenyl phenyl ketone (n_D^{25} 1.5653) with alcoholic potassium hydroxide at room temperature for fifteen hours yields a product (n_D^{25} 1.5500) on distillation which will not crystallize. The ultraviolet absorption curves for these materials cannot be used to differentiate them(n_D^{25} 1.5653 - λ_{max} 245 mμ; n_D^{25} 1.5500 - λ_{max} 244mμ). Refluxing the pure α,β-unsaturated ketone with base for two hours causes a lowering in refractive index (n_D^{25} 1.5576), but not to the same extent as that caused by prolonged treatment at room temperature. An interesting sideline of this reaction is the fact that addition of base to an alcoholic solution of the α,β-unsaturated ketone produces a red color which can be removed by neutralizing the solution with dilute acid.

VII. STEREOCHEMISTRY OF THE ADDITION OF HYDROGEN CHLORIDE TO 1-CYCLOHEXENYL PHENYL KETONE

The addition of hydrogen chloride to 1-cyclohexenyl phenyl ketone produces cis-2-chlorocyclohexyl phenyl ketone. This indicates that the hydrogen chloride addition has taken place stereospecifically to produce the cis compound. This is in agreement with work conducted concerning ionic additions and, more specifically, with those involving the addition of hydrogen chloride. Friederich[51] found that addition of hydrogen chloride to tetrolic acid yielded β-chlorocrotonic acid and Michael[52] showed that the addition of hydrogen chloride to acetylene dicarboxylic acid produced chlorofumaric acid. Van Coillie[43] extended this to the alicyclic series when he found that



the addition of hydrogen chloride to 1-cyanocyclohexene produced cis-2-cyano-1-chlorocyclohexane.

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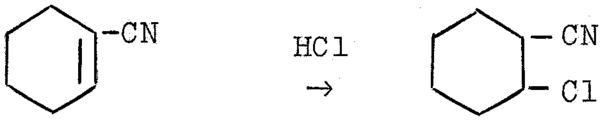
[51] R. Friederick, Ann., 219, 368 (1883).

[52] A. Michael, J. prakt. Chem., 52, 289 (1895).


CN
HCl
CN
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EXPERIMENTAL

I. FRIEDEL-CRAFTS ACYLATION OF CYCLOHEXENE WITH BENZOYL CHLORIDE

A. Attempted Preparation of trans-2-Chlorocyclohexyl Phenyl Ketone

One hundred and thirty three grams (1 mole) of powdered aluminum chloride was added slowly (ca. twenty-thirty minutes) to 150 g. (1.1 mole) of benzoyl chloride in a three-necked flask equipped with an efficient stirrer and cooled in an ice-salt bath. At the end of the addition about 2/3 of the aluminum chloride had dissolved. A dropping funnel was then attached and 82 g. (1.0 mole) of cyclohexene was added to the mixture over a two hour period. During the addition, the reaction mixture turned dark and at the end was extremely viscous. The aluminum chloride complex was decomposed by pouring it into 1500 cc. of ice-hydrochloric acid solution with stirring. The resulting oil was dissolved in 350 cc. of ether and the aqueous layer extracted with an additional 150 cc. of ether. The ethereal solution was washed with 600 cc. of ice water in 3 portions, 600 cc. of cold sodium bicarbonate solution in 4 portions and with 200 cc. of ice water in 2 portions.

The ether solution was then dried over anhydrous sodium sulfate and the solvent removed. Distillation at 0.7 mm. afforded 81 g. of yellow oil boiling at 120-140° (n_D^{25} 1.5500). Redistillation of this oil through a 10 cm. Vigreaux microdistillation apparatus at 1 mm. gave the following cuts:

A.	-130°	1.3 g.	(fore-run)	
B.	130-135°	10.0 g.	n_D^{25}	1.5582
C.	136-140°	5.2 g.	n_D^{25}	1.5558
D.	141-143°	10.9 g.	n_D^{25}	1.5537
E.	144-147°	5.5 g.	n_D^{25}	1.5532
F.	148-154°	1.8 g.	n_D^{25}	1.5545

All of the above fractions gave a positive Beilstein test for halogen and positive potassium permanganate and bromine tests for unsaturation.[53] Repeated distillation of fraction B gave an oil (n_D^{25} 1.5629) which crystallized when refrigerated (m.p. 27-30°). Recrystallization from 30-60° petroleum ether gave crystals melting at 30-31°*. This material formed a

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* All melting points are corrected.

[53] R.L. Shriner and R.C. Fuson, "Identification of Organic Compounds", John Wiley and Sons, Inc., New York, N.Y., 1948, p. 117.

semicarbazone which melts at 205-207°. After standing in the refrigerator for several weeks crystals formed in fraction F. Recrystallization from 70-90° petroleum ether gave 0.1 g. of crystals melting at 113-114°. This compound gives a positive sodium fusion test for halogen, a positive test for a carbonyl group when boiled with a methanolic solution of hydroxylamine hydrochloride and Bogen's indicator[54], and a negative test for unsaturation with potassium permanganate solution or bromine. This chloroketone is stable to heating at 200°.

Analysis*	o/o H	o/o C
Calc'd. for $C_{13}H_{15}OCl$:	6.8	70.1
Found:	7.1	70.3

The above is a description of a sample reaction. The yield of crude yellow oil, which apparently varies in constitution from run to run, was 75-95 g. The yield of chloroketone (m.p. 113-114°) varied from 0-2 per cent; the yield of crystalline unsaturated ketone 2-5 per cent.

The crude oil, obtained from the Friedel-Crafts acylation of cyclohexene with benzoyl chloride, was treated with semicarbazide hydrochloride and sodium acetate as directed by Shriner and Fuson.[55]

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* Analysis by Microchemical Laboratory University of Pittsburgh, Pittsburgh, Pennsylvania.

[54] R.L. Shriner and R.C. Fuson, ibid., p. 106.

[55] R.L. Shriner and R.C. Fuson, ibid., p. 170.

After standing at room temperature for a day, crystals formed when the side of the flask was scratched. Recrystallization of 1.1 g. of these from 70 o/o alcohol gave 0.5 g. of crystals melting at 190-197° and addition of water to the mother liquor yielded 0.3 g. of crystals melting at 160-180°. Several recrystallizations of the higher melting semicarbazone gave colorless crystals melting at 201-202°. Repeated recrystallizations, neglecting the more insoluble material, of the lower melting semicarbazone with 50 o/o alcohol afforded colorless crystals melting at 185-187°. Chromatography of the lower melting fraction using alumina as the absorbent, benzene as the solvent and 2 o/o alcohol-benzene as the eluent gave crystals melting at 185-187°. Addition of the lower melting semicarbazone to the higher melting semicarbazone gave a melting point of 196-200°.

SEMICARBAZONE A (m.p. 201-202°)

Analysis*	o/o H	o/o C
Calc'd. for $C_{14}H_{17}N_3O$:	7.0	69.1
Found:	6.7	69.1

Ultra-violet absorption (alc.): max 263-264 m

max 22,600

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* Analysis by Microchemical Laboratory, University of Pittsburgh, Pittsburgh, Pennsylvania.

SEMICARBAZONE B (m.p. 185-187°)

Analysis*	o/o H	o/o C
Calc'd. for $C_{14}H_{17}N_3O$:	7.0	69.1
Found:	6.8	68.8

Ultra-violet absorption (alc.): $_{max}$ 263-264 m

$_{max}$ 22,000

Infra red spectra show that these substances are diamorphic forms of the same compound.

The crude yellow oil obtained from the Friedel-Crafts acylation procedure was oxidized with potassium permanganate as directed by Wieland and Bettag.[13] Repeated oxidation and distillation gave 10-15 g. of yellow oil which still gave a positive test for unsaturation. A sample of the oil (n^{20}_D 1.5545) gave the following analysis*

	0/0 H	0/0 C
Found:	6.9	71.3
Calc'd. for $C_{13}H_{15}OCl$:	6.8	70.1

B. Dehydrohalogenation of Acylation Product with Potassium Hydroxide

1. Preparation of 1-Cyclohexenyl Phenyl Ketone

Cyclohexene was condensed with benzoyl chloride as directed by Christ and Fuson[14] to yield 61 g.

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* Analysis by Microchemical Laboratory, University of Pittsburgh, Pittsburgh, Pennsylvania.

(33 o/o) of yellow oil (n_D^{25} 1.5595) distilling at 115-130° at 0.7 mm. Fractionation of this gave 37 g. of oil at 125-132° (1 mm.) which was redistilled at 2 mm. to give the following:

I	134-136°,	20.9 g.,	n_D^{25} 1.5622
II	136-140°,	6.6 g.,	n_D^{25} 1.5630

(Reported[14] b.p. 147°/ 8 mm.; n_D^{22} 1.5595)
(Reported[56] n_D^{25} 1.5430)

Fraction II partially crystallized on standing in the refrigerator to give 2 g. of α,β-unsaturated ketone which, when recrystallized, melted at 31-32° (reported[26] m.p. 32-34°). This material forms a semicarbazone melting at 205-207° (reported[26] m.p. 207-209°) which, when mixed with the semicarbazone of the olefin derived from the cis-2-chlorocyclohexyl phenyl ketone causes no depression in melting point.

A solution of 39 g. of oil (from the Friedel-Crafts acylation of cyclohexene with benzoyl chloride) and 50 g. of potassium hydroxide in 200 cc. of 95 o/o alcohol was refluxed for three hours. The solution was cooled, washed with water and treated as directed by Christ and Fuson.[14] This yielded 6 g. of oil (n_D^{25} 1.5467) distilling

[56] E. Farkas and C. Stevens, J. Am. Chem. Soc., 74, 5352 (1952).

at 134-139° at 1.5 mm. After standing in the refrigerator for several weeks, some crystals formed in the oil. Filtration, followed by dissolving the residue in 60-90° petroleum ether and freezing out gave 60 mg. of crystals melting 73-77°. Recrystallization from 60-90° petroleum ether yielded colorless crystals melting 82-83°. This compound will not react with bromine in carbon tetrachloride; it will not react with a methanolic solution of hydroxylamine hydrochloride and Bogen's indicator; it will not give an active hydrogen test with isopropyl magnesium bromide; it gives a very sluggish potassium permanganate test; it gives a negative Beilstein test.

Analysis*	o/o H	o/o C	M.W.
Found:	7.7	83.6	178
Calculated for $C_{13}H_{14}O$:	7.6	83.8	186

2. Preparation of <u>cis</u>-2-Chlorocyclohexyl Phenyl Ketone

Anhydrous hydrogen chloride was passed into a solution of 42 g. of olefin in 150 cc. of anhydrous ether cooled in an ice bath. The solution turned dark during the addition and as the solution became saturated crystalline 2-chloroketone precipitated. The ether was

* Analysis by F. Schwarzkopf, Middle Village, N. Y.

removed with an aspirator and the chloroketone filtered. The dark crystals were washed several times with 60-90° petroleum ether to yield 33 g. (66 o/o) of colorless crystals melting at 90-94°. One recrystallization from 60-90° petroleum ether yielded 27 g. of chloroketone melting at 97-100°. Repeated recrystallization, avoiding prolonged heating, gave a product melting at 101-101.5°. (Reported[26] melting point 98-99°)

Analysis*	o/o H	o/o C
Found:	6.9	69.9
Calculated for $C_{13}H_{15}OCl$:	6.8	70.1

C. Dehydrohalogenation of Acylation Product with N,N-Dimethylaniline

1. Preparation of 1-Cyclohexenyl Phenyl Ketone

An acylation was run using 0.5 mole quantities and the product dehydrohalogenated with N,N-dimethylaniline as directed by Nightingale _et_. _al_.[15] Distillation yielded 22 g. (24 o/o) of oil (negative Beilstein test) boiling at 133-135° at 1 mm.

* Analysis by W. Manser, Zurick

2. Preparation of cis-2-Chlorocyclohexyl Phenyl Ketone

A solution of 22 g. (0.12 mole) of olefin in 100 cc. of anhydrous ether was saturated with anhydrous hydrogen chloride. The solvent was removed on a steam plate and the resultant crystals recrystallized from 60-90° petroleum ether to yield 15 g. (57 o/o) of cis-2-chloroketone melting at 96-99°.

II. ATTEMPTED PREPARATION OF 2-CHLOROCYCLOHEXYL 2-NAPHTHYL KETONE

A. Preparation of 2-Naphthoic Acid[57]

This material was prepared as directed in "Organic Synthesis." Forty three grams (0.25 mole) of β-acetonaphthalene was oxidized with a solution of potassium hypochlorite (prepared as directed in note 2) to yield 36 g. (83 o/o) of colorless 2-naphthoic acid after recrystallization from 95 o/o alcohol (m.p. 183-185°; reported[57] m.p. 184-185°).

B. Preparation of 2-Naphthoyl Chloride[58]

[57] A.H. Blatt, "Organic Synthesis", Coll. vol. II, John Wiley and Sons, Inc., New York, N.Y., 1943, p. 428.

[58] N.L. Drake, "Organic Synthesis", Vol. 21, John Wiley and Sons, Inc., New York, N.Y., 1941, p. 86.

Thirty five grams (0.167 mole) of phosphorous pentachloride was warmed on a steam bath with 28.7 g. (0.167 mole) of 2-naphthoic acid as directed in "Organic Synthesis." Distillation at 2 mm. afforded 27 g. (82 o/o) of colorless acid chloride (m.p. 50-51°; reported[58] m.p. 51-52°) distilling at 135-137°.

C. Reaction of Cyclohexene with 2-Naphthoyl Chloride and Aluminum Chloride

A solution of 7.6 g. (0.04 mole) of 2-naphthoyl chloride and 3.3 g. (0.04 mole) of cyclohexene dissolved in 40 cc. of nitroethane was placed in a 100 cc. three-necked flask, fitted with a mercury sealed stirrer, and cooled to -18°. To this solution 5.8 g. (0.041 mole) of powdered aluminum chloride was added with vigorous stirring over a three hour period. The reaction mixture was a light orange color so long as it was kept at -18°, but warming it to -15° or above caused considerable darkening. The mixture was decomposed by pouring it into an ice-hydrochloric acid solution and extracted with ether. After the ethereal solution had been dried over anhydrous sodium sulfate, the ether and nitroethane were removed under vacuum. Some crystalline 2-naphthoic acid was the only solid which precipitated from the remaining oil.

The above procedure was repeated except that the temperature was kept at -10 to -5°. In this instance, when the reaction mixture was poured into an ice-hydrochloric acid mixture a very viscous oil formed which solidified when scratched. The solidification was aided considerably by the addition of 5 cc. of 30-60° petroleum ether. Filtration gave 3 g. of yellow amorphous solid which did not yield to conventional recrystallization procedures. The product was purified by dissolving it in cold benzene and decolorizing with charcoal and then evaporating the benzene with a stream of air while 70-90° petroleum ether was added dropwise. This yielded an unknown compound which has the following properties:

1. Melting point - 143.8-144.5°
2. It does not react with bromine in carbon tetrachloride
3. It does not react with 2 o/o potassium permanganate solution
4. It does not react with a methanolic solution of hydroxylamine hydrochloride and Bogen's indicator
5. It does not dissolve in base
6. It does not appear to release propane from *iso*-propyl magnesium bromide
7. Heat apparently removes water and the resultant oil gives a positive test with potassium permanganate solution
8. Negative sodium fusion test for nitrogen.

Analysis*		o/o H	o/o C
Found:	1.	7.1	80.0
	2.	7.1	80.2

III. STEREOSPECIFIC SYNTHESIS OF *cis*-2-CHLOROCYCLOHEXYL PHENYL KETONE

A. Preparation of *trans*-2-Chlorocyclohexanol[59]

This material was prepared as reported in "Organic Synthesis". Sixty one grams (0.75 mole) of cyclohexene was treated with a hypochlorous acid solution and the reaction mixture handled as directed. Distillation at 16 mm. afforded 65 g. (65 o/o) of colorless *cis*-2-chlorocyclohexanol distilling at 84-85°.

B. Preparation of *trans*-2-Cyanocyclohexanol

Fifty grams (0.38 mole) of trans-2-chlorocyclohexanol was dissolved in 250 cc. of 95 o/o alcohol and a solution of 50 g. (0.77 mole) of potassium cyanide dissolved in 200 cc. of water was added and the solution held at reflux for three hours as directed by Mousseron

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* Analysis by W. Manser, Zurich

[59] H. Gilman and A.H. Blatt, "Organic Synthesis," Coll. Vol. I, John Wiley and Sons, Inc., New York, N.Y., 1941, p. 158.

et. al.[46] The reaction mixture was treated as directed and distillation gave 30 g. (65 o/o) of product boiling at 145-147° at 16 mm. (Reported[46] m.p. 46°; m.p. 45-46°)

C. Preparation of cis-2-Cyano-1-Chlorocyclohexane

1. With Thionyl Chloride

Twenty nine grams (0.23 mole) of trans-2-cyano-1-cyclohexanol was added to 55 g. (0.46 mole of thionyl chloride in a 100 cc. flask with a reflux condenser and an attached calcium chloride tube. The reaction mixture refluxed of its own accord for fifteen-twenty minutes and was then heated to reflux for an additional hour. The mixture was cooled with an ice bath and poured into an ice-hydrochloric acid solution; the resulting oil was dissolved in ether. The ether solution was washed with water and then with aqueous sodium bicarbonate until the washings were basic. After washing again with water, the ether layer was dried over anhydrous sodium sulfate. Removal of the ether and vacuum distillation gave two distinct fractions.

(1) 1-cyanocyclohexene

90-92° at 18 mm. 4.5 g. (18 o/o)

(2) cis-2-cyano-1-chlorocyclohexane

123-125° at 14 mm. 7.8 g. (24 o/o)

n_D^{30} 1.4792

Redistillation of 7.0 g. of (2) gave the following:

2.6 g.	n_D^{30} 1.4788	123-124°	at 14 mm.
2.5 g.	n_D^{30} 1.4792	124-124.5°	at 14 mm.

(Reported - b.p. 121°/12 mm.; n_D^{30} 1.4797)

2. With Thionyl Chloride and Pyridine

A solution of 25.5 g. (0.204 mole) of <u>trans</u>-2-cyano-1-cyclohexanol in 33.8 g. (0.428 mole) of pyridine was added dropwise to 48.6 g. (0.408)mole) of thionyl chloride at such a rate as to maintain the thionyl chloride solution at reflux. The solution was refluxed an additional two and one-half hours after the addition had been completed. After cooling with an ice bath the mixture was poured into an ice-hydrochloric acid solution. The resulting oil was dissolved in methylene chloride, and the solution washed several times with water, then with aqueous sodium bicarbonate solution until the washings were basic and then again with water. After the solution had been dried over anhydrous sodium sulfate, the solvent was removed and distillation of the oil yielded 18.0 g. (62 o/o) of product boiling at 123-126° at 14 mm. (n_D^{30} 1.4793). Redistillation gave the following at 1 mm:

(1)	-92°	3.5 g.	n_D^{30} 1.4788
(2)	92-93°	9.4 g.	n_D^{30} 1.4792
(3)	92-93°	3.0 g.	n_D^{30} 1.4792

(Reported[44] for cut (3) - b.p. 121°/12 mm.; n_D^{30} 1.4797)
Yield based on cuts (2) and (3) is 43 o/o.

D. Attempted Preparation of <u>trans</u>-2-Cyano-1-Chlorocyclohexane

1. Preparation of Cyclohexanone Cyanohydrin

To 1000 cc. of a saturated solution of sodium bisulfite was added, with vigorous stirring, 200 g. (2.04 mole) of cyclohexanone. Stirring was continued until the mixture cooled to room temperature (*ca*. one to one and one-half hours) at which time it was cooled in an ice-bath and filtered. The residue was washed with alcohol and ether and then dried to give 315-345 g. (76-84 o/o) of product.

A sufficient amount of water was added to 202 g. (1.0 mole) of the bisulfite addition-product to make a thick paste and 75 g. (1.2 mole) of potassium cyanide in 125 cc. of water was added. The mixture was vigorously stirred for one hour and at the end of this time the product was extracted with ether. The ether solution was thoroughly washed with water and dried over anhydrous sodium sulfate. After removal of the ether distillation at 2 mm. yielded 53 g. (70 o/o) of cyclohexanone cyanohydrin boiling at 92-94°. (m.p. 27-28°; reported[44] m.p. 26°)

2. Reaction of Thionyl Chloride with Cyclohexanone Cyanohydrin

Fifty grams (0.40 mole) of cyclohexanone cyanohydrin was treated with 52 g. (0.43 mole) of thionyl chloride as directed by Van Coillie.[44] After standing for twelve hours at room temperature, the reaction mixture was heated on a steam bath until the evolution of hydrogen chloride ceased. Seven reaction mixtures were then combined and the excess thionyl chloride removed by distillation and the material distilling at 85-125°/12 mm. collected. This material was redistilled through a 60 cm. distilling column at 12 mm. and 52 g. (7 o/o) of cis-2-cyano-1-chlorocyclohexane (n_D^{30} 1.4789; reported[44] b.p. 121°/12 mm, n_D^{30} 1.4797) was obtained, but no trans-2-cyano-1-chlorocyclohexane.

3. Preparation of trans-1,2-Dichlorocyclohexane

Eighty two grams (1.0 mole) of cyclohexene was chlorinated at 30-40° in the absence of light with chlorine gas until the increase in weight amounted to 35 g. (50 o/o theoretical) as directed by Carroll et. al.[48] Distillation through a 60 cm. column filled with glass helices yielded 36 g. (25 o/o) of trans-1,2-dichlorocyclohexane distilling at 88-89°/30 mm. (n_D^{25} 1.4879). Reported[48] refractive index n_D^{25} 1.4879.

a. Trans-1,2-Dichlorocyclohexane with Potassium Cyanide

A solution of 10.5 g. (0.16 mole) of potassium cyanide in 25 cc. of water was added to a solution of 25 g. (0.15 mole) of trans-1,2-dichlorocyclohexane in 150 cc. of 95 o/o alcohol and refluxed for three hours. The alcohol was removed by distillation and the residue extracted with ether. The ethereal solution was dried over anhydrous sodium sulfate and distilled to give 4.7 g. of dichlorocyclohexane boiling at 82-83° at 16 mm. (n_D^{25} 1.4876). Water was added to the alcoholic distillate (which was an azeotropic mixture) until the separation of oil ceased and the resulting oil distilled to yield 11.1 g. of dichlorocyclohexane boiling at 81-83° at 15 mm. (n_D^{25} 1.4878). Extraction of aqueous alcohol with 30-60° petroleum ether afforded an additional 1.5 g. of dichlorocyclohexane on distillation (n_D^{25} 1.4878). There was no evidence throughout the procedure of any higher boiling material.

The above procedure was modified in that (1) n-propyl alcohol was used as the solvent (2) 100 per cent excess potassium cyanide was employed and (3) the material was refluxed for three days. This reaction mixture was treated as previously indicated and only the 1,2-dichlorocyclohexane could be isolated with no evidence of any higher boiling material.

b. Trans-1,2-Dichlorocyclohexane with Cuprous Cyanide

Thirty two grams (0.21 mole) of trans-1,2-dichlorocyclohexane was refluxed (190-200°) with 18.7 g. (0.21 mole) of dry cuprous cyanide for four hours. The liquid was decanted from the solid and distillation gave 16.9 g. of product boiling at 81-83° at 16 mm. The cuprous cyanide residue was washed with ether and distillation of this solution gave an additional 7.4 g. of starting material boiling at 83-85° at 17 mm. There was no evidence of the formation of the nitrile.

E. Reaction of Phenylmagnesium Bromide with cis-2-Cyano-1-Chlorocyclohexane

A solution of 5.0 g. (0.035 mole) of cis-2-cyano-1-chlorocyclohexane in 35 cc. of anhydrous ether was placed, under a nitrogen atmosphere, in a 100 cc. three necked flask fitted with a mercury sealed stirrer and cooled in an ice bath. Forty cc. (0.035 mole) of phenylmagnesium bromide dissolved in ether was placed in a dropping funnel and 1-2 cc. added to the chloronitrile solution. The ice bath was removed for 2-3 minutes to start the reaction and then the remainder of the Grignard solution was added dropwise over a one and one-half hour period. This complex was decomposed by pouring into 250 cc. of ice water containing 10 cc. of concentrated sulfuric acid. The ether layer was separated and the aqueous layer extracted with 25 cc. of ether. The aqueous layer, containing the imino salts, was permitted to stand at room temperature, and in several hours crystals began to form. After standing overnight, the aqueous phase was filtered to yield 0.8 g. (14 o/o based on reacted chloronitrile) of cis-2-chloroketone melting at 96-99°. (On one occasion, the solid oiled on standing and was recrystallized by dissolving it in cold 60-90° petroleum ether and cooling the solution in a Dry Ice-acetone bath.) Recrystallization from 70-90° petroleum ether gave crystals melting at 100-101° which, when mixed with the chloroketone obtained by the addition of hydrogen chloride to 1-cyclohexenyl phenyl ketone, showed no melting point depression.

IV. ELIMINATION OF HYDROGEN CHLORIDE FROM cis-2-CHLOROCYCLOHEXYL PHENYL KETONE

A. Thermal Elimination

Eight grams (0.036 mole) of cis-2-chlorocyclohexyl phenyl ketone was heated at 120-125°, under vacuum, until the evolution of hydrogen chloride had ceased (ca. fifteen minutes) and was then distilled at 1.5 mm. to give 5.5 g. (83 o/o) of colorless oil boiling at 133-134° (n_D^{25} 1.5653). The oil easily crystallizes to give 1-cyclohexenyl phenyl ketone melting at 31-32° (λ_{max} (alc.) 245). This forms a semicarbazone melting at 201-203° and recrystallization from alcohol-water yielded a product melting at 205-207°. Dry hydrogen chloride was passed into a solution of 0.80 g. (0.0043 mole) of the olefin dissolved in 10 cc. of anhydrous ether and cooled in an ice-bath. Removal of the ether with an aspirator afforded 0.83 g. (87 o/o) of crystals melting at 90-94°. Two recrystallizations from 60-90° petroleum ether gave crystals melting at 99-100°.

B. Ionic Elimination

1. Equimolar Amount of Potassium Hydroxide

To a solution of 8.0 g. (0.036 mole) of <u>cis</u>-2-chlorocyclohexyl phenyl ketone dissolved in 60 cc. of 95 o/o alcohol was added with shaking 2.0 g. (0.036 mole) of potassium hydroxide. At the end of ten minutes, all of the potassium hydroxide had dissolved and the precipitation of potassium chloride had ceased. The neutral alcoholic solution was filtered to give 2.0 g. (74 o/o) of potassium chloride and the alcohol removed under vacuum. Distillation at 0.7 mm. afforded 5.1 g. (76 o/o) of colorless oil (n_D^{25} 1.5652) boiling at 125-128°. The oil easily crystallizes to give 1-cyclohexenyl phenyl ketone melting at 31-32°. Treatment of this with semicarbazide hydrochloride and sodium acetate gave a semicarbazone melting at 200-203°. Recrystallization from 70 o/o alcohol yielded crystals melting at 205-207° which, when mixed with the semicarbazone of the unsaturated ketone obtained by thermal decomposition of the chloroketone, showed no depression in melting point.

2. Excess Potassium Hydroxide

To a solution of 3.2 g. (0.054 mole) of potassium hydroxide in 75 cc. of alcohol was added 7.8 g. (0.035 mole) of *cis*-2-chlorocyclohexyl phenyl ketone. Potassium chloride began to precipitate immediately and within twenty minutes the solution became a dark red. After the solution had stood for one-half hour at room temperature and ten hours in the refrigerator, it was neutralized with 6 *N* hydrochloric acid. to give a light straw colored solution. The alcohol and water were removed and distillation gave 4.2 g. (65 o/o) of colorless oil (n_D^{25} 1.5578) boiling at 136-138° at 2 mm. All attempts to crystallize this oil failed.

V. REACTION OF 1-CYCLOHEXENYL PHENYL KETONE WITH ALCOHOLIC POTASSIUM HYDROXIDE

A. Room Temperature

To a solution of 0.5 g. (0.09 mole) of potassium hydroxide in 15 cc. of alcohol was added 2.5 g. (0.013 mole) of 1-cyclohexenyl phenyl ketone. The solution immediately became colored and at the end of five minutes was a dark red. After standing for fifteen hours at room temperature, the solution was neutralized with 6 N hydrochloric acid to give a light yellow solution. After the mixture had been filtered and the solvent removed, distillation at 0.5 mm. gave 1.3 g. of oil (n_D^{25} 1.5500) boiling at 115-118°. No crystalline material could be obtained from this oil.

B. At Reflux

A solution of 6.3 g. (0.034 mole) of 1-cyclohexenyl phenyl ketone and 2.0 g. of potassium hydroxide in 30 cc. of 95 o/o alcohol was refluxed for two hours. The solution was cooled and neutralized with 6 N hydrochloric acid. After the solvent had been removed, the oil was distilled to yield 3.1 g. of oil boiling at 120-123° at 0.7 mm. (n_D^{25} 1.5567). Two and seven tenths of a gram of this oil was dissolved in 10 cc. of 95 o/o alcohol containing 0.5 g. of potassium hydroxide. After the solution had been standing at room temperature for fifteen hours, it was neutralized with 6 N hydrochloric acid and the solvent removed. Distillation yielded 1.3 g. of oil distilling at 116-118° at 0.5 mm. (n_D^{25} 1.5519).

VI. PHYSICAL MEASUREMENTS

A. Dipole Moments*

The apparatus used was the same as that used by Kraus and Conciatori.[60] "The dielectric constant determinations were carried out by a resonance method with a probable error in ϵ of 0.08 o/o. The electrical apparatus consisted of a voltage regulated power supply, an electron coupled oscillator, detector, and a direct current amplifier. The plate circuit of the oscillator was tuned to the second harmonic of the grid circuit so that the frequency of oscillation would be independent of

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* The author wishes to express his gratitude to Dr. Gerard Kraus, whose considerate assistance and direction made this work possible.

[60] G. Kraus and A. Conciatori, J. Am. Chem. Soc., 72, 2283, (1950).

plate circuit tuning. The plate circuit was tuned by a 0-1400 $\mu\mu f$. precision condenser in parallel with the dielectric constant cell. The plate circuit voltage, after rectification and amplification, was read on a microammeter. The measuring cell was of the type described by Smyth[61]."

The capacitance measurements were made by tuning the apparatus to resonance with the measuring cell disconnected and the precision condenser setting at resonance was recorded. The cell was then connected in parallel with the precision condenser and the circuit again adjusted to resonance. The capacity difference between the two condenser readings represented the capacitance of the unknown cell.

Densities were measured with a 10 cc. pyknometer and the refractive indices were taken with an Abbe refractometer.

4-Chlorocyclohexyl Phenyl Ketone (30°)

W_2	ϵ	v	n_D
0.00	2.289	1.1531	1.4933
0.005659	2.309	1.1524	1.4936
0.009266	2.320	1.1516	1.4937
0.01337	2.351	1.1500	1.4939
0.01803	2.371	1.1481	1.4940

$\alpha = 4.60$ $\beta = -0.27$ $\gamma = 0.04$ $\mu = 3.08$D

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[61] C. Smyth, "Dielectric Constant and Molecular Structure", Chem. Catalog Co., New York, N.Y., 1931, p. 60.

cis-2-Chlorocyclohexyl Phenyl Ketone (30°)

w_2	ϵ	v	n_D
0.00	2.289	1.1531	1.4933
0.004370	2.320	1.1510	1.4936
0.008678	2.354	1.1516	1.4943
0.01280	2.385	1.1501	1.4947
0.01856	2.432	1.1472	1.4942

$\alpha = 7.69$ $\beta = -0.30$ $\gamma = 0.9$ $\mu = 3.95$ D

B. Infra Red Data

Infra red determinations were made by Dr. A.I. Kosak at the Cincinnati Kettering Laboratory and the Baird Laboratory in Stamford, Conneticut. He also interpreted the results with the assistance of individuals at both laboratories, especially Dr. W.A. Patterson of Baird.

C. Ultra-Violet Data

Ultra-violet measurements were made using a Beckman quartz prism spectrophotometer. Interpretation of the results were made with the able assistance of Dr. M. Orchin.

SUMMARY

A stereospecific synthesis of cis-2-chlorocyclohexyl phenyl ketone is reported. As a result of this synthesis, there is additional evidence for Van Coillie's structural assignments for the cis and trans-2-cyano-1-chlorocyclohexanes. In addition, the chloroketone obtained by the addition of hydrogen chloride to 1-cyclohexenyl phenyl ketone has been shown to be cis-2-chlorocyclohexyl phenyl ketone.

Both heterolytic and homolytic removal of hydrogen chloride from cis-2-chlorocyclohexyl phenyl ketone produce 1-cyclohexenyl phenyl ketone. This indicates that both ionic and thermal eliminations proceed via a trans mechanism.

As a consequence of the above material it can be concluded that the addition of hydrogen chloride to 1-cyclohexenyl phenyl ketone involves a stereospecific addition.

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