

THE UNIVERSITY OF MINNESOTA

GRADUATE SCHOOL

Report

of

Committee on Examination

This is to certify that we the undersigned, as a committee of the Graduate School, have given Arnold Erwin Osterberg, final oral examination for the degree of Master of Science. We recommend that the degree of Master of Science be conferred upon the candidate.

Minneapolis, Minnesota

May 24, 191²¹

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REPORT
of
Committee on Thesis

The undersigned, acting as a Committee of the Graduate School, have read the accompanying thesis submitted by Arnold Erwin Osterberg for the degree of Master of Science in Chemistry. They approve it as a thesis meeting the requirements of the Graduate School of the University of Minnesota, and recommend that it be accepted in partial fulfillment of the requirements for the degree of Master of Science in Chemistry.

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THESIS

STUDIES CONCERNING CERTAIN DERIVATIVES OF
CYCLOHEXANE

Arnold Erwin Osterberg

Submitted to the Graduate Faculty of the
University of Minnesota in partial fulfil-
ment of the requirements for the degree of
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Cyclohexane derivatives of natural and synthetic origin have been studied at considerable length by many investigators since the classic work of Baeyer¹ in 1893. Baeyer and his students definitely proved the identity of hexamethylene derivatives prepared from aliphatic compounds and of those derived by direct reduction of cyclic substances. These researches prompted many investigators among whom may be mentioned Perkin, Jr., Griess, Aschen, Markowmikoff, Ipatiew, Sabatier, Selinski, Skita, and Wallack, to continue in this field. As a result many naturally occurring terpens have been synthesized and their identity proven. Certain hydrocarbons found in Caucasian and American oils have been shown to be identical with synthetic cyclohexamethylene compounds, and numerous other related hydroaromatic substances have been produced.

The work of Baeyer and his students on the production of cyclohexamethylene derivatives from succino-succinic ester and the proof of their identity with substances obtained by direct reduction with sodium and alcohol of ring structures such as terephthalic acid was of great value and invited many workers to study ways and means for more easy and quantitative production of cyclohexane derivatives by direct reduction of the corresponding benzene compounds. The methods developed may be roughly classed into four groups. It may be generally said that each method has its own special applications and in such cases is the only procedure to be followed. However, in many instances where the same object may be obtained by two or more methods, ease of manipulation and yields are the controlling factors in choosing which to use.

1. The direct reduction by means of nascent hydrogen generated from sodium and ethyl or amyl alcohol was studied by the earlier workers, Aschen², Einhorn³, Baeyer and others. The method serves well for production of small amounts

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of substances but since large excesses of sodium and solvent are necessary to complete the reaction it is not to be preferred if a more direct catalytic method is available.

2. The method introduced by Paul⁴ accomplishes reduction by means of hydrogen and a catalyst of colloidal palladium or platinum using various solvents, such as water alcohol and acetic acid together with a small amount of a protective colloid, such as gum arabic. The pressure used may vary from slightly below atmospheric to one or two atmospheres. This procedure has been variously applied, more particularly, however, in the hydrogenation of fats and oils, reduction of aldehydes, ketones and unsaturated aliphatic compounds. Good yields of cyclohexane, cyclohexanol and derivatives of these have been obtained by this method, but have only been prepared in small quantities as the absorption of hydrogen in these cases is slow. The ease by which the catalyst may be rendered inactive is an important factor in this method. Willstatter and Hatt⁵ state that .01 mg. of thiophene per gram of benzene renders a colloidal platinum catalyst entirely inactive. The reaction proceeds smoothly and very efficiently for the preparation of small quantities of hydroaromatic compounds provided the catalyst remains active. It has a particular field in the preparation of those compounds which do not permit of high temperatures without production of side reactions.

3. The method of Sabatier and Senderens has been used quite extensively for the commercial production of cyclohexane and cyclohexanol. The vapors of the cyclic compound together with hydrogen at atmospheric pressure are passed over a suitable metallic catalyst at temperature in the neighborhood of 160° to 200°, the temperature depending on the substance. It is perhaps the most common one in use in the laboratory. In contrast to the method of Ipatiew the necessary apparatus is not of a special nature. The method gives good results if a very active catalyst is used. Considerable difficulty

has been experienced in obtaining good yields of cyclohexane and cyclohexanol from benzene and phenol respectively. This failure is due no doubt to poisoning of the catalyst by sulphur compounds ordinarily present in commercial benzene and phenol and removed only by prolonged treatment. Richards and Barry⁷ after careful attention to the many details recount the difficulties in obtaining complete reduction by this method. By passing the mixture of benzene and cyclohexane vapors through the heated coil as many as eight times the reduction is brought to completion. They give as their yield 120 gms. of pure cyclohexane from 800 gms. of benzene.

4. The method brought out by Ipatiew⁸ overcomes in a great part the difficulties of the three previous groups. The substance to be reduced together with a metal oxide catalyst being placed in a suitably constructed bomb which can be filled at intervals with hydrogen under pressure of 115 to 120 atmospheres, the whole being subjected to temperatures of approximately 250° until reduction is complete. The higher temperature and pressure used tends to counteract the decreased activity of a partially poisoned catalyst. It possesses a disadvantage, however, in that a specially constructed type of bomb is necessary. However, a very simple and serviceable one may be made from an ordinary commercial oxygen tank as shown in Figures 1 and 2.

The bomb (A) is a small oxygen tank, capacity about 1100 c.c. It is fitted with the yoke (B) and a removable piece (C) shown in cross section in Figure 2. The yoke (B) is hinged at (D) so that it may be swung back for the purpose of filling and emptying bomb when (C) is removed. Screw (E) holds (C) in place. (F) is the connection to flexible brass tubing leading to the hydrogen tank connected at (G). The dial (H) registers pressure in the hydrogen tank or bomb depending on which valves are open. Lead washers are used at all pressure connections. Figure 2 represents in detail the cross section of piece C and is self explanatory, connections being made as indicated on the diagram.

The process requires very little attention other than periodic filling and emptying of the bomb. The reaction proceeds to completion with a catalyst much less reactive than that necessary to obtain any reduction by the Sabatier method. The high pressure needed is obtained by use of commercial hydrogen sold in tanks at a pressure of 1800 pounds per square inch. Without materially slowing up the reaction the hydrogen tanks may be used without replacement until the pressure has decreased to approximately 1000 pounds.

During the past year in connection with work upon the production of hydro-heterocyclic compounds it was necessary to prepare considerable quantities of cyclohexane, cyclohexanol and some of their derivatives. These are not procurable on the market although the first two mentioned have been previously articles of commerce.

In seeking a method which could be standardized for the preparation of cyclohexane and cyclohexanol I have used for reasons given above, that of Ipatiew. By this process there has been prepared some thirty kilos of hexahydrophenol, the method being found very satisfactory. Nothing new is offered in the preparation of these compounds but they are the necessary starting materials for the production of a series of new substances which I wish to describe, I shall also outline somewhat in detail the procedure found most satisfactory for the preparation of cyclohexane, cyclohexanol, cyclohexylamine, cyclohexene and the more simple well known members of this series since even after a careful perusal of the literature one is in doubt as to which to follow.

A study of *o*-di-substituted derivatives of cyclohexane offers many opportunities in determining the effects of one group on the activity of the other, since these compounds lie intermediate to aliphatic and aromatic substances. Studies on *o*-di-substituted derivatives of the cyclohexane series are relatively few and these are confined mainly to compounds in which the groups are similar such as the di-brom and di-chlor prepared from cyclohexane.

A few compounds in which the other groups are dissimilar have brief mention in the literature. For example, *o*-iodo chlorocyclohexane,⁹ iodo-cyclohexanol,¹⁰ *o*-iodo-brom cyclohexane¹¹ and *o*-cyan iodocyclohexane.¹² In addition I shall describe the preparation of *o*-amino-cyclohexanol and *o*-chlor-cyclohexylamine together with some of their derivatives.

Experimental

Preparation of a catalyst. Metallic nickel was used almost exclusively. Pure nickel/nitrate is calcined at a dull red heat for an hour, cooled and very finely ground. It may be heated again to a red heat to insure complete decomposition of the nitrate. The powdered nickel oxide is then reduced in a stream of hydrogen at 250° for several hours. It is allowed to cool over night in an atmosphere of hydrogen and placed in a tightly stoppered flask until used. This catalyst used in proportion of one part catalyst to ten of substance remains in an active state for five or six reductions. If the reduction is proceeding too slowly it is best to replace the old by fresh unused nickel.

Cyclohexane

Commercial benzene is purified by repeated washing with concentrated sulphuric acid until the washings give a negative isatin test for thiophene. The sulphuric acid is removed by shaking with sodium carbonate and water, the benzene dried and distilled.

Three hundred grams of purified benzene and 30 gm. of nickel catalyst are placed in the bomb, and shaken well to obtain a good distribution of the nickel. The bomb is placed in an electrically heated hot air oven at 250° and filled with hydrogen at 1800 pounds pressure; at intervals of two hours during the day more hydrogen is introduced to replace that which has reacted. At night the bomb is not refilled but is allowed to remain in the oven.

At the end of forty-eight hours the reaction is complete as shown by the fact that the dial (H) registers no decrease in pressure when the valve (K) is opened. The bomb is then removed, cooled and the contents poured into a distilling flask and distilled. The fraction boiling between 80 and 85 is collected and is sufficiently pure for synthetic work. If desired the small amount of benzene present may be removed by treatment with sulphuric acid or ethyl tartrate. The nickel remaining in the flask is washed back into the bomb with the next run and used again. Yield 275 grams or 85 per cent of theory.

Cyclohexanol

Commercial U.S.P. phenol is used, purified by one distillation. Three hundred grams of the crystals are melted and poured into the bomb together with 30 gm. of nickel. The reduction is carried out precisely as given above for benzene. When completed the reaction product is fractionated, the fraction boiling at 158° at 730 mm. being practically pure cyclohexanol. A small amount of cyclohexane and water is formed and is collected in the lower fraction, boiling between 80° and 110°. If the reduction has not proceeded to completion some tetrahydrophenol, distilling at 165°, is formed. This may be returned to the bomb with the next run and the reduction completed. The nickel is also returned. Yield of cyclohexane 255 gm. or 80 per cent of theory.

Cyclohexanone

¹³Baeyer prepared this substance by the oxidation of cyclohexanol with Beckman's chronic acid mixture and proved its identity with the ketohexamethylene obtained by Perkin, Jr. ¹⁴from calcium pimelate. Baeyer used a proportion of 2 gm. of cyclohexanol to 27 gm. of the chronic acid mixture. The method used here is essentially the same, modified slightly to keep the volumes down when dealing with 100 gm. portions.

One hundred grams of cyclohexanol and 150 c.c. of water are placed in a one liter flask and cooled in ice water. To this is added gradually 35 c.c. of concentrated sulphuric acid.

One hundred grams sodium dichromate ($\text{Na}_2\text{Cr}_2\text{O}_7 \cdot 2\text{H}_2\text{O}$) are dissolved in a solution of 35 c.c. of concentrated sulphuric acid in 150 c.c. of water. The chromic acid solution is added to the cyclohexanol mixture in 10 c.c. portions over a period of two hours, shaking well after each addition. To complete the reaction the mixture is heated in a water bath for two hours, cooled and ether extracted, the extract dried with potassium carbonate and the ether distilled off. The cyclohexanone boils constantly at 155. Yield 83 gm. or 85 per cent of theoretical.

Ortho-chlor-cyclohexanone

This may be prepared by a method similar to that used by Kotz¹⁵ for the corresponding bromine compound.

Chlorin is bubbled through a mixture of 20 gm. of cyclohexanone, 15 gm. of calcium carbonate and 50 c.c. of water in a flask immersed in cold water, until the reaction is complete. The oil is extracted with ether, dried and the ether removed. The oil does not distill in vacuo without decomposition and is difficult to obtain pure and free from chlorine.

Attempts to form an aminoketone invariably led to condensation products, and secondary and tertiary amines.

Cyclohexanone oxime

¹⁶Baeyer obtained the oxime in theoretical yield allowing the ketone to react with hydroxylamine hydrochloride and excess sodium bicarbonate in alcohol at water bath temperature, extracting the residue with ether and recrystallizing from petroleum ether. It may also be obtained with equal facility and in theoretical yield in water solution by the following method.

Eight and four tenths grams of hydroxylamine sulphate in 60 c.c. of water are added in small portions in a mixture of 10 gm. of cyclohexanone and 50 c.c. of water containing 4.1 gm. of sodium hydroxide or excess bicarbonate.

The reaction flask should be continually shaken and cooled under a tap of water. When nearly all the hydroxylamine has been added the oxime separates as a crystalline solid and is filtered off immediately, washed with water and dried. If the reaction mixture is not cooled a red color is developed and the yield decreased. The dried product recrystallized from boiling ligroin melts at 88.

Cyclohexylamine

Many attempts to prepare cyclohexylamine by direct catalytic reduction of aniline have at the best resulted in very poor yields. By Paul's¹⁷ method a yield of 10 per cent has been obtained in eighty hours. The use of Sabatier and Senderens method results in destruction and numerous side reactions. Ipatiew¹⁸ reports a yield by his method of 40 to 50 per cent, using nickel oxide on a catalyst and a pressure of 115 to 120 atmospheres. I have attempted to use Ipatiew's method with a nickel catalyst but it has invariably resulted in such great destruction and production of side reactions as to cause its abandonment.

Cyclohexylamine may be obtained in good yield by reduction of ketchexamethyleneoxime by either Sabatier and Senderens¹⁹ method or that of Baeyer.²⁰ In Baeyers procedure 5 gm. of the oxime are dissolved in 200 c.c. of absolute alcohol and added to 25 gm. of sodium. It is best to dissolve all the oxime in a small amount of alcohol, and add the solution to the sodium. Additional alcohol is then poured through the reflex condenser. In this way all the oxime is present during the entire reaction.

Ten grams of cyclohexanone oxime in 30 c.c. of absolute alcohol are added through a reflex condenser to 50 gm. of sodium strips. An additional 400 c.c. of absolute alcohol is now added. When the reaction is complete the alcohol is distilled from a water bath, water is added and the solution made acid with hydrochloric acid. The acid solution is evaporated to dryness on a water bath with the help of an air blast. A small amount of water is added (20 c.c.) and excess solid potassium hydroxide. The oil which separates is

ether extracted, dried, and distilled after removal of the ether. Boiling point 133° . It distills with some decomposition and takes up carbon dioxide very rapidly, consequently is best distilled in a stream of hydrogen as Baeyer recommends. However, it is not necessary if the receiver is protected with a soda lime tube. Melting point of carbonate 110° , hydrobromide 195° , hydrochloride 204° , acetate 147° , acetyl 99° , dithiocarbamide 178° .

Cyclohexane

Many methods have been proposed for the production of cyclohexane from cyclohexanol using various dehydrating agents. It is also frequently made by treating monohalide cyclohexanes with alkalis, such as calcium oxide²¹ and quinoline. Among the dehydrating agents may be mentioned particularly oxalic acid,²² iodine,²³ sulphuric acid,²⁴ dimethyl sulphate²⁵ and potassium bisulphate.²⁶

Zelinsky using one part cyclohexanol to five parts of anhydrous oxalic acid at 100° to 110° , obtained cyclohexane. In using this method it has been found that this proportion may be considerably increased and good yields obtained. The process may be made continuous by addition of cyclohexanol as the tetrahydrogenesene and water distills over and with occasional addition of anhydrous oxalic acid to replace that which is destroyed or distills over as the ester of cyclohexanol.

The objection to using dimethyl sulphate is of course, obvious, calcium oxide requires a temperature of 350° and special apparatus, potassium bisulphate gives poor yields due to formation of cyclohexyl ether. The catalytic sulphuric acid method described by Senderens is easy of application and gives practically a 90 per cent yield. The procedure followed is precisely that of the above worker.

One hundred grams of cyclohexanol and 2 c.c. of concentrated sulphuric acid are slowly distilled until white fumes are evolved and the odor of sulphur dioxide is apparent. The water and cyclohexene in the distillate

are separated in a separating funnel, the cyclohexane dried with potassium carbonate and redistilled. Sixty grams of pure cyclohexene boiling 82° to 84° are obtained and 16 gm. of a higher boiling fraction consisting of a mixture of unacted on cyclohexanol and cyclohexene. Yield of pure cyclohexene 75 per cent. This may be increased to approximately 90 per cent by retreating the higher fraction with the next run.

In searching for other agents which would serve to dehydrate cyclohexanol to cyclohexene, phosphorous trichloride has been found to be fairly efficient. Its disadvantage lies in the amount of phosphorous trichloride necessary to be used and in the mechanical losses of cyclohexene which occur. About a kilo of cyclohexene has been prepared by the following method.

Two hundred and seventy-four grams of phosphorous trichloride are added slowly through a dropping funnel to 300 gm. of cyclohexanol in a one liter flask fitted with a reflux condenser. The temperature is maintained at 70° by immersion in a water bath. Addition of the first mole (137 gm.) of phosphorous trichloride produces a vigorous reaction but the second may be added more rapidly. When all phosphorous trichloride has been added the product is refluxed for four hours and then distilled from the phosphorous oxide. One hundred and fifty c.c. of water are added to the distillate through a reflux condenser and the mixture is refluxed for a short time to decompose all excess phosphorous trichloride. The cyclohexene is separated from the aqueous layer, dried and distilled. Yield 65 per cent of theory or 160 gm. of tetrahydrobenzene boiling between 82° and 87° and 30 gm. of a fraction boiling 87° to 160° .

It is necessary to have the cyclohexanol warm when the trichloride is added as otherwise considerable mono-chlorocyclohexane is formed which is not broken down by subsequent treatment and may be obtained in the final distillation as the fraction boiling at 143° .

Ortho-chlor-cyclohexanol

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This substance, described by Fortey, was made by shaking tetrahydrobenzene with a dilute hypochlorous acid solution. The hypochlorous acid being made by passing chlorine into water containing freshly precipitated mercuric oxide. She described it as a yellowish oil distilling with decomposition and having a characteristic odor. Prepared by the following method it is a water white oil possessing a characteristic odor, distilling in vacuum with no decomposition and at atmospheric pressure with only slight destruction.

One hundred c.c. of cyclohexene (about three times theoretical) is shaken with 1700 to 1800 c.c. of a 2 per cent hypochlorous acid solution adding the acid in 200 c.c. portions and shaking until decolorized before addition of more. When all hypochlorous acid has been added the mixture is shaken until 1 c.c. gives only a faint or not yellow color with potassium iodide solution. The hypochlorous acid has always been made by bubbling carbon dioxide through a suspension of calcium hypochlorite in water and filtering off the calcium carbonate. The reaction product is now saturated with salt and steam distilled. The distillate is saturated with salt and the upper layer of cyclohexene and ortho-chlor-cyclohexanol removed and fractionated. The first fraction, boiling, below 90 at 20 mm. is a mixture of water, unacted on cyclohexene and some ortho-chlor-cyclohexanol which may be used again. The ortho-chlor cyclohexanol boils at 92 under pressure of 20 mm. Yield 85 gm.

Substance .1236 gm. Ag Cl .1298 gm.

Calculated for $C_6H_{11}OCl$; Cl 26.35 per cent. Found 25.99 per cent.

Preparation of ortho-amino cyclohexanol

No mention of this substance has been found in the literature although it is easily prepared from ortho-chlor cyclohexanol and alcoholic

amonia the chlorine being substituted by the amino group. In aqueous solutions secondary and tertiary amines are the chief products but if sufficient strength of alcohol is used to maintain a clear solution the primary amine is the chief product.

For the preparation of the free amine the following has been found to be the best procedure; 26.8 gm. ($1/5$ mol.) of ortho-chlor cyclohexanol is placed in a pressure bottle (the ordinary citrate of magnesia bottle fitted with a rubber stopper which can be clamped down is satisfactory) and 100 c.c. of a strong solution of amonia in 50 per cent alcohol is added. If the solution is not clear a higher per cent of alcohol should be used. The bottle is shaken well and is then heated in a steam bath for three hours. The contents of five such bottles after cooling are poured into a liter distilling flask, 40 gm. of stick sodium hydroxide added and the alcohol and water distilled off, the temperature should be allowed to rise to 110° and be maintained there until the greater portion of water is removed. Two hundred c.c. of acetone are added and the mixture refluxed for one-half hour. The salts are removed by filtering the hot solution with suction, washing the precipitate well with acetone. The acetone is removed by distillation and the residue fractionated in vacuo, using the side neck of the flask as a condenser and immersing the receiver flask in ice water.

The pure ortho-amino-cyclohexanol boils at 120° at 20 mm. and crystallizes in the receiver in rosettes which melt at 65° . Yield 70 gm.

Substance 10 mg. Amino nitrogen 2.19 c.c. at 21° 734 mm.

Calculated for $C_6H_{13}ON$; N, 12.17 per cent. Found 12.00, per cent

Melting points of salts made from the corresponding acid and an ether solution of the amine. Hydrochloride 175° , hydroiodide 187° , hydrobromide 191° , carbonate 139° , sulphate not melted at 250° .

The diacetyl made by refluxing ortho amino-cyclohexanol with excess acetic anhydride in chloroform, crystallizes from ether in flat plates. m.p. 115° . The hydrochloride salt from ether m.p. 202° .

Ortho-chlor-cyclohexylamine

In attempting to prepare orthohalogen cyclohexylamine, ortho-amino cyclohexanol was treated with fuming hydriodic acid in a sealed tube at temperatures from 100° to 150°. It was found that the iodine did not replace the hydroxy group at a temperature below 130° while at higher temperatures there was a deep seated decomposition, with the separation of ammonium iodide. Hydrobromic acid also failed to substitute. Thionyl chloride does not replace the hydroxy group even when refluxed at the boiling point. Phosphorous trichloride does not substitute the hydroxy group with chlorine, producing instead an ester of phosphorous acid. The great resistance of the hydroxy group suggested the necessity of using phosphorous pentachloride. When this was tried in chloroform a very poor yield of orth-chlor-cyclohexylamine was obtained. Future investigations showed that phosphorous oxychloride readily reacts with ortho amino cyclohexanol in chloroform even at a temperature of 0°, forming the phosphoric acid ester. If however, the hydrochloride of ortho amino cyclohexanol is suspended in chloroform the reaction with phosphorous oxychloride is practically suppressed. Phosphorous pentachloride, even at 0°, reacts vigorously with the hydrochloride of ortho amino cyclohexanol.

The reaction product dissolved in water after the treatment with phosphorous pentachloride in chloroform, is made alkaline with sodium hydroxide, extracted with ether, the ether removed and the residue consisting of ortho-chlor-cyclohexylamine distilled in vacuo. Boiling point 85 at 15 m.m. pressure.

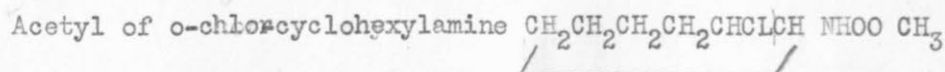
Fifty-seven and one-half grams (one-half mole) of ortho amino cyclohexanol are dissolved in 300 c.c. of chloroform. The chloroform is purified by treating first with phosphorous pentachloride, then with anhydrous ammonia and finally concentrated sulphuric acid. The chloroform solution is placed in a liter, Erlenmeyer Flask, with side neck and fitted with a one hole rubber

stopper, A few mg. of methyl orange are added and dry hydrochloride acid gas led in through a glass tube until the reaction is distinctly acid, indicating complete formation of the hydrochloride salt. The flask is cooled in ice water. One hundred and fifty grams of phosphorous pentachloride, ground in a dry mortar to a fine powder, and about 300 c.c. of purified chloroform are placed in the bottom of a one-quart mason fruit jar which is packed in an ice and salt mixture. To this suspension which is stirred mechanically and maintained below 0°C ., is added the mixture of ortho amino cyclohexylamine hydrochloride and chloroform. This will require approximately one hour. The solution may then be filtered. The hydrochloride of the ortho-chlor-cyclohexylamine is quite soluble in chloroform but a considerable portion will separate at 0° . The chloroform solution is now placed in a liter-distilling flask. One hundred c.c. of water are added and the flask placed under a reflux condenser. Occasional shaking will start the reaction, decomposing the phosphorous oxychloride. After the vigorous reaction has subsided it is refluxed in a water bath for not less than one and one-half hours, in order to decompose the last traces of phosphorous oxychloride. The chloroform is then distilled and the residue placed in a tall jar. The volume of the residue should be between 100 and 200 c.c. This is packed in ice and salt and a saturated solution of sodium hydroxide in water is added. The solution is stirred with mechanical stirrer until it becomes very thick. Ether is then added and sufficient sodium hydroxide to make the solution distinctly alkaline. Solid sodium hydroxide is now added and about 500 to 600 c.c. of ether. The salt separates in solid, dry, form and is readily extracted with ether. Three extractions are generally sufficient. The ether is dried over solid sodium hydroxide, removed by distillation and the ortho-chlor-cyclohexylamine distilled in vacuo. The yield depends upon the extent to which water is excluded and may reach 70 to 80 per cent of theory. If water is not completely

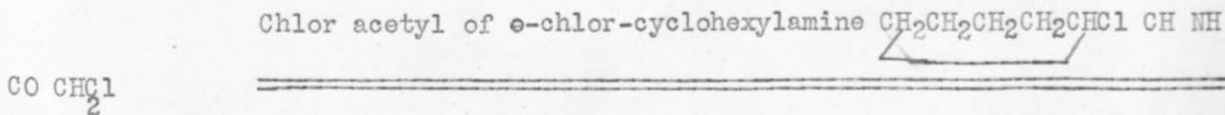
excluded the yield may drop as low as 50 per cent. The ortho-chlor-cyclohexylamine is a colorous oil of characteristic odor which does not solidify at 10°C.

Substance .1412 gm. Ag Cl.1510 gm. Calculated for C₆H₁₂NCl; Cl 26.55 per cent. Found 26.45 per cent.

Hydroanilides from o-amino cyclohexanol and o-chlor-cyclohexylamine may be quantitatively prepared by the usual methods in an indifferent solvent such as chloroform. As examples the preparation of the acetyl and chlor acetyl are given.



To 13.4 gm. of o-chlor-cyclohexylamine dissolved in 50 c.c. of anhydrous chloroform and immersed in ice water is added a solution of 12 gm. (one and one-half times theoretical) of acetyl chloride in chloroform. When all is added the solution is refluxed for about two hours. A small amount of alcohol is added to decompose the excess acetyl chloride and the chloroform distilled off on a boiling water bath. The residue may be recrystallized by dissolving in 90 per cent alcohol and diluting with water m.p. 88.



This procedure is identical to that given for the acetyl using one and one-half times the theoretical amount of chlor acetylchloride. It is recrystallized from alcohol by the addition of water. It is soluble in hot water one part in 220, in cold water one part in 2,000. The chlor acetyl of o-chlor cyclohexylamine melts at 111.

Substance .0882 gm. Ag Cl .1192 gm.

Calculated for C₈H₁₃ON Cl₂ Cl 33.76 per cent. Found 33.43 per cent.

Cyan acetyl of o-chlor cyclohexylamine $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CHCl CH NH CO}$

CH₂CN

The chlor acetyl of o-chlor-cyclohexylamine may be treated with large excesses of sodium cyanide in water at the boiling point for a short time with substitution taking place only on the side chain. The yield, however, is not particularly good since boiling in alkalis decomposes the nitrile present to some extent.

A mixture of 4 gm. of the chlor acetyl of o-chlor-cyclohexylamine and 4 gm. sodium cyanide in 400 c.c. of water is heated to boiling and boiled for ten minutes. The solution is then quickly made acid to methyl orange by addition of concentrated hydrochloric acid diluted one to one. About 15 c.c. are required. The cyan acetyl of o-chlor-cyclohexylamine crystallizes on cooling. Yield 2.3 gm. It may be purified by recrystallizing from hot water m.p. 139.

Substance .1357 gm. Ag Cl .0965 gm.

Calculated for $\text{C}_9\text{H}_{13}\text{ON}_2\text{Cl}$; Cl, 17.59 per cent. Found 17.59 per cent. Mono-ortho chlor hexahydro anilide of malonic acid $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH Cl CH NH CO CH}_2\text{COOH}$

This may be obtained by converting the corresponding cyan compound first to the ester and then hydrolyzing the ester to the sodium salt in aqueous sodium hydroxide.

Four grams of the cyan acetyl of o-chlor-cyclohexylamine are dissolved in 75 c.c. of alcohol which is then saturated with dry hydrochloric acid. It is refluxed for one hour while passing a stream of dry hydrochloric acid through the solution. The solution is concentrated to one-half, the ammonium chloride removed by filtering and the remainder of the alcohol distilled off in vacuo. The residue is taken up in water, 5 c.c. of 30 per cent sodium

hydroxide added and the product shaken until the saponification is complete. The alkaline solution is then acidified with hydrochloric acid and allowed to stand. The free acid crystallizes slowly. m.p. 132.

Substance .1598 gm. Ag Cl .1046 gm.

Calculated for $C_9H_{14}O_3CCl$; Cl 16.14 per cent. Found 16.17 per cent.

SUMMARY

Methods for obtaining cyclohexane derivatives by direct reduction of the corresponding benzenecompounds have been reviewed. The method of Ipatiew for the reduction of benzene and phenol has been particularly applied.

These methods, with some modifications which are most applicable in the laboratory production of cyclohexane, cyclohexanol, cyclohexamone and its oxime, cyclohexylamine and cyclohexene are described.

Methods for obtaining the following or the substituted cyclohexane compounds in which the ortho groups are dissimilar, chlor cyclohexane, chlor cyclohexanol, amino cyclohexanol, and chlor cyclohexylamine with certain of their derivatives are given.

BIBLIOGRAPHY

1. Baeyer, Adolf: Ueber die Constitutionen des Benzole d. deutsch chem. Gesellsch, 1886, xiv, 1797-1810. Ueber die Hydrirten Derivatives des Benzols. d. deutsch chem. Gesellsch. 1893, xxvi, 229-231. Ueber die Constitution des Benzols, Liebigs Annalen de Chemie, 1894, cclxxxviii, 88-116.
2. Aschan, Ossian: Ueber die Hydrirung der Benzoesaure. s. deutsch chem. Gesellsch. 1891, xxvi, 1864-1869, d. deutsch chem. Gesellsch, 1891, xxiv, 2617-2622.
3. Einhorn, A. und Meyenberg, A.: Ueber die Hexandroanthranilsaure und Hexahydrosalicylsaure d. deutsch. chem. Gesellsch, 1894, xxvii, 2466-2475, Ueber die Reduction der p. Dimethyl amido Benzoesaure. d. deutsch chem. Gesellsch. 1894, xxvii, 2829-2834.
4. Paul, C. und Amberger, C.: Ueber die Activirung des Wasserstoffe durch Colloidales Palladium. d. deutsch chem. Gesellsch, 1905, xxxviii, 1406-1407, Ueber katalytische Wirkungen kolloidaler metalle der Platingruppe, d. deutsch chem. Gesellsch, 1907, xl, 2201-2206.
4. Paul, C. und Gerum, J.: Ueber katalysische Wirkungen kolloidaler metalle der Platingruppe II, d. deutsch chem. Gesellsch, 1907, xl, 2209-2220.
4. Paul, C. und Roth, K.: Ueber katalysische Wirkungen kolloidaler metalle der Platingruppe V. Die Reduktion der Fette, d. deutsch chem. Gesellsch, 1909, xlii, 1541-1553.
4. Paul, C. und Gerum, J.: Ueber katalysische Wirkungen kolloidal metalle der Platingruppe VI. Reduktion katal son mit kolloidalen Palladium. d. deutsch chem. Gesellsch, 1909, xliii, 1883-1860.
4. Skita, A.: Ueber die katalytische Reduktion von Aldenhyden und Ketonen d. deutsch. chem. Gesellsch, 1915, xlviiii, 1486-1498.
4. Skita, A. Ueber die Reduktion von aromatischen Alkoholen, Aldenhyden, und Ketonen, Katalytische, Hydrungen, ungesattigten, Stoffe, d. deutsch. chem. Gesellsch, 1915, xlviiii, 1685-1698.
5. Willstatter, R.: und Hatt, D.P Hydrierung Aromatischen Verbindungen mit Platin und Wasserstoffe. d. deutsch. chem. Gesellsch, 1912, xlv, 1471-1481.
6. Sabatier, P. and Sanderens, J.B.: Nouvelle methode de preparation de l'aniline et des alcalis analoges. Compt. rend. Acad. d. sc. 1901, cxxxiii, 321-324.
6. Sabatier, P. and Sanderens, J.B.: Nouvelle methodes generales d'hydrogenation et de dedoublement moleculaire Bases sur l'emploi des metaux divises. Ann. de Chemie et de Physique. 8 s. 1905, iv, 319-488.
6. Sabatier, P. et Mailhe, A.: Syntheses d'alcohols dans la serie cyclohexanique, Ann. de chemie et de Physique, 1907, s.s. x, 527-574.

6. Sabatier, P. et Maihle, A.: Nouvelles applications de la methode generale d'hydrogenation par les metaux divises. Ann. de chemie et de Physique. 1909, 8 s. xvi, 70-107.
6. Sabatier, P. et Marat, M.: Hydrogenation directe par caralyse des ethers benziones; preparation des ethers hexahydrogenzoiques. Compt. rend. Acad. d. sc. 1912, cliv, 922-925.
7. Richards, W. and Barry, F.: Rates of combustion of aromatic substnaces. Jour. Am. Chem. Soc. 1915, xxxvii, 1002.
8. Ipatiew, W.: Katalytische Reactionen bei hohen Temperatures und Drucken. vlll, d. deutsch. chem. Gesellsch, 1904, xxxvii, 2961-2985.
ix, d. deutsch. chem. Gesellsch, 1904, xxxvii, 2986-3005.
8. Ipatiew, W.: Katalytische Reactionen bei hohen Temperatures und Drucken. xl, Reduktions katalye in Gegenwart von metalloxydes, d. deutsch chem. Gessellsch, 1907, xl, 1281-1290.
8. Ipatiew, W.: Katalytische Reationen bei hohen Temperatures und Drucken, xlll, Reduktions katalyse in Genwart von metalloxyden d. deutsch chem. Gesellsch, 1918, xli, 991-993.
8. Ipatiew, W.: Katalytische Reactionen bei hohen Temperaturen und Drucken. xiv, Reduktions katalyse in Gegenwart von Metalloxyden. d. deutsch chem. Gesellsch. 1908, xli, 993-995.
8. Ipatiew, W. und Jakowlew, W. und Sakitin, L.: Katalytische Reactionen bei hohen Temperaturen und Drucken. xv, Reduktions katalyse in Gegenwart von Metalloxyden. d. deutsch chem. Gesellsch, 1908, xli, 996-1000.
9. Brunel, Leon: Additionsprodukte des Cyclohexens. Chem. Zentrabl. 1903, i, 233.
9. Brunel, Leon: Ueber ein nosces o-Cyklohexandiol und seine Derivate. Chem. Zentralb. 1903, i, 711.
10. Brunel, Leon: Derives d'addition de cyclohexene. Compt. rend. Acad. d. sc. 1902, cxxxv, 1055-1057.
11. Brunel, Leon: Derivate des Cyklohexanes. Chem. Zentralb. 1905, ii, 1337-1339.
12. Brunel, Leon: Derivate des Cyklohexanes. Chem. Zentralb. 1905, ii, 1337-1339.
13. Baeyer, A.: Ueber die Constitutionen des Benzols. Liebigs's Ann. d. chem. 1894, cclxxviii, 100.
14. Perkin, W.H, Jr.: Ueber die Pentamethylendicarbonsäure. d. deutsch chem. Gesellsch. 1885, xviii, 3246-3252.
15. Kotz, A.: Ueber der Zinflues der Alkugruppen bei den Auf und Abbau von alkyl - 1, cyclohexanon -2, carbonsäurestern-1, Ann. d. chem. 1907, ccclviii, 194-208.

16. Baeyer, A.: Ueber die Constitution des Benzols. Ann. d. chem. 1894, cclxxviii, 102.
17. Willstatter, R. und Hatt, D.: Hydrierung aromatischer Verbindungen mit Platin und Waasserstoffe. d. deutsch chem. Gesellsch. 1912, xlv, 1471-1481.
18. Ipatiew, W.: Katalytische reaction bei hohen Temperaturen und Drucken d. deutsch chem. Gesellsch. 1908, xli, 991-993.
19. Amourex: Cyclohexylamine. Chem. Ztg. xxxv, 192.
20. Baeyer, A.: Ueber die Constitution des Benzols. Ann. d. chem. 1894, cclxxviii, 103.
21. Hochschwerder, K. and Eichler, T.U.S. patent 1,221 Chem. Abstr. 1917, xi, 1885.
22. Zelinsky, N. and Zelikow, J.: Ueber Umwandlung von Alkoholen in ungesättigte Kohlenwasserstoffe under Einwirkung der Oxalsäure. d. deutsch. chem. Gesselsch. 1901, xxxiv, 3249-3256.
23. Hibbert, H.: Britisch patent 5,408, Chem. Abstr. 1915, ix, 2291.
24. Senderens, J.B.: Catalyse des Cyclonols par voie humide au moyen de l'acide sulfurique; preparation des cyclenes. Compt. rend. Acad. f. sc. 1912, cliv, 1168-1170.
25. Chavonne, G. et Roelan, van B. Contribution a l'étude du cyclohexanol. Bull. soc. belge. chem. 1908, xxii, 410-413.
26. Brunel, Leon: Preparation du cyclohexanes a partu du cyclohexanol. Bull. de chem. 1905, 3 s. xxxiii, 270-271.
27. Fortey, Emily: Hexamethylene from American and Galician petroleum. Jour. Chem. Soc. cxxiii, 948.

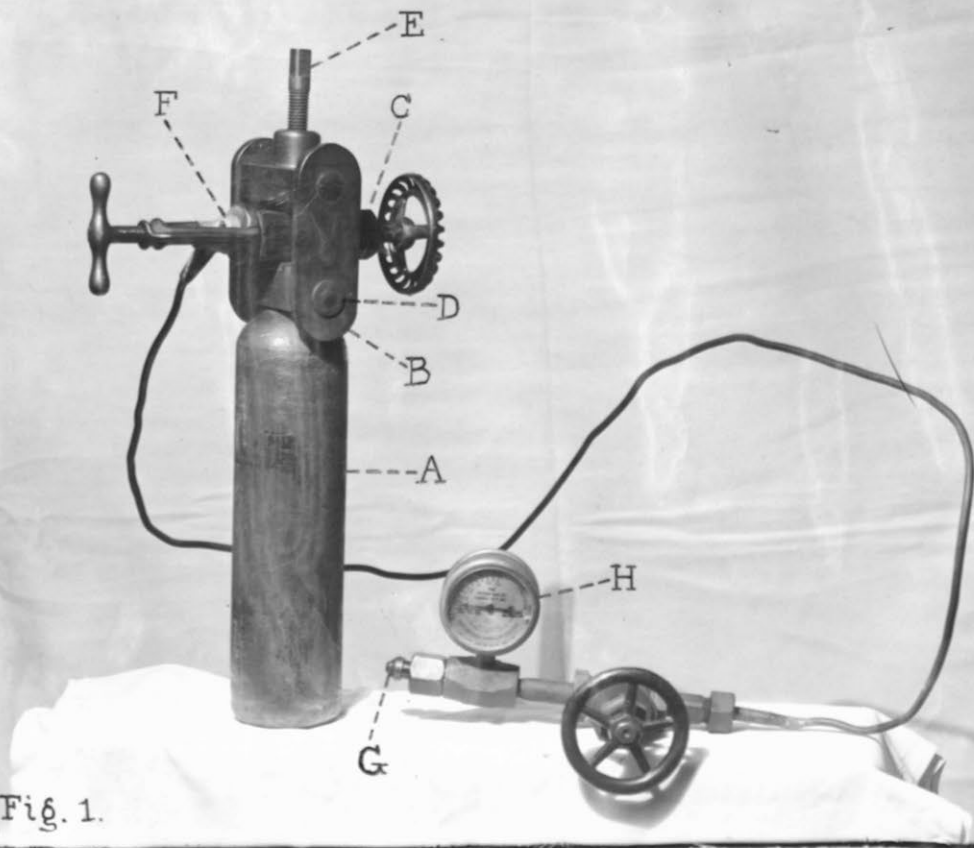


Fig. 1.

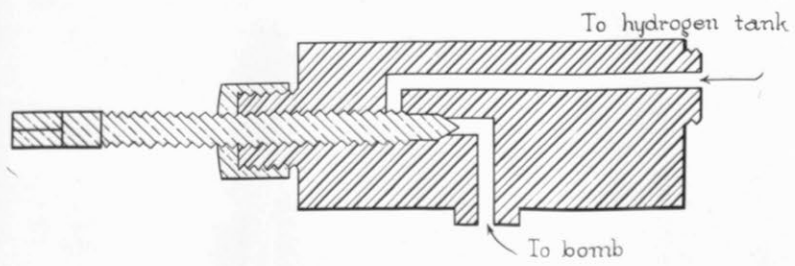


Fig. 2.

TOP

Figure No. 3004⁰⁰¹ 2 prints.

Author Mr. Osterberg

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