rate from the reaction mixture. It was then necessary to pour the mixture into 500 cc. of water and extract with benzene or ether. After the extracts were washed several times with water and dried over calcium chloride, the solvent was removed and the residue distilled *in vacuo*. The chloromethyl derivative was separated easily from the parent ketone by this method.

All but one of the chloromethylated ketones prepared were low-melting solids which, although very soluble in organic solvents, could be recrystallized from low-boiling petroleum ether or methyl alcohol.

Summary

A method has been developed for nuclear chloromethylation of certain types of aromatic ketones.

URBANA, ILLINOIS RECEIVED JANUARY 20, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF HARVARD UNIVERSITY]

Hexahydroacetomesitylene[1]

BY E. P. KOHLER, THOMAS L. JACOBS[2] AND H. M. SONNICHSEN[3]

In continuation of a series of investigations made in this Laboratory[4] as to the effect of hindrance on the stability of enols of aliphatic monoketones, it appeared of interest to study the behavior of hexahydroacetomesitylene and its derivatives from this same point of view. The results of such a study are presented herewith.

It was decided to undertake the preparation of hexahydroacetomesitylene by catalytic hydrogenation of the mesitylene nucleus because that method seemed likely to involve the fewest stereochemical complications, although it is probable that there are other easier routes to that substance.

Preliminary experiments showed that the carbonyl group of acetomesitylene is reduced catalytically before nuclear hydrogenation begins, and the alcohol produced is dehydrated under much less drastic conditions than are necessary for the hydrogenation of the ring; consequently it was necessary to find another derivative of mesitylene which could be hydrogenated in the nucleus and later transformed into an acetyl derivative, and for this purpose mesitylene carboxylic acid seemed the logical choice. The sodium salt of this acid was successfully hydrogenated in water solution using Raney nickel catalyst activated with ammonium chloroplatinate.

It was not possible to separate the isomeric hexahydromesitylene carboxylic acids by simple crystallization, due partly to their great solubility in common organic solvents, and sublimation also failed. The acids were therefore converted into a mixture of amides from which a pure amide melting at 230° and a mixture melting sharply at 167° were obtained. The mixture was shown to contain the 230° amide.

When the residues from the amide preparation were distilled under reduced pressure the principal product was the nitrile, 2,4,6-trimethylhexahydrobenzonitrile, and from the solid residue in the distillation flask was recovered more of the mixture of amides melting at 167°. The structure of the nitrile was proved by the fact that methyl alcoholic potassium hydroxide hydrolyzed it to the 230° amide. The failure of the nitrile to be hydrolyzed past the amide stage by heating with methyl alcoholic potassium hydroxide for several hours was our first indication of the hindered nature of these derivatives of trimethylcyclohexane.[5] The amide also resisted concentrated phosphoric acid and was remarkably inert toward nitrous acid, although by this means it was possible to obtain enough pure trimethylhexahydrobenzoic acid (m. p. 85–87°) for an analysis.

The mixture of amides melting at 167° gave an acid melting at 114–117° when partially hydrolyzed with nitrous acid, and the material remaining unattacked was a mixture of the 230° amide and the 167° mixture. A mixture of the acid

---

(1) Abstracted from a thesis entitled "Mesitylenic and Hexahydromesitylenic Ketones" presented by H. M. Sonnichsen to the Faculty of Arts and Sciences of Harvard University in partial fulfillment of the requirements for the degree of Doctor of Philosophy, June, 1939. The work described herein was begun under the direction of Professor Kohler and completed after his death under the direction of Dr. Jacobs.—H. M. S.

(2) Present address: Department of Chemistry, University of California, Los Angeles Branch, Los Angeles, California.

(3) Present address: R & H Chemicals Department, E. I. du Pont de Nemours Co., Niagara Falls, New York.

(4) Kohler, Tishler and Potter, THIS JOURNAL, **57**, 2517 (1935); Kohler and R. B. Thompson, *ibid.*, **59**, 887 (1937); D. T. Rogers, Harvard Ph.D. Thesis, 1938.

(5) Similar cases may be found in the following references: (a) Jacobsen, *Ber.*, **22**, 1219 (1889); (b) Küster and Stallberg, *Ann.*, **278**, 207 (1893); (c) Hantzsch and Lucas, *Ber.*, **28**, 748 (1895); (d) Sudborough, Jackson and Lloyd, *J. Chem. Soc.*, **71**, 229 (1897); (e) Sachs, *Ber.*, **35**, 3325 (1902); (f) Klages, *ibid.*, **36**, 4192 (1903); (g) Knoevenagel, *ibid.*, **37**, 4091 (1904); (h) Reich, *Bull. soc. chim.*, **21**, 222 (1917); (i) Tiemann, *Ber.*, **31**, 889 (1898).

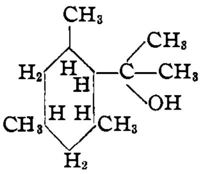
melting at 85–87° with the 114° acid melted below 80°. Carbon–hydrogen analyses showed that both had the composition of 2,4,6-trimethylhexahydrobenzoic acid. Although the troublesome separation of the amide mixture made it difficult to estimate the composition of the crude reduced acids, the fact that about 60% of the acid could be accounted for as the 230° amide in a reaction with an over-all yield not greater than 70% convinced us that the trimethylhexahydrobenzoic acid obtained by hydrogenation of mesitylene carboxylic acid was nearly all one substance, and this assumption was confirmed by the failure of any significant amount of separation of isomeric substances in subsequent reactions.

There are six possible geometric isomers of hexahydromesitylene carboxylic acid,[6] two of which are racemic mixtures separable into optical antipodes. Obviously no decisions can be made from the experimental evidence as to the configurations of the acids isolated. The rule of Skita[7] concerning the production of *cis* and *trans* isomers by hydrogenation in acid or alkaline media is of doubtful validity here because of the complicated structure of the molecule and the drastic conditions of the hydrogenation. Chavanne and Becker's observation[8] that reduction with Raney nickel favors the production of *trans*-isomers and reduction with platinum the formation of *cis*-isomers is of just as little use, not only because of the complexity of the molecule, but also because of the mixed catalyst used. Work on the configurations was not taken up because the primary object of this research was the comparison of the effect of the mesityl and the trimethylcyclohexyl radicals on the stability of enols of monoketones.

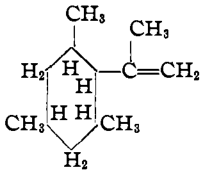
The material at hand best suited for the preparation of hexahydroacetomesitylene seemed to be the 230° amide, but when the carefully purified crystalline solid was added to a solution of methylmagnesium chloride, the main product was the nitrile obtained previously. Another possible path was the reaction of the methyl ester of hexahydrotrimethylbenzoic acid with Grignard reagent. The ester reacted slowly with methylmagnesium chloride, but the only product isolated was a small amount of 1-methyl-1-hexahydromesitylethylene (II), a hydrocarbon obtained later by the dehydration of hexahydromesityldimethylcarbinol (I).

Hexahydroacetomesitylene was finally obtained by Fuson's[9] method for preparing ketones from hindered acid chlorides. The addition of 2,4,6-trimethylhexahydrobenzoyl chloride to excess methylmagnesium chloride in benzene at the boiling point gave a mixture containing 70% hexahydroacetomesitylene, 10 or 15% hexahydromesityldimethylcarbinol (I) and 5% of the hydrocarbon obtained by dehydration of the carbinol (II). Separation by fractionation was difficult, and the chemical methods ordinarily available for the demonstration of the presence of ketone and alcohol groups failed because of hindrance. Even condensations of the ketone with aldehydes by the usual procedure failed to give more than traces of α,β-unsaturated ketone. Benzalacetohexahydromesitylene was finally prepared using sodamide as the condensing agent.

The structures of the tertiary alcohol and the hydrocarbon were more difficult to establish, for analyses do not distinguish very well between a secondary and a tertiary methyl carbinol. Of course the production of a secondary alcohol by the reaction of methylmagnesium chloride with an acid chloride seemed extremely unlikely since this reagent lacks the hydrogen in the beta-position usually associated with reductions by Grignard reagents. Reduction by metallic magnesium or magnesium–magnesium chloride mixture could be definitely ruled out, since the yield of alcohol was the same in preparations in which considerable unchanged magnesium was present and in those in which the addition of methyl chloride had been continued for several hours after the last trace of magnesium had disappeared. Nevertheless the possibility of the production of a secondary alcohol by some obscure mechanism had to be considered. The following evidence can be adduced to prove that the structures of the alcohol and the hydrocarbon are those shown below



I



II

---

[6] A similar case involving a less symmetrical molecule is the hexahydropseudocumidines investigated by Skita (*Ber.*, **53**, 1792 (1920); Hennenbruch, Dissertation, Freiburg, 1920).

[7] Skita, *ibid.*, **53**, 1792 (1920); **56**, 2234 (1923); *Ann.*, **427**, 255 (1922); **431**, 1 (1923).

[8] Chavanne and Becker, *Bull. soc. chim. Belg.*, **31**, 95 (1922).

[9] Fuson, This Journal, **59**, 1508 (1937); **60**, 2063 (1938).

The alcohol reacted rapidly with Grignard reagent in the Zerewitinoff apparatus, giving off a mole of gas in the cold. When treated with phenylisocyanate it was dehydrated and no urethan was isolated. Both acetyl chloride and acetic anhydride dehydrated the alcohol smoothly to the hydrocarbon, and when it was shaken with sodium hypobromite for a long period at room temperature the hydrocarbon was again produced in good yield. The alcohol absorbed hydrogen chloride at 0° in aqueous hydrochloric acid solution and formed an unstable chloride which boiled several degrees lower than the original alcohol. Perhaps the best evidence in favor of the tertiary alcohol structure is that when the ketone was reduced with sodium and alcohol the resulting secondary alcohol exhibited quite different properties. This might be a case of geometrical isomerism, but it is not likely.

Investigation of the hydrocarbon gave further support to the hypothesis that methylmagnesium chloride had added to the carbonyl group of hexahydroacetomesitylene. Ozonization of the hydrocarbon furnished little information, since the only product which could be detected with any certainty was formaldehyde. A trace of hexahydroacetomesitylene was detected in the ozonization products but the amount was so small that it might as reasonably be assumed to be a trace of impurity as a product of ozonolysis. No acetone could be found in the mixture, nor could any other products be isolated. Apparently ozone produced a good deal of general oxidation.

Final proof was furnished by the bromination of the unsaturated hydrocarbon, although the course of the reaction was unexpected. The hydrocarbon absorbed bromine rapidly, but almost immediately began to give off hydrogen bromide. When the product was distilled decomposition was evident, and a second distillation of the product produced further decomposition. The distillate crystallized giving a solid monobromide whose analysis, due to the introduction of the bromine, made it possible to distinguish between the various possibilities and show that the hydrocarbon resulted from dehydration of hexahydromesityldimethylcarbinol.

The above evidence shows that under the conditions of the reaction used in its synthesis hexahydroacetomesitylene adds methylmagnesium chloride to produce hexahydromesityldimethylcarbinol to the extent of about 15% of the ketone formed. Here again was an excellent opportunity to compare the hindrance of the mesityl and the trimethylcyclohexyl radicals. A large amount of 2,4,6-trimethylbenzoyl chloride was treated with methylmagnesium chloride under exactly the same conditions as had been used in the preparation of hexahydroacetomesitylene. Absolutely no evidence of any addition of Grignard reagent to the carbonyl was obtained and the yield of acetomesitylene was good enough to establish that under these conditions not more than 1 or 2% could have occurred.

The addition of Grignard reagents to hexahydroacetomesitylene was investigated further on the pure ketone. In the Zerewitinoff apparatus the hydroaromatic substance acted almost exactly the same as acetomesitylene, giving off gas slowly in the cold and requiring some heating before the reaction was complete. The hydroaromatic ketone could be recovered practically unchanged when treated with ethylmagnesium bromide in the cold, but if the ether solution was boiled for two hours 15 to 20% of by-products resulted. The treatment of the bromomagnesium enolate with acylating and alkylating agents also was undertaken but will not be reported, since the work is not complete.

Hexahydroacetomesitylene was reduced easily with sodium and alcohol to hexahydromesitylmethylcarbinol, a liquid, which was characterized by means of its phenylurethan.

Three weeks of shaking with alkaline hypobromite produced a small amount of cleavage of hexahydroacetomesitylene to hexahydromesitylene carboxylic acid. The cleavage product was found to be the geometrical isomer melting at 86–87°. The bromine-containing oil which formed the remainder of the product decomposed on distillation, and there was isolated not a tribromo but a dibromo ketone, $(CH_3)_3C_6H_8COCHBr_2$.

Benzalacetohexahydromesitylene formed a dibromide which was converted to a β-diketone by the usual treatment with alcoholic base. The liquid diketone was characterized as its copper derivative.

The preparation of the enol peroxide of β,β-diphenylpropiohexahydromesitylene was carried out according to the general method used for the preparation of peroxides of this type,[10] furnishing further evidence that di-ortho-substitution pro-

---

(10) R. B. Thompson, Harvard Ph.D. Thesis, 1938, p. 65, and ref. (4).

duces considerable hindrance in this derivative of cyclohexane. The isolation of this peroxide adds another to the list of hindered ketones whose enols are sufficiently stable in solution to permit their reaction with molecular oxygen. The list now includes β,β-diphenylpropiomesitylene,[11] β,β-diphenylpropiohexahydromesitylene, α,β,β-triphenylpropiophenone,[12] α,β-diphenylvalerophenone,[13] β,β-diphenylpropiotriphenylmethane,[14] 2-diphenylmethyl - 6 - benzalcyclohexanone,[15] and β,β-diphenylpropiotriphenylfuran.[16]

The first peroxide preparation gave two isomers, both of which behaved as peroxides with potassium iodide and on heating. In a second preparation only the lower melting isomer was obtained. It should be mentioned that there are a number of possibilities for isomers of this peroxide, and no decision can be made concerning either structure or configuration in this case. In addition to the usual problem of whether the peroxide is cyclic or in the hydroperoxide form, the existence of two carbon atoms bearing hydrogens in the alpha-position to the carbonyl introduces extra complications. The possibility of *cis* and *trans* isomers of a cyclic peroxide structure and of dimorphic crystalline forms should not be forgotten, and finally there is the stereoisomerism of the cyclohexane ring already mentioned, a list of possibilities so large that exploration seems futile. Thermal decomposition of the peroxide was attempted, but none of the products obtained could be identified.

Experimental

Mesitylene Carboxylic Acid.—Mesitylene carboxylic acid was prepared by carbonation of mesitylmagnesium bromide and purified by recrystallization from methanol. Acid which had been recrystallized only once was found to serve as well for the hydrogenation reaction as very carefully purified material.

Reduction of Mesitylene Carboxylic Acid.—A solution of the sodium salt of mesitylene carboxylic acid was prepared from 100 g. of the acid, 24.3 g. of sodium hydroxide, and 150 cc. of water, and shaken with 5 to 10 g. of Raney nickel catalyst and 0.2 g. of ammonium chloroplatinate at 250° under 3600 lb. (240 atm.) pressure of hydrogen for twenty-four hours. The catalyst was then filtered off and a fresh portion of Raney nickel and ammonium chloroplatinate added. During the first treatment the aromatic acid sometimes absorbed as much as half the theoretical amount of hydrogen, but in the majority of runs no hydrogen was taken up. The material was again shaken at the same temperature and pressure for forty-eight hours before the catalyst was again filtered off and a fresh batch added. The process ordinarily required three treatments, but in some cases without the use of ammonium chloroplatinate as many as six were required to obtain the complete conversion of the aromatic acid to the corresponding derivative of cyclohexane. The primary factor affecting the rate of absorption seemed to be the condition of the copper can used as a reaction vessel. After continued use the inside of the can became covered with a dark-colored deposit of metal and the hydrogenations were completed in much less time.

After the solution of the sodium salt had absorbed the theoretical amount of hydrogen it was filtered and acidified with concent ratedhydrochloric acid. Hexahydromesitylene carboxylic acid was precipitated in 95–99% yield as a thin oil which slowly solidified to a waxy mass from which the water could be decanted. The crude solid was taken up in petroleum ether and separated from the remaining water. If the hydrogenation had not been carried to completion most of the aromatic acid remaining was precipitated at this point.

Preparation of Trimethylhexahydrobenzamides.—A mixture of 7.5 cc. of thionyl chloride and 10 g. of trimethylhexahydrobenzoic acid was allowed to stand overnight, heated on the steam-bath to drive off excess thionyl chloride, and poured into 50 cc. of concentrated ammonium hydroxide cooled in an ice-bath. The precipitate after drying weighed 8.0 g. and consisted of 5.0 g. of an amide melting at 230°, some ammonium chloride, and some oily material containing a good deal of sulfur. From the ammonia solution was recovered 2.1 g. of unchanged acid. The amide was recrystallized from methyl alcohol.

Anal. Calcd. for $C_{10}H_{19}ON$: C, 70.94; H, 11.31. Found: C, 70.75; H, 11.04.

The above analysis is of a sample burned in air. Samples burned in oxygen exploded with an audible detonation. The results of analyses in oxygen agreed with the theoretical percentage of carbon but were four to six-tenths per cent. low in hydrogen.

The oily residues from several preparations of the 230° amide were distilled *in vacuo*. The main fraction boiled at 61–62° at 3 mm., but there was water in the distillate and considerable smell of methyl mercaptan. When the liquid boiling at 62° was heated for twelve hours with saturated methyl alcoholic potassium hydroxide, there was obtained in about 50% yield the same 230° amide which had been isolated earlier.

The flask residue crystallized, giving a solid which melted at 167° after recrystallization from benzene or ether. This substance when mixed with the 230° amide melted between 180 and 220°, different samples of apparently equal purity giving a different mixed melting point. In subsequent preparations the residues from a number of runs were combined and the 167° amide obtained by very tedious fractional crystallization from benzene. Hydrolysis with sodium nitrite in acetic acid showed that this substance was a mixture of the amide melting at 230° and an isomeric amide which it was not possible to isolate in pure form.

---

(11) Kohler, Tishler and Potter, THIS JOURNAL, **57**, 2517 (1935).

(12) Kohler and Tishler, *ibid.*, **54**, 1595 (1932).

(13) Kohler, *Am. Chem. J.*, **36**, 185 (1906).

(14) D. T. Rogers, Harvard Ph.D. Thesis, 1938, p. 61.

(15) C. E. Barnes, Harvard Ph.D. Thesis, 1935, p. 96.

(16) R. D. Cramer, unpublished work.

Anal. Calcd. for $C_{10}H_{19}ON$: C, 70.94; H, 11.31. Found: (burned in air) C, 70.75; H, 10.93.

Hydrolysis of 230° Amide.—Two grams of amide, m. p. 230°, was added to 50 cc. of glacial acetic acid. The mixture was heated until the amide dissolved, then 2 g. of solid sodium nitrite was added in small portions. The solution was heated for fifteen minutes, then neutralized with 20% sodium hydroxide and filtered. Half of the original amide was recovered. The water solution was acidified and extracted with ether. The ether solution was dried over calcium chloride, filtered and evaporated. The solid material remaining was sublimed and 0.13 g. of crystals obtained which after two more sublimations melted at 85–87°.

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.57; H, 10.65. Found: C, 70.90; H, 10.43.

Hydrolysis of the 167° Amide.—The substance melting at 167° was submitted to the same procedure as above, but its solubility in water (approximately 0.1 g. per 100 cc.) made it necessary to extract the crude hydrolysis mixture with ether, and then extract the ether solution with bicarbonate. When the bicarbonate solution was acidified there was deposited in about 15% yield a solid melting at 95–105°. The ether solution deposited a mixture of the 230° amide and the 167° substance, showing that the original 167° substance was a mixture of two amides. The acid was recrystallized twice from petroleum ether (in which it was extremely soluble) and resublimed. The analytical sample sintered slightly at 100° and melted at 114–117°.

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.57; H, 10.65. Found[17]: C, 70.63; H, 10.42.

Reaction of 230° Amide with CH_3MgCl; Preparation of Hexahydrotrimethylbenzonitrile.—A solution of methylmagnesium chloride was prepared from 7.2 g. (0.30 mole) of magnesium and to this was added in small portions 20 g. (0.12 mole) of the pure amide melting at 230°. The ether boiled vigorously during the addition and the amide went into solution. After all of the solid had been added the ether was almost all gone and a pasty mass was left. The product was allowed to stand overnight, boiled for one hour and poured into iced dilute hydrochloric acid. When the mixture was extracted with a large amount of ether, the ether solution extracted with sodium bicarbonate, dried with calcium chloride and evaporated it deposited 1.7 g. of unchanged amide. The residue, distilled through a short column, boiled 66–71° (3 mm.). The product gave a qualitative test for nitrogen.

Anal. Calcd. for $C_{10}H_{17}N$: C, 79.41; H, 11.33. Found: C, 80.32; H, 11.28.

When burned in oxygen the sample (14 mg.) exploded with such violence that it shattered the combustion tube. The above analysis is of a sample burned in air. The composition of the compound was made certain by treatment with strong alcoholic potassium hydroxide which produced in good yield the original 230° amide, leaving no doubt that the liquid was the corresponding nitrile.

Preparation of Trimethylhexahydrobenzoyl Chloride.—A mixture of 90 cc. of purified thionyl chloride and 180 g. of hexahydromesitylene carboxylic acid was allowed to stand for four hours, during which time hydrogen chloride was evolved rapidly. The acid chloride was then distilled *in vacuo* (20 mm.), and there was obtained:

Fraction	B. p., °C.	Weight, g.
Forerun		6.0
Fraction I	102–104	27.0
Fraction II	104	111.0
Flask residue	.....	42.0

The flask residue when hydrolyzed yielded 14.0 g. of a neutral fraction from which nothing could be obtained, 21.0 g. of mesitylene carboxylic acid and 7.0 g. of hexahydromesitylene carboxylic acid. This represents a yield of 79% and a recovery of 91%. In most preparations the amount of mesitylene carboxylic acid recovered was much smaller, representing more complete reduction of the original material. The acid chloride was a clear colorless liquid with a pungent odor, $n^{20}D$ 1.472, d^{20}_4 1.01.

Preparation of Methyl Ester of Trimethylhexahydrobenzoic Acid.—Methyl alcohol (75 cc.) was added to 51 g. of trimethylhexahydrobenzoyl chloride and heated in an all-glass apparatus on the steam-bath overnight. The ester was taken up in ether, washed with water and bicarbonate solution, dried over sodium sulfate and distilled. All of the material came over between 90 and 96° at 14 mm.; recovery 96%; $n^{20}D$ 1.452; b. p. 93° (14 mm.); d^{20}_4 0.934.

Anal. Calcd. for $C_{11}H_{20}O_2$: C, 71.69; H, 10.94. Found: C, 72.14; H, 11.22.

Reaction of Ester with Methylmagnesium Chloride.—In the Zerewitinoff machine the ester gave off gas very slowly at 100° and a white solid separated. The total amount of gas given off after heating for one and one-quarter hours at 100° was 0.25 mole. When 29.5 g. of the ester was added dropwise to a solution in boiling benzene of methylmagnesium chloride prepared from 24 g. of magnesium, heat was evolved and solid separated. The suspension was boiled for thirty-six hours, and decomposed with ice and hydrochloric acid. Fractionation through a 50-cm. column at 15 mm. pressure gave:

Fraction	B. p., °C.	Weight, g.
Fraction I	83–92.2	5.3
Fraction II (unchanged ester)	93.4–94.2	11.0
Flask residue	.....	4.4

Anal. of Fraction II. Calcd. for $C_{11}H_{20}O_2$: C, 71.69; H, 10.94. Found: C, 73.60; H, 11.25.

The low-boiling fraction was redistilled and the material boiling 84.5 to 86° was analyzed.

Anal. Calcd. for $C_{12}H_{22}$: C, 86.65; H, 13.33. Found: C, 86.26; H, 13.63.

Comparison of physical properties ($n^{20}D$ 1.444, d^{20}_4 0.831) with the hydrocarbon obtained by dehydration of the tertiary alcohol $(CH_3)_3C_6H_8C(OH)(CH_3)_2$ showed that the material was still impure.

Addition of $(CH_3)_3C_6H_8COCl$ to Methylmagnesium Chloride.—Methylmagnesium chloride was prepared from 60 g. of magnesium in one liter of ether solution in a two-liter three-necked flask. Dry benzene was added and the

---

[17] This analysis was performed by Mr. H. S. Wight.

solution boiled until the temperature of the vapor was 75° and the volume of the solution approximately 800 cc. Hexahydrotrimethylbenzoyl chloride (100 g.) dissolved in 200 cc. of benzene was added slowly with vigorous stirring. The resulting paste was boiled for one-half hour, then poured into iced hydrochloric acid. The mixture was extracted with ether, and the ether layer was washed with water and sodium bicarbonate. Most of the benzene was evaporated and the residue was distilled at 9 mm.

Fraction	B. p., °C.	Weight, g.
Forerun	60–86	5.0
Fraction II	86–87	46.0
Fraction III	87–95	17.0
Flask residue	...	16.8

Fraction III was redistilled along with the flask residue and there was obtained 17.0 g. more of hexahydroacetomesitylene, b. p. 86–87°, and 14.5 g. of a solid boiling at 105° at 11 mm. This represents a 5.5% yield of the low-boiling material, which was shown to be the same hydrocarbon as that obtained from the action of methylmagnesium chloride on the ester and of dehydrating agents on the alcohol, a 70% yield of hexahydroacetomesitylene and a 16% yield of the solid $(CH_3)_3C_6H_8C(OH)(CH_3)_2$; total recovery, 91% of the theoretical. The same ketone was produced when methylzinc chloride prepared by the addition of anhydrous zinc chloride to a solution of methylmagnesium chloride was treated with trimethylhexahydrobenzoyl chloride, but the yield was only 55% of the theoretical.

Hexahydroacetomesitylene, $(CH_3)_3C_6H_8COCH_3$.—The ketone was a colorless liquid, b. p. 86–87° (9 mm.), 93–94° (15 mm.), 97–98° (25 mm.), $n^{20}D$ 1.452; d^{20}_4 0.892. *MR* obsd., 50.85; calcd., 50.83; surface tension at 25°, 30.9; parachor, calcd. 445.7; found 445.

Anal. Calcd. for $C_{11}H_{20}O$: C, 78.50; H, 11.98. Found: C, 78.76; H, 12.21. Found[18]: C, 78.93; H, 12.41.

The ketone had a faint pleasant odor and was quite volatile with steam. It gave no iodoform test by Fuson's method.[19] When hexahydroacetomesitylene was treated with Grignard reagent in the Zerewitinoff apparatus it gave off gas slowly in the cold. The total amount of gas evolved was 0.84 equivalent and the total amount of reagent which added was only 0.05 equivalent.[20] When 20.0 g. of hexahydroacetomesitylene was treated with two equivalents of ethylmagnesium bromide at 0° for thirty minutes, gas was given off slowly during the addition (acetomesitylene reacts more vigorously). When distilled at 10 mm. the product of decomposition of the clear colorless Grignard solution boiled over a range of seven degrees but refractive index measurements indicated that not more than a negligible amount of addition had occurred. Boiling the ketone with ethylmagnesium bromide in ether solution for two hours produced between 12 and 25% of by-products.

Hexahydromesityldimethylcarbinol, $(CH_3)_3C_6H_8C(OH)(CH_3)_2$, was a white solid which boiled at 106° under 10 mm. pressure. It was extremely soluble in all the ordinary organic solvents, but could be recrystallized from methanol–water mixtures, forming stout needles, m. p. 67–69°.

Anal. Calcd. for $C_{12}H_{24}O$: C, 78.19; H, 13.12. Found[21]: C, 78.43, 78.66; H, 12.53, 12.58. Found[22]: C, 78.56; H, 12.91.

When treated with Grignard reagent in the Zerewitinoff apparatus,[20] the alcohol gave off 1.12 equivalents of gas rapidly in the cold. When treated with phenyl isocyanate it reacted vigorously at 120°, but the only product isolated was diphenyl urea. When treated with acetyl chloride or acetic anhydride the hydrocarbon $C_{12}H_{22}$ was produced in good yield. The sample of this hydrocarbon redistilled for analysis boiled 70.8–71.2° (10 mm.), $n^{20}D$ 1.4605, d^{20}_4 0.831, *MR* calcd. 54.97, found 54.83.

Anal. Calcd. for $C_{12}H_{22}$: C, 86.65; H, 13.33. Found[17]: C, 86.60; H, 13.43.

The same hydrocarbon was produced when 5.0 g. of the alcohol was shaken for two weeks with a mixture of 75 cc. of water, 7.5 g. of sodium hydroxide, and 7.5 g. of bromine.

When 4.0 g. of the alcohol was added to 15 cc. of concentrated hydrochloric acid at −5° and dry hydrogen chloride bubbled through the mixture, the solid disappeared and was replaced by a layer of clear liquid. This was separated from the aqueous layer, washed with water, dried over sodium carbonate and distilled through a small column. The main fraction boiled 94.6–97.1° (9 mm.) and was a clear, almost odorless liquid, $n^{20}D$ 1.472. It was allowed to stand overnight before redistillation, and this time it gave off hydrogen chloride and the sole product was the same hydrocarbon obtained in the dehydration of the alcohol. Lack of material prevented repetition of the reaction.

Determination of Structure of the Hydrocarbon $C_{12}H_{22}$.—A solution of 4.1 g. of the hydrocarbon in 30 cc. of glacial acetic acid was treated with 4% ozone at room temperature. The ozone was absorbed quantitatively at first, but after about two-thirds of the theoretical amount had been taken up absorption ceased. The ozonide was rinsed into a hydrogenation bottle with glacial acetic acid and hydrogenated with palladium catalyst. There was an induction period of nearly an hour before the catalyst began to be reduced. The solution then took up one-third of the theoretical quantity of hydrogen in about twenty minutes, after which absorption stopped. The solution, after filtering off the catalyst, gave a faint test with hypoiodite and a strong test with ammoniacal silver nitrate. When 2,4-dinitrophenylhydrazine was added to a portion of the product the dinitrophenylhydrazone of formalde-

---

[18] By H. S. Wight.

[19] R. C. Fuson, This Journal, **56**, 1638 (1934).

[20] This determination performed by Mr. Richard Cramer.

[21] These analyses by the Arlington Laboratories, Arlington, Va. The sample had been distilled three times through a 3-ft. (90-cm.) column. The boiling point was constant at 105.9° (10 mm.). Unfortunately it was necessary to distil rather rapidly to prevent the product solidifying in the condenser. The freezing point of the product was 50.4°. The material was a white waxy-looking solid.

[22] This analysis was performed by H. S. Wight. The sample had been recrystallized four times from methanol–water solution and melted at 67–69°. The analyses do not distinguish very well between the tertiary alcohol and the corresponding secondary alcohol, $(CH_3)_3C_6H_8CH(OH)CH_3$ (calcd.: C, 77.58; H, 13.03). The composition of the ketone is also very close to the same figure (calcd.: C, 78.49; H, 11.98). The chemical evidence leaves no doubt about the structure.

hyde was obtained, identified by a mixed melting point with an authentic sample. No other crystalline substance was isolated. The original solution, after oxidation with ammoniacal silver nitrate, no longer gave a detectable amount of iodoform when hypoiodite was added, proving that acetone was absent.

An attempt to isolate hexahydroacetomesitylene from the product of ozonization by condensation with benzaldehyde and formation of the dibromide of the benzal compound gave such a small amount of product (identified by a mixed melting point) that it might conceivably have come from a trace of ketone present as an impurity in the hydrocarbon before ozonization, so this cannot be considered a proof of structure.

Better evidence was furnished by bromination of the unsaturated hydrocarbon: 9.5 g. of crude material in 50 cc. of carbon tetrachloride was cooled in an ice-bath and a solution of 9.0 g. of bromine in 30 cc. of carbon tetrachloride was added slowly. Hydrogen bromide was evolved almost immediately. The solution was decolorized with sodium bisulfite, filtered, and washed with sodium bicarbonate. When the carbon tetrachloride was pumped off and the remaining oil distilled under reduced pressure, it boiled 60–135° (10 mm.) with no evidence of any pure substance being present. The distillate was mixed with methyl alcohol and cooled in dry-ice until it deposited about 1.5 g. of gummy crystals which were filtered off and recrystallized from methanol to give a product melting at 41–42°. The analysis indicated that it was the unsaturated monobromohydrocarbon $(CH_3)_3C_6H_8C(CH_3){=}CHBr$. It was not investigated further.

Anal. Calcd. for $C_{12}H_{21}Br$: C, 58.77; H, 8.63. Found[17]: C, 58.78; H, 8.38.

Reaction of Trimethylbenzoyl Chloride with CH_3MgCl.—Trimethylbenzoyl chloride was treated with methylmagnesium chloride under exactly the same conditions as had been used in the preparation of hexahydroacetomesitylene. From 103.0 g. of the acid chloride there was obtained 79.9 g. of acetomesitylene, n^{20}_D 1.517–1.519 (n^{20}_D of purest sample on hand 1.5190). There was also obtained 4.8 g. of forerun, refractive index 1.515, and 4.0 g. of high-boiling material. This high-boiling material was shaken with copper acetate and there was obtained 3.2 g. of the copper enolate of dimesitoylmethane. This represents a 90% yield of acetomesitylene and leaves only 1.25% of the liquid obtained unidentified. Therefore it is estimated that there could not have been more than 1 or 2% of addition to the carbonyl group under conditions where hexahydroacetomesitylene adds to the extent of 16%.

Reduction of Hexahydroacetomesitylene. Preparation of $(CH_3)_3C_6H_8CHOHCH_3$.—A solution of 10 g. of hexahydroacetomesitylene in 100 cc. *t*-amyl alcohol was heated on the steam-bath and metallic sodium (8 g.) was added in small pieces over a period of six hours. The mixture was heated six hours more, let stand overnight, then treated with methyl alcohol and water to destroy traces of sodium remaining. The resulting emulsion was poured into water, extracted with ether and the ether solution steam distilled. The steam distillate was extracted with ether, dried over sodium sulfate, and distilled at 8 mm. After 1.5 g. of forerun boiling at 76–97°, there was obtained 6.3 g. of secondary alcohol, b. p. 97.5–98.2°, n^{20}_D 1.470. A second distillation divided the material into three fractions boiling at 94–99.5° (8 mm.), n^{20}_D of all three fractions 1.4700, n^{20}_D of flask residue 1.4701. The fraction taken as an analytical sample boiled at 99.5°, d^{20}_4 0.905, *MR* obsd., 52.5; calcd., 52.35.

Anal. Calcd. for $C_{11}H_{22}O$: C, 77.58; H, 13.03. Found[17]: C, 77.36; H, 12.83.

Phenylurethan of Methylhexahydromesityl Carbinol.—Two cc. of the secondary alcohol was mixed with 2 cc. of phenyl isocyanate and heated in an oil-bath. Reaction began when the temperature reached 130°. The mixture was heated for one-half hour at 150° then cooled in ice, when 1.0 g. of solid material was precipitated melting around 100°. Three recrystallizations from ether–petroleum ether raised the melting point to 130–132°. Three more recrystallizations from ligroin raised the melting point slightly to 132–134°.

Anal. Calcd. for $C_{18}H_{26}O_2N$: C, 74.72; H, 9.41; N, 4.84. Found[17]: C, 74.94; H, 9.28; N, 5.24.

Alkaline Bromination of Hexahydroacetomesitylene. Preparation of $(CH_3)_3C_6H_8COCHBr_2$.—When 5 g. of hexahydroacetomesitylene was shaken for seventy-four hours with 100 cc. of a 10% solution of bromine in 10% sodium hydroxide, the organic material increased in density sufficiently to cause it to settle to the bottom of the flask. When it was distilled some decomposition was evident and on redistillation more decomposition occurred. The distillate crystallized on standing and was recrystallized three times from petroleum ether to give a substance melting at 63–65°.

Anal. Calcd. for $C_{11}H_{18}OBr_2$: Br, 49.01. Found:[21] Br, 48.90.

From the aqueous hypobromite layer was recovered a very small amount of acid which gave an amide melting at 215–225° after three recrystallizations. A mixture with the 230° amide melted at 220–228°.

Condensation of Hexahydroacetomesitylene with Benzaldehyde.—Finely ground sodamide (12 g.) was suspended in 100 cc. of benzene and 42.0 g. of hexahydroacetomesitylene was added. Benzaldehyde (30.0 g.) was added slowly to the suspension of ketone and sodamide and a vigorous reaction ensued. A gelatinous solid was produced which was allowed to stand for six hours, then extracted with ether and water. The ether layer was treated with a saturated solution of sodium bisulfite to remove excess benzaldehyde and then washed thoroughly with sodium bicarbonate solution and water. When the ether was evaporated and the residue distilled in a Claisen flask at 15 mm., 12.8 g. of unchanged ketone was recovered (30% of the starting material). The pressure was then reduced to 2.5 mm. and 43.7 g. of the unsaturated ketone distilled over as a yellow viscous oil at 160–165° (68% yield). The flask residue weighed 8.4 g. but only a trace of the dibromide of benzalacetohexahydromesitylene could be recovered from it when it was treated with bromine. Redistillation of the main fraction gave a pale yellow liquid, b. p. 148–150° (0.5 mm.). This was again distilled and an analytical sample, b. p. 148.0° (0.5 mm.), was removed, n^{20}_D 1.562, d^{20}_4 0.994; *MR* obsd., 83.62; calcd., 79.09. The yellow liquid crystallized in dry-ice but melted again below 0°.

Anal. Calcd. for $C_{16}H_{24}O$: C, 84.34; H, 9.44. Found: C, 84.59; H, 9.74.

Dibromide of Benzalacetohexahydromesitylene, C_6H_5-$CHBrCHBrCOC_6H_8(CH_3)_3$.—When the unsaturated ketone was treated with a solution of bromine in carbon tetrachloride and the carbon tetrachloride evaporated, there remained a white solid melting near 180°. Three recrystallizations from benzene brought the melting point to 211–212° (with slight decomposition).

Anal. Calcd. for $C_{16}H_{24}OBr_2$: C, 51.95; H, 5.81. Found[17]: C, 52.50; H, 6.04.

Preparation of $C_6H_5COCH_2COC_6H_8(CH_3)_3$.—A solution of 1.8 g. of the dibromide, $C_6H_5CHBrCHBrCOC_6H_8$-$(CH_3)_3$ in 10 cc. of methyl alcohol was heated for thirty minutes on the steam-bath with 0.75 g. of potassium hydroxide. The solution was acidified with hydrochloric acid and again heated for thirty minutes. Fifty cc. of water was added, the solution extracted with ether, and the ether layer shaken with saturated cupric acetate solution. The copper derivative of the beta-diketone was soluble in ether. When the ether layer was evaporated to dryness and the resulting solid recrystallized from ether–petroleum ether, there was obtained 1.2 g. of crystals, m. p. 195–200° (90% yield). Two more recrystallizations gave an analytical sample with m. p. 197–199°.

Anal. Calcd. for $C_{36}H_{46}O_4Cu$: C, 71.20; H, 7.65. Found[17]: C, 71.19; H, 7.81.

Hydrogenation of Unsaturated Ketone. Preparation of $C_6H_5CH_2CH_2COC_6H_8(CH_3)_3$.—When benzalacetohexahydromesitylene was hydrogenated with Adams catalyst it took up exactly one equivalent of hydrogen. The product boiled between 179 and 187°, and when redistilled for analysis boiled 180–182° (8 mm.), n^{20}_{D} 1.514, d^{20}_{4} 0.967; *MR* obsd., 80.4; calcd., 79.56. The analytical sample was a pale yellow liquid, indicating that the material still contained some unchanged unsaturated ketone.

Anal. Calcd. for $C_{18}H_{26}O$: C, 83.68; H, 10.15. Found[18]: C, 83.35; H, 10.34.

Reaction of Benzalacetohexahydromesitylene with Phenylmagnesium Bromide.—Five grams (0.0195 mole) of unsaturated ketone was added rapidly to a solution of phenylmagnesium bromide prepared from 1.05 g. (0.045 mole) of magnesium. The solution boiled during the addition but remained colorless and clear. It was allowed to stand for eight hours under nitrogen, then cooled in ice and decomposed by the addition of iced dilute hydrochloric acid. The mixture was allowed to stand overnight under nitrogen, then extracted with water and steam distilled to remove diphenyl and bromobenzene. The residue from the steam distillation was extracted with ether, dried over calcium chloride, evaporated, and diluted with petroleum ether. Cooling in dry-ice caused the mixture to solidify, and after allowing it to warm to room temperature 3.5 g. of an oily solid was filtered off. The remaining 2.5 g. of oil would deposit no more solid material. The solid, after three recrystallizations from petroleum ether, melted at 78–80° and a mixture with β,β-diphenylpropiomesitylene melted below 60°.

Anal. Calcd. for $C_{24}H_{30}O$: C, 86.18; H, 9.05. Found[17]: C, 86.38; H, 8.88.

Enol Peroxides of β,β-Diphenylpropiohexahydromesitylene.—A solution of phenylmagnesium bromide was prepared from 1.9 g. of magnesium, and to this was added 10 g. of $C_6H_5CH{=}CHCOC_6H_8(CH_3)_3$ dissolved in dry ether. The solution was boiled for fifteen minutes, then poured into a mixture of 500 cc. of ice, 50 cc. of concentrated hydrochloric acid, and 250 cc. of water. The mixture formed an emulsion with a clear ether layer on top. The ether layer was removed, washed three times with ice-water and diluted to 200 cc. Oxygen was passed into this solution for several hours until it had evaporated to 50 cc., then 100 cc. of petroleum ether was added and oxygen passed in until the solution had evaporated to a yellow viscous oil. The oil was allowed to stand overnight in ice, then cooled in dry-ice, when it deposited 2.0 g. of crystals melting over a wide range around 75°. Recrystallization from ether and petroleum ether gave 0.1 g. or less of material melting at 119–121° and 1.3 g. melting 83–87°. Both substances depressed the melting point of β,β-diphenylpropiohexahydromesitylene, of β,β-diphenylpropiomesitylene and its enol peroxide. Both substances liberated a small amount of iodine from acidified potassium iodide solution and both decomposed vigorously when heated slightly above the melting point. When the higher-melting substance was mixed with the lower-melting peroxide the mixture melted at the same point as the lower-melting substance alone. Both substances were soluble in ether, the higher-melting one much less than the other, and both were precipitated by petroleum ether in micro-crystalline form.

Anal. Calcd. for $C_{24}H_{30}O_3$: C, 78.65; H, 8.25. Found[17]: (87° peroxide) C, 79.51, 79.56; H, 8.83, 8.57: Found[21]: (87° peroxide) C, 79.34; H, 8.56. Found[17]. (133° peroxide) C, 78.51; H, 8.43.

There was not enough of the higher-melting peroxide to investigate further. When the preparation of the peroxide was repeated 10.8 g. of crude solid peroxide (50% yield) was obtained from 20.0 g. of benzalacetohexahydromesitylene, but this was found to be entirely the 86–87° material, and none of the higher-melting peroxide could be isolated.

Preparation of Hydroxyketone.—Both peroxides took up hydrogen very rapidly, but the amount of the higher melting substance available was so small that the quantitative results were not significant. When 0.666 g. of the 87° peroxide was dissolved in 50 cc. of absolute alcohol and hydrogenated with Adams catalyst, it took up 34.0 cc. of hydrogen (90% of the theoretical amount). When the alcohol solution was filtered and evaporated, a yellow oil was obtained which deposited 0.25 g. of white crystals melting at 81–84°. After two more recrystallizations from petroleum ether the melting point was 86–87°; mixed melting point with 87° peroxide 75–80°.

Anal. Calcd. for $C_{24}H_{30}O_2$: C, 82.23; H, 8.62. Found[17]: C, 82.00; H, 8.76.

The product is therefore a hydroxyketone, analogous to the substance $(CH_3)_3C_6H_2COCHOHCH(C_6H_5)_2$ obtained in the mesitylene series.[11]

Thermal Decomposition of the Peroxide.—When 1.5 g. of crude peroxide (m. p. 85°) was dropped into a hot test-tube it decomposed with a rush, giving off quantities of gas. When the residue was cooled and extracted with sodium bicarbonate only a trace of acidic material was obtained. This was taken up in ether, dried, evaporated to dryness and treated with thionyl chloride. When the thionyl chloride solution was poured into an excess of iced ammonium hydroxide, the precipitate was barely visible and embedded in a yellow oil. When washed with ether it melted at 165–170° and lowered the melting point of the 167° amide thirty degrees. The melting point of a mixture with the 232° amide was 180–190°. Apparently the substance was not the amide of hexahydromesitylene carboxylic acid. No conclusions can be drawn from this evidence as to the structure of the peroxide, since apparently most of the material gave up its oxygen without cleavage. The remaining neutral material when treated with hydroxylamine deposited a trace of crystalline material which analysis showed to be a hydrocarbon, m. p. 200–205°.

Anal. Found[17]: C, 92.64; H, 6.83. No other crystalline material could be isolated.

Summary

The preparation and properties of one of the six possible geometric isomers of hexahydroacetomesitylene are described.

Investigation of this isomer of hexahydroacetomesitylene and some of its derivatives indicates that this particular configuration of the trimethylcyclohexane ring offers slightly less hindrance to the reactions of a ketone group adjacent to the ring than does the mesitylene nucleus.

RECEIVED DECEMBER 8, 1939

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

The Separation of the Isomeric Hexenes by Batch Fractionation

BY ARTHUR ROSE

The maximum sharpness of separation between any two components in a batch fractionation may be estimated by an extension of the reasoning of Sydney Young[1] and of Rayleigh[2] as will soon be described in detail elsewhere.[3] The present paper applies this line of reasoning to the separation of the isomeric hexenes so as to obtain a definite idea of the fractionating efficiency required and the results to be expected in attempts at such separations.

The Vapor Pressure Ratios of the Hexenes.—In order to estimate the maximum possible sharpness of separation for any pair of substances it is necessary to know the vapor pressure ratio (α) for the pair. These may be obtained for the hexenes by using the boiling points of Schmitt and Boord[4] and the boiling point correction method cited by Eaton.[5] Thus 2-ethyl-1-butene boils at 66.45° at 760 mm. while 3-hexene boils at 66.8°. At this temperature the b. p. correction would be about 0.042° per mm., so that at 66.8° the vapor pressure of 2-ethyl-1-butene must be about 768 mm. and *alpha* for this pair must be about 768/760 = 1.011. The values in Table I were obtained in a similar manner. In every case only three significant figures are retained but in dropping excess figures the value of *alpha* was increased, except for pair A, so the other pairs are actually more difficult to separate than the values of *alpha* indicate.

TABLE I

	Hexene pair	Alpha
(A)	2-Ethyl-1-butene and 3-hexene	1.01
(B_1)	2-Methyl-2-pentene and 3-methyl-2-pentene-*trans*	1.02
(B_2)	3-Hexene and 2-methyl-2-pentene	1.02
(B_3)	3-Methyl-2-pentene-*cis* and 3-ethyl-1-butene	1.02
(C)	2-Ethyl-butene-1 and 2-methyl-2-pentene	1.03
(D)	3-Methyl-2-pentene-*cis* and -*trans*	1.07

The estimates of maximum sharpness of separation to be given below assume that α is constant over the temperature range and concentrations involved in the distillations. The temperature ranges involved are so narrow that the variation in α from this source may certainly be disregarded. The conclusions of Beatty and Calingaert[6] make it reasonable to assume that none of the hexene mixtures would depart sufficiently from ideality to alter the general nature of the conclusions to be drawn in this paper.

Distillation Curves to be Expected.—It can be shown[3] that a distillation curve with a maximum sharpness of separation approximately like that

---

(1) Sydney Young, "Distillation Principles and Processes," Macmillan Co., London, 1922, p. 117.

(2) Walker, Lewis, McAdams and Gilliland, "Principles of Chemical Engineering," p. 532, McGraw-Hill Book Co., New York, N. Y., 1937; also Badger and McCabe, "Elements of Chemical Engineering," McGraw-Hill Book Co., Inc., New York, N. Y., 1936, p. 336.

(3) Arthur Rose and L. M. Welshans, *Ind. Eng. Chem.*, **32**, May (1940).

(4) Schmitt and Boord, THIS JOURNAL, **54**, 751 (1932); **53**, 2427 (1931).

(5) E. S. Beale, "Science of Petroleum," Vol. II, Oxford University Press, Oxford, 1937, p. 1280, etc.

(6) H. A. Beatty and G. Calingaert, *Ind. Eng. Chem.*, **26**, 504 (1934).