

THE CHEMICAL AND PHYSICAL  
PROPERTIES OF 2- AND 3-BROMOMETHYLCYCLOHEXANES

by

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ESTABLISHED BROWN'S

TO MY WIFE AND CHILDREN

ADVANCE BOND

# ADVANCE BOND

W. A. BROWN, JR.

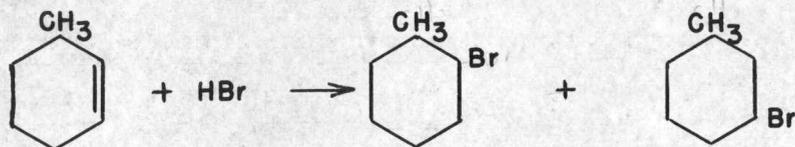
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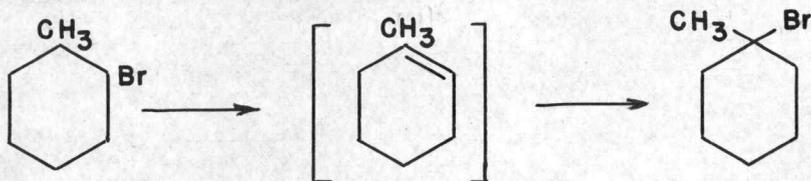
INTRODUCTION

Earlier work in this laboratory by Rogers (6) and Dickison (1) was concerned with the products obtained when HBr was added to the unsymmetrical olefin 3-methylcyclohexene. The major products expected would be:



Infrared methods were used by both Dickison and Rogers for the quantitative analysis of the addition products.

Murat (4, p. 111) observed that the 2-bromomethylcyclohexane had a tendency to split out HBr, and if this added back to the ring, Markownikoff's rule would predict the 1-bromo compound as the chief product if the double bond is localized as shown below.



Dickison showed that the reaction of HBr with 3-methylcyclohexene gave a predominance of the 3-bromomethylcyclohexane, which substantiated the work of Rogers and lends support to the theory of hyperconjugation but as in the work of Rogers, yields were rather low in some cases.

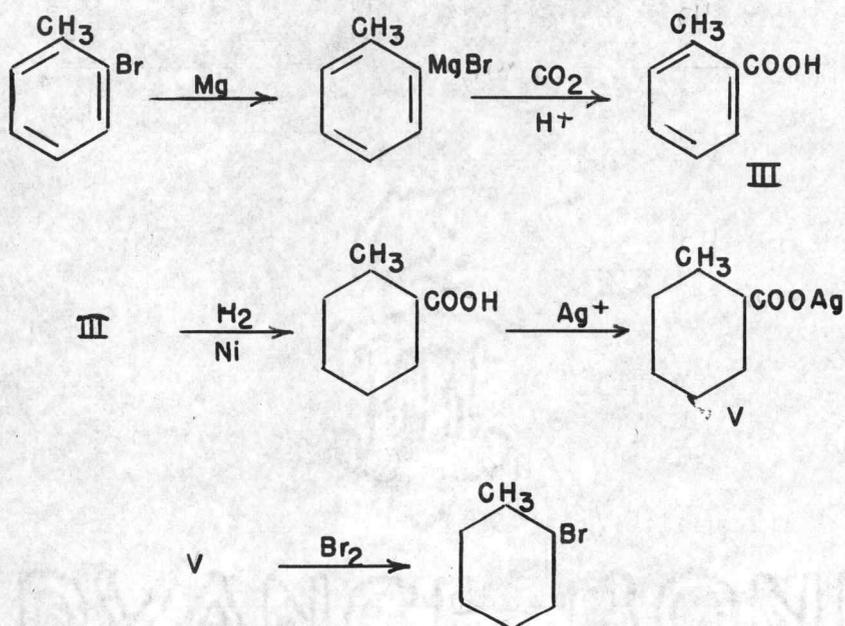
Rearrangement might yield some of the 1- and 4-bromomethylcyclohexanes and since these possibilities exist, the development of a quick method of analysis would be necessary in order to support the results obtained by Rogers and Dickison.

The infrared method used for the quantitative analysis of the addition products requires pure samples of the isomeric bromomethylcyclohexanes as model compounds and the reported instability of the 2-bromomethylcyclohexane is a particularly disturbing feature. It is desirable therefore, to develop an independent means of determining the purity of 2-bromomethylcyclohexane.

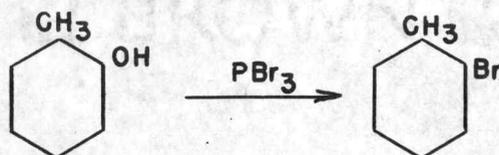
## PURPOSE OF INVESTIGATION

It was the intent of this investigation to try to prepare pure 2-bromomethylcyclohexane and to develop an analytical method other than infrared analysis for this compound.

The following sequence illustrates the first method attempted in preparing 2-bromomethylcyclohexane (Method A).



Method B is illustrated below:



## EXPERIMENTAL

## - Method A -

Ortho-Toluic Acid

Ortho-Toluic acid was prepared via the Grignard derivative from 0.1 mole o-bromo toluene.

The Grignard reagent was prepared by mixing the bromotoluene and an equivalent amount of magnesium in 200 ml of anhydrous ether in a Grignard apparatus. Heat was applied and after a short induction period, a vigorous reaction set in. When this subsided, the mixture was heated with stirring at a reflux temperature for 20-30 minutes. After cooling to room temperature, the contents of the flask were forced over by nitrogen into a dry-ice mixture.

The mixture was then decomposed while still very cold by the slow addition of an excess of dilute sulfuric acid. The product was isolated by filtration and recrystallized several times from boiling water.

Melting point 102-104°C Literature (2, p. 1098-1099)  
104-105°C

Yield 8.2 g Theoretical yield 13.6 g

Percentage yield 60%

Hexahydro-o-toluic Acid

This substance was prepared by the method of Macbeth et al. (3, p. 1012). Ortho-toluic acid (10.5 g) was added to 15 ml of hot water. Nine per cent NaOH solution was slowly added with stirring until all the acid dissolved and the mixture was made neutral to litmus. The solution was diluted with distilled water to 100 ml and then transferred to a special Parr bottle to be used in a high pressure hydrogenation apparatus.<sup>1</sup>

One milliliter of an alcohol slurry of W-4 Raney nickel was added and the material was heated at 240-250°C and 2500-psi for 14 hours.<sup>2</sup> The final pressure was 2300-psi.

The nickel residues were removed by filtration and the filtrate was acidified with dilute sulfuric acid and placed in a freezer overnight. The tan colored solid was separated and recrystallized several times from a large quantity of boiling water, dried and pressed repeatedly between filter paper in order to try to remove last traces of the oily cis isomer.

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<sup>1</sup>From previous runs, it was found that less loss occurred if the bottle had a narrow neck and was closed by a flat glass plate.

<sup>2</sup>Parlic, A. A., and Homer Adkins. Preparation of a Raney Nickel Catalyst. Journal of the American Chemical Society. 68:1471. 1946.

Melting Point	48-51°C	Literature (3, p. 1010)
		51-52°C
Yield of Crude Product	5 g	Theoretical Yield 11 g
Percentage Yield	45.4%	

#### Silver Salt of Hexahydro-o-toluic Acid

The procedure for the preparation of this compound was essentially that of Oldham and Obbelohde (5, p. 371).

Four grams of hexahydro-o-toluic acid were added to 50 ml of warm, distilled water in a beaker. The mixture was stirred with warming and reagent grade sodium carbonate was added until the solution was neutral to pH paper and remained clear. The solution was filtered while still hot and then allowed to cool.

The silver salt is light sensitive and its preparation, therefore, must be carried out in the dark. The neutral solution of sodium hexahydro-o-toluate prepared above was added with stirring to 4.8 g of reagent grade silver nitrate dissolved in 50 ml of cold distilled water while maintaining the beaker in a cold water bath. The resulting thick, white paste was covered with more cold water and stirred 1-2 minutes longer. The thick mixture was then set aside for an additional 2-3 minutes. The product was collected on a Buchner funnel with a fine filter paper and then rapidly washed with distilled water, alcohol, and finally ether.

The white precipitate was transferred to a beaker and dried in a vacuum over phosphorus pentoxide in the dark for six days.

Weight of Product 4.9 g

Brominative Decarboxylation of the Silver Salt of Hexahydro-o-toluic Acid - The Hunsdieker Reaction

The method of Winston et al. (8, p. 878) was followed.

Since it is essential that all moisture be removed, special precautions were followed in order to carry out the decarboxylation in an absolutely moisture free environment.

Inserted into the center neck of a three-neck 200 ml  $\text{F}$  flask was a  $\text{4}$  type adaptor tube carrying a reflux condenser on the side arm of the  $\text{4}$  adaptor. The assembly was placed in an oven at  $100^{\circ}\text{C}$  for three days. The other end of the condenser carried a  $\text{CaCl}_2$  drying tube. This assembled apparatus was quickly removed and a small Florence flask covered with black paper and containing 4.9 g of the dry silver salt was connected to one of the side necks of the flask by means of a short length of large diameter rubber tubing. The apparatus was placed in the oven in such a manner that the silver salt would not spill from its container and the apparatus was dried at  $100^{\circ}\text{C}$  for two additional days.

The rubber connector was clamped shut with a large screw clamp and then the assembly was removed from the oven. The top of the adaptor tube was closed by a stainless steel, packed type, high vacuum stirrer.<sup>3</sup> The third neck of the three-neck  $\text{F}$  flask was closed with a cork.

To a self-equalizing type addition funnel, previously packed with a wad of glass wool and dried at  $100^{\circ}\text{C}$  for 2 days, was quickly added ten to fifteen grams of phosphorus pentoxide. Three and two-tenths grams of reagent grade bromine dissolved in 150 ml of reagent grade carbon tetrachloride, both of which were previously dried over phosphorus pentoxide were then quickly added. The top of the funnel was closed and the funnel was assembled to the flask thus replacing the cork in the three-neck flask. Nitrogen gas, dried by passing it through a long column of glass wool and phosphorus pentoxide, was passed into the apparatus slowly via the top of the addition funnel.

The silver salt was very slowly shaken into the flask at  $15^{\circ}\text{C}$ , with stirring at high speed, in such a manner that one-third was added in a period of three hours. No reaction was noticed so the mixture was gradually heated at  $70^{\circ}\text{C}$ . At this point, the evolution of carbon dioxide was slow to moderate. The temperature was raised to the

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<sup>3</sup>Constructed by the author. This stirrer was used since it was completely moisture tight.

boiling point of the carbon tetrachloride, at which point the reaction became vigorous.

The temperature was lowered to 55-65°C and gas evolution continued at a slow rate and the solution lightened to a light orange color. All of the remaining silver salt was added in five and one-half hours at 60°C with stirring.

The silver bromide was removed by filtration and the carbon tetrachloride solution was washed with several small portions of dilute sodium bisulfite solution.

The carbon tetrachloride was removed by distillation at atmospheric pressure and the dark red-brown liquid was fractionated through a short micro Vigreux column at 10-mm pressure in which the product passed over at 78-95°C.

$n_D^{25}$  1.4870

Literature (6) 1.4871

Yield of Crude Product 2.15 g

Theoretical Yield 3.48 g

Percentage Yield 61.7%

- Method B -

### 2-Bromomethylcyclohexane

Twenty-two and eight-tenths grams (0.2 moles) of redistilled 2-methylcyclohexanol were placed in a three-necked flask equipped with a stirrer, dropping funnel and a thermometer. The alcohol was stirred and cooled to -10°C in an ice-salt bath and 19.8 grams (0.073 moles) of

phosphorous tribromide were slowly added so that the temperature did not rise above  $0^{\circ}\text{C}$ . After the phosphorus tribromide had been added (2 - 2 1/2 hours), stirring was continued and the reaction mixture was allowed to come to room temperature and left overnight. The crude bromide was distilled under vacuum, cooled to  $0^{\circ}\text{C}$  and washed with three 15 ml portions of ice cold concentrated sulfuric acid, and then shaken with 2-3 grams of anhydrous sodium carbonate until no more hydrogen bromide was evolved. The compound distilled at  $64-65^{\circ}\text{C}$  (19 mm).

$n_{\text{D}}^{25}$  1.4892

Literature (6) 1.4871

Yield 11.5 g

Theoretical Yield 35.4 g

Percentage Yield 32.5%

### 3-Bromomethylcyclohexane

The 3-bromomethylcyclohexane was also produced from 3-methylcyclohexanol by Method B and was obtained in a 28.3 per cent yield.

$n_{\text{D}}^{25}$  1.4870

Literature  $n_{\text{D}}^{25}$  (6) 1.4867

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## - Preparation of Samples for Analysis -

## A. Model Compounds

2-Methylcyclohexanone

Eight and two-tenths grams of reagent grade potassium dichromate were dissolved in 40 ml of distilled water to which was added 3.8 ml of concentrated sulfuric acid. The mixture was cooled to 30°C, and added slowly with stirring, to 4.6 g of commercial 2-methylcyclohexanol in a 125 ml flask. The temperature rises and was kept at 55-60°C for 10 minutes. At the end of this time, the mixture was allowed to stand at room temperature for one hour.

The ketone was steam distilled from the dark brown mixture and the distillate was extracted with ether. The ether was removed on a warm water bath. The ketone was obtained in a 88.7 per cent yield.

The crude ketone was then converted to the semi-carbazone and hydrolyzed by the general method of Smith and Nichols (7, p. 491) in order to obtain the purified ketone.

$n_D^{25}$  1.4461

Literature (2, p. 790)  
1.45049<sup>14.6</sup>

B.P. 162°C (760 mm Hg)

Literature (2, p. 790) 163°C

Yield 2 g

Theoretical Yield 4.5 g

Percentage Yield 67%

3-Methylcyclohexanone

3-methylcyclohexanone, prepared from 4.6 g of commercial 3-methylcyclohexanol in the same manner as used for the preparation of the 2-keto derivative, was converted to the bisulfite addition compound and hydrolyzed with 20 ml of 10 per cent sodium hydroxide in order to obtain the purified product.

$n_D^{25}$  1.4444

Literature (2, p. 790-791)  
(dl) 1.4430<sup>20</sup>

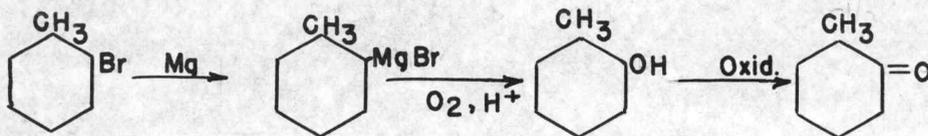
Yield 2 g

Theoretical yield 3 g

Percentage Yield 67%

## B. Reaction Products

The compound, 2-bromomethylcyclohexane, prepared by Method B, was subjected to the following sequence of reactions. By these series of reactions the 2-methylcyclohexanol and 2-methylcyclohexanone were prepared.



The 3-bromomethylcyclohexane, also produced by Method B, was likewise converted to the corresponding 3-methylcyclohexanol and 3-methylcyclohexanone.

The reaction products and the samples used in analysis were studied by gas phase methods. The samples were injected into the preheated system of a Perkin Elmer Model 154B Vapor Fractometer and most of the runs were made at temperatures ranging from 152° to 162°C. Columns used were single six-foot type A columns (dinonyl phthalate) or two six-foot columns in series.

Retention volumes were calculated for various compounds prepared or studied in this work and are tabulated in Table I.

TABLE I

## RETENTION VOLUMES OF PRODUCTS STUDIED

Substance	Retention Volume
2-Bromomethylcyclohexane	887.5 ml at 152°C (6'A)
3-Bromomethylcyclohexane	887.5 ml at 152°C (6'A)
2-Methylcyclohexanol	555 ml at 154°C (6'A)
3-Methylcyclohexanol	568 ml at 154°C (6'A)
2-Methylcyclohexanone	550 ml at 156°C (6'A)
3-Methylcyclohexanone	612.3 ml at 156°C (6'A)
2-Methylcyclohexanone	1147 ml at 160°C (12'A)
3-Methylcyclohexanone	1244 ml at 160°C (12'A)
4-Methylcyclohexanone	1272 ml at 160°C (12'A)
Cyclohexanone	905.5 ml at 160°C (12'A)

## DISCUSSION OF RESULTS

The purpose of this work was to try to prepare pure 2-bromomethylcyclohexane and to develop an analytical method to determine the purity of that substance.

Two methods were employed in the preparation of the 2-bromomethylcyclohexane. The Hunsdieker reaction (Method A) was abandoned in favor of the more direct method of reacting 2-methylcyclohexanol with phosphorus tribromide as employed by Rogers (Method B). The compound, 3-bromomethylcyclohexane, was also prepared by Method B for use in the analytical procedure.

Gas phase chromatography was chosen as a possible analytical method to supplement the quantitative infrared analysis which had been done by Rogers and Dickison. Two reference compounds, 2- and 3-methylcyclohexanones, were prepared by direct methods to provide standards for comparison with the compounds produced in the experimental work.

Freshly prepared samples of the 2- and 3-bromomethylcyclohexanes were examined separately by gas phase chromatography and each bromide gave a well defined peak indicating reasonable high purity. The retention volumes of these two compounds were identical and no separation was achieved using a mixed sample.

The two bromides were converted to the corresponding alcohols and subjected to the same procedure as that used with the bromides. Samples of separate alcohols gave sharp peaks but the peaks produced by a mixed sample had merged to such an extent that it was evident that there had been but a small amount of separation of the two alcohols.

The two alcohols were converted to the corresponding ketones. The retention volumes of the two ketones differed by approximately 100 ml and separation on a 12' type A column was effected. The physical constants for these ketones were almost identical to those for the ketones used as reference compounds.

This work is primarily concerned with the purity of the 2-bromomethylcyclohexane and the conversion of the bromides through the alcohols to the ketones might, by these fractionating steps, tend to reduce the quantity of 3-bromomethylcyclohexane impurity present in a sample of original 2-bromo compound. To test the effect of these fractionating steps, a mixture composed of ten per cent 3-bromomethylcyclohexane and ninety per cent 2-bromomethylcyclohexane was converted, through the mixed alcohols, to the mixed ketones. The chromatograph of the resulting mixture indicated the presence of approximately fifty per cent 3-methylcyclohexanone. The conversion of the bromides to the ketones had increased the amount of product obtained

from the 3-bromo impurity and thus enhances the value of this analytical method for determining the purity of the 2-bromo compound.

The results obtained with this mixture indicates that a limiting value can be placed on the amount of the 3-bromo compound present as an impurity in freshly prepared 2-bromomethylcyclohexane. It is evident that ten per cent impurity can be readily detected. The experimental data indicates that the 3-bromo compound, if present, in 2-bromomethylcyclohexane, is present in an amount not to exceed three per cent. The result of this analysis is in good agreement with the data obtained by infrared methods.

In order to ascertain whether or not 4-bromomethylcyclohexane was present in the reaction mixture, commercial 4-methylcyclohexanone was analyzed by gas phase chromatography. The 4-bromomethylcyclohexane appeared to be absent since the presence of 4-methylcyclohexanone was not shown to exist from gas phase chromatographs of the 2- and 3-methylcyclohexanones produced from the bromides.

## SUMMARY

The compounds, 2- and 3-bromomethylcyclohexanes, were prepared by the reaction of phosphorus tribromide with 2- and 3-methylcyclohexanols. The 2-bromo derivatives were converted to the corresponding Grignard reagents followed by oxidation to the alcohols and finally to the ketones.

Separation and analysis of the mixed bromides has been effected by gas phase chromatography by first converting the bromides to the ketones.

Analysis of the mixed bromides both by infrared and gas phase chromatographic methods shows that initially prepared 2-bromomethylcyclohexane is of reasonably high purity and the amount of 3-bromo impurity is probably three per cent or less.

No indication of 4-bromomethylcyclohexane was given by the analytical methods used in this work.

The refractive index of 2-bromomethylcyclohexane changes over a period of time indicating rearrangement or other chemical change.

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