

six ketones. As noted in the earlier paper, acetophenone shows an anomalous behavior.

The relationship of wave height to concentration of ketone was found to be independent of the presence of toluene, *t*-butyl alcohol, aluminum hydroxide, and another ketone, or alcohol such as was known to be present in the reaction mixtures. However, the relationship is not independent of the concentration of water or tetramethylammonium hydroxide in the polarographic cell. The relationship is not independent of the characteristics of the particular capillary electrode.

### Summary

Thirteen representative ketones have been compared with each other as oxidizing agents. A numerical statement of the result of the comparison is given in the last column of Table II. The comparisons were made by equilibrating two ketones against each other in the presence of aluminum *t*-butoxide and the alcohols corresponding to the ketones. The concentration of the ketones at equilibrium was determined by means of a polarograph.

MADISON, WISCONSIN

RECEIVED SEPTEMBER 28, 1939

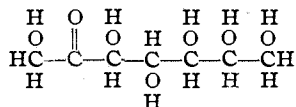
[CONTRIBUTION FROM THE LABORATORY OF BIOLOGICAL CHEMISTRY, LOYOLA UNIVERSITY SCHOOL OF MEDICINE]

## The Reduction Products of *d*-Glucoheptulose<sup>1</sup>

BY FRED L. HUMOLLER, STANLY J. KUMAN AND FRED H. SNYDER

In 1928 Bertrand and Nitzberg<sup>2</sup> prepared *l*-glucoheptulose (designated by them as  $\alpha$ -glucoheptulose) by the action of *Bact. xylinium* on  $\alpha$ -glucoheptitol. In their studies on the structure of this ketoheptose they subjected it to the action of sodium amalgam. From the reaction products they isolated  $\alpha$ -glucoheptitol and a substance which they named  $\alpha$ -glucoheptulitol. This new substance melted at 144° and showed a specific rotation of  $-2.24^\circ$ .<sup>3</sup> Later Khouvine and Nitzberg<sup>4</sup> repeated the work of Bertrand and Nitzberg and also obtained  $\alpha$ -glucoheptulitol as one of the reduction products of *l*-glucoheptulose. They assumed, though not without reservations, that  $\alpha$ -glucoheptulitol was either  $\beta$ -*d*-glucoheptitol or  $\beta$ -*l*-glucoheptitol.

In 1930 Austin<sup>5</sup> prepared *d*-glucoheptulose by the rearrangement of  $\alpha$ -*d*-glucoheptose in lime water. Because of its method of preparation and because of the identity of its osazone with that obtained from  $\alpha$ -*d*-glucoheptose, Austin assigned to *d*-glucoheptulose the formula



(1) These studies, a portion of which was reported on the program of the meeting of the American Chemical Society in Milwaukee, September, 1938, were abstracted in part from a dissertation submitted by Mr. Kuman to the Graduate School of Loyola University in partial fulfillment of the requirements for the degree of Master of Science.

(2) Bertrand and Nitzberg, *Compt. rend.*, **186**, 925 (1928).

(3) Bertrand and Nitzberg, *ibid.*, **196**, 1172 (1928).

(4) Khouvine and Nitzberg, *ibid.*, **196**, 218 (1933).

(5) Austin, *THIS JOURNAL*, **52**, 2106 (1930).

From its formula it can be seen that *d*-glucoheptulose should yield upon reduction of its ketone group  $\alpha$ -glucoheptitol or  $\beta$ -*d*-glucoheptitol, or both, provided the structure which Austin assigned to this ketose is correct.

However, when Khouvine and Nitzberg<sup>6</sup> reduced *d*-glucoheptulose with sodium amalgam, they obtained  $\alpha$ -glucoheptitol and the enantiomorph of  $\alpha$ -glucoheptulitol but not  $\beta$ -*d*-glucoheptitol as predicted by Austin's formula. This new substance, which they called  $\alpha$ -*d*-glucoheptulitol, melted at 143–143.5° and showed a specific rotation of  $+2.10^\circ$ . From their studies on the structure of this substance they came to the conclusion that it was not identical with either  $\beta$ -*d*-glucoheptitol or  $\beta$ -*l*-glucoheptitol, but that it might be a heptitol of unknown structure. They suggested that the glucoheptulitols might be formed by the local concentration of alkali during the reduction with sodium amalgam. This view was strengthened by the fact that when they reduced *d*-glucoheptulose catalytically no  $\alpha$ -*d*-glucoheptulitol was obtained but only the two glucoheptitols predicted by Austin's formula.<sup>7</sup>

In view of the findings of the French workers it seemed desirable to us to extend their studies on the structure of the glucoheptulitols. For that purpose *d*-glucoheptulose was prepared by the rearrangement of  $\alpha$ -*d*-glucoheptose, using Austin's method<sup>5</sup> with some modifications. These modifications were introduced in the separation of the

(6) Khouvine and Nitzberg, *Compt. rend.*, **198**, 985 (1934).

(7) Khouvine, *ibid.*, **204**, 983 (1937).

ketoheptose from the unchanged aldoheptose. Whereas Austin had carried out this separation by oxidizing the unchanged aldoheptose with bromine and separating the salt of the aldonic acid from the ketoheptose by alcohol, advantage was taken of the fact that diphenylmethanedimethyldihydrazine reacts very readily with certain aldoses at room temperature but does not react with ketoses.<sup>8</sup> By means of this reagent it was easily possible to separate the ketose nearly quantitatively from the aldose.

*D*-Glucoheptulose, prepared in this manner, proved to be identical with a sample left by the late Dr. Austin. The reduction of this ketose was carried out with sodium amalgam at room temperature in a medium kept faintly acid to litmus by frequent additions of sulfuric acid. Several reductions were carried out and in all but one case  $\alpha$ -*D*-glucoheptulitol was one of the products of the reaction, the only other crystalline product which could be isolated being  $\beta$ -*D*-glucoheptitol. In one case both  $\alpha$ -glucoheptitol and  $\beta$ -*D*-glucoheptitol were obtained along with  $\alpha$ -*D*-glucoheptulitol. Both glucoheptitols were identified by comparing their physical constants with those of the respective glucoheptitols prepared by the reduction of the crystalline aldoheptoses and with the constants given in the literature.

The  $\alpha$ -*D*-glucoheptulitol obtained, after having been recrystallized three times from absolute ethanol, melted at 141<sup>o</sup> and showed a specific rotation of +2.04<sup>o</sup> in water. Further recrystallizations from ethanol failed to change these constants. The molecular weight of  $\alpha$ -*D*-glucoheptulitol, as determined by the cryoscopic method, was found to be 192. An elementary analysis of this substance for carbon and hydrogen gave values which differed from those calculated for a heptitol by amounts greater than could be ac-

counted for by experimental errors (Table I). Attempts to determine the number of hydroxyl groups in  $\alpha$ -*D*-glucoheptulitol were unsuccessful, for in every attempt to prepare the acetate of glucoheptulitol only the heptaacetate of  $\alpha$ -glucoheptitol was obtained. The identity of this heptaacetate was proved by elementary analysis, melting point, absence of optical rotation and melting point when mixed with a sample of pure heptaacetate of  $\alpha$ -glucoheptitol. In the same manner every attempt to prepare a trityl derivative of  $\alpha$ -*D*-glucoheptulitol yielded as the only crystalline product a substance which was proved to be identical, according to the standards mentioned in the case of the acetate, with the ditryl derivative of  $\alpha$ -glucoheptitol.

In further studies to elucidate the structure of  $\alpha$ -*D*-glucoheptulitol it was subjected to the action of acid and alkali. Boiling  $\alpha$ -*D*-glucoheptulitol with 0.1 *N* sulfuric acid for thirty minutes left it totally unchanged. Similarly, boiling it with 10% barium hydroxide for ninety minutes did not produce any change, since the unchanged glucoheptulitol could be isolated from the solution. However, when  $\alpha$ -*D*-glucoheptulitol was boiled with 10% sulfuric acid for seventy-five minutes, some reaction did take place, for the only crystalline substance which could be isolated from the solution was  $\alpha$ -glucoheptitol besides a small quantity of unchanged glucoheptulitol.

Considering all the properties of glucoheptulitol thus far mentioned, one might be tempted to assume that this substance is an anhydride of  $\alpha$ -glucoheptitol, crystallizing as four molecules of anhydride with three molecules of water. It would be necessary to assume three molecules of water of crystallization in order to satisfy the values obtained for carbon and hydrogen in the elementary analysis of  $\alpha$ -*D*-glucoheptulitol.<sup>1</sup> It is, however, difficult to visualize a substance containing water of crystallization which can be recrystallized repeatedly from anhydrous solvents and which can be heated in a high vacuum at 100<sup>o</sup> without any loss of this water of crystallization.

The conclusion, therefore, seems justifiable that  $\alpha$ -*D*-glucoheptulitol is not a pure chemical substance but consists of mixed crystals, made up very largely of  $\alpha$ -glucoheptitol plus a small amount of an optically active impurity. This latter substance is probably a decomposition product of *D*-glucoheptulose formed during the reduction of the ketose. This conclusion has been reached in

TABLE I

ELEMENTARY ANALYSIS OF  $\alpha$ -*D*-GLUCOHEPTULITOL

% C	% H	Remarks
39.37	7.80	Bertrand and Nitzberg, <i>Compt. rend.</i> , 186, 1773 (1928)
40.54	7.51	Humoller, Kuman and Snyder, av. of 11 macro-analyses
40.50	7.40	Schoeller, Berlin, Germany (com. analyst), av. of 2 micro-analyses
39.61	7.60	Values calcd. for a heptitol

(8) Von Braun, *Ber.*, 43, 1495 (1910); 50, 42 (1917).

(9) All melting points obtained by the authors were determined in a capillary glass tube suspended in a bath of sulfuric acid and are not corrected for stem exposure. The French workers used the bloc Maquenne for their melting point determinations.

spite of three statements appearing in the literature: (a) The French workers in their several papers on the properties and structure of the glucoheptulitols state that they are pure substance and probably are heptitols of unknown structure; (b) Elsner in Tollens' "Handbook on Carbohydrates"<sup>10</sup> assumes that  $\alpha$ -glucoheptulitol is identical with  $\beta$ -*d*-glucoheptitol; (c) and the Armstrongs in their monograph on carbohydrates<sup>11</sup> state that  $\alpha$ -glucoheptulitol is a heptitol not identical with the  $\beta$ -glucoheptitols.

Proof of the validity of the conclusion that  $\alpha$ -*d*-glucoheptulitol consists of mixed crystals of  $\alpha$ -glucoheptitol with a small amount of an optically active impurity is furnished by the solubility studies shown in Table II. As can be seen from this table, when  $\alpha$ -glucoheptitol and  $\beta$ -*d*-glucoheptitol or  $\alpha$ -*d*-glucoheptulitol and  $\beta$ -*d*-glucoheptitol are dissolved together in methanol their solubilities are additive or nearly so. However, quite different results were obtained when the solubility of  $\alpha$ -glucoheptitol and of  $\alpha$ -*d*-glucoheptulitol as well as that of a mixture of these two substances was determined. A saturated solution of  $\alpha$ -*d*-glucoheptulitol contained 63.5 mg. of substance per 10 ml. and a saturated solution of  $\alpha$ -glucoheptitol in the same solvent contained 69.9 mg. of substance. If now a solution of methanol was saturated with respect to both  $\alpha$ -glucoheptitol and  $\alpha$ -*d*-glucoheptulitol, it contained 71.3 mg. of solids, or the same amount, within limits of experimental error, as a saturated solution of  $\alpha$ -glucoheptitol alone in methanol. In other words, a solution saturated with respect to  $\alpha$ -glucoheptitol is also saturated with respect to  $\alpha$ -*d*-glucoheptulitol.

### Experimental

**Preparation of *d*-Glucoheptulose.**— $\alpha$ -*d*-Glucoheptose was rearranged in lime water according to the method of Austin,<sup>8</sup> and from the rearrangement a mixture of *d*-glucoheptulose and  $\alpha$ -*d*-glucoheptose was obtained. An aqueous solution of 278 g. of this material in 1500 ml. of solution was prepared. Iodimetrically it was found that the solution contained 67.5 g. of aldoheptose. To this solution was added 58 g. of diphenylmethane-dimethyldihydrazine dissolved in 1500 ml. of 95% ethanol, and the solution allowed to stand overnight. The precipitate of the dihydrazone of  $\alpha$ -*d*-glucoheptose was filtered off and washed with 100-ml. portions of ethanol: yield 52 g.; m. p. 167°.

(10) Tollens-Elsner, "Kurzes Handbuch der Kohlenhydrate," 4th ed., Verlag Johann Ambrosius Barth, Leipzig, Germany, 1935, p. 407.

(11) E. F. Armstrong and K. F. Armstrong, "The Carbohydrates," 5th ed., Longmans, Green and Co., London, 1934, p. 148.

To the combined filtrate and washings obtained, an excess of formaldehyde was added in order to remove the uncombined diphenylmethane-dimethyldihydrazine. After standing at room temperature overnight, the dihydrazone of formaldehyde was filtered off and discarded. The filtrate was concentrated to a small volume under reduced pressure. It was then rediluted and redistilled several times to remove all traces of formaldehyde. The formaldehyde-free sirup was then taken up in 300 ml. of a 7:3 mixture of methanol and ethanol. Upon seeding and cooling the system soon solidified to a crystalline mass. In this way 212 g. of crude *d*-glucoheptulose, m. p. 163°, was obtained and recrystallized to melt at 169°.

**Reduction of *d*-Glucoheptulose.**—Twenty grams of *d*-glucoheptulose was reduced with sodium amalgam at room temperature in the usual manner. After removing the sodium sulfate with ethanol, the system was concentrated to a thin sirup which was taken up in 100 ml. of boiling anhydrous ethanol. Upon cooling, a precipitate consisting of fine needles aggregating in rosetts began to form. After standing in the refrigerator overnight, the crystals were filtered off, washed with cold ethanol and dried *in vacuo* to give 10 g. of Crop I, melting at 139°. The mother liquors were concentrated to a sirup and taken up in 50 ml. of boiling anhydrous ethanol. Upon standing in the refrigerator overnight the solution yielded 4 g. of crystalline material as Crop II, m. p. 116°, consisting of small rectangles and fine needles.

Crop I was dissolved in 20 ml. of water, filtered through hardened filter paper, concentrated to a thin sirup under reduced pressure and taken up in 100 ml. of boiling absolute ethanol. After chilling the solution for several hours 9 g. of crystalline material was obtained which melted at 141°. Three subsequent recrystallizations from ethanol as well as recrystallizations from anhydrous methanol and from aqueous dioxane failed to alter the melting point of this substance. It was optically active,  $[\alpha]_D^{20} +2.04^\circ$  (*c*, 0.760; *l*, 2; H<sub>2</sub>O). This substance is therefore  $\alpha$ -*d*-glucoheptulitol.

Crop II was dissolved in a small quantity of boiling methanol, filtered and allowed to crystallize. Its melting point after this treatment was 119°. Another recrystallization from the same solvent brought the melting point up to 125°, but under the microscope two types of crystals still could be seen. Through fractional crystallization from hot methanol four different crops were obtained: Crop IIa, m. p. 129°, Crop IIb, m. p. 128°, Crop IIc, m. p. 126°, Crop IID, m. p. 126°. Crops IIa and IIb were combined and recrystallized from methanol to yield a product which crystallized in small rectangular plates melting at 129°. Crop IIc was recrystallized twice from methanol to yield a substance melting at 129°. All three crops were combined and recrystallized from methanol to yield 1 g. of small rectangular plates, m. p. 129°. They showed a slight optical activity,  $[\alpha]_D^{20} +0.62^\circ$  (*c*, 1.004; *l*, 2; H<sub>2</sub>O). When mixed with a sample of  $\beta$ -*d*-glucoheptitol, obtained by the reduction of crystalline  $\beta$ -*d*-glucoheptose, it melted at 129°. The substance therefore is  $\beta$ -*d*-glucoheptitol.

Crystals of Crop IID when mixed with crystals of  $\beta$ -*d*-glucoheptitol melted at 115°; when mixed with crystals of  $\alpha$ -glucoheptitol (m. p. 129°) they melted at 127°. No op-

tical rotation was observed. Presumably Crop II<sub>d</sub> consisted of impure  $\alpha$ -glucoheptitol.

**Effect of Acid upon  $\alpha$ -*d*-Glucoheptulitol.**—Six grams of  $\alpha$ -*d*-glucoheptulitol was dissolved in 30 ml. of 10% sulfuric acid and boiled under the reflux for seventy-five minutes. The solution was decolorized with charcoal and its specific rotation was found to be  $[\alpha]^{25}_D -1.83^\circ$ . The filtrate, obtained after removal of the sulfate ions as barium sulfate, was concentrated to a thin sirup. This sirup was taken up in 85 ml. of hot absolute ethanol. After the solution was cooled, copious crystallization occurred. The crystals were filtered off and after having been dried *in vacuo* at room temperature they weighed 3 g. After three recrystallizations the substance melted at  $129^\circ$  and was found to be optically inactive. A mixture of some of these crystals with pure  $\alpha$ -glucoheptitol melted at  $129^\circ$ . Hence this substance is  $\alpha$ -glucoheptitol. The mother liquors from the first crystallization of this crop were concentrated to a thin sirup and taken up in absolute ethanol. On cooling a second crop, weighing 0.5 g., was obtained. This crop showed a melting point of  $138^\circ$  and a specific rotation of  $[\alpha]^{25}_D +2.4^\circ$  (*c*, 0.480; *l*, 1; H<sub>2</sub>O), hence it consisted of impure  $\alpha$ -*d*-glucoheptulitol. The mother liquors of this crop were strongly levorotatory. They were not investigated any further.

Treatment of  $\alpha$ -*d*-glucoheptulitol with 0.1 *N* sulfuric acid at boiling temperature had no effect upon the substance, for it could be recovered unchanged nearly quantitatively.

**Effect of Barium Hydroxide upon  $\alpha$ -*d*-Glucoheptulitol.**—Four grams of  $\alpha$ -*d*-glucoheptulitol was dissolved in 30 ml. of 10% barium hydroxide solution and boiled for ninety minutes. After removing the barium as the sulfate the solution was concentrated to a thin sirup under reduced pressure. The sirup was taken up in 50 ml. of boiling ethanol and allowed to crystallize. After drying *in vacuo* at room temperature the crystals weighed 3.1 g. They showed a melting point of  $139^\circ$  and when mixed with a sample of the starting material the melting point remained unchanged.

**Reaction of  $\alpha$ -*d*-Glucoheptulitol with Acetic Anhydride.**—Four grams of  $\alpha$ -*d*-glucoheptulitol was heated with acetic anhydride and fused zinc chloride in the usual manner.<sup>12</sup> The product obtained crystallized in rhombic plates, and after one recrystallization from ethanol the crystals melted at  $115^\circ$ . The yield of acetate, starting with 4 g. of  $\alpha$ -*d*-glucoheptulitol, was 6 g. The acetate was optically inactive. A mixture of this acetate with the heptaacetate prepared from crystalline  $\alpha$ -glucoheptitol did not show any depression of the melting point.

*Anal.* Calcd. for C<sub>21</sub>H<sub>30</sub>O<sub>14</sub>: C, 49.79; H, 5.97. Found: C, 49.65; H, 6.08.

Similar results were obtained when the milder pyridine method of acetylation<sup>13</sup> was used. Again the only crystalline product obtained was found to be identical with  $\alpha$ -glucoheptitol heptaacetate.

**Reaction of  $\alpha$ -*d*-Glucoheptulitol with Trityl Chloride.**—The trityl derivative of  $\alpha$ -*d*-glucoheptulitol was prepared in the usual manner.<sup>14</sup> When 2 g. of  $\alpha$ -*d*-glucoheptulitol was allowed to react with 6 g. of trityl chloride in 25 ml. of

anhydrous pyridine according to this procedure, there was isolated a crystalline substance. After three recrystallizations from a 2:1 mixture of methanol and ethanol, it weighed 3.1 g. and showed a melting point of  $142$ – $143^\circ$ . The substance was optically inactive. Mixed with a sample of the ditrityl derivative prepared from  $\alpha$ -glucoheptitol (m. p.  $142$ – $143^\circ$ ), it showed no depression of the melting point.

*Anal.* Calcd. for C<sub>48</sub>H<sub>44</sub>O<sub>7</sub>: C, 77.57; H, 6.37. Found: C, 77.82; H, 6.47.

**Solubility Studies.**—The solubility of  $\alpha$ -*d*-glucoheptulitol alone or when mixed with one of the glucoheptitols was determined by suspending an excess of the substances listed in Table II in 30 ml. of anhydrous methanol. The

TABLE II  
SOLUBILITY STUDIES ON  $\alpha$ -*d*-GLUCOHEPTULITOL<sup>a</sup>

Substance	Mg. in 10 ml. of methanol		Av.	Calcd. <sup>b</sup>
$\beta$ - <i>d</i> -Glucoheptitol	47.8	48.0	48.0	
	48.2	48.0		
$\alpha$ - <i>d</i> -Glucoheptulitol	63.2	63.5	63.5	
	63.7			
$\alpha$ -Glucoheptitol	69.7	70.0	69.9	
	69.6	70.2		
$\alpha$ -Glucoheptitol + $\alpha$ - <i>d</i> -Glucoheptulitol	70.3	71.4	71.3	133.4
	72.0	71.6		
$\beta$ - <i>d</i> -Glucoheptitol + $\alpha$ - <i>d</i> -Glucoheptulitol	110.0	109.4	109.8	111.5
	110.2	109.7		
$\beta$ - <i>d</i> -Glucoheptitol + $\alpha$ -Glucoheptitol	112.7	112.3	112.6	117.9
	112.8	112.5		

<sup>a</sup> These studies were carried out in an incubator kept at  $37.0 \pm 1^\circ$ . <sup>b</sup> These values were obtained by adding the average solubility of each constituent of the mixture.

suspensions, contained in tightly stoppered  $1 \times 8''$  ( $2.5 \times 20$  cm.) test-tubes, were placed into a shaking machine which operated within an incubator set at  $37 \pm 1^\circ$ . The suspensions were shaken for two days and then filtered as quickly as possible. Then 10-ml. portions of the filtrate were pipetted into weighed evaporating dishes and the solvent driven off by heating the dishes on a steam-bath. The dishes were then dried to constant weight in a vacuum desiccator. The results of this study are listed in Table II.

**Molecular Weight of  $\alpha$ -*d*-Glucoheptulitol.**—The molecular weight of  $\alpha$ -*d*-glucoheptulitol was determined by the cryoscopic method. When 1.0009 g. of the substance was dissolved in 24.95 g. of water, the following lowering of the freezing point of the solution was observed:  $0.388^\circ$ ;  $0.383^\circ$ ;  $0.389^\circ$ ;  $0.389^\circ$ ; average,  $0.387^\circ$ . Substituting the average value,  $0.387^\circ$ , in the formula Molecular Weight =  $kw/dW$ , where *w* is the number of grams of solute dissolved in *W* g. of solvent, thereby causing a lowering of its freezing point of *d* degrees, and using 1860 as the value for *k*, the molecular weight of  $\alpha$ -*d*-glucoheptulitol was found to be 192.3.

## Summary

1. It has been shown that diphenylmethane-dimethyldihydrazine is a convenient reagent to

(12) Fischer, *Ann.*, **270**, 64 (1892).

(13) Behrend and Roth, *Ann.*, **331**, 359 (1904).

(14) Helferich, Moog and Juenger, *Ber.*, **58**, 872 (1925).

separate mixtures of *d*-glucoheptulose and  $\alpha$ -*d*-glucoheptose.

2. When *d*-glucoheptulose was reduced with sodium amalgam  $\beta$ -*d*-glucoheptitol and a substance which Khouvine and Nitzberg have called  $\alpha$ -*d*-glucoheptulitol were obtained.

3. Evidence has been presented to show that the substance called  $\alpha$ -*d*-glucoheptulitol is not a pure chemical entity but consists of mixed crystals of  $\alpha$ -glucoheptitol plus a small amount of an optically active impurity. This evidence is, briefly:

From the values obtained in elementary analyses and in molecular weight determinations it is

not possible to write a formula which is consistent with the chemical behavior of the substance.

The substance when heated in a 10% solution of sulfuric acid goes over into  $\alpha$ -glucoheptitol.

The substance when treated with acetic anhydride and a catalyst forms the heptaacetate of  $\alpha$ -glucoheptitol.

The substance when treated with trityl chloride in the presence of pyridine forms the ditryl derivative of  $\alpha$ -glucoheptitol.

A saturated solution of  $\alpha$ -glucoheptitol in methanol is also saturated with respect to this substance.

CHICAGO, ILLINOIS

RECEIVED AUGUST 26, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE UNIVERSAL OIL PRODUCTS COMPANY]

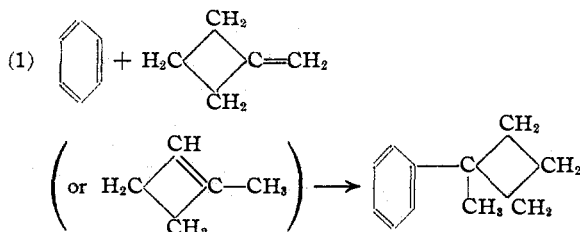
## Reaction of Benzene with Methylcyclobutene and Methylene-cyclobutane in the Presence of Sulfuric Acid<sup>1</sup>

BY V. N. IPATIEFF AND HERMAN PINES

The reaction between alkenes and aromatic hydrocarbons proceeds readily in the presence of various condensing agents.<sup>2</sup> Of the cycloalkenes only those containing five- and six-membered rings have been studied.

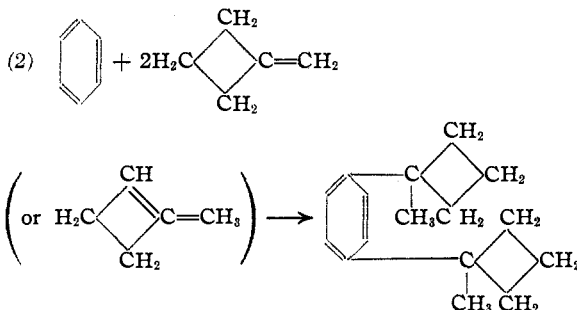
We were interested in studying the reaction of benzene with a cycloalkene containing a four-membered ring, in order to determine whether methylcyclobutylbenzene would be formed and whether a cyclobutyl group attached to a phenyl group is more stable than an unarylated cyclobutane. It was found that a mixture composed of methylcyclobutene and methylenecyclobutane reacts readily with benzene in the presence of 96% sulfuric acid at 0–10° to yield a product consisting of mono-, di- and trimethylcyclobutylbenzenes.

The reaction proceeds according to the equation



(1) Presented before the Division of Organic Chemistry of the American Chemical Society at Boston, Mass., Sept. 11–15, 1939.

(2) Ipatieff, Pines and Schmerling, paper presented before the Organic Division at the American Chemical Society meeting, Milwaukee, Wisconsin, September, 1938.



The monosubstituted benzene, which is probably 1-methyl-1-phenylcyclobutane,<sup>3</sup> contains a cyclobutyl ring which is stable toward nitrating mixture consisting of 1 vol. concentrated nitric and 2 vol. of concentrated sulfuric acid. A nitro compound was obtained from which a solid monoacetamino derivative was prepared. The cyclobutyl ring in methylcyclobutane decomposes when subjected to similar treatment.

The di-substituted benzene consists mainly of *p*-di-(1<sup>1</sup>-methylcyclobutyl)-benzene which melts at 33–34°. The higher-boiling fractions consist of tri-(1<sup>1</sup>-methylcyclobutyl)-benzene.

The cyclobutyl ring in the di-substituted benzene is stable toward 2% potassium permanganate at 100° and toward dilute nitric acid at a

(3) The position of the methyl group was not established, but on the basis of reaction of alkenes with benzene<sup>3</sup> one would expect the phenyl group to attach itself to the carbon atom of cyclobutyl containing the methyl group.