

more active than B. The substances are readily inactivated by cysteine and belong to the

thiol-reactive group of antibiotics.

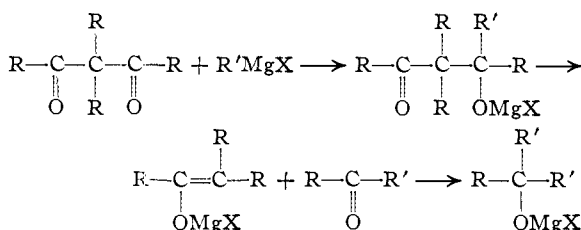
RENSSELAER, NEW YORK RECEIVED JANUARY 3, 1946

[CONTRIBUTION FROM THE COATES CHEMICAL LABORATORY OF LOUISIANA STATE UNIVERSITY]

## The Cleavage of Cyclic Beta Diketones. I. Tetramethyl-1,3-cyclobutanedione<sup>1</sup>

By J. L. E. ERICKSON AND GARRY C. KITCHENS<sup>2</sup>

It has been shown that various types of  $\beta$ -diketones<sup>3</sup> undergo a characteristic cleavage when treated with organic magnesium compounds



The ketone, formed as a primary cleavage product, does not survive in the presence of excess reagent and is converted readily to a tertiary alcohol.

Cyclic  $\beta$ -diketones have been reported to differ from open-chain  $\beta$ -diketones in their behavior toward the Grignard reagent.

Wedekind and Miller<sup>4</sup> added tetramethyl-1,3-cyclobutanedione to an excess of ethylmagnesium bromide and obtained a compound, b. p. 128–130° (30 mm.), presumably the corresponding glycol resulting from the normal addition of two moles of the reagent.

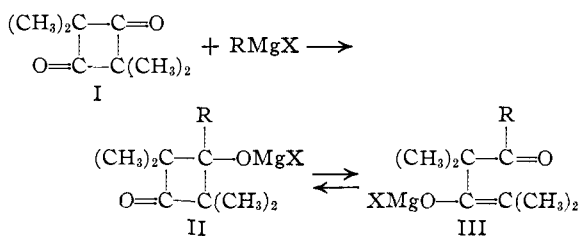
Hurd, Jones and Blunck<sup>5</sup> reported that ethyl 1,3 - diethyl - 2,4 - cyclobutanedione - 1,3 - dicarboxylate probably adds two moles of Grignard reagent to form a diaddition product, which subsequently undergoes hydrolytic rupture of the ring to yield a  $\beta$ -keto ester.

Geissman and co-workers<sup>6</sup> have observed that 2,2-dimethyl-1,3-indanedione and 8,8-dimethyl-7,9-perinaphthindanedione, compounds in which the two carbonyl groups are members of five and six-membered rings, respectively, undergo normal addition when treated with phenylmagnesium bromide.

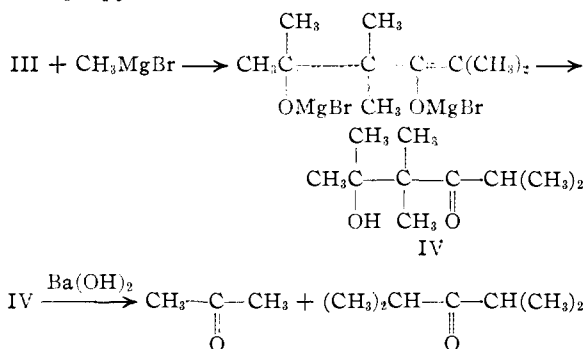
Contrary to the report of Wedekind and Miller, experiments in this Laboratory with tetramethyl-1,3-cyclobutanedione have shown conclusively that the reaction of this compound with a variety of organic magnesium and lithium compounds

(e. g., methyl, ethyl, phenyl and mesitylmagnesium bromide, phenyllithium and mesityllithium) leads to cleavage of the ring in every case where any reaction at all took place.

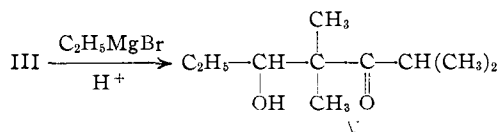
Tetramethyl-1,3-cyclobutanedione (I) reacted with an excess of Grignard reagent to yield a monoaddition product (II), which was unstable and underwent a reverse aldol condensation, resulting in cleavage of the ring with the formation of a primary cleavage product (III).



In the presence of an excess of methylmagnesium bromide, III did not survive and was converted into the  $\beta$ -hydroxy ketone, 5-hydroxy-2,4,4,5-tetramethyl-3-hexanone (IV), together with small quantities of acetone and diisopropyl ketone. When treated with barium hydroxide, IV decomposed almost quantitatively into acetone and diisopropyl ketone.



In the same manner it was found that ethylmagnesium bromide produced cleavage of I, yielding the primary cleavage product (III), which subsequently was reduced by the reagent to form 5-hydroxy-2,4,4-trimethyl-3-heptanone (V).



(1) Partly from a thesis submitted by Garry C. Kitchens to the Faculty of Louisiana State University, June, 1945, in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(2) Present address: Givaudan-Delawanna, Inc., Delawanna, N. J.

(3) Kohler and Erickson, *THIS JOURNAL*, **53**, 2301 (1931).

(4) Wedekind and Miller, *Ber.*, **44**, 3285 (1911).

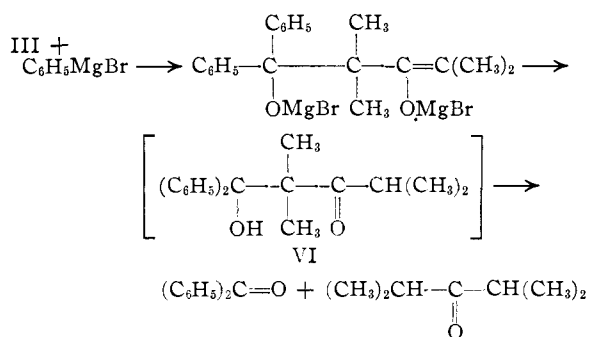
(5) Hurd, Jones and Blunck, *THIS JOURNAL*, **57**, 2033 (1935).

(6) (a) Geissman and Tulagin, *ibid.*, **63**, 3352 (1941); (b) Geissman and Morris, *ibid.*, **66**, 716 (1944).

presence of one hydroxyl and one carbonyl group was ascertained by an active hydrogen determination using the Zerewitinoff method. The identity of V was confirmed by its decomposition products with barium hydroxide, which proved to be propionaldehyde and diisopropyl ketone. Attempts to avoid reduction by adding only one mole of the reagent failed, as no other product was obtained. This type of reduction is not unusual even with ethylmagnesium bromide as the reduction of sterically hindered ketones with this reagent has been reported.<sup>7</sup>

These results differ from those of Wedekind and Miller,<sup>4</sup> who erroneously describe the product of the reaction as a cyclic glycol. In view of the fact that their presumed glycol and V had the same boiling point and approximately the same analysis, their identity was at once suspected. They failed presumably to recognize their product as the  $\beta$ -hydroxy ketone (VI), because they did not determine the number of hydroxyl groups in the molecule. In view of our results there is now no evidence for the formation of either the cyclic glycol or its reduction product. The reported b. p. (124–125°) of their cyclic hydrocarbon, corresponding to the reduction of the glycol, is probably in error, since V should reduce to 2,4,4-trimethylheptane<sup>8</sup> boiling at 151–152°.

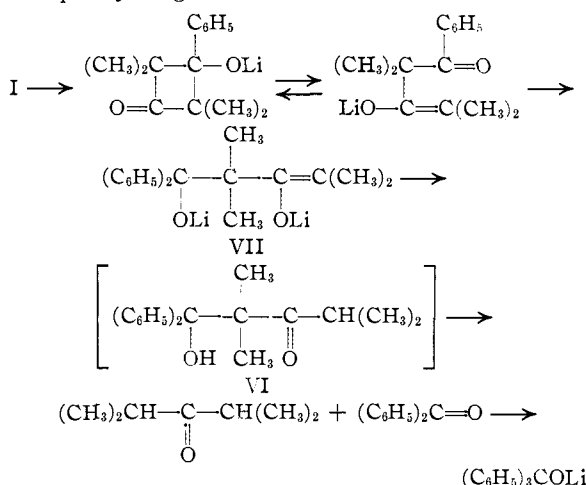
When I was added to an excess of phenylmagnesium bromide cleavage of the molecule occurred, but the expected  $\beta$ -hydroxy ketone (VI) could not be isolated by any of the various procedures used for the hydrolysis of the magnesium complex. All attempts to isolate VI led to its decomposition products, benzophenone and diisopropyl ketone.



The inverse addition of only one mole of phenylmagnesium bromide to I was carried out in an attempt to prevent further addition of the reagent to the primary cleavage product and thus render possible the formation of a diketone, which is one step nearer the cleavage process than the  $\beta$ -hydroxy ketone. This effort failed as only the decomposition products of VI, benzophenone and diisopropyl ketone, were obtained.

It has been established that the behavior of open-chain  $\beta$ -diketones toward organic lithium

compounds is the same as their behavior toward organic magnesium compounds.<sup>9</sup> It is possible, however, that phenyllithium might yield a more stable primary addition product than that obtained with phenylmagnesium bromide and in this way avoid cleavage of the ring. In order to test this hypothesis, I was treated with phenyllithium, but it was found that phenyllithium reacted in a manner comparable to phenylmagnesium bromide. In addition to diisopropyl ketone and benzophenone, triphenylcarbinol was also obtained. This was surprising, since it was not produced by any of the reactions between I and phenylmagnesium bromide.



Experiments were conducted in which phenyllithium was added slowly to an agitated mixture of iced acid and benzophenone and also to a mixture of iced acid and diisopropyl ketone. No addition occurred in the case of the diisopropyl ketone, but benzophenone competed favorably with hydrochloric acid for phenyllithium and was converted to triphenylcarbinol. When phenylmagnesium bromide was substituted for phenyllithium, no triphenylcarbinol was formed. This proved that benzophenone is capable of reverting to triphenylcarbinol during the hydrolysis process. Since only benzophenone was produced in the reaction between phenylmagnesium bromide and I, these facts indicate (1) the formation of VII and consequent absence of benzophenone, and (2) that benzophenone was formed by the decomposition of VI upon hydrolysis with hydrochloric acid.

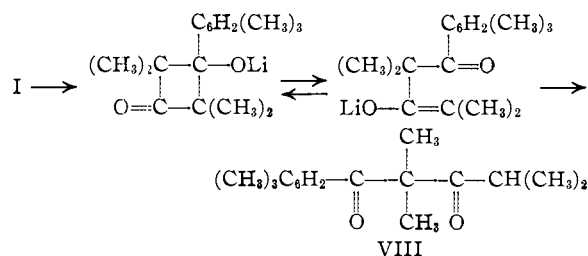
In order to establish with certainty the nature of the primary cleavage product of I, it became necessary to adopt a reagent which would produce a cleavage product having a highly sterically hindered carbonyl group and thus be incapable of reacting with more of the reagent. In this manner the cleavage process could be confined to the first stage. Our various attempts to combine I with mesitylmagnesium bromide failed, but mesityllithium produced a vigorous reaction, resulting in

(7) (a) Stas, *Bull. soc. chim. Belg.*, **35**, 379 (1926); (b) Leroide, *Ann. chim.*, [9] **16**, 354 (1921).

(8) Levina and Kagan, *J. Gen. Chem., U. S. S. R.*, **11**, 523 (1941).

(9) Erickson and Stansbury, *Proc. Louisiana Acad. Sci.*, **6**, 89 (1942).

the formation of dimethyl-isobutyryl-mesityl-methane (VIII). When treated with alcoholic potassium hydroxide, VIII was converted into isobutyric acid and isobutyrylmesitylene.



Kohler, *et al.*,<sup>10</sup> have advanced the explanation that cleavage of  $\alpha$ -oxido ketones by organic magnesium compounds involves fundamentally the same mechanism as the reversal of an aldol condensation. They recognized the possibility of explaining the instability of the magnesium complex, formed by addition of one mole of the reagent to the compound, by an application of ionization or chelation. It was shown later<sup>8</sup> that certain open-chain  $\beta$ -diketones form magnesium compounds which are unstable and decompose in a manner that is essentially the same as that of the magnesium compounds which are formed from  $\alpha$ -oxido ketones.

Geissman and co-workers<sup>6,11</sup> have applied these principles involving ionization and also chelation to cyclic  $\beta$ -diketones as possible explanations of the course of the reaction with Grignard reagents. They observed that certain cyclic  $\beta$ -diketones, which have both carbonyl groups as part of the cycle, failed to undergo cleavage with phenylmagnesium bromide and suggested that cleavage failed because a chelated intermediate could not form.

In the case of the monoaddition product (II) of tetramethyl-1,3-cyclobutanedione, chelation such as that suggested above cannot be involved, yet cleavage of the ring was observed in every case where any reaction at all occurred. Thus, our experiments with this compound have established definitely that cleavage can take place in the absence of chelation.

The cleavage of I as well as open-chain  $\beta$ -diketones can be explained on the basis of a reversible aldol condensation (II  $\rightleftharpoons$  III). Maintenance of the cyclic member of the equilibrium would lead to further addition of the reagent without cleavage, while maintenance of the open-chain member of the equilibrium results in cleavage of the cyclic ring. Since a four-membered ring represents a strained configuration, it is to be expected that it would be broken readily and that the cyclic member would not be maintained in the above equilibrium. This expectation is fulfilled by the fact that cleavage of tetramethyl-1,3-

cyclobutanedione occurs with a variety of organic magnesium and lithium compounds.

### Experimental

**Tetramethyl-1,3-cyclobutanedione (I).**—This compound was prepared by the method of Wedekind and Weisswange<sup>12</sup> by the reaction of  $\alpha$ -bromo-isobutyryl bromide and zinc with a yield of only 10%. A second method<sup>12</sup> using isobutyryl chloride and triethylamine gave only a yield of 18%. Better results can be obtained by a modification of the second method which gives a much greater yield.

To a solution of 266 g. (2.63 moles) of triethylamine in 700 ml. of anhydrous carbon disulfide under an atmosphere of dry nitrogen was added 266 g. (2.50 moles) of isobutyryl chloride with vigorous stirring over a period of one and one-half hours. The mixture was agitated for four hours and then allowed to stand for five days with periodic agitation. Upon addition of petroleum ether, triethylammonium chloride precipitated. After filtering and washing with ether, the combined liquids were evaporated. This yielded 80 g. of the crude product. After purification by distilling twice from a short-necked flask, the yield was 68 g. (0.48 mole) (38%), b. p. 159–161°, m. p. 115–116°.

This procedure was used with benzene as a solvent, without the precaution of an inert atmosphere, with no impairment of yield.

**Cleavage by Methylmagnesium Bromide. 5-Hydroxy-2,4,4,5-tetramethyl-3-hexanone (IV).**—To a solution of methylmagnesium bromide, prepared from 60 g. of methyl bromide and 12.88 g. of magnesium in anhydrous ether, was added 15 g. (0.106 mole) of I in small portions over a period of fifteen minutes. The mixture was refluxed for thirty minutes to complete the reaction and then hydrolyzed with iced hydrochloric acid. The aqueous layer was extracted three times with ether and the combined ether extract was dried over anhydrous sodium sulfate. The ether was removed by distillation through a 40-cm. column packed with  $5/32$  inch glass helices. The residual liquid was fractionated through a 20-cm. column packed in the same manner but equipped with a partial condensation type head and gave 0.8 g. of acetone, b. p. 54–57°,  $n_D^{20}$  1.3596, 2,4-dinitrophenylhydrazone, m. p. 127.5–128.2°, mixed m. p. 127–128°. The residue, upon distillation under reduced pressure, gave two fractions: (1) 2.4 g., b. p. 30–69° (2 mm.); (2) 14.64 g., b. p. 69–72° (3 mm.). Fraction 1 was refractionated yielding 1.8 g. of diisopropyl ketone, b. p. 123–127°,  $n_D^{20}$  1.4021, semicarbazone, m. p. 154–155.5°, mixed m. p. 154.2–155.3°. Fraction 2 was separated by distillation into three parts, each having the same b. p. 71–71.5° at 3 mm., and the same  $n_D^{20}$  1.4419, m. p. 16°. Yield of IV was 12 g. (65%).

*Anal.* Calcd. for  $\text{C}_{10}\text{H}_{20}\text{O}_2$ : C, 69.6; H, 11.7. Found: C, 69.4; H, 11.9.

**Identification of IV.**—A mixture of 7.0 g. of IV and 0.1 g. of barium hydroxide was heated in a small distilling flask on an oil-bath at 170–180° until the distilling flask was dry. This required about three hours with 6.8 g. of the material distilling at a vapor temperature of 56–130°. The product was fractionated and yielded 2.2 g. of acetone, b. p. 55.5–56.4°,  $n_D^{20}$  1.3581, semicarbazone, m. p. 190–191°, mixed m. p. 190.1–190.8°; 2,4-dinitrophenylhydrazone, m. p. 127.5–128°, mixed m. p. 127–128°; and 4.45 g. of diisopropyl ketone, b. p. 123–127°,  $n_D^{20}$  1.4016, semicarbazone, m. p. 153.8–155°, mixed m. p. 154.1–155°. The yield was 95.2% of acetone and 96.3% of diisopropyl ketone.

**Cleavage by Ethylmagnesium Bromide. 5-Hydroxy-2,4,4-trimethyl-3-heptanone (V).**—To a solution of ethylmagnesium bromide, prepared from 18.2 g. of magnesium and 85.0 g. of ethyl bromide in anhydrous ether, was added 21.0 g. of I in crystalline form. After the reaction ceased, the mixture was heated on a water-bath at reflux temperature for fifteen minutes, then cooled and hydrolyzed with iced hydrochloric acid. The ether extract, after drying

(10) Kohler, Richtmyer and Hester, *THIS JOURNAL*, **53**, 205 (1931).

(11) Geissman and Tulagin, *ibid.*, **66**, 719 (1944).

(12) Wedekind and Weisswange, *Ber.*, **39**, 1631 (1906).

over anhydrous sodium sulfate, was evaporated and the residue distilled under reduced pressure through a packed column, yielding 21.8 g. (84%) of V, b. p. 127–128° (30 mm.),  $n_D^{20}$  1.4449.

*Anal.* Calcd. for  $C_{10}H_{20}O_2$ : C, 69.6; H, 11.7. Found: C, 69.6; H, 12.0.

**Identification of V.**—Zerewitinoff determination: one mole of V gave 1.01 moles of methane and consumed 1.93 moles of the reagent, indicating the presence of one hydroxyl group and one carbonyl group in the molecule. A mixture of 7.3 g. of V and 0.1 g. of barium hydroxide, upon heating in a distilling flask at 180° for three hours, gave 7.1 g. of distillate, b. p. 48–127°. Upon fractional distillation, there was obtained 2.1 g. (86%) of propionaldehyde, b. p. 48–51°,  $n_D^{20}$  1.3640; 2,4-dinitrophenylhydrazone, m. p. 154.9–155.6°, mixed m. p. 154.5–155.5°; and 4.7 g. (97%) of diisopropyl ketone, b. p. 124–127°,  $n_D^{20}$  1.4018, semicarbazone, m. p. 154.6–155.2°, mixed m. p. 153.9–155.1. When V was heated without barium hydroxide, the same two products were obtained, but a much longer time was required for complete cleavage.

**Cleavage by Ethylmagnesium Bromide. Inverse Grignard Reaction.**—A solution of ethylmagnesium bromide, prepared from 2.08 g. of magnesium and 11.0 g. of ethyl bromide, was added over a period of forty-five minutes to 12.0 g. of I dissolved in ether. After hydrolysis with acid, the ether extract was evaporated to a small volume and upon addition of petroleum ether gave 7.3 g. (60%) of the starting material. The mother liquor was subjected to fractional distillation and gave 4.8 g. of a liquid, b. p. 127–131° (30 mm.),  $n_D^{20}$  1.4456, which was identified as V. The yield of V was 83%, based upon the amount of I not recovered.

**Cleavage by Phenylmagnesium Bromide.**—To a solution of phenylmagnesium bromide (18.24 g. of magnesium and 119.6 g. of bromobenzene) was added 21 g. of I over a period of fifteen minutes. After hydrolysis with iced acid, the ether extract was distilled through a packed column and separated into a distillate and a residue of 44.6 g. of material. From the distillate there was obtained 6.0 g. of diisopropyl ketone, b. p. 118–127°. The residue yielded 8.5 g. of diisopropyl ketone, b. p. 124–127°, and 26.1 g. of benzophenone, m. p. 47–48°, mixed m. p. 47–49°. The yield was 14.5 g. (85%) of diisopropyl ketone and 26.1 g. (95%) of benzophenone.

Various methods of hydrolysis were tried in order to isolate the cleavage product (VI). A reaction was carried out using the same amounts of materials and following the same procedure described above, except that the reaction mixture was hydrolyzed with a mixture of ice and ammonium chloride solution. After evaporation of the ether, the residue was distilled at room temperature using a mercury vapor pump and yielded diphenyl and 23.4 g. (86%) of benzophenone, m. p. 45–47°. No attempt was made to isolate diisopropyl ketone in this reaction.

The reaction was repeated and hydrolysis was accomplished by adding dropwise to the mixture an ether-hydrogen chloride solution, prepared by passing dry hydrogen chloride into 53 g. of ether until the weight increase amounted to 75 g. The addition required about one hour, the temperature was not allowed to rise above 2° and the mixture was agitated continuously. The magnesium chloride was removed by filtration and the filtrate was distilled under reduced pressure at room temperature. A small amount of diisopropyl ketone and 21 g. (77%) of benzophenone were obtained.

Still another reaction was carried out as described above, but at a much lower temperature (–25°) and 80% of the starting material was recovered.

**Cleavage by Phenylmagnesium Bromide. Inverse Grignard Reaction.**—A solution of phenylmagnesium bromide (2.6 g. of magnesium and 16.8 g. of bromobenzene) was added to a solution containing 12 g. of I. The addition was made over a period of one hour and the reaction mixture was hydrolyzed with hydrochloric acid. Upon working up the products in the usual way, there was obtained 7.1 g. (59%) of the starting material, 2.1 g. (53%) of diisopropyl ketone and 5.8 g. (91%) of benzophenone.

**Cleavage by Phenyllithium.**—An ethereal solution of phenyllithium was prepared by allowing 4.04 g. of lithium to react with 45 g. of bromobenzene in 150 ml. of dry ether and any unreacted lithium was then removed mechanically. To this reagent was added 5 g. of I in small portions. After the reaction subsided, the mixture was heated fifteen minutes on a water-bath. The reaction product was then hydrolyzed with iced hydrochloric acid. The aqueous layer was extracted with ether and the combined ether extracts dried over anhydrous sodium sulfate. After removal of ether under reduced pressure, petroleum ether was added causing the precipitation of 4.5 g. of triphenylcarbinol, m. p. 161–162°, mixed m. p. 161.5–162°. The filtrate, upon distillation, gave 3.8 g. of diisopropyl ketone and a residue from which there was obtained 1.4 g. of benzophenone and 0.5 g. of triphenylcarbinol. The total products obtained were 5.0 g. (54%) of triphenylcarbinol, 1.4 g. (22%) of benzophenone and 3.8 g. (94%) of diisopropyl ketone.

The following experiment was designed to show that benzophenone, if present, would not survive during the hydrolysis process, but would react with phenyllithium to produce triphenylcarbinol. A phenyllithium reagent was prepared from 1.4 g. of lithium and 15.6 g. of bromobenzene in 100 ml. of ether. A solution of 3.64 g. of benzophenone in 75 ml. of ether was added to an ice and hydrochloric acid mixture containing 0.5 mole of acid. The lithium reagent was added very slowly with vigorous stirring to this mixture and the ether layer was separated. After evaporation of the ether, the addition of petroleum ether caused 4.1 g. (79%) of triphenylcarbinol, m. p. 161–162°, to crystallize. After the evaporation of the petroleum ether from the filtrate, steam distillation of the residue yielded 0.6 g. (16%) of the original benzophenone. The hydrolysis of phenyllithium was repeated in the presence of 4.9 g. of diisopropyl ketone using the same procedure as above. After the hydrolysis, 4.1 g. (84%) of diisopropyl ketone was recovered by distillation.

The hydrolysis of phenylmagnesium bromide was carried out in the presence of benzophenone and diisopropyl ketone with the result that these two materials were recovered unchanged from the reaction mixture.

**Treatment with Mesitylmagnesium Bromide.**—The diketone (I), 5 g., was added to an ethereal solution of mesitylmagnesium bromide (5.4 g. of magnesium and 23 g. of bromomesitylene). The mixture was heated on the water-bath for thirty minutes, decanted from excess magnesium and hydrolyzed with iced acid. Upon evaporation of the ether and distillation of the residue, there was obtained 8.6 g. of mesitylene and some bromomesitylene and 4.5 g. (90%) of the starting material unchanged. A second reaction was carried out using the same amounts of materials and following the same procedure except that after the addition of I, the ether was replaced by benzene and the reaction mixture was refluxed for several hours. A total of 4.2 g. (84%) of the diketone was recovered.

**Cleavage by Mesityllithium. Dimethyl-isobutyryl-mesityl-methane (VIII).**—An ethereal solution of 10.1 g. of I was added to a solution of mesityllithium, prepared from 3.2 g. of lithium and 43.8 g. of bromomesitylene. A vigorous reaction resulted and the mixture was allowed to stand overnight. The reaction product was hydrolyzed with iced acid, the aqueous layer was extracted several times with ether, the combined ether extracts were dried over calcium chloride and the ether was removed by distillation. The residue gave 18 g. of material, b. p. 140–151° (2 mm.), which upon recrystallization from alcohol yielded 14 g. (75%) of VIII, m. p. 34–36°. Three grams of this solid was further purified by crystallizing once from petroleum ether and twice from alcohol, m. p. 35.5–36.5°.

*Anal.* Calcd. for  $C_{17}H_{24}O_2$ : C, 78.4; H, 9.3. Found: C, 78.1; H, 9.5.

**Identification of VIII.**—Zerewitinoff determination: one mole of compound consumed 2.12 moles of reagent but gave no methane indicating the absence of a hydroxyl group and suggesting cleavage of the molecule.

One gram of VIII was refluxed with 15 ml. of saturated alcoholic potassium hydroxide for twenty minutes. The

alcohol was removed by distillation, 20 ml. of water was added and the mixture was extracted several times with ether. The aqueous solution was acidified with sulfuric acid and distilled; the distillate was made alkaline and evaporated to dryness. The residue was converted to isobutyro-*p*-toluidide, m. p. 103.5–104.5°. From the ether extracts there was obtained 0.8 g. of isobutyrylmesitylene, b. p. 140–143° (20 mm.),  $n_D^{20}$  1.5086, which was converted to  $\alpha,3,5$ -tribromo-2,4,6-trimethylisobutyrophenone, m. p. 106–107°.

### Summary

Tetramethyl-1,3-cyclobutanedione has been found to undergo cleavage of the ring when treated with organic magnesium and lithium compounds. The behavior of this cyclic  $\beta$ -diketone has been found to be strictly analogous to the behavior of open-chain  $\beta$ -diketones with these reagents.

BATON ROUGE, LOUISIANA RECEIVED AUGUST 10, 1945

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AT THE OHIO STATE UNIVERSITY]

## Fluorinated Derivatives of Propane and Propylene. VI

BY ALBERT L. HENNE AND T. PHILLIP WAALKES

Electron diffraction measurements have shown that atomic distances are shrunk in polyfluorinated groups. This shrinkage is not restricted to the carbon-fluorine distance, but also affects the carbon to chlorine distance in  $\text{CCl}_2\text{F}_2$ , or the carbon to carbon distance in  $\text{CF}_3\text{CH}_3$ . To understand the behavior of polyfluorides, it would be well to learn how far this effect extends down a chain, whether the effect of two polyfluorinated groups is cumulative, and what the influence is on a double bond. For such purposes, the synthesis of  $\text{CF}_3\text{CH}_2\text{CF}_3$ ,  $\text{CF}_2=\text{CHCF}_3$ ,  $\text{CH}_2=\text{CFCF}_3$  and  $\text{CF}_2=\text{CFCF}_3$  was undertaken; these compounds were chosen in the hope that their electron diffraction patterns would not be too complicated to resolve. They were sent to Dr. L. O. Brockway at the University of Michigan, who will report the electron diffraction measurements.

The syntheses have used operations which have all been described in our previous papers.<sup>1,2,3</sup> All intermediates have been isolated and characterized as single, definite individuals. Great care was given to criteria of purity, for which whole freezing curves, not merely freezing points, were used. Compounds were regarded as adequately purified only after their freezing range had become as small as indicated in the table of physical constants.

### Experimental

**Synthesis of  $\text{CF}_3\text{CH}_2\text{CF}_3$ .**—The sequence of reactions found most convenient was:  $\text{CH}_3\text{CHClCH}_2\text{Cl} \rightarrow \text{CH}_3\text{CH}=\text{CCl}_2 \rightarrow \text{CH}_3\text{CH}_2\text{CFCl}_2$  and  $\text{CH}_3\text{CH}_2\text{CF}_2\text{Cl} \rightarrow \text{CH}_3\text{CH}_2\text{CF}_3 \rightarrow \text{CCl}_3\text{CH}_2\text{CF}_3 \rightarrow \text{CF}_3\text{CH}_2\text{CF}_3$ . The starting point was commercial  $\text{CH}_3\text{CHClCH}_2\text{Cl}$ , which an alkaline treatment transformed into  $\text{CH}_3\text{CH}=\text{CCl}_2$  with an 88% yield. The latter, heated with hydrogen fluoride<sup>4</sup> at 100° as long as a 20 atm. pressure could be maintained while bleeding off the generated hydrogen chloride, gave an average yield of 60% of  $\text{CH}_3\text{CH}_2\text{CF}_2\text{Cl}$  and 12% of  $\text{CH}_3\text{CH}_2\text{CFCl}_2$ . The passage from  $\text{CH}_3\text{CH}_2\text{CF}_2\text{Cl}$  to  $\text{CH}_3\text{CH}_2\text{CF}_3$  was easily brought about, in 90% yield, by means of

nascent mercuric fluoride<sup>5</sup>; an alternate method, calling for dehydrohalogenation to  $\text{CH}_3\text{CH}=\text{CF}_2$  followed by hydrogen fluoride addition, was found less practical, as its first step proved time-consuming. The trifluoropropane was chlorinated to  $\text{CF}_3\text{CH}_2\text{CCl}_3$ , in the manner shown before,<sup>6</sup> and the latter upon treatment with nascent mercuric fluoride<sup>5</sup> yielded the desired  $\text{CF}_3\text{CH}_2\text{CF}_3$  (84%), together with some intermediate  $\text{CClF}_2\text{CH}_2\text{CF}_3$ , (5%).

**Synthesis of  $\text{CF}_2=\text{CHCF}_3$ .**—The hydrogen atoms in  $\text{CClF}_2\text{CH}_2\text{CF}_3$  (obtained as shown in the preceding paragraph) are exceedingly acid in character,<sup>7</sup> and the compound is therefore very easily attacked by alcoholic potassium hydroxide. The action of the alkali removed only hydrochloric acid, as shown by a positive test for chlorine ions and a negative test for fluorine ions. The reaction was both intramolecular, for a 65% yield of  $\text{CF}_2=\text{CHCF}_3$ , and intermolecular as shown by the appearance of condensation products boiling about 70 and 105°, respectively.

When hydrogen fluoride was added to  $\text{CF}_2=\text{CHCF}_3$ , practically no  $\text{CF}_3\text{CH}_2\text{CF}_3$  was formed at temperatures below 100°, but at 100° or higher the addition proceeded smoothly and quantitatively.

**Synthesis of  $\text{CH}_2=\text{CFCF}_3$ .**—The following sequence was used:  $\text{CH}_2\text{ClCHClCH}_2\text{Cl} \rightarrow \text{CH}_2=\text{CClCH}_2\text{Cl} \rightarrow \text{CH}_3\text{CFClCH}_2\text{Cl} \rightarrow \text{CH}_3\text{CFClCCl}_2 \rightarrow \text{CH}_3\text{CFClCF}_2\text{Cl} \rightarrow \text{CH}_2=\text{CFCF}_2\text{Cl} \rightarrow \text{CH}_2=\text{CFCF}_3$ . The fluorine atom on the central carbon was introduced first. For that purpose, the starting point was commercial  $\text{CH}_2\text{ClCHClCH}_2\text{Cl}$ , which a caustic treatment transformed into  $\text{CH}_2=\text{CClCH}_2\text{Cl}$  in 80% yield. The addition of hydrogen fluoride proceeded normally to give about 70% of  $\text{CH}_3\text{CFClCH}_2\text{Cl}$ , with  $\text{CH}_3\text{CF}_2\text{CH}_2\text{Cl}$  as by-product.<sup>8</sup> Directed chlorination in sunlight gives the expected  $\text{CH}_3\text{CFClCCl}_2$ . In this stage, our original plans called for an alkaline treatment to remove hydrogen chloride and yield  $\text{CH}_2=\text{CFCCl}_2$ , in which the transformation of the  $\text{CCl}_2$  group into a  $\text{CF}_3$  was expected to be facilitated by its "allylic" character.<sup>9</sup> However this dehydrohalogenation (and also that of  $\text{CH}_3\text{CCl}_2\text{CCl}_3$ ) failed, because the hydrolysis of  $\text{CH}_2=\text{CXCCl}_3$  is much faster than its generation. To avoid this decomposition, partial fluorination of the saturated compound was resorted to, which yielded a mixture of 10%  $\text{CH}_3\text{CFClCFCl}_2$ , 35%  $\text{CH}_3\text{CFClCF}_2\text{Cl}$  and 35%  $\text{CH}_3\text{CF}_2\text{CFCl}_2$ , separable by distillation. After accumulating  $\text{CH}_3\text{CFClCF}_2\text{Cl}$ , the alkaline treatment was applied, and yielded very slowly (three days) the desired  $\text{CH}_2=\text{CFCF}_2\text{Cl}$ , which proved stable enough to resist hydrolysis. In view of the time consumed, the dehydrohalogenation was then tried on  $\text{CH}_3\text{CFClCFCl}_2$ . When operated under a reflux condenser maintained at about 50°, the olefin  $\text{CH}_2=\text{CF}$

(1) Henne in Gilman's "Organic Chemistry," Vol. I, John Wiley and Sons, New York, 1943, p. 944.

(2) Henne in "Organic Reactions," Vol. 2, John Wiley and Sons, New York, 1944, p. 42.

(3) Henne and Waalkes, *THIS JOURNAL*, **67**, 1639 (1945).

(4) Henne and Plueddemann, *ibid.*, **65**, 1271 (1943).

(5) Henne, *ibid.*, **60**, 1569 (1938); Henne and Flanagan, *ibid.*, **65**, 2362 (1943).

(6) Henne and Whaley, *ibid.*, **64**, 1157 (1942).

(7) Henne, Hinkamp and Zimmerschied, *ibid.*, **67**, 1906 (1945).

(8) Henne and Haeckl, *ibid.*, **63**, 2692 (1941).

(9) Henne, Whaley and Stevenson, *ibid.*, **62**, 3478 (1941).