

separated, and the aqueous layer was extracted with 100 ml. of benzene. The combined benzene-toluene solution was washed with 100-ml. portions of 5% sodium hydroxide solution, water, 5% hydrochloric acid, and saturated sodium bicarbonate solution. After drying the solvents were removed by distillation at atmospheric pressure, and the residue distilled under reduced pressure. The fore-run (17.2 g.) contained both δ -chlorovaleronitrile and *p*-isopropylphenylacetonitrile; the product was collected at 180–200° (0.5–0.7 mm.) as a light yellow viscous oil; yield 70.0 g. (58%).

Anal. Calcd. for $C_{16}H_{20}N_2$: C, 79.95; H, 8.39. Found: C, 79.94; H, 8.16.

α -Methyl- α -(*p*-isopropylphenyl)-pimelonitrile (III).—Sodamide was prepared as usual from 7.4 g. (0.32 mole) of sodium. To the stirred sodamide-ammonia mixture was added 70.0 g. (0.29 mole) of α -(*p*-isopropylphenyl)-pimelonitrile, and 100 ml. of dry ether. The mixture was stirred for twenty minutes. An additional 100 ml. of dry ether was added, a nitrogen atmosphere was provided, and the ammonia was allowed to evaporate. There was added 57 g. (0.40 mole) of methyl iodide in 60 ml. of dry ether. After the initial reaction subsided, the mixture was stirred under reflux for one hour. Methanol (25 ml.) and water (200 ml.) were added, and the ether layer was separated. The ether solution was washed with 100-ml. portions of water, 5% hydrochloric acid, water and saturated sodium bicarbonate solution. After drying, the ether was removed and the residue distilled under reduced pressure to yield 63.2 g. (85%) of light yellow viscous oil, b. p. 178–183° (0.6 mm.).

Anal. Calcd. for $C_{17}H_{22}N_2$: C, 80.26; H, 8.72; N, 11.02. Found: C, 80.18; H, 8.51; N, 11.10.

2-Methyl-2-(*p*-isopropylphenyl)-6-cyanocyclohexanone-imine (IV).—Sodamide was prepared from 6.3 g. (0.27 mole) of sodium. There was then added, in the usual way, 63.2 g. (0.25 mole) of α -methyl- α -(*p*-isopropylphenyl)-pimelonitrile, 30 ml. of dry ether, and 150 ml. of dry benzene. The mixture was allowed to stand under a nitrogen atmosphere until the ammonia had evaporated, and it was then heated to reflux and stirred (under nitrogen) for two hours. Methanol (15 ml.) and water (200 ml.) were added to the cooled solution, the benzene layer was separated, and the aqueous layer was extracted with 100 ml. of benzene and three 50-ml. portions of ethyl acetate. The combined extracts were washed with 100-ml. portions of water, 5% hydrochloric acid, water and saturated sodium bicarbonate solution, and dried. The solvents were removed by distillation, and the residue distilled under reduced pressure to yield 44.5 g. (70%) of very viscous oil, b. p. 182–185° (0.6 mm.).

Anal. Calcd. for $C_{17}H_{22}N_2$: C, 80.26; H, 8.72. Found: C, 80.18; H, 8.56.

2-Methyl-2-(*p*-isopropylphenyl)-6-cyanocyclohexanone.—A mixture of 7.5 g. of iminonitrile (IV), 110 ml. of methanol, 22 ml. of water, and 22 ml. of concentrated hydrochloric acid was heated under reflux for thirty-five minutes. The mixture was poured into 700 ml. of water and the product was extracted with four 100-ml. portions of ether. The combined extracts were washed with three 50-ml. portions of saturated sodium bicarbonate solution, with water, and dried. Evaporation of the ether at room temperature left a slightly discolored crystalline residue of crude ketonitrile in quantitative yield. Recrystallization of a small sample of this material from ether-pentane gave the colorless ketonitrile, m. p. 137–137.5°.

Anal. Calcd. for $C_{17}H_{21}ON$: C, 79.96; H, 8.29; N, 5.49. Found: C, 79.83; H, 8.25; N, 5.68.

2-Methyl-2-(*p*-isopropylphenyl)-6-carbomethoxycyclohexanone (V).—A solution of 6.50 g. of crude 2-methyl-2-(*p*-isopropylphenyl)-6-cyanocyclohexanone in 60 ml. of methanol was saturated with hydrogen chloride. After standing for twelve hours, the mixture was poured into 700 ml. of water, and the product extracted with five 100-ml. portions of ether. The combined ether extracts were washed with saturated sodium bicarbonate solution, with water, and dried. The ether was removed, and the crude ketoester was evaporatively distilled at 110–112° (0.1 mm.); yield 4.62 g. of the methyl ester as a nearly colorless viscous oil.

Anal. Calcd. for $C_{18}H_{24}O_3$: C, 74.98; H, 8.39. Found: C, 74.71, H, 8.32.

2,6-Dimethyl-2-(*p*-isopropylphenyl)-6-carbomethoxycyclohexanone (VI).—2-Methyl-2-(*p*-isopropylphenyl)-6-carbomethoxycyclohexanone was alkylated with methyl iodide by the usual sodamide procedure, using 4.27 g. of the ketoester, 0.40 g. of sodium, 4.30 g. of methyl iodide, and 150 ml. of dry ether as the solvent. A nitrogen atmosphere was employed. The crude ethereal solution of the product was washed with water, 5% hydrochloric acid, water, and saturated sodium bicarbonate solution, and dried. Evaporative distillation at 100–130° (0.07–0.1 mm.) yielded 3.00 g. of keto-ester as a viscous oil.

Anal. Calcd. for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67. Found: C, 75.28; H, 8.77.

Summary

The synthesis of 2,6-dimethyl-2-*p*-isopropylphenyl-6-carbomethoxycyclohexanone is described.

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

The Ketonic Decarboxylation Reaction¹: The Ketonic Decarboxylation of Trimethylacetic Acid² and Isobutyric Acid

BY ALFRED L. MILLER,^{3a} NEWELL C. COOK^{3b} AND FRANK C. WHITMORE⁴

Introduction

In 1944, Cook, Miller and Whitmore² reported that the ketonic decarboxylation of trimethylacetic acid yielded *t*-butyl isobutyl ketone. This was the first report of a ketonic decarboxylation

of an acid with no alpha hydrogens and also the first successful application of this reaction that did not yield a symmetrical ketone. The study of these data has led to a clearer understanding of the nature of the ketonic decarboxylation reaction. This work has been extended to isobutyric acid, and in addition to the already reported diisopropyl ketone, *n*-propyl isopropyl ketone has been isolated.

In 1913, Senderens⁵ formulated a general equation for ketonic decarboxylation

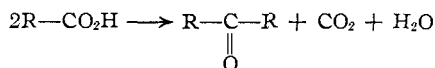
(1) Presented before the Organic Section, American Chemical Society; Atlantic City, 1947.

(2) Presented before the Organic Section, American Chemical Society; New York, N. Y., 1944.

(3) (a) Celanese Corporation of America, Summit, N. J.; (b) General Electric Co., Schenectady, N. Y.

(4) Deceased June 1947.

(5) Senderens, *Ann. chim. phys.*, [8] 28, 243 (1913).



At the same time he made the first report of an exception to the general equation, when he was unable to prepare benzophenone from benzoic acid. Farmer and Kracovski⁶ reported their inability to decarboxylate ketonically 2,2,5,5-tetramethyladipic acid. Neunhoffer and Paschke⁷ reported the thermal decomposition of calcium trimethylacetate to yield isobutylene but no ketone. These exceptions involve acids that have no alpha hydrogens.

Results and Discussion

In this investigation, trimethylacetic acid was ketonically decarboxylated by passing the acid over aerogel thoria catalyst⁸ at 490°. The major product was *t*-butyl isobutyl ketone with no evidence of di-*t*-butyl ketone. Liquid products (69%) and gaseous products (31%) were collected and analyzed and the results are shown in Table I.

TABLE I
Liquid products

Trimethylacetic acid (unreacted)	21%
<i>t</i> -Butyl isobutyl ketone	15
<i>t</i> -Butyl methyl ketone	9
<i>t</i> -Butyl ethyl ketone	0.7
Trimethylacetaldehyde	3
Crotonaldehyde	3
Ethyl trimethylacetate	Trace
Intermediate fractions	17
Total	69%
Gaseous products ^a	
Hydrogen	0.3%
Carbon monoxide	2.7
Carbon dioxide	20.0
Methane	0.6
Ethane	0.1
Ethylene	0.05
Acetylene	Trace
Propane	0.14
Propylene	0.03
Butanes	5.0
Butylenes	2.6
Total	31%

^a The authors wish to thank Dr. H. D. Zook of the Chemistry Department, The Pennsylvania State College, who performed this analysis of the gaseous products.

A variety of reaction temperatures was tried and the results are shown in Fig. 1. Above 490°, the decomposition of the ketone product increased rapidly as indicated by the decrease in liquid recovery, with corresponding increase in the gaseous products. Below 490°, the liquid recovery rose rapidly due to the rapid decrease in the reaction.

(6) Farmer and Kracovski, *J. Chem. Soc.*, **129**, 680 (1927).

(7) Neunhoffer and Paschke, *Ber.*, **72B**, 919 (1939).

(8) Swann and Appel, *Ind. Eng. Chem.*, **26**, 388 (1934).

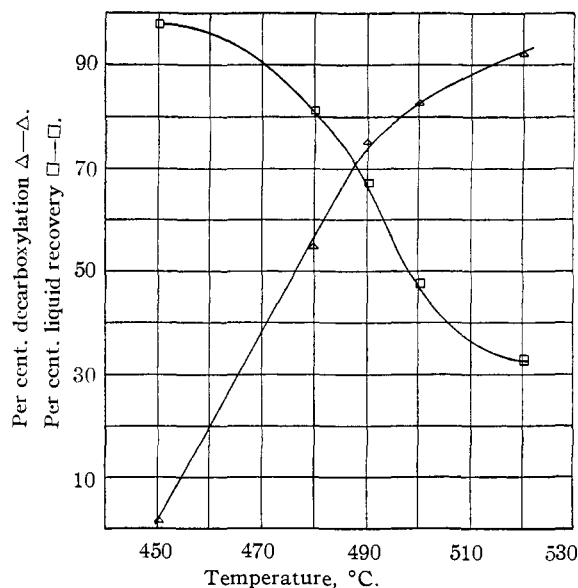
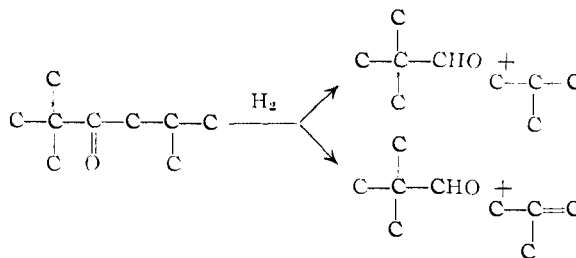


Fig. 1.—Effect of temperature on the decarboxylation of trimethylacetic acid over thoria catalyst.

t-Butyl isobutyl ketone and carbon dioxide were primary products of the ketonic decarboxylation. All other gaseous and liquid products appeared to be decomposition products of *t*-butyl isobutyl ketone. Methyl *t*-butyl ketone and ethyl *t*-butyl ketone resulted from the decomposition of the isobutyl end of the ketone product. Similar observations have been made by other workers.⁹ To confirm this, *t*-butyl isobutyl ketone was passed over thoria at 490° and pinacolone was isolated from the product.

Dilthey⁹ isolated isovaleraldehyde in his work with isovaleric acid which is analogous to the isolation of trimethylacetaldehyde in this work. This decomposition may be explained by one or both of the reactions



Ethanol was isolated from a high boiling fraction after an alkaline treatment. It must therefore have come from an ethyl ester, probably trimethylacetate. No acetaldehyde has been isolated but the presence of considerable amounts of crotonaldehyde indicates that acetaldehyde had been formed and then went through an aldol condensation followed by dehydration. It is suggested that the ethanol necessary for the ethyl

(9) Dilthey, *Ber.*, **34**, 2115 (1901); Barbaglia and Gucci, *ibid.*, **13**, 1572 (1880); M. Gluchsmann, *Monatsh.*, **16**, 817 (1895).

ester came from the reduction of acetaldehyde. The acetaldehyde may be presumed to have resulted from the decomposition of trimethylacetaldehyde, in the same manner that *t*-butyl isobutyl ketone gave pinacolone.

Since this reaction was run at 490°, pyrolysis undoubtedly accounted for the hydrogen and the hydrocarbon gases. Carbon monoxide has been shown by Mitchell and Reid¹⁰ to be a product of ketone decomposition.

The following mechanism is offered for the formation of *t*-butyl isobutyl ketone. The adsorption of the gaseous acid upon the basic catalyst is followed by the formation of a thorium salt of trimethylacetic acid. It seems most probable that the role the catalyst might play in this reaction would be one of the orientation of two or more acid molecules into reactive positions as suggested by the Fisher-Hirschfelder model of thorium trimethylacetate (a sulfur atom model was used as an approximation for thorium) in which the position of the atoms is roughly represented by Fig. 2.

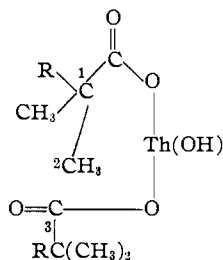


Fig. 2.

For the formation of di-*t*-butyl ketone C_3 must approach C_1 but in no way can the model be so manipulated due to the steric hindrance caused by the methyl groups attached to C_1 . However, any one of these methyl groups can approach and collide with C_3 , the carbonyl carbon. It is suggested, then, that a reaction occurs between C_2 and C_3 , probably by an aldol type of condensation with the formation of a seven member ring intermediate.

In this intermediate, C_3 has attached to it two oxo groups which is an unstable arrangement. This intermediate may then decompose to the thorium salt of a gamma keto acid which may be further decarboxylated (in the same manner that sodium acetate in the presence of sodium hydroxide is thermally decarboxylated to methane) to form *t*-butyl isobutyl ketone.

This mechanism may also be applied to the ketonic decarboxylation of acids that have alpha hydrogens. As a test, the mechanism was applied to isobutyric acid. Previous workers have reported diisopropyl ketone as the only seven carbon ketone product. We found that isobutyric acid passed over aerogel thoria at 490° gave 50% diisopropyl ketone and 5% *n*-propyl isopropyl

ketone. The same mechanism would apply here as with the trimethylacetic acid.

In this reaction however, C_3 can approach C_1 , and since C_1 has a hydrogen attached to it, an aldol type of condensation leads to the formation of diisopropyl ketone. Reaction can occur also, and does to a small extent, between C_2 and C_3 . This leads to the formation of *n*-propylisopropyl ketone.

From these data and observations the following conclusions have been drawn:

- (1) Acids which have no alpha hydrogens may be ketonically decarboxylated with reaction occurring at the beta carbon and resulting in an unsymmetrical ketone.
- (2) In the ketonic decarboxylation of acids having both alpha and beta hydrogens, reaction may occur at both the alpha and the beta carbons, with reaction at the alpha carbon taking precedence.
- (3) The role of the catalyst in ketonic decarboxylation appears to be one of orientation of two or more acid molecules into reactive positions.

Experimental

Trimethylacetic Acid.—A 100-mole copper reactor was charged with six gallons of anhydrous ether (Mallinckrodt) and 1210 g., 50 moles, of magnesium turnings. Over a period of six hours, 4600 g., 50 moles, of *t*-butyl chloride was added and the yield of Grignard reagent was 80%. Carbonation was effected by the addition of 2900 g. of small chunks of Dry Ice. When the addition was completed another gallon of ether was added because the addition product had stiffened. The product was poured on crushed ice to which 40 moles of concentrated hydrochloric acid had been added. After stripping the ether and fractionating, 3060 g. of trimethylacetic acid, n_D^{20} 1.4030, was isolated, a yield of 60%.

Isobutyric Acid.—A 15-mole preparation of isobutyric acid was made in the same manner described for trimethylacetic acid. Isopropylmagnesium chloride was carbonated and isobutyric acid isolated in 70% yield.

The Decarboxylation Reaction.—The reaction tube used in this investigation was of pyrex glass, 47 cm. long by 17 mm. bore, and was held in a horizontal position. The tube was heated by an electrically heated jacket which was insulated with magnesia lagging. The temperature was measured by means of thermocouples in a small glass tube (5 mm.) running along the center of the reaction tube. The aerogel thoria catalyst was prepared in the manner described by Kistler, Swann and Appel,⁸ and shaped in pellets of an average diameter of 0.25 cm.

Small scale preliminary decarboxylations showed the optimum ketonic decarboxylation temperature to be 490°. The extent of reaction was determined by titrating an aliquot of the liquid condensate with standard base and comparison with a blank of starting material. In a typical run 7.2 moles of trimethylacetic acid was passed through a decomposition tube at a feed rate of 0.5 cc./minute at 490°. The effluent from the tube was passed through a condenser, an ice trap, two Dry-Ice acetone traps, and two liquid air traps and the non-condensable gases were collected over a saturated brine solution.

The gases were analyzed by Dr. H. D. Zook of the Chemistry Department, The Pennsylvania State College, by low temperature distillation and combustions (Table I).

The liquid products were fractionated and identified by boiling points, refractive indices and by the preparation of derivatives: trimethylacetaldehyde b. p. 73°, n_D^{20} 1.3800, 2,4-dinitrophenylhydrazone, m. p. 209–211°; croton-

(10) Mitchell and Reid, *THIS JOURNAL*, **63**, 338 (1931).

aldehyde b. p. 85–95°, n_D^{20} 1.4025–28, 2,4-dinitrophenylhydrazone m. p. 189–190°; methyl *t*-butyl ketone b. p. 105°, n_D^{20} 1.3970, 2,4-dinitrophenylhydrazone m. p. 125°; ethyl *t*-butyl ketone b. p. 120–125, n_D^{20} 1.4051, 2,4-dinitrophenylhydrazone 144°, 2,4-dinitrophenylhydrazone 95°. All derivatives were checked with mixed m. p. of known samples.

The products from the decarboxylation of isobutyric acid were analyzed only for diisopropyl ketone, b. p. 123°, n_D^{20} 1.4000, semicarbazone m. p. 157°, mixed m. p. 157°, and *n*-propyl isopropyl ketone b. p. 135–140°, n_D^{20} 1.4060–1.4070, semicarbazone m. p. 119°, mixed m. p. 119°.

Preparation of *t*-Butyl Isobutyl Ketone.—A 2.2 mole preparation of *t*-butylmagnesium chloride was made in 60% yield. The Grignard reagent was removed to a separatory flask by pumping with nitrogen pressure. Over a period of four hours the reagent was added to 1.3 moles of methyl isovalerate, n_D^{20} 1.3920, dissolved in 0.5 liter of anhydrous ether.

A mixture of *t*-butyl isobutyl ketone and *t*-butylisobutylcarbinol b. p. 153–165° 33 g., was isolated and oxidized in the following manner: The alcohol-ketone mixture (33 g.) was added slowly with stirring to the oxidizing mixture (36 g. of $\text{Na}_2\text{Cr}_2\text{O}_7$, 290 ml. of water, 49 g. of concd. H_2SO_4), the temperature not exceeding 50°. After stirring for two hours, the reaction mixture was refluxed

for one-half hour and then steam distilled. The yield of *t*-butyl isobutyl ketone was 80%, b. p. 155°, n_D^{20} 1.4135, 2,4-dinitrophenylhydrazone m. p. 94°.

Decomposition of *t*-Butyl Isobutyl Ketone.—Twenty-three grams of *t*-butyl isobutyl ketone was passed over aerogel thoria catalyst at 490° and 20 g. of liquid condensate collected, 87%. Better than 90% of the product was unchanged *t*-butyl isobutyl ketone. Of the 10% which reacted approximately 10% was pinacolone, identified by b. p. and its 2,4-dinitrophenylhydrazone derivative.

Summary

1. The ketonic decarboxylation of trimethylacetic acid over thoria catalyst at 490° was found to yield *t*-butyl isobutyl ketone and a variety of products resulting from the decomposition of this ketone.

2. A mechanism is proposed to explain this product. This mechanism has been applied to the ketonic decarboxylation of isobutyric acid, and the formation of *n*-propyl isopropyl ketone in addition to diisopropyl ketone was confirmed.

STATE COLLEGE, PA.

RECEIVED JULY 20, 1949

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CALIFORNIA, LOS ANGELES]

The Reaction of Grignard Reagents with Di-*t*-butyl Peroxide¹

BY TOD W. CAMPBELL,² WELTON BURNEY³ AND THOMAS L. JACOBS

The reaction of dialkyl peroxides with Grignard reagents has not been examined extensively because most of these peroxides are unstable. However, it has been shown⁴ that phenylmagnesium bromide and diethyl peroxide give a 35% yield of phenetole and 18% of biphenyl. This is similar to the reaction of Grignard reagents with disulfides⁵

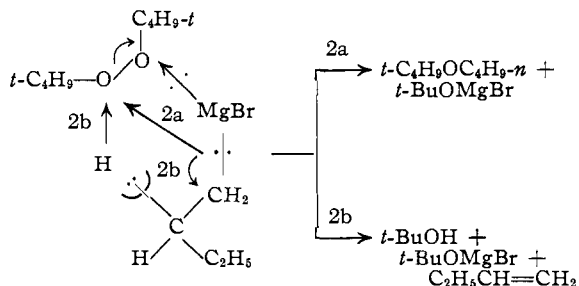


and diselenides.⁶

The availability of the relatively inert di-*t*-butyl peroxide in large amounts,⁷ has made possible investigations of the chemistry of organic peroxides heretofore impossible or very difficult. In this paper are presented the results of an investigation of the reaction of this compound with a series of Grignard reagents, including phenylmagnesium bromide as well as primary, secondary and tertiary aliphatic bromomagnesium compounds. Little or no reaction occurred in the case of the *t*-aliphatic and phenyl Grignard reagents; steric hindrance may be important in the first of these. The Grignard reagents from the primary and secondary halides reacted readily

to yield as significant products a *t*-butyl alkyl ether, which would be predicted on the basis of equation (1), an olefin derived from the Grignard reagent, and *t*-butyl alcohol. The coupling product from the Grignard reagent was also formed in low yield.

It is possible and appears attractive to postulate a course for the reaction of aliphatic Grignard reagents with the hindered peroxide similar to that for the reduction of a hindered ketone by a β -hydrogen atom in a Grignard reagent.⁸ Thus, the reaction between butylmagnesium bromide and di-*t*-butyl peroxide might involve the initial complex A, which could, by appropriate electronic shifts, decay by either path 2a or 2b to give the experimentally observed products.



(1) Taken from the thesis submitted by Welton Burney in partial fulfillment of the requirements for the M.S. degree in Chemistry, June, 1949.

(2) Western Regional Research Laboratory, Albany, California.

(3) Lockheed Aircraft, Burbank, California.

(4) Gilman and McCracken, *THIS JOURNAL*, **45**, 2462 (1923).

(5) Wuyts, *Bull. soc. chim.*, **35**, 166 (1906).

(6) Campbell and McCullough, *THIS JOURNAL*, **67**, 1965 (1945).

(7) We wish to thank the Shell Development Co., Emeryville, California, for a generous gift of this compound.

According to this formulation the moles of *t*-butyl alcohol should be equal to the moles of ether plus twice the moles of olefin. This was found to be true within experimental error.

(8) Whitmore and George, *THIS JOURNAL*, **64**, 1239 (1942).