III. **α-Methylbutyrophenone.**—This was synthesized in the following steps: (a) *s*-butyl bromide by the method of Kamm and Marvel,[17] (b) *dl*-ethylmethylacetic acid by the carbonation of the Grignard reagent of *s*-butyl bromide,[18] conversion of this acid to the acid chloride by the method of H. C. Brown,[19] and (c), the preparation of α-methylbutyrophenone in a yield of 65% from the acid chloride using the Friedel–Crafts reaction.

The 2,4-dinitrophenylhydrazone was prepared according to the method described by Shriner and Fuson[20] and melted at 128–129°.

Anal. Calcd. for $C_{17}H_{18}N_4O_4$: C, 59.64; H, 5.30. Found: C, 59.65; H, 5.32.

Attempted Mannich Reactions with α-Methylbutyrophenone. A.—To 21 g. (0.13 mole) of α-methylbutyrophenone was added 9.1 g. (0.13 mole) of piperidine, 10.8 ml. of formalin and 45 ml. of 95% alcohol. The solution was refluxed on a steam-bath for 48 hr. After removal of low boiling materials, the only material recovered was 19.5 g. of α-methylbutyrophenone.

B.—The above experiment was repeated substituting 15.7 g. (0.13 mole) of piperidine hydrochloride for the piperidine. Upon distillation of the reaction mixture, there was recovered 19.0 g. of α-methylbutyrophenone.

Acknowledgment is made to the Allied Chemical and Dye Corporation whose generous support has made much of this study possible.

SYRACUSE 10, N. Y. RECEIVED JANUARY 13, 1951

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(17) Gilman and Blatt, "Organic Syntheses," Coll. Vol. I, second edition, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 29.

(18) *Ibid.*, p. 361.

(19) H. C. Brown, THIS JOURNAL, **60**, 1325 (1938).

(20) Shriner and Fuson, "Identification of Organic Compounds," second ed., John Wiley and Sons, New York, N. Y., 1940, p. 143.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND THE DEPARTMENT OF PHYSICS, KANSAS STATE COLLEGE]

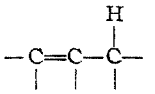
Autoxidation of Ketones. I. Diisopropyl Ketone[1]

BY DEXTER B. SHARP,[2a] LEO W. PATTON,[2a] AND STUART E. WHITCOMB[2b]

Liquid diisopropyl ketone has been oxidized by molecular oxygen in the absence of added inorganic catalysts to the primary oxidation product 2-(2,4-dimethylpentanone-3-yl) hydroperoxide, an α-hydroperoxide of the ketone. Acetone and isobutyric acid were obtained as secondary oxidation products and as decomposition products of the hydroperoxide. The progress of an oxidation was followed by chemical analysis. Infrared spectroscopic data were obtained during the oxidations. Mechanisms are suggested for the oxidation process.

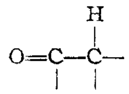
Introduction

The susceptibility to attack by molecular oxygen of a position alpha to a carbon–carbon double bond was established when the α-hydroperoxides of cyclohexene,[3] 1-methylcyclohexene[4] and 1,2-dimethylcyclohexene[4] were shown to be primary autoxidation products of these cycloölefins. A similar α-position activation by an aromatic ring system was demonstrated when α-*ac*-tetralyl hydroperoxide[5] and α,α-dimethylbenzyl hydroperoxide[6] were isolated from the autoxidized hydrocarbons. Farmer[7] has pointed out that the α-position of the olefinic system (I) was the preferential point of attack by free radicals. The similarity in bond structure of I and the α-carbon–carbonyl system (II) suggested that the α-positions of ketones also might be susceptible to attack by free radicals, and particularly by oxygen in autoxidative reactions. Two literature reports which substantiated this postulate were those of Jenkins[8] and Paquot.[9] Jenkins did not report any subsequent extensions of his results, and Paquot employed catalysts which are known to accelerate autoxidation processes. Fuson and Jackson[10] recently reported the formation of an α-hydroperoxide of β,β-dimesitylpropiophenone by action of molecular oxygen on the ketone. This ketone is similar to those for which Kohler and Thompson[11] earlier reported facile peroxide formation.



$$-\underset{|}{C}=\underset{|}{C}-\underset{|}{\overset{\overset{H}{|}}{C}}-$$

I



$$O=\underset{|}{C}-\underset{|}{\overset{\overset{H}{|}}{C}}-$$

II

In order to follow the progress of oxidation, to detect all products formed and to provide foundations for postulates of mechanisms, a multiple attack upon the problem was employed. Chemical analyses were carried out during the course of autoxidation. Infrared spectroscopic analyses were made during the reaction and such data were compared with the chemical data. Efforts were directed toward complete separation and unequivocal identification of the final products. Inorganic oxidation catalysts were excluded insofar as possible from the reaction mixtures in order to minimize acceleration or other effects which might alter the reaction or destroy sensitive intermediate products. This paper reports the results obtained in the study of the autoxidation of diisopropyl ketone (III).

Experimental

Apparatus.—The oxidations were conducted in the all-glass apparatus constructed according to the diagram shown in Fig. 1. A Chromel ribbon-wound Pyrex tube and outer Pyrex jacket (F) were concentric with the inner Pyrex oxidation chamber (E) (20 mm. i.d.). This chamber (E) was fused to a sintered disk (D) which dispersed the oxygen entering at (A) through stopcock (C). Final reaction mixtures were drained through the opening at (B). A condenser (G) and Dry Ice-cooled trap (H) were connected in series at the top of the apparatus. The sample withdrawal unit

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(1) Presented in part at the 117th Meeting of the A. C. S., Philadelphia, April 9–13, 1950. Abstracted in part from the Ph.D. thesis submitted to the Graduate Faculty of Kansas State College by Leo W. Patton, August, 1950. Supported in part by a contract with the Office of Naval Research. Contribution no. 431, Department of Chemistry, and no. 3, Department of Physics.

(2) (a) Dept. of Chemistry; (b) Dept. of Physics.

(3) R. Criegee, H. Pilz and H. Flygare, *Ber.*, **72**, 1799 (1939).

(4) E. H. Farmer and A. Sundralingam, *J. Chem. Soc.*, 121 (1942).

(5) H. Hock and W. Susemihl, *Ber.*, **66**, 61 (1933).

(6) H. Hock and S. Lang, *ibid.*, **77B**, 257 (1944).

(7) E. H. Farmer, *Trans. Faraday Soc.*, **38**, 340, 348, 356 (1942); *J. Soc. Chem. Ind.*, **66**, 86 (1947).

(8) S. S. Jenkins, THIS JOURNAL, **57**, 2733 (1935).

(9) C. Paquot, *Bull. soc. chim.*, **12**, 450 (1945).

(10) R. C. Fuson and H. L. Jackson, THIS JOURNAL, **72**, 1637 (1950).

(11) E. P. Kohler and R. B. Thompson, *ibid.*, **59**, 887 (1937).

(J) was connected to a glass tube (K) extending about halfway down the oxidation chamber. Two thermometers were suspended at different heights by glass string from the sampler tube (K) in order to measure the temperature of the oxidizing mixture directly. All pigmented marking substance had been removed from each thermometer. Samples were drawn into (J) by application of suction at the side-arm, and were removed with a pipet after removal of the standard taper plug. The oxidation chamber was about four feet tall, sufficient to hold 500–600 ml. of liquid.

Materials.—Diisopropyl ketone (Eastman Kodak Co. P3244) was fractionated through a 48-inch, 20-mm. i.d., adiabatic column packed with glass helices ($^{3}/_{8}$ inch) and fitted with a total condensation-variable takeoff stillhead. The fraction used for the oxidations had the following physical constants: b.p. (738 mm.) 118–119° (reported,[12] 123.7° at 761 mm.); d^{20}_{4} 0.806 (reported,[12] d^{20}_{4} 0.806); $n^{20}\mathrm{D}$ 1.4011 (reported,[13] $n^{20}\mathrm{D}$ 1.4010). Reagent grade chemicals were used for analyses and other operations.

Oxidation Procedure.—Before each run the oxidation chamber was cleaned thoroughly. Acetone was used to remove residual organic material and the chamber was washed with water. Sodium bisulfite solution was introduced in order to destroy residual peroxidic material; this solution was removed, and the chamber was washed again with water. Dilute nitric acid was placed in the chamber to destroy any bisulfite, the chamber was drained, and successive water-washes were employed until the wash water showed no acid reaction. Finally, the chamber was filled with hot acetone, the acetone was removed, and the chamber was dried for two hours with a current of dry air.

The oxidation chamber (Fig. 1, E) was filled with diisopropyl ketone (425 g.), and Dry Ice was placed about the trap. The ketone was heated to the desired temperature, and oxygen was introduced at such a rate that bubbles of gas always reached the top of the liquid column. Samples were removed at intervals and analyzed for peroxide by the method of Wagner, Smith and Peters[14] and for acid by titration with standard base. The infrared absorption spectrum of each sample was obtained also. At the end of the oxidation analyses were obtained for the final mixture. Runs were made at 100 and 110° in diffuse daylight and at 100° in the dark.

Separation of Products.—The final oxidation mixture was distilled at reduced pressure until 100 ml. of distillate had been collected. This distillate was added to the material caught in the Dry Ice-cooled trap during the oxidation, and the combined liquids were distilled through a 10-inch Vigreux column at ordinary pressure. A fraction, b.p. 55–57°, was collected and shown to be acetone; 2,4-dinitrophenylhydrazone, m.p. and mixed m.p. 123–124° with authentic 2,4-dinitrophenylhydrazone of acetone (reported[15] 126°), semicarbazone, m.p. 187–188° (reported[16] for acetone semicarbazone, 186°). The residual liquid was diisopropyl ketone and was added to the original distillation residue. The latter was extracted with portions of 5% sodium hydroxide solution, to which phenolphthalein had been added, until the phenolphthalein color of a subsequent portion of base was not discharged. This precaution was taken in order to avoid having an excess of base in contact with the organic phase. The aqueous extracts were combined and extracted with ether and the extract was discarded. The aqueous basic extract was evaporated to dryness, water (30 ml.) and 85% phosphoric acid (30 ml.) were added, and the solution was extracted with several portions of ether. The ether extract was dried over anhydrous sodium sulfate and the ether was removed. The residue was distilled, and a distillate was collected over the range 150–156° and was shown to be isobutyric acid (reported[17] for isobutyric acid, b.p. 154.35° at 760 mm.); Duclaux Numbers[18] were 25.3, 20.2 and 15.7 (reported[18] for isobutyric acid, 25.0, 20.9 and 16.0); anilide, m.p. 103–104° (reported[19] for isobutyranilide, 106–107°), *p*-bromophenacyl ester, m.p. 75.5–76.6° (reported[20] for *p*-bromophenacyl isobutyrate, 76.8°). The organic phase from which the acid had been extracted was fractionated through a 2-foot, 20-mm. i.d., adiabatic column at a pressure of 28 mm. The pot temperature was maintained in the range 40–60°. When the pot temperature reached 60°, the pressure was reduced to 1.0 mm. By this procedure a large amount of unchanged diisopropyl ketone was obtained. When all unchanged ketone had been distilled, a fraction of water-white liquid was collected, b.p. (0.8 mm.) 62–69°, d^{20}_{4} 1.013 and $n^{20}\mathrm{D}$ 1.4321. This liquid proved to be a hydroperoxide of diisopropyl ketone.[21]

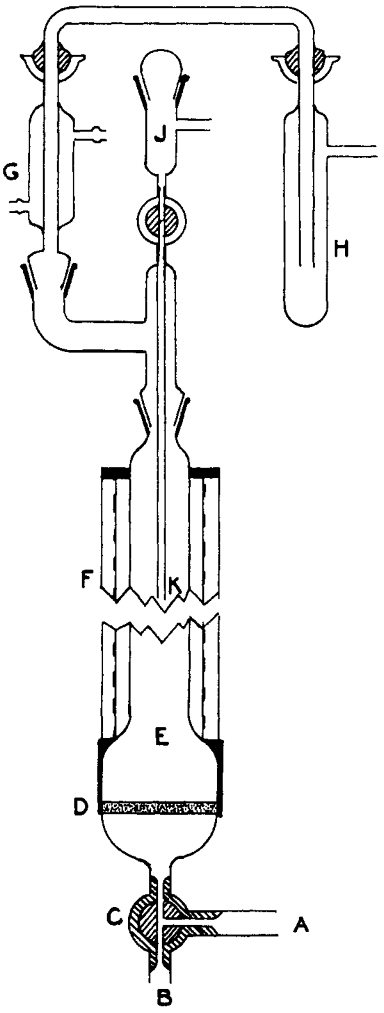

Fig. 1.—Oxidation apparatus.

Anal. Calcd. for $C_7H_{14}O_3$: C, 57.52; H, 9.65; mol. wt., 146.2; active H,[22] 1.00; addn. of Grignard,[22] 1.00. Found: C, 57.12; H, 9.55; mol. wt. (f.p. depression in benzene), 149; mol. wt. (as peroxide), 149.3, 149.8, 148.9; active H, 1.02; addn. of Grignard, 1.02.

Acetone, isobutyric acid, the hydroperoxide of diisopropyl ketone and unchanged ketone were the only organic compounds isolated from the oxidation mixtures; some water was always produced. The amounts of the oxidation products that were isolated from three oxidations are given in

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[12] G. Poletaeff, *Ber.*, **24**, 1308 (1891).

[13] V. N. Ipatieff and V. Haensel, *J. Org. Chem.*, **7**, 189 (1942).

[14] C. D. Wagner, R. H. Smith and E. D. Peters, *Anal. Chem.*, **19**, 976 (1947).

[15] C. F. H. Allen, THIS JOURNAL, **52**, 2955 (1930).

[16] A. Michael, *ibid.*, **41**, 393 (1919).

[17] J. Timmermans, *Bull. soc. chim. Belg.*, **24**, 244 (1910).

[18] R. L. Shriner and R. C. Fuson, "Identification of Organic Compounds," 3rd Ed., John Wiley and Sons, Inc., New York, N. Y., 1948, p. 146.

[19] O. Diels and K. Pflaumer, *Ber.*, **48**, 223 (1915).

[20] W. L. Judefind and E. E. Reid, THIS JOURNAL, **42**, 1043 (1920).

[21] Care should be taken when distilling the hydroperoxide. Prolonged heating of the pot charge at 65–70° generally resulted in violent decomposition. Smooth distillations resulted when the pot temperature was not allowed to exceed 70° and the distillation was completed in as short a time as possible.

[22] S. Siggia, "Quantitative Organic Analysis via Functional Groups," John Wiley and Sons, Inc., New York, N. Y., 1949, pp. 17, 41.

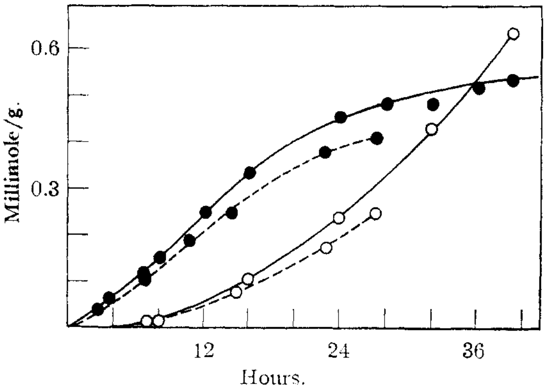


Fig. 2.—Autoxidation of diisopropyl ketone at 100°: ●, peroxide; ○, acid; light ——, dark — — — —.

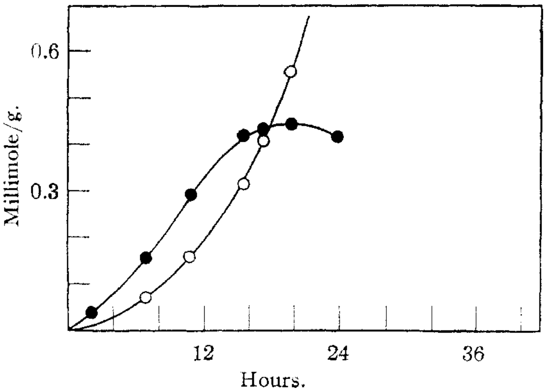


Fig. 3.—Autoxidation of diisopropyl ketone at 110°: ●, peroxide; ○, acid.

Table I, and are compared with the amounts that were indicated by the analyses.

An attempt to fractionate a 125-ml. portion of crude hydroperoxide resulted in violent decomposition of the compound.[21] The liquid (20 ml.) which was found in the fraction cutter was distilled through a 10-inch Vigreux column. Acetone (4 ml.), b.p. 53–58°, and isobutyric acid (12 ml.), b.p. 150–160°, were obtained.

Progress of Oxidation.—The concentrations of acid and peroxide were calculated as millimoles per gram of sample, and these values were plotted against time of oxidation. The curves are shown in Figs. 2 and 3 for oxidations at 100 and 110°, respectively.

Infrared Studies.—The infrared spectra from two to four microns of pure diisopropyl ketone, diisopropyl ketone oxidized for 32 hours at 110°, and of diisopropyl ketone hydroperoxide are shown in Fig. 4. The spectra were obtained using a Perkin-Elmer Model 12C Recording Spectrometer equipped with a sodium chloride prism. The sample cells were of the rock salt plate and spacer type. The spacers used were of aluminum rolled to a thickness of 0.1 mm. for the pure and oxidized ketones and 0.05 mm. for the hydroperoxide. Spectra from 4–15 μ using a sodium chloride prism and from 2–5 μ using a lithium fluoride prism were also obtained and will be discussed in a subsequent paper.

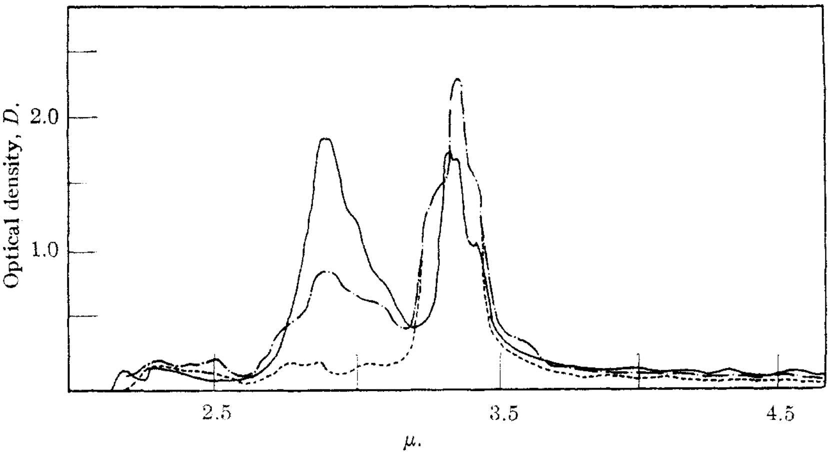


Fig. 4.—Infrared absorption spectra of diisopropyl ketone - - - - (0.1), ketone oxidized at 110° for 32 hours —·—·— (0.1), and 2-(2,4-dimethylpentanone-3-yl) hydroperoxide —— (0.05). Parenthetic numbers are cell thicknesses in mm.

Discussion of Results

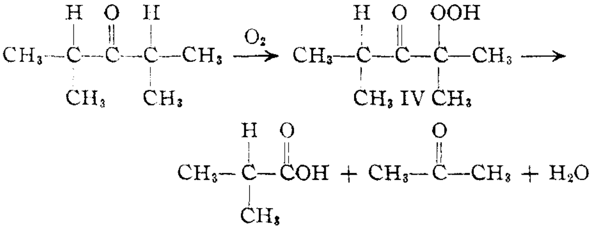
The curves in Figs. 2 and 3 are similar in form to those obtained during typical autoxidation reactions,[23] *i.e.*, rapid reaction after an induction period, and a decrease in the rate of peroxide formation after the reaction had proceeded for a time. These curves indicate that measurable peroxide appeared before detectable amounts of acid were formed. It seemed logical, therefore, that the hydroperoxide which was isolated from the final reaction mixture was the first stable compound formed during the oxidation. The analytical data and the decomposition of this hydroperoxide into acetone and isobutyric acid suggested that it is 2-(2,4-dimethylpentanone-3-yl) hydroperoxide (IV). If this hydroperoxide is the precursor of the acetone and isobutyric acid produced during the oxidation, a formulation of the reaction may be as follows.

TABLE I

QUANTITIES OF PRODUCTS ISOLATED FROM OXIDATIONS OF DIISOPROPYL KETONE[a]

	100°				110°	
	Daylight,[b] g.		Dark,[c] g.		Daylight,[d] g.	
	Found	Anal.[e]	Found	Anal.[e]	Found	Anal.[e]
Isobutyric acid	25.9	26.4	8.7	9.0	50.8	51.1
Acetone	15.5	17.4[f]	5.0	5.9[f]	33.6	33.6[f]
Hydroperoxide	24.0	32.2	18.0	26.4	19.0	18.4

[a] 425 g. of ketone for each run. [b] Thirty-nine hours. [c] Twenty-seven hours. [d] Thirty-six hours. [e] By analysis (titration) of final mixtures. [f] These values are equivalent to the mole portion of isobutyric acid. It was assumed that acetone and isobutyric acid were formed in equimolar quantities.



$$CH_3-\underset{CH_3}{\overset{H}{C}}-\overset{O}{\overset{\|}{C}}-\underset{CH_3}{\overset{H}{C}}-CH_3 \xrightarrow{O_2} CH_3-\underset{CH_3}{\overset{H}{C}}-\overset{O}{\overset{\|}{C}}-\underset{CH_3}{\overset{OOH}{C}}-CH_3 \ (IV) \longrightarrow$$

$$CH_3-\underset{CH_3}{\overset{H}{C}}-\overset{O}{\overset{\|}{C}}OH + CH_3-\overset{O}{\overset{\|}{C}}-CH_3 + H_2O$$

Water was produced in visible quantities during the oxidations and therefore is included with the products in this formulation. Since the oxidation appears to be a chain autoxidation the following

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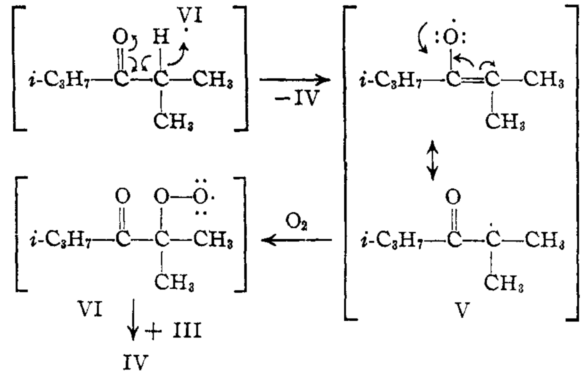
(23) W. A. Waters, "The Chemistry of Free Radicals," Oxford University Press, London, England, 1946, p. 237.

mechanism is proposed as a possible chain propagation step for the formation of the hydroperoxide.



Simple decomposition of IV into acetone and isobutyric acid can be written in a stoichiometric equation, but the appreciable production of water suggests a more involved decomposition sequence to give the final products. Studies of the kinetics of this oxidation are continuing and will be the subject of a future communication.

The infrared absorption spectra in Fig. 4 show a marked increase in absorption after 32 hours at a wave length of about 2.9 μ. Absorption in this wave length region has been designated[24] as being due to O–H stretching and the absorption at about 3.4 μ has been assigned[24] to C–H stretching. The increase of optical density at 2.9 μ with increased oxidation time indicates the development of hydroxyl groups in the form of the hydroperoxide, isobutyric acid or water or any combination of the three. The strong absorption at this region obtained with the pure hydroperoxide is confirmatory evidence for the existence of the hydroperoxy group in that molecule.

Acknowledgment.—The authors are indebted to Mr. A. Dwight Moorhead and Mr. B. L. Thompson for assistance in obtaining the spectroscopic data, and to the Office of Naval Research under whose sponsorship this investigation was conducted. We also gratefully acknowledge the aid in interpretation of the kinetic data given by Dr. M. K. Testerman and Dr. J. L. Hall of the Department of Chemistry.

(24) H. M. Randall, R. G. Fowler, N. Fuson and J. R. Dangl, "Infrared Determination of Organic Structures," D. Van Nostrand Company, New York, N. Y., 1949, p. 43.

MANHATTAN, KANSAS RECEIVED OCTOBER 16, 1950

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE UNIVERSITY OF MARYLAND]

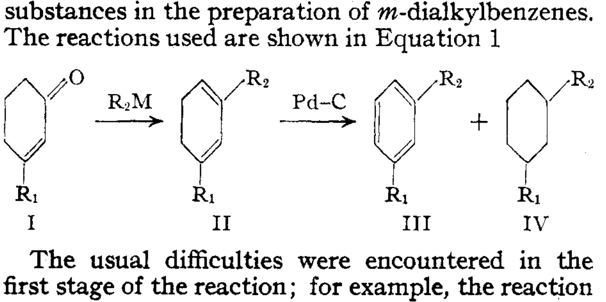
Synthesis of *m*-Dialkylbenzenes

BY G. FORREST WOODS AND ROBERT E. PLAPINGER

A number of *m*-dialkylbenzenes were prepared from 3-alkyl-Δ^2-cyclohexenones by means of the Grignard reaction followed by dehydrogenation over palladium-charcoal. Purification of the aromatic products was accomplished by sulfonation, extraction of the non-aromatic by-products and hydrolysis of the sulfonic acids.

A general method of synthesis of *m*-dialkylbenzenes has long been needed. The best approach to such a preparation has been the use of the Wurtz–Fittig or the Friedel–Crafts reaction. The former has not been useful because of the unavailability of the various *m*-haloalkylbenzenes. The numerous difficulties of the Friedel–Crafts reaction in this type of synthesis are too well known to merit mention here.

Recent publications[1] from this Laboratory have described the preparation of 3-alkyl-Δ^2-cyclohexenones from dihydroresorcinol monoethyl ether. This paper is a report on the utilization of these substances in the preparation of *m*-dialkylbenzenes. The reactions used are shown in Equation 1



The usual difficulties were encountered in the first stage of the reaction; for example, the reaction between *t*-butylmagnesium chloride and 3-*n*-butyl-Δ^2-cyclohexenone afforded none of the desired diene. Presumably the Grignard reagent reacted with the enolic form of the ketone since the ketone was recovered almost completely. However, the expected bond isomer was obtained by addition of *n*-butylmagnesium bromide to 3-*t*-butyl-Δ^2-cyclohexenone.

Table I lists the physical and analytical data for the 1,3-dialkylcyclohexadienes-1,3 (II) obtained in the course of this study.

Unlike 1,3-diarylcyclohexadienes[2] which are readily aromatized over palladium–charcoal catalyst, the 1,3-dialkylcyclohexadienes-1,3 (II) underwent severe disproportionation to yield, in addition to the benzenoid compound (III), 1,3-dialkylcyclohexane (IV).

The purification or separation of these two substances was accomplished in the following manner. The aromatic compound was sulfonated in the cold with concentrated sulfuric acid. After dilution with water, the mixture was extracted with pentane. The aromatic compound was recovered by hydrolysis of the sulfonic acid group and the dialkylcyclohexane could be recovered by fractional distillation of the pentane layer.

It was found that when a 60% sulfuric acid

(1) G. F. Woods, P. H. Griswold, B. H. Armbrecht, D. I. Blumenthal and R. E. Plapinger, THIS JOURNAL, **71**, 2028 (1949).

(2) (a) G. F. Woods and I. W. Tucker, *ibid.*, **70**, 2174 (1948); (b) *ibid.*, **70**, 3340 (1948); (c) G. F. Woods and F. T. Reed, *ibid.*, **71**, 1348 (1949); (d) G. F. Woods, A. L. Van Artsdale and F. T. Reed, *ibid.*, **72**, 3221 (1950).