$\Delta^{3,5}$-Pregnadiene-3,21-diol-7,20-dione (VII).—A solution of VIa (100 mg.) in acetone (20 ml.) was treated with 3 *N* perchloric acid (1 ml.) and allowed to stand at room temperature for 2 hours. The greenish-yellow fluorescent solution was poured into ice-water, and the precipitate was collected; 63 mg. (80% yield), m.p. 227–232° with previous softening, browning and decomposition; λ_{max} 320–321 mμ (ϵ 23,500) and 389–392 mμ (ϵ 2,700). Two crystallizations from acetone–petroleum ether gave 39 mg., m.p. 232–235° with previous softening, browning and decomposition; λ_{max} 320–321 mμ (ϵ 23,600) and 391–392 mμ (ϵ 3,800), $\lambda_{max}^{1\%\ KOH\ in\ abs.\ alc.}$ 390–391 mμ (ϵ 74,400); ν_{max}^{KBr} 3448, 3135, 1704, 1600 and 1546 cm.$^{-1}$; $[\alpha]^{27}$D −267° (*c* 0.487).

Anal. Calcd. for $C_{21}H_{28}O_4$ (344.44): C, 73.22; H, 8.19. Found: C, 73.38; H, 8.43.

PEARL RIVER, NEW YORK

[CONTRIBUTION FROM THE BAKER LABORATORY OF CORNELL UNIVERSITY]

Cyclizations Accompanying the Hydration and the Dehydration of β-Methylheptenone

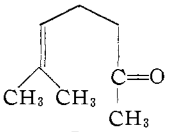
BY J. MEINWALD AND R. F. GROSSMAN

RECEIVED AUGUST 1, 1955

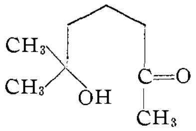
The hydration of β-methylheptenone (I) to the corresponding ketol II was observed to give some crystalline product on one occasion. This product, previously considered to be a pure sample of II, is now shown to be 1,3-dimethylcyclohexane-1,3-diol (IIIc). In connection with this structural assignment, it became necessary to reinvestigate the acid-catalyzed dehydration of I, reported by Verley to yield the "dihydro-*m*-xylene" IV. Verley's claim was discredited by Wallach, who adduced evidence in favor of the hydrocarbon consisting chiefly of a mixture of *m*-xylene and the "tetrahydro-*m*-xylene" VI. New chemical and physical evidence now supports the following conclusions regarding the disputed hydrocarbon: 1, the initial dehydration product is 1,3-dimethylcyclohexadiene-1,3 (IV); 2, under a variety of conditions, IV partially disproportionates to *m*-xylene and 1,5-dimethylcyclohexene (VI); 3, using strong sulfuric acid, the final product consists solely of IV and VI, while zinc chloride yields *m*-xylene in addition to these two components. Some rationalizations for these findings are offered.

The Hydration of β-Methylheptenone.—While carrying out Rupe's synthesis of α-cinenic acid,[1] a curious observation was made in the first step. β-Methylheptenone (I) was hydrated with 35% sulfuric acid to give the corresponding tertiary ketol II; on distillation of the ketol a crystalline material appeared as a slightly higher boiling fraction.[2] This material showed a melting range of 50–60°, but after purification it melted at 90–91°. Elementary analysis showed it to be isomeric with the normal hydration product II. Further quantities of the abnormal product were obtained from the residue remaining after the distillation of α-cinenic nitrile, formed by treating the crude ketol II with anhydrous hydrogen cyanide.[3]

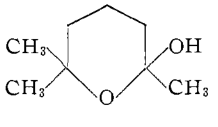
Although this abnormal product was not mentioned by Rupe, reference to its formation in one instance may be found in an early study of the action of sulfuric acid on β-methylheptenone published by Verley in 1897.[4] It was Verley's opinion that this material was simply a very pure sample of II. This hypothesis, however, is untenable. The abnormal hydration product shows no absorption in the carbonyl region of the infrared, although it does have strong hydroxylic absorption. The spectrum might be reconciled with Verley's view if we presume that the unknown is the hemiketal IIa. This possibility can be eliminated, however, by the observation that the compound fails to form a 2,4-dinitrophenylhydrazone, indicating the absence of even a potential carbonyl group.



I



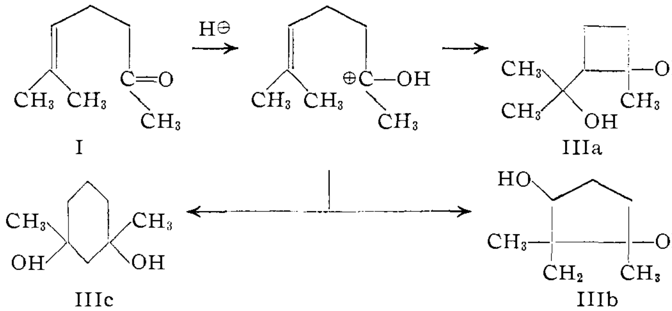
II



IIa

The following structures and modes of formation (eq. 1) for the abnormal hydration product were considered: IIIa appeared unlikely on steric grounds, while IIIb would require anti-Markownikoff addition and is not in accord with the fact that the compound is not acetylated by pyridine and acetic anhydride. IIIc, therefore, seemed most likely, even though its formation would require preliminary migration of the double bond into a terminal position. The dehydration of the diol to 1,3-dimethylcyclohexadiene-1,3 (IV) (discussed below) provides further evidence that the assignment of structure IIIc to the "anormal hydration product" is actually correct.

(1)



The Dehydration of β-Methylheptenone.—Verley's study of the β-methylheptenone–sulfuric acid reaction included a series of experiments in which the effect of acid concentration on product composition was investigated. The most interesting of his results was the finding that in 75% sulfuric acid, the chief product was a hydrocarbon, C_8H_{12},

---

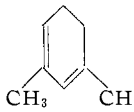
[1] H. Rupe and P. Schlochoff, *Ber.*, **38**, 1502 (1905); H. Rupe and C. Liechtenhan, *ibid.*, **41**, 1298 (1908).

[2] The formation of this product was first noticed in this Laboratory by R. Burrows.

[3] J. Meinwald, THIS JOURNAL, **77**, 1617 (1955). See especially footnote 25 in this reference.

[4] A. Verley, *Bull. soc. chim. Paris*, [3] **17**, 175 (1897).

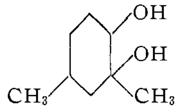
which he designated as "dihydro-*m*-xylene" and to which he assigned formula IV. We have found that the diol IIIc dehydrates to the same hydrocarbon.



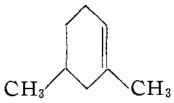
IV

The original evidence in support of structure IV was suggestive, but necessarily vague.[4] Although formation of IV from methylheptenone requires only a simple dehydration in "lasso" terms, it is obvious that the change, if correct at all, must be complex. We have chosen to reinvestigate this problem in some detail not only because of its connection with the structure of the diol discussed above, but also because of the possible general significance of the cyclization technique.

Some critical experiments on the dehydration of β-methylheptenone, using zinc chloride and phosphorus pentoxide[5a] as well as 75% sulfuric acid,[5b] led Wallach to different conclusions regarding the nature of the cyclization product.[5c] The hydrocarbon, on oxidation with potassium permanganate, gave rise to the crystalline glycol V (in unspecified yield) and *m*-xylene (in about 50% yield). On this basis Wallach reached the reasonable conclusion that the hydrocarbon was a mixture of equal amounts of the "tetrahydro-*m*-xylene" VI and *m*-xylene, *with little if any of IV present.*



V



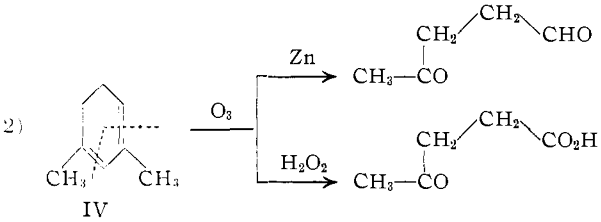
VI

These unexpected observations emphasized the need for further study of the Verley hydrocarbon. The first new insight resulted from spectral examination of the material. Its infrared spectrum showed an absence of absorption at 12.5 and 13.4 μ, although *m*-xylene was found to have definite maxima at these wave lengths. Furthermore, the product showed a λ_{max}^{EtOH} 266 mμ (log ε *ca.* 3.6), in accord with expectations for 1,3-dimethylcyclohexadiene-1,3 (IV).[6]

The crude hydrocarbon was distilled using an 85-cm. Podbielniak column. The ranges of boiling point (127–138°) and refractive index (n^{20}D 1.451–1.485) confirmed Wallach's conclusion that the material was a *mixture* of components. Infrared spectra of individual fractions were similar except in the 12–15 μ region. None of the fractions showed the maxima characteristics of *m*-xylene, however, and it is therefore safe to conclude that *m-xylene is not a component of the mixture.*

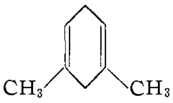
The higher boiling (135–138°) component was shown to be 1,3-dimethylcyclohexadiene-1,3 (IV) in the following way. The material showed a λ_{max}^{EtOH} 266 mμ, log ε 3.75. Infrared analysis did not show the characteristic terminal methylene absorption at 11.25–11.40 μ. Ozonolysis, followed by zinc dust reduction gave levulinaldehyde but no formaldehyde. Oxidation of the ozonide gave levulinic acid, isolated in 72% yield as its 2,4-dinitrophenylhydrazone (eq. 2).

(2)

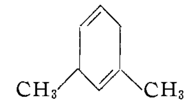


As a final check on the identity of the hydrocarbon, IV was synthesized by a modification of a method previously described by Haworth.[7] The properties of the synthetic diene were in agreement with those previously reported,[7] and spectra indicated that the synthetic diene was identical with the high boiling component of Verley's "dihydro-*m*-xylene."[8]

Attention was directed next to the low boiling (127–129°) component of Verley's hydrocarbon. This material we originally considered to be isomeric with IV. The absence of an absorption maximum above 215 mμ, coupled with the failure of reductive ozonolysis to give formaldehyde, restricted the possible double bond isomers to IVa and IVb. IVb would appear intrinsically unlikely on the basis of the genesis of the hydrocarbon.



IVa



IVb

The Birch reduction product of *m*-xylene (IVa) had been prepared previously in impure state and its structure established.[9] The reported properties seemed to preclude the identity of this compound with the low boiling hydrocarbon from β-methylheptenone; nevertheless Birch's procedure was repeated to give a sample of IVa (of about 89% purity). The non-identity of the two hydrocarbons was demonstrated by direct infrared comparison.

Having excluded the only reasonable dihydro-*m*-xylene structure (IVa) for the low boiling hydrocarbon, the tetrahydro-*m*-xylene structure VI, originally suggested by Wallach, and further indicated by the low value of its refractive index, was considered. This structure was easily confirmed when hypoiodite degradation of the ozonized hydrocarbon gave rise to β-methyladipic acid and iodoform in 34 and 70% yields, respectively (eq. 3).

---

(5) (a) O. Wallach, *Ann.*, **395**, 74 (1913); (b) **396**, 264 (1913); (c) Wallach's conclusions are not seriously affected by his failure to recognize the dependence of product composition on dehydrating agent (*vide infra*), since he performed the same key experiments on hydrocarbon samples prepared with and without sulfuric acid. Brevity dictates against any thorough historical survey at this point.

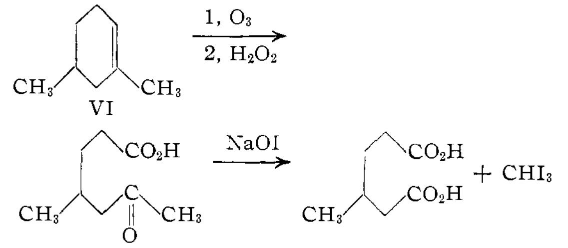
(6) For a summary and extension of "Woodward's rules" on ultraviolet spectra, see L. F. Fieser and M. Fieser, "Natural Products Related to Phenanthrene," Reinhold Publishing Corp., New York, N. Y., 1949, pp. 184 ff.

(7) W. N. Haworth, *J. Chem. Soc.*, **103**, 1242 (1913).

(8) Several attempts to prepare Diels–Alder adducts from IV were unsuccessful, probably because of the instability of the diene. An effort to prepare the diol (IIIc) by hydration of IV led only to the recovery of unchanged starting material.

(9) A. J. Birch, *J. Chem. Soc.*, 430 (1944).

(3)



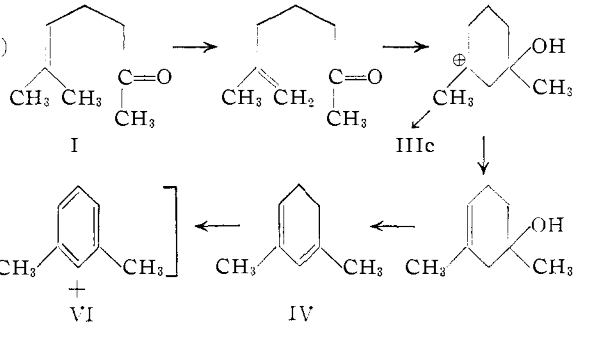
Thus the structural studies so far described indicated that the hydrocarbon produced by the dehydration of β-methylheptenone with 75% sulfuric acid consists of a mixture of 1,3-dimethylcyclohexadiene-1,3 (IV) and 1,5-dimethylcyclohexene (VI). From the intensity of the 266 mμ maximum of a typical sample of crude reaction product, the concentration of IV can be estimated to be about 70%.

There remain several unanswered questions at this point. First of all, the discrepancy between the present work and that of Wallach requires explanation. Wallach's isolation of *m*-xylene from the crude hydrocarbon (produced *via* 75% sulfuric acid[5b]) *after* treatment with permanganate must be reinterpreted to mean that dehydrogenation of IV accompanied oxidation. This explanation was verified by subjecting a sample of synthetic IV to partial permanganate oxidation. The recovered hydrocarbon contained appreciable amounts of *m*-xylene.

The formation of VI, a compound in a lower oxidation state than I, is also puzzling. Wallach's hypothesis was that the "unstable" IV disproportionates to VI and *m*-xylene. Although this explanation hardly seems tenable in view of the demonstrated absence of *m*-xylene in the sulfuric acid product, it is actually essentially correct! A trivial factor interferes with the isolation of the aromatic product; under the reaction conditions it is soluble in sulfuric acid. To demonstrate this fact a mixture of *m*-xylene and I was subjected to the dehydration conditions, and the product was shown to be free of aromatic compound. Furthermore, substitution of a Lewis acid (zinc chloride) for sulfuric acid resulted in the conversion of I into a hydrocarbon mixture containing IV, VI *and* *m*-xylene. Finally, zinc chloride was shown to bring about the disproportionation of a synthetic sample of IV into VI and *m*-xylene. (It may be noted in passing that the isolation of *m*-xylene after permanganate oxidation of products produced with zinc chloride or phosphorus pentoxide now requires no special explanation.)

Probably the most significant remaining question concerns the mechanism of the formation of these cyclic compounds. The reaction sequence portrayed below (eq. 4) is suggested as one possible path.

(4)



In continuing these studies, the exploration of the conversion of apposite unsaturated ketones into hydroaromatic and aromatic compounds is projected.

Acknowledgment.—The partial support of the work reported herein by a Research Grant from the National Science Foundation is gratefully acknowledged.

Experimental

1,3-Dimethylcyclohexane-1,3-diol (IIIc) from the Hydration of β-Methylheptenone (I).—The hydration reaction, using 35% sulfuric acid, was carried out as described previously.[1,3,4] In large scale runs, a small percentage of the product was found to crystallize in the condenser toward the end of a typical distillation. Further quantities of the same crystals were slowly deposited when the distilled hydration product was stored in the refrigerator. The initial m.p. of 50–60° was raised to 90–91° by several recrystallizations from heptane or cyclohexane. Attempts to find conditions which would produce a good, reproducible yield of the diol have been unsuccessful.

A Nujol mull of the crystals showed a broad infrared maximum at 2.9 μ, but no carbonyl absorption. Treatment with 2,4-dinitrophenylhydrazine gave no derivative, and the compound was recovered unchanged after treatment with excess acetic anhydride and pyridine for one hour at 100°.

Dehydration of β-Methylheptenone by 75% Sulfuric Acid.—One hundred grams of 75% (by weight) sulfuric acid was added slowly to 66 g. of β-methylheptenone (I). The mixture was shaken for 15 minutes, carefully neutralized with 10% aqueous sodium hydroxide and steam distilled. The organic layer of the distillate was separated and dried over anhydrous magnesium sulfate to yield about 40 g. (70%) of hydrocarbon mixture, b.p. 128–140°.

The mixture was free of appreciable amounts of *m*-xylene, since infrared maxima at 12.52 and 13.42 μ characteristic of the aromatic compound were absent in the product spectrum. The ultraviolet spectrum of the mixture ($\lambda_{\max}^{\mathrm{EtOH}}$ 266 mμ, log ε *ca.* 3.6) was distinctly different from that reported[10] for *m*-xylene ($\lambda_{\max}$ 270 mμ, log ε 2.5).

An 85-cm. Podbielniak column was used to distil 25 g. of the product. The results are recorded in Table I.

Table I

Fractionation of Hydrocarbon Mixture

Fraction	B.p., °C.	n^{20}D	Weight, g.
1	127–129	1.4518	2.5
2	129–130	1.4603	1.5
3	130–133	1.4695	7.5
4	133–135	1.4812	6.6
5	135–138	1.4858	4.4
Residue			1.6

Despite the poor separation, infrared examination of the individual fractions revealed that the middle cuts were simply mixtures of the two chief components, represented by fractions 1 and 5. Fraction 1 had a characteristic maximum at 12.31 μ, absent in both 5 and *m*-xylene, while fraction 5 had a distinct $\lambda_{\max}^{\mathrm{EtOH}}$ 266 mμ, log ε 3.75, in sharp contrast to *m*-xylene. Fraction 1 had no ultraviolet absorption maximum at all.

Characterization of Fraction 5 as 1,3-Dimethylcyclohexadiene-1,3 (IV). A.—Ozonolysis of 0.5 g. of unfractionated hydrocarbon in methylene chloride (cooled by an ice–acetone-bath) was carried out in the usual way. Zinc dust reduction of the ozonide followed by distillation into a dimedone solution containing a drop of piperidine yielded no formaldehyde–dimedone derivative. In a parallel experiment, methallylsuccinic anhydride yielded 50% recovered formaldehyde derivative.

---

[10] K. L. Wolf and W. Herold, *Z. physik. Chem.*, **B13**, 227 (1931).

B.—A solution of 5 g. of IV (fraction 5, b.p. 135–138°) in 40 ml. of methylene chloride was cooled in an acetone–ice-bath, ozonized, and finally reduced with zinc and ethanol. The resultant solution was filtered, concentrated and portions of it used to prepare a semicarbazone and *p*-nitrophenylhydrazone. Levulinic aldehyde disemicarbazone (m.p. 181–182°, reported 180–182°[11]) and levulinic aldehyde di-*p*-nitrophenylhydrazone (m.p. 282–285°, reported 284–285°[11]) were obtained.

C.—A solution of ozonide prepared as before was added to 100 ml. of glacial acetic acid and 50 ml. of 35% hydrogen peroxide, and refluxed at 90–100° for two hours. The resulting solution was concentrated and a 2,4-dinitrophenylhydrazone prepared. Levulinic acid 2,4-dinitrophenylhydrazone was isolated in 72% yield; after recrystallization from ethyl acetate it melted at 206–207° (reported m.p. 206.5°[12]) and was undepressed by admixture with an authentic sample. Infrared spectra of the two derivatives, pressed into potassium bromide pellets, were indistinguishable.

Dihydroresorcinol Ethyl Ether.—The "direct esterification" method[13] gave 45% of a product, b.p. 95–105° (5 mm.), $n^{20}\text{D}$ 1.4297. This method seemed superior to the ethyl iodide alkylation described more recently.[14]

3-Methyl-2-cyclohexenone.—An ethereal solution of lithium methyl was prepared from 0.9 g. of lithium and 20 g. of methyl iodide in the usual way. The solution was cooled to −10° and 10 g. of dihydroresorcinol ethyl ether in 100 ml. of absolute ether was added with stirring. The mixture was allowed to stand for two hours, and then poured into 50 ml. of 35% sulfuric acid diluted with 100 ml. of water and 100 ml. of ice. After an hour of standing the organic layer was separated and the aqueous layer extracted several times with ether. Evaporation of the dried ethereal solution yielded 6 g. of a red liquid from which 5 g. (63%) of clear 3-methyl-2-cyclohexenone (b.p. 95–105° (12 mm.), $n^{20}\text{D}$ 1.4958, $\lambda_{\text{max}}^{\text{EtOH}}$ 235 mμ, ϵ 12,470; reported $n^{20}\text{D}$ 1.4945, $\lambda_{\text{max}}^{\text{EtOH}}$ 235 mμ, ϵ 12,600[14,15]) was distilled.

Synthesis of 1,3-Dimethylcyclohexadiene-1,3 (IV).—A 5-g. yield (50%) of IV was obtained by the treatment of 10 g. of freshly distilled 3-methyl-2-cyclohexenone with lithium methyl as described above. The properties of the product (b.p. 135–137°, $n^{20}\text{D}$ 1.4852) were in good agreement with those previously reported (b.p. 135–136°, $n^{20}\text{D}$ 1.4856[7]). The ultraviolet spectrum of the synthetic material ($\lambda_{\text{max}}^{\text{EtOH}}$ 266, log ϵ 3.75) as well as the other physical properties were in accord with observations made on 1,3-dimethylcyclohexadiene-1,3 (IV) obtained as fraction 5 above.

Attempted Hydration of 1,3-Dimethylcyclohexadiene-1,3.—A mixture of 10 g. of the diene IV and 100 g. of 35% sulfuric acid was shaken for seven hours. The resultant clear, two-layer system was neutralized in the cold with 10% aqueous sodium hydroxide, and continuously extracted with ether. Evaporation of the ether left 8.5 g. of a clear liquid whose infrared spectrum was identical with that of the starting material.

Attempted Diels–Alder Additions to IV.—Attempts to obtain adducts from the diene IV using maleic anhydride and *n*-phenylmaleimide in benzene and xylene, even allowing reflux periods of one week, led only to the recovery of the dienophiles.

Birch Reduction of *m*-Xylene.[9]—A mixture of 200 ml. of liquid ammonia and 12 g. of finely cut sodium was stirred at −70° until solution was complete. A solution of 22 g. of *m*-xylene in 30 ml. of absolute methanol was added dropwise, and the mixture stirred until the blue color vanished. The usual work-up technique yielded 19 g. (84%) of a clear liquid, b.p. 138–142°, $n^{20}\text{D}$ 1.4737. Comparison of the ultraviolet absorption of the product with that of *m*-xylene indicated that the latter was present in the reduction product to the extent of 11%.

Degradation of 1,5-Dimethylcyclohexene (VI) to β-Methyladipic Acid and Iodoform.—A solution of 3 g. of "fraction 1" (VI) in methylene chloride was ozonized and the ozonide oxidized with hydrogen peroxide, as described above in the characterization of IV. The solution of oxidized ozonide was concentrated and added to 250 ml. of water containing 12.5 g. of potassium iodide. Clorox was added as long as a precipitate continued to form. The iodoform so produced, 7.5 g. (70%), m.p. 115–118°, was filtered and the filtrate extracted several times with ether. Evaporation of the dried ether yielded 1.5 g. (34%) of β-methyladipic acid as white crystals, m.p. 93–95° (reported 97°[16]). Treatment of the acid with thionyl chloride in benzene, followed by reaction with aniline in the usual way, yielded β-methyladipic acid dianilide as white flakes, m.p. 203–205°.

Nitrosochloride of VI.—A solution of 1 ml. of VI (b.p. 127–129°) in 2 ml. of glacial acetic acid was added to a mixture of 1.5 ml. of *n*-butyl nitrite and 0.8 ml. of concentrated hydrochloric acid, precooled to 0°. The brown color of the upper layer slowly became green as crystals appeared at the interface. White crystals with a greenish tinge were collected, m.p. 118–119° (reported 119°[5]).

Dehydration of 1,3-Dimethylcyclohexane-1,3-diol (IIIc).—A mixture of 1 g. of diol and 5 g. of 75% sulfuric acid was shaken for 15 minutes. The reaction mixture was neutralized with 10% sodium hydroxide and the organic layer extracted with ether. The dried ethereal solution yielded 0.6 g. (80%) of liquid, b.p. *ca.* 135–136°, $n^{20}\text{D}$ 1.4820. The infrared spectrum of this liquid indicated it to be a mixture of IV and VI with the former predominating; the high value of its refractive index supported this conclusion.

Permanganate Dehydrogenation of IV.—To 3 g. of synthetic IV, 20 ml. of 2% potasssium permanganate was added with vigorous shaking. Further increments of oxidant were not decolorized. An organic layer was separated and filtered to yield a clear liquid, $n^{20}\text{D}$ 1.4912, whose infrared spectrum indicated the presence of *m*-xylene but not of VI. The amount of *m*-xylene present was estimated to be about 44% from consideration of refractive indices.

Removal of *m*-Xylene by Sulfuric Acid during Dehydration of β-Methylheptenone (I).—A mixture of 10 g. of I and 3 g. of *m*-xylene was shaken with 100 g. of 75% sulfuric acid as described previously. The product (6 g.) was found to be free of *m*-xylene by inspection of its infrared spectrum.

Dehydration of β-Methylheptenone (I) by Zinc Chloride.—A mixture of 10 g. of freshly distilled I and 10 g. of anhydrous zinc chloride was warmed on a steam-bath. The temperature rose spontaneously to 150°. After cooling to room temperature, the mixture was added to 50 ml. of water and steam distilled. The distillate was extracted with ether to yield 6 g. (70%) of a mixture of *m*-xylene, IV and VI, as demonstrated by infrared examination. The *m*-xylene was removed by shaking the mixture with warm, concentrated sulfuric acid for 30 minutes. Neutralization and extraction led to the recovery of 3.5 g. of a mixture of approximately equal amounts of IV and VI (estimated from ultraviolet data).

Disproportionation of 1,3-Dimethylcyclohexadiene-1,3 (IV) over Zinc Chloride.—A mixture of synthetic IV and 5 g. of anhydrous zinc chloride was refluxed for two hours. The organic layer was decanted to give a clear liquid, $n^{20}\text{D}$ 1.4820, whose infrared spectrum showed absorption characteristic of *m*-xylene (12.52, 13.42 μ) and 1,5-dimethylcyclohexene (12.31 μ). Removal of the *m*-xylene by sulfuric acid yielded 3 g. of a liquid estimated to contain 15–20% of unreacted diene IV (on the basis of ultraviolet data).

ITHACA, NEW YORK

---

[11] I. Heilbron, "Dictionary of Organic Compounds," Oxford University Press, New York, N. Y., 1953, Vol. 3, p. 179.

[12] M. A. Cowley and H. A. Schuette, THIS JOURNAL, **55**, 3463 (1933).

[13] A. W. Crossley and N. Renouf, *J. Chem. Soc.*, **93**, 640 (1908).

[14] G. F. Woods and I. W. Tucker, THIS JOURNAL, **70**, 2174 (1948).

[15] A. Gillam and E. S. Stern, "Electronic Absorption Spectroscopy," Arnold Press, London, 1954.

[16] I. Heilbron, "Dictionary of Organic Compounds," Oxford University Press, New York, N. Y., 1953, Vol. 3, p. 290.