15 min. of refluxing. α,α-Dimethyl-δ-phthalimidolevulinic acid was recrystallized from acetone–water, m.p. 159–160°.

Anal. Calcd. for $C_{15}H_{15}NO_5$: C, 62.29; H, 5.27; N, 4.84. Found: C, 62.24; H, 5.34; N, 5.07.

Methyl β,β-dimethyl-δ-phthalimidolevulinate under the same conditions hydrolyzed to the extent of 64.8% during 5-min. reflux to yield β,β-dimethyl-δ-phthalimidolevulinic acid. It was recrystallized from acetone–water, m.p. 157–158°.

Anal. Found: C, 61.99; H, 5.41; N, 4.89.

A mixture of these two isomeric acids melted at 130–137°.

α,α-Dimethyl-δ-aminolevulinic Acid.—Methyl α,α-dimethyl-δ-phthalimidolevulinate (5 g.) and 55 ml. of 24% hydrobromic acid were refluxed for 12 hr. The α,α-dimethyl-δ-aminolevulinic acid hydrobromide obtained was recrystallized from a methanol–acetone–ether mixture to yield colorless crystals, 3.65 g. (92.1%), m.p. 150°. The yield of phthalic acid was 2.60 g. (95%).

Anal. Calcd. for $C_7H_{14}BrNO_3$: C, 35.02; H, 5.88; Br, 33.28; N, 5.83. Found: C, 34.89; H, 5.91; Br, 33.54; N, 6.02.

α,α-Dimethyl-δ-aminolevulinic acid hydrochloride was obtained as highly hygroscopic crystals. To a solution of the amino acid hydrochloride (obtained from the hydrolysis of 2.0 g. of phthalimidolevulinate) in 10 ml. of water was added a solution of 1.3 g. of disodium naphthalene-1,5-disulfonate in 15 ml. of water. The solution was warmed on the steam bath for a few minutes and allowed to cool gradually. Colorless needles of the disulfonate salt separated. It was recrystallized once again from water. It started charring at 258° and completely blackened at 262°. The yield (1.8 g.) was 90%.

Anal. Calcd. for $(C_7H_{14}NO_3)_2 \cdot C_{10}H_6O_6S_2$: C, 47.48; H, 5.65; N, 4.62. Found: C, 47.70; H, 5.63; N, 4.58; S, 10.76.

β,β-Dimethyl-δ-aminolevulinic Acid Hydrochloride.—Methyl β,β-dimethyl-δ-phthalimidolevulinate, m.p. 80° (3.7 g.), and 45 ml. of 6 *N* hydrochloric acid were refluxed for 12 hr. The yield of phthalic acid was 1.9 g. (94%). The β,β-dimethyl-δ-aminolevulinic acid hydrochloride obtained was recrystallized from an acetone–methanol–ether mixture to yield colorless crystals, 2.05 g. (86%), m.p. 182°.

Anal. Calcd. for $C_7H_{14}ClNO_3$: C, 42.96; H, 7.21; Cl, 18.12; N, 6.99. Found: C, 42.85; H, 7.14; Cl, 18.17; N, 6.96.

Methyl β,δ-Dimethyl-δ-chlorolevulinates.—β-Carbomethoxyisobutyryl chloride (25 g.) was treated with diazoethane prepared from 70 g. of N-nitrosoethyl urea. This was followed by treatment with dry hydrogen chloride for 3 hr. as usual. A small amount of ether-insoluble, water-soluble, yellow, powdery mass which formed was filtered off. The dark brown liquid product was distilled. A yellow oil boiling over a range of 53–73° (0.5 mm.), $n^{27.5}$D 1.4370–1.4480, was obtained. The yield was 14.25 g. The main fraction (12.0 g.) was redistilled and boiled at 55–63° (0.3 mm.), n^{29}D 1.4380–1.4420. A portion of the main fraction of this distillation was redistilled for analysis. The major fraction, b.p. 52° (0.1 mm.), n^{29}D 1.4415, $d^{28.5}$ 1.1057, was yellow and obviously impure.

Anal. Calcd. for $C_8H_{13}ClO_3$: C, 49.90; H, 6.77; Cl, 18.41. Found: C, 52.73; H, 7.39; Cl, 14.69.

The infrared spectrum showed no olefinic peaks even though analysis indicated some dehydrochlorination. The n.m.r. spectrum of the analytical sample showed two doublets of equal intensity at τ 8.57 and 9.0 (J = 7.2 c.p.s.) for the two CH_3CH groups (the doublet at the lower intensity showed fine splitting into four peaks); a multiplet at τ 6.7–8 for the CH_2CH– group; a singlet at τ 6.7 for OCH_3; and a finely split quadruplet at τ 5.6 for the CHCl group.

Phthalimido Derivatives.—The mixture containing methyl β,δ-dimethyl-δ-chlorolevulinate obtained after three distillations (b.p. 56–68° at 0.3 mm.) was treated with potassium phthalimide in dimethylformamide during 1 hr. at room temperature at 100° for 5 hr. In a subsequent experiment the chloro ester, obtained after one distillation, b.p. 70–90° (1 mm.), was treated likewise with potassium phthalimide at room temperature for 20 hr. The reaction mixtures were worked up as usual to yield a semisolid residue; this was taken up in methanol–petroleum ether (30–60°) and cooled. A crystalline solid separated in 16–20% yield and was recrystallized from ethyl acetate–petroleum ether (30–60°) to yield colorless plates, m.p. 125°.

Anal. Calcd. for $C_{16}H_{17}NO_5$; C, 63.37; H, 5.65; N, 4.62. Found: C, 63.28; H, 5.84; N, 4.62.

The infrared spectrum was similar to the other phthalimidolevulinates. The n.m.r. spectrum of the compound showed a single doublet for the CH_3 group at τ 8.92 (three protons), indicating that only one CH_3CH group remains in the molecule. We conclude that the compound is **methyl 3-methyl-4-oxo-6-phthalimidohexanoate**, since this structure fully explains the complex multiplet between τ 7 and 8 (five protons, $—CH_2COCHCH_2—$), the sharp singlet at τ 6.5 (three protons, OCH_3), the triplet at τ 6.2 (two protons, $>N—CH_2—$), and the doublet at τ 2.5 (four protons).

Hydrolysis.—The phthalimido derivative, m.p. 125°, on hydrolysis with 6 *N* hydrochloric acid during 5-min. reflux gave **3-methyl-4-oxo-6-phthalimidohexanoic acid**. It was recrystallized from ethyl acetate–petroleum ether, m.p. 150°.

Anal. Calcd. for $C_{15}H_{15}NO_5$: C, 62.29; H, 5.27; N, 4.87. Found: C, 62.46; H, 5.38; N, 4.78.

6-Amino-3-methyl-4-oxohexanoic Acid Hydrochloride.—The phthalimido derivative, m.p. 125° (1.0 g.), was refluxed with 15 ml. of 6 *N* hydrochloric acid for 8 hr. The product was recrystallized from a mixture of acetone, methanol, and ether to yield 0.60 g. (93.3%) of colorless crystals, m.p. 125–126°.

Anal. Calcd. for $C_7H_{14}ClNO_3$: C, 42.96; H, 7.21; Cl, 18.12; N, 6.99. Found: C, 42.93; H, 7.17; Cl, 18.08; N, 7.02.

Pyrolysis Studies. XV. Thermal Retrograde Aldol Condensation of β-Hydroxy Ketones[1a]

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This present note reports the vapor phase kinetics of a retrograde aldol condensation of 4-hydroxy-4-methyl-2-pentanone which thermally decomposes to acetone. In a very well-seasoned reactor this compound decomposes by first-order kinetics with a negative entropy of activation (−8.3 ± 1.5 e.u. at 220°) and an activation energy of 31.2 ± 1.0 kcal./mole. The reaction was shown to be homogeneous on changing the surface to volume ratio ten times by introducing a stainless steel sponge. The values of the rate constant before and after packing were 8.77×10^{-3} and 8.98×10^{-3} sec.$^{-1}$, respectively, at 243.9°. It proved difficult to obtain reproducible kinetic results, thus requiring extended treatments with 3-butenoic acid at 400° and repeated pyrolyses (50 times) of the β-hydroxy ketone to completely deactivate the walls of the stainless steel reactor. Interestingly, first-order plots of $(P_\infty - P_t)$ against time were linear up to at least 90% decomposition before the surface was completely deactivated. Normally the plots are curved when a heterogeneous reaction is occurring. Eventually reproducible results were obtained and first-order plots were linear to greater than 90% completion.

Although this vapor phase reaction was reported in Hurd's[2] book on pyrolysis, very little has been reported since as has nothing on the mechanism of the reaction.

Based on the kinetics obtained and the products formed it is proposed that β-hydroxy ketones thermally decompose in the vapor state through a six-membered cyclic transition state mechanism (I) similar to those

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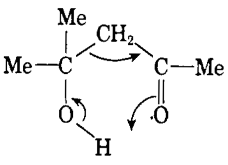
(1) (a) This paper was presented in part at the Northwest Regional Meeting of the American Chemical Society in Spokane, Wash., June 1964. (b) Postdoctoral research associate, 1963–1964.

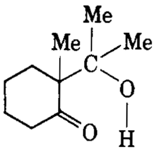
(2) C. D. Hurd, "The Pyrolysis of Organic Compounds," The Chemical Catalog Co., Inc., Reinhold Publishing Corp., New York, N. Y., 1929, p. 164.

proposed for the pyrolysis of esters,[3a] β-hydroxy olefins,[3b] and β,γ-unsaturated acids.[4]

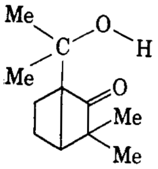
Further evidence for a cyclic transition state mechanism was presented by Mole[5] who reported the condensed phase thermal decomposition of β-hydroxy ketones. He showed that 2-methyl-2-(1-hydroxy-1-methylethyl)cyclohexanone (II) pyrolyzes into 2-methylcyclohexanone and acetone and that the rate in petroleum ether was uneffected by the nature of the surface of the reaction vessel or by small traces of acids or bases. They reported that 3,3-dimethyl-1-(1-hydroxy-1-methylethyl)bicyclo[2.2.1]heptanone (III) is essentially stable to heat. This compound cannot form a cyclic transition state and products without forming a double bond at the bridgehead.



I



II



III

As 4-hydroxy-4-methyl-2-pentanone is the only β-hydroxy ketone whose pyrolysis rate has been measured in the vapor state, comparative studies are a little premature. However, it is noteworthy that the temperature required for the pyrolysis of 4-hydroxy-4-methyl-2-pentanone (200–250°) is much lower than that for simple aliphatic esters (300–400°),[3a] β-hydroxy olefins (350–400°),[3b] and β,γ-unsaturated acids (369–378°).[4] This indicates that although the acidity of the hydrogen, which is thought to be involved in the transition state, is not particularly important,[3b] the greater basicity of the C=O bond in the β-hydroxy ketones over that of C=C bond is significant.

Experimental

4-Hydroxy-4-methyl-2-pentanone.—4-Hydroxy-4-methyl-2-pentanone was obtained commercially and fractionated before use, b.p. 65–66° (17 mm.), $n^{20}\text{D}$ 1.4215 [lit.[6] b.p. 67–69° (19 mm.), $n^{20}\text{D}$ 1.4213].

Method of Pyrolysis.—4-Hydroxy-4-methyl-2-pentanone was pyrolyzed at temperatures ranging from 221.9 to 255.2° in a stainless steel reactor of constant volume (200 ml.), whose design and operation have been described.[7] The reaction was followed automatically using a stainless steel diaphragm closing one end of the reactor as a null gauge and a pressure transducer connected to a strip chart recorder. The temperature was maintained to within 0.02° with a large glass wool lagged, electrically heated aluminum block, and was measured with two Chromel–Alumel thermocouples in series; these were calibrated to 0.1° against a platinum resistance thermometer.

Product Analysis.—The product from several pyrolyses of 4-hydroxy-4-methyl-2-pentanone was trapped in a liquid nitrogen trap attached directly to the reaction vessel, and was analyzed by v.p.c. on a Dow silicone 710 column and by fractional distillation. In the v.p.c. analysis only one peak was obtained, corresponding in retention time to acetone, and the fractionation only yielded acetone and unreacted 4-hydroxy-4-methyl-2-pentanone which were identified by their refractive indices and infrared spectra.

TABLE I

KINETIC DATA FOR THE PYROLYSIS OF 4-HYDROXY-4-METHYL-2-PENTANONE

$k \times 10^3$, sec.$^{-1}$	Temp., °C.	Activation energy, kcal.	Log A	Entropy of activation at 500°K., e.u.
16.7	255.2	32.3	11.63	−8.3
8.77	243.9			
4.05	231.1			
2.27	221.9			

Acknowledgment.—This work was supported in part by the United States Air Force, Air Force Office of Scientific Research under Grant No. AF-62-628 and by the Utah State University Research Council. Grateful acknowledgment is given for this support.

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The Reaction of Aromatic–Aliphatic Sulfones with N-Bromosuccinimide[1]

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In 1955 the author attempted to prepare 1,5-dibromo-1,2,4,5-tetrahydro-3-benzothiepine 3,3-dioxide by allowing 1-bromo-1,2,4,5-tetrahydro-3-benzothiepine 3,3-dioxide to react with N-bromosuccinimide.[2] The yields were disappointingly low (2–7%), even though the reaction conditions were varied. These results were surprising since numerous benzylic-type compounds had been successfully brominated with N-bromosuccinimide.[3]

Although Maerov[4] was unable to brominate 2,3,4,5-tetrahydrothiepine 1,1-dioxide with N-bromosuccinimide, Traynelis and Love[5] reported the successful bromination of 2,3-dihydro-1-benzothiepine 1,1-dioxide with N-bromosuccinimide. In view of these results, it seemed worthwhile to determine whether N-bromosuccinimide could be generally used for the bromination of benzylic methylene groups at least once removed from sulfone groups.

Since the 2-phenethylsulfonyl grouping in 2-phenethyl phenyl sulfone is similar to that found in 1,2,4,5-tetrahydro-3-benzothiepine 3,3-dioxide, this compound was selected for initial study. 2-Phenethyl phenyl sulfone was treated with N-bromosuccinimide and a 46% yield of 2-bromo-2-phenethyl phenyl sulfone was realized. The bromo compound was dehydrohalogenated with triethylamine to yield phenyl ω-styryl sulfone which was compared with an authentic sample.[6]

Initial attempts to form bis(2-bromo-2-phenethyl) sulfone by vigorously refluxing bis(2-phenethyl) sulfone with N-bromosuccinimide in carbon tetrachloride were

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[1] Acknowledgment is made to the American Medical Association Education and Research Foundation for partial support of this research.

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