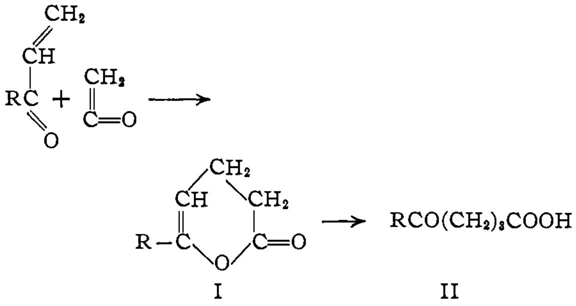
[CONTRIBUTION FROM THE RESEARCH AND DEVELOPMENT DEPARTMENT OF THE CARBIDE AND CARBON CHEMICALS CORPORATION]

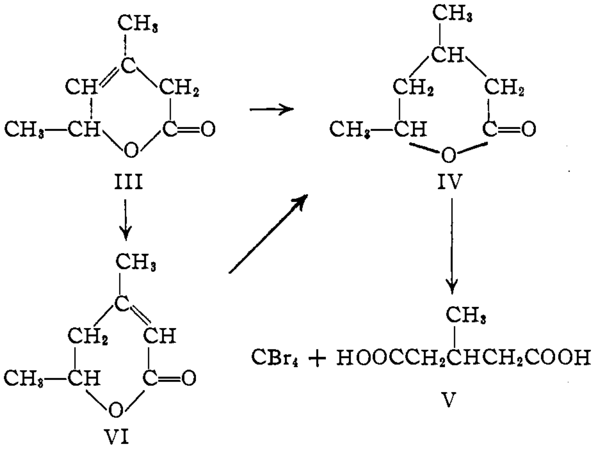
The Reaction of Ketene with Unsaturated Ketones

BY FRANK G. YOUNG

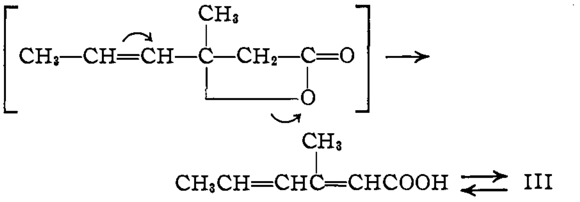
Recent patents have described the reaction of ketene with saturated aldehydes and ketones giving β-lactones[1] and α,β-unsaturated acids.[2] The reaction of vinyl methyl ketone with ketene was described in patents[3,4] by Hopff and Rapp. This reaction was carried out in absence of catalyst and the product was described as a γ,δ-unsaturated lactone (I) which was easily hydrolyzed, by water or aqueous alkali, to a δ-keto acid (II). The over-all equation proposed[3] presumably involves a 1,4-addition of ketene to the unsaturated system.



Because of the widespread physiological activity of unsaturated lactones,[5] it was of interest to determine if β-alkyl vinyl methyl ketones would undergo similar condensation with ketene. In contrast to its reaction with vinyl methyl ketone, no reaction between ketene and β-alkyl vinyl methyl ketones could be produced in the absence of a catalyst, but a trace of boron trifluoride or other acidic agent afforded rapid reaction and good yields of unsaturated lactones. The lactone isolated, after neutralization of catalyst, from the condensation of ketene and ethylidene acetone was not of type I, since it remained unchanged on treatment with boiling water, and saponification with aqueous alkalies followed by acidification of the cold solution, produced the same substance as that originally isolated. Presumably the intermediate product of the acidification was an unsaturated acid, which under the experimental conditions rapidly isomerized to the lactone. This eliminated the possibility of a β-lactone and indicated that the unsaturation was not in the γ,δ-position, an observation which was supported by its mode of hydrogenation,[6] and confirmed by reaction with iodine bromide.[7,8,9,10] Distinction among $\Delta^{\alpha,\beta}$, unconjugated, and enol-lactones can be made using this reagent.[7] Since the lactone required approximately one mole of halogen per mole, the β,γ-position of the double bond was indicated. The δ-lactone structure of the molecule (III) was proved by hydrogenation to a saturated lactone (IV), which upon oxidation with alkaline hypobromite solution gave carbon tetrabromide and β-methylglutaric acid (V).



The production of a $\Delta^{\beta,\gamma}$ rather than a $\Delta^{\gamma,\delta}$ enol-lactone indicated that 1,4-addition of ketene to the ene-one system, $-\overset{|}{C}=\overset{|}{C}-\overset{|}{C}=O$ could not represent the true reaction mechanism. An alternative mechanism involving 1,2-addition of ketene to the carbonyl group of the ketone, producing an intermediate unsatured β-lactone, analogous to the mechanism proposed for the reaction of ketene with saturated aldehydes,[1] is postulated. The β-lactone was not isolated in the present work.



The electron-donating effect of the γ-double bond would be expected to enhance the instability of the β-lactone ring, and the formation of a doubly unsaturated acid by β-displacement. The methylsorbic acid would then rapidly equilibrate with its isomeric δ-lactone (III).

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(1) Küng, U. S. Patent 2,356,459 (August 22, 1944).

(2) Boese, U. S. Patent 2,387,464 (August 14, 1945).

(3) U. S. Patent 2,265,165 (December 9, 1941).

(4) German Patent 723,277 (August 8, 1942).

(5) Haynes, *Quarterly Reviews*, **II**, 46 (1948), The Chemical Society, London.

(6) Jacobs and Scott, *J. Biol. Chem.*, **87**, 601 (1930); **93**, 139 (1931).

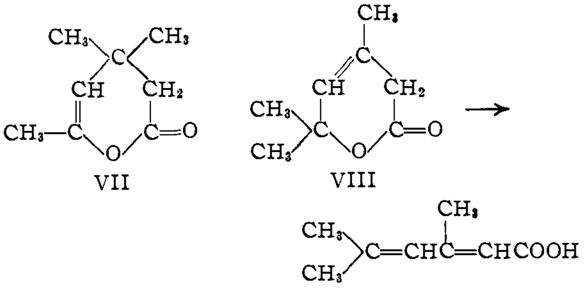
(7) Cavallito and Haskell, THIS JOURNAL, **68**, 2332 (1946).

(8) Thiele and Straus, *Ann.*, **319**, 155 (1901).

(9) Jacobs, Hoffman and Gustus, *J. Biol. Chem.*, **70**, 1 (1926).

(10) Caldwell and Piontowski, THIS JOURNAL, **56**, 2086 (1934).

Addition of ketene to ethylidene acetone by either of these mechanisms would produce an unsaturated δ-lactone, differing only in the location of the double bond. Support for the latter mechanism was found in the reaction of mesityl oxide and ketene. In this case reaction by 1,4-addition should yield VII, but VIII was formed as proved by its conversion to β,δ-dimethylsorbic acid.


VII VIII

$(CH_3)_2C{=}CHC(CH_3){=}CHCOOH$

Lactone III may be converted quantitatively to the $\Delta^{\alpha,\beta}$-isomer (VI) by heating it with a trace of an alkaline catalyst. This lactone is unreactive toward the iodine monobromide reagent, and on hydrogenation yields a saturated lactone identical with IV.

Spectrographic examination of the lactones III and VI in *n*-heptane shows a much more intense ultraviolet absorption below 220 mμ for VI, but the distinct maximum at 265 mμ, characteristic of the carbonyl group, is much weakened. Longer wave lengths are about equally absorbed by the two lactones. Molecular extinction values are 115 at 240 mμ, 130 at 265 mμ, 68 at 280 mμ, and 5 at 300 mμ for III; and ϵ = 267, 108, 60, and 10 at corresponding values for VI. The lactone III is readily soluble to the extent of 5% by volume in *n*-heptane, but VI is less than 2% soluble in the same solvent.

Experimental[11]

β-Methyl-$\Delta^{\beta,\gamma}$-δ-hexenolactone (III).—Into a solution of 800 g. (10.0 moles) of dry ethylidene acetone in 715 g. of anhydrous ether maintained at 0° by external cooling, there was diffused simultaneously 240 g. (5.7 moles) of ketene at the rate of 168 g. per hour and 10 g. of boron trifluoride at the rate of 6.6 g. per hour. Enough 0.5 *N* sodium hydroxide solution to destroy the catalyst was then added. The lower aqueous layer was separated and discarded. After removal of the ether, the residue from the upper layer was distilled. There was obtained 404 g. of unreacted ethylidene acetone and 467 g. (95% based on the ketone consumed) of the unsaturated lactone (III), b. p. 85° (5 mm.); sp. gr. $^{20}_{15.6}$ 1.043; n^{30}D 1.4640. *Anal.* Calcd. for $C_7H_{10}O_2$: C, 66.6; H, 8.0; sapn. equiv., 126.2. Found: C, 66.4; H, 8.0; sapn. equiv., 126.0.

Saponification of β-Methyl-$\Delta^{\beta,\gamma}$-δ-hexenolactone (III).—Eighty-seven grams of the lactone was stirred with 350 ml. of 10% aq. sodium hydroxide at 20° until solution was complete. The clear solution was acidified with 75 ml. of concentrated hydrochloric acid, and the oil which separated was distilled, b. p. 85° (5 mm.); sp. gr. $^{20}_{15.6}$ 1.042; n^{30}D 1.4640, identical in all respects with the original lactone (III).

Reaction of β-Methyl-$\Delta^{\beta,\gamma}$-δ-hexenolactone (III) with Iodine Bromide Reagent.—The iodine number was determined by the usual Hanus procedure[12] using the modifications suggested by Cavallito and Haskell.[7]

Anal. 0.1103 g. (III) required 9.40 ml. of 0.1001 *N* IBr = 1.07 moles of halogen per mole.

β-Methyl-δ-hexanolactone (IV).—Fifteen hundred grams of the unsaturated lactone (III) was hydrogenated at 50° and 1000 p. s. i. hydrogen in the presence of 15 g. of Raney nickel. The catalyst was filtered off and the filtrate was washed several times with 10% sodium bicarbonate solution to remove the small amount of β-methylcaproic acid formed by hydrogenolysis of the lactone ring. The neutral material was dried and distilled, b. p. 83–86° (3 mm.); sp. gr. $^{30}_{15.6}$ 1.020; n^{30}D 1.4437. *Anal.* Calcd. for $C_7H_{12}O_2$: C, 65.6; H, 9.4; sapn. equiv., 128.2. Found: C, 65.4; H, 9.4; sapn. equiv., 128.1. Iodoform test positive. The yield was 1250 g. (82%).

Oxidation of β-Methyl-δ-hexanolactone (IV).—Six and one-half grams of the saturated lactone (IV) was added to a solution of 40 g. of bromine and 20 g. of sodium hydroxide in 400 ml. water. During twelve hours standing at room temperature a heavy liquid separated which was soon converted to a white crystalline solid. The material (9.0 g., 70% of the theoretical) was filtered off and identified as carbon tetrabromide by its m. p. of 90.1°. The filtrate was extracted with ether, acidified with hydrochloric acid and re-extracted with ether. After removal of the solvent, the residue of 5 g. was distilled at 0.5 mm., 140° bath temperature. The distillate crystallized, m. p. 87–89°, undepressed by admixture with an authentic sample of β-methylglutaric acid (V).

β-Methyl-$\Delta^{\alpha,\beta}$-δ-hexenolactone (VI).—Seven hundred eighty-two grams of III and 3.7 g. (0.5%) of anhydrous potassium carbonate were heated together by means of an oil-bath to a temperature of 118°. A mild exothermic reaction set in and the temperature rose to 130° with the bath removed. The mixture was allowed to cool to 115°, and maintained at that temperature for fifteen minutes by replacing the oil-bath. Distillation gave a fraction of 743 g. (94%), b. p. 105° (5 mm.); sp. gr. $^{20}_{15.6}$ 1.045; n^{30}D 1.4746. *Anal.* Calcd. for $C_7H_{10}O_2$: C, 66.6; H, 8.0; sapn. equiv., 126.2. Found: C, 66.6; H, 8.0; sapn. equiv., 126.2. 1.9094 g. required 1.02 ml. of 0.1001 *N* IBr = 0.0067 mole of halogen per mole.

Hydrogenation of β-Methyl-$\Delta^{\alpha,\beta}$-δ-hexenolactone (VI).—Two hundred fifty-two grams (2 moles) of the lactone (VI) and 6.5 g. of Raney nickel in 400 ml. of dioxane were shaken at 80–100° and 800 p. s. i. of hydrogen until the uptake was completed. Distillation of the filtered material gave 250 g. of a liquid b. p. 84–85° (3 mm.); sp. gr. $^{30}_{15.6}$ 1.020; n^{30}D 1.4437; *Anal.* Calcd. for $C_7H_{12}O_2$: C, 65.6; H, 9.4; sapn. equiv., 128.2. Found: C, 65.5; H, 9.3; sapn. equiv., 128.2, identical in all respects with IV previously prepared.

A sample of each of the two saturated lactones from the different sources, III and VI, dissolved in cold aqueous sodium hydroxide and treated with *p*-bromophenacyl bromide, gave identical *p*-bromophenacyl esters m. p. 139–140°, undepressed when mixed.

Thirteen grams of the saturated lactone prepared from VI was oxidized with excess aqueous sodium hypobromite solution. Twelve grams of carbon tetrabromide m. p. 90.1° was collected after standing for twenty-four hours. The filtrate was acidified with hydrochloric acid and freed from bromine with a little sodium bisulfite. Extraction with ether and evaporation gave 10 g. of an acid m. p. 87°; undepressed when mixed with authentic β-methylglutaric acid or the acid from the oxidation of the saturated lactone derived from (III). *Anal.* Calcd.: neut. equiv., 73.1. Found: neut. equiv., 73.7.

Reaction of Mesityl Oxide with Ketene.—Into a well-agitated solution of 1 g. of boron trifluoride diethyl etherate in 479 g. of mesityl oxide, 185 g. of ketene was introduced over a period of two hours at 0–10°. The catalyst was destroyed by stirring with an excess of dilute (2%) sodium hydroxide solution at this temperature. Distilla-

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(11) All m. p. are corrected and b. p. uncorrected.

(12) Scott, "Standard Methods of Chemical Analysis," D. Van Nostrand Co., New York, N. Y., 1922, p. 1166.

tion of the organic layer gave 133 g. of unreacted mesityl oxide, and 396 g. (80%) of β,δ-dimethyl-$\Delta^{\beta,\gamma}$-δ-hexenolactone (VIII) b. p. 92–93° (2 mm.); sp. gr. $^{20}{}_{15.6}$ 1.012; n^{30}D 1.4600. *Anal.* Calcd. for $C_8H_{12}O_2$: C, 68.6; H, 8.6; sapn. equiv., 140.3. Found: C, 68.5; H, 8.5; sapn. equiv., 140.0.

β,δ-Dimethylsorbic Acid.—Fifty grams of VIII was refluxed eight hours with 100 ml. of 50% sodium hydroxide solution. The clear solution was cooled to 10° and strongly acidified. β,δ-Dimethylsorbic acid crystallized and was filtered off (24 g., 48%), m. p. 94–95°, undepressed by admixture with authentic material. By extraction of the filtrate with ether 25 g. of reformed VIII was isolated.

β-Methyl-$\Delta^{\beta,\gamma}$-δ-octenolactone (IX).—One hundred and nine grams of ketene was introduced at 10° into a solution of 291 g. of butylidene acetone dissolved in 800 ml. of ether containing 4 g. of boron trifluoride. The catalyst was destroyed with sodium hydroxide as previously described. Distillation gave 73 g. unreacted ketone and 298 g. (99%) of IX, b. p. 111° (3.5 mm.); sp. gr. $^{20}{}_{15.6}$ 1.002; n^{30}D 1.4660. *Anal.* Calcd. for $C_9H_{14}O_2$: C, 70.0; H, 9.2; sapn. equiv., 154.2. Found: C, 70.1; H, 9.2; sapn. equiv., 154.2.

Summary

β,γ-Unsaturated δ-lactones were readily obtained by the reaction of ketene with β-alkyl vinyl methyl ketones in the presence of boron trifluoride.

The β,γ-unsaturated lactones were transformed quantitatively to α,β-unsaturated lactones by heating with potassium carbonate.

The mechanism for the condensation reaction is discussed.

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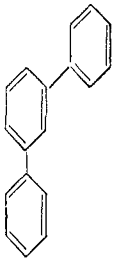
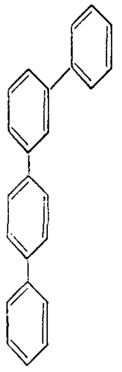
[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE UNIVERSITY OF MARYLAND]

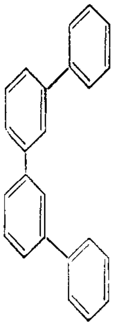
m-Diarylbenzenes

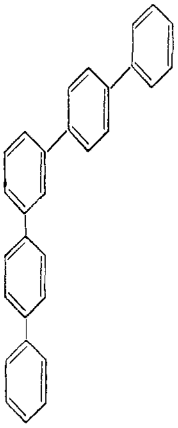
BY G. FORREST WOODS AND FRED T. REED

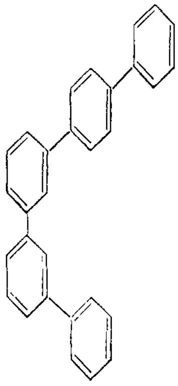
The reaction of the monoethyl ether of dihydroresorcinol with organo-metallic reagents[1] gives rise to a series of *m*-diarylbenzenes.

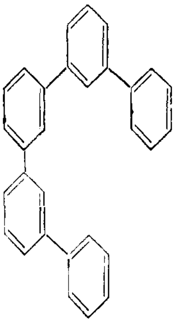

V


VI


VII


VIII


IX


X

An earlier communication[2] described the preparation of V, VI and VIII. The present study describes the preparation of VII, IX and X, these syntheses being summarized in the flow sheet.

The intermediate dienes were not isolated and identified in all cases, since they undergo oxidation very readily, presumably to the aromatic compounds. In practice, the dienes were treated directly without purification with palladium–charcoal to effect aromatization. 1-Phenyl-3-(3-xenyl)-benzene, VII, was best prepared by the reaction of IV with 3-xenylmagnesium bromide rather than by the alternate route since a Wurtz type of reaction in the preparation of 3-xenylmagnesium bromide gives VII as a product. Substance VII, obtained by either procedure, corresponds in properties with those reported by Bowden[3] for 1-phenyl-3-(3-xenyl)-benzene prepared by the treatment of 3-xenyl iodide with copper powder. Substance IX was best prepared by treating II with 3-xenylmagnesium bromide rather than by the alternate method. Substance X could be prepared only by the one series of reactions indicated.

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Experimental

Preparation of 3-Xenyl Bromide.—The synthesis of 3-xenyl bromide, first attempted without success by the Gomberg–Bachmann[4] reaction, was realized by the method of Huber, *et al.*,[5] modified by extracting the deamination reaction mixture with ether and obtaining crude 3-xenyl bromide by distillation of this extract. A solution prepared by adding an approximately equal volume of 30–60° petroleum ether to the crude 3-xenyl bromide was passed through a chromatographic column packed with activated alumina, resulting in an effective removal of colored impurities. The resulting solution was distilled, yielding

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[1] Woods and Tucker, THIS JOURNAL, **70**, 2174 (1948).

[2] Woods and Tucker, *ibid.*, **70**, 3340 (1948).

[3] Bowden, *J. Chem. Soc.*, **139**, 111 (1931).

[4] Gomberg and Bachmann, THIS JOURNAL, **46**, 2339 (1924).

[5] Huber, *et al.*, *ibid.*, **68**, 1111 (1946).