pair at 1590 and 1570 cm.$^{-1}$ These absorptions may be the N-H deformation frequencies for primary and secondary amines, respectively.[19]

1,2-Hexanediol. This material was isolated by distillation, b.p. 112–113°/12 mm., n_D^{20} 1.4400 (lit., b.p., 111°/12 mm).[20] A di-(*p*-nitrobenzoate) was prepared in high yield, m.p. 100.2–100.8°.

Anal. Calcd. for $C_{20}H_{20}N_2O_8$: N, 6.73. Found: N, 6.73.

1-Amino-2-hydroxy- and 1-hydroxy-2-aminohexane. The amino alcohol hydrochloride portion of the products from ammonolysis of the acetoxy chlorides from 1-hexene in aqueous ammonia resisted all attempts at crystallization and was isolated as a partially solid water-soluble oil. Its infrared spectrum was consistent with amino alcohol hydrochloride. A 0.5-g. portion on Schotten-Baumann benzoylation gave 0.7 g. of white plates from benzene, m.p. 105.5–106°.

Anal. Calcd. for $C_{13}H_{19}NO_2$: N, 6.33. Found: N, 6.25.

cis-1,2-Cyclohexanediol. Diol isolated from the ammonolysis of *trans*-2-chlorocyclohexyl acetate in anhydrous ammonia-*o*-xylene, m.p. 95–96.3°, mixed melting point with authentic *cis*-1,2-cyclohexanediol,[21] 98.2–99.2°, mixed melting point with authentic *trans*-1,2-cyclohexanediol,[21] 53–61°. The infrared spectra of all fractions of crystalline diol isolated, as well as the crystallization liquors, indicated the formation of only the *cis* isomers by the absence of bands at 1040, 925, and 855 cm.$^{-1}$ characteristic of the *trans* isomer.

trans-2-Aminocyclohexanol. *trans*-2-Aminocyclohexanol, isolated as its hydrochloride from the ammonolysis of *trans*-2-chlorocyclohexyl acetate in aqueous ammonia melted at 171–172.4° (lit.,[22] m.p., 175°). Schotten-Baumann benzoylation of 0.5 g. of the amino alcohol hydrochloride gave 0.75 g. of *trans*-2-benzoylaminocyclohexanol, white needles from benzene, m.p. 171.8–172° (lit.,[23] m.p. 171–172°).

Acknowledgment. We wish to thank Professor S. Winstein and Dr. Philip S. Magee for many stimulating discussions during the course of this work.

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[19] L. J. Bellamy, *The Infrared Spectra of Complex Molecules*, 2nd ed., John Wiley & Sons, New York, 1958, p. 255.

[20] P. A. Levene and A. Walti, *J. Biol. Chem.*, **94**, 361 (1931).

[21] Kindly furnished by Professor S. Winstein.

[22] G. E. McCasland, R. K. Clark, and H. E. Carter, *J. Am. Chem. Soc.*, **71**, 637 (1949).

[23] W. S. Johnson and E. N. Schubert, *J. Am. Chem. Soc.*, **72**, 2187 (1950).

[CONTRIBUTION FROM THE COLLEGE OF PHARMACY, UNIVERSITY OF MICHIGAN]

Interaction of an Ivanov and an Ivanov-Like Reagent with γ-Butyrolactone and γ-Valerolactone

F. F. BLICKE AND B. A. BROWN[1,2]

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Reactions of the α-chloromagnesium derivative of the chloromagnesium salt of phenylacetic acid with γ-butyrolactone and with γ-valerolactone, and reactions of the α-chloromagnesium derivative of *N,N*-dimethylphenylacetamide with the same two lactones were studied.

Interest in the Ivanov reaction prompted us to study the interaction of a typical Ivanov reagent, the α-chloromagnesium derivative of the chloromagnesium salt of phenylacetic acid, with γ-butyrolactone. Reactions of this lactone had been studied previously with methylmagnesium bromide,[3,4] methylmagnesium iodide,[5,6] and phenylmagnesium bromide.[7,8] In all instances the product obtained showed that one molecular equivalent of the lactone had reacted with two molecular equivalents of the Grignard reagent.

It was found that when γ-butyrolactone was treated with either one or two molecular equivalents of the Ivanov reagent, the reaction products were α-(tetrahydro-2-furylidene)phenylacetic acid (Ia) and 2-benzylidenetetrahydrofuran (IIa).

In order to account for the presence of IIa in the reaction mixture, it may be assumed that the initial reaction product, after acidification, underwent reactions with the formation of the β-keto acid, the hydroxy ketone, and the hydroxybenzyltetrahydrofuran shown in the reaction scheme; the last mentioned product then lost water to form IIa.

Compound Ia dissolved readily in sodium bicarbonate solution and precipitated unchanged after the addition of acid. The unsaturated nature of Ia was proven by the fact that it decolorized bromine and potassium permanganate. When heated to its melting point, Ia lost carbon dioxide and was converted into an oil (IIa) which also gave positive tests for unsaturation.

When Ia was hydrogenated catalytically, a saturated compound, α-(tetrahydro-2-furyl)phenyl-

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[1] Abstracted from the Ph.D. dissertation of B. A. Brown, University of Michigan, 1961.

[2] Lilly Endowment Incorporated Fellow.

[3] W. H. Urry, F. W. Stacey, E. S. Huyser, and O. O. Juveland, *J. Am. Chem Soc.*, **76**, 450 (1954).

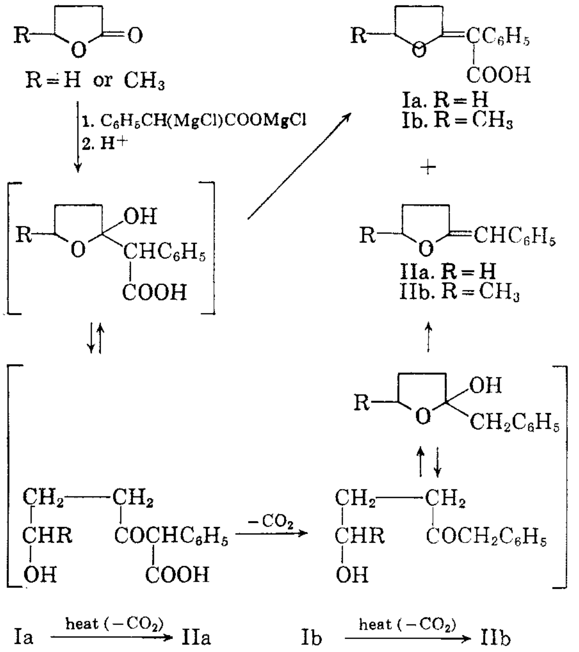
[4] G. Gamboni, H. Schinz, and A. Eschenmoser, *Helv. Chim. Acta*, **37**, 964 (1954).

[5] L. Henry, *Compt. rend.*, **143**, 1221 (1906); *Chem. Abstr.*, **1**, 714 (1907).

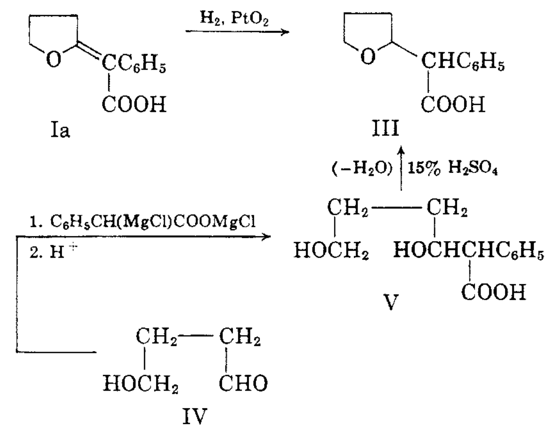
[6] M. S. Newman, W. S. Fones, and W. I. Booth, Jr., *J. Am. Chem. Soc.*, **67**, 1053 (1945).

[7] C. Weizmann and F. Bergmann, *J. Am. Chem. Soc.*, **60**, 2647 (1938).

[8] J. F. Vozza, *J. Org. Chem.*, **24**, 770 (1959).



acetic acid (III), was formed. In order to establish its structure, this acid was synthesized in the following manner. 4-Hydroxybutyraldehyde (IV)[9] was allowed to react with the Ivanov reagent whereupon 3,6-dihydroxy-2-phenylhexanoic acid (V) was obtained. This substance, when refluxed with 15% sulfuric acid, was converted into III. A portion of V was converted into its methyl ester by the use of diazomethane.

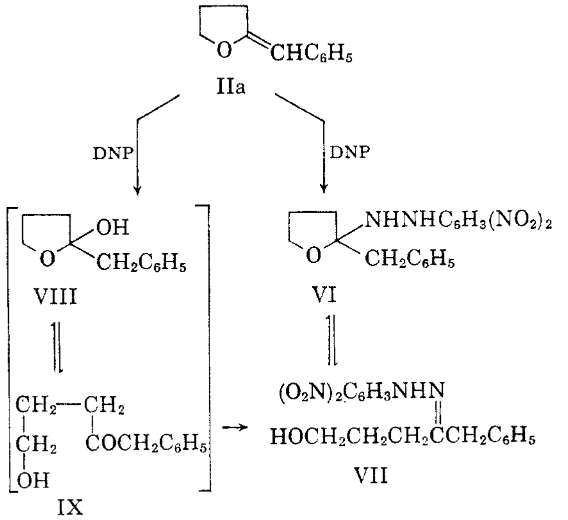


The information mentioned above proved that the substituted phenylacetic acid obtained possessed either structure Ia or the structure of an isomeric acid in which the olefinic bond was endocyclic. The ultraviolet spectrum of a solution of the substituted phenylacetic acid supplied data which is consistent with that which has been reported[10] for a double bond in conjugation with a benzene ring, a system which is present in Ia but not in the isomeric, unsaturated acid.[11]

Compound Ia yielded a methyl ester when treated with diazomethane. The molecular weight of the ester corresponded to the calculated value.

Upon catalytic hydrogenation of IIa, a liquid product was obtained. The infrared spectrum of this substance and that of an authentic sample of 2-benzyltetrahydrofuran[12] were superposable. For further identification of the liquid hydrogenation product, it was converted, successively, into (a) 1-phenyl-2,5-dibromopentane by the action of hydrogen bromide, (b) 1-phenyl-2-benzylpyrrolidine by treatment of the dibromide with aniline, and (c) the pyrrolidine picrate. After an authentic sample of 2-benzyltetrahydrofuran had been subjected to the same reactions, the two picrates were found to be identical.

Compound IIa reacted with 2,4-dinitrophenylhydrazine reagent[13] to form a solid derivative. It was recognized that IIa could react directly with the reagent to form VI, a substance which is tautomeric with the 2,4-dinitrophenylhydrazone of 5-hydroxy-1-phenyl-2-pentanone (VII) or indirectly after IIa had been converted into IX.



The infrared spectrum of a Nujol suspension of the solid derivative showed bands indicative of the hydroxyl group and also bands which have been shown to be characteristic of imino groups in other 2,4-dinitrophenylhydrazones.[14,15] It seemed

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[9] R. Paul and S. Tchelitcheff, *Bull. soc. chim. France*, 197 (1948).

[10] T. W. Campbell, S. Linden, S. Godshalk, and W. G. Young, *J. Am. Chem. Soc.*, **69**, 880 (1947).

[11] We are indebted to Drs. M. G. Van Campen and J. H. Biel who suggested the possible value of ultraviolet spectral data in this connection.

[12] R. Paul, *Bull. soc. chim. France* [5] **5**, 1053 (1938).

[13] A mixture of 2,4-dinitrophenylhydrazine, sulfuric acid, ethanol, and water (DNP). See R. L. Shriner, R. C. Fuson, and D. Y. Curtin, *The Systematic Identification of Organic Compounds*, John Wiley and Sons, Inc., New York, N. Y., Fourth Ed., 1956, p. 111.

[14] F. A. Isherwood and R. L. Jones, *Nature*, **175**, 419 (1955); *Chem. Abstr.*, **49**, 9386 (1955).

[15] L. A. Jones, J. C. Holmes, and R. B. Seligman, *Anal. Chem.*, **28**, 191 (1956).

certain, on the basis of this data, that the solid derivative of IIa which was isolated should be represented by structure VII.

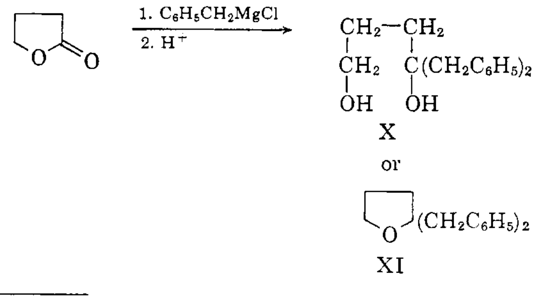
It was found possible to synthesize IIa by interaction of 4-hydroxybutyronitrile[16,17] with benzylmagnesium chloride. Although the product obtained was slightly contaminated by bibenzyl, its identity was established in the following manner: the infrared spectrum was superposable with the spectrum obtained from IIa prepared by the Ivanov reaction; the 2,4-dinitrophenylhydrazone was identical with VII.

$$\mathrm{HOCH_2CH_2CH_2CN} \xrightarrow[\text{2. H}^+]{\text{1. }\mathrm{C_6H_5CH_2MgCl}} (\mathrm{IX} \rightleftharpoons \mathrm{VIII}) \xrightarrow{-\mathrm{H_2O}}$$

$$\mathrm{IIa} \xrightarrow{\text{DNP}} \mathrm{VII}$$

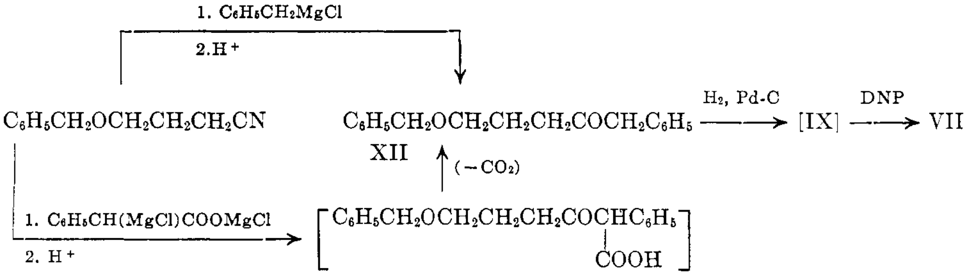
The evidence obtained from an ultraviolet spectrum of IIa showed that the olefinic bond was an exocyclic one.

In the event that benzylmagnesium chloride and γ-butyrolactone could be made to react in the molecular ratio of 1:1 and the initial reaction product lost water, IIa would be formed. However, from the structures of the products isolated from the reaction, carried out by the addition of benzylmagnesium chloride (one molecular equivalent) to the lactone, it was evident that the Grignard reagent and the lactone had reacted in the molecular ratio of 2:1. Dibenzyl-γ-hydroxypropylcarbinol (X) was obtained when the reaction mixture was hydrolyzed with 2.3M hydrochloric acid, and 2,2-dibenzyltetrahydrofuran (XI) was isolated when 3.7M hydrochloric acid was used in the hydrolysis. The effect of the concentration of the acid employed in the hydrolysis of a similar Grignard adduct has been shown by Vozza.[8] Compound XI was obtained also by reaction between benzylmagnesium chloride and ethyl 4-hydroxybutyrate.[18,19]

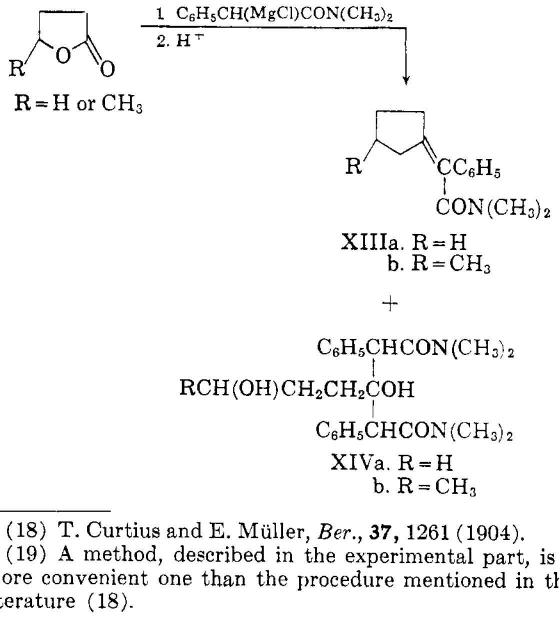


Since it was postulated that the hydroxy ketone (IX) may have been an intermediate in the conversion of IIa into VII, an attempt was made to synthesize this substance. It was found that 5-benzyloxy-1-phenyl-2-pentanone (XII) could be obtained by interaction of 4-benzyloxybutyronitrile with benzylmagnesium chloride or with the Ivanov reagent. However, after debenzylation of XII, the oily product isolated could not be purified. The crude product reacted with 2,4-dinitrophenylhydrazine reagent to form VII.

γ-Valerolactone reacted with the Ivanov reagent to yield α-(5-methyltetrahydro-2-furylidene)-phenylacetic acid (Ib) and 2-benzylidene-5-methyltetrahydrofuran (IIb), products analogous to those prepared from γ-butyrolactone. The methyl ester of Ib was prepared by the use of diazomethane.



From the interaction of the Ivanov-like reagent, the α-chloromagnesium derivative of N,N-dimethylphenylacetamide, and γ-butyrolactone two products, N,N-dimethyl-α-(tetrahydro-2-furyli-



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(16) Yu. K. Yur'ev, G. P. Michaĭlovskiĭ, and S. Z. Shapiro, *Zhur. Obshcheĭ Khim.* (*J. Gen. Chem.*), **19**, 2217 (1949); *Chem. Abstr.*, **44**, 4460 (1950).

(17) A method for the preparation of this compound, more advantageous than the one described in the literature (16), is found in the experimental part.

(18) T. Curtius and E. Müller, *Ber.*, **37**, 1261 (1904).

(19) A method, described in the experimental part, is a more convenient one than the procedure mentioned in the literature (18).

dene)phenylacetamide (XIIIa) and *N,N,N',N'*-tetramethyl-2,4-diphenyl-3-hydroxy-3-(3-hydroxypropyl)glutaramide (XIVa), were isolated.

The structure of XIIIa was proven by its hydrolysis to Ia. Upon reduction with lithium aluminum hydride, XIIIa was converted into 1-phenyl-1-(tetrahydro-2-furyl)-2-dimethylaminoethane (XV).

Compound XIVa was reduced to 1,5-bis(dimethylamino) - 2,4 - diphenyl - 3 - (3 - hydroxypropyl)-3-pentanol (XVI) with lithium aluminum hydride. When hydrolyzed, XIVa yielded 2,4-diphenyl-3-hydroxy-3-(3-hydroxypropyl)glutaric acid (XVII).

The Ivanov-like reagent and γ-valerolactone reacted to produce *N,N*-dimethyl-α-(5-methyltetrahydro-2-furylidene)phenylacetamide (XIIIb) and *N,N,N',N'*-tetramethyl-2,4-diphenyl-3-hydroxy-3-(3-hydroxybutyl)glutaramide (XIVb).

Product XIIIb was converted into Ib by hydrolysis and into 1-phenyl-1-(5-methyltetrahydro-2-furylidene)-2-dimethylaminoethane (XVIII) by reduction with lithium aluminum hydride.

Compound XIVb, when reduced with lithium aluminum hydride, was converted into 1,5-bis-(dimethylamino)-2,4-diphenyl-3-(3-hydroxybutyl)-3 - pentanol (XIX). 2,4 - Diphenyl - 3 - hydroxy-3 - (3 - hydroxybutyl)glutaric acid (XX) was obtained by hydrolysis of XIVb.

EXPERIMENTAL

α-(Tetrahydro-2-furylidene)phenylacetic acid (Ia) *and 2-benzylidenetetrahydrofuran* (IIa). A solution of isopropylmagnesium chloride was prepared from 53.5 g. (2.2 g.-atoms) of magnesium, 172.7 g. (2.2 moles) of isopropyl chloride, 2 ml. of ethyl bromide, and 500 ml. of ether. After the addition of 500 ml. of anhydrous benzene, the solution was stirred and 136.1 g. (1.0 mole) of phenylacetic acid, dissolved in 500 ml. of benzene, was added, dropwise. The mixture was stirred for 12 hr.

γ-Butyrolactone (86.0 g., 1.0 mole), dissolved in 300 ml. of benzene, was added, dropwise, to the stirred suspension of the Ivanov reagent. The mixture was stirred for 24 hr. and then was hydrolyzed with a mixture of 188 ml. of concd. hydrochloric acid and 800 g. of ice water. The insoluble Ia was removed by filtration. The solvents were removed from the organic layer in the filtrate. The residue consisted of an oily mixture of IIa, phenylacetic, acid and crystals of Ia. After removal of Ia by filtration, the combined portions of Ia were recrystallized from dioxane; yield 40.7 g. (0.2 mole); m.p. 218–220° dec.

Anal. Calcd. for $C_{12}H_{12}O_3$: C, 70.57; H, 5.92; neut equiv., 204.2. Found: C, 70.53; H, 5.77; neut. equiv., 204.9; ultraviolet spectrum in dioxane: 2500 Å (ε 12,000).

The oily mixture of IIa and phenylacetic acid was dissolved in ether and the solution was extracted with an aqueous solution of sodium bicarbonate which removed 43.5 g. (0.32 mole) of phenylacetic acid. The solvent was removed from the ether layer and the residue (IIa) was distilled; b.p. 92–96°/0.3 mm.; yield 67.3 g. (0.42 mole).

Anal. Calcd. for $C_{11}H_{12}O$: C, 82.46; H, 7.55. Found: C, 82.10; H, 7.45; ultraviolet spectrum in dioxane: 2420 Å (ε 8200).

Conversion of Ia *into* IIa. When Ia was heated at the temperature of its melting point (220°) for 20 min., carbon dioxide was evolved. The oily residue was dissolved in ether, the solution was extracted with an aqueous solution of sodium bicarbonate and the solvent was removed from the organic layer. The residue distilled at 93–96°/0.3 mm. and formed a solid derivative with 2,4-dinitrophenylhydrazine reagent; m.p. 144–145°. A mixture with VII melted at 144–145°.

α-(Tetrahydro-2-furyl)phenylacetic acid (III). (a) Compound Ia (2.0 g., 0.01 mole), dissolved in 100 ml. of acetic acid, was hydrogenated under an initial pressure of 45 lbs., in the presence of 1 g. of 5% palladium on carbon, for 2 hr. The mixture was filtered and the solvent was removed. After several days, the oily residue crystallized; yield 1.0 g. (50%); m.p. 123–124° after recrystallization from petroleum ether (b.p. 90–100°).

Anal. Calcd. for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84; neut. equiv., 206.2. Found: C, 69.85; H, 6.83; neut. equiv., 205.6.

(b) 3,6-Dihydroxy-2-phenylhexanoic acid (V), described below, (1.0 g.) was refluxed for 1.5 hr. with 35 ml. of 15% sulfuric acid. The mixture was extracted with ether, the solvent was removed from the ether layer and the residue was crystallized from petroleum ether (b.p. 90–100°); m.p. and mixed m.p. 122–124°.

3,6-Dihydroxy-2-phenylhexanoic acid (V). Phenylacetic acid (27.2 g., 0.2 mole), dissolved in 200 ml. of benzene, was added, dropwise, to a stirred solution of isopropylmagnesium chloride, which had been prepared from 10.7 g. (0.44 g.-atom) of magnesium, 34.6 g. (0.44 mole) of isopropyl chloride, 1 ml. of ethyl bromide, and 200 ml. of ether. The mixture was stirred for 12 hr.

4-Hydroxybutyraldehyde[9] (8.8 g., 0.1 mole), dissolved in 150 ml. of ether, was added, dropwise, to the stirred suspension of the Ivanov reagent. The mixture was stirred and refluxed for 12 hr. and was then hydrolyzed with a mixture of 40 ml. of concd. hydrochloric acid and 250 g. of ice. The ether layer was extracted with a 5% aqueous solution of sodium bicarbonate. The bicarbonate solution was acidified, extracted with ether, and the solvent was removed from the ether layer. Repeated extraction of the oily residue with boiling petroleum ether (b.p. 60–70°) removed 10 g. (0.07 mole) of phenylacetic acid. The material which was insoluble in petroleum ether was crystallized from nitromethane; yield 5.0 g. (24%); m.p. 129–131°.

Anal. Calcd. for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19; neut. equiv., 224.2. Found: C, 63.97; H, 7.26; neut. equiv., 225.5.

Methyl 3,6-dihydroxy-2-phenylhexanoate. Prepared with the use of diazomethane, the ester melted at 84–86° after recrystallization from toluene.

Anal. Calcd. for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.64; H, 7.65.

Methyl α-(tetrahydro-2-furylidene)phenylacetate. This ester, prepared from Ia and diazomethane, melted at 81–82° after recrystallization from petroleum ether (b.p. 90–100°).

Anal. Calcd. for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47; mol. wt., 218.2. Found: C, 71.41; H, 6.44; mol. wt. (Rast), 213.0.

2-Benzyltetraydrofuran. Compound IIa (67.0 g., 0.42 mole), dissolved in 20 ml. of acetic acid, was hydrogenated, in the presence of 1.0 g. of platinum dioxide, for 18 hr. under an initial pressure of 1000 lbs. After filtration, the solvent was removed from the filtrate and the residue was distilled. The yield of pure product, b.p. 104–107°/10 mm. (lit.,[12] b.p. 109–110°/10 mm.), was 41.7 g. (61%).

1-Phenyl-2,5-dibromopentane. (a) 2-Benzyltetrahydrofuran, obtained by hydrogenation of IIa, was treated with hydrogen bromide, in the manner described by Paul.[12] The product was obtained in 81% yield; b.p. 175–180°/15 mm. (lit.,[12] b.p. 172–175°/10 mm.).

(b) 2-Benzyltetrahydrofuran, obtained from furfural by a method described by Paul,[12] was allowed to react with hydrogen bromide in accordance with Paul's procedure.[12] The product boiled at 175–180°/15 mm.

1-Phenyl-2-benzylpyrrolidine picrate. In order to prove the identity of the liquid 1-phenyl-2,5-dibromopentane, prepared by the two methods described above, each dibromopentane was converted into the pyrrolidine picrate in the following manner.

1-Phenyl-2,5-dibromopentane (23.0 g., 0.07 mole), prepared by method (a) described above, 50 ml. of absolute ethanol, and 23.3 g. (0.25 mole) of aniline were refluxed on a steam bath for 1.5 hr.[20] The ethanol was removed on a steam bath by the use of a stream of air. The residue was poured into 100 ml. of water, the mixture was made basic with potassium bicarbonate and the mixture was extracted with ether. The ether and excess aniline were removed under reduced pressure. The residue, upon distillation, yielded 6.0 g. (35%) of 1-phenyl-2-benzylpyrrolidine; b.p. 142–145°/0.3 mm.

1-Phenyl-2-benzylpyrrolidine picrate, prepared in ethanol, melted at 167–178° after recrystallization from ethanol.

Anal. Calcd. for $C_{23}H_{22}O_7N_4$: C, 59.22; H, 4.75; N, 12.01. Found: C, 59.31; H, 4.77; N, 11.85.

Di(1-phenyl-2-benzylpyrrolidine) chloroplatinate melted at 166–168° after recrystallization from ethanol.

Anal. Calcd. for $C_{34}H_{40}N_2Cl_6Pt$: C, 46.16; H, 4.56; Pt, 22.07. Found: C, 46.44; H, 4.70; Pt, 22.50.

1-Phenyl-2,5-dibromopentane, obtained by method (b) described above, was converted into 1-phenyl-2-benzylpyrrolidine. The picrate melted at 169–177°; mixed m.p. 163–170°. The chloroplatinate melted at 166–169°; mixed m.p. 164–169°.

2,4-Dinitrophenylhydrazone of 5-hydroxy-1-phenyl-2-pentanone (VII). 2-Benzylidenetetrahydrofuran (IIa) was added to a solution of 2,4-dinitrophenylhydrazine reagent[13]; after several hours yellow crystals of the hydrazone precipitated; m.p. 144–145° after recrystallization from ethanol.

Anal. Calcd. for $C_{17}H_{18}O_5N_4$: C, 56.98; H, 5.06; N, 15.64. Found: C, 56.78; H, 4.95; N, 15.60 (Dumas); infrared spectrum of a Nujol mull on a salt plate: 3280 cm.$^{-1}$, 1618 cm.$^{-1}$, 1590 cm.$^{-1}$.

4-Hydroxybutyronitrile. Following a procedure employed for the synthesis of 3-hydroxypropionitrile,[21] a solution of 130 g. (2 moles) of potassium cyanide in 200 ml. of water was added, dropwise, to a stirred, refluxing solution of 271 g. (1.95 moles) of 3-bromo-1-propanol in 1000 ml. of ethanol. The mixture was stirred and refluxed for 8 hr. and then stirred at room temperature for an additional 18 hr. The solvents were removed, the residue was dissolved in ether, and the solution was dried thoroughly over magnesium sulfate. After filtration, the solvent was removed and the residue was distilled; b.p. 85–86°/3.0 mm. (lit.,[16] b.p. 135–136°/30 mm.); yield 100 g. (60%).

Synthesis of IIa *from 4-hydroxybutyronitrile and benzylmagnesium chloride.* 4-Hydroxybutyronitrile (25.5 g., 0.3 mole), dissolved in 150 ml. of anhydrous tetrahydrofuran, was added, dropwise, to a stirred solution of benzylmagnesium chloride, which had been prepared from 21.9 g. (0.9-g.-atom) of magnesium, 113.9 g. (0.9 mole) of benzyl chloride, and 200 ml. of ether. The mixture was stirred and refluxed for 4 hr., stirred at room temperature for 36 hr., and then hydrolyzed with a mixture of 75 ml. of concd. hydrochloric acid and 350 g. of ice. After the solvents had been removed from the organic layer, the residue was distilled. The first fraction boiled at 89–92°/0.2 mm. and consisted of 25.6 g. of bibenzyl (m.p. 50°; mixed m.p. with an authentic sample 49–51°). The second fraction, which represented all of the material which remained in the distillation flask, was collected at 92–93°/0.2 mm. and consisted of 19.0 g. of a liquid. This liquid was redistilled; the first fraction was 6 g. of bibenzyl. The infrared spectrum of the second fraction, b.p. 92–93°/0.2 mm., was superposable with that of IIa. This fraction formed a 2,4-dinitrophenylhydrazone; the m.p. and mixed m.p. with VII was 143–145°.

Dibenzyl-γ-hydroxypropylcarbinol (X). A solution of benzylmagnesium chloride, prepared from 10.7 g. (0.44 g.-atom) of magnesium, 55.4 g. (0.43 mole) of benzyl chloride, and 250 ml. of ether, was added, dropwise, to a stirred solution of 19.0 g. (0.22 mole) of γ-butyrolactone in 200 ml. of ether. The mixture was stirred and refluxed for 5 hr. and was then hydrolyzed with a mixture of 200 g. of ice and 40 ml. of hydrochloric acid. The organic layer was extracted with an aqueous solution of sodium bicarbonate. After the solvent was removed from the ether layer, the oily residue was refrigerated for 2 days whereupon crystals precipitated. The crystals were recrystallized from petroleum ether (b.p. 60–75°); m.p. 79–80°; yield 32 g. (54%).

Anal. Calcd. for $C_{18}H_{22}O_2$: C, 79.96; H, 8.20; active hydrogen, 0.746. Found: C, 79.91; H, 8.27; active hydrogen, 0.747.

2,2-Dibenzyltetrahydrofuran (XI). A solution of benzylmagnesium chloride, prepared from 10.7 g. (0.44 g.-atom) of magnesium, 55.4 g. (0.43 mole) of benzyl chloride and 250 ml. of ether, was added, dropwise, to a stirred solution of 37.8 g. (0.44 mole) of γ-butyrolactone in 300 ml. of ether. The mixture was stirred and refluxed for 4 hr. and was then hydrolyzed with a mixture of 125 g. of ice and 40 ml. of hydrochloric acid. The ether layer was extracted with an aqueous solution of sodium bicarbonate. After the solvent was removed from the ether layer, the oily residue was distilled. The crystalline material which formed in the distillate, collected at 184–220°/8 mm., was recrystallized from methanol; m.p. 58–59°; yield 33.5 g. (60%).

Anal. Calcd. for $C_{18}H_{20}O$: C, 85.67; H, 7.99. Found: C, 85.47; H, 7.85.

Ethyl 4-hydroxybutyrate. This ester was obtained in 70% yield by the procedure[22] which had been used to synthesize ethyl 2-ethyl-4-hydroxybutyrate; b.p. 67°/11 mm. (lit.,[18] b.p. 65–70°/11 mm.).

2,2-Dibenzyltetrahydrofuran (XI) *from ethyl 4-hydroxybutyrate and benzylmagnesium chloride.* Ethyl 4-hydroxybutyrate (26.4 g., 0.2 mole), dissolved in 150 ml. of anhydrous ether, was added, dropwise, to a stirred solution of benzylmagnesium chloride, prepared from 19.5 g. (0.8 g.-atom) of magnesium, 101.0 g. (0.79 mole) of benzyl chloride, and 175 ml of ether. The mixture was stirred at room temperature for 12 hr. and was then hydrolyzed with a mixture of 200 g. of ice and 68 ml. of hydrochloric acid. After removal of the solvent from the ether layer, the oily residue was distilled. Bibenzyl (20.0 g.) boiled at 145–150°/8 mm. The portion collected at 160–175°/8 mm. solidified; m.p. and mixed m.p. with XI 58–59°; yield 22.7 g. (45%).

5-Benzyloxy-1-phenyl-2-pentanone (XII). (a) 4-Benzyloxybutyronitrile[23] (14.1 g., 0.08 mole), dissolved in 100 ml. of ether, was added, dropwise to a stirred solution of benzylmagnesium chloride, prepared from 3.6 g. (0.15 g.-atom) of magnesium, 19.0 g. (0.15 mole) of benzyl chloride, and 100 ml. of ether. The mixture was stirred and refluxed for 5 hr. and was then stirred at room temperature for 12 hr. It was hydrolyzed with a mixture of 12.5 ml. of concd. hydrochloric acid and 200 g. of ice. After removal of the solvent from the ether layer, the residue was distilled; yield 7.2 g. (32%); b.p. 142–145°/0.15 mm.

Anal. Calcd. for $C_{18}H_{20}O_2$: C, 80.56; H, 7.51. Found: C, 80.50; H, 7.58.

The 2,4-dinitrophenylhydrazone melted at 99–100° after recrystallization from ethanol.

Anal. Calcd. for $C_{24}H_{24}O_5N_4$: C, 64.27; H, 5.39. Found: C, 64.12; H, 5.38.

(b) Phenylacetic acid (13.6 g., 0.1 mole), dissolved in 100 ml. of anhydrous benzene, was added, dropwise, to a stirred solution of isopropylmagnesium chloride, prepared from 5.3 g. (0.22 g.-atom) of magnesium, 18.1 g. (0.22 mole) of isopropyl chloride, 1 ml. of ethyl bromide, and 150 ml. of ether. The mixture was stirred for 12 hr.

4-Benzyloxybutyronitrile[23] (17.5 g., 0.1 mole), dissolved in 50 ml. of ether, was added, dropwise, to the stirred sus-

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(20) This method was used by M. Scholtz and P. Friemehlt [*Ber.*, 32, 848 (1899)] and J. Von Braun [*Ber.*, 42, 4541 (1909)] for the synthesis of an analogous compound.

(21) W. A. Jacobs and M. Heidelberger, *J. Am. Chem. Soc.*, 39, 1465 (1917)

(22) E. R. Meincke and S. M. McElvain, *J. Am. Chem. Soc.*, 57, 1443 (1935).

(23) G. M. Bennett and A. L. Hock, *J. Chem. Soc.*, 472 (1927).

pension of the Ivanov reagent. The mixture was stirred for 48 hr. and then it was hydrolyzed by adding it to a mixture of 25 ml. of concd. hydrochloric acid and 75 g. of ice. The ether layer was extracted with an aqueous solution of sodium bicarbonate. When the alkaline solution was acidified, 7.0 g. (0.05 mole) of phenylacetic acid precipitated. Upon distillation of the ether layer, there was obtained 13.4 g. (0.08 mole) of 4-benzyloxybutyronitrile, b.p. 160–164°/15 mm., and 4.0 g. (15%) of XII, b.p. 147°/0.2 mm. The 2,4-dinitrophenylhydrazone melted at 99–100°; mixed melting point with the hydrazone described in method (a) 99–100°.

Debenzylation of 5-benzyloxy-1-phenyl-2-pentanone (XII). The ketone (XII) (5.0 g., 0.02 mole), dissolved in 75 ml. of absolute ethanol, was hydrogenated, in the presence of 2.5 g. of 5% palladium on carbon, for 24 hr. under an initial pressure of 50 lbs. After filtration, the solvent was removed from the filtrate and the residue was treated with 2,4-dinitrophenylhydrazine reagent. The precipitated hydrazone was recrystallized from ethanol; m.p. and mixed m.p. with VII, 142–144°.

α-(5-Methyltetrahydro-2-furylidene)phenylacetic acid (Ib) *and 2-benzylidene-5-methyltetrahydrofuran* (IIb). The procedure for the preparation of Ia and IIa was followed using the following amounts of the reagents: 53.5 g. (2.2 g.-atoms) of magnesium, 172.7 g. (2.2 moles) of isopropyl chloride, 2 ml. of ethyl bromide, 136.1 g. (1.0 mole) of phenylacetic acid, and 100.0 g. (1.0 mole) of γ-valerolactone.

Compound Ib was recrystallized from ethanol; m.p. 183–184° (dec.); yield 21.6 g. (0.1 mole).

Anal. Calcd. for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47; neut. equiv., 218.2. Found: C, 71.28; H, 6.24; neut. equiv., 218.3; ultraviolet spectrum in dioxane: 2525 Å (ε 13,000).

Compound IIb boiled at 92°/0.4 mm.; yield 113.5 g. (0.65 mole).

Anal. Calcd. for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.48; H, 8.13; ultraviolet spectrum in dioxane: 2410 Å (ε 8250).

When a solution of 2,4-dinitrophenylhydrazine reagent was added to an ethanolic solution of IIb, the 2,4-dinitrophenylhydrazone of 5-hydroxy-1-phenyl-2-hexanone precipitated; m.p. 154–155° after recrystallization from ethanol.

Anal. Calcd. for $C_{18}H_{20}O_5N_4$: C, 58.06; H, 5.41; N, 15.05. Found: C, 58.10; H, 5.21; N, 15.10 (Dumas).

Methyl α-(5-methyltetrahydro-2-furylidene)phenylacetate. The ester was prepared from the acid (Ib) and diazomethane; m.p. 75–76° after recrystallization from methanol.

Anal. Calcd. for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.43; H, 6.89.

N,N-Dimethyl-α-(tetrahydro-2-furylidene)phenylacetamide (XIIIa) *and N,N,N',N'-tetramethyl-2,4-diphenyl-3-hydroxy-3-(3-hydroxypropyl)-glutaramide* (XIVa). *N,N*-Dimethylphenylacetamide[24] (81.5 g., 0.5 mole), dissolved in 200 ml. of anhydrous benzene, was added, dropwise, to a stirred solution of isopropylmagnesium chloride, prepared from 13.5 g. (0.55 g.-atom) of magnesium, 43.2 g. (0.55 mole) of isopropyl chloride, 2 ml. of ethyl bromide, and 200 ml. of ether. The mixture was stirred and refluxed for 1.5 hr.

γ-Butyrolactone (43.0 g., 0.5 mole), dissolved in 150 ml. of anhydrous benzene, was added, dropwise, to the stirred suspension of the reagent. The mixture was stirred at room temperature for 12 hr. and was then hydrolyzed with 370 ml. of a 10% solution of ammonium chloride. In order to remove the gel-like precipitate, hydrochloric acid was added, gradually, until the mixture was approximately at *p*H 5. The mixture was filtered to remove a precipitate (A). After the solvents had been distilled from the organic layer in the filtrate, the residual oil was distilled. *N,N*-Dimethylphenylacetamide (24.5 g.) was collected at 90–100°/0.2 mm. Compound XIIIa boiled at 160–162°/0.4 mm. When a concentrated ether solution of this product was cooled, crystals appeared; m.p. 80–82°; yield 44.0 g. (0.19 mole).

Anal. Calcd. for $C_{14}H_{17}O_2N$: C, 72.70; H, 7.41; N, 6.06. Found: C, 72 70; H, 7.52; N, 6.33; ultraviolet spectrum in dioxane; 2710 Å (ε 17,600).

Precipitate A was extracted with hot benzene. Product XIVa precipitated from the cooled solution; m.p. 161–162° after recrystallization from benzene; yield 24.8 g. (0.06 mole).

Anal. Calcd. for $C_{24}H_{32}O_4N_2$: C, 69.88; H, 7.82; N, 6.79. Found: C, 69.72; H, 7.98; N, 6.82.

N,N-Dimethyl-α-(5-methyltetrahydro-2-furylidene)phenylacetamide (XIIIb) *and N,N,N',N'-tetramethyl-2,4-diphenyl-3-hydroxy-3-(3-hydroxybutyl)glutaramide* (XIVb). From 50.0 g. (0.5 mole) of γ-valerolactone, by the use of the procedure described above, there were obtained 29.4 g. (0.24 mole) of XIIIb and 21.3 g. (0.05 mole) of XIVb after recrystallization from benzene.

Compound XIIIb boiled at 142–145°/0.2 mm.

Anal. Calcd. for $C_{15}H_{19}O_2N$: C, 73.44; H, 7.81; N, 5.71. Found: C, 73.26; H, 7.86; N, 5.65; ultraviolet spectrum in dioxane: 2700 Å (ε 17,500).

Compound XIVb melted at 162–163°.

Anal. Calcd. for $C_{25}H_{34}O_4N_2$: C, 70.39; H, 8.03; N, 6.57. Found: C, 70.17; H, 8.26; N, 6.33.

Hydrolysis of XIIIa *to* Ia. A mixture of 9.0 g. (0.04 mole) of XIIIa, 5.6 g. (0.1 mole) of potassium hydroxide, and 25 ml. of ethylene glycol was refluxed for 36 hr. The solution was poured into 50 ml. of water. After extraction with ether, the aqueous layer was made acidic with hydrochloric acid and then slightly basic with potassium bicarbonate. The ethylene glycol was removed by distillation. The oily residue was dissolved in 10 ml. of water, the solution was acidified and then was extracted with ether. After the solvent was removed from the ether layer, the crystalline residue weighed 0.2 g.; m.p. and mixed m.p. with Ia 217–219°.

Hydrolysis of XIIIb *to* Ib. The procedure employed for the hydrolysis of XIIIa to Ia was repeated using XIIIb; yield 0.8 g.; m.p. and mixed m.p. with Ib 179–181°.

Reduction of amides XIIIa, XIVa, XIIIb, *and* XIVb *to amines* XV, XVI, XVIII, *and* XIX, *respectively.* The amide, dissolved or suspended in 200 ml. of anhydrous ether, was added, dropwise, to a stirred suspension of lithium aluminum hydride in 150 ml. of ether. The mixture was refluxed for 15 hr., cooled in an ice bath, and 3 ml. of water was added, dropwise. The mixture was stirred at room temperature for 9 hr., filtered through Celite, and the filtrate was distilled.

1-Phenyl-1-(tetrahydro-2-furylidene)-2-dimethylaminoethane (XV), prepared from 0.07 mole of XIIIa and 0.07 mole of lithium aluminum hydride, boiled at 115–116°/0.4 mm.; yield 73%.

Anal. Calcd. for $C_{14}H_{19}ON$: C, 77.38; H, 8.81; N, 6.45. Found: C, 77.48; H, 8.96; N, 6.53; ultraviolet spectrum in dioxane: 2560 Å (ε 8370).

The picrate was prepared in ethanol; m.p. 138–140° after recrystallization from ethanol.

Anal. Calcd. for $C_{20}H_{22}O_8N_4$: C, 53.81; H, 4.97; N, 12.55. Found: C, 53.65; H, 4.86; N, 12.72.

1,5-Bis(dimethylamino)-2,4-diphenyl-3-(3-hydroxypropyl)-3-pentanol (XVI), prepared from 0.06 mole of XIVa and 0.02 mole of lithium aluminum hydride, was a viscous material which could not be distilled or crystallized.

The dihydrochloride was prepared in ether; m.p. 137° dec. after recrystallization from ethyl acetate.

Anal. Calcd. for $C_{24}H_{38}O_2N_2Cl_2$: C, 63.01; H, 8.37; N, 6.12; Cl, 15.50. Found: C, 63.14; H, 8.40; N, 6.35; Cl, 15.39.

The dipicrate was prepared in ethanol; m.p. 208–211° after recrystallization from ethanol.

Anal. Calcd. for $C_{36}H_{42}O_{16}N_8$: C, 51.30; H, 5.02; N, 13.30. Found: C, 51.42; H, 5.00; N, 13.34.

1-Phenyl-1-(5-methyltetrahydro-2-furylidene)-2-dimethylaminoethane (XVIII), prepared from 0.05 mole of XIIIb and 0.05 mole of lithium aluminum hydride, boiled at 103–106°/0.4 mm.; yield 64%.

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[24] H. Rapoport and R. M. Bonner, *J. Am. Chem. Soc.*, 72, 2783 (1950).

Anal. Calcd. for $C_{15}H_{21}ON$: C, 77.88; H, 9.15; N, 6.05. Found: C, 77.69; H, 9.32; N, 5.77; ultraviolet spectrum in dioxane: 2590 Å (ϵ 9400).

1,5-Bis(dimethylamino)-2,4-diphenyl-3-(3-hydroxybutyl)-3-pentanol (XIX), prepared from 0.075 mole of XIVb and 0.02 mole of lithium aluminum hydride, was a viscous material which could not be distilled or crystallized.

The dimethiodide was prepared in methanol; m.p. 248–249° dec. after recrystallization from methanol.

Anal. Calcd. for $C_{27}H_{44}O_2N_2I_2$: C, 47.52; H, 6.50; N, 4.11; I, 37.19. Found: C, 47.32; H, 6.56; N, 4.37; I, 37.37.

Hydrolysis of glutaramides XIVa *and* XIVb *to glutaric acids* XVII *and* XX, *respectively.* The amide (0.01 mole), suspended in a mixture of 80 ml. of water and 12 ml. of concd. sulfuric acid, was refluxed and stirred frequently for 3 hr. The precipitate was removed from the cooled mixture by filtration and was dissolved in an aqueous solution of potassium bicarbonate. After filtration, the alkaline solution was made acidic, filtered, and the precipitate was allowed to dry thoroughly.

2,4-Diphenyl-3-hydroxy-3-(3-hydroxypropyl)glutaric acid (XVII) was obtained in 80% crude yield; m.p. 198–199° recrystallization from ethanol.

Anal. Calcd. for $C_{20}H_{22}O_6$: C, 67.02; H, 6.19; neut. equiv. 179.2. Found: C, 67.04; H, 6.27; neut. equiv., 179.3.

2,4-Diphenyl-3-hydroxy-3-(3-hydroxybutyl)glutaric acid (XX) was obtained in 85% crude yield; m.p. 204–205° after recrystallization from acetic acid.

Anal. Calcd. for $C_{21}H_{24}O_6 \cdot \frac{1}{2}H_2O$: C, 66.13; H, 6.61; neut. equiv., 190.7. Found: C, 66.12; H, 6.40; neut. equiv., 190.1.

ANN ARBOR, MICH.

[CONTRIBUTION FROM ORGANIC CHEMISTRY BRANCH, CHEMISTRY DIVISION, U. S. NAVAL ORDNANCE TEST STATION]

The Base-Catalyzed Self-Condensation of α,β-Unsaturated Ketones. Condensation of Cyclopropyl Methyl Ketone with 2-Methylpropanal to Isomeric Diketones, $C_{18}H_{28}O_2$[1]

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The base-catalyzed self-condensation reactions of α,β-unsaturated ketones have been examined. It is suggested that each example may be pictured as an initial Michael condensation to an acyclic monoolefinic diketone, followed, in many instances, by a second, intramolecular Michael condensation or an aldol condensation. In the present study, cyclopropyl methyl ketone and 2-methylpropanal condense (through self-condensation of 1-cyclopropyl-4-methyl-2-penten-1-one, V) to epimeric, unconjugated, monoolefinic diketones, $C_{18}H_{28}O_2$ (X). Evidence supporting the structural assignments for these compounds is presented and discussed.

The mild base-catalyzed condensation of aldehydes with ketones, or the self-condensation of ketones, in an aldol condensation leads to ketols, or the derived α,β-unsaturated ketones. If forcing conditions, such as increased base concentration, a stronger base, elevated temperatures or prolonged reaction times are applied to this condensation, several other reactions may occur. For example, side reactions involving the aldehyde are especially favorable if the ketone is unreactive and the aldehyde has two alpha hydrogens.[2] Knoevenagel condensations leading to saturated acyclic 1,5-diketones may result when two or more mole-equivalents of ketone are employed.[3]

A less familiar possible occurrence in an aldehyde-ketone or ketone-ketone condensation under forcing conditions is the self-condensation of the initially formed α,β-unsaturated ketone itself. Several examples of the base-catalyzed self-condensation of various α,β-unsaturated ketones are now known where the structure of the (dimeric) product has been established.[4] In each case the self-condensation may be pictured as an initial Michael condensation at the α'-, α-, or γ-position (*e.g.*,

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(1) Presented at the Pacific Southwest Regional American Chemical Society Meeting, Los Angeles, Calif., December 3, 1960.

(2) α,β-Unsaturated aldehydes or polymers thereof are the products most frequently encountered. (a) S. G. Powell and A. T. Nielsen, *J. Am. Chem. Soc.*, **70**, 3627 (1948); (b) J. E. Dubois, *Ann. chim.* (*Paris*), (12), **6**, 406 (1951); (c) G. de Gaudemaris and P. Arnaud, *Compt. rend.*, **241**, 1311 (1955); (d) R. Heilmann, G. de Gaudemaris, P. Arnaud, and G. Scheuerbrandt, *Bull. soc. chim. France*, 112 (1957).

(3) These most often occur with aromatic ketones and aromatic aldehydes or alicyclic ketones and formaldehyde. They probably arise by a Michael addition of a ketone molecule to the initially formed α,β-unsaturated ketone. (a) The formation of benzamaron is an example; E. Knoevenagel and R. Weissgerber, *Ber.*, **26**, 436 (1893). For other examples see (b) W. Dilthey, *J. prakt. Chem.*, (2), **101**, 177 (1921), (c) St. v. Kostanecki and G. Rossbach, *Ber.*, **29**, 2245 (1896) and (d) J. Colonge, J. Dreux, and H. Delplace, *Bull. soc. chim. France*, 1635 (1956).

(4)(a) R. Dickinson, I. M. Heilbron, and F. Irving, *J. Chem. Soc.*, 1888 (1927); (b) E. R. H. Jones and H. P. Koch, *J. Chem. Soc.*, 393 (1942); (c) D. Iwanow and T. Iwanow, *Ber.*, **77**, 173 (1944); (d) H. Meerwein, *Ber.*, **77**, 227 (1944); (e) W. A. Ayer and W. I. Taylor, *J. Chem. Soc.*, 2227 (1955); (f) E. A. Braude, B. F. Gofton, G. Lowe, and E. S. Waight, *J. Chem. Soc.*, 4054 (1956); (g) D. B. Bright, *J. Am. Chem. Soc.*, **79**, 3200 (1957); (h) G. Büchi, J. H. Hansen, D. Knutson, and E. Koller, *J. Am. Chem. Soc.*, **80**, 5517 (1958); (i) M. N. Tilichenko and V. G. Kharchenko, *J. Gen. Chem.* (*U. S. S. R.*), **29**, 1909 (1959); (j) K. Kulka, R. J. Eiserle, J. A. Rogers, Jr., and F. W. Richter, *J. Org. Chem.*, **25**, 270 (1960); (k) R. Anet, *J. Org. Chem.*, **26**, 246 (1961). The products described in refs. (a), (i), (j), and k are derived from aldehyde-ketone condensations and those in (c), (d), and (f) from ketone-ketone condensations. Those in (b), (f), (g), and (h) are formed from various α,β-unsaturated alicyclic ketones.