benzoate (II), b.p. 142–143° (1 mm.), n_D^{25} 1.5846. The distillation residue was negligible.

Anal. Calcd. for $C_{13}H_9ClO_2$: C, 67.11; H, 3.90; Cl, 15.24; mol. wt., 234. Found: C, 66.96; H, 4.27; Cl, 15.39; mol. wt., 245 (b.p. in benzene). The infrared spectrum showed ester carbonyl absorption at 5.73 μ. Basic hydrolysis of a small sample of the product gave *o*-chlorobenzoic acid (isolated) and phenol (identified as tribromophenol).

A sample of the dark solid obtained in the pyrolysis was shown by x-ray diffraction to contain large amounts of silver chloride.

An authentic sample of II was prepared in 67% yield from *o*-chlorobenzoyl chloride and phenol in dry pyridine. The pure ester had boiled at 125–127° (0.5 mm.), n_D^{25} 1.5843, and had a satisfactory analysis. The infrared spectrum of the authentic sample was identical with that of the pyrolysis product as isolated above.

Preparation of III. *o*-Chlorobenzoic acid (20.0 g., 0.13 mole) was converted to the acid chloride with 40 ml. of thionyl chloride. The acid chloride was added dropwise to a cooled (0°) and stirred solution of salicylic acid (17.7 g., 0.13 mole) in dry pyridine (60 ml.). The mixture was allowed to stand at 3° overnight and was then poured into a large excess of cold water. The solid was collected, washed with water, and sucked dry. Pure *o*-carboxyphenyl *o*-chlorobenzoate was obtained as colorless needles after one recrystallization from benzene, m.p. 169–170°. The yield was 12.4 g. (35%).

Anal. Calcd. for $C_{14}H_9ClO_4$: C, 60.77; H, 3.28. Found: C, 61.22; H, 3.51.

The recrystallized acid (12.4 g., 0.045 mole) was finely ground and suspended in 100 ml. of water. The mixture was stirred and cooled to 5° and was then slowly neutralized by the dropwise addition of one equivalent of concd. ammonium hydroxide. The cold solution was filtered into a beaker surrounded by an ice bath, and a cold solution of silver nitrate (7.6 g., 0.045 mole) in water (30 ml.) was added slowly with vigorous stirring. The thick, white salt that precipitated was stirred for an additional hour at 0° and was then collected by suction filtration. The salt was washed well with cold water and was dried. There was obtained 12.0 g. (69%) of pure III, m.p. 177–178° dec.

Anal. Calcd. for $C_{14}H_8AgClO_4$: Ag, 28.13. Found: Ag, 27.92.

Pyrolysis of III. Salt III (10.0 g., 0.03 mole) was pyrolyzed under conditions identical with those under which silver *o*-chlorobenzoate gave phenyl *o*-chlorobenzoate. Exothermic decomposition occurred at approximately 180°, and the temperature was raised to 225° over 3 hr. No volatile product appeared on the cold finger, and on cooling there was obtained approximately 8 g. of a black, hard, insoluble mass. The apparatus was washed out with ether, and the solid was pulverized and extracted with boiling ether. The combined ether solutions gave on concentration 0.3 g. of an oil which afforded a trace of chlorobenzene on distillation. No other volatile products could be distilled even at bath temperatures over 200° at 0.05 mm. The experiment was repeated with an intimate mixture of 10 g. of III and 0.5 g. of silver chloride. The results were substantially unchanged. In neither run could any II be detected.

Pyrolysis of I (M = Ag, X = F). The dried salt I (36.5 g., 0.15 mole) was pyrolyzed in bulk in the apparatus described for I (M = Ag, X = Cl). A vigorous reaction occurred slightly above the melting point of the salt, and the products were worked up as described above. Distillation of the liquid product afforded 4.0 g. of fluorobenzene, b.p. 85°, n_D^{25} 1.4657. A residue of less than 0.5 g. could not be distilled.

Pyrolysis of I (*M* = Ag, X = I). The dried salt I (34.1 g., 0.10 mole) was pyrolyzed in bulk in the apparatus described for I (M = Ag, X = Cl). A vigorous reaction occurred at approximately 150° and appeared to be complete in a few seconds. The solid products were worked up in the usual manner to give 3.2 g. (31%) of the lactone of *o*-carboxy-*o'*-hydroxydiphenyl ether, m.p. 180–181°, from benzene/pentane.

Anal. Calcd. for $C_{13}H_8O_3$: C, 73.58; H, 3.80. Found: C, 73.29; H, 3.76. The infrared spectrum showed a sharply split carbonyl absorption at 5.65, 5.70, and 5.75 μ. Scale molecular models predict a complex carbonyl spectrum on the basis of conformation considerations. The spectrum was free from hydroxyl absorption and showed no other characteristic functionality. Strong absorption at 13.70 μ suggested *o*-disubstituted phenyl.

Attempts to prepare an authentic sample of IV by the Baeyer-Villiger oxidation of xanthone with peracetic acid using sulfuric acid and *p*-toluenesulfonic acid catalysts failed, and in both cases xanthone was recovered unchanged after treatments of 1 week.

WILMINGTON 98, DEL.

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

The Reaction of Propylene Oxide, Styrene Oxide, and Cyclohexene Oxide with an Ivanov Reagent

F. F. BLICKE AND P. E. WRIGHT[1,2]

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Propylene oxide reacted with the Ivanov reagent, the α-chloromagnesium derivative of the chloromagnesium salt of phenylacetic acid, to form α-phenyl-β-hydroxyvaleric acid and two stereoisomeric α-phenyl-β-methylbutyrolactones. From styrene oxide and the Ivanov reagent, two stereoisomeric α,γ-diphenyl-β-hydroxybutyric acids were obtained. Cyclohexene oxide and the Ivanov reagent reacted to form α-phenyl-α-(2-hydroxycyclohexyl)acetic acid.

Ethylene oxide has been found[3] to react with the α-chloromagnesium derivative of the sodium salt of phenylacetic acid (an Ivanov reagent) to produce α-phenyl-γ-hydroxybutyric acid.

This paper described the reactions of propylene oxide, styrene oxide, and cyclohexene oxide, re-

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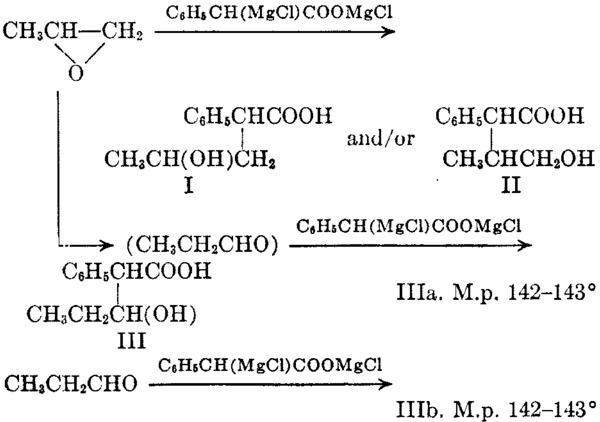
[1] (1) This paper represents part of a dissertation submitted by P. E. Wright for the Ph. D. degree in the University of Michigan.

[2] (2) The Wm. S. Merrell Fellow.

[3] (3) F. F. Blicke and H. Raffelson, *J. Am. Chem. Soc.*, **74**, 1730 (1952).

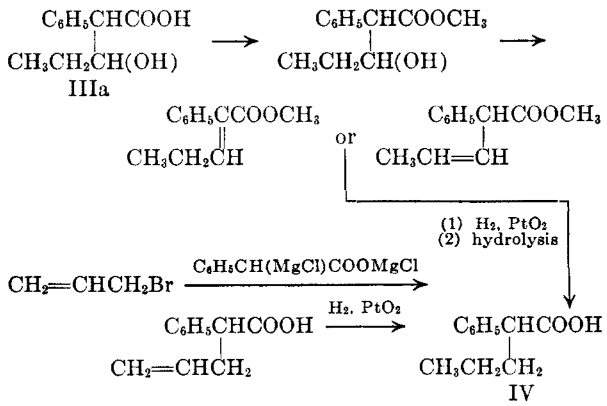
spectively, with the chloromagnesium derivative of the chloromagnesium salt of phenylacetic acid (an Ivanov reagent).

Propylene oxide can react with a Grignard reagent either in the epoxide form or as propionaldehyde.[4,5] The epoxide and the Ivanov reagent could interact to form I and/or II; from the aldehyde, III would be formed. After reaction of propylene oxide and the Ivanov reagent, α-phenyl-β-hydroxyvaleric acid (IIIa)(m.p. 142–143°) was obtained. In addition, there were isolated a solid lactone of α-phenyl-β-methyl-γ-hydroxybutyric acid (II) and a liquid product, presumably a stereoisomer.



Proof that propylene oxide had reacted, to some extent, in the aldehyde form to yield III was obtained by a separate experiment in which propionaldehyde was allowed to react with the Ivanov reagent. An acid (IIIb) which melted at 142–143°[6] was obtained from the reaction mixture; in addition, an isomeric α-phenyl-β-hydroxyvaleric acid (IIIc) was isolated which melted at 125–126°. Both stereoisomeric acids were converted into their methyl and β-diethylaminoethyl esters.

In conformity with the assigned structure, IIIa, after successive esterification dehydration, hydrogenation, and hydrolysis, was converted into α-phenylvaleric acid (IV). This same acid (IV) would have been formed if compound I had been submitted to this series of reactions; however, compound II would have been converted into α-phenylisovaleric acid.

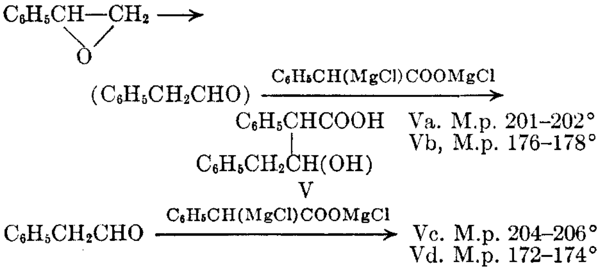


In order to obtain a sample of IV for a mixed melting point determination, it was synthesized by hydrogenation of α-phenyl-α-allylacetic acid.[7]

Oxidation of the solid lactone, isolated from the reaction mixture, with the use of bromine, sodium hydroxide and magnesium sulfate,[8] yielded α-phenyl-α′-methylsuccinic acid, a substance which could have been produced only from the lactone of II. The same succinic acid was obtained by oxidation of the liquid lactone.

Both the solid and the liquid lactone were converted by ammonia into α-phenyl-β-methyl-γ-hydroxybutyramide. Lithium aluminum hydride reduced the amide to β-phenyl-γ-methyl-δ-hydroxybutylamine.

Styrene oxide reacted in the form of phenylacetaldehyde with the Ivanov reagent to form two stereoisomeric α,γ-diphenyl-β-hydroxybutyric acids (Va, Vb). The two acids Vc and Vd were obtained from the interaction of phenylacetaldehyde and the Ivanov reagent. A mixture of Va and Vc and also a mixture of Vb and Vd showed no melting point depression.



Methyl esters were prepared from acids Va and Vb and from acids Vc and Vd. The esters of Va and Vc proved to be identical; identity was also established for the esters of Vb and Vd. Methyl esters of Va and Vb, when heated with phosphorus pentoxide in benzene solution, were dehydrated. It was not established whether the dehydration product was a methyl ester of 2,4-diphenyl-2-butenoic or of 2,4-diphenyl-3-butenoic acid.

A lactone was obtained from acid Va when it was refluxed with acetic anhydride, and a lactone was produced from Vb when it was heated in methanol solution with a small amount of concentrated sulfuric acid.

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[4] F. H. Norton and H. B. Hass, *J. Am. Chem. Soc.*, **58**, 2147 (1936).

[5] P. G. Stevens and J. A. McCoubrey, *J. Am. Chem. Soc.*, **63**, 2847 (1941).

[6] This acid has been obtained previously from propionaldehyde and the Ivanov reagent (ref. 3. R. H. Cox, Dissertation, University of Michigan, 1954.

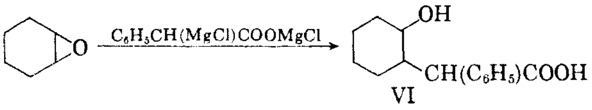
[7] G. R. Ackermann, Dissertation, University of Michigan, 1956.

[8] Lactones have been oxidized in this manner by R. R. Russell and C. A. VanderWerf (*J. Am. Chem. Soc.*, **69**, 11 (1947)) and by J. A. McRae, E. H. Charlesworth, and D. S. Alexander (*Canadian J. Res.*, **21**, Sect. B, 1 (1943)).

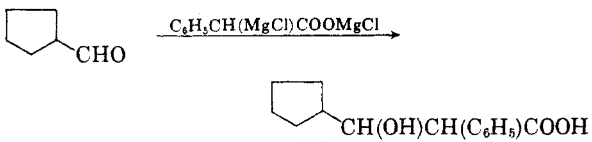
2,4-Diphenyl-1,3-butanediols were prepared from Va and Vb by the use of lithium aluminum hydride.

Incidentally, it was found that when Va was heated in acetic acid with phosphorus and iodine, in the expectation that α,γ-diphenylbutyric acid would be formed, α,γ-diphenyl-β-acetoxybutyric acid was produced.

It is believed that cyclohexene oxide reacted in the epoxide form with the Ivanov reagent to produce α-phenyl-α-(2-hydroxycyclohexyl)acetic acid (VI); the product isolated melted at 153–154°.



VI



VII

After the preparation of the methyl ester of VI, dehydration of the ester with phosphorus pentoxide in benzene solution yielded an unsaturated ester which may have been either methyl α-phenyl-α-(1-cyclohexenyl)acetate or methyl α-phenyl-α-(2-cyclohexenyl)acetate.

A lactone was obtained when VI was heated in methanol with a small amount of concentrated sulfuric acid.

In the event that cyclohexene oxide reacted in the form of cyclopentanecarboxaldehyde,[9] α-phenyl-β-cyclopentyl-β-hydroxypropionic acid (VII) would have been formed. Compound VII had already been synthesized[10] from the aldehyde and the Ivanov reagent and it was stated that VII melted at 145–148°. As the melting point (153–154°) of the product obtained from cyclohexene oxide and the melting point reported for VII are rather close, VII was synthesized from cyclopentanecarboxaldehyde and the Ivanov reagent in order to make a mixed melting point determination. The product obtained, after one recrystallization, melted at the reported melting point (145–148°). However, by the use of different solvents, it was possible to separate the product into two components; one melted at 130–131°, the other at 161–162°. The analytical data for each component corresponded to that calculated for VII.

EXPERIMENTAL

Reaction of propylene oxide with the Ivanov reagent. Formation of α-phenyl-β-hydroxyvaleric acid (IIIa) and α-phenyl-β-methylbutyrolactones. Phenylacetic acid (272.2 g., 2.0 moles), dissolved in 1500 ml. of benzene, was added, dropwise, to a stirred solution of isopropylmagnesium chloride prepared from 112 g. (4.6 g.-atom) of magnesium, 361 g. (4.6 moles) of isopropyl chloride and 1000 ml. of ether; the reaction was initiated with 5 ml. of ethyl bromide. The mixture was refluxed for 4 hr.

Propylene oxide (133.6 g., 2.0 moles), dissolved in 500 ml. of benzene, was added, dropwise, to the stirred mixture. It was stirred for 20 hr., the ether was removed by distillation, and a mixture of 400 ml. of conc. hydrochloric acid and 1500 ml. of ice water was added to the stirred material. The layers were separated and the aqueous layer was extracted with benzene. The combined benzene layers were concentrated to a volume of 400 ml. and the solution was placed in a refrigerator for 24 hr. The precipitate (IIIa) was filtered, then the filtrate was concentrated to 300 ml., cooled for 24 hr., and filtered (filtrate A) to yield more product. The combined material was washed with hot petroleum ether (60–75°); it weighed 83.0 g. (21.4% yield); m.p. 142–143° after recrystallization from toluene.

Anal. Calcd. for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27; neut. equiv., 194.2. Found: C, 68.17; H, 7.18; neut. equiv., 194.1.

The benzene filtrate (A) was stirred with 84 g. of sodium bicarbonate, dissolved in 1000 ml. of water, and the aqueous layer was separated and extracted with benzene. The benzene solutions were combined, the solvent was removed, and the residue was distilled. The fraction (123 g.) which boiled at 109° (0.3 mm.) partially solidified after 48 hr. in a refrigerator. After filtration through a sintered glass funnel, the crystals, α-phenyl-β-methylbutyrolactone, weighed 35.3 g., (10% yield); m.p. 93–94° after recrystallization from petroleum ether (60–75°).

Anal. Calcd. for $C_{11}H_{12}O_2$: C, 74.97; H, 6.86. Found: C, 74.90; H, 6.66.

The liquid filtrate which, based on analytical data, was another α-phenyl-β-methylbutyrolactone, weighed 83.8 g. (23% yield).

Anal. Calcd. for $C_{11}H_{12}O_2$: C, 74.97; H, 6.86. Found: C, 74.76; H, 6.61.

This liquid filtrate was refluxed with an aqueous sodium hydroxide solution until it dissolved. Upon acidification at 0°, an oil precipitated. The oil was separated and cooled whereupon it partially solidified. The solid material melted at 93–94° after recrystallization from petroleum ether (60–75°). The liquid portion was distilled; b.p. 109° (0.3 mm.). The distillate was refluxed with aqueous sodium hydroxide until it dissolved and the process mentioned above was repeated. Again a solid, m.p. 93–94°, and a liquid, b.p. 109° (0.3 mm.), were obtained.

Preparation of α-phenyl-β-hydroxyvaleric acids (IIIb, IIIc) *from propionaldehyde and the Ivanov reagent.* Propionaldehyde (116.2 g.), dissolved in 500 ml. of benzene, was added, dropwise, to a stirred suspension of the Ivanov reagent prepared in the manner described above from 272.2 g. of phenylacetic acid. The mixture was refluxed for 6 hr. and hydrolyzed with a mixture of 333 ml. of conc. hydrochloric acid and 1500 ml. of ice water. The layers were separated and the aqueous layer was extracted with ether and benzene. After concentration of the combined extracts, 167.5 g. (43%) of crystals precipitated; they were removed by filtration (filtrate A) and after recrystallizaton from toluene they melted at 142–143°.[6] This product (IIIb) proved to be identical with IIIa; mixed m.p. 142–143°.

After concentration and cooling of filtrate A, 65.3 g. (16%) of material (IIIc) was obtained; m.p. 125–127° after recrystallization from toluene. This product, based on an analysis and a neutralization equivalent, seems to be another stereoisomeric α-phenyl-β-hydroxyvaleric acid.

Anal. Calcd. for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27; neut. equiv., 194.2. Found: C, 68.05; H, 7.25; neut. equiv., 196.1.

Methyl and β-diethylaminoethyl esters of α-phenyl-β-hydroxyvaleric acids (IIIa, IIIc). The methyl ester of IIIa was prepared from 3.8 g. (0.02 mole) of the acid, dissolved

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(9) Reaction of cyclohexene oxide in this form has often been reported. See M. S. Kharasch and O. Reinmuth, Grignard Reactions of Nonmetallic Substances, Prentice-Hall, Inc., New York, N. Y.

(10) F. F. Blicke and H. Zinnes, *J. Am. Chem. Soc.*, **77**, 6247 (1955).

in 500 ml. of the dimethyl ether of ethylene glycol, by the addition of excess diazomethane dissolved in ether. The mixture was allowed to remain at 0° for 2 hr., then the solvent and excess diazomethane were removed in a stream of air; yield 3.3 g. (79%); m.p. 57–58°[11] after recrystallization from petroleum ether (60–75°).

Anal. Calcd. for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 69.00; H, 7.90.

The methyl ester of IIIc was obtained in 64% yield by the method described above; b.p. 90° (0.3 mm.).

Anal. Calcd. for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 69.17; H, 7.74.

The β-diethylaminoethyl ester of IIIa was prepared by dissolving 2.3 g. of sodium in 250 ml. of isopropyl alcohol, adding 19.4 g. of the acid and 17.5 g. of β-diethylaminoethyl chloride hydrochloride and refluxing the mixture for 16 hr. After filtration and removal of the solvent from the filtrate, the residue was made basic with sodium carbonate solution, extracted with ether, and the ether solution was dried with anhydrous magnesium sulfate. After removal of the ether, the residue was recrystallized from petroleum ether (60–75°); yield 15.8 g. (53%); m.p. 78–80°.

Anal. Calcd. for $C_{17}H_{27}O_3N$: C, 69.59; H, 9.28. Found: C, 69.80; H, 9.36.

The dihydrogen citrate was prepared in ether; m.p. 96–98° after recrystallization from isopropyl alcohol.

Anal. Calcd. for $C_{23}H_{35}O_{10}N$: C, 56.89; H, 7.27. Found: C, 56.92; H, 7.28.

The β-diethylaminoethyl ester of IIIc was prepared in the manner described above; yield 51%; b.p. 111° (0.5 mm.).

The dihydrogen citrate was prepared in ether; m.p. 93–94° after recrystallization from isopropyl alcohol.

Anal. Calcd. for $C_{23}H_{35}O_{10}N$: C, 56.89; H, 7.27. Found: C, 56.76; H, 7.25.

Conversion of methyl α-phenyl-β-hydroxyvalerate into α-phenylvaleric acid (IV). The methyl ester (10.4 g.) of IIIa was dissolved in 250 ml. of benzene and added, dropwise, to a stirred, refluxing mixture of 20 g. of Celite, 15 g. of phosphorus pentoxide, and 750 ml. of benzene. The mixture was stirred and heated for 4 hr., cooled and filtered. The filtrate was washed with bicarbonate solution, dried with magnesium sulfate, and evaporated to dryness. The oily dehydration product (9.2 g., 96%) boiled at 155° (20 mm.).

A portion (3.8 g.) of this oil, dissolved in absolute methanol, was hydrogenated under an initial pressure of 50 lbs., in the presence of 0.1 g. of platinum dioxide, until the calculated amount of hydrogen had been absorbed (2 hr.). The solvent was removed from the filtered mixture whereupon an oil was obtained. This liquid was allowed to remain in the presence of 2.2 g. of potassium hydroxide, dissolved in 25 ml. of 90% ethanol, for 5 days. The solution was diluted with 150 ml. of water and extracted with ether. Upon acidification of the cold, alkaline solution, 2.5 g. (70%) of IV precipitated; m.p. 51–53°[12] after recrystallization from petroleum ether (90–100°).

Preparation of α-phenylvaleric acid (IV) from 2-phenyl-4-pentenoic acid. 2-Phenyl-4-pentenoic acid[7] (3.5 g.) was dissolved in 100 ml. of absolute methanol and hydrogenated under an initial pressure of 50 pounds in the presence of 0.1 g. of platinum dioxide. After filtration, the solvent was removed from the filtrate and the residue was recrystallized from petroleum ether (90–100°); m.p. and mixed m.p. 51–53°.

Oxidation of α-phenyl-β-methylbutyrolactones. The liquid lactone (17.6 g.) was added to 15 g. of sodium hydroxide, dissolved in 75 ml. of water, and the mixture was heated until a solution was obtained. The solution was stirred and kept hot while a hot solution of 43.5 g. of hydrated magnesium sulfate in 33 ml. of water was added slowly. The mixture was cooled to 10° and 5.5 ml. of bromine was added, dropwise, over a period of 2 hr. The cold mixture was stirred for several hours and acidified with 33 ml. of 32% sulfuric acid. The precipitate was filtered and washed with toluene. The product, α-phenyl-α′-methylsuccinic acid, melted at 169–172°[13] after recrystallization from water; yield 6.2 g. (29%).

The solid lactone (17.6 g.) was treated in the manner described above. This reaction yielded 4.1 g. (19%) of the same product; m.p. 169–172°.

α-Phenyl-β-methyl-γ-hydroxybutyramide. The liquid lactone (8.8 g.) was shaken with 15 ml. of conc. ammonia water for 18 hr. The precipitated amide was filtered and the excess ammonia was removed from the filtrate by a stream of air whereby an additional amount of amide was obtained; total yield 9.4 g. (97%); m.p. 145–146° after recrystallization from methyl ethyl ketone.

Anal. Calcd. for $C_{11}H_{15}O_2N$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.35; H, 7.60; N, 7.25.

The solid lactone (4.4 g.) was dissolved in 200 ml. of absolute ethanol and ammonia was bubbled slowly into the solution for 6 hr. After evaporation of the solvent and recrystallization of the residue from methyl ethyl ketone, the amide melted at 145–146°.

β-Phenyl-γ-methyl-δ-hydroxybutylamine. α-Phenyl-β-methyl-γ-hydroxybutyramide (11.4 g.), dissolved in 100 ml. of anhydrous tetrahydrofuran, was added slowly to a stirred solution of 5.3 g. of lithium aluminum hydride in 250 ml. of the same solvent. The mixture was stirred for 4 hr., and 10 ml. of water was added, dropwise, to the stirred mixture. After filtration, the solvent was removed from the filtrate and the residue was distilled; b.p. 132° (0.7 mm.); yield 5.1 g. (48%). After some time, the pure hydroxy amine became very viscous.

Anal. Calcd. for $C_{11}H_{17}ON$: C, 73.70; H, 9.56. Found: C, 73.59; H, 9.50.

Reaction of styrene oxide with the Ivanov reagent. The formation of α,γ-diphenyl-β-hydroxybutyric acids (Va, Vb). Styrene oxide[14] (48.0 g., 0.4 mole), dissolved in 250 ml. of benzene, was added, dropwise, to a stirred suspension of the Ivanov reagent which had been prepared from 54.4 g. (0.4 mole) of phenylacetic acid. The material was refluxed for 72 hr., then hydrolyzed with a mixture of 67 ml. of conc. hydrochloric acid and 1000 ml. of ice water. The precipitate (Va), which formed between the two layers, was filtered. Partial evaporation of the organic layer in the filtrate yielded more Va; the total yield of Va, after recrystallization from ethanol, was 41.2 g. (40%); m.p. 201–202°.

Anal. Calcd. for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29; neut. equiv., 256.3. Found: C, 75.07; H, 6.30; neut. equiv., 258.5.

Further concentration of the organic layer gave material (Vb) which, after recrystallization from toluene, weighed 17.2 g. (16%); m.p. 176–178°.

Anal. Calcd. for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29; neut. equiv., 256.3. Found: C, 74.84; H, 6.40; neut. equiv., 256.4.

Methyl and β-diethylaminoethyl esters of α,γ-diphenyl-β-hydroxybutyric acids. A mixture of 128 g. of Va, 1500 ml. of methanol, and 5 ml. of conc. sulfuric acid was refluxed for 20 hr. The solution was concentrated whereupon the ester precipitated. After recrystallization from petroleum ether (60–75°), the yield was 107 g. (79%); m.p. 98–99°.[15]

Anal. Calcd. for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71. Found: C, 75.49; H, 6.68.

In order to prepare the methyl ester of Vb, about twice the calculated amount of diazomethane, dissolved in 100 ml. of ether, was added to a solution of 17.0 g. of the acid in 500 ml. of dioxane which had been cooled to 0°. After 2 hr.

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(11) In a separate experiment, IIIb was treated with diazomethane. The methyl ester produced melted at 57–58°; mixed m.p. 57–58°.

(12) H. Veldstra and C. van de Westeringh, *Rec. trav. chim.*, **70**, 1113 (1951); m.p. 51–52°.

(13) C. A. Miller, H. I. Scholl, and L. M. Long, *J. Am. Chem. Soc.*, **73**, 5608 (1951); m.p. 169–172°.

(14) Purchased from the Dow Chemical Company.

(15) A small amount of ester, prepared by the use of diazomethane, melted at 98–99°.

at this temperature, the solvent was removed; the yield, after recrystallization from petroleum ether (60–75°), was 17.0 g. (95%); m.p. 49–50°.

Anal. Calcd. for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71. Found: C, 75.48; H, 6.55.

The β-diethylaminoethyl ester of Va was prepared by the addition of 2.3 g. of sodium to 250 ml. of isopropyl alcohol and heating the mixture until the sodium had disappeared. After the addition of 25.6 g. of Va and 17.5 g. of β-diethylaminoethyl chloride hydrochloride, the mixture was refluxed for 16 hr. After filtration, most of the solvent was removed from the filtrate. The precipitated ester hydrochloride (5.0 g.) was removed by filtration (filtrate A) and recrystallized from isopropyl alcohol; m.p. 100–101°.

Anal. Calcd. for $C_{22}H_{30}O_3NCl$: C, 67.41; H, 7.72; Cl, 9.05. Found: C, 67.45; H, 7.62; Cl, 9.19.

Filtrate A was made basic with sodium carbonate solution, extracted with ether and the extract was dried over magnesium sulfate. Removal of the ether and distillation of the residue yielded the ester base of Va; b.p. 106° (0.7 mm.); yield 13.5 g.

The methobromide, prepared in ether, melted at 158–159° after recrystallization from isopropyl alcohol.

Anal. Calcd. for $C_{23}H_{32}O_3NBr$: C, 61.33; H, 7.16. Found: C, 61.35; H, 7.24.

The β-diethylaminoethyl ester of Vb was prepared in the manner described above. The precipitated ester hydrochloride was filtered; yield 8.6 g.; m.p. 100–101° after recrystallization from isopropyl alcohol.

Anal. Calcd. for $C_{22}H_{30}O_3NCl$: C, 67.41; H, 7.72; Cl, 9.05. Found: C, 67.41; H, 7.79; Cl, 9.20.

Although the basic ester hydrochlorides of Va and of Vb melted at the same temperature, the mixed melting point was 85–95°.

The methobromide was prepared in ether by the use of the crude ester base obtained from the filtrate in the manner described above; m.p. 129–130° after recrystallization from isopropyl alcohol.

Anal. Calcd. for $C_{23}H_{32}O_3NBr$: C, 61.33; H, 7.16. Found: C, 61.38; H, 7.12.

Dehydration of the methyl esters of Va and Vb. The methyl ester prepared from Va, dissolved in 250 ml. of benzene, was added, dropwise, to a stirred, refluxing mixture of 50 g. of Celite, 140 g. of phosphorus pentoxide, and 1000 ml. of benzene. The stirred mixture was refluxed for 4 hr. After filtration and evaporation of the solvent from the filtrate, the oily residue was distilled; b.p. 151° (0.5 mm.); yield 78 g. (77%). The product rapidly decolorized an aqueous solution of potassium permanganate and bromine dissolved in carbon tetrachloride. The analytical data corresponded to that calculated for the methyl ester of 2,4-diphenyl-2-butenoic or of 2,4-diphenyl-3-butenoic acid.

Anal. Calcd. for $C_{17}H_{16}O_2$: C, 80.92; H, 6.39. Found: C, 80.78; H, 6.51.

When the isomeric methyl ester, prepared from Vb, was subjected to dehydration in the manner described above, a product was isolated which boiled at 150° (0.7 mm.); yield 12.5 g. (78%). The material decolorized solutions of potassium permanganate and bromine. The analytical data corresponded to that calculated for the methyl ester of 2,4-diphenyl-2-butenoic or of 2,4-diphenyl-3-butenoic acid.

Anal. Calcd. for $C_{17}H_{16}O_2$: C, 80.92; H, 6.39. Found: C, 80.92; H, 6.30.

Preparation of α,γ-diphenyl-β-hydroxybutyric acids (Vc, Vd). Phenylacetaldehyde (18.0 g.) dissolved in 75 ml. of benzene, was added, dropwise, to a stirred suspension of the Ivanov reagent prepared from 20.4 g. of phenylacetic acid. The material was refluxed for 12 hr. and then hydrolyzed with a mixture of 25 ml. of conc. hydrochloric acid and 250 ml. of water. The precipitate (Vc), which separated between the two layers, was filtered and the filtrate (filtrate A) was retained. The product, after recrystallization from ethanol, weighed 33.0 g. (85%) and melted at 204–206°. It proved to be identical with Va; mixed melting point 201–202°.

The ether-benzene layer of filtrate A was separated, concentrated, and cooled whereupon 2.5 g. (6%) of Vd precipitated; m.p. 172–174° after recrystallization from toluene. This substance was identical with Vb; mixed melting point 172–174°.

Methyl esters of Vc and Vd. In order to obtain the methyl ester of Vc, 5.1 g. of the acid was dissolved in 750 ml. of the dimethyl ether of ethylene glycol and the solution was cooled to 0°. Excess diazomethane, dissolved in 100 ml. of ether, was added and the mixture was allowed to remain at 0° for 2 hr. After removal of the solvent the residue, after recrystallization from petroleum ether (60–75°), weighed 4.6 g. (85%) and melted at 98–99°. A mixture of the methyl esters of Va and Vc melted at 98–99°.

The methyl ester of Vd was prepared in the manner described above except that only 500 ml. of the dimethyl ether of ethylene glycol was employed. The product, after recrystallization from petroleum ether (60–75°), weighed 2.8 g. (51%) and melted at 54–55°. Although this melting point is somewhat higher than the melting point (49–50°) of the methyl ester of Vb, the mixed melting point of the two esters was 49–50°.

Lactones of α,γ-diphenyl-β-hydroxybutyric acids Va and Vb. A mixture of 25.6 g. of Va and 50 ml. of acetic anhydride was refluxed for 8 hr. After removal of the acetic anhydride, the residue was distilled; b.p. 170° (0.4 mm.); yield 6.5 g. The distillate solidified after some time, and the lactone was then recrystallized from ether; m.p. 125–126°; yield 5.9 g.

Anal. Calcd. for $C_{16}H_{14}O_2$: C, 80.64; H, 5.92. Found: C, 80.66; H, 6.02.

A mixture of 12.8 g. of Vb, 250 ml. of methanol and 1 ml. of conc. sulfuric acid was refluxed for 20 hr. After removal of the solvent, the residue was treated with hot ether. The solvent was removed from the cold, filtered ether solution and the lactone was recrystallized from ether; m.p. 82–84°; yield 9.2 g. (77%).

Anal. Calcd. for $C_{16}H_{14}O_2$: C, 80.64; H, 5.92. Found: C, 80.63; H, 5.90.

2,4-Diphenyl-1,3-butanediols. Lithium aluminum hydride (1.5 g.) was suspended in 250 ml. of ether and 10.2 g. of Va, suspended in 500 ml. of ether, was added. After the mixture had been stirred for 24 hr., 3 ml. of water was added, dropwise, to the stirred mixture. The precipitated salts were filtered, the solvent was removed from the filtrate, and the residue was recrystallized from diisopropyl ether; yield 2.8 g. (28%); m.p. 96–98°.

Anal. Calcd. for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49. Found: C, 79.33; H, 7.72.

An isomeric 2,4-diphenyl-1,3-butanediol was obtained in 35% yield, in the manner described above, from Vb; m.p. 154–155° after recrystallization from absolute ethanol.

Anal. Calcd. for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49. Found: C, 78.99; H, 7.33.

α,γ-Diphenyl-β-acetoxybutyric acid. A mixture of 12.8 g. of Va, 3.1 g. of red phosphorus, 1.2 g. of iodine, and 350 ml. of acetic acid was refluxed for 8 hr. After filtration, the acetic acid was removed from the filtrate and the residue was recrystallized from toluene; yield 8.1 g.; m.p. 124–126°.

Anal. Calcd. for $C_{18}H_{18}O_4$: C, 72.46; H, 6.08; neut. equiv., 298.3. Found: C, 72.43; H, 6.18; neut. equiv., 298.8.

Reaction of cyclohexene oxide with the Ivanov reagent. Formation of α-phenyl-α-(2-hydroxycyclohexyl)acetic acid (VI). Cyclohexene oxide[16] (196.0 g.), prepared from *trans*-2-chlorocyclohexanol,[17] was dissolved in 500 ml. of benzene and added, dropwise, to the stirred suspension of the Ivanov reagent prepared from 272.2 g. of phenylacetic acid. The stirring was continued for 48 hr. and the mixture was then hydrolyzed with a cold mixture of 333 ml. of conc. hydro-

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(16) *Org. Syntheses*, **Coll. Vol. I**, 185 (1941).

(17) Purchased from the Aldrich Chemical Company.

chloric acid and 1500 ml. of water. After removal of the solvents from the organic layer, the residue was recrystallized from toluene; yield 187.0 g. (40%); m.p. 153–154°.

Anal. Calcd. for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74; neut. equiv., 234.3. Found: C, 71.78; H, 7.51; neut. equiv., 235.1.

Dehydration of methyl α-phenyl-α-(2-hydroxycyclohexyl)-acetate. The methyl ester was prepared from 8.2 g. of VI, dissolved in 300 ml. of ether, by the addition of excess diazomethane, dissolved in ether, at 0°. After 2 hr. at this temperature, the solvent was removed; yield 7.9 g. (90%) after recrystallization from petroleum ether (60–75°); m.p. 94–95°.

Anal. Calcd. for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.27; H, 8.02.

The ester (12.4 g.), dissolved in 250 ml. of benzene, was added dropwise to a stirred, refluxing mixture of 20 g. of Celite, 15 g. of phosphorus pentoxide, and 750 ml. of benzene. The mixture was stirred and refluxed for 4 hr., cooled, and filtered, and the filtrate was shaken with an aqueous sodium bicarbonate solution. The solvent was removed from the dried benzene layer and the residue was distilled; yield 7.8 g. (67%); b.p. 166–170° (20 mm.). The product, which instantly decolorized solutions of potassium permanganate and bromine, may have been methyl α-phenyl-α-(1-cyclohexenyl)acetate or methyl α-phenyl-α-(2-cyclohexenyl)acetate.

Anal. Calcd. for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 77.82; H, 7.75.

Lactone of VI. A mixture of 9.3 g. of VI, 150 ml. of methanol, and 1 ml. of conc. sulfuric acid was refluxed for 4 hr. The solvent was removed, the residue was dissolved in ether, and the solution was extracted with aqueous sodium bicarbonate solution. The solvent was removed from the ether layer and the residue was recrystallized from petroleum ether (60–75°); m.p. 75–77°; yield 8.4 g. (97%).

Anal. Calcd. for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.75; H, 7.45.

The same lactone was isolated in at least 90% yield when attempts were made to prepare the β-diethylaminoethyl ester of VI by the following procedures: (a) a mixture of the silver salt of VI, β-diethylaminoethyl chloride, and acetone was stirred for 24 hr.; (b) attempted transesterification with the use of the methyl ester of the acid, β-diethylaminoethanol, sodium methoxide, and petroleum ether (60–75°).

The lactone was converted into VI in the following manner. A mixture of 8.4 g. of the lactone, 1.6 g. of potassium hydroxide, and 150 ml. of water was refluxed for 3 hr. The solution was extracted with ether. The cold aqueous layer was acidified and the precipitate (VI) was recrystallized from toluene; yield 8.8 g. (94%); m.p. and mixed m.p. 153–155°.

α-Phenyl-β-cyclopentyl-β-hydroxypropionic acids (VII). Cyclopentanecarboxaldehyde[18] (31.0 g.), dissolved in 100 ml. of benzene, was added dropwise to the stirred suspension of the Ivanov reagent prepared from 43.0 g. of phenylacetic acid. The material was stirred and refluxed for 4 hr. and poured into a mixture of 53 ml. of conc. hydrochloric acid and 500 ml. of ice water. After removal of the solvent from the organic layer and recrystallization of the residue from toluene, 53.5 g. (72%) of product was obtained; m.p. 145–148° (lit.[10] m.p. 145–148°). When 50 g. of this material was heated with petroleum ether (60–75°), some of the product remained undissolved. The soluble portion, obtained after removal of the solvent, was recrystallized from petroleum ether (60–75°); yield 35.5 g. (51%); m.p. 130–131°.

Anal. Calcd. for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.66; H, 7.51.

The petroleum ether-insoluble portion was recrystallized from toluene; yield 5.6 g. (8%); m.p. 161–162°.

Anal. Calcd. for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.77; H, 7.52.

ANN ARBOR, MICH.

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[18] J. English, Jr., J. D. Gregory, and J. R. Trowbridge, II, *J. Am. Chem. Soc.*, 73, 615 (1951).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF IOWA STATE UNIVERSITY]

Solvolysis of Dimethylcyclopentyl Halides

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The rates of solvolysis of 1,2-dimethylcyclopentyl halides are only slightly faster than those of 1-methylcyclopentyl halides. This observation implies that some reservation is necessary in considering the I-strain explanation of the relative reactivities of cyclopentyl halides.

In connection with another study,[3] the rates of solvolysis of mixtures of *cis*- and *trans*-1,2-dimethylcyclopentyl bromides and chlorides were measured. As a matter of collateral interest the rates of solvolysis of 1-methylcyclopentyl bromide and chloride were determined under comparable conditions.

RESULTS

The first-order rate constants for solvolysis of various cyclopentyl halides are summarized in Table I and Table II. All rates were measured at 25.00 ± 0.02° in ethanol solutions containing 0.100*N* lithium perchlorate.

Scrutiny of the data shows that the rates measured for various samples of dimethylcyclopentyl halides were not as consistent as might be desired. This was shown to be not readily resolvable into two rates because of different reactivities of *cis* and *trans* isomers. Samples prepared from dimethylcyclopentene known to be relatively rich in the *cis* isomer[3] (*ca.* 30%) were solvolyzed and the data

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[3] G. S. Hammond and C. H. Collins, *J. Am. Chem. Soc.*, submitted.