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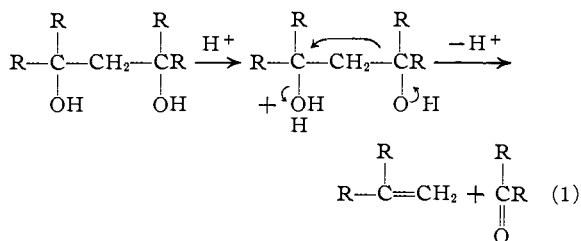
The Cleavage Reaction of 1,3-Diols.¹ I

BY HOWARD E. ZIMMERMAN AND JAMES ENGLISH, JR.

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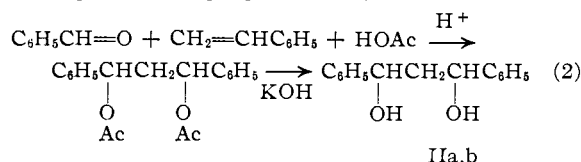
Some new 1,3-diols have been synthesized and the acid-catalyzed cleavage reaction of these compounds studied.

The acid-catalyzed cleavage of ditertiary 1,3-diols has been shown by Brucher and English^{2,3} to proceed in the following manner



It was thought to be of interest to extend this reaction to further examples of 1,3-diols and with this purpose in mind, the present work was begun.⁴ The known⁵ 1,1,3-triphenyl-1,3-propanediol (I) was prepared by the method of McKenzie and Martin as an example of a secondary-tertiary triaryl diol. 1,3-Diphenyl-1,3-propanediol (II) was chosen as a representative disecundary diaryl diol. Two diastereomeric modifications of this compound should exist. One isomer (reported m.p. 93–97°) had been obtained by Sprague and Adkins⁶ by the high pressure hydrogenation of dibenzoylmethane. The other isomer (reported m.p. 129°) had been isolated from the sodium amalgam reduction of dibenzoylacetic acid by Perkin and Stenhouse.⁷ Since both isomers were desired for

the present study, a new approach to II was sought in the Prins reaction.⁸ This reaction had been reported previously only with formaldehyde, except for the internal Prins reaction of citronella⁹ and one study⁹ in which poor yields of 1,3-diol diacetates were obtained with aliphatic aldehydes. In the present work, it was found that the reaction of benzaldehyde and styrene in acetic acid containing one-tenth its volume of sulfuric acid led, after saponification, to a mixture of the two isomers of 1,3-diphenyl-1,3-propanediol (IIa,b).



The two isomers were separated by fractional crystallization. The α -isomer (IIa)¹⁰ agreed in melting point with the compound of Perkin and Stenhouse⁷ while the β -isomer (IIb) had a somewhat higher and sharper melting point than that reported by Sprague and Adkins⁶ for their compound.

In addition to the pair of diastereomeric 1,3-diols thus prepared, it seemed of interest to attempt the

(8) E. Arundale and L. Mikeska, *Chem. Revs.*, **51**, 505 (1952).

(9) W. Emerson, *J. Org. Chem.*, **10**, 464 (1945).

(10) It has been shown by W. Herz, *This Journal*, **74**, 2928 (1952), that the catalytic reduction of chalcone oxide yields two dihydroxydiphenylpropanes, m.p. 84 and 128°, which he considered to be the diastereomeric α -glycols. His proof of structure for the 84° isomer seems indisputable and a 65° isomer of the α -glycol had been prepared by previous workers by what would seem to us to be unambiguous methods. Since only two diastereomeric α -glycols are possible, the identity of the 128° compound seems in doubt. The assignment of the α -glycol structure to this compound was based, apparently due to a lack of material, only on a carbon-hydrogen analysis and the odor of benzaldehyde on treatment with periodic acid. It seems likely to us that the 128° compound is our "alpha" 1,3-diphenyl-1,3-propanediol, m.p. 128–130°; the formation of benzaldehyde under acidic conditions would be expected.

(1) Taken from the dissertation presented by H. E. Zimmerman to the Graduate School of Yale University in partial fulfillment of the requirements for the degree of Doctor of Philosophy. We are indebted to the E. I. du Pont de Nemours Company for a fellowship in support of this work.

(2) F. V. Brucher and J. English, Jr., *This Journal*, **74**, 4279 (1952).

(3) F. V. Brucher, Ph.D. Thesis, Yale University, 1951.

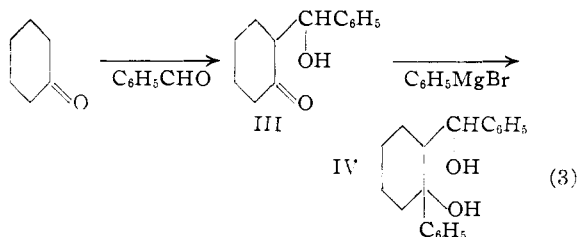
(4) For the previous paper in this series, see H. E. Zimmerman and J. English, Jr., *This Journal*, **75**, 2367 (1953).

(5) A. McKenzie and G. Martin, *J. Chem. Soc.*, 112 (1913).

(6) J. Sprague and H. Adkins, *This Journal*, **56**, 2669 (1934).

(7) W. Perkin, Jr., and J. Stenhouse, *J. Chem. Soc.*, 1010 (1891).

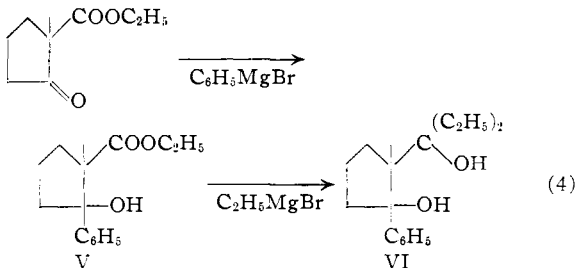
synthesis of cyclic 1,3-diols which might occur as *cis-trans* isomers, the cleavage of which might shed light on the mechanism of the reaction. 1-Phenyl-2-(α -hydroxybenzyl)-cyclohexanol (IV) was obtained by the reaction of phenylmagnesium bromide with 2-(α -hydroxybenzyl)-cyclohexanone¹¹ (III). Although there should be two diastereoisomers cor-



responding to structure III, only one isomer, m.p. 107° , was isolated. Likewise, reaction of this pure isomer III with a Grignard reagent might conceivably give rise to two (*cis-trans*) isomers of a 1,3-diol. However, a survey of the literature of the reactions of cyclic ketones with organometallic reagents indicated¹² that the major product is the isomer in which hydrocarbon portion of the reagent has attacked from the less-hindered side of the molecule. In the present work only one isomer of IV was isolated. Use of phenyllithium in lieu of phenylmagnesium bromide yielded the same isomer and the mother liquors from the pure product of the latter synthesis yielded no pure isomeric material on chromatographing on alumina with 4% methanol in benzene. It is reasonable to conclude by analogy that in IV the phenyl and hydroxybenzyl groups are *trans*.

In another attempt to obtain *cis* and *trans* isomers of a cyclic 1,3-diol, 2-carbomethoxy-2-methylcyclopentanone, was treated with one mole of phenylmagnesium bromide to give 1-phenyl-2-carbomethoxy-2-methylcyclopentanol.

This substance has been prepared by Newman¹³ who apparently did not characterize it but observed its spontaneous dehydration on distillation. Reaction of V with excess ethylmagnesium bromide gave 1-phenyl-2-(3'-hydroxy-3'-pentyl)-2-methylcyclopentanol (VI).

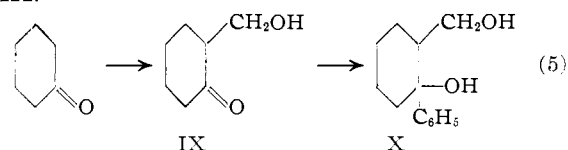


(11) D. Vorländer and K. Kunze, *Ber.*, **59**, 2079 (1926).

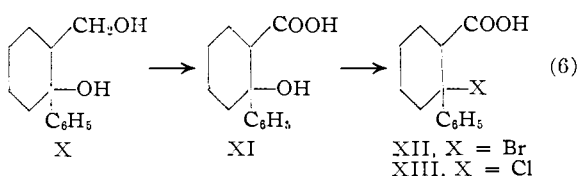
(12) For example, note the reactions of 17-ketosteroids ("Natural Products Related to Phenanthrene," Fieser and Fieser) and camphenilone (O. Aschan, *Ann.*, **410**, 222 (1915)). See the papers which follow in this series for further discussion.

(13) After completion of this work M. Newman, G. Eglinton and H. Grotta, *THIS JOURNAL*, **75**, 349 (1953), reported the abnormal saponification of this crude ester to yield α -methyl- δ -benzoylvaleric acid. Our observations were essentially the same and the properties of this substance and of Δ -1-methylcyclopentenecarboxylic acid reported by these investigators are in good agreement with those observed in this work.

Only one isomer of this diol VI could be isolated from the reaction. It is of interest to report that the abnormal saponification of V proceeds through the open chain keto ester, ethyl α -methyl- δ -benzoylvalerate (VII), to the corresponding acid (VIII). From a partial saponification there was isolated an ester (VII) whose infrared spectrum was virtually identical with that of authentic methyl α -methyl- δ -benzoylvalerate together with some α -methyl- δ -benzoylvaleric acid. This is taken to indicate that this reverse Reformatsky reaction, which is analogous to those studied by Ivanov¹⁴ and others, occurs before hydrolysis of the ester group. In a final attempt to obtain a pair of cyclic *cis-trans* 1,3-diols, phenylmagnesium bromide was treated with 2-hydroxymethylcyclohexanone (IX)¹⁵ to give 1-phenyl-2-hydroxymethylcyclohexanol (X). It was hoped that two isomers might result directly or that X might be convertible to a β -lactone which in turn would be expected¹⁶ to be convertible to a pair of *cis-trans* β -hydroxyacids. Only one isomer of X was obtained. Phenyllithium again gave the same isomer on reaction with IX.



The oxidation of X to 2-hydroxy-2-phenylcyclohexanecarboxylic acid XI was accomplished in good yield by use of dilute mildly alkaline aqueous potassium permanganate at room temperature. Reaction of this compound with saturated aqueous hydrogen bromide and with hydrogen chloride at 0° gave 2-bromo-2-phenylcyclohexanecarboxylic acid (XII) and 2-chloro-2-phenylcyclohexanecarboxylic acid (XIII), respectively.



Treatment of XII with either dilute sodium carbonate or sodium bicarbonate solution gave an oil which was shown by infrared comparison to be essentially pure phenylcyclohexene; no trace of absorption in the infrared region (5.44μ) characteristic¹⁶ of β -lactones could be detected.

The results of the acid-catalyzed cleavages of the 1,3-diols, whose syntheses have been described, are summarized in Table I and will now be considered in detail.

The dehydration of 1,1,3-triphenyl-1,3-propanediol (I) by refluxing with dilute ethanolic sulfuric acid in the presence of 2,4-dinitrophenylhydrazine could be followed by observing the precipitation of the insoluble benzaldehyde 2,4-dinitrophenylhydrazone and was complete in 85% yield within a few minutes. By running the reaction in the ab-

(14) D. Ivanov, *Bull. soc. chim.*, **7**, 569 (1940).

(15) C. Mannich and W. Brose, *Ber.*, **56**, 841 (1923).

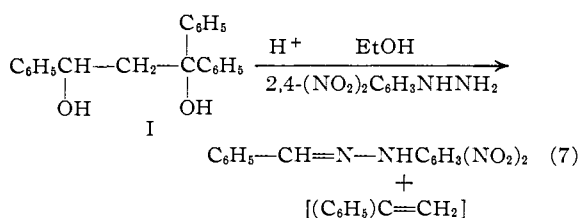
(16) P. Bartlett and P. Rylander, *THIS JOURNAL*, **73**, 4275 (1951).

TABLE I

	Compound	Cleavage products isolated	Yields, %
(I)	1,1,3-Triphenyl-1,3-propanediol	Benzaldehyde	85 ^a
		Benzaldehyde	93 ^b
(IIa)	α -1,3-Diphenyl-1,3-propanediol	Benzaldehyde	35 ^c
		Benzaldehyde	37 ^d
(IIb)	β -1,3-Diphenyl-1,3-propanediol	Benzaldehyde	23 ^c
(IV)	1-Phenyl-2-(α -hydroxybenzyl)-cyclohexanol	Benzaldehyde	23 ^b
		Benzaldehyde	39 ^c
		Phenylcyclohexene	38 ^c
		1,7-Diphenylhept-1-ene-7-one	36 ^c
(V)	1-Phenyl-2-(3'-hydroxy-3'-pentyl)-2-methylcyclopentanol	Diethyl ketone	24 ^e

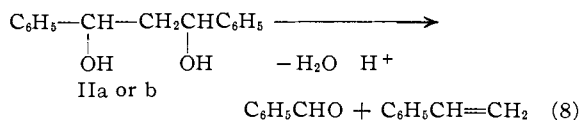
^a Dehydration with 10% ethanolic sulfuric acid + 2,4-dinitrophenylhydrazine. ^b With 10% ethanolic sulfuric acid. ^c With potassium bisulfate. ^d Steam distillation with aqueous sulfuric acid.

sence of 2,4-dinitrophenylhydrazine, neutralizing and forming benzaldehyde phenylhydrazone under neutral conditions, it was possible to show that the



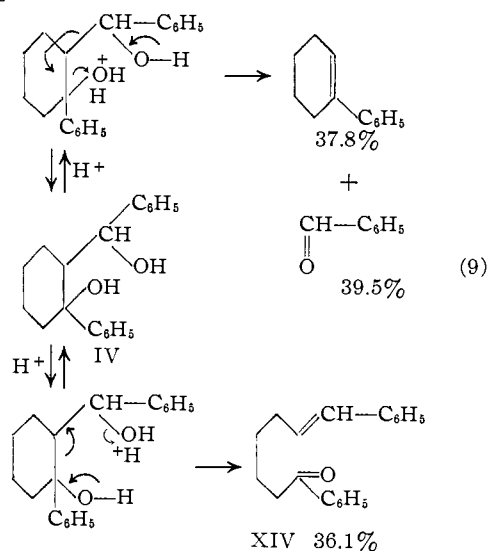
presence of 2,4-dinitrophenylhydrazine did not increase the cleavage yield; such an effect might have been observed if the yield of benzaldehyde had been determined by an equilibrium. It may be noted that of the two possible carbonyl cleavage products, benzaldehyde and benzophenone, only the former was isolated.

The dehydration of α - and β -1,3-diphenyl-1,3-propanediol (IIa and IIb) by heating with potassium bisulfate at 200° gave benzaldehyde in yields of 35 and 23%, respectively. It may be noted that the dehydration is essentially a reversal of the Prins reaction by which the isomeric 1,3-diols were prepared.

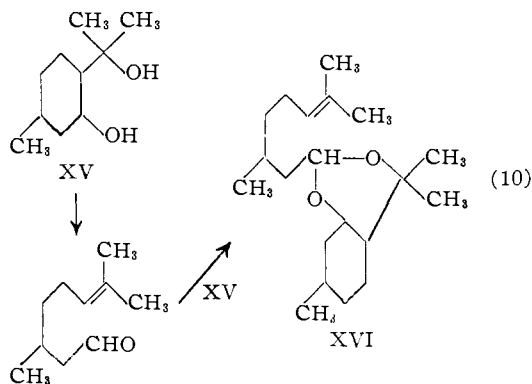


The dehydration of 1-phenyl-2-(α -hydroxybenzyl)-cyclohexanol (IV) with dilute ethanolic sulfuric acid, followed by neutralization and steam distillation gave a 23% yield of benzaldehyde isolated as the phenylhydrazone. Since a reasonable amount of this 1,3-diol IV was available, a somewhat larger scale dehydration was run. In this experiment, dehydration was effected by heating with potassium bisulfate and distilling out volatile products under reduced pressure. Distillation of the material obtained in this manner yielded three products: a 39% yield of benzaldehyde, identified as the phenylhydrazone; a 37.8% yield of phenylcyclohexene, identified by oxidation to δ -benzoylvaleric acid according to v. Auwers and

Treppmann¹⁷; and a 36.1% yield of a compound $\text{C}_{19}\text{H}_{20}\text{O}$ (XIV) which is unsaturated, as evidenced by rapid decolorization of 5% bromine in carbon tetrachloride, and ketonic. A crystalline 2,4-dinitrophenylhydrazone and oxime were obtained. The infrared spectrum of XIV had an absorption band at 6.25 $\text{m}\mu$, indicating the presence of a phenyl group, a carbonyl absorption band at 5.92 $\text{m}\mu$, indicating the presence of a benzoyl group,¹⁸ and a strong band at 10.37 $\text{m}\mu$ which, in light of report by Thompson and Whiffen¹⁹ that *trans* olefins of the type $\text{R}-\text{CH}=\text{CH}-\text{R}'$ absorb at 965 cm^{-1} (*i.e.*, 10.36 $\text{m}\mu$), seems most likely due to the absorption of the system $\text{C}_6\text{H}_5-\text{CH}=\text{CH}-$. This evidence suggests that XIV is the cleavage product resulting from fission of the carbon-oxygen bond of the hydroxybenzyl group. Although other ketonic products might be envisaged as arising by acid-catalyzed rearrangement of IV, no unsaturation would be expected to occur in their formation. The dehydration of IV may reasonably be formulated as



There does exist in the literature a close analogy to the formation of XIV. Isopulegol hydrate (XV) of unknown configuration has been found by Horiuchi²⁰ to give on dehydration with 50% sulfuric



(17) K. v. Auwers and W. Treppmann, *Ber.*, **48**, 1217 (1915).

(18) H. Gilman, "Organic Chemistry," Vol. III, John Wiley and Sons, Inc., New York, N. Y., p. 146.

(19) H. Thompson and D. Whiffen, *J. Chem. Soc.*, 1914 (1948).

(20) R. Horiuchi, *Chem. Zentr.*, **99**, II, 1326 (1928).

acid a compound $C_{20}H_{36}O_2$ (XVI) which was mono-unsaturated and non-ketonic. Such a compound has been obtained under acidic conditions from *d*-citronellal by Stoll and Bolle,²¹ who were apparently unaware of the earlier work of Horiuchi. These workers showed this compound to be the citronellidine acetal (XVI) of isopulegol hydrate (XV). It seems reasonable that the formation of XVI from XV proceeds by the cleavage reaction of XV to form citronellal which then forms a cyclic acetal with excess XV.

Discussion

Although the mechanism of the cleavage reaction of 1,3-diols will be considered in the following two papers, there are several qualitative points which may be discussed here. First, it is apparent from the present study and also from previous examples of the work of Brutcher and English^{2,2a} that the major cleavage product arises by fission of the more highly substituted (especially by aromatic groups) carbinol carbon-oxygen bond. This is analogous to the acid-catalyzed rearrangement of unsymmetrical pinacols where carbon-oxygen fission occurs at the carbinol group in which loss of the hydroxyl group is facilitated by substitution.²² Secondly, it may be seen that increased substitution of the 1,3-diol, especially by aromatic groups, favors the cleavage reaction over competing modes of dehydration, thus increasing the cleavage yield.

Experimental

The Diastereoisomeric 1,3-Diphenyl-1,3-propanediols.—To a mixture of 106 g. of benzaldehyde and 300 ml. of acetic acid in a one-liter three-neck flask fitted with a stirrer, thermometer and dropping funnel, was added 30 ml. of concentrated sulfuric acid with stirring and cooling. The temperature was kept at 20° by means of an ice-bath while 104 g. of freshly distilled styrene was added dropwise with stirring. Then the mixture was allowed to stand at room temperature overnight. The orange reaction mixture was cooled in ice and 500 ml. of water was added dropwise with stirring, whereupon an oil separated. The entire mixture was ether extracted and the ether extracts washed three times with water and dried over sodium sulfate. The ether was then removed by distillation. Saponification of the residue (acetylated diol) by means of aqueous sodium hydroxide proved to be inadequate. After refluxing with excess 20% alcoholic potassium hydroxide for 2.5 hours the reaction mixture was then subjected to distillation under water-pump vacuum to remove about half of the ethanol and was finally diluted with an equal volume of water and ether extracted. The ether extracts were washed with water and dried over sodium sulfate. The ether and some remaining ethanol were distilled off and the residue solidified almost completely. Filtering yielded 38.4 g. of solid, m.p. 88–112°. Recrystallization from 50 ml. of benzene gave fractions A, 24.8 g., m.p. 112–120°; and B, 12.2 g., m.p. 95–98°. The latter is essentially pure β -1,3-diphenyl-1,3-propanediol. Fraction A on recrystallization from benzene-petroleum ether (30–60°) yielded 11.4 g. of α -1,3-diphenyl-1,3-propanediol, m.p. 128–130° (the melting point was not altered by continued recrystallization) and 3.6 g. more of "beta" isomer, m.p. 94–96°. The β -isomer recrystallized nicely from ethanol and the melting point remained at 95.8–97.1°.

Anal. of α -isomer. Calcd. for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06. Found: C, 78.91; H, 7.18. *Anal.* of β -isomer. Found: C, 79.23; H, 7.11.

2-(α -Hydroxybenzyl)-cyclohexanone.—This compound was obtained by a slight modification of the procedure of

Vorländer and Kunze¹¹ which utilized a 0.05% sodium hydroxide solution and mechanical shaking for 3.5 hours. Several recrystallizations of the product from ethanol gave a 21.3% yield of 2-(α -hydroxybenzyl)-cyclohexanone, m.p. 105.5–107.0° (reported¹¹ m.p. is 101–102°). The infrared spectrum contained hydroxyl and carbonyl absorption bands (2.81 and 5.86 μ , respectively).

Anal. Calcd. for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.61; H, 8.01.

1-Phenyl-2-(α -hydroxybenzyl)-cyclohexanol.—To 0.20 mole of phenylmagnesium bromide in 130 ml. of ether in a 300-ml. three-neck flask fitted with reflux condenser, stirrer and dropping funnel was added with stirring 10.0 g. (0.049 mole) of 2-(α -hydroxybenzyl)-cyclohexanone dissolved in a mixture of 50 ml. of anhydrous ether and 35 ml. of dry benzene. The addition required 20 minutes and the mixture was then refluxed on the steam-bath for 30 minutes. The solution was poured onto ice and saturated ammonium chloride solution and the aqueous phase was ether extracted. The dried ether extracts were concentrated at atmospheric pressure and finely volatile material removed on the steam-bath under water-pump vacuum. After several recrystallizations of the solid residue from benzene-petroleum ether (60–90°) 4.0 g. of 1-phenyl-2-(α -hydroxybenzyl)-cyclohexanol, m.p. 147.0–147.5°, was obtained; yield 29%. The filtrates yielded more of the same isomer on concentration and recrystallization. Infrared analysis indicated the presence of hydroxyl functions (2.80 μ , 2.87–3.00 μ).

Anal. Calcd. for $C_{19}H_{22}O_2$: C, 80.81; H, 7.85. Found: C, 80.87; H, 8.06.

1-Phenyl-2-carbethoxy-2-methylcyclopentanol.—To 25 g. (0.147 mole) of α -methyl- α -carbethoxycyclopentanone in 50 ml. of anhydrous ether in a three-neck flask equipped with reflux condenser, efficient Hershberg stirrer and dropping funnel was added dropwise over 1.5 hours 0.147 mole of phenylmagnesium bromide in 55 ml. of ether. During the addition, a heavy complex separated. Stirring was continued for two hours and the reaction mixture was then decomposed with saturated ammonium chloride solution and a small quantity of ice. The ether extracts were dried over sodium sulfate and the ether removed. The residue was distilled to give 17.80 g., b.p. 106–120° at 0.18–0.20 mm. This was fractionated in a short column packed with glass helices to give seven fractions. Fractions two to seven inclusive had essentially the same refractive index (n_D^{20} 1.5221) and boiling point (119–120° at 0.20 mm.). These fractions were combined to give a total yield of 10.88 g. (30.8%) of 1-phenyl-2-carbethoxy-2-methylcyclopentanol.¹³

Anal. Calcd. for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.34; H, 8.06.

The Reaction of 1-Phenyl-2-carbethoxy-2-methylcyclopentanol with Base to Give α -Methyl- δ -benzoylvaleric Acid.—One-half gram of 1-phenyl-2-carbethoxy-2-methylcyclopentanol was mechanically shaken with 5.0 ml. of 10% aqueous sodium hydroxide. At the end of 29 hours, only one phase remained. On acidification, a crystalline product separated and was removed by ether extraction. Recrystallization of the solid product from benzene-petroleum ether (60–90°) gave 0.29 g. of δ -benzoyl- α -methylvaleric acid, m.p. 81.2°. The infrared spectrum of this compound contained carbonyl absorption bands at 5.82 and 5.94 μ and was very similar to that of the known δ -benzoylvaleric acid.¹⁷

Anal. Calcd. for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 70.56; H, 7.62.

To 1.24 g. of 1-phenyl-2-carbethoxy-2-methylcyclopentanol was added 0.56 g. of potassium hydroxide dissolved in 10 ml. of methanol and 1 ml. of water. One-half-ml. aliquots were withdrawn periodically and titrated. When the reaction was 88% complete (at the end of five hours), the reaction mixture was diluted with water and ether extracted. After drying over sodium sulfate and concentration an oil remained whose infrared spectrum was run. This was found to lack hydroxyl absorption (2.7–3.1 μ) and to be virtually identical with the spectrum of methyl δ -benzoyl- α -methylvalerate. The aqueous phase above on acidification yielded 0.65 g. of δ -benzoyl- α -methylvaleric acid.

2-(3'-Hydroxy-3'-pentyl)-1-phenyl-2-methylcyclopentanol.—To 0.30 mole of ethylmagnesium bromide in 120 ml. of ether in a 300-ml. three-neck flask fitted with reflux condenser, dropping funnel and Hershberg stirrer, was

(21) M. Stoll and P. Bolle, *Helv. Chim. Acta*, **31**, 1 (1948).

(22) G. Wheland, "Advanced Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., p. 496.

added with stirring over 80 minutes 12.4 g. (0.05 mole) of 1-phenyl-2-carbomethoxy-2-methylcyclopentanol in 50 ml. of dry ether. The mixture was allowed to stand at room temperature for one-half hour and was then decomposed on ice and saturated aqueous ammonium chloride. The dried ether extracts were concentrated *in vacuo* whereupon crystalline material separated. This was recrystallized several times from ether (30–60°) to give 2.6 g. of 2-(3'-hydroxy-3'-pentyl)-1-phenyl-2-methylcyclopentanol, m.p. 114–117°, and 0.5 g. of less pure material, m.p. 113–114°. The filtrates after solvent removal weighed 13.2 g. The infrared spectrum of this oily material contained a strong carbonyl absorption band at 5.9 μ of such intensity that it indicated the presence of little non-carbonyl material.

Anal. Calcd. for $C_{17}H_{26}O_2$: C, 77.81; H, 9.99. Found: C, 77.70, 77.78; H, 10.08, 10.06.

2-Hydroxymethylcyclohexanone.¹⁵—One liter of cyclohexanone, 333 ml. of 37% aqueous formaldehyde and 666 ml. of distilled water were mixed in a liter flask equipped with a Hershberg stirrer. The mixture was cooled in ice to 20° and the mixture was made basic to phenolphthalein by addition of calcium hydroxide, whereupon an emulsion formed. The temperature of the homogeneous mixture was maintained at 20° and stirring was continued. Additional calcium hydroxide was added to keep the mixture basic. At the end of 4.5 hours, the odor of formaldehyde was no longer apparent. The solution was neutralized with a few drops of concentrated hydrochloric acid and then saturated with ammonium chloride. The oily phase was ether extracted. The combined organic phase and ether extracts were dried over sodium sulfate and the ether was then removed under reduced pressure. The residue was distilled to give 683 g. of material, b.p. 28–51° at 4.0–26 mm. (this was largely impure cyclohexanone) and 124.55 g. of 2-hydroxymethylcyclohexanone, b.p. 77–82° at 2.0–2.5 mm. A higher boiling residue of 103.5 g. remained in the pot. Redistillation of the product gave a b.p. of 89–91° at 5.0 mm. (bath temp. 115–130°), n_D^{25} 1.4766.

1-Phenyl-2-hydroxymethylcyclohexanol.—To 2.0 moles of phenylmagnesium bromide in 750 ml. of ether in a 500-ml. three-neck flask fitted with Hershberg stirrer, reflux condenser and dropping funnel was added dropwise with cooling in ice and stirring 64.09 g. (0.5 mole) of 2-hydroxymethylcyclohexanone in 50 ml. of dry ether. The addition required one hour; stirring with cooling in ice was continued for an additional one-half hour. During this time a crystalline complex separated. The mixture was then decomposed by pouring onto ice and saturated ammonium chloride solution. The ether extracts were dried over sodium sulfate and then concentrated at atmospheric pressure. Distillation of the residue from a wide side-arm Claisen flask yielded 26.3 g. of thick oil, b.p. 126–128° at 0.10–0.12 mm. (bath temp. 152–158°) which slowly crystallized on standing. Recrystallization from ether–petroleum ether (30–60°) brought the melting point of the 1-phenyl-2-hydroxymethylcyclohexanol to 81–83°. Further recrystallization did not alter the melting point. No isomeric material could be isolated from the filtrates and chromatographic analysis of the distilled product on alumina with 4% methanol in benzene yielded only the same isomer.

Anal. Calcd. for $C_{18}H_{24}O_2$: C, 75.69; H, 8.79. Found: C, 75.82; H, 8.77.

2-Phenyl-2-hydroxycyclohexanecarboxylic Acid.—To a solution of 10 g. (0.032 mole) of potassium permanganate and 5 g. of dry sodium carbonate in 1 liter of distilled water in a two-liter flask equipped with a Hershberg stirrer was added 5 g. (0.024 mole) of finely powdered 2-phenyl-2-hydroxymethylcyclohexanol. The suspension was stirred at room temperature for 21.5 hours. The manganese dioxide was filtered off and the filtrate was decolorized with sodium bisulfite and then acidified with concentrated hydrochloric acid. Needles separated and were filtered to yield 3.6 g. of 2-phenyl-2-hydroxycyclohexanecarboxylic acid which melted at 144.5–146.5° after one recrystallization from ether–petroleum ether (60–90°). Ether extraction of the aqueous filtrate yielded 0.47 g. more of solid product, which recrystallized to give the same material.

In earlier runs, it was necessary to obtain the entire product by ether extraction, since no crystallization from the aqueous solution occurred after acidification.

Anal. Calcd. for $C_{18}H_{20}O_3$: C, 70.89; H, 7.32. Found: C, 70.95; H, 7.32.

2-Chloro-2-phenylcyclohexanecarboxylic Acid.—Four grams of 2-hydroxy-2-phenylcyclohexanecarboxylic acid was added to 40 ml. of cold aqueous hydrogen chloride solution which had been saturated with HCl at 0°. The mixture was kept in ice for ten hours and was then filtered to give 6.6 g. of white solid, m.p. 95° with decomposition. This was taken up in 40 ml. of benzene at room temperature and decanted from about one ml. of hydrochloric acid and then filtered through dry filter paper. A nitrogen stream was passed over the solution to remove residual hydrogen chloride. Concentration of the benzene gave solid in several fractions. A first crop weighed 1.8 g. and melted at 99–106° dec., a second crop weighed 1.35 g. and melted at 90° dec. Recrystallization of these from benzene yielded 2.55 g. of 2-chloro-2-phenylcyclohexanecarboxylic acid, m.p. 129.5° with decomposition. Additional material could be isolated from the original acid filtrate and also the benzene filtrates. The melting point (really a decomposition point) varied considerably on different runs.

Anal. Calcd. for $C_{18}H_{18}O_2Cl$: C, 65.41; H, 6.33. Found: C, 65.43; H, 6.36.

2-Bromo-2-phenylcyclohexanecarboxylic Acid.—To 25 ml. of an aqueous solution of hydrogen bromide saturated at 0° and kept cold by cooling in ice was added 3.56 g. of 2-phenyl-2-hydroxycyclohexanecarboxylic acid with stirring. The thick mixture was kept in ice for nine hours and then allowed to warm to room temperature and filtered. The solid was treated with benzene and the benzene solution separated from undissolved aqueous acid. The remaining dissolved HBr was removed by passing a stream of dry nitrogen into the flask containing the benzene solution. Then petroleum ether (60–90°) was added and the solution placed in the refrigerator. Two grams of crystalline material was filtered off; this melted at 107–109° with decomposition. The filtrate yielded 0.7 g. of material, m.p. 84–92° dec. No more material was obtained by dilution of the original acid filtrate with water and ether extraction. Recrystallization of the high-melting fraction yielded 1.0 g. of 2-bromo-2-phenylcyclohexanecarboxylic acid, m.p. 109–110° (decomposition with gas evolution) and the filtrate yielded 0.65 g. of slightly lower-melting material. The material melting at 84–92° was recrystallized from petroleum ether to yield 0.45 g., m.p. 92.4° dec. The infrared spectra of the 109–110° and 92–94° compounds were essentially the same; they indicated a non-hydroxylic acid. Samples of 2-bromo-2-phenylcyclohexanecarboxylic acid were extremely unstable and decomposed within a few days. Acceptable analyses were not obtained. The formulation of these substances as β -bromoacids was supported by their reaction with dilute sodium bicarbonate (1%) and also with dilute sodium carbonate (4%) to give an oil identified as phenylcyclohexene by infrared comparison with an authentic sample.

Cleavage of 1,1,3-Triphenyl-1,3-propanediol with Dilute Ethanolic Acid Containing 2,4-Dinitrophenylhydrazine.—One-third gram (0.0016 mole) of 2,4-dinitrophenylhydrazine was dissolved in 10 ml. of 95% ethanol containing 1 ml. of concentrated sulfuric acid. To the warm solution 0.50 g. (0.0016 mole) of 1,1,3-triphenyl-1,3-propanediol, prepared according to McKenzie and Martin,⁴ was added. The solution was then heated on the steam-bath almost to the boiling point for five minutes; within the first three minutes the orange crystalline product had separated. The reaction mixture was allowed to cool and the solid was filtered and then washed with ethanol. The yield was 0.40 g. (85.1% cleavage) of benzaldehyde 2,4-dinitrophenylhydrazone, m.p. 240–241°; mixed melting point with an authentic sample was 240–242°.

Cleavage of 1,1,3-Triphenyl-1,3-propanediol with Dilute Ethanolic Acid.—One-half gram (0.0016 mole) of 1,1,3-triphenyl-1,3-propanediol was dissolved in a mixture of 10 ml. of 95% ethanol and 1 ml. of concentrated sulfuric acid. The clear solution was refluxed gently on the steam-bath for ten minutes. It was then neutralized to phenolphthalein pink with 8% aqueous sodium hydroxide. After filtering the solution free of precipitated sodium sulfate 0.40 ml. of phenylhydrazine was added and the mixture heated on the steam-bath for ten minutes. The crystalline product was filtered and recrystallized from petroleum ether (60–90°) containing a little benzene to give 0.30 g. (93.5% cleavage) of benzaldehyde phenylhydrazone, needles, m.p. 156°, which showed no mixed melting point depression with an authentic sample.

A control experiment was run to show that no cleavage had occurred under the conditions of derivative formation. One-half gram (0.0016 mole) of 1,1,3-triphenyl-1,3-propanediol was dissolved in a mixture of 10 ml. of 95% ethanol and 3 ml. of water. Then 0.40 ml. of phenylhydrazine was added and the mixture was heated on the steam-bath for ten minutes. No material separated on cooling. On heating, adding water and again allowing to cool, 0.40 g. of 1,1,3-triphenyl-1,3-propanediol, m.p. 129.5–130.0°, separated. This gave no melting point depression with starting material.

Cleavage of α -1,3-Diphenyl-1,3-propanediol with Aqueous Sulfuric Acid.—One-half gram of α -1,3-diphenyl-1,3-propanediol (m.p. 128.5–130.0°) was placed in a 125-ml. distillation flask fitted with a side-arm condenser and steam inlet tube. Twenty ml. of water containing 2 ml. of concentrated sulfuric acid was then added and steam distillation begun. Three fractions of distillate were collected; the receiver was changed every 15 minutes. At the end of the first 15 minutes little more oil was steam distilled and no solid remained in the distilling flask. The distillation was stopped at the end of 45 minutes. The three fractions were individually ether extracted and the ether solutions concentrated. Fraction one yielded 0.10 g. of benzaldehyde phenylhydrazone on treatment with phenylhydrazine. Fractions two and three yielded 0.06 g. more of derivative on the same treatment. The total cleavage yield was then 0.16 g. (37.3%) of benzaldehyde phenylhydrazone, m.p. 154.5–157.0°. The non-steam volatile fraction contained a yellow oil which gave no reaction with phenylhydrazine.

Cleavage of the Stereoisomeric 1,3-Diphenyl-1,3-propanediols with Potassium Bisulfate.—One half gram of α -1,3-diphenyl-1,3-propanediol, m.p. 128.5–130.5°, and 0.50 g. of anhydrous potassium bisulfate were ground together and placed in a three-ml. flask fitted with a side-arm receiver cooled in Dry Ice. The flask was heated in an oil-bath to 190–210° for three hours; during this time a vacuum (not below 50 mm.) was applied periodically to aid in the distillation of volatile material. At the end of this time the distillate was washed from the side-arm and receiver with ethanol and excess phenylhydrazine was added and shortly thereafter a crystalline precipitate formed. The weight of benzaldehyde phenylhydrazone, needles, m.p. 154–156°, was 0.15 g. (35% cleavage).

The same procedure was followed with one-half gram of β -1,3-diphenyl-1,3-propanediol. This yielded 0.10 g. of benzaldehyde phenylhydrazone, needles, m.p. 149–151° (23% cleavage); these were recrystallized from petroleum ether (60–90°) to give a melting point of 153–154.5°.

Cleavage of 1-Phenyl-2-(α -hydroxybenzyl)-cyclohexanol with Dilute Ethanolic Sulfuric Acid.—One-half gram of 1-phenyl-2-(α -hydroxybenzyl)-cyclohexanol was dissolved in a mixture of 9 ml. of absolute ethanol, 1 ml. of water and 1 ml. of concentrated sulfuric acid and refluxed on the steam-bath for four hours. At the end of this time, the odor of benzaldehyde was apparent. The cooled mixture was neutralized with 10% sodium hydroxide solution to phenolphthalein pink and the precipitated inorganic salt filtered and washed with ethanol. The filtrates were subjected to steam distillation and the distillate was ether extracted. After removal of the ether, the residue was treated with 1 ml. of phenylhydrazine and 1 ml. of water. After three minutes, fine needles separated and were filtered. These weighed 0.08 g. and melted at 153–155° and did not depress the melting point of authentic benzaldehyde phenylhydrazone. This represented a cleavage yield of 23.0%. Oil droplets were present in the non-steam volatile fraction. This material, after isolation by ether extraction, gave a positive von Baeyer test and yielded no solid phenylhydrazone.

Cleavage of 1-Phenyl-2-(α -hydroxybenzyl)-cyclohexanol with Potassium Bisulfate.—Six grams (0.201 mole) of 1-

phenyl-2-(α -hydroxybenzyl)-cyclohexanol and 6.0 g. of potassium bisulfate were ground together and placed in a ten-ml. distilling flask with a Dry Ice-cooled receiver connected to a vacuum system. The flask was placed in an oil-bath which was gradually heated to 185°; the pressure was then lowered to 35 mm. When no more material distilled the pressure was lowered to one mm. and the oil-bath temperature raised whereupon a yellow oil distilled at 200–230°. The distillate was taken up in ether and the water phase separated. After drying over sodium sulfate, the ether solution was concentrated and the residue distilled to give three fractions: (1) 0.90 g., b.p. 76–77° at 15 mm. smelling like benzaldehyde; (2) 1.27 g., b.p. 125–126° at 16 mm. having the odor of phenylcyclohexene; and (3) 2.02 g., b.p. 184–187° at 0.70–0.75 mm., a yellow oil.

Fraction one was treated with excess phenylhydrazine and 1.25 g. of benzaldehyde phenylhydrazone, m.p. 156–157° (mixed m.p. with authentic sample, 156–157°) was obtained. This corresponds to a 30.5% yield while the yield based on benzaldehyde distilled is 39.5%.

Fraction two was shown to be phenylcyclohexene by oxidation of 0.50 g. of this fraction to δ -benzoylvaleric acid according to the method of v. Auwers and Treppmann.¹⁷ The yield was 50 mg. of acid which had been recrystallized to a m.p. of 73–75° (authentic m.p. is 76–77°). The cleavage yield based on phenylcyclohexene is 37.8%.

Fraction three, which is believed to be 1,7-diphenylhept-1-ene-7-one, gave a slow von Baeyer test and rapidly decolorized 5% bromine in carbon tetrachloride. Infrared analysis showed carbonyl absorption at 5.95 μ indicating¹⁸ the presence of the benzoyl function and a band at 10.37 μ . This material did not form a solid phenylhydrazone but did form a solid 2,4-dinitrophenylhydrazone, m.p. 137° after recrystallization from petroleum ether (60–90°)-benzene. Also a crystalline oxime was formed in the following manner. To a solution of 2.0 g. of hydroxylamine hydrochloride in 8 ml. of water with enough 10% sodium hydroxide to reach phenolphthalein pink was added 0.80 g. of fraction three. Then 10 ml. of ethanol was added and the solution refluxed for one hour. Water was added to cloudiness and the crystalline oxime separated on cooling; yield 0.50 g., m.p. 88–91°. This, on recrystallization from petroleum ether (60–90°), gave 0.36 g., m.p. 94–95°.

Anal. Calcd. for $C_{19}H_{21}NO$: C, 81.68; H, 7.58; N, 5.01. Found: C, 81.75; H, 7.80; N, 5.09.

Cleavage of 1-Phenyl-2-(3'-hydroxy-3'-pentyl)-2-methylcyclopentanol.—To a 3-ml. flask fitted with capillary and Dry Ice-cooled receiver was added a finely powdered mixture of 0.50 g. of 1-phenyl-2-(3'-hydroxy-3'-pentyl)-2-methylcyclopentanol and 0.50 g. of potassium bisulfate. The flask was heated to 150° by means of an oil-bath and the pressure of the system was gradually lowered by application of an oil-pump vacuum until it reached 15 mm. During this time, which amounted to 15 minutes, some material distilled and was condensed in the receiver; at the end of this period, no more material was distilling. The receiver was changed and the pressure lowered to 3.5 mm. to give a second fraction distilling at bath temperature 180°, 0.31 g.

Fraction one smelled like diethyl ketone. On treatment with excess 2,4-dinitrophenylhydrazine (0.38 g.) in 10 ml. of ethanol containing 1 ml. of sulfuric acid, 0.12 g. of pure diethyl ketone 2,4-dinitrophenylhydrazone, m.p. 152–154° (no mixed m.p. depression with an authentic sample) was obtained; this corresponds to 23.5% cleavage. Fraction two did not decolorize bromine immediately. The infrared spectrum contained a carbonyl absorption band at 5.85 μ which would seem to be due to an aliphatic ketone. No solid 2,4-dinitrophenylhydrazone could be obtained from this fraction.

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