[CONTRIBUTION NUMBER 1170 FROM THE STERLING CHEMISTRY LABORATORY OF YALE UNIVERSITY]

The Cleavage Reaction of 1,3-Diols. II. The Synthesis, Cleavage and Proof of Configuration of Two Pairs of Diastereomeric Secondary–Tertiary 1,3-Diols[1]

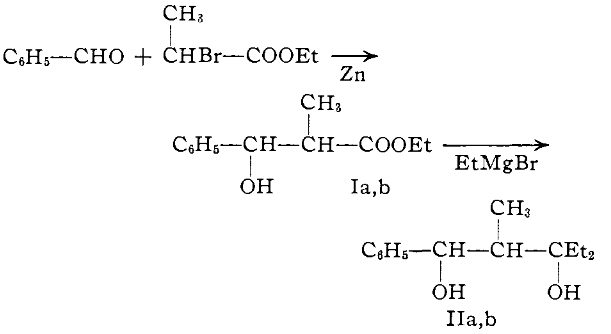
BY HOWARD E. ZIMMERMAN AND JAMES ENGLISH, JR.

RECEIVED JULY 27, 1953

Two pairs of diastereomeric secondary–tertiary 1,3-diols have been synthesized and configurations determined. The acid-catalyzed cleavage reaction of these compounds has been studied.

In the course of a study[2a,2b] of the acid-catalyzed cleavage reaction of 1,3-diols, it was deemed important to obtain a pair of stereoisomeric 1,3-diols which would undergo this reaction and to determine their configurations. A difference in cleavage behavior between two stereoisomers might throw some light on the mechanism of the cleavage reaction.

The Reformatsky reaction of benzaldehyde with ethyl α-bromopropionate is known[3] to yield ethyl β-hydroxy-α-methyl-β-phenylpropionate (I). In the present study, the mixture of isomers from this Reformatsky reaction was treated first with ethylmagnesium bromide to yield a mixture of the diastereoisomeric 1-phenyl-2-methyl-3-ethyl-1,3-pentanediols (IIa,b). Fractional crystallization from ethanol gave α-1-phenyl-2-methyl-3-ethyl-1,3-pentanediol (IIa), m.p. 139.5°. The lower melting fractions obtained from the mother liquors of the α-isomer on fractional crystallization yielded β-1-phenyl-2-methyl-3-ethyl-1,3-pentanediol (IIb), m.p. 98°. The assignment of this structure to these compounds is



$$C_6H_5-CHO + \overset{CH_3}{\overset{|}{CHBr}}-COOEt \xrightarrow[Zn]{} C_6H_5-\underset{\underset{OH}{|}}{CH}-\overset{CH_3}{\overset{|}{CH}}-COOEt \xrightarrow[EtMgBr]{} C_6H_5-\underset{\underset{OH}{|}}{CH}-\overset{CH_3}{\overset{|}{CH}}-\underset{\underset{OH}{|}}{CEt_2}$$

Ia,b IIa,b

supported by carbon–hydrogen analysis, the mode of preparation, infrared spectra and the results of the cleavage reaction. The infrared spectra of the two isomers contained O–H stretching absorption bands (2.8, 2.9 μ) and lacked carbonyl absorption bands. It is of interest that the infrared spectra of the diastereomers exhibited marked differences in the 8–12 μ region.

The cleavage of each of the pure isomers was effected by refluxing with dilute ethanolic sulfuric acid in the presence of one equivalent of 2,4-dinitrophenylhydrazine. This procedure is very convenient, since the course of the cleavage reaction may be followed visually by virtue of the precipitation of the insoluble 2,4-dinitrophenylhydrazone and a rough estimate of the relative cleavage rate may be obtained from the time required for the beginning of precipitation of the derivative and a knowledge of the cleavage yield. Where the yields are high the precipitation time should be approximately inversely proportional to the cleavage rate, assuming that the 1,3-diol reacts by processes first order with respect to itself. It was found that α-1-phenyl-2-methyl-3-ethyl-1,3-pentanediol (IIa) gave benzaldehyde in 17% yield with four minutes being required for initial precipitation of the benzaldehyde 2,4-dinitrophenylhydrazone. The β-isomer produced benzaldehyde in 33% yield, precipitation occurring in two minutes.

In view of the low yields and small differences in rate of cleavage with these substances a pair of diastereomeric 1,3-diols for which cleavage would be the major reaction was sought. In a previous paper[2b] the generalization has been made that increased substitution of 1,3-diols, especially by aromatic groups, tends to increase the cleavage yield. For this reason and because the triaryl 1,3-diol 1,1,3-triphenyl-1,3-propanediol was known[2b] to undergo the cleavage reaction in 85% yield, it was decided to study the isomeric 1,1,3-triphenyl-2-methyl-1,3-propanediols (IIIa,b). A mixture of these diastereomers was obtained by the reaction of the same mixture of ethyl β-hydroxy-α-methyl-β-phenylpropionates (Ia,b) with phenylmagnesium bromide. By fractional crystallization of the crude product from ethanol and then from benzene β-1,1,3-triphenyl-2-methyl-1,3-propanediol (IIIb), m.p. 167.5°, and α-1,1,3-triphenyl-2-methyl-1,3-propanediol (IIIa), m.p. 131°, were obtained. The infrared spectra of the α- and β-isomers of 1,1,3-triphenyl-2-methyl-1,3-propanediol are similar to each other and to that of the structurally analogous 1,1,3-triphenyl-1,3-propanediol in the region up to 8 μ, but show marked differences at higher wave lengths.

The cleavage reaction of these compounds (IIIa and IIIb) was effected under the usual conditions. Both isomers yielded benzaldehyde as the only carbonyl product isolated as had 1,1,3-triphenyl-1,3-propanediol, the α-isomer (IIIa) in 89% yield and the β(IIIb) in 65% yield. Still greater was the difference found in the time required for precipitation of the 2,4-dinitrophenylhydrazone. The α-isomer yielded a precipitate in 10 seconds while the precipitation time for the β-isomer was 75 seconds.

If the configurations of IIIa and IIIb could now be established, it was thought that some light might be shed on the mechanism of the cleavage reaction,

---

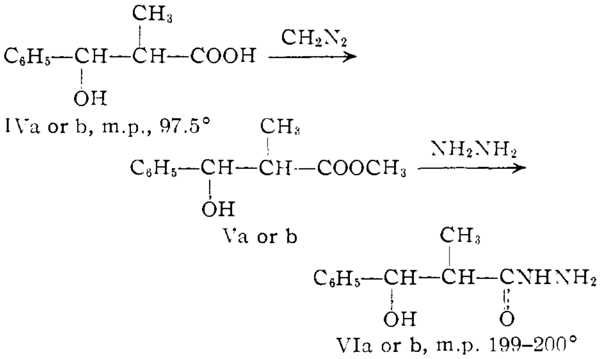
[1] Taken from the dissertation presented by H. E. Zimmerman to the Graduate School of Yale University in partial fulfillment of the requirements for the degree of Doctor of Philosophy. We are indebted to the E. I. du Pont de Nemours Company for a fellowship in support of this work.

[2] (a) H. E. Zimmerman and J. English, Jr., THIS JOURNAL, **75**, 2367 (1953); (b) *ibid.*, **76**, 2285 (1954).

[3] G. Dain, *J. Russ. Phys. Chem. Soc.*, **29**, 217 (1897).

for not all postulated mechanisms would fit the stereochemical evidence. An approach to the stereochemistry of the 1,3-diols IIIa and IIIb would logically begin with the β-hydroxyacids IVa and IVb corresponding to the β-hydroxyesters Ia and Ib from which the 1,3-diols were derived. One of these β-hydroxy-α-methyl-β-phenylpropionic acids, m.p. 95°, has been reported by several researchers. Dain[3] obtained this acid by barium hydroxide saponification of the corresponding ester which was the product of the Reformatsky reaction between acetophenone and ethyl α-bromopropionate. Posner[4] isolated this same acid from the nitrous acid treatment of β-amino-α-methyl-β-phenylpropionic acid of unknown configuration. Perkin and co-workers[5,6] again obtained this acid by the sodium amalgam reduction of ethyl α-benzoylpropionate. Farmer and Hose[7a] reported a β-hydroxy-α-methyl-β-phenylpropionic acid, m.p. 77°, by saponification of the Reformatsky ester I, while Chi and co-workers[7b] obtained a β-hydroxy-α-methyl-β-phenylpropionic acid, m.p. 116–118°, by catalytic hydrogenation of ethyl α-benzoylpropionate and saponification.

In the present work ethyl β-hydroxy-α-methyl-β-phenylpropionate (Ia,b) obtained from the Reformatsky reaction described above (equation 1) was saponified with alcoholic potassium hydroxide to give after extensive purification one isomer of β-hydroxy-α-methyl-β-phenylpropionic acid, m.p. 97.5° (IVa or b), apparently the 95° melting acid of the literature. Reaction of this acid with diazomethane yielded the corresponding methyl ester (Va or b), which was a low melting solid. This compound, by refluxing with hydrazine hydrate in ethanol for 35 minutes was converted to the corresponding hydrazide (VIa or b), m.p. 199–200°. In general, β-hydroxyesters are epimerized by base only under much more severe treatment (for example, see ref. 2a).



$$C_6H_5—\underset{OH}{CH}—\overset{CH_3}{CH}—COOH \xrightarrow{CH_2N_2}$$

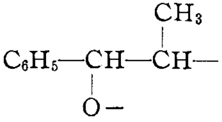
IVa or b, m.p., 97.5°

$$C_6H_5—\underset{OH}{CH}—\overset{CH_3}{CH}—COOCH_3 \xrightarrow{NH_2NH_2}$$

Va or b

$$C_6H_5—\underset{OH}{CH}—\overset{CH_3}{CH}—\underset{O}{\overset{\|}{C}}NHNH_2$$

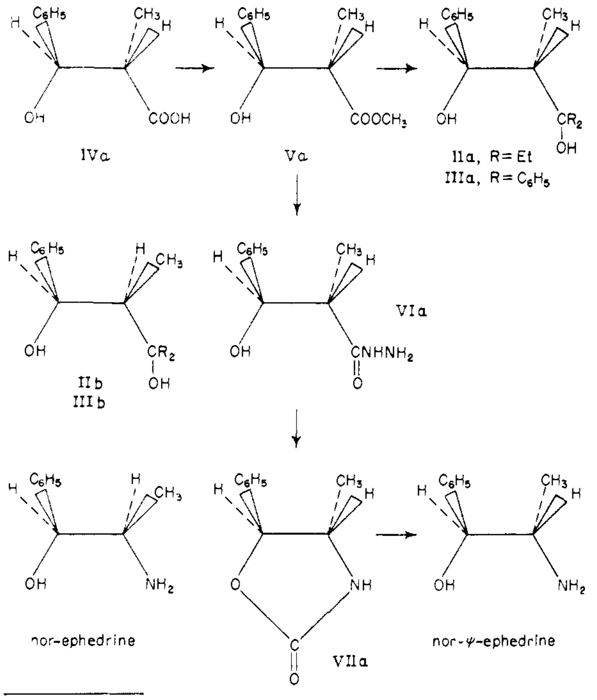
VIa or b, m.p. 199–200°

The Curtius rearrangement of β-hydroxyhydrazides has been studied by a number of researchers and shown[8-13] to give 2-oxazolidones, the products expected from internal urethan formation of the initially formed hydroxy isocyanates. Also it has been demonstrated by Kenyon and co-workers[14,15] that the Curtius rearrangement proceeds with retention of configuration of the migrating group. In the case of N-phenylacetyl-D-seryl azide, Baker and Ollis[13] have found that no racemization occurs in the Curtius rearrangement to give 4-phenylacetamido-2-oxazolidone. Therefore, it was anticipated in the present study that the Curtius rearrangement of β-hydroxy-α-methyl-β-phenylpropionic hydrazide, m.p. 199–200°, would yield the one of the two possible 4-methyl-5-phenyl-2-oxazolidones[16,17] (VIIa or b) in which the configuration of the  $C_6H_5—\underset{O—}{CH}—\overset{CH_3}{CH}—$ group had been retained.

When the 199–200° hydrazide (VIa or b) was subjected to the Curtius rearrangement, a product (VIIa or b) was obtained whose infrared spectrum was run and which was used directly in the next step. Infrared comparison of our crude product of unsharp melting point with authentic samples of the[18] isomeric 4-methyl-5-phenyl-2-oxazolidones showed it to be the lower melting (96°) isomer contaminated with a small amount of impurity having a carbonyl absorption band at 5.95 μ. Neither pure isomer absorbed at this point and this absorption may be due to some unreacted hydrazide in our product.

Saponification of the oxazolidone under relatively

CHART I



---

(4) T. Posner, *Ann.*, **389**, 75 (1912).

(5) W. Perkin, Jr., and A. Calman, *J. Chem. Soc.*, 154 (1886).

(6) W. Perkin, Jr., and J. Stenhouse, *ibid.*, 1010 (1891).

(7a) E. Farmer and C. Hose, *ibid.*, 964 (1933).

(7b) Y. Chi, C. Lueng and W. Yu, *C. A.*, **34**, 2347 (1940).

(8) G. Schroeter, *Ber.*, **42**, 2340 (1909).

(9) J. Fruton, *J. Biol. Chem.*, **146**, 463 (1942).

(10) M. Newman, THIS JOURNAL, **71**, 378 (1949).

(11) M. Newman and A. Kutner, *ibid.*, **73**, 4199 (1951).

(12) W. Close, *ibid.*, **73**, 95 (1951).

(13) W. Baker and W. Ollis, *J. Chem. Soc.*, 558 (1951).

(14) J. Kenyon and D. Young, *ibid.*, 263 (1941).

(15) A. Campbell and J. Kenyon, *ibid.*, 25 (1946).

(16) A. Homeyer, *C. A.*, **40**, 4085 (1946).

(17) W. Close, *J. Org. Chem.*, **15**, 1134 (1950).

(18) We are indebted to Dr. W. Close of the Abbott Laboratories and Dr. J. Venerable of the Mallinckrodt Chemical Works for generous gifts of authentic samples of these compounds.

mild conditions yielded, as the only isolable product, *dl*-nor-ψ-ephedrine, m.p. 77.5°, pure before recrystallization. *dl*-Norephedrine has been reported[19] to melt at 104° while *dl*-nor-ψ-ephedrine was said to melt at 71°. It is significant that the lower melting *dl*-nor-ψ-ephedrine of the literature was isolated by fractional crystallization (as the hydrochloride) of material from the filtrates of the higher melting and more insoluble *dl*-nor-ephedrine hydrochloride and hence may have been slightly impure, thus accounting for the lower literature melting point. Conversion of our sample of *dl*-nor-ψ-ephedrine to the hydrochloride gave *dl*-nor-ψ-ephedrine hydrochloride, m.p. 172–173°. The reported[19] melting points are 169° for *dl*-nor-ψ-ephedrine hydrochloride and 194° for *dl*-nor-ephedrine. Since the *dl*-nor-ephedrines have been related[19] by methylation and resolution to the ephedrines, whose configurations are known (see ref. 17 for references), the configurations of the nor-ephedrines may be considered to be firmly established. Thus, the configuration of the 97.5° β-hydroxy-α-methyl-β-phenylpropionic acid (IVa or b) has been related to that of nor-ψ-ephedrine, whose configuration is known (note Chart I[20]).

Reaction of the corresponding methyl ester (Va or b), which had already been used in the formation of the 200° hydrazide (VIa or b), with ethylmagnesium bromide and phenylmagnesium bromide in separate experiments was found to yield the α-isomers of 1-phenyl-2-methyl-3-ethyl-1,3-pentanediol (IIa), and 1,1,3-triphenyl-1,3-propanediol (IIIa), respectively, thus establishing the configurations of IIa, IIb, IIIa and IIIb. The entire reaction sequence may be written as shown in Chart I.

Experimental

Ethyl β-Hydroxy-α-ethyl-β-phenylpropionate.—Thirty-seven grams of granulated zinc (30 mesh) was activated by swirling for two minutes with 4% hydrochloric acid and washing thoroughly with water, ethanol and benzene in this order and then distilling off the final benzene until the distillate was clear. The zinc was transferred to a liter three-neck flask equipped with Hershberg stirrer, large reflux condenser and dropping funnel. Approximately 20 ml. of a mixture of 100 ml. of benzene, 58.4 ml. (0.447 mole) of ethyl α-bromopropionate and 45.4 ml. (0.448 mole) of freshly distilled benzaldehyde was added to the zinc and stirring was begun. To start the reaction the mixture was heated vigorously with a steam-bath for five minutes, whereupon an exothermic reaction began. The liquid reactants were then added to a rate to effect continued refluxing without further external heating. Near the end of the reaction, the mixture had to be heated for refluxing to continue. The total addition required 40 minutes and the mixture was refluxed on the steam-bath for an additional 110 minutes. The mixture was then cooled in ice and 200 ml. of ice-cold 20% sulfuric acid added with stirring and cooling. The benzene phase was separated and the aqueous phase was benzene extracted. The benzene extracts were washed with 10% sodium carbonate and then with water and finally dried over sodium sulfate. The benzene was removed on the steam-bath under vacuum and the residue distilled to give 72.0 g. (77.4%) of ethyl β-hydroxy-α-methyl-β-phenylpropionate,[3] b.p. 107–109° at 0.3–0.4 mm.

α and β-1-Phenyl-2-methyl-3-ethyl-1,3-pentanediol (IIa, b).—To 0.5 mole of ethylmagnesium bromide in 180 ml. of ether in a liter three-neck flask equipped with Hershberg stirrer, dropping funnel and reflux condenser, was added dropwise with stirring and cooling in ice 20.83 g. (0.10 mole) of ethyl β-hydroxy-α-methyl-β-phenylpropionate in 70 ml. of dry ether. The addition required 2.5 hours; at the end of this time, the reaction mixture was allowed to warm to room temperature and stir for an additional 3.5 hours. At the end of this time, the reaction mixture was poured onto ice and saturated ammonium chloride solution and then ether extracted. The ether extracts were dried over sodium sulfate and concentrated in vacuum leaving 21.48 g. of slightly oily solid. Recrystallization of this from aqueous ethanol yielded 3.41 g. of pure α-1-phenyl-2-methyl-3-ethyl-1,3-pentanediol, m.p. 138.0–139.5°. When the filtrates would yield no more of this isomer, recrystallization of the lower-melting fractions using ether–petroleum ether (30–60°) was begun. Large rhombic crystals of β-isomer separated first, but tended to be covered quickly by fine crystals of the α-isomer, they were therefore quickly removed and manually scraped free of the smaller crystals. Repetition of the process finally yielded 2.33 g. of pure β-1-phenyl-2-methyl-3-ethyl-1,3-pentanediol, m.p. 96.5–97.9°. Infrared analysis of the two isomers showed some differences in the 7–12 μ region.

Anal. Calcd. for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97. Found for α-isomer: C, 75.86; H, 9.70. Found for β-isomer: C, 75.68; H, 9.81.

α- and β-1,1,3-Triphenyl-2-methyl-1,3-propanediol (IIIa, b).—To 0.5 mole of phenylmagnesium bromide in 180 ml. of ether in a three-neck flask equipped with Hershberg stirrer, dropping funnel and reflux condenser, was added dropwise over two hours with cooling in ice and stirring 20.8 g. (0.1 mole) of ethyl β-hydroxy-α-methyl-β-phenylpropionate dissolved in 60 ml. of dry ether. At the end of the addition, the reaction mixture was allowed to warm to room temperature and stir for an additional two hours. Then it was cooled again in ice with stirring and a saturated solution of ammonium chloride was added slowly until the precipitation of solid began. At this point, the entire mixture was poured onto ice and saturated ammonium chloride and ether extracted. The ether extracts were dried over sodium sulfate and then concentrated on the steam-bath at atmospheric pressure to leave 33 g. of very thick oil which was induced to crystallize by dissolving a portion in petroleum ether-ether and cooling in Dry Ice, and then seeding. Two recrystallizations from ethanol gave 7.13 g., m.p. 164–166°, and one more recrystallization yielded 5.12 g. of pure β-1,1,3-triphenyl-2-methyl-1,3-propanediol, m.p. 165–166°; this isomer recrystallized best from methanol to give large crystals and the melting point finally reached 166.5–167.5°. The filtrates yielded lower melting material which on recrystallization from benzene yielded 2.88 g. of impure β-isomer, m.p. 154–162° and then several crops of material melting below 128°. This latter on benzene recrystallization yielded a total of 4.01 g. α-1,1,3-triphenyl-2-methyl-1,3-propanediol, m.p. 128.5–130.0°. Further recrystallization of a small sample from aqueous ethanol brought the melting point to 129.5–131.0°. By working up the 2.88 g. of impure β-isomer, the total yield of β-1,1,3-triphenyl-2-methyl-1,3-propanediol was brought to 6.83 g.

Anal. Calcd. for $C_{22}H_{22}O_2$: C, 82.98; H, 6.96. Found for α-isomer: C, 82.70; H, 6.71. Found for β-isomer: C, 83.24; H, 6.78.

Dehydration of Diols.—In each case the calculated amount (1 equiv.) of 2,4-dinitrophenylhydrazine was dissolved in 10 ml. of 95% ethanol and 1 ml. of concd. sulfuric acid. This solution was heated to boiling and 0.50 g. of finely powdered diol added. Heating was continued for 5 or 6 minutes after which the solution was cooled and the precipitated 2,4-dinitrophenylhydrazones filtered. They were identified by comparison with authentic samples of benzaldehyde dinitrophenylhydrazone (no m.p. depressions were observed). The yields and precipitation times are listed in Table I.

---

[19] W. Nagai and S. Kanao, *Ann.*, **470**, 157 (1929).

[20] It has been assumed that saponification of the oxazolidone proceeds by attack at the carbonyl group to give no change in configuration. In support of this, is the formation of the same oxazolidone (m.p. 96°) from nor-ψ-ephedrine by reaction with diethyl carbonate using a basic catalyst[16] and the formation of the isomeric oxazolidone (m.p. 146°) from nor-ephedrine by reaction with urea hydrochloride at elevated temperatures[17] and also by reaction with diethyl carbonate.[16] It would be difficult to write a reasonable mechanism involving inversion for the diethyl carbonate reaction and there is evidence[17] indicating that the urea reaction proceeds with no change in configuration.

TABLE I

CLEAVAGE OF ISOMERIC 1,3-DIOLS

	Cpd., -1,3-propanediol	Precipitation time	Yield, %
(IIa)	α-1-Phenyl-2-methyl-3,3-diethyl	4 min.	17.1
(IIb)	β-1-Phenyl-2-methyl-3,3-diethyl	2 min.	32.6
(IIIa)	α-1,1,3-Triphenyl-2-methyl	10 sec.	88.9
(IIIb)	β-1,1,3-Triphenyl-2-methyl	75 sec.	65.4

β-Hydroxy-α-methyl-β-phenylpropionic Acid (IVa).—To 28.05 g. of potassium hydroxide in 50 ml. of ethanol and 100 ml. of water was added 52.1 g. of ethyl β-hydroxy-α-methyl-β-phenylpropionate. The mixture was refluxed for one hour, diluted with water and ether extracted. The aqueous phase was cooled and acidified with 400 ml. of ice cold 20% hydrochloric acid and ether extracted. The ether extracts after drying and concentrating yielded 46.3 g. of an oil which crystallized. Eleven fractional crystallizations from 1:1 benzene–petroleum ether (60-90°) yielded 8.75 g., m.p. 96.5–97.5°, whose melting point was not altered by continued recrystallization. Recrystallization of non-oily material from water yielded the same melting point. From the filtrates could be isolated additional product having this melting point. The reported[3,4,6] melting point for this isomer is 95°.

β-Hydroxy-α-methyl-β-phenylpropionic Hydrazide (IVa).—To a solution of 4.0 g. β-hydroxy-α-methyl-β-phenylpropionic acid, m.p. 96.5–97.5°, in ether was added an ethereal solution of excess diazomethane. Removal of the ether by distillation left 4.35 g. of colorless oil which crystallized to give solid, m.p. 43–46°. This methyl β-hydroxy-α-methyl-β-phenylpropionate was used directly in the reactions with hydrazine hydrate and Grignard reagents.

A mixture of 1 g. of methyl β-hydroxy-α-methyl-β-phenylpropionate, 0.75 ml. of hydrazine hydrate (85%) and 1 ml. of ethanol was refluxed on the steam-bath for 30 minutes. On cooling, a solid separated and was filtered and washed with a little ethanol; yield 0.71 g. (71%) of β-hydroxy-α-methyl-β-phenylpropionic hydrazide, m.p. 199-200°.

Anal. Calcd. for $C_{10}H_{14}O_2N_2$: N, 14.42; C, 61.83; H, 7.27. Found: N, 14.54; C, 61.71; H, 7.50.

Curtius Rearrangement of β-Hydroxy-α-methyl-β-phenylpropionic Hydrazide (IVa).—One-half gram of β-hydroxy-α-methyl-β-phenylpropionic hydrazide, m.p. 199–200°, was suspended in 5.0 ml. of water and 0.44 ml. of 50% hydrochloric acid added with mechanical stirring to the mixture cooled to 5°. Then 4.0 ml. of ether was added. Finally, a cold solution of 0.20 g. of sodium nitrite in 2.0 ml. of water was added dropwise with stirring over five minutes keeping the temperature at 5°. The ether phase was separated and the aqueous phase ether extracted three times. The ether phase was diluted with 20 ml. of benzene and dried over sodium sulfate for ten minutes. The ether was removed by distillation and the benzene solution remaining was refluxed on the steam-bath for one-half hour. Removal of the benzene under reduced pressure left an oil which crystallized m.p. 100–110°; 0.35 g. (78% crude). Comparison of the infrared spectrum of the product with the spectra of the two pure isomers of 4-methyl-5-phenyl-2-oxazolidones (m.p. 96° and 146°)[16] showed it to be essentially pure lower melting isomer (96°). Both isomers and the product contained a carbonyl absorption band at 5.67 μ; however, the product exhibited a weak band also at 5.95 μ which may be due to an impurity of unreacted hydrazide. The spectrum of the higher melting isomer (146°) contained absorption bands at 7.43 and 9.99 μ. These were lacking in the spectrum of the Curtius product and that of the pure lower melting isomer (96°). An absorption band at 9.82 μ was present only in the spectrum of the product and that of the lower melting isomer. Otherwise, except for some smaller differences, the three spectra were identical.

The Curtius product was saponified on the steam-bath with 5 ml. of 20% aqueous sodium hydroxide. At the end of 70 minutes, the mixture was made definitely acid with 20% hydrochloric acid and ether extracted and then made basic with 20% sodium hydroxide solution and benzene extracted and dried over sodium sulfate. The ether extracts yielded only a very small amount of non-crystalline material. Concentration of the benzene extracts left 0.16 g. of solid, m.p. 71–75°. One recrystallization from ether-petroleum ether (30–60°) brought the melting point of the *dl*-nor-ψ-ephedrine to 76.8–77.5°; further recrystallization did not change this.

Anal. Calcd. for $C_9H_{13}NO$: N, 9.26. Found: N, 9.13.

Fifty mg. of the *dl*-nor-ψ-ephedrine was dissolved in 5 ml. of dry ether and anhydrous hydrogen chloride gas was passed into the solution to give a white precipitate weighing 48 mg., m.p. 172–173°. The melting point was not altered by recrystallization from ethanol.

Anal. Calcd. for $C_9H_{14}NOCl$: N, 7.46; Cl, 18.89; C, 57.60; H, 7.52. Found: N, 7.66; Cl, 19.05; C, 57.45; H, 7.62.

Reaction of Methyl β-Hydroxy-α-methyl-β-phenylpropionate (Va) with Ethylmagnesium Bromide and Phenylmagnesium Bromide.—These reactions were run exactly as described above for the corresponding ethyl ester Ia,b except on a much smaller scale. From the reaction with ethylmagnesium bromide only the α-isomer of 1-phenyl-2-methyl-3-ethyl-1,3-pentanediol, m.p. 138°, was isolated while from the reaction with phenylmagnesium bromide only the α-isomer of 1,1,3-triphenyl-2-ethyl-1,3-propanediol, m.p. 131°, was obtained. The yields were 37 and 31%, respectively.

NEW HAVEN, CONNECTICUT

[CONTRIBUTION NUMBER 1171 FROM THE STERLING CHEMISTRY LABORATORY, YALE UNIVERSITY]

The Cleavage Reaction of 1,3-Diols. III. The Synthesis of a Pair of Diastereomeric Ditertiary 1,3-Diols and an Effect of Configuration on Mode of Cleavage[1]

BY HOWARD E. ZIMMERMAN AND JAMES ENGLISH, JR.

RECEIVED JULY 27, 1953

The diastereomeric 2-phenyl-3-methyl-4-ethyl-2,4-hexanediols have been synthesized by several approaches, including one which is stereospecific. The results of the acid-catalyzed cleavage reaction of these compounds are explicable on the basis of the mechanism proposed in this paper.

The ease with which the cleavage reaction of 1,3-diols[2–5] proceeds to give olefins and ketones or aldehydes has been shown[5] in the case of the diastereomeric 1,1,3-triphenyl-2-methyl-1,3-propanediols to depend on the configuration of the 1,3-diol. The present paper deals with a somewhat more striking case of differing behavior of diastereomers in the cleavage reaction, that is, with the isomeric 2-phenyl-3-methyl-4-ethyl-2,4-hexanediols (IIa, b).

For the preparation of these compounds (IIa, b) three different synthetic approaches were used.

---

[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. Brutcher and J. English, Jr., THIS JOURNAL, **74**, 4279 (1952).

[3] H. E. Zimmerman and J. English, Jr., *ibid.*, **75**, 2367 (1953).

[4] *Ibid.*, **76**, 2285 (1954).

[5] *Ibid.*, **76**, 2291 (1954).