at 1665 and 1645 cm.$^{-1}$. Removal of the cyclohexane under vacuum gave a partially dimerized residue.

Anal. Calcd. for $C_9H_{12}O$: C, 79.4; H, 8.9. Found: C, 79.4; H, 8.9.

Dipole Moment Determination. Apparatus.—The apparatus used in determining the electric moment consisted of a BC-221 Frequency meter adapted in the manner described by Thompson and Rogers.[9] The cell was constructed of three stainless steel cylinders held concentrically by Teflon spacers, the assembly being mounted in a glass envelope. The cell of about 30-ml. capacity was filled and drained through a tube entering at the bottom. All such operations were carried out with the cell fixed in position in the constant temperature bath. The apparatus was calibrated by obtaining frequency readings as a function of dielectric constant of the medium in the cell; the purified liquids used for this purpose were benzene, cyclohexane and toluene. The cell was immersed in a constant temperature bath of 23.97 ± 0.02°. Density and refractive index determinations were also made at this temperature. In determining densities a 5-ml. pycnometer was used; the refractive indices were determined by use of a Bausch and Lomb precision refractometer fitted with a sodium lamp as source.

Materials.—Thiophene-free reagent-grade benzene was purified by recrystallization followed by distillation from phosphorus pentoxide in an efficient column packed with glass helices. The product of this distillation was stored over sodium wire; d_{24} 0.87435. Reagent grade toluene was purified by passing it through a 60 × 1.2 cm. column of alumina, 100 mesh, and carefully fractionating the middle portion. Storage was over sodium wire; d_{24} 0.86310. Cyclohexane was purified by passage through a 60 × 1.2 cm. column of 100 mesh alumina, followed by careful fractionation. The product, d_{24} 0.77410, was stored over sodium wire.

Procedure.—The cyclohexane solutions of II were made up by weight, and were of weight fractions 0.03829, 0.02060 and 0.00929. The dielectric constant, refractive index and density of each solution was determined, from which values of $\partial\epsilon/\partial w_2$, $\partial n^2/\partial w_2$, and $\partial\nu/\partial w_2$ of 1.048, 0.157 and −0.345 were calculated, where w_2 is mole fraction of solute, ϵ is dielectric constant, n is refractive index and ν is volume per g. The method of Halverstadt and Kumler[10] was employed in calculating the polarization per gram of solute, p_2, and the refractivity per gram, r_2. The values so obtained were 0.4915 and 0.2794, respectively, leading to values of 133.7 and 76.0 cm.^{3}, respectively, for the total molar polarization P_2 and the molar refractivity, R_2. The latter value is to be compared with the value 78.1 cm.^{3} determined from the sum of bond refractivities.[11] The difference between P_2 and R_2, 57.7 cm.^{3}, represents the sum of the orientation and atom polarizations.

If all of the net polarization, 57.7 cm.^{3}, is considered to be due to orientation polarization, a calculated moment of 1.71 D. results.

The carbonyl groups in II are pointing in nearly opposite directions, the angle between them being probably 160–170°. In *p*-benzoquinone the arrangement of oppositely directed carbonyl groups leads to an atom polarization[12] of 8–10 cm.^{3}. This presumably arises as a result of each carbonyl having one degree of bending freedom. If oppositely directed polar groups have additional degrees of freedom as a result of deformation modes peculiar to the atoms which separate them, the atom polarization is further increased. For example, 4,4′-dicyanobiphenyl has an atom polarization of 35 cm.^{3}, whereas for *p*-dicyanobenzene it is only 12 cm.^{3}.[3,13]

In the compound under consideration here there are a number of possibilities for low-frequency bending modes which would cause a change in the angle between the carbonyl groups, and thus contribute to atom polarization. If it is assumed that the atom polarization is 25 cm.^{3} a moment of 1.27 D. is calculated. This amount of atom polarization is not unlikely for the molecule under consideration. Thus, although a precise value of the moment cannot be calculated because of the uncertainty in the atom polarization, a reasonable estimate of the latter quantity leads to a value for the moment which is of the same magnitude as that estimated from models of one of the isomers. Any improved value must be smaller and therefore still consistent only with structure A.

Calculation of Theoretical Moments for Structures A-D.—The carbonyl–carbonyl angles assumed are angles shown under the structures presented in the text. They were estimated visually from "Student Molecular Models" of the O. H. Johns Glass Co., Toronto, Canada, a liberal allowance being made for distortion from what is believed to be the most stable conformation. The moments were calculated from the equation

$$u = [(2.9)^2 + (3.8)^2 + (2)(2.9)(3.8)\cos\theta]^{1/2}$$

the values of 3.8 and 2.9 D being those reported for 3,5-dimethyl-2-cyclohexenone and fenchone, respectively,[14] chosen as the closest models for which data are available.

URBANA, ILLINOIS

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[9] H. B. Thompson and M. T. Rogers, *J. Chem. Educ.*, **32**, 20 (1955).

[10] I. F. Halverstadt and W. D. Kumler, THIS JOURNAL, **64**, 2988 (1942).

[11] A. I. Vogel, W. T. Cresswell, G. H. Jeffrey and J. Leicester *J. Chem. Soc.*, 514 (1952).

[12] J. W. Smith, "Electric Dipole Moments," Butterworths, London, 1955, p. 271.

[13] Reference 12, p. 272.

[14] H. L. Donle and G. Volkert, *Z. physik. Chem.*, **B8**, 60 (1930).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF SOUTHERN CALIFORNIA]

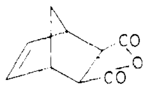
The Hydration of *exo-cis*-3,6-Endomethylene-Δ^4-tetrahydrophthalic Anhydride[1]

BY JEROME A. BERSON AND SHIGETO SUZUKI

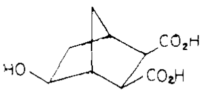
RECEIVED JANUARY 19, 1957

The hydration reaction of the title gives *exo*-4-hydroxy-*exo-cis*-3,6-endomethylenehexahydrophthalic acid. The structure of the product is proved by alternate synthesis from *exo*-4,5-epoxy-*exo-cis*-3,6-endomethylenehexahydrophthalic anhydride.

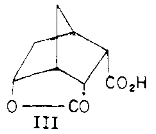
In connection with another study, it was necessary for us to prepare *exo*-4-hydroxy-*exo-cis*-3,6-endomethylenehexahydrophthalic acid (II).



I



II



III

A substance (IIα) to which this structure had been assigned had been reported by Alder and co-work-

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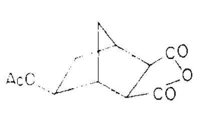
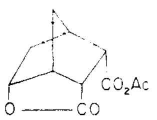
[1] This research was supported by the United States Air Force through the Air Force Office of Scientific Research of the Air Research and Development Command under contract No. AF 18(600)-1544. Reproduction in whole or in part is permitted for any purpose of the United States Government.

ers,[2] who found it among the hydration products of the corresponding olefin I. The following considerations moved us to question the structural assignment.

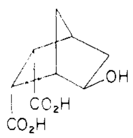
Hot 50% sulfuric acid converted I to a mixture of products, from which the known lactonic acid III, m.p. 203°, $C_9H_{10}O_4$ was isolated by taking advantage of its solubility in ethyl acetate.[2] The less soluble fraction contained a substance (IIα) that also had m.p. 203°, but had the molecular formula $C_9H_{12}O_5$, *i.e.*, III + H_2O. With boiling acetyl chloride, IIα gave an "acetoxyanhydride," formulated as IV, and with 50% sulfuric acid at 150°, IIα give III.[2] No evidence was presented to indicate that IIα and III were chemically distinguishable.[2] The possibility remained, therefore, that IIα was merely a crystal hydrate of III, and that the "acetoxyanhydride" was the mixed anhydride V. Even had IIα and III had been chemically different, the data did not eliminate the possibility that IIα was the Wagner–Meerwein relative VI, since VI would have been consistent with all the observations reported.



IV

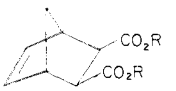


V

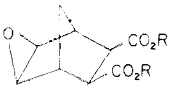


VI

We therefore undertook an independent synthesis of II. The epoxydiester VIIIa had previously been prepared by Alder[3] from the olefinic ester VIIa with perbenzoic acid. We obtained VIIIa in 70% yield by epoxidation of VIIa with peroxytrifluoroacetic acid in methylene chloride in the presence of sodium carbonate, according to the procedure of Emmons and Pagano.[4] Attempts to hydrogenolyze the oxirane ring of VIIIa with a variety of reagents known to be effective in such reactions were uniformly unsuccessful; VIIIa was recovered from attempted reductions with Raney nickel and hydrogen in ethyl acetate, palladium–charcoal and hydrogen in acetic acid, sodium borohydride in dioxane at 100°, and lithium aluminum hydride in ether at −78°.

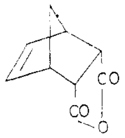


VIIa, R = CH_3
b, R = H

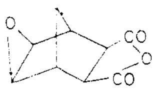


VIIIa, R = CH_3
b, R = H

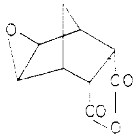
The sluggishness of the oxirane function to attack by external reagents also was manifested in a series of epoxidation experiments. Peroxytrifluoroacetic acid reacts with simple olefins to give glycol monoesters, presumably resulting from opening of the intermediate epoxide by trifluoroacetic acid,[5] the epoxides being isolated only when the reaction is carried out heterogeneously in the presence of a weakly alkaline buffering agent such as sodium carbonate.[4] Nevertheless, the dibasic acid VIIb reacted with peroxytrifluoroacetic acid in methylene chloride–chloroform in the absence of buffer to give moderate yields of epoxide VIIIb. The anhydrides I and IX gave good yields of epoxyanhydrides X and XI, respectively, when the epoxidation was carried out in the presence of anhydrous sodium sulfate. The epoxide functions of both X and XI were, however, readily subject to opening internally; XI was converted to the hydroxylactonic acid XII by hot water; X could be hydrolyzed to the dibasic acid VIIIb by brief heating in water, but prolonged treatment gave a hydroxylactonic acid $C_9H_{10}O_5$, m.p. 196–197°, which conceivably may have been the lactone (m.p. 200°) of 3-*exo*-carboxy-5-*exo*-hydroxy-4-*endo*-hydroxynorbornane-2-*endo*-carboxylic acid,[3] but more probably was the Wagner–Meerwein rearrangement product XIII. This point was not pursued.



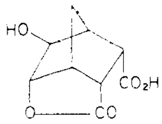
IX



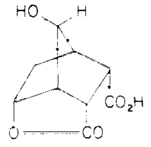
X



XI



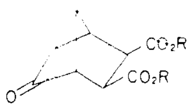
XII



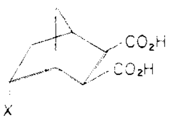
XIII

The hydrolysis also produced an uncharacterized oil, which gave a positive test for the presence of a vicinal glycol. The 197° hydroxylactonic acid was also formed as a by-product in the epoxidation of VIIb.

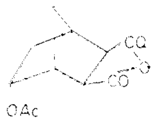
Reduction of the ketoester XIVa with sodium borohydride in methanol gave, after saponification, the dibasic hydroxyacid XVa. The latter had been obtained[6] previously by catalytic hydrogenation and hydrolysis of the anhydride of the ketoacid XIVb. Catalytic hydrogenation of the oxime of XIVb gave an amino acid XVb, whose stereochemistry was assigned by analogy to the reduction of norcamphoroxime to *endo*-norbornylamine[6] and of 4-keto-3,6-endomethylene-*trans*-hexahydrophthalic acid oxime to the lactam of the 4-*endo*-amino-*trans*-acid.[6]



XIVa,R = CH_3
b,R = H



XVa, X = OH
b, X = NH_2



XVI

The amino acid XVb, which might have been expected to give II upon diazotization (compare *endo*-norbornylamine → *exo*-norborneol[7,8]), released

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[2] K. Alder, G. Stein, F. v. Buddenbrock, W. Eckardt, W. Frercks and S. Schneider, *Ann.*, **514**, 1 (1934).

[3] K. Alder, G. Stein, W. Eckardt, R. F. v. Buddenbrock and S. Schneider, *ibid.*, **504**, 216 (1933).

[4] W. D. Emmons and A. S. Pagano, THIS JOURNAL, **77**, 89 (1955).

[5] W. D. Emmons, A. S. Pagano and J. P. Freeman, *ibid.*, **76**, 3472 (1954).

[6] K. Alder, G. Stein, S. Schneider, M. Liebmann, E. Rolland and G. Schulze, *Ann.*, **525**, 183 (1936).

[7] G. Komppa and S. Beckmann, *ibid.*, **512**, 172 (1934).

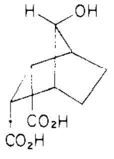
[8] K. Alder, G. Stein, E. Rolland and G. Schulze, *ibid.*, **514**, 211 (1934).

nitrogen when treated with nitrous acid, but the product was extremely soluble in water and insoluble in organic solvents, and it could not be separated from inorganic salts.

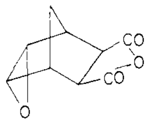
A successful synthesis of IIα was accomplished by treating the epoxyanhydride X with hydrogen bromide in chloroform–glacial acetic acid, followed by debromination of the crude product with Raney nickel in boiling water. The hydroxyacid thus obtained was identical with that (IIα) prepared by hydration of I according to Alder.[2] The derived acetoxyanhydrides (IV) from the two sources were also identical, but differed from the stereoisomeric acetoxyanhydride XVI. Compound IIα was precisely dibasic, and it strongly depressed the melting point of the authentic lactonic acid III. It therefore cannot be represented as a crystal hydrate of the latter. Oxidation of either IIα or its epimer XVa with potassium dichromate in sulfuric acid gave the *exo*-ketoacid XIVb.

The crude product from the reaction of X with hydrogen bromide might have contained rearranged bromohydrin,[9] and/or the bromohydrin might have suffered rearrangement during debromination.[10] However, IIα must have been formed from X without any net change in carbon skeleton, since rearrangement in its formation from X would require that IIα be XVII, a structure that could not also be formed in the hydration of I without the intervention of bridgehead carbonium ion intermediates. Only structure II for IIα is consistent with *both* the paths I → IIα and X → IIα; Alder's assignment[2] is confirmed.

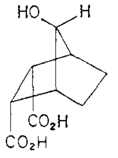
The *exo*-stereochemistry of the hydroxyl group of IIα (II) follows from the premise that epoxidation of I gave *exo*-epoxide X. This premise is supported by analogy to the epoxidation of norbornene.[11] It is independently proved by the fact that the *endo*-epoxide XVIII would have given hydroxyacid XVa or XIX. Compound IIα cannot be XIX since the latter could not be a product of the hydration of I, and IIα cannot be XVa since a substance that unambiguously has this structure is known[6] and is not identical with IIα. Epoxidation of I, therefore, gave X and not XVIII.



XVII



XVIII



XIX

Experimental[12]

Dimethyl *exo*-4,5-Epoxy-*exo-cis*-3,6-endomethylenehexahydrophthalate (VIIIa).—A solution of 45.5 g. of the diester VIIa in 180 ml. of dry methylene chloride was stirred with 122 g. of sodium carbonate under a Dry Ice–acetone condenser and treated dropwise during 30 minutes with a solution of peroxytrifluoroacetic acid[4] (from 9 ml. of 90% hydrogen peroxide and 63 g. of trifluoroacetic anhydride) in 50 ml. of dry methylene chloride. After being heated at reflux for 15 minutes, the mixture was cooled, the methylene chloride was removed and the solid material was washed several times by decantation with fresh methylene chloride. The combined methylene chloride layers were treated with a little activated charcoal (Norite) and the mixture was dried overnight with sodium sulfate. The solution was filtered, evaporated *in vacuo* at room temperature, and the crystalline residue recrystallized from hexane to give 31.1 g., m.p. 84–85° (first crop), and 3.0 g., m.p. 81–83° (second crop), of the epoxydiester VIIIa, reported[3] m.p. 86–87°. A mixture m.p. with a sample prepared by perbenzoic acid oxidation[3] of VIIa was not depressed.

Epoxidation of VIIb.—A mixture of 9.2 g. of VIIb,[13] 75 ml. of methylene chloride and 50 ml. of chloroform was stirred and treated during 45 minutes with a solution of peroxytrifluoroacetic anhydride (from 14.7 g. of trifluoroacetic anhydride, 1.67 ml. of 90% hydrogen peroxide and 25 ml. of methylene chloride). After an additional two hours, the solution was treated with 80 ml. of benzene and evaporated at room temperature *in vacuo*. The residue was leached with 500 ml. of boiling chloroform and filtered. The filtrate was concentrated and the precipitate was recrystallized from acetonitrile to give 0.9 g. of the **epoxyacid VIIIb**, m.p. 167–168° dec. The insoluble residue from the chloroform extract was recrystallized from acetonitrile to give a further quantity of VIIIb (2.2 g.), m.p. and mixed m.p. 167–168° dec.

Anal. Calcd. for $C_9H_{10}O_5$: C, 54.54; H, 5.10. Found: C, 54.68; H, 5.22.

Conversion of a sample of VIIIb to the dimethyl ester VIIIa was accomplished with ethereal diazomethane. The product had m.p. 86–88°, alone or mixed with authentic VIIIa.

The combined chloroform extract and acetonitrile mother liquors from the epoxidation experiment were evaporated and the residue recrystallized from acetonitrile to give 1.1 g. of a **hydroxylactonic acid**, m.p. 196–197°.

Anal. Calcd. for $C_9H_{10}O_5$: C, 54.54; H, 5.10. Found: C, 54.45; H, 5.08.

The hydroxylactonic acid was converted to its **methyl ester**, m.p. 145–146°, from ethyl acetate, with ethereal diazomethane. A chloroform solution of the methyl ester showed infrared absorption maxima at 3650 cm.$^{-1}$ (w) (hydroxyl), 1775 cm.$^{-1}$ (vs) (5-ring lactone carbonyl), and 1740 cm.$^{-1}$ (s) (ester carbonyl).

Anal. Calcd. for $C_{10}H_{12}O_5$: C, 56.60; H, 5.70. Found: C, 56.54; H, 5.70.

Epoxidation of I.—A mixture of 20 g. of I, 20 g. of anhydrous sodium sulfate and 30 ml. of methylene chloride was treated as in the above epoxidations with peroxytrifluoroacetic acid (from 4.0 ml. of 90% hydrogen peroxide and 29.4 g. of trifluoroacetic anhydride) in a mixture of 20 ml. of methylene chloride and 20 ml. of chloroform. After removal of the solvents, the solid residue was leached with boiling acetonitrile. The solution was filtered and concentrated to give 14.1 g. of the **epoxyanhydride X**, m.p. 203–209° dec. An analytical sample, recrystallized from chloroform, melted at 204–206° dec.

Anal. Calcd. for $C_9H_8O_4$: C, 59.99; H, 4.50. Found: C, 59.91; H, 4.52.

Hydrolysis of X.—A suspension of 3.0 g. of X in 20 ml. of water was shaken and heated on the steam-bath for 6 minutes, after which time complete solution had occurred. After an additional 10 minutes of heating, the solution was evaporated to dryness *in vacuo* at room temperature to give 3.2 g. of the dibasic epoxyacid VIIIb, m.p. 161–165° dec. The acid was dissolved in 25 ml. of water and solution was heated on the steam-bath for 6 hours. The water was removed *in vacuo*, the residual oil was taken up in acetonitrile, and the solution was dried over calcium sulfate, decolorized with charcoal, concentrated to a volume of 10 ml., and stored at 0° for 3 days. The precipitated solid was collected to give 1.75 g. of crude hydroxylactonic acid, m.p. 183–191°. Recrystallization from acetonitrile gave 1.50 g. of product melting at 194°, alone or mixed with a specimen prepared as above. A mixture m.p. with X was depressed to 170–180°.

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[9] H. M. Walborsky and D. F. Loncrini, *J. Org. Chem.*, **22**, 1117 (1957).

[10] H. Kwart and G. Null, THIS JOURNAL, **80**, 248 (1958).

[11] (a) H. M. Walborsky and D. F. Loncrini, *ibid.*, **76**, 5396 (1954); (b) H. Kwart and W. G. Vosburgh, *ibid.*, **76**, 5400 (1954).

[12] Melting points are corrected. Microanalyses are by Dr. Adalbert Elek, Elek Microanalytical Laboratories, 4763 W. Adams Blvd., Los Angeles, Calif.; Micro-Tech Laboratories, Skokie, Ill., and Mr. W. J. Schenck.

[13] D. Craig, THIS JOURNAL, **73**, 4889 (1951).

The acetonitrile mother liquors were evaporated to give a viscous oil, which gave a heavy precipitate of silver iodate when treated with periodic acid–nitric acid solution and silver nitrate. A blank test and a test with the 197° hydroxylactonic acid were both negative.

Epoxidation of IX.—This reaction was carried out under conditions similar to those used in the epoxidation of I. The product from 20 g. of IX was worked up as above to give three crops of material (total weight 17.0 g.). The crude product XI melted in the range 215–250° with pre-softening and darkening. An analytical sample, m.p. 232–233° dec., when heated slowly from room temperature, was prepared by recrystallization from acetonitrile.

Anal. Calcd. for $C_9H_8O_4$: C, 59.99; H, 4.50. Found: C, 60.33; H, 4.68.

When 1.7 g. of XI was heated on the steam-bath with 25 ml. of water, complete solution occurred in 15–20 minutes. Evaporation of the water to a volume of 5 ml. deposited 1.4 g. of material of m.p. 204–206°. It was redissolved in water and re-treated as above to give 1.2 g. of material of m.p. 205–206°. The combined filtrates were heated for 3 hours on the steam-bath and the water was evaporated. The residual oil was crystallized from acetonitrile to give an additional 0.6 g. of material of m.p. 200–204°. An analytical sample of the **hydroxylactonic acid XII**, m.p. 204–205°, was recrystallized from water.

Anal. Calcd. for $C_9H_{10}O_5$: C, 54.54; H, 5.10. Found: C, 54.50; H, 5.07.

Methylation of XII with ethereal diazomethane gave the **methyl ester**, m.p. 90–90.8°, from *dry* ether. The analytical sample was dried at 55° *in vacuo* for 30 hours.

Anal. Calcd. for $C_{10}H_{12}O_5$: C, 56.60; H, 5.70. Found: C, 56.61; H, 5.68.

The ester appeared to form a relatively stable **hydrate**, m.p. 61°, when it was allowed to crystallize slowly from ether without exclusion of moisture. The analytical sample was dried at room temperature *in vacuo*.

Anal. Calcd. for $C_{10}H_{14}O_6$: C, 52.17; H, 6.13. Found: C, 52.50; H, 6.23.

The 61° form in chloroform showed infrared maxima at 3605 cm.$^{-1}$ (w) (hydroxyl), 1778 cm.$^{-1}$ (vs) (5-ring lactone carbonyl) and 1737 cm.$^{-1}$ (s) (ester carbonyl). It was converted to the 91° form upon drying at 55° *in vacuo*.

Sodium Borohydride Reduction of the Ketoester XIVa.—The anhydride of XIVb[6] was converted to the ketoester XIVa, m.p. 84–85°, with methanolic sulfuric acid. Seven grams of XIVa was added slowly to a stirred solution of 1.13 g. of sodium borohydride in 100 ml. of absolute methanol with occasional cooling of the reaction mixture in ice-water. After completion of the addition, the reaction mixture was stirred for 15 hours at room temperature. The solvent was evaporated, the residue was taken up in dilute hydrochloric acid, and the hydroxyester was extracted with ethyl acetate. The ethyl acetate solution was evaporated and the residual oil was heated on the steam-bath for 2 hours with 50 ml. of 15% aqueous sodium hydroxide. The clear solution was acidified and exhaustively extracted with ethyl acetate and with ether. The aqueous solution was evaporated to dryness and the solid residue leached with fresh ethyl acetate. The combined extracts were dried over calcium sulfate and evaporated to give 4.03 g. of crude **hydroxyacid XVa**, m.p. 172–184° dec. Recrystallization from ethyl acetate–hexane gave pure material, m.p. 181–182° dec., reported[6] m.p. 183°. With acetyl chloride, the **acetate anhydride XVI**, m.p. 101°, reported[6] m.p. 105°, was obtained.

***endo*-4-Amino-*exo-cis*-3,6-Endomethylenehexahydrophthalic Acid (XVb).**—Twenty-one grams of the anhydride of XIVb[6] was dissolved in 100 ml. of warm water. The solution was cooled and treated with 16.7 g. of hydroxylamine hydrochloride and 25.2 g. of sodium bicarbonate. The reaction mixture was heated on the steam-bath for 5.5 hours, cooled, and acidified with hydrochloric acid, whereupon 20.6 g. of the **oxime** of the ketoacid XIVb crystallized. The oxime had m.p. 260–262° dec. An analytical sample, m.p. 260-262° dec., was prepared by recrystallization from water.

Anal. Calcd. for $C_9H_{11}O_5N$: C, 50.70; H, 5.20; N, 6.57. Found: C, 50.63; H, 5.06; N, 6.48.

A suspension of 20.6 g. of the oxime and 0.6 g. of platinum oxide in 130 ml. of glacial acetic acid was hydrogenated in a Parr apparatus at an initial pressure of 47 lb./in.^{2} After about 70 hours, hydrogen absorption had virtually ceased (*ca.* 1.7 moles were absorbed). The solution was filtered and evaporated, and the semi-solid residue crystallized from ether–methanol. The substance was purified for analysis by recrystallization from concentrated aqueous solution after treatment with charcoal. The pure **amino-acid XVb** lost water at 205–207° and decomposed above 230°. It was notably hygroscopic.

Anal. Calcd. for $C_9H_{13}O_4N$: C, 54.27; H, 6.58; N, 7.03. Found: C, 54.11; H, 6.40; N, 7.09.

Conversion of the *exo*-Epoxyanhydride X to IIα.—A suspension of 13.1 g. of X in 350 ml. of chloroform was treated with a solution of 16.2 g. of hydrogen bromide in 30 ml. of glacial acetic acid added in one portion. Heat was evolved and after 10–15 minutes, a pale yellow-brown oil began to separate. After being kept at room temperature overnight, the chloroform layer was decanted off and the insoluble oil was freed of solvent *in vacuo*. Attempts to obtain crystalline material from the resulting glassy solid so far have been unsuccessful. Evaporation of the chloroform layer also gave a pale yellow glass. This material (8 g.) was heated at reflux with 150 ml. of water and 75 g. (wet weight) of Raney nickel for 5 hours. A few drops of octyl alcohol was added to prevent foaming. The mixture was filtered through diatomaceous earth and the filter cake was thoroughly washed with hot water. The combined filtrate and washings contained ionic nickel, as was evidenced by a pale green color. The solution was decolorized with Dowex-50 cation exchange resin, filtered, the now pale yellow filtrate treated with charcoal, filtered and evaporated to give 3.45 g. of IIα (II), m.p. 196–198° dec., alone or mixed with a sample of IIα, m.p. 196–197° dec., prepared by hydration of I according to Alder.[2] An analytical sample, m.p. 196–197° dec., was recrystallized from water. Alder[2] reports m.p. 203° dec. A mixed m.p. of IIα with III[2] of m.p. 202–202.5° was depressed to 171–184°.

Anal. Calcd. for $C_9H_{12}O_5$: C, 54.00; H, 6.04; neut. equiv., 100. Found: C, 53.73; H, 6.20; neut. equiv., 101 ± 1.

The acetate anhydride IV, prepared from synthetic IIα and acetyl chloride, had m.p. 109–110° alone or mixed with a sample prepared from IIα obtained in the hydration of I. Alder[2] reports m.p. 112°. The acetate anhydride also appears to occur as an unstable dimorph, m.p. 69–70°. This form was obtained in early preparations, but once the 110° material had been obtained, the 70° form could not be prepared again. A mixture of the 110° form with the epimeric acetate anhydride XVI[6] (*vide supra*) melted at 75–90°. An analytical sample of IV (110° form) was prepared by recrystallization from ether–hexane.

Anal. Calcd. for $C_{11}H_{12}O_5$: C, 58.92; H, 5.39. Found: C, 58.81; H, 5.46.

The methyl ester acid phthalate of IIα (II) was prepared in the following manner. Twenty grams of IIα was treated with 9.7 g. of diazomethane in 330 ml. of ether at 5°. After gas evolution ceased, the excess diazomethane was decomposed with acetic acid, the reaction mixture was dried over calcium sulfate and filtered. Evaporation of the filtrate left a thick oil which was taken up in 30 ml. of dry pyridine and treated with 14.8 g. of phthalic anhydride. The mixture was heated on the steam-bath for 4 hours, cooled, treated with 600 ml. of iced water and 22 ml. of 0.45 *N* sulfuric acid, and extracted with six portions of benzene (total 1200 ml.). The extracts were dried over calcium sulfate, filtered, evaporated, and the residue oil taken up in hot ethyl acetate–hexane. After 5 days at 5°, an oil had separated, which, upon being kept at room temperature an additional 5 days, crystallized to give 29.0 g. of **methyl ester acid phthalate**, m.p. 134–136°. A mixed m.p. with phthalic anhydride (m.p. 131°) was depressed to 103–108°. Recrystallization from ethyl acetate–hexane afforded material of m.p. 136–137°.

Anal. Calcd. for $C_{19}H_{20}O_8$: C, 60.63; H, 5.37. Found: C, 60.76; H, 5.43.

Oxidation of IIα (II) to the Ketoacid XIVb.—A solution of 0.6 g. of potassium dichromate in 6 *N* sulfuric acid was added with vigorous stirring to 0.5 g. of IIα. After 7 hours, the reaction mixture was stored at 5° for two days, and then was treated with an additional 0.2 g. of potassium dichromate and warmed intermittently to 40° during five hours.

The clear solution was extracted with twelve portions (30 ml. each) of ethyl acetate. The extract was dried over calcium sulfate, filtered and evaporated and the residue was crystallized from water to give 0.3 g. of the ketoacid XIVb, m.p. 165–166° dec. The ketoacid was converted to the characteristic oxime (*vide supra*), m.p. 255–256° dec. The infrared spectrum of the oxime (KBr disk) was identical with that of an authentic sample.

Oxidation of XVIIb to XIVb.—A solution of 1.75 g. of potassium dichromate in 40 ml. of water containing 6 g. of concentrated sulfuric acid was added in one portion with stirring to 1.5 g. of XVIIb. The temperature was held at 30–40° for 2 hours, the reaction mixture was diluted with water to a volume of 100 ml. and, after standing overnight at 5°, it was extracted with ten 45-ml. portions of chloroform. This extract gave a negligible quantity of product. The aqueous solution was further extracted with ten 45-ml. portions of ethyl acetate, the extract was dried over calcium sulfate, filtered and evaporated. The residue was crystallized from water (using charcoal) to give 1.0 g. of XIVb, m.p. 165–166° dec. This sample of ketoacid gave oxime of m.p. 257–258° dec.

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Studies of Stereospecificity in the α-Phenylethylation of Phenylacetonitrile and Phenylacetic Acid and of Epimerization of the Alkylation Products[1]

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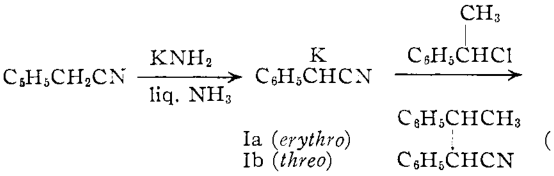
The α-phenylethylation of potassiophenylacetonitrile with α-phenylethyl chloride affords exclusively the *erythro* isomer of 2,3-diphenylbutyronitrile under certain conditions, but a mixture of the two diastereoisomers under certain other conditions. No conclusion is warranted concerning stereospecificity since relatively rapid epimerization of one or both of the diastereoisomers of the alkylation product may mask the primary reaction. Conditions were developed for effecting partial epimerization of the *erythro* or *threo* isomer and complete epimerization of the *threo* isomer. The α-phenylethylation of disodio- or dipotassiophenylacetic acid with α-phenylethyl chloride in liquid ammonia affords largely the *erythro* isomer of 2,3-diphenylbutyric acid. Since the *threo* isomer is not epimerized appreciably under similar conditions, this alkylation is considered to follow a stereospecific course. The *threo* isomer of 2,3-diphenylbutyric acid was prepared satisfactorily by the acid hydrolysis of the corresponding *threo*-nitrile.

The α-phenylethylation of phenylacetonitrile[2] and phenylacetic acid[3] with α-phenylethyl chloride has been effected recently by means of alkali amides in liquid ammonia to produce excellent yields of the *erythro* isomers[4] of 2,3-diphenylbutyronitrile[2] and 2,3-diphenylbutyric acid, respectively.

The indicated stereospecificity of these reactions as well as the possible epimerization of the diastereoisomers of the alkylation products has now been studied.

α-Phenylethylation of Phenylacetonitrile.—This reaction was effected through potassiophenylacetonitrile which was prepared by means of an equivalent of potassium amide in liquid ammonia (equation 1).



$$C_6H_5CH_2CN \xrightarrow[\text{liq. } NH_3]{KNH_2} \overset{K}{C_6H_5CHCN} \xrightarrow{C_6H_5\overset{CH_3}{\overset{|}{C}}HCl} \begin{matrix} C_6H_5CHCH_3 \\ \vdots \\ C_6H_5CHCN \end{matrix} \qquad (1)$$

Ia (*erythro*)
Ib (*threo*)

The relative proportions of the diastereoisomers of 2,3-diphenylbutyronitrile (Ia) and (Ib) afforded by this reaction are dependent on the solvents employed in the alkylation step. Thus, it was reported previously,[2] and confirmed in the present investigation, that the *erythro* isomer is obtained exclusively when the alkylation is effected in liquid ammonia containing a little ether, whereas approximately equal yields of the two isomers are realized when the reaction is carried out in ether alone. Under the former condition, the *erythro* isomer is obtained as a precipitate, while under the latter, both isomers remain in solution although a precipitate of potassium salts is present. In line with the latter result, it was found that roughly equal yields of the two isomers are also produced when the alkylation is effected in liquid ammonia containing sufficient tetrahydrofuran to keep both isomers in solution. These results are summarized in Table I.

TABLE I

DIASTEREOISOMERS OF 2,3-DIPHENYLBUTYRONITRILE FROM α-PHENYLETHYLATION OF POTASSIOPHENYLACETONITRILE

Media solvents	State of reaction mixture	Diastereoisomers, yield, % *erythro* (Ia)	*threo* (Ib)
Liq. NH_3 (little ether)	Heterogeneous[a]	99	0
Ether alone	Heterogeneous[b]	30	29
Liq. NH_3 and tetrahydrofuran	Homogeneous[b]	43	33

[a] *Erythro* isomer precipitates. [b] Both isomers remain in solution.

These results may or may not represent the proportions of the isomers produced in the alkylation step proper. Thus, the exclusive production of the *erythro*-nitrile in the first experiments in Table I might have involved the primary formation of both isomers accompanied by the complete epimerization of the *threo*-nitrile, since the latter isomer has been observed[4] to undergo such a complete epimerization under similar conditions in the presence of potassiophenylacetonitrile which is the reactive intermediate in the alkylation. Moreover, the production of the two isomers in the second and third experiments in Table I might have involved the primary formation of only the *erythro* or the *threo*

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[1] Supported by the National Science Foundation.

[2] C. R. Hauser and W. R. Brasen, THIS JOURNAL, **78**, 494 (1956).

[3] C. R. Hauser and W. J. Chambers, *ibid.*, **78**, 4942 (1956).

[4] See W. R. Brasen and C. R. Hauser, *ibid.*, **79**, 395 (1957).