The best yield of hexabenzylethane resulted when tribenzylmethyl bromide, in benzene, was acted upon by zinc. Gentle treatment at a relatively low temperature was essential. A hexanitro derivative of the desired hydrocarbon was obtained by direct nitration.

It is a pleasure to acknowledge financial aid from the Atwater Fund, and analytical assistance by Dr. Richard G. Clarke.

Experimental

Tribenzylmethyl Bromide.—Fifty grams of tribenzylcarbinol[6] was dissolved in just sufficient ether and 25 g. of phosphorus tribromide was so added that only very gentle boiling took place. Subsequently, the system was refluxed for six hours. On cooling, crystals appeared and were filtered out. Concentration of the mother liquor yielded another crop and an intractable oil. The solid product, recrystallized from ether and then from acetone, was white, melted at 158°, and weighed 33 g. The yield was 54.6%.

Anal. Calcd. for $C_{22}H_{21}Br$: Br, 21.9. Found (micro catalytic oxidation): Br, 21.79, 21.76, 21.87, 21.94.

Hexabenzylethane.—Thirty-five grams of tribenzylmethyl bromide and 18 g. of zinc dust were heated to 50° for forty-eight hours in dry benzene. The inorganic material was filtered out and the filtrate concentrated in a vacuum. The residue, a pale yellow oil, was dissolved in ether and alcohol was cautiously added until a slight permanent turbidity resulted. By seeding and standing the system yielded some very small white crystals. As concentration of the solution continued an oil, the unsaturated hydrocarbon, 2-benzyl-1,3-diphenylpropene, appeared. The solid product, separated by decantation, was recrystallized from ether and then melted at 195°. It did not contain halogen, nor did it react with a carbon tetrachloride solution of bromine or with an alkaline solution of potassium permanganate. The yield was 3 g., 5.5% of the theoretical value.

Anal. Calcd. for $C_{44}H_{42}$: C, 92.58; H, 7.42; mol. wt., 570. Found: C, 92.85, 92.79; H, 7.86, 7.34; mol. wt. (Rast method), 560, 563.

In some experiments, the unsaturated hydrocarbon was removed from the mixture of products by distillation at 5 mm. (the boiling point was 209°) and the brownish residue, less than 10% of the total product, was recrystallized. The yield of hexabenzylethane was not as large as that obtained by the other method of treatment.

Hexanitrohexabenzylethane.—To 0.8 g. of hexabenzylethane was added 8 ml. of concentrated sulfuric acid. Subsequently, 8 ml. of concentrated nitric acid was introduced carefully and the mixture refluxed for ninety minutes. After cooling, it was poured over 20 g. of cracked ice. The yellow oil, which first appeared, soon solidified. The solid was dissolved in acetone and treated with alcohol, dropwise, until a slight turbidity persisted. A yellow crystalline mass was obtained, m. p. 174–179°. The yield was not recorded.

Anal. Calcd. for $C_{44}H_{36}O_{12}N_6$: N, 10.00. Found (micro modified Kjeldahl): N, 9.94, 9.61, 9.43.

Summary

Tribenzylmethyl bromide has been prepared and converted to hexabenzylethane which in turn was characterized by nitration to a hexanitro derivative.

MIDDLETOWN, CONNECTICUT
RECEIVED FEBRUARY 10, 1941

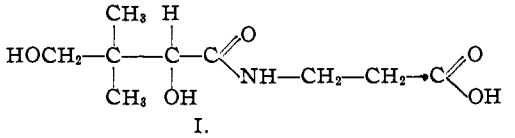
(6) Klages and Heilmann, *Ber.*, **37**, 1456 (1904).

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF MERCK & CO., INC.]

Resolution of *dl*-α-Hydroxy-β,β-dimethyl-γ-butyrolactone

BY RANDOLPH T. MAJOR AND JACOB FINKELSTEIN

In a previous publication[1] from this Laboratory, it was shown that pantothenic acid, I, consists of (+)α,γ-dihydroxy-β,β-dimethylbutyric acid and β-alanine joined through an amide linkage.



I.

The (+)α,γ-dihydroxy-β,β-dimethylbutyric acid was obtained, as previously described,[2] by resolving the racemic α-hydroxy-β,β-dimethyl-γ-butyrolactone by the application of the method of Pope and Peachey[3] involving the equilibrium of salts. In a more recent publication on this subject, Reichstein and Grüssner[4] resolved the lactone through its quinine salt by refluxing the lactone with quinine in an alcoholic solution for several hours. Although the melting point of their quinine salt is slightly lower than that re-

(1) Stiller, Keresztesy and Finkelstein, THIS JOURNAL, **62**, 1779 (1940).

(2) Stiller, Harris, Finkelstein, Keresztesy and Folkers, *ibid.*, **62**, 1785 (1940).

(3) Pope and Peachey, *J. Chem. Soc.*, **75**, 1066 (1899).

(4) Reichstein and Grüssner, *Helv. Chim. Acta*, **23**, 650 (1940).

ported from this Laboratory,[2] they succeeded, nevertheless, in preparing the salt directly.

Prior to any of these communications, it occurred to us that the resolution of the lactone could be accomplished by the use of a strong, optically active base which would readily open the lactone. This expectation was confirmed when the racemic lactone was treated with such reagents as quinine methohydroxide, quinidine methohydroxide and cinchonine methohydroxide. Each of these bases reacts in aqueous solution to form a quaternary metho salt. After concentrating *in vacuo* and recrystallizing the residue, the quaternary metho salt of the desired (+)α,γ-dihydroxy-β,β-dimethylbutyric acid was obtained in well-defined crystalline form.

The salts, using the above mentioned reagents, agreed in all their properties with the corresponding salts prepared from pure levo-rotatory α-hydroxy-β,β-dimethyl-γ-butyrolactone. They are colorless, non-hygroscopic and possess sharp melting points. The resolved lactone may be liberated from these optically pure salts by means of hydrochloric acid. After extraction with ether, purification is effected by recrystallization or distillation.

The clear colorless solutions of the above mentioned methohydroxides were obtained by shaking the corresponding methochlorides with silver oxide and filtering. The amount to be used was always freshly prepared, since, after several days, the solutions turned brown, even on exclusion of light. The freshly prepared solution was then standardized by titrating against sulfuric acid.

Commercial marketed quinine and cinchonine were found to be quite suitable for this resolution. However, commercial quinidine was contaminated with other alkaloids of the cinchona group and required purification. The purification procedure used was a combination of the methods of Thoron and Dirscherl[5] and Buttle, Henry and Travam.[6] The quinidine was separated from the di-hydro derivatives of the cinchona alkaloids by means of mercuric acetate. Then, after decomposing the derivative, the quinidine was recrystallized from alcohol until pure. The quinidine finally used had a melting point 171–172° and $(\alpha)^{26}D$ + 262.4° as compared to melting point 167–168° and $(\alpha)^{25}D$ +246.9° of the starting product.

(5) Thoron and Dirscherl, *Ann.*, **515**, 252 (1935).
(6) Buttle, Henry and Travam, *Biochem. J.*, **28**, 426 (1934).

Experimental Part

Quinine Methiodide.—To a cooled suspension of 93 g. of quinine in 100 cc. of methanol, 42 g. of methyl iodide was added. After standing overnight, the product was filtered and washed with methanol-ether (1:1) mixture and sucked dry.

Quinone Methochloride.—This compound was prepared according to the method of Jacobs and Heidelberger.[7]

Quinine Methohydroxide.—A mixture of 50 g. of quinine methochloride and 50 g. of silver oxide in 150 cc. of water was stirred in ice water for about fifteen minutes. Then, it was shaken for several hours at room temperature and filtered. The clear colorless solution had a pH > 13 and was standardized against normal sulfuric acid.

Salt from Quinine Methohydroxide and Pure Levo-rotatory α-Hydroxy-β,β-dimethyl-γ-butyrolactone.—To 1.2 g. of levo-rotatory-α-hydroxy-β,β-dimethyl-γ-butyrolactone dissolved in 3 cc. of water was added the required amount of quinine methohydroxide in aqueous solution. After standing several hours, the solution was concentrated *in vacuo* below 25° until a viscous residue was obtained. After triturating the gum with dry ether, a solid substance was obtained. This was crystallized from boiling dioxane and recovered as a colorless crystalline compound. After recrystallization from dioxane and drying at 100° in vacuum, the product was pure, m. p. 176–177°; $(\alpha)^{25}D$ −159° (*c*, 0.93%; water).

Anal. Calcd. for $C_{27}H_{38}O_6N_2$: C, 66.65; H, 7.87; N, 5.74. Found: C, 66.45; H, 7.73; N, 5.69.

Resolution of *dl*-α-Hydroxy-β,β-dimethyl-γ-butyrolactone via Quinine Methohydroxide.—Starting with 35 g. of *dl*-α-hydroxy-β,β-dimethyl-γ-butyrolactone and following the above procedure, 32 g. of crude salt is obtained. Two recrystallizations from dioxane gave the pure levo-rotatory quinine methohydroxide salt, m. p. 176-177°; $(\alpha)^{25}D$ −160.56° (*c*, 1.781%; water).

Anal. Calcd. for $C_{27}H_{38}O_6N_2$: C, 66.65; H, 7.87; N, 5.74. Found: C, 66.15; H, 7.88; N, 5.94.

A mixed melting point with compound prepared above showed no depression.

Cinchonine Methiodide.—This compound was prepared following the method of Stahlschmidt and Plettenberg.[8]

Cinchonine Methochloride.—The methochloride was prepared from the iodide, as above.

Cinchonine Methohydroxide.—The methohydroxide was prepared from the methochloride and silver oxide following the procedure outlined above for quinine methohydroxide.

Salt from Cinchonine Methohydroxide and Pure Levo-rotatory α - Hydroxy - β,β - dimethyl - γ - butyrolactone.—Five cc. of a solution of 1.05 g. of levo-rotatory α-hydroxy-β,β-dimethyl-γ-butyrolactone was mixed with cinchonine methohydroxide solution and kept overnight in a dark place. During this time, the pH changed from above 10 to about 6. The solution was then concentrated *in vacuo* at about 30° until all the water had been removed, whereupon a reddish-brown semi-solid residue was obtained. Upon triturating with dry ether, the product

(7) Jacobs and Heidelberger, THIS JOURNAL, **41**, 2090 (1919).
(8) Stahlschmidt and Plettenberg, *Ann.*, **90**, 218 (1854).

solidified completely. It was filtered and washed with ether yielding 36 g. of moist material. The product was then recrystallized several times by dissolving in a minimum amount of absolute alcohol and adding just enough dry ether to cause a slight turbidity. On standing, clusters of fine, colorless needles were formed. The crystals were filtered and dried at 100° in vacuum, m. p. 189–190°; $(\alpha)^{25}D$ + 179.5° (*c*, 0.791%: water).

Anal. Calcd. for $C_{26}H_{36}O_5N_2$: C, 68.39; H, 7.95; N, 6.13. Found: C, 68.55; H, 8.12; N, 6.27.

Resolution of *dl*-α-Hydroxy-β,β-dimethyl-γ-butyrolactone via Cinchonine Methohydroxide.—Starting with 12 g. of *dl*-α-hydroxy-β,β-dimethyl-γ-butyrolactone and following the above procedure using cinchonine methyl hydroxide, 27 g. of a crude white powder was obtained. After several recrystallizations from absolute alcohol and anhydrous ether, the product had a constant melting point at 188–189°, and a constant rotation; $(\alpha)^{31}D$ + 176.4° (*c*, 0.36%; water).

Anal. Calcd. for $C_{26}H_{36}O_5N_2$: C, 68.39; H, 7.95; N, 6.13. Found: C, 68.35; H, 8.05; N, 6.08.

Separation of Pure Quinidine and Dihydroquinidine from Commercial Quinidine.—The starting product called quinidine was a colorless, crystalline product, melting point 168° and $(\alpha)^{26}D$ + 246.9°.

A solution of 420 g. of quinidine was prepared by dissolving in 254 g. of concentrated sulfuric acid diluted with 600 cc. of water. To this solution, 589 g. of mercuric acetate in 3000 cc. of 10% acetic acid was added and the reaction mixture heated at 40–50° for four hours. After cooling, and while stirring in ice–salt mixture, 1100 cc. of concentrated ammonia was slowly added until the solution was alkaline to phenolphthalein. Then, while continuing the stirring, ammonia gas was added until the *p*H was about 9.5–10. This ammoniacal solution produced a white precipitate. The precipitate, extracted with chloroform, was dried over sodium sulfate and later worked up to obtain the dihydroquinidine.

The extracted solution was then filtered from the small amount of flocculent material. The clear filtrate was acidified by the slow addition of dilute sulfuric acid with efficient cooling to prevent any rise in temperature. Afterward 675 g. of phosphorous acid (1.12) was added and the solution heated to boiling where it was maintained for about one hour. During this operation, the solution turned dark gray and mercury was deposited. After cooling and filtering, the filtrate was made alkaline with concentrated ammonia, with cooling by stirring in an ice–salt-bath. The white precipitate which formed was extracted with chloroform. The extract was dried over sodium sulfate and treated with Norit until colorless. After removing the solvent on steam-bath, a very viscous product, which crystallized on cooling, was obtained. This product was dissolved in 500 cc. of boiling 95% alcohol. On cooling, the alkaloid crystallized in the form of colorless needles. The dried product was then recrystallized by refluxing 185 g. with 600 cc. of absolute alcohol for about forty-five minutes and filtering from the undissolved crystals. On standing, the clear filtrate deposited colorless needles of pure quinidine. The product was filtered, washed with ethanol, and dried *in vacuo* at 110°; m. p. 171–172°; $(\alpha)^{26}D$ + 262.4° (*c*, 0.61%; alcohol).

The chloroform extract which contains the dihydroquinidine was dried over sodium sulfate and concentrated. This yielded 62 g. of product which was recrystallized several times from alcohol to obtain clusters of colorless crystals. The product was dried in an oven at 115°; m. p. 167–168°; $(\alpha)^{26}D$ +230.84° (*c*, 0.699%; alcohol).

Quinidine Methiodide.—A solution of 169 g. of quinidine in 5 liters of methanol was prepared by heating on the steam-bath. When the temperature cooled to about 49°, 85 g. of methyl iodide was added. After stirring to mix intimately, the flask was well stoppered and kept at room temperature. The stopper must be very secure because the reaction mixture warms up on standing. After twenty-four hours, the solution was concentrated to about 400 cc. Crystallization set in and when the flask was cooled, the contents turned completely solid. The product was filtered and washed with a small amount of methanol and ether. Then, it was recrystallized from hot water and treated with Norit. Long silky needles separated on cooling, and were dried at 115° for two hours.

Quinidine Methochloride.—This compound was prepared from quinidine methiodide according to the method of Jacobs and Heidelberger.[7] It was recrystallized several times from alcohol–ether mixture and dried at 115°; m. p. 236–237°; $(\alpha)^{25}D$ + 257.9° (*c*, 0.8764%; H_2O).

Anal. Calcd. for $C_{21}H_{27}N_2Cl \cdot H_2O$: C, 64.19; H, 7.44; N, 7.13; Cl, 9.03. Found: C, 64.16; H, 7.15; N, 7.13; Cl, 9.09.

Salt from Quinidine Methohydroxide and Pure Levorotatory α-Hydroxy-β,β-dimethyl-γ-butyrolactone.—To 1.1 g. of levo-rotatory α-hydroxy-β,β-dimethyl-γ-butyrolactone in 5 cc. of water, a solution containing the equivalent amount of quinidine methohydroxide was added. After standing overnight at room temperature, the *p*H changed from about 10 to 7.3. The solution was concentrated in vacuum at 35° until a brownish, hard, but brittle, amorphous product was obtained.

The product was triturated with a small amount of ethyl acetate until the product seemed to be crystalline. The product was then recrystallized from alcohol–ether mixture several times until the substance was obtained in clusters of fine needles, m. p. 153–154°; $(\alpha)^{24}D$ + 213.91° (*c*, 0.4884%; water).

Anal. Calcd. for $C_{27}H_{36}O_6N_2$: C, 66.64; H, 7.87. Found: C, 66.53; H, 8.06.

Resolution of *dl*-α-Hydroxy-β,β-dimethyl-γ-butyrolactone via Quinidine Methohydroxide.—An aqueous solution of 8.2 g. of racemic α-hydroxy-β,β-dimethyl-γ-butyrolactone and a solution of quinidine methohydroxide reacted as above. The first treatment with alcohol–ether mixture gave an oily product which solidified on long standing in the ice chest. This solidified product was then dissolved in a small amount of ethyl acetate and treated with ether until a faint cloud formed. After standing in the ice chest for two days, small needles separated from solution. More ether was then added until another faint cloud formed. This also cleared up as a result of further crystallization during standing in the refrigerator. This process of fractional crystallization was continued until further cloudiness could not be effected by ether. The crystals were filtered, washed with ether, and dried at 100° in

vacuum. This drying is necessary, otherwise, a hygroscopic product is obtained. Further crystallization was performed by using absolute alcohol–ether mixture (1:10). After filtering, the product was dried at 100° and 1 mm., m. p. 152–153°; $(\alpha)^{25}D + 210.22°$ (c, 0.7064%; water).

Anal. Calcd. for $C_{27}H_{36}O_6N_2$: C, 66.64; H, 7.87; N, 5.76. Found: C, 66.41; H, 7.63; N, 5.69.

Summary

A novel application of an optically active quaternary ammonium hydroxide for resolution purposes has been demonstrated by separating the levo-rotatory α-hydroxy-β,β-dimethyl-γ-butyrolactone from its enantiomorph.

RAHWAY, NEW JERSEY RECEIVED MARCH 5, 1941

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF WASHINGTON]

Inner Complexes of Phenylazo-phenanthrol, -retenol, and -chrysenol

BY HELMUT M. HAENDLER AND GEORGE MCP. SMITH

The product formed by the action of phenylhydrazine on 9,10-phenanthrenequinone was first reported as the phenylhydrazone by Zincke,[1] and the analogous retenequinone compound was also reported as the phenylhydrazone by Bamberger and Grob.[2] "Phenanthrenequinone phenylhydrazone" was later characterized by Auwers[3] as an *o*-hydroxy azo compound on the basis of its chemical reactions, particularly those with acyl phenylhydrazines. More recently, Auwers[4] has summarized the evidence for the formulation of this type of compound as an ortho-hydroxy azo type.

Consequently, in connection with our recently published work on the inner complexes of ortho-hydroxy azo dyes,[5] it was decided to study the possible formation of copper inner complexes of phenyl-azo-phenanthrol, -retenol, and -chrysenol as compared to the previously prepared inner complexes of the naphthol series. Comparison of absorption spectra of both organic compounds and inner complexes should serve as further evidence for the existence of the ortho-hydroxy azo form.

Comparison of the spectra (Fig. 1) of phenylazophenanthrol, phenylazoretenol, phenylazochrysenol and their copper inner complexes with the spectra of 1-phenylazo-2-naphthol and its copper inner complex indicated strongly that all the organic compounds and complexes were structurally similar to those reported.[5] The structure thus appears to be, in all probability, the *o*-hydroxy azo type rather than the quinone phenylhydrazone type. In addition, the chemical and physical behavior of compounds and complexes is extraordinarily similar in both series.

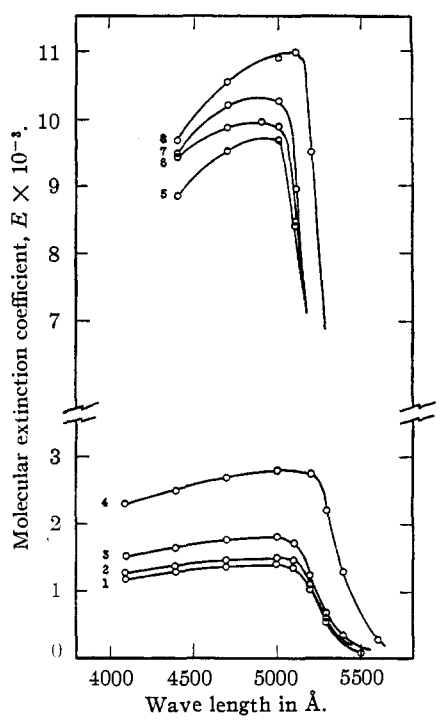


Fig. 1.—Absorption spectra of: 1, 1-phenylazo-2-naphthol; 2, 9-phenylazo-10-phenanthrol; 3, 9(10)-phenylazo-10(9)-retenol; 4, 5(6)-phenylazo-6(5)-chrysenol; 5, 1-phenylazo-2-naphtholato-copper; 6, 9-phenylazo-10-phenanthrolato-copper; 7, 9(10)-phenylazo-10(9)-retenolato-copper; 8, 5(6)-phenylazo-6(5)-chrysenolato-copper.

Experimental

9-Phenylazo-10-phenanthrol.—The azo compound was prepared from phenanthrenequinone and phenylhydrazinium chloride by the method of Auwers[3]; m. p. 162°.

9(10)-Phenylazo-10(9)-retenol.—This had been prepared originally by the violent reaction between phenylhydrazine and retenequinone,[2] but the following modification was found more satisfactory. To a solution of 5.25

(1) Zincke, *Ber.*, **16**, 1564 (1883).
(2) Bamberger and Grob, *ibid.*, **34**, 539 (1901).
(3) Auwers, *Ann.*, **378**, 214 (1911).
(4) Auwers, *ibid.*, **505**, 283 (1938).
(5) Haendler with Smith, THIS JOURNAL, **62**, 1669 (1940).