

naphthyl, 18; *p*-tolyl, 15; *p*-biphenyl, 11.5; *p*-isopropylphenyl, 9; *p*-ethylphenyl, 5; *m*-tolyl, 1.95; *p*-fluorophenyl, 1.85; *p*-iodophenyl, 1; phenyl, 1; *p*-bromophenyl, 0.71; *p*-chlorophenyl, 0.66; *m*-methoxyphenyl, 0.2; *o*-tolyl, *o*- and *m*-bromophenyl and *o*- and *m*-chlorophenyl, very small. It should be noted that the series of migration aptitudes coincides well with a similar series of affinity capacities of the same groups; this is in harmony with the observation of Tiffeneau and Orekhoff that the groups that have the greatest affinity capacity migrate most easily.

Summary

A number of pinacols have been prepared by the reaction of Gomberg and Bachmann and a study has been made of the equilibrium mixture, ketyl \rightleftharpoons pinacolate, which is found in each case.

Twelve pinacols have been subjected to the pinacol-pinacolin rearrangement and a comparison of the migration aptitudes of the phenyl, *p*-tolyl, *p*-biphenyl, anisyl, *o*-tolyl, *m*-tolyl and *p*-chlorophenyl groups has been obtained.

The migration aptitudes of a group in a symmetrical benzopinacol has been shown to be a property characteristic of that group and is not dependent on the particular pinacol in which it is found.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

OXIDATION OF UNSATURATED COMPOUNDS. VI. SYNTHESIS OF 3-BROMOTHREONIC ACID. SUPPLEMENT TO THE PROOF OF CONFIGURATION OF *dl*-1,2-DIHYDROXYBUTYRIC ACIDS

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In a recent publication of this series the proof of configuration of *dl*-1,2-dihydroxybutyric acids was presented.² The proof was based on the fact that the 3-chlorothreonic acid could be converted into racemic tartaric acid and on the other hand it could be reduced to the *dl*-1,2-dihydroxybutyric acid (m. p. 74°), which shows clearly that the *dl*-1,2-dihydroxybutyric acid (m. p. 74°) has the same configuration as the racemic acid. It was thought necessary to complete this proof with the reactions of 3-bromothreonic acid, and the results of this investigation are reported in the present paper.

I. Synthesis of 3-Bromothreonic Acid.—The 3-bromothreonic acid is prepared by the oxidation of 3-bromocrotonic acid³ with osmic acid activated barium chlorate in the same manner as was reported in the case of 3-chlorocrotonic acid.² The 3-bromothreonic acid hydrolyzes gradually in

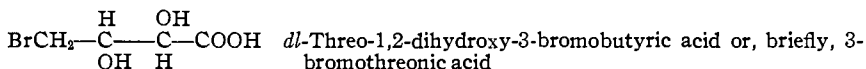
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² Géza Braun, *THIS JOURNAL*, **52**, 3176 (1930).

³ Géza Braun, *ibid.*, **52**, 3167 (1930).

aqueous solution; therefore care should be taken to protect it from the prolonged action of water. It is advisable to carry out the oxidation of 3-bromocrotonic acid in a minimum amount of water and, after the oxidation is completed, the 3-bromothreonic acid is best isolated by pouring the aqueous solution into a large amount of ether and then drying the solution completely with anhydrous sodium sulfate. The 3-bromothreonic acid is obtained then from the ethereal solution with 70% yield, whereas if the water is removed at reduced pressure in the usual manner, the yield is considerably lower.

According to analysis the hydroxylated product corresponds to a formula $C_4H_7O_4Br$. Its configuration was proved by conversion into racemic tartaric acid with dilute nitric acid. The acid can be directly oxidized with nitric acid; however, the oxidation is very slow and incomplete. It was found to be best to remove the bromine with silver acetate at first and then oxidize the resulting product with nitric acid. The oxidation yielded, except for a small amount of oxalic acid, exclusively racemic tartaric acid; therefore the compound has the same configuration as the racemic acid



The 3-bromothreonic acid has properties similar to those of 3-chlorothreonic acid, only its halogen is much more reactive, as would be expected. It precipitates sodium bromide from an acetone solution of sodium iodide and it seems to be converted into 3-iodothreonic acid by this process; but the crystalline 3-iodothreonic acid could not be isolated.

II. Reduction of 3-Bromothreonic Acid.—This was carried out in both acid and alkaline solutions, but it was possible to isolate the *dl*-1,2-dihydroxybutyric acid (m. p. 74°)—as a result of the reduction—only in alkaline solution. In acid solution there seems to be an hydrolysis rather than reduction, as for instance in case of reduction with zinc in 50% acetic acid the result of reduction is a lactone with a molecular weight of 118, which corresponds to the molecular weight of the lactone of threonic acid.

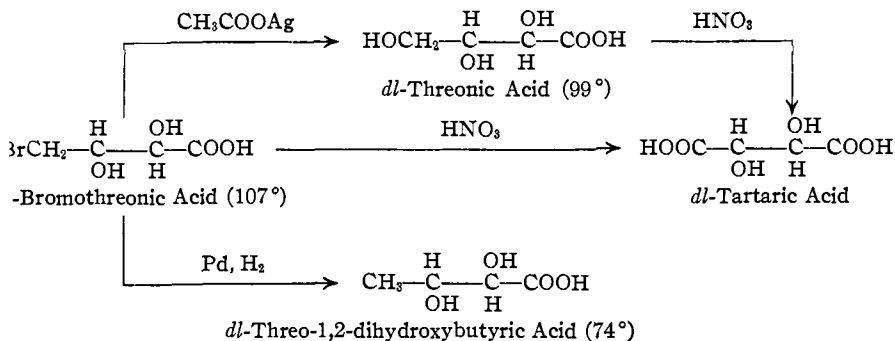
When the sodium 3-bromothreonate was reduced with palladium-activated hydrogen the reduction product showed some crystallization, after it was seeded with the crystals of *dl*-1,2-dihydroxybutyric acid (m. p. 74°), but no definite compound could be isolated. The sirupy acid according to titration had a molecular weight of 126. These experiments in acid solution show that the carboxyl group was not involved in the reduction.

The reduction of 3-bromothreonic acid in alkaline solution proceeds just as well as in the case of 3-chlorothreonic acid. The result of the reduction is the *dl*-1,2-dihydroxybutyric acid (m. p. 74°) with 70% yield.

III. *dl*-Threonic Acid.—The 3-bromothreonic acid is easily converted into *dl*-threonic (m. p. $98\text{--}99^\circ$) by treatment with silver acetate in aqueous

solution. This method, working in 10–20 g. lots, gives the threonic acid—also in the case of 3-chlorothreonic acid—in about 60% yield and is to be preferred to the previously published method through the barium salt with silver oxide.

A brief summary of the reactions carried out is given below



Experimental Part

3-Bromocrotonic acid (m. p. 74°) was prepared from 2-hydroxy-3-bromo-*n*-butyronitrile as it was previously reported.³

3-Bromothreonic Acid.—Twenty-five grams of 3-bromocrotonic acid (m. p. 74°) was suspended (partially dissolved) in 200 cc. of ice water which contained 20 cc. of 1% osmic acid solution and 11 g. of barium chlorate and this solution was kept in ice water under frequent shaking. In about seven hours at 2–3° all of the acid went into solution, whereupon the reaction mixture was allowed to warm up to room temperature. The oxidation was complete in twenty hours; the acidity of the solution corresponded to 24.5 g. of 3-bromocrotonic acid. Then the osmic acid was extracted several times with benzene, the aqueous solution poured into 1.5 liters of ether and the mixture dried with anhydrous sodium sulfate (about 900 g.). After removal of solids the ethereal filtrate was completely dried and finally the pure ethereal solution concentrated to dryness at reduced pressure. The pale yellow residue, which soon solidified to a hard crystalline mass, weighed 26.5 g. or 85% of the theoretical. This was dissolved in a mixture of 20 cc. of ethyl acetate and 10 cc. of chloroform and cooled to –10°: 18.0 g. of crystals, m. p. 105°. The mother liquor gave in a similar manner 2.2 g. of crystals; the concentrated final mother liquor still deposited 0.8 g. of crystals overnight, making a total yield of 21.0 g., or 70% of the theoretical.

Recrystallization from 30 cc. of warm ethyl acetate and 10 cc. of warm chloroform yielded 17.0 g. of crystals (m. p. 107°) in ice.

Titration. Subs., 0.5626, 0.4432: 28.35, 22.30 cc. of 0.1 *N* alkali at room temp.; 28.35, 22.24 cc. of 0.1 *N* alkali and 28.1, 22.25 cc. of 0.1 *N* silver nitrate solution for organically bound bromine after saponification on the water-bath for fifteen minutes. Calcd. for C₄H₇O₄Br: mol. wt., 198.98; Br, 40.16. Found: mol. wt., 198.55, 198.7; Br, 39.92, 40.17.

Anal. Subs., 0.5626, 0.4432: AgBr, 0.5300, 0.4136. Calcd. for C₄H₇O₄Br: Br, 40.16. Found: Br, 40.09, 39.72.

Oxidation of 3-Bromothreonic Acid with Nitric Acid

(a) **Direct Oxidation.**—One gram of 3-bromothreonic acid was dissolved in 20 cc. of nitric acid (sp. gr. 1.21) and heated for seventy-two hours at 56°, *i. e.*, until the evolu-

tion of brown gases ceased. The hydrogen bromide was precipitated with silver acetate (0.45 g. of silver bromide was obtained, about 25% of the theoretical) and then the nitric acid was removed at reduced pressure and the crystalline residue converted into potassium acid tartrate in the usual manner. Only 0.1 g. of potassium acid tartrate was isolated. This was recrystallized from water and titrated: 0.050 g. required 2.62 cc. of 0.1 *N* NaOH. Calcd. mol. wt. for $C_4H_5O_6K$: 188.1. Found: 190.1.

(b) Two grams of 3-bromothreonic acid was dissolved in 50 cc. of water and after addition of 4 g. of silver acetate the mixture was shaken at room temperature for about twenty hours. After removal of silver bromide (1.9 g.) and excess silver acetate, the pure filtrate was concentrated to dryness at reduced pressure and the residue oxidized with 10 cc. of nitric acid (sp. gr. 1.21) in the usual manner. The crystalline oxidized product gave 1.0 g. of recrystallized potassium acid tartrate (dried at 100°).

Titration. Subs., 0.5158: 27.2 cc. of 0.1 *N* of alkali. Calcd. mol. wt. for $C_4H_5O_6K$: 188.1. Found: mol. wt., 189.6.

The filtrate of potassium acid tartrate gave some calcium oxalate, but no meso-tartaric acid was found.

Reduction of 3-Bromothreonic Acid

(a) **With Zinc in Acetic Acid.**—Two grams of 3-bromothreonic acid was dissolved in 40 cc. of 50% acetic acid and under violent stirring 6 g. of zinc dust was added, in two lots, at 75°. In two and one-half hours the organic bromine was completely ionized, whereupon the hydrogen bromide was precipitated with a slight excess of silver acetate. Then the excess silver and zinc were precipitated with hydrogen sulfide and the filtrate of the sulfides was concentrated at reduced pressure. The residue was dissolved in water, concentrated again at reduced pressure and this operation repeated until the acetic acid was completely removed. The residue, 0.8 g. of pale yellow sirup, could not be crystallized.

Titration. Subs., 0.1700: 2.0 cc. of 0.1 *N* alkali at room temperature and 12.35 cc. of 0.1 *N* alkali after fifteen minutes' heating on the water-bath. Calcd. mol. wt. for threonic lactone, $C_4H_6O_4$: 118. Found: mol. wt., 118.4.

(b) **Reduction of 3-Bromothreonate.**—Two grams of 3-bromothreonic acid was dissolved in 40 cc. of water, the solution cooled in a freezing mixture until much ice appeared and then neutralized with 10 cc. of 1 *N* alkali. After addition of 5.0 g. of palladium-norit (corresponding to 0.25 g. of palladium), the mixture was shaken in a hydrogen atmosphere. The reduction proceeded rapidly at the beginning but soon stopped and started again only after neutralization of the acid formed. Altogether 225 cc. of hydrogen was consumed and 10 cc. of 1 *N* alkali used for neutralization. The solution was then filtered, and to the filtrate, which contained the theoretical amount of sodium bromide, 9 cc. of 1 *N* sulfuric acid was added and the reduction product isolated in the usual manner. About 1.0 g. of sirup was obtained, which showed some crystallization after it was seeded with the crystals of *dl*-1,2-dihydroxybutyric acid (m. p. 74°), but the amount of crystals was negligible.

Titration. Subs., 0.1700: 9.0 cc. of 0.1 *N* alkali at room temperature and 4.5 cc. after fifteen minutes' heating on the water-bath. Calcd. mol. wt. for dihydroxybutyric acid, $C_4H_8O_4$: 120. Found: mol. wt., 126.

(c) **Reduction in Alkaline Solution.**—Two grams of 3-bromothreonic acid was dissolved in 40 cc. of water, the solution cooled until much ice appeared and then 20 cc. of 1 *N* alkali and 5 g. of palladium-norit (0.25 g. of palladium) were added. Then the mixture was again cooled in ice and salt until almost solidified and was violently shaken in a hydrogen atmosphere, while the temperature was kept around 0° for about half an

hour. In about three hours 320 cc. of hydrogen was consumed and the reduction was complete.

After addition of 9 cc. of 1 *N* sulfuric acid the reaction mixture was worked up in the usual manner. There was obtained 0.85 g. of a pale yellow sirup (70% of the theoretical) which soon solidified to a hard crystalline mass. This gave 0.5 g. of crystals, m. p. 73–74°, from ethyl acetate. The mixed melting point with the *dl*-1,2-dihydroxybutyric acid (m. p. 74°) was 74°.

Titration. Subs., 0.1360: 11.02 cc. of 0.1 *N* alkali. Calcd. mol. wt. for $C_4H_8O_4$: 120. Found: mol. wt., 123.

dl-Threonic Acid.—Two grams of 3-bromothreonic acid was dissolved in 100 cc. of water and after addition of 4 g. of silver acetate the mixture was shaken at room temperature for fifteen hours. The reaction was complete by this time. To the filtrate of the silver salts 150 cc. of 0.2 *N* barium hydroxide was added and the silver oxide removed by filtration. Then the alkaline solution was heated at 75° for ten minutes and afterward allowed to stand overnight. From the filtrate of an unidentified barium salt the barium was quantitatively removed by sulfuric acid and then the clear filtrate concentrated at reduced pressure to a thick sirup. This was dissolved in a warm mixture of absolute alcohol and acetone, the clear solution poured off and concentrated at reduced pressure. The residue, about 1.1 g., soon solidified to a hard crystalline mass, which gave 0.3 g. of crystals, m. p. 99°, from acetone. A mixed melting point with *dl*-threonic acid of known purity (m. p. 98–99°) was 98–99°.

Titration. Subs., 0.1793: 13.00 cc. of 0.1 *N* alkali at room temperature and 0.07 cc. of 0.1 *N* alkali at 80°, total 13.07 cc. Calcd. for $C_4H_8O_5$: mol. wt., 136.06. Found: mol. wt. 137.1.

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Summary

1. The oxidation of 3-bromocrotonic acid (m. p. 74°) with barium chlorate is reported. The oxidation yields the *dl*-threo-1,2-dihydroxy-3-bromobutyric acid (m. p. 107°) in 70% yield. The configuration of the hydroxylated product was proved by its conversion into racemic tartaric acid by direct and indirect oxidation with nitric acid.

2. Treatment of *dl*-threo-1,2-dihydroxy-3-bromobutyric acid with silver acetate gives the *dl*-threonic acid in good yield.

3. The reduction of *dl*-threo-1,2-dihydroxy-3-bromobutyric acid with palladium-activated hydrogen gives the *dl*-threo-1,2-dihydroxybutyric acid (m. p. 74°) in 70% yield.

These results confirm that the *dl*-1,2-dihydroxybutyric acid (m. p. 74°) has the same configuration as racemic tartaric acid and consequently the *dl*-erythro-1,2-dihydroxybutyric acid (m. p. 81.5°) has a configuration corresponding to mesotartaric acid.