[Contribution from the Kent Chemical Laboratory, University of Chicago]

OXIDATION OF UNSATURATED COMPOUNDS. II. PREPARATION AND CONFIGURATION OF THE 3-HALOGENO DERIVATIVES OF CROTONIC ACID

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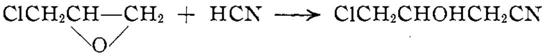
In the first publication of this series[2] the oxidation of crotonic and isocrotonic acids with chlorates and perbenzoic acid was reported. There is no known method for the establishment of the configurations of the *dl*-1,2-dihydroxybutyric acids which resulted. However, the results which were obtained were so harmonious that it was possible to assign configurations to these acids with a considerable degree of assurance. For the purpose of the exact chemical proof of configuration it would be necessary to convert these compounds into the tartaric acids in such a way that no change of configuration could take place during these operations. Unfortunately these changes could not be accomplished by direct oxidation of the dihydroxybutyric acids with dilute nitric acid because the methyl group is completely eliminated in the oxidation. It seemed therefore to be necessary to synthesize compounds having a substituent in the methyl group—these would be the derivatives of threonic and erythronic acids—the configurations of which could be shown by oxidation to the tartaric acids. Their relationship to the dihydroxybutyric acids on the other hand could be demonstrated by reduction. For this indirect proof of configuration only the 3-halogeno derivatives of threonic and erythronic acids could come into consideration, making a connection between the tartaric and 1,2-dihydroxybutyric acids.

These halogeno-tetronic acids are as yet unknown. For their synthesis the oxidation of the corresponding 3-halogeno-crotonic acids seemed to offer the most practicable method, and it became necessary therefore to study the preparation and properties of these unsaturated acids.

I. Preparation of 3-Chlorocrotonic Acid

This acid was first prepared by Lespieau[3] by means of the operations indicated



$$ClCH_2\underset{\diagdown O \diagup}{CH-CH_2} + HCN \longrightarrow ClCH_2CHOHCH_2CN \qquad (1)$$

$$ClCH_2CHOHCH_2CN \xrightarrow[\text{in alc.}]{HCl} ClCH_2CHOHCH_2COOC_2H_5 \qquad (2)$$

$$ClCH_2CHOHCH_2COOC_2H_5 \xrightarrow{P_2O_5} ClCH_2CH{=}CHCOOC_2H_5 \qquad (3)$$

$$ClCH_2CH{=}CHCOOC_2H_5 \xrightarrow{KOH} ClCH_2CH{=}CHCOOH \qquad (4)$$

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[1] International Research Fellow in Organic Chemistry from Hungary, 1926–1928.

[2] Géza Braun, This Journal, **51**, 228 (1929).

[3] Lespieau, *Bull. soc. chim.*, [3] **33**, 466 (1905).

These reactions are described by Lespieau only in a general way. The yields must have been rather low but, because all the operations involved are of general interest in the field of preparative organic chemistry, it was decided to study and, if necessary, modify the original procedure to improve the yield. A new process is reported which makes it possible to obtain the 3-chlorocrotonic acid from the 2-hydroxy-3-chloro-*n*-butyronitrile in 32% yield.

(1) **2-Hydroxy-3-chloro-*n*-butyronitrile.**—Lespieau's[3,4] original method has the great disadvantage that the handling of anhydrous hydrogen cyanide above its boiling point is very inconvenient. The new procedure avoids this; it involves the treatment of dichlorohydrin with sodium cyanide in aqueous suspension. The desired product is separated from the dinitrile, which is formed to some extent, by fractionation and is obtained in 25% yield.

(2) **Ethyl 2-Hydroxy-3-chlorobutyrate.**—The ester was prepared by treatment of the nitrile with dry hydrogen chloride in absolute alcohol according to Stieglitz and Carr[5] but without the isolation of the pure imino-ester hydrochloride. The yield of pure ester was as high as 80–85% of the theoretical.

(3) **Ethyl 3-Chlorocrotonate.**—In the preparation of this ester the best results were obtained when only 70% of the theoretical amount of phosphorus pentoxide was used for the dehydration of ethyl 2-hydroxy-3-chlorobutyrate. The purified reaction product was obtained in good yield (62.5%), but it proved to be a mixture of unsaturated halogeno esters; saponification yielded two isomeric halogeno acids. There are two possibilities in the dehydration of ethyl 2-hydroxy-3-chlorobutyrate: the reaction may involve carbon atoms 2 and 1 or carbon atoms 2 and 3, yielding ethyl 3-chlorocrotonate, $CH_2ClCH{=}CHCOOC_2H_5$, or ethyl 3-chloro-vinylacetate, $ClHC{=}CHCH_2COOC_2H_5$, respectively. There is also a possibility of the formation of ethyl 3-chloro-isocrotonate but the formation of this under the conditions is very improbable. It was estimated on the basis of the saponification results that the ester mixture contained about 80% of ethyl 3-chlorocrotonate.

(4) **Saponification of the Unsaturated Esters.**—This is the most delicate step in the synthesis. The esters are very resistant toward hydrolysis by acids. The saponification proceeds rapidly in alkaline solution but extreme care must be taken to protect the organic halogen. It was found that barium hydroxide below 0° gives excellent results. The 3-chlorocrotonic acid (m. p. 83°) is obtained in high yield and it is possible to isolate from the mother liquor an isomeric unsaturated halogeno acid of m. p. 10° (very probably the 3-chloro-vinylacetic acid). A study of this acid is in progress.

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[4] See also Hörmann, *Ber.*, **12,** 23 (1879).

[5] Carr, Doctor's Dissertation, University of Chicago, **1910.**

The barium hydroxide method may also be used in the saponification of ethyl 3-bromo- and ethyl 3-iodocrotonates; the yields of the pure acids are over 50% of the theoretical.

II. The Preparation of 3-Bromo- and 3-Iodocrotonic Acids

(1)**The 3-Bromocrotonic acid** was prepared in essentially the same manner as the 3-chlorocrotonic acid. The preparation of the dibromohydrin, which is the starting material in the preparation of 3-bromocrotonic acid, has been greatly improved. It is possible to obtain it now from glycerin in 54% yield, while the original method of Aschan[6] gave only 12% and Lespieau's method[7] about 21%. The purity of the product obtained was controlled by its conversion into epibromohydrin according to Fourneau and Tiffeneau.[8]

(2) **3-Iodocrotonic Acid.**—The preparation of this acid is based on the fact that the 3-chlorocrotonic acid precipitates sodium chloride from an acetone solution of sodium iodide and the chloro acid is converted into 3-iodocrotonic acid by this process. The same reaction may be carried out with the 3-bromocrotonic acid, when the sodium bromide precipitates instantaneously. The yields of 3-iodocrotonic acid are in both cases almost quantitative.

The ethyl 3-iodocrotonate is obtained from ethyl 3-chlorocrotonate by the procedure described above in good yield.

Thus three 3-monohalogeno derivatives of crotonic acid are known. The bromo has the lowest (74°), the iodo the highest 108.5°), and the chloro an intermediate (83°) melting point.

III. Configuration of 3-Halogeno-crotonic Acids

The 3-chlorocrotonic acid may be reduced with palladium-activated hydrogen in alkaline solution to crotonic acid according to Rosenmund and Zetzsche. This shows clearly that the 3-chlorocrotonic acid belongs to the crotonic acid series and has the *trans* configuration according to Auwers and Wissebach.[9] It is a remarkable fact that the reduction of 3-bromocrotonic acid proceeds much more slowly and the 3-iodocrotonic acid not at all under the conditions in which the 3-chlorocrotonic acid is easily reducible. This will be the subject of a future study.

The relationship between these halogeno-crotonic acids is shown by converting the 3-chloro- and 3-bromocrotonic acids into the 3-iodocrotonic acid in an acetone solution of sodium iodide, proving that all these acids have the *trans* configuration.

The preparation of 3-chlorocrotonic acid was attempted by the partial

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[6] Aschan, *Ber.*, **23**, 1826 (1890).

[7] Lespieau, *Ann. chim.*, [7] **11**, 236 (1897).

[8] Fourneau and Tiffeneau, *Compt. rend.*, **140**, 1595 (1905).

[9] Auwers and Wissebach, *Ber.*, **56**, 715 (1923).

reduction of Auwers' 3,3-dichlorocrotonic acid.[10] Unfortunately no definite compound could be isolated directly from the reduction product. However, when the crude product was treated with sodium iodide in acetone solution, the pure 3-iodocrotonic acid was isolated, which could have been derived only from the 3-chlorocrotonic acid. This established the fact that the 3-chlorocrotonic acid is an intermediate product in the reduction of 3,3-dichlorocrotonic acid to crotonic acid.

In the preparation of the 3,3-dichlorocrotonic acid the yields were invariably as high as 80–85%, whereas Auwers reports only 50–60%. The improvement is probably due to the fact that zinc was added during the reduction very slowly under violent stirring, so the possibility of local overheating was reduced to a minimum.

Experimental Part

I. Preparation of 3-Chlorocrotonic Acid

(1) **2-Hydroxy-3-chlorobutyronitrile.**—(a) A mixture of 500 g. of epichlorohydrin and 145 g. of anhydrous hydrogen cyanide was heated in a dilute sodium hydroxide bath to 75–85° in a thick-walled pyrex tube for ninety hours. The yield after two fractional distillations was 420 g. of nitrile, b. p. 138–142° at 14 mm., or 65%.

(b) **From Dichlorohydrin.**—Three hundred grams of dichlorohydrin was suspended in 500 cc. of water and, under violent stirring, 100 g. of sodium cyanide was added in the course of about twenty minutes at 60°. The temperature was then gradually raised to 100° in about two hours. The water and unchanged dichlorohydrin were now removed at reduced pressure and the residue dissolved in alcohol–ether mixture. The filtrate from the sodium chloride was concentrated at reduced pressure, the residue dissolved in ether and the ethereal solution fractionated; the yield was 60 g. of nitrile, b. p. 138–142° at 14 mm., or 25% of the theoretical on the basis of sodium cyanide. This product may be used in the preparation of 3-chlorocrotonic acid. For analysis it was redistilled at 2 mm. pressure (b. p. 110–112°).

Anal. Subs., 0.5050, 0.5863: AgCl, 0.5888, 0.6854. Calcd. for C_4H_6ONCl: Cl, 29.67. Found: Cl, 28.84, 28.92.

The residue from the above nitrile was distilled further at 2 mm. pressure; 30 g. of a viscous, yellow sirup, b. p. 160–180°, was obtained. This was not investigated at the time.

(2) **Ethyl 2-Hydroxy-3-chlorobutyrate.**—Five hundred grams of 2-hydroxy-3-chlorobutyronitrile (from epichlorohydrin) was dissolved in 260 cc. of absolute alcohol and 500 cc. of dry ether, the mixture cooled to −15° and slowly saturated with dry hydrogen chloride (in about six to eight hours). Then the ether and excess hydrochloric acid were removed under reduced pressure at room temperature as far as possible (in about five hours) and the residue—a very thick sirup—was dissolved in one liter of water and the solution kept at 45–50° for about half an hour. Then the oil was separated and united with the ethereal extract of the aqueous solution. The ethereal solution was now washed with sodium bicarbonate, dried with sodium sulfate and fractionated; yield, 564 g. of colorless ester, b. p. 120° at 15–16 mm. or 81%. In 100-g. lots the yield of ester was as high as 85%. The crude nitrile from dichlorohydrin gives the ester in about 70–75% yield.

(3) **Ethyl 3-Chlorocrotonate.**—To 200 g. of crude ethyl-2-hydroxy-3-chlorobutyrate in a 1-liter round-bottomed flask, 100 g. of phosphorus pentoxide was added in 10–20

g. lots under violent shaking. The temperature rose to about 100°. Then the flask was put in a 190° oil-bath and after ten minutes' heating the product was drawn over by vacuum as fast as the foaming of the mass permitted. The distillation was continued at reduced pressure until no more material came over. The yield of a pale yellow distillate was 125–128 g. The united distillates of two experiments gave after two fractional distillations 223 g. of unsaturated ester, b. p. 80° at 10 mm. (62.5%) and 23 g. of a fraction above 100° at 10 mm.

The unsaturated ester was redistilled at 2 mm. pressure. It distilled at 66–68° to a small residue.

Anal. Subs., 0.5161, 0.6799: (after reduction with sodium in absolute alcohol) 37.82, 45.43 cc. of 0.1 *N* $AgNO_3$. Calcd. for $C_6H_9O_2Cl$: Cl, 23.88. Found: Cl, 23.73, 23.70.

The high-boiling fraction partially crystallized during the distillation. The mixture was cooled in ice and after five hours' standing the crystals were separated by filtration, pressed between filter paper and recrystallized from 30 cc. of ligroin (60–110°); 7 g. of crystals, m. p. 83.5°, was obtained (2.5%); mixed m. p. with 3-chlorocrotonic acid (m. p. 83°), 83°.

Anal. Subs., 0.3294, 0.4514: 27.15, 37.3 cc. of 0.1 *N* $AgNO_3$. Calcd. for $C_4H_5O_2Cl$: Cl, 29.42. Found: Cl, 29.23, 29.30.

One g. of the crystals was dissolved in 7 cc. of acetone which contained 2.5 g. of sodium iodide, etc. (see below); 1.1 g. of yellow crystals, m. p. 108–108.5°, was obtained; mixed m. p. with the pure 3-iodocrotonic acid (m. p. 108°), 108°.

(4) **Saponification of Ethyl 3-Chlorocrotonate.** (A) **With Potassium Hydroxide.**—Two hundred and fifty grams of ester was dissolved in 200 cc. of absolute alcohol, the solution cooled to −15° and, under violent stirring, 100 g. of potassium hydroxide in 300 cc. of water was added in about one and one-half hours. After one and one-half hours' stirring at −15°, the stirring was continued at 0° for two hours, when all of the potassium hydroxide was used up. The mixture was diluted with 200 cc. of water and extracted three times with ether. The ethereal solution gave 50 g. of unchanged ester, b. p. 90° at 15 mm.

The aqueous solution was acidified with ice cold dilute sulfuric acid (calcd. amount) and the solution extracted with ether. (After extraction of the unsaturated acids the aqueous solution contained according to titration potassium chloride corresponding to about 15% of ester used.) The ethereal extract was dried with sodium sulfate, etc. The residue was dissolved in hot ligroin (60–110°) in the presence of sodium sulfate, the solution decanted and the operation repeated several times. The ligroin solution deposited yellowish crystals at −15° which were recrystallized from ligroin (for 50 g. of pure material about 800 cc. of boiling range 60–110° or 2 liters of 40–50°). The yield was 66 g. of white crystals, m. p. 83°, or 40%.

Titration. Subs., 0.2505, 0.2998: 20.32, 24.24 cc. of 0.1 *N* alkali. Calcd. mol. wt. for $C_4H_6O_2Cl$: 120.5. Found: 123.5, 123.6.

Anal. Subs., 0.4431, 0.3123: 36.3, 25.5 cc. of 0.1 *N* $AgNO_3$. Subs., 0.1252, 0.1499 (titrated with bromine water, see ref. 2): 20.62, 24.61 cc. of 0.1 *N* $Na_2S_2O_3$. Calcd. for $C_4H_6O_2Cl$: Cl, 29.42; iodine number, 210.6. Found: Cl, 29.06, 28.96; iodine number, 209, 208.4.

The united ligroin mother liquors of the 83° crystals gave about 40 g. of a liquid product (dried at two mm. for five hours). This acid deposited large amounts of crystals at −20°; the crystallized product showed the same analytical data as the 3-chlorocrotonic acid (see later in connection with the barium hydroxide saponification).

(B) **With Barium Hydroxide at Room Temperature.**—The procedure is the same as is described under (C) except that the temperature was 0° at the beginning and about 20° at the end of the reaction. Thirty g. of ester treated with 32 g. of barium hydroxide gave 8.5 g. of crystalline product, m. p. 82° (43% of theoretical) with 14 g. of white powder insoluble in ether and water. Six grams of unchanged ester was recovered.

(C) With Barium Hydroxide Below 0°.—One hundred grams of pure ester was emulsified by violent stirring in 700 cc. of 25% alcohol. In an apparatus fitted with mercury-sealed stirrer, and after the mixture had been cooled to −10°, 110 g. of finely powdered barium hydroxide was added in the course of about an hour. Then the mixture was stirred for ten hours at −2° and afterwards for six to ten hours at 1–2°, *i. e.*, until all of the barium hydroxide was consumed. The procedure from this point is exactly the same as described under (A). The yield was 44 g. of 3-chlorocrotonic acid, m. p. 78–80° (60%), and 18 g. of liquid acid, m. p. 2–5° (25%). Ten g. of unchanged ester was recovered. The acid 78–80° gave 40 g. of product, m. p. 83°, from low-boiling ligroin.

The liquid acid was dissolved in 25 cc. of low-boiling ligroin, the mixture cooled to −15° and the crystals separated as quickly as possible. By repetition of this crystallization 10 g. of product of m. p. 10° was obtained. The melting point could not be changed any further.

Anal. Subs., 0.3039: 24.35 cc. of 0.1 *N* alkali. Calcd. for $C_4H_5O_2Cl$, mol. wt., 120.5. Found: mol. wt., 124.8. Subs., 0.3734: 30.23 cc. of 0.1 *N* silver nitrate. Subs., 0.3092: 51.0 cc. of 0.1 *N* $Na_2S_2O_3$. Calcd. for $C_4H_5O_2Cl$: Cl, 29.42; iodine number, 210.6. Found: Cl, 28.7; iodine number, 209.3.

Preparation of 3,3-Dichlorocrotonic Acid.—Sixty grams of 3,3,3-trichlorocrotonic acid (m. p. 114°) was dissolved in 120 cc. of alcohol and then 30 cc. of water and 46 cc. of glacial acetic acid were added. In the course of about twenty minutes 27 g. of zinc dust was added in very small portions at 56° while the solution was violently stirred. After addition of zinc the solution was stirred for fifteen minutes, then cooled, extracted with ether (after addition of 600 cc. of water), and the ethereal solution washed three times with small amounts of water, etc. The residue of the ethereal solution gave 40 g. of white crystalline product at 110° under 2 mm. pressure. In other similar experiments 42–43 g. of this product was obtained, corresponding to an average yield of 85% of the theoretical. Recrystallization from low-boiling ligroin at −15° yielded 37.5–40 g. of crystals, m. p. 42–43°. The recrystallized acid is very stable and may be stored for years, whereas the crude product begins to decompose in several months.

II. Preparation of 3-Bromocrotonic Acid

(1) Preparation of Dibromohydrin.—To a mixture of 1600 g. of glycerin and 150 g. of red phosphorus, 750 cc. of bromine is added in about seven to eight hours under effective stirring and moderate cooling, so that the reaction mixture is always hot. Then the mixture is heated on the water-bath until all of the bromine disappears (three hours). After this the solution is cooled to 40–50°, 150 cc. of bromine is added in one operation and the mixture is allowed to stand at room temperature overnight. After the solution is heated for three hours on the water-bath, the reaction mixture is distilled under reduced pressure until the oil-bath reaches 180° and the residue shows the first sign of decomposition. The distillate is now neutralized with sodium bicarbonate, the aqueous solution separated from the oil and extracted with a small amount of ether. This ethereal extract is united with the oil, dried with sodium sulfate and purified by fractional distillation; yield, 2050 g. of colorless product, b. p. 110–112° at 20 mm., or 54%.

Epibromohydrin.—Four hundred and forty grams of dibromohydrin was dissolved in 1.2 liters of dry ether and, under violent stirring, 95 g. of finely powdered sodium hydroxide was gradually added in about fifteen minutes under ice cooling. The mixture was then stirred for one hour at room temperature. The sodium bromide was separated by filtration and the filtrate fractionated; yield, 204 g. of colorless mobile oil, b. p. 134–136°, or 75%.

(2) **2-Hydroxy-3-bromo-*n*-butyronitrile.**—One thousand and eighty grams of dibromohydrin was suspended in 2.5 liters of water which contained 350 g. of potassium cyanide, etc., as is described in the case of the chloronitrile under (b). The solution became dark brown. The yield of redistilled product, b. p. 154° at 14 mm., was 93 g. or 16.5%. This was redistilled under 2 mm. pressure; 80 g. of colorless distillate, b. p. 117–118°, was obtained.

Anal. Subs., 0.4938, 0.4248: AgBr, 0.5643, 0.4843. Calcd. for C_4H_6ONBr: Br, 48.72. Found: Br, 48.64, 49.00.

(3) **Ethyl 2-Hydroxy-3-bromobutyrate.**—Four hundred and thirty grams of crude 2-hydroxy-3-bromo-butyronitrile, b. p. 148–154° at 14 mm., was dissolved in 165 cc. of absolute alcohol and 250 cc. of ether and saturated with dry hydrogen chloride in exactly the same manner as in the case of ethyl 2-hydroxy-3-chlorobutyrate. The yield was 425 g. of yellow crude ester (dried at 100° for two hours at reduced pressure) or 77%. The crude ester boils at 94–96° at 2 mm. with slight decomposition. The yield of colorless distillate after two fractionations was 70% of the crude ester.

Anal. Subs., 1.0917: AgBr, 1.0750. Calcd. for $C_6H_{11}O_3Br$: Br, 37.88. Found: Br, 41.90.

(4) **Ethyl 3-Bromocrotonate.**—To 75 g. of crude ethyl 2-hydroxy-3-bromobutyrate 25 g. of phosphorus pentoxide was added, under violent shaking, in two lots. The further procedure was the same as in the case of ethyl 3-chlorocrotonate. The united crude distillates of five experiments gave 98 g. of twice distilled pure ester, b. p. 80–82° under 2 mm., or 28.5%.

Anal. Subs., 0.4403, 0.4329: 22.03, 21.70 cc. of 0.1 *N* silver nitrate (after reduction with sodium in absolute alcohol). Calcd. for $C_6H_9O_2Br$: Br, 41.4. Found: Br, 40.00, 40.06.

The ester is soluble in all of the usual organic solvents except ligroin. It has a pleasant odor but causes blisters on the skin.

The residue from the distillation of the unsaturated ester deposited a small amount of crystals (probably 3-bromocrotonic acid).

(5) **Saponification of Ethyl 3-Bromocrotonate.**—Twenty grams of ester was dissolved in 250 cc. of 25% alcohol and treated with 16 g. of powdered barium hydroxide below 0° in the same manner that is described in the case of ethyl 3-chlorocrotonate under (c). Six and a half grams of white crystals, m. p. 70–71°, was obtained from 200 cc. of ligroin (60–110°). This corresponds to 44% of the theoretical.

The mother liquor of the crystals gave about 1 g. of liquid acid which partially crystallized in a freezing mixture; the total yield of unsaturated acids was 7.5 g. or 50% of the theoretical. Three grams of ester was recovered.

The crystals, m. p. 70°, were recrystallized from 70 cc. of hot ligroin. Five and nine-tenths grams of crystals (m. p. 74°) was obtained.

Anal. Subs., 0.2335, 0.1364: 14.0, 8.2 cc. of 0.1 *N* alkali. Calcd. for $C_4H_5O_2Br$: mol. wt., 164.94. Found: mol. wt., 165.8, 165.3. Subs., 0.3737, 0.6293: 22.6, 38.00 cc. of 0.1 *N* of silver nitrate. Calcd. for $C_4H_5O_2Br$: Br, 48.45. Found: Br, 48.32, 48.25.

The 3-bromocrotonic acid (m. p. 74°) crystallizes in large plates from ligroin. The crystals are very soluble in ether, chloroform, acetone, etc., but sparingly soluble in cold ligroin. The saturated aqueous solution contains at room temperature about 3% of the acid.

III. Preparation of 3-Iodocrotonic Acid

(1) **Ethyl 3-Iodocrotonate.**—Thirty grams of ethyl 3-chlorocrotonate was dissolved in 100 cc. of acetone which contained 32 g. of sodium iodide. The precipitation of sodium chloride started immediately and was finished in about an hour. The precipitate was now separated by filtration and washed with acetone; 9.5 g. of sodium chloride (80% of the theoretical) was obtained. The filtrate from the sodium chloride was poured into 500 cc. of ether; the ethereal solution was washed with sodium thiosulfate solution and then with water and finally dried with sodium sulfate. The residue from this solution, a dark orange ester, weighed 42 g. This crude product was fractionated under 2 mm. pressure; 12 g. of distillate was obtained from 85 to 90°, the rest boiled at 90–92° with slight decomposition. The distillate was much darker than the crude product.

Anal. of the crude product. Subs., 0.7263, 0.7836: 32.0, 34.1 cc. of 0.1 *N* silver nitrate. Calcd. for $C_6H_9O_2I$: I, 52.88. Found: I, 55.92, 55.5.

Anal. of fraction 90–92° under 2 mm. Subs., 0.7936, 0.7740: 32.6, 31.7 cc. of 0.1 *N* silver nitrate. Calcd. for $C_6H_9O_2I$: I, 52.88. Found: 52.14, 51.98.

The ester is soluble in the usual organic solvents except ligroin. It is *lacrymatory* and causes blisters on the skin.

Saponification of Ethyl 3-Iodocrotonate.—Twenty-five grams of ethyl 3-iodocrotonate (b. p. 90–92° at 2 mm.) was suspended in 250 cc. of 25% alcohol and was treated with 16 g. of finely powdered barium hydroxide below 0° as is described in the case of ethyl 3-chlorocrotonate under (c). After fifteen hours' stirring a sticky mass deposited in the flask; the solution was now decanted, 250 cc. of ether-saturated water added and the stirring continued for about five to six hours, etc., as usual. The yield was 8.5 g. of yellow crystals (m. p. 104–105°) from 250 cc. of ligroin (80–110°) or 53% of the theoretical. Recrystallization yielded 7.5 g. of yellowish crystals, m. p. 108°; a mixed melting point with 3-iodocrotonic acid (m. p. 108°) made from 3-chlorocrotonic acid was 108°. Seven grams of ester was recovered.

(2) **3-Iodocrotonic Acid.**—To a cold solution of 40 g. of sodium iodide in 120 cc. of acetone, 24 g. of 3-chlorocrotonic acid (m. p. 83°) was added. In about half an hour the solution became clear. After one hour the sodium chloride was separated by filtration, etc., as in the case of ethyl 3-iodocrotonate; 11.2 g. of sodium chloride was separated (96%). From the crude crystalline residue of the ethereal solution (39.0 g.), 36.5 g. of yellow crystals (m. p. 108°) was obtained from ligroin (86%).

Anal. Subs., 0.2353, 0.6163: 11.05, 28.75 cc. of 0.1 *N* silver nitrate. Calcd. for $C_4H_5O_2I$: I, 59.8. Found: I, 59.6, 59.21.

The 3-iodocrotonic acid (m. p. 108–108.5°) crystallizes in yellow needles. It has approximately the same solubility as the 3-bromocrotonic acid. The compound is stable and may be stored for months.

IV. Reduction of 3-Chlorocrotonic Acid (m. p. 83°) with Palladium and Hydrogen

Two and four-tenths grams of 3-chlorocrotonic acid was dissolved in 20 cc. of water and cooled until much ice appeared in the solution; then 40 cc. of 1 *N* sodium hydroxide and 2.5 g. of palladium–norit (0.05 g. of Pd) was added and the mixture violently shaken in a hydrogen atmosphere. When approximately 460–480 cc. of hydrogen was consumed in the reduction (the hydrogen necessary for the saturation of palladium–norit must be taken into account), the solution contained the theoretical amount of sodium chloride and the reduction was interrupted immediately (the reduction does not stop at this point but would have gone further to the complete saturation of the compound). The products of three experiments were united and the palladium–norit was separated by filtration. The filtrate contained according to analysis the theoretical amount of sodium chloride and 4.8 g. of crotonic acid. The solution was now acidified with sulfuric acid and extracted with ether, etc. The residue of the ethereal solution was dissolved in low-boiling ligroin and the residue from this weighed 4.9 g. and was a semi-crystalline mass (95% of the theoretical). From this, 1.9 g. of recrystallized product (m. p. 71°) was obtained from low-boiling ligroin; a mixed m. p. with crotonic acid (m. p. 71.5°) was 71.5°.

Reduction of 3,3-Dichlorocrotonic Acid.—Nine and three-tenths grams of 3,3-dichlorocrotonic acid (m. p. 42–43°) was dissolved in 180 cc. of 1 *N* sodium hydroxide at −3°. Then 1.6 g. of palladium–norit was added and the mixture violently shaken in a hydrogen atmosphere. The reaction was controlled by titration for chloride and for acidity. In about six hours, when about 1500 cc. of hydrogen was taken up, the amount of sodium chloride corresponded exactly to one mol and the titration for acidity showed that one mol of sodium hydroxide was neutralized. The reaction mixture was now worked up as before in the case of the reduction of 3-chlorocrotonic acid. The residue of the ligroin solution was 7 g. of yellow sirup, which deposited about 2 g. of crystals from low-boiling ligroin at −15°. The crystals after recrystallization from ligroin melted at 58–60°; from water also at 58–60°.

Three and four-tenths grams of the mother liquor of the crystals was dissolved in 10 cc. of a saturated solution of sodium iodide in acetone and the solution was allowed to stand for twenty-four hours. The sodium chloride was separated by filtration, etc., as usual. Two-tenths gram of sodium chloride was obtained. The ethereal filtrate gave 0.1 g. of yellow crystals (m. p. 108°); a mixed melting point with pure 3-iodocrotonic acid gave 108°.

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Summary

1. An improved method of preparation of 3-chlorocrotonic acid (m. p. 83°) is reported. The acid is prepared from 2-hydroxy-3-chloro-*n*-butyronitrile in the following manner. The nitrile is esterified in absolute alcohol with hydrogen chloride and the resulting ethyl 2-hydroxy-3-chlorobutyrate is treated with phosphorus pentoxide. The ethyl 3-chlorocrotonate thus obtained is saponified with alkali in order to obtain the 3-chlorocrotonic acid (m. p. 83°). The yield of this acid from the nitrile is 32% of the theoretical.

A new method for the preparation of 2-hydroxy-3-chlorobutyronitrile is reported which involves the treatment of dichlorohydrin with sodium cyanide in aqueous suspension.

It is shown that in the treatment of ethyl 2-hydroxy-3-chlorobutyrate with phosphorus pentoxide, two isomeric unsaturated esters are obtained. The main product is ethyl 3-chlorocrotonate; the by-product is very probably ethyl 3-chloro-vinylacetate.

Saponification of ethyl 3-chlorocrotonate with barium hydroxide below 0° is reported. The yield is as high as 85%.

2. The preparation of 3-bromocrotonic acid (m. p. 74°) is reported. This acid is prepared from 2-hydroxy-3-bromobutyronitrile in the same manner as in the case of 3-chlorocrotonic acid. The yield of acid, taking the nitrile as a basis, is about 12% of the theoretical.

A greatly improved method of preparation of dibromohydrin is reported. This product may be obtained now from glycerin with 54% yield.

The preparation of 2-hydroxy-3-bromobutyronitrile from dibromohydrin is described.

The preparation of ethyl 2-hydroxy-3-bromobutyrate (b. p. 94–96° at 2 mm.) and ethyl 3-bromocrotonate (b. p. 80° under 2 mm.) is reported.

3. The preparation of ethyl 3-iodocrotonate (b. p. 92–93° at 2 mm.) and that of the 3-iodo-crotonic acid (m. p. 108°) are described.

4. The structure of the 3-halogenocrotonic acids is proved. The 3-chloro acid may be reduced to crotonic acid (m. p. 72°); the 3-chloro- and 3-bromocrotonic acids may easily be converted into 3-iodocrotonic acid.

5. It is shown that the 3-chlorocrotonic acid is an intermediate product in the reduction of 3,3-dichlorocrotonic acid to crotonic acid.

6. An improved method of preparation of 3,3-dichlorocrotonic acid is described. The reduction of 3,3,3-trichlorocrotonic acid with zinc in acetic acid yields the 3,3-dichlorocrotonic acid in 80–85% yield.

CHICAGO, ILLINOIS

[CONTRIBUTION FROM THE KENT CHEMICAL LABORATORY, UNIVERSITY OF CHICAGO]

OXIDATION OF UNSATURATED COMPOUNDS. III. OXIDATION OF 3-CHLOROCROTONIC ACID. SYNTHESIS OF *dl*-THREONIC ACID. PROOF OF CONFIGURATION OF THE *dl*-1,2-DIHYDROXYBUTYRIC ACIDS

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In the study of hydroxylation of double bonds, undoubtedly fumaric and maleic acids have the most prominent place. Their structure was determined with a considerable degree of assurance[2] and the structure of their hydroxylated products—that of the tartaric acids—was proved with the greatest accuracy. Because the configurations of both starting and end products are known, it would be a comparatively simple matter to study the mechanism of the hydroxylation and the nature of the oxidizing agent in the oxidation of fumaric and maleic acids. Unfortunately these acids have a very inactive double bond. As a matter of fact it is possible to get satisfactory results only with the strongest hydroxylating agents,

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[2] Although there might be objections, it is generally accepted that fumaric acid is the "*trans*" and maleic acid is the "*cis*" form.