Ethyl γ-Chlorobutyrate.—Thirty-five grams (77%) of this product was obtained when 40 g. of γ-ethoxybutyric acid, which boiled at 114–116° (7 mm.),[20] and 54 g. of thionyl chloride were heated on a steam-bath for four hours. The ethyl γ-chlorobutyrate boiled at 70–71° (10 mm.).[21]

When 30 g. of the ester was heated for six hours on a steam-bath with 18 cc. of concd. hydrochloric acid and the mixture extracted with ether, 8 g. of γ-chlorobutyric acid, b. p. 104–109° (6 mm.), and 18 g. of unchanged ester were obtained. Upon further fractionation, 4 g. of the acid was found to boil at 107–108° (6 mm.); m. p. 13°.[22]

The following compounds were prepared in the manner described above. Ethyl iodobutyrate was obtained in 67% yield; b. p. 69–71° (3 mm.).[23]

Ethyl γ-diethylaminobutyrate was prepared in 78% yield; b. p. 73–75° (4 mm.).[24] The hydrochloride, after recrystallization from a mixture of acetone and ether, melted at 113°.

Anal. Calcd. for $C_{10}H_{22}O_2NCl$: Cl, 15.84. Found: Cl, 15.85.

Upon hydrolysis of the ester with concd. hydrochloric acid, γ-diethylaminobutyric acid hydrochloride was produced; m. p. 166–167°.

Butyl γ-Chlorobutyrate.—When 32 g. of γ-butoxybutyric acid, which boiled at 120–125° (4 mm.),[25] and 30 g. of thionyl chloride were heated for four hours on a steam-bath, there was obtained 32 g. (90%) of butyl γ-chlorobutyrate; b. p. 93–96° (8 mm.).

Anal. Calcd. for $C_8H_{15}O_2Cl$: Cl, 19.85. Found: Cl, 19.93.

Butyl γ-iodobutyrate was obtained in 65% yield; b. p. 100–103° (4 mm.).

Butyl γ-diethylaminobutyrate was prepared in 74% yield; b. p. 105–107° (5 mm.). Upon acid hydrolysis of the ester the hydrochloride of γ-diethylaminobutyric acid was isolated; m. p. 166°.

When β-methoxypropionic acid was heated on a steam-bath with thionyl chloride, β-methoxypropionyl chloride was obtained; b. p. 34–36° (6 mm.).[26]

To a cooled mixture of 9.8 g. of the acid chloride, 7 cc. of methyl alcohol and 7 cc. of water, sodium hydroxide pellets were added, gradually, until the mixture was slightly alkaline. The alcoholic layer yielded 5.6 g. of methyl β-methoxypropionate; b. p. 145–147° (746 mm.).[27]

β-Ethoxypropionic acid and thionyl chloride yielded β-ethoxypropionyl chloride; b. p. 34–35° (5 mm.).[28] Ethyl β-ethoxypropionate, obtained from the acid chloride in 74% yield, boiled at 49–50° (6 mm.).[29]

Summary

γ-Methoxy-, γ-ethoxy- and γ-butoxybutyryl chloride are transformed, under the influence of heat, into methyl, ethyl and butyl γ-chlorobutyrates, respectively. Certain α-substituted γ-alkoxybutyryl chlorides seem to behave in a similar manner but β-alkoxypropionyl chlorides apparently are unaffected by heat under the same conditions.

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[20] Ref. 7, b. p. 116.5–117° (8 mm.).

[21] Ref. 19, p. 307, b. p. 77° (16 mm.).

[22] Cloves, ref. 13, found that the acid boiled at 115° (13 mm.) and melted at 16°.

[23] Fuson, Arnold and Cooke, THIS JOURNAL, **60**, 2273 (1938), found 84–85° (4 mm.).

[24] Ref. 19, b. p. 98° (13 mm.).

[25] Ref. 7, b. p. 122.5–123° (4 mm.).

[26] Ref. 4, b. p. 27–27.5° (3 mm.).

[27] Palomaa and Kilpi, *Chem. Zentr.*, **81**, II, 1453 (1910), found 143.4–143.6° (750 mm.).

[28] Ref. 4, b. p. 28–28.5° (2 mm.).

[29] Ref. 27, b. p. 49.5–49.8° (7 mm.).

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF BARNARD COLLEGE]

Certain Reactions of *p*-Bromocinnamic Acid

BY MARIE REIMER AND ELISE TOBIN

In the course of a study of *p*-bromobenzalpyruvic acid,[1] it became of interest to have for comparison certain derivatives of *p*-bromocinnamic acid. This acid and several related compounds have, therefore, been prepared.

p-Bromocinnamic acid has been obtained previously by the usual methods[2] and also by vacuum distillation of brominated truxillic acids[3] and, unexpectedly, as a by-product in the Friedel–Crafts reaction with the acid chloride of cinnamic acid dibromide.[4] The acid used in this study was the product of hydrogen peroxide oxidation of *p*-bromobenzalpyruvic acid. This method of preparation of various cinnamic acids has been used repeatedly in this Laboratory and found to give far better yields than those noted by other procedures.

The dibromide of *p*-bromocinnamic acid, like that of cinnamic acid, readily loses bromine as well as hydrogen bromide on heating. By treatment of the dibromide with potassium hydroxide in methanol solution, however, it has been found

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[1] Reimer and Tobin, THIS JOURNAL, **62**, 2515 (1940).

[2] Knoevenagel, *Ber.*, **31**, 2604 (1898); Gabriel, *ibid.*, **15**, 2501 (1882); Perkin's synthesis.[1]

[3] Kraus, *ibid.*, **35**, 2932 (1902); **37**, 223 (1904).

[4] Kohler, Heritage and Burnley, *Am. Chem. J.*, **44**, 60 (1910).

possible to eliminate smoothly one molecular proportion of hydrogen bromide, or two, at will. When a cooled 25% solution of potassium hydroxide in methanol was used, a nearly quantitative yield of an α-bromo-*p*-bromocinnamic acid (m. p. 148°) could be obtained. This acid is isomeric with the α-bromo-*p*-bromocinnamic acid (m. p. 221°) previously prepared by hydrogen peroxide oxidation of the yellow form of β-bromo-*p*-bromobenzalpyruvic acid.[1] If the suggested configuration of the latter is correct, the bromocinnamic acid obtained by its oxidation should be the *trans* form. That the new bromocinnamic acid is the less stable of the two and, therefore, certainly in this case the *cis* isomer, is shown by the fact that the new, lower-melting acid changes to the higher-melting on heating above the melting point, by long boiling in water or benzene and on exposure of a benzene solution to the sunlight.

When the reaction between the dibromide of *p*-bromocinnamic acid and alcoholic potash was carried out at 100°, two molecular proportions of hydrogen bromide were eliminated and *p*-bromophenylpropiolic acid was formed. The acetylenic acid dissolves readily in sulfuric acid, the solution on hydrolysis yielding *p*-bromobenzoylacetic acid. This acid loses carbon dioxide at the melting point to form *p*-bromoacetophenone.

The action of bromine on *p*-bromophenylpropiolic acid was carried out by Bergmann[5] as a step in the synthesis of 2,3,6-tribromoindone but the bromination product was not investigated nor identified except by cyclization to the required indone. We find that *p*-bromophenylpropiolic acid combines with one molecular proportion of bromine to form a mixture of acids, one, pure white, melting at 167° and proved to be α,β-dibromo-*p*-bromocinnamic acid, the other, a pale yellow isomer, melting at 154°. A mixture of either acid with phosphorus pentoxide, when distilled under diminished pressure according to Bergmann's procedure, yielded the 2,3,6-tribromoindone described by him.

When bromine is added to *p*-bromophenylpropiolic acid in aqueous suspension, α-bromo-*p*-bromophenylacetylene is formed. From this compound, by solution in sulfuric acid and subsequent hydrolysis, a good yield of *p*-bromophenacyl bromide is obtained.

Treatment of the dibromide of *p*-bromocinnamic acid with a hot dilute solution of sodium carbonate gives an α-bromo-*p*-bromostyrene (m. p. 74°) isomeric with the compound (m. p. 81°) obtained from the unstable dibromide of *p*-bromobenzalpyruvic acid.

An interesting characteristic of several of these compounds is their marked fragrance. The low-melting form of α-bromo-*p*-bromostyrene (74°) has the odor of mint although the higher-melting isomer (81°) is odorless, and α-bromostyrene, with no *para*-bromine atom, smells of hyacinths; α-bromo-*p*-bromophenylacetylene smells strongly of anise and *p*-bromoacetophenone has the exact odor of the trailing arbutus.

Experimental Part

p-Bromocinnamic Acid, 4-$BrC_6H_4CH{=}CHCOOH$.—To a mixture of 4 g. (0.015 mole) of *p*-bromobenzalpyruvic acid,[1] 0.9 g. (0.008 mole) of sodium carbonate and 750 ml. of water, 30 ml. of hydrogen peroxide (13 vol.) was added and the mixture shaken vigorously. After a few minutes the yellow color of the solution faded and a flocculent white solid began to separate. The shaking was continued and the mixture then left standing overnight or until all the yellow ketonic acid had reacted. The filtered solid, together with the acid precipitated by acidification of the filtrate, gave a 94% yield of product which represents an over-all yield of 89% calculated from the *p*-bromobenzaldehyde originally used. The acid separates in shining plates from a large volume of boiling benzene or in fine needles from boiling water in which it is only slightly soluble. The melting points given in the literature for this acid range from 251° to 265–267°. Our product melted at 257° after repeated crystallization from benzene.

p-Bromocinnamic Acid Dibromide, 4-$BrC_6H_4CHBrCHBrCOOH$ (192°).—Addition of bromine to *p*-bromocinnamic acid takes place slowly and incompletely by the usual procedure in cold chloroform or carbon bisulfide. The best results were obtained by heating to boiling a mixture of 5 g. (0.022 mole) of bromocinnamic acid in 290 ml. of carbon tetrachloride and adding to the boiling solution 1.15 ml. (0.022 mole) of bromine in 10 ml. of carbon tetrachloride over a period of one hour. Two-thirds of the liquid was then distilled off. An 88% yield of crystalline product separated from the cooled residue. After one recrystallization from carbon tetrachloride this *p*-bromocinnamic acid dibromide separated in white shining plates melting at 192°.

Anal. Calcd. for $C_9H_7O_2Br_3$: C, 27.90; H, 1.80. Found: C, 28.41; H, 2.01.

The methyl ester of the acid, prepared by action of diazomethane, crystallizes from methanol in shining rhombic crystals melting at 110°.

Anal. Calcd. for $C_{10}H_9O_2Br_3$: C, 29.92; H, 2.24. Found: C, 30.22; H, 2.26.

This ester was prepared by Bergmann[5] by bromination of methyl *p*-bromocinnamate.

The acid dibromide is readily soluble in boiling alcohols and benzene, only very slightly soluble in water. On long boiling in water decomposition occurs, the products being

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(5) Bergmann, *Ber.*, **64**, 1481 (1931).

p-bromobenzaldehyde (m. p. 57°), separated by steam distillation, *p*-bromocinnamic acid (m. p. 257°) undissolved in the boiling solution and a low-melting compound which crystallized from the solution on cooling and was identified as α-bromo-*p*-bromostyrene (m. p. 81°) by mixed melting point with an authentic sample. The residue had a strong odor of mint later recognized as that of an isomeric bromostyrene (m. p. 74°).

α-Bromo-*p*-bromostyrene, $4\text{-BrC}_6\text{H}_4\text{CH}{=}\text{CHBr}$ (74°).—The compound is best prepared by boiling *p*-bromocinnamic acid dibromide in a 2% solution of sodium carbonate. Decomposition was very rapid the liquid becoming cloudy and depositing, in 70% yield, a yellowish oil which solidified on cooling. The substance is very soluble in boiling alcohol and glacial acetic acid, less so in benzene and hexane. It crystallizes in fine branching needles from glacial acetic acid to which a few drops of water have been added.

Anal. Calcd. for $C_8H_6Br_2$: C, 36.64; H, 2.29. Found: C, 36.49; H, 2.35.

The odor of mint noted whenever the dibromide of *p*-bromocinnamic acid was prepared is accounted for by contamination with the styrene. The pure dibromide is odorless.

A sample of the dibromide (m. p. 192°) was heated for an hour in a bath of methyl benzoate (b. p. 194°). Bromine and hydrogen bromide were eliminated rapidly. The cooled solid residue was extracted repeatedly with small volumes of boiling benzene. The solutions deposited *p*-bromophenylpropiolic acid. The less soluble residue was *p*-bromocinnamic acid.

α-Bromo-*p*-bromocinnamic Acid, $4\text{-BrC}_6\text{H}_4\text{CH}{=}\text{CBrCOOH}$ (148°).—Three grams of *p*-bromocinnamic acid dibromide was shaken vigorously for fifteen minutes with 75 ml. of a cooled 25% solution of potassium hydroxide in methanol and the cloudy mixture allowed to stand with frequent shaking for forty-five minutes. It was then filtered into 150 ml. of ice-water and the solution acidified at once. The unsaturated acid thus obtained crystallizes from boiling benzene in fine cream-colored needles which soften at about 145° and melt at 148°. The substance is readily soluble in alcohols, ether, glacial acetic acid and hot benzene, less so in boiling water.

Anal. Calcd. for $C_9H_6O_2Br_2$: C, 35.29; H, 1.96. Found: C, 35.49; H, 2.28.

The methyl ester, prepared with diazomethane, separates from a very small volume of methanol in stiff, shining needles, melting at 57°.

Anal. Calcd. for $C_{10}H_8O_2Br_2$: C, 37.50; H, 2.50. Found: C, 37.46; H, 2.55.

As repeated crystallizations of the acid from benzene or from water were found to raise the melting point gradually, the following experiments were carried out with a view to isomerization of the acid. A sample of the acid (148°) was heated in the melting point bath for about five minutes at 160°, then cooled. This was repeated at successively higher temperatures to 220°. The temperature at which the melt solidified was higher after each heating and the melting point was raised to a final 219°. This substance was ground to a powder and mixed with the isomeric acid (221°). The mixture melted 219–220°. The same isomerization takes place on long boiling of the acid in water or benzene.

A saturated solution of the acid (148°) in benzene was exposed in a sunny window for five days. The quantity of hard white crystals which had then separated on the sides of the quartz test-tube, after one crystallization from benzene, melted at 220° as did a mixture of the substance with a pure sample of the 221° acid. The acid (148°) is, therefore, the unstable isomer of the acid (221°).

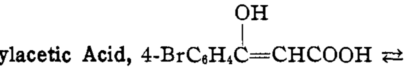
p-Bromophenylpropiolic Acid, $4\text{-BrC}_6\text{H}_4\text{C}{\equiv}\text{CCOOH}$ (201°).—Three grams of *p*-bromocinnamic acid dibromide and 50 ml. of a 25% solution of potassium hydroxide in methanol were heated over boiling water for thirty minutes. The mixture was then thoroughly chilled, the shining potassium salt filtered, washed with cold methanol and dissolved in ice-water. On acidification an 80% yield of the acetylenic acid was obtained. The acid is readily soluble in cold alcohols, in hot acetone, glacial acetic acid and benzene, very difficultly soluble in water, insoluble in ligroin. It melts at 201° to a yellow liquid which distils rapidly up the melting point tube to form a greenish-brown deposit at the top, a behavior which distinguishes it from all the other high-melting acids here described.

Anal. Calcd. for $C_9H_5O_2Br$: C, 48.00; H, 2.22. Found: C, 48.17; H, 2.47.

This acid was obtained by Bergmann by hydrolysis of the bromination product of methyl *p*-bromocinnamate but not further described.

The methyl ester of the acetylenic acid prepared by diazomethane or by heating the acid for about an hour in methanol saturated with hydrogen chloride, can be purified by crystallization from the smallest possible quantity of boiling methanol to which water is added to faint cloudiness. It separates in brilliant flat needles melting at 106°.

Anal. Calcd. for $C_{10}H_7O_2Br$: C, 50.20; H, 2.92. Found: C, 50.51; H, 3.33.



p-Bromobenzoylacetic Acid, $4\text{-BrC}_6\text{H}_4\overset{\text{OH}}{\overset{|}{\text{C}}}{=}\text{CHCOOH} \rightleftarrows 4\text{-BrC}_6\text{H}_4\text{COCH}_2\text{COOH}$.—One gram of the acetylenic acid just described was stirred into 8 ml. of 98% sulfuric acid. The clear straw-colored solution was allowed to stand overnight and was then added, drop by drop, to crushed ice. The solid product was washed with ice water till free from sulfuric acid and air dried. The acid, obtained in 90% yield, gave a brilliant wine-red color when its solution in alcohol was treated with ferric chloride. It softened at 120° and melted at 123–125° with vigorous effervescence. The residue, a clear colorless liquid, solidified in the melting point tube and then melted at 51°, the melting point of *p*-bromoacetophenone. The experiment was repeated on a larger scale and the substance proved to be that compound by melting with an authentic sample. A gradual loss of carbon dioxide takes place when the acid is boiled with water or heated in any of the usual organic solvents. A sample for analysis was purified by washing with warm hexane.

Anal. Calcd. for $C_9H_7O_3Br$: C, 44.44; H, 2.88. Found: C, 44.45; H, 3.20.

The fragrance of *p*-bromoacetophenone is present in all experiments in which the hydroxy acid is used and in the residues from the preparation of the acetylenic acid.

The methyl ester of the hydroxy acid was prepared by dissolving the washed crude acid in ether and treating with diazomethane in large excess. After evaporation of the ether a yellow oil remained. This was dissolved in boiling hexane after slow evaporation of which clear crystals and a yellow oil remained. These were separated mechanically and the crystals washed and then repeatedly recrystallized from boiling hexane. The ester separates in thick six-sided prisms melting at 45–46° with previous softening. In alcoholic solution the substance gives a red-purple color with ferric chloride.

Anal. Calcd. for $C_{10}H_9O_3Br$: C, 46.57; H, 3.50. Found: C, 46.69; H, 3.20.

The oily product may have been the methyl ether of this ester but the amount obtained was too small for proof.

α,β-Dibromo-*p*-bromocinnamic Acid, $4\text{-BrC}_6\text{H}_4\text{CBr}{=}\text{CBrCOOH}$ (166–167°).—One molecular proportion of bromine was added at room temperature to *p*-bromophenylpropiolic acid dissolved in chloroform. After the fairly rapid decolorization of the bromine, the chloroform was drawn off by a current of dry air. When about three-fourths of the liquid had evaporated, the remainder, now a yellow solution, was poured off from the crystals that had separated. These were purified by repeated crystallization from boiling benzene. The unsaturated acid separates in bunches of white, feathery needles melting at 166–167°. The acid can also be recrystallized from boiling hexane.

Anal. Calcd. for $C_9H_5O_2Br_3$: C, 28.05; H, 1.30. Found: C, 28.08; H, 1.64.

The methyl ester, prepared in ether solution with diazomethane separates from a very small volume of methanol in large, rhombic crystals of a pale cream color which melt at 69°.

Anal. Calcd. for $C_{10}H_7O_2Br_3$: C, 30.07; H, 1.75. Found: C, 30.43; H, 1.89.

α,β-Dibromo-*p*-bromocinnamic Acid, $4\text{-C}_6\text{H}_4\text{CBr}{=}\text{CBrCOOH}$ (153–154°).—The yellow chloroform solution, poured off from the bromination product just described, was evaporated to dryness in a current of dry air. The solid remaining was taken up in a small volume of hot benzene. After this had cooled to room temperature, the yellow liquid was poured off from the crystals of the white acid that had separated and allowed to evaporate spontaneously. If more colorless crystals separated, the liquid was again poured off. From it there separated gradually, stiff, single, pale yellow needles. These soften at about 145° and melt at 153–154°. Frequent crystallization from boiling benzene changes this acid to the colorless isomer. This acid is far more soluble in chloroform, carbon tetrachloride, benzene and ligroin than the higher-melting isomer.

Anal. Calcd. for $C_9H_5O_2Br_3$: C, 28.05; H, 1.30. Found: C, 28.06; H, 1.63.

The methyl ester, prepared by diazomethane reaction, separates from diluted methanol in long, cream-colored needles melting at 67°. A mixture with the isomeric ester (69°) melts from 40 to 58°.

Anal. Calcd. for $C_{10}H_7O_2Br_3$: C, 30.07; H, 1.75. Found: C, 30.11; H, 2.20.

These acids differ not only in solubility, color and crystalline form but conspicuously in the fact that the yellow acid creeps rapidly up the sides of the container. Indeed, a partial separation of the acids can be made by taking advantage of this fact. The esters show even more striking differences in crystalline form than the acids and the ester of the yellow acid also creeps.

When the colorless acid (166–167°) was mixed with an equal bulk of phosphorus pentoxide and heated under diminished pressure, according to the procedure of Bergmann,[5] a red oil distilled. This solidified on cooling. On crystallization from methanol the substance separates in firm, orange-red needles that melt at 144–145°, and form an oxime melting, with vigorous decomposition, at 231° as described by Bergmann for 2,3,6-tribromoindone. The same result was obtained with the yellow isomeric acid under similar treatment, indicating isomerization of one or the other of these acids under the conditions of the reaction. As the melting point of the white acid is not changed by repeated melting, while that of the yellow acid rapidly drops to 30–40°, the latter is the less stable of the two, in this case the *trans* form as it is certainly the *cis* acid that forms the indone.

α-Bromo-*p*-bromophenylacetylene, $4\text{-BrC}_6\text{H}_4\text{C}{\equiv}\text{CBr}$.—When bromination of *p*-bromophenylpropiolic acid was carried out in aqueous suspension or in dilute sodium carbonate solution the bromine was decolorized instantly and a copious white precipitate formed. This was crystallized from methanol to which a few drops of water were added. It separates in glistening, pale yellow plates melting at 102°. The substance rapidly becomes brown in the light.

Anal. Calcd. for $C_8H_4Br_2$: C, 36.92; H, 1.54. Found: C, 36.93; H, 1.72.

The proof that the compound has the formula given is found in the following experiment. The substance dissolved slowly in cooled 98% sulfuric acid. This was allowed to stand overnight and then poured onto ice. The white solid formed crystallizes from boiling alcohol in fine white needles, melting at 110°, and was proved to be *p*-bromophenacyl bromide by melting with an authentic sample prepared by bromination of *p*-bromoacetophenone.

Summary

Several compounds related to *p*-bromocinnamic acid have been prepared primarily for the purpose of comparison with compounds obtained in a study of *p*-bromobenzalpyruvic acid.

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