pressure; yield 1-2 g. Identification was effected by ultraviolet absorption[1,18] and by the preparation of two crystalline derivatives: the 2,4-dinitrophenylhydrazone of m. p. 198–200° (dec., Fisher–Johns apparatus) (after recrystallization from 95% ethanol; in agreement with accepted value[21]) and the condensation product with β-naphthylamine of m. p. 130–131° (after recrystallization from benzene; accepted value[22] 131–132°). These two derivatives showed no depression in melting point on admixture with authentic samples of like melting point.

Preparation of N-D-Glucosylglycine Ethyl Ester.—This compound was first recorded by Euler and Zeile.[23] The following is an improved method of preparation which makes this substance readily available. An amount (66 g.) of freshly prepared glycine ethyl ester was added to a suspension of 115 g. of anhydrous D-glucose in 200 ml. of absolute ethanol and the mixture was mechanically stirred and heated under reflux on a water-bath while protected from moisture by a guard tube. The heating was continued until all of the D-glucose had dissolved, about seventy-five minutes of heating time generally being required. The resultant solution was tea-colored. Approximately 125 ml. of ethanol was then removed under diminished pressure and *ca.* 150 ml. of acetone added to the residual sirup. The resultant solution was nucleated and allowed to stand at room temperature until crystallization was complete (overnight). The crude product was removed by filtration and washed with absolute ethanol; yield 110 g. (64%), m. p. 80°. Quite pure material was obtained on three recrystallizations from equal parts of hot absolute ethanol; yield 50 g. (30%), m. p. 108°, $[\alpha]^{25}D$ −5° (*c* 3, absolute ethanol). A significant purification could be obtained by making a slurry of the crude product with absolute ethanol, filtering and washing with a small amount of ethanol. The filtrate was discarded and the filtered material was crystallized from hot absolute ethanol.

Hydrolytic Breakdown of N-D-Glucosylglycine Ethyl Ester in Water; Ninhydrin Reaction.—An amount (0.26 g.) of D-glucosylglycine ethyl ester was heated on a water-bath in 10 ml. of water containing ninhydrin. The characteristic color developed in a few minutes and heating was continued for a total of thirty minutes. Comparison of this solution (cooled rapidly to room temperature) with a solution containing an equivalent amount of glycine by means of a photoelectric colorimeter revealed that both solutions absorbed to the same extent.

(22) W. F. Cooper and W. H. Nuttall, *J. Chem. Soc.*, **101**, 1080 (1912).

(23) H. v. Euler and K. Zeile, *Ann.*, **487**, 163 (1931).

Acknowledgment.—The assistance of Mrs. Clare B. Spitler is gratefully acknowledged. We are also pleased to acknowledge the counsel of Dr. T. L. Tan and of Professors W. R. Brode, M. S. Newman and F. H. Verhoek of this department.

Summary

1. Aqueous solutions of D-xylose form small amounts of 2-furaldehyde on being heated. The presence of a relatively large amount of glycine promotes this conversion as it does the analogous conversion of hexoses to 5-(hydroxymethyl)-2-furaldehyde.

2. The course of the formation of 2-furaldehyde from D-xylose has been followed spectroscopically and on this basis structures are postulated for several intermediates.

3. It is demonstrated that 5-(hydroxymethyl)-2-furaldehyde, in the case of D-glucose, and 2-furaldehyde, in the case of the pentoses and D-galacturonic acid, are important precursors in the formation of the brown colors developed when aqueous solutions of these substances are heated with glycine.

4. Evidence is presented which shows that the carbonyl-amino reaction could occur to only a slight extent if at all in dilute aqueous solutions of D-glucose and glycine.

COLUMBUS, OHIO RECEIVED MAY 31, 1949

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF RUTGERS UNIVERSITY AND THE DEPARTMENT OF CHEMISTRY OF COLUMBIA UNIVERSITY]

A Synthesis for 4-Bromo-7-methoxyhydrindene

BY RODERICK A. BARNES, ELISE R. KRAFT[1] AND LOUIS GORDON[2]

In a previous paper[3] the use of 4-substituted hydrindenes as starting materials for preparation of cyclopentanophenanthrene derivatives has been illustrated. The present work was undertaken in order to extend the scope of this method by making available a new 4-substituted hydrindene (IV).

The method which finally proved successful for the synthesis of IV and which was most readily applicable to large-scale preparation was based on the hydrindone synthesis of von Auwers.[4] Although halogen substituted hydrindones have not previously been prepared by this procedure, we have found that it can be used to synthesize 4-bromo-7-hydroxy-1-hydrindone (II) in 40–50% yield. The Clemmensen reduction (80% yield) to 4-bromo-7-hydroxyhydrindene (III) and methylation of III with diazomethane complete the synthesis.

The von Auwers preparation of hydrindones takes place in two steps, first a Fries rearrangement of the phenol ester of an α- or β-halopropionic acid, and second a cyclization of the intermediate haloketone. In harmony with this conception of the reaction we have found that the best yields of II were obtained when I was heated with aluminum chloride at 95–100° for five to six hours to complete the Fries rearrangement and then at 170° for one hour to cause cyclization. Extended heating at the higher temperature results in de-

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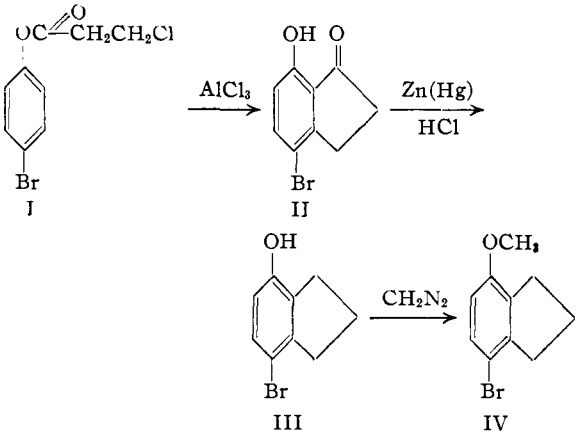
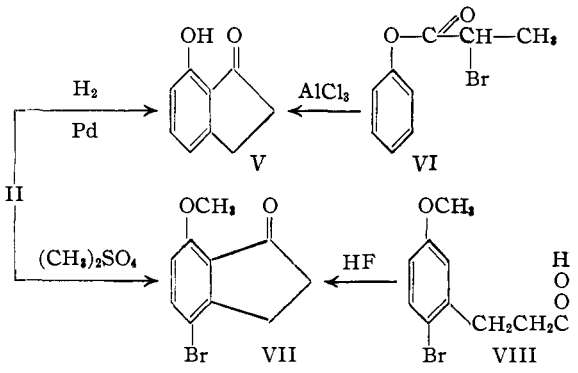
(2) A portion of this work was taken from a thesis presented by Louis Gordon in partial fulfilment of the requirements for the Ph.D. degree, Columbia University, June 1948.

(3) Barnes and Gordon, THIS JOURNAL, **71**, 2644 (1949).

(4) von Auwers, *Ann.*, **439**, 132 (1924).





struction of II; however, cyclization is very slow at the lower temperature.

The yield of II was less than has been reported[5] for *p*-cresyl β-chloropropionate (60%); however, this may be explained by a comparison of the inductive effect of the bromine atom and the methyl group. Thus, the lower electron density at the cyclization position in our case requires that a higher temperature be used for this step of the reaction with a resultant increase in destructive side reactions. The more readily available *p*-bromophenyl α-chloropropionate gave only a trace of II in spite of the fact that 7-hydroxy-1-hydrindone (V) can be prepared in small yield from phenyl α-bromopropionate (VI).[6]

In view of the rather drastic reaction conditions necessary to produce the hydrindone II, it was important to prove its structure.[7] To show that II had the desired carbon skeleton it was reduced over palladium until no more hydrogen was absorbed. It was anticipated that the known 4-hydroxyhydrindene would be formed; however, the product was 7-hydroxy-1-hydrindone (V).[6] The failure of the carbonyl group to undergo catalytic reduction is believed to be due to chelation.[8]

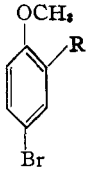
The position of the bromine atom in II was confirmed by an alternate synthesis of 4-bromo-7-methoxy-1-hydrindone from β-(2-bromo-5-methoxyphenyl)-propionic acid (VIII) which was prepared by direct bromination of β-(*m*-methoxyphenyl)-propionic acid in carbon tetrachloride at −5°.

The location of the bromine atom in VIII was determined by oxidation to the known 2-bromo-5-methoxybenzoic acid.[9] The synthesis of IV from acid VIII was not seriously considered as a preparative method because of the greater number of steps and more expensive reagents necessary to prepare VIII from *m*-hydroxybenzaldehyde. The preparation of I from acrylonitrile and *p*-bromophenol requires only two steps.

Additional proof for the position of the bromine atom was furnished by the nitration of III to produce a steam-volatile nitration product whose methyl ether did not react with a boiling alcoholic solution of silver nitrate. The steam volatility of this product indicates that the nitro group must be ortho to the phenolic hydroxyl, and the inactivity of the bromine atom indicates it to be meta to the nitro group. The indicated structure for III, with the bromine atom in the 4-position, is the only one in accord with these facts. Chromic acid oxidation of III produced a small amount of 4,7-hydrindenequinone; the bromine atom would not have been eliminated during oxidation to this product if it were in any but the 4-position.

The first approach to the preparation of IV had been based on the observation of Johnson and Shelberg[10] that β-(*p*-methoxyphenyl)-propionic acid could be cyclized in 85% yield to 5-methoxy-1-hydrindone. To this end β-(2-methoxy-5-bromophenyl)-propionic acid XII was prepared. The condensation of ethyl cyanoacetate with 2-methoxy-5-bromobenzaldehyde produced the cyanoester IX in good yield, but prolonged acid hydrolysis of IX produced only cyanoacid X. The condensation of the aldehyde with malonic acid produced the desired cinnamic acid XI but the reduction with hydrogen and Raney nickel removed the bromine atom.

IX, R = —CH=C(CN)COOEt
X, R = —CH=C(CN)COOH
XI, R = —CH=CH—COOH
XII, R = —CH_2CH_2COOH
XIII, R = —CH_2Cl



The desired acid XII was prepared in an over-all yield of 63% from *p*-bromoanisole by chlorometh-

(5) Krollpfeiffer and Schultze, *Ber.*, **57**, 600 (1924).

(6) von Auwers and Hilliger, *ibid.*, **49**, 2410 (1916).

(7) The migration of the bromine atom during the cyclization was the possibility which seemed most likely to produce a substance isomeric with the desired hydrindone. A discussion of the rearrangement of bromo compounds under acid conditions is presented by Moyle and Smith, *J. Org. Chem.*, **2**, 112 (1937).

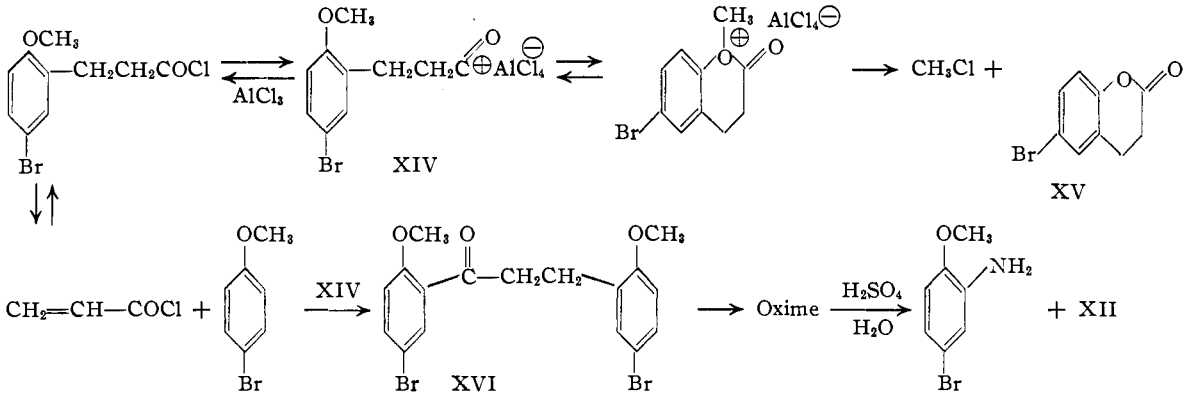
(8) Jarowski and Cramer (Washington A.C.S. Meeting, September, 1948) have observed that the carbonyl group of 2-carbethoxy-5-hydroxy-γ-chromenone is not reduced by hydrogen in the presence of Raney nickel. In this case chelation is also possible.

(9) We are indebted to Dr. Domenick Papa for a generous sample of β-(*m*-hydroxyphenyl)-propionic acid and a melting point sample of 2-bromo-5-methoxybenzoic acid. Schwenk and Papa have reported (Chicago A. C. S. meeting, September, 1948) that bromination of the silver salt of β-(*m*-methoxyphenyl)-propionic acid also produces VIII.

(10) Johnson and Shelberg, THIS JOURNAL, **67**, 1853 (1945).

ylation to 2-methoxy-5-bromobenzyl chloride (XIII) followed by alkylation of malonic ester with XIII.

Using a variety of reaction conditions we have been completely unable to cyclize either β-(2-methoxy-5-bromophenyl)-propionic acid XII or β-(*o*-methoxyphenyl)-propionic acid.[11] Neither stannic chloride nor anhydrous hydrogen fluoride caused any reaction of acid XII. With aluminum chloride in benzene or nitrobenzene the main product was 6-bromo-3,4-dihydrocoumarin (XV). When nitrobenzene was used as a solvent there was also obtained in 18% yield a ketone m. p. 93–94° (XVI). The structure assigned to this ketone is based on the analysis, molecular weight, oxidation by potassium permanganate to 2-methoxy-5-bromobenzoic acid and the Beckmann rearrangement of the oxime.



The results obtained in this attempted cyclization of the acid XII would indicate that the failure of β-(*o*-methoxyphenyl)-propionic acids to cyclize is due to preferential reaction of the positive carbon of the complex XIV with the oxygen of the methoxyl group rather than with the ring carbon meta to the methoxyl group. The relative yield of the dihydrocoumarin XV and the ketone XVI were not materially changed by the addition of a mole of *p*-bromoanisole to the cyclization mixture; this would indicate that the intramolecular reaction with oxygen was faster also than reaction with the ortho position of *p*-bromoanisole.

Acknowledgment.—The authors wish to express their appreciation for a Frederick Gardner Cottrell Research Grant which made possible the successful completion of this work.

Experimental[12]

β-Chloropropionic Acid.—Acrylonitrile (250 g.) was added to concentrated hydrochloric acid (2 liters), and the mixture refluxed for six hours. After cooling the precipitated ammonium chloride was filtered and the filtrate concentrated *in vacuo*. The residue was distilled to yield 384 g. (75%) of acid which boiled at 115–117° (32 mm.) and which solidified on standing for a short time.

***p*-Bromophenyl β-Chloropropionate.**—Phosphorus trichloride (90 ml.) was added dropwise to β-chloropropionic acid (332 g.) and the mixture heated at 110–120° for three hours. Then, a solution of *p*-bromophenol (533 g.) in toluene (500 ml.) was added and the mixture refluxed for an additional three hours. The cool reaction mixture was washed with dilute potassium hydroxide solution, dried and distilled. There was obtained 567 g. (65%) of the ester which boiled at 106–117° (0.4–0.6 mm.).

Anal. Calcd. for $C_9H_8O_2ClBr$: C, 41.02; H, 3.06. Found: C, 41.05; H, 3.11.

***p*-Bromophenyl α-Chloropropionate.**—α-Chloropropionyl chloride[13] (50.9 g.) and *p*-bromophenol (60.5 g.) were refluxed for two hours and the reaction mixture processed as for the previous ester. There was obtained 33.8 g. (53%) of the ester which boiled at 160–167° (26 mm.). This substance crystallized on standing and after recrystallization from ligroin (b. p. 90–110°) melted at 56.2–56.8°.

Anal. Calcd. for $C_9H_8O_2ClBr$: C, 41.02; H, 3.06. Found: C, 40.88; H, 3.20.

4-Bromo-7-hydroxy-1-hydrindone.—A mixture of *p*-bromophenyl β-chloropropionate (131.5 g.) and aluminum chloride (250 g.) was stirred while the temperature was maintained at 95–100° for six hours; the temperature was then raised to 170° and the reaction mixture was heated at this temperature for one hour. After cooling, the mixture was treated with ice water and then steam distilled. The steam distillate was chilled and filtered to yield 70.2 g. of yellow crystals. After drying and recrystallization from ligroin (b. p. 90–110°) there was obtained 49.8 g. (44%) of the hydrindone which melted at 142–145°.[14] This substance was obtained analytically pure by alternate recrystallization from methyl ethyl ketone and ligroin, m. p. 146.2–146.9°.

Anal. Calcd. for $C_9H_7O_2Br$: C, 47.60; H, 3.11; Br, 35.19. Found: C, 47.37; H, 3.18; Br, 35.32.

This compound can be preserved pure only if kept in a sealed evacuated container. Without this precaution surface oxidation of the crystals takes place; however, on standing in air only a small percentage of the compound is oxidized by this process. Thus, a sample left exposed to air for two weeks had the following analysis: C, 46.82; H, 3.20; Br, 33.97.

p-Bromophenyl α-chloropropionate was allowed to react with aluminum chloride at temperatures from 140–185° for periods of time varying from one-half hour to five hours, but the main steam volatile product was an oil.

(11) Heinzelmann, Kolloff and Hunter, THIS JOURNAL, **70**, 1386 (1948), have reported that β-(*o*-methoxyphenyl)-propionic acid could not be cyclized by anhydrous hydrogen fluoride, aluminum chloride or phosphorus pentoxide.

(12) All melting points are corrected. Microanalyses are by W. Manser and Lois E. May.

(13) Prepared by the method of Henry, *Compt. rend.*, **100**, 116 (1885).

(14) These conditions, which produce a maximum yield of the hydrindone, were worked out by Dr. G. L. Shoemaker, Cottrell Grant Research Fellow.

By extraction of an ether solution of the oil with sodium hydroxide and subsequent neutralization of the aqueous solution a very small amount of hydrindone II could be isolated.

4-Bromo-7-hydroxyhydrindene.—4-Bromo-7-hydroxy-1-hydrindone (65 g.) was refluxed with amalgamated zinc (75 g.) and alcohol (200 ml.) while hydrochloric acid (250 ml.) was added in portions during eight hours. After filtration and dilution with water the product was extracted with ether. Recrystallization from ligroin produced 49.6 g. (81%) of product which melted at 106–107°. The pure substance melts at 108–108.8°.

Anal. Calcd. for C_9H_9OBr: C, 50.73; H, 4.26. Found: C, 50.46: H, 4.39.

4-Bromo-7-methoxyhydrindene.—4-Bromo-7-hydroxyhydrindene (15 g.) was allowed to stand with a solution of diazomethane in ether (prepared from 16 g. of nitrosomethylurea) for twenty-four hours. The ether solution was washed with dilute sodium hydroxide (0.2 g. of the phenol was recovered) and the solvent was removed on the water pump. The crystalline residue was recrystallized from petroleum ether (30–60°). There was obtained 13.2 g. (82%) of product which melted at 66–66.5°.

Anal. Calcd. for $C_{10}H_{11}OBr$: C, 52.88; H, 4.88. Found: C, 52.47; H, 4.85.

β-(2-Bromo-5-methoxyphenyl)-propionic Acid.—β-(*m*-Methoxyphenyl)-propionic acid (5.0 g.) prepared by methylation of β-(*m*-hydroxyphenyl)-propionic acid[9] with dimethyl sulfate, was dissolved in carbon tetrachloride (100 ml.) and cooled to −10° while a solution of bromine (4.8 g.) in carbon tetrachloride (15 ml.) was added dropwise with mechanical stirring. On processing of the reaction mixture there was obtained 5.4 g. (75%) of product which melted at 81–83°. The purified acid melted at 83.7–84.4°.[15]

Oxidation of 0.5 g. of this substance by boiling with potassium permanganate solution produced 2-bromo-5-methoxybenzoic acid, melting point and mixed melting point with an authentic sample[9] 160–160.8°.

4-Bromo-7-methoxy-1-hydrindone.—**A.** β-(2-Bromo-5-methoxyphenyl)-propionic acid (4 g.) was dissolved in anhydrous hydrogen fluoride (100 ml.) contained in a copper reaction bottle and allowed to stand at room temperature until all of the hydrogen fluoride had evaporated. Recrystallization of the residual solid from alcohol produced 2.2 g. (60%) of product which melted at 133.6–134.2°.

B. The methylation of 4-bromo-7-hydroxy-1-hydrindone (1.8 g.) by reaction with dimethyl sulfate (2.9 ml.) and a slight excess of sodium hydroxide in methanol solution produced 1 g. of material which melted at 134.5–135°. The melting point of a mixture of this substance and the product obtained in part A was 133.5–134.5°.

Anal. Calcd. for $C_{10}H_9O_2Br$: C, 49.81; H, 3.84. Found: C, 49.67; H, 3.78.

7-Hydroxy-1-hydrindone.—**A.** 4-Bromo-7-hydroxy-1-hydrindone (5 g.) was shaken with hydrogen in the presence of palladium on barium sulfate (1 g.) at atmospheric pressure until no more hydrogen was absorbed (twenty hours). The catalyst was filtered off, the filtrate evaporated and the residue crystallized from petroleum ether. The product melted at 112–113°.[16]

B. Phenyl α-bromopropionate (20 g.) was treated with aluminum chloride (40 g.) according to the procedure of von Auwers.[6] There was obtained 1.55 g. (12%) of the steam-volatile 7-hydroxy-1-hydrindone. The melting point of this substance and also of a mixture of it and the product from part A was 112–113°.

4-Bromo-6-nitro-7-hydroxyhydrindene.—Fuming nitric acid (1 ml.) dissolved in acetic acid (10 ml.) was added dropwise to a solution of 4-bromo-7-hydroxyhydrindene (2.4 g.) in acetic acid (25 ml.) at 5°. When the addition was complete the reaction mixture was allowed to stand fifteen minutes and then poured into cold water. The crude product was filtered and purified first by steam distillation and then by recrystallization from ethanol. There was obtained 2.3 g. (80%) of the bright yellow nitrophenol which melted at 101.8–102.6°.

Anal. Calcd. for $C_9H_8O_3NBr$: C, 41.88; H, 3.12; N, 5.43. Found: C, 41.99; H, 3.23; N, 5.32.

The methyl ether was prepared by allowing the nitrophenol to stand for twenty-four hours with a solution of diazomethane. After recrystallization from ethanol the nearly colorless product melted at 81.7–82.2°.

Anal. Calcd. for $C_{10}H_{10}O_3NBr$: C, 44.14; H, 3.70; N, 5.15. Found: C, 44.16; H, 3.82; N, 5.03.

There was no reaction when this methyl ether was boiled with an alcoholic solution of silver nitrate.

4,7-Dihydroxyhydrindene.—4-Bromo-7-hydroxyhydrindene (1 g.) dissolved in 70% acetic acid (100 ml.) was treated with chromic anhydride (6 g.) for ten minutes at 70–75°. The product was isolated by dilution of the reaction mixture with cold water and ether extraction. The ether extract was concentrated and the quinone sublimed *in vacuo*. The oily sublimate was shaken with ether and aqueous sodium hydrosulfite. Evaporation of the ether left the crystalline hydroquinone (28 mg.) which was purified by crystallization from methyl ethyl ketone and ligroin. When heated under a microscope the product began to melt at 155–160°; however, at this temperature a new crystalline form appeared which melted sharply at 186–187°.

This same behavior was noted with an authentic sample prepared by the method of Arnold and Zaugg[17] and there was no lowering of the melting point when the two samples were mixed and heated.

Ethyl α-Cyano-2-methoxy-5-bromocinnamate.—2-Methoxy-5-bromobenzaldehyde[18] (50 g.) was treated with ethyl cyanoacetate (30 g.), ammonium acetate (3.9 g.), acetic acid (12 g.) and benzene (50 ml.) according to the directions of Cope, *et al.*[19] After recrystallization from ethanol there was obtained 65 g. (91%) of product which melted at 103–104°.

Anal. Calcd. for $C_{13}H_{12}O_3NBr$: C, 50.34; H, 3.90. Found: C, 50.60; H, 4.04.

α-Cyano-2-methoxy-5-bromocinnamic Acid.—Ethyl α-cyano-2-methoxy-5-bromocinnamate (31 g.) was refluxed for thirty hours with a mixture of hydrochloric acid (150 ml.) and acetic acid (300 ml.). After filtration of the cold reaction mixture there was obtained 27 g. (96%) of the acid which crystallized as yellow needles from alcohol, m. p. 240–242° (dec.).

Anal. Calcd. for $C_{11}H_8O_3NBr$: C, 46.83; H, 2.86; N, 4.97; Br, 28.33. Found: C, 46.91; H, 2.79; N, 4.53; Br, 28.16.

A repetition of the treatment with acid produced no further change in this substance. When a solution of this acid in potassium hydroxide was allowed to stand at room temperature, crystals of 2-bromo-5-methoxybenzaldehyde (m. p. and mixed m. p. with an authentic sample 117–118°) were slowly deposited.

2-Methoxy-5-bromocinnamic Acid.—The condensation of 2-methoxy-5-bromobenzaldehyde (13.6 g.) with malonic acid (6.5 g.) produced only 2.1 g. (13%) of the desired acid, m. p. 223–226°.[20] The starting aldehyde was recovered in 62% yield (8.5 g.).

The reduction of 2-methoxy-5-bromocinnamic acid (1 g.) in alkaline solution with hydrogen (40 lb.) and Raney nickel produced β-(*o*-methoxyphenyl)-propionic acid, m. p. and mixed m. p. with an authentic sample 87–88°.

(15) Schwenk and Papa (ref. 9) report a melting point of 83-84° for this substance.

(16) von Auwers and Hilliger, ref. 6, report the melting point of this substance to be 111-112°.

(17) Arnold and Zaugg, THIS JOURNAL, **63**, 1317 (1941), report the melting point to be 184–185°.

(18) Graebe, *Ann.*, **340**, 210 (1905).

(19) Cope, Hoffman, Wyckoff and Hardenbergh, *ibid.*, **63**, 3452 (1941).

(20) Billmann and Rimbert, *Bull. soc. chim.*, **33**, 1473 (1923), report the melting point of this substance as 222-223°.

β-(2-Methoxy-5-bromophenyl)-propionic Acid.—**A.** 2-Methoxy-5-bromobenzyl chloride[21] (250 g.) was slowly added to a cold (5–10°) solution of sodium (25 g.) and malonic ester (250 g.) in absolute ethanol (800 ml.). The mixture was stirred for twelve hours at room temperature and then refluxed for an additional three hours. The crude alkylated malonic ester was isolated by pouring the reaction mixture into water (3 liters) and extracting with ether. The ether and excess malonic ester were removed by distillation until the vapor temperature of the distillate reached 95° (6 mm.). The residue (371 g.) was refluxed for twenty hours with potassium hydroxide (145 g.) water (100 ml.) and methanol (400 ml.). The mixture was poured into water and extracted with ether. The aqueous solution was acidified and the solid malonic acid filtered and decarboxylated by heating to 180°. The crude acid was purified by dissolving in dilute potassium hydroxide, washing the aqueous solution with ether, reprecipitating with hydrochloric acid and finally recrystallizing from benzene and petroleum ether. There was obtained 226 g. (82%), of the acid which melted at 117–118°.

Anal. Calcd. for $C_{10}H_{11}O_3Br$: C, 46.35; H, 4.28. Found: C, 45.74; H, 4.37.

B. β-(*o*-Methoxyphenyl)-propionic acid was brominated by the same procedure as for the meta isomer. The product from this reaction melted at 117–118° and when mixed with the acid obtained in part A caused no depression of the melting point. The oxidation of this acid with aqueous potassium permanganate produced 2-methoxy-5-bromobenzoic acid, m. p. 119°. A mixture of this oxidation product (m. p. 119°) and β-(2-methoxy-5-bromophenyl)-propionic acid (m. p. 117–118°) melted at 84–95°.

Cyclization Attempts with *o*-Methoxyphenylpropionic Acid.—Seven experiments using variations of the procedure developed by Johnson and Shelberg[10] for the para isomer, were carried out but in each case there was obtained either recovered acid or an amorphous precipitate (m. p. *ca.* 230–280°) which was insoluble in both organic and inorganic reagents (presumably a polymer). In three experiments small amounts (0.5–5%) of an oil were isolated which reacted with 2,4-dinitrophenylhydrazone. The small amounts of partially purified 2,4-dinitrophenylhydrazones obtained (m. p. 113–118°, 153–156° and 245–250°) were not further investigated.

Cyclization Attempts with β-(2-Methoxy-5-bromophenyl)-propionic Acid.—This acid (24 g.) was recovered quantitatively after standing for thirty hours at room temperature with anhydrous hydrogen fluoride (200 g.).

The acid chloride when treated with stannic chloride in benzene solution at room temperature did not undergo any reaction.

The acid chloride (prepared from 79 g. of acid and thionyl chloride) was dissolved in benzene (400 ml.) and aluminum chloride (40 g.) was added slowly to the cold solution. The mixture was stirred for six hours at room temperature, then after washing with water the organic layer was extracted with dilute potassium hydroxide. Acidification of this alkaline solution liberated 21 g. of β-(2-hydroxy-5-bromophenyl)-propionic acid which melted at 139–140°.[22] Evaporation of the benzene and recrystallization of the residue from ethanol produced 18 g. of 6-bromo-3,4-dihydrocoumarin, m. p. 106–106.5°.[23] It was subsequently observed that the dihydrocoumarin can be completely extracted from an organic layer by warm potassium hydroxide solution. Both the dihydrocoumarin and the hydroxy acid were reconverted to β-(2-methoxy-5-bromophenyl)-propionic acid (m. p. and mixed m. p. 117–118°) by reaction with dimethyl sulfate and potassium hydroxide.

The acid chloride (60 g., b. p. 152–155° (3 mm.)) was dissolved in nitrobenzene (200 ml.) and treated with a solution of aluminum chloride (29 g.) in nitrobenzene (100 ml.) at room temperature for nine hours. The dihydrocoumarin was removed by shaking with warm potassium hydroxide solution to yield 37 g. (70%) of β-(2-hydroxy-5-bromophenyl)-propionic acid. After removing solvents and recrystallizing from ethanol there was obtained 9 g. (18%) of a substance melting at 93–94°.

Anal. Calcd. for $C_{17}H_{16}O_3Br_2$: C, 47.69; H, 3.77; Br, 37.33. Found: C, 47.18, 47.72; H, 3.76, 3.79; Br, 36.87.

In an attempt to prepare larger quantities of the above substance β-(2-methoxy-5-bromophenyl)-propionic acid (14 g.) was treated with aluminum chloride in nitrobenzene as above except that one equivalent of *p*-bromoanisole (10 g.) was added. By extraction of the reaction mixture with sodium bicarbonate solution 0.89 g. (6%) of the starting acid was recovered. Most of the dihydrocoumarin was removed by recrystallization from alcohol (7.3 g., 60%), the remainder by washing with warm potassium hydroxide solution (acidification liberated 0.9 g. of crude hydroxy acid). The residual ketone (2.2 g., 9%) was contaminated with a small amount of another substance (0.09 g., m. p. 149–151°) which was obtained by concentration of the mother liquors after most of the ketone (m. p. 92–94°) had been removed.

Structure Proof for β-(2-Methoxy-5-bromophenyl)-ethyl 2′-Methoxy-5′-bromophenyl Ketone.—The molecular weight determined by the depression of the freezing point of benzene was 412 (calcd. 428). Oxidation with aqueous potassium permanganate produced only 2-methoxy-5-bromobenzoic acid, m. p. and mixed m. p. 118–119° (the authentic sample was prepared by oxidation of 2-methoxy-5-bromobenzaldehyde). The following derivatives were prepared by standard procedures; oxime, m. p. 141–142°.

Anal. Calcd. for $C_{17}H_{17}O_3NBr$: C, 46.07; H, 3.87. Found: C, 46.10; H, 4.18.

Phenylhydrazone, m. p. 159–161°.

Anal. Calcd. for $C_{23}H_{22}O_2N_2Br_2$: C, 53.30; H, 4.28. Found: C, 53.07; H, 4.00.

p-Nitrophenylhydrazone, m. p. 187–188°.

Anal. Calcd. for $C_{23}H_{21}O_4N_3Br_2$: C, 49.04; H, 3.76. Found: C, 49.22; H, 3.96.

The oxime (0.4 g.) was mixed with 85% sulfuric acid (10 ml.) and heated to 180° during five minutes. After dilution with water (100 ml.) the solution was boiled for five hours. The cool hydrolysis mixture was extracted with ether and the aqueous layer made alkaline and extracted with ether to remove the amine. There was obtained 0.13 g. of amine which after recrystallization from petroleum ether melted at 94.8–95.6°. The melting point of a mixture of this substance and an authentic sample of 2-amino-4-bromoanisole was 95–96.2°. The 2-amino-4-bromoanisole was prepared by reduction with iron and acetic acid of 2-nitro-4-bromoanisole (m. p. 84–85°) which had been prepared by the method of Reverdin and Düring.[24] The ether extract of the original hydrolysis mixture was shaken with sodium bicarbonate solution to remove the acid. Acidification of the aqueous solution followed by ether extraction and evaporation of the ether yielded 0.04 g. of crude acid. After purification by sublimation and recrystallization from petroleum ether this substance melted at 116–118° and was found by mixed melting to be identical with β-(2-methoxy-5-bromophenyl)-propionic acid.

Summary

A satisfactory method for the preparation of 4-bromo-7-methoxyhydrindene has been worked out using the von Auwers hydrindone synthesis.

The structure of the intermediate 4-bromo-7-hydroxy-1-hydrindone has been proven by an alternate synthesis.

(21) Prepared in 78% yield by the method of Quelet, *Bull. soc. chim.*, [5] **1**, 539 (1934).

(22) Lasch, *Monatsh.*, **34**, 1662 (1913), reports the melting point as 142°.

(23) Fittig and Hochstetter, *Ann.*, **226**, 362 (1884), report the melting point as 106°.

(24) Reverdin and Düring, *Ber.*, **32**, 161 (1899).

It has been established that attempted cyclization of β-(2-methoxy-5-bromophenyl)-propionic acid produces 6-bromo-3,4-dihydrocoumarin as the main product.

The structure of a minor product (β-(2-methoxy-5-bromophenyl)-ethyl 2′-methoxy-5′-bromophenyl ketone) of the cyclization has been proved. This substance must have been formed by the elimination of a propionic side chain in the presence of aluminum chloride.

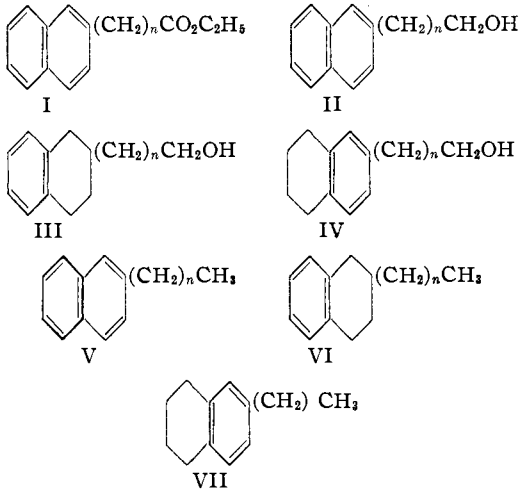
NEW BRUNSWICK, N. J., AND NEW YORK, N. Y. RECEIVED MAY 14, 1949

[A COMMUNICATION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Selective Hydrogenation of Esters Containing a Naphthalene Nucleus

BY HOMER ADKINS AND EDWARD E. BURGOYNE[1]

The selective hydrogenation of a carbethoxy to a carbinol group, in an ester containing a naphthalene nucleus, has not seemed a feasible process. This was true because the naphthalene nucleus is rather rapidly and quantitatively hydrogenated to a tetralin over the copper chromium oxide catalyst at 150–190°. A further complication arises from the fact that the unsaturation of the rings labilizes an attached carbinol group toward hydrogenolysis. Thus the hydrogenation of esters of the type shown in I may give one or all of the three types of alcohols II, III and IV, and the hydrocarbons V, VI and VII resulting from hydrogenolysis.



Ethyl and methyl esters where "*n*" has a value of 0, 1, 2 and 3, and the chain is in the 1- or the 2-position of the nucleus, have been subjected to hydrogenation over a copper chromium oxide catalyst.[2] A summary of the numerical results of several of the more significant hydrogenations is given in Table I. The extent of hydrogenation is indicated in the fourth column of the table by stating the percentage to which the carbethoxy group reacted, as well as the moles of hydrogen absorbed during the period of reaction. A hydrogenation of ethyl benzoate to benzyl alcohol is also listed in the table. The result at 125° was similar to that reported at 165° by Mozingo and Folkers, who were the first to hydrogenate a carbethoxy group on a benzenoid nucleus to a carbinol group.[3]

The experimental conditions, as well as the structure of the ester, make important differences in the rates and relative rates of the various types of hydrogenation and hydrogenolysis. The compounds, where *n* equals 1, 2 or 3 in formula I, underwent hydrogenation to alcohols smoothly at 190–200°. The yield of alcohols when *n* equals 1 was lower (77%) than where *n* equals 2 or 3 (90%). There was no significant difference in behavior between the esters containing the 1- as compared with the 2-naphthyl group. However, in all the four esters just mentioned, four moles of hydrogen per mole of ester were absorbed so that the alcohol produced contained a tetrahydronaphthyl, rather than a naphthyl, group. That is to say, the naphthalene nucleus is sufficiently labile toward hydrogenation in the presence of the copper oxide–chromite catalyst so that hydrogenation of the ring took place under the same conditions required for the hydrogenation of the carbethoxy to a carbinol group. The relative distribution of hydrogen between the substituted and unsubstituted rings during catalytic hydrogenation, will be considered in more detail below, but it will suffice for the present to state that the tetrahydronaphthyl alcohols of structure IV predominate with lesser amounts of alcohols of type III.

In compounds where *n* equals zero in I, hydrocarbons are almost the only products resulting when the esters are hydrogenated at 190–200°. Fortunately, the esters where *n* equals 0 or 1, can be hydrogenated under milder conditions than when *n* equals 2 or 3. The naphthoates and naphthylacetates may be hydrogenated at tempera-

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(2) The catalyst was prepared as described by Adkins, "Reactions of Hydrogen," University of Wisconsin Press, Madison, 1937, p. 13, except the decomposition step was carried out by a procedure recommended by Dr. Ralph Mozingo. This consisted of decomposing 2 g. of copper ammonium chromate, stirring in another 2 g. and carefully decomposing, then adding 4 g., etc., each time doubling the amount added and carrying out the decomposition at the minimum temperature with constant stirring until a total of 60-100 g. of material was used.

(3) Mozingo and Folkers, THIS JOURNAL, 70, 230 (1948).