40°; 10% NaOH (20 ml) was added; and this temperature was kept for 0.5 hr. The mixture was cooled and poured into 1500 ml of ice water containing 10 ml of glacial HOAc. The white precipitate after drying and recrystallizing weighed 56 g (67%), mp 167–168°. The yield of cyanohydrin can be raised to 85% of theoretical by running the reaction overnight at room temperature. An infrared spectrum of this solid exhibited absorptions *inter alia* at 3400 (OH stretching vibration) and at 2265 cm^{-1} ($C\equiv N$ stretching vibration).

Anal. Calcd for $C_8H_{10}O_2N_2$: C, 57.85; H, 6.07; N, 16.85. Found: C, 57.54; H, 6.14; N, 16.97.

Dimethyl 1,4-dihydroxy-1,4-cyclohexanedicarboxylate (3) was prepared by slowly adding HCl (Matheson, reagent grade) to a solution of **2** (8.4 g, 0.05 mol) in methanol (100 ml) until no more gas was absorbed. The mixture was stirred for an additional 2 hr and the resulting precipitate was collected and reacted with water (200 ml) overnight. The recrystallized white solid weighed 9.1 g (81% yield), mp 162–175°. An infrared spectrum of this material exhibited absorptions *inter alia* at 3510 (OH stretching vibration) and at 1730 cm^{-1} (C=O stretching vibration). The diester (2.0 g) was saponified under usual conditions[10] and the white crystals collected after acidification were recrystallized to obtain 1.5 g of 1,4-dihydroxy-1,4-cyclohexanedicarboxylic acid, mp 224–237°. An infrared spectrum of this solid (KBr pellet) exhibited absorptions *inter alia* at 3415 and 1720 cm^{-1}.

Anal. Calcd for $C_8H_{12}O_6$: C, 47.06; H, 5.93. Found: C, 46.92; H, 5.81.

Dimethyl 1,4-Diacetoxy-1,4-cyclohexanedicarboxylate (4).—To acetic anhydride (16.4 g, 0.16 mol) at 80° was slowly added a solution of compound **3** (9.2 g, 0.04 mol) in HOAc (80 ml). The reaction mixture was refluxed overnight, cooled, and poured into ice water. After drying and recrystallization 11.4 g (90% yield) of a white solid was obtained, mp 168–182°.

An infrared spectrum of this solid exhibited an absorption, *inter alia*, at 1750 cm^{-1} (acetate C=O stretching vibration).

Anal. Calcd for $C_{14}H_{20}O_8$: C, 53.16; H, 6.38. Found: C, 53.14; H, 6.27.

Dimethyl Cyclohexa-1,3-diene-1,4-dicarboxylate (5).—Pyrolyses[11] were conducted in a 0.75 × 18 in. quartz column, filled with 0.25-in.-diameter glass beads, mounted vertically and surrounded by an electric heating oven. A slow stream of nitrogen was passed through the column during the pyrolysis. The temperature was controlled by means of a "Pyro-O-Vane" temperature controller. The temperature inside the column was measured with a thermocouple inserted in a well near the center of the column. The pyrolysate was collected in two traps connected in series and immersed in a Dry Ice–perchloroethylene mixture.

In a typical run, 5.0 g of dimethyl 1,4-diacetoxy-1,4-cyclohexanedicarboxylate was dissolved in 300 ml of methyl acetate at 50°, maintained at this temperature throughout the reaction by means of flexible heating tape, and was dropped through the column at 400° and at a rate of *ca.* 2.5 ml/min. When the addition was complete, the column was allowed to cool and was washed with additional methyl acetate.

Removal of the solvent afforded 3.8 g of a slightly yellow product. Vapor phase chromatographic analysis[12] revealed that 95% of the starting material had been converted into two major products with retention times of 5.8 and 6.2 min. The first peak accounted for 18% of the pyrolysate, whereas the latter represented a 75% yield. Samples of both materials were collected from the gas chromatograph. The product with a retention time of 5.8 min melted at 139–141°, identical with the melting point of dimethyl terephthalate.[13] Comparison of the infrared spectrum and vpc retention time with an authentic sample[14] completed the identification. The 6.2-min product melted at 83.5–84.2° (lit.[2] mp 83.1–84.6°). Comparison of the infrared and ultraviolet spectra with those of authentic samples helped confirm the identification.[15] To complete the identification, the adduct of the pyrolysate with maleic anhydride was prepared by a previously described procedure.[16] The adduct melted at 185–192° (lit. mp 188.0–188.6°,[16] 191.5°[17]) and its infrared spectrum, as a KBr pellet, exhibited absorptions at 1865, 1780, 1745, and 1620 cm^{-1} identical with the published spectrum[17] of 1,4-bis(methoxycarbonyl)bicyclo[2.2.2]oct-5-ene-*endo*-2,3-dicarboxylic anhydride.

Registry No.—**2**, 16273-48-6; **3**, 16273-49-7; **3**, free acid, 16273-50-0; **4**, 16273-51-1; **5**, 1659-95-6.

Acknowledgment.—The author is grateful to Dr. J. W. Way for many valuable discussions.

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[10] J. Cason and H. Rapoport, "Laboratory Text in Organic Chemistry," Prentice-Hall, Inc., Englewood Cliffs, N. J., 1950, p 83.

[11] W. J. Bailey, R. Barclay, and R. A. Baylouney, *J. Org. Chem.*, **27**, 1851 (1962).

[12] A 6 ft. × 0.25 in. diameter 10% XE-60 on 60/80 mesh Chromosorb W column was used. No corrections were made for differences in thermal conductivities.

[13] I. Heilbron, "Dictionary of Organic Compounds," Vol. 5, Oxford University Press, New York, N. Y., 1965, p 2,949.

[14] Du Pont dimethyl terephthalate, refined grade.

[15] The author is grateful to Dr. J. C. Kauer for supplying these spectra.

[16] J. C. Kauer, U. S. Patent 3,071,597 (Jan 1, 1963).

[17] G. Smith, C. L. Warren, and W. R. Vaughan, *J. Org. Chem.*, **28**, 3323 (1963).

Synthesis of α-Hydroxyarylacetic Acids from Bromoform, Arylaldehydes, and Potassium Hydroxide, with Lithium Chloride Catalyst

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A one-step preparation of α-methoxyarylacetic acids from arylaldehydes, bromoform (or chloroform), and potassium hydroxide in methanol has been described.[1] The preparative method for the α-hydroxyarylacetic acids given here is a modification of that procedure, differing in that lithium chloride serves as an additional catalyst along with the potassium hydroxide,[2] and a 50:50 mixture of water and 1,4-dioxane acts as solvent, instead of methanol. The yields in these α-hydroxy compound syntheses (quantitative) are decidedly better than those obtained in the preparations of α-methoxy compounds (1–80%).

There are a number of articles in the literature wherein others have reported preparation of trihalomethyl carbinols (a proposed intermediate in this reaction) in heterogeneous media, and/or treated trihalomethylcarbinols with nucleophilic reagents to obtain α-substituted acids, but none of these procedures[2,3] produces a quantitative yield of product.

In some of these cases[2] the yields are less because side reactions, such as the Cannizzaro, are occurring simultaneously or exclusively. In fact, when the preparations of the α-hydroxyarylacetic acids were attempted in pure 1,4-dioxane and with lithium hydroxide as a base catalyst (a heterogeneous mixture), with six different aryl aldehydes only the corresponding arylcarboxylic acids were isolated.

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[1] W. Reeve and C. W. Woods, *J. Amer. Chem. Soc.*, **82**, 4062 (1960); W. Reeve and E. L. Compere, Jr., *ibid.*, **83**, 2755 (1961).

[2] The potassium hydroxide is a reagent as well as a catalyst; see E. D. Bergmann, D. Ginsburg, and D. Lavie, *ibid.*, **72**, 5012 (1950).

[3] (a) P. Hebert, *Bul. Soc. Chim. Fr.*, **27**, 45 (1920); (b) J. W. Howard, *J. Amer. Chem. Soc.*, **47**, 455 (1925); (c) J. W. Howard, *ibid.*, **52**, 5059 (1930); (d) J. Jocicz, *Zh. Russ. Fiz. Khim. Obshchest.*, **29**, 100 (1897); *Chem. Zentr.*, **1**, 1013 (1897).

TABLE I

SPECIFIC DATA ON THE α-HYDROXYARYLACETIC ACID SYNTHESES

Compd[j]	Mp, °C		Quantity of starting aldehydes	Crude yields of hydroxy acids[c]	Recrystn solvent	Analytical data					
						Carbon, %		Hydrogen, %		Neut equiv	
	Obsd	Lit.				Calcd	Found	Calcd	Found	Calcd	Found
α-Hydroxyphenylacetic acid	118–119.5	118–119[d]	26.5 g (0.25 mol), benzaldehyde	34.2–35.1 g or 90.0–92.3% 28.5 g of 75.0%[b]	5:1 Chloroform–ligroin (60–90°)	63.16	63.12	5.29	5.37	152	153
2-Chloro-α-hydroxyphenylacetic acid	82–83	85–85.5[e]	35.1 g (0.25 mol), 2-chlorobenzaldehyde	45.9–47.2 g or 98.3–100%	Chloroform	51.49	51.71	3.78	3.97	186.5	188
3-Chloro-α-hydroxyphenylacetic acid	106.5–107	115–115.5[e]	10 g (0.07 mol), 3-chlorobenzaldehyde	13.2–13.7 g or 99.5–100%	Chloroform	51.49	51.63	3.78	3.70	186.5	186
4-Chloro-α-hydroxyphenylacetic acid	119–120	120.5–121[e]	35.1 g (0.25 mol), 4-chlorobenzaldehyde	45.1–46.8 g or 96.8–100%	Chloroform–ligroin (60–90°)	51.49	51.36	3.78	3.94	186.5	187
2-Fluoro-α-hydroxyphenylacetic acid	114–115	116.5[f]	10 g (0.08 mol), 2-fluorobenzaldehyde	12.5–13.7 g or 91.3–100% 7.6 g of 60.8%	Chloroform	56.48	56.46	4.15	4.27	170	171
3-Fluoro-α-hydroxyphenylacetic acid	98–99	101[f]	10 g (0.08 mol), 3-fluorobenzaldehyde	12.2–14.5 g or 89.0–100% 12.2 g of 89.0%	Chloroform	56.48	56.50	4.15	4.17	170	168
4-Fluoro-α-hydroxyphenylacetic acid	138–139.5	133[f]	10 g (0.08 mol), 4-fluorobenzaldehyde	12.7–14.1 g or 92.7–100% 10.2 g of 74.5%[b]	Chloroform	56.48	56.51	4.15	4.16	170	171
4-Methoxy-α-hydroxyphenylacetic acid	100–101	108–109[g]	17 g (0.125 mol), 4-methoxybenzaldehyde	10.3–10.8 g or 44.3–47.5%	Chloroform	59.34	59.39	5.53	5.51	182	181
α-Hydroxy-α-(1-naphthalene)acetic acid	87–88	91–93[h]	25 g (0.16 mol), 1-naphthaldehyde	25.2–26.6 g or 77.8–82.2%	5:1 Chloroform–ligroin (60–90°)	71.28	71.36	4.93	5.12	202	203
α-Hydroxy-α-(2-naphthalene)acetic acid	155–156	158[i]	10 g (0.07 mol), 2-naphthaldehyde	10.7–12.3 g or 82.6–95.2% 8.7 g of 67.2%[b]	5:1 Chloroform–ligroin (60–90°)	71.28	71.36	4.93	4.86	202	202

[a] Analyses (C–H) were by Spang Microanalytical Laboratory, Ann Arbor, Mich. 48109. [b] Yields obtained when the reaction systems were diluted twofold with solvent. [c] Infrared spectra of the "crudes" are identical with those of the analytical samples. [d] G. Dorner, *Chem. Zentr.*, 4901 (1959). [e] S. S. Jenkins, *J. Amer. Chem. Soc.*, **53**, 2341 (1931). [f] R. Belcher, A. Sykes, and J. C. Tatlow, *Anal. Chim. Acta*, **10**, 34 (1954). [g] R. Quelet and J. Gavarret, *Bull. Soc. Chim. Fr.*, 1075 (1950). [h] A. McKenzie and W. S. Dennler, *J. Chem. Soc.*, 1599 (1926). [i] R. Quelet, C. Borgel, and R. Durand, *Compt. Rend.*, **240**, 1900 (1955). [j] The respective registry numbers are 90-64-2, 10421-85-9, 16273-37-3, 492-86-4, 389-31-1, 395-05-1, 395-33-5, 10502-44-0, 6341-54-4, 14289-44-2.

Certain other variations in the reaction conditions were shown to affect the product yields. In six cases (see Table I), when a twofold dilution of the reactants was made by adding more solvent, the yields were reduced to 55–89% instead of being quantitative. In the case of mandelic acid preparation, if the lithium chloride was excluded, the yields in three trials were less (62% average) even than in the cases above where the twofold dilutions were made without the exclusion of this catalyst. These data suggest that the lithium chloride exerts a significant catalyzing effect, presumably by a loose attachment of the lithium ion to the carbonyl oxygen.

Aside from the utility of this method of preparation, the products were of interest because it was thought that they might have the ability to form relative insoluble crystalline sodium[1] and cesium[4] acid salts from aqueous solution, a property which mandelic acid and α-methoxyarylacetic acids share.[5,6]

Experimental Section

General Procedure for Preparing α-Hydroxyarylacetic Acids.—In a 600–800-ml erlenmeyer flask were placed 0.5 mol of lithium chloride, 1.0 mol of potassium hydroxide, and 200 g of ice. To this mixture were added 200 ml of 1,4-dioxane, 0.25 mol of arylaldehyde, and 0.25 mol of bromoform. The mixture (containing some undissolved solids) was placed in a refrigerator (5–10°) and was stirred magnetically for 24 hr. If the pH was then below 12, 0.125 mol potassium hydroxide was added. Then the mixture was allowed to stir outside the refrigerator at 30–35° for another 24 hr.

The solution was then transferred to an 800-ml beaker, diluted to 600-ml volume with water. This solution was extracted three times with 50-ml portions of ether.[7] The aqueous layer was then acidified to a pH of 1 and extracted four times with 50-ml portions of ether. The combined ether extract was dried over magnesium sulfate, filtered, and evaporated to obtain the crude acid (usually a colored oil which solidified over several days time). These crude materials were recrystallized in an appropriate solvent; see Table I.

Registry No.—Bromoform, 75-25-2; potassium hydroxide, 1310-58-3; lithium chloride, 7447-41-8.

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(4) Only the α-methoxyarylacetic acids do this: E. L. Compere, Jr., unpublished results.

(5) Many alkali acid salts of monobasic acids have been known for over a century [N. V. Sidgwick, *J. Chem. Soc.*, **127**, 2379 (1925)], but a survey of the literature [J. C. Speakman, *ibid.*, 3357 (1949), and references therein] shows that, excepting those referred to above, most are easily dissolved in water.

(6) All of the α-hydroxyarylacetic acids form initially soluble sodium acid salts, excepting the 1-naphthyl derivative; the two least soluble sodium acid salts were the 2-naphthyl (0.12 g/100 g of H_2O) and the *p*-chlorophenyl (0.37 g/100 g of H_2O) derivatives, whose solubilities were determined after the salts had been kept dry for 6 months. Other alkali-metal acid salts are not easily formed, just as in the case of those of mandelic acid: A. McKenzie and N. Walker, *ibid.*, 356 (1922).

(7) In several of the preparations, notably the cases of *p*-methoxy-α-hydroxyphenylacetic and mandelic acids, a precipitate occurred which is presumed to be a normal lithium salt of the respective acid. In these cases the reaction mixture was acidified and extracted with ether, and the ether extract was extracted twice with 5% sodium hydroxide, to remove the acid. This basic solution was then treated according to the general procedure. In the *p*-methoxy case, the precipitate may be the cause of the lower yield.