absolute alcohol (adding in all 50 cc. of the latter) and fractionating, 9 g. (72% of theoretical) of pure glycerol β-methyl ether, b. p. 125 (14 mm.), was obtained; $d^{17°}_{4°} = 1.1300$; $n^{17°}_{D} = 1.4500$.

In like manner, 17 g. of 1,2-ethylidene glycerol methyl ether yielded 10 g. of glycerol α-methyl ether, b. p. 111–112° (13 mm.), and a small higher fraction containing some β-isomer. That the main fraction was a practically pure α-ether was shown by its refractive index and density, $n^{17°}_{D} = 1.4462$ and $d^{17°}_{4°} = 1.1191$, compared with $n^{17°}_{D} = 1.4460$ and $d^{17°}_{4°} = 1.1197$ reported by Irvine for pure glycerol methyl ether.

Hydrolysis of the Isomeric Ethylidene Glycerols.—Twenty g. of each of the acetals was heated at 130° for one hour with 10 cc. of 5% phosphoric acid, using a reflux condenser maintained at 40°. The latter in turn was connected to a well cooled spiral condenser to collect the acetaldehyde. 20.26 g. of 1,2-ethylidene glycerol (A) gave 7.53 g. of acetaldehyde; yield, 99%. 18.81 g. of 1,3-ethylidene glycerol (B), treated in like manner, gave 6.93 g. of acetaldehyde; yield, 98%.

Summary

1. The preparation, isolation and quantitative separation of the two isomeric ethylidene glycerols are described.

2. The corresponding methyl ethers and benzoates have been prepared and their physical constants determined.

Montreal, Canada

[Contribution from the Morley Chemical Laboratory of Western Reserve University]

THE SYNTHESIS OF CERTAIN IODO-ALKOXY ACIDS AND THE MECHANISM OF THE REACTIONS BY WHICH THEY ARE FORMED

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Received April 16, 1928 Published August 4, 1928

The ready substitution of the chlorine atom in α-iodo-β-chlorophenylpropionic acid by the hydroxyl, methoxyl and ethoxyl groups was demonstrated by Erlenmeyer[1] in 1896. The reaction of α-iodo-β-chlorophenylpropionic acid with water was shown to produce α-iodo-β-hydroxyphenylpropionic acid, while its reaction with solutions of potassium hydroxide in absolute methyl and ethyl alcohols gave, respectively, α-iodo-β-methoxyphenylpropionic acid and α-iodo-β-ethoxyphenylpropionic acid.

In applying the procedure of Erlenmeyer to the synthesis of a variety of α-iodo-β-alkoxyphenylpropionic acids, the fact soon came to our attention that the use of potassium hydroxide is unnecessary. When solutions of α-iodo-β-chlorophenylpropionic acid in a number of different alcohols were allowed to stand for several hours, the α-iodo-β-alkoxyphenylpropionic acids resulted. The yields of the iodo-alkoxy acids depend upon the alcohol, being lowest in the case of *iso*propyl and *tert.*-butyl alcohols. The reaction is not precluded by the substitution of the

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[1] Erlenmeyer, *Ann.*, **289**, 259 (1896).

α-hydrogen atom in α-iodo-β-chlorophenylpropionic acid by the methyl group, since α-iodo-α-methyl-β-chlorophenylpropionic acid was shown to react with absolute methyl alcohol to yield α-iodo-α-methyl-β-methoxyphenylpropionic acid. Although the methyl ester of α-iodo-β-chlorophenylpropionic acid does not react with water,[1] it reacts readily with absolute methyl alcohol to give methyl α-iodo-β-methoxyphenylpropionate.

A more suitable method for the preparation of the α-iodo-β-alkoxyphenylpropionic acids was found to be the reaction of iodine monochloride with cinnamic acid and the appropriate alcohol. In order to avoid esterification of the acids, the reaction was carried out in the presence of calcium carbonate. The methoxy and ethoxy acids were also prepared by the introduction of chlorine into solutions of cinnamic acid and iodine, or an alkali iodide, in the appropriate alcohol. The reaction of iodine monochloride and absolute methyl alcohol with crotonic acid yields iodomethoxybutyric acid.

In addition to the synthesis of α-iodo-β-hydroxyphenylpropionic acid by the reaction of water with α-iodo-β-chlorophenylpropionic acid, Erlenmeyer showed that the compound may be prepared by the reaction of the hydrochloride of iodine monochloride with sodium cinnamate in aqueous solution. We have found the introduction of chlorine into a suspension of iodine and cinnamic acid in water to be a convenient procedure for the preparation of the iodohydroxy acid.

For the synthesis of the iodo-alkoxy acids by the reaction of α-iodo-β-chlorophenylpropionic acid with the various alcohols, it was necessary to prepare the iodochloro acid in large quantities. The addition of iodine monochloride to cinnamic acid in carbon tetrachloride[2] solution proved to be more convenient and to produce higher yields than the procedure of Erlenmeyer,[1] who treated cinnamic acid in ether solution with the hydrochloride of iodine monochloride. Also, the reaction of iodine monochloride with α-methylcinnamic acid in carbon tetrachloride solution is a satisfactory method for the preparation of α-iodo-α-methyl-β-chlorophenylpropionic acid.

The yields of the iodo-alkoxy acids by the different methods of preparation are given in Table I.

Erlenmeyer assumed the methoxyl group in the iodomethoxyphenylpropionic acid to be in the β-position by analogy with the corresponding iodohydroxy acid. We confirmed this structure by the reaction of the iodomethoxy acid with zinc and absolute methyl alcohol to give β-methoxyphenylpropionic acid. One would expect the alkoxyl groups in the other acids, which were prepared from α-iodo-β-chlorophenylpropionic acid, to be in the β-position from the method by which the compounds were prepared. It will be shown below, in the discussion of the mechanism

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[2] Compare James, *J. Chem. Soc.*, **103**, 1372 (1913).

TABLE I

THE PREPARATION OF IODO-ALKOXY ACIDS

Der. of α-iodo-β-phenylpropionic acid	Method[a]	Cryst. solvent	M. p. (uncorr.), °C.	Yield, %	Analyses		
						Calcd., %	Found, %
β-Methoxy	1	$CHCl_3$	168–169[b]	75	OCH_3,	10.1	9.4
	2	or	.....	88		...	......
	3	C_6H_6	.....	34–48		...	......
β-Methoxy methyl ester	1	CCl_4	68–69	79	OCH_3,	19.38	18.58
					I,	39.66	39.93, 40.08
α-Methyl-β-methoxy	1	CCl_4	169–170[c]	46	OCH_3,	9.69	9.10
					I,	39.66	39.93
β-Ethoxy	3	C_6H_6	137–138	?		...	......
β-*n*-Propoxy	1	C_6H_6	110–111	28	I,	37.99	37.82
	2	C_6H_6	.....	62		...	......
β-*Iso*propoxy	1	$CHCl_3$	113–114	11	I,	37.99	38.44
	2	$CHCl_3$	.....	22		...	......
β-*n*-Butoxy	1	C_6H_6	93–94	25	I,	36.46	36.55
	2	C_6H_6	.....	42		...	......
β-*Iso*butoxy	2	$CHCl_3$	89–90	38	I,	36.46	36.77
β-*Tert.*-butoxy	1	$CHCl_3$	113–114	8	I,	36.46	36.66
	2	$CHCl_3$	.....	15		...	......
Iodomethoxybutyric acid	2	C_6H_6	83–84	33	OCH_3,	12.71	12.35
					I,	52.01	52.05

[a] **Methods.**—(1) The reaction of the appropriate alcohol with the α-iodo-β-chloro acid, or ester; (2) the reaction of iodine monochloride with the unsaturated acid and the appropriate alcohol in the presence of calcium carbonate; (3) the reaction of chlorine with a solution of the unsaturated acid and iodine, or alkali iodide, in the appropriate alcohol.

[b] Erlenmeyer gives 164–165°.

[c] Obtained by rapid heating (melting point varies with rate of heating).

of the reactions, that the compounds result either from the direct replacement of the chlorine atom by the alkoxyl groups, or from the addition of the alkyl hypoiodites to cinnamic acid. In the first case, there could be no question of the structure of the iodo-alkoxy acids. In the latter case, the alkoxyl groups would be in the β-position, if the mode of addition of the alkyl hypoiodites to cinnamic acid is the same as that of the alkyl hypobromites and hypochlorites.[3] As a check we have proved the compound, prepared with *iso*propyl alcohol, to be α-iodo-β-*iso*propoxyphenylpropionic acid by the preparation of acetophenone[3c] through its reaction with alcoholic potassium hydroxide, followed by hydrolysis of the product with dilute sulfuric acid solution. By similar reactions, the iodomethoxy acid, obtained from α-iodo-α-methyl-β-chlorophenylpropionic acid, was shown to yield propiophenone. The formation of propiophenone from α-iodo-α-methyl-β-methoxyphenylpropionic acid is shown by the following reactions.

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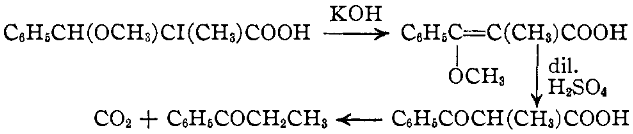
[3] (a) Conant and Jackson, THIS JOURNAL, **46**, 1727 (1924); (b) Jackson, *ibid.*, **48**, 2166 (1926); (c) Jackson and Pasiut, *ibid.*, **49**, 2071 (1927).



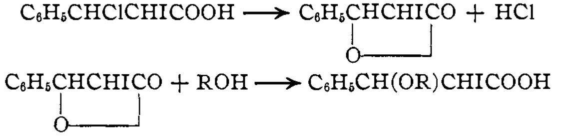
$$C_6H_5CH(OCH_3)CI(CH_3)COOH \xrightarrow{KOH} \underset{\displaystyle OCH_3}{C_6H_5C}{=}C(CH_3)COOH \xrightarrow{dil.\ H_2SO_4} C_6H_5COCH(CH_3)COOH \longrightarrow CO_2 + C_6H_5COCH_2CH_3$$

The structure of the iodomethoxybutyric acid, which was prepared from crotonic acid, has not yet been established.

The Mechanism of the Reactions

The formation of the α-iodo-β-alkoxy acids from α-iodo-β-chlorophenylpropionic acid could result from any of the following mechanisms

$$C_6H_5CHClCHICOOH + ROH \longrightarrow C_6H_5CH(OR)CHICOOH + HCl \qquad (1)$$



$$C_6H_5CHClCHICOOH \longrightarrow C_6H_5\underset{\llcorner O \lrcorner}{CHCHICO} + HCl \qquad (a)\quad (2)$$

$$C_6H_5\underset{\llcorner O \lrcorner}{CHCHICO} + ROH \longrightarrow C_6H_5CH(OR)CHICOOH \qquad (b)$$

$$C_6H_5CHClCHICOOH \longrightarrow C_6H_5CH{=}CICOOH + HCl \qquad (a)\quad (3)$$

$$C_6H_5CH{=}CICOOH + ROH \longrightarrow C_6H_5CH(OR)CHICOOH \qquad (b)$$

$$C_6H_5CHClCHICOOH \longrightarrow C_6H_5CH{=}CHCOOH + ICl \qquad (a)\quad (4)$$

$$ROH + ICl \longrightarrow ROI + HCl \qquad (b)$$

$$C_6H_5CH{=}CHCOOH + ROI \longrightarrow C_6H_5CH(OR)CHICOOH \qquad (c)$$

Erlenmeyer[1] considered the formation of α-iodo-β-hydroxyphenylpropionic acid, as well as the corresponding methoxy and ethoxy acids, to proceed through the β-lactone as shown in mechanism (2). In the case of the hydroxy acid, he regarded the direct replacement of the chlorine atom by the hydroxyl group improbable, since the methyl ester of α-iodo-β-chlorophenylpropionic acid failed to react with water. Mechanism (3), as well as the direct substitution of the chlorine atom by the alkoxyl groups as shown in mechanism (1), was considered unlikely for the lack of analogous examples. Erlenmeyer did not take mechanism (4) into consideration.

By the preparation of methyl α-iodo-β-methoxyphenylpropionate through the reaction of absolute methyl alcohol with the methyl ester of α-iodo-β-chlorophenylpropionic acid, we have shown that a β-lactone need not be an intermediate compound in the formation of the iodo-alkoxy acids. We have also eliminated mechanism (3) by the synthesis of α-iodo-α-methyl-β-methoxyphenylpropionic acid through the reaction of absolute methyl alcohol with α-iodo-α-methyl-β-chlorophenylpropionic acid, which has not the necessary hydrogen atom on the α-carbon atom. The iodo-alkoxy acids are formed, therefore, either according to mechanism (1) or mechanism (4).

Although we have no decisive experiments to distinguish between mechanisms (1) and (4), we nevertheless have obtained certain facts which favor mechanism (4). In the reaction of α-iodo-β-chlorophenylpropionic acid with the various alcohols, there was formed in each instance a certain amount of cinnamic acid, the quantity varying with the alcohol used. In the case of methyl alcohol the amount of cinnamic acid was small, while with *iso*propyl alcohol 75% of the iodochloro acid was converted into cinnamic acid. The data given in Table I show that the yields of the iodo-alkoxy acids, obtained by this method, vary from 75% with methyl alcohol to 8% with *tert.*-butyl alcohol. Erlenmeyer has shown that α-iodo-β-hydroxyphenylpropionic acid is almost completely changed into cinnamic acid by means of 25% hydrochloric acid solution, a reaction which he interprets as proceeding through α-iodo-β-chlorophenylpropionic acid. The production of cinnamic acid in the reaction of the alcohols with α-iodo-β-chlorophenylpropionic acid might, therefore, be attributed to the accumulation of hydrochloric or hydriodic acid in the solution. This, however, seems unlikely in view of the fact that the reactions were carried out in the presence of calcium carbonate. The simplest explanation of the formation of cinnamic acid is the elimination of a molecule of iodine monochloride from α-iodo-β-chlorophenylpropionic acid, as shown in Equation (a) of mechanism (4). This hypothesis is in accord with the usual practice of employing a considerable excess of the reagent in the determination of iodine values by the methods which involve the addition of iodine monochloride. In the presence of methyl alcohol the cinnamic acid, which was formed by the dissociation of iodine monochloride, is almost completely converted into α-iodo-β-methoxyphenylpropionic acid, as shown by Equations (b) and (c) of mechanism (4). When, however, the solvent is *iso*propyl or *tert.*-butyl alcohol, most of the iodine monochloride, formed in the initial reaction, is used up in side reactions with the alcohols, while a small amount simultaneously reacts to produce the alkyl hypoiodite, which by addition to the double linkage of the unsaturated acid gives a low yield of the α-iodo-β-alkoxy acid. This view is consistent with the results of experiments in which the iodo-alkoxy acids were synthesized by the reaction of iodine monochloride with cinnamic acid and the alcohols. Thus, when cinnamic acid reacts with methyl alcohol and iodine monochloride (1.25 moles), α-iodo-β-methoxyphenylpropionic acid results in 88% yield, while under similar conditions the reactions with *iso*propyl and *tert.*-butyl alcohols give the iodo-alkoxy acids in only 22 and 15% yields, respectively. In this connection it should be mentioned that the yields obtained in the reaction of an excess of iodine monochloride with cinnamic acid and the various alcohols were in each case higher than resulted in the reaction of α-iodo-β-chlorophenylpropionic acid with the corresponding alcohol. In the latter case a low concentration of iodine monochloride would be maintained throughout the reaction by the gradual elimination of iodine monochloride from the molecule of the iodochloro acid. In order to approximate these conditions, the calculated amount of iodine monochloride was added, a few drops at a time, to a dilute solution of cinnamic acid in *iso*propyl alcohol over approximately the same period that was used for the reaction of α-iodo-β-chlorophenylpropionic acid with *iso*propyl alcohol. The yield of α-iodo-β-*iso*propoxyphenylpropionic acid thus obtained was comparable to that produced in the reaction with α-iodo-β-chlorophenylpropionic acid.

The formation of the iodo-alkoxy acids according to mechanism (4) involves the assumption that iodine monochloride reacts with the various alcohols to give the alkyl hypoiodites. That iodine monochloride reacts with the alcohols in this manner seems practically certain from our experiments with *tert.*-butyl alcohol. *Tert.*-butyl alcohol was found to be almost without action on α-iodo-β-chlorophenylpropionic acid in the time which was used for the preparation of α-iodo-β-*tert.*-butoxyphenylpropionic acid by the reaction of cinnamic acid with iodine monochloride and *tert.*-butyl alcohol. Also, in the latter reaction no α-iodo-β-chlorophenylpropionic acid was recovered. This indicates that α-iodo-β-chlorophenylpropionic acid is not formed as an intermediate compound in the production of α-iodo-β-*tert.*-butoxyphenylpropionic acid by the reaction of cinnamic acid with iodine monochloride and *tert.*-butyl alcohol. The iodo-*tert.*-butoxy acid is probably formed by the addition of *tert.*-butyl hypoiodite to cinnamic acid, the *tert.*-butyl hypoiodite being a product of the reaction of iodine monochloride with *tert.*-butyl alcohol. The production of the other iodo-alkoxy acids, by the reaction of iodine monochloride with the unsaturated acids and the different alcohols, probably involves a similar mechanism.

Although the facts outlined are in accord with mechanism (4), we do not consider the direct replacement of the chlorine atom excluded. If the iodo-alkoxy acids are formed according to mechanism (1), the slow rate of reaction of *tert.*-butyl alcohol, as well as *iso*propyl alcohol, with α-iodo-β-chlorophenylpropionic acid would be expected as a consequence of the small reactivity of the hydroxyl hydrogen atoms[4] in these alcohols. However, this slow rate of reaction could equally well be interpreted as a solvent effect on the reactions of mechanism (4).

In previous papers[3a,b,c] it has been shown that bromine and chlorine react with ethylene derivatives and certain alcohols to give bromo and chloro-alkoxyl compounds. This reaction was interpreted as involving the addition of the alkyl hypobromites and hypochlorites to the double linkage of the unsaturated compounds. In connection with the reaction of the different alcohols with α-iodo-β-chlorophenylpropionic acid to give the iodo-alkoxy acids, the question arises whether the bromo and chloro-

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[4] (a) Norris and Ashdown, THIS JOURNAL, **47**, 837 (1925); (b) Norris and Cortese, *ibid.*, **49**, 2640 (1927).

alkoxyl compounds are formed in a similar manner by the reaction of the alcohols with the appropriate dibromides or dichlorides. The latter possibility is eliminated by the fact that cinnamic acid dibromide was shown by Werner[5] to be unchanged on heating with methyl alcohol, while we have found the dichloride of cinnamic acid in absolute methyl alcohol solution, containing hydrogen chloride, to undergo only the esterification reaction after standing for sixty-five hours. Under similar conditions the high-melting isomer of α,β-dichloro-β-phenylpropiophenone was shown to be unchanged.

Experimental Part

Preparation of the Iodochloro Acids

Ten g. of the unsaturated compound, cinnamic acid, methyl cinnamate or α-methyl cinnamic acid, was dissolved in carbon tetrachloride. To this was added 1.25 moles of iodine monochloride, which was prepared by the method of Hannay.[6] After standing for about fifteen hours, the solid material was filtered off and washed with carbon tetrachloride. The α-iodo-β-chlorophenylpropionic acid, obtained from cinnamic acid, melted with decomposition at 124–126°; yield, 92%. It was further purified by recrystallization from chloroform containing a small amount of petroleum ether. The methyl α-iodo-β-chlorophenylpropionate resulting from methyl cinnamate was recrystallized from carbon tetrachloride; yield, 77%. It melted at 97–98°, which is the melting point given by Erlenmeyer.[1] The yield of α-iodo-α-methyl-β-chlorophenylpropionic acid prepared from α-methyl cinnamic acid was 74%. After recrystallization from carbon tetrachloride, the compound melted at 104–105° with decomposition.

Anal. Calcd. for $C_{10}H_{10}ClIO_2$: Cl and I, 50.04. Found: 49.99.

Synthesis of Iodo-alkoxy Acids by the Reaction of Alcohols with the Iodochloro Acids.—Two and one-half to 10 g. of the α-iodo-β-chloro acid or ester was dissolved in the appropriate alcohol. In order to avoid esterification of the acids, there was added precipitated calcium carbonate (3 to 12 g.). After standing at room temperature for thirty-five to ninety-eight hours, the calcium carbonate was filtered off and washed with the proper alcohol. The filtrate was poured into a large volume of water. This in some cases precipitated solid material and in others an oil, which crystallized after standing for several hours. Saturation of the filtrate from this material with sodium chloride gave a small amount of crystals. By dissolving the calcium carbonate in hydrochloric acid, an additional quantity of solid was obtained. For purification the substance was dissolved in sodium carbonate solution and treated with potassium permanganate solution in small excess. By filtering off the manganese dioxide, extracting the filtrate with ether and acidifying, the somewhat impure compound was obtained. Recrystallization from the solvent given in Table I yielded the pure substance.

In the preparation of methyl α-iodo-β-methoxyphenylpropionate and α-iodo-α-methyl-β-methoxyphenylpropionic acid, the general procedure was varied in that the solvent was distilled under diminished pressure at 25–35° instead of pouring into water. The resulting products were purified by recrystallization from the solvents specified.

The principal product in the reaction of *iso*propyl alcohol with α-iodo-β-chlorophenylpropionic acid was cinnamic acid. Thus, from 2.5 g. of α-iodo-β-chlorophenylpropionic acid there was obtained 0.9 g. of cinnamic acid melting at 130–131° (75%

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[5] Werner, *Ber.*, **39**, 27 (1906).

[6] Hannay, *J. Chem. Soc.*, **26**, 815 (1873).

of the calculated amount). The substance was shown to be cinnamic acid by a mixed melting point determination and by its complete oxidation by potassium permanganate solution.

The rate of the reaction of *tert.*-butyl alcohol with α-iodo-β-chlorophenylpropionic acid was found to be very slow. After a solution of 10 g. of the iodochloro acid in 75 cc. of *tert.*-butyl alcohol had stood for twenty-two hours, it was poured into water. The solid thus precipitated weighed 7 g. and melted with decomposition at 126–127°. It was shown to be principally unchanged α-iodo-β-chlorophenylpropionic acid by a mixed melting point determination and by its reaction with methyl alcohol to produce α-iodo-β-methoxyphenylpropionic acid; m. p. 167–168°. However, when a solution of the iodochloro acid in *tert.*-butyl alcohol, containing calcium carbonate in suspension, was allowed to stand for ninety-eight hours, the products were cinnamic acid and α-iodo-β-*tert.*-butoxyphenylpropionic acid (8% yield).

The compounds prepared by this method together with the yields, melting points and analyses are given in Table I.

Structure of the Iodomethylmethoxyphenylpropionic Acid.—To a solution of 4.3 g. of potassium hydroxide in 25 cc. of absolute alcohol there was added 3.6 g. of the iodomethylmethoxyphenylpropionic acid melting at 169–170°. After boiling under a reflux condenser for eight hours, the alcohol was distilled off, the residue dissolved in water and acidified. The oil thus precipitated was extracted with ether. The ether was distilled and to the residue was added 100 cc. of 10% sulfuric acid solution. It was then steam distilled until oil ceased to pass over. By extracting the distillate with ether, drying over sodium sulfate and distillation of the solvent, an oil was obtained which partially crystallized on cooling to about 18°. It was shown to be propiophenone by the preparation of its semicarbazone. To a solution of the substance in alcohol was added a concd. aqueous solution of 0.5 g. of semicarbazide hydrochloride and 0.8 g. of sodium acetate. After boiling under a reflux condenser for about ten minutes, the solution was set aside overnight. Needle-shaped crystals resembling propiophenone semicarbazone as described by Stobbe[7] had then separated. It is insoluble in water. The crude product melted at 168–171°. After recrystallization from alcohol, it melted at 173–174°, which agrees with the melting point of propiophenone semicarbazone given in the literature. The formation of propiophenone by these reactions shows that the methoxyl group is in the β-position to the carboxyl group and the substance is α-iodo-α-methyl-β-methoxyphenylpropionic acid.

Structure of the Iodo-*iso*propoxy Acid.—One g. of the iodo-*iso*propoxy acid melting at 113–114° was treated with alcoholic potassium hydroxide and sulfuric acid according to the procedure described for the iodomethylmethoxyphenylpropionic acid. The product was an oil (0.3 g.) resembling acetophenone in appearance and odor. It reacted with semicarbazide hydrochloride and sodium acetate to give acetophenone semicarbazone; m. p. 195–196°. The melting point was unchanged when mixed with known acetophenone semicarbazone. The formation of acetophenone by these reactions shows that the *iso*propoxyl group is in the β-position to the carboxyl group.

Synthesis of Iodo-alkoxy Acids by the Reaction of Unsaturated Acids with Iodine Monochloride and Alcohols.—To a solution of 5 to 10 g. of cinnamic acid or crotonic acid in the appropriate alcohol, containing in suspension 7 to 15 g. of calcium carbonate, there was added 1.25 moles of iodine monochloride. After standing for sixteen to forty-two hours, the calcium carbonate was filtered off and washed with the appropriate alcohol. However, in the case of crotonic acid the reaction mixture was stirred for ten hours. The filtrate from the calcium carbonate was poured into a large volume of water and decolorized with sodium sulfite. The products from cinnamic acid were

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[7] Stobbe, *Ann.*, **321**, 103 (1902).

precipitated as solids, except those resulting from the reactions with *n*-butyl and *iso*butyl alcohols. Crotonic acid and methyl alcohol gave material soluble in water. The solids thus precipitated were filtered off and the filtrate saturated with sodium chloride, which yielded a small amount of crystals. Additional substance was obtained by dissolving the calcium carbonate in hydrochloric acid. The compounds were purified by dissolving in sodium carbonate solution and treating with potassium permanganate as previously described. Recrystallization from the solvents given in Table I yielded the pure substances. After recrystallization of α-iodo-β-*tert.*-butoxyphenylpropionic acid from chloroform, it was found to retain the solvent and its correct melting point was obtained only after standing in a vacuum desiccator for about twenty-four hours. The compound also combines with benzene.

The product obtained by pouring into water the solution resulting from the reaction of cinnamic acid, iodine monochloride and *n*-butyl alcohol was an oil which did not crystallize after standing for fifteen hours. The oil was separated from the aqueous solution and dissolved in ether. After drying the ethereal solution over calcium chloride and distillation of the solvent, an oil was recovered which crystallized, in part, on cooling in ice. The substance was partially dissolved in benzene and allowed to stand in an open beaker for several days. The crystals were then separated from the oil by suction filtration and recrystallized from benzene.

Likewise, the product of the reaction of cinnamic acid, iodine monochloride and *iso*butyl alcohol was an oil which did not crystallize on standing in water for two days. Most of the aqueous layer was decanted from the oil, which was then combined with a small amount of oil obtained by dissolving the calcium carbonate in hydrochloric acid. By extracting the oil with ether, drying over sodium sulfate and distillation of the ether, a solution of the substance in *iso*butyl alcohol was obtained. The *iso*butyl alcohol was distilled off under diminished pressure, the bath temperature being 85–95°. The resulting product was dissolved in sodium carbonate solution and treated with potassium permanganate in the usual manner. Acidification of the sodium carbonate solution precipitated colorless crystals which were then recrystallized from chloroform.

The iodine precipitated by pouring the solution obtained in the reaction of crotonic acid, iodine monochloride and absolute methyl alcohol into water was filtered off. The excess of iodine monochloride was removed by precipitation with quinoline.[8] The solution was made distinctly acid with hydrochloric acid and quinoline added until precipitation ceased. The solid material was then filtered off and discarded. The filtrate was strongly acidified with hydrochloric acid and thoroughly extracted with ether. The calcium carbonate was dissolved in hydrochloric acid and the solution extracted with ether, which was then combined with the main portion. After drying over sodium sulfate and distillation of the ether, an oil was obtained which partially crystallized on standing overnight. The crystals were separated from the oil by filtration and recrystallized from benzene.

The reaction of 10 g. of cinnamic acid and 1.25 moles of iodine monochloride in 90 cc. of *iso*propyl alcohol during forty-two hours produced a 22% yield of α-iodo-β-*iso*propoxyphenylpropionic acid, as given in Table I. In order to test the effect of the concentration of the reacting substances on the yield of the iodo-*iso*propoxy acid, one mole of iodine monochloride was added in small portions at intervals of several hours to a more dilute solution of cinnamic acid in *iso*propyl alcohol. To a solution of 5 g. of cinnamic acid in 105 cc. of *iso*propyl alcohol, containing in suspension 12 g. of calcium carbonate, there was added two or three drops of iodine monochloride; it was then allowed to stand for several hours. This process was repeated until one mole of iodine monochloride had been added during ninety-seven hours. The product was separated

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[8] German patent, 30,358.

as described under the general procedure and purified by treatment with potassium permanganate solution. The yield of α-iodo-β-*iso*propoxyphenylpropionic acid melting at 108–112° was 0.6 g. or 5.3%.

The reaction of unsaturated acids with iodine monochloride and alcohols in the absence of calcium carbonate produces the esters of the iodo-alkoxy acids. Thus, a solution of 10 g. of cinnamic acid and 11 g. of iodine monochloride in 82 cc. of absolute methyl alcohol, after about forty-eight hours, gave 12 g. of solid melting at 65–74° and a small amount of higher melting material. By recrystallization from carbon tetrachloride, or petroleum ether, the pure methyl ester of α-iodo-β-methoxyphenylpropionic acid melting at 68–69° was obtained.

The compounds prepared by this method and the yields are summarized in Table I.

Synthesis of Certain Iodo-alkoxy Acids by the Reaction of Chlorine with Unsaturated Acids, Iodine and Alcohols.—On chlorinating a solution of cinnamic acid and iodine, or an alkali iodide, in absolute methyl alcohol, α-iodo-β-methoxyphenylpropionic acid results. The introduction of chlorine (about 2 liters) into a vigorously stirred solution of 10 g. of cinnamic acid in 50 cc. of absolute methyl alcohol, to which 9 g. of iodine was added in small portions during ten hours, gave a 34% yield of α-iodo-β-methoxyphenylpropionic acid. In a similar manner, a 48% yield of the iodomethoxy acid was obtained by the reaction of about 2 liters of chlorine with a solution of 10 g. of cinnamic acid and 2.4 g. of potassium iodate in 75 cc. of absolute methyl alcohol, to which 8.2 g. of sodium iodide was added over a period of ten hours. Continuation of the reaction over a relatively long period of time yields the ester of the iodomethoxy acid. Thus, the introduction of about 12 liters of chlorine, during two days, into a solution of 20 g. of cinnamic acid in 190 cc. of absolute methyl alcohol, to which 46 g. of potassium iodide was gradually added, produced methyl α-iodo-β-methoxyphenylpropionate (37% yield).

α-Iodo-β-ethoxyphenylpropionic acid was prepared by the reaction of chlorine with cinnamic acid and sodium iodide in absolute ethyl alcohol solution. To a thoroughly stirred solution of 20 g. of cinnamic acid in 200 cc. of absolute ethyl alcohol was added 20 g. of sodium iodide in small portions, chlorine being simultaneously introduced until the iodine had completely reacted, about 4.5 liters being required. After recrystallization of the product from alcohol, there was obtained 6.5 g. of substance melting at 75–125° and 2.5 g. melting at 70–105°. Another crystallization of the material melting at 75–125° from benzene gave 2 g. of crystals melting at 128–138° and some lower melting substance. By dissolving the material melting at 128–138° in sodium carbonate solution and treating with potassium permanganate in the usual manner, crystals melting at 137–138° resulted. No depression of the melting point was produced on mixing with known α-iodo-β-ethoxyphenylpropionic acid, which was prepared by the procedure of Erlenmeyer.[1]

The reaction of chlorine with crotonic acid and iodine in absolute methyl alcohol solution, containing calcium carbonate in suspension, gave iodomethoxybutyric acid. However, the yield by this method was less than that obtained with the use of iodine monochloride and the product was more difficult to purify. When the reaction was carried out in the absence of calcium carbonate, the product was a liquid consisting of esters which could not be obtained in the solid state. To a thoroughly stirred solution of 5 g. of crotonic acid in 50 cc. of absolute methyl alcohol, in which was suspended 7 g. of calcium carbonate, there was added 8 g. of iodine in portions of about 1 g. each. The solution was treated with about 2 liters of chlorine during six hours, the iodine color having then disappeared. The resulting oil was distilled at 5 mm. pressure until the boiling point reached 125°. The residue in the distilling flask partially crystallized on standing overnight. The yield of substance melting at 50–60° was 3 g. After several recrystallizations from benzene, pure iodomethoxybutyric acid was obtained.

α-Iodo-β-hydroxyphenylpropionic acid was prepared by treating a suspension of iodine and cinnamic acid in water with chlorine. To a vigorously stirred suspension of 10 g. of cinnamic acid in 1.3 liters of water, there was added 11 g. of finely powdered iodine in small portions, chlorine being simultaneously introduced until the iodine had completely reacted. About 3.5 liters of chlorine were required. The solid was filtered off and the filtrate extracted with ether. After recrystallization of the product from chloroform, 9 g. of slightly impure α-iodo-β-hydroxyphenylpropionic acid melting at 136–142° resulted. Further recrystallization gave the pure compound; m. p. 141–142°.

Summary

α-Iodo-β-chlorophenylpropionic acid has been shown to react with methyl, *n*-propyl, *iso*propyl, *n*-butyl and *tert.*-butyl alcohols to yield the corresponding α-iodo-β-alkoxyphenylpropionic acids.

A more suitable method for the preparation of the iodo-alkoxy acids was found to be the reaction of iodine monochloride with cinnamic acid and the appropriate alcohol. This reaction has been applied to methyl, *n*-propyl, *iso*propyl, *n*-butyl, *iso*butyl and *tert.*-butyl alcohols. By the reaction of crotonic acid, iodine monochloride and absolute methyl alcohol, iodomethoxybutyric acid was formed. The iodomethoxy and iodoethoxyphenylpropionic acids were also prepared by reaction of chlorine with solutions of cinnamic acid and iodine, or an alkali iodide, in the appropriate alcohol.

That a β-lactone is not an intermediate compound in the formation of the iodo-alkoxy acids from α-iodo-β-chlorophenylpropionic acid was shown by the preparation of methyl α-iodo-β-methoxyphenylpropionate through the reaction of methyl alcohol with the methyl ester of α-iodo-β-chlorophenylpropionic acid. Also, the iodo-alkoxy acids are not formed by the elimination of hydrogen chloride from α-iodo-β-chlorophenylpropionic acid followed by the addition of the alcohols to the double linkage thus produced, since methyl alcohol reacts with α-iodo-α-methyl-β-chlorophenylpropionic acid to give α-iodo-α-methyl-β-methoxyphenylpropionic acid. The iodo-alkoxy acids are produced either by the direct replacement of the chlorine atom by the alkoxyl groups, or by the dissociation of iodine monochloride from the molecule of the iodochloro acid, followed by its reaction with the alcohols to produce the alkyl hypoiodites, which then add to the double linkage of the unsaturated acid. Facts supporting the latter mechanism have been submitted.

Evidence has been given which indicates that in the reaction of iodine monochloride with the alcohols and unsaturated acids, the iodo-alkoxy acids are probably formed by the addition of the alkyl hypoiodites to the unsaturated acids.

The preparation of α-iodo-β-chlorophenylpropionic acid and α-iodo-α-methyl-β-chlorophenylpropionic acid, by the addition of iodine monochloride to the unsaturated acids in carbon tetrachloride solution, has been found to be more convenient than the procedure of Erlenmeyer,

who used an ether solution of the hydrochloride of iodine monochloride. The introduction of chlorine into a suspension of iodine and cinnamic acid in water proved to be a convenient method for the preparation of α-iodo-β-hydroxyphenylpropionic acid.

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REDUCTION OF PYRIDINE HYDROCHLORIDE AND PYRIDONIUM SALTS BY MEANS OF HYDROGEN AND PLATINUM-OXIDE PLATINUM BLACK. XVIII[1]

BY T. S. HAMILTON[2] AND ROGER ADAMS

RECEIVED APRIL 17, 1928 PUBLISHED AUGUST 4, 1928

Although the catalytic reduction of pyridine and pyridine derivatives has been described in the literature,[3] no systematic work has been done which makes possible a prediction of satisfactory conditions for reducing compounds which contain the pyridine nucleus. A study has therefore been made of the reduction with hydrogen and platinum-oxide platinum black, of pyridine hydrochloride and pyridonium salts, quinoline and benzyl quinolonium chloride.

It has been found that pyridine alone in most solvents poisons platinum-oxide platinum black and no reduction takes place. On the other hand pyridine hydrochloride can be reduced readily. The selection of the proper solvent, however, is important. Absolute alcohol proved to be the best of those used, with glacial acetic acid second. Peculiarly enough, water in the alcohol inhibits the reduction very markedly and no satisfactory results were obtained using 95% ethyl alcohol or commercial methyl alcohol as a solvent. Absolute methyl alcohol could be used but it did not give such consistent results as absolute ethyl alcohol. Acetone and ethyl acetate do not dissolve the pyridine hydrochloride readily and, therefore, are not suitable.

As a standard run, 0.1 mole of pyridine hydrochloride in 150 cc. of solvent with 0.15 g. of platinum-oxide platinum black from C. P. chloroplatinic acid was used. The time required for the complete reduction was six to seven hours. In fact 0.15 g. of catalyst was the minimum which would allow complete reduction. Increase of the amount of catalyst to 0.3 g. lowered the reduction time to one hour and using 0.5 g. of catalyst lowered

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[1] The last paper in this series was Adams and Marshall, THIS JOURNAL, **50**, 1970 (1928).

[2] This paper is a portion of a thesis submitted by T. S. Hamilton in partial fulfilment of the requirements for the degree of Doctor of Philosophy in Chemistry at the University of Illinois.

[3] Skita and Brunner, *Ber.*, **49**, 1597 (1916); Darzens, *Compt. rend.*, **149**, 1001 (1909); Ipatiew, *Ber.*, **41**, 992 (1908).