(dipicrate of hydroxy compound VIII): C, 37.75; H, 4.00; N, 18.53. Calcd. for $C_{20}H_{26}N_8O_{15}$ (dipicrate of VII): C, 38.34; H, 4.24; N, 18.12. Found: C, 38.94, 38.83; H, 4.25, 4.19; N, 17.70, 17.82.

β-*i*-Butylaminopropionitrile.—Acrylonitrile (29 g.) was added dropwise with stirring to 40 g. of redistilled *i*-butylamine (b. p. 66.5–67.5°). After the addition was complete, the mixture stood for four hours at room temperature, was then refluxed for one hour, and stood overnight. Vacuum distillation yielded only a very small amount of starting material, and 62.97 g. (91%) of product was obtained, b. p. 82–88° (7 mm.). The analytical sample had the following properties: b. p. 107° (11 mm.), $n^{20}D$ 1.4352.

Anal. Calcd. for $C_7H_{14}N_2$: C, 66.62; H, 11.20; Found: C, 66.67; H, 11.03.

The **phenylcarbamyl derivative,** $(CH_3)_2CHCH_2N(CONHC_6H_5)CH_2CH_2CN$, was prepared by mixing 1 cc. of the propionitrile and 1 cc. of phenyl isocyanate in 10 cc. of petroleum ether. The product, which precipitated immediately in crystalline form, was best recrystallized from about 6 cc. of benzene, and melted, when recrystallized for analysis, at 117.5–118°.

Anal. Calcd. for $C_{14}H_{19}N_3O$: C, 68.53; H, 7.81. Found: C, 68.40; H, 7.75.

γ-(*i*-Butylamino)-propylamine (VI).—The corresponding nitrile (45 g.) was reduced by procedure C described above for II, and the product VI was obtained in 64% yield; the analytical sample had these properties: b. p. 95–97° (31 mm.); $n^{20}D$ 1.4452.

Anal. Calcd. for $C_7H_{18}N_2$: C, 64.52; H, 13.95. Found: C, 64.55; H, 13.66.

The **dipicrate** melted, after recrystallization from methanol, at 171–172°.

Anal. Calcd. for $C_{19}H_{24}N_8O_{14}$: C, 38.77; H, 4.11. Found: C, 38.31; H, 4.13.

Summary

2,2-Dimethylethylenimine has been added to acrylonitrile, and the product has been reduced, with sodium–alcohol, and with Raney nickel-hydrogen, to 2,2-dimethyl-1-(γ-aminopropyl)-ethylenimine. The evidence on which this structure is based is presented. The imine ring of the dipicrate undergoes methanolysis when recrystallized from methanol. γ-(*i*-Butylamino)-propylamine and several compounds related to it have been prepared and characterized.

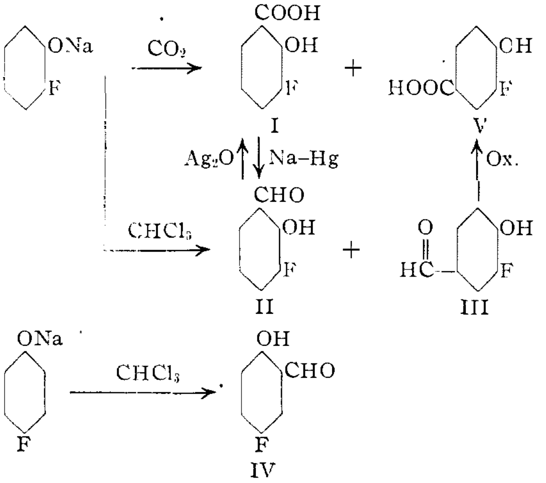
ROCHESTER, NEW YORK RECEIVED JULY 11, 1946

[CONTRIBUTION FROM THE CHEMICAL LABORATORY, UNIVERSITY OF CALIFORNIA]

Some New Fluorinated Phenolic Aldehydes and Acids

BY LLOYD N. FERGUSON,[1] JAMES C. REID AND MELVIN CALVIN

In connection with the preparation of oxygen-carrying chelates,[2] it was desired to test 3-fluorosalicylaldehyde (II), and 5-fluorosalicylaldehyde (IV). 3-Fluorosalicylic acid (I) was prepared as an intermediate and 3-fluoro-4-hydroxybenzaldehyde (III) and 3-fluoro-4-hydroxybenzoic acid (V) were obtained as by-products according to the scheme



Experimental[3]

o-**Fluorophenol** was prepared by the method of Schiemann.[4]

p-**Fluorophenol** was prepared by demethylation of Eastman Kodak Co. *p*-fluoranisole by refluxing for forty-eight hours with a four-fold *M* excess of 48% hydrobromic acid. The yield was 90%.

Preparation of 3-Fluorosalicyladehyde (II) and 3-Fluoro-4-hydroxybenzaldehyde (III) by the Reimer–Tiemann Reaction.—A solution of 77.2 g. (1.93 mole) of sodium hydroxide and 32.4 g. (0.29 mole) of *o*-fluorophenol in 260 ml. of water was brought to 55° and 76.8 g. (0.645 mole) of chloroform was run in during thirty minutes with efficient stirring, holding the temperature at 55°. After seventy minutes, the temperature was raised to 65° for an additional period of sixty minutes. The mixture was then acidified with sulfuric acid and steam distilled. Chloroform and unchanged phenol came out first, followed by solid II. When solid appeared, the receiver was changed and the pure product was collected. The hot residue remaining in the distillation flask was decanted away from a heavy tar on the bottom of the flask, and III crystallized out on cooling. An additional quantity of III was obtained by ether extraction of the mother liquor. Distillation of the recovered chloroform–phenol solution was carried out, reducing the pressure when the chloroform had been removed, and gave back 19.8 g. (61%) of the unchanged phenol in pure form. An additional quantity of II was obtained from the residue from this distillation by sublimation.

The yield of II was 5.3 g. (13%); white plates, m. p. 66.7–68.2° cor. *Anal.* Calcd. for $C_7H_5O_2F$: C, 59.98; H, 3.63. Found: C, 59.8; H, 3.80. The phenylhydrazone was prepared by the customary procedure, using phenylhydrazine in acetate buffer in alcohol at room temperature. Dilution with water threw down the phenylhydrazone as yellow plates; m. p. after recrystallization from dilute alcohol, 156.0–157.5° cor. The 2,4-dinitrophenylhydrazone was made in the usual way, using 2,4-dinitrophenylhydrazine in hot alcoholic hydrochloric acid solution. It was obtained as orange needles; m. p. after recrystallization from alcohol, 282–283° cor.

The yield of III was 6.1 g. (15%); white needles, m. p.

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[1] Present address: Howard University, Washington, D. C.

[2] THIS JOURNAL, **68**, 2254, ff. (1946).

[3] All melting points are uncorrected unless otherwise noted.

[4] G. Schiemann, *Z. physik. Chem.*, **A156**, 397 (1931).

after recrystallization from hot water, 121.1–122.9°. *Anal.* C, 59.97; H, 3.65.

Dinitrophenylhydrazone: scarlet needles, m. p. 291–292° cor. The phenylhydrazone was obtained as yellow plates which could not be purified.

5-Fluorosalicylaldehyde (IV).—This compound was prepared by the Reimer–Tiemann reaction using *p*-fluorophenol instead of *o*-fluorophenol as starting material. To a vigorously stirred solution of 270 g. (6.7 mole) of sodium hydroxide and 110 g. (1.0 mole) of *p*-fluorophenol in 890 ml. of water at 50° was slowly run in 270 g. (2.23 mole) of chloroform, and the mixture held at 40–50° for six hours. No other reaction conditions were tried. Working up the product in the usual way produced 70.5 g. (64.2%) of unchanged phenol and 10.8 g. (7.8%) of IV. The rest was tar. The aldehyde was obtained as white plates, m. p. 82.0–84.0 cor.

Anal. C, 59.12; H, 3.68.

Phenylhydrazone: yellow plates, m. p. 144.0–145.2° cor.

2,4-Dinitrophenylhydrazone: orange needles, m. p. 285–287° cor.

Copper Chelate of the Ethylenediamine Schiff Base of II.—Equimolar quantities of 3-fluorosalicylaldehyde and ethylenediamine were mixed in 95% ethanol and a two-fold excess of copper acetate, dissolved in water, was added. Dilution of the mixture with water threw down the chelate in purple plates. It was crystallized once from dilute alcohol containing a little ethylenediamine, then dried for two hours at 120° *in vacuo.*

Anal. Calcd. for $C_{16}H_{12}O_2N_2F_2Cu$: C, 52.52; H, 3.30; Cu, 17.38. Found: C, 52.71; H, 3.22; Cu, 17.72.

Preparation of 3-Fluorosalicylic Acid (I) **from 3-Fluorosalicylaldehyde** (II).—Two grams of aldehyde were boiled with slightly more than the theoretical amount of freshly precipitated silver oxide in 50 cc. of water for one hour. The hot solution was filtered, allowed to cool and the acid was filtered off. Recrystallization from water gave white plates, m. p. 144–145°.

Anal. Calcd. for $C_7H_5O_3F$: C, 53.85; H, 3.23. Found: C, 53.57; H, 3.79.

Oxime of 3-Fluoro-4-hydroxybenzaldehyde (III).—To a solution of 5 g. of the aldehyde in 20 cc. of ethanol was added 4.1 g. of hydroxylamine hydrochloride dissolved in a little water. The solution was made basic with sodium carbonate and allowed to stand overnight. It was then concentrated somewhat on a steam-bath and neutralized with hydrochloric acid. The oxime was filtered off and recrystallized from hot water; white crystals, m. p. 140–141°.

Preparation of 3-Fluoro-4-hydroxybenzoic Acid (V) **from the Oxime of III.**—To a solution of 4 g. of oxime in 25 cc. of acetic anhydride was added five drops of concentrated sulfuric acid and the solution was refluxed for six hours. The nitrile was not isolated but was converted directly to V by distilling off most of the acetic anhydride, then adding 20 cc. of 5 *N* hydrochloric acid and heating on a steam-bath for one hour. The crude acid was filtered from the cooled solution, then recrystallized from water, using charcoal; white crystals, m. p. 154–157. This substance was the monohydrate of the acid as the analysis shows. Co-distillation with kerosene raised the melting point to 160–161°.

Anal. Found: C, 48.74; H, 4.12. Calcd. for $C_7H_5O_3F \cdot H_2O$: C, 48.3; H, 4.03.

Preparation of 3-Fluorosalicylic Acid (I) **and 3-Fluoro-4-hydroxybenzoic Acid** (V) **by the Kolbe–Schmidt Reaction.**—Sodium *o*-fluorophenolate was prepared by mixing 118 g. (1.05 mole) of *o*-fluorophenol into a solution of 40 g. (1.00 mole) of C. P. sodium hydroxide in 150 ml. of water. The resulting solution became yellow, then a clear red in color. It was concentrated over a flame, taking care to avoid charring. When the mixture had been reduced to a thick slush it was allowed to cool, when it set to a hard solid. The solid was pulverized and dried overnight at 100° under vacuum. It was then reground and placed in a steel pressure vessel. The vessel was fitted with a valve carrying a pressure gage, and was heated with an oil-bath. With the bath at 150° the solid was dried eight hours more under vacuum. Then tank carbon dioxide was admitted to a pressure of 800 p. s. i. while the temperature was maintained at 150–160°. After six hours at this temperature and pressure the vessel was cooled and the product was dissolved in water.

The solution was transferred to a distilling apparatus, acidified with sulfuric acid and steam distilled. From the distillate was recovered 14.7 g. (13%) of unchanged fluorophenol. The residue in the distilling flask was cooled and the mixed I and V were filtered off. It was determined that negligible amounts were present in the filtrate. The yield of mixed acids was 132 g. (0.848 mole). This amounts to a yield of 97% based on phenol unrecovered. Of the mixed acids, 71% was I, as determined by titration with the glass electrode.

Separation of the isomeric acids was done only for purposes of identification. The crude mixture was dissolved in the minimum amount of boiling water, allowed to cool to 40° and filtered. By repetition of this process I was obtained as white crystals, m. p. 143–144°. Two crystallizations from benzene raised the melting point to 145–147°. The equivalent weight of the higher melting form, determined with the glass electrode, was 157: calcd. for $C_7H_5O_3F$, 156.

The combined filtrates were cooled in ice, bringing down solid enriched in V. This was purified by recrystallization from benzene. White crystals were obtained, m. p. 161–162°. The equivalent weight was 166, the high value no doubt being due to the presence of some hydrate.

Recrystallization from water gave white needles, m. p. 154–157°, showing no depression when mixed with a specimen of V prepared from the oxime of III. Co-distillation of the lower melting form with kerosene, followed by two crystallizations from benzene raised the melting point to 161–162 again. This specimen showed an equivalent weight of 161.

Assay of Mixed Acids from Kolbe–Schmidt Reaction.—The amount of each of the isomeric acids in the Kolbe–Schmidt product can be determined by titration with alkali, using a glass electrode. This is possible because the phenolic hydroxyl of V is acidic enough to give a break in the titration curve, while that of I is not.[5] The determination is carried out by dissolving a weighed amount of the mixed acids in 10 ml. of methanol, diluting with 50 ml. of water and titrating with tenth normal alkali. A first inflection point occurs at *p*H 6, which corresponds to neutralization of the carboxyl of both acids and indicates the total amount of acid present. Continuing the titration gives a second break at *p*H 10, as the phenolic hydroxyl of the carboxylate ion of V is neutralized. The distance between the breaks indicates the amount of V in the mixture.

Preparation of 3-Fluorosalicylaldehyde (II) **by Reduction[6] of 3-Fluorosalicylic Acid** (I).—A suspension of 156 g. (1.00 mole) of I or a quantity of the crude mixed I and V containing 1.00 mole of I in 2 liters of water was neutralized with sodium hydroxide. To this solution was added 360 g. (3.36 mole) of *p*-toluidine[7] and the mixture was heated until the toluidine melted. The mixture was then poured into 7 liters of water in a ten-gallon crock. Vigorous mechanical stirring was provided to finely disperse the solidifying toluidine. Following this, 2500 g. of sodium chloride and 400 g. of boric acid were added, and the mixture cooled to 13° by the addition of crushed ice.

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(5) The *pK*'s determined from the mid-points of the titration curves in dilute methanol are: for the carboxyl of I, 2.6; for the carboxyl of V, 4.6; and for the phenolic hydroxyl of the carboxylate ion of V, 8.0.

(6) Weil, *Ber.*, **41,** 4147 (1908).

(7) The quantities of reagents used for the reduction were based on the amount of I present, irrespective of the amount of V. It has been established that V is not reduced to the corresponding aldehyde, although it cannot be recovered from the reaction mixture.

Then 4600 g. of sodium amalgam made from 90.2 g. (3.92 mole) of sodium and 4510 g. of mercury by direct union of the elements was added at the rate of 400 g. every five minutes. Concurrently, an additional 800 g. of boric acid was added in portions alternating with those of amalgam. During the entire course of the operation the temperature was held at 13–15° by judicious addition of ice and very efficient mechanical stirring was provided. The reduction took about two hours. After all the reactants were added, the fluffy yellow Schiff base and excess toluidine were filtered off, acidified with cold 18 *N* sulfuric acid and steam distilled. The distillate was cooled to about 10° and filtered. No appreciable amount of aldehyde remained in the filtrate. The yield of II so obtained was 80.0 g., 57.0%; m. p. 67–68°.

The *p*-toluidine was recovered almost quantitatively from the residue from the steam distillation by carefully making it alkaline with 40% sodium hydroxide and continuing the distillation. The mercury was also recovered after decanting off the Schiff base and could be used to prepare more amalgam after being washed and dried.

Descriptive Information on the Aldehydes.—The aldehydes are stable, colorless crystalline solids. II and IV are volatile in steam and give a purple ferric complex. III is not volatile in steam and gives a sherry ferri-complex. All give a positive Schiff test, which soon fades. They reduce cold Tollens reagent only after several hours. Warming gives a black granular deposit of silver. None reduce boiling Fehling solution.

Discussion

Attempts to prepare II by the N-methylformanilide reaction[8] were entirely unsuccessful. The hexamethylenetetramine reaction[9] gave a 0.5% yield. A synthesis based upon the oxidation of 2-fluoro-6-Δ^1-propenylphenol[10] gave somewhat better yields but was still unsatisfactory.

The reaction conditions described for the synthesis of I, II, III and V were arrived at by systematic investigation of the effects of varying molar ratios, temperature, time, etc. Deviation from them may result in seriously lowered yields.

The structures of the isomeric II and III, both of which were obtained in the Reimer–Tiemann reaction were assigned by showing that II reacts with ethylenediamine to form a Schiff base which forms a chelate with cupric ion, while III does not.

The structure of V was established by a mixed melting point showing its identity with the acid formed by oxidation of III synthesized by the Reimer–Tiemann reaction. The oxidation was accomplished by making the oxime of the aldehyde, dehydrating it to the nitrile and hydrolyzing the nitrile. A specimen of I was prepared by silver oxide oxidation of II and shown to melt at the same temperature as the Kolbe–Schmidt product.

Acknowledgment.—We are indebted to Mr. Charles W. Koch for the carbon–hydrogen analyses and to Mr. Richard R. Holmes for working out the procedure for assaying the mixed acids in the Kolbe–Schmidt product and for carrying out a number of these analyses.

Summary

The preparation of 3-fluorosalicyclic acid, 3-fluoro-4-hydroxybenzoic acid, 3-fluorosalicylaldehyde, 3-fluoro-4-hydroxybenzaldehyde and 5-fluorosalicylaldehyde, all hitherto unreported, has been accomplished and their synthesis is described.

BERKELEY, CALIFORNIA RECEIVED JULY 22, 1946

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[8] L. F. Fieser and J. E. Jones, THIS JOURNAL, **54**, 1666 (1942).

[9] V. C. Duff, *J. Chem. Soc.*, 547 (1941).

[10] Developed by Richard R. Holmes and Dr. Warren G. Miller, unpublished.

[CONTRIBUTED FROM KEDZIE CHEMICAL LABORATORY, MICHIGAN STATE COLLEGE]

Isomeric Esters Produced by the Dehydration of Ethyl 3-Hydroxy-2,3-dimethylbutanoate

BY RALPH C. HUSTON AND GORDON L. GOERNER

In the preparation of a certain alcohol in our laboratory, it became necessary to prepare ethyl 2,3-dimethylbutanoate (IV). The path chosen was through the Reformatsky[1] reaction, using propanone and ethyl 2-bromopropanoate to prepare ethyl 3-hydroxy-2,3-dimethylbutanoate (I). The latter was dehydrated to the unsaturated esters (II and III) which were then reduced to IV.

$$\underset{\text{I}}{(CH_3)_2C(OH)CH(CH_3)COOC_2H_5} \longrightarrow$$

$$\underset{\text{II}}{CH_2{=}C(CH_3)CH(CH_3)COOC_2H_5}, \text{ and}$$

$$\underset{\text{III}}{(CH_3)_2C{=}C(CH_3)COOC_2H_5}$$

$$\text{II or III} \xrightarrow[\text{Pt}]{H_2} \underset{\text{IV}}{(CH_3)_2CHCH(CH_3)COOC_2H_5}$$

Shriner[2] states that β-hydroxy esters are generally unstable, many of them dehydrating upon distillation. Ester I, which contains a tertiary hydroxyl group, proved to be exceptionally stable. Dehydration by dry hydrogen chloride[3] failed completely. Iodine[4] likewise proved unsatisfactory, 10 g. being required to dehydrate one mole of the ester. Phosphorus pentoxide[5] in benzene gave satisfactory results.

Only one unsaturated ester corresponding to compounds II and III is recorded in the literature[6] with a boiling point of 153 to 157°.

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[1] (a) Gilaroff, *J. Russ. Phys.-Chem. Soc.*, **28**, 501 (1896); (b) Perkin and Thorpe, *J. Chem. Soc.*, 1482 (1896).

[2] "Organic Reactions," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1942, p. 11.

[3] Natelson and Gottfried, THIS JOURNAL, **61**, 970 (1939).

[4] Whitmore and Laughlin, *ibid.*, **54**, 4392 (1932); Hibbert, *ibid.*, **37**, 1748 (1915).

[5] Kon and Nargund, *J. Chem. Soc.*, 2461 (1932).

[6] Merling and Welde, *Ann.*, **366**, 140 (1909); v. Auwers and Eisenlohr, *J. prakt. Chem.*, [2] **82**, 167 (1910); Jupp, Kon and Lockton, *J. Chem. Soc.*, 1642 (1928).