γ-Di-*n*-butylaminopropyl 3-Bromo-4-*n*-propylaminobenzoate.—γ-Di-*n*-butylaminopropyl 3-bromo-4-aminobenzoate, 26 g., was refluxed in *n*-propyl alcohol solution with 13 g. of *n*-propyl bromide until no longer alkaline to litmus, more bromide being added if necessary at the end of about twenty hours. The propyl alcohol was removed by vacuum distillation and the residue neutralized with alcoholic hydrochloric acid and placed in a desiccator, where it crystallized. The product was recrystallized three times from water; m. p. 146–148°.

Anal. Calcd. for $C_{21}H_{35}N_2O_2Br \cdot HCl$: N, 6.04. Found: N, 6.00.

γ-Di-*n*-butylaminopropyl 3-Bromo-4-*n*-butylaminobenzoate.—γ-Di-*n*-butylaminopropyl 3-bromo-4-aminobenzoate, 24.3 g., was refluxed in *n*-butyl alcohol solution with 15 g. of *n*-butyl bromide. The product was worked up in the same manner as the *n*-propyl analog. The hydrochloride was recrystallized from water; m. p. 116–117°.

Anal. Calcd. for $C_{22}H_{37}N_2O_2Br \cdot HCl$: N, 5.86. Found: N, 5.90.

γ-Di-*n*-butylaminopropyl 2-Bromo-3-*n*-butylaminobenzoate.—γ-Di-*n*-butylaminopropyl 2-bromo-3-aminobenzoate was alkylated by refluxing with *n*-butyl bromide in *n*-butyl alcohol solution. The hydrochloride was prepared and purified by leaching with acetone; m. p. 169–171°.

Anal. Calcd. for $C_{22}H_{37}N_2O_2Br \cdot HCl$: N, 5.86. Found: N, 5.77.

γ-Di-*n*-butylaminopropyl 3,5-Dibromo-4-aminobenzoate.—Butyn base, 10 g., was dissolved in chloroform and a solution of bromine in chloroform containing 0.75 g. of bromine per cc. was gradually added with cooling and stirring until no more bromine appeared to be absorbed. The flask became filled with crystals. After standing and cooling, these were filtered off and recrystallized from alcohol (four times); m. p. 162.5–163°; yield 8.5 g., 48%.

Anal. Calcd. for $C_{18}H_{28}N_2O_2Br_2 \cdot HBr$: N, 5.14; Br, 43.98. Found: N, 4.80; Br, 43.74.

γ-Di-*n*-butylaminopropyl 3,5-Dibromo-4-*n*-propylaminobenzoate.—γ-Di-*n*-butylaminopropyl 3,5-dibromo-4-aminobenzoate, 6 g., was refluxed in *n*-propyl alcohol solution with a slight excess of *n*-propyl bromide in a total time of refluxing of eighteen hours. The product was made alkaline with sodium carbonate solution, shaken out in ether, the ether dried and evaporated. The residue in acetone solution was acidified with hydrochloric acid, and benzene added to precipitate the hydrochloride. This precipitate was twice recrystallized from alcohol; m. p. 117–118°; yield 2 g., 29%.

Anal. Calcd. for $C_{21}H_{34}N_2O_2Br_2 \cdot HCl$: N, 5.16. Found: N, 5.10.

The authors wish to thank Mr. E. F. Shelberg for the microanalyses reported in this work.

Summary

For the purpose of testing as local anesthetics, a series of esters of aminobenzoic and N-alkylaminobenzoic acids containing one or two bromine atoms in the aromatic nucleus have been prepared.

The water insolubility of the hydrochlorides of these esters limits their usefulness as local anesthetics.

NORTH CHICAGO, ILLINOIS RECEIVED JULY 12, 1940

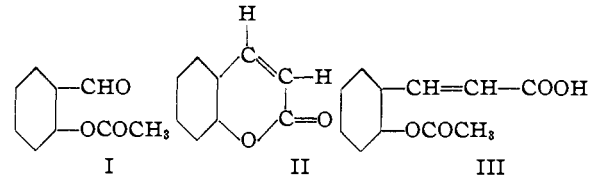
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF MARYLAND]

The Reactions of Ketene with Salicylaldehyde and *p*-Hydroxybenzaldehyde

BY JONATHAN W. WILLIAMS[1] AND ALEXANDER SADLE[2]

It has been shown by Hurd and Thomas[3] that ketene reacts with aromatic aldehydes in the presence of anhydrous potassium acetate to form β-aryl-substituted acrylic acids in a type of Perkin synthesis. It is shown in the present work that, although the same type of reaction may be accomplished with phenolic aldehydes, acetylation of the phenol group is the predominant reaction, and the substituted cinnamic acid obtained in small yield contains an acetylated phenol group.

Ketene and Salicylaldehyde.—The reaction of ketene with salicylaldehyde gives, under various conditions, acetylsalicylaldehyde (I), coumarin (II), and *o*-acetoxycinnamic acid (III). I may be obtained in 84% yield, along with a 9% yield



I II III

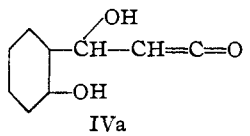
of II as a by-product, by the direct reaction of ketene and salicylaldehyde at room temperature in the absence of a catalyst. By running the reaction in the presence of a drop of sulfuric acid, the yield of II may be increased to 31%. III is obtained in the reaction products only when fused sodium or potassium acetate is present with the reactants, and then only in a 1–2% yield.

(1) Present address: Chemistry Department, University of North Carolina, Chapel Hill, North Carolina.

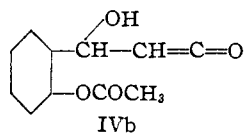
(2) Taken from the M.S. Thesis of Alexander Sadle.

(3) Hurd and Thomas, THIS JOURNAL, **55**, 275 (1933).

Mechanism of the Reaction.—The formation of II may be explained either by the direct dehydration of I, or by the intermediate formation of an unstable compound such as IVa or IVb.[3] Formation of II from I in the quantities actually ob-



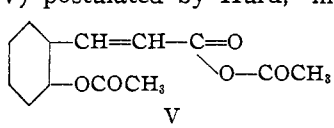
IVa



IVb

tained seems unlikely, since experiments show that ketene has practically no effect on I, except in the presence of sulfuric acid or sodium acetate. When I is subjected to the action of ketene in the presence of a drop or two of sulfuric acid at room temperature, only a 2–5% yield of II is obtained, as contrasted to the 31% yield of II from salicylaldehyde.

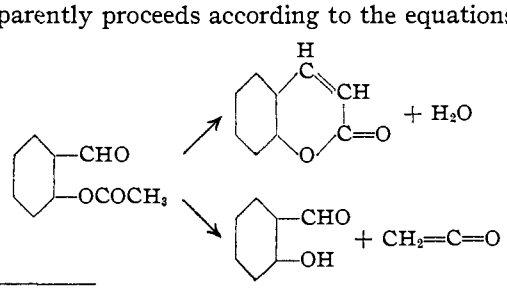
The formation of *o*-acetoxycinnamic acid is most easily explained by a rearrangement of the "three carbon system" type on IVb. No evidence was found for the mixed anhydride type of intermediate (V) postulated by Hurd,[3] inasmuch as



V

analysis with dry oxalic acid and pyridine[4] gave no measurable volume of gas.

Pyrolysis of Acetylsalicylaldehyde.—When heated to refluxing temperature for five to ten hours, approximately 10% of I is converted to II. Most of the remainder may be recovered as unchanged I. Pyrolysis in the presence of one drop of sulfuric acid increases the yield of II to 16%. In each case some acetic acid and acetic anhydride are obtained. By carrying out the pyrolysis in the presence of 5 g. of fused sodium acetate, much larger amounts of acetic acid and anhydride are obtained, and, in addition to a 16% yield of II, and a recovery of 20% of I, salicylaldehyde is formed in a 29% yield. The thermal decomposition at refluxing temperatures, therefore, apparently proceeds according to the equations



$$CH_2{=}C{=}O + H_2O \longrightarrow CH_3COOH$$
$$2\ CH_2{=}C{=}O + H_2O \longrightarrow (CH_3CO)_2O$$

Ketene and *p*-Hydroxybenzaldehyde.—Ketene reacts easily with *p*-hydroxybenzaldehyde in acetone solution at room temperature to give *p*-acetoxybenzaldehyde (VI) in a 91% yield. In the presence of fused sodium acetate a 5% yield of *p*-acetoxycinnamic acid (VII) results. Starting with VI, the action of ketene and sodium acetate produces VII in a 6% yield.

p-Acetoxybenzaldehyde is sensitive to oxidation by the air, and, on standing, is converted to *p*-acetoxybenzoic acid (VIII). VI, VII, and VIII are all easily saponified by the action of cold 10% sodium hydroxide solution.

Experimental Part

Ketene was prepared in a ketene lamp which delivered 0.45 mole per hour.[5]

Acetylsalicylaldehyde.—Ketene was passed for three and one-half hours (1.6 moles) into one mole of salicylaldehyde (122 g., "Eastman pure," recovered from the bisulfite compound) at room temperature. The color change was from pale yellow to deep red. On distillation there was obtained 138 g. (0.84 mole) of acetylsalicylaldehyde at 134–136° (13 mm.) and a fraction boiling at 138–160° (13 mm.) from which 10 g. (0.07 mole) of coumarin was obtained on crystallization from water.

The purity of the starting material is important in this preparation. With ordinary salicylaldehyde, even though freshly distilled, the highest yield of acetylated product was 60%.

Coumarin.—The highest yield of coumarin was obtained when ketene was passed for ten hours (4.5 moles) into one mole of salicylaldehyde to which had been added one drop of sulfuric acid. From the fraction boiling at 138–160° (13 mm.), 45 g. (0.31 mole) of coumarin was isolated by crystallization from water.

***o*-Acetoxycinnamic Acid.**—Ketene was passed for twenty hours (9 moles) into a mixture of one mole of salicylaldehyde (122 g.), 28.5 g. of fused sodium acetate and 200 ml. of acetone. The acetone was removed on the steam-bath, the residue taken up in ether and the solution extracted with 10% aqueous sodium bicarbonate. Acidification with phosphoric acid yielded about 2 g. (0.01 mole) of a precipitate of *o*-acetoxycinnamic acid, which after three recrystallizations from water melted at 156–157°, and was identified by a mixed m. p. with known *o*-acetoxycinnamic acid.

Effect of Ketene on Acetylsalicylaldehyde.—Treatment of 98.7 g. of acetylsalicylaldehyde with ketene for five hours at room temperature gave a reaction mixture from which 67.4 g. (68%) of the starting material was recovered by distillation at 13 mm. The residue was a tar from which 0.5 g. of coumarin resulted on crystallization from water. In a similar run to which a drop of sulfuric acid was added, 58% of the acetylsalicylaldehyde was recovered and 3 g. of coumarin was obtained.

(4) (a) Whitford, THIS JOURNAL, **47**, 2939 (1925); (b) Hurd and Dull, *ibid.*, **54**, 3427 (1932).

(5) Williams and Hurd, *J. Org. Chem.*, **5**, 122 (1940).

Pyrolysis of Acetylsalicylaldehyde.—Freshly distilled acetylsalicylaldehyde (91.7 g.) was refluxed for ten hours. The refluxing temperature at first was 255° but, as the pyrolysis proceeded, the refluxing became more vigorous, and the temperature had to be reduced. At the end of the run it was 225°. The products, separated by distillation at reduced pressure, were 6 g. of acetic acid and acetic anhydride, 53 g. of recovered acetylsalicylaldehyde, and 7.6 g. of coumarin.

Refluxing 50.7 g. of acetylsalicylaldehyde and one drop of sulfuric acid for ten hours produced 7.0 g. of coumarin, yields of other products being comparable to those in the above run.

Refluxing 53.0 g. of acetylsalicylaldehyde with 5.0 g. of fused sodium acetate for five hours produced about 6 g. of a mixture of acetic acid and acetic anhydride, 11.6 g. of salicylaldehyde, 10.6 g. of acetylsalicylaldehyde, and 7.5 g. of coumarin.

***p*-Acetoxybenzaldehyde.**—Ketene was passed for five hours (2.5 moles) into a solution of 55 g. (0.45 mole) of *p*-hydroxybenzaldehyde in 300 ml. of acetone. On distillation the reaction mixture yielded a 67 g. fraction (0.408 mole, 91% yield) of *p*-acetoxybenzaldehyde, b. p. 119–120° (6 mm.). This substance formed a 2,4-dinitrophenylhydrazone, m. p. 241°. The acetylated aldehyde was very sensitive to the action of aqueous alkali, the acetyl group being removed on short exposure to cold 10% aqueous sodium hydroxide solution. The acetylated aldehyde was also found to be oxidized easily by the action of air, forming *p*-acetoxybenzoic acid, m. p. 118°, a compound which is easily hydrolyzed by the action of cold 10% aqueous sodium hydroxide solution to *p*-hydroxybenzoic acid.

***p*-Acetoxycinnamic Acid.**—Ketene was passed for ten hours (4.5 moles) into a mixture of 61 g. (0.5 mole) of *p*-hydroxybenzaldehyde, 10.6 g. of fused sodium acetate and 300 ml. of benzene. Extraction of the reaction mixture with a 10% aqueous sodium bicarbonate solution, followed by acidification of the extract with phosphoric acid, yielded 18 g. of a crude product from which, after several recrystallizations from water and several treatments with Norit, 6 g. (5% yield) of pure *p*-acetoxycinnamic acid, m. p. 207°, was obtained.

A comparable run in which *p*-acetoxybenzaldehyde was the starting material gave a 6% yield of *p*-acetoxycinnamic acid.

Summary

The reaction of ketene with salicylaldehyde yielded acetylsalicylaldehyde, coumarin (especially in the presence of sulfuric acid), and, only in the presence of sodium acetate, *o*-acetoxycinnamic acid. The mechanism of the formation of these compounds is discussed.

Pyrolysis of acetylsalicylaldehyde at its boiling point yielded salicylaldehyde, acetic acid, acetic anhydride and coumarin. The presence of sulfuric acid catalyzed the formation of coumarin.

Ketene reacted with *p*-hydroxybenzaldehyde to give a good yield of *p*-acetoxybenzaldehyde. When the reaction was carried out in the presence of sodium acetate, it was possible to isolate some *p*-acetoxycinnamic acid from the reaction mixture.

RECEIVED JULY 26, 1940

[CONTRIBUTION FROM THE DIVISION OF INDUSTRIAL AND CELLULOSE CHEMISTRY, MCGILL UNIVERSITY]

Studies on Lignin and Related Compounds. XLIX. Occurrence of the Guaiacyl and Syringyl Groupings in the Ethanolysis Products from Various Plants

BY A. S. MACINNES, EINAR WEST, JOSEPH L. MCCARTHY AND HAROLD HIBBERT

It has been shown that ethanolysis[1] (*i. e.*, treatment with boiling anhydrous ethanol containing hydrogen chloride) of spruce wood,[2] maple wood,[3] and of oak lignin,[4] results in a conversion of a part of the lignin constituents into water-soluble oils. The remainder either remains in the residual plant tissue, or is isolated as the water-insoluble, amorphous, non-distillable "ethanol lignin."

In the present investigation[5] these findings have been extended by subjecting various types of plant materials to ethanolysis[1] and then determining the degree of lignin removal, as well as the amounts of "crude oils" and ethanol lignin formed. The products investigated were California redwood, Douglas fir, red oak, jute, corn stalks, rye straw and bamboo. The water-soluble "crude oils" were separated by the previous method[1] into a bisulfite, bicarbonate, and alkali soluble, as well as a "neutral" fraction. The yields obtained are based on the Klason lignin originally present and are compared with previously published results[1] obtained with spruce and maple (Table I).

It is apparent that each of these lignin-con-

(1) Brickman, Pyle, McCarthy and Hibbert, THIS JOURNAL, **61**, 868 (1939).

(2) Cramer, Hunter and Hibbert, *ibid.*, **61**, 509 (1939).

(3) Hunter, Cramer and Hibbert, *ibid.*, **61**, 516 (1939).

(4) Peniston, McCarthy and Hibbert, *ibid.*, **61**, 530 (1939).

(5) Preliminary results dealing with the present investigation have been reported previously, see ref. 1 and West, MacInnes, McCarthy and Hibbert, *ibid.*, **61**, 2556 (1939).