

liters. Both the C_4 and the β -glucometasaccharinic anilide fractions crystallized spontaneously on concentration *in vacuo* to sirups.

Fractionation of Saccharinic Anilides Derived from L-Arabinose.—This mixture, derived from 20 g. of L-arabinose, was fractionated on the 6-inch column. A fore-run of 7.5 liters was taken, and then 310 fractions of 100 cc. each. The C_4 fraction was obtained at 6–9.5 liters effluent volume, and the C_5 -anilides at 10–21 liters. A slower " C_6 -fraction," taken at 21–31 liters, was a sirup.

The C_5 -anilide fraction was a mixture, weighing 7.5 g., and crystallized spontaneously on concentration *in vacuo*. Crystallization from ethyl acetate-ligroin gave 1.5 g. of crystalline product III, and a levorotatory mother liquor.

Fractionation of Saccharinic Anilides Derived from Cellobiose.—Fractionation of saccharinic anilides derived from

1 g. of cellobiose was carried out on a 2-inch cellulose column at 650 cc. per hour. After a fore-run of 750 cc., 52 fractions of 43 cc. each and 48 fractions of 86 cc. each were taken. A total of 940 mg. crude yield of anilides was recovered, including: C_3 , 170 mg.; C_4 , 130 mg.; C_5 , 180 mg.; α -isosaccharinic anilide, 215 mg.; and β -glucometasaccharinic anilide, 105 mg.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE OHIO STATE UNIVERSITY]

Ethyl Hydrogen DL-Galactarate and Ethyl DL-Galactarate Lactone, and Their Conversion to a Derivative of α -Pyrone¹

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The preparation of ethyl hydrogen DL-galactarate and ethyl DL-galactarate lactone is described. The two compounds are also formed as by-products in the synthesis of diethyl di-*O*-isopropylidene-galactarate. Acetic anhydride in the presence of sodium acetate reacts with either of them at 100° to give a compound described tentatively as 4-acetoxy-6-ethoxycarbonyl- α -pyrone.

During the course of the preparation of diethyl galactarate by the action of ethanol and sulfuric acid on galactaric (mucic) acid, the crude crystalline product obtained from the reaction mixture was dried overnight at 100°. Though the melting point of diethyl galactarate is 172°, the product fused to a sirup during this time. A sample of pure diethyl galactarate heated under the same conditions was recovered unchanged, hence the change in the first instance was attributed to the crude product's being contaminated with acid. Some small amount of unchanged diethyl ester was found in the sirup and, in addition, two other compounds were isolated. One compound reduced hot Fehling solution, gave galactaramide when treated with concentrated ammonia, and was identified by elemental analysis as ethyl DL-galactarate lactone, m.p. 103–104°. The other compound, which did not reduce Fehling solution, gave DL-galactaramic acid with concentrated ammonia, and elemental analysis showed it was ethyl hydrogen DL-galactarate, m.p. 181–182°. These two compounds, which are described here for the first time, are also formed as by-products when diethyl galactarate is treated with acetone and sulfuric acid, the main product being diethyl di-*O*-isopropylidene-galactarate.

When either ethyl hydrogen DL-galactarate or its monolactone was heated for a few minutes at 100° with acetic anhydride and sodium acetate, a solid product was obtained from which ethyl tri-*O*-acetyl-DL-galactarate lactone (II, probable structure) was isolated in small amount. The triacetate, which also reduced hot Fehling solution, had been ob-

tained previously by Skraup² by heating diethyl galactarate with acetyl chloride. In the present work it was found that if the reaction time in the acetic anhydride-sodium acetate reaction is increased to ninety minutes, the product obtained is an acetoxy-ethoxycarbonyl- α -pyrone. The compound reduces warm Fehling solution, and its alcoholic solution does not color ferric chloride. It dissolves slowly in cold 10% aqueous sodium hydroxide to give a yellow solution. If this solution is acidified the yellow color is diminished, and the resulting solution gives a deep-red coloration with ferric chloride, decolorizes bromine water and reduces alkaline permanganate. Acetylation of diethyl galactarate under the same conditions gave only diethyl tetra-*O*-acetyl-galactarate.

The dilactones of mannaric and glucaric acids, and the ester lactones of glucaric acid are known to exhibit reducing properties after treatment with alkaline reagents.³ This has been shown to be due to an opening of the lactone ring together with the formation of an enol by α,β -dehydration. By analogy, the enol I is probably responsible for the reducing properties of the ethyl DL-galactarate lactone now prepared. It is reasonable to assume that one molecule of the triacetate II of this compound (which also reduces Fehling solution) by further action of acetic anhydride and sodium acetate, forms the intermediate enol ester III which then cyclizes by splitting out two molecules of acetic acid. If this is true, the product obtained is either 3-acetoxy-6-ethoxycarbonyl- α -pyrone (IV) or 4-acetoxy-6-ethoxycarbonyl- α -pyrone (V). The compound, after having been de-esterified by acid or alkali,

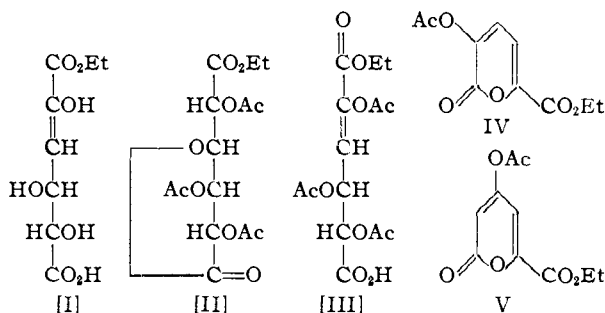
(1) This work was carried out under contract (DA-33-019-ord-1466; supervising agency, Ballistic Research Laboratories, Aberdeen Proving Ground, Md.) between the Ordnance Corps and The Ohio State University Research Foundation (Project 589).

(2) Z. H. Skraup, *Monatsh.*, **14**, 470 (1893); P. Fortner and Z. H. Skraup, *ibid.*, **15**, 200 (1894).

(3) F. Smith, *Advances in Carbohydrate Chem.*, **2**, 101 (1946).

does not give, with ferric chloride, the deep-green color which is typical of 3-hydroxy- α -pyrones⁴ and which is given by 6-carboxy-3-hydroxy- α -pyrone in particular.⁵ It is tentatively suggested, therefore, that the compound's structure is that represented by V rather than IV.

Several instances of the formation of α -pyrone derivatives from carbohydrate sources have been reported in the literature, and these have been reviewed by Fried.⁶ Only one other instance is known, however, of this occurring during acetylation. In 1902, Neuberg reported that he obtained a crystalline compound from the reaction of 2-amino-2-deoxy-D-gluconic (D-glucosaminic) acid with acetic anhydride and sodium acetate.⁷ Nearly 30 years elapsed before this was identified as 3-acetamido-6-acetoxymethyl- α -pyrone.⁸



Experimental

Preparation of Diethyl Galactarate; Ethyl Hydrogen DL-Galactarate, Ethyl DL-Galactarate Lactone.—A suspension of galactaric acid (mucic acid, 400 g.) in absolute ethanol (2000 ml.) containing concentrated sulfuric acid (40 ml.) was boiled under reflux, with stirring, overnight. Unchanged galactaric acid (200 g.) was removed by filtering the hot reaction mixture, and the filtrate on cooling deposited crystals of diethyl galactarate (200 g.). These were collected, washed thoroughly with 95% ethanol, dried at room temperature, and recrystallized from 95% ethanol as pure diethyl galactarate, m.p. 172° after softening at 160°, in agreement with recorded values.^{2,10}

In another experiment, using the same quantities and reaction conditions, the crude diethyl galactarate, which separated from the filtered, cooled reaction mixture, was collected and washed once in a beaker with 95% ethanol. The crystals were then filtered and dried overnight at 100°, during which time they were reduced to a sirup. When this was triturated with ethanol (250 ml.) most of the sirup dissolved leaving a solid which, recrystallized from ethanol, was identified as diethyl galactarate, yield 11 g., m.p. (and mixed m.p.) 171–172°. The alcoholic solution was evaporated to a sirup (159 g.) which, when stirred with acetone (750 ml.) at room temperature, left a white solid (48 g.) undissolved. This was collected, dried, and recrystallized from aqueous ethanol as ethyl hydrogen DL-galactarate, yield 30 g., m.p. 181–182° (with foaming). The compound did not reduce hot Fehling solution; it was sparingly soluble in water and was insoluble in the common organic solvents.

Anal. Calcd. for $C_8H_{14}O_8$: C, 40.30; H, 5.88. Found: C, 40.04; H, 6.18.

The acetone solution was evaporated to a sirup (106 g.)

(4) L.-J. Simon, *Compt. rend.*, **130**, 255 (1900); E. Votoček and S. Malachta, *Collection Czechoslov. Chem. Commun.*, **8**, 66 (1936).

(5) E.-E. Blaise and H. Gault, *Compt. rend.*, **147**, 198 (1908).

(6) J. Fried in "Heterocyclic Compounds," R. C. Elderfield, ed., John Wiley and Sons, Inc., New York, N. Y., 1950, Vol. 1, p. 367.

(7) C. Neuberg, *Ber.*, **35**, 4014 (1902).

(8) M. Bergmann, L. Zervas and E. Silberkweit, *ibid.*, **64**, 2428 (1931).

(9) All melting points are corrected (Fisher-Johns apparatus).

(10) R. S. Tipson and Mary A. Clapp, *J. Org. Chem.*, **18**, 952 (1953).

which crystallized. The solid was washed with a little chloroform and then dissolved in boiling ethyl acetate. Some insoluble ethyl hydrogen DL-galactarate (9 g.) was filtered from the hot solution which on cooling deposited granular crystals. These were again dissolved in ethyl acetate, and the process was repeated several times to obtain pure ethyl DL-galactarate lactone, yield 30 g., m.p. 103–104°. The compound reduced hot Fehling solution, it was soluble in water and ethanol but was insoluble in chloroform, ether and hexane.

Anal. Calcd. for $C_8H_{12}O_7$: C, 43.64; H, 5.46. Found: C, 43.64; H, 5.67.

A sample of pure diethyl galactarate, heated at 100° for 24 hr., was unchanged at the end of this time.

Diethyl Di-O-isopropylidene-galactarate; Ethyl Hydrogen DL-Galactarate, Ethyl DL-Galactarate Lactone.—Diethyl galactarate (100 g.), acetone (1000 ml.) and concentrated sulfuric acid (10 ml.) were stirred together for 6 hr. at room temperature. The acid was then removed by shaking the solution with powdered, anhydrous potassium carbonate, the point of neutralization being indicated by the disappearance of the yellow color of the solution. The filtered acetone solution was evaporated to a sirup which was extracted five times with boiling hexane¹¹ (total vol. 500 ml.). The combined extracts were evaporated to a colorless crystalline solid, which was washed with water, dried and recrystallized from hexane as diethyl di-O-isopropylidene-galactarate, yield 25 g., m.p. 85°. The substance was insoluble in water and was soluble in alcohol, ether, chloroform, and hexane.

Anal. Calcd. for $C_{26}H_{42}O_8$: C, 55.50; H, 7.51. Found: C, 55.69; H, 7.58.

The sirupy residue which did not dissolve in the hexane was triturated with ether (500 ml.) to effect solidification. The solid, after having been washed with a further 100 ml. of ether, was dissolved in hot ethyl acetate and the cooled solution was diluted to 500 ml. with cold ethyl acetate. The solution was allowed to stand at room temperature for 2 days, after which the solid which had separated was removed by filtration, and the filtrate was concentrated. Some ethyl hydrogen DL-galactarate (2.4 g.) was filtered from the hot concentrate, and was identified, after recrystallization from water, by its melting point and mixed melting point of 181–182°. The ethyl acetate solution on cooling deposited crystals of ethyl DL-galactarate lactone (16.5 g.) m.p. (and mixed m.p.) 103–104°. A further 2 g. of this compound was obtained by concentrating the ethereal solution.

When it was desired to obtain only diethyl di-O-isopropylidene-galactarate from this reaction, the sirupy reaction product was shaken with water. The acetonated compound remained undissolved and the other products of the reaction passed into solution.

Action of Ammonia on Ethyl DL-Galactarate Lactone.—Ethyl DL-galactarate lactone (1 g.) was stirred into concentrated ammonium hydroxide (3 ml.) and immediately a white precipitate appeared. The suspension was agitated for 5 min. and then diluted with ethanol (10 ml.). The solid obtained by filtration was recrystallized from a large volume of water as micro needles of galactaramide, m.p. 230° dec. (coloration at 220°). A sample of galactaramide, prepared in the same way from diethyl galactarate, exhibited the same behavior on heating.

Action of Ammonia on Ethyl Hydrogen DL-Galactarate.—The above procedure was followed using 1 g. of ethyl hydrogen DL-galactarate instead of the lactone. The crude product was suspended in cold water and 5% hydrochloric acid was added dropwise until the solution was faintly acid. The filtered solid was washed with water, and recrystallized from water as granular crystals of DL-galactaramic acid, m.p. 195° dec. (coloration at 180°). Bergmann,¹² who prepared this compound from the monolactone of galactaric acid, described it as browning at 175° and foaming at 192°.

Ethyl Tri-O-acetyl-DL-galactarate Lactone.—Ethyl DL-galactarate lactone (5 g.), acetic anhydride (15 ml.) and sodium acetate (1.5 g.) were heated at 100° for 7 min. The reaction mixture was then poured onto crushed ice and water, and a solid was obtained, yield 6 g. Three wasteful recrystallizations from ethanol gave stout needles of ethyl tri-O-acetyl-DL-galactarate lactone, yield 0.5 g., m.p. 125°

(11) Skellysolve B, b.p. 65–69°.

(12) M. Bergmann, *Ber.*, **54**, 1362 (1921).

(Skraup² recorded 122°). The same product was obtained when the reaction was repeated using ethyl hydrogen DL-galactarate and a reaction time of 3 min. The compound reduced hot Fehling solution.

Anal. Calcd. for C₁₄H₁₈O₁₀: C, 48.57; H, 5.21; CH₃CO, 37.3. Found: C, 48.66; H, 5.46; CH₃CO, 37.3.¹³

4-Acetoxy-6-ethoxycarbonyl- α -pyrone.—When the reaction mixture (from ethyl DL-galactarate lactone) described in the preceding experiment was heated at 100° for 90 min., the solution became a very dark brown. On pouring the mixture onto ice and water a brown solid was obtained which, having been washed and dried, was boiled with hexane. The dark color remained in the insoluble residue from which the solution was decanted. Long needles of 4-acetoxy-6-ethoxycarbonyl- α -pyrone separated from the cooled solution, yield 2.5 g., m.p. 68°. Pure material was obtained on one recrystallization from hexane, m.p. 69°. The substance was insoluble in water and was soluble in alcohol, ether, hexane and chloroform.

When ethyl hydrogen DL-galactarate (5 g.) was used as

(13) The authors are indebted to Mr. A. Chaney of this Laboratory for the acetyl analysis.

the starting compound, the same product was obtained, yield 1.5 g., m.p. 68°.

Anal. Calcd. for C₁₀H₁₀O₆: C, 53.20; H, 4.43. Found: C, 53.42; H, 4.48.

The compound decomposed slowly at room temperature, losing acetic acid, but it could be stored at 0°. It reduced warm Fehling solution; an alcoholic solution of it gave no color with ferric chloride. The compound dissolved in cold 10% aqueous sodium hydroxide to give a yellow solution. When hydrochloric acid was added dropwise until the solution was slightly acid, the yellow color became paler, and the resulting solution gave a deep-red coloration with ferric chloride, decolorized bromine water and reduced alkaline potassium permanganate.

Diethyl Tetra-O-acetyl-galactarate.—Diethyl galactarate (5 g.) was heated with acetic anhydride (15 ml.) and sodium acetate (1.5 g.) for 90 min. The solid obtained on decomposing the reaction mixture with ice and water was insoluble in hexane, and was recrystallized from methanol as needles of diethyl tetra-O-acetyl-galactarate, m.p. 195° (Skraup² recorded 189°).

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[CONTRIBUTION FROM PULP MILLS RESEARCH AND THE DEPARTMENTS OF CHEMISTRY AND CHEMICAL ENGINEERING, UNIVERSITY OF WASHINGTON]

Lignin. VII. Distribution in Molecular Weight of Certain Lignin Sulfonates^{1a}

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Several lignin sulfonate preparations, representative of nearly all of the lignin in gymnosperm woods, have been fractionated and estimates have been made of the average molecular weights of the lignin sulfonates in the fractions. It is found that the molecular weights of the lignin sulfonates range from a few hundred to about one hundred thousand, average around ten or twenty thousand, and are distributed somewhat differently in the several preparations studied. An ordered change in the ultraviolet absorption spectrum and presumably in phenolic hydroxyl content occurs with increase in the molecular weight. In fractions of the lowest molecular weight, the presence of several individual lignin sulfonates, or of closely related groups of lignin sulfonates, has been observed by use of an electrophoresis technique.

Introduction

Several investigations of the molecular weight of lignins have been carried out but the results so far reported²⁻⁴ have in most cases been obtained using lignin preparations which seem to have been representative of only a part of the total lignin available from the wood, or to have been incompletely purified or inadequately fractionated.

Thus, one of the objectives of research conducted in this Laboratory over the last several years has been to develop methods by which molecular weights of lignins could be estimated under such conditions that the above-mentioned difficulties could be minimized or avoided. Investigations have been carried out with the sulfonate derivatives of lignin in part because (a) nearly all of the lignin in xylem tissue can be converted to these derivatives, (b) the conversion takes place under mildly acidic conditions whereby the possibilities of alkaline rearrangements are avoided although

acidic condensation reactions may proceed to a limited degree,⁵ and (c) almost the total lignin sulfonates are soluble and are thereby amenable to investigation by well established procedures. It has been found^{2,6} that an aqueous solution of total lignin sulfonates and other wood components is separated by dialysis into dialyzable material consisting of some lignin sulfonates, sugars and other substances of low molecular weight, and also into non-dialyzable material consisting of higher molecular weight lignin sulfonates in a good state of purity. These non-dialyzable lignin sulfonates were fractionated⁷ and the fractions proved to be of approximately constant composition and to manifest progressively different diffusion coefficients⁸ as expected for a polymeric series of lignins. Recently, the molecular weights of some carefully purified and fractionated non-dialyzable lignin sulfonates have been determined by a light scattering method.⁹ The diffusion coefficients of the same samples were also measured. The relationship found between the diffusion coefficients and the molecular weights, along with other evidence,

(5) V. F. Felicetta and J. L. McCarthy, unpublished research.

(6) Q. P. Peniston and J. L. McCarthy, *THIS JOURNAL*, **70**, 1324 (1948).

(7) A. E. Markham, Q. P. Peniston and J. L. McCarthy, *ibid.*, **71**, 3599 (1949).

(8) V. F. Felicetta, A. E. Markham, Q. P. Peniston and J. L. McCarthy, *ibid.*, **71**, 2839 (1949).

(9) J. Moacanin, V. F. Felicetta, W. Haller and J. L. McCarthy, *ibid.*, **77**, 3470 (1955).

(1) (a) Presented in part at American Chemical Society Lignin Symposium in New York in September, 1950, and at the Pacific Northwest Regional Meeting in Eugene, Oregon, in June, 1955. (b) American Association of University Women and Fullbright Research Fellow. Urheilukatu 4, Helsinki-Toolo, Finland.

(2) (a) F. Brayns, "The Chemistry of Lignin," Academic Press, Inc., New York, N. Y., 1952; (b) N. Gralen, *J. Colloid Sci.*, **1**, 453 (1946).

(3) (a) E. Olleman and D. M. Ritter, *THIS JOURNAL*, **69**, 665 (1947); (b) E. Olleman, D. Pennington and D. M. Ritter, *J. Colloid Sci.*, **3**, 185 (1948).

(4) B. Ivarsson, *Svensk Papperstidn.*, **54**, 1 (1951).