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A Second Synthesis of Glucosidoferulic Acid[1]

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The initial synthesis[2] of glucosidoferulic acid (3-methoxy-4-β-*d*-glucosidocinnamic acid) was accomplished by the simultaneous saponification and deacetylation of the acetylated methyl ester resulting from the condensation of methyl ferulate and acetobromoglucose. In an effort to shorten the procedure we have studied the condensation of tetra-acetyl-β-*d*-glucosidovanillin and malonic acid by the Knoevenagel reaction, and find that it leads to a quantitative yield of tetraacetylglucosidoferulic acid. The acetylated acid may be smoothly deacetylated by sodium methylate and the glycosidic acid obtained either as the monohydrate previously isolated or as the anhydrous acid described herewith for the first time.

Experimental

β-*d*-Glucosidovanillin (3-Methoxy-4-β-*d*-glucosidobenzaldehyde).—A convenient simplification of the method of Fischer and Raske,[3] obviating the isolation of acetobromoglucose, was employed. A solution of acetobromoglucose in chloroform was prepared by saturating a solution of 38.5 g. of β-glucose pentaacetate in 50 cc. of glacial acetic acid with dry hydrobromic acid gas, allowing the reaction to proceed overnight, extracting with 150 cc. of chloroform and washing the chloroform layer with weak sodium bicarbonate solution and water. This chloroform solution was mixed with a paste prepared from 16.5 g. of vanillin (10% excess) and 103.2 cc. of 0.95 *N* alcoholic potassium hydroxide and the mixture refluxed gently for one-half hour; some darkening occurred and potassium bromide precipitated. After cooling it 500 cc. of ice water was added, the chloroform layer separated, washed with ice water, dried with calcium chloride and concentrated *in vacuo* to a dry mass of crystals, which were then recrystallized from 25 cc. of 95% alcohol; yield 24 g. (50%); the properties of the substance agree with the data of Fischer and Raske.

β-Tetraacetyl-*d*-glucosidoferulic Acid (3-Methoxy-4-β-tetraacetyl-*d*-glucosidocinnamic Acid).—β-Tetraacetyl-*d*-glucosidovanillin (5 g.), malonic acid (2.7 g.), pyridine (5 cc.) and piperidine (5 drops) were heated under reflux on the steam-bath for one and one-half hours, then heated just to boiling, and the cooled solution treated with 75 cc. of water. The thick yellow sirup which separated crystallized after trituration with water and was recrystallized from 95% alcohol; yield 5.4 g. (quantitative).

β-Tetraacetyl-*d*-glucosidoferulic acid crystallizes in glistening platelets melting at 207° (corr.) to a clear, colorless oil. It is levorotatory, showing an $[\alpha]^{20}_{D}$ value of −33.9° (0.2428 g. in 25 cc. of chloroform in a 2-dm. tube gave a reading 0.658° to the left) which was unchanged upon recrystallization. Titration showed the presence of one carboxyl and four acetyl groups (0.1056 g. consumed 2.01 cc. 0.1 *N* alkali immediately and 9.94 cc. upon standing in an excess of alkali for one hour; calcd. 2.01, 10.07 cc.).

Anal. Calcd. for $C_{24}H_{28}O_{13}$: C, 54.94; H, 5.38. Found: C, 54.81; H, 5.48.

β-*d*-Glucosidoferulic Acid (3-Methoxy-4-β-*d*-glucosidocinnamic Acid).—Twenty-five cubic centimeters of *N* sodium methylate solution was slowly added to a solution of 2.9 g. of the acetylated acid in 100 cc. of dry chloroform at −3°, causing a white precipitate; after one-half hour an equivalent quantity of 5 *N* sulfuric acid was added and the solution was concentrated *in vacuo* to dryness. The glucosido acid was separated from the sodium sulfate by extraction with hot 95% alcohol, the solvent was distilled off and the residue was recrystallized from 25 cc. of hot water; yield 1.9 g. (96%). A second recrystallization from water gave the monohydrate previously described, m. p. 198–199°. Upon recrystallization from absolute alcohol the substance loses its water of crystallization, separating in glistening elongated prisms melting at 227° (corr.) with marked decomposition. This anhydrous form is only sparingly soluble in alcohol. In pyridine solution it shows $[\alpha]^{20}_{D}$ −45.4° (0.1825 g. in 25 cc. of pyridine in a 2-dm. tube rotated 0.831° to the left).

Anal. Calcd. for $C_{16}H_{20}O_9$: C, 53.91; H, 5.66. Found: C, 53.83; H, 5.72; 59.1 mg. consumed 1.65 cc. of 0.1 *N* alkali; calcd. 1.66.

Summary

A shorter and improved method has been described for the preparation of glucosidoferulic acid, by utilizing β-*d*-glucosidovanillin in the Knoevenagel synthesis for cinnamic acids.

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[2] Hann, THIS JOURNAL, **52**, 5049 (1930).

[3] Fischer and Raske, *Ber.*, **42**, 1474 (1909).