fluxed for four hours, poured into water, the precipitated piperidino derivative was filtered and recrystallized three times from dilute methanol. The compound appeared as lustrous colorless plates; m. p. 124–125°.

Anal. Calcd. for $C_{15}H_{17}ClN_2$: C, 69.09; H, 6.57. Found: C, 69.26; H, 7.41.[11]

The **picrate** crystallized from ethanol as yellow needles, m. p. 161–163°.

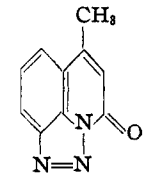
8-Chloro-4-methoxyquinaldine.—A solution of 0.043 g. of sodium in 2 cc. of methanol was added to a solution of 0.4 g. of 4,8-dichloroquinaldine in 30 cc. of methanol, and the mixture was refluxed for twelve hours. The reaction product was precipitated as an almost colorless solid by dilution with water, and purified by fractional sublimation at 90° and 3 mm. The small colorless plates melted at 122–124°.

Anal. Calcd. for $C_{11}H_{10}ClNO$: C, 63.62; H, 4.85. Found: C, 64.30; H, 5.39.

2-Chlorolepidine and Sodium Diethyl Malonate.—A solution of 9 g. of diethyl malonate in 10 cc. of absolute ethanol was refluxed with a solution of 1.3 g. of sodium in 30 cc. of absolute ethanol for five minutes; 10 g. of 2-chlorolepidine in 10 cc. of absolute ethanol was added, and the mixture boiled for fifty hours. The separated sodium chloride was filtered, 7.6 g. of potassium hydroxide was added, and the alkaline mixture refluxed for four hours to complete hydrolysis of the ester. Neutralization with dilute acetic acid precipitated an oil which crystallized on cooling. It was recrystallized from dilute alcohol and appeared as colorless needles, m. p. 49–50°. Analysis showed it to be 2-ethoxylepidine.[12]

Anal. Calcd. for $C_{12}H_{13}NO$: C, 76.97; H, 7.00. Found: C, 76.33; H, 6.91.

2-Oxo-4-methylquinoline-1,8-diazoimide.—The method of preparation of this diazoimide which we had interpreted[2] as 5-hydroxy-3-pyrido-[4,3,2-*de*]-cinnoline, has now been improved. A hot solution of 8-amino-2-hydroxylepidine



in 21 cc. of 10% hydrochloric acid was cooled, and the suspension of the finely divided hydrochloride was diazotized with sodium nitrite solution. The diazoimide separated as a brown amorphous precipitate. It was filtered, suspended in hot water, and the mixture heated on a steam-bath for one hour. The tan solid was filtered; the yield was 1.0 g. (47.5%); m. p. 236–237.5° (dec.).

The diazoimide could be recrystallized from boiling ethanol without decomposition, in contrast to other diazoimides (aryl azides)[13] which decompose under these conditions with the loss of one molecule of nitrogen. However, when our diazoimide was boiled in ethanol solution with "darco" a strong odor of acetaldehyde was noted, and 2-hydroxylepidine crystallized on dilution with water. It was identified by a melting point and a mixture melting point with an authentic sample.

Summary

1. The structure of the lepidine derivatives substituted in position 8 prepared by Johnson and Hamilton has been confirmed. These compounds are identical with those previously interpreted by us as the isomeric 5-substituted derivatives of lepidine.

2. The compound described by us as 5-hydroxy-3-pyrido-[4,3,2-*de*]-cinnoline is therefore 2-oxo-4-methylquinoline-1,8-diazoimide.

3. The 8-chloro derivatives of lepidine reported by Kermack and Muir apparently are 8-chloro derivatives of quinaldine.

(11) The values for hydrogen for our quinaldine derivatives ran high due to weather conditions. The daily test microanalyses of known compounds showed the same tendency.

(12) Knorr, *Ann.*, **236**, 69 (1886).

(13) Sah and Wen-Hou Yin, *Rec. trav. chim.*, **59**, 238 (1940).

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[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF COLUMBIA UNIVERSITY]

The Synthesis of Phenolic Glycosides

BY THOMAS H. BEMBRY AND GARFIELD POWELL[1]

In the course of work in this Laboratory on derivatives of tetrahydrocannabinol, we had occasion to attempt the preparation of the glucoside. The method of Helferich and Schmitz-Hillebrecht,[2] employing zinc chloride or *p*-toluenesulfonic acid as catalyst in a fused mixture of phenol and sugar pentaacetate, was first used. It was not possible in the case of the difficultly accessible phenol, tetrahydrocannabinol, to use the large excess ordinarily employed in this procedure, and poor results were obtained when equimolar quantities of the reactants were used.

On the other hand, we found that tetrahydrocannabinol and a number of other phenols condense smoothly with fully acetylated sugars in benzene solution in the presence of moist phosphorus oxychloride, giving high yields of acetyl-

(1) We are indebted to Smith, Kline and French Laboratories, and one of us (T. H. B.) to the Julius Rosenwald Fund for generous grants to support this work.

(2) Helferich and Schmitz-Hillebrecht, *Ber.*, **66**, 378 (1933).

ated β-glycosides based on the amount of phenol used. We believe that this method gives distinct promise of general usefulness for the preparation of the phenolic glycosides.

The present work describes the application of the method to the preparation of the glycosides of a number of representative phenols, using various fully acetylated sugars. The preparation of the glucoside of tetrahydrocannabinol will be described elsewhere.

Experimental

Pure phosphorus oxychloride appeared to be unsatisfactory as a catalyst, and we used as a standard a reagent made by the addition of 1% by volume of distilled water to a redistilled analytical reagent grade of the material.

Procedure

A solution of phenol (1 mole), the fully acetylated sugar (1 mole), and the phosphorus oxychloride reagent (1/3 mole) in dry benzene was heated under reflux for three hours. After cooling, the reaction mixture was shaken with ice water, and the benzene layer was separated, washed with dilute sodium hydroxide solution, then with water, and then dried over calcium chloride. After evaporation of the solvent under reduced pressure, the residue was crystallized from an appropriate solvent, usually 95% ethanol.

In this way we prepared tetraacetyl-phenol-β-*d*-glucoside[2,3] (44%), m. p. 125–126° (cor.), $[\alpha]^{26}D$ −23° ($CHCl_3$), from phenol and β-pentaacetyl glucose; tetraacetyl-phenol-β-*d*-galactoside[2,4] (44%), m. p. 123–124° (cor.), $[\alpha]^{21}D$ −26° (C_6H_6), from phenol and β-pentaacetylgalactose; triacetylphenol-β-*d*-xyloside[2] (57%), m. p. 147–148° (cor.), $[\alpha]^{22}D$ −52° ($CHCl_3$), from phenol and tetraacetylxylose; tetraacetyl-α-naphthol-β-*d*-glucoside[3,5] (58%), m. p. 178–179° (cor.), $[\alpha]^{22}D$ −72° ($CHCl_3$), from α-naphthol and β-pentaacetyl glucose; and the new tetraacetyl-(*o*-hydroxydiphenyl)-β-*d*-glucoside[6] (35%), long white needles form 95% ethanol, m. p. 155–156° (cor.), $[\alpha]^{22}D$ −56° ($CHCl_3$), from *o*-hydroxydiphenyl and β-pentaacetylglucose.

Anal.[7] Calcd. for $C_{26}H_{28}O_{10}$: C, 62.40; H, 5.60. Found: C, 62.56; H, 5.59.

The latter derivative was deacetylated by the method of Zemplén[8] to give *o*-diphenyl-β-*d*-glucoside (90%) as shining needles from water, m. p. 76–77° (cor.), $[\alpha]^{25}D$ −42° (EtOH).

Anal.[7] Calcd. for $C_{18}H_{20}O_6$: C, 65.06; H, 6.02. Found: C, 64.81; H, 6.07.

For the preparation of tetraacetyl-phenol-β-*d*-fructoside,[2] m. p. 129–130° (cor.), $[\alpha]^{22}D$ −147° ($CHCl_3$), it was found that the reaction mixture darkened less and a somewhat better yield (33%) was obtained if (1) the benzene solution of the reactants was allowed to stand at room temperature for twenty-four hours, rather than being heated under reflux for three hours as in the general procedure, and (2) the benzene extract was washed with bicarbonate rather than sodium hydroxide.

As a further check on the identity of the known glycosides, quantitative carbon–hydrogen determinations were run[7] on all samples; satisfactory agreement with theory was obtained in each case.

Summary

A method for the condensation of phenols with the fully acetylated sugars in the presence of phosphorus oxychloride in benzene solution to form glycosides of phenols has been described. The physical constants of *o*-diphenyl-β-*d*-glucoside are reported.

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(3) Fisher and Mechel, *Ber.*, **49**, 2813 (1916); Carter, *ibid.*, **63**, 586 (1930); Montgomery, Richtmyer and Hudson, THIS JOURNAL, **64**, 690 (1942).

(4) Fisher and Armstrong, *Ber.*, **35**, 833 (1902).

(5) Drouin, *Bull. soc. chim.*, **13**, 5 (1895).

(6) These substances were assigned the β-configuration on the basis of the analogy with the other cases, in which the configuration was established by comparison with authentic samples prepared by other methods.

(7) We are indebted to Mr. Saul Gottlieb for carrying out these analyses.

(8) Zemplén, *Ber.*, **62**, 1613 (1929).