Experimental

Each of the substances gave ultimate analyses[3] for carbon and hydrogen that were within the usually accepted limits, indicating the absence of significant amounts of extraneous material or moisture. As a further check, each was analyzed[4] for moisture with the Karl Fischer reagent and showed a maximum moisture content of 0.01%. The active hydrogen determinations were made[3] using *methyl Grignard* reagent in the customary manner with 7–8 mg. samples.

(3) By Drs. G. Weiler and F. B. Strauss, Oxford, England.

(4) By Miss Linda Einstein of these laboratories.

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The Synthesis of Glucofuranosides

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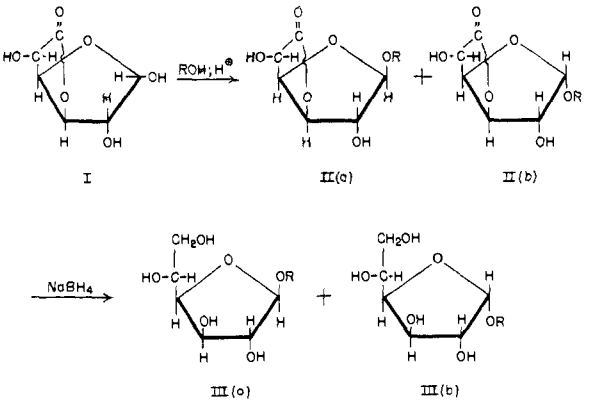
A short and convenient synthesis of glucofuranosides of general formula III was needed in these laboratories. A survey of the recorded methods indicated that none was applicable in a general way to the preparation of substantial quantities of the desired furanosides. For example, the original Fischer procedure for glycoside formation usually yields an inseparable sirupy mixture of isomeric glycosides from which a crystalline glycofuranoside has been separated only in rare instances.[1] Haworth and co-workers have developed another method involving the use of carbonates and acetonides as protecting groups but the procedure is long and over-all yields are quite low.[2] More recently it has been shown[1b] that the selective removal of thioalkyl groups from sugar mercaptals by the action of mercuric salts may give rise to glycofuranosides but yields are often poor and the sirupy mixture obtained in the case of the ethyl D-glucofuranosides (IIIa and b, R = C_2H_5) could not be crystallized, although both epimers are known to be crystalline.[2a]

Since the principal difficulty in all of these synthetic schemes rests in the formation of a furanose ring in a sugar that exists preferentially in a pyranose structure, it seemed probable to us that if a readily available intermediate containing a *preformed* furanose ring could be found, this difficulty might be circumvented. Such an intermediate is D-glucuronolactone (I), which has recently become commercially available in this country.[3] The furanose nature of this compound has been adequately demonstrated[4] and we have found it to be most useful for the preparation of furanosides.

Recent work of Osman, *et al.*,[5] has shown that D-glucuronolactone (I) gives rise to two epimeric glycosides in the presence of methanol when the reaction is catalyzed by a cationic exchange resin. A similar result has been found in these laboratories



when the more usual methanolic hydrogen chloride procedure is employed. The mixture consisted principally of the β-form (IIa, R = CH_3), but a small amount of the α-isomer (IIb, R = CH_3) could be recovered from the mother liquor by mechanical separation of the two crystalline products. These glucofururonosides were reduced by sodium borohydride to the corresponding glucofuranosides (IIIa and b, R = CH_3) according to the procedure of Wolfrom and Wood.[6a] The properties of the furanosides were in excellent agreement with those recorded in the literature.

The use of ethanol in the scheme above gave rise to a sirupy mixture of ethyl D-glucofururonosides (IIa and b, R = C_2H_5) which also contained principally the β-isomer as indicated by the reduction to crystalline ethyl β-D-glucofuranoside (IIIa, R = C_2H_5). None of the α-isomer could be isolated from either reaction.

We are currently preparing a series of glucofuranosides by this convenient two-step procedure and the hydrolysis and mutarotation studies will form the basis for a future communication.

Acknowledgment.—We wish to thank the Corn Products Refining Company, New York, for providing the D-glucuronolactone used in this work.

Experimental[7]

Methyl α- and β-D-Glucofururonoside (IIa and b, R = CH_3).—A mixture of 61.3 g. (0.35 mole) of D-glucuronolactone in 450 ml. of anhydrous 0.5% methanolic hydrogen chloride was allowed to stand with occasional shaking at room temperature for three days. The homogeneous solution was neutralized with silver carbonate, the silver chloride filtered off and the filtrate concentrated under reduced pressure to a clear, colorless sirup. Trituration of this residue with ether containing a small amount of ethyl acetate gave 62.5 g. of crude glycoside, m.p. 120–138°. Recrystallization from ethyl acetate gave 37.0 g. (56%) of methyl β-D-glucofururonoside as stout prisms, m.p. 138–139°, $[\alpha]^{20}D$ −58° (*c* 2.8, water), λ_{max}^{nujol} 5.61 μ; lit.[6] $[\alpha]^{23}D$ −59° (*c* 1.0, water).

Anal. Calcd. for $C_7H_{10}O_6$: C, 44.21; H, 5.29. Found: C, 44.33; H, 5.29.

The filtrate was concentrated to a sirup which was taken up and decolorized in absolute ethanol and 6.0 g. of a second

(1) (a) E. Fischer, *Ber.*, **26**, 2400 (1893); **47**, 1980 (1914); (b) J. W. Green and E. Pacsu, THIS JOURNAL, **59**, 1205 (1937).

(2) (a) W. N. Haworth and C. R. Porter, *J. Chem. Soc.*, 2796 (1929); 649 (1930); (b) W. N. Haworth, C. R. Porter and A. C. Waine, *ibid.*, 2254 (1932).

(3) D-Glucuronolactone is a product of the Chemical Division, Corn Products Sales Co., 17 Battery Place, New York 4, N. Y.

(4) F. Smith, *J. Chem. Soc.*, 584 (1944).

(5) E. M. Osman, K. C. Hobbs and W. E. Walston, THIS JOURNAL, **73**, 2726 (1951).

(6) (a) M. L. Wolfrom and H. B. Wood, *ibid.*, **73**, 2933 (1951). (b) After this paper had been submitted, R. E. Reeves, THIS JOURNAL, **76**, 934 (1954), reported a similar reduction of 2,5-dimethyl-α-D-glucurone to the corresponding furanoside using lithium aluminum hydride.

(7) Melting points were obtained on a Nalge-Axelrod melting block and are uncorrected. Analyses are by the Du-Good Labs., St. Louis, Mo.

crop, m.p. 131–140°, was collected. Recrystallized from ethyl acetate this material formed a mixture of the α- and β-isomers as well-defined crystalline products which were separated mechanically. The long, hair-like needles of the α-isomer obtained in this manner were crystallized from ethyl acetate to give 0.8 g. of methyl α-D-glucofururonoside, m.p. 146–148°, $[\alpha]^{25}D$ +148° (*c* 0.3, water), λ_{max}^{nujol} 5.70 μ; lit.[6] m.p. 148°, $[\alpha]^{23}D$ +149° (*c* 1.0, water).

Anal. Calcd. for $C_7H_{10}O_6$: C, 44.21; H, 5.29. Found: C, 44.20; H, 5.26.

An additional 4.0 g. of the β-isomer, m.p. 137–139°, was obtained in this operation, raising the total yield of purified product to 62%.

Ethyl β-D-Glucofururonoside (IIa, R = C_2H_5).—Treatment of 30.0 g. (0.17 mole) of D-glucuronolactone with anhydrous ethanolic hydrogen chloride as described above gave 30.0 g. (89%) of crude, sirupy glycoside, $[\alpha]^{25}D$ −20° (*c* 1.5, water), λ_{max} 5.62 μ. All attempts to crystallize this material failed.

Anal. Calcd. for $C_8H_{12}O_6$: C, 47.06; H, 5.93. Found: C, 46.86; H, 6.04.

The *p*-nitrobenzoate formed small warts from ethanol, m.p. 201–202°, $[\alpha]^{25}D$ −20° (*c* 0.2, ethanol).

Anal. Calcd. for $C_{22}H_{18}O_{12}N_2$: C, 52.60; H, 3.62. Found: C, 52.86; H, 3.60.

Methyl β-D-Glucofuranoside (IIIa, R = CH_3).—To a stirred solution of 2.71 g. (0.074 mole) of sodium borohydride in 40 ml. of water was added over ten minutes a solution of 12.6 g. (0.0664 mole) of methyl β-D-glucofururonoside in 40 ml. of water. A maximum temperature of 50° was obtained during the addition. The reaction mixture was allowed to stand for ten minutes at 40–45° when the excess reducing agent was quenched with a few drops of dilute sulfuric acid. The solution was then diluted to 200 ml. with distilled water and passed successively through 200 g. of Amberlite IR-120 ion exchange resin (strong cation type) and 200 g. of IR4B resin (weak anion type).[8] The percolate was concentrated under reduced pressure at room temperature to 9.1 g. (71%) of a pale yellow sirup, $[\alpha]^{23}D$ −77° (*c* 3.0, water); lit.[2b] $[\alpha]^{23}D$ −77° (water).

The tetracarbanilate, prepared according to Wolfrom's procedure[9] formed felt-like needles from ethanol, m.p. 218–219°, $[\alpha]^{20}D$ +14° (*c* 2.5, acetone); lit.[9] m.p. 215–217°, $[\alpha]^{26}D$ +7.6° (*c* 1.2, acetone).

Anal. Calcd. for $C_{35}H_{34}O_{10}N_4$: C, 62.66; H, 5.11. Found: C, 62.96; H, 5.23.

Methyl α-D-Glucofuranoside (IIIb, R = CH_3).—Reduction of 0.7 g. (3.7 millimoles) of methyl α-D-glucofururonoside as described above gave 0.32 g. of a yellow sirup which crystallized from ethyl acetate yielding 0.24 g. (34%) of methyl α-D-glucofuranoside as rosettes, m.p. 60–62°, $[\alpha]^{25}D$ +110° (*c* 0.5, water); lit.[2a] m.p. 62–63°, $[\alpha]^{20}D$ +118° (*c* 4.5, water)

Ethyl β-D-Glucofuranoside (IIIa, R = C_2H_5).—Reduction of 14.07 g. (0.069 mole) of sirupy ethyl β-D-glucofururonoside as described above for the methyl analog gave 7.3 g. of a sirup which crystallized after drying one week over phosphorus pentoxide. The crystals so obtained were extremely hygroscopic and crystallized with difficulty from ethyl acetate to give the furanoside as prisms, m.p. 61–63°, $[\alpha]^{25}D$ −76° (*c* 1.0, water).

(8) These resins were kindly supplied by Resinous Products Division, Rohm and Haas Co., Philadelphia 5, Pa.

(9) M. L. Wolfrom, D. I. Weisblat and A. R. Hanze, THIS JOURNAL, **66**, 2065 (1944).

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The Synthesis of Ethyl Adipamate and 2-Keto-6,6-dihydroperfluorohexamethylenimine

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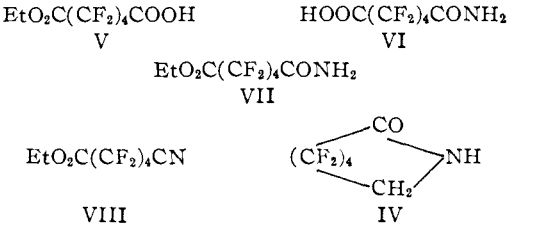
A synthesis of ethyl adipamate (I) could not be found in the literature and since the compound was of interest for comparison with its fluorinated analog, ethyl perfluoroadipamate (VII), methods for its synthesis were investigated. The best method proved to be the reaction of 5-carbethoxyvaleryl chloride (II) in dioxane solution with gaseous ammonia. Under these conditions the acid chloride function of II was preferentially attacked to yield I in 75% yield. However, when the ammonolysis was carried out in aqueous solution, I and adipamide were isolated in approximately equal amounts. This is in conformity with the findings of Day, Gordon and Miller concerning the effect of solvents on the ammonolysis of esters.[1]

Adipamic acid (III) also was used as a starting material for the preparation of I but with less success. Direct esterification of III with ethanol using an acid catalyst and azeotropic distillation of water produced I in only 36% yield. The silver salt of III reacted with ethyl iodide to form I in low yield.

A fluorinated derivative of ε-caprolactam, 2-keto-6,6-dihydroperfluorohexamethylenimine (IV) was prepared for the purpose of studying its polymerization. The compound was synthesized from ethyl perfluoroadipate through the intermediates V, VI, VII and VIII.



Ethyl perfluoroadipate[2] was converted to ethyl hydrogen perfluoroadipate (V) by heating it with perfluoroadipic acid and separating the mixture by fractional distillation. Perfluoroadipamic acid (VI) was obtained from V by ammonolysis. The esterification of VI was accomplished using diazoethane and the ethyl perfluoroadipamate (VII) formed was dehydrated by heating with phosphorus pentoxide. The ethyl 5-cyanoperfluorovalerate thus obtained was catalytically hydrogenated to produce IV.

Ethyl perfluoroadipamate was also prepared in low yield from silver perfluoroadipamate and ethyl iodide. An attempt to obtain VII by the ammonolysis of 5-carbethoxyperfluorovaleryl chloride produced only perfluoroadipamide. This is in contrast to our successful synthesis of ethyl adipamate in this manner from 5-carbethoxyvaleryl chloride. The failure to obtain a preferential reaction of ammonia with the acid chloride function in the case of the fluorinated compound demonstrates the greater reactivity of fluorinated esters.

Attempts to polymerize IV by using sodium or water as catalysts were unsuccessful.

Experimental

5-Carbethoxyvaleryl Chloride (II).—Ethyl hydrogen adipate[3] (168 g., 0.96 mole) and 114 g. (0.6 mole) of thionyl

(1) A. R. Day, M. Gordon and J. G. Miller, THIS JOURNAL, **71**, 1245 (1949).

(2) E. T. McBee, P. A. Wiseman and G. B. Bachman, *Ind. Eng. Chem.*, **39**, 415 (1947).

(3) G. T. Morgan and E. Walton, *J. Chem. Soc.*, 91 (1933).