of IIIb and IIIe, an initial heating to reflux for 1 or 2 min. was desirable. Compounds IIIb, IIIc, and IIIe formed a heavy precipitate within 3–4 hr., which prevented further stirring. Finally, the reaction mixture was chilled in ice and the product collected on a filter, washed with water, and dried; occasionally more material could be crystallized from the mother liquor. See Table III for further data.

Method B.—A solution of 2,4-diamino-6-*p*-fluorostyryltriazine (XVIIIb) (0.23 g., 1.0 mmole) in 25 ml. of 2-methoxyethanol was stirred with 0.10 g. of 5% palladium-on-carbon under hydrogen at 1 atm. for 35 min.; uptake ceased after 20 min. The catalyst was removed by filtration through a pad of Celite and the filtrate was concentrated *in vacuo* to 8 ml. Dilution with water formed a white precipitate, which was collected on a filter, washed with water (two 5-ml. portions), and dried *in vacuo*. See Table III for further data (and results with XVIIIa→IIIa). Loss of ultraviolet absorption at 292 mμ characteristic of XVIIIb and infrared absorption at 10.19 μ (—C=C=C—) verified complete saturation of the double bond (XVIIIa lost bands at 297 mμ and 10.18 μ). Reduction of 2.5 g. of XVIIIb as a suspension in 2-methoxyethanol (200 ml.) formed a solution of the product, but pure IIIb could not be isolated from it.

2,4-Diamino-6-styryl-*s*-triazines (XVIII).—An intimate mixture of 0.04 mole of 2,4-diamino-6-methyltriazine (XVI) and 0.04 mole of a halobenzaldehyde (XVII) was suspended in 7.5 ml. of concd. sulfuric acid and heated on the steam bath. After 15 min., an additional 1.5 ml. of sulfuric acid was added, and the suspension was stirred briefly, then heated again for 45 min. The mixture was cooled to room temperature and 20 ml. of water was added cautiously, with ice cooling. The yellow product, a sulfate salt, was collected on a filter. This solid, pulverized and suspended in 20 ml. of water, was neutralized by treatment with saturated aqueous sodium bicarbonate while stirring until a *p*H of 7 was maintained. The free base was a white solid, removed by filtration and dried *in vacuo*. See further data in Table IV. Melting points are characteristically broad and somewhat variable and should not be used as sole criteria of purity.

Paper Chromatography.—All of the pyrimidines and triazines prepared (II, XIV, XV, III, XVIII) were, when purified, homogeneous by the descending paper chromatographic technique and, except for XIV, distinguishable from the immediate precursors in Schemes I and II. The following solvent systems were effective with Whatman No. 1 paper: A, 1-butanol–acetic acid–water (4:1:5); B, isopropyl alcohol–2 *M* hydrochloric acid (65:35); C, 2-methoxyethanol–water (9:1); D, benzene–methanol–water (2:6:1); E, water–saturated 1-butanol. Systems A, B, C, and E were used with pyrimidine derivatives, systems A, B, and D with the triazines. Spots were detected by visual examination under ultraviolet light.

Acknowledgment.—The authors are indebted to Peter Lim for infrared interpretations, to his group for paper chromatography and spectrophotometric determinations, and to Mr. O. P. Crews and his group for large-scale preparation of intermediates.

Potential Anticancer Agents.[1] LXXIII. Synthesis of Derivatives of 1-Deoxypsicose

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The synthesis of 3,4,5,6-tetra-*O*-acetyl-1-deoxy-D-psicose (XII) via a condensation between 2,3,4,5-tetra-*O*-acetyl-D-ribonoyl chloride and dibenzyl malonate is described, together with its subsequent conversion to a series of ethyl β-thiopsicofuranosides. Certain analogies are made between derivatives of 1-deoxy-D-psicose and the corresponding derivatives of 2-deoxy-D-ribose.

A previous paper[3] from this laboratory described some model studies which were concerned with the synthesis of nucleosides derived from ketose sugars. It was demonstrated that D-fructose (IIa) could be readily transformed into either a furanose nucleoside (I) or pyranose nucleoside (III). The report by Schroeder and Hoeksema[4] of the successful synthesis of the antibiotic 9-β-D-psicofuranosyl adenine (VIa) (psicofuranine) from the blocked D-psicose (Va) suggests the generality of the nucleoside condensation with ketose sugars.

This convincing demonstration[3,4] of the ability of the ketose sugars to undergo nucleoside condensations, together with the report[4] that psicofuranine (VIa) showed marked antibacterial and antitumor activity, made it of interest to prepare some other ketose nucleosides as potential anticancer agents. The nucleoside chosen for study in the present work was 1′-deoxypsicofuranine (VIb).

The synthesis of a nucleoside such as VIb would be interesting from both the chemical and biological aspects. The presence of a methyl group vicinal to the potential reducing carbon of the sugar moiety may give a nucleoside such as VIb a chemical reactivity more closely related to that of the 2′-deoxynucleosides than to that of the ribonucleosides. If this should be true, this structural re-

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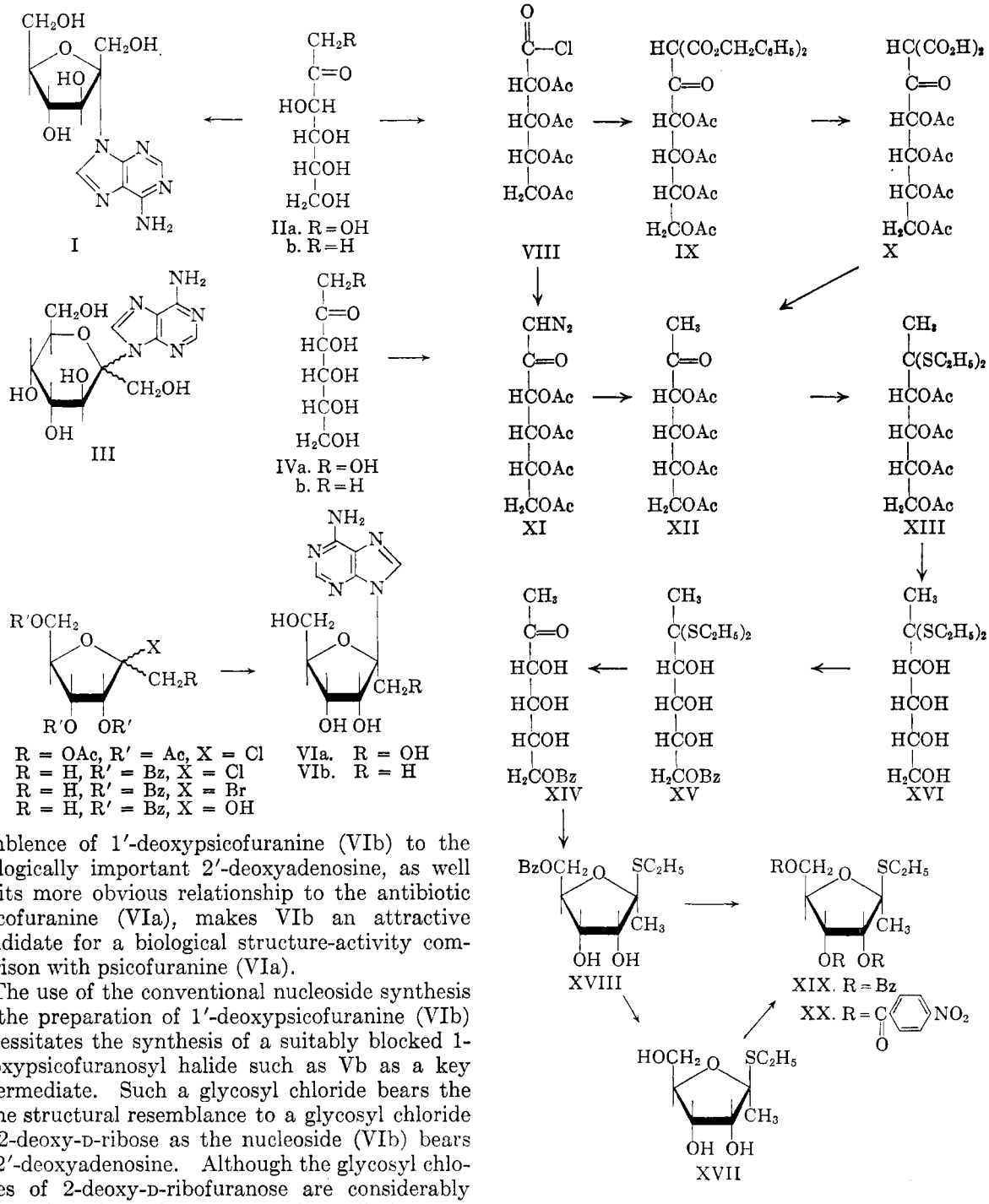
(3) E. J. Reist, P. A. Hart, and B. R. Baker, *J. Org. Chem.*, **24**, 1640 (1959).

(4) W. Schroeder and W. Hoeksema, *J. Am. Chem. Soc.*, **81**, 1767 (1959).



semblence of 1′-deoxypsicofuranine (VIb) to the biologically important 2′-deoxyadenosine, as well as its more obvious relationship to the antibiotic psicofuranine (VIa), makes VIb an attractive candidate for a biological structure-activity comparison with psicofuranine (VIa).

The use of the conventional nucleoside synthesis in the preparation of 1′-deoxypsicofuranine (VIb) necessitates the synthesis of a suitably blocked 1-deoxypsicofuranosyl halide such as Vb as a key intermediate. Such a glycosyl chloride bears the same structural resemblance to a glycosyl chloride of 2-deoxy-D-ribose as the nucleoside (VIb) bears to 2′-deoxyadenosine. Although the glycosyl chlorides of 2-deoxy-D-ribofuranose are considerably less stable than the corresponding ribofuranose glycosyl chlorides,[5] the syntheses of a number of them that are sufficiently stable to withstand the rigors of a nucleoside condensation have been reported[6] recently. It could be hoped that a glycosyl chloride such as Vb would be equally able to undergo a successful nucleoside condensation. The course of a condensation with Vb should be sterically controlled by the neighboring benzoate on C-3 to give predominantly the desired β-isomer (VIb).[7]

Little has been reported concerning the synthesis and chemistry of 1-deoxyketose sugars. Wolfrom and his co-workers have prepared a number of 1-

(5) J. J. Fox and I. Wempen in "Advances in Carbohydrate Chemistry," Vol. XIV, Academic Press, Inc., New York, N. Y., 1959, p. 283.

(6) (a) M. Hoffer, R. Duschinsky, J. J. Fox, and N. Yung, *J. Am. Chem. Soc.*, **81**, 4112 (1959); (b) R. K. Ness and H. G. Fletcher, Jr., *J. Am. Chem. Soc.*, **81**, 4752 (1959).

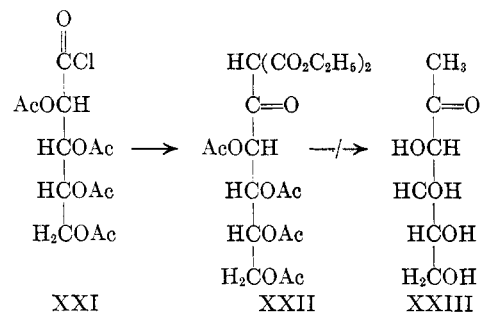
(7) B. R. Baker, Ciba Foundation Sympsoium on "The Chemistry and Biology of Purines," J. and A. Churchill Ltd., London, 1957, pp. 120–130.

(8) M. L. Wolfrom, A. Thompson, and E. F. Evans, *J. Am. Chem. Soc.*, **67**, 1793 (1945).

(9) M. L. Wolfrom, D. I. Weisblat, W. H. Zophy, and S. W. Waisbrot, *J. Am. Chem. Soc.*, **63**, 201 (1941).

deoxyketose sugars, among them 1-deoxy-D-psicose[8] (IVb) and 1-deoxy-D-fructose (IIb).[9] The synthesis of 1-deoxy-D-psicose (IVb) was accomplished by the reaction of diazomethane with 2,3,4,-5-tetra-*O*-acetyl ribonoyl chloride (VIII), followed by reduction of the resulting diazo ketone (XI) with hydrogen iodide to give the tetra-*O*-acetyl-1-deoxy-D-psicose (XII) in 56% yield from the acid chloride (VIII). The reaction of diazomethane with 2,3,4,5-tetra-*O*-acetyl-D-arabinose gave 3,4,5,6-tetra-*O*-acetyl-1-deoxy-D-fructose[9] in 62% yield. The large-scale preparation of XII by a method involving the use of diazomethane, however, was unattractive.

An alternative route to tetra-*O*-acetyl-1-deoxy-D-psicose (XII) that was adaptable to large-scale synthesis involved initially the condensation of 2,3,4,5-tetra-*O*-acetyl-D-ribonoyl chloride (VIII) with dibenzyl malonate[10] to afford the crude diester (IX). Without further purification, compound IX was hydrogenolyzed to the malonic acid (X), then directly decarboxylated[11] to give a 30% over-all



XXI XXII XXIII

yield (from VIII) of tetra-*O*-acetyl-1-deoxy-D-psicose (XII).

Treatment of the tetra-*O*-acetyl-1-deoxy-D-psicose (XII) with ethyl mercaptan and zinc chloride gave a 97% yield of 2,3,4,5-tetra-*O*-acetyl-1-deoxy-D-psicose diethyl mercaptal (XIII) as an analytically pure sirup. Deacetylation of the mercaptal tetraacetate (XIII) with methanolic sodium methoxide yielded 82% of 1-deoxy-D-psicose diethyl mercaptal (XVI) as a low-melting crystalline solid. Selective benzoylation of the crystalline diethyl mercaptal (XVI) afforded 97% of a sirup that analyzed fairly well for a monobenzoate of 1-deoxy-D-psicose diethyl mercaptal and is assumed to contain 6-benzoate (XV).[13]

Treatment of the mercaptal (XV) with mercuric chloride and cadmium carbonate in water gave 6-*O*-benzoyl-1-deoxy-D-psicose (XIV) as a crystalline solid, m.p. 96–98°, in 24% yield. It is interesting to note that the ethylthio groups of XV could be easily removed by short treatment with warm 50% aqueous acetic acid to give a 24% yield of a crystalline product, m.p. 86–87°, that also analyzed for a monobenzoate of 1-deoxy-D-psicose; its melting point and infrared spectrum, however, were distinctly different from the 6-*O*-benzoyl-1-deoxy-D-psicose obtained from the treatment of the mercaptal (XV) with mercuric chloride. A small amount of what appears to be a third crystalline form of the monobenzoate (XIV) was isolated from the hydrolysis of XV with aqueous acetic acid, but sufficient material for complete characterization could not be obtained.

The hydrolysis of the mercaptal grouping of XV by 50% aqueous acetic acid is in marked contrast to the behavior of aldose mercaptals with acetic acid. In a control experiment, 5-*O*-benzoyl-D-arabinose diethyl mercaptal[13b] was recovered unchanged when treated with 50% aqueous acetic acid in the manner described for XV. Zinner and his co-workers[14] commented on the great ease with which the mercaptal grouping of fully benzoylated 2-deoxy-D-ribose diethyl mercaptal could be removed with mercuric chloride under neutral conditions, compared with the corresponding fully benzoylated D-ribose diethyl mercaptal. They attributed this greater reactivity of the mercaptal grouping of 2-deoxy-D-ribose to the presence of the adjacent methylene group. Such an argument should be equally valid for the 1-deoxy-D-psicose mercaptal (XV).

Treatment of the crystalline 6-*O*-benzoyl-1-deoxy-D-psicose (XIV), m.p. 86–87°, with ethyl mercaptan and zinc chloride gave a 45% yield of crystalline ethyl 6-*O*-benzoyl-1-deoxy-β-D-thiopsicofuranoside (XVIII), plus an additional 35% yield of the α-anomer of XVIII as a sirup.[15] Treatment of the crystalline 6-benzoate (XIV), m.p. 96–98°, with ethyl mercaptan and zinc chloride gave a 32% yield of the same crystalline thioglycoside (XVIII). The formation of the same thioglycoside from both forms of the monobenzoate ketose (XIV) shows that both had the benzoate on the same position—

(10) B. R. Baker, R. E. Schaub, M. V. Querry, and J. H. Williams *J. Org. Chem.*, **17**, 77 (1952).

(11) It should be noted in passing that the use of diethyl malonate was unsuccessful as a means of synthesizing the deoxyketoses. The condensation of 2,3,4,5-tetra-*O*-acetyl-D-arabonoyl chloride[12] (XXI) with the magnesio salt of diethyl malonate in benzene gave a 22% yield of crystalline diethyl α-(2,3,4,5-tetra-*O*-acetyl-D-arabinoyl)-malonate (XXII). Efforts to remove the ethyl ester in order to generate the methyl ketone (XXIII) were fruitless and extensive decomposition always occurred. This sensitivity towards saponification is in agreement with the base sensitivity of the ketose acetates mentioned by Wolfrom and co-workers.[8]

(12) M. L. Wolfrom, S. W. Waisbrot, and R. L. Brown, *J. Am. Chem. Soc.*, **64**, 1701 (1942).

(13) There are numerous references to the selective acylation of the terminal hydroxyl of sugar mercaptals—*e.g.*, (a) H. Zinner, K. Wessely, W. Bock, K. Rieckhoff, F. Strandt, and W. Nimmich, *Ber.*, **90**, 500 (1957); (b) E. J. Reist, P. A. Hart, L. Goodman, and B. R. Baker, *J. Am. Chem. Soc.*, **81**, 5176 (1959).

(14) H. Zinner, H. Nimz, and H. Venner, *Ber.*, **91**, 148 (1958).

(15) For convenience, the β-configuration is assigned to the crystalline anomer of XVIII on the basis of the high negative rotation compared with the rotation of the sirupy residue. Such an assignment is by no means unequivocal in the light of certain exceptions to Hudson's rules of isorotation pointed out by Lemieux and Hoffer.[16] Similarly, the thioglycoside recovered from the mother liquors of the crystallization is assigned the α-configuration. These mother liquors may not be anomerically pure.

(16) R. U. Lemieux and M. Hoffer, *Can. J. Chem.*, **39**, 110 (1961).

most likely at C-6. Regeneration of the 6-benzoate (XIV) from the thioglycoside (XVIII) with 50% aqueous acetic acid gave a 75% recovery of the benzoate with m.p. 86–87°. Similarily, treatment of the thioglycoside (XVIII) with mercuric chloride and cadmium carbonate gave the benzoate (XIV) with m.p. 96–98°. It is interesting to speculate that the two forms are anomeric to one another or that one is an open-chain ketose sugar while the other is a furanose anomer, and that the form obtained is dependent on the *p*H at which the desulfurization is run. The third monobenzoate isolated in trace amounts could conceivably be the third member of the trio of possible 6-*O*-benzoyl-1-deoxy-D-psicose structures—*i.e.*, two furanoses and one open-chain ketose.

Benzoylation of the thioglycoside (XVIII) with benzoyl chloride gave a quantitative yield of ethyl 3,4,6-tri-*O*-benzoyl-1-deoxy-β-D-thiopsicofuranoside (XIX) as an analytically pure sirup. There are several reports in the literature which describe the direct conversion of a thioglycoside to a glycosyl bromide by the reaction of the thioglycoside with bromine in ether.[17] When this reaction was attempted with the thioglycoside tribenzoate (XIX) in order to prepare the glycosyl bromide (Vc), extensive decomposition resulted and the infrared spectrum of the product showed the presence of considerable quantities of benzoic acid. The reaction of chlorine in ether with the thioglycoside was investigated in the hope that the resulting glycosyl chloride (Vb) would be sufficiently more stable than the glycosyl bromide (Vc) to permit its isolation and subsequent reaction with chloromercuri-6-benzamidopurine. Again considerable quantities of benzoic acid were liberated and the product did not contain any active chlorine. Acetolysis[18] of the thioglycoside (XIX) was unsuccessful and water-soluble products resulted. Treatment of the thioglycoside (XIX) with mercuric chloride and cadmium carbonate gave a sulfur-free oil that had a fair analysis for the tribenzoate (Vd). Treatment of this oil (Vd) with hydrogen chloride in dichloromethane[19] again resulted in extensive decomposition and liberation of benzoic acid.

The successful use of the *p*-nitrobenzoyl blocking group to prepare a reasonably stable glycosyl chloride of 2-deoxyribose[6b] suggested a similar modification for the 1-deoxy-D-psicofuranose series. Debenzoylation of the thioglycoside 6-benzoate (XVIII) with methanolic ammonia gave the crystalline ethyl 1-deoxy-β-D-thiopsicofuranoside (XVII). The unblocked thioglycoside (XVII) showed an uptake of [illegible] of neutral periodate; however, essentially no formic acid was liberated. The absence of formic acid is added confirmation that the thioglycoside (XVII) possesses a furanose ring. The extra mole of periodate uptake for XVII is probably due to the presence of the sulfur atom of the thioglycoside (XVII).[20] An attempt was made to desulfurize the thioglycoside (XVII) with Raney nickel to give a hydroxytetrahydrofuran, a compound whose periodate oxidation would not be complicated by the presence of a sulfur atom. The product obtained from the desulfurization, although free of sulfur, gave a very poor analysis for the desired tetrahydrofuran and gave a very strong reducing sugar test with Benedict's reagent.

Treatment of the thioglycoside (XVII) with *p*-nitrobenzoyl chloride gave ethyl 1-deoxy-3,4,6-tri-*O*-(*p*-nitrobenzoyl)-β-D-thiopsicofuranoside (XX) as a crystalline solid in 82% yield. Reaction of the crystalline thioglycoside (XX) with chlorine in ether gave a sulfur-free precipitate which contained very little active chlorine and which failed to give any demonstrable amounts of nucleoside when coupled with chloromercuri-6-benzamidopurine. Other attempts to prepare a chlorosugar tri-*p*-nitrobenzoate were equally abortive and gave varying amounts of *p*-nitrobenzoic acid. At no time was there any appreciable amount of active chlorine, indicative of a chlorosugar.

Ness[21] reported that pure crystalline 2-deoxy-3,5-*O*-*p*-nitrobenzoyl-D-ribosyl chloride could be stored at room temperature for some weeks. However, when heated at its melting point, it rapidly lost the elements of hydrogen chloride and *p*-nitrobenzoic acid to give a furan derivative. The formation of some *p*-chlorobenzoic acid has been observed[22] during the preparation of 2-deoxy-3,5-di-*O*-*p*-chlorobenzoyl ribosyl chloride from the methyl glycoside. Thus, in the deoxyribose series there is ample precedent for the elimination of blocking groups with, in at least one case, concomitant formation of an olefin.

The complete failure to isolate a glycosyl chloride of 1-deoxy-D-psicofuranose is somewhat surprising and would suggest that the sensitivity of the 1-deoxyketose glycosyl chlorides may be even greater than that of the analogous 2-deoxyaldofuranose sugars. Since the stability of deoxyribofuranosyl halides varies so drastically with changes in the blocking groups, it is possible that certain blocking groups may lend sufficient stability to deoxypsicofuranosyl halides to permit their useful application to nucleoside syntheses.

(17) (a) F. Weygand, H. Ziemann, and H. J. Bestmann, *Ber.*, **91**, 2534 (1958); (b) H. Zinner, A. Koine, and H. Nimz, *Ber.*, **93**, 2705 (1960).

(18) (a) B. R. Baker, J. P. Joseph, and R. E. Schaub, *J. Am. Chem. Soc.*, **77**, 5905 (1955); (b) N. K. Richtmeyer and C. S. Hudson, *J. Am. Chem. Soc.*, **63**, 1727 (1941).

(19) R. K. Ness and H. G. Fletcher, Jr., *J. Am. Chem. Soc.*, **78**, 4710 (1956).

(20) (a) A. Wickstrom and J. K. Wold, *Acta Chem. Scand.*, **14**, 1419 (1960); (b) L. Hough and M. I. Taha, *J. Chem. Soc.*, 3994 (1957).

(21) R. K. Ness, D. L. MacDonald, and H. G. Fletcher, Jr., *J. Org. Chem.*, **26**, 2895 (1961).

(22) E. M. Acton, R. H. Iwamoto, and L. Goodman, unpublished data.

Experimental[23]

2,3,4,5-Tetra-*O*-acetyl-1-deoxy-D-psicose (XII).—To a stirred, chilled (0°) suspension of 0.136 g. (5.68 mmoles) of sodium hydride in 6 ml. of dry, freshly distilled tetrahydrofuran was added 1.65 g. (5.8 mmoles) of dibenzyl malonate[10] at a rate such that the temperature in the flask never exceeded 25°. After the addition was complete, the resulting solution of the sodio salt of dibenzyl malonate was cooled to 5° and 2.0 g. (5.68 mmoles) of 2,3,4,5-tetra-*O*-acetyl-D-ribonoyl chloride (VIII)[8] was added. The mixture was stirred at 0–5° for 15 min., then at room temperature for 2 hr.

The reaction mixture was poured into 50 ml. of ice water and the aqueous mixture was extracted with two 30-ml. portions of chloroform. The chloroform extracts were washed with 25 ml. of saturated aqueous sodium bicarbonate and 25 ml. of water, then dried over magnesium sulfate, and evaporated to dryness *in vacuo* to give 3.44 g. of crude dibenzyl α-(2,3,4,5-tetra-*O*-acetyl-D-ribonoyl)malonate (IX) as a viscous sirup; $\lambda_{max(\mu)}^{film}$ 5.68 (C=O).

The crude malonate (IX) was dissolved in a mixture of 4 ml. of ethyl acetate and 4 ml. of acetic acid and treated at room temperature with hydrogen in a Parr apparatus at 17 lb. pressure with 0.58 g. of 5% palladium-on-charcoal. After hydrogen uptake had ceased (1.5–2 hr.), the catalyst was removed by filtration and the solution of α-(2,3,4,5-tetra-*O*-acetyl-D-ribonoyl)malonic acid (X) was decarboxylated by being heated at reflux for 1 hr., by which time carbon dioxide evolution had ceased. The solution was evaporated to dryness *in vacuo* to give 0.85 g. (43%) of crude 2,3,4,5-tetra-*O*-acetyl-1-deoxy-D-psicose (XII) as a white solid. Recrystallization from diethyl ether gave 0.51 g. (26%) of white crystals, m.p. 69–70°. The analytical sample had m.p. 69–71°; $[\alpha]^{32}D$ −44° (1% in chloroform); $\lambda_{max(\mu)}^{Nujol}$ 5.69 (C=O).

Anal. Calcd. for $C_{14}H_{20}O_9$: C, 50.6; H, 6.07. Found: C, 50.7; H, 6.17.

Wolfrom[8] reported m.p. 75–77°, $[\alpha]^{28}D$ −47° (3% in chloroform).

A large-scale preparation of XII using 13.7 g. of tetra-*O*-acetyl ribonoyl chloride gave a 30% yield of XII, m.p. 70–71°, after 1 recrystallization.

2,3,4,5-Tetra-*O*-acetyl-1-deoxy-D-psicose Diethyl Mercaptal (XIII).—A mixture of 1.0 g. (3 mmoles) of 2,3,4,5-tetra-*O*-acetyl-1-deoxy-D-psicose (XII) and 0.88 g. of sodium sulfate was added to a solution of 0.45 g. (3.3 mmoles) of anhydrous zinc chloride in 3.5 ml. of ethyl mercaptan in an ice-salt bath.

The mixture was stirred at 0° for 3.5 hr., then poured into 10 ml. of saturated aqueous sodium bicarbonate. The precipitated solid was filtered and washed with two 10-ml. portions of hot chloroform. The filtrate was extracted with two 10-ml. portions of chloroform. The combined chloroform fractions were washed with 10 ml. of water, then dried over magnesium sulfate and evaporated to dryness *in vacuo* to yield 1.27 g. (96%) of the product (XIII) as a nearly colorless oil; $\lambda_{max(\mu)}^{film}$ 5.68 (acetate C=O), 8.00 (S—C_2H_5).

Anal. Calcd. for $C_{18}H_{30}O_8S_2$: C, 49.3; H, 6.90; S, 14.6. Found: C, 49.4; H, 7.03; S, 14.3.

1-Deoxy-D-psicose Diethyl Mercaptal (XVI).—A solution of 1.0 g. (2.28 mmoles) of 2,3,4,5-tetra-*O*-acetyl-1-deoxy-D-psicose diethyl mercaptal (XIII) in 16 ml. of absolute methanol was cooled to 0° in an ice–salt bath, while protected from moisture. To the cooled solution was added 1 ml. of 1*N* methanolic sodium methoxide. The solution was kept in the refrigerator for 18 hr., then carefully neutralized with glacial acetic acid to *p*H 7. Care must be taken to prevent overacidification, since the ethylthio groups are extraordinarily acid-labile.

The neutralized solution was evaporated to dryness *in vacuo*. The residue was dissolved in 10 ml. of ether and the ether solution was washed with two 2-ml. portions of water. The ether solution was dried over magnesium sulfate, then evaporated to dryness to give 0.5 g. (82%) of product that crystallized when seeded. Recrystallization from ethyl acetate–petroleum ether (b.p. 62–70°) gave the analytical sample, m.p. 47–48°; $[\alpha]^{23}D$ +12° (1% in 95% ethanol); $\lambda_{max(\mu)}^{Nujol}$ 3.08 (OH), 7.83 (S—C_2H_5).

Anal. Calcd. for $C_{10}H_{22}O_4S_2$: C, 44.4; H, 8.20; S, 23.7. Found: C, 44.2; H, 8.07; S, 23.6.

A large-scale deacetylation of 80 g. of XIII gave a 71% yield of crystalline XVI, m.p. 47–48°.

6-*O*-Benzoyl-1-deoxy-D-psicose Diethyl Mercaptal (XV).—A solution of 33.0 g. (0.11 mole) of 1-deoxy-D-psicose diethyl mercaptal (XVI) in 500 ml. of dry pyridine was cooled to 0° in an ice–salt bath, and 15 ml. (18.1 g., 0.13 mole) of benzoyl chloride was added over about a 10-min. period. The reaction mixture was kept at 0° for 18 hr., then decomposed by being added slowly and with vigorous stirring to 600 ml of ice-cold saturated aqueous sodium bicarbonate. The aqueous layer was extracted with three 150-ml. portions of chloroform. The combined extracts were washed with two 100-ml. portions of water, then dried over magnesium sulfate and evaporated to dryness *in vacuo* to yield 44.2 g. (97%) of product (XV) as a pale yellow sirup; $\lambda_{max(\mu)}^{film}$ 2.91 (OH), 5.80 (benzoate C=O).

Anal. Calcd. for $C_{17}H_{26}O_5S_2$: C, 54.5; H, 7.00; S, 17.1. Found: C, 54.7; H, 6.81; S, 16.2.

6-*O*-Benzoyl-1-deoxy-D-psicose (XIV). Method A.—A suspension of 115 g. (0.308 mole) of 6-*O*-benzoyl-1-deoxy-D-psicose diethyl mercaptal (XV), 240 g. (0.885 mole) of mercuric chloride, and 180 g. (1.05 moles) of cadmium carbonate in 1 l. of water was stirred at room temperature for 2 hr., then at 50° for 2 hr. The mixture was filtered and the filtrate was treated with hydrogen sulfide until precipitation was complete. The precipitated sulfides were removed by filtration and the filtrate was continuously extracted with chloroform for 18 hr. The chloroform extract was evaporated *in vacuo* to give 36.0 g. (44%) of crude product (XIV) as a sirup that was satisfactory for the preparation of the thioglycoside (XVIII); $\lambda_{max(\mu)}^{film}$ 2.90 (OH), 5.80 (benzoate C=O). The product was homogeneous on paper chromatography in solvents A and B with R_{Ad} 2.44 and 1.93, respectively.

Recrystallization of the crude ketose from benzene gave 20.0 g. [24% from the mercaptal (XV)] of product as white crystals with m.p. 95–97°; $[\alpha]^{31}D$ 0° (1% in water); $\lambda_{max(\mu)}^{Nujol}$ 2.82, 2.88, 2.98 (OH), 5.83 (benzoate C=O), 7.80 (benzoate C—O—C).

Anal. Calcd. for $C_{13}H_{16}O_6$: C, 58.2; H, 6.01. Found: C, 58.3; H, 5.85.

Method B.—A solution of 8.68 g. (23.2 mmoles) of sirupy 6-*O*-benzoyl-1-deoxy-D-psicose diethyl mercaptal (XV) in 320 ml. of 50% aqueous acetic acid was heated in an oil bath at 75° for 1 hr. The solution was evaporated to dryness *in vacuo* and the residue was dissolved in 150 ml. of water. The aqueous solution was extracted with two 20-ml. portions of ether to remove unchanged starting material and over-benzoylated material, then was continuously extracted for 20 hr. with chloroform to remove the desired product from unbenzoylated 1-deoxy-D-psicose. The chloroform extract was evaporated *in vacuo* to give 3.8 g. (61%) of product (XIV) as a pale yellow sirup that crystallized on standing.

Recrystallization from benzene, then acetonitrile, gave 1.5 g. (24%) of white crystals, m.p. 80–83°. The analytical sample had m.p. 86–87°; $[\alpha]^{29}D$ +5° → 0.64° (over 48 hr.)

(23) Melting points were taken on a Fisher-Johns apparatus and are uncorrected. Optical rotations were measured with a Standard polarimeter Model D attachment to the Beckman DU spectrophotometer calibrated with standard sucrose solutions. Paper chromatograms were run by the descending technique with water–saturated butanol (solvent A), butanol–benzene–water (5:2:3) (solvent B), and 5% aqueous sodium hydrogen phosphate (solvent C). The spots were located by a bromine spray for mercaptals[12b] or by an aniline citrate spray for reducing sugars.

(1% in water); $\lambda_{max(\mu)}^{Nujol}$ 2.97 (OH), 5.81 (benzoate C=O); $\lambda_{max(m\mu)}^{C_2H_5OH}$ 229 (ε 12,500).

Anal. Calcd. for $C_{13}H_{16}O_6$: C, 58.2; H, 6.01. Found: C, 57.9; H, 6.39.

In a similar run, a 3% yield of an isomer with m.p. 126–127° was obtained. This isomer had $[\alpha]^{30}D$ −3° → −14° (5 hr.) (1% in water); $\lambda_{max(\mu)}^{Nujol}$ 2.90, 2.97 (OH), 5.85 (benzoate C=O), 7.77 (benzoate C—O—C); $\lambda_{max(m\mu)}^{C_2H_5OH}$ 230 (ε 12,600).

Anal. Calcd. for $C_{13}H_{16}O_6$: C, 58.2; H, 6.01. Found: C, 58.8; H, 5.87.

Both isomers had identical behavior on paper chromatography in solvent systems A and C, with R_{Ad} 1.85 and 2.10, respectively.

Method C.—A solution of 50 mg. of ethyl 6-*O*-benzoyl-1-deoxy-β-D-thiopsicofuranoside (XVIII) in 2 ml. of 50% aqueous acetic acid was heated at 75° for 2 hr. The colorless solution was evaporated to dryness *in vacuo* to give 44 mg. (98%) of product (XIV) as a colorless sirup that crystallized when triturated with benzene. The crystals were filtered to give 27 mg. (60%) of the product (XIV) as white crystals, m.p. 80.5–81.5°, essentially identical with the material from procedure B according to infrared spectral comparison. There was no depression on a mixed melting point with material from procedure B.

Ethyl 6-*O*-Benzoyl-1-deoxy-β-D-thiopsicofuranoside (XVIII).—A mixture of 0.50 g. (1.86 mmoles) of 6-*O*-benzoyl-1-deoxy-D-psicose (XIV) (m.p. 86–87°) and 0.55 g. of anhydrous sodium sulfate was treated with a solution of 0.28 g. (2.1 mmoles) of freshly fused zinc chloride in 3.0 ml. of ethyl mercaptan at 0°. The reaction was stirred for 3.5 hr. at 0°, then poured into 15 ml. of saturated aqueous sodium bicarbonate. The mixture was filtered and the filter cake was washed with five 5-ml. portions of hot chloroform. The aqueous layer was separated from the filtrate and was extracted with two 10-ml. portions of chloroform. The combined chloroform extracts were washed with 10 ml. of water, then dried over magnesium sulfate and evaporated to dryness *in vacuo* to give 0.50 g. (86%) of crude thioglycoside (XVIII) as a colorless sirup that partially crystallized on standing; $\lambda_{max(\mu)}^{film}$ 2.90, 2.95 (OH), 5.80, 5.88 (benzoate C=O).

The thioglycoside was dissolved in 10 ml. of benzene, then petroleum ether (b.p. 88–99°) was added to the cloud point and the solution was cooled to give 0.26 g. (45%) of white crystals, m.p. 98–105°. The analytical sample had m.p. 110–112°; $[\alpha]^{31}D$ −110° (1% in 95% ethanol); $\lambda_{max(\mu)}^{Nujol}$ 2.90, 2.97 (OH), 5.88 (benzoate (C=O).

Anal. Calcd. for $C_{15}H_{20}O_5S$: C, 57.7; H, 6.46; S, 10.2. Found: C, 58.1; H, 6.33; S, 10.1.

The filtrate after removal of the crystalline thioglycoside (XVIII) was evaporated *in vacuo* to give 0.20 g. (35%) of a sirup; $[\alpha]^{27}D$ +63° (1% in 95% ethanol); $\lambda_{max(\mu)}^{film}$ 2.90 (OH), 5.78 (benzoate C=O).

Anal. Calcd. for $C_{15}H_{20}O_5S$: C, 57.7; H, 6.46; S, 10.2. Found: C, 57.1; H, 6.52; S, 10.6.

Ethyl 3,4,6-Tri-*O*-benzoyl-1-deoxy-β-D-thiopsicofuranoside (XIX).—To a solution of 100 mg. (0.32 mmole) of ethyl 6-*O*-benzoyl-1-deoxy-β-D-thiopsicofuranoside (XVIII) in 1 ml. of dry pyridine was added 0.09 ml. (0.80 mmole) of benzoyl chloride. The solution was left at room temperature for 18 hr., then was poured into 10 ml. of saturated aqueous sodium bicarbonate. The resulting mixture was extracted with three 5-ml. portions of chloroform. The chloroform extracts were combined, washed with 5 ml. of water, then dried over magnesium sulfate and evaporated to dryness *in vacuo* to yield 171 mg. (102%) of product (XIX) as a yellow sirup; $\lambda_{max(\mu)}^{film}$ 5.76 (benzoate C=O); there was no OH band near 2.9 μ.

Anal. Calcd. for $C_{29}H_{28}O_7S$: C, 66.9; H, 5.42; S, 6.14. Found: C, 67.1; H, 5.15; S, 6.12.

Ethyl 1-Deoxy-β-D-thiopsicofuranoside (XVII).—A solution of 3.0 g. (9.6 mmoles) of ethyl 6-*O*-benzoyl-1-deoxy-β-D-thiopsicofuranoside (XVIII) in 75 ml. of absolute methanol was saturated with ammonia at room temperature. The solution was stored at room temperature for 18 hr., then filtered to remove a small amount of insoluble material. The filtrate was evaporated to dryness *in vacuo* to give a yellow sirup. Trituration with water gave a gummy solid, which was recrystallized from benzene to afford 0.7 g. of starting material (XVIII), m.p. 108–109° (no depression on mixed melting point with pure XVIII).

Evaporation of the aqueous filtrate *in vacuo* gave 1.3 g. (85% based on unrecovered starting material) of crude product (XVII) as a yellow solid. Recrystallization from benzene gave 1.0 g. (65%) of a white solid, m.p. 74–76°. The analytical sample had m.p. 74–75°; $[\alpha]^{24}D$ −111° (1% in 95% ethanol); $\lambda_{max(\mu)}^{Nujol}$ 2.96, 3.16 (OH); there was no carbonyl band near 5.8 μ.

Anal. Calcd. for $C_8H_{16}O_4S$: C, 46.1; H, 7.75; S, 15.4. Found: C, 45.8; H, 7.77; S, 15.6.

After 2 hr., the product (XVII) had consumed 2.2 moles of periodate with generation of 0.06 mole of formic acid.

Ethyl 1-Deoxy-3,4,6-tri-*O*-(*p*-nitrobenzoyl)-β-D-thiopsicofuranoside (XX).—To an ice-cold solution of 0.64 g. (3.08 mmoles) of ethyl 1-deoxy-β-D-thiopsicofuranoside (XVII) in 17 ml. of dry pyridine was added 3.00 g. (16.2 mmoles) of freshly distilled *p*-nitrobenzoyl chloride. The reaction mixture was allowed to warm to room temperature, then was stirred for 18 hr. The solution was decomposed with a few drops of water, then poured slowly into 75 ml. of saturated aqueous sodium bicarbonate. The product (XX), which separated as a yellow solid, was filtered to give 2.0 g. (100%) of material, m.p. 139–141°. Recrystallization from ethyl acetate–petroleum ether (b.p. 62–70°) gave 1.65 g. (82%) of pale yellow solid, m.p. 142–144°.

The analytical sample had m.p. 144–145°; $[\alpha]^{20}D$ +6° (1% in ethyl acetate); $\lambda_{max(\mu)}^{Nujol}$ 5.74 (ester C=O), 6.50 and 7.36 (NO_2).

Anal. Calcd. for $C_{29}H_{25}N_3O_{13}S$: C, 53.1; H, 3.85; N, 6.42; S, 4.90. Found: C, 53.2; H, 3.60; N, 6.30; S, 4.84.

Ethyl α-(2,3,4,5-Tetra-*O*-acetyl-D-arabonoyl)malonate (XXII).—A solution of 2.0 g. (5.7 mmoles) of 2,3,4,5-tetra-*O*-acetyl-D-arabonoyl chloride[12] in 11 ml. of dry benzene was added over 30 min. to a vigorously stirred suspension of 3.60 g. (22.4 mmoles) of diethyl malonate and 1.64 g. (17.3 mmoles) of magnesium methoxide hemimethanolate. After the addition was complete, the reaction mixture was stirred for 1 hr., then was acidified with 3 ml. of acetic acid and washed with 10 ml. of 3*N* aqueous hydrochloric acid and 10 ml. of water. The organic layer was evaporated to dryness *in vacuo* to yield 2.1 g. of an orange oil.

The oil was extracted with 20 ml. of petroleum ether (b.p. 88–99°) and the residue was dissolved in 15 ml. of ethyl acetate. The ethyl acetate solution was diluted with 40 ml. of petroleum ether (b.p. 88–99°) then cooled at 0° for 18 hr. The white crystals of the product (XXII) were removed by filtration, yield 0.61 g. (22%), m.p. 58–59°. Two more recrystallizations from ethyl acetate–petroleum ether gave the analytical sample, m.p. 61–62°; $[\alpha]^{25}D$ +7° (1.7% in chloroform); $\lambda_{max(\mu)}^{Nujol}$ 5.66, 5.70 (C=O); there was no OH band near 2.9 μ.

Anal. Calcd. for $C_{20}H_{28}O_{13}$: C, 50.5; H, 5.92. Found: C, 50.7; H, 6.41.

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