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SYNTHESES OF *p*-AMINOPHENYL 1-THIO-α- AND -β-D-IDOPYRANOSIDES AS ANALOGS OF GLYCOSIDASE SUBSTRATES*

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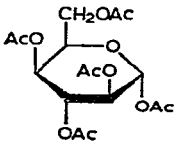
ABSTRACT

The *p*-nitrophenyl and *p*-aminophenyl 1-thio-α- and -β-D-idopyranosides were synthesized for use in structure–activity studies of glycosidases. Zinc chloride-catalyzed fusion of α-D-idopyranose pentaacetate with *p*-nitrobenzenethiol gave *p*-nitrophenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-α-D-idopyranoside as an amorphous glass in 67% yield, and the crystalline β anomer in 13% yield. Deacetylation with catalytic amounts of sodium methoxide in methanol, followed by hydrogenation under pressure over palladium-on-barium sulfate catalyst, afforded *p*-aminophenyl 1-thio-α- and -β-D-idopyranosides.

INTRODUCTION

The requirements for binding of glycosides to glycosidases are considered to be more stringent pertaining the sugar than they are for the aglycon[1]. However, examples of glycosidases hydrolyzing the glycosides of more than one sugar have been known for some time[2,3]. Recently, evidence has come to light indicating that glycosides



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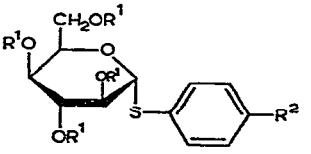
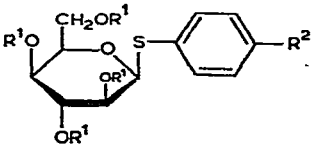


2 R^1 = Ac, R^2 = NO_2
3 R^1 = H, R^2 = NO_2
4 R^1 = H, R^2 = NH_2
5 R^1 = Ac, R^2 = NHAc



6 R^1 = Ac, R^2 = NO_2
7 R^1 = H, R^2 = NO_2
8 R^1 = H, R^2 = NH_2
9 R^1 = Ac, R^2 = NHAc

other than the substrate may bind to a given glycosidase, provided certain specificity requirements are met, without undergoing hydrolysis as a consequence. Thus, the β-D-mannosidase of human synovial fluid is inhibited[4] by *p*-nitrophenyl β-D-galactopyranoside, and the α-D-mannosidase of *Medicago sativa* is reported[5] to bind both

*Part II of the series.

to α-D-mannosides and α-D-glucosides. In order to study the structure–activity relationship of glycosidases, we have synthesized the aryl glycosides and 1-thioglycosides of aldohexoses not commonly found in Nature. In this connection, we have recently described the synthesis of *p*-nitrophenyl and *p*-aminophenyl α-D-talopyranoside and 1-thio-α-D-talopyranoside[6]. We now report the synthesis of the analogous *p*-nitrophenyl and *p*-aminophenyl 1-thio-α- (**3**, **4**) and -β-D-idopyranosides (**7**, **8**).

RESULTS AND DISCUSSION

Fusion[7,8] of α-D-idopyranose pentaacetate[9] (**1**) with *p*-nitrobenzenethiol at 125° in the presence of anhydrous zinc chloride gave a mixture containing the anomeric *p*-nitrophenyl 1-thio-D-idopyranoside tetraacetates (**2** and **6**). Part of the β anomer **6** crystallized from benzene. The crystalline **6** thus obtained and the α anomer (**2**) present in benzene solution were purified on a column of silica gel to remove traces of the other anomer. *p*-Nitrophenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-idopyranoside (**6**) was obtained crystalline in 13% yield. The α anomer (**2**) could not be crystallized, and was isolated as a foam in a yield of 67%. The i.r. spectra of **2** and **6** showed all of the requisite absorption maxima. Their anomeric configurations were assigned on the basis of Hudson's isorotation rules[10]. Confirmation of these assignments was obtained from 250-MHz n.m.r. spectra, which showed that both **2** and **6** exist almost exclusively in the $^4C_1$(D) conformation[11].

Deacetylation of **2** and **6** with catalytic amounts of sodium methoxide[12] in methanol afforded *p*-nitrophenyl 1-thio-α- (**3**) and -β-D-idopyranosides (**7**) in 83.5 and 87.8% yields, respectively. Reduction of **3** and **7** to *p*-aminophenyl 1-thio-α- (**4**) and -β-D-idopyranosides (**8**) was achieved by pressure hydrogenation over palladium-on-barium sulfate as catalyst. The *p*-aminophenyl glycosides **4** and **8** were isolated in > 95% yields as syrups that could not be crystallized, but were essentially homogeneous on t.l.c. Both **4** and **8** were characterized by conversion into the acetylated *p*-acetamidophenyl 1-thioidosides **5** and **9**.

Tables I and II show Hudson's 2A values for various acetylated and non-acetylated *p*-nitrophenyl 1-thio-D-glycopyranosides, respectively. It has been suggested[13] that the 2A values of pyranosides may be grouped into two categories according to the configuration of the substituent at C-2. Thus, glycosides of glucose, galactose, gulose, and allose on the one hand, and those of mannose, talose, idose, and altrose on the other would be expected to have similar 2A values. This generalization appears to hold true for alkyl glycopyranosides[13–15]. It was of interest to compare the 2A values for the *p*-nitrophenyl 1-thioglycosides of sugars belonging to the two aforementioned groups, as the 2A values for the *p*-nitrophenyl 1-thioidopyranosides (**2**, **3**, **6**, and **7**) and *p*-nitrophenyl 2,3,4,6-tetra-*O*-acetyl-1-thiotalopyranosides[6] have now become available. For the acetylated derivatives, it may be seen from Table I that the 2A-values for the *p*-nitrophenyl thiomannopyranosides, thiotalopyranosides, and thioidopyranosides are lower than those of the glucosides. The differ-

ence is least (100°) for the idosides, the most (220°) for the mannosides, and the talosides fall in between (171°). It may be of relevance that talosides differ from the mannosides in the configuration at C-4, whereas in the idosides, the configurations at C-3 and C-4 are inverted from those in the mannosides. The 2A values for *p*-nitrophenyl 1-thioglycosides of sugars other than glucose (for sugars belonging to this group) are not available. In Table I, the 2A value for *p*-nitrophenyl 2,3,4-tri-*O*-acetyl-6-deoxy-1-thiogalactosides is included as, for the methyl aglycon, the 2A value is identical for the fucosides and galactosides and of the same magnitude as that of the glucosides[13,14]. For the acetylated *p*-nitrophenyl 1-thioglycosides, however, the 2A values of the fucosides resemble those of the mannosides and not the glucosides (Table I).

For the non-acetylated *p*-nitrophenyl 1-thioglycosides listed in Table II, it is noteworthy that the mannosides and glucosides possess similar 2A values (difference 19°), whereas the 2A value of the galactosides is less than that of the mannosides (by 62°) and glucosides (by 80°). The idosides **3** and **7** have the lowest of the 2A values listed in Table II. Thus, for the nonacetylated *p*-nitrophenyl 1-thioglycopyranosides, the rule[13] concerning the 2A values of glycosides does not appear to be valid. The optical-rotation data for the remaining *p*-nitrophenyl 1-thioaldohexosides should help to settle this question conclusively.

The optical-rotation data for acetylated and nonacetylated *p*-nitrophenyl D-glycopyranosides recorded in Tables III and IV, respectively, show that the 2A value for the *p*-nitrophenyl group in the mannosides is considerably less than that in the glucosides and galactosides. However, it is not possible to determine unequivocally

TABLE I

CONTRIBUTION OF AGLYCON TO THE OPTICAL ROTATION OF ACETYLATED *p*-NITROPHENYL 1-THIO-D-GLYCOPYRANOSIDES IN CHLOROFORM SOLUTION[a]

p-Nitrophenyl tetra-O-acetyl-1-thio-D-glycopyranoside	$[\alpha]_D$ *(degrees)*	$[M]_D$[b] *(degrees)*	$M_\alpha - M_\beta$ *(2A)*	$M_\alpha + M_\beta$ *(2B)*	*Reference*
α-gluco	+254.0	+1232	1397	1067	16
β-gluco	−34.1	−165.4			17
α-galacto					
β-galacto	−7.0	−34.0			18
6-Deoxy-*α-galacto*[c]	+273.5	+1167	1185	1149	19
6-Deoxy-*β-galacto*	−4.3	−18.4			18
α-manno	+142.6	+691.6	1177	207	18
β-manno	−100.0	−485.0			16
α-talo	+162.4	+787.6	1226	349	6
β-talo	−90.4	−438.4			6
α-ido (2)	+187.8	+910.8	1297	525	
β-ido	−79.6	−386.1			

[a]Molecular rotations and 2A and 2B values were calculated from $[\alpha]_D$ values given in the references cited. [b]$[M]_D = [\alpha]_D \times$ mol. wt./100. [c]The reference cited gives $[\alpha]_D$ for the L enantiomer.

TABLE II

CONTRIBUTION OF AGLYCON TO THE OPTICAL ROTATION OF *p*-NITROPHENYL 1-THIO-D-GLYCOPYRANOSIDES[a]

p-Nitrophenyl 1-thio-D-glyco-pyranoside	*Solvent*	$[\alpha]_D$ *(degrees)*	$[M]_D$[b] *(degrees)*	$M_\alpha - M_\beta$ *(2A)*	$M_\alpha + M_\beta$ *(2B)*	*Reference*
α-gluco	water	+333.0	+1055.6	1408	704	16
β-gluco	water	−111.0	−351.9			20
α-galacto	water	+295.0	+935.2	1326	544	20
β-galacto	water	−123.3	−390.9			20
α-manno	water	+258.0	+817.9	1389	247	20
β-manno	water	−180.0	−570.6			20
α-ido (3)	water	+240.8	+763.3	1302	225	
β-ido (7)	water	−169.8	−538.3			
α-ido (3)	methanol	+332.6	1054.3	1583	526	
β-ido (7)	methanol	−166.8	−528.8			
α-talo	methanol	+330.9	+1049.0			6
β-talo						
6-Deoxy-*α-galacto*[c]	methanol	+382.0	+1149.8	1499	801	19
6-Deoxy-*β-galacto*[c]	methanol	−116.0	−349.2			19

[a]Molecular rotations and 2A and 2B values were calculated from $[\alpha]_D$ values given in the references cited. [b]$[M]_D = [\alpha]_D \times$ mol. wt./100. [c]The reference cited gives $[\alpha]_D$ for the L enantiomer.

TABLE III

CONTRIBUTION OF AGLYCON TO THE OPTICAL ROTATION OF ACETYLATED *p*-NITROPHENYL D-GLYCOPYRANOSIDES IN CHLOROFORM SOLUTION[a]

p-*Nitrophenyl* D-*glycopyranoside tetraacetate*	$[\alpha]_D$ *(degrees)*	$[M]_D$[b] *(degrees)*	$M_\alpha - M_\beta$ *(2A)*	$M_\alpha + M_\beta$ *(2B)*	*Reference*
α-gluco	+200.0	+938.0	1130	746	8
β-gluco	−41.0	−192.3			8, 21
6-Thio-*α-gluco*	+230.0	+1115.5	1169	1063	22
6-Thio-*β-gluco*	−10.9	−52.9			22
α-galacto	+207.7	+974.1	1013	935	23
β-galacto	−8.3	−38.9			24
α-manno	+103.0	+483.1	952	14	23
β-manno	−100.0	−469.0			25
α-talo	+116.0	+544.0			6
β-talo					

[a]Molecular rotations and 2A and 2B values were calculated from $[\alpha]_D$ values given in the references cited. [b]$[M]_D = [\alpha]_D \times$ mol. wt./100.

whether *p*-nitrophenyl glycosides and their acetates comply with the proposed rule[13] concerning the classification of the 2A values according to the configuration at C-2 of the sugar moiety until data for other *p*-nitrophenyl hexopyranosides become available.

Pigman and Isbell[21], and Pigman[27], have demonstrated that the 2A and 2B values for both acetylated and nonacetylated aryl glycopyranosides are considerably

TABLE IV

CONTRIBUTION OF AGLYCON TO THE OPTICAL ROTATION OF *p*-NITROPHENYL D-GLYCOPYRANOSIDES[a]

p-Nitrophenyl D-*glycopyranoside*	*Solvent*	$[\alpha]_D$ *(degrees)*	$[M]_D$[b] *(degrees)*	$M_\alpha - M_\beta$ *(2A)*	$M_\alpha + M_\beta$ *(2B)*	*Reference*
α-gluco	water	+232.0	+698.3	1008	388	26
β-gluco	water	−103.0	−310.0			8, 26, 27
α-galacto	water	+305.0	+918.1	1234	602	28
β-galacto	water	−105.0	−316.0			26
α-manno	water	+155.0	+466.6	843	90	29
β-manno	water	−125.0	−376.3			29
α-talo	methanol	+187.4	+564.1			6
β-talo						

[a]Molecular rotations and 2A and 2B values were calculated from $[\alpha]_D$ values given in the references cited. [b]$[M]_D = [\alpha]_D \times$ mol. wt./100.

higher than those of the analogous alkyl glycopyranosides. Likewise, comparison of the data for acetylated (Table I) and nonacetylated (Table II) *p*-nitrophenyl 1-thioglycosides with those in Tables III and IV, respectively, for the corresponding *p*-nitrophenyl 1-oxygenated glycosides shows that, with the exception of the 2B value of the nonacetylated galactosides, the 2A and 2B values of 1-thioglycosides are considerably higher than the analogous values for 1-oxygenated glycosides. For acetylated *p*-nitrophenyl glycopyranosides, replacement of the glycosidic oxygen (Table III) by sulfur (Table I) causes a change in the molecular rotation of the α anomer that is more than 10 times that in the molecular rotation of the β anomer. In keeping with this observation, the molecular rotation of *p*-nitrophenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-α-D-talopyranoside (Table I) is more positive by 244° as compared with its 1-oxygenated analog (Table III), whereas, for the 1-oxygenated (Table III) and 1-thio (Table I) analogs of acetylated *p*-nitrophenyl β-galactosides, a difference in the molecular rotations of ~5° is observed.

The non-acetylated *p*-nitrophenyl glycopyranosides apparently do not conform with this pattern. Thus, although substitution of the glycosidic oxygen by sulfur in *p*-nitrophenyl α-glucoside brings about a change in the molecular rotation nearly 8.5 times that observed for the β-glucosides, the corresponding ratio is less than 2-fold for the mannosides, and the *p*-nitrophenyl β-galactosides experience a change in the molecular rotation more than four times than do the α-galactosides (Tables II and IV).

Pigman and Isbell[21] have shown that a linear correlation exists between the molecular rotations of various substituted aryl glucopyranosides and the dissociation constant of the corresponding phenols. Whether such correspondence extends to sugars other than glucose, and to variously substituted aryl 1-thioglycosides, remains to be established.

Although acetylated and nonacetylated *p*-nitrophenyl glycosides[21,27] and their 1-thio analogs (Tables I–IV) display molecular rotations considerably higher than

those of the corresponding alkyl glycosides, no example of the violation of rule 1 of Hudson's isorotation rules[10] has been observed thus far with these glycosides; in all examples studied, the α anomer is invariably found to be more dextrorotatory than the β anomer (for the D series).

EXPERIMENTAL

General methods. — Melting points were determined on a Fisher–Johns apparatus and are uncorrected. Optical rotations were measured at ambient temperature in a 1-dm cell with a Perkin–Elmer Model 241 automatic polarimeter. I.r. spectra were recorded with a Perkin–Elmer Model 257 spectrophotometer. T.l.c. was performed on plates coated with a 0.25-mm layer of silica gel G (Sigma Chemical Co., St. Louis, Missouri). The components on t.l.c. plates were detected by exposure to iodine vapor and/or by charring with sulfuric acid. Unless otherwise mentioned, the solvent system employed for t.l.c. of acetylated derivatives was 5:2:1 benzene–ethyl acetate–heptane, and 15:5:1 ethyl acetate–acetic acid–water for deacetylated derivatives. Column chromatography was performed on Hi-Flosil (Applied Science Laboratories, State College, Pennsylvania). All evaporations were carried out under diminished pressure below 40°. Elementary analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tennessee.

*1,2,3,4,6-Penta-*O*-acetyl-α-*D*-idopyranose* (**1**). — α-D-Idopyranose pentaacetate (**1**) was prepared from 1,2,3,4,6-penta-*O*-acetyl-β-D-glucopyranose by a slight modification of the acetoxonium-ion rearrangement procedure of Paulsen[9]; a yield of 43.6% of **1** was obtained as compared to the reported[9] 23%. According to the modification, the crude crystalline 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl chloride (prepared[30] in ~88% yield from β-D-glucopyranose pentaacetate) was converted into the 4,6-*O*-acetoxonium-1,2,3-tri-*O*-acetyl-α-D-idopyranose hexachloroantimonate by treatment with antimony pentachloride at 0° (instead of −10°). The complex was dried under vacuum over phosphorus pentaoxide for ~1.5 h, and then used the same day for reaction with sodium acetate in water at 0°. The latter reaction was allowed to proceed overnight (instead of the prescribed[9] 15 min), and the aqueous layer containing a separated gum was exhaustively extracted with chloroform (10 × 50 ml); an emulsion was formed, and it was necessary to be on guard against losses of product at this stage. The combined chloroform extracts were washed with cold water (5 × 50 ml), dried (sodium sulfate), and evaporated to a syrup. Conventional acetylation with acetic anhydride and pyridine afforded 8.72 g (43.6% overall) of crystalline **1** (from 95% ethanol); m.p. 92–93°, $[\alpha]_D$ +56° (chloroform) [reported[9] m.p. 94–95°, $[\alpha]_D^{20}$ +55° (chloroform)].

p-*Nitrophenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-α-* (**2**) *and -β-*D*-idopyranoside* (**6**). — To a mixture of α-D-idopyranose pentaacetate[9] (**1**, 3.00 g) and *p*-nitrobenzenethiol (3.60 g) was added a solution of freshly fused zinc chloride (0.720 g) in 3 ml of 19:1 acetic acid–acetic anhydride. The mixture was fused[7,8] for 15 min at 125° under diminished pressure. At the end of the reaction, the residue was dissolved in chloro-

form (75 ml), and washed with cold water (3 × 30 ml), cold saturated sodium hydrogencarbonate solution (5 × 30 ml), and cold water (4 × 30 ml). The dried (sodium sulfate) chloroform solution was evaporated to a yellowish-orange syrup that crystallized from benzene to give 0.622 g of the crude β-idoside **6**, m.p. 150–160°.

The benzene filtrate from the crystallization of **6** was evaporated to dryness, and the residue was chromatographed on silica gel. The column was washed with benzene to remove fast-migrating by-products. Subsequent elution with 20:1 benzene–ethyl acetate and pooling of appropriate fractions (monitored by t.l.c.) afforded 2.49 g (66.7%) of the α-idoside **2** as a pale-yellow foam that could not be crystallized; $[\alpha]_D$ +187.8° (*c* 0.2, chloroform); R_F 0.42; ν_{max}^{KBr} 1750 (C=O) 1599 and 1580 (aromatic), 1517 and 1343 (NO_2), 1225 (acetate C-O-C), 855, and 747 cm^{-1}.

Anal. Calc. for $C_{20}H_{23}NO_{11}S$: C, 49.48; H, 4.78; N, 2.89. Found: C, 50.37; H, 5.11; N, 2.82.

Chromatography of crude **6** (0.622 g) thus obtained, on silica gel with chloroform as solvent, separated **6** from byproducts and traces of the α anomer **2**. The β-idoside **6** was isolated as almost colorless crystals; yield 0.299 g (8.0%), m.p. 178–179°. An additional 5% of **6** was recovered from the chromatography of the α anomer **2** (see foregoing). An analytical sample of **6** was prepared by recrystallization from methanol; it had m.p. 179–180°, $[\alpha]_D$ −79.6° (*c* 0.21, chloroform); R_F 0.33; ν_{max}^{KBr} 1750 (C=O), 1600 and 1582 (aromatic), 1515 and 1345 (NO_2), 1240 and 1215 (acetate C-O-C), 859, and 750 cm^{-1}.

Anal. Calc. for $C_{20}H_{23}NO_{11}S$: C, 49.48; H, 4.78; N, 2.89. Found: C, 49.56; H, 4.90; N, 2.92.

p-*Nitrophenyl 1-thio-α-*D*-idopyranoside* (**3**). — To a solution of *p*-nitrophenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-α-D-idopyranoside (**2**, 0.724 g) in dry methanol (5 ml) was added 0.25 ml of 0.45M sodium methoxide in methanol. After 4.5 h, the clear-yellow solution was neutralized with methanol-washed Dowex-50 (H^+) resin, and evaporated to a yellow, foamy residue that crystallized on being kept. The crystalline mass was triturated with anhydrous ether and filtered to afford 0.395 g (83.5%) of yellow crystals of **3**; m.p. 151–155°, $[\alpha]_D$ +332.6° (*c* 0.22, methanol), +240.8° (*c* 0.18, water); R_F 0.80; ν_{max}^{KBr} 3500–3330 (OH), 1592, 1576, and 1497 (aromatic), 1510 and 1342 (NO_2), 859, 850 (shoulder), 842, 823, 777, and 745 cm^{-1}.

Anal. Calc. for $C_{12}H_{15}NO_7S$: C, 45.42; H, 4.76; N, 4.41. Found: C, 45.50; H, 4.90; N, 4.47.

p-*Nitrophenyl 1-thio-β-*D*-idopyranoside* (**7**). — Deacetylation of **6** (0.200 g) with sodium methoxide in methanol, and processing as described for **3**, afforded 0.115 g (87.8%) of pale-yellow crystals of **7**, m.p. 160–165°, $[\alpha]_D$ −166.8° (*c* 0.18, methanol), −169.8° (*c* 0.16, water); R_F 0.78; ν_{max}^{KBr} 3500–3300 (OH), 1600, 1580, and 1505 (aromatic), 1520 and 1340 (NO_2), 858, 847, 819, and 748 cm^{-1}.

Anal. Calc. for $C_{12}H_{15}NO_7S$: C, 45.42; H, 4.76; N, 4.41. Found: C, 45.34; H, 4.80; N, 4.35.

p-*Acetamidophenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-α-*D*-idopyranoside* (**5**). — The *p*-nitrophenyl 1-thio-α-D-idopyranoside (**3**, 0.150 g) was hydrogenated for 18 h in

methanol (50 ml) solution with 5% palladium-on-barium sulfate (0.100 g) as catalyst at an initial pressure of 50 lb.in^{-2}. The catalyst was filtered off through Celite and washed with methanol. The combined methanolic filtrates were evaporated to obtain yellow, syrupy *p*-aminophenyl 1-thio-α-D-idopyranoside (**4**) which could not be crystallized; yield 0.126 g (92.6%); t.l.c. showed a single spot (R_F 0.48).

The syrupy **4** was acetylated with pyridine (3 ml) and acetic anhydride (1.1 ml) for 24 h. Evaporation with the aid of toluene gave a yellow syrup (0.209 g, 95.9%) that was essentially homogeneous on t.l.c. The syrup was dissolved in methanol and decolorized with Nuchar. Evaporation of methanol left a colorless, chromatographically homogeneous syrup (0.155 g, 71.1%), which, on crystallization from methanol–water, afforded 0.113 g (51.8%) of colorless crystals of **5**, m.p. 161–163°, $[\alpha]_D$ +140.3° (*c* 0.20, chloroform); R_F (25:1 chloroform–methanol) 0.63; ν_{max}^{KBr} 3345 (NH), 1750 and 1735 (ester C=O), 1703 (amide, type I band), 1595 and 1499 (aromatic), 1522 (amide, type II band), 1250–1225 (acetate C-O-C), 872, 845, 830, 818, and 778 cm^{-1}.

Anal. Calc. for $C_{22}H_{27}NO_{10}S$: C, 53.11; H, 5.47; N, 2.82. Found: C, 53.27; H, 5.40; N, 2.86.

p-*Acetamidophenyl 2,3,4,6-tetra*-O-*acetyl-1-thio-β*-D-*idopyranoside* (**9**). — Hydrogenation of 0.100 g of *p*-nitrophenyl 1-thio-β-D-idopyranoside (**7**) was performed with 5% palladium-on-barium sulfate (70 mg) as catalyst in methanol (35 ml) as described for **3**. Chromatographically homogeneous (R_F 0.47) **8** was obtained as a syrup that could not be induced to crystallize; yield, 99 mg (109%). Syrupy **8** was acetylated with pyridine and acetic anhydride as described for **4** to afford syrupy **9**, which solidified on standing. The solid residue was triturated with cold water, and filtered to give 0.134 g (85.3%) of **9** as a yellow powder; m.p. 95–105°. T.l.c. (25:1 chloroform–methanol) showed this product to be homogeneous (R_F 0.57), except for traces of two components near the solvent front; no suitable solvent could be found for its recrystallization.

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