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Note

A one-step method for the preparation of 2-pyridyl 2-deoxy-1-thiohexopyranosides from glycal esters*

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Glycosyl fluorides[1], glycal esters[2], and glycosyl thiopyridyl ethers[3–5] of 2-deoxy sugars have been used for the formation of glycosides. The 2-pyridylthio moiety is a good leaving-group and glycosidation occurs under mild conditions[3,6]. 2-Pyridyl 2-deoxy-1-thioglycosides can be prepared by reaction[3,4] of the corresponding 2-deoxy sugars with $(2\text{-Py-S})_2/PBu_3/CH_2Cl_2/0°$ and a simple, one-step method for their preparation from glycal esters is now reported.

3,4,6-Tri-*O*-acetyl-D-glucal (**1**), 3,4,6-tri-*O*-acetyl-D-galactal (**7**), and 3,4-di-*O*-acetyl-L-rhamnal (**8**), when reacted severally with 2-mercaptopyridine (**2**), either with or without anhydrous toluene-*p*-sulfonic acid in dichloromethane, afforded the 1,2-addition products **3**, **4**, and **9–12**, respectively (69–73% yield). Normally, nucleophilic reagents, in the presence of Lewis acid, react[7] with **1** to give 2,3-unsaturated compounds **5**. The use of protic or Lewis acid catalysts promotes allylic displacement with and without allylic rearrangement[8], and even benzylic protected glycals show the allylic rearrangement[9]. No allylic rearranged product (**6**) was detected in the above reaction of **1**. However, the use of BF_3–Et_2O as the catalyst resulted in the formation only of **6**.

Each of products **3**, **4**, and **9–12** was isolated by flash chromatography[10] and characterised on the basis of spectral data. The $J_{1,2a}$ values of 6 and 12 Hz, respectively, of **4** and **3** established the α and β-configurations, respectively, as did the respective $[\alpha]_D$ values of +26° and −35° (chloroform). The structures of **9–12** were confirmed similarly.

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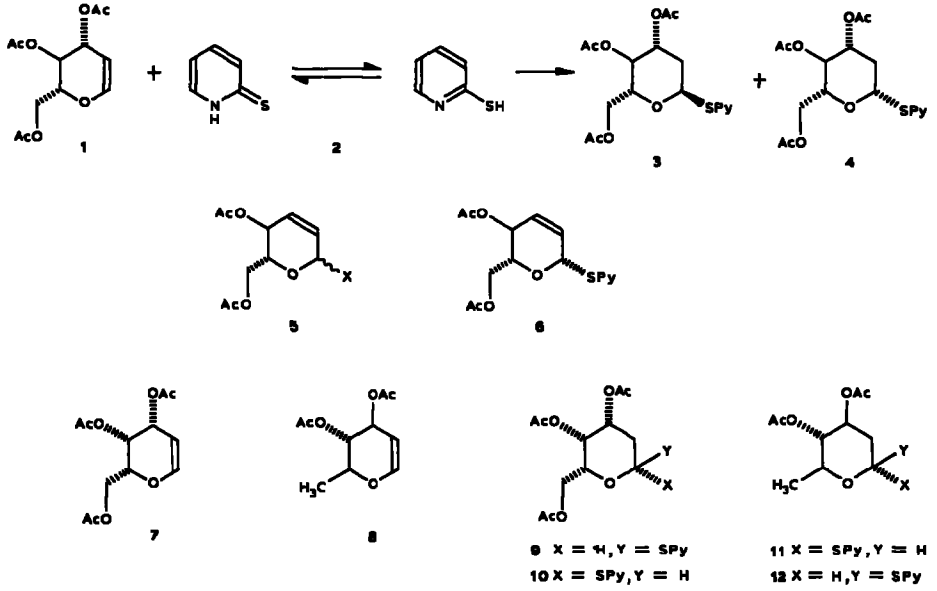

EXPERIMENTAL

General methods. — Melting points were determined with a Kofler hot-plate and are uncorrected. Boiling points were determined by bulb-to-bulb distillation. N.m.r. spectra were recorded for solutions in $CDCl_3$ (internal Me_4Si) with Bruker WH-300-FT (^1H, 300 MHz) and WH-90-FT (^{13}C, 22.63 MHz) spectrophotometers. Silica Gel 60 (230–400 mesh ASTM) (Merck) was used for flash-column chromatography[10]. T.l.c. was performed on Silica Gel-G (Acme) with detection by iodine vapour. All reactions were carried out with dry solvents under anhydrous conditions unless otherwise stated.

*2-Pyridyl 3,4,6-tri-*O*-acetyl-2-deoxy-1-thio-α-* (**4**) *and -β-*D-arabino-*hexopyranoside* (**3**). — To a solution of **1** (5 g, 18.4 mmol) in dry dichloromethane (100 mL) were added 2-mercaptopyridine (**2**; 2.65 g, 23.9 mmol) and anhydrous toluene-*p*-sulfonic acid (1 g, 6 mmol). The mixture was heated under reflux for 30 min (8 h in the absence of catalyst) and then poured into cold water, and the organic phase was washed with cold aqueous 2% potassium hydroxide and water, dried, and concentrated. Flash chromatography (light petroleum–ethyl acetate, 2:1) of the residue gave, first, **4** (2.07 g, 29%), m.p. 103° (from hexane–ether), $[\alpha]_D$ +26° (*c* 0.1, chloroform). N.m.r. data: ^1H, δ 1.99, 2.04, 2.05 (3 s, 9 H, 3 OAc), 2.33 (ddd, 1 H, $J_{2a,2e}$ 13, $J_{2a,3}$ 11 Hz, H-2*a*), 2.46 (ddd, 1 H, $J_{2e,3}$ 5.5 Hz, H-2*e*), 3.97 (dd, 1 H, $J_{6,6'}$ 12, $J_{5,6}$ 2 Hz, H-6), 4.33 (dd, 1 H, $J_{5,6'}$ 4.5 Hz, H-6′), 4.37 (ddd, 1 H, $J_{4,5}$ 9.5 Hz, H-5), 5.06 (t, 1 H, H-4), 5.27 (ddd, 1 H, $J_{3,4}$ 9.5 Hz, H-3), 6.46 (dd, 1 H, $J_{1,2a}$ 6, $J_{1,2e}$ 2 Hz, H-1), 7.08–8.48 (4 H, thiopyridyl); ^{13}C, δ 20.7, 20.9, 21.0 (3 q, 3 $OCOCH_3$), 35.5 (t, C-2), 62.1 (t, C-6), 69.4, 69.7, 69.8 (3 d, C-3,4,5), 79.8 (d,

C-1), 120.8, 123.7, 136.6, 149.8 (4 d, C-3″,4″,5″,6″), 156.2 (s, C-2″), and 169.8, 170.0, 170.5 (3 s, 3 $OCOCH_3$).

Anal. Calc. for $C_{17}H_{21}NO_7S$: C, 53.26; H, 5.52; N, 3.65; S, 8.35. Found: C, 53.39; H, 5.59; N, 3.68; S, 8.37.

Eluted second was **3** (3.06 g, 43%), b.p. 160°/0.01 Torr, $[\alpha]_D$ −35° (*c* 0.05, chloroform). N.m.r. data: ^1H, δ 1.98–2.10 (m, 1 H, H-2*a*), 2.06, 2.07, 2.13 (3 s, 9 H, 3 OAc), 2.54 (ddd, 1 H, $J_{2a,2e}$ 12, $J_{2e,3}$ 5 Hz, H-2*e*), 3.78 (ddd, 1 H, $J_{4,5}$ 10, $J_{5,6}$ 5, $J_{5,6'}$ 2.5 Hz, H-5), 4.06 (dd, 1 H, $J_{6,6'}$ 12 Hz, H-6), 4.27 (dd, 1 H, H-6′), 5.05 (t, 1 H, H-4), 5.14 (dt, 1 H, $J_{3,4} = J_{2a,3}$ = 10 Hz, H-3), 5.71 (dd, 1 H, $J_{1,2a}$ 12, $J_{1,2e}$ 2 Hz, H-1), 7.06–8.45 (4 H, thiopyridyl); ^{13}C, δ 20.7, 20.9 (3 q, 3 $OCOCH_3$), 36.0 (t, C-2), 62.5 (t, C-6), 68.8, 71.8, 76.1 (3 d, C-3,4,5), 78.3 (d, C-1), 120.7, 123.1, 136.6, 149.6 (4 d, C-3″,4″,5″,6″), 155.8 (s, C-2″), and 169.8, 170.2, 170.6 (3 s, 3 $OCOCH_3$).

Anal. Found: C, 53.29; H, 5.55; N, 3.69; S, 8.39.

2-Pyridyl 3,4,6-tri-O-acetyl-2-deoxy-1-thio-α- (**10**) *and -β-*D-lyxo-*hexopyranoside* (**9**). — Compound **7** (5 g, 18.4 mmol) was treated with **2** (2.65 g, 23.9 mmol) and anhydrous toluene-*p*-sulfonic acid (1 g, 6 mmol) in dichloromethane (100 mL), as described above. Column chromatography (light petroleum–ether, 2:3) of the product gave, first, **10** (2.15 g, 30%), b.p. 170°/0.01 Torr, $[\alpha]_D$ +256° (*c* 0.05, chloroform). N.m.r. data: ^1H, δ 1.90, 2.01, 2.14 (3 s, 9 H, 3 OAc), 2.09 (dt, 1 H, $J_{2,2'}$ 13, $J_{2a,3} = J_{1,2a}$ = 6 Hz, H-2*a*), 2.59 (dt, 1 H, $J_{2e,3} = J_{1,2e}$ = 6 Hz, H-2*e*), 4.04 (dd, 1 H, $J_{6,6'}$ 18, $J_{5,6}$ 11 Hz, H-6), 4.08 (dd, 1 H, $J_{5,6'}$ 5 Hz, H-6′), 4.54 (t, 1 H, $J_{3,4}$ 6 Hz, H-3), 5.25 (ddd, 1 H, $J_{4,5}$ 3 Hz, H-5), 5.36 (d, 1 H, H-4), 6.51 (d, 1 H, H-1), 7.07–8.48 (4 H, thiopyridyl); ^{13}C, δ 20.5, 20.6, 20.8 (3 q, 3 $OCOCH_3$), 30.7 (t, C-2), 62.0 (t, C-6), 66.4, 67.0, 68.5 (3 d, C-3,4,5), 81.0 (d, C-1), 120.8, 123.8, 136.6, 149.8 (4 d, C-3″,4″,5″,6″), 156.5 (s, C-2″), 169,9, 170.2, 170.3 (3 s, 3 $OCOCH_3$).

Anal. Calc. for $C_{17}H_{21}NO_7S$: C, 53.26; H, 5.52; N, 3.65; S, 8.35. Found: C, 53.31; H, 5.68; N, 3.43; S, 8.41.

Eluted second was **9** (3.15 g, 44%), m.p. 113° (from hexane–ether), $[\alpha]_D$ −58° (*c* 0.1, chloroform). N.m.r. data: ^1H, δ 2.00, 2.02, 2.16 (3 s, 9 H, 3 OAc), 2.10–2.40 (m, 2 H, H-2,2′ overlapped with acetate signal), 3.98 (t, 1 H, $J_{5,6} = J_{4,5}$ = 6.5 Hz, H-5), 4.12 (d, 2 H, H-6,6′), 5.13 (ddd, 1 H, $J_{2a,3}$ 12, $J_{3,4}$ 5, $J_{2e,3}$ 3 Hz, H-3), 5.33 (d, 1 H, H-4), 5.71 (dd, $J_{1,2a}$ 12, $J_{1,2e}$ 3 Hz, H-1), 7.08–8.45 (4 H, thiopyridyl); ^{13}C, δ 20.6 (3 q, 3 $OCOCH_3$), 31.2 (t, C-2), 61.9 (t, C-6), 65.4, 69.4, 74.7 (3 d, C-3,4,5), 78.8 (d, C-1), 120.7, 123.1, 136.6, 149.6 (4 d, C-3″,4″,5″,6″), 156.3 (s, C-2″), 169.9, 170.3, 170.4 (3 s, 3 $OCOCH_3$).

Anal. Found: C, 53.11; H, 5.52; N, 3.63; S, 8.43.

2-Pyridyl 3,4-di-O-acetyl-2,6-dideoxy-1-thio-α- (**11**) *and -β-*L-arabino-*hexopyranoside* (**12**). — Compound **8** (5 g, 23.4 mmol) was treated with **2** (3.37 g, 30.4 mmol) and anhydrous toluene-*p*-sulfonic acid (1.26 g, 7.6 mmol) in dichloromethane (100 mL) as described above. Column chromatography (light petroleum–ethyl acetate, 2:1) of the product gave, first, **11** (2.2 g, 29%), m.p. 109° (from dichloromethane–ether), $[\alpha]_D$ −281° (*c* 0.13, chloroform). N.m.r. data: ^1H, δ 1.16

(d, 3 H, $J_{5,6}$ 6.2 Hz, H-6,6′,6″), 2.02, 2.06 (2 s, 6 H, 2 OAc), 2.30 (ddd, 1 H, $J_{2a,2e}$ 13, $J_{2a,3}$ 11 Hz, H-2*a*), 2.46 (ddd, 1 H, $J_{2e,3}$ 5, $J_{1,2e}$ 1.5 Hz, H-2*e*), 4.20 (dq, 1 H, $J_{4,5}$ 9.5, $J_{5,6}$ 6.2 Hz, H-5), 4.80 (t, 1 H, $J_{3,4} = J_{4,5}$ = 9.5 Hz, H-4), 5.25 (ddd, 1 H, H-3), 6.42 (dd, 1 H, $J_{1,2e}$ 6 Hz, H-1), 7.05–8.50 (4 H, thiopyridyl); ^{13}C, δ 17.6, 20.8, 21.0 (3 q, C-6 and 2 OCO*C*H$_3$), 36.1 (t, C-2), 68.2, 69.7, 74.8 (3 d, C-3,4,5), 79.5 (d, C-1), 120.6, 123.4, 136.6, 149.8 (4 d, C-3‴,4‴,5‴,6‴), 156.9 (s, C-2‴), 170.1 (2 s, 2 O*C*OCH$_3$).

Anal. Calc. for $C_{15}H_{19}NO_5S$: C, 55.38; H, 5.89; N, 4.31; S, 9.84. Found: C, 55.60; H, 6.03; N, 4.32; S, 9.88.

Eluted second was **12** (3.4 g, 45%), m.p. 131° (from dichloromethane–ether), $[\alpha]_D$ +50° (*c* 0.1, chloroform). N.m.r. data: ^{1}H, δ 1.25 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6,6′,6″), 2.03, 2.06 (2 s, 6 H, 2 OAc), 1.95–2.10 (m, 1 H, H-2*a*), 2.55 (ddd, 1 H, $J_{2a,2e}$ 12.5, $J_{2e,3}$ 5.4 Hz, H-2*e*), 3.65 (dq, 1 H, $J_{4,5}$ 9.5, $J_{5,6}$ 6.2 Hz, H-5), 4.80 (t, 1 H, $J_{3,4}$ 9.5 Hz, H-4), 5.10 (dt, 1 H, $J_{2a,3}$ 9.5, $J_{2e,3}$ 5.4 Hz, H-3), 5.70 (dd, 1 H, $J_{1,2a}$ 13.2, $J_{1,2e}$ 2 Hz, H-1), 7.00–8.50 (4 H, thiopyridyl); ^{13}C, δ 17.8, 20.7, 20.8 (3 q, C-6, 2 OCO*C*H$_3$), 36.3 (t, C-2), 71.6, 73.8, 74.3 (3 d, C-3,4,5), 77.7 (d, C-1), 120.5, 122.8, 136.5, 149.6 (4 d, C-3‴,4‴,5‴,6‴), 156.3 (s, C-2‴), and 169.9, 170.0 (2 s, 3 O*C*OCH$_3$).

Anal. Found: C, 54.95; H, 5.82; N, 4.25; S, 9.90.

*2-Pyridyl 4,6-di-O-acetyl-2,3-dideoxy-1-thio-α-*D*-*erythro*-hex-2-enopyranoside* (**6**). — To a solution of **1** (0.5 g, 1.8 mmol) and **2** (0.26 g, 2.3 mmol) in dry chloroform (5 mL) was added boron trifluoride–ether (0.1 mL) at room temperature. After 15 min, the catalyst was neutralised with anhydrous sodium carbonate (0.2 g). Removal of the solids and the solvent left a residue (α,β mixture ~4:1 based on n.m.r. data) which crystallised from chloroform–hexane to give **6** (0.42 g, 70%), m.p. 117°, $[\alpha]_D$ +362° (*c* 0.07, chloroform). N.m.r. (90 MHz) data: ^{1}H, 1.95, 2.12 (2 s, 6 H, 2 OAc), 4.0–4.4 (m, 3 H, H-5,6,6′), 5.41 (dd, 1 H, $J_{3,4}$ ~1, $J_{4,5}$ 8 Hz, H-4), 5.85 (dd, 1 H, $J_{2,3}$ 10, $J_{1,2}$ 3 Hz, H-2), 6.12 (dd, 1 H, H-3), 6.63 (bs, 1 H, H-1), 6.92–8.65 (4 H, thiopyridyl); ^{13}C, δ 20.3, 20.7 (2 q, 2 OCO*C*H$_3$), 62.8 (t, C-6), 65.1, 68.5 (2 d, C-4,5), 79.9 (d, C-1), 120.5, 123.3, 128.5, 127.8, 136.3, 149.6 (6 d, C-2,3,3″,4″,5″,6″), 157.2 (s, C-2″), 169.8, 170.7 (2 s, 2 O*C*OCH$_3$).

Anal. Calc. for $C_{15}H_{17}NO_5S$: C, 55.72; H, 5.30; N, 4.33; S, 9.90. Found: C, 55.67; H, 5.27; N, 4.31; S, 9.95.

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