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Note

Synthesis of 3-amino-3-deoxy-5-thio-D-allose and 3-amino-3-deoxy-1,2-*O* : 5,6-*S*,*O*-di-isopropylidene-5-thio-α-D-glucofuranose

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The syntheses have been described of the 2-acetamido-2-deoxy derivatives of 5-thio-D-glucose[1–3], 5-thio-D-mannose[4], 5-thio-D-allose[5], 3-acetamido-3-deoxy-5-thio-D-xylose[6], and 4-acetamido-4-deoxy-5-thio-L-lyxose[6]. We now report the syntheses of 3-amino-3-deoxy-5-thio-D-allose hydrochloride and a derivative of the *gluco* analogue.

Treatment of the syrupy ketone[7] **1** with hydroxylamine in pyridine–ethanol gave two products which were separated by chromatography. The first was identified tentatively as the oxime **2**, the structure of which was based on the ^{1}H NMR data (Table I). Reduction of **2** with lithium aluminium hydride in dry ether gave a single product identified as 3-amino-3-deoxy-1,2-*O* : 5,6-*S*,*O*-di-isopropylidene-5-thio-α-D-allofuranose (**3**). The ^{1}H NMR spectrum of **3** (Table I) showed some resemblance to that of the *allo* alcohol[7] **4**.

Treatment of **3** with toluene-*p*-sulphonyl chloride in dry pyridine gave the crystalline *N*-tosylate **5** (58%). The corresponding acetamido (**7**) and benzamido (**8**) derivatives were obtained as syrups.

Hydrolysis of **3** in hot aqueous hydrochloric acid gave crystalline 3-amino-3-deoxy-5-thio-D-allose hydrochloride (**9**), the mutarotation of which [$-12° \rightarrow +65°$ (H_2O)] indicated the β-pyranose form, and this was confirmed by the conversion into the penta-acetate **10**. The ^{1}H NMR spectrum of **10** (Table I) demonstrated the $^4C_1$ conformation ($J_{1,2}$ 9.0, $J_{4,5}$ 10.0 Hz).

Treatment of the 3-mesylate[7] **6** with lithium azide in dry *N*,*N*-dimethylfor-

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TABLE I

^{1}H NMR data [a]

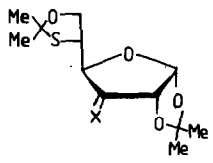
Compound	Chemical shifts (δ in ppm)							Other signals
	H-1	H-2	H-3	H-4	H-5	H-6a	H-6b	
2	6.12	5.53		4.97	3.88	4.50	4.41	8.44 (OH), 1.82, 1.82, 1.71, 1.60 (2 CMe_2)
3	5.70	4.54	4.24		3.06	3.65	3.73	6.42 (NH), 1.63, 1.59, 1.50, 1.30 (2 CMe_2)
4[7]	5.61	4.46			4.2–3.6			2.34 (OH), 1.62, 1.58, 1.52, 1.31 (2 CMe_2)
5	5.79	4.61	5.10	4.30	3.48	3.85	3.76	5.11 (NH), 2.39 (ArMe), 1.56, 1.45, 1.25, 1.17 (2 CMe_2)
6[7]	5.12	4.14	4.49	4.08	3.49	3.81	3.65	2.39 (SO_2Me), 1.53, 1.37 (2), 1.00 (2 CMe_2)
7	5.75	4.30	4.58	4.26	3.67	4.10	3.83	5.82 (NH), 2.01 (COMe), 1.62, 1.60, 1.55 (2 CMe_2)
8	5.69	4.33	4.62	4.27	3.57	4.08	3.77	5.82 (NH), 7.71–7.23 (H-Ar), 1.59, 1.53, 1.30, 1.22 (2 CMe_2)
10	6.13	5.61	5.10	5.40	3.67	4.35	4.17	5.95 (NH), 2.18, 2.12 (2), 2.08, 2.04 (NHAc, OAc)
11	5.81	4.58	3.85	4.31	3.62	3.81	3.72	1.64, 1.58, 1.47, 1.24 (2 CMe_2)
12	5.81	4.36	4.28–4.16		3.57	4.00		5.74 (NH), 1.63, 1.59, 1.45, 1.25 (2 CMe_2)
13[7]	5.83	4.42			4.4–3.5			2.69 (OH), 1.66, 1.60 (2), 1.47 (2 CMe_2)
14	5.91	4.69	5.32	4.38	3.56	3.86	3.76	5.72 (NH), 2.31 ArMe), 1.68, 1.61, 1.58, 1.45, 1.36 (2 CMe_2)

[a] For solutions in $CDCl_3$, except **5** and **13** (CCl_4), and **6** (C_6D_6).

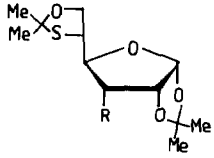
mamide gave a single compound which was identified as the expected 3-azido-3-deoxy-1,2-*O*:5,6-*S*,*O*-di-isopropylidene-5-thio-α-D-glucofuranose (**11**), the structure of which was indicated by the ^{1}H NMR spectrum (Table I).

Coupling constants (J in Hz)						
$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6a}$	$J_{5,6b}$	$J_{6a,6b}$
4.0			7.0	5.0	10.0	12.0
4.4	4.0			4.8	7.2	12.0
4.0	4.5					
4.0	4.5	4.1	8.8	3.8	4.8	9.5
4.0	5.0	9.0	6.0	4.0	6.5	10.5
4.1	4.4	5.7	8.0	3.5	5.6	10.0
6.0	7.2	9.0	7.0	3.5	5.8	10.0
9.0	3.0	2.6	10.0	5.5	5.0	12.0
3.5	0	3.0	9.5	3.0	4.5	11.0
4.5	0		10.0	3.0	5.0	12.0
3.5	0					
4.0	0	3.5	10.5	2.5	4.5	11.5

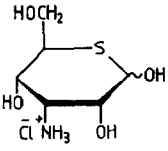
Reduction of **11** with lithium aluminium hydride in dry ether afforded the syrupy amine **12**. The $J_{2,3}$ value in the ^{1}H NMR spectrum of **12** (Table I) had a value similar to that (0 Hz) of the *gluco* alcohol[7] **13**. The amine **12** was characterised as the crystalline *N*-tosylate **14**, the ^{1}H-NMR spectrum (Table I) of which confirmed the *gluco* configuration.



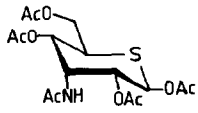
1 X = O
2 X = NOH



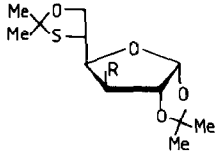
3 R = NH_2
4 R = OH
5 R = NHTs
6 R = OMs
7 R = NHAc
8 R = NHBz



9



10



11 R = N_3
12 R = NH_2
13 R = OH
14 R = NHTs

EXPERIMENTAL

Melting points were measured with a Gallenkamp apparatus and are uncorrected. The ^1H NMR spectra (internal Me_4Si) were recorded with Perkin–Elmer R32 (90 MHz) and Varian EM-390 (80 MHz) spectrometers. The ^1H NMR data are reported in Table I. Optical rotations were determined with a Perkin–Elmer 141 polarimeter. The purity of products was monitored by TLC on Kieselgel 60 (Merck). Column chromatography was performed on silica gel (Merck, 70–230 mesh). Amino sugars were detected with ninhydrin.

*1,2-O : 5,6-S,O-Di-isopropylidene-5-thio-α-*D-ribo-*hexofuranos-3-ulose oxime* (**2**). —The ketone[7] **1** (7.0 g, 23.94 mmol) was heated under reflux in 1 : 1 EtOH–pyridine (70 mL) containing hydroxylamine (3.6 g, 109.9 mmol) for 3 h. The mixture was then concentrated under vacuum and the residue was partitioned between $CHCl_3$ and water. The organic layer was dried ($MgSO_4$), then filtered, and the solvent was evaporated. Column chromatography (4 : 1 benzene–ether) of the residue (6.0 g) gave, first, **2** (2.4 g, 33%), mp 102–103°C (from di-isopropyl ether), $[\alpha]_D$ + 10° (*c* 0.6, $CHCl_3$) (Found: C, 49.75; H, 6.71; N, 4.92. $C_{12}H_{19}NO_5S$ calcd: C, 49.81; H, 6.62; N, 4.84%).

Further elution with 2 : 1 benzene–ether afforded an unidentified syrupy product (0.5 g).

3-Amino-3-deoxy-1,2-O : 5,6-S,O-di-isopropylidene-5-thio-α-D-allofuranose (**3**).—A solution of **2** (1.0 g, 3.45 mmol) in dry ether (50 mL) was heated under reflux with $LiAlH_4$ (0.8 g, 21.4 mmol) for 2 h. TLC (4:1 benzene–MeOH) then revealed a single product (R_f 0.65). Ethyl acetate was added followed by water to destory the excess of $LiAlH_4$, and the organic phase was dried ($MgSO_4$), filtered, and concentrated. Column chromatography (9:1 benzene–MeOH) of the residue afforded crystalline **3** (0.51 g, 53%). Recrystallisation from cyclohexane gave **3**; mp 96–97°C; $[\alpha]_D$ −20° (*c* 1.1, $CHCl_3$) (Found: C, 51.64; H, 8.01; N, 4.90. $C_{12}H_{21}NO_4S$ calcd: C, 52.34; H, 7.69; N, 5.09%).

3-Deoxy-1,2-O : 5,6-S,O-di-isopropylidene-3-O-toluene-p-sulphonamido-5-thio-α-D-allofuranose (**5**).—A solution of **3** (50 mg, 0.18 mmol) in dry pyridine (5 mL) was treated with toluene-*p*-sulphonyl chloride (75 mg, 0.39 mmol) at room temperature overnight. A few drops of water were added and, after 15 min, the mixture was partitioned between water and $CHCl_3$. The organic extract was washed successively with dil H_2SO_4 and dil aq $NaHCO_3$, dried ($MgSO_4$), filtered, and concentrated. Column chromatography (9:1 benzene–MeOH) of the residue and recrystallisation from di-isopropyl ether gave **5** (45 mg, 58%); mp 155–157°C; $[\alpha]_D$ −14° (*c* 0.5, $CHCl_3$) (Found: C, 52.69; H, 6.16; N, 2.96. $C_{19}H_{29}NO_6S_2$ calcd: C, 53.12; H, 6.34; N, 3.26%).

3-Acetamido-3-deoxy-1,2-O : 5,6-S,O-di-isopropylidene-5-thio-α-D-allofuranose (**7**).—To a solution of **3** (130 mg, 0.47 mmol) in dry pyridine (5 mL) was added acetic anhydride (3 mL). The solution was heated at 70°C for 30 min, then worked-up as above. Column chromatography (9:1 benzene–MeOH) of the product yielded syrupy **7** (61 mg, 70%); $[\alpha]_D$ −7° (*c* 1.2, $CHCl_3$). Mass spectrum: *m/z* 317.4042 (M^+) ($C_{14}H_{23}NO_5S$ calcd 317.4029).

3-Benzamido-3-deoxy-1,2-O : 5,6-S,O-di-isopropylidene-5-thio-α-D-allofuranose (**8**).—To a solution of **3** (63 mg, 0.23 mmol) in dry pyridine (5 mL) was added benzoyl chloride (0.03 mL). The solution was heated at 70°C for 30 min, then worked-up as above. Column chromatography (9:1 benzene-MeOH) of the product yielded syrupy **8** (61 mg, 70%); $[\alpha]_D$ −13° (*c* 0.56, $CHCl_3$). Mass spectrum: *m/z* 379.4710 (M^+) ($C_{19}H_{25}NO_5S$ calcd 379.4753).

3-Amino-3-deoxy-5-thio-D-allose hydrochloride (**9**).—A solution of **3** (236 mg, 0.92 mmol) in 2 M HCl (12 mL) was kept at 100°C for 1 h. TLC (3:2 benzene–MeOH) then revealed a component with R_f 0.28. The mixture was neutralised with Dowex 1-X8-100 (HO^-) resin, filtered, and concentrated. The residue was recrystallised from EtOH to give **9** (172 mg, 80%); mp 236–241°C; $[\alpha]_D$ −12 → +65° (equil.; *c* 0.78, H_2O) (Found: C, 30.64; H, 5.59; N, 5.85. $C_6H_{14}NO_4SCl$ calcd: C, 31.09; H, 6.09; N, 6.04%).

3-Acetamido-1,2,4,6-tetra-O-acetyl-3-deoxy-5-thio-β-D-allopyranose (**10**).—A solution of **9** (110 mg, 0.47 mmol) in water (15 mL) was passed through a column of Amberlite IRA-400 (HO^-) resin, then concentrated, and the residue was treated for 2 days at room temperature with pyridine (4 mL) and acetic anhydride (2 mL). The solvents were removed and the residue was crystallised from EtOH–di-isopro-

pyl ether to yield **10** (187 mg, 82%); mp 84–88°C; $[\alpha]_D$ −13° (*c* 0.95, $CHCl_3$) (Found: C, 47.58; H, 5.70; N, 3.24. $C_{16}H_{23}NO_9S$ calcd: C, 47.39; H, 5.72; N, 3.45%).

3-Azido-3-deoxy-1,2-O : 5,6-S,O-di-isopropylidene-5-thio-α-D-glucofuranose (**11**). —To a solution of the 3-mesylate[7] **6** (1.1 g, 3.41 mmol) in dry *N,N*-dimethylformamide (28 mL) were added sodium azide (3.7 g, 56.92 mmol) and ammonium chloride (2.0 g, 37.38 mmol). The mixture was heated under reflux for 3 h, then partitioned between $CHCl_3$ and water, and the organic phase was dried ($MgSO_4$), filtered, and concentrated. Column chromatography (2:1 benzene–ether) of the residue gave syrupy **11** (0.62 g, 66%); $[\alpha]_D$ −45° (*c* 0.97, $CHCl_3$). Mass spectrum: *m/z* 259.3395 ($M^+ - N_3$) ($C_{12}H_{19}N_3O_4S$ calcd 259.3442).

3-Amino-3-deoxy-1,2-O : 5,6-S,O-di-isopropylidene-5-thio-α-D-glucofuranose (**12**). —A solution of **11** (200 mg, 0.65 mmol) in dry ether (15 mL) containing $LiAlH_4$ (50 mg) was heated under reflux for 5 h, then cooled. Ethyl acetate (2 mL) was added, followed by ether (15 mL) and a few drops of water. The mixture was boiled for 10 min, filtered (Hyflo), dried ($MgSO_4$), filtered, and concentrated to give the amine **13** (117 mg, 64%) as a syrup; $[\alpha]_D$ −37° (*c* 0.62, $CHCl_3$). Mass spectrum: *m/z* 275.3589 (M^+) ($C_{12}H_{21}NO_4S$ calcd: 275.3671).

*3-Deoxy-1,2-O : 5,6-S,O-di-isopropylidene-3-toluene-*p*-sulphonamido-5-thio-α-D-glucofuranose* (**14**).—Compound **12** (70 mg, 0.25 mmol) was treated with toluene-*p*-sulphonyl chloride (96 mg, 0.50 mmol) in pyridine (7 mL) overnight at room temperature and the mixture was worked-up in the usual way. Column chromatography (9:1 benzene–MeOH) of the product and crystallisation from di-isopropyl ether gave **15** (65 mg, 67%); mp 142–144°C; $[\alpha]_D$ −88° (*c* 0.6, $CHCl_3$) (Found: C, 53.07; H, 6.31; N, 3.41. $C_{19}H_{27}NO_6S_2$ calcd: C, 53.14; H, 6.34; N, 3.26%).

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