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1-ARYL(GLYCOFURANO)IMIDAZOLIDINE-2-THIONES DERIVED FROM NEW 2-(ALKYLAMINO)-2-DEOXYHEPTOSES HAVING D-*glycero*-D-*galacto* AND D-*glycero*-D-*talo* CONFIGURATIONS

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ABSTRACT

The aminonitrile synthesis applied to D-mannose gave, in good yield, a mixture of the two epimeric heptosamines 2-deoxy-2-(ethylamino)-D-*glycero*-α-D-*galacto*-heptopyranose and 2-deoxy-2-(ethylamino)-D-*glycero*-β-D-*talo*-heptopyranose that could be fractionated by recrystallization. The stereochemistry at C-2 of both amino sugars, and of their acyl derivatives, was established from their ^{1}H-n.m.r. spectra. This stereochemistry was also demonstrated by the preparation of the 3-alkyl-1-aryl(glycofurano)imidazolidine-2-thiones, whose structures were assigned from the ^{1}H-n.m.r. spectra of their tetra-*O*-acetyl-derivatives. In a similar way, hemihydrogenation of the epimeric mixture of 2-deoxy-2-(propylamino)-heptononitriles gave an amorphous mixture of 2-deoxy-2-(propylamino)heptoses having the D-*glycero*-D-*galacto* and D-*glycero*-D-*talo* configurations. By reaction of this mixture with phenyl isothiocyanate, 1-phenyl-3-propyl-(1,2-dideoxy-D-*glycero*-β-D-*talo*-heptofurano)[2,1-*d*]imidazolidine-2-thione (**21**) was obtained. The structure of **21** was also demonstrated from the ^{1}H-n.m.r. spectrum of its acetyl derivative.

INTRODUCTION

In our current work on the synthesis of *C*-nucleoside analogs, we have made use of the reaction between 2-amino-2-deoxyheptoses and β-dicarbonyl compounds in order to obtain acyclic *C*-nucleosides that can be transformed into cyclic *C*-nucleosides by intramolecular dehydration of their pentahydroxypentyl chains[1–4]. We now describe the preparation of new 2-(ethylamino)- and 2-(propylamino)-2-deoxyheptoses having D-*glycero*-D-*galacto* and D-*glycero*-D-*talo* con-

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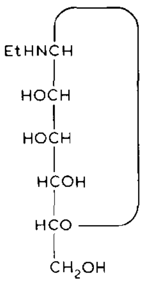
figurations which will be used in that synthesis of the corresponding *C*-nucleosides.

In order to confirm the stereochemistry at C-2 of these amino sugars, we prepared 3-alkyl-1-aryl(glycofurano)imidazolidine-2-thiones by their reaction with aryl isothiocyanates. These compounds are also interesting, because of their facile isomerization to acyclic *C*-nucleosides of the imidazole[5,6].

RESULTS AND DISCUSSION

Treatment of *N*-ethyl-β-D-mannopyranosylamine (**1**) with dry hydrogen cyanide in methanol gave a crystalline mixture of the epimeric heptononitriles **2** and **3** that could not be fractionated. Catalytic hydrogenation of this epimeric mixture gave a mixture of the heptosamines **6** and **8** which was separated by crystallization and recrystallization. The structures of **6** and **8** were assigned on the basis of their elemental analyses, i.r. and ^{1}H-n.m.r. spectra, and chemical properties. The ^{1}H-n.m.r. spectrum of **6** in D_2O, recorded immediately after it had dissolved, showed only an anomeric-proton signal corresponding to the equatorial proton of the α anomer ($J_{1,2}$ 3.4 Hz). In the spectrum recorded when mutarotational equilibrium had been reached, the signals of both anomers could be detected ($J_{1,2}$ for the β anomer, 8.3 Hz). These facts suggest that the α anomer was the crystalline product isolated from the reaction mixture; the α-anomeric configuration was also proved from its mutarotation to less positive values[7]. The D-*glycero*-D-*galacto* configuration was deduced from the large $J_{1,2}$ value of the β anomer, in agreement with a *trans*-diaxial disposition of these protons which is indicative of that configuration in the $^4C_1$(D) conformation. This configuration was confirmed by the ^{1}H-n.m.r. spectrum of its benzoyl derivative (**7**), which showed $J_{2,3}$ 9.3 Hz, in agreement with a *trans*-diaxial disposition of these protons.



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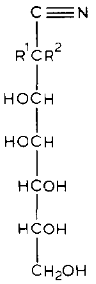


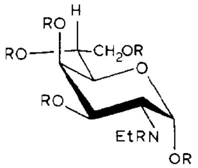
2 R^1 = NHEt, R^2 = H

3 R^1 = H, R^2 = NHEt

4 R^1 = NHPr, R^2 = H

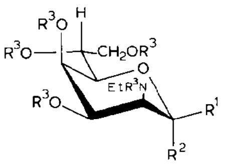
5 R^1 = H, R^2 = NHPr

The D-*glycero*-D-*talo* configuration assigned to **8** was based on the ^{1}H-n.m.r. spectrum of its acetyl derivative (**9**), which exhibited a double-doublet signal for H-



6 $R = H$

7 $R = Bz$



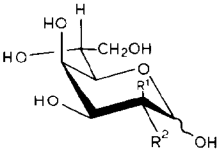
8 $R^1 = OH, R^2 = R^3 = H$

9 $R^1 = H, R^2 = OAc, R^3 = Ac$

10 $R^1, R^2 = H, OBz, R^3 = Bz$

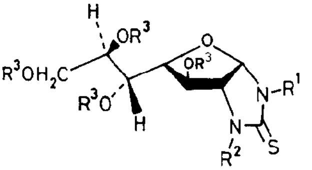
2 whose coupling constants ($J_{1,2}$ 3.1 and $J_{2,3}$ 1.0 Hz) suggested the equatorial disposition of H-2, in agreement with the assigned configuration in the $^4C_1$(D) conformation. The α-anomeric configuration is only tentatively assigned, in accordance with the high-positive, specific rotatory power. The β-anomeric configuration assigned to the free amino sugar **8** was based on its mutarotation to more positive values. On the other hand, the $J_{1,2}$ value (4.9 Hz) measured on the spectrum recorded in D_2O immediately after dissolving may be indicative of an axial–equatorial disposition for these protons, because this value is out of the range of values normally exhibited by the coupling constants of equatorial–equatorial protons[8].

The structures proposed for **6** and **8** were confirmed by the preparation of 1-aryl(glycofurano)imidazolidine-2-thiones (**13**, **15**, **17**, and **19**) by reaction with aryl isothiocyanates. By reaction of **6** with phenyl and 4-bromophenyl isothiocyanates, the 3-ethyl-1-phenyl-(1,2-dideoxy-D-*glycero*-α-D-*galacto*-heptofurano)[2,1-*d*]imidazolidine-2-thione (**13**) and the 1-(4-bromophenyl)-3-ethyl-(1,2-dideoxy-D-*glyc*-



11 $R^1 = H, R^2 = NHPr$

12 $R^1 = NHPr, R^2 = H$



13 $R^1 = Ph, R^2 = Et, R^3 = H$

14 $R^1 = Ph, R^2 = Et, R^3 = Ac$

15 $R^1 = 4\text{-}BrC_6H_4, R^2 = Et, R^3 = H$

16 $R^1 = 4\text{-}BrC_6H_4, R^2 = Et, R^3 = Ac$

TABLE I

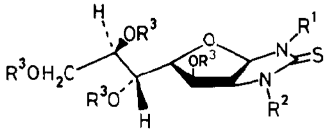
90-MHz, ^{1}H-N.M.R. DATA[a] FOR **14, 16, 18, 20,** AND **22**

Compound No	*H-1'*[b]	*H-2'*	*H-3'*	*H-4'*	*H-5'*	*H-6'*	*H-7'*	*H-7''*[b]	*OAc*	*Aryl*	*Et*	*Pr*
14	5.94[c] d[d] $J_{1',2'}$ 6.9	4.36 d $J_{2',3'}$ 0.0	5.29 d $J_{3',4'}$ 2.0	4.42 dd $J_{4',5'}$ 2.7	5.39 dd $J_{5',6'}$ 7.0	5.22 m $J_{6',7'}$ 2.7 $J_{6',7''}$ 5.0	4.39 dd $J_{7',7''}$ −12.3	4.12 dd	2.20 s (3H) 2.13 s (3 H) 2.04 s (3H) 2.02 s (3 H)	7.70–7.23 m	4.30–4.10 m (1H) 3.54 m (1 H) 1.22 t (3H)	
16	5.91 d $J_{1',2'}$ 6.9	4.37 d $J_{2',3'}$ 0.0	5.28 d $J_{3',4'}$ 2.0	4.31 dd $J_{4',5'}$ 2.7	5.38 dd $J_{5',6'}$ 7.0	5.22 m $J_{6',7'}$ 2.7 $J_{6',7''}$ 5.0	4.39 dd $J_{7',7''}$ −12.3	4.10 dd	2.18 s (3H) 2.16 s (3 H) 2.06 s (3H) 2.03 s (3 H)	7.50 s	4.23 m (1H) 3.47 m (1 H) 1.21 t (3H)	
18	5.85 d $J_{1',2'}$ 6.7	4.54 t $J_{2',3'}$ 5.7	5.02 dd $J_{3',4'}$ 9.3	4.40–4.10 dd $J_{4',5'}$ 2.3	5.41 m $J_{5',6'}$ 6.8	5.14 m $J_{6',7'}$ 2.3 $J_{6',7''}$ 5.0	4.42–4.00 m $J_{7',7''}$ −12.3		2.18 s (3H) 2.10 s (3 H) 2.04 s (3H) 2.02 s (3 H)	7.39 s	4.18 m (1H) 3.31 m (1 H) 1.23 t (3H)	
20	5.83 d $J_{1',2'}$ 6.6	4.55 t $J_{2',3'}$ 5.7	5.04 dd $J_{3',4'}$ 9.3	4.40–4.10 dd $J_{4',5'}$ 2.3	5.41 m $J_{5',6'}$ 6.8	5.20 m $J_{6',7'}$ 2.3 $J_{6',7''}$ 5.0	4.40–4.00 m $J_{7',7''}$ −12.3		2.17 s (3H) 2.10 s (3 H) 2.04 s (3H)	7.44 q	4.17 m (1H) 3.32 m (1 H) 1.22 t (3H)	
22	5.87 d $J_{1',2'}$ 6.3	4.58 dd $J_{2',3'}$ 5.7	5.05 dd $J_{3',4'}$ 9.2	4.40–4.20 m	5.50–5.20 m		4.60–4.00 m		2.20 s (3H) 2.13 s (3 H) 2.07 s (3H) 2.06 s (3H)	7.50–7.28 m		4.19 m (1H) 3.20 m (1 H) 1.70 m (2H) 0.93 t (3H)

[a] Recorded in $CDCl_3$ at 35.5°; δ scale (internal Me_4Si); J in Hz, with assignments verified by selective proton-decoupling. [b] Single primes denote numbering of atoms on the sugar ring-atoms. Double primes are reserved for the labeling of the upfield proton (usually) of a methylene group. [c] Values obtained by extrapolation back to zero concentration of $Eu(fod)_3$. [d] Signal multiplicities: d, doublet; dd, double doublet; m, multiplet; q, quartet; s, single, t, triplet.

ero-α-D-*galacto*-heptofurano)[2,1-*d*]imidazolidine-2-thione (**15**) were respectively obtained. In the same way, the reaction of **8** with the same isothiocyanates afforded the 3-ethyl-1-phenyl-(1,2-dideoxy-D-*glycero*-β-D-*talo*-heptofurano)[2,1-*d*]imidazolidine-2-thione (**17**) and the 1-(4-bromophenyl)-3-ethyl-(1,2-dideoxy-D-*glycero*-β-D-*talo*-heptofurano)[2,1-*d*]imidazolidine-2-thione (**19**). The structures assigned to these compounds were in agreement with their elemental analyses, spectral data (u.v. and i.r.), and periodate oxidation of the glycofuranoid ring, ~1 molar equivalent of formic acid being produced in each case. Acetylation of these compounds gave the tetra-*O*-acetyl derivatives **14**, **16**, **18**, and **20**, whose ^{1}H-n.m.r. spectra are shown in Table I. Compounds having the D-*glycero*-α-D-*galacto* configuration (**14** and **16**), with a *trans* disposition of H-2 and H-3, show $J_{2,3}$ ~0 Hz, whereas compounds with a D-*glycero*-β-D-*talo* configuration (**18** and **20**), which have a *cis* arrangement of H-2 and H-3, exhibit $J_{2,3}$ 5.7 Hz. These values are in good agreement with those previously reported[9–14] for other bicyclic compounds having similar structures.

By hydrogenation of the epimeric mixture of the aminonitriles **4** and **5**, the heptosamines **11** and **12** were obtained as an amorphous powder. By reaction of this epimeric mixture of amino sugars with phenyl isothyocyanate, the 1-phenyl-3-propyl-(1,2-dideoxy-D-*glycero*-β-D-*talo*-heptofurano)[2,1-*d*]imidazolidine-2-thione (**21**) was obtained. Its epimer having the D-*glycero*-D-*galacto* configuration could not be isolated from the reaction mixture. The structure of **21** was demonstrated as described for **17** and **19**. The proposed D-*glycero*-β-D-*talo* configuration is in agreement with the medium value (5.7 Hz) observed for $J_{2,3}$ in the ^{1}H-n.m.r. spectrum of its tetra-*O*-acetyl derivative **22**.



17 R^1 = Ph, R^2 = Et , R^3 = H
18 R^1 = Ph, R^2 = Et , R^3 = Ac
19 R^1 = 4-BrC_6H_4 , R^2 = Et , R^3 = H
20 R^1 = 4-BrC_6H_4 , R^2 = Et , R^3 = Ac
21 R^1 = Ph , R^2 = Pr , R^3 = H
22 R^1 = Ph , R^2 = Pr , R^3 = Ac

EXPERIMENTAL

General methods. — Solutions were evaporated *in vacuo* at temperatures below 50°. Melting points were determined with a Gallenkamp apparatus, and are uncorrected. Optical rotations were measured at 22 ±4° with a Perkin–Elmer 141 polarimeter (10-cm, 5-mL cell). I.r. spectra (KBr discs) were recorded with a Perkin–Elmer 399 spectrophotometer, and u.v. spectra with a Pye–Unicam SP8-250 instrument. Paper chromatography was performed on Whatman No. 1 paper by the ascending technique, with 1:1:1 1-butanol–pyridine–water as the eluant, and silver nitrate–sodium hydroxide as the indicator. T.l.c. was conducted on silica gel GF_{254} (Merck) with 3:1 ethyl acetate–ethanol (Solvent *A*) or 3:2 benzene–ether (Solvent *B*), and detection with u.v. light or iodine vapor. Formic acid produced in the oxidation with sodium periodate was determined as previously described[15,16]. ^{1}H-N.m.r. spectra at 90 MHz, with internal Me_4Si or sodium 4,4-dimethyl-4-silapentane-1-sulfonate (DSS) were recorded with a Perkin–Elmer R-32 spectrometer, and coupling constants were measured directly from spectra recorded at 300 Hz sweep-width (temperature of the probe 35.5°). Assignments were confirmed by double resonance (spin–spin decoupling and spin-tickling), and overlapping signals were gradually shifted and separated from one another by incremental additions of $Eu(fod)_3$.

N-*Ethyl-β-*D-*mannopyranosylamine* (**1**). — The method previously described[17] has been modified in the following procedure. To a suspension of D-mannose (60 g, 0.33 mol) in abs. ethanol (240 mL) was added ethylamine (50 mL, 0.75 mol), and the mixture was stirred until dissolution occurred. It was kept at room temperature and the product crystallized in a solid mass. The crystals were filtered off, and successively washed with cooled abs. ethanol and ether (yield 67.8 g, 99%); m.p. 124–126° (lit.[17] m.p. 126.6°); $[\alpha]_D$ −16°, $[\alpha]_{578}$ −16°, $[\alpha]_{546}$ −18°, $[\alpha]_{436}$ −27.5°, $[\alpha]_{365}$ −33.5° (*c* 1.0, 1:9 NH_4OH-H_2O); $[\alpha]_D$ −15.5°, $[\alpha]_{578}$ −16.5°, $[\alpha]_{546}$ −19°, $[\alpha]_{436}$ −29°, $[\alpha]_{365}$ −41° (*c* 1.0, 2.5M HCl).

*2-Deoxy-2-(ethylamino)-*D-glycero-D-talo-*heptononitrile* (**2**) *and 2-deoxy-2-(ethylamino)-*D-glycero-D-galacto-*heptononitrile* (**3**). — To a solution of **1** (67.8 g, 0.33 mol) in abs. methanol (324 mL) was added dry hydrogen cyanide (30 mL). After several min, crystallization began, and the flask was kept for 2 h at room temperature and then for 24 h at 0°. The crystals were filtered off, successively washed with cold abs. methanol and ether, and dried over sodium hydroxide *in vacuo*, to give a mixture of **2** and **3** (57.6 g, 75%). An analytical sample was obtained by recrystallization from abs. methanol; m.p. 137–139°, $[\alpha]_D$ −40°, $[\alpha]_{578}$ −42°, $[\alpha]_{546}$ −48°, $[\alpha]_{436}$ −68°, $[\alpha]_{365}$ −133° (*c* 1.6, pyridine); ν_{max} 3500–3100 (OH, NH) and 2220 cm^{-1}(C≡N).

Anal. Calc. for $C_9H_{18}N_2O_5$: C, 46.15; H, 7.75; N, 11.96. Found: C, 45.98; H, 8.04; N, 11.72.

*2-Deoxy-2-(propylamino)-*D-glycero-D-talo-*heptononitrile* (**4**) *and 2-deoxy-2-(propylamino)-*D-glycero-D-galacto-*heptononitrile* (**5**). — To a solution of *N*-propyl-*β*-D-mannopyranosylamine[18,19] (3.3 g, 14.9 mmol) in abs. methanol (20 mL) was added dry hydrogen cyanide (3 mL). The reaction mixture was processed as described for the preparation of **2** and **3**, to give a mixture of **4** and **5** (2.2 g, 59%);

m.p. 133–135°, $[\alpha]_D$ −59°, $[\alpha]_{578}$ −61°, $[\alpha]_{546}$ −69°, $[\alpha]_{436}$ −118°, $[\alpha]_{365}$ −184° (*c* 1.2, pyridine); ν_{max} 3500–3100 (OH, NH) and 2220 cm^{-1}(C≡N).

Anal. Calc. for $C_{10}H_{20}N_2O_5$: C, 48.37; H, 8.12; N, 11.28. Found: C, 48.60; H, 8.37; N, 11.25.

*2-Deoxy-2-(ethylamino)-*D-glycero-α-D-galacto-*heptopyranose hydrochloride* (**6**) *and 2-deoxy-2-(ethylamino)-*D-glycero-β-D-talo-*heptopyranose hydrochloride* (**8**). — A solution of the mixture of **2** and **3** (48 g, 0.21 mol) in M hydrochloric acid (550 mL) was hydrogenated at atmospheric pressure and room temperature in the presence of 10% palladium-on-barium sulfate (25 g). After 5 days, the catalyst was filtered off, and the filtrate was concentrated until crystals of ammonium chloride appeared. These were filtered off, and the residue was dissolved in ethanol; benzene was added and the solution was evaporated under diminished pressure. The resulting, thick syrup was thinned with abs. ethanol, and kept at 0°. After 20 days, compound **6** crystallized; it was filtered off, washed with abs. ethanol, and dried *in vacuo* over calcium chloride (yield 12.3 g, 22%). An analytical sample was obtained by dissolving the crude product (1 g) in hot 90% ethanol (16 mL) and gradually adding acetone (20 mL); m.p. 185–187°, $[\alpha]_D$ +111°, $[\alpha]_{578}$ +115°, $[\alpha]_{546}$ +129°, $[\alpha]_{436}$ +213°, $[\alpha]_{365}$ +318° (*c* 1.0, water; 5 min); $[\alpha]_D$ +95°, $[\alpha]_{578}$ +99°, $[\alpha]_{546}$ + 117°, $[\alpha]_{436}$ +194°, $[\alpha]_{365}$ +291° (3 h, final value); ν_{max} 3600–2300 (OH, NH_2^+) and 1560 cm^{-1} (NH_2^+); ^{1}H-n.m.r. data (1:1 D_2O–CF_3CO_2H): δ 5.61 (d, H-1, $J_{1,2}$ 3.4 Hz, α anomer) and 5.16 (d, H-1, $J_{1,2}$ 8.3 Hz, β anomer).

Anal. Calc. for $C_9H_{20}ClNO_6$: C, 39.49; H, 7.37; Cl 12.95; N, 5.12. Found: C, 39.74; H, 7.71; Cl, 13.33; N, 5.13.

The mother liquors of compound **6** were kept for one month at 0°, and product **8** crystallized; it was filtered off, washed with cold abs. ethanol, and dried *in vacuo* over calcium chloride (yield 30.0 g, 54%); m.p. 138–140°, $[\alpha]_D$ −42°, $[\alpha]_{578}$ −43°, $[\alpha]_{546}$ −48°, $[\alpha]_{436}$ −78°, $[\alpha]_{365}$ −113° (*c* 1.0, water; 5 min); $[\alpha]_D$ −29°, $[\alpha]_{578}$ −30°, $[\alpha]_{546}$ −34°, $[\alpha]_{436}$ −55°, $[\alpha]_{365}$ −81° (4.5 h, final value); ν_{max} 3600–2300 (OH, NH_2^+) and 1535 cm^{-1} (NH_2^+); ^{1}H-n.m.r. data (D_2O): δ 5.69 (d, 1 H, H-1, $J_{1,2}$ 4.9 Hz, β anomer).

Anal. Calc. for $C_9H_{20}ClNO_6$: C, 39.49; H, 7.37; Cl 12.95; N, 5.12. Found: C, 39.35; H, 7.67; Cl, 13.19; N, 5.22.

*1,3,4,6,7-Penta-*O*-benzoyl-2-deoxy-2-(*N*-ethylbenzamido)-*D-glycero-α-D-galacto-*heptopyranose* (**7**). — To a suspension of **6** (1 g, 3.7 mmol) in pyridine (10 mL) at 0° was added benzoyl chloride (3.8 mL, 32.9 mmol), and the mixture was kept for 4 days at 0°, and poured into ice–water (300 mL) containing sodium hydrogencarbonate (9 g). After 4 days at room temperature, the solid was filtered off, washed with cold water, and dried *in vacuo* over sodium hydroxide (yield 2.9 g, 92%). The crude product was purified by dissolution in hot, 96% ethanol (15 mL), treatment with charcoal, and addition of cold water until precipitation of **7** occurred; this was filtered off, and dried *in vacuo* over silica gel (yield 1.86 g, 59%); m.p. 106–108°, $[\alpha]_D$ +50°, $[\alpha]_{578}$ +52°, $[\alpha]_{546}$ +58°, $[\alpha]_{436}$ +88°, $[\alpha]_{365}$ +140° (*c* 1.0, chloroform); ν_{max} 1720 (C=O ester), 1640 (C=O amide), 1595, 1580, and 710 cm^{-1} (phenyl); ^{1}H-n.m.r. data (CDCl$_3$): δ 8.30–6.90 (m, 30 H, 6 Ph), 6.73 (m, 1 H, H-1, $J_{1,2}$ 2 Hz), 6.30–6.00 (m, 2 H, H-4,6), 5.48 (m, 1 H, H-3), 5.13 (m, 1 H, H-2, $J_{2,3}$ 9.3 Hz). 4.90–4.40 (m, 3 H, H-5,7,7′), 3.56 (m, 2 H, CH$_2$), and 0.95 (m, 3 H, CH$_3$).

Anal. Calc. for $C_{51}H_{43}NO_{12}$: C, 71.07; H, 5.03; N, 1.63. Found: C, 71.07; H, 5.06; N, 1.78.

*1,3,4,6,7-Penta-O-acetyl-2-deoxy-2-(N-ethylacetamido)-*D-glycero-α-D-talo-*heptopyranose* (**9**). — To a suspension of **8** (1 g, 3.7 mmol) in pyridine (2.7 mL) was added acetic anhydride (3.3 mL) without cooling, and the mixture was kept for 24 h at room temperature, poured into ice water, and extracted with chloroform (5 × 20 mL). The extracts were combined, washed successively with 1.5M sulfuric acid (3 × 15 mL), saturated sodium hydrogencarbonate solution (3 × 15 mL), and water, dried (anhydrous magnesium sulfate), and evaporated under diminished pressure, to give a yellow syrup that crystallized on dissolving in 96% ethanol and storing for 20 days at 0° (yield 0.39 g, 19%); m.p. 138–140°, $[\alpha]_D$ +116°, $[\alpha]_{578}$ +121°, $[\alpha]_{546}$ +137°, $[\alpha]_{436}$ +224°, $[\alpha]_{365}$ +330° (*c* 0.4, chloroform); ν_{max} 1750, 1730 (C=O ester), and 1640 cm^{-1} (C=O amide); ^{1}H-n.m.r. data (CDCl$_3$): δ 6.19 (d, 1 H, H-1, $J_{1,2}$ 3.1 Hz), 5.65–5.40 (m, 2 H, H-3,4, $J_{2,3}$ 1, $J_{4,5}$ 0.0 Hz), 5.29 (dd, 1 H, H-2), 5.10 (m, 1 H, H-6, $J_{5,6}$ 10.0, $J_{6,7}$ 2.3, $J_{6,7'}$ 3.7 Hz), 4.43 (dd, 1 H, H-7, $J_{7,7'}$ −12.3 Hz, 4.23 (d, 1 H, H-5), 4.07 (dd, 1 H, H-7′), 3.30 (q, 2 H, CH$_2$, J 7.3 Hz), 2.17 (s, 3 H, Ac), 2.13 (s, 3 H, Ac), 2.12 (s, 3 H, Ac), 2.10 (s, 3 H, Ac), 2.04 (s, 3 H, Ac), 1.99 (s, 3 H, Ac), and 1.09 (t, 3 H, CH$_3$).

Anal. Calc. for $C_{21}H_{31}NO_{12}$: C, 51.53; H, 6.38; N, 2.86. Found: C, 51.20; H, 6.53; N, 2.88.

*1,3,4,6,7-Penta-O-benzoyl-2-deoxy-2-(N-ethylbenzamido)-*D-glycero-D-talo-*heptopyranose* (**10**). — The benzoylation of compound **8** (1 g, 3.7 mmol) was conducted as for the preparation of **7**, to give **10** (3.1 g, 97%). The crude product was dissolved in hot, 96% ethanol, and the solution treated twice with charcoal. From the filtrate, crystals of **10** were isolated, washed with abs. ethanol, and dried *in vacuo* over sodium hydroxide. An analytical sample was obtained by several recrystallizations from 96% ethanol; m.p. 141–143°, $[\alpha]_D$ −39°, $[\alpha]_{578}$ −42°, $[\alpha]_{546}$ −47.5°, $[\alpha]_{436}$ −82°, $[\alpha]_{365}$ −132.5° (*c* 0.8, chloroform); ν_{max} 1715 (C=O ester), 1635 (C=O amide), 1590, 1570, and 710 cm^{-1} (phenyl); ^{1}H-n.m.r. data (CDCl$_3$): δ 8.30–6.90 (m, 30 H, 6 Ph), 7.02 (d, 1 H, H-1, $J_{1,2}$ 4.7 Hz), 6.20 (dd, 1 H, H-5, $J_{4,5}$ 2.7, $J_{5,6}$ 5.5 Hz), 5.93 (m, 1 H, H-6, $J_{6,7}$ 3.0, $J_{6,7'}$ 6.0 Hz), 5.76 (dd, 1 H, H-3, $J_{2,3}$ 7.0, $J_{3,4}$ 3.3 Hz), 5.13 (dd, 1 H, H-4), 4.96 (dd, 1 H, H-7, $J_{7,7'}$ −12.0 Hz), 4.76 (dd, 1 H, H-2), 4.61 (dd, 1 H, H-7′), 3.60 (q, 2 H, CH$_2$, J 7.0 Hz), and 0.88 (t, 3 H, CH$_3$).

Anal. Calc. for $C_{51}H_{43}NO_{12}$: C, 71.07; H, 5.03; N, 1.63. Found: C, 71.20; H, 5.02; N, 1.37.

*2-Deoxy-2-(propylamino)-*D-glycero-D-galacto-*heptopyranose hydrochloride* (**11**) *and 2-deoxy-2-(propylamino)-*D-glycero-D-talo-*heptopyranose hydrochloride* (**12**). — A solution of a mixture of **4** and **5** (20.3 g, 82 mmol) in M hydrochloric acid

(170 mL) was hydrogenated at atmospheric pressure and room temperature in the presence of 10% palladium-on-barium sulfate (8.5 g). After 7 days, the catalyst was filtered off, and the filtrate was concentrated until crystals of ammonium chloride appeared; these were filtered off, and the thick syrup was repeatedly evaporated with abs. ethanol and benzene, to give an amorphous mixture of **11** and **12** (21.8 g, 93%) that was used without purification in the preparation of **21**.

*3-Ethyl-1-phenyl-(1,2-dideoxy-*D-glycero-α-D-galacto-*heptofurano)[2.1-*d]*-imidazolidine-2-thione* (**13**). — To a solution of **6** (2.0 g, 7.3 mmol) in water (5 mL) were added sodium hydrogencarbonate (0.7 g, 8.3 mmol), phenyl isothiocyanate (1.5 mL, 12.4 mmol), and 96% ethanol (18 mL). The mixture was heated, with stirring, for 2 h at 40°; acetic acid (2.5 mL) was added, and the solution was heated for 1 h more at 40°, cooled, evaporated under diminished pressure, the residue treated with water (12 mL), and the solution washed with ether (4 × 25 mL). Compound **13** was isolated from the aqueous layer by extraction with ethyl acetate (5 × 15 mL); the extracts were combined, dried (anhydrous magnesium sulfate), evaporated, and the residue crystallized by addition of a small volume of ethyl acetate (yield 1.9 g, 72%); m.p. 131–133°, $[\alpha]_D$ +14°, $[\alpha]_{578}$ +15°, $[\alpha]_{546}$ +17°, $[\alpha]_{436}$ +26°, $[\alpha]_{365}$ +23°, (*c* 1.0, pyridine); λ_{max}^{EtOH} 245 nm (ε_{mM} 17.7); ν_{max} 3500–3100 (OH), 760, and 690 cm^{-1} (phenyl).

Anal. Calc. for $C_{16}H_{22}N_2O_5S$: C, 54.22; H, 6.26; N, 7.90; S, 9.05. Found: C, 54.43; H, 6.39; N, 7.98; S, 9.32. Formic acid produced: 1.0 mol.

*3-Ethyl-1-phenyl-(3,5,6,7-tetra-O-acetyl-1,2-dideoxy-*D-glycero-α-D-galacto-*heptofurano)[2,1-*d]*imidazolidine-2-thione* (**14**). — To a solution of **13** (0.78 g, 2.2 mmol) in pyridine (4 mL) was added acetic anhydride (4.7 mL), and the mixture was kept for 24 h at room temperature, poured into ice-water, and the resulting syrup extracted with chloroform (3 × 15 mL). The extracts were combined, successively washed with 1.5M sulfuric acid (3 × 15 mL), saturated sodium hydrogencarbonate solution (3 × 15 mL), and water, dried (anhydrous magnesium sulfate), and evaporated under diminished pressure, to give a colorless syrup which was dissolved in ethanol, and the solution evaporated, to yield a thick syrup which solidified after several days at 0° (yield 1.0 g, 90%); m.p. 47–49°, $[\alpha]_D$ +17°, $[\alpha]_{578}$ +17°, $[\alpha]_{546}$ +18°, $[\alpha]_{436}$ +18°, $[\alpha]_{365}$ +33°, (*c* 1.0, chloroform); ν_{max} 1735 (C=O ester), 1590, 760, and 695 cm^{-1} (phenyl); ^{1}H-n.m.r. data are given in Table I.

Anal. Calc. for $C_{24}H_{30}N_2O_9S$: C, 55.16; H, 5.79; N, 5.36; S, 6.14. Found: C, 54.81; H, 5.70; N, 5.43; S, 6.08.

*1-(4-Bromophenyl)-3-ethyl-(1,2-dideoxy-*D-glycero-α-D-galacto-*heptofurano)[2,1-*d]*imidazolidine-2-thione* (**15**). — To a solution of **6** (4.0 g, 14.6 mmol) in water (8 mL) were added sodium hydrogencarbonate (1.23 g, 14.6 mmol), 4-bromophenyl isothiocyanate (3.14 g, 14.6 mmol), and 96% ethanol (20 mL). The mixture was heated with stirring for 2 h at 40°, acetic acid (2.5 mL) was added, and the solution was heated for 1 h more at 40°, cooled, evaporated under diminished pressure, the residue treated with water (20 mL), and the solution washed with ether (3 × 25 mL). From the aqueous phase spontaneously separated a thick syrup that solidified on standing overnight at room temperature. The solid was filtered off, washed with cold water, and dried *in vacuo* over sodium hydroxide (yield 4.23 g, 76%). Recrystallization from ethyl acetate gave needles, m.p. 156–158°, $[\alpha]_D$ +45°, $[\alpha]_{578}$ +47°, $[\alpha]_{546}$ +54°, $[\alpha]_{436}$ +95°, $[\alpha]_{365}$ +146°, (*c* 1.0, pyridine); λ_{max}^{EtOH} 245 nm (ε_{mM} 20.1); ν_{max} 3600–3000 cm^{-1} (OH).

Anal. Calc. for $C_{16}H_{21}BrN_2O_5S$: C, 44.35; H, 4.89; Br, 18.44; N, 6.46; S, 7.40. Found: C, 44.09; H, 4.86; Br, 18.82; N, 6.65; S, 7.33. Formic acid produced: 1.2 mol.

*1-(4-Bromophenyl)-3-ethyl-(3,5,6,7-tetra-O-acetyl-1,2-dideoxy-*D-glycero-*α*-D-galacto-*heptofurano)[2,1-*d*]imidazolidine-2-thione* (**16**). — To a solution of **15** (0.86 g, 2.0 mmol) in pyridine (3 mL) was added acetic anhydride (4.4 mL), and the mixture was processed as described for the preparation of **14**, to give an amorphous product (1.16 g, 97%); m.p. 52-54°, $[\alpha]_D$ +13.5°, $[\alpha]_{578}$ +14°, $[\alpha]_{546}$ +15°, $[\alpha]_{436}$ +15°, $[\alpha]_{365}$ −29°, (*c* 1.0, chloroform); ν_{max} 1735 (C=O ester), 1580, and 825 cm^{-1} (aryl); ^{1}H-n.m.r. data are given in Table I.

Anal. Calc. for $C_{24}H_{29}BrN_2O_9S$: C, 47.93; H, 4.86; Br, 13.29; N, 4.66; S, 5.33. Found: C, 47.70; H, 4.91; Br 13.48; N, 4.67; S, 5.40.

*3-Ethyl-1-phenyl-(1,2-dideoxy-*D-glycero-*β*-D-talo-*heptofurano)[2,1-*d*]imidazolidine-2-thione* (**17**). — To a solution of **8** (5 g, 18.3 mmol) in water (10 mL) were added sodium hydrogencarbonate (1.54 g, 18.3 mmol), phenyl isothiocyanate (2.2 mL, 18.3 mmol), and 96% ethanol (25 mL). The mixture was heated with stirring for 4 h at 40°; acetic acid (4 mL) was added, and the solution was heated for 1.5 h more, cooled, and evaporated under diminished pressure, to give **17** as a crystalline product (4.7 g, 72%). Recrystallization from water, and then from 25% ethanol, gave needles; m.p. 208–210°, $[\alpha]_D$ −89°, $[\alpha]_{578}$ −93°, $[\alpha]_{546}$ −105°, $[\alpha]_{436}$ −171°, $[\alpha]_{365}$ −273°, (*c* 0.3, pyridine); λ_{max}^{EtOH} 245 nm (ε_{mM} 17.9); ν_{max} 3600–3100 (OH), 765, and 695 cm^{-1} (phenyl).

Anal. Calc. for $C_{16}H_{22}N_2O_5S$: C, 54.22; H, 6.26; N, 7.90; S, 9.05. Found: C, 54.39; H, 6.30; N, 7.85; S, 9.42. Formic acid produced: 1.2 mol.

*3-Ethyl-1-phenyl-(3,5,6,7-tetra-O-acetyl-1,2-dideoxy-*D-glycero-*β*-D-talo-*heptofurano)[2,1-*d*]imidazolidine-2-thione* (**18**). — Conventional treatment of **17** (1.0 g, 2.8 mmol) with pyridine (6 mL) and acetic anhydride (6 mL) gave **18** (1.47 g, quant.). Crystallized from 96% ethanol, it had m.p. 155–157°, $[\alpha]_D$ −84°, $[\alpha]_{578}$ −88°, $[\alpha]_{546}$ −100°, $[\alpha]_{436}$ −168°, $[\alpha]_{365}$ −253°, (*c* 1.0, chloroform); ν_{max} 1735 (C=O), 1590, 760, and 695 cm^{-1} (phenyl); ^{1}H-n.m.r. data are given in Table I.

Anal. Calc. for $C_{24}H_{30}N_2O_9S$: C, 55.16; H, 5.79; N, 5.36; S, 6.14. Found: C, 54.98; H, 5.81; N, 5.35; S, 6.41.

*1-(4-Bromophenyl)-3-ethyl-(1,2-dideoxy-*D-glycero-*β*-D-talo-*heptofurano)-[2,1-*d*]imidazolidine-2-thione* (**19**). — To a solution of **8** (5.0 g, 18.3 mmol) in water (10 mL) were added sodium hydrogencarbonate (1.54 g, 18.3 mmol), 4-bromophenyl isothiocyanate (3.9 g, 18.3 mmol), and 96% ethanol (25 mL). The mixture was heated with stirring for 4 h at 40°; acetic acid (4 mL) was added, and the solution was heated for 1.5 h more. After 12 h at 0°, a crystalline product (0.48 g) was isolated, and identified as ethyl 4-bromophenylthiocarbamate. The mother liquors were evaporated under diminished pressure, and the residue was treated with water and ether, crystallization being spontaneous (yield 1.76 g). Several crops of crystals were obtained from the mother liquors by evaporation of the solvent (total yield 4.28 g, 54%). Recrystallization from 96% ethanol and then from 30% ethanol gave needles; m.p. 211–213°, $[\alpha]_D$ −90°, $[\alpha]_{578}$ −94°, $[\alpha]_{546}$ −108°, $[\alpha]_{436}$ −186°, $[\alpha]_{365}$ −287°, (*c* 0.5, pyridine); λ_{max}^{EtOH} 246 nm (ε_{mM} 20.5); ν_{max} 3600–3100 (OH) and 830 cm^{-1} (aryl).

Anal. Calc. for $C_{16}H_{21}BrN_2O_5S$: C, 44.35; H, 4.89; Br, 18.44; N, 6.46; S, 7.40. Found: C, 44.05; H, 5.20; Br, 18.28; N, 6.53; S, 7.80. Formic acid produced: 1.0 mol.

*1-(4-Bromophenyl)-3-ethyl-(3,5,6,7-tetra-O-acetyl-1,2-dideoxy-*D-glycero-*β*-D-talo-*heptofurano)[2,1-*d*]imidazolidine-2-thione* (**20**). — Conventional treatment of **19** (1.0 g, 2.3 mmol) with pyridine (4 mL) and acetic anhydride (5 mL) gave **20** (1.4 g, quant.). Crystallized twice from 96% ethanol, it had m.p. 165–167°, $[\alpha]_D$ −83°, $[\alpha]_{578}$ −86.5°, $[\alpha]_{546}$ −98.5°, $[\alpha]_{436}$ −169°, $[\alpha]_{365}$ −267°, (*c* 1.0, chloroform); ν_{max} 1735 (C=O) and 835 cm^{-1} (aryl); ^{1}H-n.m.r. data are given in Table I.

Anal. Calc. for $C_{24}H_{29}BrN_2O_9S$: C, 47.93; H, 4.86; Br, 13.29; N, 4.66; S, 5.33. Found: C, 48.14; H, 4.91; Br, 13.30; N, 4.60; S, 5.56.

*1-Phenyl-3-propyl-(1,2-dideoxy-*D-glycero-*β*-D-talo-*heptofurano)[2,1-*d*]imidazolidine-2-thione* (**21**). — To a solution of a mixture of **11** and **12** (3.55 g, 12.3 mmol) in water (10 mL) were added sodium hydrogencarbonate (1.0 g, 12.3 mmol), phenyl isothiocyanate (1.5 mL, 12.3 mmol), and 96% ethanol (20 mL). The reaction mixture was processed as described for the preparation of **17**, to give a crystalline product (1.9 g, 42%) which was purified by recrystallization from ethanol; m.p. 203–204°, $[\alpha]_D$ −68°, $[\alpha]_{578}$ −71°, $[\alpha]_{546}$ −80°, $[\alpha]_{436}$ −127°, $[\alpha]_{365}$ −162°, (*c* 0.4, pyridine); λ_{max}^{EtOH} 253 nm (ε_{mM} 7.9); ν_{max} 3500–3200 (OH), 1590, 760, and 695 cm^{-1} (phenyl).

Anal. Calc. for $C_{17}H_{24}N_2O_5S$: C, 55.43; H, 6.52; N, 7.61; S, 8.66. Found: C, 55.67; H, 6.74; N, 7.68; S, 9.00. Formic acid produced: 1.2 mol.

*1-Phenyl-3-propyl-(3,5,6,7-tetra-O-acetyl-1,2-dideoxy-*D-glycero-*β*-D-talo-*heptofurano)[2,1-*d*]imidazolidine-2-thione* (**22**). — Conventional treatment of **21** (0.1 g, 0.3 mmol) with pyridine (1 mL) and acetic anhydride (1 mL) gave **22** (0.14 g, 72%). Crystallized twice from ethanol, it had m.p. 80–81°, $[\alpha]_D$ −77°, $[\alpha]_{578}$ −80°, $[\alpha]_{546}$ −90.5°, $[\alpha]_{436}$ −150°, $[\alpha]_{365}$ −221°, (*c* 0.4, chloroform); ν_{max} 1740 (C=O), 1590, 765, and 695 cm^{-1} (phenyl); ^{1}H-n.m.r. data are given in Table I.

Anal. Calc. for $C_{25}H_{32}N_2O_9S$: C, 55.96; H, 6.01; N, 5.22; S, 5.97. Found: C, 55.97; H, 6.03; N, 4.99; S, 6.23.

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