(ii) The dynamic process present in compound 1c involves a rotation about the anthryl-C(sp^2)/substituent-C(sp^3) bond with a barrier of 14.5 kcal mol^{-1}.

(iii) Allinger's MM2 calculations provided an excellent estimation of the barrier, 15 kcal mol^{-1}; moreover, the origin of the barrier and the most stable conformation were ascertained.

(iv) The calculated most stable conformation, explains the NOE results at low temperature ($H_1 \leftarrow\!\!\sim\!\!\rightarrow H_{11}$).

Experimental Section

Materials. (*R*)-(−)-2,2,2-Trifluoro-1-(9-anthryl)ethanol was purchased from Aldrich and used without further purification.

NMR Measurements. The NMR spectra at variable temperatures were taken with a Bruker AM 400 WB spectrometer, in a 5-mm dual probe with $CDCl_3$ as solvent, operating at 400.13 MHz for ^1H and 100.62 MHz for ^{13}C.

The temperature of the probe was calibrated by the methanol standard method, and a delay of 600 s was used before registering the NMR spectra at each temperature. NOE difference spectra were obtained using a low decoupler setting (typically 40 L, 5 mW approximately) with a total presaturation time resulting from the three times irradiation during 1 s in each individual quartet signals of H_{11}, following a NOEMULT sequence. In the case of the irradiation of H_1 or H_8 a single frequency was used during 10 s. A 512 number of transients was acquired using 16K points and a sweep width of 5000 Hz in alternate groups of eight, irradiating on/off resonance. A 90° pulse was used during acquisition.

In the 2D experiments, the standard Bruker sequences were applied. The COSY experiment was carried out with 1024 and 512 points along *f*2 and *f*1, respectively. The *f*1 time domains were zero filled and both directions multiplied by a sine square bell function before Fourier transformation.[12] The $^1H/^{13}C$ correlation spectrum was obtained from 256 time increments, each of 2K points, and Fourier transformed after zero filling to 256 points along *f*1 and exponential multiplication in *f*2.

Computational Details. Calculations were performed on a VAX-8820 computer in the Computer Center of the Universitat Autònoma de Barcelona, using the MM2PRIME program.[13] Allinger's MM2 (77) force field together with all MM2 (85) parameters have been used throughout this work.[14]

Acknowledgment. This work was supported by CICYT of Spain (Project Number PB87-0094-CO2-00). Servei d'Espectroscopia RMN of UAB is greatly acknowledged for allocating spectrometer time.

Registry No. (*R*)-(−)-1c, 53531-34-3.

Supplementary Material Available: MM2 contour map of the torsional energy surface obtained by driving ω_1 (C_{9a}–C_9–C_{11}–OH) and ω_2 (C_9–C_{11}–O–H), ^1H NMR spectra between 260 and 340 K, NOE difference experiments at 245 and 292 K, plot of proton chemical shifts vs concentrations at 245 K, and heteronuclear ^1H–^{13}C correlation spectra at 245 and 340 K (6 pages). Ordering information is given on any current masthead page.

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(13) Osawa, E.; Jaime, C.; Fujiyoshi, T.; Goto, H.; Imai, K. *JCPE Newsletter* **1989**, *1*, program No. 9 (VAX version).
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Total Synthesis of 6-Deoxy-6-aminoheptopyranuronic Acid Derivatives[1]

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Two enantio couples of terminal *C*-glycopyranosyl α-amino acids, namely the aminopyranuronic acids L-**9**, D-**9** and L-**10**, D-**10**, have been synthesized from the serine-derived pair L-**2**, D-**2** by exploiting enantiomerically pure butenolide intermediates **3** and **4**. The key synthetic steps involved the sequential antiselective cis dihydroxylation of the butenolide double bond and the clean furanose-to-pyranose ring expansion to construct the sugar skeleton with the proper stereochemistry. In our best performance, homogeneous L-**9** was prepared from L-**2** in four steps and 10 reactions in 20% overall yield.

Glycopyranosyl α-amino acids, where the α-aminoacyl residue is appended at the nonanomeric terminal of a pyranose via a carbon–carbon link, are the core components of a quite rare subclass of nucleoside antibiotics including amipurimycin[2] and the miharamycins,[3] both displaying activity against the causative agent for rice blast disease *Pyricularia oryzae*.[4]

A totally synthetic approach to amipurimycin, recently reported by Garner,[5] utilizes L-serine-derived oxazolidine aldehyde L-**2** as the homochiral progenitor, according to the Danishefsky's diene–aldehyde cyclocondensation protocol, while a nonnatural pyranosyl representative, 6-acetamido-2,3,4-tri-*O*-allyl-6-deoxy-α-D-*gluco*-heptopyranosiduronic acid, was synthesized by Antonakis[6] by

(1) A preliminary report of this work has appeared: Casiraghi, G.; Colombo, L.; Rassu, G.; Spanu, P. *J. Chem. Soc., Chem. Commun.* **1991**, 603.
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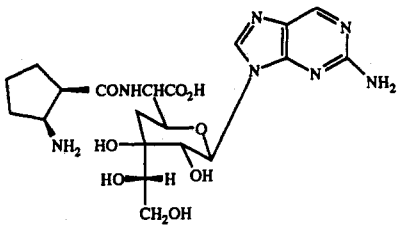
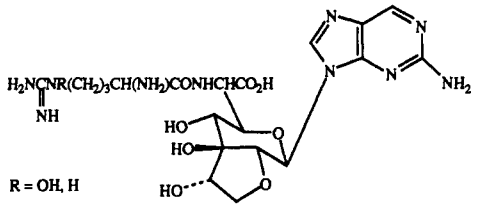
(4) A review dealing with synthetic approaches to complex nucleoside antibiotics including the furanosyl α-amino acid system of the polyoxins and the pyranosyl system of amipurimycin has recently been published: Garner, P. In *Studies in Natural Products Chemistry, Vol. 1 Stereoselective Synthesis, Part A*; Atta-ur-Rahman, Ed.; Elsevier: Amsterdam, 1988; pp 397–434.
(5) See ref 4, pp 404–408.

0022-3263/91/1956-6523$02.50/0



Amipurimycin



Miharamycins

exploiting, in the key stage of the sequence, the Sharpless asymmetric epoxidation of glucose-based allylic alcohols.

We had planned to prepare novel 6-deoxy-6-amino-heptopyranuronic acids de novo by exploiting our butenolide approach to higher carbon sugars[7] and the available L- and D-serine aldehydes L-**2** and D-**2**[8] to introduce the correct stereocenters at the pyranose rings carbons. We report herein a full account[1] of the diastereoselective synthesis of two enantio couples of terminal *C*-glycopyranosyl glycine derivatives, namely the glycero-talo and glycero-allo pairs L-**9**, D-**9** and L-**10**, D-**10**.

Our synthetic plan (Scheme I) called for **9** and **10** to be generated from the arabino- and ribo-configurated butenolide couples **3** and **4**, respectively. The opening move was the preparation of substantial amounts of enantiomerically pure butenolides L-**3**, D-**3** and L-**4**, D-**4**, and this was achieved via four-carbon elongation of L-**2** and D-**2** using 2-(trimethylsiloxy)furan (**1**).[9] Although commercially available, **1**[10] was routinely prepared following the good protocols of Näsman[11] and Brimble[12] via oxidation of furfural and subsequent silyl enol ether formation; the fresh material proved in our hand to work as well as the commercial substance. This reacted with L-**2** and D-**2** in CH_2Cl_2 in the presence of BF_3 etherate at −80 °C, providing, after aqueous $NaHCO_3$ quenching, crystalline seven-carbon arabino-configurated butenolides L-**3** and D-**3** in 88% and 84% yield, respectively, along with only marginal amounts (3–5%) of the ribo-counterparts L-**4** and D-**4**.

Base-catalyzed C-4 epimerization of the arabino-butenolides L-**3** and D-**3** using Et_3N and catalytic DMAP in CH_2Cl_2 provided equilibrium mixtures of ribo and arabino epimers in a ratio of ca. 65:35, from which the more abundant components L-**4** and D-**4** were obtained in a pure state by flash chromatography. Having enantiomerically pure **3** and **4**, we first elaborated the lactone fragments according to a highly stereoselective three-step sequence consisting of protection of the free OH at C-5 as TMS ether, anti-cis dihydroxylation of the butenolide double bond using solid $KMnO_4$ in CH_2Cl_2 in the presence of dicyclohexano-18-crown-6 ether,[13] and persilylation. This provided heptonolactones L-**5**, D-**5** and L-**6**, D-**6** in 60–62% overall yield for the three steps. They were purified by flash chromatography and fully characterized. As expected, for all the butenolides **5** and **6** a definite NOE was observed between the two cis hydrogens H-2 and H-3, while no effect between anti-disposed H-2 and H-4 was detected, and this substantiates the stereochemical assignments.

The ring expansion to pyranoses **7** and **8** required three further operations. DIBALH reduction in CH_2CL_2 at −80 °C generated γ-lactol intermediates, which, by citric acid–methanol treatment and subsequent peracetylation, were converted to pyranoses **7** and **8** in 55–58% overall yield.

While compounds **7** were obtained as single α-anomers, pyranoses **8** consisted of ca. 30:70 mixtures of α- and β-pyranoses, with only trace amounts of furanose forms. The major β-anomers L-**8** and D-**8** were easily separated from the mixtures by flash chromatography providing homogeneous samples which were used in the subsequent steps. The pyranose nature and stereochemistry of **7** and **8** were deduced on the basis of detailed analysis of the ^1H NMR spectra and difference NOE measurements of the L-enantiomers. For L-**7**, which mainly exists in the stable $^1C_4$(L) conformation, the strong NOE between axial C-3 and C-5 protons and the presence of a four-bond W coupling between equatorial H-2 and H-4 provided clear evidence supporting the L-talo structure of the ring, while for L-**8** the L-allo configuration was deduced based on the presence of large coupling constants between axially disposed H-1 and H-2 (J = 8.4 Hz) and H-4 and H-5 (J = 10.2 Hz) and the strong NOE's between H-1 and H-5 and between H-2 and H-4.

In the final stages of the synthesis, the remaining carbon to be elaborated in compounds **7** and **8** was the terminal hydroxymethylene group, and this was cleanly performed paralleling the chemistry reported by Garner for the synthesis of the nucleosidic component of the polyoxins.[14]

Treatment of **7** and **8** with 70% aqueous acetic acid at 60 °C resulted in selective removal of the acetonide groups, giving compounds with unprotected terminal CH_2OH functions. The crude primary alcohols were subjected to oxidation using $NaIO_4$ and catalytic $RuO_2{\cdot}H_2O$, resulting in formation of the expected carboxylic acids, which were finally transformed into the corresponding methyl esters by CH_2N_2 treatment. There were obtained two enantio pairs of virtually homogeneous methyl heptopyranuronates L-**9**, D-**9** and L-**10**, D-**10** in isolated yields ranging from 64 to 66% for the final set of reactions.

The α-glycero-talo configuration of **9** and the β-glycero-allo configuration of **10** follows directly from the ^1H NMR coupling constants and NOE measurements, the diagnostic parameters being $J_{1,2}$ = 1.2 Hz, $J_{2,4}$ = 0.9 Hz, $J_{2,3} = J_{3,4}$ = 3.6 Hz, and positive NOE between H-3 and H-5 for the couple L-**9**, D-**9** and $J_{1,2}$ = 9.0 Hz, $J_{2,3} = J_{3,4}$ = 3.0 Hz, $J_{4,5}$ = 9.5 Hz, and positive NOE's between H-2 and H-4 and between H-1 and H-5 for the couple L-**10**, D-**10**.

Each enantio pair showed superimposable ^1H NMR spectra with optical rotations nearly equal but opposite.

(6) Bessodes, M.; Komiotis, D.; Antonakis, K. *J. Chem. Soc., Perkin Trans. 1* **1989**, 41.

(7) (a) Casiraghi, G.; Colombo, L.; Rassu, G.; Spanu, P. *J. Org. Chem.* **1990**, *55*, 2565. (b) Casiraghi, G.; Colombo, L.; Rassu, G.; Spanu, P. *J. Org. Chem.* **1991**, *56*, 2135.

(8) Garner, P.; Park, J. M. *J. Org. Chem.* **1987**, *52*, 2361.

(9) Casiraghi, G.; Colombo, L.; Rassu, G.; Spanu, P.; Gasparri Fava, G.; Ferrari Belicchi, M. *Tetrahedron* **1990**, *46*, 5807.

(10) 2-(Trimethylsiloxy)furan is sold by both Fluka and Aldrich at Lit. 34 600 and 30 500 per gram, respectively.

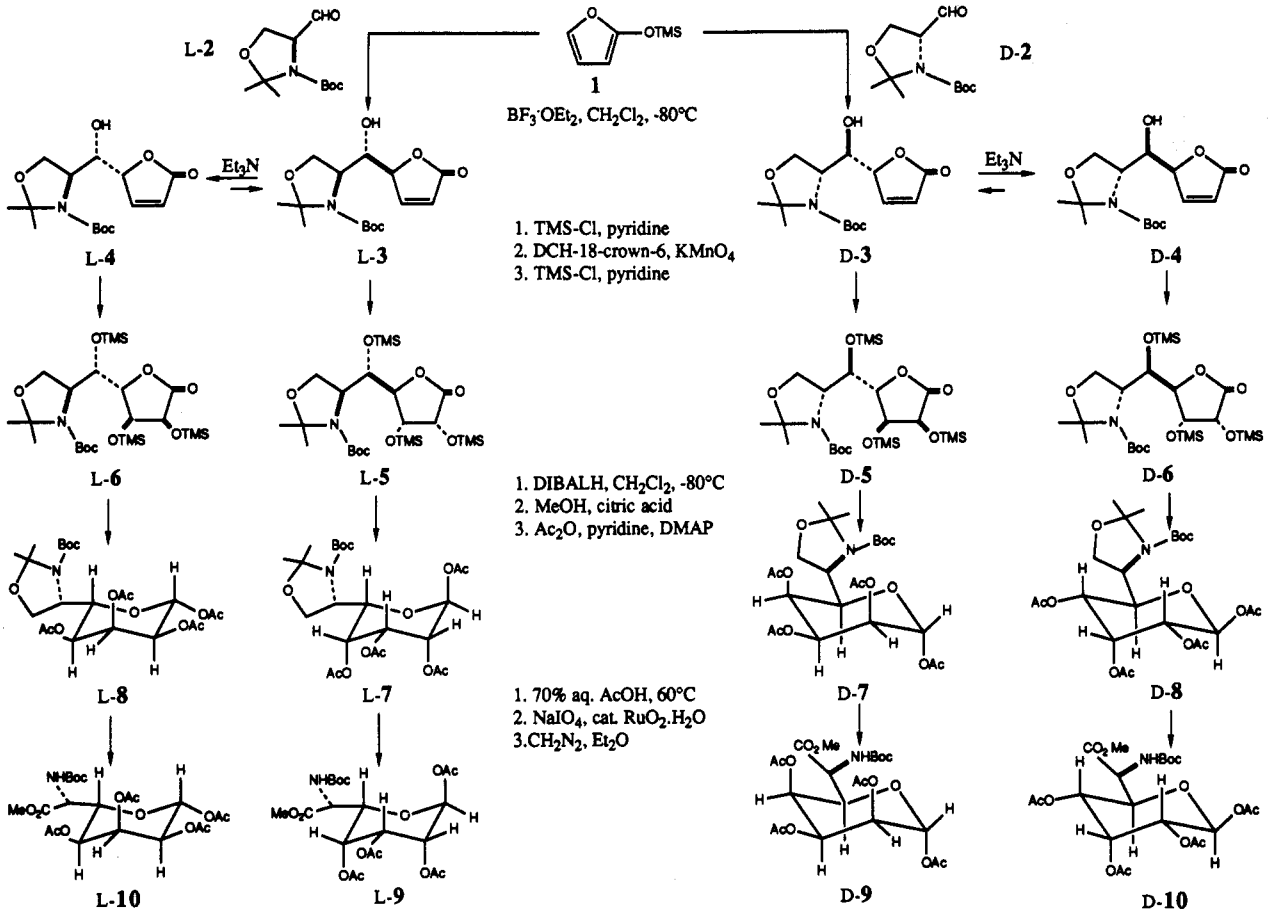
(11) Näsman, J.-A. H.; Göran Pensar, K. *Synthesis* **1985**, 787.

(12) Brimble, M. A.; Brimble, M.; Gibson, J. *J. Chem. Soc., Perkin Trans. 1* **1989**, 179.

(13) Mukaiyama, T.; Tabusa, F.; Suzuki, K. *Chem. Lett.* **1983**, 173. Mukaiyama, T.; Suzuki, K.; Yamada, T.; Tabusa, F. *Tetrahedron* **1990**, *46*, 265.

(14) Garner, P.; Park, J. M. *J. Org. Chem.* **1990**, *55*, 3772.

Scheme I



For the couple L-9/D-9, examination of the individual ^1H NMR spectra in $CDCl_3$ at 25 °C in presence of 0.9 equiv of the chiral shift reagent Eu(hfc)$_3$ established that only a single enantiomer is present, since the ester methyl group of racemic **9**, obtained by mixing equal amounts of pure enantiomers, absorbed as two 1:1 singlets at δ 3.79 and 3.83 in the presence of this chiral reagent. This established that no detectable racemization had occurred during the preparation and subsequent reactions of serine aldehydes L-2 and D-2.

In summary, we have established that substantial quantities of certain terminal *C*-glycopyranosyl α-amino acid derivatives,[15] possessing structural features present in rare pyranose nucleoside antibiotics, can be easily prepared by short and efficient routes. In our best performance, an overall yield of 20% was obtained for the complete sequence generating L-9 from L-2. Quantitative transfer of stereogenicity from the single chirality of **2**, creating all the six stereocenters of the target amino acids, was achieved by a sequence which exploits the merits of butenolides **3** and **4** as versatile homochiral building blocks. Additional aminoheptopyranuronic acid stereoisomers and analogues are also attainable, in principle, since the unsaturated carbon in **3** and **4** could be hydroxylated with other relative configurations and substituted by functions other than hydroxy groups.[16]

(15) Two synthetic approaches to related "anomeric" *C*-glycopyranosyl α-amino acids have recently been explored: Colombo, L.; Casiraghi, G.; Pittalis, A.; Rassu, G. *J. Org. Chem.* **1990**, *56*, 3897. Simchen, G.; Pürkner, E. *Synthesis* **1990**, 525.

(16) We are actively pursuing these objectives by studying, on simple model, the butenolide double-bond epoxidation and the conjugate addition of oxygen and nitrogen nucleophiles to the α,β-unsaturated lactone system.

Experimental Section

For general remarks, see ref 7b. Optical rotations are reported as α_D (*c* in g/100 mL). 2-(Trimethylsiloxy)furan (**1**) was prepared from furfural via H_2O_2 oxidation and subsequent silyl enol ether formation following the procedures of Näsman[11] and Brimble.[12] Serine-derived oxazolidine aldehydes L-2 and D-2 were prepared from the commercial *N*-*t*-Boc-serines (Aldrich) via methyl ester formation and protection, according to the protocol of Garner.[8] *J* values are given in Hz.

6,7-*N*,*O*-Isopropylidene-6-[(*tert*-butoxycarbonyl)amino]-2,3,6-trideoxy-L-*arabino*-hept-2-enono-1,4-lactone (L-3). 2-(Trimethylsiloxy)furan (**1**) (7.81 g, 0.05 mol) and serinal L-2 (11.5 g, 0.05 mol) were dissolved in anhydrous CH_2Cl_2 (150 mL) under argon, and the mixture was cooled to −80 °C. With stirring, BF_3 etherate (7.0 g, 0.05 mol) cooled to the same temperature was added via cannula over 10 min, and the solution was stirred for 8 h. The reaction was then quenched at this temperature by adding an excess of a saturated aqueous $NaHCO_3$ solution. After ambient temperature was reacted, the mixture was extracted with CH_2Cl_2 (3 × 25 mL) and the organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. This furnished crude lactone L-3 contaminated by ca. 5% of C-4 epimer L-4. The major component was purified by flash chromatography by using 7:3 diethyl ether/hexane as the eluant to afford L-3 (14.0 g, 88%) as a white solid: mp 127–128 °C; $[\alpha]_D$ −83.1° (*c* 1.3, $CHCl_3$); IR ($CHCl_3$) 1763 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6, 60 °C) δ 7.71 (dd, *J* = 5.7, 1.5, 1 H, H-3), 6.18 (dd, *J* = 5.7, 2.1, 1 H, H-2), 5.20 (d, *J* = 6.9, 1 H, OH), 5.05 (ddd, *J* = 3.0, 2.1, 1.5, 1 H, H-4), 4.05 (dd, *J* = 8.7, 2.4, 1 H, H-7a), 3.97 (m, 1 H, H-5), 3.90 (m, 1 H, H-6), 3.88 (dd, *J* = 8.5, 6.0, 1 H, H-7b), 1.49 (s, 3 H, Me), 1.45 (s, 3 H, Me), 1.43 (s, 9 H, Bu^t); ^{13}C NMR (75.4 MHz, DMSO-d_6, 60 °C) δ 172.9, 156.0, 151.6, 121.1, 93.1, 83.7, 68.8, 63.3, 58.8, 27.8, 26.4, 23.9; MS *m*/*z* 313 (M^+). Anal. Calcd for $C_{15}H_{23}NO_6$: C, 57.50; H, 7.40; N, 4.47. Found: C, 57.72; H, 7.66; N, 4.67.

D-*arabino*-Lactone D-3. This was prepared from D-2 (4.0 g, 0.017 mol) according to the previous procedure: yield 4.5 g (84%);

white solid; mp 129–131 °C; $[\alpha]_D$ +79.1° (*c* 1.2, $CHCl_3$). Anal. Calcd for $C_{15}H_{23}NO_6$: C, 57.50; H, 7.40; N, 4.47. Found: C, 57.80; H, 7.55; N, 4.70.

6,7-*N*,*O*-Isopropylidene-6-[(*tert*-butoxycarbonyl)amino]-2,3,6-trideoxy-L-*ribo*-hept-2-enono-1,4-lactone (L-4). To a solution of L-3 (14.0 g, 0.044 mol) in CH_2Cl_2 (100 mL) were added Et_3N (15 mL) and (*N*,*N*-dimethylamino)pyridine (0.1 g, 0.8 mmol), and the mixture was allowed to react for 4 h at room temperature. Then, after addition of water (20 mL) and extraction with CH_2Cl_2 (3 × 10 mL), the organic layer was dried over $MgSO_4$ and concentrated in vacuo. The oily residue was directly subjected to flash chromatography by using an 8:2 diethyl ether/hexane eluant mixture, giving pure L-4 (8.4 g, 60%) along with unconverted L-3 (5.0 g, 36%). For L-4: white solid; mp 162 °C; $[\alpha]_D$ +66.7° (*c* 0.5, $CHCl_3$); IR ($CHCl_3$) 1762 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6, 60 °C) δ 7.78 (dd, *J* = 5.7, 1.2, 1 H, H-3), 6.23 (dd, *J* = 5.7, 1.8, 1 H, H-2), 5.52 (d, *J* = 6.6, 1 H, OH), 4.97 (ddd, *J* = 4.1, 1.8, 1.2, 1 H, H-4), 3.7–4.2 (m, 4 H, H-5, H-6, and H_2-7), 1.50 (s, 3 H, Me), 1.46 (s, 3 H, Me), 1.43 (s, 9 H, Bu^t); ^{13}C NMR (75.4 MHz, DMSO-d_6, 60 °C) δ 172.8, 156.1, 151.6, 121.2, 93.2, 83.5, 68.6, 63.3, 58.8, 27.8, 26.4, 24.0; MS *m*/*z* 313 (M^+). Anal. Calcd for $C_{15}H_{23}NO_6$: C, 57.50; H, 7.40; N, 4.47. Found: C, 57.67; H, 7.65; N, 4.70.

D-*ribo*-Lactone D-4. This was prepared from D-3 (4.6 g, 0.015 mol) and purified according to the previous procedure: yield 3.0 g (65%); white solid; mp 163–164 °C; $[\alpha]_D$ −65.6° (*c* 1.5, $CHCl_3$). Anal. Calcd for $C_{15}H_{23}NO_6$: C, 57.50; H, 7.40; N, 4.47. Found: C, 57.75; H, 7.55; N, 4.62.

2,3,5-Tris-*O*-(trimethylsilyl)-6,7-*N*,*O*-isopropylidene-6-[(*tert*-butoxycarbonyl)amino]-6-deoxy-L-*glycero*-L-*talo*-heptono-1,4-lactone (L-5). To a solution of L-3 (4.0 g, 0.013 mol) in dry pyridine (60 mL) was added chlorotrimethylsilane (1.7 g, 0.015 mol), and the mixture was allowed to stir at room temperature until compound L-3 could not be detected by TLC (3 h). The solution was concentrated under vacuum, and the residue was dissolved in CH_2Cl_2 (100 mL). Dicyclohexane-18-crown-6 ether (600 mg, 1.6 mmol) and powdered $KMnO_4$ (2.4 g, 0.015 mol) were added at 0 °C with stirring, and the mixture was allowed to react at 15 °C while the progress of the reaction was monitored by TLC. After 3 h, further portions of $KMnO_4$ (240 mg, 1.5 mmol) and crown ether (60 mg, 0.16 mmol) were added, and the mixture was stirred for additional 3 h at room temperature. Next, solid sodium sulfite (4 g) and water (50 mL) were added, and the brown mixture was filtered through a Celite pad. The Celite pad was washed with CH_2Cl_2 (4 × 10 mL), and the combined filtrates were dried ($MgSO_4$) and evaporated under vacuum. The residue was dissolved in pyridine (125 mL) and treated with TMSCl (3.3 g, 0.03 mol). After being stirred at room temperature for 5 h, the mixture was concentrated under vacuum and the residue was flash chromatographed on silica by using 8:2 ethyl acetate/hexane as the eluant to yield 4.5 g (60%) of L-5 as a colorless solid: mp 85–87 °C; $[\alpha]_D$ −11.42° (*c* 1.1, $CHCl_3$); ^1H NMR (300 MHz, DMSO-d_6, 50 °C) δ 4.42 (d, *J* = 5.4, 1 H), 4.31 (dd, *J* = 5.1, 0.9, 1 H), 4.21 (dd, *J* = 4.5, 1.5, 1 H), 3.7–4.1 (m, 4 H), 1.49 (s, 3 H), 1.44 (s, 9 H), 0.17 (s, 9 H), 0.14 (s, 9 H), 0.12 (s, 9 H); ^{13}C NMR (75.4 MHz, DMSO-d_6, 25 °C) δ 176.6, 151.8, 93.2, 79.5, 70.6, 68.9, 68.4, 63.9, 58.2, 27.9, 27.1, 2.0; MS *m*/*z* 563 (M^+). Anal. Calcd for $C_{24}H_{49}NO_8Si_3$: C, 51.12; H, 8.76; N, 2.48. Found: C, 50.91; H, 8.60; N, 2.62.

D-*glycero*-D-*talo*-Lactone D-5. This was prepared from D-3 (3.6 g, 0.011 mol) and purified according to the previous procedure: yield 3.8 g (62%); colorless solid; mp 75–79 °C; $[\alpha]_D$ +15.38° (*c* 1.3, $CHCl_3$). Anal. Calcd for $C_{24}H_{49}NO_8Si_3$: C, 51.12; H, 8.76; N, 2.48. Found: C, 51.18; H, 8.42; N, 2.53.

L-*glycero*-L-*allo*-Lactone L-6. This was prepared from L-4 (2.2 g, 0.007 mol) and purified according to the previous procedure: yield 2.37 g (60%); colorless oil; $[\alpha]_D$ −51.03° (*c* 1.2, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, 25 °C) δ 4.47 (m, 1 H), 4.36 (m, 2 H), 3.8–4.3 (m, 4 H), 1.55 (s, 3 H), 1.51 (s, 3 H), 1.48 (s, 9 H), 0.23 (s, 9 H), 0.16 (s, 18 H); ^{13}C NMR (75.4 MHz, DMSO-d_6, 25 °C) δ 176.5, 155.1, 93.2, 79.6, 70.6, 68.9, 68.5, 64.1, 59.0, 27.9, 27.2, 2.1; MS *m*/*z* 563 (M^+). Anal. Calcd for $C_{24}H_{49}NO_8Si_3$: C, 51.12; H, 8.76; N, 2.48. Found: C, 51.18; H, 8.43; N, 2.35.

D-*glycero*-D-*allo*-Lactone D-6. This was prepared from L-4 (2.5 g, 0.008 mol) and purified according to the previous procedure: yield 2.75 g (61%); colorless oil; $[\alpha]_D$ +49.05° (*c* 1.57, $CHCl_3$). Anal. Calcd for $C_{24}H_{49}NO_8Si_3$: C, 51.12; H, 8.76; N, 2.48. Found: C, 51.21; H, 8.42; N, 2.85.

1,2,3,4-Tetra-*O*-acetyl-6,7-*N*,*O*-isopropylidene-6-deoxy-6-[(*tert*-butoxycarbonyl)amino]-α-L-*glycero*-L-*talo*-heptopyranose (L-7). To a stirred solution of the lactone L-5 (1.5 g, 2.6 mmol) in 50 mL of anhydrous CH_2Cl_2 was slowly added a 1 M solution of DIBALH in CH_2Cl_2 (7.9 mL, 7.9 mmol) via cannula at −90 °C. After the reaction was stirred at this temperature for 5 h, methanol (2 mL) and then sodium–potassium tartrate (2 g) and water (15 mL) were added and the mixture was stirred at room temperature overnight. The mixture was extracted with CH_2Cl_2 (3 × 15 mL), which was dried over $MgSO_4$ and then evaporated. The residue was dissolved in methanol (40 mL), and then solid citric acid (0.5 g) was added. After being stirred at room temperature for 3 h, the solvent was removed and the residue dissolved in pyridine (1.5 mL). To this solution Ac_2O (1.63 g, 0.016 mol) and a catalytic amount of DMAP (100 mg) were added, and the mixture was stirred at room temperature for 5 h. The solution was evaporated under reduced pressure, and the residue was chromatographed on silica (1:1 hexane/ethyl acetate) to afford 0.79 g (58% yield) of heptopyranose L-7 as a single α-anomer, an oil: $[\alpha]_D$ −79.13° (*c* 1.2, $CHCl_3$); ^1H NMR (300 MHz, C_6D_6, 65 °C) δ 6.33 (d, *J* = 0.8, 1 H, H-1), 5.53 (m, 1 H, H-4), 5.46 (t, *J* = 3.9, 1 H, H-3), 5.28 (ddd, *J* = 3.9, 1.5, 0.9, 1 H, H-2), 4.47 (bd, *J* = 4.6, 1 H, H-5), 4.25 (m, 2 H, H-6 and H-7a), 3.36 (dd, *J* = 9.0, 6.1, 1 H, H-7b), 1.96, 1.78, 1.73, and 1.62 (four s, each 3 H, OAc), 1.40 (m, 15 H, Me_2 and Bu^t); ^{13}C NMR (75.4 MHz, C_6D_6, 25 °C) δ 170.3, 169.8, 168.3, 153.3, 92.7, 80.7, 71.3, 67.6, 67.4, 66.4, 65.2, 57.6, 28.8, 28.7, 28.4, 25.3, 21.6, 20.9, 20.7, 20.4; MS *m*/*z* 517 (M^+). Anal. Calcd for $C_{23}H_{35}NO_{12}$: C, 53.38; H, 6.82; N, 2.71. Found: C, 52.85; H, 6.63; N, 2.83.

α-D-*glycero*-D-*talo*-Heptopyranose D-7. This was obtained by starting with D-5 (0.35 g, 0.62 mmol) according to the above protocol: yield 0.17 g (55%)' colorless oil; $[\alpha]_D$ +81.82° (*c* 0.66, $CHCl_3$). Anal. Calcd for $C_{23}H_{35}NO_{12}$: C, 53.38; H, 6.82; N, 2.71. Found: C, 54.01; H, 6.36; N, 2.93.

β-L-*glycero*-L-*allo*-Heptopyranose L-8. The reaction was conducted as described for L-7 by starting with 0.59 g (1.04 mmol) of lactone L-6. This furnished a crude product essentially consisting of a 72:28 mixture (^1H NMR), of the β- and α-anomers. The major less polar β-anomer was purified by flash chromatography (1:1 hexane/ethyl acetate) to afford pure L-8 (0.2 g) as a colorless oil: $[\alpha]_D$ −10° (*c* 4, $CHCl_3$); ^1H NMR (300 MHz, C_6D_6, 65 °C) δ 6.25 (d, *J* = 8.4, 1 H, H-1), 5.98 (t, *J* = 3.0, 1 H, H-3), 5.19 (dd, *J* = 8.7, 3.0, H-2), 4.96 (dd, *J* = 10.2, 3.0, 1 H, H-4), 4.30 (dd, *J* = 10.2, 3.2, 1 H, H-5), 4.21 (m, 1 H, H-6), 4.13 (dd, *J* = 9.6, 2.4, 1 H, H-7a), 3.78 (dd, *J* = 9.6, 6.6, 1 H, H-7b), 1.93, 1.84, 1.73, and 1.66 (four s, each 3 H, OAc), 1.42 (m, 15 H, Me_2 and Bu^t); ^{13}C NMR (75.4 MHz, C_6D_6, 65 °C) δ 170.1, 169.7, 169.6, 168.1, 150.4, 92.8, 80.7, 71.4, 69.2, 67.7, 67.3, 64.6, 58.4, 28.9, 28.8, 25.4, 21.3, 20.7, 20.6, 20.4; MS *m*/*z* 517 (M^+). Anal. Calcd for $C_{23}H_{35}NO_{12}$: C, 53.38; H, 6.82; N, 2.71. Found: C, 54.13; H, 6.41; N, 2.84.

β-D-*glycero*-D-*talo*-Heptopyranose D-8. This was obtained by starting with D-6 (0.5 g, 0.88 mmol) according to the above protocol: yield 0.13 g; colorless oil; $[\alpha]_D$ +15°. Anal. Calcd for $C_{23}H_{35}NO_{12}$: C, 53.38; H, 6.82; N, 2.71. Found: C, 52.79; H, 6.71; N, 2.62.

Methyl 1,2,3,4-Tetra-*O*-acetyl-6-deoxy-6-[(*tert*-butoxycarbonyl)amino]-α-L-*glycero*-L-*talo*-heptopyranuronate (L-9). Compound L-7 0.5 g, 0.97 mmol) was dissolved in 25 mL of 70% aqueous acetic acid, and the solution was allowed to stir at 60 °C until TLC indicated that the starting material was almost completely consumed with formation of a less mobile spot (ca. 6 h). The solvent was evaporated under vacuum, and the residue was dissolved in acetone (15 mL) and water (10 mL). Solid $NaIO_4$ (3.5 g, 1.6 mmol) was then added followed by $RuO_2 \cdot H_2O$ (30 mg). The mixture was stirred at room temperature for 3 h then quenched by addition of 5 mL of 2-propanol. The suspension was filtered through the Celite pad, and the filtrate was concentrated under vacuum to give the crude acid as a white foam. This was dissolved in Et_2O (20 mL) and treated with an excess of an ethereal diazomethane solution. The solution was concentrated under vacuum and the oily residue was flash chromatographed on silica gel, eluting with 1:1 hexane/ethyl acetate giving pure methyl ester L-9 (0.32 g, 66% yield) as a glass: $[\alpha]_D$ −60.07°

(c 1.5, $CHCl_3$); IR ($CHCl_3$) 3682, 1751, 1522, 1425 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, 25 °C) δ 6.08 (d, J = 1.2, 1 H, H-1), 5.39 (td, J = 3.8, 0.9, 1 H, H-4), 5.29 (t, J = 3.6, 1 H, H-3), 5.07 (ddd, J = 3.9, 1.5, 0.9, 1 H, H-2), 4.81 (d, J = 10.2, 1 H, NH), 4.67 (t, J = 9.6, 1 H, H-6), 4.11 (m, 1 H, H-5), 3.74 (s, 3 H, CO_2Me), 2.16, 2.15, 2.12, and 2.00 (four s, each 1 H, OAc), 1.39 (s, 9 H, Bu^t); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C) δ 171.5, 170.1, 169.8, 169.7, 167.7, 154.1, 91.3, 80.8, 71.3, 66.2, 65.3, 63.7, 52.7, 52.1, 28.1, 20.8, 20.6, 20.5, 20.4; MS m/z 505 (M^+). Anal. Calcd for $C_{21}H_{31}NO_{13}$: C, 49.90; H, 6.18; N, 2.77. Found: C, 50.07; H, 6.24; N, 2.91.

Methyl α-D-*glycero*-D-*talo*-Heptopyranuronate D-9. This was obtained by starting with D-7 (0.12 g, 0.23 mmol) according to the above three-reaction protocol: yield 75 mg (64%); glassy solid; $[\alpha]_D$ +59.06° (c 1.27, $CHCl_3$). Anal. Calcd for $C_{21}H_{31}NO_{13}$: C, 49.90; H, 6.18; N, 2.77. Found: C, 49.69; H, 6.34; N, 2.40.

Methyl β-L-*glycero*-L-*allo*-Heptopyranuronate L-10. The reaction was conducted as described for L-9 by starting with 0.15 g (0.29 mmol) of heptopyranose L-8. Flash chromatography eluting with 1:1 hexane/ethyl acetate gave 95 mg (65% yield) of pure L-10 as a glass: $[\alpha]_D$ −5.0° (c 0.47, $CHCl_3$); IR ($CHCl_3$) 3682, 1753, 1524, 1425 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, 25 °C) δ 5.93 (d, J = 9.0, 1 H, H-1), 5.70 (t, J = 3.0, 1 H, H-3), 5.08 (dd, J = 10.5, 2.7, 1 H, H-4), 4.96 (dd, 9.0, 2.8, 1 H, H-2), 4.58 (d, J = 6.6, 1 H, NH), 4.30 (dd, J = 10.5, 2.7, 1 H, H-5), 4.15 (dd, J = 6.5, 3.0, 1 H, H-6), 3.76 (s, 3 H, CO_2Me), 2.17, 2.16, 2.14, and 2.05 (four s, each 1 H, OAc), 1.46 (s, 9 H, Bu^t); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C) δ 172.43, 170.4, 169.,9, 168.8, 167.7, 154.2, 90.8, 81.2, 75.5, 66.4, 65.3, 63.4, 52.8, 52.3, 28.8, 20.8, 20.6, 20.5, 20.3; MS m/z 505 (M^+). Anal. Calcd for $C_{21}H_{31}NO_{13}$: C, 49.90; H, 6.18; N, 2.77. Found: C, 49.61; H, 6.40; N, 2.43.

Methyl β-D-*glycero*-D-*allo*-Heptopyranuronate D-10. This was obtained by starting with D-8 (100 mg, 0.19 mmol) according to the previous protocol: yield 63 mg (65%); a glass; $[\alpha]_D$ +5.6° (c 0.9, $CHCl_3$). Anal. Calcd for $C_{21}H_{31}NO_{13}$: C, 49.90; H, 6.18; N, 2.77. Found: C, 50.02; H, 6.06; N, 2.59.

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Registry No. 1, 61550-02-5; D-2, 95715-87-0; L-2, 102308-32-7; D-3, 127997-05-1; L-3, 131613-93-9; D-4, 127997-06-2; L-4, 131613-94-0; D-5, 135086-50-9; L-5, 136597-86-9; D-6, 136597-87-0; L-6, 136597-85-8; D-7, 135086-52-1; L-7, 136597-88-1; D-8, 136597-89-2; L-8, 136598-84-0; D-9, 135086-55-4; L-9, 136489-91-3; D-10, 136489-92-4; L-10, 136523-34-7; citric acid, 27-92-9.

Horsfiline, an Oxindole Alkaloid from *Horsfieldia superba*

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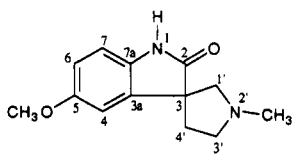
Horsfiline (1), a new oxindole alkaloid, was isolated from *Horsfieldia superba* together with the known alkaloids 6-methoxy-2-methyl-1,2,3,4-tetrahydro-β-carboline **2** and 5-methoxy-*N*,*N*-dimethyltryptamine. The structure of 1 was determined by spectral analysis and confirmed by partial synthesis from **2**.

Introduction

Several Myristicaceae are used as sources of intoxicating snuffs, and some of them have been shown to contain hallucinogenic alkaloids, especially those from *Virola*, which contain tryptamine derivatives.[1] The *Horsfieldia* genus, which encompasses several woody species growing in South East Asia, is sometime used as a medicinal plant.[2] Previous phytochemical investigations of the group led to isolation of trimyristin,[3] arylalkanones,[4] and lignans.[5,6] Alkaloids were not previously reported in the genus. From *H. superba*, a small tree indigenous to Malaysia, we isolated from the leaves three bases including a new oxindole alkaloid, horsfiline (1).



Horsfiline 1

Results and Discussion

Extraction of alkaloids was carried out in the usual way and the three main constituents of the alkaloid fraction were separated by column chromatography and further purified by TLC or crystallization. Two known compounds, 6-methoxy-2-methyl-1,2,3,4-tetrahydro-β-carboline (**2**) and 5-methoxy-*N*,*N*-dimethyltryptamine (**3**), were identified on the basis of their spectral data. Horsfiline (1) was obtained as colorless crystals from acetone, mp 125–126 °C, optically active, $[\alpha]^{20}_D$ −7.2° (MeOH).

The molecular formula $C_{13}H_{16}N_2O_2$ for horsfiline (1) was determined by HRMS. The ^{13}C NMR spectrum displayed signals of 13 carbon atoms: two methyl and three methylene groups, six sp^2 carbons, three among them protonated, one carbonyl at δ_C 183.32, and one quaternary carbon atom at δ_C 54.17 (Table I). The ^1H NMR spectrum revealed one methoxyl (δ_H 3.732) and one *N*-methyl group (δ_H 2.412), three aromatic protons of an ABX spin system, and six protons analyzed from the ^1H–^1H and ^1H–^{13}C COSY data as one methylene and two vicinal methylene groups; one exchangeable proton, detected at lower field (δ_H 9.52), was assigned to an NH group. The NMR chemical shifts of two of the three methylene groups in-

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