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Asymmetric Synthesis of 4-Amino-2,3,4-trideoxyaldonic Acids: Novel GABA *C*-Glycoconjugates

Gloria Rassu, Luigi Pinna, Pietro Spanu, Fausta Ulgheri, Mara Cornia, Franca Zanardi, and Giovanni Casiraghi*

Dipartimento di Chimica dell'Università and Istituto per l'Applicazione delle Tecniche Chimiche Avanzate del CNR, Via Vienna 2, I-07100 Sassari, Italy.

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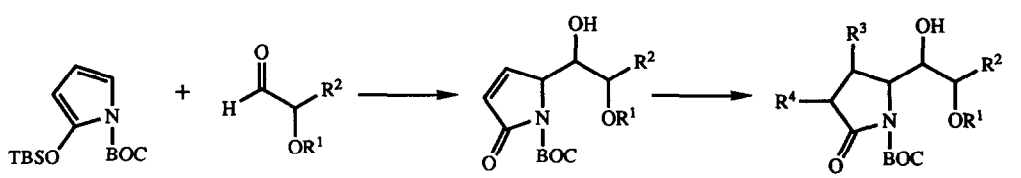
Abstract: *Stereochemically defined 4-amino-2,3,4-trideoxyaldonic acids* ***4****, representatives of a new progeny of C-glycosylated GABAs, have been synthesized from the readily available aldehydo precursors* ***1*** *in three steps and 60-75% overall yields. The key reaction is the $SnCl_4$-assisted regio- and diastereoselective homologation of* ***1*** *with the nitrogen-containing five-membered ring siloxydiene TBSOP.*

Hybrid structures with carbon-carbon joined amino acids and carbohydrates are often encountered in Nature as individual molecules[1] or as the core components of highly functionalized nucleoside antibiotics.[2] In connection with our approach to complex polyhydroxylated compounds, we recently introduced *N-tert*-butoxycarbonyl-2-(*tert*-butyldimethylsiloxy)pyrrole (TBSOP) as a tool to assemble nitrogen-containing carbohydrates and alkaloids.[3]

Scheme 1



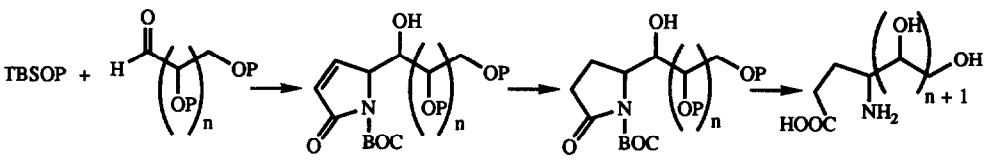
TBSOP A B C

As shown in Scheme 1, TBSOP reacts with aldehydo derivatives **A** in the presence of Lewis acids to give unsaturated and saturated lactams **B** and **C** which can be subsequently employed for a number of proposals, including synthesis of aracemic hydroxylated pyrrolidine[3a], pyrrolizidine,[3b] and indolizidine derivatives.[3c]

One possible application of products like **C** could be the hydrolitic ring opening to stereochemically defined 4-amino-2,3,4-trideoxyaldonic acids **4** which

can be envisioned as hybrids between a sugar (alditol) and γ-aminobutyric acid (GABA), an important neurotransmitter in mammalian systems.[4] Treatment of neurological disorders with GABA[5] is limited due to the inability of GABA to cross the blood-brain barrier efficiently;[6] conjugating in one molecule GABA with a sugar would result in novel hybrids with promising application in the GABA-related inhibitors domain. To this end, the three-step plan outlined in Scheme 2 was devised and executed.

Scheme 2



1 **2** **3** **4**

Regio- and diastereospecific homologation of aldehydo sugars **1a-e** with TBSOP was optimally performed in anhydrous diethyl ether in the presence of 1.5 equiv. of $SnCl_4$ at -85° C. This procedure led invariably to unsaturated lactams **2a-e** (77-90%) as enantiomerically pure compounds, as judged by ^1H NMR analyses of the respective crude reaction products (Table 1).

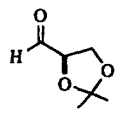
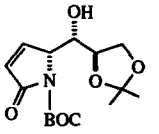
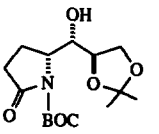
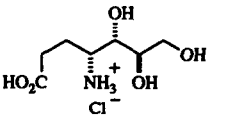
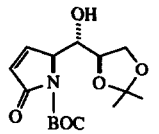
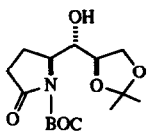
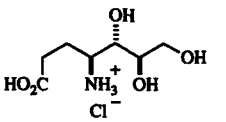
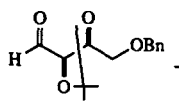
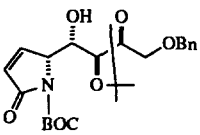
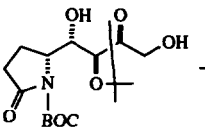
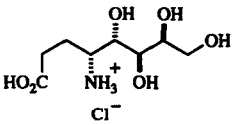
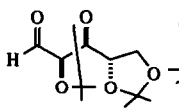
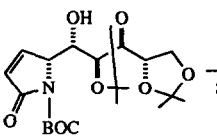
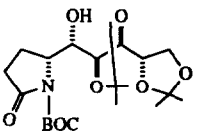
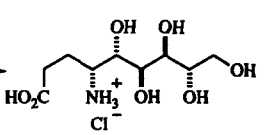
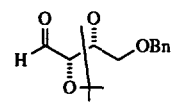
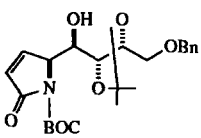
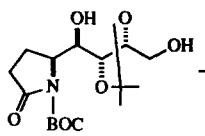
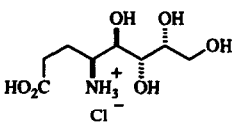
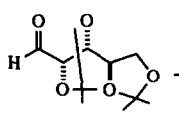
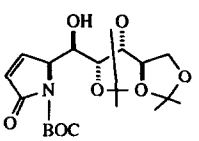
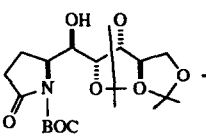
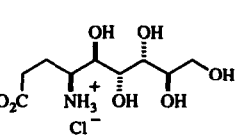
The success of this approach lies in the ability to transfer the chirality at C-2 in **1** to the centers at C-4 and C-5 in **2**. Indeed, 2*R*-configurated aldehydes **1a**, **1b**, and **1c**, gave rise to 4*R*,5*S*-configurated lactams **2a**, **2b**, and **2c**, exclusively, whereas 2*S*-configurated sugars **1d** and **1e** produced solely lactams with 4*S*,5*R* configuration, **2d** and **2e**.[7] Enhancing the synthetic scope of this chemistry, 4-*epi*-**2a**, having 4*S*,5*S* configuration, was easily obtained from **2a** (90%) via Et_3N-promoted C-4 epimerization; and this intermediate was subsequently exploited for the preparation of the corresponding 4-*epi* GABA derivative.

As a rule, irrespective of the side-chain substitution and chirality, 4*R*-configurated lactams show large dextrorotation while 4*S*-configurated compounds display large levorotation;[8] and this assumption allowed immediate configurational assignments for all the unsaturated intermediates **2** in Table 1. That 4*R* lactam **2a** and 4*S* lactam 4-*epi*-**2a** possess indeed the absolute configurations shown has been previously confirmed by single-crystal X-ray analyses.[3b]

Next, unsaturated lactams **2** were subjected to catalytic hydrogenation (Pd on carbon) at ambient temperature and pressure in NaOAc-buffered THF solutions. This reaction cleanly ensured double bond saturation with concomitant removal of the *O*-benzyl protecting groups (if present), affording saturated lactams **3** in excellent yields (84-95%).

The remaining step of the synthesis was straightforward. It is well known that 2-pyrrolidinone reacts with 6N HCl to give GABA.[9] This suggested direct hydrolitic ring opening of **3** with concomitant deprotection using this acidic medium; and this reaction (12 h at reflux) afforded the expected 4-amino-2,3,4-trideoxyaldonic acids **4** as hydrochloride salts in high yields (80-88%). Passage through basic DOWEX provided the corresponding free amino acids, but also gave 5-substituted-2-pyrrolidinones as substantial (20-35%) by-products.

Table 1. Synthesis of *C*-Glycosylated γ-Aminobutyric Acids **4**[a]

Entry/ Series	Aldehydo Sugar (1)	Unsaturated Lactam (2)	Saturated Lactam (3)	*C*-Glycosyl GABA (4)
a				
4-*epi*-a				
b				
c				
d				
e				

[a]**Conditions**: (i) 1.0 equiv. TBSOP, 1.5 equiv. $SnCl_4$, Et_2O, -85°C; (ii) 10% Pd-C, THF, NaOAc, r.t.; (iii) 6N HCl, reflux; (iv) Et_3N, DMAP, CH_2Cl_2, r.t.

In summary, this paper describes the preparation of 4-amino-2,3,4-trideoxyaldonic acids, a novel progeny of *C*-glycosylated GABAs, by a short sequence and good overall yields. The chemistry herein sets the stage for the synthesis of many other analogues of GABA-related *C*-glycosyl-γ-amino acids, by adopting a strategy which meet the criteria of atom economy and synthetic efficiency. Introduction of oxygen functionalities in the unsaturated five-membered ring of **2** could provide an eventual entry to statine-related glycoconjugates.

EXPERIMENTAL SECTION

Materials. *N*-(*tert*-Butoxycarbonyl)-2-(*tert*-butyldimethylsiloxy)pyrrole (TBSOP) was prepared on a multigram scale from pyrrole following the procedure recently reported by us.[3a,b] 2,3-*O*-Isopropylidene-4-*O*-benzyl-L- and D-threose (**1b** and **1d**) were prepared from diethyl-L- and D-tartrate via the corresponding 2,3-*O*-isopropylidenethreitols.[10] 2,3;4,5-Di-*O*-isopropylidene-L- and D-arabinose (**1c** and **1e**) were prepared from the corresponding sugars via dithioacetal formation, acetonidation, and liberation of the aldehyde function, by following the procedures of Zinner.[11]

***N*-*tert*-Butoxycarbonyl-6,7-*O*-isopropylidene-2,3-dideoxy-D-*arabino*-hept-2-enono-1,4-lactam (2a)** (Typical Condensation Procedure). To a solution of 2,3-*O*-isopropylidene-D-glyceraldehyde (**1a**) (3.0 g, 23 mmol) in anhydrous Et_2O (150 mL), TBSOP (6.8 g, 23 mmol) and $SnCl_4$ (1M in CH_2Cl_2, 34 mL, 34 mmol) were added under argon at -85°C. The mixture was stirred at this temperature for 3 h then a saturated aqueous $NaHCO_3$ solution was added at -85°C and, after ambient temperature was reached, the resulting mixture was extracted with Et_2O (3x30 mL). After drying ($MgSO_4$), the solution was evaporated under reduced pressure and the crude product was crystallized from CH_2Cl_2/hexane: 2.9 g (80%), white solid, mp 138-140 °C; $[\alpha]_D$ +197.59° (*c* 0.83, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.43 (dd, 1H, *J*=6.3, 2.1 Hz, H-3), 6.13 (dd, 1H, *J*=6.3, 1.5 Hz, H-2), 4.81 (dt, 1H, *J*=5.7, 2.4 Hz, H-4), 4.09 (ddd, 1H, *J*=6.0 , 5.7, 3.9 Hz, H-5), 4.01 (q, 1H, *J*=6.0, H-6), 3.94 (dd, 1H, *J*=8.1, 6.0 Hz, H-7a), 3.86 (dd, 1H, *J*=8.1, 6.0 Hz, H-7b), 3.63 (d, 1H, *J*=3.9 Hz, OH), 1.57 (s, 9H, Bu^t), 1.37 and 1.32 (2s, each 3H, Me); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 168.90, 150.91, 148.23, 126.94, 109.23, 83.79, 75.63, 72.59, 66.43, 65.57, 27.99, 26.40, 25.08. Anal. Calcd for $C_{15}H_{23}NO_6$: C, 57.15; H, 7.40; N, 4.47. Found: C, 56.93; H, 7.35; N, 4.32.

By following exactly the above protocol, the following unsaturated lactams **2b-e** were prepared from the corresponding aldehydo sugars **1b-e**:

***N*-*tert*-Butoxycarbonyl-6,7-*O*-isopropylidene-8-*O*-benzyl-2,3-dideoxy-L-*galacto*-oct-2-enono-1,4-lactam (2b)**. Yield 90%, colorless oil; $[\alpha]_D$ + 134.66° (*c* 0.88, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.2-7.4 (m, 6H, CH_2Ph and H-3), 6.12 (dd, 1H, *J*=6.0, 1.8 Hz, H-2), 4.77 (dt, 1H, *J*=4.8, 1.8 Hz, H-4), 4.58 (m, 2H, CH_2Ph), 4.30 (d, 1H, *J*=3.0 Hz, OH), 4.14 (ddd, 1H, *J*=9.0, 5.1, 3.3 Hz, H-5), 4.07 (td, 1H, *J*=6.9, 4.5 Hz, H-7), 3.73 (dd, 1H, *J*=9.3, 4.5 Hz, H-8a), 3.53 (dd, 1H, *J*=9.0, 6.9 Hz, H-6), 3.50 (dd, 1H, *J*=9.3, 6.9 Hz, H-8a), 1.53 (s, 9H, Bu^t), 1.31, 1.29 (2s, each 3H, Me); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 169.06, 150.31, 147.38, 136.78, 128.49, 128.09, 127.90, 127.65, 109.86, 82.99, 79.56, 78.93, 73.83, 72.38, 70.54, 65.65, 28.05, 26.52. Anal. Calcd. for $C_{23}H_{31}NO_7$: C, 63.73; H, 7.21; N, 3.23. Found: C, 63.90; H, 7.19; N, 3.29.

***N*-*tert*-Butoxycarbonyl-6,7;8,9-di-*O*-isopropylidene-2,3-dideoxy-L-*glycero*-L-*galacto*-non-2-enono-1,4-lactam (2c).** Yield 79%; white solid, mp 147-149°C; $[\alpha]_D$ +128.48° (*c* 1.12, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ7.39 (dd, 1H, *J*=6.0, 2.1 Hz, H-3), 6.19(dd, 1H, J=6.0, 1.8 Hz, H-2), 4.83 (dt, 1H, *J*=4.2, 2.1 Hz, H-4), 4.32 (ddd, 1H, *J*=9.0, 4.2, 1.8 Hz, H-5), 4.26 (d, 1H, *J*=1.8, OH), 4.02 (m, 3H, H-6, H-7 and H-8), 3.72(m, 1H, H-9a), 3.55(m, 1H, H-9b), 1.56(s, 9H, Bu^t), 1.48, 1.38, 1.31, 1.26 (4s, each 3H, Me); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 169.58, 150.12, 147.33, 128.75, 110.85, 110.58, 83.06, 82.15, 80.75, 77.84, 71.44, 68.35, 65.60, 28.56, 26.93, 26.78, 26.67, 25.35. Anal. Calcd for $C_{20}H_{31}NO_8$: C, 58.10; H, 7.56; N, 3.39. Found: C, 57.82; H, 7.45; N, 3.50.

***N*-*tert*-Butoxycarbonyl-6,7-*O*-isopropylidene-8-*O*-benzyl-2,3-dideoxy-D-*galacto*-oct-2-enono-1,4-lactam (2d).** Yield 88%, a syrup; $[\alpha]_D$ -133.9° (*c* 0.9, $CHCl_3$); ^1H and ^{13}C NMR identical to those reported for its enantiomer **2b**. Anal. Calcd. for $C_{23}H_{31}NO_7$: C, 63.73; H, 7.21; N, 3.23. Found: C, 63.80; H, 7.16; N, 3.25.

***N*-*tert*-Butoxycarbonyl-6,7;8,9-di-*O*-isopropylidene-2,3-dideoxy-D-*glycero*-D-*galacto*-non-2-enono-1,4-lactam (2e).** Yield 81%, white solid, mp 150-152°C; $[\alpha]_D$=-127.90° (*c* 1.7, $CHCl_3$); ^1H and ^{13}C NMR identical to those reported for its enantiomer **2c**. Anal. Calcd. for $C_{20}H_{31}NO_8$: C, 58.10; H, 7.56; N, 3.39. Found: C, 58.22; H, 7.50; N, 3.45.

***N*-*tert*-Butoxycarbonyl-6,7-*O*-isopropylidene-2,3-dideoxy-D-*ribo*-hept-2-enono-1,4-lactam (4-*epi*-2a).** Lactam **2a** (2.0 g, 6.4 mmol) was dissolved in CH_2Cl_2 (15 mL), then Et_3N (2.0 mL) and *N*,*N*-dimethylaminopyridine (200 mg) were added. The solution was stirred at room temperature for 5 h, water (10 mL) was added and the mixture was extracted with CH_2Cl_2 (3x30 mL). The combined extracts, dried over $MgSO_4$, were evaporated under vacuo. The crude product was purified by flash chromatography on SiO_2 (EtOAc/MeOH 98:2): 1.8 g (90%); white solid, mp 118-120°C; $[\alpha]_D$ -119.7° (*c* 0.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.29 (dd, 1H, *J*=6.3, 2.1 Hz, H-3), 6.16 (dd, 1H, *J*=6.3, 2.0 Hz, H-2), 4.97 (q, 1H, *J*=2.1 Hz, H-4), 4.20 (m, 1H, H-6), 4.15 (td, 1H, *J*=6.6, 2.2 Hz, H-5), 4.03 (m, 2H, H_2-7), 3.49 (d, 1H, *J*=6.6 Hz, OH), 1.56 (s, 9H, Bu^t), 1.46 and 1.37 (2s, each 3H, Me); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 169.98, 149.67, 147.24, 128.01, 109.90, 83.50, 76.27, 71.40, 67.89, 65.07, 28.07, 26.70, 24.50. Anal. Calcd for: $C_{15}H_{23}NO_6$: C, 57.15; H, 7.40; N, 4.47. Found: C, 57.03; H, 7.30; N, 4.25.

***N*-*tert*-Butoxycarbonyl-6,7-*O*-isopropylidene-2,3-dideoxy-D-*arabino*-heptono-1,4-lactam (3a)** (Typical Reduction Procedure). A solution of **2a** (1.42 g, 4.54 mmol) in THF (50 mL) was hydrogenated in the presence of 10% Pd on carbon (150 mg) and NaOAc (200 mg) at room temperature for 24 h. After the catalyst was filtered, the solution was evaporated and the crude product was purified by flash chromatography on silica gel (AcOEt/hexane 8/2): 1.31 g (92%), white solid, mp 99-103°C; $[\alpha]_D$ +59.24° (*c* 1.26, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 4.31 (ddd, 1H, *J*=5.7, 5.4, 3.9 Hz, H-4), 4.05 (m, 2H, H-7a and H-7b), 3.97 (ddd, 1H, *J*=5.5, 4.8, 1.2 Hz, H-6), 3.69 (q, 1H, *J*=5.7 Hz, H-5), 3.54 (d, 1H, *J*=6.3 Hz, OH), 2.71 (dt, 1H, *J*=17.1, 10.5 Hz, H-2a), 2.32 (ddd, 1H, *J*=17.7, 6.0, 4.8 Hz, H-2b), 2.10 (m, 2H, H-3a and H-3b), 1.48 (s, 9H, Bu^t), 1.36, 1.30 (2s, each 3H, Me); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 174.52, 151.73, 109.39, 83.60, 77.74, 74.48, 66.80, 60.36, 31.96, 27.99, 26.56, 25.07, 21.71. Anal. Calcd. for $C_{15}H_{25}NO_6$: C, 57.13; H, 7.99; N, 4.44. Found C, 57.26; H, 8.15; N, 4.59.

By using this same reduction protocol, the following saturated lactams **3b-e** and 4-*epi*-**3a** were produced by starting with **2b-e** and 4-*epi*-**2a**, respectively:

***N*-*tert*-Butoxycarbonyl-6,7-*O*-isopropylidene-2,3-dideoxy-L-*galacto*-octono-1,4-lactam (3b).** Yield 95%, colorless oil; $[\alpha]_D$ +45.83° (*c* 0.24, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 4.37 (ddd, 1 H, *J*=8.1, 5.7, 1.8 Hz, H-4), 4.08 (td, 1 H, *J*=6.3, 6.3, 3.9 Hz, H-7), 3.86 (dd, 1 H, *J*=11.7, 3.9 Hz, H-8a), 3.70-3.81 (m, 3 H, H-5, H-6, H-8b), 2.66 (ddd, 1 H, *J*=16.2, 12.0, 9.0 Hz H-2a), 2.37 (ddd, 1 H, *J*=17.7, 9.0, 1.5 Hz, H-2b), 2.07- 2.28 (m, 2 H, H-3a and H-3b), 1.52 (s, 9H, Bu^t), 1.41, 1.39 (2s, each 3H, CH_3). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 174.90, 151.76, 109.54, 83.62, 80;93, 79.34, 74.29, 63.07, 61.20, 31.81, 27.97, 26.82, 26.68, 20.87. Anal. Calcd. for $C_{16}H_{27}NO_7$: C, 55.62; H, 7.88; N, 4.06. Found: C, 55.38; H, 7.76; N, 4.04.

***N*-*tert*-Butoxycarbonyl-6,7;8,9-di-*O*-isopropylidene-2,3-dideoxy-L-*glycero*-L-*galacto*-nonono-1,4-lactam (3c).** Yield 87%, white solid, mp 103-105°C; $[\alpha]_D$ +24.32° (*c* 0.93, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 4.45 (m, 1H, H-4), 4.22 (d, 1H *J*=2.7 Hz, OH), 4.04 (m, 2H), 3.91 (m, 2H), 3.76 (m, 2H), 2.67 (m, 1H, H-2a), 2.38 (m, 1H, H-2b), 2.13 (m, 2H, H-3a and H-3b), 1.52 (s, 9H, Bu^t), 1.46, 1.37, 1.34, 1.32 (4s, each 3H, Me); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 175.21, 152.00, 110.46, 110.04, 82.52, 81.93, 80.28, 76.28, 72.93, 68.03, 59.57, 32.07, 28.01, 26.47, 26.25, 24.92, 19.93. Anal. Calcd. for: $C_{20}H_{33}NO_8$: C, 57.82; H, 8.01; N, 3.37. Found: C, 58.03; H, 7.95; N, 3.32.

***N*-*tert*-Butoxycarbonyl-6,7-*O*-isopropylidene-2,3-dideoxy-D-*galacto*-octono-1,4-lactam (3d).** Yield 91%, colorless oil; $[\alpha]_D$ -45.6° (*c* 0.2, $CHCl_3$); ^1H and ^{13}C NMR identical to those reported for its enantiomer **3b**. Anal. Calcd. for $C_{16}H_{27}NO_7$: C, 55.62; H, 7.88; N, 4.06. Found: C, 55.58; H, 7.92; N, 4.14.

***N*-*tert*-Butoxycarbonyl-6,7;8,9-di-*O*-isopropylidene-2,3-dideoxy-D-*glycero*-D-*galacto*-nonono-1,4-lactam (3e).** Yield 88%, white solid, mp 106-108°C; $[\alpha]_D$ -24.70° (*c* 1.05, $CHCl_3$); ^1H and ^{13}C NMR identical to those reported for its enantiomer **3c**. Anal. Calcd. for $C_{20}H_{33}NO_8$: C, 57.82; H, 8.01; N, 3.37. Found: C, 57.75; H, 7.80; N, 3.40.

***N*-*tert*-Butoxycarbonyl-6,7-*O*-isopropylidene-2,3-dideoxy-D-*ribo*-hepto-no-1,4-lactam** (4-*epi*-**3a**). Yield 84%, white solid, mp 176-178°C; $[\alpha]_D$ -40.46° (*c* 1.48, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 4.42 (d, 1H, *J*=9.3 Hz, OH), 4.17 (dd, 1H, *J*=6.9, 5.4 Hz), 3.98 (m, 4H), 2.77 (dt, 1H, *J*=17.7, 10.5 Hz, H-2a), 2.33 (ddd, 1H, *J*=18.0, 10.5, 1.8 Hz, H-2b), 2.06 (m, 2H, H-3a and H-3b), 1.52 (s, 9H, Bu^t), 1.43, 1.35 (2s, each 3H, Me). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 176.27, 150.02, 109.54, 83.02, 75.39, 73.42, 67.79, 59.78, 32.48, 28.03, 26.61, 25.00, 17.65. Anal. Calcd. for $C_{15}H_{25}NO_6$: C, 57.13; H, 7.99; N, 4.44. Found: C, 57.40; H, 8.10; N, 4.50.

4-Amino-2,3,4-trideoxy-D-*arabino*-heptonic Acid Hydrochloride (4a) (Typical Ring-Opening Procedure). A suspension of **3a** (1.4 g, 4.44 mmol) in 10% aqueous HCl (20 mL) was refluxed for 12h. The clear solution was cooled to room temperature and the solvent was evaporated under reduced pressure to give a brown oil. The oil was dissolved in 30 mL of water, refluxed for 10 min with about 2 g of activated charcoal, and filtered. Evaporation of the water under reduced pressure gave 0.83 g of **4a** (81%) as a white solid, mp 210°C (dec); $[\alpha]_D$ -1.25° (*c* 0.80, H_2O); ^1H NMR (300 MHz, D_2O) δ 3.95 (m, 1H), 3.65 (m, 1H), 3.49 (m, 3H), 2.35 (m, 2H, H-2a and H-2b), 2.20 (m, 1H, H-3a), 1.89 (m, 1H, H-3b); ^{13}C NMR (75.4 MHz, D_2O) δ 181.57, 71.78, 70.86, 61.66, 55.35, 29.00, 21.99; IR (KBr) 3402,

3144, 2359, 2340, 1721, 1618 cm-1. Anal. Calcd. for $C_7H_{16}ClNO_5$: C, 36.61; H, 7.02; N, 6.10. Found: C, 36.52; H, 7.10; N, 6.15.

The following amino acids **4b-e** and 4-*epi*-**4a** were prepared by the same above procedure by starting with the corresponding lactams **3b-e** and 4-*epi*-**3a**:

4-Amino-2,3,4-trideoxy-L-*galacto*-octonic Acid Hydrochloride (4b). Yield 88%, a glass; $[\alpha]_D$ -2.78° (*c* 0.76, H_2O); ^1H NMR (300 MHz, D_2O) δ 4.2-3.5 (m, 6H), 2.52 (m, 2H), 1.93 (m, 2H); ^{13}C NMR (75.4 MHz, D_2O) δ 174.05, 73.70, 70.77, 68.10, 60.16, 49.06, 26.94, 21.99; IR (KBr) 3404, 3155, 1736, 1618 cm-1. Anal. Calcd. for $C_8H_{18}ClNO_6$: C, 37.00; H, 6.99; N, 5.39. Found: C, 37.10; H, 7.05; N, 5.50.

4-Amino-2,3,4-trideoxy-L-*glycero*-L-*galacto*-nononic Acid Hydrochloride (4c). Yield 86%, a foam, mp 98-100°C; $[\alpha]_D$ -5.97 (*c* 1.17, H_2O); ^1H NMR (300 MHz, D_2O) δ 4.5-4.0 (m, 2H), 3.5-4.0 (m, 5H), 2.5 (m, 2H), 2.0 (m, 2H); ^{13}C NMR (75.4 MHz, D_2O) δ 174.05, 68.00, 66.65, 66.40, 65.06, 60.27, 49.06, 26.94, 22.00; IR (KBr) 3397, 2923, 1725, 1624 cm-1. Anal. Calcd for $C_9H_{20}ClNO_7$: C, 37.31; H, 6.96; N, 4.83. Found: C, 37.44; H, 7.05; N, 4.78.

4-Amino-2,3,4-trideoxy-D-*galacto*-octonic Acid Hydrochloride (4d). Yield 87%, a glass; $[\alpha]_D$ +2.65 (*c*, 0.82, H_2O); IR, ^1H NMR, and ^{13}C NMR identical to those reported for its enantiomer **4b**. Anal. Calcd. for $C_8H_{18}ClNO_6$: C, 37.00; H, 6.99; N, 5.39. Found: C, 36.95; H, 7.02; N, 5.28.

4-Amino-2,3,4-trideoxy-D-*glycero*-D-*galacto*-nononic Acid Hydrochloride (4e). Yield 83%, a foam; $[\alpha]_D$ +5.72° (*c* 0.98, H_2O); IR, ^1H NMR, and ^{13}C NMR identical to those reported for its enantiomer **4c**. Anal. Calcd. for $C_9H_{20}ClNO_7$: C, 37.31; H, 6.96; N, 4.83. Found: C, 37.28; H, 6.93; N, 4.86.

4-Amino-2,3,4-trideoxy-D-*ribo*-heptonic Acid Hydrochloride (4-*epi*-4a). Yield 80%, a glass, $[\alpha]_D$ -4.50° (*c* 1.40, H_2O); ^1H NMR (300 MHz, D_2O) δ 4.0-4.4 (m, 1H), 3.57 (m, 4H), 2.49 (m, 2H), 1.79-2.00 (m, 2H); ^{13}C NMR (75.4 MHz, D_2O) δ 175.37, 71.95, 70.58, 63.36, 53.28, 30.82, 22.01; IR (KBr) 3402, 3150, 2368, 2350, 1720, 1620 cm-1. Anal. Calcd. for $C_7H_{16}ClNO_5$: C, 36.61; H, 7.02; N, 6.10. Found: C, 36.58; H, 7.09; N, 6.07.

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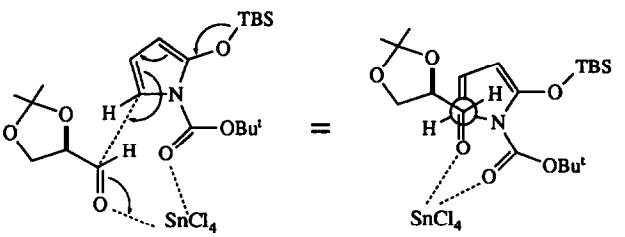
7. A chelate transition state model, $TS_A^{\neq} = TS_{A'}^{\neq}$, between **1a** and TBSOP can be suggested accounting for the observed diastereoselective behaviour:



$TS_A^{\neq}$ $TS_{A'}^{\neq}$

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