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THE TOTAL SYNTHESIS OF L-DAUNOSAMINE

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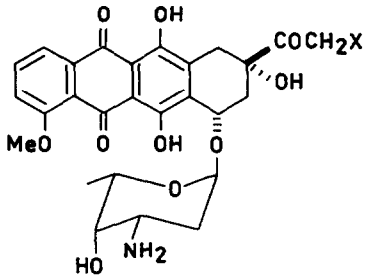
Abstract - *N,O*-Dibenzyl-*N*-*tert*-butoxycarbonyl-L-homoserinal (**7**), obtained from L-aspartic acid, reacts with vinylmagnesium chloride to afford with high stereoselectivity compound **6** which is subsequently transformed into the derivative of L-daunosamine **15**.

L-Daunosamine, a naturally occurring 2,3,6-trideoxy-3-aminohexose, is an important component of the anthracycline antibiotics daunorubicin (**1**) and adriamycin (**2**), exhibiting high activity against a wide range of solid tumors and soft tissue sarcomas.[1-3]

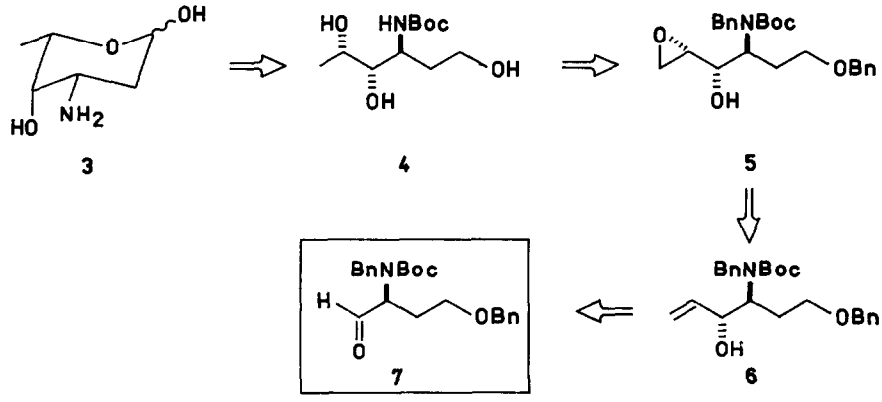


1; X=H
2; X=OH

The importance of the anthracycline antibiotics as antineoplastic agents and the high cost of the microbially produced antibiotics containing L-daunosamine have been the major factors contributing to the great synthetic interest in this sugar.[4,5]

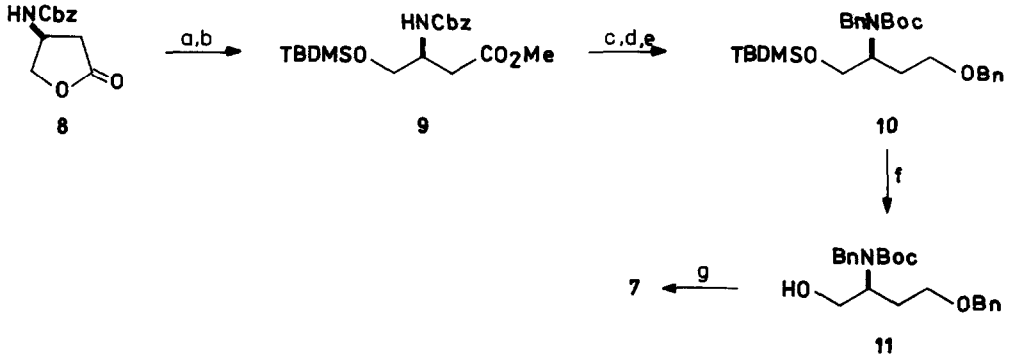
During our studies on applications of *N*-protected α-amino aldehydes in organic synthesis we have found that they are very convenient and versatile chirons.[6] For example, addition of furyllithium to variously *N,N*-diprotected D-alaninals opens a highly stereoselective route to aminosugar precursors - chiral uloses.[7] On the other hand, Reetz *et al.* have recently demonstrated high stereoselectivity in additions of a variety of metalloorganic reagents,[8] trimethylsilylcyanide,[9] and lithiated heterocycles[10] to *N,N*-dibenzyl α-amino aldehydes.

Now we report a new application of this methodology for the total synthesis of L-daunosamine. Retrosynthetic analysis shown in Scheme 1 suggests that *N,O*-dibenzyl-*N*-*tert*-butoxycarbonyl-L-homoserinal (**7**) could serve as a starting material.



Scheme 1

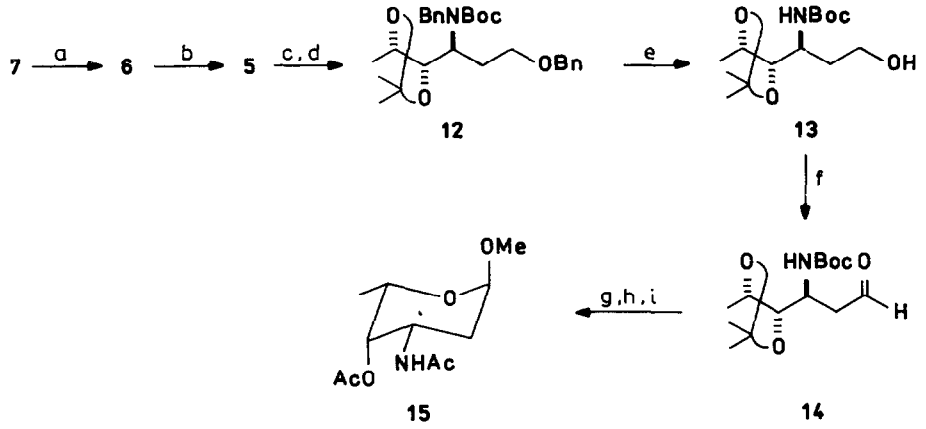
Compound **7** was prepared from lactone **8** by the reaction sequence shown in Scheme 2. The starting lactone **8** was obtained from L-aspartic acid in two steps by literature methods.[11-13] Transesterification of **8** with methanol, followed by protection of the hydroxy group led to compound **9**. The *N*-carbobenzoxy protecting group was then transformed into the *N-tert*-butoxycarbonyl one,[14] and reduction of the ester group, followed by benzylation afforded product **10**. Cleavage of the silyl functionality and subsequent oxidation[15] led to the key derivative **7** of L-homoserinal.



Scheme 2. Reagents and reaction conditions: (a) DCC, MeOH, RT, 5 days, 83%; (b) TBDMSCl, imidazole, DMF, 40°C, 2h, 94%; (c) H_2, 5% Pd/C, $(Boc)_2O$, MeOH, RT, 12h, 98%; (d) $LiAlH_4$, Et_2O, -25°C, 1h, 82%; (e) BnBr, NaH, DMF, -10°C → RT, 2h, 74%; (f) Bu_4NF, THF, RT, 0.5h, 97%; (g) SO_3/Py, DMSO, RT, 0.5h, 95%

The addition reaction of vinylmagnesium chloride to homoserinal **7** afforded the expected adduct **6** with an excellent *anti*-diastereoselectivity (Scheme 3). Epoxidation of the chromatographically pure allylic alcohol **6** gave as a single product the epoxide **5** of

syn-configuration.[16] Reductive ring-opening of the epoxide **5**, followed by protection of the resulting 1,2-diol system afforded the isopropylidene derivative **12**. Chromatographically pure compound **12** was treated with sodium in liquid ammonia to give alcohol **13** which was then subjected to oxidation with the sulphur trioxide - pyridine complex,[6] furnishing the aldehyde **14**. Final treatment of compound **14** with methanolic hydrochloride, followed by acetylation, led to a mixture of methyl α- and β-glycosides of *N*,*O*-diacetyl-L-daunosamine in a 95:5 ratio. The α-glycoside **15** has, after chromatographic purification, mp 186 - 187°C and $[\alpha]_D$ -207° (*c* 1.3, $CHCl_3$); lit.[17] mp 188 - 189°C and $[\alpha]_D$ -202° (*c* 1.0, $CHCl_3$).



Scheme 3. Reagents and reaction conditions: (a) vinylMgCl, Et_2O, -78°C, 1h, 82%; (b) mCPBA, CH_2Cl_2, +5°C, 4 days, 70%; (c) DIBAL, Et_2O, -78 → -40°C, 1.5h, 78%; (d) DMP, acetone, *p*-TsOH, 0 → 15°C, 1h, 91%; (e) Na, NH_3(liq.), 0.5h, 92%; (f) SO_3·Py, DMSO, RT, 0.5h, 96%; (g) HCl/MeOH (pH≈1), RT, 12h, 91%; (h) Ac_2O/Py, RT, 12h, 93%; (i) Column chromatography, Kieselgel 60, 230-400 mesh, Merck, hexane - ethyl acetate - methanol 6:4:1.

The presented total synthesis of L-daunosamine proves to be a practical alternative to the known approaches.[4,5,18] Moreover, it exemplifies the usefulness of *N*-protected α-amino aldehydes in the synthesis of natural products.

Experimental

^1H NMR spectra were recorded with a Varian-GEMINI (200 MHz) or a Bruker AM-500 (500 MHz) spectrometer for $CDCl_3$ solutions (δ scale, TMS=0). ^{13}C NMR spectra were measured at 50 MHz with a Varian-GEMINI spectrometer. The IR spectra were taken with a Beckman IR-4240 spectrophotometer. Optical rotations were determined using JASCO D/P-360 spectropolarimeter. High-resolution mass spectra were recorded with an AMD 604 spectrometer (70

eV).

Column chromatography was performed according to the method described by Still et al.[19] on Merck Kieselgel 60 (230-400 mesh). All the reactions were followed by TLC using Merck DC Alufolien Kieselgel 60 F-254. The reported yields refer to chromatographically pure compounds.

3(*S*)-Benzyloxycarbonylamino-4-*tert*-butyldimethylsilyloxypropancarboxylic acid methyl ester (9). Lactone **8** (500 mg, 2 mmol) was dissolved in methanol (10 mL) and dicyclohexylcarbodiimide (490 mg, 2.2 mmol) was added. The reaction mixture was kept at ambient temperature for 3 days. After evaporation of the solvent under reduced pressure, the residue was dissolved in ethyl acetate (20 mL) and passed through a short column of silica gel. The solution was evaporated to dryness, and the residue was dissolved in DMF (20 mL). Then imidazole (272 mg, 4 mmol) and *tert*-butyldimethylsilyl chloride (452 mg, 3 mmol) were added. The reaction mixture was stirred at 40°C for 2 h and then it was diluted with ethyl ether (100 mL) and washed with 2N HCl (2 x 50 mL), water (2 x 50 mL), and brine (30 mL). The solution was dried over $MgSO_4$, filtered, evaporated and chromatographed, yielding ester **9** (650 mg, 85%) as colorless oil: $[\alpha]_D^{23}$ -4.1° (c 1.0, $CHCl_3$). HR MS M^+ found 381.19659. $C_{19}H_{31}NO_5Si$ requires 381.19709. M^+-OMe found 350.1740. $C_{18}H_{28}NO_4Si$ requires 350.1780. ^1H NMR (500 MHz): 7.35-7.25 (m, 5H), 5.38 (bd, J=8.6 Hz, 1H), 5.14 (s, 2H), 4.09 (m, 1H), 3.72-3.60 (m, 5H), 2.68-2.60 (m 2H), 0.85 (s, 9H), 0.01 (s, 6H). ^{13}C NMR (50 MHz): 172.1, 155.9, 136.6, 128.6, 128.2, 66.6, 63.8, 51.5, 49.2, 35.2, 25.6, 18.0, -5.9. IR, ν (cm^{-1}): 3560, 3100-2880, 1740, 1720, 1515, 1260, 1220, 1120.

2(*S*)-(*N*-Benzyl-*N*-*tert*-butyloxycarbonyl)amino-4-benzyloxy-1-*tert*-butyldimethylsilyloxybutane (10). Di-*tert*-butyldicarbonate (850 mg, 3.9 mmol) and ester **9** (1.40 g, 3.5 mmol) were dissolved in methanol (20 mL) and 5% Pd-C catalyst (0.5 g) was added. The mixture was hydrogenated at ambient temperature for 8 h. The catalyst was filtered off, and the filtrate was evaporated under reduced pressure. The residue containing crude NH-Boc derivative of ester **9** was dissolved in dry ethyl ether (15 mL) and cooled down under argon stream to -25°C (CO_2/CCl_4-bath), and lithium aluminum hydride (130 mg, 3.5 mmol) was added in small portions. Reduction was carried out at 0°C for complete conversion of substrate (TLC, 2 h.). An excess of hydride was quenched with methanol (ca. 2mL), and the mixture was treated with saturated solution of sodium-potassium tartrate (20 mL). After 2 h. of vigorous stirring, the organic layer was separated, washed with water (10 mL), brine (10 mL), and dried ($MgSO_4$). After filtration, the solution was evaporated, and the residue was dissolved in dry DMF (10 mL). The solution was cooled down under argon (-10°C), and 50% NaH suspension in mineral oil (504 mg, 10.5 mmol) was added. The reaction mixture was warmed up and stirred at room temperature for 2 h. An excess of hydride was quenched with methanol, and the reaction mixture was diluted with water (100 mL). Product was extracted with ethyl ether (3 x 50 mL), and combined organic extracts were washed with water (2 x 30 mL), brine (30 mL), dried over $MgSO_4$, and evaporated under reduced pressure. Chromatographic purification gave **10** (1.14 g, 65%) as pale-yellow oil: $[\alpha]_D^{25}$ -8.8° (c 0.9,

$CHCl_3$). Anal. calcd for $C_{29}H_{45}NO_4Si$:C, 69.70; H, 9.08; N, 2.80. Found: C, 69.58; H, 9.12; N, 2.73. ^1H NMR (500 MHz, 25°C): 7.35-7.19 (m, 10H), 4.53-4.29 (m, 4H), 3.84-3.54 (m, 3H), 3.43-3.21 (m, 2H), 1.89 (dbt, J_1=6.5, J_2=43.3 Hz, 2H), 1.42 (bd, J=73.8 Hz, 9H), 0.85 (s, 9H), -0.03 (s, 6H). ^1H NMR (500 MHz, 60°C): 7.46-6.98 (m, 10H), 4.52 (bs, 1H), 4.31 (s, 2H), 3.82 (bs, 1H), 3.41 (bt, J=5.6 Hz, 1H), 2.18 (s 2H), 2.05-1.98 (m, 2H), 1.52-1.30 (m, 2H), 1.46 (s, 9H), 0.98 (s, 9H), 0.05 (s, 6H). ^{13}C NMR (50 MHz): 138.6, 128.4, 128.3, 127.8, 127.6, 72.8, 67.6, 64.3, 56.5, 50.0, 29.5, 28.2, 25.7, 18.0, -5.8. IR, ν (cm^{-1}): 3100-2880, 1705, 1465, 1380, 1260, 1180, 1110.

***N*-Benzyl-*N*-*tert*-butyloxycarbonyl-*O*-benzyl-L-homoserinal (7).** Compound **10** (1.23 g, 2.47 mmol) was dissolved in 20 mL of THF, and tetrabutylammonium fluoride (1.56 g, 4.94 mmol) was added in one portion. Deprotection was carried out at ambient temperature for 1h. Reaction mixture was diluted with ethyl ether, and washed with water (2 x 30 mL) , brine (30 mL), and dried ($MgSO_4$). Ether was evaporated in-vacuo, and the residue containing alcohol **11** ($[\alpha]_D^{22}$ -17.6° (c 0.8, $CHCl_3$)), was dissolved in DMSO (15 mL). Triethylamine (1.65 mL, 12.3 mmol) and SO_3-pyridine complex (1.59 g, 10 mmol) in 5 mL DMSO was added. Oxidation was carried out for 15 minutes at ambient temperature. The reaction mixture was transferred into the separatory funnel, diluted with ethyl ether and washed with saturated $NaHCO_3$ (3 x 50 mL), water (3 x 50 mL) and finally with brine (50 mL). Ether solution was dried over $MgSO_4$ and evaporated in-vacuo. Crude **7** was purified with "flash" chromatography giving slightly yellow oil (850 mg, 94%) $[\alpha]_D^{25}$ -50.1° (c 2.2, $CHCl_3$). ^1H NMR (200 MHz): 9.42-9.30 (s, 1H), 7.38-7.20 (m, 10H), 5.10 - 4.84 ($\frac{1}{2}$ABq, J=14.7 Hz, 1H), 4.48 (s, 2H), 4.09 - 3.97 ($\frac{1}{2}$ABq, J=14.8 Hz 1H), 3.80-3.62 (m, 1H), 3.61-3.44 (m, 2H), 2.30-2.28 (m, 1H), 2.10-1.80 (m, 1H), 1.47 + 1.43 (s, 9H). ^{13}C NMR (50 MHz): 199.9, 138.4, 128.9, 128.6, 127.9, 112.5, 73.0, 66.5, 66.4, 51.8, 28.7, 28.1. Since α-amino aldehydes are unstable this product was used immediately in the next step.

4(*S*)-(*N*-Benzyl-*N*-*tert*-butyloxycarbonyl)amino-6-benzyloxy-3(*R*)-hydroxyhexene-1 (6). L-homoserinal **7** (800 mg, 2.09 mmol) was dissolved in 20 mL of dry ethyl ether. The solution was cooled down to -78°C (CO_2/acetone bath) under argon stream, and vinyl magnesium chloride in THF (15%, 1.5 mL, 2.5 mmol) was added dropwise. The reaction mixture was stirred at the same temperature for 1h. Water (125 mL) was added, and organic phase was separated. Aqueous solution was extracted with ether (2 x 50 mL), and combined organics were washed with water (2 x 30 mL), brine (30 mL), and dried over $MgSO_4$. Filtration and evaporation of solvents under reduced pressure gave the crude adduct **6** which was chromatographed yielding colorless oil (695 mg, 81%). $[\alpha]_D^{25}$ -8.2° (c 1.0, $CHCl_3$). (Found: C, 72.79; H, 8.16; N, 3.33. $C_{25}H_{33}NO_4$ requires C, 72.96; H, 8.08; N, 3.40).

For the spectroscopic reasons adduct **6** has been transformed into its *O*-acetyl derivative: ^1H NMR (500 MHz, 25°C): 7.36-7.18 (m, 10H), 5.62 (bs, 1H), 5.49 (bs, 1H), 5.25-5.05 (m, 2H), 4.47-4.26 (m, 5H), 3.43-3.15 (m, 2H), 2.08-1.84 (m, 5H), 1.44 (bd, J=70.2 HZ, 9H).

^{1}H NMR (500 MHz, 70°C): 7.32-6.92 (m, 10H), 5.75 (dd, J_1=J_2=7.0 Hz, 1H), 5.72-5.54 (m, 1H), 5.18 (dd, J_1=17.1, J_2=1.1 Hz, 1H), 4.96 (dd, J_1=10.5, J_2=1.1 Hz, 1H), 4.43-4.18 (m, 4H), 3.29 (bs, 2H), 1.95 (m, 1H), 1.64 (s, 3H), 1.38 (s, 9H).
^{13}C NMR (50 MHz): 138.9, 128.5, 127.9, 127.8, 127.5, 115.4, 80.7, 75.4, 72.8, 67.3, 62.0, 53.7, 29.6, 28.3.
IR, ν (cm^{-1}): 3370, 3100-2870, 1690, 1670, 1460, 1370, 1210, 1165.

4(*S*)-(*N*-benzyl-*N*-*tert*-butyloxycarbonyl)amino-6-benzyloxy-1,2-(2*S*)-epoxy-3(*S*)-hydroxyhexane (5). Olefin **6** (414 mg, 1.01 mmol) was dissolved in dry CH_2Cl_2 (10 mL) and 3-chloroperoxybenzoic acid (85%, 408 mg, 2 mmol) was added. Reaction flask was allowed to stay at +5°C for 4 days, then the reaction mixture was transferred into the separatory funnel, diluted with ethyl ether (100 mL), and washed with saturated $NaHCO_3$ (3 x 20 mL) and brine (20 mL). Ether solution was dried ($MgSO_4$), concentrated in-vacuo, and purified with "flash" chromatography to give **5** as colorless oil (300 mg, 70%). $[\alpha]_D^{24}$ -12.3° (c 0.7, $CHCl_3$). (Found: C, 70.07; H, 7.91; N, 3.09. $C_{25}H_{33}NO_5$ requires C, 70.23; H, 7.78; N, 3.28).
Spectroscopic data for *O*-acetyl derivative:
^{1}H NMR (500 MHz, 25°C): 7.36-7.24 (m, 10H), 4.60-4.53 (m, 1H), 4.49 ($\frac{1}{2}$ABq, J=14.9 Hz, 1H), 4.35 (ABq, J=12.5 Hz, 2H), 4.26 ($\frac{1}{2}$ABq, J=14.9 Hz, 1H), 3.41-3.09 (m, 2H), 2.67 (bs, 1H), 2.51 (bt, J=33.1, 1H), 2.20-2.09 (bs, 1H), 2.01 (d, J=12.8 Hz, 3H), 1.96-1.78 (m, 2H), 1.48 (bd, J=30.9 Hz, 9H).
^{1}H NMR (500 MHz, 70°C): 7.30-6.96 (m, 10H), 5.17 ($\frac{1}{2}$ABq, 14.9 Hz, 1H), 5.10 (dd, J_1=5.1, J_2=2.1 Hz, 1H), 4.24 (s, 2H), 3.91 (dd, J_1=5.1, J_2=4.1 Hz, 1H), 3.82 ($\frac{1}{2}$ABq, 14.8 Hz, 1H), 3.54 (d$\frac{1}{2}$ABq, J_1=12.2, J_2=4.0 Hz, 1H), 3.47 (d$\frac{1}{2}$ABq, J_1=12.1, J_2=5.1 Hz, 1H), 3.44-3.37 (m, 1H), 3.35-3.21 (m, 2H), 1.82-1.64 (m, 2H), 1.61 (s, 3H), 1.38 (s, 9H).
^{13}C NMR (50 MHz): 156.8, 138.8, 138.6, 128.9, 128.8, 128.1, 128.0, 81.1, 75.2, 73.1, 67.3, 59.7, 53.8, 53.5, 44.3, 29.8, 28.5. IR, ν (cm^{-1}): 3440, 3100-2840, 1700, 1460, 1370, 1170.

4(*S*)-(*N*-benzyl-*N*-*tert*-butyloxycarbonyl)amino-6-benzyloxy-2,3-(2*S*,3*S*)-izopropylidenedioxyhexane (12). The epoxide **5** (210 mg, 0.49 mmol) was dissolved in dry ethyl ether (10 mL). The solution was cooled under argon stream to -78°C and diisobutylaluminium hydride (DIBAL) (1 mL, 1.5M toluene solution, 1.5 mmol) was added dropwise. Reduction was carried out at -40°C for 1.5 h. An excess of hydride was decomposed with methanol, and saturated sodium-potassium tartrate (20 mL) was added. After 1.5 h of vigorous stirring organic layer was separated, and aqueous one was extracted with ethyl ether (2 x 20 mL). Combined organic extracts were washed with water (3 x 20 mL), brine (20 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. Residue containing crude 2,3-diol ($[\alpha]_D^{25}$ -21.5° (c 1.2, $CHCl_3$)) was dissolved in acetone (5 mL), and dimethoxypropane (DMP) (125 µL, 1mmol) with catalytic amount of *p*-toluenesulphonic acid (*p*-TsOH) was added. Reaction mixture was maintained at room temperature for 45 min., diluted with ethyl ether (50 mL), and washed with saturated $NaHCO_3$ (3 x 20 mL) and brine (20 mL). Dried ($MgSO_4$) ether

solution was finally concentrated in-vacuo, and chromatographed to give **12** (166 mg, 72%) as colorless oil. $[\alpha]_D^{27}$ -32.2° (c 0.8, $CHCl_3$). (Found: C, 71.67; H, 8.43; N, 3.06. $C_{28}H_{39}NO_5$ requires C, 71.61; H, 8.37, N, 2.98).
^1H NMR (200 MHz, 25°C): 7.37-7.24 (m, 10H), 4.52 (d, J=15.0 Hz, 1H), 4.40 (s, 2H), 4.29 ($\frac{1}{2}$ABq, J=15.1 Hz, 1H), 3.86-3.52 (m, 2H), 3.48-3.22 (m, 3H), 2.10-1.92 (m, 2H), 1.45 (bd, J=16.7 Hz, 9H), 1.32-1.23 (m, 6H), 1.18 (bd, J=5.3 Hz, 3H).
^1H NMR (500 MHz, 55°C): 7.20-6.95 (m, 10H), 4.55 ($\frac{1}{2}$ABq, J=15.1 Hz, 1H), 4.34 ($\frac{1}{2}$ABq, J=15.0 Hz, 1H), 4.32 (s, 2H), 4.17-4.10 (m, 1H), 3.89 (dd, J_1=7.7, J_2=6.1 Hz, 1H), 3.76 (dq, J_1=7.7, J_2=6.0 Hz, 1H), 3.46-3.40 (m, 2H), 1.41 (s, 9H), 1.30 (s, 6H), 1.18 (d, J=6.0, 3H).
^{13}C NMR (50 MHz): 136.7, 128.5, 127.8, 127.6, 127.0, 108.1, 83.9, 80.1, 75.1, 67.5, 67.0, 55.2, 29.5, 28.3, 27.1, 26.7, 18.1. IR, ν (cm^{-1}): 3100-2860, 1680, 1370, 1210, 1170.

4(*S*)-(*N-tert*-butyloxycarbonyl)amino-6-hydroxy-2,3-(2*S*,3*S*)-izopropylidenedioxyhexane (13). Compound **12** (85 mg, 0.18mmol) was dissolved in dry THF (0.5 mL). The solution was cooled down under argon to -40°C, and the reaction flask was protected with condenser containing dry ice. Liquid ammonia was added slowly (ca. 2 mL), and then few small pieces of metal sodium to the stable violet color of the reaction mixture. After 15 minutes stirring, the reaction was quenched with saturated ammonium chloride (1 mL). Cooling bath and condenser were removed, and the mixture was allowed to warm up to the room temperature without any extra heating. The reaction mixture was diluted with ethyl ether (20 mL), washed with water (3 x 5 mL), brine (5 mL), and dried over $MgSO_4$. Solvents were evaporated in-vacuo, and the residue was subjected to "flash" column chromatography to yield colorless oil of **13** (48 mg, 92%). $[\alpha]_D^{25}$ -8.8° (c 1.0, $CHCl_3$). (Found: C, 58.11; H, 9.41; N, 4.84. $C_{14}H_{27}NO_5$ requires C, 57.96; H, 9.63; N, 4.65). ^1H NMR (200 MHz): 4.86 (bd, J=9.9 Hz, 1H), 3.94-3.81 (m, 2H), 3.78-3.57 (m, 3H), 1.99-1.73 (m, 2H), 1.62 (bt, J=8.3 Hz, 1H), 1.45 (s, 9H), 1.40 (s, 3H), 1.37 (s, 3H), 1.31 (d, J=5.9 Hz, 3H). ^{13}C NMR (50 MHz): 156.2, 108.4, 80.2, 74.2, 58.6, 48.1, 33.1, 28.1, 27.2, 26.7, 18.0. IR, ν (cm^{-1}): 3450, 1700, 1510, 1375, 1210, 1170.

(5*S*)-4(*S*)-*O*- acetyl- 3(*S*)- acetylamino- α-methyl- 2,3,6,- trideoxyhexapyranoside (15). Alcohol **13** (55 mg, 0.19 mmol) was dissolved in DMSO (1.5 mL), triethylamine (130 μL, 0.95 mmol), and SO_3-pyridine (120 mg, 0.76 mmol) in 0.5 mL DMSO was added. Oxidation was performed at ambient temperature for 30 min. Reaction mixture was transferred into the separatory funnel, diluted with ethyl ether (20 mL), and washed with saturated $NaHCO_3$ (3 x 10 mL), brine (10 mL), and dried ($MgSO_4$). Solvents were removed under reduced pressure. The residue aldehyde **14** was then dissolved in 0.1N methanolic HCl (6 mL), and the mixture was maintained at room temperature for 12 hr. Solvents were carefully evaporated in-vacuo, and the oily residue was treated with pyridine (0.5 mL) and acetic anhydride (100 μl, 1mmol). Reaction was carried out for 12 hr at room temperature. The mixture was then diluted with ethyl ether (20 mL). Pyridine was washed out with 1N HCl (2 x 10 mL). Ether solution was neutralized with saturated $NaHCO_3$ (2 x 10 mL), and washed with brine (10 mL).

Solvent was dried ($MgSO_4$) and evaporated under reduced pressure, and the residue was purified with "flash" column chromatography yielding **15** (42 mg, 90%) as colorless crystals: mp 186 - 187°C and $[\alpha]^{25}$ -207° (*c* 1.3, CHCl); lit.[17] mp 188 - 189°C and $[\alpha]^{25}$ -202° (*c* 1.0, $CHCl_3$). (Found: C, 53.59; H, 7.76; N, 6.05. $C_{11}H_{19}NO_5$ requires C, 53.87; H, 7.81; N, 5.71%. HR M^+: found 214.10797. $C_{11}H_{19}NO_5$ requires 214.1079). ^{1}H NMR (200 MHz): 5.44 (bd, J=8.7 Hz, 1H), 5.09 (dd, J_1=2.7, J_2=0.7 Hz, 1H), 4.81 (t, J=2.4 Hz, 1H), 4.65-4.44 (m, 1H), 4.06 (qd, J_1=6.6, J_2=0.7 Hz, 1H), 3.35 (s, 3H), 2.19 (s, 3H), 1.94 (s, 3H), 1.82 (ABq, J_1=9.9, J_2=2.4 Hz, 2H), 1.11 (d, J=6.6 Hz, 3H). ^{13}C NMR (50 MHz): 171.1, 169.6, 98.1, 71.5, 65.0, 54.7, 43.8, 30.5, 23.1, 20.6, 16.7. IR, ν (cm^{-1}): 3460, 1750, 1680, 1515, 1370, 1220, 1050.

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