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Synthesis of α-Azido Aldehydes Stereoselective Access to a Protected Lincosamine Analogue

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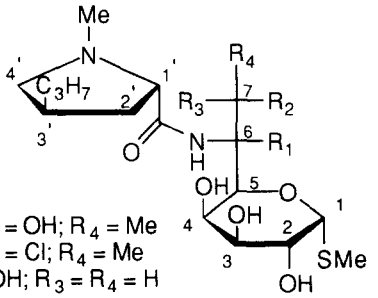
Abstract - Reaction of ketone **3** with dichloromethyllithium gave a unique branched-chain dichloromethyl sugar **7** whose structure was ascertained by X-ray crystallography. Transformation of **7** in seven steps, involving the key-intermediate α-azido-aldehyde **9**, afforded the protected lincosamine analogue **14**. © 1997 Elsevier Science Ltd.

INTRODUCTION

The clinically important antibiotic lincomycin **1a** exerts its antibacterial activity by the inhibition of protein synthesis at the ribosomal level[1]. Early work has demonstrated that modification of either the substituent or the stereochemistry at positions 1, 2, 3 or 4 of the pyranose ring of the carbohydrate fragment of lincomycin resulted in drastic reduction of its antibacterial activity[2-4]. However, modifications of its side-chain brought about some improvement and was at the origin of the development of the clinical applications of clindamycin **1b**[3,4].

In view of these results and the continuing interest for lincomycin[5], we decided to apply our methodology to the synthesis of the novel branched-chain lincosamine analogue **14**. In the latter, the configuration of the amino group of lincosamine is preserved while the C-8 methyl group of the natural product is displaced to C-6.



1a $R_1 = R_2 = H$; $R_3 = OH$; $R_4 = Me$
1b $R_1 = R_3 = H$; $R_2 = Cl$; $R_4 = Me$
17 $R_1 = Me$; $R_2 = OH$; $R_3 = R_4 = H$

In an attempt to synthesize some natural products of biological interest, we have constructed stereoselectively, years ago[6] and recently[7-10], branched-chain amino sugars in which the nitrogen atom was attached to a quaternary carbon center. The key step in two independent strategies towards such molecules involved : a.- lithium aluminium hydride treatment of ketone-derived cyanomesylates followed by Raney nickel mediated regiospecific opening of intermediate aziridines[6]; b.- Darzens type condensation of ketones with

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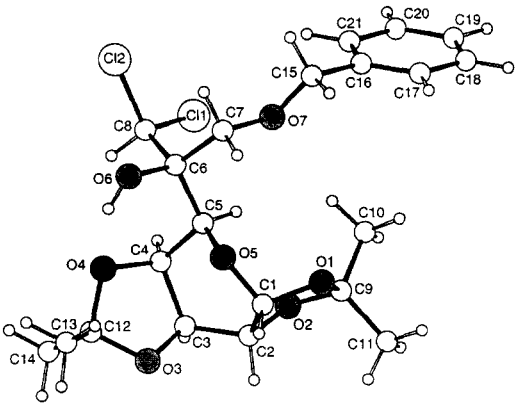
chloromethyl *p*-tolylsulfone[7,9,11] or with dichloromethyllithium[12,13] followed by azide ion treatment of intermediate α,β-epoxy sulfones or chlorides[8,10], furnishing α-azido aldehydes.

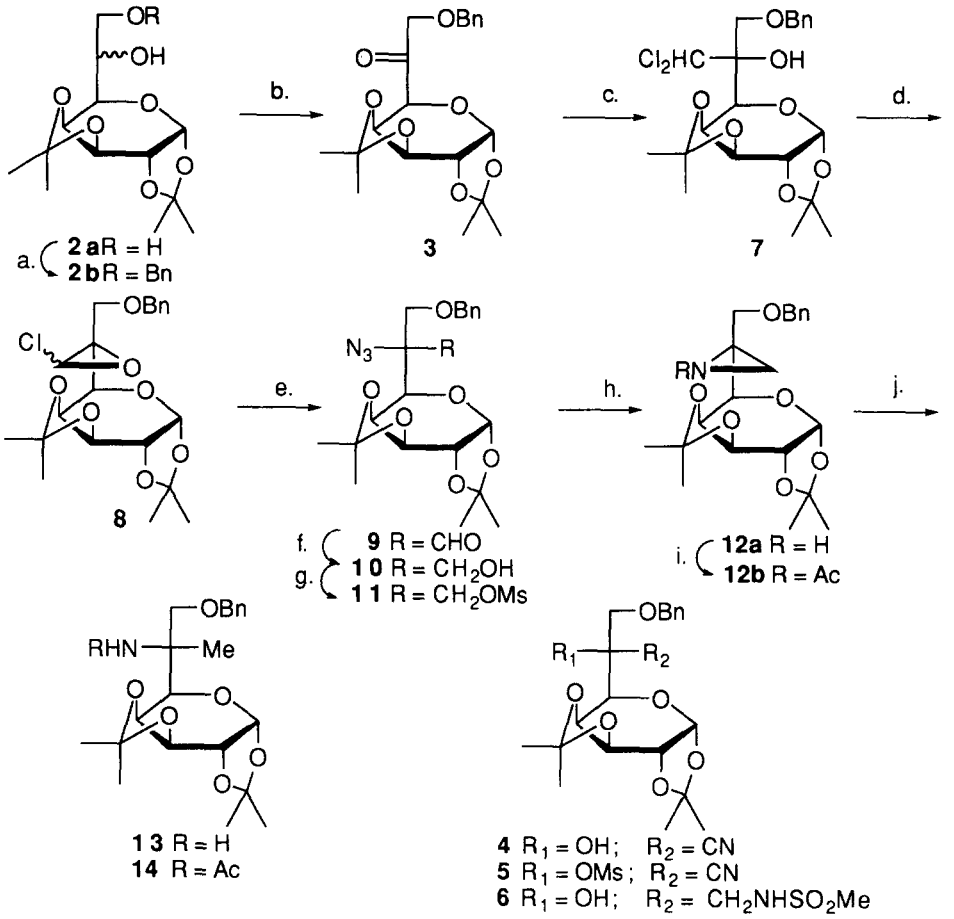
As an initial attempt towards our target molecule **14**, ketone **3** appeared to be the appropriate starting material (scheme 1). The latter was prepared in two steps by regioselective benzylation at C-7 of a diastereomeric mixture of diols **2a**[14] followed by Swern oxidation. The unique cyanohydrine **4**, prepared from ketone **3** was mesylated. The desired stereochemistry of this cyanomesylate **5** could be assigned only at a later stage of our work (*vide infra*). However, lithium aluminium hydride treatment of **5**, instead of giving the expected aziridine **12a**, furnished only a complex mixture. An analysis of this crude reaction mixture seems to indicate the presence of sulfonamide **6** [mass spectrum FAB : m/z 494 (M^+ + Na); ^{1}H NMR δ 2.92 (s) $NHSO_2Me$; ^{13}C NMR δ 40.0 ($NHSO_2Me$)] which could not be isolated in a pure state. When ketone **3** was treated, in the presence of potassium *t*-butoxide, with chloromethyl *p*-tolylsulfone as described[7,9], only decomposition of the starting material was observed.

Therefore, the reaction of ketone **3** with dichloromethyllithium, according to the method of Sato et al [12,13] was investigated. This reaction afforded the unique branched-chain dichloromethyl sugar **7** in 82%[15] whose stereochemistry could be ascertained by X-ray crystallography (figure)[16]. The stereochemistry at C-6 of **7** appeared to be the desired one in the light of its projected transformation towards our target molecule **14** .



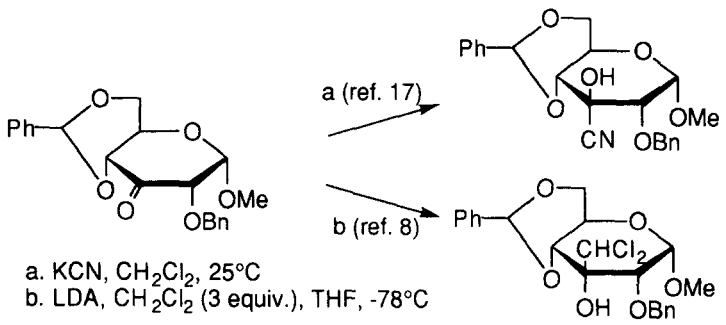
FIGURE

This X-ray crystallographic structural determination permitted to assign also the stereochemistry of the above mentioned cyanomesylate **5**. Results on carbohydrate ketones furnish informations about the stereochemical outcome for the considered two different reactions. If a unique cyanohydrine is formed from a ketone under thermodynamical conditions (see experimental section for the preparation of **4**), the stereochemistry of its cyano group will be the opposite to that of the dichloromethyl group of the branched-chain sugars obtained from the same ketone in the Darzens type condensation reactions investigated[8,17] (scheme 2).



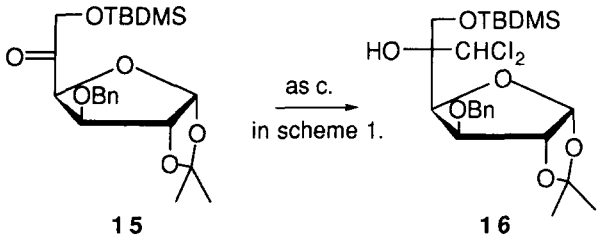
a. $(Bu_3Sn)_2O/C_6H_6$, thenBnBr, Bu_4NBr, Δ; b. Swern oxdn; c. LDA/THF, CH_2Cl_2, -78° then rt; d. NaH/THF, rt; e. HMPA, NaN_3, 15 crown-5/ether, Δ; f. $NaBH_4$/EtOH, 0°; g. MsCl, NEt_3/CH_2Cl_2, 0°; h. $NaBH_4$/iPrOH, Δ; i. Ac_2O/pyridine; j. H_2, Raney Ni, rt, then Ac_2O/pyridine

SCHEME 1



a. KCN, CH_2Cl_2, 25°C
b. LDA, CH_2Cl_2 (3 equiv.), THF, -78°C

SCHEME 2



15 16

SCHEME 3

Deducing the stereochemistry of the cyanomesylate **5** from the X-ray structure of **7** and the considerations developed above, if its reaction with lithium aluminium hydride had given an aziridine, the latter would have been precisely of the desired configuration[6] **12a** for our target **14**. However, these arguments are based only on a unique example.

The stereochemical outcome, respectively, of the cyanohydrine and the Darzens type reactions, affording the unique branched-chain sugars **4** and **7**, is quite surprising and difficult to rationalize[18,19]. Tentative stereochemical interpretation of a Sakurai-type reaction on related and less complex carbohydrate aldehydes afforded contradictory results[19]. Furthemore, in our previous investigations[8,10], under similar reaction conditions, ketone **15** afforded stereoselectively a dichloromethyl sugar **16** whose configuration at C-6 - based on both chemical correlation with synthetic myriocin and nOe experiments - was the opposite (scheme 3) to that obtained from **3**. As a consequence, α-azido aldehydes of both (*R*) and (*S*) configuration, highly useful for transformations directed to the synthesis of α-substituted α-amino acids can be stereoselectively prepared from the two different open-chain carbohydrate ketones **3** and **15**.

The α-hydroxy dichloromethyl sugar **7** was converted, in the presence of sodium hydride into a 2 : 1 mixture of α,β-epoxy chlorides **8** which could be only partially separated. However, the stereochemistry of these compounds **8** at the chlorine bearing carbon could not be determined. Each, contaminated with about 10% of its isomer, was treated in HMPA solution, in the presence of 15-crown-5 with sodium azide, giving the same α-azido aldehyde **9** (87%) by S_N2 reaction at the β-carbon relative to the chlorine.

In the presence of 1 equiv. of sodium borohydride, reduction of **9** at O°C gave quantitatively the α-azido methylalcohol **10**. The latter was mesylated and the resulting compound **11** treated with sodium borohydride at 80°C affording the spiro aziridine **12a** (93%). Regioselective opening of this aziridine was effected by Raney nickel treatment giving **13** (90%) and the crude product was acetylated affording the protected amino sugar **14**, a close analogue of lincosamine[5], our target molecule.

The transformation of **14** into the corresponding lincomycin analogue **17** and the antibacterial activity of the latter will be reported upon permission from our industrial partner.

EXPERIMENTAL PART

General procedures. A Perkin-Elmer Model 141 MC polarimeter and 1-dm tubes were used for measurement of specific rotations. ^1H NMR spectra were recorded in chloroform-d solution. The ^{13}C NMR spectra were measured in chloroform-d solution at 50.31 MHz with a Bruker WP-200 spectrometer. Chemical

shifts are given in parts per million, and tetramethylsilane was the internal standard (δ 0.000). Carbon-13 chemical shifts for aromatic carbons are not given. Isopropylidene carbon and proton shifts are, as follows : (carbon shifts) two quaternary carbon signals between 109 and 110 ppm and four methyl signals between 26.0 and 23.5 ppm; (proton shifts) four methyl singlets between 1.50 and 1.25 ppm. Microanalyses were performed by the Service Central de Microanalyse du CNRS. Silica gel 60 PF_{254} (Merck) activated at 120°C was the support for TLC and for column chromatography. The term usual work-up means dichloromethane extraction, washing of the organic layer with a saturated solution of $NaHCO_3$, drying over Na_2SO_4 followed by evaporation under reduced pressure.

7-O-Benzyl-1,2:3,4-di-O-isopropylidene-α-D- and β-L-glycero-D-galacto-heptopyranose (2b). To a diastereomeric mixture of diol 2a (9.98 g, 34.4 mmol) in benzene (100 mL) was added bis-tributylstannyl oxide (27.6 mL, 51.6 mmol) and the solution was refluxed for 4 h with azeotropic elimination of water. After concentration to 50 mL, was added to the mixture benzyl bromide (12.3 mL, 100 mmol) and tetrabutyl ammonium bromide (5.54 g, 17.2 mmol) and reflux was continued for another 24h. After the usual work-up and chromatography of the residue using heptane/ethyl acetate 7 : 3, 2b (11.5 g, 89%) was obtained, mass spectrum (C.I.) : m/z 381 ($M^+ + H$).

7-O-Benzyl-1,2:3,4-di-O-isopropylidene-α-D-galacto-heptopyran-6-ulose (3). To a solution of oxalyl chloride (2.48 mL, 27.7 mmol) in dichloromethane (80 mL), in an argon atmosphere at -78°C was added dropwise a solution of DMSO (4.26 mL, 60 mmol) in dichloromethane (12 mL) and stirring was maintained for 20 min. To this mixture was added, slowly under stirring, monobenzyl derivative 2b (8.8 g, 23.1 mmol) in dichloromethane (20 mL). Stirring was maintained for another 30 min then triethylamine (19.2 mL) was added. After stirring for 2 h the temperature was allowed to raise slowly to +20°C. The usual work-up gave a residue from which chromatography with heptane/ethyl acetate 7 : 3 afforded 3 (8.28 g, 95%), m.p. 95-96°C, $[\alpha]_D$ -109 ($CHCl_3$, c 1.48), mass spectrum (C.I.) : m/z 379 ($M^+ + H$); ^1H NMR (200 MHz, $CDCl_3$) δ 7.30 (5H, m, Ph), 5.55 (1H, d, $J_{1,2}$ = 4 Hz, H-1), 4.65-4.28 (m, 8H, H-2,3,4,5,7,7' and OCH_2Ph); ^{13}C NMR (50.33 MHz, $CDCl_3$) δ 205.1 (C-6), 96.1 (C-1), 74.0 and 73.1 (C-7 and OCH_2Ph), 73.5, 72.2, 70.4 and 70.3 (C-2,3,4 and 5). Anal. Calcd for $C_{20}H_{26}O_7$: C, 63.15; H, 6.87. Found : C, 63.12; H, 6.91.

7-O-Benzyl-6-cyano-1,2:3,4-di-O-isopropylidene-6-O-methane-sulfonyl-α-D-glycero-D-galacto-heptopyranose (5). To a solution of ketone 3 (0.34 g, 1 mmol) in dichloromethane (5 mL) was added first $NaHCO_3$ (0.18 g, 2 mmol) in water (1.5 mL), then KCN (0.14 g, 2.14 mmol) and the mixture was stirred overnight at room temperature. After the usual work-up crude cyanohydrine 4 (0.40 g, 96%) was dissolved in dichloromethane (5 mL) and to this solution was added at 0°C triethylamine (1.5 mL) and then mesyl chloride (0.43 mL), 5.5 mmol). Stirring was maintained for two hours and the usual work-up followed. Chromatography with heptane/ethyl acetate 7 : 3 gave 5 (0.46 g, 94%), m.p. 192°C, $[\alpha]_D$ -82 ($CHCl_3$, c 1.10), mass spectrum (C.I.) : m/z 484 ($M^+ + H$); ^1H NMR (200 MHz, $CDCl_3$) δ 7.30 (5H, m, Ph), 5.58 (1H, d, $J_{1,2}$ = 4 Hz, H-1), 4.68 (2H, 2d, J_{gem} = 12 Hz, OCH_2Ph), 4.45- 4.36 (4H, m, H-2,3,4,and 5), 4.22 and 3.95 (2H, 2d, J_{gem} = 12 Hz, H-7,7'), 3.28 (3H, s, SO_2Me); ^{13}C NMR (50.33 MHz, $CDCl_3$) δ 114.0 (CN), 95.5 (C-1), 79.6 (C-6), 74.3 (OCH_2Ph), 70.8-66.0 (C-2,3,4,5 and 7), 40.1 (SO_2Me). Anal. Calcd for $C_{22}H_{29}NO_9S$: C, 54.65; H, 6.00; N, 2.89; S, 6.62. Found : C, 54.70; H, 6.03; N, 2.87; S, 6.66.

Reduction of cyanomesylate 5. To a solution of 5 (0.37 g, 0.76 mmol) in THF (2 mL) was added at -15°C in an argon atmosphere $LiAlH_4$ (58 mg, 1.52 mmol) in THF (10 mL). After stirring for 30 min the temperature was allowed to raise to + 20°C. The mixture was diluted with ether (10 mL) and the usual work-up gave a complex residue as judged by T.L.C., ^1H and ^{13}C NMR as well as mass spectrometry. Although, sulfonamide 6 could not be isolated pure from this mixture its presence in it is highly suspected : mass spectrum (C.I.) : m/z 494 (M^+ + Na); ^1H NMR (200 MHz, $CDCl_3$) δ 2.92 (3H, s, $NHSO_2Me$); ^{13}C NMR (50.33 MHz, $CDCl_3$) δ 40.0 ($NHSO_2Me$).

7-O-Benzyl-1,2:3,4-di-O-isopropylidene-6-C-dichloromethyl-β-L-glycero-D-galacto-heptopyranose (7). To a solution of diisopropylamine (5.68 mL, 40.23 mmol) in THF (30 mL) was added slowly, under stirring at -78°C in an argon atmosphere, n-butyllithium in hexane (1.6 M) (25.2 mL, 40.23 mmol). After 30 min was added slowly dichloromethane (2.6 mL, 40.23 mmol) in THF (5 mL). After another 30 min was added dropwise ketone 3 (5.07 g, 13.4 mmol) in THF (30 mL). The temperature was then allowed to raise slowly to +20°C and the usual work-up followed. Chromatography using heptane/ethyl acetate 8 : 2 furnished 7 (5.08 g, 82%), m.p. 116-117°C, $[\alpha]_D$ -45 ($CHCl_3$, c 2.45), mass spectrum (C.I.) : m/z 463 (M^+ + H); ^1H NMR (200 MHz, $CDCl_3$) δ 7.30 (5H, m, Ph), 6.15 (1H, s, $CHCl_2$), 5.60 (1H, d, $J_{1,2}$ = 4 Hz, H-1), 4.73 (1H, dd, $J_{1,2}$ = 4 Hz, $J_{2,3}$ = 8 Hz, H-2), 4.60 (3H, m, H-3,5 and OH), 4.35 (2H, s, OCH_2Ph), 4.30 (1H, m, H-4), 3.85 (2H, dd, J_{gem} = 10 Hz, H-7,7'); ^{13}C NMR (50.33 MHz, $CDCl_3$) δ 96.8 (C-1), 79.0 (C-6), 75.3, 72.4, 71.1 and 70.7 (C-2,3,4 and 5), 73.7 and 70.7 (C-7 and OCH_2Ph), 65.1 ($CHCl_2$). Anal. Calcd for $C_{21}H_{28}Cl_2O_7$: C, 54.54; H, 6.06; Cl, 15.15. Found : C, 54.60; H, 6.05; Cl, 15.17.

7-O-Benzyl-1,2:3,4-di-O-isopropylidene-6-C-(α-chloro-epoxides)-β-L-glycero-D-galacto-heptopyranose (8). To a mixture of sodium hydride (0.15 g) in THF (30 mL) was added, at room temperature, slowly 7 (1.41 g, 2.81 mmol) in THF (5 mL). After stirring for 12 h the usual work-up followed, giving a residue consisting of a 2 : 1 diastereomeric mixture of 8 (1.22 g, 93%); mass spectrum (C.I.) : m/z 427 (M^+ + H). Chromatography of this mixture with heptane/ethyl acetate 7 : 3 gave each of its components contaminated with about 10% of its epimer.

6-Azido-7-O-benzyl-6-deoxy-1,2:3,4-di-O-isopropylidene-6-C-formyl-α-D-glycero-D-galacto-heptopyranose (9). To a solution of either isomers of 8 (85 mg, 0.2 mmol) , in two separate experiments, in HMPA (1 mL) were added sodium azide (65 mg, 1 mmol) and 15-crown-5 (20 μL, 0.1 mmol) and the mixture was heated for 3h at 100°C. Chromatography of the crude reaction mixture, first with heptane and then with ether, gave azido-aldehyde 9 (80 mg, 93%), m.p. 87-88°C, $[\alpha]_D$ -56 ($CHCl_3$, c 1.12), mass spectrum (C.I.) : m/z 434 (M^+ + H); ^1H NMR (200 MHz, $CDCl_3$) δ 9.68 (1H, s, CHO), 7.30 (5H, m, Ph), 5.55 (1H, d, $J_{1,2}$ = 4 Hz, H-1), 4.60 (4H, m, H-3, OCH_2Ph, OH), 4.40 (1H, dd, $J_{1,2}$ = 4 Hz, $J_{2,3}$ = 8 Hz, H-2), 4.30 (1H, m, H-4), 4.10 (1H, bs, H-5), 3.83 (2H, dd, J_{gem} = 10 Hz, H-7,7'); ^{13}C NMR (50.33 MHz, $CDCl_3$) δ 196.0 (CHO), 96.8 (C-1), 73.9 (OCH_2Ph), 71.4 (C-6), 70.7-69.1 (C-2,3,4,5 and 7). Anal. Calcd for $C_{21}H_{27}N_3O_7$: C, 58.19; H, 6.23; N, 9.69. Found : C, 58.24; H, 6.19; N, 9.71.

6-Azido-7-O-benzyl-6-deoxy-1,2:3,4-di-O-isopropylidene-6-C-hydroxymethyl-α-D-glycero-D-galacto-heptopyranose (10). To a solution of 9 (2.17 g, 5 mmol) in ethanol (10 mL) was added at 0°C $NaBH_4$ (126 mg, 3.33 mmol). Stirring was applied for 30 min. The usual work-up gave 10 (2.17 g, 99%) as a syrup, $[\alpha]_D$ -74 ($CHCl_3$, c 1.09), mass spectrum (C.I.) : m/z 436 ($M^+ + H$); ^1H NMR (200 MHz, $CDCl_3$) δ 7.35 (5H, m, Ph), 5.52 (1H, d, $J_{1,2}$ = 4 Hz, H-1), 4.58 (3H, m, H-3, OCH_2Ph), 4.40 (1H, dd, $J_{1,2}$ = 4 Hz, $J_{2,3}$ = 8 Hz, H-2), 4.25 (1H, m, H-4), 4.02 (1H, bs, H-5), 3.80 (2H, bs, CH_2OH), 3.70 (2H, dd, J_{gem} = 10 Hz, H-7,7'); ^{13}C NMR (50.33 MHz, $CDCl_3$) δ 96.7 (C-1), 73.7 (OCH_2Ph), 71.4-68.0 (C-2,3,4,5 and 7) 67.0 (C-6), 62.6 (CH_2OH). Anal. Calcd for $C_{21}H_{29}N_3O_7$: C, 57.93; H, 6.66; N, 9.65. Found : C, 57.87; H, 6.69; N, 9.70.

6-Azido-7-O-benzyl-6-deoxy-1,2:3,4-di-O-isopropylidene-6-C-(hydroxymethyl-methanesulfonate)-α-D-glycero-D-galacto-heptopyranose (11). To a solution of 10 (1 g, 2.29 mmol) in dichloromethane (10 mL) containing triethylamine (638 µL) was added dropwise at 0°C methanesulfonyl chloride (213 µL, 2.74 mmol). Stirring was applied for 2h and then the usual work-up followed giving, after chromatography with heptane/ethyl acetate 8 : 2, 11 (1.11 g, 95%) as a syrup, $[\alpha]_D$ -66 ($CHCl_3$, c 1.1), mass spectrum (C.I.) : m/z 513 ($M^+ + H$); ^1H NMR (200 MHz, $CDCl_3$) δ 7.30 (5H, m, Ph), 5.50 (1H, d, $J_{1,2}$ = 4 Hz, H-1), 4.75 and 4.30 (2H, dd, J_{gem} = 10 Hz, CH_2OMs), 4.60 (3H, m, H-3 and OCH_2Ph), 4.35 (1H, dd, $J_{1,2}$ = 4 Hz, $J_{2,3}$ = 8 Hz, H-2), 4.30 (1H, m, H-4), 4.22 (1H, bs, H-5), 3.52 (2H, s, H-7,7'), 3.00 (3H, s, OMs); ^{13}C NMR (50.33 MHz, $CDCl_3$) δ 96.7 (C-1), 73.7 (OCH_2Ph), 71.2-66.9 (C-2,3,4,5, and 7), 69.6 (C-6), 66.9 (CH_2OMs), 37.2 (OMs). Anal. Calcd for $C_{22}H_{31}N_3O_9S$: C, 51.36; H, 6.04; N, 8.18; S, 6.23. Found : C, 51.40; H, 5.98; N, 8.17; S, 6.24.

6-(N-Acetyl-2-aziridine)-7-O-benzyl-6-deoxy-1,2:3,4-di-O-isopropylidene-α-D-glycero-D-galacto-heptopyranose (12b). To a solution of 11 (0.26 g, 0.5 mmol) in isopropanol (5 mL) was added $NaBH_4$ (19 mg, 0.5 mmol) and the mixture was heated to 80°C overnight. After the usual work-up aziridine 12a (0.20 g, 93%) was obtained and characterized as its N-acetyl derivative 12b. Acetylation was carried out from 12a (45mg, 0.12 mmol) in pyridine solution (2 mL) containing acetic anhydride (0.2 mL) followed by the usual work-up; $[\alpha]_D$ -96 ($CHCl_3$, c 1.23), mass spectrum (C.I.) : m/z 434 ($M^+ + H$); ^1H NMR (200 MHz, $CDCl_3$) δ 7.27 (5H, m, Ph), 5.54 (1H, d, $J_{1,2}$ = 4 Hz, H-1), 4.50 (3H, m, H-3 and OCH_2Ph), 4.30 (2H, m, H-2,4), 3.96 (1H, bs, H-5), 3.70 (2H, dd, J_{gem} = 10 Hz, H-7,7'), 2.46 (2H, dd, J_{gem} = 14 Hz, aziridine), 2.16 (3H, s, $NCOCH_3$); ^{13}C NMR (50.33 MHz, $CDCl_3$) δ 181.3 ($NCOCH_3$), 96.6 (C-1), 73.1 (OCH_2Ph), 71.1-67.5 (C-2,3,4,5 and 6), 67.3 (C-7), 45.8 (CH_2-aziridine), 28.8 ($NCOCH_3$). Anal. Calcd for $C_{23}H_{31}NO_7$: C, 63.74; H, 7.15; N, 3.23. Found : C, 63.80; H, 7.16; N, 3.22.

6-N-Acetyl-7-O-benzyl-6-deoxy-1,2:3,4-di-O-isopropylidene-6-C-methyl-α-D-glycero-D-galacto-heptopyranose (14). To a solution of aziridine 12a (0.15 g, 0.38 mmol) in ethyl acetate (5 mL) was added Raney nickel (0.15 g) and the mixture was hydrogenated for four days under pressure (120 bars). After filtration and evaporation of the solvent the crude residue 13 was acetylated in pyridine solution (0.5 mL) containing acetic anhydride (50 µL). After the usual work-up and chromatography of this residue with heptane/ethyl acetate 7 : 3, pure syrupy 14 (0.15 g, 90%) was obtained, $[\alpha]_D$ -56 ($CHCl_3$, c

1.14), mass spectrum (C.I.) : m/z 436 ($M^+ + H$); ^1H NMR (200 MHz, $CDCl_3$) δ 7.30 (5H, m, Ph), 6.62 (1H, bs, NH), 5.55 (1H, d, $J_{1,2}$ = 4 Hz, H-1), 4.58 and 4.45 (2H, dd, J_{gem} = 12 Hz, OCH_2Ph), 4.50 (1H, dd, $J_{2,3}$ = 8 Hz, $J_{3,4}$ = 2 Hz, H-3), 4.30 (1H, dd, $J_{1,2}$ = 4 Hz, $J_{2,3}$ = 8 Hz, H-2), 4.25 (1H, m, H-4), 4.10 and 3.65 (2H, 2d, J_{gem} = 10 Hz, H-7,7'), 4.00 (1H, s, H-5), 1.88 (3H, s, $NHCOCH_3$), 1.62 (3H, s, C-6 Me); ^{13}C NMR (50.33 MHz, $CDCl_3$) δ 169.8 ($NHCOCH_3$), 97.0 (C-1), 73.2 (OCH_2Ph), 71.9 (C-7), 71.5-68.6 (C-2,3,4,5 and 6), 22.7 ($NHCOCH_3$), 19.6 (C-6 Me). Anal. Calcd for $C_{23}H_{33}NO_7$: C, 63.44; H, 7.58; N, 3.21. Found : C, 63.49; H, 7.61; N, 3.28.

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