ХИМИЯ ГЕТЕРОЦИКЛИЧЕСКИХ СОЕДИНЕНИЙ. — 2000. — № 1. — С. 45—52

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NOVEL OPTICALLY ACTIVE 1,3-AMINOALCOHOLS DERIVED FROM D-GLUCAL

A series of ethyl(phenyl) 6-amino-2,3,6-trideoxy-α-D-glucopyranosides (amino = piperidino (Pip), pyrrolidino (Pyr), azetidino (Az), Bu_2N) have been prepared from tri-O-acetyl-D-glucal to obtain catalysts for asymmetric synthesis and the starting compounds for the syntheses of other bidentate ligands.

Keywords: ethyl(phenyl) 6-amino-2,3,6-trideoxy-α-D-glucopyranosides, tri-O-acetyl-D-glucal, piperidine, pyrrolidine, azetidine.

The synthesis of new chiral ligands is essential for the development of asymmetric catalysis [1–3]. Various kinds of chiral aminoalcohols, mainly 1,2-aminoalcohols, are used in enantioselective catalysis and asymmetric synthesis [1–6]. Chiral 1,3-aminoalcohols are rare and less studied. On the other hand, carbohydrates including monosaccharides (the largest natural pool of chiral enantiopure synthons [7]) were used hitherto as a starting material for the preparation of some bidentate ligands for asymmetric catalysis, mainly diphenylphosphinites and diphenylphosphines [8–12].

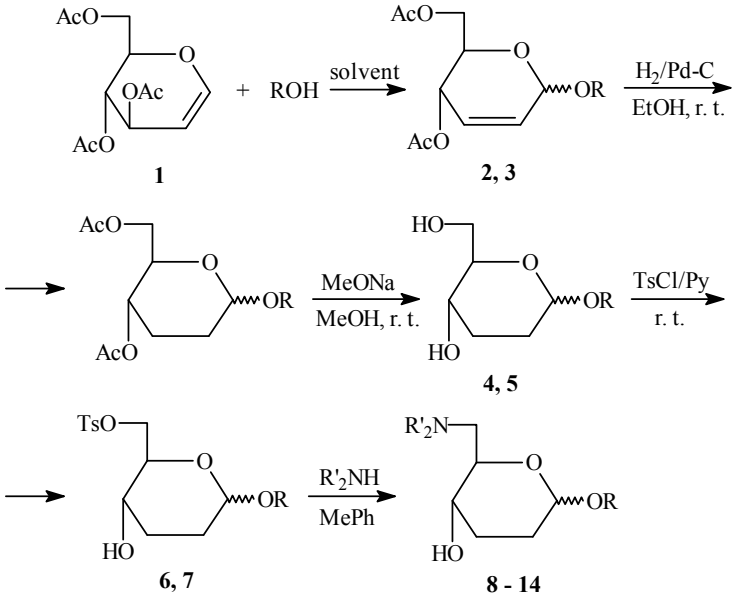
Recently, we have prepared optically active ligands and complexes and studied their behaviour in various enantioselective catalytic reactions (hydrosilylation, hydrogen transfer reduction, trimethylsilylcyanation and alkylation) [13–16].

Herein we report a five-step procedure (Scheme) for transformation of commercially available tri-O-acetyl-D-glucal (1,2-dideoxy-3,4,6-tri-O-acetyl-D-*arabino*-hex-1-enopyranose) (**1**) to a series of new optically active bidentate ligands, 1,3-aminoalcohol derivatives of tetrahydropyran (**8–14**). The synthesized ligands were tested in the asymmetric addition of dialkylzinc reagents to (hetero)aromatic aldehydes and shown to give optical induction up to 72% *ee* in the presence of phenyl 6-pyrrolidino-2,3,6-trideoxy-α-D-glucopyranoside (**13**) (catalytic experiments were presented in Ref. [17]).

One of the main routes to hex-2-enopyranosides, e.g. **2** and **3**, (see Reviews [18–20]) developed by Ferrier is a reaction at enhanced temperature or, alternatively, acid-catalyzed reaction at room-temperature [21–25] of alcohols with glucal **1**. It proceeds through allylic rearrangement of the double bond and displacement of the C(3) functionality. Processes at enhanced temperature gave mixtures of α- and β-anomers. The following catalytic (Pd or Pt) hydrogenation and hydrolysis of various 2,3-unsaturated glycosides yielded alkyl 2,3-dideoxy-α-D-glucopyranosides (6-alkoxy-3-hydroxy-2-hydroxymethyltetrahydropyrans) [26–33].

In the present work seven novel optically active aminocarbinols containing tetrahydropyran ring were prepared (Scheme). Totally, thirteen chiral compounds (only three of which, **2–4**, were previously known) were

synthesized, isolated (mainly by column chromatography) and characterized by spectral methods, elemental analyses and optical rotation. Diacetyl compounds (**2**, **3**: R = Et, Ph, respectively) were obtained from **1**, $[\alpha]_D^{25}$ –12 (c = 2, EtOH), using the methods described in Ref. [21, 33]. They were converted into the dicarbinols **4** and **5** under catalytic hydrogenation and then deacetylated with methanolic sodium methoxide.



2, 4, 6, 8–11: R = Et; **3, 5, 7, 12–14**: R = Ph; **8**: R' = Bu; **9, 12**: R'$_2$ = –$(H_2C)_5$–; **10, 13**: R'$_2$ = –$(H_2C)_4$–; **11, 14**: R'$_2$ = –$(H_2C)_3$–

Scheme. Synthesis of chiral compounds derived from tri-O-acetyl-D-glucal

Compounds **4** and **5** reacted with TsCl to give the tosylates **6** and **7**, which were converted into the corresponding aminocarbinols (**8**–**14**) using the reactions with four amines: dibutylamine, piperidine, pyrrolidine and azetidine.

All synthesized compounds were characterized by a series of spectral methods: FT-IR, MS and GC-MS (EI and FAB), ^{1}H and ^{13}C NMR (using DEPT, ^{1}H,^{1}H- and ^{13}C,^{1}H-COSY techniques). IR and mass spectra of products (**2**–**14**) have been found in good agreement with their structures (mass spectrum of **2** was given in Ref. 25). Some of the signals in the ^{1}H and ^{13}C NMR spectra of the compounds obtained were assigned taking into account data from Ref. [22–33].

The analysis of NMR spectra showed that all compounds, excluding **3**, were α-anomers. For **4**–**14**, the values of coupling constants $J_{H-1,H-2ax}$ were 3.0–3.5 Hz, the values $J_{H-1,H-2eq}$ were < 1.0 Hz, which exclude an axial position of H(1). In the ^{1}H and ^{13}C spectra of compounds **5** and **13** signals of the β-isomer (ca 10%) were found. The NMR data of the minor products (**5**: δ_{H-1} = 5.18, dd, $J_{H-1ax,H-2ax}$ = 9.2 Hz, $J_{H-1ax,H-2eq}$ = 2.5 Hz, δ_{C-1} = 100.9; **13**: δ_{H-1} = 5.11, dd, $J_{H-1ax,H-2ax}$ = 9.5 Hz, $J_{H-1ax,H-2eq}$ = 2.5 Hz, δ_{C-1} = 99.7) prove the assignment of signals to the β-anomers (bis-axial coupling, high-field shift of H(1), low-field shift of C(1) compared to the α-anomer).

For compound **3**, both α- and β-anomers were isolated (α- as major and β- as minor isomer). The values of $J_{H\text{-}1,H\text{-}2}$ for both isomers were ≈ 0. Therefore, an unambiguous distinction between α- and β-forms based on coupling constants was impossible. However, in the NOESY spectra recorded for both anomers, only in one case a correlation between H(1) and H(5) was found proving the axial position of H(1) (β-anomer). Based on the assignments for **3** the ^{1}H and ^{13}C NMR data for **2** correspond to the α-anomer. The results correlate with the data previously reported [25–33].

EXPERIMENTAL

Materials and Methods. All the reagents were purchased from Fluka, Merck and Aldrich and were used without additional purification. Thin-layer chromatography (t.l.c.) was performed on a Merck silica gel 60 F_{254} with various eluents using UV, iodine-reagent and acidic vanillin (methanol-acetic acid-concentrated sulphuric acid-vanillin = 25ml : 2.5ml : 1ml : 0.1g) as a spray reagent. Column chromatography was carried out on a Merck silica gel 60 (230–400 mesh) using various eluents. Melting points were determined with a Kofler micro-stage apparatus. Optical rotations were detected with a Gyromat-HP polarimeter. Elemental analyses were carried out on a LECO CHNS-932 automatic instrument. GC analysis was performed on a Hewlett-Packard (5890 series II) chromatograph equipped with a flame-ionization detector, on a capillary column packed with HP-1 or HP-5 nonpolar phase (1 or 5% phenyl substituted methyl polysiloxane, 30m × 0.25mm), carrier gas was helium (1 ml/min); the temperature programme was from 35–50 to 260–280 °C (8 °C/min). GC-MS spectra were obtained by means of an HP 5890 (II) chromatograph with an HP 101 capillary column (Methyl Silicon Fluid, 25m × 0.2mm), connected to an HP Engine 5989-A mass spectrometer (70 eV). High-resolution mass spectra were registered with an AMD 402/3 (70 eV) instrument. FT-IR data were recorded in KBr pellets on a Nicolet Magna 550 spectrometer. NMR spectroscopy was performed using Bruker AC 250, ARX 300 or ARX 400 instruments on solutions of compounds in $CDCl_3$. The calibration of spectra was carried out by means of solvent peaks ($CDCl_3$: δ^1H = 7.25; δ^{13}C = 77.0).

Procedures. **Ethyl 2,3-dideoxy-4,6-di-O-acetyl-α-D-*erythro*-hex-2-enopyranoside (2).** A solution of glucal **1** (5.44 g, 20 mmol) and ethanol (2.28 ml, 40 mmol) in dry 1,2-dichloroethane (100 ml) was treated with $SnCl_4$ (0.48 ml, 4.1 mmol) at ambient temperature. After 1 h the t.l.c. (petroleum ether–diethyl ether 4 : 1) of the mixture showed the disappearance of glucal and the formation of a single product. The mixture was quenched with 4.2 ml triethylamine, diluted with chloroform (200 ml), washed twice with water, dried ($MgSO_4$), and concentrated to give a solid. It was recrystallized from 10 ml 90% aq. ethanol as colourless needles (3.23 g, 62%), *mp* 72–79 °C, $[\alpha]_D^{22}$ 122 (*c* = 1.0, CH_2Cl_2). Lit.: 78–79 °C (aq. EtOH) [22, 24, 26, 33]; $[\alpha]_D^{22}$ 105–107 (*c* = 1.0–2.1, C_6H_6) [22, 24, 26]; $[\alpha]_D^{22}$ 133 (*c* = 1.0, CH_2Cl_2) [33]. Found, %: C 55.88; H 7.06. $C_{12}H_{18}O_6$. Calculated, %: C 55.80; H 7.02. ^{1}H NMR (250.13 MHz, δ, ppm): 1.20 (3H, t, *J* = 7.1 Hz, CH_3(Et)); 2.03 (3H, s, Ac); 2.06 (3H, s, Ac); 3.56 (1H, m, CH_2(Et)); 3.70 (1H, m, CH_2(Et)); 4.05–4.28 (3H, m, 5-H, 6-H); 5.03 (1H, s, 1-H); 5.28 (1H, m, $J_{4,5}$ = 9.5 Hz, 4-H); 5.78–5.90 (2H, m, 2-H, 3-H). ^{13}C NMR (62.86 MHz, δ, ppm): 15.2, CH_3 (Et); 20.7, 20.9, 2 CH_3(Ac); 63.0, CH_2 (Et); 64.2, $C_{(6)}$; 65.3, $C_{(4)}$; 66.9, $C_{(5)}$; 94.2, $C_{(1)}$; 128.0, $C_{(2)}$; 129.0, $C_{(3)}$; 170.2, 170.6, 2 CO.

Phenyl 2,3-dideoxy-4,6-di-O-acetyl-α(β)-D-*erythro*-hex-2-enopyranoside (3). Glucal **1** (10.0 g, 36.3 mmol) and phenol (33.3 g, 35.4 mmol) reacted in boiling chlorobenzene (100 ml). The t.l.c. (petroleum ether–diethyl ether 1 : 1) of the mixture showed the disappearance of glucal after 4 h. Then chlorobenzene was evaporated (60–80 °C/13–20 mm), and the excess of phenol was removed by vacuum distillation (50 °C/4.5×10^{-2} mm). The oily residue (11.56 g) was eluted from silica gel (150 g) with petroleum ether–diethyl ether (4 : 1) to give **3** in three colourless fractions (α-, β-anomers and their mixture): 1. fine needles (4.23 g, 38%), *mp* 50–52 °C, $[\alpha]_D^{24}$ 172.5 (*c* = 3.1, EtOH), $[\alpha]_D^{24}$ 174.5 (*c* = 3.1, acetone); 2. syrup (a mixture of α- and β-anomers) (2.6 g, 23%); 3. syrup (0.84 g, 7.5%), $[\alpha]_D^{22}$ 53.7 (*c* = 0.9, EtOH). Lit. [21] data for α-**3**: syrup, $[\alpha]_D^{20}$ 132 (*c* = 1.5, EtOH). Found for solid, %: C, 62.66; H, 5.77. $C_{12}H_{18}O_6$. Calculated, %: C, 62.73; H, 5.92. GC-MS, *m/z* (rel. int., %): 305 ($[M–H]^+$, 1), 277 ($[M–H–CO]^+$, 1), 246 ($[M–H–OAc]^+$, 1), 213 ($[M–OPh]^+$, 19), 173 ($[M–H–OAc–CH_2OAc]^+$, 4), 153

([M–H–OAcOPh]$^+$, 22), 111 ([M–OAc–OPh–Ac]$^+$, 55), 94 ([PhOH]$^+$, 18), 81 ([M–OAc–CH_2OAc–OPh]$^+$, 15), 43 (Ac, 100). NMR data of α-anomer: ^{1}H NMR (400.13 MHz, δ, ppm): 1.97 (3H, s, Ac); 2.10 (3H, s, Ac); 4.10–4.30 (3H, m, 5-H, 6-CH_2); 5.38 (1H, m, $J_{4,5} \approx$ 9.5 Hz, 4-H); 5.69 (1H, m, 1-H); 5.96–6.04 (2H, m, 2-H, 3-H); 7.00–7.12 (3H, m, *o*-Ph; *p*-Ph); 7.25–7.32 (2H, m, *m*-Ph). ^{13}C NMR (100.58 MHz, δ, ppm): 20.7, 21.0, 2 CH_3; 62.7, $C_{(6)}$; 65.1, $C_{(4)}$; 67.8, $C_{(5)}$; 93.0, $C_{(1)}$; 117.1, *o*-Ph; 122.5, *p*-Ph; 127.1, $C_{(2)}$; 129.5, *m*-Ph; 130.1, $C_{(3)}$; 157.1, *i*-Ph; 170.3, 170.8, 2 CO. NMR data of β-anomer: ^{1}H NMR (400.13 MHz, δ, ppm): 1.83 (3H, s, Ac); 2.10 (3H, s, Ac); 4.19 (1H, m, 6a-H); 4.25 (1H, m, 5-H); 4.31 (1H, m, 6b-H); 5.15 (1H, m, 4-H); 5.80 (1H, s, 1-H); 6.13 (2H, m, 2-H, 3-H); 6.95–7.05 (3H, m, *o*-Ph, *p*-Ph); 7.25–7.30 (2H, m, *m*-Ph). ^{13}C NMR (100.58 MHz, δ, ppm): 20.4, 21.0, 2 CH_3; 63.3, $C_{(6)}$; 63.4, $C_{(4)}$; 72.8, $C_{(5)}$; 91.6, $C_{(1)}$; 116.2, *o*-Ph; 122.1, *p*-Ph; 125.4, $C_{(2)}$; 129.4, *m*-Ph, $C_{(3)}$; 156.7, *i*-Ph; 170.2, 170.5, 2 CO.

Ethyl 2,3-dideoxy-α-D-glucopyranoside (4). Compound **4** was synthesized from **2** *via* hydrogenation in ethanol under catalysis with 10% palladium-charcoal at ambient temperature followed by deacetylation with sodium methoxide in dry methanol by a modified procedure from Ref. 24. Diacetyl derivative **2** (2.24 g, 8.7 mmol) dissolved in dry ethanol (30 ml) was hydrogenated at room temperature in the presence of Pd catalyst (20 mg). The solution was filtered, and ethanol evaporated. The residue (2.2 g) was dissolved in dry methanol (50 ml) and treated with 3 ml sodium methoxide solution in methanol (3.5 mmol/ml) at 25 °C. T.l.c. (petroleum ether–diethyl ether 2 : 1) showed the disappearance of the starting saturated diacetyl compound for 1.5 h. The mixture was neutralized with Amberlite IRC-50 and filtered off. After evaporation of methanol, the residue was eluted from silica gel (50 g) with chloroform–methanol (4 : 1) to yield **4** as a syrup which could not be crystallized (1.22 g, 82%), $[\alpha]_D^{23}$ 107 (*c* = 0.8, H_2O). Lit.: *mp* 67–70 °C (benzene–light petroleum ether) [22, 24, 26, 27]; $[\alpha]_D^{20}$ 141 (*c* = 0.7, H_2O) [26], 113 ($CHCl_3$) [27], 135 (H_2O), 151 (EtOH) [22], 154 (EtOH) [24]. ^{1}H NMR (250.13 MHz, δ, ppm): 1.23 (3H, t, $J \approx$ 7.2 Hz, CH_3); 1.64–1.98 (4H, m, 2 2-H, 2 3-H); 2.55 (1H, brs, OH); 3.00 (1H, brs, OH); 3.34–3.85 (6H, m, 4-H, 5-H, CH_2(Et), 6-H); 4.76 (1H, d, $J \approx$ 3.5 Hz, 1-H). ^{13}C NMR (62.86 MHz, δ, ppm): 15.0, CH_3; 27.1, $C_{(3)}$; 29.4, $C_{(2)}$; 62.4, CH_2(Et); 63.0, $C_{(6)}$; 67.1, $C_{(4)}$; 72.8, $C_{(5)}$; 95.9, $C_{(1)}$.

Phenyl 2,3-dideoxy-α-D-glucopyranoside (5). The synthesis of **5** was carried out analogously to the preparation of **4.** Compound **3** (4.23 g, 13.81 mmol) absorbed hydrogen (308 ml) under catalysis with 10% palladium-charcoal (40 mg) in ethanol (60 ml) at 25 °C, and followed by deacetylation with sodium methoxide in methanol, was converted to **5**. The t.l.c. (chloroform–methanol 4 : 1) evidenced for the disappearance of the starting saturated diacetyl compound for 2.5 h. The mixture was neutralized with Amberlite IRC-50 and filtered off. After evaporation of methanol, the residue was dissolved in 20 ml of the mixture hexane–chloroform (1 : 1) and filtered off. The filtrate was concentrated to give a solid. After recrystallization from 20 ml of petroleum ether–chloroform (4 : 1) and drying *in vacuo* (60–70 °C/0.1 mm), colourless needles of **5** were obtained (2.70 g, 87%), *mp* 93–94 °C; $[\alpha]_D^{24}$ 128.5 (*c* = 1.03, EtOH). MS, *m/z* (rel. int., %): 224 (M$^+$, 1), 207 ([M –OH]$^+$, 1), 189 ([M–H–2OH]$^+$, 2), 131 ([M–OPh]$^+$, 100), 113 ([M–H–OH–OPh]$^+$, 17), 94 ([PhOH]$^+$, 18), 71 (10). ^{1}H NMR (400.13 MHz, δ, ppm): 1.80–2.10 (4H, m, 2 2-H, 2 3-H); 2.42 (2H, brs, 2 OH); 3.61–3.87 (4H, m, 4-H, 5-H, 2 6-H); 5.52 (1H, dd, $J \approx$ 3.5 Hz, $J \approx$ 1.0 Hz, 1-H); 6.95–7.30 (5H, m, Ph). ^{13}C NMR (100.58 MHz, δ, ppm): 26.9, $C_{(3)}$; 29.3, $C_{(2)}$; 62.9, $C_{(6)}$; 66.8, $C_{(4)}$; 73.4, $C_{(5)}$; 94.5, $C_{(1)}$; 116.4, *o*-Ph; 121.9, *p*-Ph; 129.4, *m*-Ph; 156.6, *i*-Ph.

Ethyl 2,3-dideoxy-6-O-tosyl-α-D-glucopyranoside (6). Tosyl chloride (1.35 g, 7.1 mmol) was added under stirring to a solution of diol **4** (1.2 g, 6.8 mmol) in dry pyridine (10 ml). After 20 h at room temperature, the t.l.c. (chloroform–methanol 9 : 1) showed the disappearance of the starting **4**, and pyridine was evaporated. The solution of the residue in chloroform (50 ml) was washed with water (3 × 20 ml), dried ($MgSO_4$), filtered off and concentrated. The residue was eluted from silica gel (90 g) with chloroform–methanol (9 : 1) to give an oily product **6** (1.1 g, 46%), $[\alpha]_D^{22}$ 60 (*c* = 1.075, chloroform). Found, %: C 53.33; H 6.73; S 9.20. $C_{15}H_{22}O_6S$. Calculated, %: C 54.53; H 6.71; S 9.70. MS, *m/z* (rel. int., %): 329 ([M–H]$^+$, 1), 299 ([M–2H–Et]$^+$, 2), 285 ([M–OEt]$^+$, 9), 267 ([M–H–OEt–OH]$^+$, 2), 172 ([TsOH]$^+$, 9), 155 (Ts, 23)$^+$, 115 ([M–H–Et–$TsOCH_2$]$^+$, 100), 91 ([Ts–SO_2]$^+$, 55), 87 (39), 72 (90), 69 (18), 65 (18), 57 (14), 43 (38), 41 (19), 39 (10). ^{1}H NMR (250.13 MHz, δ, ppm): 1.15 (3H, t, $J \approx$ 7.2 Hz, CH_3(Et)); 1.60–1.90 (4H, m, 2 2-H, 2 3-H); 2.43 (3H, s, CH_3(Ts)); 3.35–3.75 (4H, m, OCH_2, 4-H, 5-H); 4.20 (1H, dd, $J_{6a,6b} \approx$ 11.3 Hz, $J_{5,6a} \approx$ 3.0 Hz, 6a-H); 4.35 (1H, dd, $J_{6a,6b} \approx$ 11.3 Hz, $J_{5,6b} \approx$ 3.5 Hz, 6b-H); 4.70 (1H, d, $J \approx$ 3.0 Hz, 1-H); 7.32 (2H, m, 3'-Ts); 7.78 (2H, m, 2'-Ts); 8.58 (1H, d,

$J \approx 4.5$ Hz, OH). ^{13}C NMR (62.86 MHz, δ, ppm): 15.1, CH_3(Et); 21.6, CH_3(Ts); 27.1, $C_{(3)}$; 29.2, $C_{(2)}$; 62.5, CH_2(Et); 65.6, $C_{(4)}$; 69.9, $C_{(6)}$; 71.6, $C_{(5)}$; 95.9, $C_{(1)}$; 127.9, 2'-Ts; 129.8, 3'-Ts; 133.1, 4'-Ts; 144.8, 1'-Ts.

Phenyl 2,3-dideoxy-6-O-tosyl-α-D-glucopyranoside (7). A solution of diol **5** (2.60 g, 11.6 mmol) in pyridine (20 ml) was stirred with tosyl chloride (2.32 g, 12.2 mmol) at ambient temperature. After 2 h the t.l.c. (chloroform–methanol 8 : 1) of the mixture showed the disappearance of the starting **5** and the formation of a single product. Pyridine was evaporated (50 °C/15 mm, then 70 °C/0.5 mm), the residue was dissolved in 10 ml of chloroform–methanol (1 : 1) and filtered off. After evaporation of the solvents, the residue was eluted from silica gel (120 g) with chloroform–methanol (9.5 : 0.5) to give a solid (3.8 g). After recrystallization from petroleum ether–chloroform (4 : 1) and drying *in vacuo* the colourless crystals of **7** were obtained (3.03 g, 69%), *mp* 74–77 °C; $[\alpha]_D^{22}$ 68 (c = 0.73, EtOH), $[\alpha]_D^{25}$ 61 (c = 5.5, chloroform). Found, %: C 61.60; H 5.75; S 8.10. $C_{19}H_{22}O_6S$. Calculated, %: C 60.30; H 5.86; S 8.47. MS, *m/z* (rel. int., %): 378 (M^+, 1), 285 ($[M–OPh]^+$, 95), 267 ($[M–H–OH–OPh]^+$, 15), 176 ($[M–OH–TsO]^+$, 1), 173 ($[TsOH_2]^+$, 12), 155 ($[Ts]^+$, 63), 113 ($[M–H–OPh–TsO]^+$, 94), 95 ($[PhOH_2]^+$, 97), 94 ($[PhOH]^+$, 66), 91 ($[Ts–SO_2]^+$, 100), 85 (21), 83 ($[M–OH–OPh–TsOCH_2]^+$, 19), 81 (30), 77 ($[Ph]^+$, 18), 71 (19), 69 (45), 67 (43), 65 (28), 57 (27), 43 (32), 39 (15). ^{1}H NMR (400.13 MHz, δ, ppm): 1.83–2.06 (4H, m, 2-H, 3-H); 2.29 (1H, d, $J \approx 5.0$ Hz, OH); 2.43 (3H, s, CH_3); 3.71 (1H, m, 5-H); 3.76 (1H, m, 4-H); 4.03 (1H, dd, $J_{6a,6b} \approx 11.4$ Hz, $J_{5,6a} \approx 2.0$ Hz, 6a-H); 4.40 (1H, dd, $J_{6a,6b} \approx 11.4$ Hz, $J_{5,6b} \approx 3.2$ Hz, 6b-H); 5.45 (1H, d, $J \approx 3.2$ Hz, 1-H); 6.95–7.02 (3H, m, *o*-Ph, *p*-Ph); 7.20–7.27 (2H, m, *m*-Ph); 7.31 (2H, m, 3'-Ts); 7.76 (2H, m, 2'-Ts). ^{13}C-NMR (100.58 MHz, δ, ppm): 21.7, CH_3; 26.6, $C_{(3)}$; 29.3, $C_{(2)}$; 65.0, $C_{(4)}$; 69.2, $C_{(6)}$; 72.2, $C_{(5)}$; 94.7, $C_{(1)}$; 116.3, *o*-Ph; 121.9, *p*-Ph; 128.0, 2'-Ts; 129.4, *m*-Ph; 129.9, 3'-Ts; 132.8, 4'-Ts; 145.0, 1'-Ts; 156.5, *i*-Ph.

Ethyl 6-dibutylamino-2,3,6-trideoxy-α-D-glucopyranoside (8). Compound **8** was obtained from **6** (1.07 g, 3.24 mmol) and an excess of dibutylamine (5.5 ml, 32.4 mmol). The reagents were heated at 100 °C. The t.l.c. of mixture showed the disappearance of the starting **6** in 6 h. The mixture was filtered and evaporated, and the residue was eluted from silica gel (30 g) with chloroform-methanol (9 : 1) to yield an oily product **8** (0.28 g, 30%), $[\alpha]_D^{22.5}$ 33 (c = 1.08, chloroform). ^{1}H NMR (250.13 MHz, δ, ppm): 0.90 (6H, t, $J \approx 7.1$ Hz, CH_3(Bu)); 1.19 (3H, t, $J \approx 7.1$ Hz, CH_3(Et)); 1.20–1.48 (8H, m, CH_2(Bu)); 1.60–1.85 (4H, m, 2-H, 3-H); 2.25–2.40 (2H, m, 6-H); 2.50–2.75 (4H, m, CH_2N(Bu)); 3.45 (2H, m, $J \approx 7.1$ Hz, OCH_2); 3.60–3.75 (2H, m, 4-H, 5-H); 4.70 (1H, d, $J \approx 3.0$ Hz, 1-H). ^{13}C-NMR (75.43 MHz, δ, ppm): 14.0, 2 CH_3(Bu); 15.2, CH_3(Et); 20.5, 2 CH_2(Bu); 26.1, $C_{(3)}$; 28.8, $C_{(2)}$; 28.9, 2 CH_2(Bu); 54.9, 2 CH_2(Bu); 59.8, $C_{(6)}$; 62.4, OCH_2) 67.2, $C_{(4)}$; 72.9, $C_{(5)}$; 96.2, $C_{(1)}$.

Ethyl 6-piperidino-2,3,6-trideoxy-α-D-glucopyranoside (9). Compound **9** was obtained from **6** (1.42 g, 4.3 mmol) and an excess of piperidine (1.28 ml, 12.9 mmol) in 10 ml of toluene at 80 °C. The t.l.c. (methylene chloride–methanol 9 : 1) of the mixture showed the disappearance of starting **6** in 7 h. Then the remaining toluene and the piperidine were evaporated, toluene (20 ml) was added, the obtained precipitate filtered off, and the filtrate was concentrated. The residue was eluted from silica gel (100 g) with methylene chloride–methanol (9 : 1) to give oily **9** (0.6 g, 57%), $[\alpha]_D^{24}$ 64 (c = 0.74, chloroform). Found, %: C 64.16; H 10.45; N 5.64. $C_{13}H_{25}NO_3$. Calculated, %: C 64.16; H 10.35; N 5.76. MS, *m/z* (rel. int., %): 243 (M^+, 8), 226 ($[M–OH]^+$, 2), 198 ($[M–OEt]^+$, 52), 114 ($[M–OEt–Pip]^+$, 12), 98 ($[PipCH_2]^+$, 100), 85 ($[PipH]^+$, 49), 84 ($[Pip]^+$, 16), 69 (20), 67 (12), 45 (20). ^{1}H NMR (300.13 MHz, δ, ppm): 1.18 (3H, t, $J \approx 7.2$ Hz, CH_3); 1.39–1.52 (2H, m, 2 3'-H); 1.52–1.68 (4H, m, 4 2'-H); 1.68–1.85 (4H, m, 2-H, 3-H); 2.45 (2H, br, 2 1'-H); 2.62 (2H, d, $J \approx 6.0$ Hz, 2 6-H); 2.70 (2H, br, 2 1'-H); 3 .34–3.75 (4H, m, CH_2(Et), 4-H, 5-H); 4.70 (1H, d, $J \approx 3.0$ Hz, 1-H); 6.40 (1H, brs, OH). ^{13}C NMR (75.43 MHz, δ, ppm): 15.1, CH_3; 23.7, $C_{(3')}$; 25.6, $C_{(2')}$; 26.2, $C_{(3)}$; 28.9, $C_{(2)}$; 55.6, $C_{(1')}$; 62.5, OCH_2; 63.3, $C_{(6)}$; 67.0, $C_{(4)}$; 72.3, $C_{(5)}$; 96.2, $C_{(1)}$.

Ethyl 6-pyrrolidino-2,3,6-trideoxy-α-D-glucopyranoside (10). A solution of **6** (0.32 g, 0.97 mmol) in 10 ml toluene was treated with pyrrolidine (0.42 ml, 5.0 mmol) and heated in a Schlenk tube at 70 °C under argon for 4 h, when the t.l.c. of the mixture showed the disappearance of the starting **6**. The mixture was concentrated, diluted with chloroform (50 ml), washed twice with water, dried ($MgSO_4$), filtered, and the solvent was evaporated. The residue was eluted from silica gel (50 g) with methylene chloride–methanol (7 : 3) to give an oily **10** (0.09 g, 38%), $[\alpha]_D^{23}$ 64 (c = 0.81, chloroform). Found, %: C 63.90; H 10.10; N 6.00. $C_{12}H_{23}NO_3$. Calculated, %: C 62.85; H 10.11; N 6.11%). MS (FAB), *m/z* (rel. int., %): 230 ($[M+H]^+$, 100), 228 ($[M–H]^+$, 18), 213 ($[M–OH]^+$, 4), 184 ($[M–OEt]^+$, 53), 154 (12), 114 ([M–

OEt–Pyr]$^+$, 7), 84 ([PyrCH$_2$]$^+$, 98), 72 (12), 71 ([PyrH]$^+$, 13), 70 ([Pyr], 8), 67 (2). ^{1}H NMR (250.13 MHz, δ, ppm): 1.19 (3H, t, $J \approx 7.1$ Hz, CH$_3$); 1.60–1.90 (8H, m, 4 2'-H, 2 2-H, 2 3-H); 2.45–2.60 (3H, m, 6b-H, 2 1'-H); 2.60–2.75 (2H, m, 2 1'-H); 2.88 (1H, dd, $J_{6a,6b} \approx 11.5$ Hz, $J_{5,6a} \approx 10.5$ Hz, 6a-H); 3.38–3.72 (4H, m, OCH$_2$, 4-H, 5-H); 4.72 (1H, d, $J \approx 3.3$ Hz, 1-H); 5.35 (1H, brs, OH). ^{13}C NMR (62.86 MHz, δ, ppm): 15.1, CH$_3$; 23.4, 2 C$_{(2')}$; 26.1, C$_{(3)}$; 28.8, C$_{(2)}$; 54.9, 2 C$_{(1')}$; 60.9, C$_{(6)}$; 62.3, OCH$_2$; 68.0, C$_{(4)}$; 73.4, C$_{(5)}$; 96.1, C$_{(1)}$.

Ethyl 6-azetidino-2,3,6-trideoxy-α-D-glucopyranoside (11). In a Schlenk tube an excess of azetidine (0.95 ml, 14 mmol) was added to a solution of the tosylate **6** (1.54 g, 4.68 mmol) in toluene (15 ml). The mixture was stirred and heated at 50 °C under argon. The t.l.c. (chloroform–methanol 2 : 1) showed the disappearance of the starting compound **6** after 10 h. Toluene and unreacted azetidine were evaporated, and hexane (20 ml) was added. After filtration and concentration of the mixture, the residue was eluted from silica gel (50 g) with chloroform–methanol (2 : 1) to give solid **11** (0.24 g, 24%), *mp* 76 °C, $[\alpha]_D^{23}$ 78 ($c = 1.02$, chloroform). Found, %: C 60.61; H 9.75; N 6.33. $C_{11}H_{21}NO_3$. Calculated, %: C 61.37; H 9.83; N 6.51. MS (FAB), *m/z* (rel. int., %): 216 ([M+H]$^+$, 100), 214 ([M–H]$^+$, 12), 198 ([M–OH]$^+$, 3), 170 ([M–OEt]$^+$, 66), 154 ([M–H–OH–OEt]$^+$, 44), 93 (12), 79 (11), 70 ([AzCH$_2$]$^+$, 56), 69 ([AzCH]$^+$, 17), 67 (15), 61 (11). ^{1}H NMR (300.13 MHz, δ, ppm): 1.18 (3H, t, $J \approx 7.0$ Hz, CH$_3$); 1.60–1.80 (4H, m, 2-H, 3-H); 2.04 (2H, quintet, $J \approx 7.2$ Hz, 2'-H); 2.56 (1H, dd, $J_{6a,6b} \approx 11.5$ Hz, $J_{5,6b} \approx 4.0$ Hz, 6b-H); 2.65 (1H, dd, $J_{6a,6b} \approx 11.5$ Hz, $J_{5,6a} \approx 10.5$ Hz, 6a-H); 3.20 (2H, q, $J \approx 7.0$ Hz, OCH$_2$); 3.24–3.46 (5H, m, 1'-H, 4-H); 3.63 (1H, m, 5-H); 4.68 (1H, m, $J \approx 3.2$ Hz, 1-H); 5.8 (1H, brs, OH). ^{13}C-NMR (75.43 MHz, δ, ppm): 15.1, CH$_3$; 17.8, C$_{(2')}$; 26.2, C$_{(3)}$; 28.8, C$_{(2)}$; 56.0, C$_{(1')}$; 62.3, OCH$_2$; 64.4, C$_{(6)}$; 67.7, C$_{(4)}$; 72.8, C$_{(5)}$; 96.1, C$_{(1)}$.

Phenyl 6-piperidino-2,3,6-trideoxy-α-D-glucopyranoside (12). Compound **12** was synthesized from **7** (0.42 g, 1.12 mmol) and piperidine (2.5 ml, 2.53 mmol) in 10 ml toluene at 80 °C. The t.l.c. showed the disappearance of the starting **6** after 6 h. The mixture was concentrated, diethyl ether was added and the obtained precipitate filtered off, then the filtrate was concentrated. The residue was eluted from silica gel (60 g) with methylene chloride–methanol (9 : 1) to give solid **12** (0.27 g, 84%), *mp* 84 °C, $[\alpha]_D^{22.5}$ 107 ($c = 0.97$, chloroform). Found, %: C 68.70; H 8.79; N 4.84. $C_{17}H_{25}NO_3$. Calculated, %: C 70.07; H 8.64; N 4.81. MS, *m/z* (rel. int., %): 291 (M$^+$, 10), 275 ([M–O]$^+$, 1), 273 (2), 234 (2), 213 (1), 199 (14), 198 ([M–OPh]$^+$, 79), 196 (5), 128 (10), 112 ([M–OPh–Pip–2H]$^+$, 16), 99 ([PipCH$_3$]$^+$, 43), 98 ([PipCH$_2$]$^+$, 100), 94 ([PhOH]$^+$, 22), 85 ([PipH]$^+$, 53), 84 ([Pip]$^+$, 34), 77 ([Ph]$^+$, 11), 69 (22), 55 (28), 41 (51), 28 (21). ^{1}H NMR (250.13 MHz, δ, ppm): 1.30–1.60 (6H, m, 4 2'-H, 2 3'-H); 1.75–2.10 (4H, m, 2 2-H, 2 3-H); 2.30 (2H, br, 2 1'-H); 2.42–2.65 (4H, m, 2 6-H, 2 1'-H); 3.50–3.82 (4H, m, OCH$_2$, 4-H, 5-H); 5.50 (1H, d, $J \approx 3.2$ Hz, 1-H); 6.90–7.10 (3H, m, *o*-Ph, *p*-Ph); 7.20–7.33 (2H, m, *m*-Ph). ^{13}C NMR (62.86 MHz, δ, ppm): 23.9, C$_{(3')}$; 25.9, C$_{(2')}$; 25.9, C$_{(3)}$; 28.8, C$_{(2)}$; 55.6, C$_{(1')}$; 63.7, C$_{(6)}$; 67.5, C$_{(4)}$; 72.8, C$_{(5)}$; 94.9, C$_{(1)}$; 116.5, *o*-Ph; 121.6, *p*-Ph; 129.3, *m*-Ph; 157.0, *i*-Ph.

Phenyl 6-pyrrolidino-2,3,6-trideoxy-α-D-glucopyranoside (13). A mixture of pyrrolidine (2.5 ml, 30 mmol) and a solution of **7** (2.07 g, 5.47 mmol) in 20 ml toluene was stirred under reflux at 70 °C under argon. After 5 h the t.l.c. (chloroform–methanol 9 : 1) showed the disappearance of starting **7**. The mixture was concentrated, diluted with chloroform (100 ml), washed twice with water, dried (MgSO$_4$), filtered, and then the solvent was evaporated. The residue (1.7 g) was eluted from silica gel (80 g) with chloroform–methanol (20 : 1) to give an oily **13** (0.95 g, 63%), $[\alpha]_D^{22}$ 89 ($c = 0.95$, chloroform). Found, %: C 68.42; H 8.31; N 5.10. $C_{16}H_{23}NO_3$. Calculated, %: C 69.29; H 8.36; N 5.05. GC-MS, *m/z* (rel. int., %): 277 (M$^+$, 8), 260 ([M–OH]$^+$, 2), 206 ([M–H–Pyr]$^+$, 1), 184 ([M–OPh]$^+$, 82), 114 ([M–OPh–Pyr]$^+$, 8), 98 ([M–OPh–Pyr–OH+H]$^+$, 12), 94 ([PhOH]$^+$, 15), 84 ([PyrCH$_2$]$^+$, 100), 77 ([Ph]$^+$, 7), 70 ([Pyr]$^+$, 18), 55 (16), 42 (25). MS (FAB), *m/z* (rel. int., %): 278 ([M+H]$^+$, 72), 277 (M, 10)$^+$, 276 ([M–H]$^+$, 13), 260 ([M–OH]$^+$, 2), 194 ([M–PyrCH$_2$+H]$^+$, 1), 185 ([M–OPh+H]$^+$, 12), 184 ([M– OPh]$^+$, 100), 114 ([M–OPh–Pyr]$^+$, 2), 94 ([PhOH]$^+$, 15), 84 ([PyrCH$_2$]$^+$, 51), 71 ([PyrH]$^+$, 8), 70 ([Pyr]$^+$, 7). ^{1}H NMR (400.13 MHz, δ, ppm): 1.67–1.76 (4H, m, 2'-H); 1.75–2.05 (4H, m, 2-H, 3-H); 2.42–2.52 (3H, m, 1'-H, 6a-H); 2.62–2.73 (2H, m, 1'-H); 2.90 (1H, dd, $J_{6a,6b} \approx 11.7$ Hz, $J_{5,6b} \approx 10.5$ Hz, 6b-H); 3.60 (1H, m, 4-H); 3.75 (1H, m, 5-H); 5.48 (1H, dd, $J \approx 3.5$ Hz, $J < 1.0$ Hz, 1-H); 6.96–7.01 (1H, m, *p*-Ph); 7.03–7.07 (2H, m, *o*-Ph); 7.24–7.30 (2H, m, *m*-Ph). ^{13}C-NMR (100.58 MHz, δ, ppm): 23.4, C$_{(2')}$; 25.9, C$_{(3)}$; 28.9, C$_{(2)}$; 54.9, 2 C$_{(1')}$; 60.7, C$_{(6)}$; 68.9, C$_{(4)}$; 72.5, C$_{(5)}$; 95.0, C$_{(1)}$; 116.6, *o*-Ph; 121.7, *p*-Ph; 129.4, *m*-Ph; 157.0, *i*-Ph.

Phenyl 6-azetidino-2,3,6-trideoxy-α-D-glucopyranoside (14). Azetidine (0.32 ml, 4.75 mmol) was added to a solution of the tosylate **7** (0.36 g, 0.95 mmol) in toluene (5 ml). The mixture was stirred and heated at 60 °C in a Schlenk tube under argon for 10 h, then the t.l.c.

(methylene chloride–methanol 8 : 2) showed the disappearance of the starting **7**. Toluene and unreacted azetidine were evaporated, and the residue was eluted from silica gel (30 g) with chloroform–methanol (2 : 1) giving a solid **14** (0.15 g, 60%), *mp* 75 °C, $[\alpha]_D^{23}$ 135 ($c = 0.6$, chloroform). Found, %: C 67.15; H 8.05; N 5.31. $C_{15}H_{21}NO_3$. Calculated, %: C 68.42; H 8.04; N 5.32. GC-MS, *m/z* (rel. int., %): 263 (M^+, 1), 246 ($[M–OH]^+$, 1), 206 ($[M–Az]^+$, 1), 170 ($[M–OPh]^+$, 57), 100 ($[M–OPh–AzCH_2]^+$, 6), 94 ($[PhOH]^+$, 6), 70 ($[AzCH_2]^+$, 100), 57 ($[AzH]^+$, 8), 56 ($[Az]^+$, 8), 42 (18), 41 (15), 39 (4). ^{1}H NMR (300.13 MHz, δ, ppm): 1.73–2.00 (6H, m, 2-H, 2'-H, 3-H); 2.49 (1H, dd, $J_{6a,6b} \approx 11.5$ Hz, $J_{5,6b} \approx 3.8$ Hz, 6b-H); 2.59 (1H, dd, $J_{6a,6b} \approx 11.5$ Hz, $J_{5,6a} \approx 10{,}5$ Hz, 6a-H); 3.15 (4H, m, 1'-H); 3.34–3.52 (2H, m, 4-H, 5-H); 5.40 (1H, d, $J \approx 3.5$ Hz, 1-H); 5.90 (1H, brs, OH); 6.85–7.07 (3H, m, *o*-Ph, *p*-Ph); 7.10–7.25 (2H, m, *m*-Ph). ^{13}C NMR (75.43 MHz, δ, ppm): 17.8, $C_{(2')}$; 28.9, $C_{(2)}$; 29.9, $C_{(3)}$; 55.9, 2 $C_{(1')}$; 64.0, $C_{(6)}$; 68.5, $C_{(4)}$; 72.7, $C_{(5)}$; 95.0, $C_{(1)}$; 116.6, *o*-Ph; 121.7, *p*-Ph; 129.4, *m*-Ph; 157.0, *i*-Ph.

Acknowledgements: The authors are grateful to Mrs. H. Baudisch, Mrs. M. Diehr and Mrs. K. Kortus for assistance and performance of analytical work. Thanks also to the Fonds der chemischen Industrie for financial support.

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Received July 5, 1999

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