Synthesis and Reactions of Highly Protected Mannosamines

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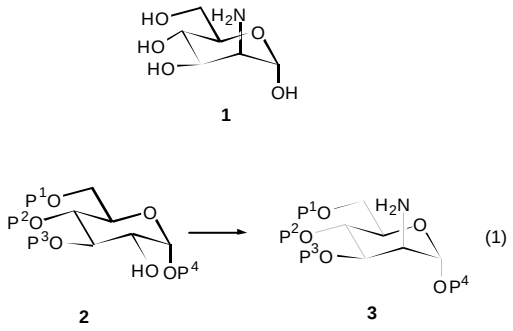
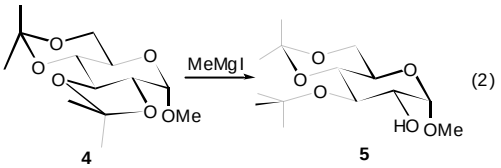
Highly protected mannosamine derivatives are synthesized from protected glucose derivatives having a free hydroxy group at C_2 position. Indium-mediated allylation of protected mannosamine derivatives is investigated.

Mannosamine **1** is an important aminosugar and is present in a number of naturally occurring oligosaccharides.[1] The compound can also serve as an important precursor for a number of higher homologues of sugar derivatives having different kinds of biological activities.[2] Most published syntheses of **1** use arabinose[3] or glucal[4] as starting materials. Separation of stereoisomers of intermediates is generally required in these procedures. Equilibraton of 2-glucosamine with **1** under basic conditions has been reported, but in low overall conversion.[5] An ideal approach for the synthesis of mannosamine derivative **3** is to start with a glucose derivative **2** having a free hydroxy group at C_2. Inversion of configuration by displacement of this hydroxy group with an amino group would lead to a convenient synthesis of mannosamine derivatives **3** (eq 1).

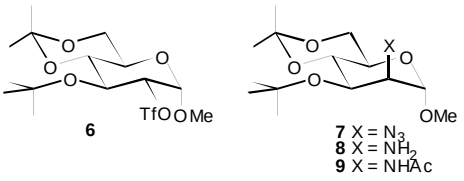


We recently reported a convenient procedure for the synthesis of the highly protected glucose derivative **5** having the desired free hydroxy group at C_2 from the corresponding bisacetonide **4** (eq 2).[6] Accordingly, this will be an ideal starting point for the synthesis of highly protected mannosamine derivatives **3**. In this paper, we address the details for the synthesis and reactions of highly protected mannosamine derivatives.



RESULTS AND DISCUSSION

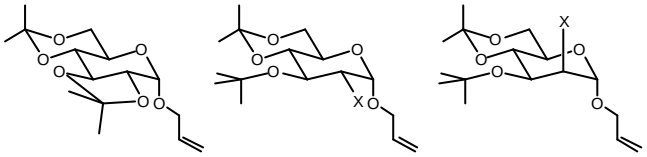
In the beginning of this research, methyl glucoside **5** was treated with triflic anhydride to give the corresponding triflate **6** in excellent yield. Without further purification, **6** was allowed to react with sodium azide to afford azide **7**. Catalytic hydrogenolysis of **7** yielded amine **8** which was further transformed into the corresponding amide **9** upon treatment with acetic anhydride.



This promising preliminary investigation prompted us to tackle several related systems, in particular, those having a labile anomeric protective group. Allyl glucosides **10** was subjected to the reaction with the MeMgI in refluxing benzene for 1.5 h to give the corresponding ring opening product **11** having a free hydroxy group at the C_2 position. Similar transformation as described above yielded the mannosamide derivative **15**. It is noteworthy that triphenylphosphine was required for the reduction of **13**.[7] Attempts to use other reducing agents resulted in low isolation yield of the amine **13**.

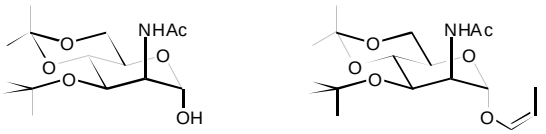
Several procedures in the literature are known to re-

Dedicated to Professor Sheng-lieh Liu on the occasion of his ninetieth birthday.



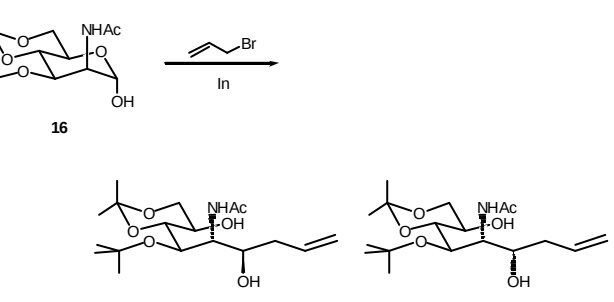
10 **11** X = OH; 12 X = **OTf** **13** X = N_3; **14** X = NH_2; **15** X = NHAc

move the allyl pro tec tive group at the anomeric po si tion. How ever, treat ment of **15** with $Pd(PPh_3)4$ in ace tic acid at 80 °C did not yield **16**. The acetonide pro tec tive group was also re moved un der these con di tions. In a sim i lar man ner, re action of **15** with $PdCl_2$ in MeOH at room tem per a ture also produced a mix ture of prod ucts while the acetonide moi ety was gone. Pre sum ably, the pro duc tion of the HCl from this transformation would facilitate further deprotection process. Gigg's pro ce dure was then adopted to isomerize the allyl protec tive group to the cor re spond ing 1-propenyl moi ety.[8] It is in ter est ing to note that the re ac tion was stereoselective and only cis-isomer **17** was ob tained. Di rect treat ment of crude **17** with $HgO/HgCl_2$ af forded **16** in 80% over all yield.

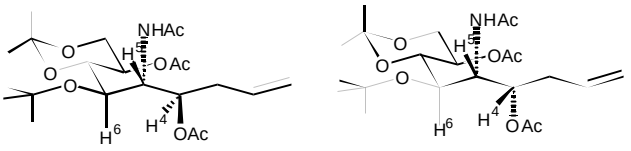


16 **17**

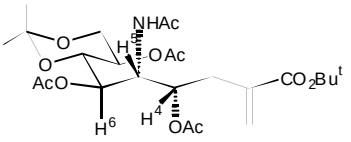
In cor po ra tion of an allyl substituent at the anomeric cen ter fur nishes a use ful en try for the ex ten sion of a three-carbon unit to a sugar mol e cule. Many pro ce dures are known to ac com plish this goal. Re ac tions of car bon nucleophiles with a sugar de riv a tive are well doc u mented. More re cently the use of in dium pro vides a pow er ful ar se nal for this purpose. In par tic u lar, the re ac tion can be car ried out in aque ous me dium and ex hib its high stereoselectivity.[9] Ac cord ingly, the in dium-mediated allylation of **16** in acetonitrile-water (1:1) or THF-water (1:1) yielded an in sep a ra ble mix ture of **18** and **19** (eq 3). It is note wor thy that wa ter is es sen tial for this re ac tion. In the ab sence of wa ter, no de sired prod uct was obtained at all. Acetylation of **18** and **19** af forded the re spec tive ac e tates **20** and **21**, the ma jor iso mer **20** be ing ob tained as a crys tal line solid. The stereochemistry as sign ment was based on the NMR data. The cou pling con stants $J_{H4,H5}$ and $J_{H5,H6}$ in **20** were 10.2 and 4.8 Hz, re spec tively. In a re lated com pound **22**, the acetoxy group at C^4 and the acetamido group at C^5 are syn. The cou pling con stants $J_{H4,H5}$ and $J_{H5,H6}$ in **22** were 4.0 and 8.5 Hz, re spec tively.[10] Con se quently, the ab so lute configu ration at C^4 of the ma jor prod uct **20** should be *R* and that of the mi nor prod uct **21** should be *S*.



16 **18** **19**



20 **21**



22

In sum mary, we have dem on strated a con ve nient pro ce dure for the syn the sis of highly pro tected mannosamine deriv a tives which can be ex tended to the syn the sis of a va ri ety of higher homo logues of sugar de riv a tives. Fur ther ex ten sion of this re search is in prog ress in our lab o ra tory.

EXPERIMENTAL SECTION

Methyl 2-O-trifluoromethanesulfonyl-4,6-O-isopropylidene-α-D-glucopyranoside (6)

To a so lu tion of **5** (0.29 g, 1.0 mmol) in dried CH_2Cl_2 (4.0 mL) at -75 °C was added pyridine (0.24 g, 3.0 mmol) and Tf_2O (0.85 g, 3.0 mmol). The mix ture was stirred from -75 °C to 0 °C for 2.5 h, quenched with wa ter (10 mL), and ex tracted with ether (10 mL × 2). The com bined or ganic layer was dried ($MgSO_4$), fil tered and the sol vent of the fil trate was evap o-rated *in vacuo* to give the crude **6** (0.35 g, 82%), which was un sta ble and used for the next re ac tion im me di ately.[1]H NMR (300 MHz, $CDCl_3$) δ 1.19 (s, 9H), 1.37 (s, 3H), 1.45 (s, 3H), 3.40 (s, 3H), 3.42-3.47 (m, 1H), 3.60-3.72 (m, 2H), 3.80-3.88 (m, 1H), 3.98 (t, *J* = 9.2 Hz, 1H), 4.51 (dd, *J* = 9.2, 3.6 Hz,

1H), 4.91 (d, J = 3.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.0, 28.9, 29.3, 55.5, 62.2, 63.9, 64.2, 68.9, 73.8, 75.8, 84.4, 97.8, 99.5; ^{19}F NMR (300 MHz, $CDCl_3$) δ -75.9.

Methyl 2-azido-2-deoxy-4,6-O-isopropylidene-3-O-tert-butyl-α-D-mannopyranoside (7)

A DMF solution (5 mL) of **6** (0.35 g, 0.83 mmol) was treated with NaN_3 (0.26 g, 4.2 mmol) and the mixture was stirred at 80 °C for 16 h. Water (10 mL) was added and the mixture was extracted with ether (10 mL). The organic phase was dried ($MgSO_4$), filtered and the solvent of the filtrate was removed *in vacuo* to give the residue which was chromatographed on silica gel (Hexane/EtOAc = 19/1) to afford **7** as a white solid (0.20 g, 77%): mp 54-56 °C; $[\alpha]_D^{24}$ = +72.4 (*c* 0.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.20 (s, 9H), 1.35 (s, 3H), 1.48 (s, 3H), 3.31 (s, 3H), 3.56 (br q, J = 8.5 Hz, 1H), 3.71-3.84 (m, 4H), 3.82 (dd, J = 9.5, 9.4 Hz, 1H), 3.95 (dd, J = 9.4, 3.8 Hz, 1H), 4.54 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.3, 28.4, 29.2, 54.8, 62.3, 65.1, 69.3, 70.1, 75.0, 99.7, 100.3; IR (neat) ν 2928, 2865, 2107, 1759, 1463, 1374, 1308, 1264, 1197, 1134, 1026, 970, 893, 864, 801 cm^{-1}; Anal. calcd for $C_{14}H_{25}O_5N_3$: C, 53.32; H, 7.99. Found: C, 52.72; H, 7.91.

Methyl 2-amino-2-deoxy-4,6-O-isopropylidene-3-O-tert-butyl-α-D-mannopyranoside (8)

A mixture of **7** (0.42 g, 1.3 mmol) and Pd/C (0.76 g) in ethanol (50.0 mL) was stirred under an atmosphere of H_2 for 8 h. The mixture was filtered through Celite and the solvent of the filtrate was evaporated *in vacuo* to afford the crude **8** (0.22 g, 58%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.11 (s, 9H), 1.28 (s, 3H), 1.42 (s, 3H), 3.16 (m, enbodied singlet for CH_3 group at 3.24, 4H), 3.52-3.60 (m, 1H), 3.60-3.88 (m, 4H), 4.80 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.4, 28.4, 29.0, 54.6, 55.9, 62.2, 64.8, 67.0, 69.4, 74.8, 99.7, 100.5; IR (neat) ν 3375, 3306, 2975, 2938, 2912, 2878, 2835, 1594, 1471, 1381, 1367, 1329, 1199, 1172, 1089, 971, 946, 885 cm^{-1}.

Methyl 2-acetamido-2-deoxy-4,6-O-isopropylidene-3-O-tert-butyl-α-D-mannopyranoside (9)

A mixture of **8** (0.22 g, 0.75 mmol), acetic anhydride (1.42 g, 13.9 mmol) and pyridine (0.93 g, 11.6 mmol) in CH_2Cl_2 (20 mL) was stirred at 40 °C for 13 h. The mixture was quenched with water (10 mL) and extracted with ether (20 mL). The organic phase was dried ($MgSO_4$), filtered and the solvent of the filtrate was removed *in vacuo* to give the residue which was chromatographed on silica gel (Hexane/EtOAc = 19/1) to afford **9** as a white solid (0.2 g, 77%): mp 88-90 °C; $[\alpha]_D^{27}$ = +72.4 (*c* 2.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.15 (s, 9H), 1.36 (s, 3H), 1.47 (s, 3H), 1.98 (s, 3H), 3.31 (s, 3H), 3.52 (t, J = 10.0 Hz, 1H), 3.64 (dt, J = 10.0, 4.8 Hz, 1H), 3.73 (t, J = 10.0 Hz, 1H), 3.80 (dd, J = 10.0, 4.8 Hz, 1H), 3.91 (dd, J = 10.0, 5.2 Hz, 1H), 4.20 (ddd, J = 6.8, 5.2, 0.8 Hz, 1H), 4.71 (d, J = 0.8 Hz, 1H), 5.78 (d, J = 6.8 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 19.2, 23.3, 28.2, 29.1, 54.3, 62.3, 64.2, 66.3, 70.5, 74.8, 99.6, 100.7, 170.6; IR (KBr) ν 3262, 3201, 3080, 2981, 2951, 2908, 2876, 2834, 2250, 1654, 1632, 1562, 1472, 1443, 1380, 1269, 1202, 1129, 1074, 1040, 985, 957, 918, 887, 863, 731 cm^{-1}; HRMS calcd for $C_{16}H_{29}O_6N$ 331.1995. Found 331.1998; Anal. calcd for $C_{16}H_{29}NO_6$: C, 57.97; H, 8.82. Found: C, 57.67; H, 8.54.

Allyl O^2,O^3;O^4,O^6-Bis-isopropylidene-α-D-glucopyranoside (10)

A mixture of allyl α-D-glucopyranoside (3.82 g, 17.3 mmol), TsOH (0.04 g, 0.21 mmol) and 2-methoxypropene (10 mL, 69 mmol), in dry DMF (50 mL) was stirred for 2 h at 20 °C. The mixture was poured into water (100 mL) and extracted with ether (50 mL × 2). The organic phase was dried ($MgSO_4$) and the solvent was removed *in vacuo* to afford **10** as an oil (4.56 g, 88%): $[\alpha]_D^{27}$ +86.6 (*c* 0.05, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.38 (s, 3H), 1.39 (s, 3H), 1.42 (s, 3H), 1.49 (s, 3H), 3.45-3.59 (m, 2H), 3.71-3.88 (m, 3H), 3.97-4.23 (m, 3H), 5.11-5.18 (m, 2H, embodied a doublet, J = 3.0 Hz), 5.27 (dq, J = 17.2, 1.4 Hz, 1H), 5.89 (ddt, J = 17.2, 10.9, 5.3 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 19.0, 26.3, 26.7, 28.9, 62.2, 65.0, 68.7, 73.7, 73.9, 76.7, 96.9, 99.5, 111.3, 117.4, 133.4; Anal calcd for $C_{15}H_{24}O_6$: C, 59.98; H, 8.05. Found C, 59.94; H, 8.12.

Allyl O^3-tert-Butyl-O^4,O^6-isopropylidene-α-D-glucopyranoside (11)

A benzene solution (20 mL) of **10** (0.92 g, 3.06 mmol) was allowed to react with MeMgI (2.4 mL, 2 M ether, 6.1 mmol) at 50-60 °C for 1.5 h. The mixture was quenched with NH_4Cl solution. The organic layer was separated, and the aqueous solution was extracted with ether. The combined organic layers were washed successively with water and brine and dried ($MgSO_4$) to afford **11** (0.83 g, 86%) as a color less oil: $[\alpha]_D^{27}$ +110.8 (*c* 0.05, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.21 (s, 9H), 1.37 (s, 3H), 1.44 (s, 3H), 2.06 (d, J = 7.9 Hz, 1H), 3.30-3.35 (m, 2H), 3.55-3.88 (m, 4H), 4.04 (dd, J = 12.8, 6.4 Hz, 1H), 4.22 (dd, J = 12.8, 5.4 Hz, 1H), 4.92 (d, J = 3.8 Hz, 1H), 5.21 (dd, J = 10.2, 1.5 Hz, 1H), 5.29 (dd, J = 17.3, 1.5 Hz, 1H), 5.92 (ddt, J = 17.3, 10.2, 5.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 19.0, 29.0, 29.3, 62.5, 64.3, 68.5, 72.2, 72.4, 73.3, 74.5, 98.3, 99.1, 118.0, 133.6; HRMS calcd for $C_{16}H_{28}O_6$: 316.1886, found: 316.1889; Anal calcd: C, 60.74; H, 8.92. Found C, 60.74; H, 9.06.

Allyl 2-Azido-2-deoxy-*O*^{3}-tert-butyl-*O*^{4},*O*^{6}-isopropylidene-α-D-mannopyranoside (13)

To a CH_2Cl_2 so lu tion (60 mL) of **11** (3.0 g, 9.5 mmol) and pyridine (1.5 mL, 19.0 mmol) at -10 °C was added Tf_2O (1.2 mL, 11.4 mmol) over a pe riod of 30 min, and the mix ture was stirred for 2 h at 0 °C. Ice-cooled wa ter (20 mL) was then in tro duced. The aque ous layer was ex tracted with ether (50 mL), and the com bined or ganic lay ers were dried ($MgSO_4$). The sol vent was re moved *in vacuo* to yield the crude **12** (3.6 g, 8.8 mmol, 93%) which was dis solved in DMF (60 mL). NaN_3 (2.86 g, 44.0 mmol) was added, and the mix ture was stirred at 80 °C for 18 h. Then wa ter was in tro duced, and the mix ture was ex tracted with ether (60 mL). The or ganic layer was suc ces sively washed with wa ter and brine and dried ($MgSO_4$). The sol vent was re moved *in vacuo* to give the res i-due which was chromatographed on silica gel (Hexane/EtOAc = 4/1) to af ford the **13** (2.17 g, 72%) as a col or less oil: $[\alpha]_D^{29}$ +72.4 (*c* 0.05, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.22 (s, 9H), 1.36 (s, 3H), 1.49 (s, 3H), 3.50-4.05 (m, 7H), 4.13 (ddt, *J* = 12.9, 5.3, 1.2 Hz, 1H), 4.50 (d, *J* = 1.2 Hz, 1H), 5.20 (dq, *J* = 11.5, 1.5 Hz, 1H), 5.27 (dq, *J* = 17.1, 1.5 Hz, 1H), 5.88 (dddd, *J* = 17.1, 11.5, 6.2, 5.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 19.3, 28.4, 29.2, 62.2, 65.3, 65.4, 68.1, 69.3, 70.2, 75.0, 98.4, 99.7, 117.9, 133.4; IR (neat) ν 2110 cm^{-1}; Anal calcd for $C_{16}H_{27}N_3O_5$: C, 56.29; H, 7.97; N, 12.31. Found C, 56.34; H, 8.32; N, 12.14.

Allyl 2-Amino-2-deoxy-*O*^{3}-tert-butyl-*O*^{4},*O*^{6}-isopropylidene-α-D-mannopyranoside (14)

Ph_3P (2.52 g, 9.60 mmol) was added to a so lu tion of **13** and the mix ture was stirred at am bi ent tem per a ture for an ad-di tional 12 h. Hex ane (50 mL) was in tro duced, and the slurry was fil tered. The fil trate was dried ($MgSO_4$), and the sol vent was re moved *in vacuo* to give the res i due which was chro-matographed on sil ica gel (Hex ane/EtOAc = 2/1) to af ford **14** (2.34 g, 78%) as a col or less oil: $[\alpha]_D^{29}$ +57.4 (*c* 0.05, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.17 (s, 9H), 1.35 (s, 3H), 1.46 (s, 3H), 3.11 (br, 1H), 3.60-3.85 (m, 7H), 3.39 (ddt, *J* = 13.0, 6.1, 1.2 Hz, 1H), 4.13 (ddt, *J* = 13.0, 5.2, 1.2 Hz, 1H), 4.73 (br s, 1H), 5.14-5.31(m, 2H), 5.89 (ddt, *J* = 17.3, 10.4, 5.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 19.2, 28.6, 29.2, 56.2, 62.5, 65.1, 67.9, 68.6, 69.8, 74.3, 99.5, 100.9, 117.3, 133.9; HRMS calcd for $C_{16}H_{29}NO_5$: 315.2046, found: 315.2034; Anal calcd: C, 60.93; H, 9.27; N, 4.44. Found C, 60.92; H, 8.99; N, 3.95.

Allyl 2-Acetamido-2-deoxy-4,6-O-isopropylidene-3-O-tert-butyl-α-D-mannopyranoside (15)

To a so lu tion of **14** (3.01 g, 9.55 mmol) in CH_2Cl_2 (30 mL) was added pyridine (0.9 mL, 11.5 mmol), and the mix-ture was cooled to 0 °C. Af ter a brief stir ring, ace tic an hy-dride (1.3 mL, 14.3 mmol) was added, and the mix ture was stirred overnight at room tem per a ture. The re ac tion was quenched with wa ter (10 mL) and di luted with CH_2Cl_2 (100 mL). The or ganic layer was washed with acqueous $CuSO_4$ so-lu tion (0.2 M, 50 mL), wa ter (100 mL), and brine (50 mL) and the or ganic layer was dried ($MgSO_4$). Sol vent was re moved *in vacuo* to yield **15** (3.23 g, 95%) as a white solid: mp 113-114 °C (hex ane); $[\alpha]_D^{26}$ +38.2 (*c* 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.16 (s, 9H), 1.36 (s, 3H), 1.48 (s, 3H), 2.03 (s, 3H), 3.50 (t, *J* = 8.7 Hz, 1H), 3.60-3.88 (m, 3H), 3.95 (dd, *J* = 8.7, 6.3 Hz, 1H), 3.88-4.05 (m, 1H), 4.05-4.18 (m, 1H), 4.23 (t, *J* = 6.3 Hz, 1H), 4.87 (s, 1H), 5.19 (dd, *J* = 10.3, 1.4 Hz, 1H), 5.28 (dd, *J* = 17.3, 1.4 Hz, 1H), 5.75 (d, *J* = 6.3 Hz, 1H), 5.89 (ddt, *J* = 17.3, 10.3, 5.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 70 MHz) δ 19.3, 23.5, 28.3, 29.2, 54.6, 62.4, 64.5, 66.4, 68.4, 70.7, 75.0, 99.0, 99.8, 117.5, 133.7, 170.7; HRMS calcd for $C_{18}H_{31}NO_6$: 357.2151, found: 357.2135.

2-Acetamido-2-deoxy-4,6-O-isopropylidene-3-O-tert-butyl-α-D-mannopyranose (16)

To a so lu tion of **15** (0.50 g, 1.59 mmol) in dry DMSO (25 mL) was added t-BuOK (0.54 g, 4.77 mmol) and the mix-ture was stirred at 70 °C for 30 min. Af ter cool ing to rt, the mix ture was poured into ice-water (50 mL) and ex tracted with EtOAc (100 mL). The or ganic layer was washed with water (2 × 100 mL), dried ($MgSO_4$) and concentrated *in vacuo* to give crude **17** which was treated with $HgCl_2$ (0.86 g, 3.18 mmol) and HgO (0.69 mg, 3.18 mmol) in ac e tone-water (4:1, 25 mL) for 30 min. The mix ture was fil tered through char coal and the fil trate was di luted with EtOAc (200 mL) and washed suc ces sively with H_2O (50 mL) and brine (2 × 50 mL), and dried ($MgSO_4$). Sol vent was re moved *in vacuo* to yield the res i due which was chromatographed on sil ica gel (EtOAc/Hex ane = 1/1) to af ford **16** ($MgSO_4$) as a mix ture of anomeric iso mers (0.35 g, 79%, ma jor:mi nor = 4:1): $[\alpha]_D^{26}$ -25.0 (*c* 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.16 (s, 7.2H), 1.16 (s, 1.8H), 1.35 (s, 3H), 1.45 (s, 0.6H), 1.46 (s, 2.4H), 2.02 (s, 2.4H), 2.12 (s, 0.6H), 3.25 (dt, *J* = 9.9, 5.2 Hz, 0.2H), 3.42-3.57 (m, 1H, em bod ied a trip let, *J* = 9.8 Hz), 3.62-4.07 (m, 3.8H), 4.19 (t, *J* = 6.1 Hz, 1H), 4.47 (d, *J* = 4.1 Hz, 0.8H), 4.82 (d, *J* = 7.3 Hz, 0.2H), 5.21 (d, *J* = 4.1 Hz, 0.8H), 5.92 (d, *J* = 6.1 Hz, 0.8H), 6.04 (d, *J* = 4.4 Hz, 0.2H), 6.79 (d, *J* = 7.3 Hz, 0.2H); ^{13}C NMR ($CDCl_3$, 70 MHz) δ 19.2, 19.3, 23.2, 23.4, 28.3, 28.4, 29.0, 29.1, 55.4, 57.3, 62.2, 62.4, 64.4, 66.1, 68.8, 69.2, 70.4, 70.7, 75.1, 75.5, 93.9, 96.1, 99.7, 99.8, 171.3, 174.2; Anal calcd for $C_{15}H_{27}NO_6$: C, 56.77; H, 8.57; N, 4.41. Found C, 56.35; H, 8.62; N, 4.38.

Allylation of 16

To a solution of **16** (0.10 g, 0.32 mmol) and allyl bromide (60 μL, 0.64 mmol) in 10 mL of aqueous acetonitrile (v/v 1:1) was added indium power (0.06 g, 0.48 mmol) in one portion. The mixture was stirred for 1 h at 0 °C and an additional 6 h at ambient temperature. After filtration, the solvent was removed *in vacuo* and the residue was triturated with EtOAc. The organic solution was washed with brine, dried ($MgSO_4$), filtered, and concentrated. The residue was purified by column chromatography on SiO_2 (EtOAc/Hexane = 3/1) to afford a diasteroemeric mixture of **18** and **19** (3.8:1, 0.06 g, 49%), as colorless oil: $[\alpha]_D^{25}$ = +16.2 (*c* 2.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ (selected signals) 1.20 (s, t-Bu, minor product), 1.21 (s, t-Bu, major product), 1.35, 1.43 (s, Me, minor product), 1.41, 1.47 (s, Me, major product), 1.97 (s, CH_3-N-acetyl, major product), 2.02 (s, CH_3-N-acetyl, minor product), 5.0-5.2 (m, 2H), 5.70-5.95 (m, 1H,), 6.38 (d, *J* = 7.9 Hz, NH-acetamide, minor product), 6.68 (d, *J* = 7.9 Hz, NH-acetamide, major product);^{13}C NMR ($CDCl_3$, 70 MHz) δ 19.1, 19.5, 23.2, 23.4, 27.9, 28.5, 28.6, 28.8, 38.5, 38.8, 53.6, 57.7, 62.2, 64.9, 65.0, 66.8, 69.8, 71.6, 74.1, 74.7, 74.8, 75.1, 75.7, 98.6, 98.9, 117.5, 117.8, 134.3, 135.0, 170.8, 171.0; IR (neat, cm^{-1}) 526, 684, 912, 995, 1069, 1165, 1195, 1231, 1373, 1530, 1659, 2882, 2943, 2981, 3082, 3407; HRMS calcd for $C_{18}H_{33}NO_6$: 359.2308, found: 359.2326.

Acetate 20

To a CH_2Cl_2 (2 mL) solution of **18** and **19** (0.15 g, 0.42 mmol) and pyridine (90 μL, 0.1 mmol) was added Ac_2O (100 μL, 0.1 mmol), and the mixture was stirred at room temperature over night. The solution was diluted with CH_2Cl_2 (10 mL), then quenched with water (10 mL). The organic layer was washed with brine, dried ($MgSO_4$), filtered, and concentrated. The crude product was purified by column chromatography on SiO_2 (EtOAc/Hexane = 1/1) to afford **20** (0.12 g, 64.3%) as a white solid: mp 97-98 °C; $[\alpha]_D^{25}$ -21.5 (*c* 0.50, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.13 (s, 9H), 1.41 (s, 3H), 1.52 (s, 3H), 1.94 (s, 3H), 1.99 (s, 3H), 2.03 (s, 3H), 2.19-2.33 (m, 1H), 2.40-2.53 (m, 1H), 3.58 (dd, *J* = 11.9, 6.4 Hz, 1H), 3.80 (dd, *J* = 4.8, 2.0 Hz, 1H), 4.00 (dd, *J* = 8.8, 2.0 Hz, 1H), 4.09 (dd, *J* = 11.9, 5.0 Hz, 1H), 4.49 (ddd, *J* = 10.2, 8.8, 4.8 Hz, 1H), 4.74-4.89 (m, 2H), 5.00 (d, *J* = 7.9 Hz, 1H), 5.03 (d, *J* = 15.2 Hz, 1H), 5.62-5.80 (m, 1H), 6.72 (d, *J* = 8.9 Hz, 1H);^{13}C NMR ($CDCl_3$, 70 MHz) δ 20.9, 20.9, 23.6, 27.3, 28.4, 37.2, 54.6, 61.7, 65.3, 66.8, 72.2, 73.2, 74.6, 99.7, 117.9, 133.6, 169.9, 170.2, 170.7; HRMS calcd for $C_{22}H_{37}NO_8$: 443.2519, found: 443.2519. Anal calcd: C, 59.58; H, 8.41; N, 3.16. Found C, 59.51; H, 8.34; N, 3.79.

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Key Words

Mannosamines; Indium; Allylation.

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