Communication

Facile and Effective Synthesis of Glucopyranosyl Oligosacchardes with Alternative (1→3)-α- and -β-Linkages in the Presence of C-2 Ester Capable of Neighboring Group Participation†

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Coupling of acetylated α-(1→3)-linked glucobiosyl trichloroacetimidate with acetylated α-(1→3)-linked glucobioside acceptor gave a β-linked tetrasaccharide, while coupling of acetylated β-(1→3)-linked glucobiosyl trichloroacetimidate with acetylated β-(1→3)-linked glucobioside acceptor gave an α-linked tetrasaccharide in spite of the C-2 neighboring group participation. Two hexasaccharides with alternative (1→3)-α- and -β-linkges were synthesized by these reactions via remote control exerted by the glycosylation bond in either donor or acceptor.

Keywords oligosaccharide, remote control, regio- and stereoselective synthesis

β-(1→3)-Linked glucans occur in a variety of biologically important natural products, such as antitumor schizophyllan, sceroglucan and lentinan,[1] while α-(1→3)-linked glucans exist in some medically important fungi such as *Cryphonectrini parasitica* and *Ganoderma lucidum*.[2] For a study on the structure-function relationships, a series of synthetic β- and α-(1→3)-linked glucooligosaccharides is needed as probes. Our previous communication[3] reported that pure α-linked products can be obtained in high yields in glycosylation with glucosyl trichloroacetimidate donors with a C-2 ester capable of neighboring group participation. Based on this finding, further studies were carried out with disaccharide donors and acceptors as indicated in Scheme 1. It was found that coupling of 2,4,6-tri-*O*-acetyl-3-*O*-allyl-α-*D*-glucopyranosyl trichloroacetimidate (**1**) with *p*-methoxyphenyl 2,4,6-tri-*O*-acetyl-β-*D*-glucopyranoside (**2**) produced a disaccharide mixture **3** consisting of α and β anomer in a 7:3 ratio. The two anomers were well separated and defined as **3α** and **3β** respectively. Deallylation of **3α** or **3β** with $PdCl_2$ in CH_3OH-CH_2Cl_2 at room temperature gave **4** (82%) or **7** (85%), while oxidative cleavage of 1-OMP of **3α** or **3β** with CAN in CH_3CN-H_2O, followed by trichloroacetimidation with CCl_3CN afforded **5** (76% for two steps) or **6** (75% for two steps) readily.

Coupling of the α-linked disaccharide donor **5** with the α-linked disaccharide acceptor **4** gave a β-linked tetrasaccharide **8**, while coupling of the β-linked disaccharide donor **6** with the β-linked disaccharide acceptor **7** gave an α-linked tetrasaccharide **10** in spite of the C-2 neighboring group participation. These coupling reactions revealed that glycosylation bond in donor and acceptor controlled the stereoselectivity of the forthcoming bond in (1→3)-glucosylation by through bond interaction, *i.e.*, the glycosylation bond in the donor and acceptor lead to a forthcoming bond having configuration opposite to that of glycosylation bond in the donor and acceptor. This through bond interaction, or called remote control is very specific and, apparently, overwhelms the C-2 neighboring group participation. Coupling of **4** with **6**, and coupling of **5** with **7** were also carried out giving decomposed product and unreacted acceptor in substantial amount. This indi-

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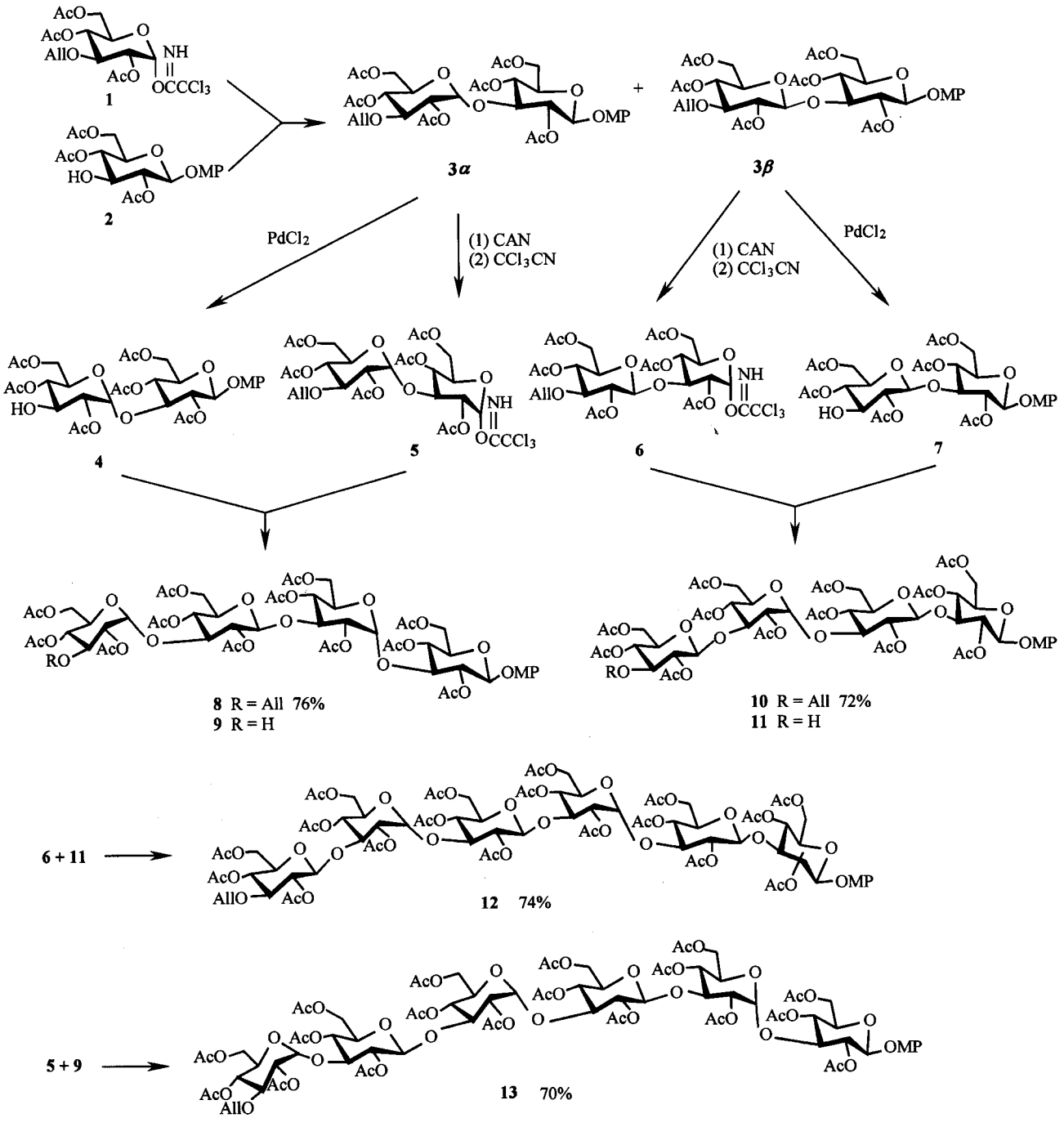
Scheme 1



cated that the donor and acceptor with contradictory remote control effect could not be coupled effectively.

Control of glycosylation linkage by remote substituent was discussed by several reports,[4] and in which, no C-2 neighboring group participation was involved. However, van Boeckel reported that double stereodifferentioation affected α/β ratio in carbohydrate coupling reactions in the presence of neighboring group participation.[5] All of the above reported reactions did not show good stereospecificity.

Our new findings could be used in the syntheses of (1→3)-linked high oligosaccharides with alternative α- and β-linkages. For example, hexasaccharide **12** (74%) was synthesized readily by coupling of the disaccharide

donor **6** with the tetrasaccharide acceptor **11**, while hexasaccharide **13** (70%) was obtained by coupling of the disaccharide donor **5** with the tetrasaccharide acceptor **9**. The coupling reactions described above were carried out under normal conditions with catalytic TMSOTf as the promoter at − 10 ℃ to room temperature for several hours. The obtained oligosaccharides were characterized with ^{1}H and ^{13}C NMR spectra,[6] mass spectroscopy and elemental analysis. For the di- and trisaccharides, ^{1}H NMR spectra usually gave clear identification since the signals at δ 4—6 region were well resolved and H-1α, H-1β showed coupling constants of ~ 3 Hz and ~ 8 Hz respectively. For higher oligosaccharides, ^{13}C NMR spectra were also recorded, giving the C-1-α at δ 94.80—96.05 with $J_{C1\text{-}H1}$ at 174—177 Hz, and the C-1-β at δ 99.70—100.80 with $J_{C1\text{-}H1}$ at 161—166 Hz.

In summary, an effective method for the synthesis of glucooligosaccharides with alternative α- and β-(1→3)-linkges by remote control is described. It should be possible to be used in large scale preparation employing this method.

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6 All of the new compounds involved in the study were identified by optical rotations, ^{1}H or ^{13}C NMR spectra and elemental analyses. Selected spectral data:

3β $[\alpha]_D$ − 72.5 (*c* 0.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 6.92—6.79 (m, 4H, C_6H_4), 5.76—5.74 (m, 1H, −CH=), 5.29—5.11 (m, 3H), 5.05 (t, *J* = 9.6 Hz, 1H), 5.02 (t, *J* = 9.2 Hz, 1H), 4.90 (t, *J* = 9.0 Hz, 1H), 4.81 (d, *J* = 8.0 Hz, 1H, β-H-1), 4.53 (d, *J* = 8.4 Hz, 1H, β-H-1), 4.32—4.29 (m, 1H), 4.28—4.26 (m, 2H), 4.17—4.06 (m, 3H), 3.96—3.94 (m, 1H), 3.81—3.77 (m, 4H), 3.59—3.53 (m, 2H), 2.16 (s, 3H, CH_3CO), 2.10 (s, 3H, CH_3CO), 2.08 (s, 6H, $2CH_3CO$), 2.06 (s, 3H, CH_3CO), 2.04 (s, 3H, CH_3CO).

3α $[\alpha]_D$ + 44.2 (*c* 0.6, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 6.93—6.79 (m, 4H, C_6H_4), 5.78—5.74 (m, 1H, −CH=), 5.27 (d, *J* = 4.0 Hz, 1H, α-H-1), 5.27—5.11 (m, 4H), 5.05 (t, *J* = 9.6 Hz, 1H), 4.80 (d, *J* = 8.0 Hz, 1H, β-H-1), 4.70 (dd, *J* = 3.4, 10.4 Hz, 1H, H-2′), 4.24—3.95 (m, 8H), 3.75 (s, 3H, CH_3CO), 3.74—3.72 (m, 2H), 2.11 (s, 3H, CH_3CO), 2.10 (s, 3H, CH_3CO), 2.08 (s, 3H, CH_3CO), 2.07 (s, 3H, CH_3CO), 2.06 (s, 3H, CH_3CO), 2.04 (s, 3H, CH_3CO); ^{13}C NMR ($CDCl_3$) δ: 170.65, 170.65, 170.65, 169.97, 169.94, 169.62, 156.00, 152.10, 134.43, 118.69, 116.69, 114.68, 100.65 (β-C-1, $J_{C1—H1}$ = 161 Hz), 96.05 (α-C-1, $J_{C1—H1}$ = 176 Hz), 76.25, 73.96, 73.17, 72.18, 71.88, 70.30, 69.47, 68.42, 62.12, 61.70, 55.71, 20.93.

8 $[\alpha]_D$ + 42 (*c* 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: (5.76—574 (m, 1H, −CH=), 5.28—5.17 (m, 5H, 2α-H-1), 4.80 (d, *J* = 7.8 Hz, 1H, β-H-1), 4.73 (dd, *J* = 3.6, 10.2 Hz, 1H, H-2′), 4.66 (dd, *J* = 4.0, 10.2 Hz, 1H, H-2‴), 4.49 (d, *J* = 8.4 Hz, 1H, β-H-1); ^{13}C NMR ($CDCl_3$) δ: 100.21 (β-C-1, $J_{C1—H1}$ = 161 Hz), 100.14 (β-C-1, $J_{C1—H1}$ = 161 Hz), 95.50 (α-C-1, $J_{C1—H1}$ = 177 Hz), 94.89 (α-C-1, $J_{C1—H1}$ = 174 Hz).

10 $[\alpha]_D$ + 9.9 (*c* 0.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 5.77—5.74 (m, 1H, −CH=), 5.23—5.09 (m, 5H, α-H-1), 4.82 (m, *J* = 8.0 Hz, 1H, β-H-1), 4.71 (dd, *J* = 3.6, 10.2 Hz, 1H, H-2″), 4.50 (d, *J* = 8.4 Hz, 2H, 2β-H-1); ^{13}C NMR δ: 100.76 (β-C-1), 100.69 (β-C-1), 100.01 (β-C-1), 94.96 (α-C-1).

12 $[\alpha]_D$ + 17.2 (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 5.77—5.73 (m, 1H, −CH=), 5.25—5.12 (m, 6H, 2α-H-1), 4.85 (d, *J* = 8.0 Hz, 1H, β-H-1), 4.78—4.58 (m, 4H, β-H-1), 4.56—4.52 (m, 4H, 2β-H-1); ^{13}C NMR δ: 100.77 (β-C-1), 100.65 (β-C-1), 100.48 (β-C-1), 100.02 (β-C-1), 95.12 (α-C-1), 94.90 (α-C-1).

13 $[\alpha]_D$ + 98.7 (*c* 0.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 5.76—5.73 (m, 1H, −CH=), 5.26—5.17 (m, 5H, 3α-H-1), 4.81 (d, *J* = 8.0 Hz, 1H, β-H-1), 4.51 (d, *J* = 8.4 Hz, 1H, β-H-1), 4.44 (d, *J* = 8.4 Hz, 1H, β-H-1); ^{13}C NMR δ: 100.54 (β-C-1), 100.44 (2β-C-1), 95.81 (α-C-1), 95.20 (α-C-1), 95.00 (α-C-1).

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