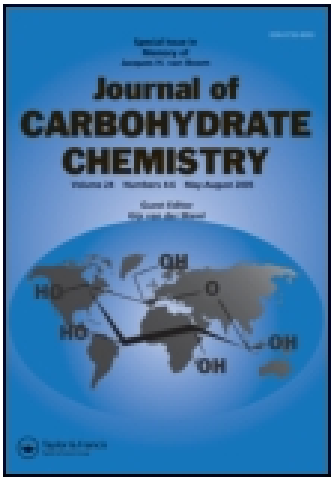

Journal of Carbohydrate Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lcar20

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Published online: 17 Nov 2009.

To cite this article: Chinmoy Mukherjee & Anup Kumar Misra (2009) Synthesis of (6,6′)-C-Linked Pseudodisaccharides, Journal of Carbohydrate Chemistry, 28:9, 475-482

To link to this article: http://dx.doi.org/10.1080/07328300903267577

Journal of Carbohydrate Chemistry, 28:475–482, 2009

ISSN: 0732-8303 print / 1532-2327 online
DOI: 10.1080/07328300903267577

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A series of (6,6′)-*C*-linked pseudodisaccharides has been prepared using a general synthetic strategy of olefin metathesis in the presence of Grubbs second-generation catalyst. Yields were excellent in every case.

Keywords C-glycoside; Pseudodisaccharide; Grubbs catalyst; Olefin metathesis

INTRODUCTION

Pseudodisaccharides are structural analogs of natural disaccharides in which the linkage is formed without involvement of the anomeric center of the monosaccharides. Two monosaccharide units may be connected together through an ether, thio, carbo, or imino linkage.[1] In general, sugars in which the ether linkage region is replaced by a methylene group are termed carbasugars.[2] Carbasugars can act as stable glycosidase inhibitors because of their stability in the enzymatic reaction conditions.[3] A few years back, Perez and coworkers[4] reported a compound named "Coyolosa" from the root extract of *Acrocomia mexicana* having significant hypoglycemic activity (Fig. 1). In the preliminary report, they also suggested that Coyolosa is a pseudodisaccharide in which two D-allose units were interconnected through a 6,6′-ether linkage. Afterward, Haines[5] carried out extensive studies for the verification of the structure of Coyolosa and confirmed that it is not a 6,6′-ether-linked disaccharide. In an independent chemical approach, Ikegami et al.[6] proposed the structure of Coyolosa as 6,6′-ether-connected D-mannose. In the recent past, a number of elegant methods appeared in the literature for the synthesis of ether-linked pseudodisaccharides for their possible use as glycosidase inhibitors.[7,8] It is expected that replacement of an ether linkage by a methylene

Received July 10, 2009; accepted August 17, 2009.
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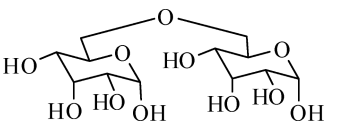
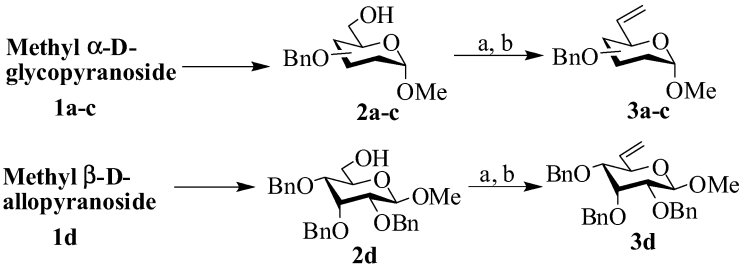


Figure 1: Proposed structure of Coyolosa.[4]

group could result stable glycomimetics for their bioevaluation. However, reports of preparation of 6,6′-carbon-linked pseudodisaccharides are scarce in literature. A few reports for the preparation of (1,1′)- and (1,6′)-carbon-linked pseudodisaccharides are available in the literature[2] using olefin metathesis. As part of the ongoing program toward the preparation of stable glycomimetics, we report herein the synthesis of four (6,6′)-carbon-linked pseudodisaccharides applying the olefin metathesis[9] technique.

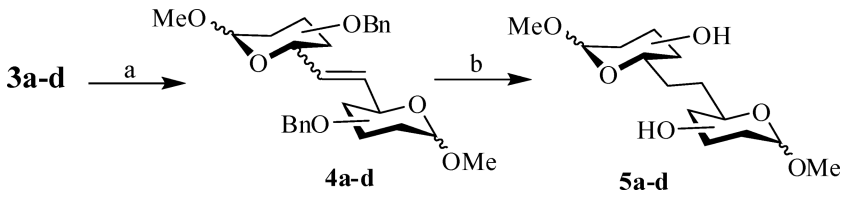
RESULTS AND DISCUSSION

A general synthetic approach has been adopted for the preparation of (6,6′)-carba pseudodisaccharides starting from a series of suitably functionalized monosaccharide units. Following literature-reported methods, methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (**3a**), methyl 2,3,4-tri-*O*-benzyl-α-D-galactopyranoside (**3b**), methyl 2,3,4-tri-*O*-benzyl-α-D-mannopyranoside (**3c**), and methyl 2,3,4-tri-*O*-benzyl-β-D-allopyranoside (**3d**) were prepared in excellent yield starting from compounds **2a–d**.[10–13] Swern oxidation followed by Wittig olefination of compounds **2a–d** furnished compounds **3a**,[14] **3b**,[15] **3c**,[16] and **3d** in excellent yield (Sch. 1). Homo-coupling of olefin derivatives (**3a–d**) in the presence of Grubbs second-generation catalyst[17] afforded (1,6′)-carba-linked pseudodisaccharide derivatives (**4a–d**) in satisfactory yield, which on hydrogenation over Pearlmann's catalyst[18] furnished deprotected pseudodisaccharide derivatives (**5a–d**) in excellent yield. Structures of all



Sugar: a: D-glucose; b: D-galactose; c: D-mannose

Scheme 1: Reagent: (a) $(CH_3)_2SO$, $(COCl)_2$, Et_3N, CH_2Cl_2, −78°C; (b) CH_3PPh_3I, n-BuLi, THF, −78°C (72% for **3a**, 70% for **3b**, 73% for **3c**, 69% for **3d**).



Scheme 2: Reagents: (a) Grubbs 2nd cat. (10 mol%), CH_2Cl_2, 45°C, 8 h (69% for **4a**, 70% for **4b**, 69% for **4c**, 67% for **4d**); (b) 20% $Pd(OH)_2/C$, CH_3OH-EtOAc (3:1), rt, 24 h (85% for **5a**, 82% for **5b**, 82% for **5c**, 78% for **5d**).

compounds were confirmed by NMR and mass spectral analysis (Sch. 2, Fig. 2).

In summary, a general synthetic approach for the preparation of a series of pseudo-*C*-disaccharide derivatives was developed using olefin metathesis in the presence of second-generation Grubbs catalyst. The reaction condition is high yielding and reproducible. Following a similar approach, a large number of hydrolytically stable *C*-disaccharide derivatives can be synthesized.

EXPERIMENTAL

General Methods

All the reactions were monitored by thin layer chromatography over silica gel-coated TLC plates. The spots on TLC were visualized by warming ceric sulphate (2% $Ce(SO_4)_2$ in 2N H_2SO_4) sprayed plates on a hot plate. Silica gel 230–400 mesh was used for column chromatography. ^1H and ^{13}C NMR was recorded on a Bruker Advance DPX 300 MHz using TMS as internal reference. Chemical shift value is expressed in δ ppm. Elementary analysis was carried out on Carlo ERBA-1108 analyzer. Optical rotations were measured at 25°C

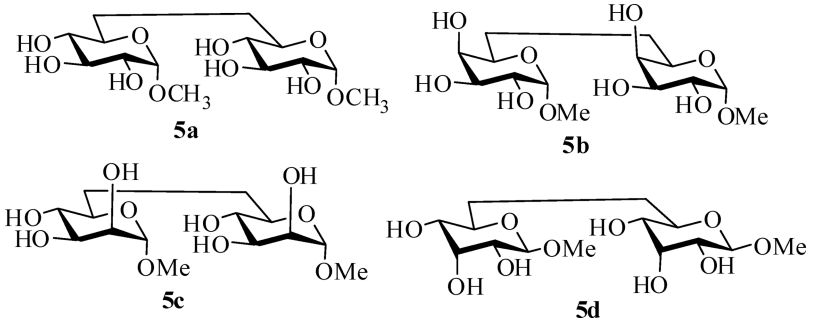


Figure 2: Deprotected (6,6′)-carbon-linked pseudodisaccharide derivatives.

on a Rudolf Autopol III polarimeter. Commercially available grades of organic solvents of adequate purity are used in many reactions.

General Experimental Procedure for the Preparation of methyl 2,3,4-tri-O-benzyl-6,7-dideoxy-α/β-D-glyco-hept-6-enopyranoside (3a–d)

A solution of oxalyl chloride (455 μL, 5.4 mmol) in THF (2 mL) and CH_2Cl_2 (2 mL) was cooled to −78°C. A solution of Me_2SO (765 μL, 10.8 mmol) in CH_2Cl_2 (3 mL) was slowly added to the cooled reaction mixture at −78°C and the mixture was stirred for 10 min at same temperature. A solution of compound **2a–d** (1 g, 2.15 mmol) in CH_2Cl_2 (5 mL) was added slowly to the reaction mixture and it was stirred for 1 h at −60°C. The mixture was cooled to −78°C and a solution of Et_3N (3 mL, 21.5 mmol) in CH_2Cl_2 (3 mL) was added during 15 min. After stirring at −78°C for 30 min, the reaction mixture was warmed to rt and H_2O (4 mL) was added. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layer was then dried (Na_2SO_4), filtered, and concentrated under reduced pressure to give the crude aldehyde. The crude aldehyde was then used directly for the next step. To a suspension of methyl triphenylphosphonium iodide (5.2 g, 12.9 mmol) in dry THF (30 mL) at −78°C was added n-BuLi (4 mL, 1.6 M solution in THF) and the mixture was stirred for 15 min at the same temperature. The dried crude aldehyde in dry THF (10 mL) was then added to it and the reaction mixture was warmed to rt. After 1 h of stirring at rt, water (15 mL) was added and the reaction mixture was extracted with ethyl acetate (3 × 30 mL). The combined organic layer was dried (Na_2SO_4), filtered, and concentrated under reduced pressure and the crude product was purified over SiO_2 using hexane-EtOAc (8:1) as eluant to give pure product **3a–d** as colorless oil. All known compounds **(3a–c)** gave acceptable NMR spectra that matched data reported in the cited references.

Methyl 2,3,4-tri-O-benzyl-6,7-dideoxy-β-D-allo-hept-6-enopyranoside (3d)

Yield: 685 mg, 69%; $[\alpha]_D^{25}$ + 39.2 (*c* 1.0, $CHCl_3$); IR (neat): 3020, 2361, 1593, 1216, 762, 670 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.38–7.21 (m, 15 H, Ar-H), 5.99–5.88 (m, 1 H, H-6), 5.45–5.38 (m, 1 H, H-7_a), 5.23–5.19 (m, 1 H, H-7_b), 4.88–4.78 (m, 4 H, H-1, PhCH_2), 4.58 (d, J = 12.2 Hz, 1 H, PhCH_2), 4.46 (d, J = 11.7 Hz, 1 H, PhCH_2), 4.40 (d, J = 11.8 Hz, 1 H, PhCH_2), 4.37–4.32 (m, 1 H, H-5), 4.03–4.01 (m, 1 H, H-3), 3.55 (s, 3 H, OCH_3), 3.17 (dd, J = 7.9, 2.6 Hz, 1 H, H-2), 3.10 (dd, J = 9.6, 2.4 Hz, 1 H, H-4); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 139.0–116.9 (aromatic and olefinic carbons), 101.8 (C-1), 80.0, 79.1,

75.1, 74.4, 73.0, 72.7, 71.9, 56.8; ESI-MS: $m/z = 483.2$ $[M+Na]^+$; Anal. Calcd. for $C_{29}H_{32}O_5$ (460.22): C, 75.63; H, 7.00. Found: C, 75.45; H, 7.20.

General Experimental Procedure for the Olefin Metathesis of Compounds 3a–d: Preparation of Compounds 4a–d

The solution of compound **3a–d** (650 mg, 1.41 mmol) in CH_2Cl_2 (5 mL) was bubbled with argon gas, followed by the addition of Grubbs second-generation ruthenium catalyst (60 mg, 0.07 mmol). After stirring for 8 h at 45°C, the reaction mixture was concentrated in vacuo and purified over SiO_2 using hexane-EtOAc (6:1) as eluant to give pure compound **4a–d** as colorless oil, which was directly used for the next step without further purification of the isomers.

General Experimental Procedure for the Preparation of Methyl (6-deoxy-α/β-D-glycopyranosyl)-(6→6′)-C-6-deoxy-α/β-D-glycopyranoside (5a–d)

To the solution of compound **4a–d** (400 mg, 0.45 mmol) in CH_3OH:EtOAc (3:1, 20 mL) was added 20% $Pd(OH)_2/C$ (50 mg) and the reaction mixture was allowed to stir at rt under a positive pressure of hydrogen for 24 h. The reaction mixture was filtered through a Celite bed and evaporated to dryness to give compound **5a–d** as white amorphous powder.

Methyl (Methyl 6-deoxy-α-D-gluco-hept-6-enopyranosyl)-6-deoxy-α-D-gluco-hept-6-enopyranoside (5a)

Yield: 135 mg, 85%; $[\alpha]_D^{25} + 135.7$ (*c* 1.0, H_2O). The proton integration in the ^1H NMR and carbon signals in the ^{13}C NMR spectra appeared as monomer because of the presence of the plane of symmetry in the molecule; ^1H NMR (D_2O, 300 MHz): δ 4.81 (d, $J = 3.6$ Hz, 2 H), 3.69–3.58 (m, 6 H), 3.45 (s, 6 H), 3.26 (t, $J = 9.2$ Hz each, 2 H), 2.04–1.95 (m, 2 H), 1.74–1.62 (m, 2 H); ^{13}C NMR (D_2O, 75 MHz): δ 99.1, 73.3, 73.0, 71.4, 70.4, 55.0, 26.1; ESI-MS: $m/z = 377.3$ $[M+Na]^+$; Anal. Calcd. for $C_{14}H_{26}O_{10}$ (354.15): C, 47.45; H, 7.40. Found: C, 47.30; H, 7.60.

Methyl (Methyl 6-deoxy-α-D-galacto-hept-6-enopyranosyl)-6-deoxy-α-D-galacto-hept-6-enopyranoside (5b)

Yield: 130 mg, 82%; $[\alpha]_D^{25} + 146$ (*c* 1.0, H_2O). The proton integration in the ^1H NMR and carbon signals in the ^{13}C NMR spectra appeared as monomer because of the presence of the plane of symmetry in the molecule; ^1H NMR (D_2O, 300 MHz): δ 4.82–4.81 (m, 2 H), 3.89–3.87 (m, 4 H), 3.83–3.82 (m, 4 H), 3.42 (s, 6 H), 1.80–1.76 (m, 2 H), 1.69–1.66 (m, 2 H); ^{13}C NMR (D_2O, 75 MHz):

δ 99.5, 70.6, 70.0, 69.7, 68.2, 55.1, 26.1; ESI-MS: $m/z = 377.2$ $[M+Na]^+$; Anal. Calcd. for $C_{14}H_{26}O_{10}$ (354.15): C, 47.45; H, 7.40. Found: C, 47.32; H, 7.65.

Methyl (Methyl 6-deoxy-α-D-manno-hept-6-enopyranosyl)-6-deoxy-α-D-manno-hept-6-enopyranoside (5c)

Yield: 130 mg, 82%; $[\alpha]_D^{25}$ + 87.1 (*c* 1.0, H_2O). The proton integration in the ^1H NMR and carbon signals in the ^{13}C NMR spectra appeared as monomer because of the presence of the plane of symmetry in the molecule; ^1H NMR (D_2O, 300 MHz): δ 4.74 (d, $J = 1.6$ Hz, 2 H), 3.95 (dd, $J = 3.4$, 1.7 Hz, 2 H), 3.74 (dd, $J = 9.1$, 3.4 Hz, 2 H), 3.60–3.46 (m, 4 H), 3.43 (s, 6 H), 2.06–1.96 (m, 2 H), 1.79–1.68 (m, 2 H); ^{13}C NMR (D_2O, 75 MHz): δ 100.8, 71.4, 70.4, 70.3, 69.9, 54.7, 26.3; ESI-MS: $m/z = 377.3$ $[M+Na]^+$; Anal. Calcd. for $C_{14}H_{26}O_{10}$ (354.15): C, 47.45; H, 7.40. Found: C, 47.32; H, 7.60.

Methyl (Methyl 6-deoxy-β-D-allo-hept-6-enopyranosyl)-6-deoxy-β-D-allo-hept-6-enopyranoside (5d)

Yield: 125 mg, 78%; $[\alpha]_D^{25}$—17.1 (*c* 1.0, H_2O). The proton integration in the ^1H NMR and carbon signals in the ^{13}C NMR spectra appeared as monomer because of the presence of the plane of symmetry in the molecule; ^1H NMR (D_2O, 300 MHz): δ 4.61 (d, $J = 8.2$ Hz, 2 H), 4.17 (brs, 2 H), 3.77 (t, $J = 9.3$ Hz, 2 H), 3.58 (s, 6 H), 3.49–3.38 (m, 4 H), 2.05–2.00 (m, 2 H), 1.72–1.67 (m, 2 H); ^{13}C NMR (D_2O, 75 MHz): δ 101.1, 72.2, 71.2, 70.8, 70.6, 56.9, 26.5; ESI-MS: $m/z = 377.2$ $[M+Na]^+$; Anal. Calcd. for $C_{14}H_{26}O_{10}$ (354.15): C, 47.45; H, 7.40. Found: C, 47.30; H, 7.58.

ACKNOWLEDGEMENTS

C.M. thanks CSIR, New Delhi, for providing a Senior Research Fellowship. This project was funded by the Department of Science and Technology (DST), New Delhi, through the Ramanna Fellowship (AKM) (Project no. SR/S1/RFPC-06/2006).

REFERENCES

1. (a) Roy, R.; Dominique, R.; Das, S.K. Extended alkenyl glycosides by Ruthenium-catalyzed cross-metathesis reaction and application toward novel C-linked pseudodisaccharides. *J. Org. Chem.* **1999**, *64*, 5408–5412; (b) Maity, J.K.; Mukherjee, S.; Drew, M.G.B.; Achari, B.; Mandal, S.B. First example of 5/6-*O*-linked pseudosaccharides: synthesis of bicyclic nucleosides containing azido or extended carbohydrate moiety. *Carbohydr. Res.* **2007**, *342*, 2511–2521; (c) Szilagyi, L.; Illyes, T.-Z.; Herczegh, P. Elaboration of a novel type of interglycosidic linkage: syntheses of disulfide disaccharides. *Tetrahedron Lett.* **2001**, *42*, 3901–3903; (d) McCort, I.; Dureault, A.; Depezay, J.-C. Synthesis of ester-and amide-linked pseudo-azadisaccharides via coupling of D-glucose

with 6-amino-6-deoxy-2,5-imino-D-glucitol. *Tetrahedron Lett.* **1998**, *39*, 4463–4466; (e) Uhrig, M.L.; Szilagyi, L.; Kover, K.E.; Varela, O. Synthesis of non-glycosidic 4,6′-thioether-linked disaccharides as hydrolytically stable glycomimetics. *Carbohydr. Res.* **2007**, *342*, 1841–1849; (f) Kroutil, J.; Budesinsky, M. Preparation of diamino pseudodisaccharide derivatives from 1,6-anhydro-β-D-hexopyranoses via aziridine-ring cleavage. *Carbohydr. Res.* **2007**, *342*, 147–153; (g) Suzuki, K.; Hashimoto, H. Synthesis of ethyl 2-acetamido-6-*S*-(5-amino-5-deoxy-β-D-arabinopyranosyl)-2-deoxy-1,6-dithio-β-D-glucopyranoside: a sulfur-linked 5-amino-5-deoxyglycopyranosyl disaccharide. *Carbohydr. Res.* **2000**, *323*, 14–17.

2. (a) Angelaud, R.; Landais, Y.; Parra-Rapado, L. Stereocontrolled access to Carba-C-disaccharides via functionalized dienylsilanes. *Tetrahedron Lett.* **1997**, *38*, 8845–8848; (b) Bleriot, Y.; Giroult, A.; Mallet, J.-M.; Rodriguez, E.; Vogel, P.; Sinay, P. Synthesis of seven- and eight-membered carbasugar analogs via ring-closing metathesis and their inhibitory activities toward glycosidases. *Tetrahedron Asymm.* **2002**, *13*, 2553–2565; (c) Ferritto, R.; Vogel, P. Synthesis of an α-C-galactoside of a carbasugar: a new class of disaccharide mimics. *Tetrahedron Lett.* **1995**, *36*, 3517–3518; (d) Mehta, G.; Lakshminath, S.; Talukdar, P. A norbornyl route to aminocyclohexitols: syntheses of diverse aminocarbasugars and 'confused' aminocarbasugars. *Tetrahedron Lett.* **2002**, *43*, 335–338. (e) Frigell, J.; Cumpstey, I. First synthesis of 4a-carba-β-D-galactofuranose. *Tetrahedron Lett.* **2007**, *48*, 9073–9076.

3. (a) Haines, A.H.; Carvalho, I. Synthesis of a novel pseudodisaccharide glycoside as a potential glycosidase inhibitor. *Chem. Commun.* **1998**, 817–818; (b) Ogawa, S.; Yokoi, S.; Kimura, N.; Shibata, Y.; Chida, N. Synthesis of pseudo-trehaloses: [(1,2,4/3,5)-2,3,4-trihydroxy-5-hydroxymethyl-1-cyclohexyl]-D-glucopyranosides. *Carbohydr. Res.* **1988**, *181*, 57–66; (c) Carvalho, I.; Haines, A.H. N-Linked carba-disaccharides as potential inhibitors of glucosidases I and II. *J. Chem. Soc. Perkin Trans. 1* **1999**, 1795–1800; (d) Blériot, Y.; Dintinger, T.; Guillo, N.; Tellier, C. Synthesis of an amidine pseudo-(1→6)-dimannoside and evaluation as a glycosidase inhibitor. *Tetrahedron Lett.* **1995**, *36*, 5175–5178; (e) Saotome, C.; Kanie, Y.; Kanie, O.; Wong, C.-H. Synthesis and enzymatic evaluation of five-membered iminocyclitols and a pseudodisaccharide. *Bioorg. Med. Chem.* **2000**, *8*, 2249–2261.

4. Pérez, G.S.; Pérez, G.R.M.; Pérez, G.C.; Zavala, S.M.A.; Vargas, S.R. Coyolosa, a new hypoglycemic from *Acrocomia mexicana*. *Pharm. Acta Helv.* **1997**, *72*, 105–111.

5. (a) Haines, A.H. Evidence on the structure of Coyolosa. Synthesis of 6,6′-ether linked hexoses. *Tetrahedron Lett.* **2004**, *45*, 835–837; (b) Haines, A.H. Synthesis of 6,6-ether linked disaccharides from D-allose, D-galactose, D-glucose and D-mannose; evidence on the structure of Coyolosa. *Org. Bioorg. Chem.* **2004**, *2*, 2352–2358.

6. Takahashi, H.; Fukuda, T.; Mitsuzuka, H.; Namme, R.; Miyamoto, H.; Ohkura, Y.; Ikegami, S. Development of a novel sugar linkage: 6,6′-ether-connected sugars. *Angew. Chem. Int. Ed.* **2003**, *42*, 5069–5071.

7. Akhtar, T.; Eriksson, L.; Cumpstey, I. Unusual synthesis of carbohydrate *sec–sec* ether-linked pseudodisaccharides. *Carbohydr. Res.* **2008**, *343*, 2094–2100.

8. Takahashi, H.; Mitsuzuka, H.; Nishiyama, K.; Ikegami, S. A facile synthesis of neosaccharides: 2,6′-and 3,6′-ether-linked sugars. *Synthesis* **2006**, 1415–1418.

9. Scholl, M.; Ding, S.; Lee, C.W.; Grubbs, R.H. Synthesis and activity of a new generation of Ruthenium-based olefin metathesis catalysts coordinated with 1,3-dimesityl-4,5-dihydroimidazol-2-ylidene ligands. *Org. Lett.* **1999**, *1*, 953–956.

10. Lam, S.N.; Gervay-Haque, J. Solution- and solid-phase oligosaccharide synthesis using glucosyl iodides: a comparative study. *Carbohydr. Res.* **2002**, *337*, 1953–1965.

11. Chambers, D.J.; Graham, R.E.; Fairbanks, A.J. An approach to the synthesis of α-(1–6)-*C*-disaccharides by tandem Tebbe methylenation and Claisen rearrangement. *Tetrahedron* **2005**, *61*, 7184–7192.

12. Belakhov, V.; Dovgolevsky, E.; Rabkin, E.; Shulami, S.; Shoham, Y.; Baasov, T. Synthesis and evaluation of a mechanism-based inhibitor of KDO8P synthase. *Carbohydr. Res.* **2004**, *339*, 385–392.

13. Kim, M.; Grzeszczyk, B.; Zamojski, A. Homologation of protected hexoses with Grignard C_1 reagents. *Tetrahedron* **2000**, *56*, 9319–9337.

14. Wang, W.; Zhang, Y.; Sollogoub, M.; Sinaÿ, P. From glucose to cyclooctanic carbaglucose: a new class of carbohydrate mimetics. *Angew. Chem. Int. Ed.* **2000**, *39*, 2466–2467.

15. Tatsuta, K.; Niwata, Y.; Umezawa, K.; Toshima, K.; Nakata, M. Total syntheses of glucosidase inhibitors, cyclophellitols. *Carbohydr. Res.* **1991**, *222*, 189–203.

16. Boons, G.J.P.H.; Van DerMarel, G.A.; van Boom, J.H. A versatile and new highly stereoselective approach to the synthesis of L-*glycero*-D-*manno*-heptopyranosides. *Tetrahedron Lett.* **1989**, *30*, 229–232.

17. (a) Tarnk, T.M.; Grubbs, R.H. The development of $L_2 \times_2 Ru = CHR$ olefin metathesis catalysts: an organometallic success story. *Acc. Chem. Res.* **2001**, *34*, 18–29; (b) Grubbs, R.H.; Chang, S. Recent advances in olefin metathesis and its application in organic synthesis. *Tetrahedron* **1998**, *54*, 4413–4696; (c) Chatterjee, A.K.; Morgan, J. P.; Scholl, M.; Grubbs, R.H. Synthesis of functionalized olefins by cross and ring-closing metatheses. *J. Am. Chem. Soc.* **2002**, *122*, 3783–3784.

18. Pearlman, W.M. Noble metal hydroxides on carbon nonpyrophoric dry catalysts. *Tetrahedron Lett.* **1967**, *8*, 1663–1664.