Pergamon

Tetrahedron: *Asymmetry* 11 (2000) 393–396

TETRAHEDRON:
ASYMMETRY

Ring-closing metathesis as a new strategy for the C–C coupling of monosaccharide derivatives via silicon tethering

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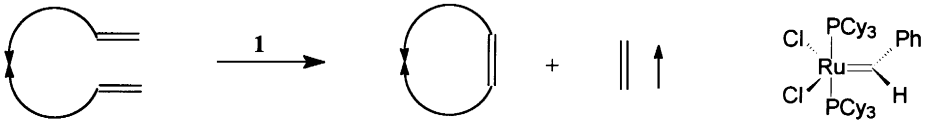
Received 29 October 1999; accepted 11 November 1999

Abstract

Suitable carbohydrate-derived terminal olefins have been coupled by ring-closing metathesis reaction following a silicon tethering strategy, generating very long contiguous chains of carbon atoms each equipped with specific stereochemistry and functionality.

During the last couple of years the olefin metathesis reaction[1] has been established as a significant synthesis strategy in organic chemistry, in which unsatured carbon–carbon bonds are rearranged in the presence of metal carbene complexes. Especially due to Grubbs[2] and his benzylidene-bis(tricyclohexylphosphine)dichlororuthenium catalyst **1**, this approach has become a powerful ring-closing tool for open chain dienes, mostly simultaneously delivering ethylene, thus shifting an equilibration in one direction (Scheme 1). However, similar intermolecular reactions, which could lead to very long carbon chains, proved to be difficult in many cases. Recently, Evans and Murthy[3] reported on a method to combine temporary silicon tethering methodology with the ring-closing metathesis reaction in order to obtain C_2-symmetric 1,4-diols. The advantage of this strategy is the clipping of two allylic alcohols to form a diene, which can then be employed in a ring-closing metathesis reaction. However, the olefin metathesis reaction has rarely been used in carbohydrate chemistry.[4] Thus, we began to adopt this strategy for the preparation of long chain monosaccharides.



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Scheme 1.

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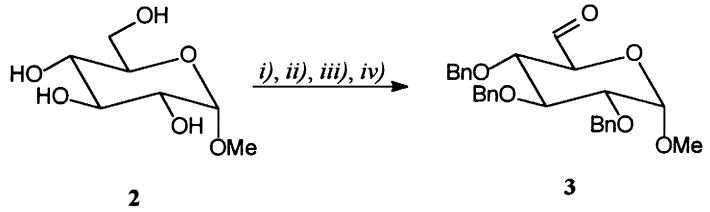
0957-4166/00/$ - see front matter
PII: S0957-4166(99)00504-2

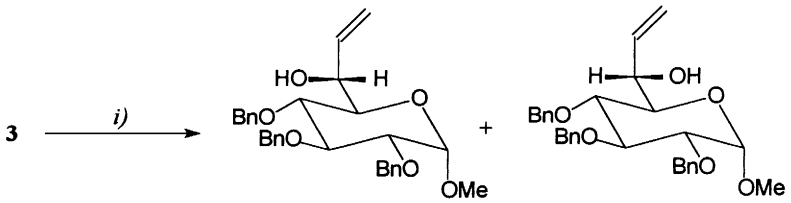
We started with the benzylidenation of commercially available methyl α-D-glucopyranoside **2** with benzaldehyde and anhydrous zinc chloride,[5] as shown in Scheme 2, to first obtain methyl 4,6-*O*-benzylidene-α-D-glucopyranoside. The subsequent benzylation under standard conditions with sodium hydride in DMF gave methyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside. Necessary cleavage of the benzylidene acetal was achieved by reduction employing $LiAlH_4/AlCl_3$ in dichloromethane/ether.[6] Finally, oxidation of the obtained intermediate, primary 6-OH-free, to aldehyde **3** succeeded with Dess–Martin periodinane[7] in dichloromethane in high yield.



2 **3**

Scheme 2. *Reagents*: (i) $ZnCl_2$, benzaldehyde (81%); (ii) benzyl bromide, sodium hydride in DMF (80%); (iii) $LiAlH_4/AlCl_3$ in dichloromethane/ether (75%); (iv) Dess–Martin periodinane in dichloromethane (92%)

Grignard-reaction[8] of **3** (Scheme 3) at −60°C in THF with commercially available vinylmagnesium bromide solution afforded the two allylic alcohols **4a** as an oil and **4b** as white crystals in 20 and 22% yields, respectively, after column chromatography.



4a **4b**

Scheme 3. *Reagents*: (i) 2.0 equiv. vinylmagnesium bromide solution, 1.0 M in THF

Treatment of **4a** and **4b** with diphenyldichlorosilane at 0°C for 20 h furnished the C_2-symmetrical bis-alkoxysilanes **5a** and **5b** in 18 and 30% isolated yields, respectively (Scheme 4). In the last step we succeeded in ring-closing metathesis reaction using 15 mol% of Grubbs' catalyst benzylidene-bis-(tricyclohexylphosphine)dichlororuthenium **1** (40°C, 24 h) in a small amount of degassed dichloromethane to give the seven-membered ring diphenyl silaketals **6a** (31%) and **6b** (19%). The structures af **6a** and **6b** were corroborated as those of the other new compounds by ^1H and ^{13}C NMR spectroscopy.[9]

In conclusion, we were able to show a new strategy in carbohydrate chemistry for the coupling of monosaccharides to obtain very long chain sugars, with properties almost unexplored.

References

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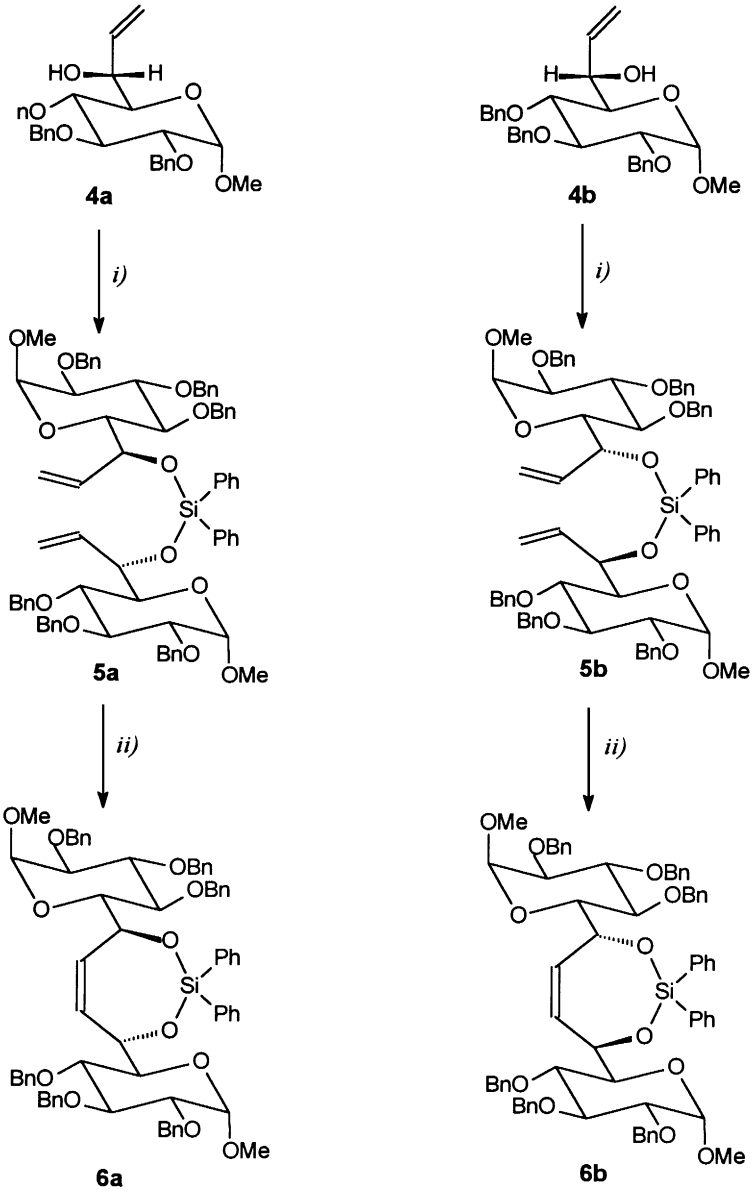

Scheme 4. *Reagents*: (i) Ph_2SiCl_2, 2,6-lutidine; (ii) 15 mol% Grubbs' catalyst **1** in dichloromethane

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9. Compound **6a**: ^{1}H NMR (500 MHz/$CDCl_3$): δ=3.298 (s, 6H, OCH_3), 3.480 (m, 6H, H2, H5, H4), 3.823 (d, 2H, ^2J=10.4 Hz, CH_2-Ph_a), 3.914 (dd, 2H, $^3J_{3,2}$=9.4 Hz, $^3J_{3,4}$=8.8 Hz, H3), 4.373 (d, 2H, ^2J=10.9 Hz, CH_2-$Ph_{a'}$), 4.539 (d, 2H, $^3J_{1,2}$=3.3 Hz, H1), 4.581 (d, 2H, ^2J=11.5 Hz, CH_2-Ph_b), 4.668 (d, 2H, ^2J=10.9 Hz, CH_2-Ph_c), 4.688 (d, 2H, ^2J=12.0 Hz, CH_2-$Ph_{b'}$), 4.854 (d, 2H, ^2J=10.9 Hz, CH_2-$Ph_{c'}$), 5.039 (s, 2H, H6), 5.701 (s, 2H, H7), 6.720 (m, 4H, Ar-H), 7.124 (m, 6H, Ar-H), 7.298 (m, 26H, Ar-H), 7.688 (m, 4H, Ar-H); ^{13}C NMR ($CDCl_3$): δ=138.27–127.27 (Ar-C, C7), 97.73 (C1), 82.25 (C3), 80.00 (C2), 78.10 (C4), 75.88 (Bn-C_c), 74.55 (Bn-C_a), 74.02 (Bn-C_b), 70.25 (C6), 54.91 (OCH_3). Compound **6b**: ^{1}H NMR (500 MHz/$CDCl_3$): δ=3.399 (s, 6H, OCH_3), 3.583 (dd, 2H, $^3J_{2,1}$=3.3 Hz, $^3J_{2,3}$=9.8 Hz, H2), 3.666 (d, 2H, $^3J_{5,4}$=8.8 Hz, H5), 3.743

(dd, 2H, $^{3}J_{4,3}$=9.3 Hz, $^{3}J_{4,5}$=8.8 Hz, H4), 3.867 (d, 2H, ^{2}J=10.4 Hz, CH_2-Ph_a), 3.996 (dd, 2H, $^{3}J_{3,2}$=9.8 Hz, $^{3}J_{3,4}$=9.3 Hz, H3), 4.559 (d, 2H, ^{2}J=10.4 Hz, CH_2-$Ph_{a'}$), 4.676 (d, 2H, ^{2}J=11.9 Hz, CH_2-Ph_b), 4.736 (d, 2H, $^{3}J_{1,2}$=3.3 Hz, H1), 4.742 (d, 2H, ^{2}J=10.4 Hz, CH_2-Ph_c), 4.810 (d, 2H, ^{2}J=11.9 Hz, CH_2-$Ph_{b'}$), 4.943 (d, 2H, ^{2}J=10.4 Hz, CH_2-$Ph_{c'}$), 5.209 (s, 2H, H6), 5.800 (s, 2H, H7), 6.720 (m, 4H, Ar-H), 7.124 (m, 6H, Ar-H), 7.298 (m, 26H, Ar-H), 7.688 (m, 4H, Ar-H); ^{13}C NMR ($CDCl_3$): δ=138.54–127.30 (Ar-C, C7), 98.23 (C1), 82.20 (C3), 80.06 (C2), 77.32 (C4), 75.88 (Bn-C_c), 74.26 (Bn-C_a), 73.65 (C5), 73.41 (Bn-C_b), 68.70 (C6), 55.26 (OCH_3).