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# Carbohydrate-Modified Fused Pyranosylidene Complexes via Radical Addition of Epoxides to Unsaturated Metal Carbenes[1]

Karl Heinz Dötz* and Edite Gomes da Silva

*Kekulé-Institut für Organische Chemie und Biochemie der Rheinischen Friedrich-Wilhelms-Universität, D-53121 Bonn, Germany*

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**Abstract**—Alkenyl and alkynyl carbene complexes of chromium and tungsten undergo a diastereoselective cyclization upon reaction with epoxides in presence of $[Cp_2TiCl]_2$. *trans*-Fused tetrahydropyranosylidene complexes are obtained from the radical addition of cyclohexene oxide to monosaccharide-derived vinylcarbene tungsten complexes. The benzyl-protected 1,2-anhydro-α-D-glucopyranose adds to styryl and alkynyl carbene complexes to give bicyclic *trans*-fused tetrahydro- and dihydropyranosylidene complexes as well as the acyclic addition products. 

## Introduction

*trans*-Fused cyclic polyether skeletons are characteristic building blocks for a series of important biologically active compounds.[2] Among them, various toxins, e.g. brevetoxins[3] and ciguatoxins[4] which selectively activate voltage-sensitive sodium channels in nerves, heart and muscles,[5] as well as less complicated structures such as okadaic acid[6] containing pyranopyran subunits have been recognized as valuable compounds in biomedical research.[7] Their biosynthesis is discussed in terms of an epoxidation of polyenes followed by a cascade of epoxide ring-opening processes.[8] Two main synthetic strategies towards *trans*-fused polyethers have been developed which are based on the heterocyclization via intramolecular formation of either C–C or, more common, C–O bonds.[9] The latter approach often involves the alkylation of oxiranyl anions followed by an acid-catalyzed cyclization.[10] Alternatively, ring-closing metathesis (RCM)[11] has been exploited for the construction of pyran rings.

## Results and Discussion

We aimed at an organometallic route to bicyclic *trans*-fused oxygenated diethers based on the radical addition of epoxides to electron-deficient carbon–carbon multiple bond systems[12] as present in vinyl and alkynyl metal carbenes. This type of carbene complexes has been widely used in stereoselective synthesis.[13] Reflecting the isolobal analogy[14] of the pentacarbonyl metal fragment $M(CO)_5$ (M=Cr, Mo, W) and an oxygen atom, they represent organometallic analogues of acrylates and propiolates which, however, are even more electrophilic than their ester counterparts. Following our interest in carbohydrate-modified organometallics[15] we focused on a strategy based on a $Ti^{III}$-mediated ring-opening of epoxides[16] and their subsequent radical addition to α,β-unsaturated carbene complexes (Scheme 1).[17]

We extended this methodology to carbohydrate-derived metal carbenes and epoxides, and now report on the synthesis of dihydro- and tetrahydropyranosylidene chromium and tungsten complexes labeled with cyclic or acyclic sugar functionalities. The reactivity of titanocenium(III) chloride towards polar functional groups, especially towards epoxides, provides a radical access to polyfunctional structures. The ring-opening of epoxides via C–O homolysis occurs regio- and diastereoselectively, and is controlled by the relative stability of the radical intermediates. Their stability increases in the order of primary<secondary< tertiary radicals, and is further influenced by stereoelectronic effects.[12]

The $(Cp_2TiCl)_2$-mediated addition of cyclohexene oxide to sugar-derived vinylcarbene complexes **1**–**4**, accessible from condensation of the perbenzyl-protected arabinose, ribose, glucose and galactose with pentacarbonyl[methoxy(methyl)carbene]tungsten[18] afforded the bicyclic pyranosylidene complexes **5**–**8** (Scheme 2). Whereas the arabinose-based cycloadduct could be isolated as a single diastereomer **5a** in low yield, the ribose, glucose and galactose analogues were obtained in moderate to excellent yields as approximate 2:1 mixtures of diastereomers **6a/b**, **7a/b** and **8a/b**. Separation of the diastereomers by analytical HPLC was achieved for the hexose derivatives **7a/b** and **8a/b**, but failed in the ribose case. The cycloaddition is diastereoselective; the six-membered rings in the bicyclic

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* Corresponding author. Tel.: +49-228-735608; fax: +49-228-735813; e-mail: doetz@uni-bonn.de

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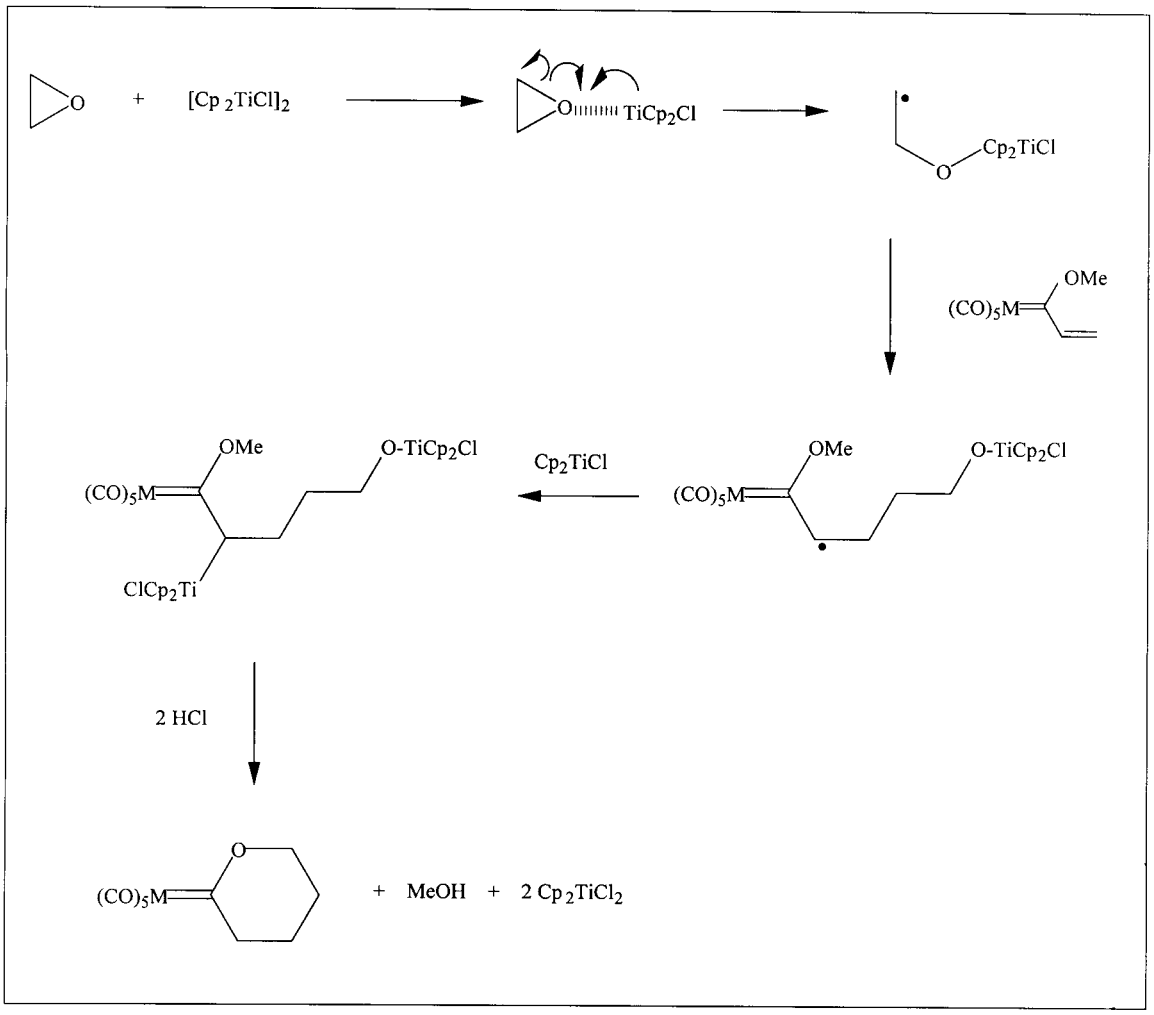
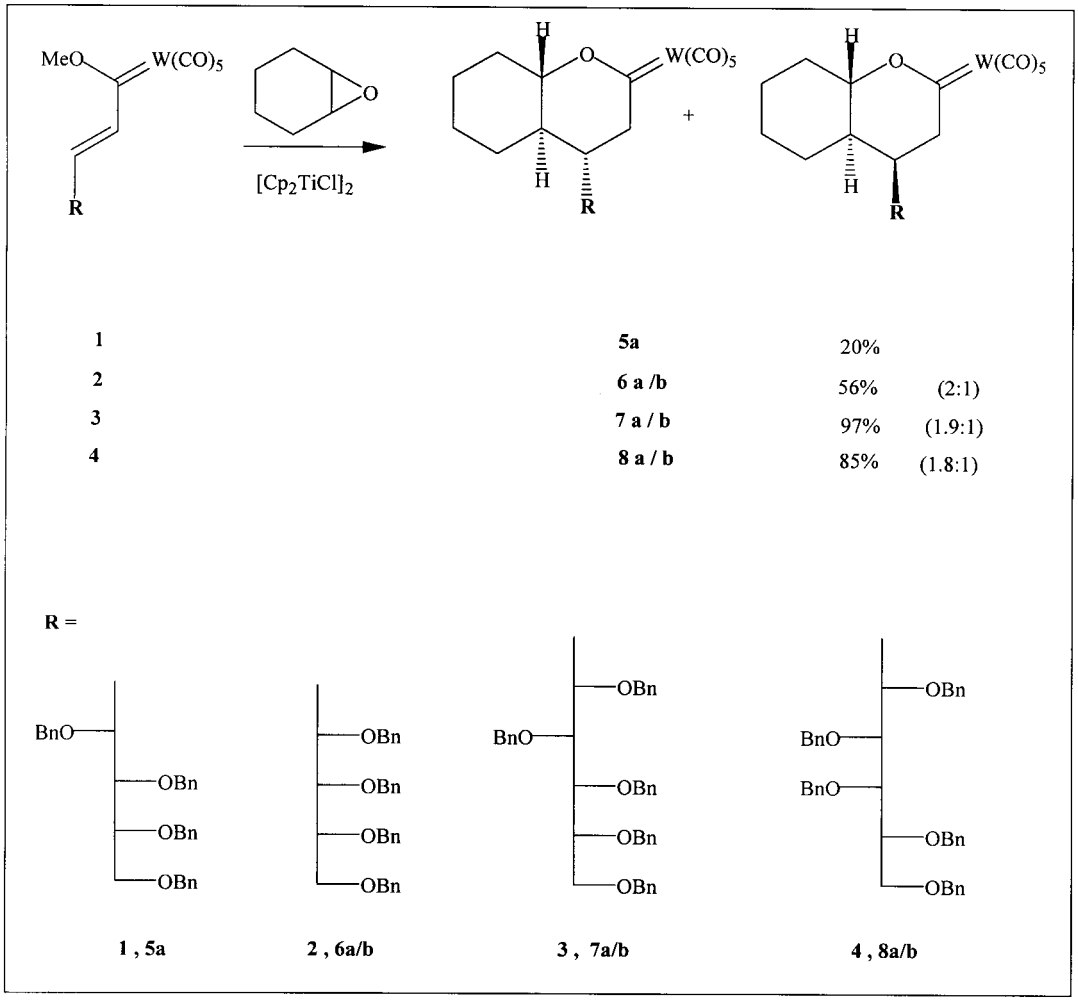



**Scheme 1.** $Ti^{III}$-mediated radical addition of epoxides to α,β-unsaturated carbene complexes.

pyranosylidene ligands are *trans*-fused as indicated by coupling constants $^3J_{H1-H6}$=9.9–10.6 Hz (Fig. 1). Similarly, the configuration of the sugar-substituted pyranosylidene ring carbon atom was established by $^1$H NMR spectroscopy which on the basis of the vicinal coupling constants $^3J_{H5-H6}$=7.4–12.7 Hz allowed an assignment to diastereomers **5a**–**8a** or, evident from coupling constants $^3J_{H5-H6}$=3.9–4.0 Hz, suggest a *cis* H5–H6 configuration in diastereomers **6b**–**8b**.

A complementary approach to carbohydrate-derived pyranosylidene complexes involves the combination of a non-sugar metal carbene and an anhydrosugar. The 1,2-anhydroglucose[19] **10** provides two alternatives for the homolytic opening of the epoxide ring (Scheme 3). Cleavage of the C–O bond according to path (a) involves a carbon-centered secondary radical which is supposed to add to the styrylcarbene complex **11** and finally to produce the bicyclic acetal pyranosylidene complex **C** after hydrolysis of the titaniumoxy radical intermediate **A** and nucleophilic substitution of the methoxy group for the hemiacetalic hydroxy substituent. An alternative homolytic cleavage of the epoxide referred to as path (b) leads to a secondary anomeric carbon radical[20] which profits by a stabilization by the adjacent pyran oxygen atom and thus is expected to be the favoured product of the homolytic ring-opening. It is supposed to add to the carbene complex to give the titaniumoxy radical intermediate **B** which finally affords pyranosylidene complex **D** bearing a vicinal dioxy substitution pattern. The cycloaddition is regio- and diastereoselective. A signal at δ=4.88 ppm characterized as a doublet of doublets with a vicinal coupling constant of $^3J_{H1-H6}$=10.96 Hz is in line with both the pyranopyran skeleton **D** resulting from path (b) and a *trans*-fusion of both pyrane rings. In contrast, the stereocontrol over the formation of the stereogenic center bearing the phenyl substituent is only moderate. NMR-analysis of the products indicates the formation of an approximate 1.5:1 mixture of diastereomers **12a/b** along with a minor amount of the monocyclic addition product **12c** (Scheme 4).

The observed selectivity according to path (b) may be explained with the formation of a more stable intermediate **B**, in which the sugar ligand chelates the metal forming a 5-membered titanacycle that leads to the final *trans*-fused product. The titanocenium fragment shields the upper side of the sugar ring, and thus favours the addition of the Fischer carbene complex from the more accessible bottom side. The chelation hypothesis is supported by the observation that the synthesis of the pyranopyran is considerably improved if




**Scheme 2.** Synthesis of sugar-labeled bicyclic pyranosylidene tungsten complexes.

tetrahydrofuran is replaced as a solvent by dichloromethane. Presumably, the formation of the titanium chelate is hampered in the presence of the strongly coordinating solvent THF which competes as a ligand for the metal (Fig. 2).

The radical addition of 1,2-anhydroglucose **10** to vinyl carbene complex **11** can be extended to alkynyl carbene complexes of chromium and tungsten. The propensity for the formation of the pyranopyranosylidene complex depends both on the metal and the alkyne substitution pattern. Under our standard reaction conditions the phenylethynyl carbene chromium **13** and the silylethynyl carbene tungsten **15** underwent addition of epoxide **10** affording either pyranopyranosylidene chromium **14** or acyclic vinyl carbene tungsten **16** in 76 or 30% yields, respectively. The addition of the sugar epoxide to the silyl carbene tungsten complex stopped at the vinyl carbene stage which was formed in the *Z*-configuration and thus prevents subsequent cyclization via nucleophilic substitution of the methoxy for the unprotected hydroxy group. In contrast, it was surprising to note that the phenylethynyl carbene tungsten complex **17**

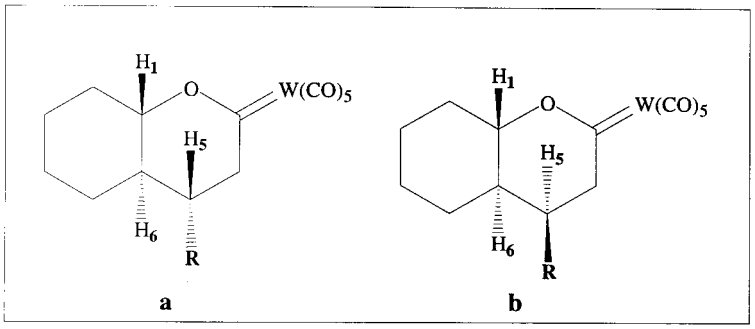
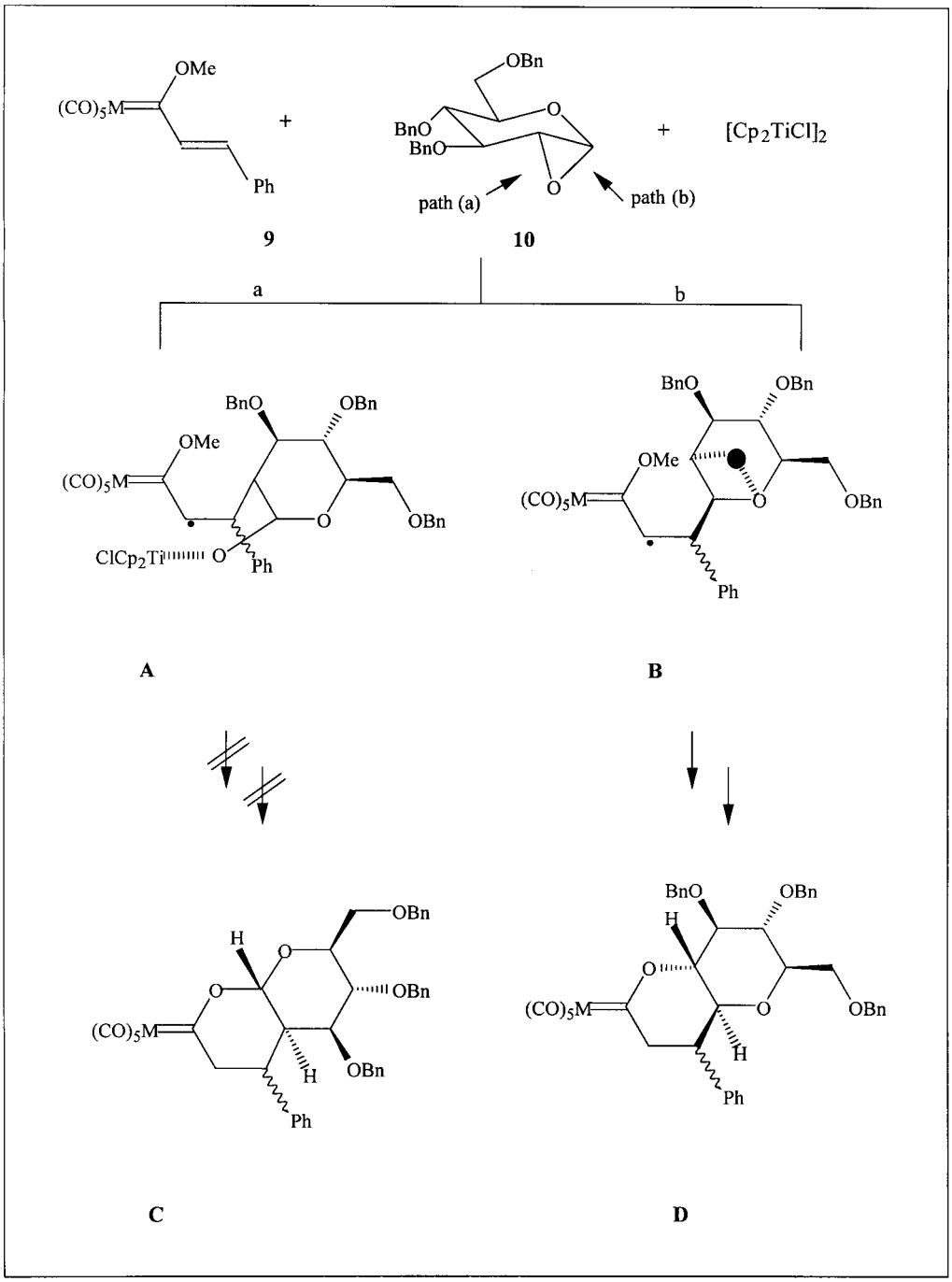



**Figure 1.** Stereochemical assignment of *trans*-fused diastereomeric cycloaddition products **a** and **b**.

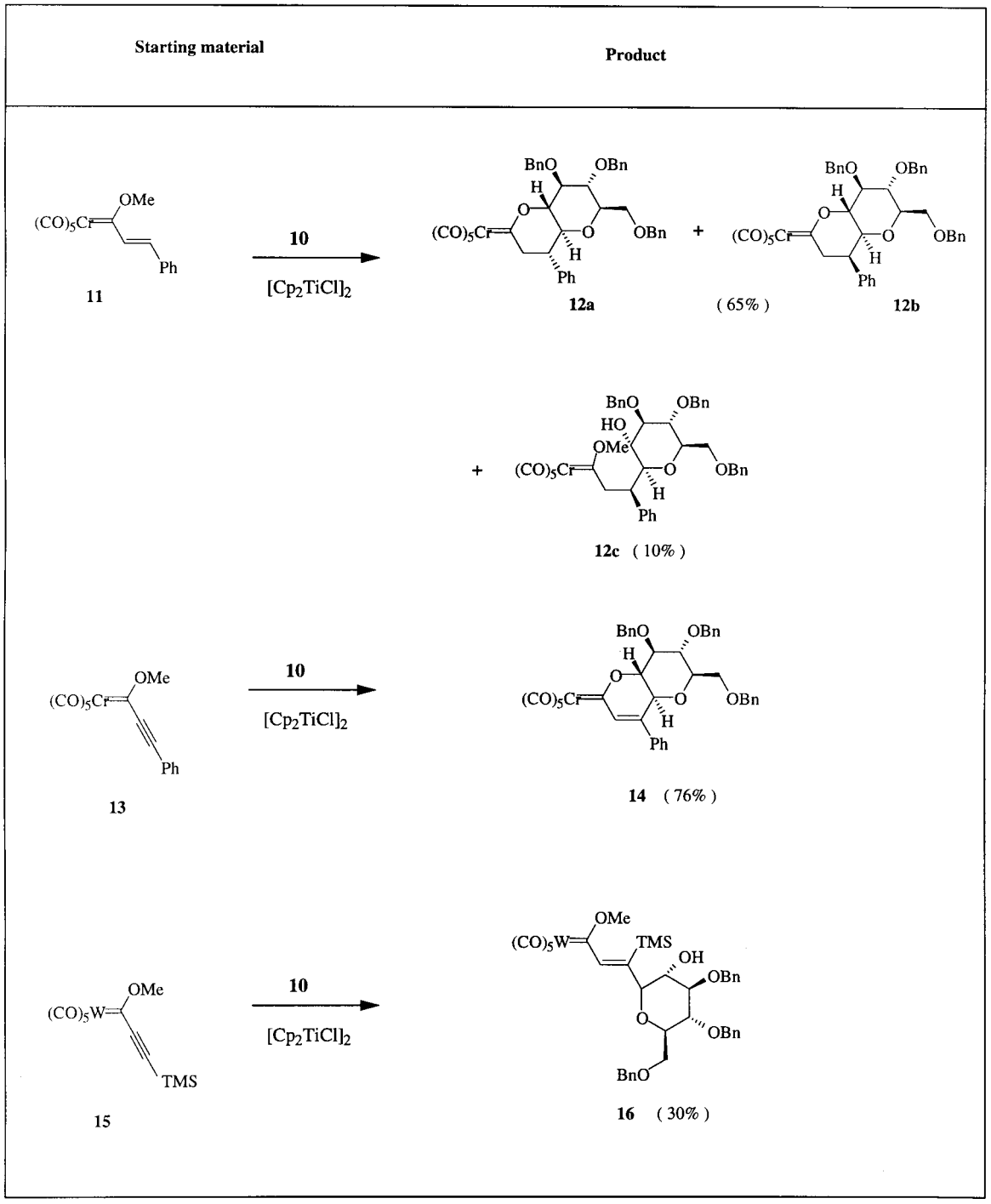



**Scheme 3.** Regioselective homolytic ring-opening of 1,2-anhydroglucose **10** and cycloaddition to styrylcarbene complex **9** (●=$Cp_2TiOCl$).

and the silylethynyl chromium complex **18** failed to give analogous addition products upon reaction with 1,2-anhydroglucose **10** under identical conditions. This behaviour was corroborated by four independent competition experiments applying different pairs of complementary carbene complexes **13/15**, **13/17**, **15/18** and **17/18**, respectively, under our standard conditions. $^{13}C$ NMR spectra recorded for the raw materials isolated after quenching the reaction with ethereal HCl and removal of the solvent revealed the conversion of chromium carbene **13** and tungsten carbene **15** to pyranopyranosylidene chromium **14** and vinyl carbene tungsten **16** while the complementary metal carbene starting materials **17** and **18** remained unreacted. The $^{13}C$ NMR spectrum of a representative competition experiment revealing the metal carbene and metal carbonyl signals is shown in Fig. 3 for the addition of sugar epoxide **10** to the pair of complementary metal carbene starting materials **13** and **17**.

## Conclusion

Novel pyranosylidene complexes bearing acyclic or cyclic monosaccharide labels have been synthesized via titanocenium monochloride-mediated radical addition of epoxides to α,β-unsaturated carbene complexes. The reaction is regio- and diastereoselective, compatible with a




**Scheme 4.** Radical addition of 1,2-anhydroglucose **10** to alkenyl and alkynyl carbene complexes.

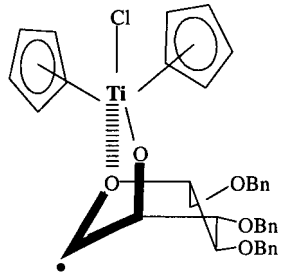



**Figure 2.** Stereopreference for C–C coupling of the anomeric radical intermediate.

range of oxygen functional groups and provides a straightforward access to organometallic pyranopyrane skeletons. However, it depends significantly on the cooperative choice of the metal and the alkyne substitution pattern.

## Experimental

All operations involving organometallic compounds were performed in an inert gas atmosphere under rigorous exclusion of air and water. The solvents were dried using standard

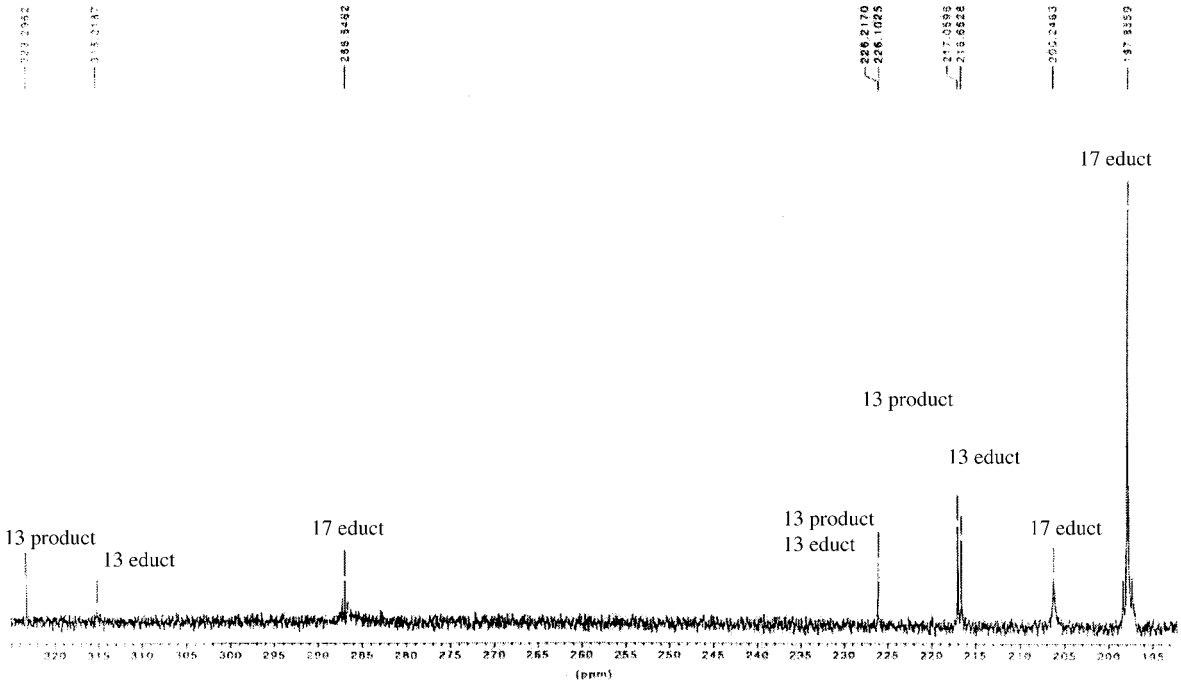



**Figure 3.** $^{13}C$ NMR (metal carbene and metal carbonyl range) spectrum obtained from the competition experiment using complementary metal carbene starting materials **13** and **17**.

methods and distilled under argon. Tetrahydrofuran was dried over $LiAlH_4$ and Na/K alloy, diethyl ether over NaH, $CH_2Cl_2$ and petroleum ether (40 to 60°C) over $CaH_2$. In all our experiments freshly prepared isolated bis(cyclopentadienyl)titanium(III)chloride was used which resulted in considerably better yields compared with those obtained with the radical source generated in situ via zinc reduction.[21]

Photochemical reactions were performed in a quartz apparatus using a mercury lamp (Fa. Philips, 125 HPK). Column chromatography of organometallic compounds was performed using silica gel (Merck 60, 0.063–0.200 mm) which was dried in vacuo and stored under argon. HPLC was performed using a column Knauer Eurospher (16×250 mm) and precolumn Knauer Eurospher 100 (5 μm particle size). Thin layer chromatography was performed using foils from Merck (Typ 60, F 254) with UV-detection. Carbohydrates were detected by a spray containing sulfuric acid (20%), acetic acid (50%), and ethanol (30%). FT-IR: Nicolet Magna. EI-MS: Kratos MS 50. NMR: Bruker AM-250, Bruker AM-400; Bruker DRX 500.

## General procedure for the preparation of carbene complexes 1–4

A suspension of 5 mmol hexacarbonyltungsten in 250 ml tetrahydrofuran was irradiated at −10°C over a period of 5 h. Then the solution was concentrated in vacuo to half volume, and a solution of 3 mmol of 1,2-dideoxy-3-(*R*/*S*)-hydroxy-4,5,6,7,8-penta-*O*-benzyl-D-oct-1-initol or the corresponding galacto compound[22] in 10 ml methanol were added at room temperature. After stirring for 24 h the solution was concentrated in vacuo, and the residue was purified by chromatography over silica gel (petroleum ether/diethyl ether, 6:1) at 10°C to give **3** (1.52 g, 51%) and **4** (1.73 g, 58%), respectively, as red oils. Complexes **1** and **2** have been prepared as previously described.[18]

**Pentacarbonyl[1-(1,2-dideoxy-3,4,5,6,7-penta-*O*-benzyl-D-gluco-hept-1-(*E*)-enitolyl)methoxycarbene]tungsten (3).** IR (PE): 2067, 1942 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$): δ 7.44 (1H, d, *J*=15.0 Hz, H-1), 7.33–7.30 (25H, m, Ph), 6.25 (1H, dd, *J*=15.0, 6.3 Hz, H-2), 4.60–4.38 (10H, m, $OCH_2Ph$), 4.65 (3H, s, $OCH_3$), 4.40 (1H, dd, *J*=6.0, 2.5 Hz, H-3), 3.90–3.81 (4H, m, H-4, 5, 6, 7), 3.70 (1H, dd, *J*=4.0 Hz, H-7′); $^{13}C$ NMR (500 MHz, $CDCl_3$): δ 308.5, 204.0, 197.3, 147.0, 134.5, 137.5, 138.2, 138.1, 137.9, 137.8, 128.0–127.4 (20C), 81.0, 80.0, 79.5, 78.2, 74.0, 73.4, 72.0, 71.5, 70.4, 69.0, 68.2; FAB-MS: *m*/*z*: 993.6 $[M]^+$, 853.6 $[M-5CO]^+$.

**Pentacarbonyl[1-(1,2-dideoxy-3,4,5,6,7-penta-*O*-benzyl-D-galacto-hept-1-(*E*)-enitolyl)methoxycarbene]tungsten (4).** IR (PE): 2067, 1945, 1958 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$): δ 7.44 (1H, *J*=15.1 Hz, H-1), 7.30–7.24 (25H, m, Ph), 6.20 (1H, dd, *J*=15.1, 6.0 Hz, H-2), 4.60–4.35 (10H, m, $OCH_2Ph$), 4.66 (3H, s, $OCH_3$), 4.20 (1H, dd, *J*=6.0, 2.2 Hz, H-3), 3.90–3.80 (4H, m, H-4, 5, 6, 7), 3.75 (1H, dd, *J*=3.3 Hz, H-7′); $^{13}C$ NMR (500 MHz, $CDCl_3$): δ 309.0, 204.1, 197.3, 146.1, 138.1, 138.0, 137.5, 137.3, 137.2, 134.4, 128.0–127.3 (20C), 81.8, 80.4, 79.6, 78.3, 74.0, 73.2, 72.3, 72.0, 69.5, 68.1; FAB-MS: *m*/*z*: 993.6 $[M]^+$, 853.6 $[M-5CO]^+$.

## General procedure for the preparation of the tetrahydropyranosylidene complexes 5–8

A solution of 4 equiv. cyclohexene oxide in 5 ml

dichloromethane and a green solution of 4 equiv. $[Cp_2TiCl]_2$ in 10 ml tetrahydrofuran were added simultaneously over 1 h to a solution of carbene complex **1**–**4** (1.5 mmol) in 10 ml dichloromethane at −30°C. After stirring for additional 2 h the solution was cooled to −78°C, and the reaction was quenched with 8 equiv. of HCl (1 M) dissolved in diethyl ether. The solvent was removed in vacuo, the residue was resuspended in diethyl ether and filtered to recover $[Cp_2TiCl]_2$. After concentrating the filtrate in vacuo the residue was purified by chromatography over silica gel to give tetrahydropyranosylidene complexes **5**–**8**.

**Pentacarbonyl[2-oxa-bicyclo[4.4.0]-1′,2′,3′,4′-tetra-*O*-benzyl-D-*arabino*-dec-3-ylidene]tungsten (5a).** Chromatography over silica gel (petroleum ether/diethyl ether, 6:1) at −10°C gave 282.7 mg (20%) of **5a** as a yellow-orange oil. IR (PE): 2071, 1968, 1943 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.40–7.20 (20H, m, Ph), 4.64–4.34 (8H, m, OC$H_2$Ph), 4.22 (1H, dd, $J$=6.4, 3.1 Hz, H-1′), 3.85 (1H, dd, $J$=5.4, 2.8 Hz, H-2′), 3.81 (1H, 'dd', $J$=10.2, 4.0 Hz, H-1), 3.78 (1H, 'd', $J$=2.8 Hz, H-3′), 3.70 (1H, dd, $J$=3.0, 5.0 Hz, H-4′), 2.20 (2H, 'd', $J$=0.4 Hz, H-4), 1.35 (1H, dd, $J$=0.2, 11.3 Hz, H-5), 0.84–0.89 (9H, m, H-6, 7, 8, 9, 10); $^{13}C$ NMR (500 MHz, $CDCl_3$): $\delta$ 335.8, 203.8, 197.5, 138.5–137.9, 128.5–127.7, 80.8, 79.0, 78.1, 74.8–71.9, 69.3, 68.8, 66.0, 38.9, 30.5, 29.1, 28.5, 25.6, 23.9; FAB-MS: *m/z*: 942.2 $[M]^+$, 858.3 $[M-3CO]^+$, 767 $[M-3CO-C_7H_7]^+$, 699.2 $[M-W(CO)_2]^+$, 643.2 $[M-W(CO)_4]^+$.

**Pentacarbonyl[2-oxa-bicyclo[4.4.0]-1′,2′,3′,4′-tetra-*O*-, benzyl-D-*ribo*-dec-3-ylidene]tungsten (6a/6b).** Chromatography over silica gel (petroleum ether/diethyl ether, 2:1) at −10°C gave 791.4 mg (56%) of an orange syrup containing an approximate 2:1 mixture of diastereomers **6a**:**6b**. $R_f$ (**6a**) 0.85 (petroleum ether/diethyl ether, 2:1); $R_f$ (**6b**) 0.76 (petroleum ether/diethyl ether, 2:1); IR (PE): 2069, 1967, 1940 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.40 −7.20 (40H, m, **6a** and **6b**, Ph), 5.01–4.40 (16H, m, **6a** and **6b**, $OCH_2Ph$), 4.35 (1H, dd, $J$=4.6, 4.0 Hz, 6b, H-1′), 4.30 (1H, 't', $J$=5.8 Hz, **6a**, H-1′), 3.95 (2H, m, **6a** and **6b**, H-2′), 3.86 (1H, dd, $J$=10.0, 8.2 Hz, **6a**, H-1), 3.75 (1H, dd, $J$=9.9, 2.7 Hz, **6b**, H-1), 3.78 (1H, 'd', $J$=3.9 Hz, **6a**, H-3′), 3.68 (1H, dd, $J$=3.9, 7.2 Hz, **6a**, H-4′), 3.62 (1H, dd, $J$=3.1, 6.8 Hz, **6b**, H-3′), 3.53 (1H, d, $J$=6.7 Hz, **6b**, H-4′), 2.20 (4H, m, **6a** and **6b**, H-4), 1.51 (1H, dd, $J$=7.4, 5.5 Hz, **6a**, H-5), 1.43 (1H, dd, $J$=6.5, 3.9 Hz, **6b**, H-5), 0.90–1.10 (18H, m, **6a** and **6b**, H-6, 7, 8, 9, 10); $^{13}C$ NMR (400 MHz, $CDCl_3$): **6a**: $\delta$ 335.8, 205.2, 198.5, 139.1–138.3 (4C, **6a** and **6b**), 128.9–127.5 (20C), 82.6, 80.6, 79.0, 74.2–72.9 (**6a** and **6b**), 71.0, 68.2, 66.4, 38.8, 30.4, 29.7, 29.0, 25.9, 23.8; $^{13}C$ NMR (400 MHz, $CDCl_3$): **6b**: $\delta$ 335.0, 204.1, 197.3, 139.1–138.3 (4C, **6a** and **6b**), 128.9–127.5 (20C, **6a** and **6b**), 81.9, 80.3, 78.7, 74.2–72.9 (**6a** and **6b**), 70.1, 67.2, 64.1, 38.6, 29.8, 29.5, 28.6, 25.1, 23.1; FAB-MS: *m/z*: 942.2 $[M]^+$, 830.2 $[M-4CO]^+$, 802.2 $[M-5CO]^+$.

**Pentacarbonyl[2-oxa-bicyclo[4.4.0]-1′,2′,3′,4′,5′-penta-*O*-benzyl-D-*gluco*-dec-3-ylidene]tungsten (7a/7b).** Chromatography over silica gel (petroleum ether/diethyl ether, 1:1) gave 1.56 g (97%) of an orange syrup containing a 64:36 mixture of diastereomers **7a**:**7b** (HPLC). $R_f$ (**7a**) 0.84 (petroleum ether/diethyl ether, 1:1); $R_f$ (**7b**) 0.75 (petroleum ether/diethyl ether); IR (PE): 2069, 1967, 1940 $cm^{-1}$; $^1H$ NMR (500 MHz, $C_6D_6$): $\delta$ 7.56–7.14 (50H, m, **7a** and **7b**, Ph), 5.14–4.3 (20H, m, **7a** and **7b**, OC$H_2$Ph), 4.20–4.03 (2H, m, **7a** and **7b**, H-1′), 3.93 (1H, dd, $J$=10.6, 7.4 Hz, **7a**, H-1), 3.84 (1H, dd, $J$=10.3, 5.8 Hz, **7b**, H-1), 3.79–3.72 (2H, m, **7a** and **7b**), 3.71–3.61 (2H, m, **7a** and **7b**, H-3′), 3.52 (1H, td, $J$=4.5, 4.3, 11.5 Hz, **7a**, H-4′), 3.32 (1H, td, $J$=4.3, 4.6, 10.9 Hz, **7b**, H-4′), 3.22 (1H, t, $J$=6.5, 12.0 Hz, **7a**, H-5′), 3.1 (1H, m, **7b**, H-5′), 1.97–1.92 (4H, m, **7a** and **7b**, H-4), 1.38 (1H, ddd, $J$=3.9, 4.8, 12.7 Hz, **7a**, H-5), 1.15 (1H, ddd, $J$=3.6, 3.9, 12.8 Hz, **7b**, H-5), 1.08–0.90 (18H, m, **7a** and **7b**, H-6, 7, 8, 9, 10); $^{13}C$ NMR (500 MHz, $C_6D_6$): **7a**: $\delta$ 333.8, 203.7, 197.5, 138.9–137.8 (5C, **7a** and **7b**), 128.0–126.6 (30C, **7a** and **7b**), 83.2, 80.2, 78.2, 74.6, 71.5, 69.8, 67.8, 66.6, 38.4, 34.8, 31.8, 28.6, 25.2, 23.9; $^{13}C$ NMR (500 MHz, $C_6D_6$): **7b**: $\delta$ 332.8, 202.8, 197.1, 139.9–137.8 (5C, **7a** and **7b**), 128.0–126.6 (30C, **7a** and **7b**), 80.7, 78.9, 78.0, 73.0, 71.2, 68.9, 67.6, 64.3, 35.0, 33.0, 29.1, 27.2, 25.1, 23.6; FAB-MS: *m/z*: 1062.4 $[M]^+$, 950.4 $[M-4CO]^+$, 738.4 $[M-5CO]^+$.

**Pentacarbonyl[2-oxa-bicyclo[4.4.0]-1′,2′,3′,4′,5′-penta-*O*-benzyl-D-*galacto*-dec-3-ylidene]tungsten (8a/8b).** Chromatography over silica gel (petroleum ether/diethyl ether, 1:1) gave 1.36 g (85%) of an orange syrup as a 65:35 mixture of diastereomers **8a**:**8b** (HPLC). $R_f$ (**8a**) 0.80 (petroleum ether/diethyl ether, 1:1); $R_f$ (**8b**) 0.78 (petroleum ether/diethyl ether, 1:1); IR (PE): 2069, 1982, 1942 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$): $\delta$ 7.50–7.10 (50H, m, **8a** and **8b**, Ph), 4.90–4.40 (20, m, **8a** and **8b**, OC$H_2$Ph), 4.20–3.52 (overlapping signals, **8a** and **8b**, H-1′, 1, 3′,3), 3.48 (1H, td, $J$=3.3, 7.1, 4.5 Hz, **8a**, H-4′), 3.29 (1H, td, $J$=9.0, 4.9, 5.1 Hz, **8b**, H-4′), 3.21 (1H, t, $J$=7.1, 6.6 Hz, **8a**, H-5′), 3.18 (1H, t, $J$=6.6, 6.4 Hz, **8a**, H-5′), 3.09 (1H, t, $J$=3.3, 5.1 Hz, **8b**, H-5′), 3.07 (1H, t, $J$=3.2 Hz, **8b**, H-5′) 2.65 (2H, m, **8a** and **8b**, H-4), 2.30–1.50 (overlapping signals, **8a** and **8b**, H-4, 5), 1.40–1.10 (18H, m, **8a** and **8b**, H-6, 7, 8, 9, 10); $^{13}C$ NMR (250 MHz, $C_6D_6$): **8a**: $\delta$ 334.1, 203.9, 197.7, 138.9–137.3 (5C, **8a** and **8b**), 128.3–126.9 (30C, **8a** and **8b**), 83.6, 79.6, 78.4, 75.1, 71.8, 68.1, 67.2, 64.9, 38.6, 35.1, 29.4, 27.4, 25.4, 23.9; $^{13}C$ NMR (250 MHz, $C_6D_6$,): **8b**: $\delta$ 333.2, 203.1, 197.3, 138.9–137.3 (5C, **8a** and **8b**), 128.3–126.9 (30C, **8a** and **8b**), 80.9, 79.2, 78.2, 72.7, 70.1, 67.7, 66.9, 61.7, 35.4, 31.1, 28.9, 25.5, 24.1, 23.7; FAB-MS: *m/z*: 1062.4 $[M]^+$, 922.4 $[M-5CO]^+$, 794.4 $[M-W(CO)_3)]^+$.

## General procedure for the preparation of carbene complexes 12, 14 and 16

A solution of 3.5 equiv. anhydroglucose **10** in 5 ml dichloromethane and a green solution of 3.5 equiv. $[Cp_2TiCl]_2$ in 10 ml dichloromethane were added over 1 h simultaneously to a solution of carbene complex **11**, **13**, **15** (1.5 mmol) in dichloromethane (10 ml) at −30°C. After stirring for additional 2 h the solution was cooled to −78°C, and the reaction was quenched with a solution of 7 equiv. HCl (1 M) in diethyl ether. After removal of the solvent the residue was suspended in diethyl ether and filtered. The product was purified by flash chromatography. The mixture **12a**–**c** was purified by chromatography over silica gel at −10°C in (petroleum ether/diethyl ether, 6:1) to

give 722 mg (65%) of a 1.5:1 mixture of **12a**:**12b** and 116 mg (10%) of **12c** as orange oils.

**Pentacarbonyl[2,7-dioxa-bicyclo[4.4.0]-9-(*R*), 10-(*S*)-dibenzyloxy-8-(*R*)-(benzyloxymethyl)-5-(*S*)-phenyl-dec-3-ylidene]chromium (12a).** IR (PE): 2066, 1946, 1934 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$, 0°C): $\delta$ 7.40–7.10 (20H, m, Ph), 5.01 (1H, 't', $J$=10.6, 10.9 Hz, H-1), 4.75 (1H, dd, $J$=10.4, 9.0 Hz, H-6), 4.36 (1H, 'dd', $J$=8.2, 9.0 Hz, H-8), 4.60–4.43 (m, 6H, OC$H_2$Ph), 4.15–4.09 (1H, dd, $J$=12.5, 9.0 Hz, H-5), 3.92 (1H, t, $J$=9.0, 8.2 Hz, H-9), 3.83 (1H, t, $J$=9.0, 9.4 Hz, H-11), 3.64 (1H, dd, $J$=3.5, 12.0 Hz, H-4), 3.52 (1H, t, $J$=10.6, 8.2 Hz, H-10), 3.47 (1H, 't', 1.9, 4.7 Hz, H-4′), 3.32 (1H, t, $J$=9.0, 3.5 Hz, H-11′); $^{13}C$ NMR (400 MHz, $CDCl_3$, 0°C): $\delta$ 354.6, 223.8, 216.7, 139.1–138.3 (3C), 129.0–127.9 (20C), 87.5, 83.9, 79.8, 78.2, 77.7, 76.4, 76.2, 75.7, 73.8, 68.5, 61.5.

**Pentacarbonyl[2,7-dioxa-bicyclo[4.4.0]-9-(*R*), 10-(*S*)-dibenzyloxy-8-(*R*)-(benzyloxymethyl)-5-(*R*)-phenyl-dec-3-ylidene]chromium (12b).** IR (PE): 2066, 1946, 1934 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$, 0°C): $\delta$ 7.14–6.92 (20H, m, Ph), 4.88 (1H, dd, $J$=11.0, 3.5 Hz, H-6), 4.81 (1H, t, $J$=11.2, 4.2 Hz, H-1), 4.30 (1H, m, H-8), 4.59–4.46 (6H, m, OC$H_2$Ph), 4.23–4.10 (1H, dd, $J$=3.5, 5.1 Hz, H-5), 3.75 (1H, t, $J$=4.0, 3.1 Hz, H-9), 3.60 (1H, 't', $J$=7.0, 9.0 Hz, H-11), 3.58 (1H, dd, $J$=1.9, 10.3 Hz, H-4), 3.48 (1H, t, $J$=4.2, 2.4 Hz, H-10), 3.30 (1H, 't', $J$=9.0, 9.4 Hz, H-4′), 3.31 (1H, dd, $J$=3.1, 9.9 Hz, H-11′), 3.13 (1H, t, $J$=3.1, 9.0 Hz, H-11); $^{13}C$ NMR (400 MHz, $CDCl_3$) $\delta$ 353.2, 223.8, 216.7, 133.5–130.1 (4C), 129.1–128.0 (20C), 84.6, 81.9, 78.6, 77.9, 73.5, 73.0, 73.7, 73.8, 69.1, 67.1, 57.6; FAB-MS (diastereomeric mixture **12a/b**): *m/z*: 740.1 $[M]^+$, 656 $[M-3CO]^+$, 600.1 $[M-5CO]^+$, 509.1 $[M-5CO-C_7H_7]^+$.

**Pentacarbonyl [3-(3′,4′,6′-tribenzyl-α-D-*glucopyranos*-1′-*yl*]-1-methoxy-3-phenylprop-1-ylidene]chromium (12c).** IR (PE): 2071, 1968, 1942 $cm^{-1}$; $^1H$ NMR (500 MHz, $d_6$-acetone): $\delta$ 7.45–7.28 (5H, m, Ph), 5.10–4.83 (overlapping signals, H-1′, 2′, 5′), 4.79 (3H, s, $OCH_3$), 4.74–4.62 (6H, m, OC$H_2$Ph), 4.60–4.31 (overlapping signals, H-3, 4′), 3.70 (2H, dd, $J$=9.00, 4.2 Hz, C$H_2$OBn, H-6′), 3.60–3.39 (3H, m, H-2, 3′); $^{13}C$ NMR (400 MHz, $d_6$-acetone): $\delta$ 360.8, 224.1, 216.7, 139.2–139.8, 128–127.8, 87.7, 83.3, 79.5, 78.5, 78.0, 75.2, 74.9, 73.4, 73.1, 72.4, 72.3, 69.4; FAB-MS: *m/z*: 772.3 $[M]^+$, 688.3 $[M-3CO]^+$, 632.3 $[M-5CO]^+$.

**Pentacarbonyl[2,7-dioxa-bicyclo[4.4.0]-9-(*R*),10-(*S*)-dibenzyloxy-8-(*R*)-(benzyloxymethyl)-5-phenyl-dec-4-en-3-ylidene]chromium(0) (14).** Chromatography over silica gel (petroleum ether/diethyl ether, 2:1) gave 841 mg (76%) of a violet powder. IR (PE): 2058, 1964, 1952 $cm^{-1}$; $^1H$ NMR (500 MHz, $d_6$-acetone): $\delta$ 7.44–7.27 (20H, m, Ph), 5.46 (1H, d, $J$=11 Hz, H-6), 5.41 (1H, s, H-4), 5.20 (1H, dd, $J$=11.0, 10.7 Hz, H-1), 4.96 (1H, 't', $J$=11.03 12.5 Hz, H-10), 4.74–4.36 (6H, m, OC$H_2$Ph), 4.15 (1H, dd, $J$=13.0, 5.2 Hz, H-9), 3.91 (1H, dd, $J$=5.6, 1.7 Hz, H-8), 3.74 (1H, dd, $J$=5.2, 4.3 Hz, H-11), 3.66 (1H, dd, $J$=11.1, 5.6 Hz, H-11′); $^{13}C$ NMR (400 MHz, $CDCl_3$): $\delta$ 323.5, 226.1, 217.1, 138.4, 138.3, 138.2, 137.2, 133.9, 132.7, 131.5–128.0 (20C), 83.6, 81.5, 80.5, 78.2, 76.3, 75.9, 73.6, 72.0, 69.1; FAB-MS: *m/z*: 738.1 $[M]^+$, 654.1 $[M-3CO]^+$, 508.1 $[M-5CO-C_7H_7]^+$.

**Pentacarbonyl[3-(3′,4′,6′-tribenzyl-α-D-*glucopyranos*-1′-*yl*)-1-methoxy-3-(trimethylsilyl)-prop-2-(*Z*)-en-1-ylidene]tungsten(0) (16).** Chromatography over silica gel (petroleum ether/diethyl ether, 6:1) gave 404 mg (30%) of an orange oil. IR (PE): 2070, 1955, 1945 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.36–7.30 (20H, m, Ph), 5.45 (1H, s, H-2), 5.08 (1H, d, $J$=2.7 Hz, H-1′), 5.04 (1H, dd, $J$=10.6, 1.9 Hz, H-2′), 4.91 (1H, 't', $J$=10.6, 11.4 Hz, H-3′), 4.74–4.45 (6H, m, OC$H_2$Ph), 4.65 (3H, s, $OCH_3$), 4.46 (1H, d, $J$=11.8, 2.4 Hz, H-4′), 4.09–4.01 (1H, m, H-5′), 3.75 (1H, dd, $J$=3.1, 9.0 Hz, H-6′), 3.65 (1H, dd, $J$=9.4, 5.1 Hz, H-6′), 0.06 (9H, s, $Si(CH_3)_3$); $^{13}C$ NMR (400 MHz, $CDCl_3$): $\delta$ 316.0, 204.0, 197.3, 139.1–138.6 (3C), 139.2, 137.7, 129.0–128.1 (20C), 97.3, 85.0, 78.8, 78.1, 75.7, 73.9, 72.3, 69.4, 1.2; FAB-MS: *m/z*: 898.1 $[M]^+$, 814.1 $[M-3CO]^+$, 786.1 $[M-4CO]^+$.

## Competition experiments

A solution of 3.5 equiv. anhydroglucose **10** in 5 ml dichloromethane and a green solution of 3.5 equiv. $[Cp_2TiCl]_2$ in 10 ml dichloromethane were added over 1 h simultaneously to a solution of carbene complex **13** (0.75 mmol) and carbene complex **15** (0.75 mmol) in dichloromethane (10 ml) at −30°C. After stirring for additional 2 h the solution was cooled at −78°C, and the reaction was quenched with a solution of 7 equiv. HCl (1 M) in diethyl ether. After removal of the solvent the residue was suspended in diethyl ether, filtered and purified over a short (5 cm) column of silica gel. The same procedure were performed for the pairs of metal carbenes **13/17**, **15/18** and **17/18**.

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## References

1. Organotransition Metal Modified Sugars, Part 18. For Part 17, see: Dötz, K. H.; Otto, F.; Nieger, M. *J. Organomet. Chem.* in press.
2. For reviews, see: Faulkner, D. J. *Nat. Prod. Rep.* **1984**, *1*, 251, 551; Faulkner, D. J. *Nat. Prod. Rep.* **1984**, *10*, 497; Faulkner, D. J. *Nat. Prod. Rep.* **1994**, *11*, 355.
3. (a) Prasad, A. V. K.; Shimizu, Y. *J. Am. Chem. Soc.* **1989**, *111*, 6476. (b) Van Duyne, G. D. In *Marine Toxins: Origin, Structure and Molecular Pharmacology*; Hall, S., Strichartz, G., Eds.; ACS Symposium Series 418; American Chemical Society: Washington, DC, 1990; p 144.
4. (a) Nagai, H.; Murata, M.; Torigoe, K.; Satake, M.; Yasumoto, T. *J. Org. Chem.* **1992**, *57*, 5448. (b) Satake, M.; Murata, M.; Yasumoto, T. *J. Am. Chem. Soc.* **1993**, *115*, 361. (c) Satake, M.; Murata, M.; Yasumoto, T. *Tetrahedron Lett.* **1993**, *34*, 1975.

5. (a) Edwards, R. A.; Trainer, V. L.; Baden, D. G. *Brain Res. Mol. Brain Res.* **1992**, *14*, 64. (b) Richards, I. S.; Kulkarni, A. P.; Brooks, S. M.; Pierce, R. *Toxicon* **1990**, *28*, 1105.
6. (a) Murakami, Y.; Oshima, Y.; Yasumoto, T. *Bull. Jpn. Soc. Sci. Fish.* **1982**, *48*, 69. (b) Norte, M.; González, R.; Fernández, J. J.; Rico, M. *Tetrahedron* **1991**, *47*, 7437.
7. Robinson, J. A. *Prog. Chem. Org. Nat. Prog.* **1991**, *58*, 1.
8. (a) Baldwin, J. E.; Silusik, M. *Tetrahedron* **1982**, *19*, 2939. (b) Alvarez, E.; Rodríguez, M. L.; Zurita, D.; Martín. J. D. *Tetrahedron Lett.* **1991**, *32*, 2253.
9. Alvarez, E.; Candenas, M.-L.; Pérez, R.; Ravelo, J. L.; Martín, J. D. *Chem. Rev.* **1995**, *95*, 1953.
10. Mori, Y. *Chem. Eur. J.* **1997**, *3*, 849.
11. Leeuwenburgh, M. A.; Overkleeft, H. S.; van der Marel, G. A.; van Boom, J. H. *Synlett* **1997**, 1263.
12. Giese, B. *Angew. Chem.* **1983**, *95*, 771; *Angew. Chem. Int. Ed. Engl.* **1983**, *22*, 753.
13. For reviews, see: (a) Dötz, K. H.; Fischer, H.; Hofmann, P.; Kreissl, F. R.; Schubert, U.; Weiss, K. *Transition Metal Carbene Complexes*, Verlag Chemie: Weinheim, 1983. (b) Wulff, W. D. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Paquette, L. A., Eds.; Pergamon: Oxford, 1991; Vol. 5, pp 1065; Zaragoza-Dörwald, F. *Metal Carbenes in Organic Synthesis*; Wiley-VCH: Weinheim, 1999. (c) de Meijere, A. *Pure Appl. Chem.* **1996**, *68*, 61.
14. (a) Hoffmann, R. *Angew. Chem.* **1982**, *94*, 725; *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 711. (b) Stone F. G. A. *Angew. Chem.* **1984**, *96*, 85; *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 89.
15. For reviews, see: (a) Dötz, K. H.; Ehlenz, R. *Chem. Eur. J.* **1997**, *3*, 175; (b) Dötz, K. H.; Jäkel, C.; Haase, W.-C. *J. Organomet. Chem.* in press.
16. (a) Nugent, W. A.; Rajan Babu, T. V. *J. Am. Chem. Soc.* **1988**, *110*, 8561. (b) Rajan Babu, T. V.; Nugent W. A. *J. Am. Chem. Soc.* **1989**, *111*, 4525. (c) Rajan Babu, T. V.; Beattie, M. S. *J. Am. Chem. Soc.* **1990**, *112*, 6408.
17. For a radical addition of non-functionalized epoxides to α,β-unsaturated metal carbenes, see: (a) Merlic, C. A.; Xu, D. *J. Am. Chem. Soc.* **1991**, *113*, 9855. (b) Merlic, C. A.; Xu, D.; Nguyen, M. C.; Truong, U. *Tetrahedron Lett.* **1993**, *34*, 227.
18. Dötz, K. H.; Paetsch, D.; Bozec, L. H. *J. Organomet. Chem.* **1999**, *589*, 11.
19. (a) Blackburne I. D.; Fredericks P. M.; Gutherie R. D. *J. Aust. Chem.* **1976**, *29*, 381. (b) Halcomb, R. L.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1989**, *111*, 6661.
20. Giese, B. *Angew. Chem.* **1989**, *101*, 993; *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 969.
21. Gansäuer, A.; Bluhm, H.; Pierobon, M. *J. Am. Chem. Soc.* **1998**, *120*, 12849.
22. Kraus, G. A.; Molina, M. T. *J. Org. Chem.* **1988**, *53*, 742.