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From Glycals to Metal Pyranosylidenes: Diastereoselective Addition of Electrophiles to Metal Carbene Enolate Intermediates[1]

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Dedicated to Professor Sandhoff on the occasion of his 60th birthday

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Abstract—Lithiated glucals react smoothly with $Cr(CO)_5THF$ at the metal center to generate the corresponding vinyl chromate intermediates which represent chromium carbene enolate equivalents. Trapping by electrophiles provides an entry to novel chromium 2-deoxypyranosylidenes. Deuteration and allylation proceed with an approximately 90% d.e. in preference of the C-2-*manno* complexes.

Introduction

Carbohydrates are among the three vital classes of compounds that form the basis of life science processes. The carbohydrate units of glycoconjugates take part in molecular recognition at cell walls,[2] in intracellular enzyme transport,[3] infection[4] and cell adhesion processes.[5] Polysaccharides serve as food and energy storage or construction materials.[6] The stereoselective formation of glycosidic bonds which requires an appropriate activation of the anomeric carbon atom remains a synthetic challenge although a series of powerful glycosylation procedures have been developed.[7] Beyond the classical *O*-glycosides their *C*-glycoside analogues have recently gained considerable attention due to their inherent stability toward hydrolysis.[8] The polyfunctionality of carbohydrates requires elaborate synthetic techniques to allow stereoselective manipulations both within the sugar backbone and its functional group periphery. In this respect, it is surprising that the impact of organometallic reagents which have revolutionalized selective organic synthesis over the past three decades is still marginal. Beyond a few main group metals such as lithium or tin the application of transition metals—which are known to allow for a sensitive tuning of the reactivity of coordinated carbon species[9]—in the activation of the anomeric center for carbon–carbon bond formation is mainly restricted to samarium and palladium so far.[10] Glycosyl manganese and iron carbonyl complexes bearing carbohydrate anion equivalents have been developed and applied to the synthesis of *C*-glycosides;[11] however, the high-pressure conditions required for an efficient insertion of alkenes and alkynes into the anomeric carbon to metal bond have prevented wider applications.[12] We became interested in organometallic glycosyl *donors* and focused on a metal carbene functionalization of the anomeric center.[13] Over two decades, *Fischer* type carbene complexes bearing an electrophilic carbene carbon atom[14] have been developed to valuable reagents for stereoselective carbon–carbon bond formation.[15] They have been applied to either carbene ligand-centered cycloaddition reactions such as Diels–Alder reactions which are facilitated by the electron–acceptor pentacarbonyl metal fragment[16] or metal-centered cycloaddition reactions such as benzannulation[17] and cyclopropanation[18] which proceed at the metal carbonyl template.[19] Moreover, they serve as precursors for photo-generated ketene equivalents which have been used in stereoselective syntheses of amino acids and β-lactams.[20] Alkylcarbene ligands undergo ready α-deprotonation to give enolate-type carbene complex anions which have been exploited in diastereoselective aldol- and Michael-type reactions.[21]

The most general synthetic access to carbonyl carbene complexes is the *Fischer* route which is based on the sequential addition of an organolithium nucleophile and a carbon electrophile across a carbonyl ligand.[14] This approach is limited to the synthesis of acyclic metal carbenes; complementary routes to cyclic carbene analogues are provided by the metal carbonyl template assisted cycloisomerization of alkynols to give metal oxacycloalkylidenes[22] or by the formal substitution of an amide

Keywords: carbenes and carbenoids; carbohydrates; chromium and compounds; glycals.

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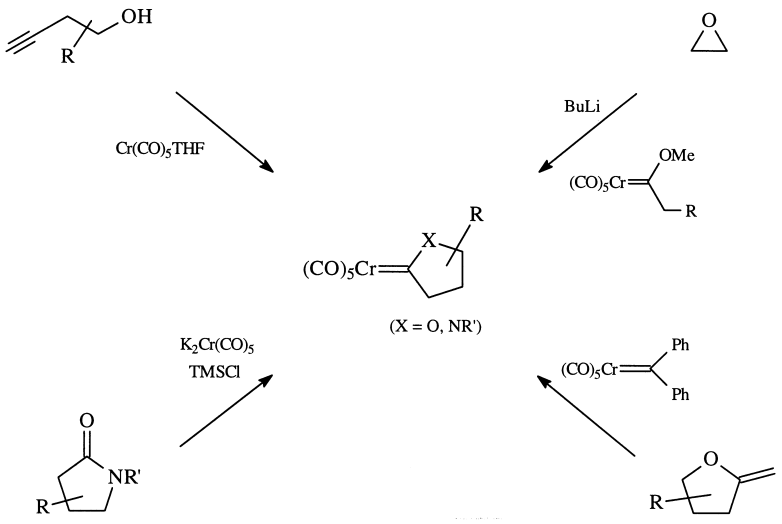


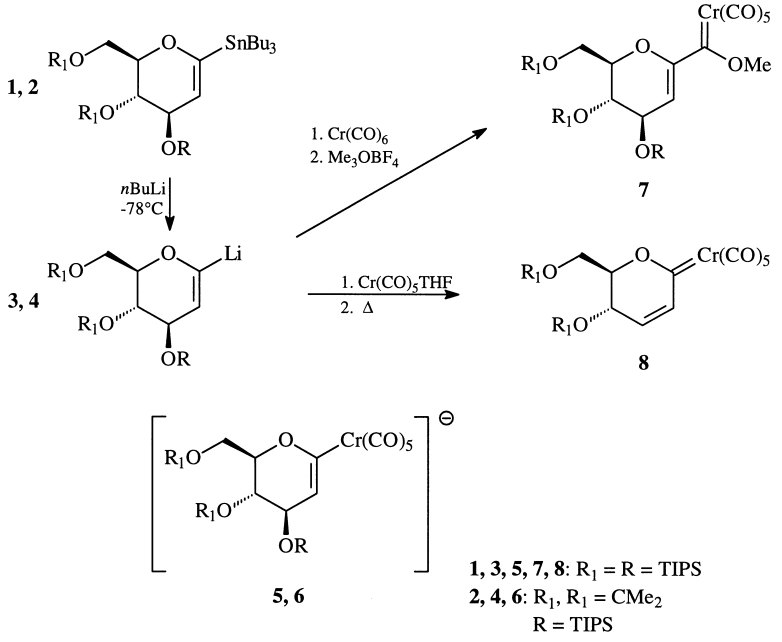
Scheme 1. Alternative routes to cyclic *Fischer*-type carbene chromium complexes.

oxygen atom by the isolobal[23] pentacarbonyl fragment which occurs along the reaction of *N*-alkyl lactams with pentacarbonyl metalate dianions in the presence of TMS chloride[24] (Scheme 1). However, both routes are not attractive for the elaboration of glycosylidene complexes either due to the tedious access to appropriately oxygenated alkynol precursors[25] or to the pronounced basicity of the carbonyl metalates which results in a deprotonation at the sugar skeleton rather than in metal carbonyl transfer.[20c] A more promising strategy relies on a stoichiometric olefin metathesis reaction[18b,26] of an electron-rich *exo*-methylene sugar and an electron-deficient diphenylcarbene pentacarbonyl complex. This approach provided a straightforward access to chromium furanosylidenes[27] but attempts to extend it to their pyranosylidene homologues were complicated by elimination processes occurring under the reaction and work-up conditions. Thus, we focused on glycals as starting materials which are readily available and allow an organometallic functionalization at the anomeric center. We now report on their modification to glycosylidene complexes bearing a 2-deoxy substitution pattern which is encountered in various biologically active compounds.[28]

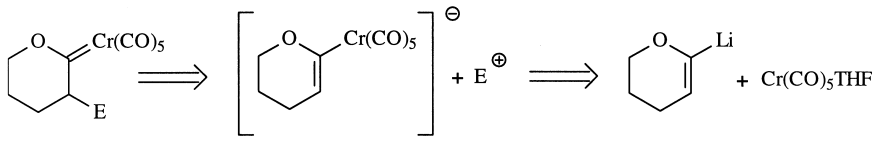
Results and Discussion

Protection and metalation of D-glucal

Glycals can be metalated in 1-position;[29] however, a great excess of the strong base *tert*-butyllithium is required for this process which complicates further transformations and purification. Thus, it is advantageous to purify the resulting lithioglycal by transmetalation to the tri-*n*-butyl tin



Scheme 2. Competing addition of lithioglucals to chromium carbonyl complexes.



Scheme 3. Retrosynthetic concept for 2-deoxy-glycosylidene complexes.

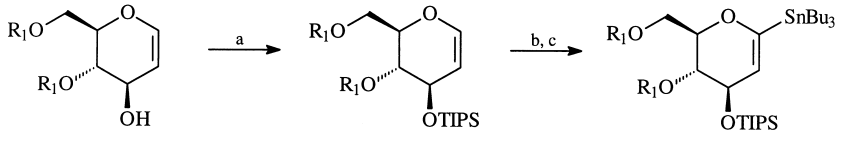
derivatives (which can be stored for weeks without decomposition) and regenerate the lithioglycal prior to use by a retransmetalation using *n*-butyl lithium.[30] The reaction of 1-lithioglucal **1** with group six metal carbonyl complexes is controlled by the substitution pattern of the carbonyl complex (Scheme 2).[31] Their addition to hexacarbonyl chromium occurs at the carbonyl carbon atom as expected for the *Fischer* metal carbene synthesis to give—after methylation of the acyl chromate intermediate—the α,β-unsaturated carbene complex **7**. However, if a single carbonyl ligand is replaced by a ligand combining good donor and leaving group properties such as triphenylphosphine or tetrahydrofuran, the lithioglucal rather adds at the metal to generate an enolate-type pentacarbonyl chromium intermediate **5**. Above 0°C a *Ferrier*-type rearrangement occurs, and elimination of trialkylsilyloxide affords the α,β-unsaturated glucosylidene complex **8**. We anticipated that the chromium enolate intermediate **5** may be applied to the addition of electrophiles. This approach is expected to offer a straightforward access to 2-deoxy-glucosylidene complexes starting from readily available $(CO)_5$CrTHF and lithioglucals (Scheme 3).

D-Glucal **9a** was metalated after stepwise protection by 2,2′-dimethoxypropane (to give **9b**[32]) and triisopropylsilyl triflate (to give **10a**,**b**) using the *tert*-butyllithium/tri-*n*-butyl(chloro)stannane protocol (Scheme 4); under *Friesen*'s conditions the stannylated glucal **2** was obtained in good yields provided that the deprotonation was limited to 30 min. Longer reaction times caused side reactions, and the yields dropped dramatically. ^{1}H NMR studies indicated that the conformation of the stannylated glucals **1**[29b] and **2** is controlled by the protecting groups. Whereas the *per*-TIPS-protected glucal **1** reveals medium and small coupling constants $J_{2,3}$ (ca. 5 Hz) and $J_{3,4}$ (ca. 2 Hz) suggesting a preferred $^5H_4$ conformation, the 4,6-diprotection by the isopropylidene group in analogue **2** shows an opposite trend ($J_{2,3}$=2.0 Hz, $J_{3,4}$=7.4 Hz) indicative for a $^4H_5$ conformation. Both stannyl glucals were readily transmetalated upon reaction with *n*-butyl lithium.

2-Deoxypyranosylidene complexes

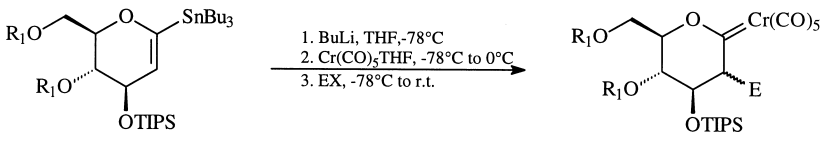
Following previous reports[33] on the addition of nucleophilic organometallics to the solvent-stabilized pentacarbonyl-chromium fragment the reaction of the lithioglucals with $(CO)_5$CrTHF was expected to generate glucalyl pentacarbonylchromium intermediates. These species may be regarded as chromium enolates which are susceptible to subsequent addition of electrophiles. Accordingly, the low-temperature addition of lithioglucals generated from stannanes **1** and **2** to $(CO)_5$THF[34] followed by protonation with hydrogen chloride in ether afforded 2-deoxypyranosylidene complexes **11** and **12** in good yields after chromatography on silica gel (Scheme 5). To elucidate the stereoselectivity of the protonation we applied deuterated trifluoroacetic acid as electrophile. A >90% incorporation of deuterium along with a >95:5 preference in favour of the *manno* configuration was observed for the tris-TIPS-protected 2-deuteroglycosylidene complex **13**. Supposed that there is no conformational change along the formation of the intermediate **5** from the stannane **1**, the stereochemical outcome may be rationalized in terms of a *si*-side attack to the chromium enolate in its $^5H_4$ conformation.We are unable at the moment to decide whether the deuteration occurs metal-mediated or directly at the β-carbon atom of the enolate.[35] Upon chromatography on silica gel the degree of deuterium incorporation dropped to 75% while the d.e. value of 90% remained unchanged. The diastereoselectivity of the deuteration strongly depends on the substitution pattern provided by the protecting groups. Substitution of the tris-TIPS-protection for the less bulky isopropylidene mono-TIPS-pattern results in a dramatic decrease in selectivity, and an only slight 58:42 preference in favour of the *gluco*-diastereomer **14e** was observed. Moreover, the formation of a 10% amount of 2,2-dideuterated material suggests that the addition of the electrophile is subject to an equilibrium process under the deuteration conditions.

The addition of electrophiles to the chromium enolates can be extended to *C*-alkylation. Allylation of intermediates **5** and **6** with allyl iodide resulted in the diastereoselective formation of C-2-deoxypyranosylidene complexes **15** and **16** in good yields. In the TIPS-series the allylation afforded complex **15** as a 94:6 mixture of diastereomers which could not be separated by chromatography. A small coupling constant $^3J_{2,3}$ (1.9 Hz) was observed for the major isomer suggesting a *manno*-configuration at C-2. The isopropylidene complex **16** was obtained as a single diastereomer

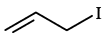
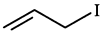


R1 = H, **9a**
R1, R1 = CMe2, **9b**
R1 = TIPS, **10a**
R1, R1 = CMe2, **10b**
R1 = TIPS, **1**
R1, R1 = CMe2, **2**

Scheme 4. Synthesis of protected stannanes **1** and **2**. Reaction conditions: (a) TIPSOTf, 2,6-lutidine, CH_2Cl_2, 0°C to RT, 2 h; (b) 4 eq. *t*-BuLi, THF, −78°C to 0°C, 30 min; (c) 3.5 eq. Bu_3SnCl, −78°C.



1, 2 **11-16**

	EX	2-*R*/*S*	Yield [%]	
1: R_1 = TIPS		6 : 94	74	**(15)**
	CF_3COOD	< 5 : 95	64	**(13a/e)**
	HCl	---	70	**(11)**
2: R_1, R_1 = CMe_2		only *S* detectable	59	**(16)**
	CF_3COOD	58 : 42	50	**(14a/e)**
	HCl	---	71	**(12)**

Scheme 5. Synthesis of 2-deoxy-glycosylidene complexes **11**–**16,** axial (**a**) and equatorial (**e**) refers to the position of deuterium.

as indicated within the limits of ^{1}H NMR spectroscopy. The configuration of the newly formed chiral center was characterized as *S*-C-2 reflecting again the *manno*-configuration according to the small coupling constant $^3J_{2,3}$ (1.4 Hz). These two examples demonstrate that the allylation of the chromium enolate intermediates occurs predominantly from the *si*-side independent of the protecting group periphery.[36]

Conclusion

The tandem nucleophilic alkylation/electrophilic addition methodology provides a novel functionalization of solvent-stabilized $Cr(CO)_5$ fragments to oxacycloalkylidene complexes. This strategy has been applied in the synthesis of chromium 2-deoxypyranosylidenes. The easy access to stannyl enol ethers and their straightforward in situ C-2 functionalization render this approach a valuable alternative to well established synthetic protocols in metal carbene chemistry. The metal carbene moiety of the pyranosylidene complexes enhances the α-CH acidity and allows for metal-centered cycloaddition reactions, providing additional opportunities for the elaboration of more complex carbohydrate skeletons.

Experimental

All transformations were performed under argon using degassed solvents dried by standard procedures. All reagents were used as supplied commercially; chromatography was carried out with degassed solvents on silica gel (Merck 60 (0.063–0.200)). All ^{1}H and ^{13}C NMR spectra were recorded on either the Bruker DRX-500 or AM-400 spectrometer. Chemical shifts refer to those of residual solvent signals based on δ_{TMS}=0.00 ppm. Chemical ionization mass spectra were recorded on a Kratos MS 50 spectrometer; FAB mass spectra were recorded on a Kratos Concept 1H spectrometer. Elemental analyses were obtained from a Heraeus CHN-O-Rapid.

1,5-Anhydro-4,6-*O*-isopropylidene-3-*O*-triisopropylsilyl-2-deoxy-D-*arabino*-hex-1-enitol (10). 3.26 ml (30.8 mmol) 2,6-Lutidine and 5.6 ml (21 mmol) TIPSOTf were added sequentially to a solution of 2.6 g (14 mmol) **3** in 15 ml CH_2Cl_2 at 0°C. The reaction mixture was allowed to warm to room temperature and stirred for 3 h. After dilution with 100 ml of water the organic layer was separated and the aqueous layer was extracted three times with 50 ml portions of CH_2Cl_2. The combined organic fractions were washed with brine, dried over $MgSO_4$ and evaporated to dryness. Column chromatography of the residue (SiO_2, CH_2Cl_2) afforded 2.86 g (8.35 mmol, 60%) of a colourless oil. R_f (CH_2Cl_2): 0.85; ^{1}H NMR (400 MHz, $CDCl_3$): δ=6.21 (dd, ^3J=6.2 Hz, ^4J=1.6 Hz, 1H, H-1), 4.63 (^3J=6.2 Hz, ^3J=1.9 Hz, 1H, H-2), 4.38 (ddd, ^3J=7.2 Hz, ^3J=1.9 Hz, ^2J=1.6 Hz, 1H, H-3), 3.88 (dd, ^2J=10.7 Hz, ^3J=5.6 Hz, 1H, H-6$_e$), 3.78 (dd, ^3J=10.4 Hz, ^3J=7.2 Hz, 1H, H-4), 3.76 (dd, ^2J=10.7 Hz, ^3J=10.2 Hz, 1H, H-6$_a$), 3.66 (ddd, ^3J=10.4 Hz, ^3J=10.2 Hz, ^3J=5.6 Hz, 1H, H-5), 1.46 (s, 3H, –CH_3), 1.35 (s, 3H, –CH_3), 1.07–0.99 (m, 21H, –Si–[CH(CH_3)$_2$]$_3$); DEPT 135 (62.8 MHz, $CDCl_3$): δ=143.3 (C-1), 105.9 (C-2), 73.5 (C-3), 69.9 (C-4), 67.9 (C-5), 61.9 (C-6), 29.1 (–CH_3), 19.0 (–CH_3), 18.1–17.8 (–Si–[CH(CH_3)$_2$]$_3$), 12.4 (–Si– [CH(CH$_3$)$_2$]$_3$); EI-MS (70 eV): *m*/*z* (%)=327.2 [M$^+$−CH$_3$], 299.2 [M$^+$−C$_3$H$_7$], 241.1 [M$^+$−C$_3$H$_7$−C$_3$H$_6$O]; HR-MS Calcd for $C_{15}H_{27}O_4Si$ [M$^+$−CH$_3$]: 327.1992; Found: 327.1984.

1,5-Anhydro-4,6-*O*-isopropylidene-3-*O*-triisopropylsilyl-2-deoxy-1-(tri-*n*-butyl)stannyl-D-*arabino*-hex-1-enitol (2). 21 ml (33.4 mmol) *t*-BuLi (15% in hexane) were added dropwise to a solution of 2.86 g (8.35 mmol) **10** in 30 ml THF at −78°C. The dry ice bath was removed and stirring was continued at 0°C for 30 min. After recooling to −78°C, 6.8 ml (25.1 mmol) tri-*n*-butylstannyl chloride was added dropwise and stirring was continued at this temperature

for 30 min. The reaction mixture was diluted with 50 ml water, the organic layer was separated and the aqueous phase was extracted three times with 60 ml portions of Et_2O. The combined organic fractions were washed twice with 20 ml water, once with brine, dried over $MgSO_4$ and evaporated to dryness. Column chromatography of the residue (SiO_2, CH_2Cl_2/petroleum ether: 3:2) afforded 4.49 g (7.1 mmol, 85%) of a colourless oil. R_f (CH_2Cl_2/petroleum ether: 3:2): 0.89; ^{1}H NMR (400 MHz, $CDCl_3$): δ=4.66 (d, ^3J=2.0 Hz, 1H, H-2), 4.35 (dd, ^3J=7.4 Hz, ^3J=2.0 Hz, 1H, H-3), 3.86 (dd, ^2J=10.8 Hz, ^3J=5.7 Hz, 1H, H-6$_e$), 3.77 (dd, ^3J=10.4 Hz, ^3J=7.4 Hz, 1H, H-4), 3.74 (dd, ^2J=10.8 Hz, ^3J=10.4 Hz, 1H, H-6$_a$), 3.58 (ddd, ^3J=10.4 Hz, ^3J=10.4 Hz, ^3J=5.7 Hz, 1H, H-5), 1.48 (s, 3 H, –CH_3), 1.37 (s, 3 H, –CH_3), 1.55–0.84 (m, 48H, –Si[CH(CH_3)$_2$]$_3$, –Sn(C$_4H_9$)$_3$); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ=162.7 (C-1), 116.4 (C-2), 99.3 (*C*(CH$_3$)$_2$), 73.6 (C-3), 69.9 (C-4), 68.6 (C-5), 62.1 (C-6), 29.1 (C(*C*H$_3$)$_2$), 29.0 (–Sn(*C*$_4$H$_9$)$_3$), 27.2 (–Sn(*C*$_4$H$_9$)$_3$), 19.0 (C(*C*H$_3$)$_2$), 18.0 (–Si[CH(*C*H$_3$)$_2$]$_3$), 13.7 (–Sn(*C*$_4$H$_9$)$_3$), 12.3 (–Si[*C*H(CH$_3$)$_2$]$_3$), 9.7 (–Sn(*C*$_4$H$_9$)$_3$); EI-MS (70 eV): *m/z* (%)=631.2 [M$^+$], 589.2 [M$^+$–C$_3$H$_6$], 575.2 [M$^+$–C$_3$H$_6$O], 401.1 [M$^+$–C$_3$H$_6$O–C$_9$H$_{22}$SiO]; Anal. Calcd for $C_{30}H_{60}O_4SiSn$: C, 56.93; H, 9.56; Found: C, 57.12; H, 9.66.

General procedure for the synthesis of complexes 11 and 12

1.2 equiv. *n*-BuLi (2.5 M in hexane) was added dropwise to a solution of 1 equiv. stannylglucal in 10 ml of dry THF at −78°C. After stirring for 1 h, a solution of 1.5 equiv. Pentacarbonyl(η^2-*cis*-cyclooctene)chromium(0) in 10 ml of dry THF precooled to −78°C was added via a transfer needle. The reaction mixture was warmed to 0°C and stirred at this temperature for 20 min. After recooling to −78°C, a solution of hydrogen chloride (1.2 equiv.) in diethyl ether (1 M) was added dropwise. The solvent was removed in vacuo, and the crude product was purified by column chromatography at −10°C using petroleum ether/dichloromethane mixtures as eluent to give the carbene complexes as analytically pure samples.

Pentacarbonyl[3,4,6-tri-*O*-triisopropylsilyl-2-deoxy-D-*arabino*-hexopyranosylidene]chromium(0) (11). 11 was prepared from 0.85 g (0.94 mmol) (**1**), 0.45 ml (1.13 mmol) *n*-BuLi, 0.42 g (1.38 mmol) $(CO)_5Cr(C_8H_{14})$ and 1.13 ml (1.13 mmol) of the HCl solution to give a 70% yield (0.53 g, 0.66 mmol) of a yellow oil, R_f (petroleum ether/CH_2Cl_2, 20:1): 0.87; ^{1}H NMR (500 MHz, C_6D_6): δ=5.08 (ddd, ^3J=6.5 Hz, ^3J=6.1 Hz, ^3J=1.0 Hz, 1H, H-5), 4.51 (d, ^2J=19.5 Hz, 1H, H-2$_e$), 4.41 (dd, ^2J=10.8 Hz, ^3J=6.5 Hz, 1H, H-6), 4.33 (dd, ^3J=4.4 Hz, ^3J=1.0 Hz, 1H, H-4), 4.25 (dd, ^2J=10.8 Hz, ^3J=6.1 Hz, 1H, H-6′), 3.83 (s, br, 1H, H-3), 3.72 (dd, ^2J=19.5 Hz, ^3J=3.7 Hz, 1H, H-2$_a$), 1.20–0.90 (m, 63 H, –Si[CH(CH_3)$_2$]$_3$); ^{13}C NMR (125.6MHz, C_6D_6): δ=351.5 (C-1), 224.1 (CO_{trans}), 217.3 (CO_{cis}), 94.6 (C-5), 67.2 (C-4), 65.3 (C-3), 64.6 (C-6), 58.1 (C-2), 18.1, 18.0 (–Si[CH(*C*H$_3$)$_2$]$_3$), 12.5, 12.3, 12.2 (–Si[*C*H(CH$_3$)$_2$]$_3$); DEPT 135 (62.8 MHz, C_6D_6): *sec.*- C: δ=64.6 (C-6), 58.1 (C-2); FAB-MS (mNBA): *m/z* (%)=806.4 [M$^+$], 752.4 [MH$_2^+$–2CO], 694.3 [M$^+$–4CO], 666.3 [M$^+$–5CO], 623.2 [M$^+$–5CO–C$_3$H$_7$], 581.1 [MH$^+$–5CO–2C$_3$H$_7$], 537.1 [M$^+$–5CO–3C$_3$H$_7$], 485.2 [M$^+$–Cr(CO)$_5$–3C$_3$H$_7$]; Anal. Calcd for $C_{38}H_{70}O_9Si_3Cr$: C, 56.54, H, 8.74; Found: C, 56.38, H, 8.87.

Pentacarbonyl[4,6-*O*-isopropylidene-3-*O*-triisopropylsilyl-2-deoxy-D-*arabino*-hexopyranosylidene]chromium(0) (12). 12 was prepared from 0.72 g (1.14 mmol) (**2**), 0.55 ml (1.37 mmol) *n*-BuLi, 0.60 g (1.98 mmol) $(CO)_5Cr(C_8H_{14})$ and 1.37 ml (1.37 mmol) of the HCl solution to give a 71% yield (0.43 g, 0.80 mmol) of an orange oil which solidified over night at −6°C. R_f (petroleum ether/CH_2Cl_2, 2:3): 0.87; ^{1}H NMR (400 MHz, $CDCl_3$): δ=4.39 (dd, ^2J=17.8 Hz, ^3J=2.2 Hz, 1H, H-2$_e$), 4.37 (dd, ^2J=11.0 Hz, ^3J=5.6 Hz, 1H, H-6$_e$), 4.11 (dd, ^2J=11.0 Hz, ^3J=10.5 Hz, 1H, H-6$_a$), 3.96 (ddd, ^3J=8.2 Hz, ^3J=6.8 Hz, J=2.1 Hz, 1 H, H-3), 3.95 (ddd, ^3J=10.5 Hz, ^3J=10.1 Hz, ^3J=5.6 Hz, 1H, H-5), 3.55 (dd, ^3J=10.1 Hz, ^3J=6.8 Hz, 1H, H-4), 3.28 (dd, ^2J=17.8 Hz, ^3J=8.2 Hz, 1H, H-2$_a$), 1.52 (s, 3H, –CH_3), 1.40 (s, 3 H, –CH_3), 1.12–0.91 (m, 21H, –Si[CH(CH_3)$_2$]$_3$); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ=355.7 (C-1), 224.0 (CO_{trans}), 216.0 (CO_{cis}), 100.2 (–*C*(CH$_3$)$_2$), 76.0 (C-3), 75.0 (C-4), 68.7 (C-5), 64.4 (C-6), 61.4 (C-2), 28.7 (–C(*C*H$_3$)$_2$), 18.8 (–C(*C*H$_3$)$_2$), 17.8, 17.7 (–Si[CH(*C*H$_3$)$_2$]$_3$), 12.0 (–Si[*C*H(CH$_3$)$_2$]$_3$); EI-MS (70 eV): *m/z* (%)=534.2 [M$^+$], 506.2 [M$^+$–CO], 478.1 [M$^+$–2CO], 450.0 [M$^+$–3CO], 422 [M$^+$–4CO], 394 [M$^+$–5CO], 299.2 [M$^+$–Cr(CO)$_5$–C$_3$H$_7$], 241.1 [M$^+$–Cr(CO)$_5$–C$_3$H$_7$–C$_3$H$_6$O]; HR-MS Calcd for $C_{23}H_{34}O_9SiCr$ [M$^+$]: 534.1424, Found: 534.1387; Anal. Calcd for $C_{23}H_{34}O_9SiCr$: C, 51.67, H, 6.41; Found: C, 51.69, H, 6.48.

General procedure for the synthesis of complexes 13 and 14

1.2 equiv. *n*-BuLi (2.5 M in hexane) was added dropwise to a solution of 1 equiv. stannylglucal in 10 ml of dry THF at −78°C. After stirring for 1 h, a solution of 1.5 equiv. Pentacarbonyl(η^2-*cis*-cyclooctene)chromium(0) in 10 ml of dry THF precooled to −78°C was added via a transfer needle. The reaction mixture was warmed to 0°C and stirred at this temperature for 20 min. After recooling to −78°C, 1.2 equiv. of a CF_3COOD solution in diethyl ether (1 M) was added in one portion. The solvent was removed in vacuo, and the crude product was purified by column chromatography at −20°C using petroleum ether/dichloromethane mixtures as eluent to give the 2-deutero deoxypyranosylidene complexes.

Pentacarbonyl[2-deutero-3,4,6-tri-*O*-triisopropylsilyl-2-deoxy-mannosylidene]chromium(0) (13a). 1.07 g (1.18 mmol) of **1** was deuterated according to the general procedure, using 0.57 ml (1.42 mmol) *n*-BuLi, 0.50 g (1.66 mmol) $(CO)_5Cr(C_8H_{14})$ and 1.42 ml (1.42 mmol) of the D^1-TFA-solution. After chromatographic purification (SiO_2, petroleum ether, −20°C) 0.61 g (0.76 mmol, 64%) of a yellow oil was obtained. Integration of the ^{1}H NMR signals at δ=4.51, 4.48, 3.72 and 3.68 ppm were used to determine the degree of deuterium incorporation and the diastereomeric ratio. ^{1}H NMR (500 MHz, C_6D_6): δ=4.51 (d, ^2J=19.7 Hz, 0.35 H, H-2$_e$, **11**), 4.48 (s, 0.75 H, H-2$_e$, **13a**), 3.72 (dd, ^2J=19.7 Hz, ^3J=4.0 Hz, 0.25H, H-2$_a$, **11**), 3.68 (d, ^3J=4.0 Hz, 0.025H, H-2$_a$, **13e**); ^{13}C NMR (125.6 MHz, C_6D_6): δ=58.1 (s, C-2, **11**), 57.8 (t, $^1J_{C,D}$=19 Hz, C-2, **13a**).

Deuteration of chromium enolate intermediate 2 with D^1-TFA

0.64 g (1.02 mmol) of **2** was deuterated according to the general procedure, using 0.70 ml (1.42 mmol) *n*-BuLi (1.6 M), 0.34 g (1.13 mmol) $(CO)_5Cr(C_8H_{14})$ and 1.13 ml (1.13 mmol) of the D^1-TFA-solution. After chromatographic work-up (SiO_2, petroleum ether, −20°C) 0.27 g (0.50 mmol, 50%) of an orange oil was obtained. Integration of the ^1H NMR signals at δ=4.39, 3.55, 3.28 and 3.21 ppm were used to determine the degree of deuterium incorporation and the diastereomeric ratio. ^1H NMR (500 MHz, $CDCl_3$): δ=4.39 (dd, ^2J=17.7 Hz, ^3J=2.2 Hz, 0.23H, H-2_e, **12**), 3.55 (dd, ^3J=10.1 Hz, ^3J=6.8 Hz, 1.00H (reference), H-4, **12**), 3.28 (dd, ^2J=17.8 Hz, ^3J=8.2 Hz, 0.26H, H-2_e, **12**), 3.21 (d, ^3J=7.9 Hz, 0.35H, H-2_a, **14e**). The signal of H-2_e of compound **14a** was covered by the signal of H-6_e. By subtraction, its integral was determined to correspond to 0.30H. The degree of 2,2-dideuteration was found to be 10% by comparison of the reference integral with the combined integrals of the signals at 3.28, 3.21 ppm and H-2_a of compound **14a**.

Pentacarbonyl[2-allyl-3,4,6-tri-*O*-triisopropylsilyl-2-deoxy-mannosylidene]chromium(0) (15). 0.48 ml (1.19 mmol) *n*-BuLi (2.5 M in hexane) was added dropwise to a solution of 898 mg (0.99 mmol) of **1** in 10 ml of dry THF at −78°C. After stirring for 1 h, a solution of 450 mg (1.49 mmol) pentacarbonyl(η^2-*cis*-cyclooctene)chromium(0) in 10 ml of dry THF precooled to −78°C was added via a transfer needle. The reaction mixture was warmed to 0°C and stirred at this temperature for 20 min. After recooling to −78°C, 200 mg (1.19 mmol) allyl iodide were added dropwise. The reaction mixture was allowed to reach room temperature slowly overnight. The solvent was removed in vacuo and the crude product was purified by column chromatography at −6°C (SiO_2, petroleum ether) to afford 619 mg (0.73 mmol, 74%) of an orange oil. It solidified overnight at −6°C, and ^1H NMR analysis indicated a 96:4 mixture of diastereomers in favour of the '*manno*'-isomer. A separation of the diastereomers by chromatography failed. R_f (petroleum ether): 0.78; ^1H NMR (500 MHz, $CDCl_3$): δ=5.97 (dddd, 1H, ^3J=17.1 Hz, ^3J=10.0 Hz, ^3J=7.8 Hz, ^3J=6.4 Hz, H-2′), 5.24 (ddd, 1H, ^3J=17.1 Hz, ^4J=3.1 Hz, ^4J=1.6 Hz, H-3′$_1$), 5.17 (ddd, 1H, ^3J=10.0 Hz, ^4J=1.6 Hz, ^4J=1.6 Hz, H-3′$_2$), 4.76 (ddd, 1H, ^3J=7.1 Hz, ^3J=4.7 Hz, ^3J=1.6 Hz, H-5), 4.15 (dd, 1H, ^2J=11.1 Hz, ^3J=7.1 Hz, H-6_1), 4.13 (dd, 1H, ^3J=3.4 Hz, ^3J=1.6 Hz, H-4), 4.09 (ddd, 1H, ^3J=11.5 Hz, ^3J=1.8 Hz, ^3J=1.6 Hz, H-2), 4.05 (dd, 1H, ^3J=11.1 Hz, ^3J=4.7 Hz, H-6_2), 3.91 (dd, 1H, ^3J=3.4 Hz, ^3J=1.8 Hz, H-3), 2.90 (ddddd, 1H, ^2J=14.1 Hz, ^3J=6.36 Hz, ^4J=3.1 Hz, ^3J=1.6 Hz, ^4J=1.6 Hz, H-1′$_1$), 2.50 (ddddd, 1H, ^2J=14.1 Hz, ^3J=11.5 Hz, ^3J=7.8 Hz, ^4J=1.6 Hz, ^4J=1.6 Hz, H-1′$_2$), 1.2–0.8 (m, 63H, TIPS); ^{13}C NMR (125 MHz, $CDCl_3$): δ=355.8 (C-1), 223.9 (CO_{trans}), 216.6 (CO_{cis}), 135.6 (C-2′), 118.5 (C-3′), 94.1 (C-5), 68.4 (C-4), 67.3 (C-2), 65.8 (C-3), 65.3 (C-6), 33.2 (C-2′), 18.2–17.5 (Si[CH(*C*H$_3$)$_2$), 12.5–11.8 (Si[*C*H(CH$_3$)$_2$); FAB-MS (mNBA): *m/z* (%)=846.3 (M^+), 803.3 ($M^+-C_3H_7$), 706.4 (M^+−5CO); Anal. Calcd for $C_{41}H_{75}O_9Si_3Cr$: C, 58.05; H, 8.91; Found: C, 58.05; H, 8.83.

Pentacarbonyl[2-allyl-4,6-*O*-isopropylidene-3-*O*-triisopropylsilyl-2-deoxy-mannosylidene]chromium(0) (16). 0.60 ml (1.50 mmol) *n*-BuLi (2.5 M in hexane) was added dropwise to a solution of 790 mg (1.25 mmol) of **2** in 20 ml of dry THF at −78°C. After stirring for 1 h, a solution of 492 mg (1.63 mmol) pentacarbonyl(η^2-cis-cyclooctene)chromium(0) in 10 ml of dry THF precooled to −78°C was added via a transfer needle. The reaction mixture was warmed to 0°C and stirred at this temperature for 20 min. After recooling to −78°C, 252 mg (1.50 mmol) allyl iodide was added dropwise. The reaction mixture was allowed to reach room temperature slowly overnight. The solvent was removed in vacuo, and the crude product was purified by column chromatography at −6°C (SiO_2, CH_2Cl_2/petroleum ether, 2:3) to afford 421 mg (0.73 mmol, 59%) of a red-orange oil which solidified overnight at −6°C. R_f (CH_2Cl_2/petroleum ether, 2:3): 0.60; ^1H NMR (500 MHz, $CDCl_3$): δ=5.76 (dddd, 1H, ^3J=16.8 Hz, ^3J=10.2 Hz, ^3J=7.8 Hz, ^3J=6.8 Hz, H-2′), 5.22 (ddd, 1H, ^3J=16.8 Hz, ^4J=∼2 Hz, ^4J=∼1 Hz, H-3′$_1$), 5.21 (ddd, 1H, ^3J=10.2 Hz, ^4J=∼1 Hz, ^4J=∼1 Hz, H-3′$_2$), 4.41 (ddd, 1H, ^3J=9.4 Hz, ^3J=4.0 Hz, ^3J=1.4 Hz, H-2), 4.35 (m, 1H, H-6_e), 3.95–4.05 (m, 2 H, H-5, H-6_a), 3.84 (dd, 1H, ^3J=7.4 Hz, ^3J=1.4 Hz, H-3), 3.51 (dd, 1H, ^3J=9.8 Hz, ^3J=7.4 Hz, H-4), 2.54 (ddddd, 1H, ^2J=14.1 Hz, ^3J=6.8 Hz, ^3J=4.0 Hz, ^4J=∼2 Hz, ^4J=∼1 Hz, H-1′$_1$), 2.26 (ddddd, 1H, ^2J=14.1 Hz, ^3J=9.4 Hz, ^3J=7.8 Hz, ^4J=∼1 Hz, ^4J=∼1 Hz, H-1′$_2$), 1.49 (s, 3 H, CH_3), 1.39 (s, 3H, CH_3), 1.1–1.0 (m, 21H, TIPS); ^{13}C NMR (125 MHz, $CDCl_3$): δ=359.7 (C-1), 223.8 (CO_{trans}), 216.0 (CO_{cis}), 140.0 (C-2′), 120.2 (C-3′), 100.1 (*C*(CH$_3$)$_2$), 75.8 (C-4), 75.0 (C-2, C-5), 71.9 (C-3), 61.9 (C-6), 35.7 (C-1′), 29.1 (C(*C*H$_3$)$_2$), 19.2 (C(*C*H$_3$)$_2$), 18.8–17.9 (Si[CH(*C*H$_3$)$_2$]$_3$), 12.3–12.0 (Si[*C*H(CH$_3$)$_2$]$_3$); EI-MS (70 eV): *m/z* (%)=574.2 [M^+], 518.2 [M^+−2CO], 490.2 [M^+−3CO], 462.2 [M^+−4CO], 434.2 [M^+−5CO], 339.2 [$M^+-Cr(CO)_5-C_3H_7$]; HR-MS Calcd for $C_{21}H_{38}O_4SiCr$ [M^+−5CO]: 434.1944, Found: 434.1954; Anal. Calcd for $C_{26}H_{38}O_9SiCr$: C, 54,34; H, 6.67; Found: C, 54.33; H, 6.77.

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