Metal modified carbohydrates: syntheses of furanosylidene complexes and their aza analogues[1]

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Alkene metathesis and a sugar lactam electrophile/metalate nucleophile combination have been exploited in the synthesis of furanosylidene complexes and their aza analogues.

Fischer-type carbene complexes $(CO)_5M{=}C(XR')R$ (M = Cr, W; X = O, NR″) have been developed as useful reagents in stereoselective organic synthesis. Their synthetic potential covers cycloaddition reactions,[2] including benzannulation,[2a] cyclopropanation,[2b,c] and—based on the photolytic generation of ketene equivalents[2d]—addition of imines or oxygen nucleophiles, affording β-lactams or α-amino acids, as well as aldol- and Michael-type addition reactions.[2e,f]

Exploiting the synthetic potential of organometallics in the developing field of C-glycoside chemistry[3] has generally been limited to stannylated and lithiated compounds. Although some encouraging examples of transition metal mediated C-glycosidations have been reported,[4b,c] well-characterized glycosyl complexes are to date only known for manganese,[4c,d] cobalt[4e] and iron.[4f] In this type of compound the anomeric centre behaves as a nucleophile; in contrast, we aimed at the incorporation of an electrophilic metal-carbene functionality into the carbohydrate skeleton. Recently, we reported on the synthesis of the first C-1 carbene complex-functionalized sugars of chromium, iron, molybdenum and tungsten[5] exploiting a strategy that can be applied to acyclic carbohydrates. We now describe two independent routes to cyclic metal glycosylidenes bearing a transition metal-stabilized carbene functionality at the former anomeric carbon atom.

Our first approach is based on the Hegedus route[6] which allows modification of amides and unsubstituted lactams into metal aminocarbenes. We have extended this strategy to a sugar lactam electrophile/metalate nucleophile combination: the reaction of *N*-methyl-2,3-*O*-isopropylidene-D-erythronolactam **1**[7] with $K_2M(CO)_5$ (M = Cr, W) affords the pentacarbonyl[1,4-dideoxy-2,3-*O*-isopropylidene-1,4-methylimino-D-erythrofuranosylidene] complexes **2** and **3** in good yields (Scheme 1).

As neither the classical Fischer route[8] nor the dianion route turned out to be suited for the preparation of oxacycloalkylidene complexes, we focussed on an alkene metathesis approach.[9] The reaction of 2,5-anhydro-1-deoxy-3,4 : 6,7-di-*O*-isopropylidene-D-*manno*-hept-1-enitol **4**[10] with pentacarbonyl(diphenylcarbene) complexes of chromium and tungsten (**5** and **6**)[11] gave the pentacarbonyl(2,3 : 5,6-di-*O*-isopropylidene-D-mannofuranosylidene) complexes **7** and **8** in yields which strongly depend on the metal used (Scheme 2). Glycosylidene complexes **7** and **8** may be regarded as metal-stabilized analogues of the furanoic 'glycosylidene–carbene' intermediates reported by Vasella and co-workers.[12] The pronounced electrophilicity of the metal-carbene moiety favours the addition of nucleophiles. Thus, aminolysis of **7** with ammonia or methylamine generates the open-chain amino(glycosyl)carbene complexes **9a**,**b** offering an unprotected hydroxy group for further functionalization. They readily undergo an intramolecular Mitsunobu reaction[13] and thus provide an access to N-protected and N-deprotected azatalofuranosylidene complexes **10a**,**b** in moderate to good yields. According to X-ray structure analyses† established for **7** and **10b** (Figs. 1 and 2) both complexes adopt a similar envelope-like conformation in the solid state with C(3) being out of plane. Obviously, the epimerization at C(4), which arises from the ring opening/cyclization sequence, has no significant influence on the conformation of the glycosylidene ring. The asymmetric unit of **7** contains two independent molecules which slightly differ in their C(1)–O(1) and C(1)–C(2) bond lengths.

The novel transition metal-stabilized glycosylidene complexes are stable at room temperature and can be handled briefly in air. Their spectroscopic data‡ show the typical characteristics of electrophilic Fischer-type carbene complexes, and as such they are promising reagents for the elaboration of more complex C-glycosidic structures.

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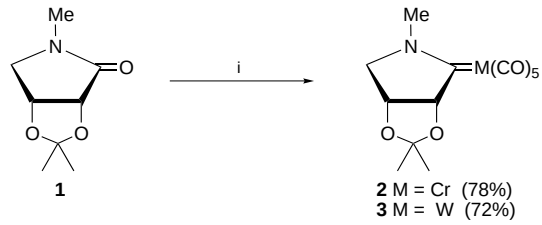
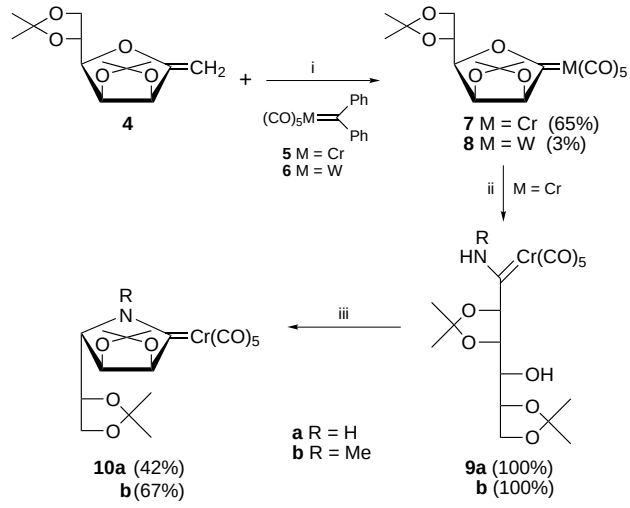


Scheme 1 *Reagents and conditions*: i, $K_2M(CO)_5$, THF, −78 °C, Me_3SiCl



Scheme 2 *Reagents and conditions*: i, *n*-heptane, 20 °C; ii, CH_2Cl_2, −78 °C, RNH_2; iii, THF, 20 °C, PPh_3, diethyl azodicarboxylate

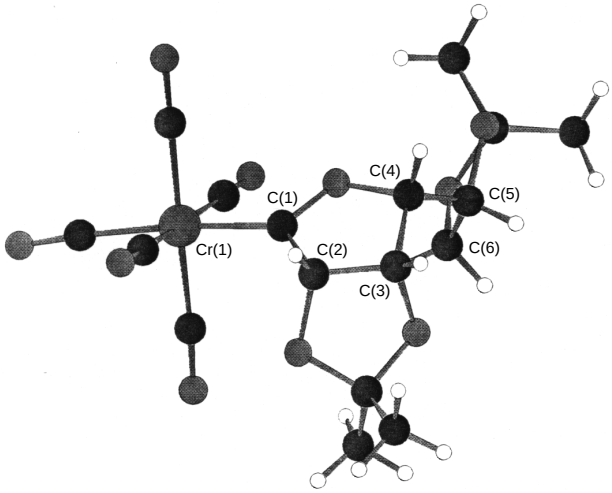


Fig. 1 Molecular structure of furanosylidene complex **7** (one of two independent molecules). Selected distances (Å) and bond angles (°) (the second independent molecule in brackets): Cr(1)–C(1) 1.979(6) [1.980(6)], C(1)–O(1) 1.302(7) [1.332(7)], C(1)–C(2) 1.560(7) [1.535(8)], O(1)–C(4) 1.483(7) [1.482(7)], Cr(1)–C(1)–O(1) 125.0(4) [123.3(4)], Cr(1)–C(1)–C(2) 128.6(4) [121.8(4)], C(2)–C(1)–O(1) 106.4(5) [106.9(5)].

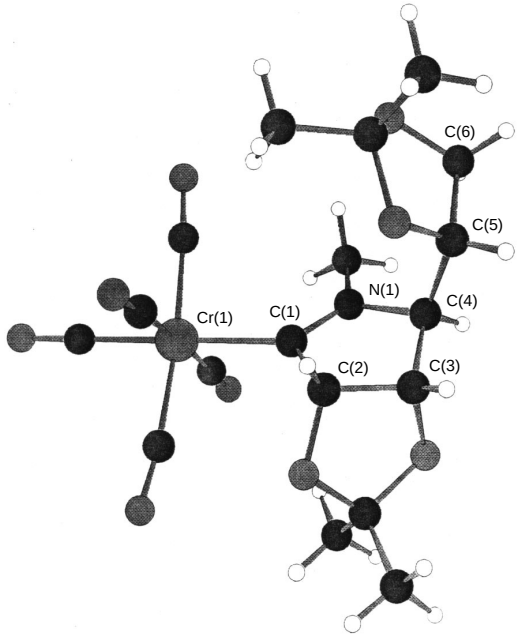


Fig. 2 Molecular structure of 1,4-iminofuranosylidene complex **10b**. Selected distances (Å) and bond angles (°): Cr(1)–C(1) 2.097(3), C(1)–N(1) 1.313(4), C(1)–C(2) 1.524(4), N(1)–C(4) 1.495(3), Cr(1)–C(1)–N(1) 130.8(2), Cr(1)–C(1)–C(2) 123.7(2), C(2)–C(1)–N(1) 105.4(2).

Footnotes

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† *Crystal data* for **7**: $C_{17}H_{18}O_{10}Cr$, M = 434.3, monoclinic, space group $P2_1$ (no. 4), orange crystals, dimensions 0.10 × 0.18 × 0.25 mm, a = 9.648(1), b = 21.872(2), c = 10.271(1) Å, β = 112.92(1)°, U = 1996.3(3) Å^3, D_c = 1.45 Mg m^{-3}, Z = 4, μ(Cu-Kα) = 5.19 mm^{-1}, T = 200(2) K, F(000) = 896; 3053 symmetry independent reflections were used for the structure solution (direct methods) and refinement (full-matrix least-squares on F^2, 523 parameters, 15 restraints), non-hydrogen atoms were refined anisotropically, H atoms localized by difference electron density and refined using a 'riding' model. $wR2$ = 0.112 {R_1 = 0.041 [$I > 2\sigma(I)$]}. The absolute configuration was determined by Flack's x-refinement x = 0.00(1) (ref. 14). An empirical absorption correction and an extinction correction were applied (ref. 15).

For **10b**: $C_{18}H_{21}NO_9Cr$, M = 447.4, orthorhombic, space group $P2_12_12_1$ (no. 19), yellow crystals, dimensions 0.20 × 0.30 × 0.50 mm, a = 9.935(4), b = 10.834(3), c = 19.526(11) Å, U = 2102(2) Å^3, D_c = 1.41 Mg m^{-3}, Z = 4, μ(Mo-Kα) = 0.59 mm^{-1}, T = 293(2) K, F(000) = 928; 3718 symmetry independent reflections were used for the structure solution (direct methods) and refinement (full-matrix least-squares on F^2, 267 parameters), non-hydrogen atoms were refined anisotropically, H atoms localized by difference electron density and refined using a 'riding' model $wR2$ = 0.100 {R_1 = 0.038 [$I > 2\sigma(I)$]}. The absolute configuration was determined by Flack's x-refinement x = 0.00(2) (ref. 14).

Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Information for Authors, Issue No. 1. Any request to the CCDC for this material should be quoted the full literature citation and the reference number 182/473.

‡ *Selected spectroscopic data* for **2**: ^{13}C NMR (125 MHz, CD_3OD, 273 K): δ 265.1 (1C, C-1), 224.7 (1C, CO_{trans}), 219.5 (4C, CO_{cis}), 112.8 (1C, C_{acetal}), 100.2, 75.9, 69.5 (3C, C-2, C-3, C4), 43.3 (1C, NMe), 27.7, 26.2 (2C, CH_3). For **3**: ^{13}C NMR (125 MHz, CD_3OD, 273 K): δ 247.0 (1C, C-1), 204.0 (1C, CO_{trans}), 199.3 (4C, CO_{cis}), 112.5 (1C, C_{acetal}), 100.9, 76.1, 68.3 (3C, C-2, C-3, C-4), 44.8 (1C, NCH_3), 27.5, 26.0 (2C, CH_3). For **7**. ^{13}C NMR (100 MHz, $CDCl_3$, 273 K): δ 342.3 (1C, C-1), 223.9 (1C, CO_{trans}), 215.7 (4C, CO_{cis}), 114.0 (1C, C_{acetal}), 109.9 (1C, C_{acetal}), 99.1, 97.4, 74.6, 72.5, 65.9 (5C, C-2, C-3, C-4, C-5, C-6), 26.7, 26.4, 25.4, 25.3, (4C, CH_3). For **8**: ^{13}C NMR (125 MHz, $CDCl_3$, 273 K): δ 314.1 (1C, C-1), 204.6 (1C, CO_{trans}), 196.5 (4C, CO_{cis}), 114.0 (1C, C_{acetal}), 109.9 (1C, C_{acetal}), 101.5, 97.8, 74.8, 72.4, 66.0 (5C, C-2, C-3, C-4, C-5, C-6), 26.75, 26.73, 25.6, 25.3 (4C, CH_3). For **10a**: ^{13}C NMR (125 MHz, $CDCl_3$, 273 K): δ 279.1 (1C, C-1), 222.8 (1C, CO_{trans}), 217.4 (4C, CO_{cis}), 112.0 (1C, CO_{acetal}), 110.8 (1C, C_{acetal}), 95.2, 77.3, 75.7, 75.3, 65.9 (5C, C-2, C-3, C-4, C-5, C-6), 26.8, 26.3, 25.7, 24.8 (4C, CH_3). For **10b**: ^{13}C NMR (125 MHz, $CDCl_3$, 273 K): δ 272.3 (1C, C-1), 223.1 (1C, CO_{trans}), 217.7 (4C, CO_{cis}) 111.6 (1C, C_{acetal}), 110.9 (1C, C_{acetal}), 96.6, 82.0, 78.0, 75.8, 66.3 (5C, C-2, C-3, C-4, C-5, C-6), 43.8 (1C, NCH_3), 27.0, 26.3, 26.1, 24.6 (4C, CH_3).

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