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Enantioselective catalysis. Part 148: Carbohydrate-derived oxime ethers stable towards hydrolysis—syntheses of ligands and complexes and a study of their catalytic properties☆

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Abstract—The synthesis of new hydrolytically stable oxime ether ligands by condensation of various aldehydes with *O*-β-D-glucopyranosylhydroxylamine **1** or *O*-β-D-galactopyranosylhydroxylamine **4** is described. After peracetylation of the hydroxyl groups, ligands soluble in organic solvents were obtained. The ligands have been tested in transition metal-catalysed reactions. Phosphorus-containing ligands gave high yields in palladium-catalysed allylic alkylation and rhodium-catalysed hydrosilylation reactions although the enantioselectivities were low. A 1,3-diphenylallyl–palladium(II) complex of ligand **2b** was prepared and its structure was established by X-ray diffraction analysis.

1. Introduction

The design of new chiral ligands for enantioselective transition metal catalysis is currently one of the major interests in organometallic chemistry. Considerable efforts continue to be made to prepare ligands by modification of compounds available in the chiral pool, such as amino acids and carbohydrates. The hydroxyl groups of sugar substituents often make such ligands water-soluble, allowing catalysis in aqueous solution.[1–6]

Saccharide derivatives with primary amino groups have been reacted with aldehydes and ketones leading to imines.[7] However, these Schiff bases suffer from their tendency towards hydrolysis. In contrast, oxime ethers are less susceptible to unwanted hydrolysis. Our previous work showed that *O*-β-D-glucopyranosylhydroxylamine **1** (Scheme 1) can be condensed with functionalised aldehydes to give oxime ethers which are not only stable towards hydrolysis, but can also be prepared in water.[8,9]

The oxime ethers **2a** and **3a** were synthesised by condensation of **1** with 2-diphenylphosphanylbenzaldehyde and 2-pyridinecarbaldehyde in water. Acetylation of the hydroxyl groups with acetic anhydride then afforded **2b** and **3b** (Scheme 1).[8,9]

Herein, we describe the extension of the oxime ether concept to other carbonyl compounds as well as to galactose, which leads to a broad variety of carbohydrate-containing ligands that are stable towards hydrolysis. The ligands were tested in different enantioselective catalysis systems and a Pd–allyl complex of **3b** was prepared and characterised by X-ray crystallography.[9]

2. Results

2.1. Ligand synthesis

O-β-D-Galactopyranosylhydroxylamine **4** was formed in a reaction similar to that for **1**[8,10] and obtained in 70% yield after recrystallisation from methanol. Condensation of **4** with 2-diphenylphosphanylbenzaldehyde **5** and with 2-pyridinecarbaldehyde **6** led to *O*-(β-D-galactopyranosyl)-2-diphenylphosphanylbenzaldoxime **7a** and *O*-(β-D-galactopyranosyl)pyridine-2-carbaldoxime **8a**, respectively (Scheme 2).

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† X-Ray structure analysis.

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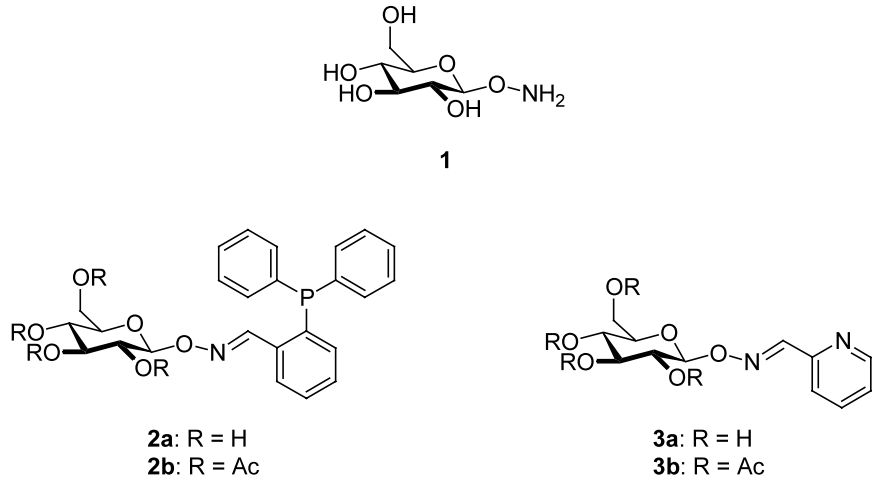
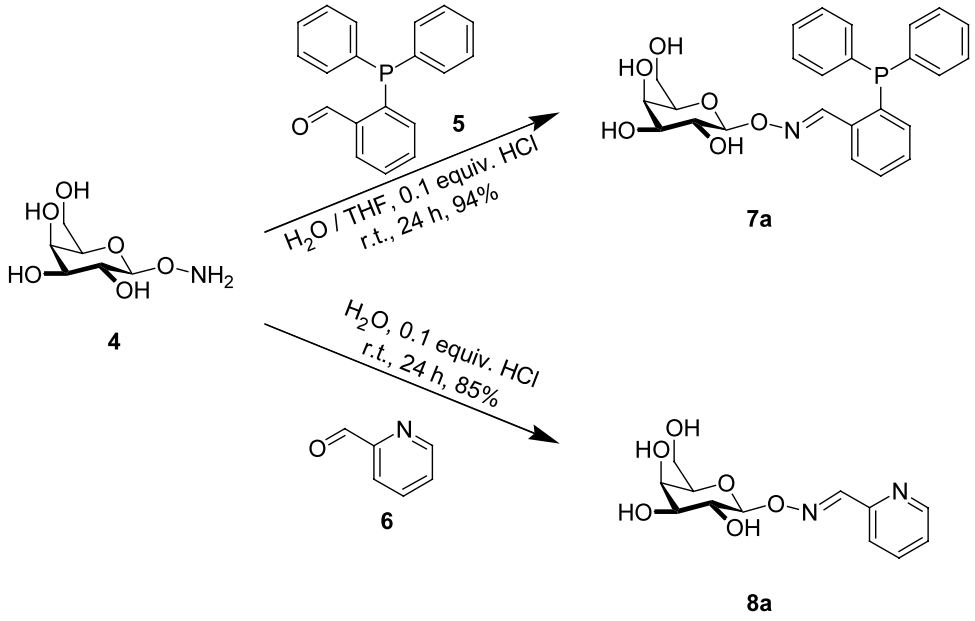


Scheme 1.

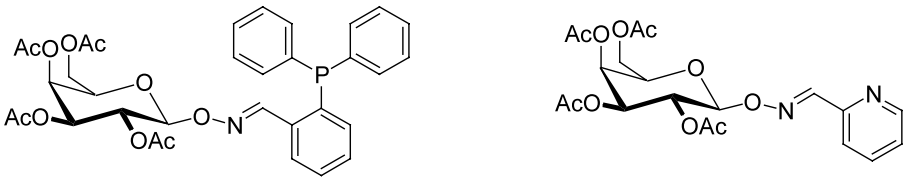


Scheme 2.

The galactose analogues of **2a** and **3a** were esterified with acetic anhydride in pyridine, resulting in the peracetylated oxime ethers **7b** and **8b** (Scheme 3).

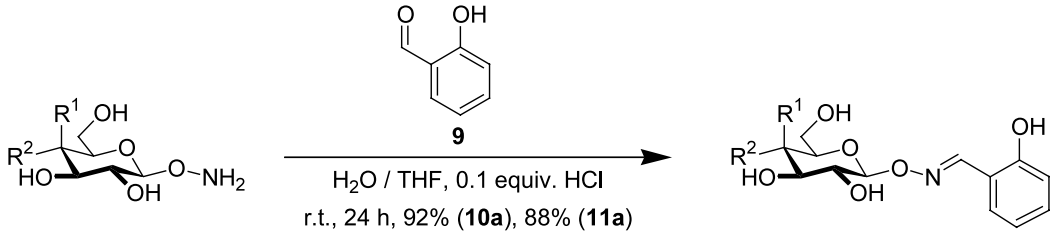
Another carbonyl compound that was used for condensation with **1** and **4** was salicylaldehyde **9**. While **7a**/**b** and **8a**/**b** are non-ionic ligands, derivatives of **9** should easily form anionic ligands. **1** and **4** were reacted with excess **9** in a water–THF mixture and 0.1 equiv. HCl (Scheme 4). After evaporation of the solvents, the residue was washed with ethyl acetate. The products *O*-β-D-glucopyranosylsalicylaldoxime **10a** and *O*-β-D-galactopyranosylsalicylaldoxime **11a** were isolated by filtration, as both substances are insoluble in non-protic solvents. The oxime ethers **10a** and **11a** form hygroscopic white powders that are soluble in water and alcohols.

To extend the concept to ligands with more than one sugar functionality, **1** was used to form oxime ethers with phthalic aldehyde **12**, glyoxal **13** and 2,6-pyridinedicarbaldehyde **14** (Scheme 5). The reactions were carried out as for **5** and **6**, except that 2–2.5 equiv. of **1** were used. For bis-*O*-(β-D-glucopyranosyl)-benzene-1,2-dicarbaldoxime **15a** the excess of **1** (2.5 equiv.) could be filtered off by warming the crude product mixture to 30°C in a small amount of methanol. **1** remained insoluble under these conditions. Removal of the solvent afforded pure **15a** in 96% yield. Compound **13** was reacted with 2 equiv. of **1**. The crude product was washed several times with hot methanol to give bis-*O*-(β-D-glucopyranosyl)ethane-1,2-dicarbaldoxime **16a** in 92% yield, which was found to be soluble in water and DMSO only.



7b **8b**

Scheme 3.



1: R^1=H, R^2=OH
4: R^1=OH, R^2=H

10a: R^1=H, R^2=OH
11a: R^1=OH, R^2=H

Scheme 4.

Dialdehyde **14** was reacted with **1** (2.2 equiv.) affording bis-*O*-(β-D-glucopyranosyl)pyridine-2,6-dicarbaldoxime **17a**, which was purified by column chromatography over silica gel. Reaction of **15a**, **16a** and **17a** with acetic anhydride in pyridine gave the peracetylated oxime ethers **15b**, **16b** and **17b** in good yields. We assume that in all of these syntheses the β-configuration of the glucose and galactose components of **7**, **8**, **10**, **11** and **15**–**17** did not change, as there were no new ^{1}H NMR signals assignable to the α-isomers.

2.2. Palladium-catalysed allylic alkylation

Palladium-catalysed allylic alkylation with soft carbon nucleophiles is a useful tool for C–C bond formation.[11–13] In the reaction of 1,3-diphenylallylacetate **18** with dimethyl malonate **19** chiral ligands may lead to enantioselectivity (Scheme 6). The new ligands were tested in this catalytic system to see if they are able to bind to a suitable palladium precursor and interact with the allylic substrate.

Table 1 shows the results for the ligands **2a**, **2b**, **7a** and **7b** containing phosphorus. All of the other ligands did not exhibit catalytic activity together with **20** due to their inability to coordinate to the Pd precursor. Thus, the oxime ether functionality is not acting as a potent binding site for the metal. However, experiments with the *P*,*N*-ligands showed that fast reactions occur even with Pd ligand ratios of 1:1 indicating bidentate coordination.

In addition, the ligands **22** and **23** (Scheme 7) developed for the Pd-catalysed allylic alkylation of barbiturates including Methohexital[14,15] were tested in the catalytic system shown in Scheme 6 to compare imine ligands with amino acid-derived backbones with the new oxime ethers bearing carbohydrate functionalities.

In all cases yields were high (>90%) but only the imines **22** and **23** induced significant stereoselectivities (Table 1). The enantioselectivity of 66% obtained with **22** dropped to 50% ee on addition of 1 equiv. of PPh_3 indicating that the Pd complex of **22** is much more stable than that of the monodentate PPh_3. When 1-methyl-3-phenylallylacetate was used as a substrate instead of **18**, the yields remained high (>90%), but no enantioselectivity was observed with either the oxime ethers **2a**, **2b**, **7a**, and **7b** nor the imines **22** and **23**.

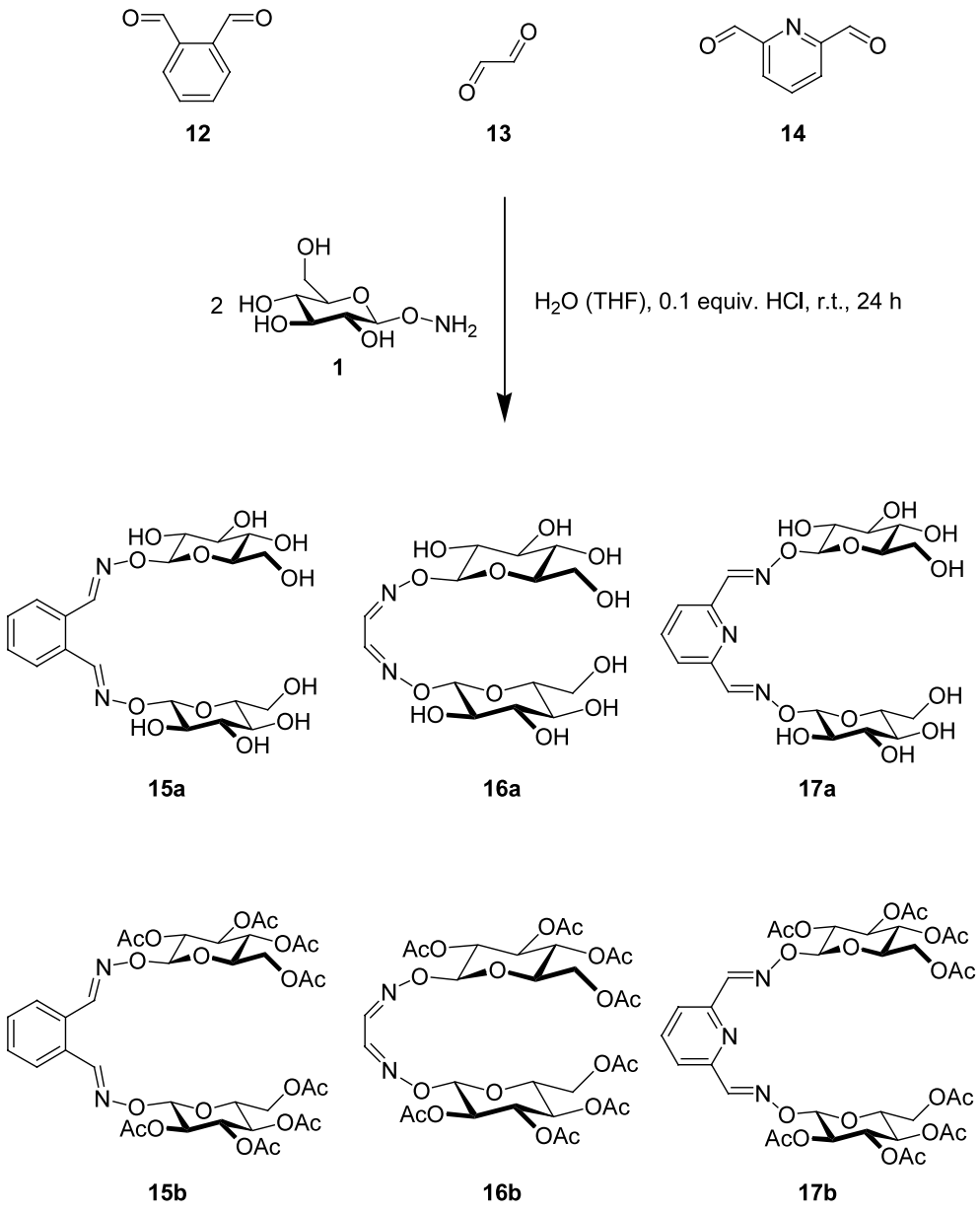
2.3. Hydrosilylation and transfer hydrogenation reactions

The oxime ether ligands were tested in the rhodium-catalysed hydrosilylation of acetophenone with diphenylsilane.[18,19] Yields were high with in situ catalysts consisting of $[Rh(cod)Cl]_2$ and ligands containing phosphorus (>80%), although the highest enantioselectivity observed was only 5.6% for ligand **7a**. Ligands without phosphorus afforded low yields of the product and did not induce any enantioselectivity.[9]

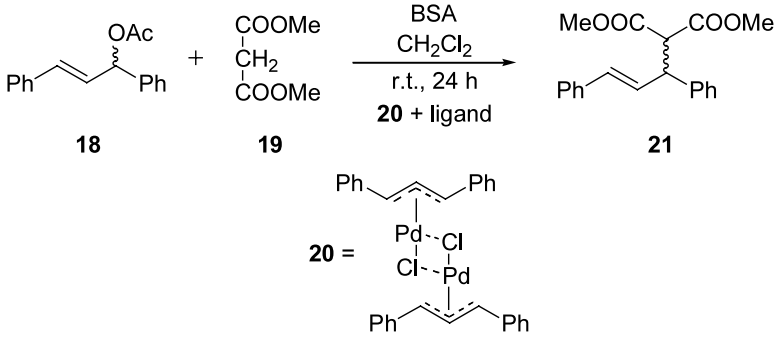
In the $RuCl_2(PPh_3)_3$-catalysed transfer hydrogenation of acetophenone with 2-propanol[20,21] at room temperature ligand **2b** gave 8.2% ee with poor conversion (2.2%). When the reaction was carried out at elevated temperatures (83°C) higher yields were obtained (10.4%), but the enantioselectivity dropped to 1.2%.[9]

2.4. X-Ray structure analysis of a Pd–allyl complex with ligand 2b

To investigate the binding properties of the oxime ether ligands, a 1,3-diphenylallyl–palladium(II) complex of **2b** was prepared. Ligand **2b** was added to a solution of **20** in ethanol. Exchange of the counter ion with $AgBF_4$ and filtration of the precipitated AgCl gave a clear



Scheme 5.



Scheme 6.

yellow solution. Removal of the solvent and recrystallisation from CH_2Cl_2/ethanol/diethyl ether then afforded yellow crystals suitable for X-ray analysis. Figure 1 shows the molecular structure of the Pd complex **24**. As expected, ligand **2b** shows a bidentate coordination to palladium with a torsion angle N(1)–C(34)–C(33)–C(32) of 166.52(47)° compared to 29.79(1)° in the free ligand.[8,9] The allyl system including

Table 1. The ligands **2a**, **2b**, **7a**, **7b**, **22** and **23** in in situ catalysts together with **20** in the enantioselective allylic alkylation of Scheme 6

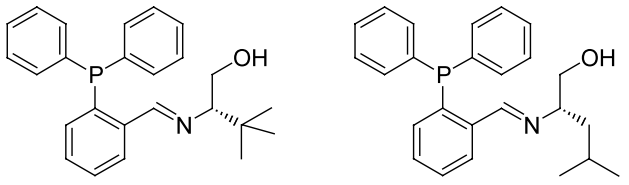
Entry	Ligand	Pd–ligand ratio	Yield (%)[a]	Ee (%)[b] (conf.[c])
1	**2a**	1:1	97	0.3 (*R*)
2	**2a**	1:2	96	0.4 (*R*)
3	**2b**	1:1	94	0.6 (*S*)
4	**7a**	1:1	96	1.3 (*R*)
5	**7a**	1:2	91	1.1 (*R*)
6	**7b**	1:1	96	2.7 (*S*)
7	**22**	1:1	93	66 (*R*)
8	**22**	1:1[d]	90	50 (*R*)
9	**23**	1:1	95	53 (*R*)
10	**23**	1:2	94	52 (*R*)

[a] Isolated yields.

[b] Enantiomeric excess was determined by HPLC on a Daicel Chiralcel OD-H column: *n*-hexane:2-propanol 99:1, $T=18$°C, 0.6 ml min^{-1} ($t_R=19.1$ min (*S*) and 20.2 min (*R*) for **21**) or by addition of 12 equiv. of (*S*)-(+)-1-(9′-anthryl)-2,2,2-trifluoroethanol to a solution of **21** (3 mg) in 1 mL of $CDCl_3$. The ^{1}H NMR signal at $\delta=3.51$ ppm shifted and showed baseline separation with peaks at $\delta=3.470$ ppm (*S*) and $\delta=3.464$ (*R*).

[c] Configuration assignment was based on the t_R values for catalysis with (2*S*,3*S*)-bis(diphenylphosphanyl)butane ((*S*,*S*)-Chiraphos) as ligand and comparison with the literature.[16,17]

[d] 1 equiv. of PPh_3 was added.



22 **23**

Scheme 7.

the *ipso*-C atoms of the phenyl substituents is almost planar with torsion angles C(1)–C(7)–C(8)–C(9) and C(7)–C(8)–C(9)–C(10) of 178.87(44)° and 175.30(45)°, respectively. In addition, the planes of the two phenyl rings are aligned with the allyl plane. The phenyl ring with *ipso*-C10 is rotated by 13.40(77)° indicating only weak interaction with the sugar moiety in accord with the low enantioselectivities obtained in the catalytic reactions with ligands of the type **2b**. The rotation of 20.13(75)° of the phenyl ring with *ipso*-C1 is probably due to π-stacking with one of the phenyl groups attached to the phosphorus (ring distance: 4.267(3) Å). As has been found for other Pd–allyl complexes with *P*,*N* ligands,[22,23] the bond distances of 2.170(4) Å for Pd(1)–C(7) and 2.257(5) Å for Pd(1)–C(9) are significantly different, demonstrating the *trans* effect of the phosphorus atom with respect to the imine nitrogen atom.

3. Experimental

3.1. General remarks

^{1}H NMR (*i*-TMS): Bruker AC 250 and ARX 400, ^{31}P NMR (ext. 85% H_3PO_4): Bruker ARX 400. Melting points: Büchi SMP-20. Optical rotations: Perkin–Elmer polarimeter 241. Mass spectra: Varian MAT 95. The glucose derivatives **1**, **2a**, **2b**, **3a** and **3b** were synthesised as described before.[8] Compounds **20**, **22** and **23** were prepared according to the literature.[14,15,24]

3.2. *O*-β-D-Galactopyranosylhydroxylamine, 4

Compound **4** was prepared from *O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-*N*-hydroxysuccinimide as described for *O*-β-D-glucopyranosylhydroxylamine **1**.[8–10] White crystalline powder, 70% yield. Mp 156°C; $[\alpha]_D^{25}=+68.0$ (*c* 3, H_2O); ^{1}H NMR (250 MHz, D_2O): $\delta=3.44$ (dd, 1H, $J_{2,3}=9.9$, $J_{2,1}=8.0$, H_{galac}-2), 3.56 (dd, 1H, $J_{3,4}=3.4$, H_{galac}-3), 3.60 (ddd, 1H, $J_{5,6b}=7.9$, $J_{5,6a}=4.0$, $J_{5,4}=0.9$, H_{galac}-5), 3.65 (dd, 1H, $J_{6a,6b}=11.3$, H_{galac}-6a), 3.71 (dd, 1H, H_{galac}-6b), 3.81 (dd, 1H, H_{galac}-4), 4.41 (d, 1H, H_{galac}-1).

3.3. *O*-(β-D-Galactopyranosyl)-2-diphenylphosphanylbenzaldoxime, 7a

Compound **7a** was prepared by condensation of **4** and **5** as described for *O*-(β-D-glucopyranosyl)-2-diphenylphosphanylbenzaldoxime **2a**.[8,9] White crystalline powder, 94% yield. Mp 132°C; $[\alpha]_D^{25}=+15.8$ (*c* 1, CH_2Cl_2); ^{1}H NMR (400 MHz, DMSO-d_6): $\delta=3.10$–3.55 (m, 5H, H_{galac}), 3.64–3.68 (m, 1H, H_{galac}), 4.34–4.47 (s, 1H, OH), 4.50–4.65 (s, 1H, OH), 4.69–4.87 (s, 1H, OH), 4.79 (d, 1H, $J_{1,2}=8.1$, H_{galac}-1), 4.95–5.12 (s, 1H, OH), 6.83–6.88 (m, 1H, H_{ar}), 7.16–7.35 (m, 4H, H_{ar}), 7.38–7.47 (m, 7H, H_{ar}), 7.50–7.68 (m, 1H, H_{ar}), 7.83–7.89 (m, 1H, H_{ar}), 8.74 (d, 1H, $J_P=4.3$, CH=N); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): $\delta=-14.80$ (s).

3.4. *O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-2-diphenylphosphanylbenzaldoxime, 7b

Compound **7b** was prepared from **7a** as described for *O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-2-diphenylphosphanylbenzaldoxime **2b**.[8,9] White crystalline powder, 62% yield. Mp 65–67°C; $[\alpha]_D^{25}=+5.7$ (*c* 1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=1.96$ (s, 3H, CH_3), 1.97 (s, 3H, CH_3), 2.02 (s, 3H, CH_3), 2.13 (s, 3H, CH_3), 3.96 (ddd, 1H, $J_{5,6a}=9.9$, $J_{5,6b}=6.8$, $J_{5,4}=1.2$, H_{galac}-5), 4.06–4.20 (m, 2H, H_{galac}-6a,6b), 5.04 (dd, 1H, $J_{3,2}=10.4$, $J_{3,4}=3.4$, H_{galac}-3), 5.11 (d, 1H, $J_{1,2}=8.5$, H_{galac}-1), 5.33 (dd, 1H, H_{galac}-2), 5.38 (dd, 1H, H_{galac}-4), 6.90–6.95 (m, 1H, H_{ar}), 7.18–7.24 (m, 4H, H_{ar}), 7.25–7.38 (m, 8H, H_{ar}), 7.83–7.87 (m, 1H, H_{ar}), 8.84 (d, 1H, $J_P=4.4$, CH=N); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): $\delta=-13.99$ (s); MS (CI): $m/z=636.4$ (MH^+, 92), 288.3 (100). Anal. calcd for $C_{33}H_{34}NO_{10}P$ (635.61): C, 62.36; H, 5.39; N, 2.20. Found: C, 62.44; H, 5.67; N, 2.09%.

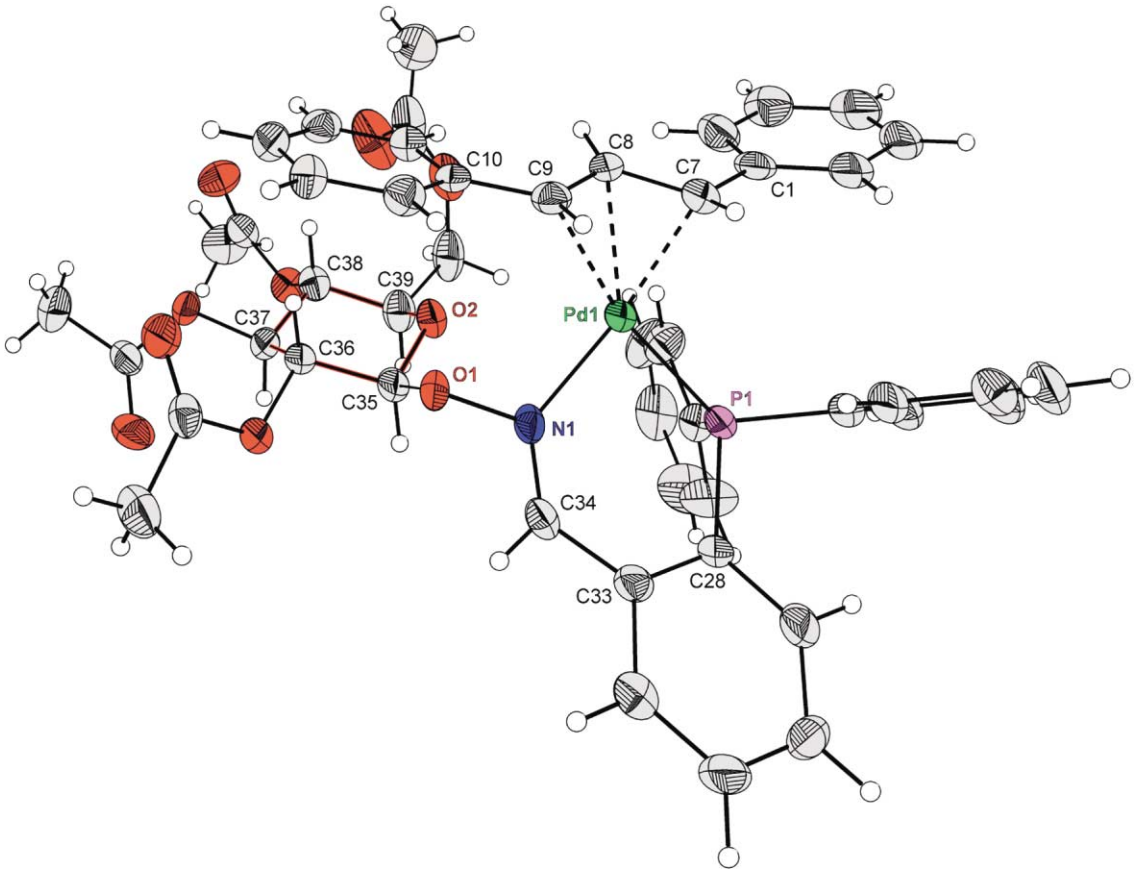


Figure 1. Molecular structure of **24**.

3.5. *O*-(β-D-Galactopyranosyl)pyridine-2-carbaldoxime, 8a

Compound **8a** was prepared by condensation of **4** and **6** as described for *O*-(β-D-glucopyranosyl)pyridine-2-carbaldoxime **3a**.[8,9] White crystalline powder, 85% yield. Mp 68°C; $[\alpha]_D^{25} = -15.0$ (*c* 3, H_2O); ^{1}HNMR (250 MHz, D_2O): $\delta = 3.60$–3.78 (m, 5H, H_{galac}), 3.85–3.90 (m, 1H, H_{galac}), 4.97–5.09 (m, 1H, H_{galac}-1), 7.39 (ddd, 1H, $J_{3,b} = 7.6$, $J_{3,d} = 5.0$, $J_{3,a} = 1.2$, H_{py}-3), 7.68 (ddd, 1H, $J_{1,2} = 8.0$, $J_{1,4} = 0.9$, H_{py}-1), 7.81 (ddd, 1H, $J_{2,4} = 1.7$, H_{py}-2), 8.29 (s, 1H, CH=N), 8.45 (ddd, 1H, H_{py}-4).

3.6. *O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-pyridine-2-carbaldoxime, 8b

Compound **8b** was prepared from **8a** as described for *O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)pyridine-2-carbaldoxime **3b**.[8,9] White crystalline powder, 62% yield. Mp 114°C; $[\alpha]_D^{25} = +9.6$ (*c* 1, CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 1.97$ (s, 3H, CH_3), 1.98 (s, 3H, CH_3), 2.05 (s, 3H, CH_3), 2.12 (s, 3H, CH_3), 3.96 (ddd, 1H, $J_{5,6a} = 8.8$, $J_{5,6b} = 6.5$, $J_{5,4} = 1.4$, H_{galac}-5), 4.16–4.24 (m, 2H, H_{galac}-6a,6b), 5.09 (dd, 1H, $J_{3,2} = 10.4$, $J_{3,4} = 3.4$, H_{galac}-3), 5.15 (d, 1H, $J_{1,2} = 8.5$, H_{galac}-1), 5.37 (dd, 1H, H_{galac}-2), 5.42 (dd, 1H, H_{galac}-4), 7.31 (ddd, 1H, $J_{3,2} = 6.6$, $J_{3,4} = 4.9$, $J_{3,1} = 2.2$, H_{py}-3), 7.75 (ddd, 1H, $J_{2,1} = 7.8$, $J_{2,4} = 1.7$, H_{py}-2), 7.74 (ddd, 1H, $J_{1,4} = 0.9$, H_{py}-1), 8.28 (s, 1H, CH=N), 8.64 (ddd, 1H, H_{py}-4); MS (CI): $m/z = 453.4$ (MH^+, 100), 366.4 (54). Anal. calcd for $C_{20}H_{24}N_2O_{10}$ (452.42): C, 53.10; H, 5.35; N, 6.19. Found: C, 52.85; H, 5.45; N, 5.97%.

3.7. *O*-β-D-Glucopyranosylsalicylaldoxime, 10a

To a solution of **1** (400 mg, 2.05 mmol) in H_2O (20 mL) and THF (25 mL) salicylaldehyde **9** (1.0 mL, 10.6 mmol) was added and the reaction mixture was stirred at room temperature for 5 h. After removal of the solvents ethyl acetate (50 mL) was added. The suspension was stirred until the excess of **9** had dissolved. The product was filtered off and dried to afford **10a** as a white hygroscopic powder in 92% yield. Mp 67°C; $[\alpha]_D^{25} = -20.7$ (*c* 2, MeOH); ^{1}H NMR (250 MHz, D_2O): $\delta = 3.30$–3.57 (m, 4H, H_{gluc}-2–5), 3.65 (dd, 1H, $J_{6a,6b} = 12.3$, $J_{6a,5} = 5.7$, H_{gluc}-6a), 3.83 (dd, 1H, $J_{6b,5} = 2.1$, H_{gluc}-6b), 5.09 (d, 1H, $J_{1,2} = 8.05$, H_{gluc}-1), 6.91 (m, 1H, $J_{4,3} = 8.3$, $J_{4,2} = 1.0$, $J_{4,1} = 0.4$, H_{ar}-4), 6.93 (m, 1H, $J_{2,1} = 7.8$, $J_{2,3} = 7.4$, H_{ar}-2), 7.31 (m, 1H, $J_{3,1} = 1.7$, H_{ar}-3), 7.40 (m, 1H, H_{ar}-1), 8.45 (s, 1H, CH=N).

3.8. *O*-β-D-Galactopyranosylsalicylaldoxime, 11a

Compound **11a** was prepared by condensation of **4** and **9** as described for **10a**. White hygroscopic powder, 88% yield. Mp 65°C; $[\alpha]_D^{25} = -10.7$ (*c* 2, MeOH); ^{1}H NMR (250 MHz, D_2O): $\delta = 3.57$–3.75 (m, 5H, H_{galac}), 3.84–3.88 (m, 1H, H_{galac}), 4.95–5.10 (m, 1H, H_{galac}-1), 6.88 (m, 1H, $J_{4,3} = 8.3$, $J_{4,2} = 1.0$, $J_{4,1} = 0.4$, H_{ar}-4), 6.90 (m,

1H, $J_{2,1}=7.8$, $J_{2,3}=7.4$, H_{ar}-2), 7.28 (m, 1H, $J_{3,1}=1.6$, H_{ar}-3), 7.37 (m, 1H, H_{ar}-1), 8.43 (s, 1H, CH=N).

3.9. Bis-*O*-(β-D-glucopyranosyl)benzene-1,2-dicarbaldoxime, 15a

To a solution of phthalic aldehyde **12** (52.7 mg, 0.4 mmol) and **1** (195 mg, 1 mmol) in H_2O (25 mL) and THF (5 mL) was added 0.1 M HCl (1 mL) and the mixture was stirred at room temperature for 24 h. After removal of the solvents methanol (15 mL) was added and the suspension was warmed to 30°C. Excess **1** was filtered off and after removal of the solvent pure **15a** was obtained as a white crystalline powder in 96% yield. Mp 167°C; $[\alpha]_D^{25}=-32.8$ (*c* 3, H_2O); ^{1}H NMR (250 MHz, D_2O): $\delta=3.31$–3.58 (m, 8H, H_{gluc}-2–5), 3.65 (dd, 2H, $J_{6a,6b}=12.3$, $J_{6a,5}=5.6$, H_{gluc}-6a), 3.83 (dd, 2H, $J_{6b,5}=2.1$, H_{gluc}-6b), 5.03–5.14 (m, 2H, H_{gluc}-1), 7.44–7.53 (m, 2H, Ar-H), 7.59–7.68 (m, 2H, Ar-H), 8.63 (s, 2H, CH=N).

3.10. Bis-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-benzene-1,2-dicarbaldoxime, 15b

Compound **15b** was prepared from **15a** as described for **2b**.[8,9] White crystalline powder, 98% yield. Mp 152–154°C; $[\alpha]_D^{25}=-31.9$ (*c* 2, CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): $\delta=2.03$ (s, 6H, CH_3), 2.04 (s, 6H, CH_3), 2.06 (s, 6H, CH_3), 2.08 (s, 6H, CH_3), 3.90 (ddd, 2H, $^3J_{5,4}=9.8$, $^3J_{5,6a}=4.3$, $^3J_{5,6b}=2.3$, H_{gluc}-5), 4.17 (dd, 2H, $^3J_{6b,6a}=12.4$, H_{gluc}-6b), 4.36 (dd, 2H, H_{gluc}-6a), 5.17 (dd, 2H, $^3J_{4,3}=9.1$, H_{gluc}-4), 5.22 (dd, 2H, $^3J_{2,3}=9.3$, $^3J_{2,1}=8.1$, H_{gluc}-2), 5.32 (dd, 2H, H_{gluc}-3), 5.33 (d, 2H, H_{gluc}-1), 7.39–7.48 (m, 2H, H_{Ar}), 7.65–7.75 (m, 2H, H_{Ar}), 8.56 (s, 2H, CH=N).

3.11. Bis-*O*-(β-D-glucopyranosyl)ethane-1,2-dicarbaldoxime, 16a

To a solution of **1** (390 mg, 2 mmol) in H_2O (10 mL) was added a 40% aqueous solution of glyoxal **13** (150 μL, 1 mmol) and 0.1 M HCl (2 mL). The mixture was stirred for 24 h and the solvent was removed. The crude product was washed with hot methanol (3×30 mL) and dried to give **16a** in 92% yield. Mp 112–114°C; $[\alpha]_D^{25}=-32.0$ (*c* 3, H_2O); ^{1}H NMR (250 MHz, D_2O): $\delta=3.30$ (dd, 2H, $J_{4,5}=9.9$, $J_{4,3}=9.3$, H_{gluc}-4), 3.38 (dd, 2H, $J_{2,3}=9.4$, $J_{2,1}=8.3$, H_{gluc}-2), 3.41 (ddd, 2H, $J_{5,6a}=5.6$, $J_{5,6b}=2.1$, H_{gluc}-5), 3.43 (dd, 2H, H_{gluc}-3), 3.60 (dd, 2H, $J_{6a,6b}=12.4$, H_{gluc}-6a), 3.75 (dd, 2H, H_{gluc}-6b), 4.98 (d, 2H, H_{gluc}-1), 7.94 (s, 2H, CH=N).

3.12. Bis-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-ethane-1,2-dicarbaldoxime, 16b

Compound **16b** was prepared from **16a** as described for **2b**.[8,9] White crystalline powder, 98% yield. Mp 152–154°C; $[\alpha]_D^{25}=-29.0$ (*c* 1, CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): $\delta=2.05$ (s, 6H, CH_3), 2.06 (s, 6H, CH_3), 2.08 (s, 6H, CH_3), 2.09 (s, 6H, CH_3), 3.82 (ddd, 2H, $J_{5,4}=9.9$, $J_{5,6a}=4.3$, $J_{5,6b}=2.4$, H_{gluc}-5), 4.15 (dd, 2H, $J_{6b,6a}=12.6$, H_{gluc}-6b), 4.31 (dd, 2H, H_{gluc}-6a), 5.12 (dd, 2H, $J_{4,3}=9.2$, H_{gluc}-4), 5.22 (dd, 2H, $J_{2,3}=9.4$, $J_{2,1}=8.0$, H_{gluc}-2), 5.25 (d, 2H, H_{gluc}-1), 5.32 (dd, 2H, H_{gluc}-3), 8.47 (s, 2H, CH=N).

3.13. Bis-*O*-(β-D-glucopyranosyl)pyridine-2,6-dicarbaldoxime, 17a

To a solution of 2,6-pyridinedicarbaldehyde **14** (270 mg, 2 mmol) and **1** (895 mg, 4.4 mmol) in H_2O was added 0.1 M HCl (4 mL) and the mixture was stirred at room temperature for 24 h. After removal of the solvent the crude product was purified by column chromatography on silica gel with methanol/ethyl acetate 1:1 to give **17a** in 85% yield. Mp 131–134°C; $[\alpha]_D^{25}=+27.4$ (*c* 3, H_2O); ^{1}H NMR (250 MHz, D_2O): $\delta=3.30$–3.55 (m, 8H, H_{gluc}-2–5), 3.63 (dd, 2H, $J_{6a,6b}=12.4$, $J_{6a,5}=5.5$, H_{gluc}-6a), 3.82 (dd, 2H, $J_{6b,5}=2.0$, H_{gluc}-6b), 5.04–5.15 (m, 2H, H_{gluc}-1), 7.74 (m, 2H, $J_{1/3,2}=7.94$, H_{py}-1/3), 7.88 (m, 1H, H_{py}-2), 8.31 (s, 2H, CH=N); MS (CI): $m/z=490.16$ (MH^+, 5), 107.4 (100). Anal. calcd for $C_{19}H_{27}N_3O_{12}$ (489.43): C, 46.63; H, 5.56; N, 8.59. Found: C, 46.31; H, 5.72; N, 8.32%.

3.14. Bis-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-pyridine-2,6-dicarbaldoxime, 17b

17b was prepared from **17a** as described for **2b**.[8,9] White crystalline powder, 99% yield. Mp 142–145°C; $[\alpha]_D^{25}=-35.1$ (*c* 1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=2.02$ (s, 6H, CH_3), 2.036 (s, 6H, CH_3), 2.039 (s, 6H, CH_3), 2.7 (s, 6H, CH_3), 3.85 (ddd, 2H, $J_{5,4}=9.7$, $J_{5,6a}=4.3$, $J_{5,6b}=2.4$, H_{gluc}-5), 4.16 (dd, 2H, $J_{6b,6a}=12.5$, H_{gluc}-6b), 4.33 (dd, 2H, H_{gluc}-6a), 5.14–5.34 (m, 8H, H_{gluc}-1–4), 7.76 (m, 2H, $J_{1/3,2}=7.63$, H_{py}-1/3), 7.84 (m, 4H, H_{py}-2), 8.26 (s, 2H, CH=N); MS (CI): $m/z=826.26$ (MH^+, 2), 107.4 (100). Anal. calcd for $C_{35}H_{43}N_3O_{20}$ (825.73): C, 50.91; H, 5.25; N, 5.09. Found: C, 50.78; H, 5.51; N, 4.95%.

3.15. (η^3-1,3-Diphenylallyl)-*P*,*N*-[*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl]-2-diphenylphosphanylbenzaldoxime)palladium(II) tetrafluoroborate ethanol solvate, 24

Ligand **2b** (253 mg, 398 μmol) and **20** (117 mg, 175 μmol) were dissolved in ethanol (2 mL) under N_2 and the mixture was stirred for 2 h. $AgBF_4$ (70 mg, 410 μmol) was added and the precipitated AgCl was filtered off. The clear orange solution was evaporated under reduced pressure and the crude product was recrystallised from CH_2Cl_2/ethanol/diethyl ether to give **24** as orange crystals in 34% yield.

3.15.1. Crystal data for compound 24. $C_{48}H_{47}NO_{10}PPd$, C_2H_6O, BF_4: Small yellow plates, Fw = 1068.13, monoclinic, space group $P2_1$ (no. 4), $a=10.1531(6)$, $b=24.300(2)$, $c=10.0213(6)$ Å, $\beta=81.416(7)°$, $V=2444.7(3)$ Å^3, $Z=2$, $D_{calcd}=1.451$ Mg/m^3, μ(Mo Kα) = 0.488 mm^{-1}, crystal dimensions 0.40×0.36×0.08 mm^3, $\lambda=0.71073$ Å (Mo Kα radiation, graphite monochromator, STOE imaging plate diffraction system). Data collection at $T=173$ K, $2.06<\theta<25.88°$, h −12→12, k −29→29, l −12→12, 34333 reflections mea-

sured, 9380 unique, merging $R_{int}=0.0456$. The structure was solved by direct methods (SIR-97[25]) and refined by full-matrix least-squares based on F^2 (SHELXL-97[26]) with weights $w=1/[\sigma^2(F_o^2)+(0.0951P)^2+0.7174P]$, $P=(F_o^2+2F_c^2)/3$. Most of the H atoms were calculated geometrically and a riding model was used during the refinement process; the H atoms at C7, C9 and C34 were located by difference Fourier synthesis and refined isotropically. The final consistency indexes for all data were $R_1=0.0515$, $wR_2=0.1262$ and goodness-of-fit = 1.062. The last difference Fourier map showed peaks between 4.177 and −0.446 e Å^{-3}. The correct absolute configuration was confirmed by the Flack parameter −0.03(2). Crystallographic data (excluding structure factors) for the structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-199089. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.)+44-1223/336-033; email: deposit@ccdc.cam.ac.uk].

3.16. General procedure for the allylic alkylation of 18

A dry Schlenk tube, charged with **20** (6.7 mg, 10 μmol) and phosphine ligand (20 μmol), was flushed with nitrogen and CH_2Cl_2 (10 mL) was added. After stirring for 30 min, 1,3-diphenylacetate **18** (120 μL, 1 mmol), dimethyl malonate **19** (345 μL, 3 mmol) and BSA (745 μl, 3 mmol) were subsequently added. The reaction progress was monitored by TLC and the reaction was found to be complete after 24 h in all cases. After the solution was diluted with diethyl ether (30 mL) and washed with water (3×20 mL) and brine (20 mL), the organic layer was separated, dried over $MgSO_4$ and the solvent was removed. To the crude product ethyl acetate/hexane 1:8 was added and the precipitated by-product (white solid) was filtered off. Column chromatography of the filtrate on silica gel with ethyl acetate/hexane 1:8 yielded **21**.

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