The synthesis and biological applications of photo-activated ruthenium anticancer drugs

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Chapter 2:

The synthesis of *O*-1 to *O*-6 substituted positional isomers of D-glucose-thioether ligands and their ruthenium polypyridyl conjugates

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2.1 Introduction

Carbohydrates are a class of biomolecules ubiquitously present in nature, comprising monosaccharides, oligosaccharides and polysaccharides, of which monosaccharides cannot be hydrolyzed further into smaller units. These molecules are recognized as important building blocks in the cell wall of bacteria (peptidoglycan),[1] in plants (pectins),[2] in the exoskeleton of insects (chitin),[3] in cell recognition processes (lectins),[4] or in the backbone of RNA and DNA.[5] Among them, D-glucose is is the most well-known monosaccharide as it serves as the primary source of chemical energy in eukaryotic cells for the production of ATP.[6] Otto Warburg found that cancer cells have an increased glycolysis rate for the production of ATP compared to normal cells.[7] As a consequence, glucose transporters (GLUTs) 1 and 3 are overexpressed in cancer cells.[8] In recent years there has been a growing interest in using this effect to selectively deliver molecules of interest to cancer cells. In the field of diagnostic imaging the well-known radiotracer 2-deoxy-2-[^{18}F]fluoroglucose (2-FDG) selectively accumulates in cancer cells since its metabolic breakdown is hampered by the replacement of a hydroxyl group on the 2-position of D-glucose by fluoride.[9] This clinically approved agent allows PET imaging of tumors anywhere in the whole body. In the field of medicinal chemistry, glufosfamide has shown some success as a safer alternative for ifosfamide, an alkylating agent used in cancer treatment. The therapeutic efficiency of glufosfamide is thought to be higher due to its increased water solubility and preferred uptake in malignant cells versus normal cells.[10] Recently Palay et. al. have demonstrated that a series of glucose conjugates of platinum-based medicines are taken up *via* GLUT1.[11] This result is in contrast to the observation of Schubiger, who found that none of their radiodiagnostic glycoconjugates based on ^{99m}Tc were taken up via glucose transporters.[12] For ruthenium(II) polypyridyl-based drugs this effect has not been thoroughly investigated. We have therefore designed a series of glycoconjugates of every positional isomers of D-glucose, containing different lengths of ethylene glycol-based spacers bearing one or two coordinating methylthioether groups. New routes towards these positional isomers were developed that are compatible with sulfur based ligands, since the existing routes use palladium-based catalysts that are deactivated by donor atoms.[13] As traces of palladium also often interfere with the biological activity of pharmaceuticals,[14] we herein describe a palladium-free synthesis for every PEGylated positional isomer of D-glucose-thioether ligands, and their coordination to ruthenium(II) polypyridyl complexes to afford eleven ruthenium-glycoconjugates (see structures in Figure 2.1) aimed at studying the structure-uptake relationship in cancer cells.

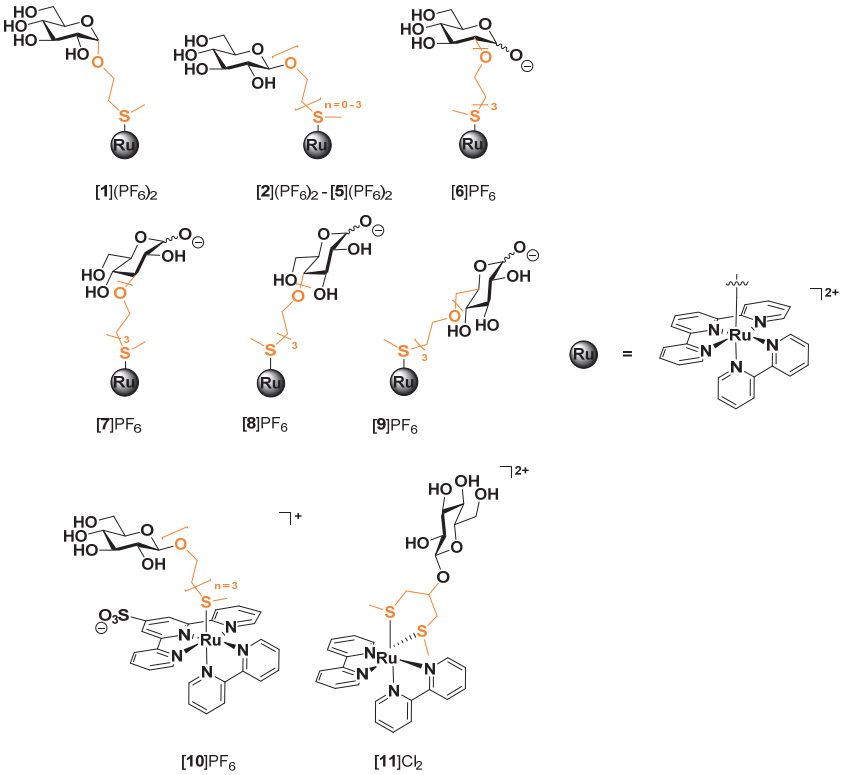
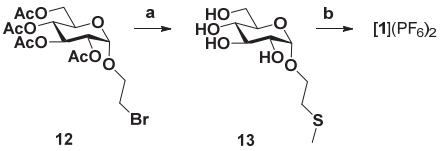


Figure 2.1. Schematic overview of *O*-1 to *O*-6 positional D-glucose ruthenium(II) polypyridyl conjugates presented in this study.

2.2 Results and discussion

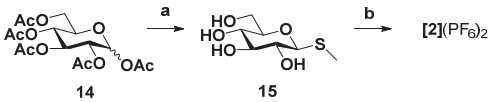
2.2.1 1-*O* substitution

Five hydroxyl groups are available for modification in D-glucose, of which the 1-*O* position is modified *via* chemical glycosylation.[15] Recently Patra *et. al.* have demonstrated that the spacer length exerts influence over GLUT mediated uptake of platinum complexes in cells,[11] however there is currently no established understanding of this effect in cationic ruthenium(II) polypyridyl compounds. Therefore oligoethyleneglycol spacers $[OCH_2CH_2]_n$ with varying length (n = 0 – 3) were introduced in glycoconjugates [**1**](PF$_6$)$_2$ – [**5**](PF$_6$)$_2$ (Figure 2.1). The first complex in this series ([**1**](PF$_6$)$_2$) was synthesized starting from precursor **12** (Scheme 2.1).[16] This building block and NaSMe were used in a S_N2 reaction ensuring the installment of the thioether group, affording **13**. This ligand was then reacted with [Ru(tpy)(bpy)Cl]Cl, affording glycoconjugate [**1**](PF$_6$)$_2$.



Scheme 2.1. a). *i.* NaSMe in DMF, rt, 16 h *ii.* NaOMe in MeOH, 66% over two steps; b). [Ru(tpy)(bpy)Cl]Cl in H_2O, 80 °C, 16 h, 39%.

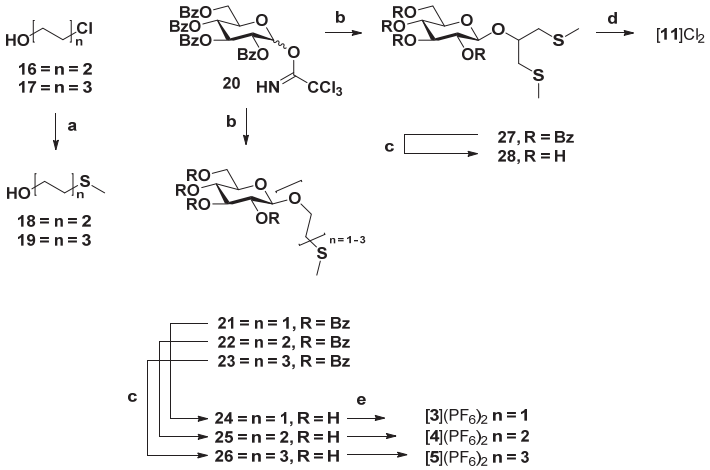
For complex [**2**]$(PF_6)_2$, a three-step one-pot synthesis starting from *per*-acetylated glucose (**14**) was adapted from Valerio *et. al.*,[17] which afforded the *trans* glucopyranoside as the only diastereoisomer. Treatment of this compound with sodium methoxide in methanol afforded fully deprotected **15** in 55% overall yield. Subsequent reaction of this ligand with [Ru(tpy)(bpy)Cl]Cl then gave [**2**](PF_6).



Scheme 2.2. a). *i.* I_2, Et_3SiH in DCM, rt., 10 min; *ii.* Thiourea in MeCN, 80 °C, 30 min; *iii.* MeI, Et_3N, rt., 10 min.; *iv.* cat. NaOMe in MeOH, rt., overnight. 57% over four steps; d). [Ru(tpy)(bpy)Cl]Cl in H_2O, 80 °C, 48 h, 28%.

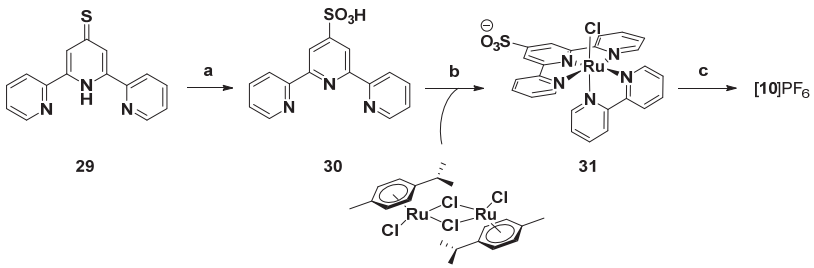
A different approach was employed for the installment of the ethylene glycol-based linkers (n = 1 – 3) for complexes [**3**]$(PF_6)_2$-[**5**]$(PF_6)_2$ and [**11**]$(PF_6)_2$ (Scheme 2.3). The disarmed Schmidt donor **20** (Scheme 2.3) was chosen due to its straightforward synthesis and robustness. The benzoyl protecting group in this building block was favored over the more common acetyl group, due to the lower reactivity – and therefore higher stability – of the benzoyl imidate.[18] Furthermore, the benzoyl group was chosen to reduce the possible formation of orthoesters, a common side reaction when using acetyl-bearing donors.[19] Commercially available 2-(methylthio)ethanol was used as acceptor and condensed with donor **20** (Scheme 2.3), affording **21** which after de-*O*-benzoylation acquired deprotected **24**. Compounds **25**, **26** and **28** were acquired in a similar fashion using acceptor **18**, **19** and 1,3-bis(methylthio)propan-2-ol respectively. The synthesis of their ruthenium complexes was found to be straightforward, by reacting excess ligand with the ruthenium species [Ru(tpy)(bpy)Cl]Cl or $[Ru(bpy)_2Cl_2]$. Their purification however, was found arduous due to the increased water-solubility of these compounds. Although hydrophilicity is a highly desired property in medicinal chemistry, it also decreases the number of available work-up techniques. Common workup methods for metal complexes such as extraction and precipitation were not applicable, since both the ligand and product are water-soluble. Also, the lability of these compounds on C-18 columns prevented reverse-phase chromatographic purification. The most reproducible approach was by purification over silica using a mixture of acetone, water and aqueous KPF_6, followed by a methanol Sephadex LH-20 size exclusion purification to remove excess salt

and minor impurities. This method afforded ruthenium polypyridyl derivatives [**3**]$(PF_6)_2$-[**5**]$(PF_6)_2$ and [**11**]Cl_2 in moderate to good yield (28 – 66%).



Scheme 2.3. a). 2-(2-chloroethoxy)ethanol, NaSMe in THF, reflux, 6 h, 94%; b). 2-(methylthio)ethanol, 1,3-bis(methylthio)propanol, **18** or **19**, cat. TMSOTf in DCM, 4Å molsieves, rt, 4 h, 81% for **21**, 66% for **22**, 85% for **23,** 90% for **27**; c). NaOMe in MeOH, rt, 88% for **24**, 86% for **25**, 91% for **26**, 70% for **28;** d). $[Ru(bpy)_2Cl_2]$ in H_2O, 80 °C, 59% for [**11**]Cl_2; e). [Ru(tpy)(bpy)Cl]Cl in H_2O, 80 °C, 39% for [**3**]$(PF_6)_2$, 66% for [**4**]$(PF_6)_2$, 65% for [**5**]$(PF_6)_2$.

Park and coworkers have demonstrated that glucose bioprobes with a formal charge of +1 are taken up preferentially over neutral and negatively charged probes.[20] To allow future study of the effect on the overall charge for ruthenium(II) polypyridyl drugs on uptake and toxicity, a derivative of [Ru(tpy)(bpy)Cl]Cl bearing a negative charge on the spectator terpyridine ligand was also synthesized. Compound **31** (Scheme 2.4) was prepared starting from thione **29**,[21] which was oxidized using *in situ* generated per-acetic acid followed by hydrogenation using 10% palladium on carbon to reverse partial overoxidation to its *N*-oxide, affording ligand **30**. A one-pot synthesis using (*p*-cymene)ruthenium(II) chloride dimer, **30** and bpy provided complex **31**. Reaction of ligand **26** (Scheme 2.3) with this complex then gave complex [**10**]$(PF_6)_2$.

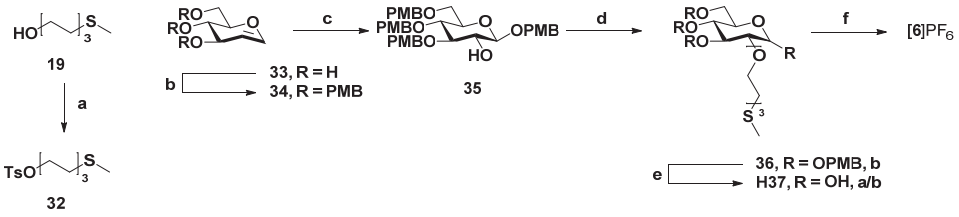


Scheme 2.4. a). *i.* H_2O_2 in AcOH, 70 °C, 6 hr.; *ii.* H_2, Pd/C, 40 °C, overnight, 24% over two steps; b). bpy in MeOH, 60 °C, 72%; c). **25**, in H_2O, 80 °C, 16 h, 38%.

2.2.2 2-*O* substitution

Demonstrations of the covalent modification of the 2-O position of D-glucose with an alkyl-based linker have been given by Dumas *et. al* and Patray and coworkers.[11, 22] Both groups chose a similar approach starting from methyl 3,5,6-*tri*-*O*-benzyl-*α/β*-D-glucofuranoside followed by installment of the linker and subsequent deprotection of the protection groups using dihydrogen and palladium on carbon. Sulfur based linkers however, poisoned the palladium catalysts which made removal of the benzyl protecting groups impossible following this approach.[13, 23] Other methods to remove benzyl groups, such as Birch reductions, have been reported to cleave thioethers.[24] Therefore all described approaches for the functionalization of the *O*-2 position in D-glucose with a metal-binding moiety, including the glucofuranoside approach described by Schubiger or Lippard, or the approach *via* a benzylorthoacetate intermediate described by Miao *et. al.*[25] were found unsuitable for thioether-containing compounds.

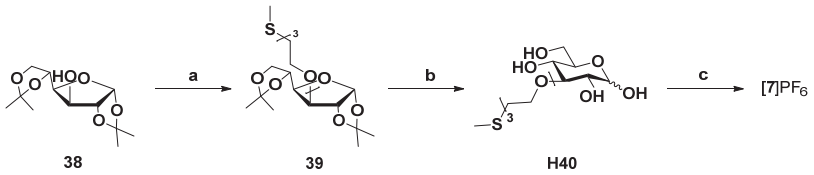
We therefore devised a new protecting group strategy improving the 10-step, 5% yield procedure published by Lippard et al,[11] and employing the α-oxirane method developed by the group of Danishefsky[26] and attempted by Dumas *et. al* (Scheme 2.5).[22] Using this method, D-glucal was protected using the *p*-methoxy benzyl (PMB) group, affording **34**. Treatment of this compound with freshly prepared dimethyldioxirane (DMDO) afforded its corresponding 1,2-anhydrosugar which was then condensed with *p*-methoxy benzyl alcohol (PMB-OH) in the presence of anhydrous $ZnCl_2$ in THF, afforded β-substituted **35** while simultaneously liberating the 2-*O* position. This compound was then treated with tosylate **32** (Scheme 2.5) for the installment of the thioether moiety. This conversion proceeded smoothly, which is in contrast to the observation of Schubiger et al who had to divert to the furanoside approach due to difficulties encountered during the installment of their iminodiacetic acid based spacer.[22] With compound **36** in hand, a recently described method[27] employing a catalytic amount of 37% hydrochloric acid in hexafluoroisopropanol (HFIP) was used to remove all four PMB groups simultaneously. After quenching the reaction using Et_3N an intermediate species was observed (m/z = 463.4 found, 463.2 calculated) corresponding to the desired product **H37** and a PMB group. This same intermediate was also observed in the presence of a mild reducing agent such as Et_3SiH. However, when this intermediate was treated with $MeNH_2$ in MeOH,[28] the methyl thioether could be liberated, acquiring hemiacetal **H37** in five steps (18% overall yield). After reaction of this compound with $[Ru(tpy)(bpy)(H_2O)](PF_6)_2$ glycoconjugate $[Ru(tpy)(bpy)(\mathbf{37})]PF_6$, ($[\mathbf{6}]PF_6$) was acquired instead of $[Ru(tpy)(bpy)(\mathbf{H37})](PF_6)_2$. This is most likely due to the relatively protic nature of the anomeric proton, resulting in deprotonation during purification on Sephadex and replacement of one of the PF_6 counterions by the 'charged' deprotonated glucose species as interpreted by elemental analysis. On mass however, only the +2 species is observed, indicating that reprotonation occurs in solution. This behavior was observed for all hemiacetal glucose derivatives.



Scheme 2.5. a). **19**, TsCl, Et_3N in DCM, 0 °C to rt, 16 h, 92%; b). PMB-Cl, NaH in DMF, 0° C to rt, 16 h, 84%; c). *i.* DMDO (0.088M in acetone) in DCM, 0 °C to rt, 3 h; *ii.* PMB-OH, $ZnCl_2$ in THF, -78 °C to rt, 16 h, 39% over two steps; d). **32**, NaH in DMF, 0 °C to rt, 6 h, 80%; e). *i.* cat. HCl in HFIP/DCM, 5 min; *ii.* $MeNH_2$ in MeOH/H_2O, 60 °C, 30 min, 67%; f). [Ru(tpy)(bpy)(H_2O)](PF_6)$_2$ in acetone/H_2O, 80 °C, 24 h, 36%.

2.2.3 3-*O* substitution

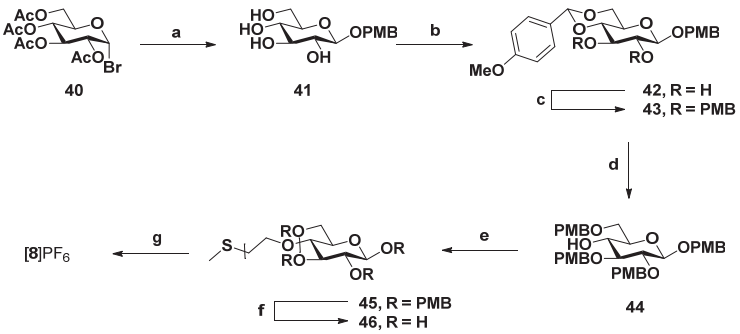
The most straightforward thioether functionalization in these series of ligands was the modification of the 3-*O* position of D-glucose. Starting from diacetone glucose **38** (Scheme 2.6),[29] the thioether moiety was installed using **32** (Scheme 2.5), affording compound **39**, which was subsequently hydrolyzed using Amberlite® IR-120 H^+, affording **H40** in 42% overall yield. Glycoconjugation of **H40** with [Ru(tpy)(bpy)Cl]Cl gave [Ru(tpy)(bpy)(40)]PF_6 ([**7**]PF_6).



Scheme 2.6. a). **32**, NaH in DMF, 0 °C to rt, 16 h, 91%; b). Amberlite IR-120 H^+ in H_2O, 60 °C, 24 h, 46% ; c). [Ru(tpy)(bpy)Cl]Cl in H_2O, 80 °C, 16 h, 37%.

2.2.4 4-*O* substitution

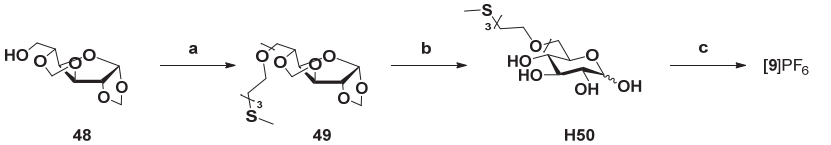
The 4-*O* position of D-glucose was modified starting from acetobromo-α-D-glucose **40** (Scheme 2.7). Using a procedure first described by Kaji et. al., this building block was converted *in situ* to its anomeric iodide, followed by a Koenigs-Knorr type glycosylation with *p*-methoxy benzyl alcohol as an acceptor and Ag_2CO_3 as a base.[30] De-*O*-acetylation furnished intermediate **41**, followed by 4,6-*O*-benzylidenation and installment of PMB groups affording fully protected **43**. With this building block in hand, a reductive opening using $NaCNBH_3$ and TFA, liberated the 4-*O* position, which could then be alkylated *via* a Williamson etherification using **32** described in the previous sections, affording **45**. Global deprotection was achieved by treatment with HFIP/HCl, which gave thioether ligand **H46** in 11% overall yield. The subsequent reaction of **H46** with [Ru(tpy)(bpy)(H_2O)](PF_6)$_2$, afforded glycoconjugate [Ru(tpy)(bpy)(46)]PF_6 ([**8**]PF_6). The synthesis of **H46** was also attempted via an alternative approach using α-methyl glucose following a similar protecting group strategy. However, this proved to be unsuccessful due to the inertness of the anomeric methyl acetal towards acid.



Scheme 2.7. a). *i*. PMB-OH, I_2, Ag_2CO_3 in Et_2O, rt, 24 h,; *ii*. NaOMe in MeOH, rt, 4 h, 72% over two steps; b). α,α,4-Trimethoxytoluene, cat. *p*-TsOH.H_2O in DMF, 60 °C, 16 h, 89%; c). PMB-Cl, NaH in DMF, 0 °C to rt, 78%; d). $NaCNBH_3$, TFA in DMF, 0 °C to rt, 16 h, 95%; e). **32**, NaH in DMF, 0 °C to rt, 6 h, 78%; f). cat. HCl in HFIP/DCM, 30 min, 29%; g). [Ru(tpy)(bpy)Cl]Cl in H_2O, 80 °C, 64%.

2.2.5 6-*O* substitution

Finally, the 6-*O* position of D-glucose was easily modified starting from dimethyl glucose **48** (Scheme 2.8),[31] which could be converted to **49** using a Williamson etherification with tosylate **32**, followed by acid hydrolysis using dilute hydrochloric acid affording methyl thioether **H50** in 55% over two steps. Glycoconjugation with [Ru(tpy)(bpy)Cl]Cl afforded [Ru(tpy)(bpy)(50)]PF_6 ([**9**]PF_6).



Scheme 2.8. a). **31**, NaH in DMF, 0 °C to rt, 3 h, 78%; b). 2M HCl in H_2O, 60 °C, 1 h, 70%; c). [Ru(tpy)(bpy)Cl]Cl in H_2O, 80 °C, 16 h, 17%.

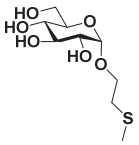
2.3 Conclusion

In this work, we have presented efficient and robust routes to all positional isomers of D-glucose bearing a thioether ligand bound to a light-cleavable ruthenium(II) polypyridyl complex. The general protecting-deprotecting group strategy presented in this work is compatible with compounds bearing donor atoms such as sulfur, as no transition metals catalysts were used until final coordination to the functional ruthenium compound. These routes could possibly be extended to application with other functionalized ligands, such as carboxylates, amines, or pyridines. The study of this library of ruthenium(II) glycoconjugates might shed light on the influence of the stereochemistry of glucose functionalization on GLUT-mediated uptake and the metabolism of the ruthenium-glucose conjugates by enzymes such as hexokinase II.

2.4 Experimental

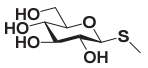
2.4.1 General

Reagents were purchased from Sigma-Aldrich and used without further purification. 2,2′:6′,2′′-Terpyridine (tpy) was ordered from ABCR GmbH & Co. Dry solvents were collected from a Pure Solve MD5 solvent dispenser from Demaco. For all inorganic reactions solvents were deoxygenated by bubbling dinitrogen through the solution for 30 minutes. All organic reactions were carried out under a diniotrogen atmosphere at rt. Flash chromatography was performed on silica gel (Screening devices B.V.) with a particle size of 40 - 64 µM and a pore size of 60 Å. TLC analysis was conducted on TLC aluminium foils with silica gel matrix (Supelco, silica gel 60, 56524) with detection by UV-absorption (254 nm), by spraying with 10% H_2SO_4 in ethanol or with a solution of $NH_4Mo_7O_{24}.4H_2O$ 25 g/L, $NH_4CeSO_4.H_2O$ 10 g/L, 10% H_2SO_4 in H_2O, followed by charring at ~250 °C on a heating plate. Optical rotation measurements were performed on a Propol automated polarimeter (sodium D-line, λ = 589 nm) with a concentration of 10 mg/mL (c = 1) unless stated otherwise. Infrared spectra were recorded on a Perkin Elmer UATR (Single Reflection Diamond) Spectrum Two device (4000-700 cm^{-1}; resolution 4 cm^{-1}). ^{1}H NMR and ^{13}C NMR were recorded in CD_3OD and $CDCl_3$ with chemical shift (δ) relative to the solvent peak on a Bruker AV 400 or AV 500. High resolution mass spectra were recorded by direct injection (2 µl of 2 µM solution in water/acetonitrile; 50/50; v/v and 0.1% formic acid) in a mass spectrometer (Thermo Finnigan LTQ Orbitrap) equipped with an electrospray 250 °C) with resolution R = 60,000 at m/z 400 (mass range m/z = 150 – 2000) and dioctylphtalate (m/z = 391.28428) as a lock mass. The high-resolution mass spectrometer was calibrated prior to measurements with a calibration mixture (Thermo Finnigan). Combustion analysis for glycoconjugates [**1**]$(PF_6)_2$ - [**5**]$(PF_6)_2$, [**6**]PF_6 - [**10**]PF_6, and [**11**]$(PF_6)_2$ was performed at Mikrolab Kolbe Germany.

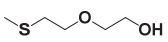


(2-Methylthio)ethyl-α-D-glucopyranoside, 13: 2,3,4,6-Tetra-*O*-acetyl-(2-bromo)ethyl-α-D-glucopyranoside[16] (135 mg, 0.297 mmol) was dissolved in dry DMF (3 mL) and to this solution was added fresh NaSMe (23 mg, 0.33 mmol). The reaction was stirred overnight after which it was diluted with EtOAc (25 mL), washed with water (2x), aq. $NaHCO_3$ (2x), and dried (Na_2SO_4). Concentration *in vacuo* was followed by purification of the residue by silica column chromatography (10% MeOH in DCM), affording the title compound (50.0 mg, 0.197 mmol, 66% over two steps) as a colorless oil. R_f = 0.84 (20% MeOH in DCM); IR (neat): 3350, 2918, 1639, 1426, 1018; ^{1}H NMR (400 MHz, CD_3OD) δ = 4.80 (d, *J* = 3.8 Hz, 1H, H-1), 3.91 – 3.75 (m, 2H, C*H*H H-6, C*H*H OCH_2), 3.69 – 3.58 (m, 4H, H-4, H-5, C*H*H H-6, C*H*H OCH_2), 3.37 (dd, *J* = 9.7, 3.8 Hz, 1H, H-2), 3.25 (d, *J* = 9.3 Hz, 1H, H-3), 2.73 (td, *J* = 6.9, 1.8 Hz, 2H, O*CH*$_2$SMe), 2.12 (s, 3H, OCH_2S*Me*). ^{13}C NMR (101 MHz, CD_3OD) δ = 100.3 (C-1),

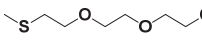
75.1 (C-4), 73.9 (C-5), 73.5 (C-2), 71.8 (C-3), 68.4 (O*C*H_2), 62.7 (C-6), 34.3 (O*C*H_2SMe), 15.8 (OCH$_2$S*Me*); HRMS: m/z calcd for $[C_9H_{18}O_6S + Na]^+$: 277.07163; found: 277.07108.



Methylthio-β-D-glucopyranoside, 15: α/β-D-Glucose pentaacetate (4.99 g, 12.4 mmol) was dissolved in anhydrous DCM (20 mL) and to this solution was added I_2 (4.84 g, 19.0 mmol) and Et_3SiH (2.90 mL, 18.2 mmol) this mixture was allowed to stir for 10 minutes after which it was diluted with DCM (100 mL) and washed with aqueous saturated $Na_2S_2O_3$ (1x) and Na_2CO_3 (1x). Layers were separated, the organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. The crude was coevaporated with toluene (3x) and redissolved in dry MeCN (20 mL), followed by the addition of thiourea (1.46 g, 19.2 mmol). The mixture was then heated for 30 minutes at 80 °C, concentrated *in vacuo*, followed by purification of the residu over silica (0 to 50% Et_2O in PE) yielding methyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside as a yellow foam (2.71 g, 7.24 mmol). This compound was then dissolved in dry MeOH (70 mL) followed by the addition of a catalytic amount of NaOMe, which after stirring overnight was quenched upon the addition of Amberlite IR-120 H^+. Filtration was followed by concentration *in vacuo*, yielding the title compound as a colourless oil (1.48 g, 7.04 mmol, 57% over four steps). R_f = 0.63 (20% MeOH in DCM); IR (neat): 3336, 2923, 2881, 1425, 1017; ^{1}H NMR (400 MHz, CD_3OD) δ = 4.35 (d, *J* = 9.6 Hz, 1H, H-1), 3.93 (d, *J* = 11.8 Hz, 1H, C*H*H H-6), 3.77 – 3.68 (m, 1H, C*H*H H-6), 3.48 – 3.35 (m, 3H, H-3, H-4, H-5), 3.31 (t, *J* = 9.1 Hz, 1H, H-2), 2.26 (s, 3H, S*Me*). ^{13}C NMR (101 MHz, CD_3OD) δ = 87.1 (C-1), 81.8 (C-3), 79.3 (C-4), 73.5 (C-2), 71.3 (C-5), 62.7 (C-6), 12.0 (S*Me*). HRMS: m/z calcd for $[C_7H_{14}O_5S + Na]^+$: 233.04542; found: 233.04442.

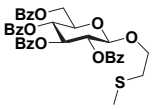


2-(Methylthio)ethoxy)ethanol, 18: To a flame-dried round-bottom flask was added freshly prepared NaSMe[32] (1.21 g, 15.5 mmol) under argon. Deoxygenated THF (50 mL) was added, followed by the addition of 2-(2-(2-chloroethoxy)ethanol (1.50 mL, 14.2 mmol). This solution was heated at 60 °C for 6 h, after which it was allowed to cool to room temperature. The mixture was diluted with EtOAc (100 mL) and washed with aqueous $NaHCO_3$ (2x) and water (1x). Layers were separated, the organic layer was dried (Na_2SO_4) and concentrated *in vacuo* affording a slightly yellowish oil (1.89 g, 13.9 mmol, 89%). IR (neat): 3480, 2907, 2866, 1611, 1512; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.68 (m, 2H, CH_2), 3.62 (t, *J* = 6.7 Hz, 2H, CH_2), 3.54 (d, *J* = 5.1 Hz, 2H, CH_2), 2.94 – 2.81 (s, 1H, OH), 2.66 (t, *J* = 6.6 Hz, 2H, -S*C*H_2), 2.10 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 72.1 (*C*H_2), 69.9 (*C*H_2), 61.5 (*C*H_2), 33.6 (S*C*H_2), 15.8 (S*C*H_3); HRMS: m/z calcd for $[C_5H_{12}O_2S + Na]^+$: 159.04502; found: 159.04566.

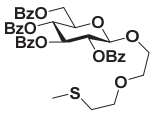


2-[2-(2-(Methylthio)ethoxy)ethoxy]ethanol, 19: The procedure was followed as described for **18** using NaSMe[32] (4.23 g, 60.4 mmol) and 2-(2-(2-chloroethoxy)ethoxy)ethanol (10.0 g, 59.3 mmol). **19** was afforded as a colourless oil (9.25

g, 51.0 mmol, 85%). IR (neat): 3427, 2915, 2869, 1105, 1063; ^{1}H NMR: (400 MHz, $CDCl_3$) δ = 3.61 – 3.42 (m, 10H, 5 x CH_2), 3.09 (s, 1H, -OH), 2.60 – 2.50 (m, 2H, 1 x CH_2), 2.03 – 1.94 (s, 3H, CH_3). ^{13}C NMR: (100 MHz, $CDCl_3$) δ = 72.4 (-*C*H_2), 70.2 (*C*H_2), 70.1 (*C*H_2), 70.0 (*C*H_2), 61.3 (*C*H_2) 33.13 (-S*C*H_2), 15.7 (-S*C*H_3). HRMS: m/z calcd for $[C_7H_{16}O_3S + Na]^+$: 203.07124; found: 203.07134.

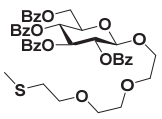


(2-Methylthio)ethyl 2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranoside, 21: *2,3,4,6*-Tetra-*O*-benzoyl-β-D-glucopyranosyl trichloroacetimidate[33] (370 mg, 0.364 mmol) and 2-(methylthio)ethanol (100 µL, 1.15 mmol) were coevaporated three times with anhydrous toluene after which they were dissolved in anhydrous DCM (36 mL). Freshly activated 4 Å molsieves were added, and the mixture was allowed to stir for 15 minutes after which a catalytic amount of TMSOTf (20.0 µL, 111 µmol) was added. After stirring for 4 h at room temperature, the reaction was quenched upon the addition of Et_3N (100 µL, 0.714 mmol) and concentrated *in vacuo* followed by purification of the residue over silica (10% to 50% EtOAc in PE), affording the title compound as a clear oil (270 mg, 0.410 mmol, 81%). R_f = 0.74 (30% EtOAc in PE); IR (neat): 3064, 2922, 2853, 1720, 1258; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.07 – 8.02 (m, 2H, H_{arom}), 8.00 – 7.96 (m, 2H, H_{arom}), 7.94 – 7.90 (m, 2H, H_{arom}), 7.87 – 7.81 (m, 2H, H_{arom}), 7.60 – 7.25 (m, 12H, H_{arom}), 5.93 (t, *J* = 9.7 Hz, 1H, H-3), 5.70 (t, *J* = 9.7 Hz, 1H, H-4), 5.56 (dd, *J* = 9.8, 7.8 Hz, 1H, H-2), 4.93 (d, *J* = 7.8 Hz, 1H, H-1), 4.67 (dd, *J* = 12.2, 3.2 Hz, 1H, C*H*H H-6), 4.52 (dd, *J* = 12.1, 5.4 Hz, 1H, C*H*H H-6), 4.19 (ddd, *J* = 8.6, 5.4, 3.2 Hz, 1H, H-5), 4.09 (dt, *J* = 10.2, 6.7 Hz, 1H, C*H*H OCH_2), 3.78 (dt, *J* = 10.3, 7.3 Hz, 1H, C*H*H OCH_2), 2.67 (t, *J* = 6.9 Hz, 2H, C*H*$_2$SMe), 2.01 (s, 3H, CH_2S*Me*). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 166.2 (C=O Bz), 165.9 (C=O Bz), 165.3 (C=O Bz), 165.2 (C=O Bz), 133.6 (C_H Arom), 133.4 (C_H Arom), 133.3 (C_H Arom), 129.9 (C_H Arom), 129.9 (C_H Arom), 129.9 (C_H Arom), 129.8 (C_H Arom), 129.7 (C_q Arom), 129.4 (C_q Arom), 128.9 (C_q Arom), 128.8 (C_q Arom), 128.5 (C_H Arom), 128.5 (C_H Arom), 128.5 (C_H Arom), 128.4 (C_H Arom), 101.4 (C-1), 73.0 (C-3), 72.4 (C-5), 71.9 (C-2), 69.8 (C-4), 69.8 (O*C*H_2) 63.2 (C-6), 33.4 (*C*H_2SMe), 16.1 (CH_2S*Me*); HRMS: m/z calcd for $[C_{37}H_{34}O_{10}S + NH_4]^+$: 688.22109; found: 688.22223.

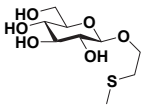


[2-(2-(Methylthio)ethoxy)]ethyl 2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranoside, 22: The general procedure described for **21** was followed, with *2,3,4,6*-tetra-*O*-benzoyl-β-D-glucopyranosyl trichloroacetimidate (6.00 g, 8.14 mmol) and 2-(2-(methylthio)ethoxy)ethanol (1.24 g, 9.10 mmol). Purification of the residue by silica column purification (0 – 25% EtOAc in PE) afforded the title compound as a clear oil (3.86 g, 5.40 mmol, 66%). R_f = 0.34 (33% EtOAc in PE); IR (neat): 3064, 2919, 1722, 1602, 1249; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.05 – 8.01 (m, 2H, H_{arom}), 8.00 – 7.96 (m, 2H, H_{arom}), 7.93 – 7.88 (m, 2H, H_{arom}), 7.86 – 7.81 (m, 2H, H_{arom}), 7.58 – 7.24 (m, 12H, H_{arom}), 5.92 (t, *J* = 9.7 Hz, 1H, H-3), 5.69 (t, *J* = 9.7 Hz, 1H, H-4), 5.54 (dd, *J* = 9.9, 7.7 Hz, 1H, H-2), 4.99 (d, *J* = 7.8 Hz, 1H, H-1), 4.65 (dd, *J* = 12.1, 3.2 Hz, 1H,

C*H*H 6-H), 4.51 (dd, *J* = 12.1, 5.1 Hz, 1H, C*H*H 6-H), 4.18 (ddd, *J* = 10.1, 5.2, 3.1 Hz, 1H, H-5), 4.00 (dt, *J* = 11.4, 4.1 Hz, 1H, C*H*H OCH_2), 3.81 (ddd, *J* = 11.1, 6.9, 3.8 Hz, 1H, C*H*H OCH_2), 3.58 (dt, *J* = 6.7, 3.7 Hz, 2H, OCH_2), 3.48 (t, *J* = 6.7 Hz, 2H, OCH_2), 2.44 (t, *J* = 6.7 Hz, 2H, CH_2SMe), 2.03 (s, 3H, CH_2S*Me*). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 166.3 (C=O Bz), 165.9 (C=O Bz), 165.3 (C=O Bz), 165.2 (C=O Bz), 133.6 (C_H Arom), 133.4 (C_H Arom), 133.3 (C_H Arom), 129.9 (C_H Arom), 129.9 (C_H Arom), 129.9 (C_H Arom), 129.9 (C_H Arom), 129.7 (C_q Arom), 129.4 (C_q Arom), 128.9 (C_q Arom), 128.9 (C_q Arom), 128.5 (C_H Arom), 128.5 (C_H Arom), 128.4 (C_H Arom), 101.4 (C-1), 73.0 (C-3), 72.3 (C-5), 72.0 (C-2), 70.6 (O*C*H_2), 70.2 (O*C*H_2) , 69.8 (C-4), 69.4 (O*C*H_2), 63.2 (C-6), 33.5 (*C*H_2SMe), 16.1 (CH_2S*Me*); HRMS: m/z calcd for $[C_{39}H_{38}O_{11}S+ NH_4]^+$: 732.24731; found: 732.24836.

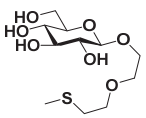


2-[2-(2-(Methylthio)ethoxy)ethoxy]ethyl 2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranoside, 23: The general procedure described for **21** was followed, with *2,3,4,6*-tetra-*O*-benzoyl-β-D-glucopyranosyl trichloroacetimidate[33] (2.65 g, 3.58 mmol) and **19** (792 mg, 4.39 mmol). Purification of the residue over silica (10% to 50% EtOAc in PE) afforded the title compound as a clear oil (2.32 g, 3.06 mmol, 85%). R_f = 0.16 (20% EtOAc in PE); $[\alpha]_D^{20}$ ($CHCl_3$): +18.0 ; IR (neat): 3063, 2918, 2869, 1722, 1451; ^{1}H-NMR: (400 MHz, $CDCl_3$) δ = 8.03 (d, J = 8.6 Hz, 2H, H_{arom}), 7.97 (d, J = 8.6 Hz, 2H, H_{arom}), 7.90 (d, J = 8.7 Hz, 2H, 2H, H_{arom}), 7.83 (d, J = 8.6 Hz, 2H, H_{arom}), 7.58 – 7.43 (m, 3H, H_{arom}), 7.43 – 7.29 (m, 7H, H_{arom}), 7.29 – 7.21 (m, 2H, H_{arom}), 5.93 (t, J = 9.7 Hz, 1H, H-3), 5.70 (t, J = 9.7 Hz, 1H, H-4), 5.55 (dd, J = 9.7, 7.8 Hz, 1H, H-2), 5.01 (d, J = 7.8 Hz, 1H, H-1), 4.66 (dd, J = 12.1, 3.1 Hz, 1H, CH*H* H-6), 4.51 (dd, J = 12.1, 5.1 Hz, 1H, CH*H* H-6), 4.20 (ddd, J = 9.9, 5.1, 3.1 Hz, 1H, H-5), 4.03 – 3.95 (m, 1H, CH*H* –OCH_2), 3.83 (m, 1H, CH*H* –OCH_2), 3.69 – 3.56 (m, 2H, -OCH_2), 3.55 (t, J = 6.9 Hz, 2H, -OCH_2), 3.50 – 3.42 (m, 2H, -OCH_2), 3.37 (t, J = 4.6 Hz, 2H, -OCH_2), 2.64 (t, J = 6.9 Hz, 2H, -CH_2SMe), 2.11 (s, 3H, -S*CH*$_3$). ^{13}C NMR: (101 MHz, CD_3OD) δ = 166.1 (C=O Bz), 165.8 (C=O Bz), 165.2 (C=O Bz), 165.1 (C=O Bz), 133.5 (CH Arom), 133.3 (CH Arom), 133.2 (CH Arom), 129.8 (CH Arom), 129.8 (CH Arom), 129.6 (C_q Arom), 129.4 (C_q Arom), 128.8 (C_q Arom), 128.4 (CH Arom), 128.4 (CH Arom), 101.3 (C-1), 73.0 (C-3), 72.2 (C-5) 72.0 (C-2), 70.7 (O*C*H_2), 70.5 (O*C*H_2), 70.2 (O*C*H_2), 69.8 (C-4), 69.4 (O*C*H_2), 63.2 (O*C*H_2), 33.4 (*C*H_2SMe), 16.0 (CH_2S*Me*). HRMS: m/z calcd for $[C_{41}H_{42}O_{12}S + Na]^+$: 781.22892; found: 781.22795.

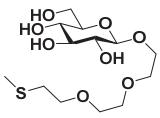


(2-Methylthio)ethyl-β-D-glucopyranoside, 24: The protected glucoside **23** (240 mg, 0.410 mmol) was dissolved in MeOH (6 mL) after which a catalytic amount of NaOMe was added. The solution was allowed to stir for 16 h, after which Amberlite IR-120 H^+ was added, until neutral pH. The resin was filtered off and the mixture was concentrated *in vacuo*. Purification of the residue over silica (0 to 10% MeOH in DCM) afforded the title compound as a colorless oil (80.0 mg, 0.315 mmol, 88%). R_f = 0.15 (5% MeOH in DCM); IR (neat): 3351, 2919, 2881, 1072, 1016; ^{1}H NMR (400 MHz, CD_3OD) δ = 4.30 (d, *J* = 7.8 Hz, 1H, H-1), 4.03 (dt, *J* = 10.1, 7.1 Hz, 1H, C*H*H OCH_2), 3.87 (dd,

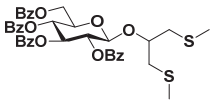
J = 11.9, 1.8 Hz, 1H, C*H*H 6), 3.74 (dt, *J* = 10.1, 7.1 Hz, 1H, C*H*H OCH_2), 3.69 – 3.64 (m, 1H, C*H*H 6), 3.39 – 3.33 (m, 1H, 4), 3.29 – 3.26 (m, 2H, 3, 5), 3.21 – 3.15 (m, 1H, 2), 2.73 (t, *J* = 7.1 Hz, 2H, CH_2SMe), 2.13 (s, 3H, CH_2SMe). ^{13}C NMR (101 MHz, CD_3OD) δ = 104.4 (1), 77.9 (3), 77.9 (4), 75.0 (2), 71.6 (5), 70.0 (OCH_2), 62.7 (6), 34.3 (CH_2SMe), 15.7 (CH_2SMe); HRMS m/z calcd for $[C_9H_{18}O_6S + Na]^+$: 277.07136; found: 277.07160.



[2-(2-(Methylthio)ethoxy)]-ethyl-β-D-glucopyranoside, 25: The procedure as described for **24** was followed, using protected glycoside **22** (560 mg, 0.780 mmol) and THF/MeOH (10 mL, 1:1). Purification of the crude over silica (0 to 20% acetone in DCM) afforded the title compound as a white solid (200 mg, 0.670 mmol, 86%). R_f = 0.19 (10% acetone in DCM); IR (neat): 3304, 2919, 1075, 1354, 1028; ^{1}H NMR (400 MHz, CD_3OD) δ = 4.31 (d, *J* = 7.8 Hz, 1H, 1), 4.05 – 3.96 (m, 1H, C*H*H OCH_2), 3.87 (dd, *J* = 11.9, 1.8 Hz, 1H, C*H*H 6), 3.78 – 3.62 (m, 6H, C*H*H 6, C*H*H OCH_2, 2 x OCH_2), 3.40 – 3.25 (m, 3H, 3, 4, 5), 3.19 (dd, *J* = 9.3, 7.5 Hz, 1H, 2), 2.68 (t, *J* = 6.8 Hz, 2H, CH_2SMe), 2.13 (s, 3H, CH_2SMe). ^{13}C NMR (101 MHz, CD_3OD) δ = 104.4 (1), 78.0 (3), 78.0 (4), 75.1 (2), 71.6 (5), 71.5 (OCH_2), 71.2 (OCH_2), 69.7 (OCH_2), 62.8 (6), 34.2 (CH_2SMe), 15.8 (CH_2SMe). HRMS: m/z calcd for $[C_{11}H_{22}O_7S + Na]^+$: 321.09784; found: 321.09760.

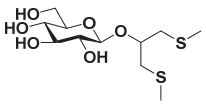


2-[2-(2-(Methylthio)ethoxy)ethoxy]ethyl β-D-glucopyranoside, 26: The protected glucoside **23** (973 mg, 1.28 mmol) was dissolved in MeOH (10 mL) after which a catalytic amount of NaOMe was added. The solution was allowed to stir for 16 h, after which Amberlite IR-120 H^+ was added, until reaching neutral pH. The resin was filtered off and the mixture was concentrated *in vacuo*. Purification of the residue over silica (0 - 10% MeOH in DCM) afforded the title compound as a colorless oil (400 mg, 1.17 mmol, 91%). R_f = 0.29 (10% MeOH in DCM): $[\alpha]_D^{20}$ (MeOH): -10.0; IR: 3371, 2915, 2874, 1073, 1031; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.35 (d, J = 7.8 Hz, 1H, 1), 4.06 (ddd, J = 10.2, 5.0, 3.0 Hz, 1H, C*H*H OCH_2), 3.90 (dd, J = 11.9, 1.7 Hz, 1H, C*H*H OCH_2), 3.82 – 3.65 (m, 10H, C*H*H OCH_2, 5, 6, 3 x CH_2 OCH_2), 3.45 – 3.37 (m, 1H, 3), 3.37 – 3.28 (m, 1H, 4), 3.24 (dd, J = 9.1, 7.8 Hz, 1H, 2), 2.72 (t, J = 6.8 Hz, 2H, -O*CH*$_2$), 2.17 (s, 3H, -S*CH*$_3$). ^{13}C NMR (101 MHz, CD_3OD) δ = 104.4 (1), 77.9 (3), 75.0 (4), 71.6 (OCH_2), 71.5 (5), 71.5 (2 x OCH_2), 71.1 (OCH_2), 69.6 (OCH_2), 62.7 (6), 34.2 (CH_2SMe), 15.9 (CH_2SMe). HRMS m/z calcd for $[C_{13}H_{30}O_8S + Na]^+$: 365.12406; found: 365.12376

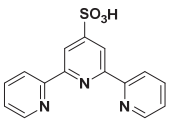


[1,3-Bis(methylthio)]-propyl-2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranoside, **27**: The general procedure described for **21** was followed, with *2,3,4,6*-tetra-*O*-benzoyl-β-D-glucopyranosyl trichloroacetimidate (5.00 g, 6.75 mmol) and 1,3-bis(methylthio)propanol (830 µL, 6.09

mmol). Purification of the residue by silica column purification (0 – 20% EtOAc in PE) afforded the title compound as a clear oil (3.95 g, 5.40 mmol, 90%). R_f = 0.55 (20% EtOAc in PE); IR (neat): 2919, 2853, 1722, 1601, 1259; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.07 – 8.00 (m, 2H, H_{arom}), 7.99 – 7.94 (m, 2H, H_{arom}), 7.91 (d, *J* = 7.8 Hz, 2H, H_{arom}), 7.85 – 7.79 (m, 2H, H_{arom}), 7.60 – 7.24 (m, 12H, H_{arom}), 5.91 (t, *J* = 9.7 Hz, 1H, H-3), 5.65 (t, *J* = 9.7 Hz, 1H, H-4), 5.52 (dd, *J* = 10.1, 7.7 Hz, 1H, H-2), 5.09 (d, *J* = 7.9 Hz, 1H, H-1), 4.67 (dd, *J* = 12.1, 3.1 Hz, 1H, C*H*H H-6), 4.48 (dd, *J* = 12.2, 5.6 Hz, 1H, C*H*H H-6), 4.18 (ddd, *J* = 9.3, 5.7, 3.0 Hz, 1H, H-5), 4.04 – 3.91 (m, 1H, C*H*($CH_2SMe)_2$), 2.86 (dd, *J* = 13.8, 4.4 Hz, 1H, C*H*H CH($CH_2SMe)_2$), 2.81 – 2.71 (m, 2H, CH_2 CH($CH_2SMe)_2$), 2.61 (td, *J* = 13.5, 7.4 Hz, 1H, C*H*H CH($CH_2SMe)_2$), 2.06 (s, 3H, S*Me*), 1.90 (s, 3H, S*Me*). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 166.2 (C=O Bz), 165.9 (C=O Bz), 165.4 (C=O Bz), 165.3 (C=O Bz), 133.6 (C_H Arom), 133.4 (C_H Arom), 133.4 (C_H Arom), 133.3 (C_H Arom), 130.0 (C_H Arom), 129.9 (C_H Arom), 129.9 (C_H Arom), 129.9 (C_H Arom), 129.6 (C_q Arom), 129.5 (C_q Arom), 128.9 (C_q Arom), 128.8 (C_q Arom), 128.6 (C_H Arom), 128.4 (C_H Arom), 101.7 (C-1), 80.2 (*C*H($CH_2SMe)_2$), 73.0 (C-3), 72.4 (C-5), 72.1 (C-2), 69.9 (C-4), 63.2 (C-6), 38.4 (*C*H_2 CH($CH_2SMe)_2$), 37.8 (*C*H_2 CH($CH_2SMe)_2$), 16.7 (2 x S*Me*); HRMS m/z calcd for $[C_{39}H_{38}O_{10}S_2 + NH_4]^+$: 748.22446; found: 748.22543.

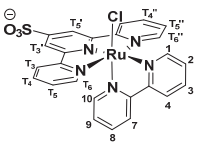


[1,3-bis(methylthio)]-propyl-β-D-glucopyranoside, 28: The procedure as described for **22** was followed, using protected glycoside **27** (3.20 g, 4.38 mmol) and DCM/MeOH (50 mL, 1:50). Purification of the residue over silica (0 to 10% MeOH in DCM) afforded **28** as a white foam (960 mg, 3.05 mmol, 70%). R_f = 0.24 (100% EtOAc); IR (neat): 3368, 2916, 1424, 1071, 1016; ^{1}H NMR (400 MHz, CD_3OD) δ = 4.45 (d, *J* = 7.8 Hz, 1H, H-1), 4.06 (p, *J* = 5.8 Hz, 1H, C*H*($CH_2SMe)_2$), 3.90 – 3.83 (m, 1H, C*H*H H-6), 3.70 – 3.63 (m, 1H, C*H*H H-6), 3.41 – 3.33 (m, 1H, H-3), 3.33 – 3.26 (m, 2H, H-4, H-5), 3.24 – 3.14 (m, 1H, H-2), 2.94 – 2.83 (m, 3H, C*H*H, CH_2 CH($CH_2SMe)_2$), 2.79 (dd, *J* = 13.8, 5.6 Hz, 1H, C*H*H CH($CH_2SMe)_2$), 2.15 (s, 6H, 2 x S*Me*). ^{13}C NMR (101 MHz, CD_3OD) δ = 104.1 (C-1), 79.4 (*C*H($CH_2SMe)_2$), 77.9 (C-3), 77.9 (C-4), 75.2 (C-2), 71.5 (C-5), 62.7 (C-6), 39.0 (CH_2 CH($CH_2SMe)_2$) 37.9 (CH_2 CH($CH_2SMe)_2$), 16.6 (S*Me*), 16.4 (S*Me*); HRMS m/z calcd for $[C_{11}H_{22}O_6S_2 + Na]^+$: 337.07500; found: 337.07520

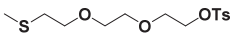


[2,2':6',2''-Terpyridine]-4'-sulfonic acid, 30 (HS-tpy): [2,2':6',2''-terpyridine]-4'(1'*H*)-thione[34] (534 mg, 2.01 mmol) was suspended in acetic acid (6 mL) and to this mixture was added 30% H_2O_2 (1 mL). The resulting purple mixture was heated at 70 °C for 12 h, and concentrated *in vacuo*. The crude was then redissolved in H_2O, followed by the addition of 10% Pd/C (32 mg) and purged with H_2 (5 min). After stirring overnight at 40 °C under a H_2 atmosphere, the reaction was filtered over Celite®, concentrated and purified over silica (0 to 10% MeOH in DCM), affording the title compound as a bright yellow powder. R_f = 0.37 (20% MeOH in DCM); IR (neat): 3391, 3064, 1622, 1398, 1189; ^{1}H NMR (400 MHz, D_2O) δ = 8.09 (dd, *J* = 4.9, 1.9 Hz, 2H, T_3, T_3''), 7.84 (s, 2H, T_3', T_5'), 7.61 (d, *J* = 7.4 Hz, 2H, T_6, T_6''), 7.54 (td,

J = 7.7, 1.9 Hz, 2H, T_4, T_4"), 7.15 (ddd, *J* = 7.4, 5.0, 1.4 Hz, 2H, T_5, T_5"). ^{13}C NMR (101 MHz, D_2O) δ = 154.9 (C_q Arom), 152.7 (C_q Arom), 152.7 (C_q Arom), 148.1 (T_3, T_3") , 138.1 (T_4, T_4"), 124.9 (T_5, T_5") , 121.8 (T_6, T_6"), 116.5 (T_3, T_3"); HRMS m/z calcd for $[C_{15}H_{11}N_3O_3S + H]^+$: 314.05939; found: 314.05999.



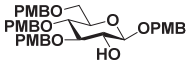
[Ru(S-tpy)(bpy)(Cl)], **31**: Compound **30** (134 mg, 0.426 mmol) was dissolved in MeOH (10 mL) and to this solution was added 100 mg washed Amberlite® Na^+. After stirring for 5 minutes at rt, the ion exchange resin was filtered off and the filtrate was concentrated *in vacuo,* affording a pinkish solid. This compound was then together with *p*-cymene dimer, redissolved in deoxygenated MeOH (5 mL) and heated to 60 °C. A solution of bpy in MeOH (2.3 mL) was then added dropwise over 10 minutes from which the color of the solution changed from purple to red. After stirring for 2 h under nitrogen, the solution was allowed to cool to rt, after which Et_2O (20 mL) was added. The resulting precipitate was filtered and washed with Et_2O (3x) affording a brown powder (185 mg, 0.306 mmol, 72%). R_f = 0.29 (10% MeOH in DCM); HRMS: m/z calcd for $[M]^+$: 605.99351; found: 605.99462.



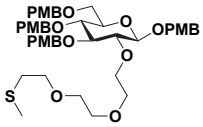
2-(2-(2-(methylthio)ethoxy)ethoxy)ethyl 4-methylbenzenesulfonate, 32: Compound **19** (715 mg, 3.97 mmol) was dissolved in dry DCM (40 mL) and cooled to 0 °C. To this solution were added Et_3N (850 ul, 6.09 mmol) and Ts-Cl (1.12 g, 5.87 mmol). The reaction was allowed to stir overnight after which it was diluted with DCM (100 mL) and transferred to a separatory funnel. After washing with water (1x) and brine (1x), layers were separated, the organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by silica column chromatography (0 to 50% EtOAc in PE) afforded the title compound as a colorless oil (1.22 g, 3.64 mmol, 92%). R_f = 0.78 (50% EtOAc in PE); IR (neat): 2917, 2868, 1598, 1353, 1174; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.73 (d, *J* = 8.3 Hz, 2H, H_{arom}), 7.30 (d, *J* = 8.1 Hz, 2H, H_{arom}), 4.18 – 4.02 (m, 2H, CH_2), 3.65 – 3.61 (m, 2H, CH_2), 3.57 (t, *J* = 6.8 Hz, 2H, CH_2), 3.51 (m, 4H, 2 x CH_2), 2.60 (t, *J* = 6.8 Hz, 2H, CH_2), 2.39 (s, 3H, CH_3 Tosyl), 2.07 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 144.7 (C_q Arom), 132.7 (C_q Arom), 129.7 (C_H Arom), 127.7 (C_H Arom), 70.5 (*C*H_2), 70.4 (*C*H_2), 70.0 (*C*H_2), 69.2 (*C*H_2), 68.5 (*C*H_2), 33.2 (S*C*H_2), 21.5 (*C*H_3 Tosyl), 15.8 (SCH_3); HRMS: m/z calcd for $[C_{14}H_{22}O_5S_2 + Na]^+$: 357.08009; found: 357.08003.

3,4,6-Tri-*O*-(4-methoxybenzyl)-D-glucal, 34: To a cooled solution (0 °C) of D-glucal in dry DMF (230 mL) was slowly added NaH (60% dispersion in mineral oil, 3.10 g, 77.5 mmol) followed by the addition of 4-methoxybenzyl chloride (10.1 mL, 74.5 mmol). After stirring overnight under a dinitrogen atmosphere, H_2O (10 mL) was added and the mixture was allowed to stir for another 10 minutes. The mixture was further diluted with EtOAc (200 mL) and transferred to a separatory funnel, washed with

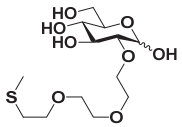
water (3x) and brine (3x). The organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. Purification by silica column chromatography (0 to 15% EtOAc in PE) afforded **34** (9.82 g, 19.4 mmol, 84%) as a clear oil that solidified upon standing over a longer time. R_f = 0.66 (10% EtOAc in PE); IR (neat): 2999, 2863, 2907, 1647, 1512; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.16 (d, *J* = 8.3 Hz, 4H, H_{arom}), 7.04 (d, *J* = 8.5 Hz, 2H, H_{arom}), 6.75 (dd, *J* = 11.9, 8.1 Hz, 6H, H_{arom}), 6.31 (d, *J* = 6.2 Hz, 1H, H-1), 4.74 (dd, *J* = 6.2, 3.2 Hz, 1H, H-2), 4.64 (d, *J* = 10.9 Hz, 1H, C*H*H PMB), 4.52 – 4.35 (m, 5H, C*H*H PMB, 2 x CH_2 PMB), 4.07 (dd, *J* = 6.5, 2.2 Hz, 1H, H-3), 3.92 (dt, *J* = 8.6, 4.1 Hz, 1H, H-5), 3.70 (s, 3H, CH_3 PMB), 3.69 (s, 4H, CH_3 PMB, H-4), 3.69 (s, 3H, CH_3 PMB), 3.66 – 3.58 (m, 2H, CH_2 H-6). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 159.3 (C_H Arom), 159.3 (C_H Arom), 159.3 (C_H Arom), 144.7 (C-1), 130.6 (C_q Arom), 130.4 (C_q Arom), 130.1 (C_q Arom), 129.7 (C_H Arom), 129.6 (C_H Arom), 129.5 (C_H Arom), 113.9 (C_H Arom), 113.9 (C_H Arom), 100.2 (C-2), 76.9 (C-5), 75.6 (C-2), 74.2 (C-4), 73.5 (CH_2 PMB), 73.2 (CH_2 PMB), 70.3 (CH_2 PMB), 68.3 (C-6), 55.4 (3 x CH_3 PMB); HRMS m/z calcd for $[C_{30}H_{34}O_7 + NH_4]^+$: 524.26428; found: 524.26551



(4-Methoxybenzyl)-3,4,6-Tri-*O*-(4-methoxybenzyl)-β-d-glucopyranoside, 35: To a solution of protected glycoside **35** (821 mg, 1.62 mmol) in dry DCM (8 mL) under a dinitrogen atmosphere, were added freshly activated 4Å molsieves. After stirring for 15 minutes, the mixture was allowed to cool to 0 °C and freshly prepared dimethyldioxirane in acetone (20 mL, 88 mM) was slowly added. The mixture was stirred for 3 h and allowed to reach rt, after which it was filtered over Celite® and concentrated *in vacuo*. The crude was then, together with 4-methoxyl benzyl alcohol (335 mg, 2.42 mmol) redissolved in dry THF under a dinitrogen atmosphere, followed by the addition of freshly activated 4Å molsieves. After stirring for 15 minutes, the mixture was cooled down to -78 °C and a cooled solution (10 °C) of $ZnCl_2$ in THF (2.43 mL, 1M) was added dropwise over ten minutes. The mixture was allowed to stir overnight at rt after which it was filtered over Celite®, concentrated *in vacuo* and purified by silica column chromatography (0 to 20% EtOAc in PE) to afford **35** (413 mg, 0.625 mmol, 39% over two steps) as a colorless oil. R_f = 0.48 (40% EtOAc in PE); IR (neat): 3480, 3000, 2907, 1611, 1511; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.30 (dd, *J* = 8.5, 4.8 Hz, 6H, H_{arom}), 7.08 (d, *J* = 8.6 Hz, 2H, H_{arom}), 6.98 – 6.77 (m, 8H, H_{arom}), 4.87 (dd, *J* = 15.4, 11.2 Hz, 2H, CH_2 PMB), 4.76 (dd, *J* = 10.7, 6.4 Hz, 2H, CH_2 PMB), 4.63 – 4.42 (m, 4H, 2 x CH_2 PMB), 4.32 (d, *J* = 7.3 Hz, 1H, H-1), 3.80 (s, 6H, 2 x CH_3 PMB), 3.79 (s, 3H, CH_3 PMB), 3.79 (s, 3H, CH_3 PMB), 3.70 (m, 2H, H-6), 3.62 – 3.50 (m, 3H, H-2, H-3, H-4), 3.45 (dd, *J* = 9.9, 4.1 Hz, 1H, H-5), 2.41 (s, 1H, OH). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 159.5 (C_q Arom), 159.3 (C_q Arom), 159.3 (C_q Arom), 130.9 (C_q Arom), 130.4 (C_q Arom), 130.3 (C_q Arom), 130.0 (C_H Arom), 129.7 (C_H Arom), 129.7 (C_H Arom), 129.6 (C_H Arom), 129.3 (C_q Arom), 114.0 (C_H Arom), 113.9 (C_H Arom), 113.9 (C_H Arom), 101.5 (C-1), 84.3 (C-2), 77.4 (C-3), 75.3 (C-4), 74.9 (CH_2 PMB), 74.7 (C-5), 73.2 (CH_2 PMB), 70.8 (CH_2 PMB), 68.5 (C-6), 55.4 (4 x CH_3 PMB); HRMS m/z calcd for $[C_{38}H_{44}O_{10} + NH_4]^+$: 678.32727; found: 678.33019.

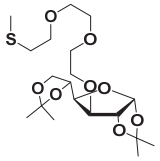


(4-Methoxybenzyl)-2-*O*-(2-[2-(2-(methylthio)ethoxy)ethoxy]ethyl)-3,4,6-Tetra-*O*-(4-methoxybenzyl)-β-D-glucopyranoside, 36: Glycoside **35** (333 mg, 0.504 mmol) was dissolved in dry DMF (5 mL) and cooled to 0 °C. To this solution was added NaH (60% dispersion in mineral oil, 26 mg, 0.65 mmol) portionwise followed by the addition of tosylate **31** (185 mg, 0.554 mmol). After stirring for 6 h at rt under a dry atmosphere, MeOH was added (1 mL). The mixture was then diluted with EtOAc (50 mL), transferred to a separatory funnel and washed with water (3x) and brine (3x). The organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by column chromatography (0 to 30% EtOAc in PE) afforded the title compound **36** as milky oil (334 mg, 0.405 mmol, 80%). R_f = 0.39 (40% EtOAc in PE); IR (neat): 2999, 2864, 2835, 1612, 1512; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.39 – 7.18 (m, 6H, H_{arom}), 7.07 (dd, *J* = 8.7, 4.8 Hz, 2H, H_{arom}), 6.92 – 6.75 (m, 8H, H_{arom}), 4.96 – 4.80 (m, 2H, CH_2 PMB), 4.78 – 4.66 (m, 2H, CH_2 PMB), 4.62 – 4.37 (m, 5H, CH_2 PMB, H-1), 4.06 (dt, *J* = 9.9, 4.6 Hz, 1H, C*H*H OCH_2), 3.85 (q, *J* = 5.2 Hz, 1H, C*H*H OCH_2), 3.81 (s, 3H, CH_3 PMB), 3.80 (s, 3H, CH_3 PMB), 3.79 (s, 3H, CH_3 PMB), 3.79 (s, 3H, CH_3 PMB), 3.74 – 3.66 (m, 2H, H-6), 3.66 – 3.53 (m, 9H, H-3, 4 x OCH_2), 3.49 (t, *J* = 9.2 Hz, 1H, H-4), 3.40 (ddd, *J* = 9.7, 5.1, 2.2 Hz, 1H, H-5), 3.29 (t, *J* = 8.3 Hz, 1H, H-2), 2.62 (t, *J* = 7.0 Hz, 2H, CH_2S*Me*), 2.10 (s, 3H, CH_2SMe). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 159.3 (C_q arom), 159.3 (C_q arom), 159.3 (C_q arom), 159.3 (C_q arom), 131.1 (C_q arom), 130.5 (C_q arom), 130.4 (C_q arom), 129.8 (C_H arom), 129.7 (C_H arom), 129.7 (C_H arom), 129.6 (C_H arom), 113.8 (C_H arom), 102.1 (C-1), 84.4 (C-4), 83.3 (C-2), 77.6 (C-4), 75.3 (CH_2 PMB), 74.9 (C-5), 74.7 (CH_2 PMB), 73.2 (CH_2 PMB), 72.1 (O*C*H_2), 70.9 (O*C*H_2), 70.9 (CH_2 PMB), 70.6 (O*C*H2), 70.5 (O*C*H2), 70.4 (O*C*H2), 68.7 (C-6), 55.4 (4 x CH_3 PMB), 33.4 (*C*H_2SMe), 16.1 (CH_2S*Me*); HRMS m/z calcd for $[C_{45}H_{58}O_{12}S + NH_4]^+$: 840.39872; found: 840.40019.

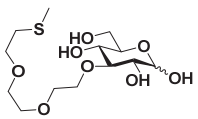


2-*O*-(2-[2-(2-(methylthio)ethoxy)ethoxy]ethyl)-α/β-D-glucopyranoside, H37: Compound **36** (241 mg, 0.293 mmol) was dissolved in a mixture of DCM/HFIP (3 mL) and to this solution were added 5 drops of 37% HCl in H_2O. The color immediately changed to dark red, and after stirring for 5 minutes the mixture was quenched upon the addition of Et_3N (500 uL, 3.57 mmol). The mixture was then concentrated *in vacuo* and redissolved in H_2O (5.8 mL), followed by the addition of a solution of $MeNH_2$ in MeOH (145 µL, 2M). After heating the reaction mixture for 30 minutes at 60 °C, solvents were removed under reduced pressure and the resulting residue was purified by silica column chromatography (0 to 20% MeOH in DCM) to afford fully deprotected hemiacetal **H37** (67 mg, 0.196 mmol, 67%) as a clear oil. R_f = 0.54 (25% MeOH in DCM); IR (neat): 3411, 2917, 2865, 1115, 1042; ^{1}H NMR (400 MHz, CD_3OD) δ = 5.29 (d, *J* = 3.5 Hz, 1H, H-1α), 4.53 (d, *J* = 7.8 Hz, 1H, H-1β), 4.04 (dt, *J* = 11.3, 4.4 Hz, 1H, C*H*H H-6), 3.89 – 3.70 (m, 8H), 3.70 – 3.59 (m, 19H), 3.42 – 3.32 (m, 1H, H-3β), 3.30 – 3.20 (m, 2H), 3.03 – 2.86 (m, 1H, H-2β), 2.68 (t, *J* = 6.8 Hz, 4H, 2 x *CH*$_2$SMe), 2.13 (s, 6H, 2 x

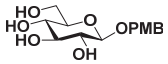
CH_2SMe). ^{13}C NMR (101 MHz, CD_3OD) δ = 98.1 (C-1β), 91.8 (C-1α), 85.1 (C-1β), 82.4, 77.9, 77.5, 73.9, 72.8, 72.6, 71.9, 71.9, 71.6, 71.6, 71.5, 71.5, 71.4, 71.2, 71.1, 71.0, 62.8 (C-6α), 62.7 (C-6β), 34.2 (2 x CH_2SMe), 15.9 (2 x CH_2SMe); HRMS m/z calcd for $[C_{13}H_{26}O_8S + Na]^+$: 365.12406; found: 365.12513.



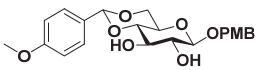
1,2:5,6-di-*O*-isopropylidene-3-*O*-(2-[2-(2-(methylthio)ethoxy)ethoxy]ethyl)-α-D-glucofuranose, 38: To a cooled solution of diacetone glucose (200 mg, 0.768 mmol) in dry DMF (8 mL) was added 60% NaH in mineral oil (80.0 mg, 2.00 mmol). After stirring for 5 min, tosylate **32** was added and the mixture was overnight. After quenching the reaction with MeOH (1 mL), Et_2O (50 mL) was added and the reaction was transferred to a separatory funnel. After washing with water (1x), aq. $NaHCO_3$ (1x) and brine (1x), layers were separated and the organic layer was dried (Na_2SO_4) and concentrated in vacuo. Purification of the residue over silica (0 -50% EtOAc in PE) gave **38** as a clear oil. (294 mg, 0.700 mmol, 91%). R_f = 0.73 (50% EtOAc in PE); IR (neat): 2985, 2871, 1456, 1371, 1058; ^1H NMR (400 MHz, $CDCl_3$) δ = 5.87 (d, *J* = 3.8 Hz, 1H, H-1), 4.57 (d, *J* = 3.6 Hz, 1H, H-2), 4.31 (dt, *J* = 7.8, 5.9 Hz, 1H, H-5), 4.14 – 4.10 (m, 1H, H-3), 4.09 – 4.05 (m, 1H, C*H*H H-6), 3.99 (dd, *J* = 8.6, 5.8 Hz, 1H, C*H*H H-6), 3.92 (d, *J* = 3.1 Hz, 1H, H-4), 3.79 – 3.71 (m, 2H, OCH_2), 3.68 – 3.60 (m, 8H, 4 x OCH_2), 2.69 (t, *J* = 6.9 Hz, 2H, CH_2SMe), 2.14 (s, 3H, CH_2SMe), 1.49 (d, *J* = 2.7 Hz, 3H, CH_3 isopropylidene), 1.42 (s, 3H, CH_3 isopropylidene), 1.34 (s, 3H, CH_3 isopropylidene), 1.31 (d, *J* = 3.6 Hz, 3H, CH_3 isopropylidene). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 111.9 (C_q isopropylidene), 109.0 (C_q isopropylidene), 105.4 (C-1), 82.8 (C-2), 82.7 (C-4) , 81.2 (C-3), 72.7 (C-5), 70.8 (O*C*H_2), 70.7 (O*C*H_2), 70.6 (O*C*H_2), 70.5 (O*C*H_2), 70.28, 67.3 (C-6), 33.5 (*C*H_2SMe), 27.0 (*C*H_3 isopropylidene), 27.0 (*C*H_3 isopropylidene), 26.4 (*C*H_3 isopropylidene), 25.6 (*C*H_3 isopropylidene), 16.2 (CH_2SMe); HRMS m/z calcd for $[C_{19}H_{34}O_8S + NH_4]^+$: 440.23126; found: 440.23203.



3-*O*-(2-[2-(2-(methylthio)ethoxy)ethoxy]ethyl)-α/β-D-glucopyranoside, H40: To a suspension of compound **38** in H_2O, was added Amberlite® IR-120 H^+ and this mixture was stirred for 24 h at 60 °C after which it was filtered and concentrated *in vacuo*. Purification of the residue over silica (0 to 10% MeOH in DCM) afforded the title compound **H40** as a clear oil (α/β = 1:1, 81 mg, 0.24 mmol, 46%). R_f = 0.32 (10% MeOH in DCM); IR (neat): 3369, 2918, 2873, 1104, 1077; ^1H NMR (400 MHz, CD_3OD) δ = 5.08 (d, *J* = 3.6 Hz, 1H, H-1α), 4.47 (d, *J* = 7.7 Hz, 1H, H-1β), 4.24 – 3.13 (m, 40H), 2.67 (t, *J* = 6.9 Hz, 4H, 2 x CH_2SMe), 2.11 (s, 6H, 2 x CH_2SMe). ^{13}C NMR (101 MHz, CD_3OD) δ = 98.1 (C-1β), 94.0 (C-1α), 87.6, 84.5, 77.8, 76.1, 73.7, 73.1, 73.0, 72.2, 72.1, 71.6, 71.4, 71.4, 71.3, 71.1, 62.8 (C-6β), 62.6 (C-6α), 34.2 (2x O*C*H_2SMe), 15.9 (2x OCH_2SMe); HRMS m/z calcd for $[C_{13}H_{26}O_8S + Na]^+$: 365.12406; found: 365.12434.

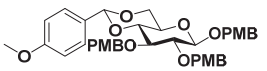


(4-Methoxybenzyl)-β-D-glucopyranoside, 41: To a solution of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (3.00 g, 7.30 mmol) and 4-methoxybenzyl alcohol (5.04 g, 36.5 mmol) in dry Et_2O (75 mL) were added freshly activated 4Å molsieves. The resulting mixture was allowed to stir for ten minutes, after which Ag_2CO_3 (6.00 g, 21.8 mmol) and I_2 (1.85 g, 7.30 mmol) were added. After stirring an additional 24 h under a dinitrogen atmosphere at rt in the dark, the reaction mixture was filtered over Celite®, diluted with EtOAc (200 mL), washed with 1M $Na_2S_2O_3$ (3x), aq. $NaHCO_3$ (3x) and brine (3x). The organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by silica column chromatography (20% EtOAc in DCM) afforded (4-methoxybenzyl)-2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (2.39 g), which was then redissolved in dry MeOH (70 mL) followed by the addition of a catalytic amount of NaOMe. The resulting mixture was allowed to stir for 4 h, after which Amberlite® IR-120 H^+ was added until neutral pH, filtered and concentrated in vacuo, affording the title compound **41** as a clear oil (1.57 g, 5.23 mmol, 72% over two steps). R_f = 0.57 (20% MeOH in DCM); IR (neat): 3335, 2924, 1612, 1027, 819; ^{1}H NMR (400 MHz, CD_3OD) δ = 7.32 (d, *J* = 8.6 Hz, 2H, H_{arom}), 6.95 – 6.71 (m, 2H, H_{arom}), 4.85 (d, *J* = 18.0 Hz, 1H, C*H*H PMB), 4.58 (d, *J* = 11.3 Hz, 1H, C*H*H PMB), 4.31 (d, *J* = 7.8 Hz, 1H, H-1), 3.89 (dd, *J* = 12.0, 2.2 Hz, 1H, C*H*H H-6), 3.68 (dd, *J* = 12.0, 5.5 Hz, 1H, C*H*H H-6), 3.42 – 3.14 (m, 4H, H-2, H-3, H-4, H-5). ^{13}C NMR (101 MHz, CD_3OD) δ = 160.8 (C_q Arom), 130.9 (C_H Arom), 130.9 (C_q Arom), 114.6 (C_H Arom), 102.9 (C-1), 78.0 (C-3), 78.0 (C-4), 75.1 (C-2), 71.7 (C-5), 71.4 (CH_2 PMB), 62.8 (C-6), 55.7 (CH_3 PMB). HRMS m/z calcd for $[C_{14}H_{20}O_7 + Na]^+$: 365.12406; found: 365.12513.

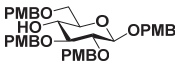


(4-Methoxybenzyl)-4,6-*O*-(4-methoxybenzylidene)-β-D-glucopyranoside, 42: To a solution of **41** (309 mg, 1.03 mmol) in dry DMF (5 mL) were added 4-methoxybenzaldehyde dimethyl acetal (135 uL, 0.793 mmol) and *p*-TsOH.H_2O (10 mg, 0.05 mmol). The resulting reaction mixture was heated at 60 °C for 16, after which it was concentrated *in vacuo*. Saturated aqueous $NaHCO_3$ (50 mL) was added, and the mixture was further diluted with EtOAc (200 mL) and transferred to a separatory funnel. After washing with aq. $NaHCO_3$ (3x), water (3x) and brine (3x), layers were separated, the organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. Compound **43** (382 mg, 0.910 mmol, 89%) was obtained after silica column chromatography (0 to 10% MeOH in DCM) as a white powder. R_f = 0.48 (10% MeOH in DCM); IR (neat): 3480, 2869, 1612, 1516, 1244; ^{1}H NMR (400 MHz, CD_3CN) δ = 7.39 (d, *J* = 8.8 Hz, 2H, H_{arom}), 7.31 (d, *J* = 8.7 Hz, 2H, H_{arom}), 7.00 – 6.86 (m, 4H, H_{arom}), 5.50 (s, 1H, CH PMB acetal), 4.76 (d, *J* = 11.5 Hz, 1H, C*H*H PMB), 4.55 (d, *J* = 11.5 Hz, 1H, C*H*H PMB), 4.43 (d, *J* = 7.8 Hz, 1H, H-1), 4.24 (dd, *J* = 10.3, 4.6 Hz, 1H, C*H*H H-6), 3.78 (s, 6H, 2 x CH_3 OMe) 3.72 (t, *J* = 9.9 Hz, 1H, C*H*H H-6), 3.62 – 3.50 (m, 1H, H-3), 3.49 – 3.33 (m, 2H, H-4, H-5), 3.26 (td, *J* = 8.1, 3.7 Hz, 1H, H-2). ^{13}C NMR (101 MHz, CD_3CN) δ = 161.1 (C_q Arom), 160.4 (C_q Arom), 131.3 (C_q Arom), 130.7 (C_H Arom), 128.6 (C_H Arom), 114.6 (C_H Arom), 114.4 (C_H Arom), 103.4 (C-1), 102.1 (*C*H PMB acetal), 81.6 (C-4), 75.6 (C-2), 74.3 (C-3), 71.4 (CH_2

PMB), 69.3 (C-6), 67.2 (C-5), 55.9 (2 x CH_3 PMB). HRMS m/z calcd for $[C_{22}H_{26}O_8 + H]^+$: 419.17004; found: 419.17101.

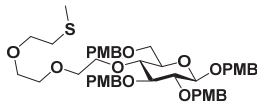


(4-Methoxybenzyl)-2,3-di-*O*-(4-methoxybenzyl)-4,6-*O*-(4-methoxybenzylidene)-β-D-glucopyranoside, 43: To a cooled solution (0 °C) of *p*-methoxy benzylidene protected **42** (377 mg, 0.900 mmol) in dry DMF (9 mL) was slowly added NaH (60% dispersion in mineral oil, 80.0 mg, 2.00 mmol) followed by the addition of 4-methoxybenzyl chloride (255 µL, 1.89 mmol). After stirring for 5 h under a dinitrogen atmosphere, the reaction was quenched upon the addition of MeOH (3 mL). The mixture was further diluted with Et_2O (200 mL) and transferred to a separatory funnel, washed with water (1x), aq. $NaHCO_3$ (1x) and brine (1x). The organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. Purification by silica column chromatography (0 to 20% EtOAc in PE) yielded the title compound **43** as a clear oil (447 mg, 0.680 mmol, 76%). R_f = 0.74 (40% EtOAc in PE); IR (neat): 3480, 2869, 1612, 1516, 1244; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.43 (d, *J* = 8.9 Hz, 2H, H_{arom}), 7.36 – 7.18 (m, 5H, H_{arom}), 7.00 – 6.78 (m, 6H, H_{arom}), 5.54 (s, 1H, CH benzylidene), 4.89 (d, *J* = 11.4 Hz, 1H, C*H*H PMB), 4.82 (dd, *J* = 10.8, 5.6 Hz, 2H, CH_2 PMB), 4.71 (dd, *J* = 16.0, 10.7 Hz, 2H, CH_2 PMB), 4.65 – 4.57 (m, 2H, C*H*H PMB, H-1), 4.37 (dd, *J* = 10.5, 5.0 Hz, 1H, C*H*H H-6), 3.82 (s, 6H, 2 x CH_3 PMB), 3.82 (s, 3H, CH_3 PMB), 3.80 (s, 3H, CH_3 PMB), 3.69 (p, *J* = 9.1 Hz, 2H, H-3, H-4), 3.49 (t, *J* = 7.9 Hz, 1H, H-2), 3.40 (td, *J* = 9.5, 5.0 Hz, 1H, H-5). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 160.1 (C_q Arom), 159.5 (C_q Arom), 159.3 (C_q Arom), 159.3 (C_q Arom), 130.8 (C_q Arom), 130.6 (C_q Arom), 129.9 (C_H Arom), 129.8 (C_H Arom), 129.8 (C_H Arom), 129.3 (C_q Arom), 127.4 (C_H Arom), 113.9 (C_H Arom), 113.8 (C_H Arom), 113.7 (C_H Arom), 103.0 (C-1), 101.2 (CH PMB acetal), 81.9 (C-2), 81.5 (C-3), 80.7 (C-4), 75.1 (CH_2 PMB), 74.9 (CH_2 PMB), 71.4 (CH_2 PMB), 68.9 (C-6), 66.2 (C-5), 55.4 (3 x CH_3 PMB), 55.3 (CH_3 PMB acetal); HRMS m/z calcd for $[C_{38}H_{42}O_{10} + Na]^+$: 681.26702; found: 681.26706.

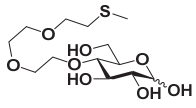


(4-Methoxybenzyl)-2,3,6-tri-*O*-(4-methoxybenzyl)-β-D-glucopyranoside, 44: Fully protected glycoside **43** (400 mg, 0.610 mmol) was dissolved in DMF (12 mL) and to this solution were added freshly activated 4Å molsieves and fresh $NaCNBH_3$ (385 mg, 6.13 mmol). After stirring for 15 minutes the solution was cooled to 0 °C and a precooled solution (0 °C) of trifluoroacetic acid (1.2 mL) in DMF (3 mL) on 4Å molsieves was then added dropwise over 15 minutes. The reaction mixture was maintained at rt for 48 h at rt and filtered over Celite®, diluted with EtOAc (100 mL) and transferred to a separatory funnel. After washing with water (1x), aq. $NaHCO_3$ (1x) and brine (1x), the organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by column chromatography over silica (0 to 30% EtOAc in PE) afforded **44** (385 mg, 0.580 mmol, 95%) as a clear oil. R_f = 0.48 (40% EtOAc in PE); IR (neat): 3480, 3000, 2907, 1612, 1512; ^{1}H NMR (400 MHz, CD_3Cl_3) δ = 7.42 – 7.16 (m, 8H, H_{arom}), 6.87 (tdd, *J* = 8.9, 4.7, 2.6 Hz, 8H, H_{arom}), 4.92 – 4.82 (m, 3H, C*H*H PMB, CH_2 PMB),

4.67 – 4.53 (m, 5H, C*H*H PMB, 2 x CH_2 PMB), 4.49 (d, *J* = 7.2 Hz, 1H, H-1), 3.82 (s, 3H, CH_3 PMB), 3.81 (s, 3H, CH_3 PMB), 3.81 (s, 3H, CH_3 PMB), 3.80 (s, 3H, CH_3 PMB), 3.79 – 3.66 (m, 2H, H-6), 3.59 – 3.51 (m, 1H, H-5), 3.48 – 3.36 (m, 3H, H-2, H-3, H-4). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 159.4 (C_q Arom), 152.7 (C_q Arom), 152.5 (C_q Arom), 130.7 (C_H Arom), 130.0 (C_H Arom), 129.9 (C_H Arom), 129.8 (C_H Arom), 129.5 (C_H Arom), 114.1 (C_H Arom), 113.9 (C_H Arom), 102.5 (C-1), 83.8 (C-4), 81.6 (C-2), 75.0 (CH_2 PMB), 74.5 (CH_2 PMB), 74.2 (C-3), 73.4 (CH_2 PMB), 71.7 (C-5), 71.1 (CH_2 PMB), 70.2 (C-6), 55.4 (4 x CH_3 PMB); HRMS m/z calcd for $[C_{38}H_{44}O_{10} + NH_4]^+$: 678.32727; found: 678.33206.

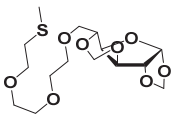


(4-Methoxybenzyl)-2-O-(2-[2-(2-(methylthio)ethoxy)ethoxy]ethyl)-3,6-tri-*O*-(4-methoxybenzyl)-β-D-glucopyranoside, 45: Compound **44** (300 mg, 0.454 mmol) was dissolved in dry DMF and cooled to (0 °C) after which 60% NaH in mineral oil (31 mg, 0.77 mmol) was added. This mixture was allowed to stir for 5 min, after which tosylate **32** (177 mg, 0.530 mmol) was added dropwise. The reaction was allowed to stir for 6 h, after which it was quenched upon the addition of MeOH (2 mL), diluted with Et_2O and transferred to a separatory funnel. After washing with aq. $NaHCO_3$ (1x), water (1x) and brine (1x), layers were separated, the organic layer dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by column chromatography (0 to 40% EtOAc in PE) afforded the title compound **45** as a clear oil (291 mg, 0.354 mmol, 78%). R_f = 0.38 (40% EtOAc in PE); IR (neat): 2998, 2907, 2836, 1612, 1513; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.36 – 7.18 (m, 8H, H_{arom}), 6.94 – 6.79 (m, 8H, H_{arom}), 4.97 – 4.50 (m, 8H, 4 x CH_2 PMB), 4.46 (d, *J* = 7.8 Hz, 1H, H-1), 3.95 (dt, *J* = 9.8, 4.5 Hz, 1H, C*H*H OCH_2), 3.81 – 3.74 (m, 1H, C*H*H H-6), 3.76 – 3.63 (m, 3H, C*H*H H-6, 2 x C*H*H OCH_2), 3.65 – 3.50 (m, 8H, H-5, C*H*H OCH_2, 3 x OCH_2), 3.46 – 3.38 (m, 3H, H-2, H-3, H-4), 2.66 (t, *J* = 6.9 Hz, 2H, CH_2SMe), 2.12 (s, 3H, CH_2S*Me*). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 159.7 (C_q Arom), 159.4 (C_q Arom), 131.1 (C_q Arom), 130.8 (C_q Arom), 130.6 (C_q Arom), 130.0 (C_H Arom), 129.8 (C_H Arom), 129.5 (C_H Arom), 113.9 (C_H Arom), 113.8 (C_H Arom), 102.5 (C-1), 84.3 (C-5), 82.0 (C-2), 78.7 (C-3), 75.4 (CH_2 PMB), 75.0 (C-4), 74.6 (CH_2 PMB), 73.2 (CH_2 PMB), 72.2 (O*C*H_2), 71.0 (CH_2 PMB), 70.9 (O*C*H_2), 70.7 (O*C*H_2), 70.6 (O*C*H_2), 70.4 (*C*H_2SMe), 68.8 (C-6), 33.5 (4 x CH_3 PMB), 16.2 (CH_2S*Me*). HRMS m/z calcd for $[C_{45}H_{58}O_{12}S + NH_4]^+$: 840.39872; found: 840.40276.

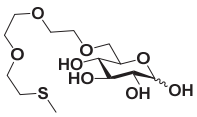


4-*O*-(2-[2-(2-(methylthio)ethoxy)ethoxy]ethyl)-α/β-D-glucopyranoside, H46: Compound **45** (108 mg, 0.131 mmol) was dissolved in a mixture of DCM/HFIP (1:1, 2 mL) and to this solution was added a catalytic amount of 37% HCl (4 drops). The mixture slowly turned red to deep purple in 30 minutes, after which it was quenched with Et_3N (0.5 mL) and concentrated *in vacuo*. The crude was redissolved in MeOH, Amberlite IR-120 H^+ was added and the mixture was stirred for 5 minutes, filtered and concentrated. Purification of the resulting residue over silica (0 to 15% MeOH in DCM) afforded the title compound **H46** as a clear oil

(13 mg, 0.038 mmol, 29%). R_f = 0.57 (20% MeOH in DCM); IR (neat): 3370, 2918, 2873, 1104, 1077; ^{1}H NMR (400 MHz, CD_3OD) δ = 5.09 (d, *J* = 3.7 Hz, 1H, H-1α), 4.45 (d, *J* = 7.7 Hz, 1H, H-1β), 4.02 – 3.58 (m, 28H), 3.47 (t, *J* = 8.9 Hz, 1H, H-3β), 3.29 – 3.19 (m, 2H), 3.13 (dd, *J* = 9.2, 7.9 Hz, 1H, H-2β), 2.68 (t, *J* = 6.8 Hz, 4H, 2 x O*CH*$_2$SMe), 2.13 (s, 6H, 2 x OCH_2S*Me*). ^{13}C NMR (100 MHz, CD_3OD) δ = 98.2 (C-1β), 93.9 (C-1α), 80.5, 80.3, 78.2, 77.0, 76.3, 75.0, 73.9, 72.9, 72.0, 71.7, 71.5, 71.2, 62.5 (C-1β), 62.4 (C-1α), 34.3 (2x O*CH*$_2$SMe), 15.9 (OCH_2S*Me*); HRMS m/z calcd for $[C_{13}H_{26}O_8S + Na]^+$: 365.12406; found: 365.12513.

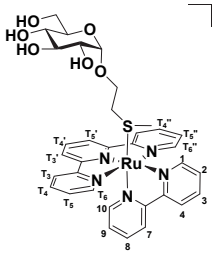


1,2:3,5-bis(O-methylidene)-6-*O*-(2-[2-(2-(methylthio)ethoxy)ethoxy]ethyl)α-D-glucofuranose, 49: To a cooled (0 °C) solution of 1,2:3,5-bis(*O*-methylidene)-α-D-glucofuranose (206 mg, 1.00 mmol) in dry DMF (10 mL) was added 60% NaH in mineral oil (57 mg, 1.42 mmol). After 10 minutes, **19** (385 mg, 1.15 mmol) was added dropwise and the resulting mixture was stirred for 3 hr at rt, after which it was quenched upon the addition of MeOH (2 mL). The reaction mixture was extracted with Et_2O (50 mL), washed with aq. $NaHCO_3$ (2x), water (2x) and brine (2x). Layers were separated, the organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. The resulting residue was then purified by silica column chromatography (0 to 60% EtOAc in PE) affording **49** as a colorless oil. R_f = 0.57 (50% EtOAc in PE); IR (neat): 2867, 1455, 1082, 1184, 1058; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.03 (d, *J* = 3.8 Hz, 1H, H-1), 5.12 (d, *J* = 5.9 Hz, 1H, C*H*H methylene), 5.08 (s, 1H, CH_2 methylene), 5.03 (s, 1H, CH_2 methylene), 4.78 (d, *J* = 6.0 Hz, 1H, C*H*H methylene), 4.46 (d, *J* = 3.9 Hz, 1H, H-2), 4.37 (d, *J* = 3.0 Hz, 1H, H-3), 4.14 (t, *J* = 4.4 Hz, 1H, H-5), 4.03 (d, *J* = 2.7 Hz, 1H, H-4), 3.85 (dd, *J* = 10.5, 3.9 Hz, 1H, C*H*H H-6), 3.75 (dd, *J* = 10.5, 4.8 Hz, 1H, C*H*H H-6), 3.64 (dd, *J* = 11.8, 5.6 Hz, 10H, 4 x OCH_2), 2.69 (t, *J* = 6.9 Hz, 2H, CH_2SMe), 2.14 (s, 3H, CH_2SMe). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 104.4 (C-1), 96.6 (CH_2 methylene), 88.2 (*C*H_2 methylene), 83.9 (C-2), 76.8 (C-3), 76.1 (C-4), 72.5 (C-6), 71.6 (C-5), 71.0 (O*C*H_2), 70.7(O*C*H_2), 70.7 (O*C*H_2), 70.7 (O*C*H_2), 70.4 (O*C*H_2), 33.5 (O*C*H_2SMe), 16.2 (OCH_2S*Me*). HRMS m/z calcd for $[C_{15}H_{26}O_8S + H]^+$: 367.14211; found: 367.14295.

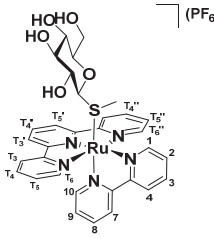


6-*O*-(2-[2-(2-(methylthio)ethoxy)ethoxy]ethyl)-α/β-D-glucopyranoside, H50: Compound **49** was dissolved in 2M HCl (5 mL) and this mixture was heated at 100 °C for 1 h after which the reaction was neutralized with 1M NaOH (10 mL) and concentrated in vacuo. Purification of the residu by silica column chromatography (0 to 20% MeOH in DCM) afforded **H50** as a colorless oil (101 mg, 0.295 mmol, 70%). R_f = 0.50 (20% MeOH in DCM); IR (neat): 3368, 2917, 2874, 1427, 1078; ^{1}H NMR (500 MHz, CD_3OD) δ = 5.13 (d, J = 3.7 Hz, 1H, H-1α), 4.52 (d, J = 7.7 Hz, 1H, H-1β), 4.06 – 3.94 (m, 4H), 3.91 – 3.87 (m, 1H, CHH H-6α/β), 3.86 – 3.77 (m, 2H), 3.75 – 3.64 (m, 20H, 10 x OCH_2), 3.49 – 3.38 (m, 3H), 3.41 (ddd, J = 9.8, 8.8, 6.0 Hz, 2H), 3.34 – 3.30 (m, 1H), 3.25 – 3.22 (m, 2H), 2.72 (t, J = 6.8 Hz, 4H, 2 x CH_2SMe), 2.16 (s, 6H, 2 x CH_2SMe). ^{13}C NMR (126 MHz, CD_3OD) δ = 98.1 (C-1β), 94.0 (C-

1α), 87.6, 84.4, 77.8, 76.1, 73.6, 73.0 (O*C*H_2), 73.0 (O*C*H_2), 73.0, 72.1 (O*C*H_2), 72.1 (O*C*H_2), 71.6 (O*C*H_2), 71.6 (O*C*H_2), 71.4 (O*C*H_2), 71.4 (O*C*H_2), 71.3, 71.1 (O*C*H_2), 71.1 (O*C*H_2), 62.8 (C-6α/β), 62.7 (C-6α/β), 34.2 (2 x *C*H_2SMe), 15.9 (2 x CH_2S*Me*). HRMS m/z calcd for $[C_{13}H_{26}O_8S + Na]^+$: 365.12406; found: 365.12519.

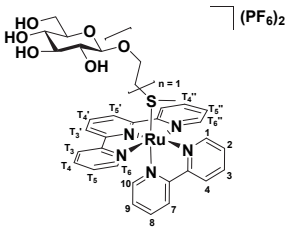


[Ru(tpy)(bpy)(13)](PF$_6$)$_2$, [1](PF$_6$)$_2$: [Ru(tpy)(bpy)Cl]Cl (63 mg, 0.112 mmol) and **13** (93 mg, 0.366 mmol) were dissolved in deoxygenated H_2O (18 mL) and this mixture was heated at 80 °C for 16 h, after which it was concentrated *in vacuo*. Purification of the residue by silica column chromatography (100/0/0 to 100/80/20 aceton/water/aq. KPF_6), followed by purification over Sephadex LH-20 (MeOH), afforded the title compound as a red solid (44 mg, 42.4 umol, 39%). R_f = 0.69 (100/80/20 aceton/water/aq. KPF_6); ^{1}H NMR (400 MHz, CD_3OD) δ = 9.85 (d, *J* = 5.7 Hz, 1H, 1), 8.81 (d, *J* = 8.0 Hz, 1H, 4), 8.77 (d, *J* = 8.2 Hz, 2H, T_3', T_5'), 8.62 (d, *J* = 8.1 Hz, 2H, T_6, T_6"), 8.58 (d, *J* = 7.8 Hz, 1H, 10), 8.44 – 8.34 (m, 2H, T_4', 3), 8.18 – 8.04 (m, 3H, T_5, T_5", 2), 7.92 (td, *J* = 7.8, 1.6 Hz, 1H, 9), 7.79 (d, *J* = 5.6 Hz, 2H, T_3, T_3"), 7.45 (ddd, *J* = 7.3, 5.6, 1.4 Hz, 2H, T_4, T_4"), 7.34 – 7.26 (m, 1H, 7), 7.23 (ddd, *J* = 7.3, 5.7, 1.3 Hz, 1H, 8), 4.69 (d, *J* = 3.7 Hz, 1H, H-1), 3.79 – 3.68 (m, 2H, C*H*H H-6, C*H*H OCH_2), 3.64 – 3.34 (m, 5H, C*H*H H-6, C*H*H OCH_2, H-2, H-3, H-5), 3.29 – 3.20 (m, 1H, H-4), 2.12 – 1.91 (m, 2H, *C*H_2SMe), 1.39 (s, 3H, CH_2*SMe*). ^{13}C NMR (101 MHz, CD_3OD) δ = 159.3 (C_q Arom), 158.7 (C_q Arom), 158.1 (C_q Arom), 157.9 (C_q Arom), 154.3 (C_H T_3, T_3"), 153.5 (C_H 1), 150.8 (C_H 7), 140.1 (C_H T_5, T_5"), 139.4 (C_H T_4'), 139.3 (C_H 9), 138.3 (C_H 3), 129.8 (C_H T_4, T_4"), 129.4 (C_H 2), 128.4 (C_H 8), 126.2 (C_H T_6), 126.2 (C_H T_6"), 125.9 (C_H 4), 125.5 (C_H T_3', T_5'), 125.1 (C_H 10), 100.2 (C-1), 75.1 (C-5), 74.3 (C-3), 73.1 (C-2), 71.7 (C-4), 64.8 (OCH_2), 62.8 (C-6), 35.9 (*C*H_2SMe), 14.8 (CH_2S*Me*); HRMS m/z calcd for $[M]^{2+}$: 372.57485; found: 372.57558; Elemental analysis calcd (%) for [**1**](PF_6)$_2$.2MeOH: C, 39.35; H, 4.13; N, 6.37; found: 41.45; H, 4.18; N, 6.35.

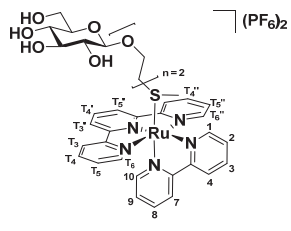


[Ru(tpy)(bpy)(15)](PF$_6$)$_2$, [2](PF$_6$)$_2$: The title compound was synthesized analogous according to the procedure described for [**1**](PF_6)$_2$ using [Ru(tpy)(bpy)Cl)]Cl (200 mg, 0.357 mmol) and **15** (100 mg, 0.476 mmol) in H_2O (60 mL) affording [**2**](PF_6)$_2$, as an orange powder (98.4 mg, 99.3 µmol, 28%). R_f = 0.15 (100/80/20 acetone/water/aq. KPF_6); ^{1}H NMR (400 MHz, CD_3OD) δ = 10.01 (d, *J* = 4.1 Hz, 1H, 1), 8.82 (dt, *J* = 8.2, 1.1 Hz, 1H, 4), 8.76 (ddd, *J* = 8.2, 4.3, 0.9 Hz, 2H, T_3', T_5'), 8.66 – 8.56 (m, 3H, T_6, T_6", 10), 8.43 – 8.36 (m, 2H, T_4', 3), 8.13 – 8.02 (m, 3H, T_5, T_5", 2), 7.93 (ddd, *J* = 8.2, 7.0, 2.1 Hz, 1H, 9), 7.86 (ddd, *J* = 5.5, 1.5, 0.7 Hz, 1H, T_3), 7.80 (ddd, *J* = 5.5, 1.5, 0.7 Hz, 1H, T_3"), 7.44 (ddt, *J* = 7.8, 5.5, 1.3 Hz, 2H, T_4, T_4"), 7.27 – 7.18 (m, 2H, 7, 8), 3.52 (d, *J* = 9.1 Hz, 1H, H-1), 3.43 (t, *J* = 3.6 Hz, 2H, H-6), 3.02 – 2.90 (m, 3H, H-2, H-3, H-4), 2.48 (d, *J* = 8.7 Hz, 1H, H-5), 1.39 (s, 3H, S*Me*). ^{13}C NMR (101

MHz, CD_3OD) δ = 163.4 (C_q Arom), 160.7 (C_q Arom), 160.0 (C_q Arom), 159.8 (C_q Arom), 158.9 (C_q Arom), 158.2 (C_q Arom), 158.0 (C_q Arom), 154.5 (C_H T_3), 154.3 (C_H T_3"), 153.8 (C_H 1), 150.4 (C_H 7), 140.2 (C_H T_5), 140.1 (C_H T_5"), 139.6 (C_H T_4'), 139.5 (C_H 9), 138.2 (C_H 3), 129.7 (C_H T_4), 129.6 (C_H T_4"), 129.0 (C_H 2), 128.5 (C_H 8), 126.1 (C_H 4), 126.0 (C_H T_6), 125.9 (C_H T_6") 125.3 (C_H T_3', T_5'), 125.1 (C_H 10), 85.7 (C-1), 82.7 (C-5), 78.6 (C-2), 71.3 (C-3), 70.0 (C-4), 61.8 (C-6), 9.0 (S*Me*). HRMS m/z calcd for $[M]^{2+}$: 350.56175; found: 350.56289. Elemental analysis calcd (%) for [**2**]$(PF_6)_2$: C, 38.18; H, 3.30; N, 6.96; found: 38.93; H, 3.39; N, 7.19.

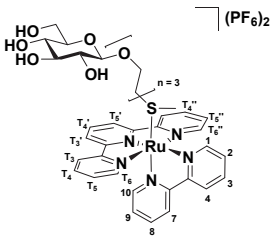


[Ru(tpy)(bpy)(24)](PF$_6$)$_2$, [3](PF$_6$)$_2$: The title compound was synthesized analogous according to the procedure described for [**1**]$(PF_6)_2$ using [Ru(tpy)(bpy)Cl)]Cl (101 mg, 0.180 mmol) and **24** (75.7 mg, 0.298 mmol) in H_2O (30 mL) affording the title compound as a hygroscopic orange powder (73.3 mg, 70.7 µmol, 39%). R_f = 0.36 (100/10/20 aceton/water/aq. KPF_6); ^{1}H NMR (500 MHz, CD_3OD) δ = 9.85 (dd, *J* = 5.6, 0.7 Hz, 1H, 1), 8.81 (dd, *J* = 17.9, 8.2 Hz, 3H, 4, T_3', T_5'), 8.63 (d, *J* = 8.1 Hz, 2H, T_6, T_6"), 8.59 (d, *J* = 8.2 Hz, 1H, 10), 8.45 – 8.36 (m, 2H, T_4', 3), 8.14 – 8.04 (m, 3H, T_5, T_5", 2), 7.93 (td, *J* = 7.8, 1.5 Hz, 1H, 9), 7.80 (td, *J* = 5.4, 0.8 Hz, 2H, T_3, T_3"), 7.45 (ddd, *J* = 7.6, 5.5, 1.3 Hz, 2H, T_4, T_4"), 7.30 (ddd, *J* = 5.7, 1.5, 0.7 Hz, 1H, 7), 7.23 (ddd, *J* = 7.2, 5.7, 1.3 Hz, 1H, 8), 4.15 (d, *J* = 7.8 Hz, 1H, H-1), 3.88 – 3.76 (m, 2H, C*H*H H-6, C*H*H OCH_2), 3.57 (ddd, *J* = 12.7, 11.5, 5.6 Hz, 2H, C*H*H H-6, C*H*H OCH_2), 3.26 (m, 1H, H-3), 3.23 – 3.17 (m, 2H, H-2, H-4), 3.09 (dd, *J* = 9.2, 7.8 Hz, 1H, H-5), 1.98 (t, *J* = 5.6 Hz, 2H, CH_2SMe), 1.39 (s, 3H, CH_2S*Me*). ^{13}C NMR (126 MHz, CD_3OD) δ = 159.3 (C_q Arom), = 159.3 (C_q Arom), 158.8 (C_q Arom), 158.2 (C_q Arom), 158.0 (C_q Arom), 154.4 (C_H T_3), 154.4 (C_H T_3"), 153.6 (C_H 1), 150.8 (C_H 7), 140.1 (C_H T_5, T_5"), 139.5 (T_4'), 139.4 (C_H 9), 138.3 (C_H 3), 129.8 (C_H T_4, T_4"), 129.2 (C_H 2), 128.4 (C_H 8), 126.2 (T_6, T_6"), 125.9 (C_H 4), 125.5 (T_3', T_5'), 125.1 (C_H 10), 104.2 (C-1), 78.2 (C-3), 78.1 (C-4), 74.9 (C-2), 71.5 (C-5), 66.6 (OCH_2), 62.6 (C-6), 35.8 (*C*H_2SMe), 14.8 (CH_2S*Me*). HRMS m/z calcd for $[M]^{2+}$: 372.57485; found: 372.57581; Elemental analysis calcd (%) for [**3**]$(PF_6)_2$: C, 39.47; H, 3.60; N, 6.77; found: 40.57; H, 3.53; N, 7.00.

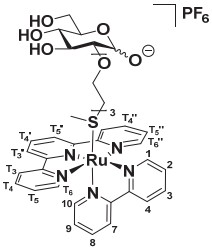


[Ru(tpy)(bpy)(25)](PF$_6$)$_2$, [4](PF$_6$)$_2$: The title compound was synthesized analogous according to the procedure described for [**1**]$(PF_6)_2$ using [Ru(tpy)(bpy)Cl)]Cl (94.2 mg, 0.168 mmol) and **25** (71.0 mg, 0.238 mmol) in H_2O (28 mL) affording the title compound as a hygroscopic orange powder (120 mg, 111 µmol, 66%). R_f = 0.56 (50/30/20 acetone/water/aq. KPF_6); ^{1}H NMR (400 MHz, CD_3OD) δ = 9.83 (d, *J* = 5.7 Hz, 1H, 1), 8.79 (dd, *J* = 14.9, 8.1 Hz, 3H, 4, T_3', T_5'), 8.60 (dd, *J* = 16.6, 8.1 Hz, 2H, T_6, T_6"), 8.43 – 8.34 (m, 2H, T_4', 3), 8.10 (m, 3H, T_5, T_5", 2), 7.91 (td, *J* = 7.8, 1.5 Hz, 1H, 9), 7.80 (d, *J* = 4.7 Hz, 1H, T_3, T_3"), 7.51 – 7.41 (m, 2H, T_4, T_4"), 7.32 – 7.27 (m, 1H, 7), 7.23 (ddd, *J* = 7.2, 5.7, 1.3 Hz, 1H,

8), 4.27 (d, *J* = 7.8 Hz, 1H, H-1), 3.97 – 3.89 (m, 1H, C*H*H OCH$_2$), 3.85 (dd, *J* = 11.8, 1.7 Hz, 1H, C*H*H H-6), 3.71 – 3.58 (m, 2H, C*H*H H-6, C*H*H OCH$_2$), 3.54 (dd, *J* = 5.4, 3.8 Hz, 2H, OCH$_2$), 3.46 (t, *J* = 5.5 Hz, 2H, OCH$_2$), 3.35 (m, *J* = 2.4 Hz, 1H, H-3), 3.28 – 3.22 (m, 3H, H-4, H-5), 3.12 (dd, *J* = 9.0, 7.8 Hz, 1H,), 1.96 – 1.88 (m, 2H, *CH$_2$*SMe), 1.40 (s, 3H, CH$_2$S*Me*). ^{13}C NMR (101 MHz, CD_3OD) δ = 159.3 (C_q Arom), 158.7 (C_q Arom), 158.1 (C_q Arom), 157.9 (C_q Arom), 154.4 (C_H T_3, T_3"), 153.4 (C_H 1), 150.8 (C_H 7), 140.1 (T_5, T_5"), 139.5 (C_H T_4'), 139.3 (C_H 9), 138.3 (C_H 3), 129.8 (C_H T_4, T_4"), 129.3 (C_H 2), 128.4 (C_H 8), 126.2 (C_H T_6), 125.9 (C_H T_6"), 125.5 (C_H 4), 125.1 (C_H T_3', T_5'), 104.4 (C-1), 78.1 (C-3), 78.0 (C-4), 75.1 (C-2), 71.6 (C-5), 71.4 (O*C*H$_2$), 69.7 (O*C*H$_2$), 68.2 (O*C*H$_2$), 62.7 (C-6), 35.6 (*C*H$_2$SMe), 15.2 (CH$_2$S*Me*). HRMS m/z calcd for $[M]^{2+}$: 394.58796; found: 394.58870; Elemental analysis calcd (%) for [**4**]$(PF_6)_2$: C, 40.08; H, 3.83; N, 6.49; found: 40.78; H, 3.97; N, 6.34.

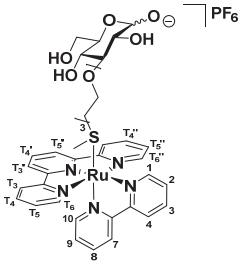


[Ru(tpy)(bpy)(26)](PF$_6$)$_2$, [5](PF$_6$)$_2$: The title compound was synthesized analogous according to the procedure described for [**1**](PF$_6$)$_2$ using [Ru(tpy)(bpy)Cl)]Cl (102 mg, 0.182 mmol) and **26** (100 mg, 0.292 mmol) in H_2O (30 mL) affording the title compound as a red solid (130 mg, 116 µmol, 65%). R_f = 0.35 (100/80/20 acetone/water/aq. KPF_6); ^{1}H NMR (400 MHz, CD_3OD) δ = 9.83 (d, *J* = 5.8 Hz, 1H, 1), 8.81 (dd, *J* = 12.6, 7.9 Hz, 3H, 4, T_3', T_5'), 8.62 (dd, *J* = 17.9, 8.1 Hz, 3H, T_6, T_6", 10), 8.46 – 8.35 (m, 2H, T_4', 3), 8.10 (t, *J* = 8.3 Hz, 3H, T_5, T_5", 2), 7.93 (t, *J* = 7.9 Hz, 1H, 9), 7.80 (d, *J* = 5.8 Hz, 2H, T_3, T_3"), 7.47 (t, *J* = 6.6 Hz, 2H, T_4, T_4"), 7.30 (d, *J* = 5.8 Hz, 1H, 7), 7.23 (t, *J* = 6.6 Hz, 1H, 8), 4.26 (d, *J* = 7.8 Hz, 1H, H-1), 4.06 – 3.91 (m, 1H, C*H*H OCH$_2$), 3.86 (d, *J* = 11.8 Hz, 1H, C*H*H H-6), 3.73 – 3.39 (m, 10H, C*H*H H-6, C*H*H OCH$_2$, 4 x OC*H$_2$*), 3.35 (m, 1H, H-5), 3.26 (d, *J* = 6.3 Hz, 2H, H-3, H4), 3.10 (t, *J* = 8.5 Hz, 1H, H-2), 1.90 (d, *J* = 5.6 Hz, 2H, OC*H$_2$*SMe), 1.41 (s, 3H, OCH$_2$S*Me*). ^{13}C NMR (101 MHz, CD_3OD) δ = 157.9 (C_q Arom), 157.4 (C_q Arom), 156.8 (C_q Arom), 156.6 (C_q Arom), 153.1 (C_H T_3, T_3"), 152.1 (C_H 1), 149.5 (C_H 7), 138.8 (C_H T_5,T_5"), 138.2 (C_H 9), 138.0 (C_H T_4'), 136.9 (C_H 3), 128.5 (C_H T_4, T_4"), 127.9 (C_H 8), 127.1 (C_H 2), 124.9 (C_H T_6, T_6"), 124.6 (C_H 4), 124.1 (C_H T_3, T_5'), 123.8 (C_H 10), 103.1 (C-1), 76.6 (C-3, C-5), 73.7 (C-2), 70.3 (C-4), 70.0 (O*C*H$_2$), 69.9 (O*C*H$_2$), 69.8 (O*C*H$_2$), 68.3 (O*C*H$_2$), 67.0 (O*C*H$_2$), 61.3 (C-6), 34.1 (O*C*H$_2$SMe), 14.00 (OCH$_2$S*Me*). HRMS: m/z calcd for $[M]^{2+}$: 416.60107; found: 416.60252; Elemental analysis calcd (%) for [**5**](PF$_6$)$_2$.3H$_2$O: C, 38.78; H, 4.37; N, 5.95; found: 39.27; H, 4.68; N, 5.95.

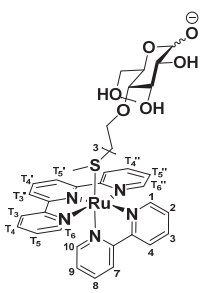


[Ru(tpy)(bpy)(37)]PF$_6$, [6]PF$_6$: [Ru(tpy)(bpy)(H_2O)](PF$_6$)$_2$ (35.9 mg, 45.0 µmol) and **H37** (30.3 mg, 44.7 µmol) were dissolved in a deoxygenated mixture of acetone/H_2O (4:1, 8 mL) and heated at 50 °C for 16 h, after which the reaction mixture was concentrated *in vacuo* and purified over Sephadex LH-20 (MeOH), affording the title compound as a red solid (18 mg, 18.4 µmol, 41%). *Rf* = 0.52

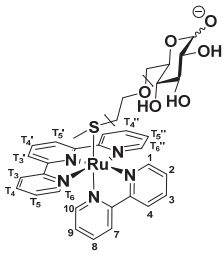
(acetone/water/aq. KPF_6 100/80/20); ^{1}H NMR (500 MHz, CD_3OD) δ = 9.84 (d, *J* = 5.6 Hz, 1H, 1), 8.88 – 8.80 (m, 3H, 4, T_3', T_5'), 8.67 (d, *J* = 7.1 Hz, 2H, T_6, T_6"), 8.62 (d, *J* = 7.5 Hz, 1H, 10), 8.43 (q, *J* = 7.9 Hz, 2H, T_4', 3), 8.17 – 8.08 (m, 3H, T_5, T_5", 2), 7.95 (td, *J* = 7.8, 1.5 Hz, 1H, 9), 7.81 (d, *J* = 5.5 Hz, 2H, T_3, T_3"), 7.48 (ddd, *J* = 7.2, 5.5, 1.3 Hz, 2H, T_4, T_4"), 7.36 – 7.28 (m, 1H, 7), 7.24 (ddd, *J* = 7.2, 5.7, 1.3 Hz, 1H, 8), 5.23 (d, *J* = 3.5 Hz, 0.5H, H-1α), 4.45 (d, *J* = 7.8 Hz, 0.5H, H-1β), 3.99 (dt, *J* = 11.1, 4.6 Hz, 0.5H C*H*H OCH_2 α/β), 3.86 (dd, *J* = 11.8, 2.3 Hz, 0.5H, C*H*H H-6α), 3.81 – 3.55 (m, 7.5H, C*H*H H-6α, CH_2 H-6β, H-3α, H-5α, H-5β, C*H*H OCH_2 α/β, 1 x OCH_2 α/β, 2 x OCH_2 α+β), 3.51 – 3.47 (m, 2H, OCH_2), 3.45 (ddd, *J* = 6.4, 5.2, 1.6 Hz, 2H, OCH_2), 3.30 – 3.20 (m, 1.5H, H-3β, H-4β, H-4α), 3.16 (dd, *J* = 9.6, 3.5 Hz, 0.5H, H-2α), 2.91 (dd, *J* = 8.9, 7.8 Hz, 0.5H, H-2β), 1.97 – 1.89 (m, 2H, *CH*$_2$SMe), 1.43 (s, 1.5H, CH_2S*Me* α), 1.42 (s, 1.5H, CH_2S*Me* β). ^{13}C NMR (126 MHz, CD_3OD) δ = 159.3 (C_q Arom), 158.8 (C_q Arom), 158.2 (C_q Arom), 158.0 (C_q Arom), 154.4 (C_H T_3, T_3"), 153.4 (C_H 1), 150.8 (C_H 7), 140.2 (C_H T_5, T_5"), 139.6 (C_H T_5, T_5"), 139.4 (C_H T_4', 9), 138.4 (C_H 3), 129.9 (C_H T_4, T_4"), 129.3 (C_H 2), 128.4 (C_H 8), 126.3 (C_H T_6, T_6"), 126.0 (C_H 4), 125.5 (C_H T_3', T_5'), 125.2 (C_H 10), 98.1 (C-1β), 91.8 (C-1α), 85.2 (C-2β), 82.5 (C-2α), 78.0, 77.6, 73.9, 72.9, 72.6, 71.8, 71.8, 71.6, 71.3, 71.3, 71.2, 70.9, 68.4, 68.3, 62.8 (C-6α/β), 62.7 (C-6α/β), 35.7 (*C*H_2SMe), 35.6 (*C*H_2SMe), 15.4 (CH_2S*Me*), 15.4 (CH_2S*Me*). HRMS: m/z calcd for $[M]^{2+}$: 416.60107; found: 416.60278; Elemental analysis calcd (%) for [**6**]PF_6.3H_2O: C, 44.27; H, 4.89; N, 6.79; found: 44.70; H, 4.73; N, 6.49.



[Ru(tpy)(bpy)(40)]PF_6, [7]PF_6: The title compound was synthesized analogous according to the procedure described for [**1**]$(PF_6)_2$ using [Ru(tpy)(bpy)Cl)]Cl (59.1 mg, 0.105 mmol) and **H40** (40.0 mg, 0.117 mmol) in H_2O (18 mL) affording the title compound as a red solid (44.2 mg, 39.3 µmol, 37%); R_f = 0.55 (100/80/20 acetone/water/aq. KPF_6); ^{1}H NMR (500 MHz, CD_3OD) δ = 9.86 (d, *J* = 5.9 Hz, 1H, 1), 8.96 – 8.80 (m, 3H, 4, T_3', T_5'), 8.74 – 8.69 (m, 2H, T_6, T_6"), 8.67 – 8.62 (m, 1H, 10), 8.51 – 8.40 (m, 2H, T_4', 3), 8.15 (dtd, *J* = 9.6, 4.4, 2.4 Hz, 3H, T_5, T_5", 2), 8.01 – 7.93 (m, 1H, 9), 7.87 – 7.79 (m, 2H, T_3, T_3"), 7.55 – 7.46 (m, 2H, T_4, T_4"), 7.36 – 7.32 (m, 1H, 7), 7.27 (ddt, *J* = 7.3, 5.7, 1.5 Hz, 1H, 8), 5.10 (d, *J* = 3.6 Hz, 0.5H, H-1α), 4.51 (d, *J* = 7.6 Hz, 0.5H, H-1β), 4.29 – 3.08 (m, 15H), 1.96 (t, *J* = 5.4 Hz, 2H, 2 x C*H*$_2$SMe), 1.45 (s, 3H, 2 x CH_2S*Me*). ^{13}C NMR (126 MHz, CD_3OD) δ = 159.3 (C_q Arom), 158.8 (C_q Arom), 158.2 (C_q Arom), 158.0 (C_q Arom), 154.4 (C_H T_3, T_3"), 153.4 (C_H 1), 150.8 (C_H 7), 140.2 (C_H T_5, T_5"), 139.6 (C_H T_4'), 139.4 (C_H 9), 138.3 (C_H 3), 129.9 (C_H T_4, T_4"), 129.3 (C_H 2), 128.4 (C_H 8), 126.3 (C_H T_6, T_6"), 126.0 (C_H 4), 125.5 (C_H T_3', T_5'), 125.2 (C_H 10), 98.2 (C-1β), 94.0 (C-1α), 87.6, 84.4, 77.8, 76.1, 73.7, 73.0, 73.0, 72.0, 72.0, 71.6, 71.4, 71.3, 71.2, 71.2, 71.1, 71.1, 68.4, 68.3, 62.6 (C-6α/β), 62.5 (C-6α/β), 35.7 (2 x *C*H_2SMe), 15.4 (2 x CH_2S*Me*); HRMS: m/z calcd for $[M]^{2+}$: 416.60107; found: 416.60242; Elemental analysis calcd (%) for [**7**]PF_6.2H_2O: C, 45.02; H, 4.87; N, 6.91; found: C, 44.82; H, 4.61; N, 6.79.

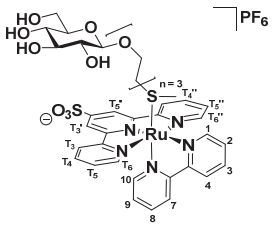


[Ru(tpy)(bpy)(46)]PF_6, [8]PF_6: [Ru(tpy)(bpy)(H_2O)](PF_6)$_2$ (25.8 mg, 32.0 µmol) and **H46** (11.0 mg, 32.1 µmol) were dissolved in a deoxygenated mixture of acetone/H_2O (4:1, 6 mL) and heated at 50 °C for 48 h, after which the reaction mixture was concentrated *in vacuo* and purified over Sephadex LH-20 (MeOH), affording the title compound as a red solid (23 mg, 23.5 µmol, 73%). R_f = 0.61 (100/80/20 acetone/water/aq. KPF_6); ^{1}H NMR (500 MHz, CD_3OD) δ = 9.85 (dd, *J* = 5.5, 1.1 Hz, 1H, 1), 8.86 (d, *J* = 8.3 Hz, 1H, 4), 8.83 (d, *J* = 8.1 Hz, 2H, T_3', T_5'), 8.69 – 8.66 (m, 2H, T_6, T_6"), 8.63 (dt, *J* = 8.2, 1.1 Hz, 1H, 10), 8.47 – 8.41 (m, 2H, T_4', 3), 8.13 (td, *J* = 7.8, 1.5 Hz, 3H, T_5, T_5", 2), 7.96 (td, *J* = 7.9, 1.5 Hz, 1H, 9), 7.82 (dd, *J* = 5.7, 1.6 Hz, 2H, T_3, T_3"), 7.49 (ddt, *J* = 7.3, 5.4, 1.8 Hz, 2H, T_4, T_4"), 7.31 (ddd, *J* = 5.7, 1.6, 0.8 Hz, 1H, 7), 7.25 (ddd, *J* = 7.2, 5.7, 1.3 Hz, 1H, 8), 5.11 (d, *J* = 3.7 Hz, 0.5H, H-1α), 4.44 (d, *J* = 7.8 Hz, 0.5H, H-1β), 3.98 – 3.05 (m, 15H), 1.95 (t, *J* = 5.5 Hz, 2H, 2 x C*H*$_2$SMe), 1.43 (s, 1.5H, CH_2S*Me*), 1.43 (s, 1.5H, CH_2S*Me*). ^{13}C NMR (126 MHz, CD_3OD) δ = 159.3 (C_q Arom), 158.8 (C_q Arom), 158.2 (C_q Arom), 158.0 (C_q Arom), 154.4 (C_H T_3), 154.4 (C_H T_3'), 153.4 (C_H 1), 150.8 (C_H 7), 140.2 (C_H T_5, T_5"), 139.6 (C_H T_4'), 139.4 (C_H 9), 138.3 (C_H 3), 129.9 (C_H T_4, T_4"), 129.3 (C_H 2), 128.4 (C_H 8), 126.3 (C_H T_6, T_6"), 125.9 (C_H 4), 125.5 (C_H T_3', T_5'), 125.2 (C_H 10), 98.3 (C-1β), 93.9 (C-1α), 80.6, 80.4, 78.1, 77.0, 76.3, 74.9, 73.8, 72.8, 72.0, 71.9, 71.3, 71.2, 71.2, 68.4, 68.4, 62.5 (C-6 α/β), 62.4 (C-6α/β), 35.7 (*C*H_2SMe), 35.6 (*C*H_2SMe), 15.3 (2x CH_2S*Me*); HRMS: m/z calcd for $[M]^{2+}$: 416.60107; found: 416.60261; Elemental analysis calcd (%) for [**8**]PF_6.2.5H_2O: C, 44.62; H, 4.93; N, 6.85; found: 45.17; H, 5.16; N, 6.55.

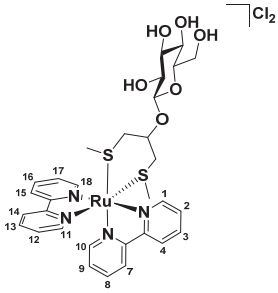


[Ru(tpy)(bpy)(50)]PF_6, [9]PF_6: The title compound was synthesized analogous according to the procedure described for [**1**](PF_6)$_2$ using [Ru(tpy)(bpy)Cl)]Cl (58.8 mg, 0.105 mmol) and **H50** (42.0 mg, 123 µmol) in H_2O (18 mL) affording the title compound as a red solid (23.5 mg, 24.1 µmol, 23%). R_f = 0.36 (16/4/1 acetone/water/1M HCl); ^{1}H NMR (500 MHz, CD_3OD) δ = 9.86 (ddd, *J* = 5.6, 1.5, 0.7 Hz, 1H, 1), 8.89 – 8.87 (m, 1H, 4), 8.85 (d, *J* = 8.2 Hz, 2H, T_3', T_5'), 8.69 (dd, *J* = 8.2, 1.2 Hz, 2H, T_6, T_6"), 8.67 – 8.62 (m, 1H, 10), 8.50 – 8.41 (m, 2H, T_4', 3), 8.16 – 8.10 (m, 3H, T_5, T_5", 2), 7.97 (td, *J* = 7.8, 1.5 Hz, 1H, 9), 7.84 (ddd, *J* = 5.6, 1.5, 0.7 Hz, 2H, T_3, T_3"), 7.50 (ddd, *J* = 7.2, 5.6, 1.4 Hz, 2H, T_4, T_4"), 7.33 (dq, *J* = 5.9, 0.9 Hz, 1H, 7), 7.26 (ddd, *J* = 7.2, 5.7, 1.3 Hz, 1H, 8), 5.10 (d, *J* = 3.6 Hz, 0.5H, H-1α), 4.50 (d, *J* = 7.6 Hz, 0.5H, H-1β), 3.99 – 3.08 (m, 15H), 1.96 (t, *J* = 5.5 Hz, 2H, 2 x C*H*$_2$SMe), 1.44 (s, 3H, 2 x CH_2S*Me*). ^{13}C NMR (126 MHz, CD_3OD) δ = 159.3 (C_q Arom), 158.8 (C_q Arom), 158.2 (C_q Arom), 158.0 (C_q Arom), 154.4 (C_H T_3'), 153.4 (C_H 1), 150.8 (C_H 7), 140.2 (C_H T_5, T_5"), 139.6 (C_H T_4'), 139.4 (C_H 9), 138.3 (C_H 3), 129.9 (C_H T_4, T_4"), 129.3 (C_H 2), 128.4 (C_H 8), 126.3 (C_H T_6, T_6"), 126.0 (C_H 4), 125.6 (C_H T_3'), 125.5 (C_H T_5'), 125.1 (C_H 10), 98.2 (C-1β), 94.0 (C-1α), 87.6, 84.4, 77.8, 76.1, 73.7, 73.0, 73.0, 73.0, 72.0, 72.0, 71.3, 71.3,

71.2, 71.2, 71.1, 68.4, 68.3, 62.6 (C-6α/β), 62.5 (C-6α/β), 35.7 (2 x CH_2SMe), 15.4 (2 x CH_2SMe); HRMS: m/z calcd for $[M]^{2+}$: 416.60107; found: 416.60264; Elemental analysis calcd (%) for [**9**]PF_6.2H_2O: C, 45.02; H, 4.87; N, 6.91; found: C, 44.88; H, 4.59; N, 6.78.



[Ru(S-tpy)(bpy)(26)]PF_6, [10]PF_6: A deoxygenated solution of **31** (40.0 mg, 0.0661 mmol) and **26** (48.0 mg, 0.140 mmol) in H_2O (11 mL) was heated at 80 °C for 16 h after which it was concentrated *in vacuo*. The resulting residue was then purified over silica (100/0/0 to 100/95/5 in acetone/water/aq. KPF_6), followed by purification over Sephadex LH-20 (MeOH) to afford the title compound as a red microcrystalline solid (18 mg, 24.4 µmol, 37%). R_f = 0.46 (100/80/20 acetone/water/aq. KPF_6); ^{1}H NMR (500 MHz, CD_3OD) δ = 9.84 (d, *J* = 5.9 Hz, 1H, 1), 9.03 (s, 2H, T_3', T_5'), 8.81 (d, *J* = 8.2 Hz, 1H, 4), 8.73 (d, *J* = 8.1 Hz, 2H, T_6, T_6"), 8.58 (d, *J* = 8.2 Hz, 1H, 10), 8.43 (t, *J* = 7.9 Hz, 1H, 3), 8.13 (dt, *J* = 13.2, 7.4 Hz, 3H, 2, T_4, T_4"), 7.95 (t, *J* = 7.7 Hz, 1H, 9), 7.81 (d, *J* = 5.9 Hz, 2H, T_3, T_3"), 7.60 – 7.43 (m, 2H, T_5, T_5"), 7.25 (dt, *J* = 12.7, 6.0 Hz, 2H, 8, 7), 4.30 (d, *J* = 7.8 Hz, 1H, H-1), 4.00 (dd, *J* = 10.6, 5.3 Hz, 1H, C*H*H OCH_2), 3.86 (d, *J* = 12.0 Hz, 1H, C*H*H H-6), 3.67 (m, 4H, C*H*H H-6, C*H*H OCH_2, 2 x OCH_2), 3.57 (dd, *J* = 5.7, 3.4 Hz, 2H, OCH_2), 3.48 (dd, *J* = 5.8, 3.4 Hz, 2H, OCH_2), 3.44 (t, *J* = 5.5 Hz, 2H, OCH_2), 3.41 – 3.36 (m, 1H, H-3), 3.29 (m, 2H, H-4, H-5), 3.14 (t, *J* = 8.5 Hz, 1H, H-2), 1.91 (t, *J* = 5.5 Hz, 2H, CH_2SMe), 1.41 (s, 3H, CH_2SMe). ^{13}C NMR (126 MHz, CD_3OD) δ = 159.2 (C_q Arom), 158.7 (C_q Arom), 157.9 (C_q Arom), 157.7 (C_q Arom), 154.8 (C_q Arom), 154.2 (C_H T_3, T_3"), 153.2 (C_H 1), 150.6 (C_H 7), 140.4 (C_H T_4, T_4"), 139.8 (C_H 3), 139.6 (C_H 9), 130.2 (C_H T_5, T_5"), 129.3 (C_H 8) 128.5 (C_H 2), 126.7 (C_H T_6, T_6"), 125.9 (C_H 4), 125.1 (C_H 10), 121.7 (CH T_3', T_5'), 104.2 (C-1), 77.8 (C-3, C-5), 74.9 (C-2), 71.4 (C-5), 71.1 (OCH_2), 71.0 (OCH_2), 69.7 (OCH_2), 68.0 (OCH_2), 62.5 (C-6), 35.2 (CH_2SMe), 15.2 (CH_2SMe). HRMS: m/z calcd for $[M]^+$: 912.15167; found: 912.15427; Elemental analysis calcd (%) for [**10**]PF_6.0.5KPF_6.5H_2O: C, 36.84; H, 4.39; N, 5.65; found: 36.83; H, 4.40; N, 5.36.



Δ/Λ-[Ru(tpy)(bpy)(28)]$(PF_6)_2$, [11]Cl_2: [Ru(bpy$_2$)Cl_2] (73.0 mg, 0.151 mmol) and **28** (46.0 mg, 0.146 mmol) were dissolved in deoxygenated H_2O (10 mL) and this mixture was heated at 80 °C for 16 h, after which the mixture was concentrated in *vacuo*. Purification by Sephadex LH-20 (MeOH) afforded the title compound as an inseparable mixture of diastereomers (69.0 mg, 0.0864 mmol, 59%). R_f = 0.28 (16/4/1 acetone/water/1M HCl); ^{1}H NMR (500 MHz, CD_3OD) δ = 10.02 (dd, *J* = 5.7, 1.4 Hz, 1H), 9.86 (dd, *J* = 5.7, 1.4 Hz, 1H), 9.50 (dd, *J* = 5.7, 1.4 Hz, 1H), 9.42 (dd, *J* = 5.7, 1.3 Hz, 1H), 8.81 (d, *J* = 8.2 Hz, 2H), 8.79 – 8.76 (m, 2H), 8.69 – 8.62 (m, 4H), 8.45 – 8.36 (m, 4H), 8.12 (tt, *J* = 8.0, 1.8 Hz, 4H), 8.06 (dddd, *J* = 13.5, 7.3, 5.6, 1.4 Hz, 5H), 7.63 (td, *J* = 5.7, 1.4 Hz, 2H), 7.57 (ddd, *J* = 7.5, 5.7, 1.4 Hz, 2H), 7.49 – 7.42 (m, 4H), 4.65 (d, *J* =

7.8 Hz, 1H), 4.58 (d, *J* = 7.8 Hz, 1H), 3.92 (ddd, *J* = 19.8, 11.8, 1.9 Hz, 2H), 3.78 – 3.70 (m, 1H), 3.62 (dd, *J* = 11.9, 6.4 Hz, 1H), 3.50 – 3.35 (m, 10H), 3.30 (t, *J* = 8.2 Hz, 1H), 3.27 – 3.20 (m, 2H), 3.13 (dd, *J* = 14.0, 6.4 Hz, 1H), 3.02 (dd, *J* = 13.9, 7.1 Hz, 1H), 2.92 (dd, *J* = 13.1, 2.1 Hz, 1H), 2.80 (dd, *J* = 13.1, 1.7 Hz, 1H), 1.53 (s, 3H), 1.50 (s, 3H), 1.25 (s, 3H), 1.23 (s, 3H). ^{13}C NMR (126 MHz, CD_3OD) δ = 159.1, 159.1, 159.0, 158.9, 158.1, 158.0, 157.9, 155.4, 155.0, 154.9, 154.8, 152.0, 152.0, 151.9, 151.9, 140.3, 140.2, 130.8, 130.0, 129.9, 129.5, 129.3, 129.0, 129.0, 128.9, 126.2, 126.1, 126.0, 125.6, 125.6, 125.5, 125.4, 104.2, 103.6, 78.4, 78.3, 78.3, 78.2, 75.3, 75.3, 75.2, 71.6, 71.6, 62.7, 40.5, 38.6, 38.4, 37.4, 18.5, 18. 1, 16.1, 16.0; HRMS: m/z calcd for $[M]^{2+}$: 364.06326; found: 364.06459; Elemental analysis calcd (%) for [**11**]$Cl_2.3H_2O$: C, 43.66; H, 5.20; N, 6.57; found: 43.34; H, 5.35; N, 6.29.

References

[1] K. H. Schleifer, O. Kandler, *Bacteriol Rev* **1972**, *36*, 407-477.

[2] K. H. Caffall, D. Mohnen, *Carbohyd Res* **2009**, *344*, 1879-1900.

[3] H. Merzendorfer, L. Zimoch, *J Exp Biol* **2003**, *206*, 4393-4412.

[4] B. K. Brandley, R. L. Schnaar, *J Leukocyte Biol* **1986**, *40*, 97-111.

[5] J. D. Watson, F. H. Crick, *Nature* **1953**, *171*, 737-738.

[6] S. Tornroth-Horsefield, R. Neutze, *P Natl Acad Sci USA* **2008**, *105*, 19565-19566.

[7] M. G. Vander Heiden, L. C. Cantley, C. B. Thompson, *Science* **2009**, *324*, 1029-1033.

[8] L. Szablewski, *Biochim Biophys Acta* **2013**, *1835*, 164-169.

[9] J. S. Fowler, T. Ido, *Semin Nucl Med* **2002**, *32*, 6-12.

[10] E. C. Calvaresi, P. J. Hergenrother, *Chem Sci* **2013**, *4*, 2319-2333.

[11] M. Patra, S. G. Awuah, S. J. Lippard, *J Am Chem Soc* **2016**, *138*, 12541-12551.

[12] J. Petrig, R. Schibli, C. Dumas, R. Alberto, P. A. Schubiger, *Chem Eur J* **2001**, *7*, 1868-1873.

[13] N. T. Kulishkin, A. V. Mashkina, *React Kinet Catal L* **1991**, *45*, 41-47.

[14] J. C. Hermann, Y. Chen, C. Wartchow, J. Menke, L. Gao, S. K. Gleason, N. E. Haynes, N. Scott, A. Petersen, S. Gabriel, B. Vu, K. M. George, A. Narayanan, S. H. Li, H. Qian, N. Beatini, L. Niu, Q. F. Gan, *ACS Med Chem Lett* **2013**, *4*, 197-200.

[15] S. van der Vorm, T. Hansen, H. S. Overkleeft, G. A. van der Marel, J. D. C. Codee, *Chem Sci* **2017**, *8*, 1867-1875.

[16] B. G. Davis, M. A. T. Maughan, M. P. Green, A. Ullman, J. B. Jones, *Tetrahedron: Asymmetry* **2000**, *11*, 245-262.

[17] S. Valerio, A. Iadonisi, M. Adinolfi, A. Ravida, *J Org Chem* **2007**, *72*, 6097-6106.

[18] B. Fraser-Reid, Z. Wu, U. E. Udodong, H. Ottosson, *J Org Chem* **1990**, *55*, 6068-6070.

[19] Z. Yang, W. Lin, B. Yu, *Carbohyd Res* **2000**, *329*, 879-884.

[20] J. Park, J. I. Um, A. Jo, J. Lee, D. W. Jung, D. R. Williams, S. B. Park, *Chem Commun* **2014**, *50*, 9251-9254.

[21] C. W. Machan, M. Adelhardt, A. A. Sarjeant, C. L. Stern, J. Sutter, K. Meyer, C. A. Mirkin, *J Am Chem Soc* **2012**, *134*, 16921-16924.

[22] C. Dumas, R. Schibli, P. A. Schubiger, *J Org Chem* **2003**, *68*, 512-518.

[23] Y. Li, G. Manickam, A. Ghoshal, P. Subramaniam, *Synth Commun* **2006**, *36*, 925-928.

[24] G. Grue-Sørensen, E. Kelstrup, A. Kjær, J. Ø. Madsen, *J Chem Soc, Perkin Trans 1* **1984**, 1091-1097.

[25] Y. Miao, C. Rousseau, A. Mortreux, P. Martin, P. Zinck, *Polymer* **2011**, *52*, 5018-5026.

[26] a). J. Gervay, S. Danishefsky, *J Org Chem* **1991**, *56*, 5448-5451; b). R. L. Halcomb, S. J. Danishefsky, *J Am Chem Soc* **1989**, *111*, 6661-6666.

[27] A. G. Volbeda, H. A. Kistemaker, H. S. Overkleeft, G. A. van der Marel, D. V. Filippov, J. D. C. Codee, *J Org Chem* **2015**, *80*, 8796-8806.

[28] J. T. Doi, G. W. Luehr, *Tetrahedron Lett* **1985**, *26*, 6143-6146.

[29] a). F. Hu, Z. Chen, L. Zhang, Y. Shen, L. Wei, W. Min, *Angew Chem Int Ed* **2015**, *54*, 9821-9825; b). X. Xue, Z. Yin, X. Meng, Z. Li, *J Org Chem* **2013**, *78*, 9354-9365; c). T. K. M. Shing, Y. L. Zhong, *Tetrahedron* **2001**, *57*, 1573-1579.

[30] E. Kaji, F. W. Lichtenthaler, Y. Osa, K. Takahashi, S. Zen, *Bull Chem Soc Jpn* **1995**, *68*, 2401-2408.

[31] C. Morin, L. Ogier, *Carbohydr Res* **1998**, *310*, 277-282.

[32] T. A. Wark, D. W. Stephan, *Organometallics* **1989**, *8*, 2836-2843.

[33] U. Muhlhausen, R. Schirrmacher, M. Piel, B. Lecher, M. Briegert, A. Piee-Staffa, B. Kaina, F. Rosch, *J Med Chem* **2006**, *49*, 263-272.

[34] Q. Wang, P. Day, J. P. Griffiths, H. Nie, J. D. Wallis, *New J Chem* **2006**, *30*, 1790-1800.