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FULL PAPER

Synthesis of water soluble *O*-glycosides of *N*-(hydroxyalkyl)-aminomethylferrocenes †

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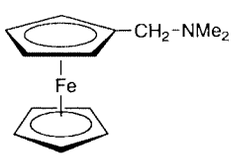
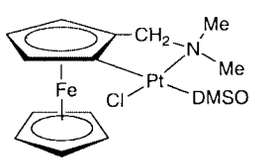
A series of water soluble ferrocenylamine–glucose conjugates, [*N*-2-(β-D-glucopyranosyloxy)ethyl-, [*N*-3-(β-D-glucopyranosyloxy)propyl-, [*N*-5-(β-D-glucopyranosyloxy)pentyl-*N*-methylaminomethyl]ferrocene, has been synthesized from the methiodide salt of *N*,*N*-dimethylaminomethylferrocene and *N*-(3,4,6-tri-*O*-benzyl-β-D-glucopyranosyloxy-ethyl, -propyl and -pentyl)amine respectively. *N*-Methylation of the products from the latter reaction was achieved by formylation followed by reduction with lithium aluminium hydride. Catalytic hydrogenolysis over palladium removed the benzyl protecting groups from the carbohydrate moiety to give the target conjugates. An alternative synthesis of [*N*-2-(β-D-glucopyranosyloxyethyl)aminomethyl]ferrocene using boron trifluoride–diethyl ether promoted glycosylation of penta-*O*-acetyl-D-glucopyranose and [*N*-(2-hydroxyethyl)-*N*-methylaminomethyl]ferrocene followed by deacetylation of the carbohydrate protecting group using basic ion exchange resin was also developed. The pK_a values of the water soluble conjugates were determined.

Introduction

In previous work we have shown the versatility of ferrocenylamines as ligands for transition metals such as platinum(II).[1] Reaction of FMA and $PtCl_2(DMSO)_2$ readily gives the cyclometallated complex **1** which showed useful activity against cisplatin, $PtCl_2(NH_3)_2$, resistant tumours and low liver dysfunction.[2] Unfortunately, it and a series of analogues did not offer significant advantages in comparison to other potential drugs.



FMA



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Ferrocenylamines themselves exhibit biological activity. Redox mechanisms have been proposed for metallocene antitumour and drug activity[3] and there is now strong evidence that ferrocenium salts bind directly to DNA *via* preferential interaction with the 5′-phosphate.[4] Experimental data for ferrocenylamines and the cycloplatinated complexes are inconclusive however. Their low oxidation potentials[5,6] could allow *in vivo* oxidation to the ferrocenium species but cell culture experiments do not support this perception.[7]

If the efficacy of the ferrocenylamines and their metal complexes is to be improved, it is desirable to probe the nature of their *in vivo* and cellular interactions in an aqueous environment. Unfortunately, the hydrophobic character of the ferrocene compounds poses a problem for biological investigations. Apart from solubility factors, hepatotoxicity and histology data have shown[2] that there is gross internal irritation from solids with either non-aqueous or peanut oil intravenous injection in mice. Increased aqueous solubility has been achieved in the cyclometallated complexes by incorporation of anionic carboxylate leaving groups *cis* to the Pt–C bond but internal aggravation was again evident with buffered aqueous injections.[8] We therefore looked for alternative methodology which would allow us to use ferrocenylamines and their complexes as bioprobes. Carbohydrates were attractive because they are structurally diverse, generally neutral and water soluble. A range of compounds where the ferrocenyl group and sugar residues are linked *via* a heteroatom have been reported. These include cyclodextrin complexes[9] and ferrocene connected *via* anomeric-*O*[10] and -*S*[11,12] and non-anomeric-*O*,-*N*[11,13] linkages; however many of these have low solubility in water. Alternatively, the ferrocenylsugar can be synthesized directly from cyclopentadienyl *C*-glycosyls.[7] There is one example where a perbenzylated glucopyranosyl unit is attached to the Cp ring of a ferrocene by a carbon–carbon bond.[14] Although there are no cytotoxicity data reported for these ferrocenylsugars, there is an expectation that the pharmacological utility of the ferrocenylamines will be enhanced with a carbohydrate substituent endowing them with greater water solubility.

Our synthetic strategy was designed to lead to a general preparation of water-soluble ferrocenylamine–carbohydrate conjugates with functionalities which could be adapted for co-ordination to Pt^{II} for studies on biological activity, directed to specific protein interactions, or linked with metal clusters and polyaromatic fluorophores to form ion-selective sensors. This paper describes the synthesis of water soluble analogues of FMA where one of the *N*-methyl groups has been replaced by an alkyl substituent attached to a glucopyranosyloxy unit. The following paper[15] reports the syntheses and structures of aminomethylferrocene–carbohydrate conjugates where a methylferrocene unit is attached to the nitrogen of the amine group of an amino-sugar (*i.e.* the *N*-ferrocenyl-*N*-glycosyl amine). The electrochemistry of both systems, *N*- and *O*-ferrocenylamine glycosides, is also described in that paper.

Results and discussion

Three possible routes to ferrocenylamine–carbohydrate conjugates of type **2** based on the retrosynthetic bond disconnections (**A**, **B** and **C**, Fig. 1) were investigated. It was envisaged that the first, based on bond disconnection **A**, could be achieved using a

† Ferrocenylamine–carbohydrate conjugates. Part 1. Electronic supplementary information (ESI) available: IR and ^{13}C NMR data. See http://www.rsc.org/suppdata/dt/a9/a908512b/

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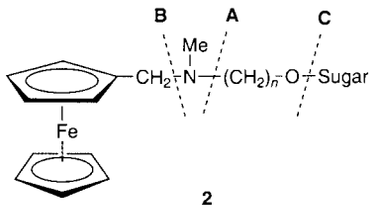

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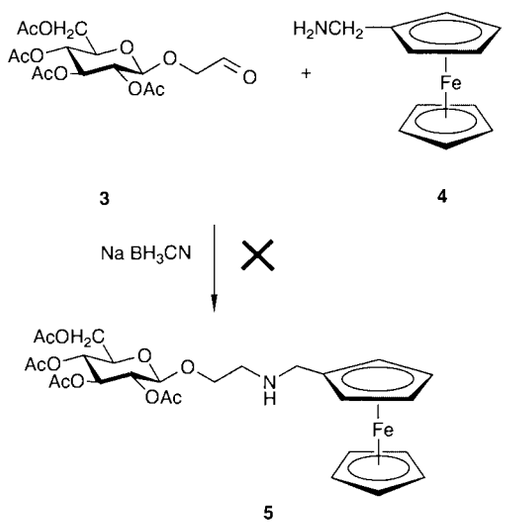
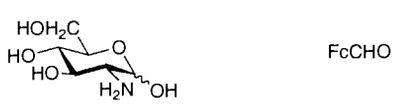
Fig. 1 Strategic bond disconnections.



Scheme 1

modification of a reductive amination process developed by Bernstein and Hall[16] for the preparation of model glycoproteins. Our approach, outlined in Scheme 1, utilised an *in situ* sodium cyanotrihydroborate reduction of the Schiff base formed from the glucopyranosyloxyacetaldehyde **3** and ferrocenylamine **4** to link the carbohydrate and organometallic units. Unfortunately, reaction of **3** and ferrocenylamine **4** under these conditions gave a complex mixture of products, none of which was identified as the target molecule **5**. Similar problems were encountered by Adam and Hall[11] on attempted reduction of a Schiff base derived from glucosamine **6** and ferrocenecarbaldehyde **7**. These researchers succeeded in synthesizing a variety of acetylated carbohydrate–ferrocene conjugates but attempts to deacetylate the sugar moiety under basic conditions generally proved unsuccessful.



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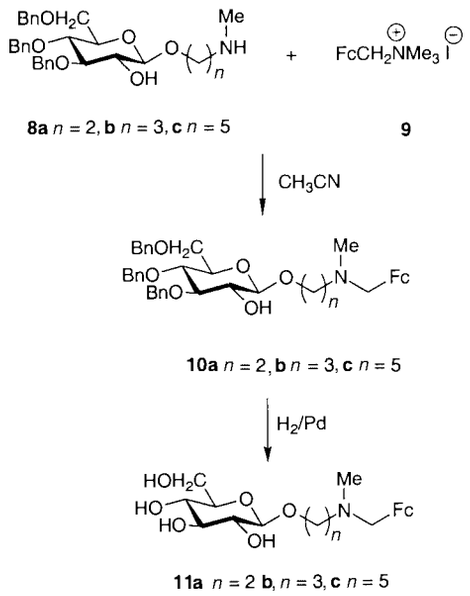
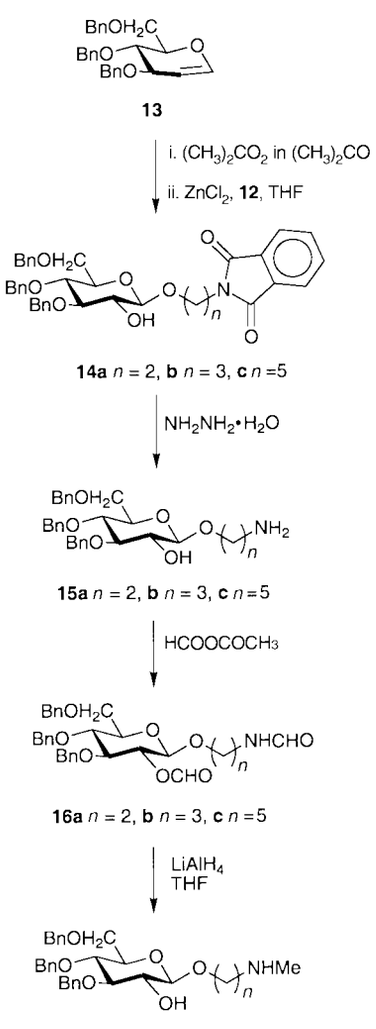
On the basis of the latter results, a strategy (using bond disconnection **B**) was developed which avoided the use of acetyl protection of the carbohydrate and reductive amination processes for coupling a ferrocene unit to the sugar. The synthetic sequence, outlined in Scheme 2, relies on a nucleophilic substitution reaction of *O*-glucosylated *N*-methylalkanolamines **8** with the methiodide salt **9** to provide the protected carbohydrate–ferrocenylamine conjugate. The choice of benzyl (Bn) protecting groups, which are easily removed by catalytic hydrogenolysis, would circumvent inter- and intra-molecular acyl transfer reactions which were presumably complicating the chemistry described in Scheme 1.

The synthetic sequence to the glucosylated alkanolamine precursors **8a** to **8c** is depicted in Scheme 3 and utilises the glucal glycosylation procedure developed by Danishefsky.[17] This method was chosen because of the high stereoselectivity

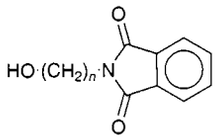


Scheme 2



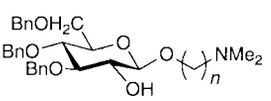
Scheme 3

reported for coupling processes using benzylated glycosyl donors. *N*-Hydroxyalkylphthalimides **12a** to **12c** were prepared from the corresponding alkanolamine and phthalic anhydride.[18] Their zinc chloride promoted glycosylations with the 1,2-epoxide of tri-*O*-benzyl-D-glucal **13** afforded after silica-gel column chromatography the β-glycosides **14a** to **14c** in yields of



12a $n=2$, **b** $n=3$, **c** $n=5$

34, 63 and 45% respectively. In each case assignment of the β-anomeric configuration was confirmed by the magnitude of the coupling constant ($J_{1',2'}$ 7–8 Hz).[19] Deblocking the amino functionality of the phthalimides with hydrazine hydrate gave the primary amines **15a** to **15c** in yields of 79, 67 and 78% respectively. It was envisaged that methylation of the amine functionality of compounds **15** could best be achieved by formylation of both the amine and alcohol functionality. Subsequent treatment with lithium aluminium hydride should reduce the formyl ester to an alcohol and the formamide to the desired secondary amine. Formylation of **15a** to **15c** proceeded smoothly and reduction of formamide **16a** gave the desired glycosylated secondary amine **8a** with the two-carbon spacer in 77% yield. Unfortunately the reductions of formamides **16b** and **16c** were relatively low yielding processes. In the latter cases it was found that after initial formation of secondary amine functionality an intramolecular transfer of a formyl group from the C-2 ester group was a competing process. Subsequent reduction gave the *N*,*N*-dimethylamines **17b** and **17c** as by-products. This problem was circumvented by initial base hydrolysis of the ester followed by lithium aluminium hydride reduction of the formamide. Using this approach **16b** was converted into **8b** in 77% yield (Scheme 3).

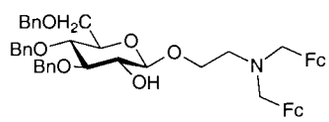


17b $n = 3$, **c** $n = 5$

With the series of *O*-glucosylated *N*-methylalkanolamines in hand the coupling reactions to the ferrocene unit were investigated (Scheme 2). Reaction of **8a** to **8c** with methiodide salt **9** and potassium carbonate in acetonitrile gave the corresponding conjugates **10a** to **10c** in yields of 78, 80 and 70% respectively. Their formation was confirmed by spectral and microanalytical data. The ^{1}H and ^{13}C NMR spectral data were consistent with the proposed structures and showed the typical resonances of benzylated β-glucosides and also those of substituted ferrocenes.

The remaining step in the strategy towards water soluble ferrocenylamine–carbohydrate conjugates was the hydrogenolytic removal of the protecting groups of the sugar unit. Careful monitoring of the catalytic hydrogenolyses of **10a** to **10c** was required as reductive cleavage of the benzylic ferrocene CH_2–N bond of each substrate was a possibility. Treatment of **10a** to **10c** in glacial acetic acid with 10% palladium on carbon gave the target conjugates **11a** to **11c** in yields of 91, 73 and 90% respectively after purification by reversed phase column chromatography and treatment of the residue with basic ion exchange in methanol to ensure complete deprotonation of the amine (Scheme 2). Compound **11a** analysed for $C_{20}H_{29}FeNO_6$ and this was confirmed by high resolution mass spectral data. All the NMR data were assigned to the relevant ^{1}H and ^{13}C nuclei with the aid of 2-D experiments. The ^{1}H NMR spectrum recorded in D_2O (**11a** was also slightly soluble in $CDCl_3$) showed a three proton singlet at δ 2.19 assigned to the resonance of the N-methyl protons. A two proton multiplet at δ 3.54 was attributed to the α-protons of the cyclopentadienyl ring whilst the remaining Cp protons resonated as a seven proton multiplet at δ 3.84. The anomeric proton of the D-glucopyranose residue appeared as a doublet at δ 4.40. The coupling constant ($J_{1',2'}$ 8 Hz) confirmed the assignment of β-anomeric configuration. The ^{13}C NMR spectrum was consistent with the proposed structure of **11a**. Signals at δ 71.5 and 69.0 were assigned to the α- and β-carbons of the Cp ring while a large signal at δ 69.5 was attributed to the Cp carbons. The anomeric carbon resonated at δ 103.0. Conjugates **11b** and **11c** showed similar spectral data. However, a notable feature of these compounds was that they were soluble in both D_2O and $CDCl_3$.

Although avoiding the use of acetyl protecting groups on the carbohydrate was pivotal in the success of this approach it was unclear to us whether the reductive amination process was instrumental in the failure of the chemistry depicted in Scheme 1. To test this, reductive aminations of the secondary amine **8a** and primary amine **15a** and carbaldehyde **7** were investigated. Treatment of a mixture of **8a** and **7** with sodium cyanotrihydroborate in acetonitrile gave the target conjugate **10a** in 82% yield after column chromatography. Surprisingly however, treatment of an equimolar mixture of primary amine **15a** and **7** under similar reaction conditions gave the bis(ferrocenyl)amine conjugate **18** as the only ferrocene containing product in a 38% yield. The mechanism of its formation is unclear as the secondary amine **20**, formed by the cyanotrihydroborate reduction of the Schiff base **19**, should be the major product on the basis of the stoichiometry of the reactants. Changing the ratio of **15a** to **7** to 1:2 gave an increased yield of **18** (71%).



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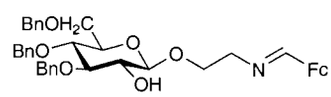

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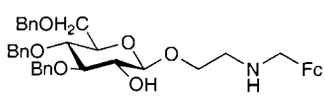

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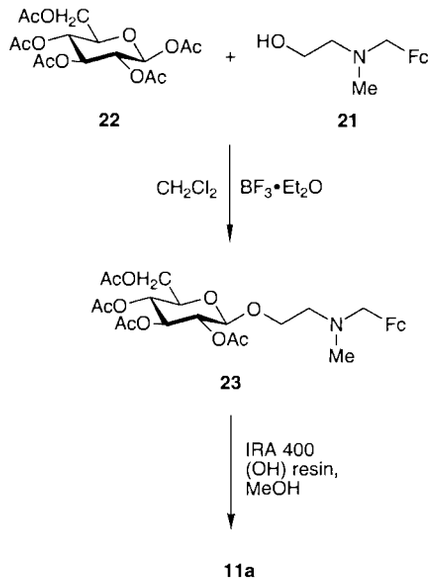
The success of the above syntheses was limited by the number of synthetic steps and the moderate yield of the Danishefsky glycosylation process. An alternative approach would be to use a strategy based on disconnection **C**. Such an approach is shown in Scheme 4 and involves the *O*-glycosylation of ferrocenylethanolamine derivative **21**. It was felt that acetyl protection of the carbohydrate could be tolerated in this system as the tertiary amine group should not participate in acyl transfer reactions.

Reaction of *N*-methylethanolamine with the methiodide **9** and potassium carbonate in acetonitrile at reflux gave the ferrocene adduct **21** in 72% yield. *O*-Glycosylation of **21** and penta-*O*-acetyl-β-D-glucospyranose **22**, promoted by boron trifluoride–diethyl ether (1:1),[20] gave the target conjugate **23** in 34% yield after chromatographic purification. The coupling constant ($J_{1',2'}$ 8 Hz) confirmed the assignment of the β-anomeric configuration of the glucopyranosyl unit. All other spectral data were consistent with the proposed structure. Although Adam and Hall[11] reported poor results for the sodium methoxide *O*-deacetylation of carbohydrate–ferrocene conjugates we felt that hydrolysis using methoxide should give the desired result. To this end a solution of the acetylated conjugate in methanol was treated with IRA 400 (OH) resin using the protocol of Pathok.[21] After filtration, removal of



Scheme 4

methanol gave the target water soluble ferrocenylamine–carbohydrate conjugate **11a** in excellent yield (85%). Even though the overall yield of **11a** from *N*-methylethanolamine was 23% it is superior to that obtained using the sequence described in Schemes 2 and 3 (*i.e.* 10%). Furthermore the brevity, three steps from a commercially available amine, makes this the synthesis of choice.

As the principal aim of this work was to produce water soluble ferrocenylamine systems the solubilities of compounds **11a**–**11c** in water were investigated. That of **11a** was measured as 5.4 g l^{-1}. The much greater solubilities of **11b** and **11c**, 54 and 84 g l^{-1} respective, were attributed to micelle formation. Of note was the fact that the NMR data for **11a**–**11c** were recorded in D_2O. Furthermore, amines **11b** and **11c** were also soluble in $CDCl_3$. The basicity of the target ferrocenylamines was also investigated as this appears to be an important factor for their use as ligands. Thus the pK_a values of **11a** and **11b** were determined by standard potentiometric methods and found to be 9.2 and 9.8 respectively. These compare well with the data for a range of ferrocenyl amines including that of FMA (8.8) reported by Duffy *et al.*[5]

Conclusion

This paper reports the successful syntheses of three water soluble ferrocenylamine–carbohydrate conjugates **11a**–**11c**. The preferred route to **11a** involved the boron trifluoride–diethyl ether reaction of per-acetylated glucose with the substituted ethanolamine derivative **21**. Deacetylation gave the target conjugate **11a** in 23% overall yield from *N*-methylethanolamine. An alternative route using the reactions of benzylated *N*-glycosyloxy-*N*-methylamines **8a**–**8c** with methiodide salt **9**, followed by hydrogenolytic debenzylation, also afforded the target conjugates **11a**–**11c**. Although the latter route is clearly longer and less efficient, it could easily be adapted to allow the synthesis of more complex ferrocenylamine–carbohydrate conjugates.

Experimental

Dichloromethane was distilled from P_2O_5 and tetrahydrofuran (THF) from sodium–benzophenone under nitrogen. All other solvents and reagents were purified using standard methods.[22] The IR spectra were recorded on a Digilab FX60, NMR spectra on a Varian VSR300 MHz spectrometer (^1H and ^{13}C as solutions in deuteriochloroform at 300 and 75 MHz respectively and referenced to residual chloroform unless otherwise stated). Microanalyses were carried out by the Campbell Microanalytical Laboratory, University of Otago. The FAB and EI mass spectra were recorded on a Kratos MS80RFA instrument with an Iontech ZN11NF atom gun. Optical rotations were recorded on a JASCO DIP-1000 digital polarimeter.

Preparation of phthalimides 14a–14c

***N*-[2-(3,4,6-Tri-*O*-benzyl-β-D-glucopyranosyloxy)ethyl]-phthalimide 14a.** An acetone solution of dimethyldioxirane (76 ml, 6.0 mmol) was added to tri-*O*-benzyl-D-glucal (**13**) (1.00 g, 2.40 mmol) and 4 Å powdered molecular sieves (1.50 g) in dichloromethane (10 ml) and the mixture stirred for 1 hour at 0 °C. The solvent was removed and the residue dried *in vacuo* for 3 hours. THF (15 ml) was added to the residue and the mixture cooled to −78 °C. A solution of 2-hydroxyethylphthalimide **12a** (920 mg, 4.80 mmol) in THF (10 ml) was then added followed by the addition of an ether solution of anhydrous zinc chloride (9 ml, 0.53 M, 4.80 mmol). The mixture was stirred and allowed to warm slowly to room temperature over 17 hours before being poured into water (150 ml) and filtered. The filtrate was washed with dichloromethane (2 × 100 ml) and the organic layer was dried ($MgSO_4$) and evaporated to dryness. The crude product mixture was purified by silica gel column chromatography (1:19 Et_2O–CH_2Cl_2, R_F 0.33) to give compound **14a** (1.03 g, 34%) as a clear oil which solidified on standing. Crystallisation of the solid from dichloromethane and hexanes gave white crystals, mp 103–105 °C; $[a]_D^{25} = -63.6$ (*c* 0.4 g dl^{-1}, CH_2Cl_2) (Found: C, 70.95; H, 6.04; N, 2.50%; MNa *m*/*z* 646, $MH^+ - 2H$ 622. $C_{37}H_{37}NO_8$ requires: C, 71.25; H, 5.98; N, 2.25%; M^+ 623); $\delta_H(CDCl_3)$ 3.28 (1 H, s, OH), 3.43–4.05 (9 H, m), 4.10–4.20 (1 H, m, 2-H), 4.29 (1 H, d, *J* 7, 1′-H), 4.47–4.60 (3 H, m, OC*H*HPh), 4.80 (1 H, d, *J* 11, OC*H*HPh), 4.83 (1 H, d, *J* 6, OC*H*HPh), 5.02 (1 H, d, *J* 11 Hz, OC*H*HPh), 7.11–7.41 (15 H, m, Ph) and 7.66–7.87 (4 H, m).

***N*-[3-(3,4,6-Tri-*O*-benzyl-β-D-glucopyranosyloxy)propyl]-phthalimide 14b.** By a similar method to that for compound **14a** using **13** (3.00 g, 7.20 mmol) and 3-hydroxypropylphthalimide **12b** (3.00 g, 14.2 mmol), **14b** was obtained as a white foam (2.90 g, 63%) (1:19 Et_2O–CH_2Cl_2, R_F 0.37); $[a]_D^{25} = 16.6$ (*c* 0.4, CH_2Cl_2) (Found: C, 71.77; H, 6.22; N, 2.02%; MH^+ *m*/*z* 638, $MH^+ - 2H$ 636. $C_{38}H_{39}NO_8$ requires: C, 71.57; H, 6.16; N, 2.30%; M^+ 637); $\delta_H(CDCl_3)$ 1.97–2.17 (2 H, m, 2-H_2), 3.39 (1 H, s, OH), 3.44–3.83 (8 H, m), 3.94–4.04 (2 H, m, 3-H_2), 4.24 (1 H, d, *J* 7, 1′-H), 4.49–4.62 (3 H, m, OC*H*HPh), 4.83 (1 H, d, *J* 11, OC*H*HPh), 4.85 (1 H, d, *J* 11, OC*H*HPh), 5.07 (1 H, d, *J* 11 Hz, OC*H*HPh), 7.15–7.45 (15 H, m, Ph) and 7.66–7.88 (4 H, m).

***N*-[5-(3,4,6-Tri-*O*-benzyl-β-D-glucopyranosyloxy)pentyl]-phthalimide 14c.** Similarly, using compound **13** (3.00 g, 7.2 mmol) and 5-hydroxypentylphthalimide **12c** (3.36 g, 14.2 mmol), **14c** was obtained as a foam (2.17 g, 45%) (1:19 Et_2O–CH_2Cl_2, R_F 0.37); $[a]_D^{25} = -10.4$ (*c* 0.4, CH_2Cl_2) (Found: C, 72.21; H, 6.81; N, 2.05%; MH^+ *m*/*z* 666, $MH^+ - 2H$ 664. $C_{40}H_{43}NO_8$ requires: C, 72.16; H, 6.51; N, 2.10%; M^+ 665); $\delta_H(CDCl_3)$ 1.48–1.50 (2 H, m, 3-H_2), 1.60–1.79 (4 H, m, 2-H_2 and 4-H_2), 2.62 (1 H, d, *J* 2, OH), 3.44–3.78 (9 H, m), 3.93 (1 H, dt, *J* 10 and 6, 5-H), 4.24 (1 H, d, *J* 8, 1′-H), 4.49–4.64 (3 H, m, OCH_2Ph), 4.84 (2 H, d, *J* 11 Hz, OC*H*HPh), 4.97 (1 H, d, *J* 11 Hz, OC*H*HPh), 7.12–7.41 (15 H, m, Ph) and 7.66–7.87 (4 H, m).

Preparation of amines 15a–15c

2-Aminoethyl 3,4,6-tri-*O*-benzyl-β-D-glucopyranoside 15a. Hydrazine monohydrate (1 ml) was added to compound **14a** (130 mg, 0.21 mmol) in methanol (30 ml) and the solution stirred at room temperature overnight. The solvent was removed

by rotary evaporation until a syrup remained. Dilution with ethanol and removal of the solvent by rotary evaporation was repeated several times to remove residual hydrazine until a white solid remained. The product was extracted into chloroform (100 ml), the solvent removed and the solid residue crystallised from dichloromethane and hexanes to give white crystals of **15a** (81 mg, 79%), mp 79–81 °C, $[\alpha]_D^{25} = 2.7$ (*c* 0.4, CH_2Cl_2) (Found: MH^+ *m*/*z* 494.2538. $C_{29}H_{35}NO_6$ requires 494.2543); $\delta_H(CDCl_3)$ 2.87–2.95 (2 H, m, 2-H_2), 3.46–3.77 (7 H, m), 3.91–4.00 (1 H, m, 1-H), 4.30 (1 H, d, *J* 7, 1′-H), 4.50–4.64 (3 H, m, OCH_2Ph), 4.84 (2 H, d, *J* 11, OCH_2Ph), 5.00 (1 H, d, *J* 11 Hz, OC*H*HPh) and 7.12–7.43 (15 H, m, Ph).

3-Aminopropyl 3,4,6-tri-*O*-benzyl-β-D-glucopyranoside 15b. From compound **14b** (1.60 g, 3.2 mmol) by a similar method to that for **15a**; as white crystals (1.07 g, 67%); mp 95 °C; $[\alpha]_D^{25} = -7.4$ (*c* 0.4, CH_2Cl_2) (Found: C, 70.64; H, 7.53; N, 3.08%; MH^+ *m*/*z* 508, $MH^+ - H_2O$ 490. $C_{32}H_{41}NO_6$ requires: C, 70.98; H, 7.35; N, 2.76%; MH^+ *m*/*z* 508); $\delta_H(CDCl_3)$ 1.66–1.87 (2 H, m, 2-H_2), 2.79–3.00 (2 H, m, 3-H_2), 3.46–3.78 (7 H, m), 4.04–4.13 (1 H, m, 1-H), 4.29 (1 H, d, *J* 7, 1′-H), 4.49–4.63 (3 H, m, OCH_2Ph), 4.83 (1 H, d, *J* 11, OC*H*HPh), 4.84 (1 H, d, *J* 11, OC*H*HPh), 5.00 (1 H, d, *J* 11 Hz, OC*H*HPh) and 7.12–7.43 (15 H, m, Ph).

5-Aminopentyl 3,4,6-tri-*O*-benzyl-β-D-glucopyranoside 15c. From compound **14c** (1.67 g, 2.5 mmol) as a clear syrup (1.30 g, 78%). $[\alpha]_D^{25}$ −1.2 (*c* 0.4, CH_2Cl_2) (Found: MH^+ *m*/*z* 536.3029. $C_{32}H_{41}NO_6$ requires: 536.3012); $\delta_H(CDCl_3)$ 1.37–1.55 (4 H, m), 1.60–1.73 (2 H, m), 2.71 (2 H, t, *J* 7, 5-H_2), 3.47–3.80 (7 H, m), 3.98 (1 H, dt, *J* 10 and 6, 1-H), 4.27 (1 H, d, *J* 7, 1′-H), 4.53–4.66 (3 H, m, C*H*HPh), 4.86 (2 H, d, *J* 11, OC*H*HPh), 5.00 (1 H, d, *J* 11 Hz, OC*H*HPh) and 7.17–7.44 (15 H, m, Ph).

Preparation of formamides 16a–16c

2-Formamidoethyl 3,4,6-tri-*O*-benzyl-2-*O*-formyl-β-D-glucopyranoside 16a. Pyridine (5 ml) was added slowly to a stirred solution of compound **15a** (200 mg, 0.41 mmol) in formic acetic anhydride (6 ml). A cold water bath was used to control the temperature of the initial reaction and the mixture stirred at room temperature overnight. The solvent was removed and the crude product dissolved in dichloromethane (60 ml) and washed with water (2 × 100 ml). The organic layer was dried ($MgSO_4$), evaporated to dryness and the residue crystallised from dichloromethane and hexanes to give white crystals of **16a** (156 mg, 70%), mp 78–80 °C, $[\alpha]_D^{25} = -12.63$ (*c* 0.4, CH_2Cl_2) (Found: C, 67.71; H, 6.32; N, 2.56%; MH^+ *m*/*z* 550, $MH^+ - CO$ 522. $C_{31}H_{35}NO_8$ requires: C, 67.74; H, 6.42; N, 2.55%; MH^+ *m*/*z* 550); $\delta_H(CDCl_3)$ 3.22–3.33 (1 H, m, 2-H), 3.49–3.74 (7 H, m), 3.81–3.89 (1 H, m, 1-H), 4.35 (1 H, d, *J* 8, 1′-H), 4.53 (2 H, s, OCH_2Ph), 4.54 (1 H, d, *J* 11, OC*H*HPh), 4.68 (1 H, d, *J* 11, OC*H*HPh), 4.81 (2 H, d, *J* 11 Hz, 2 × OC*H*HPh), 6.61 br (1 H, s), 7.15–7.38 (15 H, m, Ph), 7.90 (1 H, s, CHO) and 7.99 (1 H, s),

3-Formamidopropyl 3,4,6-tri-*O*-benzyl-2-*O*-formyl-β-D-glucopyranoside 16b. From compound **15b** (550 mg, 1.1 mmol) by a similar method except that the crude product was purified by silica gel column chromatography (1:1 Et_2O–CH_2Cl_2, $R_F = 0.24$) to give **16b** (519 mg, 85%) as a foam; $[\alpha]_D^{25} = -27.4$ (*c* 0.4, CH_2Cl_2) (Found: C, 67.93; H, 6.52; N, 2.64%; MH^+ *m*/*z* 564. $C_{32}H_{37}NO_8$ requires: C, 68.19; H, 6.62; N, 2,49%; MH^+ *m*/*z* 564); $\delta_H(CDCl_3)$ 1.71–1.82 (2 H, m, 2-H_2), 3.25–3.37 (1 H, m, 3-H), 3.38–3.46 (1 H, m, 3-H), 3.47–3.77 (6 H, m), 3.84–3.93 (1 H, m, 1-H), 4.39 (1 H, d, *J* 8, 1′-H), 4.52 (1 H, d, *J* 17, OC*H*HPh), 4.54 (1 H, d, *J* 11, OC*H*HPh), 4.58 (1 H, d, *J* 17, OC*H*HPh), 4.69 (1 H, d, *J* 11, OC*H*HPh), 4.81 (1 H, d, *J* 11, OC*H*HPh), 4.82 (1 H, d, *J* 11, OC*H*HPh), 4.91 (1 H, t, *J* 8, 2′-H), 6.36–6.44 (1 H, N*H*CHO), 7.12–7.40 (15 H, m, Ph), 7.91 (1 H, d, *J* 2) and 8.00 (1 H, d, *J* 1 Hz).

5-Formamidopentyl 3,4,6-tri-*O*-benzyl-2-*O*-formyl-β-D-glucopyranoside 16c. Compound **15c** (1.20 g, 2.2 mmol) as for **16b** gave **16c** as a white foam (0.80 g, 60%) after purification by silica gel column chromatography (1:4 Et_2O–CH_2Cl_2); $[\alpha]_D^{25} = -8.8$ (*c* 0.4, CH_2Cl_2) (Found: C, 69.08; H, 7.09; N, 2.43%; MH^+ *m*/*z* 592. $C_{34}H_{41}NO_8$ requires: C, 69.01; H, 6.98; N, 2.34%; MH^+ *m*/*z* 592); $\delta_H(CDCl_3)$ 1.31–1.43 (2 H, m), 1.46–1.64 (4 H, m), 3.27 (2 H, apparent q, *J* 4, 5-H_2), 3.42–3.52 (2 H, m, 1-H and 6′-H), 3.65–3.78 (4 H, m), 3.89 (1 H, dt, *J* 10 and 6, 1-H), 4.37 (1 H, d, *J* 8, 1′-H), 4.54 (1 H, d, *J* 12, OC*H*HPh), 4.56 (1 H, d, *J* 11, OC*H*HPh), 4.62 (1 H, d, *J* 12, OC*H*HPh), 4.69 (1 H, d, *J* 11, OC*H*HPh), 4.71 (1 H, t, *J* 10, 2-H), 4.81 (1 H, d, *J* 11, OC*H*HPh), 4.82 (1 H, d, *J* 11, OC*H*HPh), 5.93 (1 H, s, N*H*CHO), 7.18–7.40 (15 H, m, Ph), 8.03 (1 H, d, *J* 1) and 8.13 (1 H, d, *J* 2 Hz).

Preparation of methylamines 8a–8c

2-(*N*-Methylamino)ethyl 3,4,6-tri-*O*-benzyl-β-D-glucopyranoside 8a. Compound **16a** (1.5 g, 2.7 mmol) was dissolved in dry THF (200 ml), lithium aluminium hydride (800 mg) added carefully then the mixture was heated at reflux for 3 hours. Excess of lithium aluminium hydride was quenched by adding water dropwise. The mixture was then poured into dichloromethane (200 ml) and water (200 ml), filtered and the residue washed with dichloromethane (200 ml) and water (200 ml). The organic layer was separated, washed with water (300 ml), dried ($MgSO_4$) and evaporated to dryness. The crude product was purified by silica gel column chromatography (1:1 MeOH–ethylacetate; $R_F = 0.12$) to give **8a** (1.06 g, 77%) as a white foam; $[\alpha]_D^{25} = -0.5$ (*c* 0.4, CH_2Cl_2) (Found: C, 70.61; H, 7.52; N, 2.55%; MH^+ *m*/*z* 508. $C_{30}H_{37}NO_6$ requires: C, 70.98; H, 7.35; N, 2.76%; MH^+ *m*/*z* 508); $\delta_H(CDCl_3)$ 2.45 (3 H, s, CH_3), 2.82 (2 H, t, *J* 5, 2-H_2), 3.46–3.77 (7 H, m), 4.04 (1 H, dt, *J* 11 and 5, 1-H), 4.29 (1 H, d, *J* 7, 1′-H), 4.52 (1 H, d, *J* 11, OC*H*HPh), 4.53 (1 H, d, *J* 12, OC*H*HPh), 4.60 (1 H, d, *J* 12, OC*H*HPh), 4.83 (1 H, d, *J* 11, OC*H*HPh), 4.84 (1 H, d, *J* 11, OC*H*HPh) and 5.00 (1 H, d, *J* 11 Hz, OC*H*HPH).

3-(*N*-Methylamino)propyl 3,4,6-tri-*O*-benzyl-β-D-glucopyranoside 8b. From compound **16b** (3.20 g, 6.1 mmol) by the same method as for **8a** but two products were found **8b** and **17b**. Crystallisation and recrystallisation from dichloromethane and hexanes gave **8b** (1.35 g, 46%) as fine long white needles, mp 93 °C; $[\alpha]_D^{25} = -6.7$ (*c* 0.52, CH_2Cl_2) (Found: C, 71.31; H, 7.83; N, 2.69%; MH^+ *m*/*z* 522. $C_{31}H_{39}NO_6$ requires: C, 71.37; H, 7.54; N, 2.69%; MH^+ *m*/*z* 522); $\delta_H(CDCl_3)$ 1.76–1.86 (2 H, m, 2-H_2), 2.41 (3 H, s, CH_3), 2.66–2.84 (2 H, m, 3-H_2), 3.46–3.79 (7 H, m), 4.06–4.13 (1 H, m, 1-H), 4.27 (1 H, d, *J* 7, 1′-H), 4.51 (1 H, d, *J* 11, OC*H*HPh), 4.53 (1 H, d, *J* 12, OC*H*HPh), 4.61 (1 H, d, *J* 12, OC*H*HPh), 4.82 (1 H, d, *J* 11, OC*H*HPh), 4.84 (1 H, d, *J* 11, OC*H*HPh) and 5.03 (1 H, d, *J* Hz, OC*H*HPh). Removal of solvent from the mother liquors gave 3-(*N*,*N*-dimethylamino)propyl 3,4,6-tri-*O*-benzyl-β-D-glucopyranoside **17b** (0.63 g, 21%) as a colourless oil. $[\alpha]_D^{25} = 3.75$ (*c* 0.44, CH_2Cl_2) (Found: C, 71.91; H, 7.99; N, 2.61%; MH^+ *m*/*z* 537. $C_{32}H_{41}NO_6$ requires: C, 71.75; H, 7.72; N, 2.62%; MH^+ *m*/*z* 537); $\delta_H(CDCl_3)$ 1.64–1.77 (1 H, m, 2-H), 1.80–1.94 (1 H, m, 2-H), 2.23 (6 H, s, $N(CH_3)_2$), 2.41–2.47 (2 H, m, 3-H_2), 3.46–3.78 (7 H, m), 4.07–4.14 (1 H, m, 1-H), 4.26 (1 H, d, *J* 7, 1′-H), 4.50 (1 H, d, *J* 11, OC*H*HPh), 4.53 (1 H, d, *J* 12, OC*H*HPh), 4.60 (1 H, d, *J* 12, OC*H*HPh), 4.81 (1 H, d, *J* 11, OC*H*HPh), 4.84 (1 H, d, *J* 11, OC*H*HPh) and 5.03 (1 H, d, *J* 11 Hz, OC*H*HPh).

5-(*N*-Methylamino)pentyl 3,4,6-tri-*O*-benzyl-β-D-glucopyranoside 8c. From compound **16c** (1.75 g, 3.0 mmol) by the method for **8a** except that the crude product was crystallised from dichloromethane and hexanes to give **8c** (0.90 g, 56%) as fine long white needles; mp 96 °C; $[\alpha]_D^{25} = -6.5$ (*c* 0.42, CH_2Cl_2) (Found: C, 72.21; H, 8.06; N, 2.53%; MH^+ *m*/*z* 550. $C_{33}H_{43}NO_6$

requires: C, 72.10; H, 7.89; N, 2.55%; MH^+ *m/z* 550); $\delta_H(CDCl_3)$ 1.40–1.51 (2 H, m, 3-H_2), 1.51–1.62 (2 H, m, 4-H_2), 1.62–1.74 (2 H, m, 2-H_2), 2.43 (3 H, s, CH_3), 2.46–2.65 (2 H, m, 5-H_2), 3.46–3.62 (5 H, m), 3.68 (1 H, dd, *J* 11 and 5, 6′-H), 3.73 (1 H, dd, *J* 11 and 2, 6′-H), 4.00 (1 H, dt, *J* 10 and 6, 1-H), 4.25 (1 H, d, *J* 7, 1′-H), 4.53 (1 H, d, *J* 11, OC*H*HPh), 4.55 (1 H, d, *J* 12, OC*H*HPh), 4.62 (1 H, d, *J* 12, OC*H*HPh), 4.83 (1 H, d, *J* 11, OC*H*HPh), 4.84 (1 H, d, *J* 11, OC*H*HPh) and 4.99 (1 H, d, *J* 11 Hz, OC*H*HPh).

An alternative preparation of compound 8b. IRA 400 (OH) resin (2 g) was added to a stirred solution of compound **16b** (0.90 g, 1.7 mmol) in MeOH (150 ml). After 1 hour the solution was filtered and evaporated to dryness. Lithium aluminium hydride (400 mg) was added carefully to the residue dissolved in THF (45 ml) and the mixture heated at reflux for 2 hours. Water was added dropwise until the remaining lithium aluminium hydride had been quenched and the mixture poured into dichloromethane (150 ml) and water (150 ml). After filtration the residue was washed with dichloromethane (200 ml) and water (200 ml), the organic layer separated, washed with water (200 ml), dried ($MgSO_4$) and evaporated to dryness. Crystallisation from dichloromethane and hexanes gave **16b** (0.64 g, 77%) as fine long white needles identical to that described above.

Preparation of ferrocenes 10a–10c

***N*-Methyl-*N*-[2-(3,4,6-tri-*O*-benzyl-β-D-glucopyranosyloxy)-ethyl]aminomethylferrocene 10a.** Anhydrous K_2CO_3 (470 mg, 3.4 mmol) and the methiodide salt **9** (440 mg, 1.1 mmol) were added to compound **8a** (190 mg, 0.37 mmol) in CH_3CN (90 ml) and the mixture was refluxed overnight. After filtering off the K_2CO_3 the CH_3CN was removed by rotary evaporation. The residue was dissolved in dichloromethane (200 ml), washed with water (2 × 300 ml), dried ($MgSO_4$) and evaporated to dryness. The crude product was purified by silica gel column chromatography (1:39 MeOH–CH_2Cl_2, R_F 0.33) to give **10a** (347 mg, 78%) as a yellow foam; $[a]_D^{25} = -18.9$ (*c* 0.3, CH_2Cl_2) (Found: C, 69.94; H, 6.61; N, 1.71%; M^+ *m/z* 705. $C_{41}H_{47}FeNO_6$ requires: C, 69.78; H, 6.71; N, 1.99%; M^+ 705); $\delta_H(CDCl_3)$ 2.23 (3 H, s, CH_3), 2.50–2.68 (2 H, m, 1-H_2), 3.45–3.77 (9 H, m), 3.98–4.07 (1 H, m, 2-H), 4.1–4.22 (9 H, m, Cp), 4.26 (1 H, d, *J* 8, 1′-H), 4.50 (1 H, d, *J* 11, OC*H*HPh), 4.53 (1 H, d, *J* 12, OC*H*HPh), 4.59 (1 H, d, *J* 12, OC*H*HPh), 4.81 (1 H, d, *J* 11, OC*H*HPh), 4.85 (1 H, d, *J* 11, OC*H*HPh) and 5.01 (1 H, d, *J* 11 Hz, OC*H*HPh).

***N*-Methyl-*N*-[3-(3,4,6-tri-*O*-benzyl-β-D-glucopyranosyloxy)-propyl]aminomethylferrocene 10b.** From compound **8b** (200 mg, 0.38 mmol) as for **10a**, except for column chromatography the eluent was 1:19 MeOH–CH_2Cl_2 ($R_F = 0.15$), as a yellow foam (220 mg, 80%); $[a]_D^{25} = -1.3$ (*c* 0.4, CH_2Cl_2) (Found: C, 69.75; H, 6.92; N, 1.82%; MH^+ *m/z* 720. $C_{42}H_{49}FeNO_6$ requires: C, 70.09; H, 6.86; N, 1.95%; MH^+ *m/z* 720); $\delta_H(CDCl_3)$ 1.68–1.80 (1 H, m, 2-H), 1.81–1.95 (1 H, m, 2-H), 2.18 (3 H, s, CH_3), 2.41–2.58 (2 H, m, 1-H_2), 3.45–3.77 (9 H, m), 4.03–4.10 (1 H, m, 3-H), 4.10–4.15 (7 H, m, Cp), 4.20–4.24 (2 H, m, Cp), 4.28 (1 H, d, *J* 8, 1′-H), 4.52 (1 H, d, *J* 11, OC*H*HPh), 4.53 (1 H, d, *J* 12, OC*H*HPh), 4.61 (1 H, d, *J* 12, OC*H*HPh), 4.83 (1 H, d, *J* 11, OC*H*HPh), 4.86 (1 H, d, *J* 11, OC*H*HPh) and 5.06 (1 H, d, *J* 11 Hz, OC*H*HPh).

***N*-Methyl-*N*-[5-(3,4,6-tri-*O*-benzyl-β-D-glucopyranosyloxy)-pentyl]aminomethylferrocene 10c.** From compound **8c** (500 mg, 0.91 mmol) using 1:19 MeOH–CH_2Cl_2 ($R_F = 0.18$) as the eluent, as a yellow foam (480 mg, 70%); $[a]_D^{25} = -14.1$ (*c* 0.4, CH_2Cl_2) (Found: C, 70.41; H, 7.43; N, 1.87%; MH^+ *m/z* 748. $C_{44}H_{53}FeNO_6$ requires: C, 70.67; H, 7.14; N, 1.87%; MH^+ *m/z* 748); $\delta_H(CDCl_3)$ 1.35–1.49 (2 H, m, 3-H_2), 1.53–1.77 (4 H, m, 2-H_2 and 4-H_2), 2.09 (3 H, s, *N*-CH_3), 2.13 (1 H, dt, *J* 12 and 8, 4-H), 2.51 (1 H, dt, *J* 12 and 8, 4-H), 3.39 (2 H, s, CH_2Fc), 3.41–3.61 (5 H, m), 4.02–4.11 (8 H, m, Cp), 4.14–4.16 (1 H, m, Cp), 4.17–4.20 (1 H, m, Cp), 4.23 (1 H, d, *J* 8, 1′-H), 4.52 (1 H, d, *J* 11, OC*H*HPh), 4.54 (1 H, d, *H* 12, OC*H*HPh), 4.62 (1 H, d, *J* 12, OC*H*HPh), 4.81 (1 H, d, *J* 11, OC*H*HPh), 4.85 (1 H, d, *J* 11, OC*H*HPh) and 5.00 (1 H, d, *J* 11 Hz, OC*H*HPh).

Preparation of water soluble ferrocenes 11a–11c

***N*-[2-(β-D-Glucopyranosyloxy)ethyl]-*N*-methylaminomethyl-ferrocene 11a.** Compound **10a** (100 mg, 0.14 mmol) was dissolved in distilled concentrated acetic acid (25 ml), 10% palladium on carbon (35 mg) added and the mixture stirred under an atmosphere of hydrogen for 24 hours. The Pd/C was removed by filtration through Celite®, and a further portion of 10% Pd/C (35 mg) added. The mixture was stirred under an atmosphere of hydrogen for 24 hours. The solids were removed by filtration and the solution was evaporated to dryness. The residue was subjected to reversed-phase C-18 silica gel column chromatography (3:7 water–MeOH), the solvent removed and the crude product dissolved in Me(OH) (25 ml) and stirred in the presence of IRA 400 (OH) resin (200 mg) to ensure that the amino group had not been protonated. The mixture was filtered and evaporated to dryness to give **11a** (52 mg, 91%) as a yellow foam; $[a]_D^{25} = -8.0$ (*c* 0.4, CH_2Cl_2) (Found: C, 54.53; H, 6.59; N, 3.02%; M^+ *m/z* 435.1349. $C_{20}H_{29}FeNO_6$ requires: C, 55.18; H, 6.72; N, 3.22%; M^+ *m/z* 435.1344); $\delta_H(D_2O)$ 2.19 (3 H, s, CH_3), 2.54–2.73 (2 H, m, 1-H_2), 3.23–3.51 (4 H, m), 3.54 (2 H, s, CH_2Fc), 3.67–3.76 (2 H, m, 2-H and 6′-H), 3.90 (1 H, dd, *J* 12 and 2, 6′-H), 3.94–4.23 (1 H, m, 2-H), 4.21–4.26 (7 H, m, Cp), 4.30–4.34 (2 H, m, Cp) and 4.40 (1 H, d, *J* 8 Hz, 1′-H).

***N*-[3-(β-D-Glucopyranosyloxy)propyl]-*N*-methylaminomethyl-ferrocene 11b.** From compound **10b** (200 mg, 0.28 mmol) as for **10a**, except column chromatography was carried out on silica gel using 2:9 MeOH–CH_2Cl_2 ($R_F = 0.10$) as eluent, as a yellow foam (91 mg, 73%); $[a]_D^{25} = -10.9$ (*c* 0.5, CH_2Cl_2) (Found: C, 55.52; H, 7.63; N, 2.81%; M^+ *m/z* 449, MH^+ 450. $C_{21}H_{31}FeNO_6$ requires: C, 56.13; H, 6.95; N, 3.12%; M^+ *m/z* 449); $\delta_H(D_2O)$ 1.73–1.86 (2 H, m, 2-H_2), 2.13 (3 H, s, CH_3), 2.36–2.46 (2 H, m, 1-H_2), 3.26 (1 H, t, *J* 9, 2′-H), 3.34–3.52 (5 H, m, 3′-, 4′-, 5′-H and CH_2Fc), 3.56–3.77 (2 H, m, 3-H and 6′-H), 3.84–3.94 (2 H, m, 3-H and 6′-H), 4.22 br (7 H, s, Cp), 4.27s (2 H, s, Cp) and 4.38 (1 H, d, *J* 8 Hz, 1′-H).

***N*-[5-(β-D-Glucopyranosyloxy)pentyl]-*N*-methylaminomethyl-ferrocene 11c.** From compound **10c** (278 mg, 0.37 mmol), except column chromatography was carried out on silica gel with 2:9 MeOH–CH_2Cl_2 ($R_F = 0.12$) as the eluent, as a yellow foam (160 mg, 90%); $[a]_D^{25} = -22.0$ (*c* 0.5, CH_2Cl_2) (Found: C, 57.26; H, 6.87; N, 2.71%; M^+ *m/z* 477, MNa^+ 500. $C_{23}H_{35}FeNO_6$ requires: C, 57.86; H, 7.39; N, 2.93%; M^+ 477); $\delta_H(D_2O)$ 1.24–1.39 (2 H, m, 3-H_2), 1.41–1.55 (2 H, m, 2-H_2), 1.56–1.69 (2 H, m, 4-H_2), 1.97 (3 H, s, CH_3), 2.23–2.35 (2 H, m, 1-H_2), 3.26 (1 H, t, *J* 8, 2′-H), 3.35–3.52 (5 H, m), 3.55–3.66 (1 H, m, 5-H), 3.69–3.78 (1 H, m, 6′-H), 3.84–3.94 (2 H, m, 5-H and 6′-H), 4.14–4.26 (9 H, m, Cp) and 4.38 (1 H, d, *J* 8 Hz, 1′-H).

Preparation of compound 10a *via* reductive amination of ferrocenecarbaldehyde 7

A mixture of ferrocenecarbaldehyde **7** (51 mg, 0.13 mmol), glycoside **8a** (45 mg, 0.09 mmol), and sodium cyanotrihydroborate (40 mg, 0.63 mmol) in acetonitrile (10 ml) was stirred for 18 hours. Dichloromethane (50 ml) was added and the organic layer washed with a saturated aqueous solution of sodium hydrogencarbonate (50 ml) and water (50 ml). The organic layer was then dried ($MgSO_4$) and evaporated to dryness. The residue was purified by silica gel column chromatography (1:39 MeOH–CH_2Cl_2, $R_F = 0.33$) to give compound **10a** (51 mg, 82%) as a yellow foam identical to that reported above.

Preparation of bis(ferrocene) 18

A mixture of ferrocenecarbaldehyde **7** (650 mg, 1.67 mmol), glycoside **15a** (330 mg, 0.67 mmol), and sodium cyanotrihydroborate (295 mg, 4.7 mmol) in CH_3CN (25 ml) was stirred for 18 hours at room temperature. Dichloromethane (100 ml) was then added and the organic layer washed with a saturated aqueous solution of sodium hydrogencarbonate (150 ml) and water (150 ml). The organic layer was then dried ($MgSO_4$) and evaporated to dryness. The residue was purified by silica gel column chromatography (1 : 39 MeOH–CH_2Cl_2) to give compound **18** (155 mg, 27%) as a yellow foam (Found: C, 68.84; H, 6.51; N, 1.76%; MH^+ *m*/*z* 890, $MH^+ - CH_2 - Fc$ 758. $C_{51}H_{55}FeNO_6$ requires C, 68.85; H, 6.23; N, 1.57%; MH^+ *m*/*z* 890); $\delta_H(CDCl_3)$ 1.27 (3 H, s, CH_3), 2.45–2.65 (2 H, m, 1-H_2), 3.41–3.79 (10 H, m), 3.90–4.01 (1 H, m, 2-H), 4.09–4.30 (20 H, m, Cp and 6′-H_2), 4.51 (1 H, d, *J* 11, OCH*H*Ph), 4.53 (1 H, d, *J* 12, OCH*H*Ph), 4.60 (1 H, d, *J* 12, OCH*H*Ph), 4.83 (1 H, d, *J*, OCH*H*Ph), 4.88 (1 H, d, *J* 7, OCH*H*Ph), 5.11 (1 H, d, *J* 11 Hz, OCH*H*Ph) and 7.14–7.48 (15 H, m, Ph).

Preparation of *N*-(2-hydroxyethyl)-*N*-methylaminomethylferrocene 21

N-Methylethanolamine (820 mg, 11 mmol) was dissolved in dry acetonitrile (100 ml). Anhydrous potassium carbonate (2 g, 14 mmol) and methiodide salt **9** (5 g, 13 mmol) were added and the mixture was heated under reflux overnight. After filtering the solvent was removed by rotary evaporation. The remaining crude product was dissolved in dichloromethane (200 ml), washed with water (2 × 300 ml), dried ($MgSO_4$) and evaporated to dryness. The crude product mixture was purified by silica gel column chromatography (1 : 39 MeOH–CH_2Cl_2) to give compound **21** (2.55 g, 72%) as a yellow solid, mp 96–97 °C (Found: M^+ *m*/*z* 273.0817; $C_{14}H_{19}FeNO$ requires 273.0816); $\delta_H(CDCl_3)$ 2.19 (3 H, s, CH_3), 2.52 (2 H, t, *J* 5, 1-H_2), 3.37 br (1 H, s, OH), 3.48 (2 H, s, $FcCH_2$), 3.57 (2 H, t, *J* 5 Hz, 2-H_2), 4.11 (5 H, s, Cp), 4.12–4.13 (2 H, m, Cp) and 4.15–4.16 (2 H, m, Cp).

Preparation of ferrocenylamine-glucose conjugate 23

Penta-*O*-acetyl-D-glucopyranose **22** (500 mg, 1.28 mmol) and compound **21** (1.00 g, 3.60 mmol) were dissolved in dry CH_2Cl_2 (10 ml) in a 50 ml round bottom flask. Boron trifluoride–diethyl ether (5 ml) was added and the mixture stirred under a $CaCl_2$ drying tube for 18 hours. The mixture was poured into water (200 ml) and extracted into CH_2Cl_2 (150 ml). The organic layer was washed with a saturated aqueous solution of sodium hydrogencarbonate (150 ml) and then water (150 ml). The organic layer was dried ($MgSO_4$) and evaporated to dryness. The crude product mixture was purified by silica gel column chromatography (1 : 39 MeOH–CH_2Cl_2) to give **23** (264 mg, 34%) as a yellow solid, mp 117–119 °C (Found: C, 55.02; H, 5.96; N, 2.31%; MH^+ *m*/*z* 603. $C_{28}H_{37}FeNO_{10}$ requires C, 55.73; H, 6.18; N, 2.32%; MH^+ *m*/*z* 603); $\delta_H(CDCl_3)$ 2.00 (3 H, s, OAc), 2.02 (3 H, s, OAc), 2.04 (3 H, s, OAc), 2.08 (3 H, s, OAc), 2.33 (3 H, s, NCH_3), 2.72 (2 H, t, *J* 6, 1-H_2), 3.63 (2 H, s, C*H*$_2$Fc), 3.67–3.76 (2 H, m, 2-H and 5′-H), 3.92–4.01 (1 H, m, 2-H), 4.14 (5 H, s, Cp), 4.15–4.29 (6 H, m, Cp and 6′-H_2), 4.55 (1 H, d, *J* 8 Hz, 1′-H), 4.94–5.23 (3 H, m, 2′-H, 3′-H and 4′-H).

Preparation of compound 11a

Peracetate **22** (70 mg, 0.12 mmol) was dissolved in MeOH (20 ml) and stirred with OH^- IRA 400 resin (800 mg) for 3 hours. The reaction mixture was filtered and evaporated to dryness to give the target product **11a** (43 mg, 85%) as a yellow foam. The spectral and physical data were identical to those of a sample prepared above.

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