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Mild and efficient synthesis of 5,6-diamino-5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-β-L-idofuranose: precursor of the first carbohydrate-derived chiral Mn(III)–salen complex

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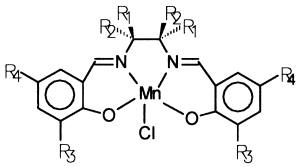
Abstract—Carbohydrates as multifunctional naturally occurred chiral products were used for the first time as chiral building blocks in Mn(III)–salen complexes as catalysts for the enantioselective epoxidation of alkenes. The pathways of the mild and efficient synthesis of a Mn(III)–salen complex and its diamino precursor 5,6-diamino-5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-β-L-idofuranose starting from D-(+)-glucose are described. The complex efficiently catalyzed the epoxidation of styrene and 1,2-dihydronaphthalene, using aqueous sodium hypochlorite in CH_2Cl_2 as terminal oxidant. The enantiomeric excesses were 13 and 33%, respectively. Mn(III)–salen catalyst with only one stereogenic carbon atom that is adjacent to nitrogen atom proved to be able to show enantioselectivity. © 2002 Elsevier Science Ltd. All rights reserved.

1. Introduction

Since Jacobsen's pilot work in 1990,[1] chiral Mn(III)–salen complexes (Scheme 1) have emerged as highly efficient biomimetic catalysts for the asymmetric epoxidations of unfunctionalized *cis*-disubstituted, tri- and tetra-substituted alkenes,[2] giving rise to optically active epoxides, which are valuable intermediates for a wide variety of biologically and pharmaceutically important compounds.[3]



Scheme 1.

The past decade has witnessed an explosive growth in the chemistry of these chiral Mn(III)–salen species, with the research topics varying from design and synthesis of salen ligands, investigation of the steric and electronic effects of the catalyst structure on stereoselectivity to rationales of the mechanism of the asymmetric induction. Satisfactory progress has been made toward catalytic enantiospecific epoxidation of certain types of alkene substrates, however, the development of high enantioselective catalysts of more general sense, especially for the asymmetric epoxidation of *trans*-substituted alkenes and terminal alkenes, still constitutes a challenge for organic chemists, furthermore, the controversial mechanism[2c] needs to be elucidated.

Among the structural units in Mn(III)–salen catalysts that affect the asymmetric induction in epoxidation reactions, the diimine moiety plays an important role. Catalysts with different diamine parts show not only different reactivity and enantioselectivity but also different enantiofacial selection, resulting in reversed enantioselectivity in some cases. On the other hand, carbohydrates as naturally occurring multifunctional products are cheap starting materials with chiral molecule structures, these characteristics make them ideal precursors for the introduction of chiral building blocks into the molecule structures of the catalysts. Surprisingly, while the derivatives of *trans*-1,2-diaryldiamines and *trans*-1,2-diaminocyclohexane as precursors of the diimine units attracted much attention, carbohydrate-derived Mn(III)–salen catalysts have never been reported before, to our best knowledge.

As a part of our research project 'metal-mediated reactions modelled after nature', we have incorporated chiral carbohydrate building blocks into the catalyst molecules either as the diamine part or as the salicyaldehyde part or both, in the hope of clarifying the catalytic mechanism and obtaining chiral catalysts with generally good activity and enantioselectivity. Here we report the preparation of the first carbohydrate-based Mn(III)–salen complex and the facile synthesis of its precursor 5,6-diamino-5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-β-L-idofuranose starting from

Keywords: diamino sugars; (salen)manganese(III) complexes; Mn(III)–salen catalysts; asymmetric reactions; enantiomeric epoxidations; carbohydrate; Jacobsen's catalyst.

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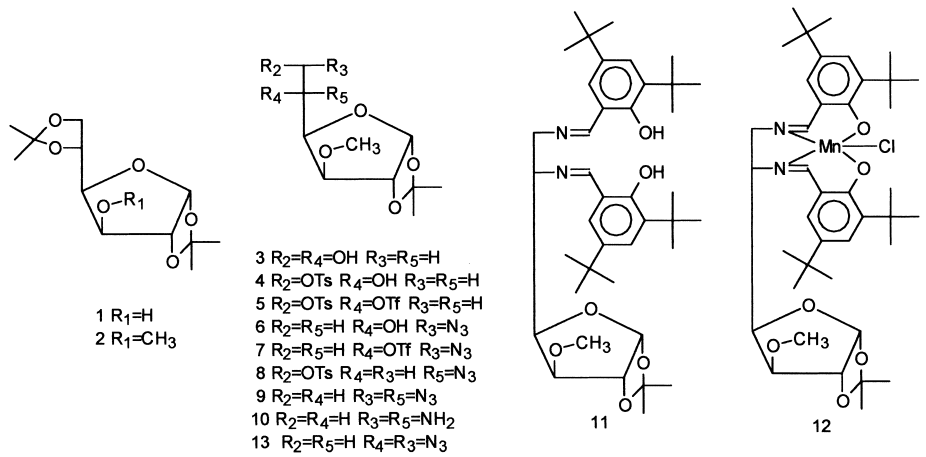


Scheme 2.

D-(+)-glucose, followed by the evaluation of the catalytic performance of this new type of complex in the epoxidation of styrene and 1,2-dihydronaphthanene.

2. Results and discussion

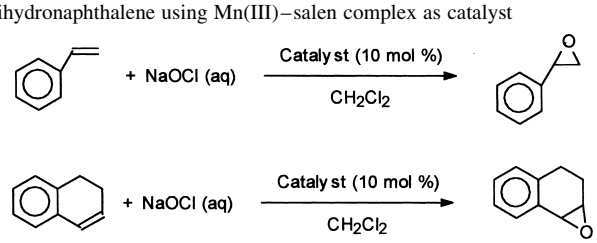
D-(+)-Glucose as a starting material was treated with catalytic amounts of sulfuric acid in acetone for 5 h at room temperature to give 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**1**) (Scheme 2) according to literature.[4] The hydroxyl group at C-3 in (**1**) was methylated with CH_3I by the method of Bessodes[5] with slight modifications. In our preparation, the cheaper tetrabutylammonium bromide was used as phase transfer catalyst instead of 18-crown-6, the reaction completed smoothly within 40 min at room temperature to give 1,2;5,6-di-*O*-isopropylidene-3-*O*-methyl-α-D-glucofuranose (**2**) with the yield of 94%. Selective hydrolysis of (**2**) in 75% aqueous acetic acid under water bath (bath temperature 60°C) for 50 min gave 1,2-isopropylidene-3-*O*-methyl-α-D-glucofuranose (**3**) in 90% yield.

The regioselective tosylation of the 6-OH group of (**3**) was carried out in pyridine by reacting the diol (**3**) with tosyl chloride at −18°C for 4 h in 94% yield, giving rise to 1,2-isopropylidene-3-*O*-methyl-6-*O*-tosyl-α-D-glucofuranose (**4**). Under this conditions, no ditosylate was found in the final reaction mixture, trace of starting diol can be easily removed by extracting with water, as it is water soluble. Extended reaction time led to formation of ditosylate resulting in a lower yield of the mono tosylate and the separation of products became more troublesome.

The monotosylate (**4**) was allowed to react with NaN_3 in DMF at about 100°C for 1 h to give chromatographically pure 6-azido-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-glucofuranose (**6**) in 96% yield. The conversion of (**6**) into idoazide (**9**) requires the introduction of another azido group at C-5 position with a single inversion of configuration. Thus, treatment of the mono-azide (**6**) with trifluoromethanesulphonic anhydride in dichloromethane in the presence of pyridine at −18°C gave quantitatively the corresponding triflate ester **7**, which is kinetically stable and easily handled. Compound **7** exhibited strong absorption at 1411 and 1206 cm^{-1} ($-SO_2-$) in IR spectrum and the peaks of −OH group disappeared. When the triflate **7** in dimethylformamide was treated with a suspension of sodium azide at room temperature, a smooth nucleophilic displacement reaction occurred within 35 min leading to the diazido idofuranose derivative **9** in a yield of 92%, with no concurrent formation of the epimeric gluco-azide **13**.

Alternatively, compound **9** can also be prepared from **4** following another route. On treatment with trifluoromethanesulphonic anhydride in dichloromethane in the

Table 1. Epoxidation of styrene and 1,2-dihydronaphthalene using Mn(III)–salen complex as catalyst



Entry	Substrate	Catalyst	Time (h)	Ee (%)	Yield (%)
1	Styrene	Compound **12**	3	13	75
2	1,2-Dihydronaphthalene	Compound **12**	6	33	52
3	Styrene	(*S*,*S*)-Jacobsen's catalyst	3	52	59
4	Styrene	Without catalyst	16	–	0
5	1,2-Dihydro-naphthalene	Without catalyst	16	–	0

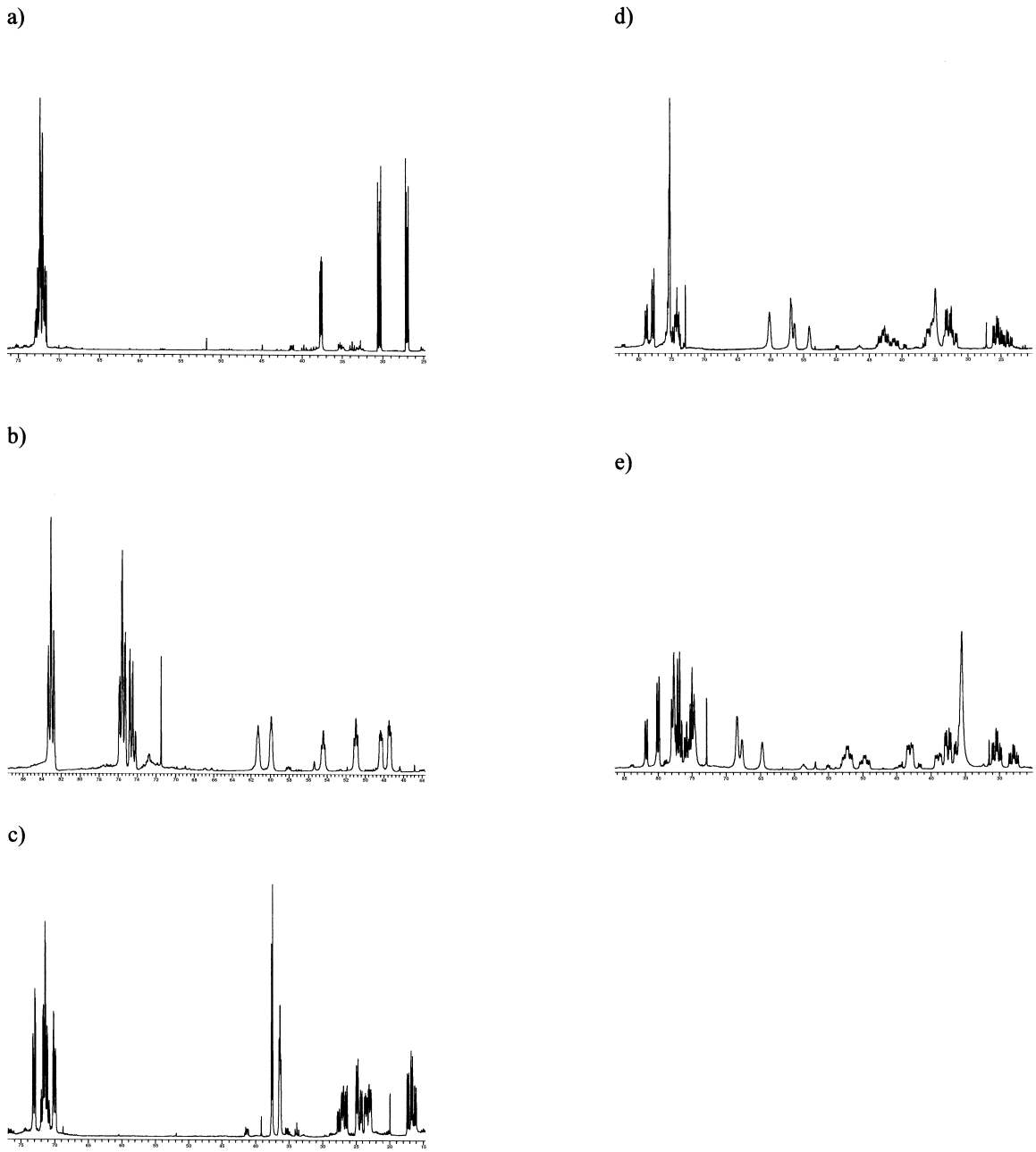


Figure 1. NMR spectra of the epoxides obtained by using compound **12** as catalyst: (a) styrene oxide without $Eu(hfc)_3$, (b) styrene oxide with 150 wt% $Eu(hfc)_3$, (c) 1,2-dihydronaphthalene oxide without $Eu(hfc)_3$, (d) 1,2-dihydronaphthalene oxide with 50 wt% $Eu(hfc)_3$, (e) 1,2-dihydronaphthalene oxide with 100 wt% $Eu(hfc)_3$.

presence of pyridine, the tosylate **4** produced the triflate **5** within 1 h in quantitative yield. Compound **5** is a yellow syrup, but slowly turns black on storage, and should be kept at low temperature under Argon protection and light prevention. Further analytical work and chemical treatment should be done shortly. However, good analytical results were also achieved 1 month later after passing the sample though a column of silica gel, about 10% of the original triflate has been degraded. The compound **5** showed characteristic IR absorption for tosyl group at 1372 and 1177 cm^{-1} as well as triflyl group at 1412 and 1209 cm^{-1}. When a solution of **5** in dimethylformamide was treated with sodium azide at room temperature for 4 h, the S_N2 substitution reaction occurred selectively at the C-5 position giving rise to 5-azido-1,2-isopropylidene-3-*O*-methyl-6-*O*-tosyl-β-L-idofuranose (**8**) in a yield of 95%. The characteristic absorption of triflyl group disappeared in IR spectrum after the formation of ido-azide while the characteristic absorption peaks of tosyl group remained at 1365 and 1176 cm^{-1}, the newly incorporated 5-azido group accounts for the additional strong peak at 2099 cm^{-1}. Compound **8** reacted with sodium azide in dimethylformamide at 100°C for 1 h gave the diazido idofuranose derivative **9** in 94% yield. Compound **9** can be obtained by treatment of **5** with sodium azide in excess, without separation of the intermediate **8**, thus shortened the synthetic pathway to final product.

Reduction of compound (**9**) with hydrazine hydrate in methanol catalyzed by Raney-nickel at room temperature

led to the formation of the diamine **10**, whose IR spectrum showed new peaks at 3375, 3317, 1597 cm^{-1} (6-NH_2) and 3244, 3151, 1565 cm^{-1} (5-NH_2), while the strong azido-absorption in IR spectrum disappeared. The yield of the diamine **10** was 87%. The Schiff base **11** was prepared in 81% yield by refluxing the ethanol solution of the diamine **10** and 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde for 3 h. Compound **11** showed strong absorption at 1628 cm^{-1}, which was attributed to the imine structure unit. Heating the solution of the Schiff base **11** in ethanol with $Mn(OAc)_2 \cdot 4H_2O$ in an atmosphere of oxygen under reflux, following by treatment with lithium chloride gave the Mn(III)–salen complex **12** in a yield of 92%.

For the evaluation of the catalytic performance of the new carbohydrate-based Mn(III)–salen catalyst, styrene as a terminal alkene and 1,2-dihydronaphthalene as a *cis*-di-substituted alkene were chosen as the substrates of the catalytic epoxidation. NaOCl solution was used as the terminal oxidant. The oxidation reactions were carried out at 20°C. Table 1 summarizes the results obtained in the epoxidation. Although carbohydrate structures are thought to be sensitive to oxidative environment, its catalytic behavior did not suggest of such kind of influence. Both substrates in entries 1 and 2 were consumed completely when 10 mol% of compound **12** was used as catalyst. Entries 4 and 5 show that, when the oxidations were carried out without any catalysts, no epoxidaton products could be detected. The substrates could be recovered nearly quantitatively.

Interestingly, although compound **12** has only one stereogenic center (C-5) that is adjacent to nitrogen atom in the diamine unit, it also showed definitely positive enantioselectivity. In the cases of styrene and 1,2-dihydronaphthalene, the enantiomeric excesses of the oxidative products were calculated to be 13 and 33%, respectively, from ^1H NMR spectra in the presence of europium tris[3-(heptafluoropropylhydoxymethylene)-(+)-camphorate] ($Eu(hfc)_3$) as the chiral shift reagent. Fig. 1 clearly shows that the peaks of the enantiomers separated with the addition of $Eu(hfc)_3$. Spectrum (b) indicates that, in the case of epoxidation of styrene, compound **12** showed the same enantiofacial selection as (*S*,*S*)-Jacobsen's catalyst, the major enantiomer has the absolute configuration of *S*-(−), as was determined by comparing the experimental results of entries 1 and 3 in Table 1.

3. Conclusion

In summary, this paper reports the preparation of the first carbohydrate-derived chiral Mn(III)–salen complex, it can efficiently catalyze the epoxidation of simple unfunctionalized olefins with positive enantioselectivity. Mn(III)–salen catalyst with only one stereogenic center that is adjacent to the nitrogen atom can also asymmetrically catalyze the epoxidation of olefins, this helps to clarify the mechanism of the epoxidation in the presence of chiral Mn(III)–salen catalysts. The facile synthesis of its precursor 5,6-diamino-5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-β-L-idofuranose from D-(+)-glucose following two different pathways is described. The reaction conditions are mild and the yields vary from high to excellent.

In view of the versatility of the derivatives of carbohydrate and other natural chiral compounds, this work opens a wide prospect of utilizing natural products as chiral templates for the asymmetric epoxidative catalysis. Further synthesis and investigations of the catalytic behavior of other types of carbohydrate-based chiral Mn(III)–salen catalysts will be published shortly.

4. Experimental

4.1. General

Melting points were determined on a Krüss apparatus, the Digital Melting Point Analyzer KSPS 1000 or on a microscopic analyzer DAW IMEJ Jena and were not corrected. NMR spectra were recorded in $CDCl_3$ at 250 MHz on a Bruker AC-200 spectrometer. IR spectra were measured on a Perkin–Elmer 2000 spectrometer. Mass spectra were carried out on a Finnigan MAT SSQ710 or a Finnigan MAT 95XLTRAP. Elemental analyses were acquired by use of a Leco CHNS 932. Optical rotation was measured with a Schmidt+Haensch product, the Polartronic E, at ambient temperature using a 50 mm sample tube, the samples were dissolved in $CHCl_3$ with concentration of 1 g/100 ml unless otherwise stated. TLC was conducted on Merck glass plates coated with silica gel 60, the plates were cut into small plates (2 cm×5 cm), the solvent front was allowed to run 4 cm, sample spots were visualized by spraying 1% vanillin/conc. H_2SO_4 solution with subsequent heating at 200°C unless otherwise stated. Chromatography was performed using silica gel 60 (particle size 0.063–0.2 mm) from Fluka Chemie GmbH. Solvents were distilled prior to use. Ethanol and pyridine were dried before distillation. Other chemicals including D-(+)-glucose were obtained from Fluka Chemie GmbH and were used directly. 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde was purchased from Aldrich Chem. Co. 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose **1** was prepared according to literature.[4]

4.1.1. 1,2;5,6-Di-*O*-isopropylidene-3-*O*-methyl-α-D-glucofuranose (2). To a magnetically stirred solution of 26.3 g (101.0 mmol) (**1**) in 150 ml acetone were added 7.4 g newly powdered KOH and 1.2 g tetrabutylammonium bromide, the mixture was cooled to 0°C, 21.5 g CH_3I (151.5 mmol) was added within 20 min, the reaction was allowed to be carried out at room temperature for a further 40 min, TLC (ethyl acetate–*n*-hexane 1:1, R_f of starting sugar: 0.55, R_f of product: 0.83) showed complete consumption of the starting sugar. Acetone was evaporated under reduced pressure, water was added and the mixture was three times extracted with CH_2Cl_2, the combined organic phase was washed with NH_4Cl solution and water, dried over anhydrous Na_2SO_4, filtered, evaporated under reduced pressure. Pure product was obtained as a colorless syrup after vacuum distillation, yield: 26.1 g (94%), $[\alpha]_D = -38.0°$. IR(ATR): 2987, 2937, 2896, 2834, 1457, 1373, 1254, 1215, 1165, 1124, 1073, 1018, 847, 641 cm^{-1}. ^1H NMR: δ 5.83 (d, 1H, J=3.7 Hz), 4.53 (d, 1H, J=3.7 Hz), 4.27 (td, 1H, J=7.8, 5.8 Hz), 3.96

(dd, 1H, J=8.6, 5.5 Hz), 4.01 (m, 2H), 3.74 (d, 1H, J=3.0 Hz), 3.42 (s, 3H), 1.47 (s, 3H), 1.40 (s, 3H), 1.33 (s, 3H), 1.29 (s, 3H). ^{13}C NMR: δ 112.0, 109.3, 105.5, 84.0, 82.3, 81.4, 72.7, 67.6, 58.5, 27.1, 27.1, 26.6, 25.7. MS(EI): m/z 275 (58%, $[M+H]^+$). Anal. calcd for $C_{13}H_{22}O_6$: C, 56.92; H, 8.08. Found: C, 56.90; H, 7.87.

4.1.2. 1,2-*O*-Isopropylidene-3-*O*-methyl-α-D-glucofuranose (3). 345 ml acetic acid and 115 ml water were added to a one-neck-round flask containing 33 g (120.3 mmol) (**2**) and a magnetic stirrer, the flask was heated with a bath, the temperature of the bath was adjusted to 60°C, the reaction mixture was stirred for 50 min until TLC showed the completion of the reaction (ethyl acetate–*n*-hexane 1:1, R_f of product: 0.10). Acetic acid and water were then removed at 40°C under reduced pressure, small amounts of toluene were added repeatedly into the flask and were distilled under reduced pressure to remove the remaining acetic acid. The crude product was dried at 40°C under vacuum to remove trace of acetic acid. The product was purified by chromatography (ethyl acetate–*n*-hexane 3:1) to give **3** as colorless syrup, yield: 25.4 g (90%). $[\alpha]_D$=−52.0°. IR(ATR): 3412, 2986, 2937, 2834, 1458, 1376, 1297, 1256, 1215, 1195, 1164, 1120, 1074, 1012, 955, 891, 852, 642, 620 cm^{-1}. ^{1}H NMR: δ 5.85 (d, 1H, J=3.8 Hz), 4.54 (d, 1H, J=3.8 Hz), 4.05 (dd, 1H, J=8.2, 3.2 Hz), 3.92 (m, 1H), 3.84 (d, 1H, J=3.1 Hz), 3.76 (m, 1H), 3.64 (m, 2H), 3.46 (m, 1H), 3.42 (s, 3H), 1.45 (s, 3H), 1.28 (s, 3H). ^{13}C NMR: δ 112.1, 105.4, 84.5, 81.8, 80.1, 69.4, 64.7, 58.2, 27.0, 26.5. MS(EI): m/z 235 (70%, $[M+H]^+$). Anal. calcd for $C_{10}H_{18}O_6$: C, 51.27; H, 7.75. Found: C, 50.71; H, 7.62.

4.1.3. 1,2-*O*-Isopropylidene-3-*O*-methyl-6-*O*-tosyl-α-D-glucofuranose (4). 10.22 g (43.6 mmol) (**3**) was dissolved in 50 ml pyridine, the solution was then cooled with a NaCl/ice bath to −18°C, 9.1 g (47.2 mmol) tosyl chloride in 10 ml pyridine was added dropwise within 15 min, the reaction mixture was kept in the cool bath for a further 4 h, TLC (ethyl acetate–*n*-hexane 1:1, R_f of product: 0.49) showed that only a very small amount of starting diol remained and no ditosylate occurred, terminated the reaction by adding water and extracting with ethyl acetate, the organic phase was washed with 0.5 M HCl several times, the inorganic phase was extracted once with ethyl acetate, combined the organic phase and washed with brine. Organic phase was dried over anhydrous Na_2SO_4, filtered, evaporated under reduced pressure, the crude product was purified by passing it through a column of silica gel giving a colorless syrup, yield: 15.9 g (94%). $[\alpha]_D$=−28.0°. IR(ATR): 3483, 2989, 2938, 2833, 1599, 1454, 1356, 1217, 1174, 1075, 1020, 967, 883, 614, 765, 666, 616 cm^{-1}. ^{1}H NMR: δ 7.78 (d, 2H, J=8.3 Hz), 7.33 (m, 2H), 5.83 (d, 1H, J=3.7 Hz), 4.55 (d, 1H, J=3.8 Hz), 4.26 (dd, 1H, J=9.6, 2.2 Hz), 4.10 (m, 3H), 3.86 (d, 1H, J=3.1 Hz), 3.41 (s, 3H), 3.00 (s, 1H), 2.43 (s, 3H), 1.44 (s, 3H), 1.30 (s, 3H). ^{13}C NMR: δ 145.4, 133.0, 130.3, 128.4, 112.2, 105.4, 84.4, 81.7, 79.5, 72.8, 67.6, 56.3, 27.1, 26.6, 22.0. MS(DCI): m/z 389 (88%, $[M+H]^+$). Anal. calcd for $C_{17}H_{24}O_8S$: C, 52.57; H, 6.23; S, 8.26. Found: C, 52.72; H, 6.24; S, 8.43.

4.1.4. 6-*O*-Azido-6-deoxy-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-glucofuranose (6). To a one-necked round-bottom flask containing 1.535 g (3.95 mmol) (**4**) and 10 ml DMF was added 0.385 g (5.92 mmol) NaN_3, the mixture was magnetically stirred and the flask was heated with an oil bath (bath temperature: 100°C) for 1 h, TLC (ethyl acetate–*n*-hexane 1:1, R_f of product: 0.61, yellow spot) showed completion of the reaction, DMF was evaporated under reduced pressure, 20 ml water was added, followed by extracting the mixture with 100 ml ethyl acetate twice, organic phase was combined and washed with 30 ml brine three times, the inorganic phase was extracted once with ethyl acetate, organic phased were combined, dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure, the product was then dried in vacuo to give **6** as a colorless syrup which is chromatographically pure, yield 0.98 g (96%). $[\alpha]_D$=−28.0°. IR(ATR): 3470, 2989, 2938, 2835, 2100, 1445, 1376, 1295, 1257, 1217, 1194, 1164, 1119, 1075, 1019, 956, 889, 855, 665, 642, 622 cm^{-1}. ^{1}H NMR: δ 5.85 (d, 1H, J=3.8 Hz), 4.56 (d, 1H, J=3.8 Hz), 4.05 (s, 2H), 3.86 (d, 1H, J=2.2 Hz), 3.51 (m, 1H), 3.42 (s, 3H), 3.38 (m, 1H), 2.98 (s, 1H), 1.45 (s, 3H), 1.29 (s, 3H). ^{13}C NMR: δ 112.2, 105.4, 84.5, 81.7, 80.3, 68.8, 62.5, 58.1, 55.0, 27.1, 26.6. MS(EI): m/z 260 (26%, $[M+H]^+$). Anal. calcd for $C_{10}H_{17}O_5N_3$: C, 46.33; H, 6.61; N, 16.21. Found: C, 46.59; H, 6.59; N, 15.80.

4.1.5. 6-*O*-Azido-6-deoxy-1,2-*O*-isopropylidene-3-*O*-methyl-5-*O*-trifluromethanesulfonyl-α-D-glucofuranose (7). A solution of 1.3 ml (16.2 mmol) pyridine in 20 ml CH_2Cl_2 was cooled to −18°C with NaCl/ice bath. 1.3 ml (7.88 mmol) Tf_2O in 10 ml CH_2Cl_2 was added dropwise with stirring into the solution in an atmosphere of Argon, 10 min later, 1.0 g (3.86 mmol) azide (**6**) in 10 ml CH_2Cl_2 was added slowly into the reaction vessel, the reaction continued at that temperature with stirring, while moisture was prevented by the inlet of Argon. 1.5 h later, TLC (ethyl acetate–toluene 1:3, R_f of product: 0.78) showed the reaction to be complete. 50 ml CH_2Cl_2 and 50 ml water were added into the reaction mixture, after the extraction, the organic phase was washed twice with 50 ml water, organic phase was combined, dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure, the product was purified by chromatography (ethyl acetate–toluene 1:6) and then dried in vacuo at room temperature to give **7** as a yellow liquid with low viscosity, yield 1.51 g (100%). $[\alpha]_D$=−44.0°. IR(ATR): 2993, 2942, 2841, 2110, 1411, 1379, 1294, 1244, 1206, 1164, 1141, 1123, 1081, 1027, 918, 851, 760, 624 cm^{-1}. ^{1}H NMR: δ 5.87 (d, 1H, J=3.6 Hz), 5.22 (m, 1H), 4.63 (d, 1H, J=3.6 Hz), 4.46 (dd, 1H, J=8.2, 3.3 Hz), 3.84 (m, 2H), 3.68 (dd, 1H, J=14.3, 4.6 Hz), 3.43 (s, 3H), 1.50 (s, 3H), 1.33 (s, 3H). ^{13}C NMR: δ 121.2, 116.1, 113.0, 105.9, 82.9, 81.8, 81.0, 57.8, 51.9, 27.2, 26.6. MS(DCI): m/z 392 (13%, $[M+H]^+$). Anal. calcd for $C_{11}H_{16}O_7N_3F_3S$: C, 33.76; H, 4.12; N, 10.74; S, 8.19. Found: C, 33.59; H, 4.19; N, 10.68; S, 8.23.

4.1.6. 5,6-Di-azido-5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-glucofuranose (9). *Method A*, *from* **7**. To a solution of 1.32 g (3.37 mmol) (**7**) in 9 ml DMF was added 0.37 g (5.69 mmol) NaN_3, the reaction continued at room temperature for 35 min, TLC (ethyl acetate–toluene 1:4, products ran slightly slower than starting sugar) showed the complete consumption of **7**, 10 ml water was added, the mixture was extracted with 80 ml ethyl acetate, the organic phase was washed once with 30 ml water and once with

30 ml brine, organic phase was then combined, dried over anhydrous Na_2SO_4, filtered, the solvent was removed under reduced pressure and the product was dried in vacuo to give pure **9** as a syrup, yield 0.88 g (92%). $[\alpha]_D=-62°$. IR(ATR): 2990, 2938, 2835, 2094, 1453, 1375, 1258, 1216, 1193, 1163, 1114, 1076, 1017, 959, 888, 851, 667, 621 cm^{-1}. ^1H NMR: δ 5.93 (d, 1H, J=3.8 Hz), 4.61 (d, 1H, J=3.8 Hz), 4.21 (dd, 1H, J=8.4, 3.5 Hz), 3.86 (m, 1H), 3.67 (d, 1H, J=3.5 Hz), 3.40 (s, 3H), 3.28 (dd, 2H, J=12.8, 6.6 Hz), 1.50 (s, 3H), 1.33 (s, 3H). ^{13}C NMR: δ 112.4, 105.2, 84.1, 81.6, 80.9, 61.5, 57.8, 52.0, 27.2, 26.6. MS(EI): *m/z* 28 (31%), 43 (54%), 45 (12%), 59 (45%), 71 (13%), 84 (20%), 87 (99%), 98 (13%), 115 (54%), 145 (22%), 173 (99%), 174 (21%), 199 (30%), 269 (9%), 285 (2%, $[M+H]^+$). Anal. calcd for $C_{10}H_{16}O_4N_6$: C, 42.25; H, 5.67; N, 29.56. Found: C, 43.49; H, 5.66; N, 25.95.

Method B, *from* **8**. A round-bottom flask containing 0.84 g (2.0 mmol) (**8**) in 4 ml DMF and 0.4 g (6.2 mmol) NaN_3 was heated with an oil bath (bath temperature: 100°C) with stirring. 1 h later, TLC (ethyl acetate–toluene 1:4, R_f of starting sugar: 0.66, R_f of product: 0.74) showed the reaction to be complete. Water was added and the reaction mixture was extracted with ethyl acetate, organic phase was washed with water and brine, dried over anhydrous Na_2SO_4, filtered, the solvent was removed under reduced pressure and the product was dried in vacuo to give pure **9**, yield 0.54 g (94%). The analytical data were the same as in method A.

Method C, *from* **5**. 1.36 g (20.9 mmol) NaN_3 was added to a solution of 3.6 g (6.9 mmol) (**5**) in 15 ml DMF, the mixture was stirred at room temperature for 4 h, TLC (ethyl acetate–toluene 1:4) showed that the intermediate product was slightly more polar than starting sugar. Then the reaction mixture was heated with an oil bath, the bath temperature was adjusted to be 100°C, the reaction was terminated 1 h later, TLC (ethyl acetate–toluene 1:4) showed that the final product was slightly less polar than the intermediate product. DMF was removed under reduced pressure, 50 ml water was added and the mixture was extracted with 100 ml ethyl acetate twice, the combined organic phase was washed with brine (3×30 ml), the inorganic phase was washed with 100 ml ethyl acetate, the organic phase was once again combined and dried over anhydrous Na_2SO_4, the solution was decolorized by filtering it through a short pad of silica gel to give a chromatographically pure (**9**) 1.87 g (yield: 95%), the analytical data were the same as in method A.

4.1.7. 1,2-*O*-Isopropylidene-3-*O*-methyl-6-*O*-tosyl-5-*O*-trifluromethanesulfonyl-α-D-glucofuranose (5). A 500 ml three-necked round-bottom flask was equipped with a electric stirrer, an addition funnel and a device for Argon introduction. The flask was charged with 5.7 ml pyridine and 160 ml CH_2Cl_2, the solution was stirred and was cooled to −18°C with a NaCl/ice bath. A solution of triflic anhydride (4.73 ml, 28.67 mmol) in 40 ml CH_2Cl_2 was slowly added though the funnel under Argon protection, 10 min later, 5.514 g (14.2 mmol) (**4**) in 40 ml CH_2Cl_2 was added dropwise through the funnel. The yellow reaction mixture was stirred under argon atmosphere while cooled with the bath for 1 h, TLC (ethyl acetate–toluene 1:4, R_f of product: 0.67) showed the disappearance of the starting sugar, 100 ml ice water and 50 ml CH_2Cl_2 were added and vigorously shaken in a separating funnel, the organic phase was separated and washed with 80 ml ice brine three times, the inorganic phase was extracted once with CH_2Cl_2, the combined organic phase was dried over anhydrous Na_2SO_4 and decolorized by filtering though a short pad of silica gel, the solution was then evaporated under reduced pressure to give, after being dried in vacuo, a yellow syrup, which turned brown easily on storage, yield: 7.4 g (100%). The product should be kept at low temperature with prevention of light and air. Immediate analyses or further chemical treatments are recommended. $[\alpha]_D=-16°$. IR(ATR): 2992, 2939, 2840, 1412, 1372, 1244, 1209, 1192, 1177, 1141, 1080, 1005, 986, 918, 891, 856, 815, 792, 758, 661, 623, 617 cm^{-1}. ^1H NMR: δ 7.79 (d, 2H, J=8.3 Hz), 7.35 (d, 2H, J=8.1 Hz), 5.82 (d, 1H, J=4.4 Hz), 5.28 (m, 1H), 4.59 (d, 1H, J=3.6 Hz), 4.46 (dd, 1H, J=12.0, 2.0 Hz), 4.39 (dd, 1H, J=7.3, 2.0 Hz), 4.23 (dd, 1H, J=12.0, 3.3 Hz), 3.83 (d, 1H, J=3.4 Hz), 3.41 (s, 3H), 2.45 (s, 3H), 1.47 (s, 3H), 1.32 (s, 3H). ^{13}C NMR: δ 145.7, 132.5, 130.3, 128.5, 113.0, 105.8, 83.0, 81.1, 80.9, 67.9, 57.9, 27.2, 26.6, 22.0. MS(DCI): *m/z* 521 (19%, $[M+H]^+$). Anal. calcd for $C_{18}H_{23}O_{10}F_3S_2$: C, 41.54; H, 4.45; S, 12.32. Found: C, 42.06; H, 4.37; S, 12.37.

4.1.8. 5-Azido-5-deoxy-1,2-*O*-isopropylidene-3-*O*-methyl-6-*O*-tosyl-α-D-glucofuranose (8). To a one-necked round-bottom flask containing 1.6 g (3.07 mmol) (**5**) and 8 ml DMF was added 0.29 g NaN_3, the reaction mixture was stirred at room temperature for 4 h, until TLC (ethyl acetate–toluene 1:4, R_f of starting sugar: 0.67, R_f of product: 0.60) showed complete consumption of the starting sugar, 20 ml water was added, the mixture was extracted with 80 ml ethyl acetate, the inorganic phase was extracted once with 50 ml ethyl acetate, the organic phase was combined and wash successively with brine (3×30 ml), then dried over anhydrous Na_2SO_4, filtered and then was passed through a short pad of silica gel to decolorize the product, solvent was removed under reduced pressure, the product was dried in vacuo to give **8** as a yellow syrup, yield 1.21 g (95%). $[\alpha]_D=40.0°$. IR(ATR): 2989, 2938, 2835, 2099, 1456, 1365, 1310, 1259, 1216, 1190, 1176, 1116, 1076, 1018, 987, 939, 889, 854, 815, 770, 664, 615 cm^{-1}. ^1H NMR: δ 7.79 (d, 2H, J=8.3 Hz), 7.35 (d, 2H, J=8.1 Hz), 5.89 (dd, 1H, J=11.6, 3.8 Hz), 4.56 (d, 1H, J=3.8 Hz), 4.16 (dd, 1H, J=8.1, 3.4 Hz), 4.05 (m, 2H), 3.88 (m, 1H), 3.62 (d, 1H, J=3.4 Hz), 3.31 (s, 3H), 2.43 (s, 3H), 1.45 (s, 3H), 1.29 (s, 3H). ^{13}C NMR: δ 145.7, 132.7, 130.4, 128.4, 112.4, 105.1, 83.9, 81.6, 79.8, 69.0, 60.0, 57.7. MS(DCI): *m/z* 69 (41%), 75 (36%), 93 (100%), 98 (20%), 115 (16%), 145 (16%), 173 (87%), 199 (46%), 242 (13%), 328 (23%), 386 (11%), 414 (3%, $[M+H]^+$). Anal. calcd for $C_{17}H_{23}O_7N_3S$: C, 49.39; H, 5.61; N, 10.16; S, 7.76. Found: C, 49.34; H, 6.18; N, 10.57; S, 6.99.

4.1.9. 5,6-Di-amino-5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-glucofuranose (10). To a stirred solution of 4.511 g (15.87 mmol) (**9**) in 30 ml methanol and 5.0 ml $N_2H_4{\cdot}H_2O$ was added catalytic Raney-nickel (freshly made) slowly, gas evolved immediately, the reaction was allowed to be carried out at room temperature over night. TLC (ethyl acetate–toluene 1:4, product spot remained at the baseline) showed no starting sugar was present. The reaction mixture was filtered under suction, the filter and Raney-nickel were

rinsed thoroughly with small amounts of methanol, solvents and excess $N_2H_4{\cdot}H_2O$ were removed under reduced pressure, the product was then dried at 40°C in vacuo to give 3.21 g (87%) **10** as a pink wax. $[\alpha]_D=-46.0°$. IR(ATR): 3375, 3317, 3244, 3151, 2986, 2935, 2830, 1597, 1565, 1457, 1375, 1316, 1256, 1214, 1194, 1164, 1116, 1074, 1010, 886, 851, 777, 682, 661, 615 cm^{-1}. ^1H NMR (400 MHz): δ 5.80 (s, 1H), 4.49 (s, 1H), 3.82 (s, 1H), 3.56 (s, 1H), 3.29 (s, 3H), 2.96 (s, 1H), 2.68 (s, 1H), 2.49 (s, 1H), 1.39 (s, 3H), 1.22 (s, 3H), broad peaks between 1.65 and 0.96 (4H). ^{13}C NMR (400 MHz): δ 111.4, 104.5, 84.2, 82.8, 81.6, 57.5, 52.5, 45.0, 26.7, 26.1. MS(EI): *m/z* 233 (24%, $[M+H]^+$). Anal. calcd for $C_{10}H_{20}O_4N_2$: C, 51.71; H, 8.68; N, 12.06. Found: C, 51.60; H, 8.91; N, 11.86.

4.1.10. 5,6-Di(*N*-3,5-di-*tert*-butylsalicylidene)amino-5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-glucofuranose (11). 20 ml ethanol solution containing 0.572 g (2.46 mmol) (**10**) and 1.15 g (4.92 mmol) 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde was reflux for 3 h with stirring, TLC (ethyl acetate–toluene 1:15 R_f of product: 0.50) showed the disappearance of the starting sugar. Ethanol was removed under reduced pressure, the residue was purified by chromatography (ethyl acetate–toluene 1:15) to give, after removal of the solvents, the Schiff base (**11**) as a yellow solid, yield: 1.33 g (81%). Melting point: 94.0–96.1°C. IR(ATR): OH-absorption occurred as shoulder of 2955, 2955, 2905, 2869, 1628, 1597, 1466, 1441, 1362, 1250, 1209, 1167, 1117, 1079, 1021, 854, 802, 772, 729, 703, 668, 645, 619 cm^{-1}. ^1H NMR: 13.59 (d, 2H, J=11 Hz), 8.45 (d, 2H, J=4.3 Hz), 7.41 (m, 1H), 7.27 (m, 1H), 7.12 (m, 2H), 5.99 (d, 1H, J=3.9 Hz), 4.73 (d, 1H, J=3.9 Hz), 4.44 (dd, 1H, J=8.0, 3.2 Hz), 3.95 (m, 4H), 3.56 (s, 3H), 1.3–1.5 (m, 42H). δ ^{13}C NMR: δ 168.72, 168.67, 158.49, 158.47, 140.44, 140.32, 136.96, 136.74, 132.30, 129.47, 128.66, 128.28, 127.50, 127.39, 126.93, 126.57, 118.41, 118.25, 112.13, 105.11, 84.48, 81.79, 81.04, 68.71, 61.21, 57.90, 35.42, 35.14, 34.51, 34.49, 31.89, 31.77, 29.93, 29.85, 29.73, 27.18, 26.76. MS(DCI): *m/z* 665 (33%, $[M+H]^+$). Anal. calcd for $C_{40}H_{60}O_6N_2$: C, 72.25; H, 9.10; N, 4.21. Found: C, 72.12; H, 8.93; N, 4.11.

4.1.11. [5,6-Di(*N*-3,5-di-*tert*-butylsalicylidene)-amino-5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-glucofuranose]chloromanganese(III) (12). To a two-necked round-bottom flask containing a magnetic stirrer, 10 ml ethanol, 0.38 g (0.57 mmol) (**11**) was added 0.36 g $Mn(OAc)_2{\cdot}4H_2O$ (1.47 mmol), the mixture was refluxed while bubbling into oxygen slowly, shortly after adding into $Mn(OAc)_2{\cdot}4H_2O$, the solution became dark brown, 30 min later, the introduction of oxygen was stopped, and air was bubbled into the reaction system. Another 30 min later, anhydrous LiCl 0.07 g was added, and the reflux continued for an additional 2 h, water was added resulting in a dark brown precipitate, which was collected by suction filtration. The collected powder was re-dissolved in CH_2Cl_2 and extracted with water and brine. The organic phase was dried over anhydrous Na_2SO_4, and solvent evaporated to afford a dark brown crystal, yield 0.396 g (92%). Mp >300°C. IR(ATR): 2955, 2869, 1608, 1535, 1413, 1387, 1362, 1304, 1273, 1252, 1175, 1114, 1080, 1025, 882, 840, 812, 781, 750, 643, 616 cm^{-1}. ^1H NMR (400 MHz): δ 5.36, 3.66, 2.45, 1.33, from 0 to 4.4 ppm a very broad absorption occurred. δ MS(DEI): *m/z* 753 ($[M+H]^+$). Anal. calcd for $C_{40}H_{58}O_6N_2MnCl$: C, 63.78; H, 7.76; N, 3.72; Cl, 4.71. Found: C, 63.95; H, 7.87; N, 3.49; Cl, 4.41.

4.2. General procedure for the catalytic epoxidaton

To a solution of 0.1 g styrene or 0.125 g 1,2-dihydronaphthalene and 10% equiv. Mn(III)–salen catalyst in 2 ml CH_2Cl_2 were added 8 ml 0.05 M Na_2HPO_4 and 8 ml sodium hypochlorite solution (from Fluka, active chlorine: 13%), the PH of the resulted buffered solution was adjusted to 11.3 by adding 1.3 g, 1.078 M HCl. The reaction flask was capped with a cork, and the reaction mixture was violently stirred at 20°C with a magnetic bar until TLC showed the completion of the reaction. The organic phase was separated, CH_2Cl_2 was added to extract the inorganic phase twice, the organic phase was combined, washed with brine twice, dried over anhydrous Na_2SO_4, filtered, solvent was evaporated under reduced pressure and the products were purified by preparative TLC. The enantiomeric excess of the products was determined by ^1H NMR analysis[6] in the presence of $Eu(hfc)_3$ as chiral shift reagent.

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