DOI: 10.1002/ejoc.200801035

Sweets for Catalysis – Facile Optimisation of Carbohydrate-Based Bis(oxazoline) Ligands

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Keywords: Asymmetric catalysis / Carbohydrates / Ligand design / N ligands

A new type of carbohydrate-based bis(oxazoline) ligands was prepared from inexpensive D-glucosamine and tested in asymmetric cyclopropanation reactions. For optimisation, modified ligands with 3-*O* substituents of varying size and electronic properties were prepared as well as a 3-OH unprotected and a perpivaloylated derivative. All new ligands were tested in asymmetric cyclopropanation, revealing a strong dependence of enantioselectivity on steric demand and electronic properties of the 3-*O* residue. Also, a significant influence of the pyranose conformation, which is determined by the presence or absence of the cyclic acetal group, was observed. Thus, it was easily possible to tune the new carbohydrate bis(oxazoline) ligands to a given reaction.

Introduction

Carbohydrates are the most abundant compounds of the chiral pool, but unlike amino acids, terpenes and alkaloids, they are far less frequently employed for the preparation of chiral ligands for metal-catalysed asymmetric synthesis. This is mainly because they contain both stereocentres and functional groups galore, which is often regarded rather more of an obstacle than an advantage. In contrast, since the first examples of efficient carbohydrate-based ligands were reported 30 years ago,[1] many interesting structures have emerged and application of such complexing agents has recently met with increasing attention.[2] Bis(oxazolines)[3] (box) and pyridylbis(oxazolines)[4] (pybox) are among the most successful classes of chiral ligands, as they are of great utility in a wide range of asymmetric transformations.[3,4] They are commonly prepared from chiral β-amino alcohols originating from mainly nonnatural sources. The inexpensive amino sugar D-glucosamine, whose *N*-acyl derivatives easily form oxazolines, has rarely been used for the synthesis of oxazoline-containing ligands. Examples are several mono(oxazolines) containing additional phosphorus-based donor sites.[5] The first examples of carbohydrate bis(oxazolines) were reported in 2005, but without any application in asymmetric synthesis.[6]

Results and Discussion

We recently introduced the new ligands *gluco*Box[7] and *gluco*Pybox,[8] which are accessible from inexpensive D-glucosamine through four efficient steps, outlined for the box ligand in Scheme 1.

Ligand Ac *gluco*Box (**5**) was employed in copper(I)-catalysed cyclopropanations of alkenes with diazoacetates,[7] a reaction first reported by Evans[9a] and Masamune[9b] (cf. Table 1). The reaction of styrene with ethyl diazoacetate, which is a benchmark for this transformation, gave diastereomeric cyclopropanation products *trans*-**8** and *cis*-**8** in a 70:30 ratio, typical for this transformation using ethyl diazoacetate, good yields and encouraging 82%*ee* (Table 1, Entry 1). Good enantioselectivities were also obtained with 4-methoxystyrene, 1,1-diphenylethylene and 2,5-dimethylhexa-2,4-diene (Table 1, Entries 3, 5 and 7). As the *trans*/*cis* ratio can sometimes be improved by employing bulky *tert*-butyl diazoacetate,[9] we repeated the reactions with this ester. For styrene, this led to a drop in both the yield and the enantioselectivity, as well as a complete loss of diastereoselectivity (Table 1, Entry 2) and a slight rise in diastereoselectivity for 4-methoxystyrene (Table 1, Entry 4). An increase in enantioselectivity was only observed for 1,1-diphenylethylene (Table 1, Entry 6). Because of these results, no further experiments were performed with *tert*-butyl diazoacetate.

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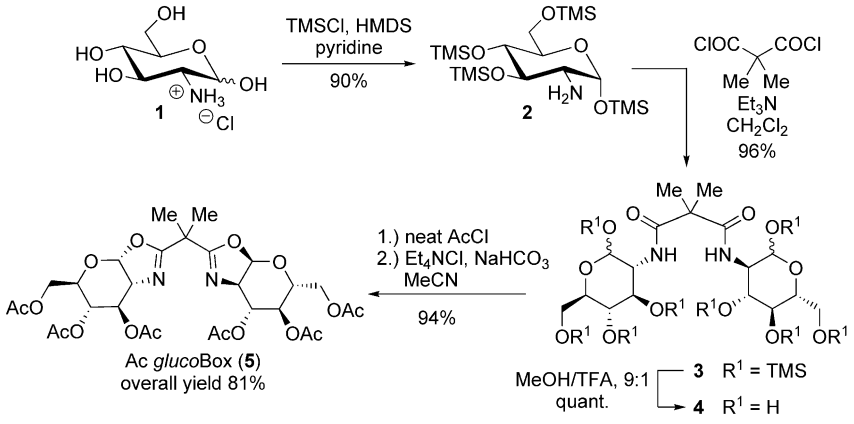
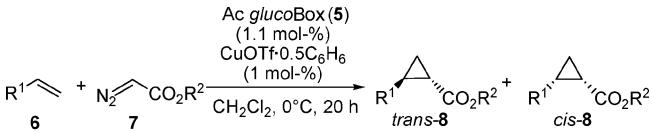
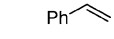
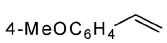
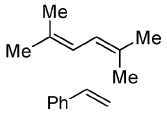
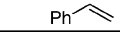


Scheme 1. Preparation of the bidentate *gluco*Box ligand (**5**) based on D-glucosamine.[7]

Table 1. Asymmetric cyclopropanations with the use of *gluco*Box ligands.



	Alkene	R^2	Yield [%][b]	*trans*/*cis*	ee_{trans} [%]	ee_{cis} [%]
1[a]		Et	60	70:30[c]	**82**[d]	**82**[d]
2		*t*Bu	44	68:32[c]	74[d]	64[d]
3[a]		Et	72	65:35[c]	77[e]	80[d]
4		*t*Bu	63	73:27[c]	76[e]	68[d]
5[a]		Et	85	–	70[e]	–
6		*t*Bu	36	–	79[e]	–
7		Et	51	75:25[d]	**82**[e]	46[e]
8[f]		Et	56	71:29[c]	68[d]	58[d]

[a] Results reported previously.[7] [b] Isolated yields after chromatography. [c] Determined after separation of the isomers by chromatography. [d] Determined by GC on a chiral stationary phase. [e] Determined by ^{1}H NMR spectroscopy with $Rh_2[(R)$-(+)-MTPA$]_4$ as chiral reagent (dirhodium method).[10] [f] TMS *gluco*Box (**10**) as ligand.

To increase the stereoselectivity for the cyclopropanations, we next set out to prepare derivatives of Ac *gluco*Box (**5**). The new carbohydrate ligand offers plentiful options for structural modifications and therefore optimisation. The pyranose unit can be modified by introduction of a wide range of residues on the hydroxy groups varying in steric and in electronic properties. It should be noted that by this approach the numerous polar functional groups prove to be an advantage: rapid access to a lot of variations of a given carbohydrate architecture is possible, something that is not nearly as easily achieved with amino alcohols conventionally employed for bis(oxazolines) synthesis.

First we studied the possibility to directly derivatise ligand **5**. Removal of the acetate groups under mildly basic conditions[11] yielded **9** with six free hydroxy groups. Reaction with TMSCl and HMDS in pyridine[12] gave ligand TMS *gluco*Box (**10**) in good yield (Scheme 2). Attempts to prepare either the corresponding pivaloylated or the benzylated ligand were unsuccessful and led to decomposition of unprotected ligand **9**.

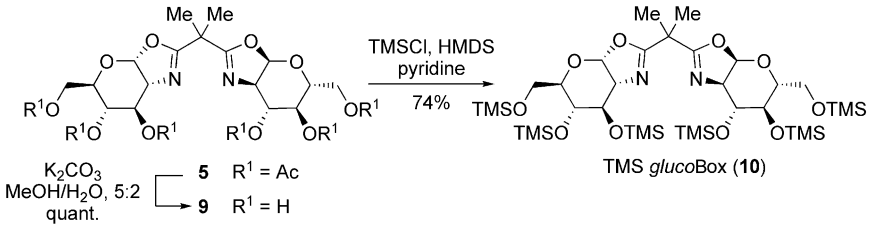
Employing TMS *gluco*Box (**10**) in the test reaction revealed this ligand to be clearly inferior to Ac *gluco*Box (**5**) (Table 1, Entry 8), and it was therefore not used for further experiments.

Even more attractive than modification of all hydroxy functions with the same residue is selective introduction of single *O*-substituents. Here, the 3-position of the pyranose ring is at the focus of interest, as it is in direct vicinity of the oxazoline nitrogen atoms. Thus, the 3-*O*-substituents should profoundly influence the steric shielding of the coordinated metal centres, and in consequence, they should have a fundamental impact on the stereoselectivity of reactions catalysed with these complexes. Therefore, we decided to selectively modify this position by attachment of ether and ester groups with varying steric demands; this strategy is illustrated in Figure 1.

In order to address the 3-*O* position, introduction of cyclic 4,6-*O*-benzylidene acetals into deprotected ligand **9** was attempted, only leading to either decomposition or recovery of the starting material. Next, unprotected bis(amide) **4** was benzylidene-protected; cyclisation to the corresponding bis(oxazoline) was tried with the use of the one-pot reaction employed for the preparation of *gluco*Box.[7] Because of the acidic conditions used in the first reaction of this sequence, only decomposition was observed.

We therefore devised a new route to 3-*O*-modified ligands with thioglycosides as key intermediates.[13] The use of thioglycosides has several advantages, as they are easily accessible, highly stable against all conditions necessary for the introduction of a broad range of 3-*O* substituents and, above all, can be activated for the cyclisation reaction under mild and specific conditions. Thus, bis(amide) **16** with free 3-hydroxy groups was prepared from D-glucosamine hydrochloride (**1**) as a key intermediate for the synthesis of 3-*O*-modified *gluco*Box ligands (Scheme 3).[13]

Starting from **16**, three ester- (Ac, Bz, Piv) and three ether-modified (Me, Bn, TES) bis(amides) (**17a**–**f**) were pre-



Scheme 2. Preparation of an *O*-TMS modified *gluco*Box ligand.

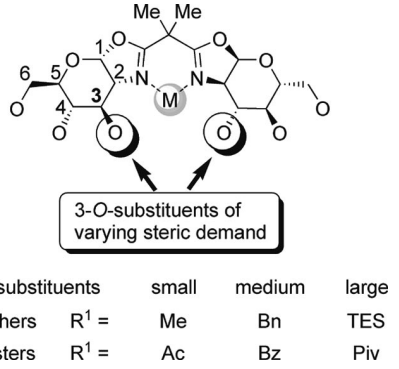
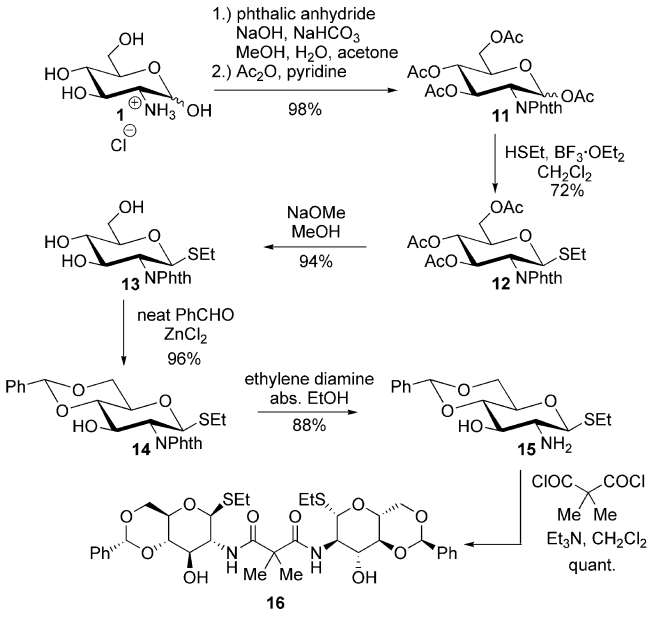


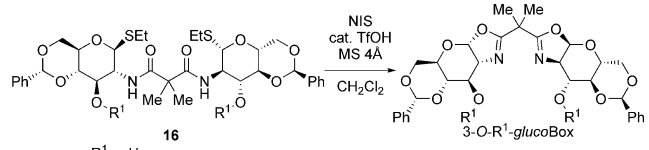
Figure 1. The 3-*O* position of *gluco*Box as a starting point for modification.



Scheme 3. Preparation of 3-*O*-modified *gluco*Box ligands by thioglucosylbis(amide) **16**.[13]

pared in good to excellent yield by using the conditions given in Table 2. Cyclisation was first attempted with acetylated bis(amide) **17a** by addition of elemental bromine to form anomeric bromides,[14] followed by treatment with Et_4NCl and $NaHCO_3$, previously described for the synthesis of Ac *gluco*Box (**5**).[7] By this method, the target bis(oxazoline) was obtained in only 20% yield, which made us look for an alternative cyclisation sequence. Next, we tried a cyclisation mediated by *N*-iodosuccinimide (NIS) and a catalytic amount of trifluoromethanesulfonic acid (TfOH), conditions originally described for the preparation of monomeric carbohydrate oxazolines from thioglycosides.[15] With the use of this protocol, all bis(amides) could be cyclised to the corresponding 3-*O*-R^1-*gluco*Box ligands **18a**–**f** in good to excellent yields irrespective of the 3-*O* substituent (Table 2).[13]

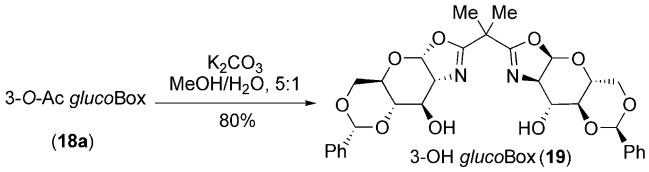
Table 2. Conditions and yields for the preparation of 3-*O* modified bis(amides) **17a**–**f** and yields of the corresponding 3-*O*-R^1-*gluco*Box ligands **18a**–**f** in the NIS-promoted cyclisation.



R^1	Bis(amide)	Yield [%]	*gluco*Box		Yield [%]
Ac[a]	**17a**	97	3-*O*-Ac	**18a**[g]	92
Bz[b]	**17b**	93	3-*O*-Bz	**18b**	84
Piv[c]	**17c**	93	3-*O*-Piv	**18c**	82
Me[d]	**17d**	94	3-*O*-Me	**18d**[g]	90
Bn[e]	**17e**	84	3-*O*-Bn	**18e**[g]	79
TES[f]	**17f**	83	3-*O*-TES	**18f**[g]	85

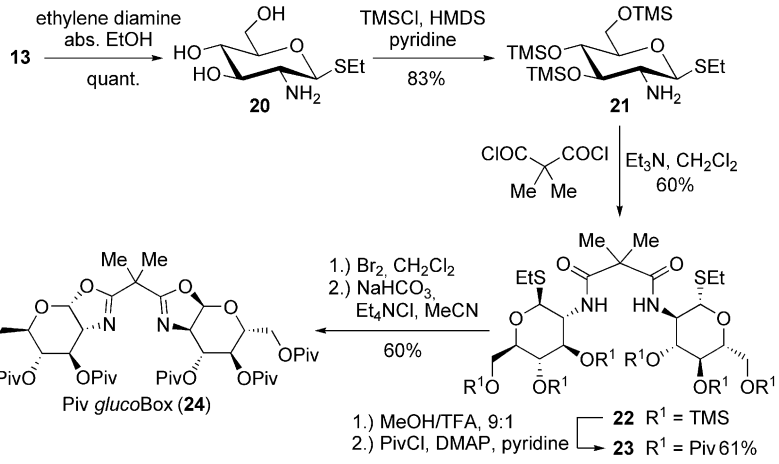
[a] Ac_2O, pyridine. [b] BzCl, pyridine.[16] [c] PivCl, DMAP, pyridine.[17] [d] MeI, NaH, DMF.[18] [e] BnBr, NaH, TBAI, DMF.[19] [f] TESOTf, Et_3N, CH_2Cl_2.[20] [g] Ligands reported previously.[13]

Additionally 3-*O*-acetylated ligand **18a** was deacetylated under basic conditions[11] to yield 3-OH *gluco*Box **19** (Scheme 4).



Scheme 4. Preparation of a 3-OH-unsubstituted *gluco*Box ligand.

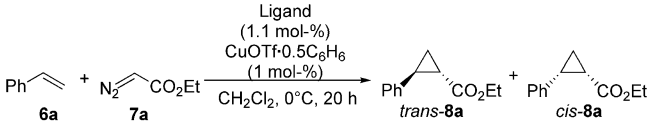
Next, a fully pivaloylated ligand was prepared from thioethyl glucoside **13**. Phthaloyl deprotection[19] followed by *O*-TMS protection[12] and coupling with dimethylmalonyl dichloride[7] yielded bis(amide) **22**. After desilylation and pivaloylation, resulting bis(amide) **23** was treated first with elemental bromine[14] and subsequently with Et_4NCl under basic conditions[7] to yield Piv *gluco*Box (**24**) (Scheme 5).



Scheme 5. Preparation of a perpivaloylated ligand Piv *gluco*Box (**24**).

With this set of eight new carbohydrate bis(oxazoline) ligands in hand, we started our evaluation studies concerning their efficiency in enantioselective copper(I)-catalysed cyclopropanation of styrene with ethyl diazoacetate (Table 3). All ligands **18a**–**f** gave products *trans*-**8a** and *cis*-**8a** in good to very good yields, but the ligands differed notably with regard to diastereoselectivity and substantially with regard to enantioselectivity. The best result was obtained with 3-*O*-Ac *gluco*Box ligand (**18a**), which yielded the products in a good *trans*/*cis* ratio of 79:21 and in 93%*ee* for the major *trans* and 82%*ee* for the minor *cis* diastereomer. The other 3-*O*-acyl, 3-*O*-alkyl and 3-*O*-silyl modified ligands **18b**–**f** did not nearly reach comparable levels of enantioselectivity. Also, ligand 3-OH *gluco*Box ligand (**19**) only gave moderate selectivity, whereas Piv *gluco*-Box (**24**) yielded another good result with *trans*-**8a** in 84%*ee* and the minor diastereomer *cis*-**8a** in 94%*ee*.

Table 3. Cyclopropanations with the use of *gluco*Box ligands **18a**–**f** and **19** and **24**.



	*gluco*Box		Yield [%][a]	*trans*/*cis*[b]	ee_{trans} [%][c]	ee_{cis} [%][c]
1	3-*O*-Ac	**18a**	90	79:21	**93**	**82**
2	3-*O*-Bz	**18b**	74	69:31	64	36
3	3-*O*-Piv	**18c**	90	64:36	62	49
4	3-*O*-Me	**18d**	87	77:23	73	39
5	3-*O*-Bn	**18e**	95	62:38	48	28
6	3-*O*-TES	**18f**	71	64:36	33	7
7	3-OH	**19**	87	68:32	51	44
8	Piv	**24**	86	63:37	**84**	**94**

[a] Isolated yields after chromatography. [b] Determined after separation of the isomers by chromatography. [c] Determined by GC on a chiral stationary phase.

From comparison of the results obtained with **18a**–**f** (Figure 2) a clear trend emerges for the ester- and ether-modified *gluco*Box ligands: in both ligand families an increase in steric demand of the 3-*O* substituent has a detrimental effect on the enantioselectivity of the cyclopropanation reaction (*ee* for 3-*O*-Ac > 3-*O*-Bz > 3-*O*-Piv; *ee* for 3-*O*-Me > 3-*O*-Bn > 3-*O*-TES), but it also becomes clear that not only steric factors are important for ligand efficiency. Ligand **18a** bearing a 3-*O* acetyl substituent yields considerably better enantioselectivity than ligand **18d** with a smaller 3-*O* methyl residue. It appears that apart from steric factors also electronic influences of the 3-*O*-R^1 group play an important role for the stereoselectivity of the reaction, with electron-withdrawing ester groups having a favourable influence. The reason for the beneficial effect of 3-*O*-acyl residues is as yet not fully understood.

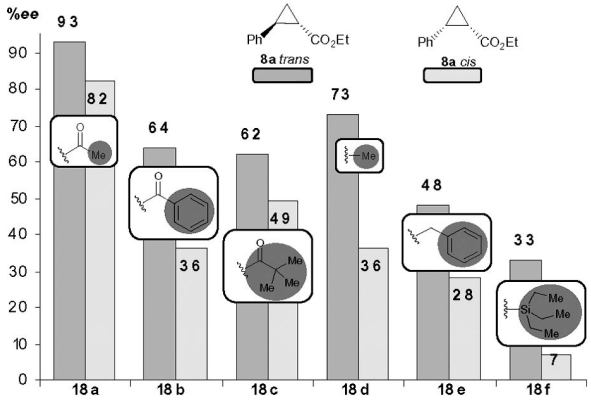


Figure 2. Impact of 3-*O* substituents on the stereoselectivity of cyclopropanation reactions with *gluco*Box ligands **18a**–**f**.

Apart from the steric and electronic influences of the 3-*O* substituents, the conformation of the pyranose units will have an impact on the structure of the metal complexes formed with the ligands. This in turn will affect the stereo-

selectivity of any reaction catalysed by such systems. As a result of the 1,2-*cis* annulated ring, oxazolines with acyclic protective groups deviate significantly from the $^4C_1$ conformation (Figure 3, **A**) commonly found for glucopyranose derivatives. Instead, they adopt a $^OS_1$ twist-like conformation (Figure 3, **B**), which was first deduced from ^1H NMR spectroscopic studies[21a] and later proved by X-ray structure analysis.[21b] The ^3J coupling constants of ligands Ac *gluco*Box (**5**) and Piv *gluco*Box (**24**) are in good agreement with those reported for simple oxazolines with acyclic protecting groups[21b] and also with those reported for the first carbohydrate bis(oxazoline).[6] Thus, we can assume with good approximation that these two ligands adopt the identical conformation as that of simple carbohydrate oxazolines. By introduction of a 4,6-*O* benzylidene group into a glucopyranose derivative a conformationally rigid *trans* decaline system is formed (Figure 3, **C**). When this cyclic acetal group is incorporated into a carbohydrate oxazoline the *trans* decaline-like system partly fixes a chair-like conformation (Figure 3, **D**). Thus, ligands with and without benzylidene groups adopt different conformations, which is also borne out by their ^1H NMR spectroscopic data.

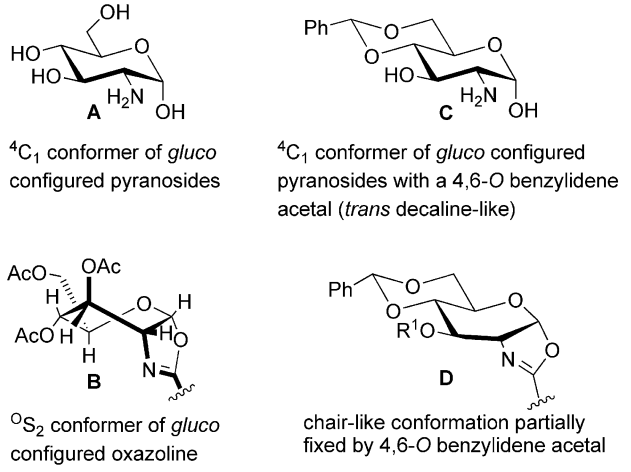


Figure 3. Pyranose conformations in the presence and absence of annulated ring systems.

Figure 4 illustrates the effects of 4,6-*O* benzylidene acetals on stereoselectivity by comparing the cyclopropanation results obtained for ligands 3-*O*-Ac (**18a**) and 3-*O*-Piv *gluco*Box (**18c**) with those of their peracetylated and perpivaloylated counterparts **5** and **24**. Whereas 3-*O*-Ac *gluco*Box (**18a**) containing a benzylidene group led, in comparison to Ac *gluco*Box (**5**), to substantially increased enantioselectivity, the reverse trend was observed for 3-*O*-Piv *gluco*Box (**18c**) and Piv *gluco*Box (**24**). Obviously, steric influences of the 3-*O* substituents are overlaid with a conformational effect caused by the benzylidene group. The cyclic acetal, partly fixing a chair-like conformation, combined with a small 3-*O*-acetyl group has a beneficial effect on stereoselectivity, whereas larger *O*-pivalates give good results when no cyclic acetal group is present and the pyranose adopts a $^OS_1$ twist-like conformation.

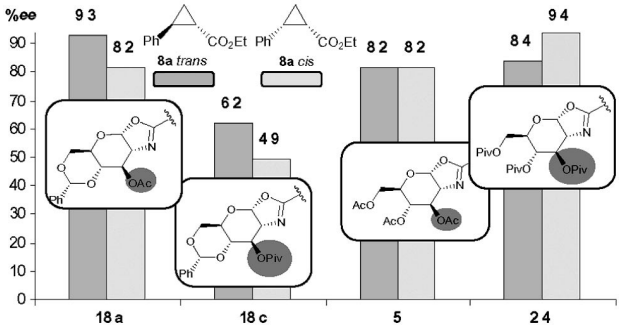


Figure 4. Impact of the pyranose conformation on stereoselectivity of cyclopropanation reactions with *gluco*Box ligands **18a**, **18c**, **5** and **24**.

Conclusions

We developed new type of carbohydrate-based bis(oxazoline) ligand based on inexpensive D-glucosamine, which as a result of the polyfunctional pyranose scaffold could successfully be optimised for asymmetric cyclopropanation by attaching 3-*O* substituents of varying steric and electronic properties in a facile manner. With benzylidene-protected ligands, considerable steric and electronic effects of the 3-*O* substituent are observed, with the small acetyl group giving far better results than those obtained with more bulky acyl residues and ether groups irrespective of their steric demand. Exploiting this strategy, the stereoselectivity of cyclopropanations with carbohydrate bis(oxazoline) ligands could be successfully increased; the major *trans* diastereomer was obtained in up to 93%*ee*, in comparison to 82%*ee* obtained with original peracetylated ligand **5**. Additionally, a conformational effect is in operation: ligands with a benzylidene moiety partly fixing the pyranose ring in a chair-like conformation give best results in combination with the rather small 3-*O* acetyl group. Peracylated ligands adopting a twist-like conformation, in contrast, give better results with bulky pivalate residues. The causes for the electronic and conformational effects are, as of yet, not fully understood and are currently under investigation. To this end, a series of ligands with other acyl-based 3-*O* residues such as carbamates, carbonates and electron-deficient esters will be prepared and tested. Further, the successful optimisation strategy of varying steric, electronic and conformational properties of the basic ligand structure will also be applied to the corresponding *gluco*Pybox scaffold.

Experimental Section

General Methods: Dry solvents were obtained by distillation over appropriate drying reagents under a nitrogen atmosphere (CH_2Cl_2 and acetonitrile distilled from calcium hydride, THF distilled from sodium/benzophenone ketyl) or were purchased in dry form from commercial sources (DMF from Acros, pyridine from Fluka, absolute ethanol from VWR) and used as received. All reactions involving reagents sensitive to air and moisture were carried out under a nitrogen atmosphere (glove box and/or Schlenk techniques). Reac-

tions were monitored by TLC on 60 F254 aluminum plates (Merck) with detection by UV light and/or charring with 10% sulfuric acid in ethanol or a mixture of cerium(IV) sulfate and molybdophosphoric acid in 8% sulfuric acid. Flash chromatography was performed on Merck silica (grain size 40–63 μM). NMR spectra were recorded with an AVS 400 instrument (Bruker) at 400 MHz (^{1}H) or at 100 MHz (^{13}C). Deuterated chloroform and methanol were used as solvents and spectra were calibrated against the residual solvent peak ($CHCl_3$: 7.24 ppm, CD_2HOD: 3.35 ppm). Electrospray mass (ESI) spectra were recorded with a Micromass LCT device (Waters), injection into the HPLC instrument (Waters) was performed in loop modus. Optical rotations were recorded with a Perkin–Elmer 451 instrument under the following standard conditions: room temperature, wavelength 589.3 nm (sodium D line), cell length 1 dm, solvent and sample concentration (in 10 mg mL^{-1}) are given with the individual experiment. Chiral GC experiments were carried out with an HP 5890-II device (Hewlett–Packard) with a flame ionisation detector and hydrogen as carrier gas in constant flow modus. Starting temperature was 50 °C 1.1 °C min^{-1}. A Hydrodex-β PM capillary column (50 m, 0.25 mm, 723370, Macherey–Nagel) was used for separation of the enantiomers. Determination of enantiomeric excesses by ^{1}H NMR spectroscopy was done with $Rh_2[(R)$-(+)-MTPA$]_4$ as chiral complexing reagent, dirhodium method.[13]

2-Amino-2-deoxy-1,3,4,6-tetra-*O*-trimethylsilyl-α-D-glucopyranose (2): To a suspension of glucosamine hydrochloride (**1**; 10.00 g, 43.36 mmol) in pyridine (500 mL) was added HMDS (90 mL, 70.00 g, 433.60 mmol) followed by TMSCl (55 mL, 47.11 g, 433.60 mmol). The resulting mixture was stirred at room temperature, and the reaction was monitored by TLC [petroleum ether (PE)/EtOAc, 5:1]. During the reaction, a lot of salt precipitated. After completion of the reaction (approx. 4 h), the mixture was evaporated in vacuo with a cooling trap placed between the rotary evaporator and the pump stand. The residue was coevaporated with toluene (2×) to remove residual pyridine. The raw material was then submitted to short column filtration through silica gel (PE/EtOAc, 5:1) to remove the pyridinium salts. Acid-sensitive **2** was obtained as a colourless crystalline solid after refrigerating overnight (19.53 g, 41.72 mmol, 90%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.08, 0.17, 0.15, 0.20, (each s, each 9 H, $SiCH_3$), 1.38 (br. s, 2 H, NH_2), 2.52 (dd, $J_{1,2}$ = 3.3 Hz, $J_{2,3}$ = 9.7 Hz, 1 H, 2-H), 3.44 (dd, $J_{3,4}$ = 8.7 Hz, $J_{4,5}$ = 9.4 Hz, 1 H, 4-H), 3.52 (dd, $J_{2,3}$ = 9.7 Hz, $J_{3,4}$ = 8.7 Hz, 1 H, 3-H), 3.61 (ddd, $J_{4,5}$ = 9.4 Hz, $J_{5,6}$ = 4.3 Hz, $J_{5,6'}$ = 2.5 Hz, 1 H, 5-H), 3.64–3.75 (m, 2 H, 6-H, 6′-H), 5.12 (d, $J_{1,2}$ = 3.3 Hz, 1 H, 1-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 0.2, 0.4, 0.9, 1.4, (each CH_3, $SiCH_3$), 57.7 (CH, C-2), 62.0 (CH_2, C-6), 78.2, 72.9, 72.0, (CH, C-3, C-4, C-5), 95.8 (CH_3, C-1) ppm. HRMS (ESI+): calcd. for $C_{18}H_{46}O_5NSi_4$ $[M + H]^+$ 468.2453; found 468.2456. $[\alpha]_D^{25}$ = +87 (c = 3.4, $CHCl_3$).

***N*,*N*′-Bis(2-deoxy-1,3,4,6-tetra-*O*-trimethylsilyl-α-D-glucopyranosid-2-yl)dimethylmalonamide (3):** Under a nitrogen atmosphere, sugar **2** (18.52 g, 39.58 mmol) was dissolved in dry CH_2Cl_2 (250 mL), and the resulting solution was cooled to 0 °C. Then, triethylamine (11 mL, 8.02 g, 79.17 mmol) followed by dimethylmalonoyl dichloride (2.6 mL, 3.35 g, 19.79 mmol) was added. Progress of the reaction was monitored by TLC (PE/EtOAc, 2:1). After approx. 2 h, the solvent was evaporated in vacuo, and the raw product was subjected to short column filtration through silica gel (PE/EtOAc, 3:1). Bis(amide) **3** was isolated as a colourless foam (19.60 g, 19.00 mmol, 96%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.10, 0.17, 0.19, 0.21, (each s, each 18 H, $SiCH_3$), 1.48 [s, 6 H, $(CH_3)_2C$], 3.61 (dd ≈ t, $J_{3,4} \approx J_{4,5}$ = 8.4 Hz, 2 H, 4-H), 3.65–3.81 (m, 8 H, 3-H, 5-H, 6-H, 6′-H), 3.99 (ddd ≈ td, $J_{1,2}$ = 3.1 Hz, $J_{2,3} \approx J_{2,NH}$ = 9.2 Hz, 2 H, 2-H), 5.06 (d, $J_{1,2}$ = 3.1 Hz, 2 H, 1-H), 7.08 (d, $J_{2,NH}$ = 9.2 Hz, 2 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = –0.43, –0.27, 0.60, 0.98, (each CH_3, $SiCH_3$), 24.4 [CH_3, $(CH_3)_2C$], 49.1 [C, $(CH_3)_2C$], 54.8 (CH, C-2), 61.5 (CH_2, C-6), 71.5, 73.1, 73.6 (CH, C-3, C-4, C-5), 91.7 (CH, C-1), 173.6 (C, CONH) ppm. HRMS (ESI+): calcd. for $C_{41}H_{95}N_2O_{12}Si_8$ $[M + H]^+$ 1031.5039; found 1031.5077. HRMS (ESI+): calcd. for $C_{41}H_{94}N_2O_{12}Si_8Na$ $[M + Na]^+$ 1053.4858; found 1053.4911. $[\alpha]_D^{25}$ = +83 (c = 1.6, $CHCl_3$).

Bis(2-amino-2-deoxy-D-glucopyranosido)dimethylmalonamide (4): Bis(amide) **3** (9.96 g, 9.66 mmol) was treated with MeOH/TFA (9:1, 150 mL) at room temperature. TLC ($MeOH/CH_2Cl_2$, 1:9) indicated the complete consumption of all staring material after 2 h. The solvent was removed in vacuo, and the residue was coevaporated with toluene until it solidified to a colourless mass. The powdery raw product was stirred with ethyl acetate (100 mL), filtered and washed with some more ethyl acetate to remove residual organosilicon byproducts. Colourless product **4** was isolated in quantitative yield and used for the next step without further purification. As each of the two carbohydrate moieties of bis(amide) **4** can individually occur in both anomeric forms, a total of three bis(amides) with different anomeric configurations is obtained. The (α,α)-, (α,β)- and (β,β)-configured compounds have all slightly different chemical shifts in the ^{1}H and ^{13}C NMR spectra, complicating interpretation. Therefore, full NMR characterisation of **4** was not attempted. HRMS (ESI): calcd. for $C_{17}H_{30}O_{12}N_2Na$ $[M + Na]^+$ 477.1696; found 477.1700. $[\alpha]_D^{25}$ = +41 (c = 1.02, MeOH).

Ac *gluco*Box (5): Bis(amide) **4** (1.00 g, 2.20 mmol) was taken up in neat acetyl chloride (10 mL) (note: the acetyl chloride should not be distilled prior to use, as a catalytic amount of hydrogen chloride is necessary for the reaction!) and stirred for 16 h. Reaction progress was monitored by TLC (CH_2Cl_2/acetone, 5:1). The acetyl chloride was then removed in vacuo, and the crude product was coevaporated with toluene (2×) to remove residual acetyl chloride and then directly used for the next step. To a solution of the crude product dissolved in dry acetonitrile (10 mL) was added Et_4NCl (860 mg, 5.20 mmol) and solid $NaHCO_3$ (860 mg, 10.48 mmol), and the resulting mixture was stirred at room temperature for 16 h. Reaction progress can be monitored by TLC (CH_2Cl_2/acetone, 3:1). The solvent was removed in vacuo, and the residue taken up in CH_2Cl_2 (20 mL) and washed with water (20 mL). The organic phase was dried with Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography on silica gel (PE/EtOAc, 1:1) to afford **5** as a yellow foam (1.40 g, 2.12 mmol, 94%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.58 [s, 6 H, $(CH_3)_2C$], 1.98, 2.16, 2.05 (each s, each 6 H, CH_3CO), 3.86 (ddd, $J_{4,5}$ = 9.2 Hz, $J_{5,6}$ = 4.8 Hz, $J_{5,6'}$ = 2.9 Hz, 2 H, 5-H), 4.13 (dd, $J_{5,6'}$ = 2.7 Hz, $J_{6,6'}$ = 12.3 Hz, 2 H, 6′-H), 4.18 (ddd, $J_{1,2}$ = 7.5 Hz, $J_{2,3}$ = 2.4 Hz, $J_{2,4}$ = 1.3 Hz, 2 H, 2-H), 4.22 (dd, $J_{5,6}$ = 4.8 Hz, $J_{6,6'}$ = 12.3 Hz, 2 H, 6-H), 4.94 (ddd, $J_{3,4}$ = 2.4 Hz, $J_{2,4}$ = 1.3 Hz, $J_{4,5}$ = 9.2 Hz, 2 H, 4-H), 5.31 (dd ≈ t, $J_{2,3} = J_{3,4}$ = 2.4 Hz, 2 H, 3-H), 6.05 (d, $J_{1,2}$ = 7.5 Hz, 2 H, 1-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.7, 20.8, 20.9 (CH_3, CH_3CO), 23.8 [CH_3, $(CH_3)_2C$], 39.2 [C, $(CH_3)_2C$], 62.8 (CH_2, C-6), 64.8 (CH, C-2), 67.8 (CH, C-5), 68.3, (CH, C-4), 70.1, (CH, C-3), 100.0 (CH, C-1), 169.2, 169.5, 170.2, 170.6 (C, CH_3CO, O-C=N) ppm. HRMS (ESI+): calcd. for $C_{29}H_{39}O_{16}N_2$ $[M + H]^+$ 671.2300; found 671.2298. $[\alpha]_D^{25}$ = +53 (c = 1.9, $CHCl_3$).

OH *gluco*Box (9): To a solution of **5** (100 mg, 150 μmol) dissolved in $MeOH/H_2O$ (5:2, 20 mL) was added potassium carbonate (40 mg, 29 μmol), and the resulting suspension was stirred at room temperature (TLC: PE/EtOAc, 1:3). After completion of the reaction, the solvent was evaporated in vacuo. The residue was coevaporated with MeOH to yield **9** (62 mg, 150 μmol, quant.) as a yellow

foam, which was employed in the next step without further purification. ^{1}H NMR (400 MHz, D_2O): δ = 1.45 [s, 6 H, $(CH_3)_2C$], 3.34–3.42 (m, 2 H, 5-H), 3.51–3.62 (m, 4 H, 6-H, 4-H), 3.70–3.74 (m, 2 H, 6′-H), 3.90–3.93 (m, 2 H, 3-H), 4.08–4.12 (m, 2 H, 2-H), 6.08 (d, $J_{1,2}$ = 7.2 Hz, 2 H, 1-H) ppm. ^{13}C NMR (100 MHz, D_2O): δ = 23.0 [CH_3, $(CH_3)_2C$], 39.1 [C, $(CH_3)_2C$], 61.5 (CH_2, C-6), 66.0 (CH, C-2), 68.7 (CH, C-4), 71.8 (CH, C-5), 73.1 (CH, C-3), 101.1 (CH, C-1), 170.2 (C, O-C=N) ppm. HRMS (ESI+): calcd. for $C_{17}H_{26}N_2O_{10}Na$ $[M + Na]^+$ 441.1485; found 441.1808. $[\alpha]_D^{20}$ = +88 (c = 1.8, H_2O).

TMS *gluco*Box (10): To a suspension of unprotected bis(oxazoline) **9** (100 mg, 240 μmol) in dry pyridine (5 mL) was added HMDS (550 μL, 4.78 mmol) followed by the addition of TMSCl (610 μL, 4.78 mmol). The resulting mixture was stirred at room temperature (TLC: PE/EtOAc, 5:1). After completion of the reaction (approx. 2 h), the mixture was evaporated in vacuo. The residue was coevaporated with toluene. The crude product was then purified by column filtration through silica gel (PE/EtOAc, 5:1) to yield compound **10** as a white solid (150 mg, 170 μmol, 74%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.08–0.21 (18 H, $SiCH_3$), 1.53 [s, 6 H, $(CH_3)_2C$], 3.40–3.45 (m, 2 H, 5-H), 3.66–3.78 (m, 8 H, 3-H, 4-H, 6-H, 6′-H), 3.85–3.89 (m, 2 H, 2-H), 6.02 (d, $J_{1,2}$ = 7.5 Hz, 2 H, 1-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 0.2, 0.5, 1.3 (CH_3, $SiCH_3$), 24.2 [CH_3, $(CH_3)_2C$], 39.5 [C, $(CH_3)_2C$], 62.2 (CH_2, C-6), 68.1 (CH, C-2), 70.0 (CH, C-4), 74.2 (CH, C-5), 76.5 (CH, C-3), 102.8 (CH, C-1), 168.4 (C, O-C=N) ppm. HRMS (ESI+): calcd. for $C_{35}H_{74}N_2O_{11}Si_6$ $[M + H]^+$ 851.3959; found 851.3556. $[\alpha]_D^{20}$ = +88 (c = 1.8, $CHCl_3$).

1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-phthalimido-D-glucopyranoside (11): To a stirred solution of D-glucosamine hydrochloride (**1**; 50.00 g, 231.88 mmol) in methanol (100 mL) and water (200 mL) was added NaOH (12.05 g, 301.44 mmol) at 0 °C. Then, phthalic anhydride (49.76 g, 336.23 mmol) dissolved in acetone (400 mL) was added while maintaining the temperature below 15 °C. More phthalic anhydride (20.59 g, 139.13 mmol) and $NaHCO_3$ (49.86 g, 593.61 mmol) were added, and the solution was subsequently stirred at room temperature overnight (TLC: EtOAc/HOAc/MeOH/H_2O, 12:3:3:2). The mixture was then brought to pH 1 with concentrated hydrochloric acid, concentrated in vacuo and left at 2 °C in the refrigerator overnight. The resulting precipitate was filtered off, washed with cold water and dried under vacuum. The crude product was dissolved in pyridine (700 mL) and treated with acetic anhydride (568.14 g, 525 mL, 5.57 mol), and the mixture was stirred at room temperature overnight (TLC: toluene/EtOAc, 3:2). The solvents were evaporated, and the product was coevaporated with toluene (2×). The residue was dried under reduced pressure to yield compound **11** as a colourless solid (108.42 g, 227.24 mmol, 98%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.83, 2.02, 2.05, 2.08 (each s, each 3 H, CH_3CO), 4.10 (dd, $J_{5,6'}$ = 2.0 Hz, $J_{6,6'}$ = 12.2 Hz, 1 H, 6′-H), 4.28 (ddd ≈ td, $J_{4,5}$ = 10.2 Hz, $J_{5,6}$ = 3.7 Hz, $J_{5,6'}$ = 2.0 Hz, 1 H, 5-H), 4.33 (dd, $J_{5,6}$ = 3.7 Hz, $J_{6,6'}$ = 12.2 Hz, 1 H, 6-H), 4.68 (dd, $J_{1,2}$ = 3.4 Hz, $J_{2,3}$ = 11.6 Hz, 1 H, 2-H), 5.13 (dd ≈ t, $J_{3,4}$ = 9.2 Hz, $J_{4,5}$ = 10.2 Hz, 1 H, 4-H), 6.24 (d, $J_{1,2}$ = 3.4 Hz, 1 H, 1-H), 6.53 (dd, $J_{2,3}$ = 11.6 Hz, $J_{3,4}$ = 9.2 Hz, 1 H, 3-H), 7.70–7.73 (m, 2 H, Phth), 7.79–7.83 (m, 2 H, Phth) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.5, 20.6, 20.9 (CH_3, CH_3CO), 52.7 (CH, C-2), 61.4 (CH_2, C-6), 66.9 (CH, C-3), 69.3 (CH, C-4), 70.1 (CH, C-5), 90.4 (CH, C-1), 132.6 (CH, Phth), 131.0 (C, Phth), 134.4 (CH, Phth), 167.3, 168.5 (C, NCO), 169.2, 169.4, 169.7, 170.5 (C, CH_3CO) ppm. HRMS (ESI+): calcd. for $C_{22}H_{24}NO_{11}$ $[M + H]^+$ 478.1344; found 478.1354. $[\alpha]_D^{20}$ = +112 (c = 0.9, $CHCl_3$).

Ethyl-3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (12): Compound **11** (5.00 g, 10.50 mmol) and ethane thiol (1.70 g, 2.03 mL, 27.30 mmol) were dissolved in dry CH_2Cl_2 (20 mL). The mixture was cooled to 0 °C and borontrifluoride diethyl ether complex (970 μL, 930 mg, 7.50 mmol) was added by syringe. The mixture was stirred for 1 h at 0 °C and then 16 h at room temperature (TLC: PE/EtOAc, 3:1). The reaction was quenched by the addition of a saturated solution of $NaHCO_3$ in water. The organic layer was separated, dried with Na_2SO_4, concentrated and purified by flash chromatography on silica gel (PE/EtOAc, 3:1) to yield **12** (3.71 g, 7.74 mmol, 74%) as colourless crystals. M.p. 118 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.18 (t, J = 7.5 Hz, 3 H, SCH_2CH_3), 1.82, 1.99, 2.06 (each s, each 3 H, CH_3CO), 2.58–2.70 (m, 2 H, SCH_2CH_3), 3.86 (ddd ≈ td, $J_{4,5}$ = 10.2 Hz, $J_{5,6}$ = 5.1 Hz, $J_{5,6'}$ = 2.0 Hz, 1 H, 5-H), 4.13 (dd, $J_{5,6'}$ = 2.0 Hz, $J_{6,6'}$ = 12.2 Hz, 1 H, 6′-H), 4.27 (dd, $J_{5,6}$ = 5.1 Hz, $J_{6,6'}$ = 12.2 Hz, 1 H, 6-H), 4.36 (dd ≈ t, $J_{1,2}$ = 10.5 Hz, $J_{2,3}$ = 10.2 Hz, 1 H, 2-H), 5.14 (dd ≈ t, $J_{3,4}$ = 9.2 Hz, $J_{4,5}$ = 10.2 Hz, 1 H, 4-H), 5.45 (d, $J_{1,2}$ = 10.5 Hz, 1 H, 1-H), 5.79 (dd, $J_{2,3}$ = 10.2 Hz, $J_{3,4}$ = 9.2 Hz, 1 H, 3-H), 7.70–7.73 (m, 2 H, Phth), 7.81–7.83 (m, 2 H, Phth) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.8 (CH_3, SCH_2CH_3), 20.4, 20.5, 20.7 (CH_3, CH_3CO), 24.3 (CH_2, SCH_2CH_3), 53.6 (CH, C-2), 62.2 (CH_2, C-6), 68.8 (CH, C-4), 71.5 (CH, C-3), 75.8 (CH, C-5), 81.4 (CH, C-1), 123.6 (CH, Phth), 131.1 (C, Phth), 134.2 (CH, Phth), 167.1, 167.7 (C, NCO), 169.4, 170.0, 170.6 (C, CH_3CO) ppm. HRMS (ESI+): calcd. for $C_{22}H_{26}NO_9S$ $[M + H]^+$ 480.1323; found 480.1319. $[\alpha]_D^{20}$ = +44 (c = 1.0, $CHCl_3$).

Ethyl-2-Deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (13): To a solution of **12** (18.00 g, 37.53 mmol) dissolved in dry methanol (380 mL) was dropwise added freshly prepared sodium methoxide solution (170 mg of Na in 10 mL of dry methanol, 7.51 mmol). The reaction mixture was stirred for 6 h (TLC: EtOAc) and then neutralized with Dowex® HCR-W2 ion-exchange resin. The resin was filtered off, and the solution was concentrated. The residue was purified by flash chromatography on silica gel (EtOAc) to yield **13** (12.40 g, 35.10 mmol, 94%) as colourless crystals. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.11 (t, J = 7.5 Hz, 3 H, SCH_2CH_3), 2.61–2.70 (m, 2 H, SCH_2CH_3), 3.41 (m, 1 H, 5-H), 3.47 (br. s, 1 H, OH), 3.62 (dd ≈ t, $J_{3,4}$ = 9.2 Hz, 1 H, 4-H), 3.77–3.85 (m, 2 H, 6-H, 6′-H), 4.09 (dd ≈ t, $J_{1,2} \approx J_{2,3}$ = 10.2 Hz, 1 H, 2-H), 4.27 (dd ≈ t, $J_{2,3} \approx J_{3,4}$ = 9.2 Hz, 1 H, 3-H), 4.43 (br. s, 1 H, OH), 4.75 (br. s, 1 H, OH), 5.26 (d, $J_{1,2}$ = 10.2 Hz, 1 H, 1-H), 7.64–7.69 (m, 2 H, Phth), 7.75–7.80 (m, 2 H, Phth) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.8 (CH_3, SCH_2CH_3), 24.3 (CH_2, SCH_2CH_3), 55.7 (CH, C-2), 61.7 (CH_2, C-6), 70.9 (CH, C-4), 72.4 (CH, C-3), 79.6 (CH, C-5), 81.1 (CH, C-1), 123.6, 123.7 (CH, Phth), 131.5, 131.6 (C, Phth), 134.0 (CH, Phth), 168.0, 168.2 (C, NCO) ppm. HRMS (ESI+): calcd. for $C_{16}H_{20}NO_6S$ $[M + H]^+$ 354.1006; found 354.1012. $[\alpha]_D^{20}$ = +6 (c = 0.9, $CHCl_3$).

Ethyl-4,6-*O*-Benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (14): Compound **13** (11.00 g, 31.13 mmol) and finely powdered anhydrous zinc chloride (4.67 g, 34.24 mmol) were suspended in freshly distilled benzaldehyde (30 mL). The solution was stirred for 16 h at room temperature (TLC: PE/EtOAc, 1:1). After adding water (300 mL) the semi-crystalline reaction mixture was cooled to 0 °C for 2 h. The precipitate was filtered off, washed with water and petroleum ether and dried in vacuo. Flash chromatography on silica gel (PE/EtOAc, 1:1) yielded **14** (13.13 g, 29.74 mmol, 96%) as colourless crystals. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.17 (t, J = 7.5 Hz, 3 H, SCH_2CH_3), 2.59–2.70 (m, 2 H, SCH_2CH_3), 2.76 (br. s, 1 H, OH), 3.56 (dd ≈ t, $J_{3,4}$ = 9.2 Hz, $J_{4,5}$ = 9.9 Hz, 1 H, 4-H), 3.65 (ddd ≈ td, $J_{4,5} \approx J_{5,6'}$ = 9.9 Hz, $J_{5,6}$ = 4.7 Hz, 1 H, 5-H), 3.77 (dd ≈ t, $J_{5,6'} \approx J_{6,6'}$ = 10.2 Hz, 1 H, 6′-H), 4.28 (t ≈ dd, $J_{1,2}$ = 10.2 Hz, $J_{2,3}$ = 8.8 Hz, 1 H, 2-H), 4.36 (dd, $J_{5,6}$ = 4.7 Hz, $J_{6,6'}$ = 10.2 Hz, 1 H, 6-H), 4.62 (dd, $J_{2,3}$ = 8.8 Hz, $J_{3,4}$ = 9.2 Hz, 1 H, 3-

H), 5.37 (d, $J_{1,2}$ = 10.2 Hz, 1 H, 1-H), 5.54 (s, 1 H, CHPh), 7.33–7.35 (m, 3 H, Ph), 7.45–7.48 (m, 2 H, Ph), 7.67–7.71 (m, 2 H, Phth), 7.80–7.85 (m, 2 H, Phth) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.8 (CH_3, SCH_2CH_3), 24.1 (CH_2, SCH_2CH_3), 55.4 (CH, C-2), 68.5 (CH_2, C-6), 69.4 (CH, C-3), 70.5 (CH, C-5), 81.8 (CH, C-1), 82.0 (CH, C-4), 101.8 (CH, PhCH), 123.2, 123.8, 126.2, 128.3, 129.3 (CH, arom.), 131.4, 131.6 (C, arom.), 134.1 (CH, arom.), 136.8 (C, arom.), 167.2, 168.2 (C, NCO) ppm. HRMS (ESI+): calcd. for $C_{23}H_{23}NO_6SNa$ [M + Na]$^+$ 464.1138; found 464.1139. $[\alpha]_D^{20}$ = –7 (c = 1.0, $CHCl_3$).

Ethyl-2-Amino-4,6-*O*-benzylidene-2-deoxy-1-thio-β-D-glucopyranoside (15): Compound **14** (5.00 g, 11.32 mmol) and ethylene diamine (28.00 mL, 25.17 g, 679.8 mmol) were dissolved in absolute ethanol (400 mL). The mixture was heated at reflux for 16 h (TLC: EtOAc). The solvent was evaporated, and the product was coevaporated with toluene (2×). Flash chromatography on silica gel (EtOAc) yielded **15** (13.13 g, 29.74 mmol, 88%) as a colourless solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.26 (t, J = 7.5 Hz, 3 H, SCH_2CH_3), 2.35 (br. s, 1 H, OH), 2.61–2.70 (m, 2 H, SCH_2CH_3), 2.74 (dd, $J_{1,2}$ = 9.9 Hz, $J_{2,3}$ = 8.8 Hz, 1 H, 2-H), 3.39 (ddd ≈ td, $J_{4,5} \approx J_{5,6'}$ = 9.9 Hz, $J_{5,6}$ = 4.7 Hz, 1 H, 5-H), 3.48 (dd ≈ t, $J_{2,3}$ = 8.8 Hz, $J_{3,4}$ = 9.2 Hz, 1 H, 3-H), 3.62 (dd, $J_{3,4}$ = 9.2 Hz, $J_{4,5}$ = 9.9 Hz, 1 H, 4-H), 3.70 (dd ≈ t, $J_{5,6} \approx J_{6,6'}$ = 10.2 Hz, 1 H, 6′-H), 4.26 (dd, $J_{5,6}$ = 4.7 Hz, $J_{6,6'}$ = 10.2 Hz, 1 H, 6-H), 5.28 (d, $J_{1,2}$ = 9.9 Hz, 1 H, 1-H), 5.49 (s, 1 H, CHPh), 7.33–7.36 (m, 3 H, Ph), 7.44–7.47 (m, 2 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.1 (CH_3, SCH_2CH_3), 24.5 (CH_2, SCH_2CH_3), 56.9 (CH, C-2), 68.5 (CH_2, C-6), 70.4 (CH, C-3), 74.4 (CH, C-5), 81.0 (CH, C-4), 87.6 (CH, C-1), 101.8 (CH, PhCH), 126.2, 128.2, 129.2 (CH, Ph), 137.0 (C, Ph) ppm. HRMS (ESI+): calcd. for $C_{15}H_{21}NO_4SNa$ [M + Na]$^+$ 334.1083; found 334.1056. $[\alpha]_D^{20}$ = –65 (c = 1.0, $CHCl_3$).

***N,N′*-Bis(ethyl-2-amino-4,6-*O*-benzylidene-2-deoxy-1-thio-β-D-glucopyranosid-2-yl)dimethylmalonamide (16):** Under a nitrogen atmosphere, compound **15** (2.60 g, 8.25 mmol) was dissolved in dry CH_2Cl_2 (40 mL), and the resulting solution was cooled to 0 °C. Then, Et_3N (2.30 mL, 1.70 g, 16.70 mmol) followed by dimethylmalonyl dichloride (560 µL, 710 mg, 4.18 mmol) was added (TLC: EtOAc). After approximately 2 h, the solvent was evaporated in vacuo, and the product was purified by flash chromatography on silica gel (EtOAc) to yield bis(amide) **16** (3.00 g, 4.18 mmol, quant.) as a colourless solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.17 (J = 7.5 Hz, 6 H, SCH_2CH_3), 1.47 [s, 6 H, $(CH_3)_2C$], 2.61–2.70 (m, 4 H, SCH_2CH_3), 3.44 (ddd ≈ td, $J_{4,5} \approx J_{5,6'}$ = 9.7 Hz, $J_{5,6}$ = 4.9 Hz, 2 H, 5-H), 3.55 (dd ≈ t, $J_{3,4}$ = 9.2 Hz, $J_{4,5}$ = 9.7 Hz, 2 H, 4-H), 3.64 (dd ≈ t, $J_{5,6'} \approx J_{6,6'}$ = 10.2 Hz, 2 H, 6′-H), 3.88 (ddd ≈ td, $J_{1,2}$ = 10.4 Hz, $J_{2,3}$ = 9.5 Hz, $J_{2,NH}$ = 9.0 Hz, 2 H, 2-H), 4.11 (dd ≈ t, $J_{2,3}$ = 9.5 Hz, $J_{3,4}$ = 9.2 Hz, 2 H, 3-H), 4.20 (dd, $J_{5,6}$ = 4.9 Hz, $J_{6,6'}$ = 10.2 Hz, 2 H, 6-H), 4.81 (d, $J_{1,2}$ = 10.4 Hz, 2 H, 1-H), 5.39 (s, 2 H, CHPh), 7.21–7.25 (m, 6 H, Ph), 7.35–7.40 (m, 4 H, Ph), 7.45 (d, $J_{2,NH}$ = 9.0 Hz, 2 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.0 (CH_3, SCH_2CH_3), 23.8 [CH_3, $(CH_3)_2C$], 24.2 (CH_2, SCH_2CH_3), 50.4 [C, $(CH_3)_2C$], 55.7 (CH, C-3), 68.2 (CH_2, C-6), 70.5 (CH, C-5), 73.0 (CH, C-2), 80.6 (CH, C-4), 84.5 (CH, C-1), 101.0 (CH, PhCH), 126.2, 128.1, 128.9 (CH, Ph), 137.2 (C, Ph), 173.0 (C, CONH) ppm. HRMS (ESI+): calcd. for $C_{35}H_{47}N_2O_{10}S_2$ [M + H]$^+$ 719.2667; found 719.2689. $[\alpha]_D^{20}$ = –106 (c = 1.0, $CHCl_3$).

***N,N′*-Bis(ethyl-3-*O*-acetyl-4,6-*O*-benzylidene-2-deoxy-1-thio-β-D-glucopyranosid-2-yl)dimethylmalonamide (17a):** To a solution of **16** (2.00 g, 2.78 mmol) dissolved in pyridine (100 mL) was slowly added acetic anhydride (2.63 mL, 2.84 g, 27.80 mmol), and the solution was stirred at room temperature for 16 h (TLC: PE/EtOAc, 1:1). The solvent was evaporated, and the product was coevaporated with toluene (2×). Flash chromatography on silica gel (PE/EtOAc, 1:1) yielded **17a** (2.17 g, 2.70 mmol, 97%) as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.24 (t, J = 7.5 Hz, 6 H, SCH_2CH_3), 1.35 [s, 6 H, $(CH_3)_2C$], 2.07 (s, 6 H, CH_3CO), 2.61–2.74 (m, 4 H, SCH_2CH_3), 3.58 (ddd ≈ td, $J_{4,5} \approx J_{5,6'}$ = 9.5 Hz, $J_{5,6}$ = 4.7 Hz, 2 H, 5-H), 3.74 (dd, $J_{5,6'} \approx J_{6,6'}$ = 10.5 Hz, 2 H, 6′-H), 3.77 (dd ≈ t, $J_{3,4}$ = 9.2 Hz, $J_{4,5}$ = 9.5 Hz, 2 H, 4-H), 4.21 (ddd ≈ td, $J_{1,2}$ = 10.5 Hz, $J_{2,3}$ = 10.5 Hz, $J_{2,NH}$ = 9.2 Hz, 2 H, 2-H), 4.33 (dd, $J_{5,6}$ = 4.7 Hz, $J_{6,6'}$ = 10.5 Hz, 2 H, 6-H), 4.79 (d, $J_{1,2}$ = 10.5 Hz, 2 H, 1-H), 5.29 (dd, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 9.2 Hz, 2 H, 3-H), 5.51 (s, 2 H, CHPh), 6.61 (d, $J_{2,NH}$ = 9.2 Hz, 2 H, NH), 7.32–7.37 (m, 6 H, Ph), 7.43–7.46 (m, 4 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.8 (CH_3, SCH_2CH_3), 21.2 (CH_3, CH_3CO), 23.8 (CH_2, SCH_2CH_3), 24.3 [CH_3, $(CH_3)_2C$], 51.1 [C, $(CH_3)_2C$], 53.4 (CH, C-2), 68.5 (CH_2, C-6), 70.4 (CH, C-5), 74.3 (CH, C-3), 78.3 (CH, C-4), 84.0 (CH, C-1), 101.5 (CH, PhCH), 126.1, 128.2, 129.1 (CH, Ph), 136.8 (C, Ph), 172.5 (C, CH_3CO), 173.0 (C, CONH) ppm. HRMS (ESI+): calcd. for $C_{39}H_{51}N_2O_{12}S_2$ [M + H]$^+$ 803.2883; found 803.2883. $[\alpha]_D^{20}$ = –107 (c = 1.0, $CHCl_3$).

***N,N′*-Bis(ethyl-3-*O*-benzoyl-4,6-*O*-benzylidene-2-deoxy-1-thio-β-D-glucopyranosid-2-yl)dimethylmalonamide (17b):** Bis(amide) **16** (500 mg, 700 µmol) was dissolved in pyridine (10 mL), and the mixture was cooled to 0 °C. Benzoyl chloride (250 µL, 300 mg, 2.10 mmol) was added dropwise, and the mixture was stirred for ca. 2 h (TLC: PE/EtOAc, 1:1). The solution was diluted with CH_2Cl_2, washed with water and concentrated. The crude product was dissolved in CH_2Cl_2 and washed with hydrochloric acid (1 M), saturated aqueous solution of $NaHCO_3$, dried, filtered and concentrated. Flash chromatography on silica gel (PE/EtOAc, 1:1) gave **17b** (600 mg, 650 µmol, 93%) as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.07 [s, 6 H, $(CH_3)_2C$], 1.23 (t, J = 7.5 Hz, 6 H, SCH_2CH_3), 2.66–2.74 (m, 4 H, SCH_2CH_3), 3.63 (ddd ≈ td, $J_{4,5} \approx J_{5,6'}$ = 9.5 Hz, $J_{5,6}$ = 4.7 Hz, 2 H, 5-H), 3.81 (dd ≈ t, $J_{5,6'} \approx J_{6,6'}$ = 10.5 Hz, 2 H, 6′-H), 3.90 (dd ≈ t, $J_{3,4} = J_{4,5}$ = 9.5 Hz, 2 H, 4-H), 4.32 (dd, $J_{1,2}$ = 10.5 Hz, $J_{2,3}$ = 9.5 Hz, 2 H, 2-H), 4.38 (dd, $J_{5,6}$ = 4.7 Hz, $J_{6,6'}$ = 10.5 Hz, 2 H, 6-H), 4.82 (d, $J_{1,2}$ = 10.5 Hz, 2 H, 1-H), 5.55 (s, 2 H, CHPh), 5.68 (dd ≈ t, $J_{2,3} = J_{3,4}$ = 9.5 Hz, 2 H, 3-H), 6.71 (d, $J_{2,NH}$ = 9.2 Hz, 2 H, NH), 7.28–7.31 (m, 6 H, Ph), 7.40–7.45 (m, 8 H, Ph), 7.53–7.58 (m, 2 H, Ph), 8.00–8.34 (m, 4 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.8 (CH_3, SCH_2CH_3), 23.8 (CH_2, SCH_2CH_3), 23.9 [CH_3, $(CH_3)_2C$], 50.7 [C, $(CH_3)_2C$], 53.7 (CH, C-2), 68.5 (CH_2, C-6), 70.6 (CH, C-5), 74.1 (CH, C-3), 78.7 (CH, C-4), 84.2 (CH, C-1), 101.4 (CH, PhCH), 126.1, 128.1, 128.5, 128.8, 129.2, 129.8, 130.5 (CH, Ph), 134.4, 136.7 (C, Ph), 167.5 (C, PhCO), 173.1 (C, CONH) ppm. HRMS (ESI+): calcd. for $C_{49}H_{54}N_2O_{12}S_2Na$ [M + Na]$^+$ 949.3016; found 949.3016. $[\alpha]_D^{20}$ = –97 (c = 1.0, $CHCl_3$).

***N,N′*-Bis(ethyl-4,6-*O*-benzylidene-2-deoxy-3-*O*-pivaloyl-1-thio-β-D-glucopyranosid-2-yl)dimethylmalonamide (17c):** To a solution of **16** (500 mg, 700 µmol) in dry pyridine (45 mL) was added pivaloyl chloride (35 µL, 340 mg, 2.80 mmol) and DMAP (100 mg). The reaction mixture was heated at 80 °C for 5 h (TLC: PE/EtOAc, 3:1). After evaporation of the pyridine, the residue was purified by flash column chromatography on silica gel (PE/EtOAc, 3:1) to give **17c** (580 mg, 650 µmol, 93%) as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.20 [s, 18 H, $(CH_3)_3CCO$], 1.22 (t, J = 7.5 Hz, 6 H, SCH_2CH_3), 1.35 [s, 6 H, $(CH_3)_2C$], 2.61–2.73 (m, 4 H, SCH_2CH_3), 3.61 (ddd ≈ td, $J_{4,5} \approx J_{5,6'}$ = 9.5 Hz, $J_{5,6}$ = 4.7 Hz, 2 H, 5-H), 3.78 (dd ≈ t, $J_{5,6'} \approx J_{6,6'}$ = 10.2 Hz, 2 H, 6′-H), 3.81 (dd, $J_{3,4} = J_{4,5}$ = 9.5 Hz, 2 H, 4-H), 4.33 (dd ≈ t, $J_{1,2}$ = 10.2 Hz, $J_{2,3}$ = 9.5 Hz, 2 H, 2-H), 4.39 (dd, $J_{5,6}$ = 4.7 Hz, $J_{6,6'}$ = 10.2 Hz, 2 H, 6-H), 4.85 (d, $J_{1,2}$ = 10.2 Hz, 2 H, 1-H), 5.33 (dd ≈ t, $J_{2,3}$ = 9.5 Hz, $J_{3,4}$ = 9.2 Hz,

2 H, 3-H), 5.56 (s, 2 H, CHPh), 6.57 (d, $J_{2,NH}$ = 9.5 Hz, 2 H, NH), 7.29–7.35 (m, 6 H, Ph), 7.39–7.45 (m, 4 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.6 (CH_3, SCH_2CH_3), 23.0 (CH_2, SCH_2CH_3), 24.6 [CH_3, $(CH_3)_2C$], 27.1 [CH_3, $(CH_3)_3CCO$], 39.1 [C, $(CH_3)_3CCO$], 51.5 [C, $(CH_3)_2C$], 52.8 (CH, C-2), 68.5 (CH_2, C-6), 70.2 (CH, C-5), 74.9 (CH, C-3), 78.6 (CH, C-4), 83.9 (CH, C-1), 101.1 (CH, PhCH), 125.8, 128.1, 128.9 (CH, Ph), 136.8 (C, Ph), 172.6 [C, $(CH_3)_3CCO$], 180.5 (C, CONH) ppm. HRMS (ESI+): calcd. for $C_{45}H_{62}N_2O_{12}NaS_2$ [M + Na]$^+$ 909.3642; found 909.3628. $[\alpha]_D^{20}$ = –98 (c = 1.0, $CHCl_3$).

***N*,*N*′-Bis(ethyl-4,6-*O*-benzylidene-2-deoxy-3-*O*-methyl-1-thio-β-D-glucopyranosid-2-yl)dimethylmalonamide (17d):** To a solution of **16** (500 mg, 700 μmol) dissolved in dry THF (5 mL) was first added sodium hydride (60% dispersion in paraffin oil, 170 mg, equalling 4.20 mmol of NaH) and second methyl iodide (400 mg, 175 μL, 2.80 mmol), and the resulting mixture was heated at reflux for 6 h (TLC: PE/EtOAc, 1:1). The mixture was diluted with CH_2Cl_2 (10 mL) and washed with hydrochloric acid (3 M, 2 × 5 mL) and saturated aqueous $NaHCO_3$ solution (2 × 5 mL). The organic layer was dried with Na_2SO_4, concentrated and purified by flash chromatography on silica gel (PE/EtOAc, 1:1) to yield **17d** (490 g, 660 μmol, 94%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.24 (t, J = 7.5 Hz, 6 H, SCH_2CH_3), 1.49 [s, 6 H, $(CH_3)_2C$], 2.65–2.75 (m, 4 H, SCH_2CH_3), 3.49 (ddd ≈ td, $J_{4,5} \approx J_{5,6'}$ = 9.9 Hz, $J_{5,6}$ = 5.1 Hz, 2 H, 5-H), 3.53 (s, 6 H, OCH_3), 3.62 (dd ≈ t, $J_{2,3}$ = 9.2 Hz, $J_{3,4}$ = 8.8 Hz, 2 H, 3-H), 3.68 (m, 6 H, 2-H, 4-H, 6′-H), 4.33 (dd, $J_{5,6}$ = 5.1 Hz, $J_{6,6'}$ = 10.2 Hz, 2 H, 6-H), 4.88 (d, $J_{1,2}$ = 9.9 Hz, 2 H, 1-H), 5.52 (s, 2 H, CHPh), 6.81 (d, $J_{2,NH}$ = 8.1 Hz, 2 H, NH), 7.32–7.37 (m, 6 H, Ph), 7.43–7.46 (m, 4 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.0 (CH_3, SCH_2CH_3), 24.2 (CH_2, SCH_2CH_3), 24.3 [CH_3, $(CH_3)_2C$], 50.1 [C, $(CH_3)_2C$], 55.5 (CH, C-2), 60.7 (CH_3, OCH_3), 68.6 (CH_2, C-6), 70.6 (CH, C-5), 80.5 (CH, C-4), 82.0 (CH, C-3), 84.1 (CH, C-1), 101.1 (CH, PhCH), 126.0, 128.2, 129.0 (CH, Ph), 137.1 (C, Ph), 173.8 (C, CONH) ppm. HRMS (ESI+): calcd. for $C_{37}H_{50}N_2O_{10}NaS_2$ [M + Na]$^+$ 769.2805; found 769.2797. $[\alpha]_D^{20}$ = –38 (c = 1.0, $CHCl_3$).

***N*,*N*′-Bis(ethyl-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-1-thio-β-D-glucopyranosid-2-yl)dimethylmalonamide (17e):** To a mixture of **16** (250 mg, 350 μmol) and tetrabutylammonium iodide (30 mg, 70 μmol) in dry DMF (5 mL) was added sodium hydride (60% dispersion in paraffin oil, 50 mg, equalling 1.19 mmol NaH) at 0 °C. The mixture was stirred for 30 min and benzyl bromide (250 μL, 360 mg, 2.10 mmol) was added by syringe (TLC: PE/EtOAc, 2:1). After 2 h, the reaction was quenched by the addition of acetic acid and filtered. Et_2O (20 mL) was added to the filtrate, which was extracted with saturated aqueous NH_4Cl solution (20 mL) and saturated aqueous $NaHCO_3$ solution (20 mL). The organic layer was separated and dried with Na_2SO_4. Flash chromatography on silica gel (PE/EtOAc, 2:1) gave **17e** (260 mg, 290 μmol, 84%) as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.20 (t, J = 7.5 Hz, 6 H, SCH_2CH_3), 1.39 [s, 6 H, $(CH_3)_2C$], 2.61–2.70 (m, 4 H, SCH_2CH_3), 3.39 (ddd ≈ td, $J_{4,5} \approx J_{5,6'}$ = 9.5 Hz, $J_{5,6}$ = 5.1 Hz, 2 H, 5-H), 3.68–3.89 (m, 8 H, 2-H, 3-H, 4-H, 6′-H), 4.32 (dd, $J_{5,6}$ = 5.1 Hz, $J_{6,6'}$ = 10.2 Hz, 2 H, 6-H), 4.54 (d, $J_{1,2}$ = 9.5 Hz, 2 H, 1-H), 4.62 (d, J = 11.2 Hz, 2 H, CH_2Ph), 4.87 (d, J = 11.2 Hz, 2 H, CH_2Ph), 5.55 (s, 2 H, CHPh), 6.40 (d, $J_{2,NH}$ = 7.8 Hz, 2 H, NH), 7.22–7.47 (m, 20 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.9 (CH_3, SCH_2CH_3), 24.0 (CH_2, SCH_2CH_3), 24.2 [CH_3, $(CH_3)_2C$], 50.4 [C, $(CH_3)_2C$], 54.7 (CH, C-2), 68.6 (CH_2, C-6), 70.4 (CH, C-5), 73.7 (CH_2, $PhCH_2$), 78.5 (CH, C-3), 82.0 (CH, C-4), 83.9 (CH, C-1), 101.1 (CH, PhCH), 125.9, 127.8, 127.8, 128.2, 128.4, 129.0, 137.1, 138.3 (C, Ph), 173.68 (C, CONH) ppm. HRMS (ESI+): calcd. for $C_{49}H_{58}N_2O_{10}NaS_2$ [M + Na]$^+$ 921.3431; found 921.3432. $[\alpha]_D^{20}$ = –25 (c = 1.0, $CHCl_3$).

***N*,*N*′-Bis(ethyl-4,6-*O*-benzylidene-2-deoxy-1-thio-β-3-*O*-triethylsilyl-D-glucopyranosid-2-yl)dimethylmalonamide (17f):** To a stirred solution of **16** (250 mg, 350 μmol) in dry CH_2Cl_2 (25 mL) at –78 °C was dropwise added Et_3N (500 μL, 350 mg, 3.50 mmol) by syringe. Then, TESOTf (460 μL, 560 mg, 2.10 mmol) was added. The mixture was stirred for 2 h at –78 °C (TLC: PE/EtOAc, 2:1) and then brought to room temperature, and the solvent was removed under reduced pressure. Flash chromatography on silica gel (PE/EtOAc, 2:1) gave **17f** (270 mg, 290 μmol, 83%) as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.51 (q, J = 7.8 Hz, 12 H, $SiCH_2CH_3$), 0.82 (t, J = 7.8 Hz, 18 H, $SiCH_2CH_3$), 1.25 (t, J = 7.5 Hz, 6 H, SCH_2CH_3), 1.46 [s, 6 H, $(CH_3)_2C$], 2.68–2.78 (m, 4 H, SCH_2CH_3), 3.42–3.52 (m, 4 H, 4-H, 5-H), 3.70–3.85 (m, 4 H, 2-H, 6′-H), 4.06 (dd ≈ t, $J_{2,3} \approx J_{3,4}$ = 8.8 Hz, 2 H, 3-H), 4.31 (dd, $J_{5,6}$ = 4.7 Hz, $J_{6,6'}$ = 10.5 Hz, 2 H, 6-H), 4.83 (d, $J_{1,2}$ = 10.2 Hz, 2 H, 1-H), 5.46 (s, 2 H, CHPh), 6.63 (d, $J_{2,NH}$ = 7.2 Hz, 2 H, NH), 7.32–7.45 (m, 10 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 5.1 (CH_2, $SiCH_2CH_3$), 6.8 (CH_3, $SiCH_3CH_2$), 14.8 (CH_3, SCH_2CH_3), 23.9 (CH_2, SCH_2CH_3), 24.5 [CH_3, $(CH_3)_2C$], 50.5 [C, $(CH_3)_2C$], 57.0 (CH, C-2), 68.6 (CH_2, C-6), 70.7 (CH, C-5), 73.0 (CH, C-3), 82.3 (CH, C-4), 83.9 (CH, C-1), 102.1, 126.2, 128.1, 129.1 (CH, Ph), 137.0 (C, Ph), 173.9 (C, CONH) ppm. HRMS (ESI+): calcd. for $C_{47}H_{74}N_2O_{10}NaSi_2S_2$ [M + Na]$^+$ 969.4221; found 969.4230. $[\alpha]_D^{20}$ = –35 (c = 1.0, $CHCl_3$).

Representative Procedure for the Cyclisation of Thioglucoside Bis(amides) to Bis(oxazolines): A mixture of **17a**–**f** (1 equiv.) and 4 Å MS (approx. 1 mg per mg **17a**–**f**) in dry CH_2Cl_2 (5 mL for 400 μmol **17a**–**f**) was stirred for 1 h under a nitrogen atmosphere in a flame-dried flask. To this was added NIS (2.5 equiv.), and the mixture was cooled to –30 °C. Then, TfOH (5 μL for 400 μmol **17a**–**f**) was added, and the mixture was stirred for 1 h at –30 °C. The reaction was quenched with Et_3N (100 μL for 400 μmol **17a**–**f**), and the mixture was filtered through Celite, diluted with CH_2Cl_2, washed with saturated aqueous $NaHCO_3$ solution, aqueous sodium thiosulfate solution (3 M) and dried with Na_2SO_4. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography on silica gel (eluants for TLC and column given with the respective compound) to yield the desired product.

3-*O*-Ac *gluco*Box (18a): Starting from **17a** (1.25 g, 1.56 mmol), yielding ligand **18a** (970 mg, 1.43 mmol, 92%). Eluant: EtOAc. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.52 [s, 6 H, $(CH_3)_2C$], 2.10 (s, 6 H, CH_3CO), 3.61 (dd ≈ t, $J_{5,6'} \approx J_{6,6'}$ = 9.9 Hz, 2 H, 6′-H), 3.75 (ddd ≈ td, $J_{4,5} = J_{5,6'}$ = 9.9 Hz, $J_{5,6}$ = 5.1 Hz, 2 H, 5-H), 3.81 (dd, $J_{3,4}$ = 7.5 Hz, $J_{4,5}$ = 9.9 Hz, 2 H, 4-H), 4.14 (dd, $J_{1,2}$ = 7.1 Hz, $J_{2,3}$ = 2.7 Hz, 2 H, 2-H), 4.39 (dd, $J_{5,6}$ = 5.1 Hz, $J_{6,6'}$ = 10.2 Hz, 2 H, 6-H), 5.28 (dd, $J_{2,3}$ = 2.7 Hz, $J_{3,4}$ = 7.5 Hz, 2 H, 3-H), 5.51 (s, 2 H, CHPh), 5.98 (d, $J_{1,2}$ = 7.1 Hz, 2 H, 1-H), 7.32–7.37 (m, 6 H, Ph), 7.44–7.46 (m, 4 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.1 (CH_3, CH_3CO), 23.4 [CH_3, $(CH_3)_2C$], 38.9 [C, $(CH_3)_2C$], 62.9 (CH, C-5), 67.8 (CH_2, C-6), 68.2 (CH, C-2), 73.5 (CH, C-3), 78.4 (CH, C-4), 101.4 (CH, PhCH), 101.4 (CH, C-1), 126.1, 128.2, 129.0 (CH, Ph), 136.8 (C, Ph), 169.6 (C, O–C=N), 169.8 (C, CH_3CO) ppm. HRMS (ESI+): calcd. for $C_{35}H_{39}N_2O_{12}$ [M + H]$^+$ 679.2503; found 679.2511. $[\alpha]_D^{20}$ = +106 (c = 1.0, $CHCl_3$).

3-*O*-Bz *gluco*Box (18b): Starting from **17b** (400 mg, 430 μmol), yielding ligand **18b** (290 mg, 360 μmol, 84%). Eluant: PE/EtOAc (2:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.57 [s, 6 H, $(CH_3)_2C$], 3.66 (dd ≈ t, $J_{5,6'} \approx J_{6,6'}$ = 10.2 Hz, 2 H, 6′-H), 3.84 (ddd ≈ td, $J_{4,5} \approx J_{5,6'}$ = 9.9 Hz, $J_{5,6}$ = 5.4 Hz, 2 H, 5-H), 4.06 (dd ≈ t, $J_{3,4}$ = 7.1 Hz, $J_{4,5}$ = 9.9 Hz, 2 H, 4-H), 4.34 (dd ≈ t, $J_{1,2}$ = 7.1 Hz, $J_{2,3}$ = 2.0 Hz,

2 H, 2-H), 4.47 (dd, $J_{5,6}$ = 5.4 Hz, $J_{6,6'}$ = 10.2 Hz, 2 H, 6-H), 5.54 (dd, $J_{2,3}$ = 2.0 Hz, $J_{3,4}$ = 7.1 Hz, 2 H, 3-H), 5.55 (s, 2 H, CHPh), 6.08 (d, $J_{1,2}$ = 7.1 Hz, 2 H, 1-H), 7.31–7.35 (m, 6 H, Ph), 7.42–7.48 (m, 8 H, Ph), 7.55–7.58 (m, 2 H, Ph), 8.07–8.09 (m, 4 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.4 [CH_3, (CH_3)$_2$C], 38.8 [C, (CH_3)$_2$*C*], 62.8 (CH, C-5), 68.2 (CH, C-2), 68.6 (CH_2, C-6), 74.2 (CH, C-3), 78.7 (CH, C-4), 101.2 (CH, C-1), 101.4 (CH, PhCH), 126.1, 128.2, 128.3, 129.0, 129.6, 129.8 (2 CH, Ph), 133.2, 136.8 (C, Ph), 165.6 (C, Ph*C*O), 169.8 (C, O-C=N) ppm. HRMS (ESI+): calcd. for $C_{45}H_{43}N_2O_{12}$ [M + H]$^+$ 803.2816; found 803.2817. $[\alpha]_D^{20}$ = +94 (*c* = 0.9, $CHCl_3$).

3-*O*-Piv *gluco*Box (18c): Starting from **17c** (250 mg, 280 μmol), yielding ligand **18c** (170 mg, 230 μmol, 82%). Eluant: PE/EtOAc (2:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.22 [s, 18 H, (CH_3)$_3$CCO], 1.52 [s, 6 H, (CH_3)$_2$C], 3.61 (dd ≈ t, $J_{5,6'}$ = 9.9 Hz, $J_{6,6'}$ = 10.2 Hz, 2 H, 6′-H), 3.74 (ddd ≈ td, $J_{4,5}$ = $J_{5,6'}$ = 9.9 Hz, $J_{5,6}$ = 5.1 Hz, 2 H, 5-H), 3.85 (dd, $J_{3,4}$ = 7.1 Hz, $J_{4,5}$ = 9.9 Hz, 2 H, 4-H), 4.12 (dd, $J_{1,2}$ = 7.1 Hz, $J_{2,3}$ = 2.0 Hz, 2 H, 2-H), 4.41 (dd, $J_{5,6}$ = 5.1 Hz, $J_{6,6'}$ = 10.2 Hz, 2 H, 6-H), 5.24 (dd, $J_{2,3}$ = 2.0 Hz, $J_{3,4}$ = 7.1 Hz, 2 H, 3-H), 5.52 (s, 2 H, CHPh), 5.60 (d, $J_{1,2}$ = 7.1 Hz, 2 H, 1-H), 7.31–7.37 (m, 6 H, Ph), 7.44–7.47 (m, 4 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.4 [CH_3, (CH_3)$_2$C], 27.0 [CH_3, (CH_3)$_3$-CCO], 38.7 [C, (CH_3)$_3$*C*CO], 38.8 [C, (CH_3)$_2$*C*], 62.7 (CH, C-5), 68.1 (CH, C-2), 68.6 (CH_2, C-6), 73.5 (CH, C-3), 78.7 (CH, C-4), 101.2 (CH, C-1), 101.2 (CH, PhCH), 126.0, 128.2, 128.9 (CH, Ph), 136.9 (C, Ph), 169.7 (C, O-C=N), 177.4 [C, (CH_3)$_3$C*C*O] ppm. HRMS (ESI+): calcd. for $C_{41}H_{50}N_2O_{12}Na$ [M + Na]$^+$ 785.3261; found 785.3262. $[\alpha]_D^{20}$ = +102 (*c* = 1.0, $CHCl_3$).

3-*O*-Me *gluco*Box (18d): Starting from **17d** (280 mg, 380 μmol), yielding ligand **18d** (210 mg, 340 μmol, 90%). Eluant: PE/EtOAc (1:2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.53 [s, 6 H, (CH_3)$_2$C], 3.54 (s, 6 H, OCH_3), 3.60–3.71 (m, 8 H, 3-H, 4-H, 5-H, 6′-H), 4.11 (dd, $J_{1,2}$ = 7.5 Hz, $J_{2,3}$ = 2.4 Hz, 2 H, 2-H), 4.33–4.41 (m, 2 H, 6-H), 5.56 (s, 2 H, CHPh), 5.97 (d, $J_{1,2}$ = 7.5 Hz, 2 H, 1-H), 7.32–7.37 (m, 6 H, Ph), 7.44–7.47 (m, 4 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.4 [CH_3, (CH_3)$_2$C], 39.0 [C, (CH_3)$_2$*C*], 58.5 (CH_3, OCH_3), 62.6 (CH, C-5), 67.8 (CH, C-2), 68.2 (CH_2, C-6), 80.1 (CH, C-3), 81.7 (CH, C-4), 101.3 (CH, PhCH), 102.2 (CH, C-1), 126.1, 128.2, 129.0 (CH, Ph), 137.1 (C, Ph), 168.8 (C, O–C=N) ppm. HRMS (ESI+): calcd. for $C_{33}H_{39}N_2O_{10}$ [M + H]$^+$ 623.2599; found 623.2521. $[\alpha]_D^{20}$ = +124 (*c* = 1.0, $CHCl_3$).

3-*O*-Bn *gluco*Box (18e): Starting from **17e** (250 mg, 280 μmol), yielding ligand **18e** (170 mg, 220 μmol, 79%). Eluant: PE/EtOAc (1:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.51 [s, 6 H, (CH_3)$_2$C], 3.63 (dd ≈ t, $J_{5,6'} \approx J_{6,6'}$ = 9.6 Hz, 2 H, 6′-H), 3.68 (ddd ≈ td, $J_{4,5} \approx J_{5,6'}$ = 9.6 Hz, $J_{5,6}$ = 4.1 Hz, 2 H, 5-H), 3.78 (dd, $J_{3,4}$ = 7.5 Hz, $J_{4,5}$ = 9.6 Hz, 2 H, 4-H), 3.93 (dd, $J_{2,3}$ = 3.0 Hz, $J_{3,4}$ = 7.5 Hz, 2 H, 3-H), 4.23 (dd, $J_{1,2}$ = 7.5 Hz, $J_{2,3}$ = 3.0 Hz, 2 H, 2-H), 4.38 (dd, $J_{5,6}$ = 4.1 Hz, $J_{6,6'}$ = 9.6 Hz, 2 H, 6-H), 4.77 (d, *J* = 12.0 Hz, 2 H, CH_2Ph), 4.82 (d, *J* = 12.0 Hz, 2 H, CH_2Ph), 5.57 (s, 2 H, CHPh), 5.98 (d, $J_{1,2}$ = 7.5 Hz, 2 H, 1-H), 7.25–7.46 (m, 20 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.4 [CH_3, (CH_3)$_2$C], 38.9 [C, (CH_3)$_2$*C*], 62.8 (CH, C-5), 68.4 (CH, C-2), 68.6 (CH_2, C-6), 72.4 (CH_2, PhCH_2), 79.7 (CH, C-3), 80.1 (CH, C-4), 101.1 (CH, PhCH), 102.2 (CH, C-1), 126.0, 127.6, 127.8, 128.1, 128.2, 128.9 (CH, Ph), 137.1, 137.9 (C, Ph), 168.8 (C, O-C=N) ppm. HRMS (ESI+): calcd. for $C_{45}H_{47}N_2O_{10}$ [M + H]$^+$ 775.3231; found 775.3234. $[\alpha]_D^{20}$ = +82 (*c* = 1.0, $CHCl_3$).

3-*O*-TES *gluco*Box (18f): Starting from **17f** (250 mg, 260 μmol), yielding ligand **18f** (180 mg, 220 μmol, 85%). Eluant: PE/EtOAc (1:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.65 (q, *J* = 7.8 Hz, 12 H, SiC*H*$_2$CH$_3$), 0.93 (t, *J* = 7.8 Hz, 18 H, SiCH$_2$C*H*$_3$), 1.50 [s, 6 H, (CH_3)$_2$C], 3.55–3.66 (m, 6 H, 4-H, 5-H, 6′-H), 3.93 (dd, $J_{2,3}$ = 3.8 Hz, $J_{3,4}$ = 7.2 Hz, 2 H, 3-H), 3.98 (dd, $J_{1,2}$ = 7.2 Hz, $J_{2,3}$ = 3.8 Hz, 2 H, 2-H), 4.36 (dd, $J_{5,6}$ = 3.1 Hz, $J_{6,6'}$ = 8.9 Hz, 2 H, 6-H), 5.53 (s, 2 H, CHPh), 5.95 (d, $J_{1,2}$ = 7.2 Hz, 2 H, 1-H), 7.32–7.37 (m, 6 H, Ph), 7.45–7.49 (m, 4 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 4.7 (CH_2, Si*C*H$_2$CH$_3$), 6.7 (CH_3, SiCH$_2$*C*H$_3$), 23.4 [CH_3, (CH_3)$_2$C], 39.0 [C, (CH_3)$_2$*C*], 63.2 (CH, C-5), 68.6 (CH_2, C-6), 70.8 (CH, C-2), 74.4 (CH, C-3), 81.1 (CH, C-4), 101.4 (CH, PhCH), 102.7 (CH, C-1), 126.0, 128.0 (CH, Ph), 128.8, 137.3 (C, Ph), 168.5 (C, O-C=N) ppm. HRMS (ESI+): calcd. for $C_{43}H_{63}N_2O_{10}Si_2$ [M + H]$^+$ 823.4021; found 823.4003. $[\alpha]_D^{20}$ = +106 (*c* = 0.9, $CHCl_3$).

3-OH *gluco*Box (19): A mixture of compound **18a** (500 mg, 740 μmol) and potassium carbonate (200 mg, 1.48 mmol) in MeOH/H_2O (5:2, 42 mL) was stirred for 1 h at room temperature (TLC: EtOAc). The reaction mixture was neutralized by the addition of a saturated solution of hydrogen chloride in MeOH. After concentration under vacuum, the product was purified by flash chromatography on silica gel (EtOAc) to yield **19** (350 mg, 59 μmol, 80%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.41 [s, 6 H, (CH_3)$_2$C], 3.53–3.67 (m, 6 H, 4-H, 5-H, 6′-H), 3.72 (dd, $J_{2,3}$ = 5.4 Hz, $J_{3,4}$ = 8.5 Hz, 2 H, 3-H), 3.95 (dd, $J_{1,2}$ = 7.8 Hz, $J_{2,3}$ = 5.4 Hz, 2 H, 2-H), 4.31 (dd, $J_{5,6}$ = 3.4 Hz, $J_{6,6'}$ = 8.8 Hz, 2 H, 6-H), 4.81 (br. s, 2 H, OH), 5.52 (s, 2 H, CHPh), 5.89 (d, $J_{1,2}$ = 7.8 Hz, 2 H, 1-H), 7.30–7.35 (m, 6 H, Ph), 7.44–7.48 (m, 4 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.2 [CH_3, (CH_3)$_2$C], 39.4 [C, (CH_3)$_2$*C*], 63.5 (CH, C-5), 68.3 (CH_2, C-6), 68.9 (CH, C-2), 73.9 (CH, C-3), 79.0 (CH, C-4), 101.7 (CH, PhCH), 103.6 (CH, C-1), 126.2, 128.2, 129.1 (CH, Ph), 136.9 (C, Ph), 169.3 (C, CONH) ppm. HRMS (ESI+): calcd. for $C_{31}H_{35}N_2O_{10}$ [M + H]$^+$ 595.2292; found 595.2294. $[\alpha]_D^{20}$ = +167 (*c* = 1.0, $CHCl_3$).

Ethyl-2-Amino-2-deoxy-1-thio-β-D-glucopyranose (20): Under a nitrogen atmosphere, **13** (10.00 g, 28.00 mmol) was dissolved in absolute ethanol (800 mL). To this solution was added ethylene diamine (112 mL, 100.90 g, 1.70 mol), and the resulting reaction mixture was heated at reflux for 2.5 h (TLC: CH_2Cl_2/MeOH, 9:1). The solvent was evaporated in vacuo, and the residue was coevaporated with toluene (2×) to yield **20** (6.25 g, 28.00 mmol, quant.) as a brownish foam, which was employed for the next step without further purification and characterization.

Ethyl-2-Amino-2-deoxy-1-thio-3,4,6-tris-*O*-trimethylsilyl-β-D-glucopyranose (21): Compound **20** (8.90 g, 40.00 mmol) was dissolved in pyridine (220 mL) and then treated with HMDS (82.80 mL, 64.60 g, 400.00 mmol) and TMSCl (51.10 mL, 43.40 g, 400.00 mmol). The mixture was then stirred for 16 h at room temperature (TLC: PE/EtOAc, 7:1). After completion of the reaction the remaining TMSCl as well as the solvent were removed in vacuo (a cooling trap was placed between the rotary evaporator and the pump stand). The crude product was purified by column filtration through silica gel (PE/EtOAc, 7:1) to yield **21** as a yellow oil (14.60 g, 33.00 mmol, 83%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.08, 0.14, 0.19, (each s, each 9 H, $SiCH_3$), 1.22 (t, *J* = 7.5 Hz, 3 H, SCH$_2$C*H*$_3$), 1.48 (br. s, 2 H, NH_2), 2.60–2.74 (m, $J_{2,3}$ = 8.5 Hz, 3 H, 2-H, SC*H*$_2$CH$_3$), 3.19 (ddd, $J_{4,5}$ = 9.2 Hz, $J_{5,6}$ = 4.4 Hz, $J_{5,6'}$ = 1.7 Hz, 1 H, 5-H), 3.36 (dd ≈ t, $J_{2,3}$ = 8.5 Hz, $J_{3,4}$ = 8.9 Hz, 1 H, 3-H), 3.56 (dd ≈ t, $J_{3,4}$ = 8.9 Hz, $J_{4,5}$ = 9.2 Hz, 1 H, 4-H), 3.72 (dd, $J_{5,6}$ = 4.4 Hz, $J_{6,6'}$ = 11.6 Hz, 1 H, 6-H), 3.78 (dd, $J_{5,6'}$ = 1.7 Hz, $J_{6,6'}$ = 11.6 Hz, 1 H, 6′-H), 4.23 (d, $J_{1,2}$ = 9.6 Hz, 1 H, 1-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 0.2, 0.7, 1.2 (CH_3, $SiCH_3$) 15.4 (CH_3, SCH$_2$*C*H$_3$), 23.8 (CH_2, S*C*H$_2$CH$_3$), 56.8 (CH, C-2), 62.1 (CH_2, C-6), 71.3 (CH, C-4), 80.9 (CH, C-3), 80.9 (CH, C-5), 86.3 (CH, C-1) ppm. HRMS (ESI+): calcd. for $C_{17}H_{41}NO_4SSi_3Na$ [M + Na]$^+$ 462.1962; found 462.1960. $[\alpha]_D^{20}$ = –12 (*c* = 1.2, $CHCl_3$).

***N*,*N*′-Bis(ethyl-2-deoxy-1-thio-3,4,6-tri-*O*-trimethylsilyl-β-D-glucopyranosid-2-yl)dimethylmalonamide (22):** Under a nitrogen atmosphere, **21** (5.00 g, 11.40 mmol) was dissolved in dry CH_2Cl_2 (75 mL). The solution was cooled to 0 °C and Et_3N (3.2 mL, 2.30 g, 22.80 mmol) and dimethylmalonyl dichloride (800 μL, 1.00 g, 5.70 mmol.) were added. The reaction mixture was warmed to room temperature and subsequently stirred for 72 h (TLC: PE/EtOAc, 7:1). After completion of the reaction the solvent was evaporated and the raw product purified by flash chromatography on silica gel (PE/EtOAc, 9:1→7:1). Compound **22** (3.40 g, 3.50 mmol, 60%) was isolated as a colourless solid. M.p. 118 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.08, 0.09, 0.13 (each s, each 18 H, $SiCH_3$), 1.23 (t, J = 7.5 Hz, 6 H, SCH_2CH_3), 1.45 [s, 6 H, $C(CH_3)_2$], 2.61–2.71 (m, 4 H, SCH_2CH_3), 3.41 (dd, $J_{5,6}$ = 5.1 Hz, $J_{6,6'}$ = 10.9 Hz, 2 H, 6-H), 3.60 (ddt, $J_{2,3} \approx J_{3,4}$ = 6.2 Hz, 2 H, 3-H), 3.68–3.73 (m, 4 H, 4-H, 5-H), 3.92 (dd, $J_{5,6'}$ = 4.8 Hz, $J_{6,6'}$ = 10.9 Hz, 2 H, 6′-H), 4.04 (ddd ≈ q, $J_{1,2} \approx J_{2,3} \approx J_{2,NH}$ = 8.2 Hz, 2 H, 2-H), 4.49 (d, $J_{1,2}$ = 8.2 Hz, 2 H, 1-H), 7.35 (d, J_{NH} = 9.6 Hz, 2 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 0.4, 0.4, 0.7, (each CH_3, $SiCH_3$), 14.9 (CH_3, SCH_2CH_3), 24.5 [CH_3, $(CH_3)_2C$], 24.7 (CH_2, SCH_2CH_3), 49.6 (CH, C-2), 54.3 [C, $(CH_3)_2C$], 62.5 (CH_2, C-6), 70.6 (CH, C-4), 75.4 (CH, C-3), 81.1 (CH, C-5), 83.2 (CH, C-1), 173.7 (C, CONH) ppm. HRMS (ESI+): calcd. for $C_{39}H_{88}N_2O_{10}S_2Si_2Na$ [M + Na]$^+$ 997.4237; found 997.4249. $[\alpha]_D^{20}$ = –22 (c = 1, $CHCl_3$).

***N*,*N*′-Bis(ethyl-2-deoxy-3,4,6-tri-*O*-pivaloyl-1-thio-β-D-glucopyranosid-2-yl)dimethylmalonamide (23):** Compound **22** (300 mg, 300 μmol) was dissolved in MeOH/TFA (9:1, 10 mL). The mixture was stirred at room temperature for 45 min (TLC: CH_2Cl_2/MeOH, 9:1). After removal of the solvents and coevaporation with toluene, the crude product was treated with EtOAc, filtered and washed with more EtOAc to remove organosilicon byproducts. The crude product was taken up in CH_2Cl_2 and MeOH, dried with Na_2SO_4, filtered and concentrated to yield bis(ethyl-2-amino-2-deoxy-1-thio-β-D-glucopyranosido)dimethylmalonamide (164 mg, 300 μmol, quant.) as a white foam which was used for the next step without any further purification. ^{1}H NMR (400 MHz, CD_3OD): δ = 1.29 (t, J = 7.5 Hz, 6 H, SCH_2CH_3), 1.47 [s, 6 H, $(CH_3)_2C$], 2.65–2.83 (m, 4 H, SCH_2CH_3), 3.33–3.36 (m, 2 H, 5-H), 3.42 (dd ≈ t, $J_{3,4}$ = 8.5 Hz, $J_{4,5}$ = 9.9 Hz, 2 H, 4-H), 3.57 (dd, $J_{2,3}$ = 9.9 Hz, $J_{3,4}$ = 8.5 Hz, 2 H, 3-H), 3.72 (dd, $J_{5,6}$ = 5.5 Hz, $J_{6,6'}$ = 12.3 Hz, 2 H, 6-H), 3.85–3.90 (m, 4 H, 2-H, 6′-H), 4.61 (d, $J_{1,2}$ = 10.2 Hz, 2 H, 1-H) ppm. ^{13}C NMR (100MHz, CD_3OD): δ = 15.6 (CH_3, SCH_2CH_3), 24.4 [CH_3, $(CH_3)_2C$], 25.2 (CH_2, SCH_2CH_3), 52.1 (CH, C-2), 56.6 [C, $(CH_3)_2C$], 63.2 (CH_2, C-6), 72.1 (CH, C-4), 77.6 (CH, C-3), 82.4 (CH, C-5), 85.5 (CH, C-1), 176.3 (C, CONH) ppm. HRMS (ESI+): calcd. for $C_{21}H_{38}N_2O_{10}S_2Na$ [M + Na]$^+$ 565.1866; found 565.1873. The deprotected bis(amide) (160 mg, 300 μmol) was dissolved in dry pyridine (8 mL) and pivaloyl chloride (500 μL, 440 mg, 3.60 mmol) and a catalytic amount of DMAP (10 mg) were added. The suspension was stirred for 8 h at 80 °C (TLC: PE/EtOAc, 2:1). After completion of the reaction the solvent was evaporated in vacuo and the residue was purified by flash chromatography on silica gel (PE/EtOAc, 7:1→2:1). Compound **23** (192 mg, 163 mmol, 61%) was isolated as a colourless crystalline solid. M.p. 96 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.12, 1.14, 1.18 [each s, each 18 H, $(CH_3)_3CCO$], 1.24 (t, J = 7.5 Hz, 6 H, SCH_2CH_3), 1.30 [s, 6 H, $(CH_3)_2C$], 2.58–2.78 (m, 4 H, SCH_2CH_3), 3.70 (ddd, $J_{4,5}$ = 9.9 Hz, $J_{5,6}$ = 5.1 Hz, $J_{5,6'}$ = 1.7 Hz, 2 H, 5-H), 4.03 (dd, $J_{5,6'}$ = 5.5 Hz, $J_{6,6'}$ = 12.3 Hz, 2 H, 6′-H), 4.15–4.23 (m, 4 H, 2-H, 6-H), 4.75 (d, $J_{1,2}$ = 10.6 Hz, 2 H, 1-H), 5.18 (dd ≈ t, $J_{3,4}$ = 9.6 Hz, $J_{4,5}$ = 9.9 Hz, 2 H, 4-H), 5.28 (dd ≈ t, $J_{2,3} = J_{3,4}$ = 9.6 Hz, 2 H, 3-H), 6.35 (d, $J_{2,NH}$ = 9.2 Hz, 2 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.9 (CH_3, SCH_2CH_3), 23.3 [CH_3, $(CH_3)_2C$], 24.5 (CH_2, SCH_2CH_3), 27.0, 27.1, 27.2 [CH_3, $(CH_3)_3$ CCO], 38.7, 38.8, 39.0 [C, $(CH_3)_3CCO$], 51.2 (CH, C-2), 54.6 [C, $(CH_3)_2C$], 62.1 (CH_2, C-6), 67.6 (CH, C-5), 74.7 (CH, C-4), 76.3 (CH, C-3), 83.2 (CH, C-1), 172.8, 176.3, 178.1 [C, $(CH_3)_3CCO$], 179.6 (C, CONH) ppm. HRMS (ESI+): calcd. for $C_{51}H_{86}N_2O_{16}Na$ [M + Na]$^+$ 1069.5316; found 1069.5306. $[\alpha]_D^{20}$ = –26 (c = 1, $CHCl_3$).

Piv *gluco*Box (24): Under a nitrogen atmosphere, **23** (500 mg, 500 μmol) was taken up in dry CH_2Cl_2 (5 mL) and cooled to 0 °C. Bromine (100 μL; 229 mg; 1.40 mmol) was slowly added, and the mixture was stirred for 1.5 h (TLC: PE/EtOAc, 4:1). After complete conversion of the starting material, the solvent was removed in vacuo and the raw product was coevaporated with toluene (3×). The crude product was used in the next step without further purification. The crude product of the previous reaction was dissolved in dry MeCN (10 mL) and treated with Et_4NCl (199 mg, 1.20 mmol). Subsequently, solid $NaHCO_3$ (190 mg, 2.30 mmol) was added, and the mixture was stirred for 16 h at room temperature (TLC: PE/EtOAc, 4:1). Then, the solvent was removed in vacuo, and the residue was taken up in CH_2Cl_2 (15 mL) and washed with water (15 mL). The organic phase was dried with Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (PE/EtOAc, 4:1) to yield **24** (278 mg, 300 μmol, 60%) as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.17, 1.17, 1.18 [each s, each 18 H, $(CH_3)_3CCO$], 1.54 [s, 6 H, $C(CH_3)_2$], 3.77 (ddd, $J_{4,5}$ = 9.2 Hz, $J_{5,6}$ = 4.8 Hz, $J_{5,6'}$ = 2.4 Hz, 2 H, 5-H), 4.02 (dd, $J_{5,6'}$ = 2.4 Hz, $J_{6,6'}$ = 12.6 Hz, 2 H, 6′-H), 4.17 (ddd, $J_{1,2}$ = 7.2 Hz, $J_{2,3}$ = 2.7 Hz, $J_{2,4}$ = 1.4 Hz, 2 H, 2-H), 4.23 (dd, $J_{5,6}$ = 4.8 Hz, $J_{6,6'}$ = 12.6 Hz, 2 H, 6-H), 4.94 (ddd ≈ dt, $J_{3,4}$ = 2.7 Hz, $J_{4,5}$ = 9.2 Hz, $J_{2,4}$ = 1.4 Hz, 2 H, 4-H), 5.22 (dd ≈ t, $J_{2,3} \approx J_{3,4}$ = 2.7 Hz, 2 H, 3-H), 5.95 (d, $J_{1,2}$ = 7.2 Hz, 2 H, 1-H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 26.9, 26.9, 27.1 [CH_3, $(CH_3)_3CCO$, $(CH_3)_2C$] 38.6 [C, $(CH_3)_2C$, $(CH_3)_3CCO$], 38.8, 39.1 [C, $(CH_3)_3CCO$], 62.5 (CH_2, C-6), 64.6 (CH, C-2), 67.6 (CH, C-5), 67.8 (CH, C-4), 69.8 (CH, C-3), 100.1 (CH, C-1), 170.1 (C, O-C=N), 176.4, 176.7, 177.9 [C, $(CH_3)_2CCO$] ppm. HRMS (ESI+): calcd. for $C_{47}H_{75}N_2O_{16}$ [M + H]$^+$ 923.5117; found 923.5112. $[\alpha]_D^{20}$ = +20 (c = 1, $CHCl_3$).

General Procedure for Cu^I-Catalysed Asymmetric Cyclopropanation of Olefins with Diazoacetates by using *gluco*Box Ligands: In a glove box, CuOTf·0.5C_6H_6 (1.8 mg, 7.2 μmol, 1 mol-%) and the respective *gluco*Box ligand (8 μmol, 1.1 mol-%) were placed into a flame-dried flask. Under a nitrogen atmosphere, dry CH_2Cl_2 (2 mL) was added, and the resulting mixture was stirred for 2 h at room temperature. To this preformed catalyst solution was added the alkene component (5 mmol). The mixture was cooled to 0 °C, and the respective diazoacetate (700 μmol) dissolved in dry CH_2Cl_2 (1 mL) was slowly added over a period of 2.5 h with a syringe pump at the same temperature. After stirring for another 16 h at 0 °C the solvent was removed under reduced pressure, and the residue was purified by flash chromatography on silica gel.

Supporting Information (see footnote on the first page of this article): Determination of enantiomeric excesses for the cyclopropanation products by either chiral GC or NMR spectroscopic methods and analytical data of these cyclopropanation products.

Acknowledgments

We thank Deutsche Forschungsgemeinschaft (grant BO 1938/2-1), VolkswagenStiftung and Fonds der Chemischen Industrie for financial support of our research and Anja Glinschert for her help with the cover design.

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Received: October 22, 2008
Published Online: January 2, 2009

