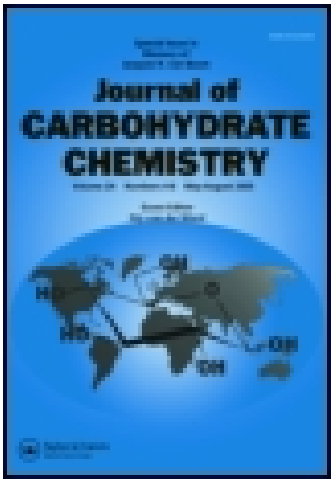

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Protecting Group Manipulation on d-Glucosamine Propane-1,3-diyl Dithioacetal

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Protecting Group Manipulation on D-Glucosamine Propane-1,3-diyl Dithioacetal

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D-glucosamine propane-1,3-diyl dithioacetal is a versatile synthetic building block, especially when being incorporated with the Corey-Seebach method. Hence, exploring compatible protecting group patterns on this compound mainly for use with the Corey-Seebach method is a fundamental work. Various protecting group strategies were applied. Typically, *N*-protection of D-glucosamine propane-1,3-diyl dithioacetal yielded *N*-phthaloyl, *N*-Boc, and *N*-Ac derivatives. On the *N*-Ac derivative, experiments differentiating 3,4- and 5,6-hydroxyls by basic stable protecting groups yielded useful intermediates. Selective protections of the 6-hydroxyl of the *N*-Ac derivative were also applied. The remaining secondary hydroxyls of the resulting *N*-Ac-6-*O*-acyl D-glucosamine propane-1,3-diyl dithioacetals could be methoxymethylated to tri-*O*-MOM derivatives or protected by a unique one-pot discriminating protection to form the *N*-acyl-6-*O*-acyl- 3,4-*O*-methylene-5-*O*-methoxymethyl D-glucosamine propane-1,3-diyl dithioacetals as useful intermediates.

Keywords D-Glucosamine propane-1,3-diyl dithioacetal, Protecting group, Selective protection

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This is part 5 of a series of work on the chemistry of propane-1,3-diyl dithioacetals of carbohydrates; for the former parts, see references 2(c), 2(d), 2(e), 2(f), 3 in this paper.
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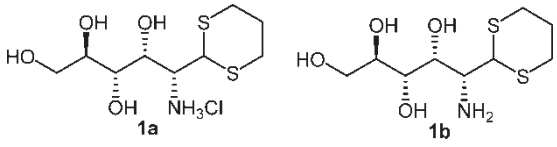


Figure 1

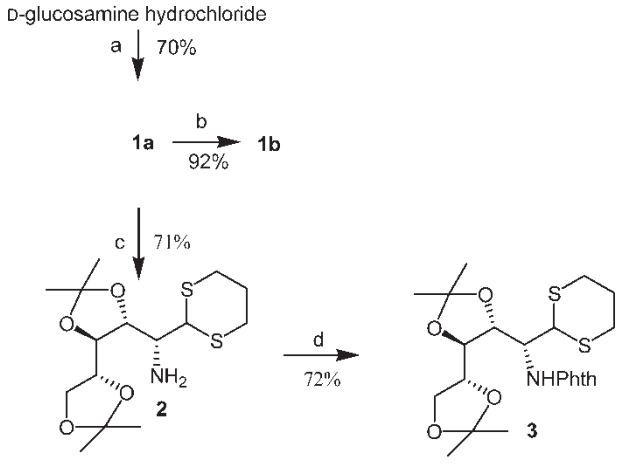
INTRODUCTION

D-Glucosamine propane-1,3-diyl dithioacetal (**1b**, and compound **1a** as its hydrochloric salt, Fig. 1) has been known for a long time[1] and is a potential precursor for the widely-used Corey-Seebach method.[2] However, to date, there has been no report in this field except two papers[3] from our group, which proved that with proper protecting groups, compound **1b** serves as an excellent precursor for the Corey-Seebach method and as a versatile building block for natural product and bioactive compound synthesis. The congenital amino group of compound **1b**, on one hand, offers great advantage for natural product and bioactive compound synthesis; on the other hand, it may cause serious problems when extreme reaction conditions are used (i.e., with BuLi in the Corey-Seebach method). Therefore, it is our first task to develop a series of robust protecting group patterns (especially toward strong basic conditions) on compound **1b** for the later application in organic synthesis. This will be reported herein.

RESULTS AND DISCUSSION

Direct isopropylidenation of hydrochloric salt **(1a)** according to the known procedure[1(b), 1(c)] gave the 3,4;5,6-di-*O*-isopropylidene derivative **2** in 71% yield. The amino group on compound **2** was further converted to phthalimide **3** in 72% yield (Sch. 1). In later experiments using the Corey-Seebach method,[3] the isopropylidene group was proved to be very stable, but the phthalimide group was eliminated when the dithian anion was formed.

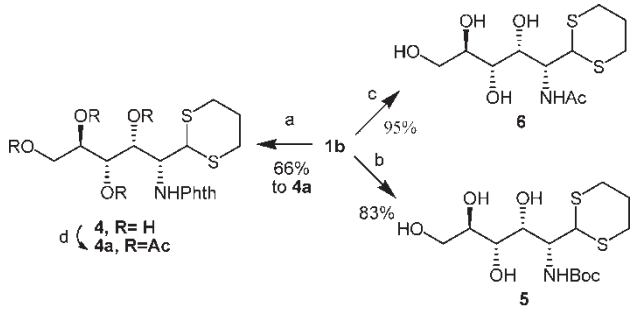
The free amine **1b**, easily available by basifying compound **1a** with aqueous sodium hydroxide, allowed the protection first of the amino function and then of the hydroxyls. By reacting compound **1b** with phthalic anhydride ($Phth_2O$), di-*tert*-butyl dicarbonate (Boc_2O), and acetic anhydride (Ac_2O), *N*-acyl compounds **4**, **5**, and **6** were prepared with good to excellent yields (Sch. 2). Different *N*-protected derivative **4**, **5**, and **6** served as important starting material for further protecting group manipulation on hydroxyls and gave useful information during the exploration of their use in the Corey-Seebach method.[3]



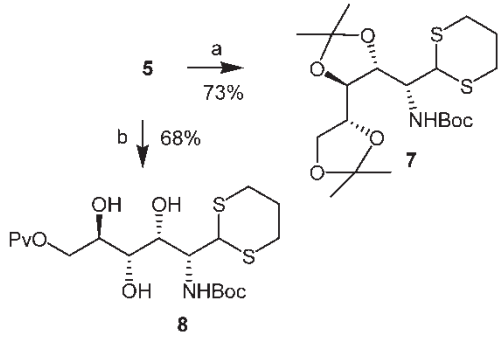
Scheme 1: Reagents and conditions: (a) 1,3-propane dithiol; (b) aqueous NaOH; (c) 2,2-dimethoxy propane, *p*-toluenesulfonic acid (cat.), reflux; (d) phthalic anhydride, pyridine.

Isopropylidenation of *N*-Boc derivative **5** with 2,2-dimethoxypropane catalyzed by pyridinium *p*-toluenesulfonate (PPTS) and selective esterification of the 6-hydroxyl gave compound **7** and **8** with the yield of 73% and 68%, respectively (Sch. 3). The Boc protection is sensitive to acid but quite stable toward nonaqueous base. In principle, the typical protecting group pattern can be applied on *N*-Boc derivative **5** if no strong acid is involved. The model compound **7** proved less efficient, though was still viable, for the Corey-Seebach method.[3]

The main work was done on the *N*-acetyl derivative **6**. This compound was found to be the easiest to handle. It also tolerated various rigorous reaction conditions including *n*-butyl lithium for the Corey-Seebach method as well as strong Lewis acids.[3] Regioselective protection and deprotection of compound



Scheme 2: Reagents and conditions: (a) NaOMe, phthalic anhydride; (b) Boc_2O, MeOH; (c) Ac_2O, MeOH; (d) Ac_2O, pyridine, for analytical reson.

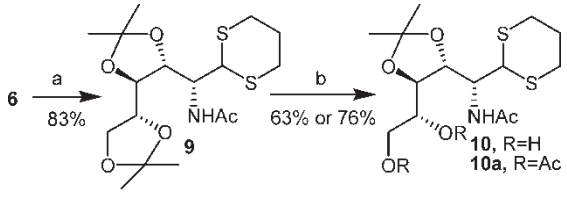


Scheme 3: Reagents and conditions: (a) 2,2-dimethoxy propane, PPTS (cat.); (b) pivaloyl chloride (PvCl), pyridine, DMF.

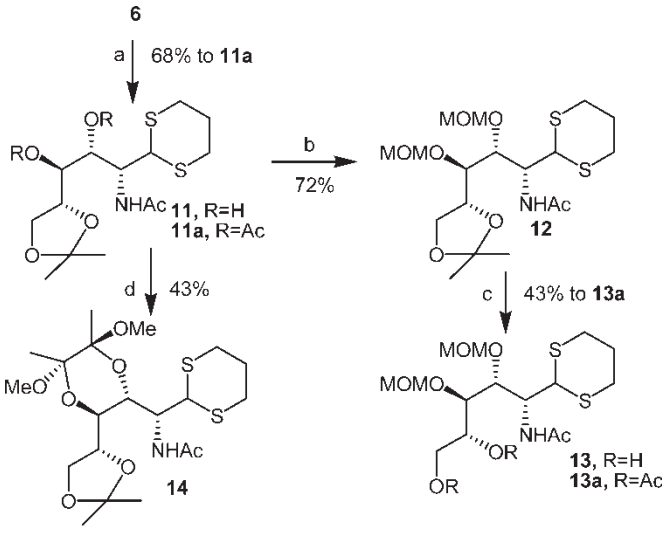
6 offers important intermediates for later synthesis[3(b)] and will be described in detail as follows.

Of compound **6**, the 3,4- and 5,6-hydroxyls could be protected simultaneously by isopropylidenation to give the 3,4;5,6-di-*O*-isopropylidene derivative **9** in 83% isolated yield. Kinetically controlled selective cleavage of the 5,6-*O*-isopropylidene group of compound **9** was realized by using 0.5 N HCl or 80% acetic acid. The resulting compound **10** was acetylated to compound **10a** for the convenience of analysis (Sch. 4).

Alternatively, the 5,6-hydroxyls of compound **6** allowed the selective protection by kinetically controlled isopropylidenation to give compound **11** at 68% yield. The remaining unprotected hydroxyls on *C*-atom 3 and 4 were subjected to further manipulation, for example, by 3,4-*O*-methoxymethylation to give the 3,4-*O*-methoxymethyl (MOM) derivative **12** or by Ley's *O*-butane diacetal (BDA) formation[4] to give compound **14**. The 5,6-*O*-isopropylidene on compound **12** could be removed selectively by 80% aqueous acetic acid to give compound **13** (Sch. 5). Attempts of removing isopropylidene acetal from compound **14** under the same condition with 80% acetic acid were not successful due to the initial cleavage of the methoxy group on the *O*-butane diacetal protection. All the above protecting groups are stable toward very basic conditions and may be used as synthetic intermediates for the Corey-Seebach method.



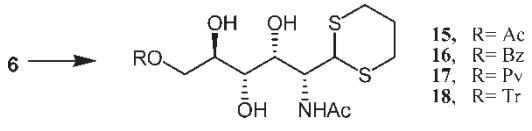
Scheme 4: Reagents and conditions: (a) con. HCl, acetone; (b) 0.5N HCl or 80% HOAc.



Scheme 5: Reagents and conditions: (a) 2-methoxypropene, *p*-toluenesulfonic acid (cat.); (b) MOMCl, diisopropyl ethylamine; (c) 0.7N HCl; (d) 2,3-butadione, trimethoxy orthoformiate, $BF_3 \cdot Et_2O$.

The differentiation of the primary and the secondary hydroxyls of compound **6** is illustrated in Scheme 6.

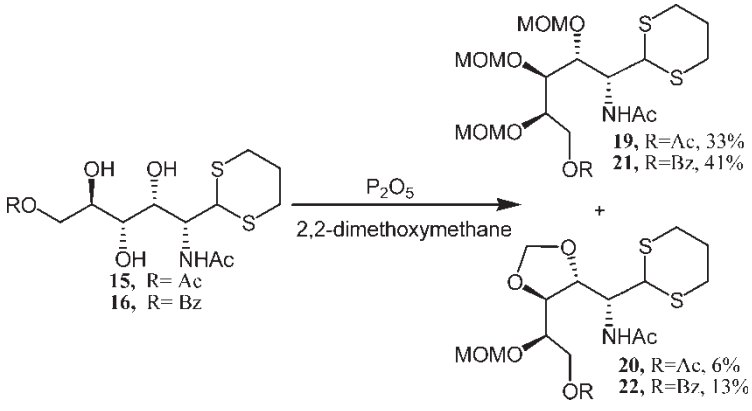
Acetylation by Ac_2O and benzoylation by BzCl of compound **6** produced compounds **15** and **16** in moderate yield. However, the pivaloylating reaction by pivaloyl chloride gave compound **17** in good yield. Furthermore, tritylation gave compound **18** almost quantitatively (Table 1).



Scheme 6

Table 1: Selective acylation and tritylation of 6-O.

Reagent	Equiv.	T(°C)	Time	Product and yield
Ac_2O	2.1	−10	1.5 h	**15**, 68%
BzCl	25.0	0	30 sec	**16**, 52%, with 32% di-*O*-benzoyl product
BzCl	1.1	0	45 min	**16**, 38%, with 28% di-*O*-benzoyl product
BzCl	1.0	−15	2.5 h	**16**, 48%, with no di-*O*-benzoyl product
PvCl	1.0	−50	3 h	**17**, 71%
TrCl	1.5	rt	12 h	**18**, 95%

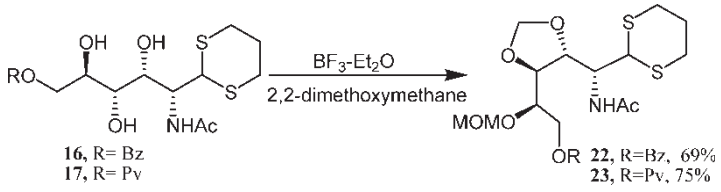


Scheme 7

By treating compounds **15** and **16** with dimethoxymethane and phosphorus pentoxide according to literature,[5] the 3,4,5-tri-*O*-methoxymethyl derivatives **19** and **21** were produced in moderate yields. Additionally, it was observed that the 3,4-di-*O*-methylene derivatives[6] **20** and **22** were formed in a considerable amount too (Sch. 7). Optimization with the aim to increase the ratio of compounds **19** and **21** to compounds **20** and **22** failed.

However, the formation of the 3,4-di-*O*-methylene derivative could be improved dramatically by applying boron trifluoride instead of diphosphopentoxide. Thus, compounds **22** and **23** were synthesized from compounds **16** and **17** in 69% and 75% yields, respectively (Sch. 8).

The compounds (**19**, **20**, **21**, **22**, and **23**), combining the base-sensitive 6-*O*-ester protection and the base-resistant 3,4,5-*O*-acetal protections, were demonstrated to be crucial intermediates, from which interesting natural product analogs were synthesized.[3] Furthermore, the *O*-MOM group is generally more labile (to acidic conditions) than the vicinal di-*O*-methylene group and can be cleaved selectively. The vicinal di-*O*-methylene group can also be opened in a regioselective way. Hence, the unique 3,4-di-*O*-methylene 5-*O*-MOM protecting pattern on compounds **20**, **22**, and **23** should offer great advantage during later synthetic applications.



Scheme 8

CONCLUSION

For the sake of exploring suitable protecting group patterns on D-glucosamine propane-1,3-diyl dithioacetal (**1b**) for later synthetic applications (especially for the Corey-Seebach method), various protecting group strategies, mainly including base stable protections and regioselective protections as well as deprotections, were tested. Three different protecting groups were applied on the amino group to yield compound **4**, **5**, and **6**, which made it possible to install various *O*-protecting groups on the remaining free hydroxyls. Differentiating protections on 3,4- and 5,6-hydroxyls, 3,4,5- and 6-hydroxyls, or 3,4- and 5-, and 6-hydroxyls were proved viable by acid or base stable protecting groups. Most of them have the advantage of easy preparation and high yields. As it has been known,[3] with proper protecting groups, D-glucosamine propane-1,3-diyl dithioacetal (**1b**) is an excellent building block when being incorporated with the Corey-Seebach procedure in natural product and bioactive compound synthesis. The protecting group manipulation described above furnishes the fundament for further exploration of the synthetic use of D-glucosamine propane-1,3-diyl dithioacetal (**1b**).

EXPERIMENTAL

Nuclear magnetic resonance spectra were recorded on a Bruker AMX 300 or 400 spectrometer. The chemical shift is specified as δ in ppm and the signal of the solvent was used as the internal standard ($CDCl_3$ ^1H: $\delta = 7.24$ ppm, ^{13}C: $\delta = 77.23$ ppm, C_6D_6 ^1H: $\delta = 7.16$ ppm, ^{13}C: $\delta = 128.39$ ppm, CD_3OD ^1H: $\delta = 4.85$ ppm, ^{13}C: $\delta = 49.15$ ppm). Electrospray ionization mass spectra (MS-ESI) were recorded on a Quattro LCZ or on a MicroTof. MALDI-TOF spectra were recorded on a REFLEX IV.

General Procedure for *O*-Acetylation

The compound with free hydroxyls was dissolved in a mixture of dry pyridine and acetic anhydride (2:1 v/v). The reaction mixture was stirred at rt until the compound was completely converted, which can take from hours to several days (monitored by TLC). The reaction may be accelerated by the addition of a catalytic amount of *N*,*N*-dimethyl aminopyridine (DMAP). The solvent was then evaporated under reduced pressure and traces of pyridine were removed by coevaporation with toluene. The crude product was purified by extraction from water with CH_2Cl_2 and, if necessary, by column chromatography.

2-Amino-2-deoxy-D-glucose Propane-1,3-diyldithioacetal Hydrochloride (1a)

D-Glucosamine hydrochloride (50.1 g, 0.23 mol) and 1,3-propanedithiol (26.0 mL, 0.24 mol) were placed in a 1-L round-bottom flask with concentrated hydrochloric acid (400 mL). The mixture was vigorously stirred at rt for 4 d and subsequently the solvent was evaporated under reduced pressure. The remaining solid was recrystallized by solving the solid in boiling water (20 mL) and adding 300 mL of ethanol during cooling of the mixture. The dithian compound **1a** (49.3 g, 0.16 mmol, 70%) precipitated as a colorless crystalline solid. mp: 219°C. (Lit. [1(a)] 204 − 206°C). $[\alpha]_D^{20} = -9.5^\circ$ (c = 1.00, H_2O). (Lit. [1(a)] $[\alpha]_D^{16} = -8.9^\circ$ (c 1.45, H_2O)).

Anal. Calcd. for $C_9H_{21}ClNO_4S_2$: C, 35.34; H, 6.59; N, 4.58. Found: C, 35.41; H, 6.50; N, 4.43.

2-Amino-2-deoxy-D-glucose Propane-1,3-diyldithioacetal (1b)

To a solution of the hydrochloride **1a** (50.6 g, 0.17 mol) in boiling water (150 mL) was added an aqueous solution of 3.3 N NaOH (50 mL, 0.17 mol). A white solid precipitated, which dissolved again after the addition of water (100 mL). During cooling of the solution the free amine compound **1b** (39.3 g, 14.6 mmol, 86%) precipitated as a colorless crystalline solid. The yield was extended to 92% by the recrystallization of the product that remained in the filtrate. mp: 174°C. $[\alpha]_D^{20} = -7.4^\circ$ (c = 1.00, H_2O).

MS-ESI (+) $m/z = 270.1\ [M + H]^+$, $292.1\ [M + Na]^+$.

Anal. calcd. for $C_9H_{19}NO_4S_2$: C, 40.13; H, 7.11; N, 5.20. Found: C, 39.93; H, 7.03; N, 5.07.

HRMS-ESI (+): m/z found $[M + Na]^+$ 292.0649. $C_9H_{19}NNaO_4S_2$ requires 292.0648.

2-Amino-2-deoxy-3,4;5,6-di-*O*-isopropylidene-D-glucose Propane-1,3-diyldi-thioacetal (2)

To a suspension of D-glucosamine 1,3-propane-diyl dithioacetal hydrochloride **1a** (3.06 g, 10.0 mmol) in 2,2-dimethoxypropane (20 mL) was added *p*-toluenesulfonic acid monohydrate (200 mg, 0.1 equiv.) at reflux temperature. The reaction was followed by TLC (EtOAc) and quenched after 3 h with a saturated aqueous sodium bicarbonate. After phase separation, the aqueous layer was extracted with Et_2O several times. The combined organic phases were washed with water and dried over $MgSO_4$, and the solvent was evaporated under reduced pressure. The purification by MPLC (cyclohexane:EtOAc = 7:1)

yielded the di-*O*-isopropylidene compound **2** (2.48 g, 7.1 mmol, 71%) as a yellowish syrup. $[\alpha]_D^{20} = +0.7^\circ$ (c = 1.00, MeOH). [Lit.[1(b)]] $+ 89^\circ$ (c = 1.3, $CHCl_3$)].

^{1}H NMR (C_6D_6, 300 MHz): δ 4.04 (dd, $J = 7.9$ Hz, $J = 1.7$ Hz, 1H, H-3), 4.37 (dd, $J = 7.9$ Hz, $J = 7.8$ Hz, 1H, H-4), 4.04 (ddd, $J = 7.8$ Hz, $J = 6.2$ Hz, $J = 4.5$ Hz, 1H, H-5), 3.99 (dd, $J = 8.3$ Hz, $J = 4.5$ Hz, 1H, H-6a), 3.94 (dd, $J = 8.3$ Hz, $J = 6.2$ Hz, 1H, H-6b), 3.91 (d, $J = 9.1$ Hz, 1H, H-1), 3.34 (dd, $J = 9.1$ Hz, $J = 1.7$ Hz, 1H, H-2), 2.59–2.42 (m, 2H, dithian-SCH_{ax}), 2.31–2.19 (m, 2H, dithian-SCH_{eq}), 1.59–1.48 (m, 2H, dithian-$SCCH_2CS$), 1.50 (s, 2H, NH_2), 1.38 (s, 3H, CH_3-*i*-pr), 1.36 (s, 3H, CH_3-*i*-pr), 1.33 (s, 3H, CH_3-*i*-pr), 1.23 (s, 3H, CH_3-*i*-pr).

^{13}C NMR (C_6D_6, 75 MHz): δ 110.0 (C_q-*i*-pr), 109.7 (C_q-*i*-pr), 80.4 (C-3), 78.8 (C-5), 78.4 (C-4), 68.5 (C-6), 54.2 (C-2), 52.9 (C-1), 28.5 (dithian-S<u>C</u>H$_2$C), 28.2 (CH_3-*i*-pr), 27.8 (dithian-S<u>C</u>H$_2$C), 27.5 (dithian-SC<u>C</u>H$_2$CS), 27.3 (CH_3-*i*-pr), 26.4 (CH_3-*i*-pr), 25.9 (CH_3-*i*-pr).

MS-ESI (+): $m/z = 350.2$ $[M + H]^+$, 372.2 $[M + Na]^+$, 388 $[M + K]^+$.

HRMS-ESI (+): m/z found $[M + H]^+$ 350.1434. $C_{15}H_{27}NNaO_4S_2$ requires 350.1454.

2-Deoxy-3,4;5,6-di-*O*-isopropylidene-2-phthalimido-D-glucose Propane-1,3-diyldithioacetal (3)

Phthalic anhydride (305 mg, 2.06 mmol) was added to a solution of the di-*O*-isopropylidene derivative **2** (719 mg, 2.06 mmol) in 20 mL dry pyridine. The reaction mixture was stirred overnight at rt. Another portion of phthalic anhydride (305 mg, 2.06 mmol) was added and the reaction mixture was stirred until TLC showed a complete conversion. Acetic anhydride was then added and again the reaction mixture was stirred until TLC showed the complete conversion to a higher running product. The solvent was then evaporated under reduced pressure and coevaporated with toluene. The purification of the remaining syrup by chromatography (cyclohexane:EtOAc = 10:1) yielded the *N*-phthalimide protected product **3** (716 mg, 1.49 mmol, 72%) as colorless crystals (from cyclohexane and EtOAc. mp: 109 − 110°C; $[\alpha]_D^{20} = -64.0^\circ$ (c = 1.00, $CHCl_3$).

^{1}H NMR (C_6D_6, 300 MHz): δ 7.53 (dd, $J = 5.5$ Hz, $J = 3.0$ Hz, 2H, H-Phth), 6.88 (dd, $J = 5.5$ Hz, $J = 3.0$ Hz, 2H, H-Phth), 5.42 (dd, $J = 7.5$ Hz, $J = 2.1$ Hz, 1H, H-3), 5.38 (d, $J = 2.3$ Hz, 1H, H-2), 5.34 (broad s, 1H, H-1), 4.14 (ddd, $J = 7.4$ Hz, $J = 6.3$ Hz, $J = 5.4$ Hz, 1H, H-5), 4.04 (dd, $J = 7.4$ Hz, $J = 7.5$ Hz, 1H, H-4), 4.02 (d, $J = 5.4$ Hz, 1H, H-6a), 4.02 (d, $J = 6.3$ Hz, 1H, H-6b), The H6a and H6b in this compound are very close to each other; therefore, the J value for them could not be determined. 2.87 (ddd, $J = 13.5$ Hz, $J = 10.2$ Hz, $J = 2.9$ Hz, 1H, dithian-SCH_{ax}-a), 2.70 (ddd, $J = 13.6$ Hz, $J = 10.2$ Hz, $J = 2.8$ Hz, 1H, dithian-SCH_{ax}-b), 2.15 (ddd, $J = 14.4$ Hz, $J = 6.4$ Hz, $J = 3.1$ Hz, 1H, dithian-SCH_{eq}-a), 2.03 (ddd, $J = 14.1$ Hz, $J = 6.4$ Hz, $J = 3.0$ Hz, 1H, dithian-SCH_{eq}-b), 1.72 (s, 3H, CH_3-*i*-pr),

1.57–1.39 (m, 2H, dithian-SCCH_2CS), 1.31 (s, 3H, CH_3-*i*-pr), 1.29 (s, 3H, CH_3-*i*-pr), 1.26 (s, 3H, CH_3-*i*-pr).

^{13}C NMR (C_6D_6, 75 MHz): δ 179.4 (CO-Phth), 179.3 (CO-Phth), 134.2 (2C, CH-Phth), 131.5 (2C, C_q-Phth), 123.7 (2C, CH-Phth), 110.7 (C_q-*i*-pr), 110.6 (C_q-*i*-pr), 80.2 (C-4), 79.4 (C-3), 78.3 (C-5), 68.4 (C-6), 54.7 (C-2), 43.5 (C-1), 27.7 (2C, CH_3-*i*-pr), 27.1 (dithian-S<u>C</u>H_2C), 26.5 (dithian-S<u>C</u>H_2C), 26.0 (2C, CH_3-*i*-pr), 25.9 (dithian-SC<u>C</u>H_2CS).

MS-ESI (+) $m/z = 502.6$ $[M + Na]^+$.

Anal. calcd. for $C_{23}H_{29}NO_6S_2$: C, 57.60; H, 6.09; N, 2.92. Found: C, 57.63; H, 5.96; N, 2.75.

HRMS-ESI (+): m/z found $[M + Na]^+$ 502.1301. $C_{23}H_{29}NNaO_6S_2$ requires 502.1329.

3,4,5,6-Tetra-*O*-acetyl-2-deoxy-2-phthalimido-D-glucose Propane-1,3-diyldithioacetal (4a)

Sodium methylate (0.89 g, 16.5 mmol) was added to a solution of D-glucosamine dithioacetal hydrochloride **1a** (5.00 g, 16.4 mmol) in MeOH (160 mL) at 40°C, after which a white solid precipitated. After 30 min of stirring, phthalic anhydride (2.67 g, 18.0 mmol) was added and the white precipitate slowly dissolved again. After 45 min TLC (EtOH) analysis showed that no starting material remained and another portion of phthalic anhydride (2.67 g, 18.0 mmol) was added. The reaction mixture was stirred overnight at rt and subsequently the solvent was evaporated. Compound **4** was crystallized from ethyl acetate and analyzed by its peracetylated derivative **4a**, produced according to the general *O*-acetylation procedure. The combined two steps yielded **4a** 6.13 g (10.8 mmol, 66%) as colorless crystals (from cyclohexane and EtOAc. mp: 162 − 163°C; $[\alpha]_D^{20} = -30.0°$ (c = 1.00, $CHCl_3$).

^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.80 (broad s, 2H, H-Phth), 7.70 (dd, $J = 5.5$ Hz, $J = 3.1$ Hz, 2H, H-Phth), 6.07 (dd, $J = 3.1$ Hz, $J = 2.5$ Hz, 1H, H-3), 5.49 (dd, $J = 8.4$ Hz, $J = 3.1$ Hz, 1H, H-4), 5.06 (ddd, $J = 8.3$ Hz, $J = 5.4$ Hz, $J = 2.9$ Hz, 1H, H-5), 4.80 (dd, $J = 11.6$ Hz, $J = 2.5$ Hz, 1H, H-2), 4.47 (d, $J = 11.6$ Hz, 1H, H-1), 4.17 (dd, $J = 12.4$ Hz, $J = 2.9$ Hz, 1H, H-6a), 4.05 (dd, $J = 12.5$ Hz, $J = 5.4$ Hz, 1H, H-6b), 3.15 (ddd, $J = 14.3$ Hz, $J = 11.3$ Hz, $J = 2.9$ Hz, 1H, dithian-SCH_{ax}-a), 2.73 (ddd, $J = 14.2$ Hz, $J = 11.3$ Hz, $J = 2.8$ Hz, 1H, dithian-SCH_{ax}-b), 2.64–2.56 (broad m, 1H, dithian-SCH_{eq}-a), 2.34–2.26 (broad m, 1H, dithian-SCH_{eq}-b), 2.04 (s, 3H, Me-OAc), 2.02 (s, 3H, Me-OAc), 2.02–1.97 (m, 2H, dithian-SCCH_2CS), 2.00 (s, 3H, Me-OAc), 1.92 (s, 3H, Me-OAc).

^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.8 (OC═O), 170.7 (OC═O), 170.3 (OC═O), 170.1 (OC═O), 168.3 (2C, O═C-Phth), 134.4 (2C, CH-Phth), 131.6 (2C, C_q-Phth), 123.6 (2C, CH-Phth), 72.1 (C-4), 68.7 (C-5), 68.0 (C-3), 62.1

(C-6), 52.0 (C-1), 42.6 (C-2), 25.2 (dithian-S$\underline{C}H_2$C), 25.0 (dithian-S$\underline{C}H_2$C), 24.5 (dithian-SC$\underline{C}H_2$CS), 21.2 (Me-OAc), 21.0 (Me-OAc), 20.8 (2C, Me-OAc).

MS-ESI (+): $m/z = 590$ $[M + Na]^+$.

Anal. calcd. for $C_{25}H_{29}NO_{10}S_2$: C, 52.90; H, 5.15; N, 2.47. Found: C, 52.85; H, 4.80; N, 2.29.

HRMS-ESI (+): m/z found $[M + Na]^+$ 590.1080. $C_{25}H_{29}NNaO_{10}S_2$ requires 590.1125.

2-*tert*-Butoxycarbonylamino-2-deoxy-D-glucose Propane-1,3-diyldithioacetal (5)

Compound **1b** (0.5 g, 1.85 mmol) was suspended in 10 mL dry MeOH and di-*tert*-butyl dicarbonate (0.6 g, 2.75 mmol) was added at rt. The reaction mixture was then stirred overnight. All volatile components were removed under vacuum, and the remained solid was recrystallized from ethyl acetate to give compound **5** (0.57 g, 1.35 mmol, 83%) as a white solid. mp: 135.8 − 136.9°C; $[\alpha]_D^{20} = -8.9°$ (c = 1.00, MeOH).

^{1}H NMR ($CDCl_3$ + DMSO-d_6, 400 MHz): δ 5.44 (d, 1H, NH), 4.25 (brs, 2H, H-6), 4.14 (m, 2H, H-2 and H-1), 3.74 (m, 1H, H-3), 3.69 (m, 1H, H-4), 3.62 (m, 1H, H-5), 3.3–4.5 (br, 4H, OH), 2.95 (m, 2H, dithian), 2.72 (m, 2H, dithian), 2.01 (m, 1H, dithian), 1.91 (m, 1H, dithian), 1.44 (s, 9H, Me-Boc).

^{13}C NMR ($CDCl_3$ + DMSO-d_6, 100 MHz): δ 152.2 (CO-Boc), 79.2 ($Me_3\underline{C}$-Boc), 73.2 (C-5), 72.0 (C-4), 69.2 (C-6), 63.5 (C-3), 54.7 (C-2), 48.4 (C-1), 28.2 (3C, Me-Boc), 27.9 (2C, dithian), 25.5 (dithian).

MS-ESI (+): $m/z = 392.1$ $[M + Na]^+$.

Anal. calcd. for $C_{14}H_{27}NO_6S_2$: C, 45.51; H, 7.37; N, 3.79. Found: C, 45.52; H, 7.26; N, 3.61.

2-Acetamido-2-deoxy-D-glucose Propane-1,3-diyldithioacetal (6)

To a suspension of the free amine compound **1b** (26.9 g, 0.10 mol) in MeOH (800 mL) was added acetic anhydride (45 mL, 4.8 mol). The reaction was followed by TLC (EtOH) and after 1.5 h of stirring at rt the solution was filtered. Evaporation of the solvent under reduced pressure yielded the *N*-acetylated compound **6** (29.4 g, 94.6 mmol, 95%) as a white solid. mp: 167−168°C; $[\alpha]_D^{20} = +1.2°$ (c = 1.00, H_2O).

NMR spectroscopic data were recorded from the *O*-peracetylated derivative.

^{1}H NMR (C_6D_6, 300 MHz): δ 5.98 (dd, $J = 5.1$ Hz, $J = 5.0$ Hz, 1H, H-3), 5.88 (d, $J = 10.2$ Hz, 1H, NHC = O), 5.78 (dd, $J = 7.0$ Hz, $J = 4.7$ Hz, 1H, H-4), 5.50 (ddd, $J = 7.0$ Hz, $J = 6.0$ Hz, $J = 3.1$ Hz, 1H, H-5), 5.06 (ddd, $J = 10.2$ Hz, $J = 6.7$ Hz, $J = 5.3$ Hz, 1H, H-2), 4.46 (dd, $J = 12.4$ Hz, $J = 3.1$ Hz, 1H, H-6a), 4.18 (dd, $J = 12.4$ Hz, $J = 6.0$ Hz, 1H, H-6b), 4.14 (d, $J = 6.7$ Hz, 1H, H-1), 2.75 (m, 2H, dithian-SCH_{ax}), 2.38–2.67 (m, 2H, dithian-SCH_{eq}), 1.83

(s, 3H, Me-OAc), 1.81 (s, 3H, Me-OAc), 1.79 (s, 3H, Me-OAc), 1.75 (s, 3H, Me-OAc), 1.74 (s, 3H, Me-NAc), 1.53-1.45 (m, 2H, dithian-SCCH$_2$CS).

^{13}C NMR (C_6D_6, 75 MHz): δ 170.7 (OC═O), 170.6 (OC═O), 170.5 (OC═O), 170.4 (OC═O), 170.0 (NC═O), 71.1 (C-4), 71.0 (C-5), 70.1 (C-3), 62.4 (C-6), 51.7 (C-2), 48.4 (C-1), 28.7 (dithian-S<u>C</u>H$_2$C), 28.4 (dithian-S<u>C</u>H$_2$C), 26.0 (dithian-SC<u>C</u>H$_2$CS), 23.1 (Me-NAc), 20.9 (Me-OAc), 20.9 (Me-OAc), 20.7 (Me-OAc), 20.7 (Me-OAc).

MS-ESI: $m/z = 334.1$ $[M + Na]^+$, 645.2 $[2M + Na]^+$.

HRMS-ESI (+): m/z calcd for $C_{11}H_{21}NNaO_5S_2$: 334.0753, found $[M + Na]^+$: 334.0712.

Anal. calcd. for $C_{11}H_{21}NO_5S_2$: C, 42.42; H, 6.80; N, 4.50. Found: C, 42.43; H, 6.76; N, 4.39.

2-*tert*-Butoxycarbonylamino-2-deoxy-3,4;5,6-di-*O*-isopropylidene-D-glucose Propane-1,3-diyldithioacetal (7)

Compound **5** (3.50 g, 9.47 mmol) was mixed with dry DMF 10 mL, dry acetone 50 mL, and 2,2-dimethoxy propane 200 mL. Then 50 mg pyridinium *p*-toluene sulfonate was added to the mixture. The resulting solution was stirred overnight. Then the solvent was removed under vacuum and the remained syrup was purified by MPLC to give compound **7** (3.10 g, 6.90 mmol, 73%) as a white solid. mp: 127.0−128.2°C; $[\alpha]_D^{20} = -17.8^\circ$ (c = 1.00, MeOH).

^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.97 (d, $J = 10.2$ Hz, 1H, NH), 4.66 (pseudo-d, $J = 7.88$ Hz, 1H, H-3), 4.34 (pseudo-t, $J = 9.9$ Hz, 1H, H-2), 4.13 (m, 2H, H-6), 3.99 (m, 1H, H-5), 3.81 (d, $J = 9.2$ Hz, 1H, H-1), 3.71 (m, 1H, H-4), 3.15 (m, 1H, H-dithian), 2.99 (m, 1H, H-dithian), 2.65 (m, 2H, H-dithian), 2.01 (m, 2H, H-dithian), 1.49 (s, 3H, CH$_3$-*i*-pr), 1.41 (s, 3H, CH$_3$-*i*-pr), 1.45 (s, 9H, Me-Boc), 1.37 (s, 3H, CH$_3$-*i*-pr), 1.35 (s, 3H, CH$_3$-*i*-pr).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 155.6 (CO-Boc), 109.9 (C_q-*i*-pr), 109.5 (C_q-*i*-pr), 79.4 (Me$_3$<u>C</u>-Boc), 78.3 (C-4), 78.1 (C-3), 77.0 (C-6), 67.4 (C-5), 51.6 (C-2), 48.0 (C-1), 28.2 (3C, CH$_3$-Boc), 27.5 (CH$_3$-*i*-pr), 26.9 (dithian-SC<u>C</u>H$_2$CS), 26.8 (2C, dithian-S<u>C</u>H$_2$), 26.5 (CH$_3$-*i*-pr), 25.4 (CH$_3$-*i*-pr), 24.2 (CH$_3$-*i*-pr).

HRMS-ESI (+): m/z found $[M + Na]^+$ 472.1798. $C_{20}H_{35}NNaO_6S_2$ requires 472.1804.

2-*tert*-Butoxycarbonylamino-6-*O*-pivaloyl-2-deoxy-D-glucose Propane-1,3-diyldithioacetal (8)

Compound **5** (50 mg, 0.135 mmol) was dissolved in dry pyridine 1.0 mL and cooled to 0°C with stirring. Pivaloyl chloride (0.025 mL, 0.203 mmol, 1.5equiv.)

in 0.5 mL dry DMF was added dropwise to the above solution. The stirring was kept for 1 more h at 0°C and MeOH was added to quench the reaction. All volatile components were removed under vacuum, and the remained syrup was purified by MPLC (EtOAc:cyclohexane = 1:5) to give compound **8** (41 mg, 0.092 mmol, 68%) as a white solid. mp: 155.0−156.5°C; $[\alpha]_D^{20} = +1.0^\circ$ (c = 1.00, MeOH).

^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.29 (d, $J = 7.2$ Hz, 1H, NH), 4.30 (m, 2H, H-6), 4.27 (brs, 1H, H-3), 4.21 (m, 2H, H-2 and H-1), 3.89 (dd, $J = 5.0$ Hz, $J = 10.5$ Hz, 1H, H-5), 3.63 (dd, $J = 5.0$ Hz, $J = 6.5$ Hz, 1H, H-4), 2.94 (m, 2H, H-dithian), 2.77 (m, 2H, H-dithian), 2.06 (m, 1H, H-dithian), 1.92 (m, 1H, H-dithian), 1.45 (s, 9H, Me-Pv), 1.22 (s, 9H, Boc).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 179.1 (CO-Pv), 156.9 (CO-Boc), 80.2 ($Me_3\underline{C}$-Boc), 72.1 (C-4), 71.4 (C-5), 70.2 (C-3), 66.1 (C-6), 55.5 (C-2), 48.7 (C-1), 39.0 ($Me_3\underline{C}$-Pv), 28.7 (C-dithian), 28.6 (C-dithian), 28.4 (3C, Me-Pv), 27.3 (3C, Me-Boc), 25.7 (C-dithian).

MS-ESI (+): $m/z = 476.2$ $[M + Na]^+$.

Anal. calcd. for $C_{19}H_{35}NO_7S_2$: C, 50.31; H, 7.78; N, 3.09. Found: C, 50.67; H, 7.78; N, 2.90.

2-Acetamido-2-deoxy-3,4;5,6-di-*O*-isopropylidene-D-glucose Propane-1,3-diyldithioacetal (9)

Concentrated hydrochloric acid (2 mL) was added to a suspension of the dithian compound **6** (3.0 g, 9.6 mmol) in dry acetone (300 mL). After 3 h of vigorous stirring at rt the reaction mixture was poured into a saturated aqueous sodium bicarbonate solution and the organic solvent was evaporated under reduced pressure. The suspension was extracted with CH_2Cl_2 several times and the combined organic layers were washed once with water. Drying the solution over $MgSO_4$ and evaporation of the solvent under reduced pressure yielded the di-*O*-isopropylidene protected compound **9** (3.1 g, 8.0 mmol, 83%) as a pale yellow solid. Further purification is possible by recrystallization from a cyclohexane-EtOAc mixture, yielding large colorless crystals. mp: 141−142°C; $[\alpha]_D^{20} = -38.1^\circ$ (c = 1.00, MeOH).

^{1}H NMR (C_6D_6, 400 MHz): δ 5.48 (d, $J = 10.1$ Hz, 1H, NHC═O), 5.09 (ddd, $J = 10.2$ Hz, $J = 10.1$ Hz, $J = 0.8$ Hz, 1H, H-2), 5.04 (dd, $J = 8.1$ Hz, $J = 0.7$ Hz, 1H, H-3), 4.05 (ddd, $J = 7.8$ Hz, $J = 7.7$ Hz, $J = 4.2$ Hz, 1H, H-5), 4.04 (dd, $J = 10.1$ Hz, $J = 4.2$ Hz, 1H, H-6a), 3.93 (dd, $J = 10.1$ Hz, $J = 7.8$ Hz, 1H, H-6b), 3.79 (dd, $J = 7.7$ Hz, $J = 7.7$ Hz, 1H, H-4), 3.76 (d, $J = 9.8$ Hz, 1H, H-1), 3.06 (ddd, $J = 13.9$ Hz, $J = 10.2$ Hz, $J = 2.7$ Hz, 1H, dithian-SCH_{ax}-a), 2.87 (ddd, $J = 13.7$ Hz, $J = 10.1$ Hz, $J = 2.7$ Hz, 1H, dithian-SCH_{ax}-b), 2.21 (ddd, $J = 14.6$ Hz, $J = 6.7$ Hz, $J = 2.9$ Hz, 1H, dithian-SCH_{eq}), 2.18 (ddd, $J = 14.4$ Hz, $J = 6.7$ Hz, $J = 2.9$ Hz, 1H, dithian-

SCH_{eq}), 1.70–1.60 (m, 1H, dithian-$SCCH_2CS$), 1.65 (s, 3H, CH_3-*i*-pr), 1.62 (s, 3H, Me-NAc), 1.55–1.47 (m, 1H, dithian-$SCCH_2CS$), 1.30 (s, 3H, CH_3-*i*-pr), 1.28 (s, 3H, CH_3-*i*-pr), 1.25 (s, 3H, CH_3-*i*-pr).

^{13}C NMR (C_6D_6, 100 MHz): δ 169.5 (NC=O), 110.7 (C_q-i-pr), 109.9 (C_q-i-pr), 79.5 (C-4), 79.2 (C-3), 78.1 (C-5), 68.1 (C-6), 50.4 (C-2), 48.1 (C-1), 27.6 (dithian-S<u>C</u>H_2C), 27.5 (CH_3-*i*-pr), 27.5 (CH_3-*i*-pr), 27.3 (CH_3-*i*-pr), 26.8 (dithian-S<u>C</u>H_2C), 26.1 (dithian-SC<u>C</u>H_2CS), 25.7 (CH_3-*i*-pr), 23.2 (Me-NAc).

MS-ESI (+): $m/z = 392.3$ $[M + H]^+$, 414.2 $[M + Na]^+$.

Anal. calcd. for $C_{17}H_{29}NO_5S_2$: C, 52.15; H, 7.47; N, 3.58. Found: C, 52.36; H, 7.30; N, 3.39.

HRMS-ESI (+): m/z found $[M + Na]^+$ 414.1331. $C_{17}H_{29}NNaO_5S_2$ requires 414.1385.

2-Acetamido-5,6-di-*O*-acetyl-2-deoxy-3,4-*O*-isopropylidene-D-glucose Propane -1,3-diyldithioacetal (10a)

Method A: To a solution of the di-*O*-isopropylidene derivative **9** (630 mg, 1.6 mmol) was added 0.5 N hydrochloric acid (10 mL, 5 mmol). The reaction was followed by TLC (EtOAc) and after 4.5 h the reaction was quenched with aqueous sodium bicarbonate. The solvent was then evaporated under reduced pressure and the remaining syrup was put in water and extracted with CH_2Cl_2 (3×20 mL). The combined organic phases were dried with $MgSO_4$ and filtered, and the solvent was evaporated under reduced pressure. Purification by MPLC (EtOAc) yielded the 5,6-dihydroxy derivative **10** (355 mg, 1.0 mmol, 63%) as a colorless syrup. The analysis was performed on 5,6-di-*O*-acetyl derivative **10a**, produced according to the general *O*-acetylation procedure.

Method B: A solution of the di-*O*-isopropylidene derivative **9** (393 mg, 1.0 mmol) in 80% aqueous acetic acid (10 mL) was heated to 50°C. After 1.5 h a TLC analysis showed complete conversion and the solvent was evaporated under reduced pressure. *O*-Acetylation of the remaining crude **10** according to the general procedure and purification by MPLC (cyclohexane/EtOAc, 1:1) yielded the di-*O*-acetyl derivative **10a** (320 mg, 0.76 mmol, 76%) as a colorless syrup. The analysis was again performed on compound **10a** and gave the same result as in method A.

$[\alpha]_D^{20} = -1.6^\circ$ (c = 1.00, MeOH).

^1H NMR (C_6D_6, 300 MHz): δ 5.63 (d, $J = 10.0$ Hz, 1H, NHC=O), 5.48 (ddd, $J = 7.7$ Hz, $J = 6.1$ Hz, $J = 3.2$ Hz, 1H, H-5), 4.89 (dd, $J = 7.9$ Hz, $J = 1.0$ Hz, 1H, H-3), 4.80 (ddd, $J = 10.1$ Hz, $J = 9.1$ Hz, $J = 1.1$ Hz, 1H, H-2), 4.72 (dd, $J = 12.1$ Hz, $J = 3.2$ Hz, 1H, H-6a), 4.15 (dd, $J = 12.1$ Hz, $J = 6.1$ Hz, 1H, H-6b), 4.01 (dd, $J = 7.8$ Hz, $J = 7.8$ Hz, 1H, H-4), 3.89 (d, $J = 9.2$ Hz, 1H, H-1), 2.79–2.61 (m, 2H, dithian-SCH_{ax}), 2.26–2.14 (m, 2H, dithian-SCH_{eq}),

1.96 (s, 3H, Me-NAc), 1.75 (s, 3H, Me-OAc), 1.65 (s, 3H, Me-OAc), 1.56–1.49 (m, 2H, dithian-SCCH$_2$CS), 1.28 (s, 3H, CH$_3$-*i*-pr), 1.25 (s, 3H, CH$_3$-*i*-pr).

^{13}C NMR (C_6D_6, 75 MHz): δ 170.4 (C=O), 170.2 (C=O), 169.8 C=O), 110.4 (C_q-*i*-pr), 78.6 (C-4), 76.6 (C-3), 72.6 (C-5), 63.5 (C-6), 51.1 (C-2), 48.3 (C-1), 30.5 (CH$_3$-*i*-pr), 28.2 (CH$_3$-*i*-pr), 27.4 (dithian-S<u>C</u>H$_2$C), 27.0 (dithian-S<u>C</u>H$_2$C), 26.0 (dithian-SC<u>C</u>H$_2$CS), 23.0 (Me-NAc), 21.1 (Me-OAc), 20.7 (Me-OAc).

MS-ESI (+): m/z = 436.2 $[M + H]^+$, 458.2 $[M + Na]^+$.

HRMS-ESI (+): m/z found $[M + Na]^+$ 458.1289. $C_{18}H_{29}NNaO_7S_2$ requires 458.1278.

Anal. calcd. for $C_{18}H_{29}NO_7S_2$: C, 49.64; H, 6.71; N, 3.22. Found: C, 49.81; H, 6.49; N, 3.06.

2-Acetamido-3,4-di-*O*-acetyl-2-deoxy-5,6-*O*-isopropylidene-D-glucose Propane- 1,3-diyldithioacetal (11a)

To a solution of acetamido derivative **6** (6.10 g, 16.5 mmol) and 2-methoxypropene (3.0 mL, 30.0 mmol) in DMF (250 mL) was added *p*-toluenesulfonic acid monohydrate (210 mg, 1.1 mmol) at 0°C. After stirring for 1 h the reaction was quenched with concentrated aqueous NH_3. The solvent was evaporated under reduced pressure and codistilled with toluene. The purification of the remaining syrup by MPLC (cyclohexane:EtOAc = 1:2) yielded the 5,6-*O*-isopropylidene derivative **11** (3.93 g, 11.2 mmol, 68%) as a colorless syrup. The analysis was performed on 3,4-di-*O*-acetyl derivative **11a,** produced according to the general *O*-acetylation procedure. mp: 100−102°C; $[\alpha]_D^{20} = -11.1^\circ$ (c = 1.00, MeOH).

^{1}H NMR (C_6D_6, 400 MHz): δ 5.95 (dd, J = 5.3 Hz, J = 4.9 Hz, 1H, H-3), 5.85 (d, J = 10.0 Hz, 1H, NHC=O), 5.55 (dd, J = 6.6 Hz, J = 4.9 Hz, 1H, H-4), 5.07 (ddd, J = 10.2 Hz, J = 6.6 Hz, J = 5.4 Hz, 1H, H-2), 4.30 (ddd, J = 6.6 Hz, J = 6.4 Hz, J = 5.3 Hz, 1H, H-5), 4.20 (d, J = 6.6 Hz, 1H, H-1), 3.95 (dd, J = 8.6 Hz, J = 5.3 Hz, 1H, H-6a), 3.86 (dd, J = 8.6 Hz, J = 6.3 Hz, 1H, H-6b), 2.66–2.60 (m, 1H, dithian-SCH$_{ax}$-a), 2.56–2.50 (m, 1H, dithian-SCH$_{ax}$-b), 2.33–2.25 (m, 2H, dithian-SCH$_{eq}$), 1.76 (s, 3H, Me-OAc), 1.75 (s, 3H, Me-OAc), 1.66 (s, 3H, Me-NAc), 1.48 (s, 3H, CH$_3$-*i*-pr), 1.47–1.42 (m, 2H, dithian-SCCH$_2$CS), 1.24 (s, 3H, CH$_3$-*i*-pr).

^{13}C NMR (C_6D_6, 100 MHz): δ 170.4 (OC=O), 169.9 (2C, OC=O/NC=O), 110.3 (C_q-*i*-pr), 75.6 (C-5), 72.2 (C-3), 72.1 (C-4), 66.6 (C-6), 51.9 (C-2), 49.0 (C-1), 28.8 (dithian-S<u>C</u>H$_2$C), 28.6 (dithian-S<u>C</u>H$_2$C), 27.2 (CH$_3$-*i*-pr), 26.0 (dithian-SC<u>C</u>H$_2$CS), 25.8 (CH$_3$-*i*-pr), 23.0 (Me-NAc), 20.7 (2C, Me-OAc).

MS-ESI (+): m/z = 436.1 $[M + H]^+$, 458.1 $[M + Na]^+$, 893.3 $[2M + Na]^+$.

HRMS-ESI (+): m/z found $[M + Na]^+$ 458.1273. $C_{18}H_{29}NNaO_7S_2$ requires 458.1278.

2-Acetamido-2-deoxy-5,6-*O*-isopropylidene-3,4-di-*O*-methoxy-methyl-D-glucose propane-1,3-diyldithioacetal (12)

To a solution of the 5,6-*O*-isopropylidene derivative **11** (2.26 g, 6.4 mmol) in DIPEA (9.5 mL, 64.3 mmol) and dry CH_2Cl_2 (15 mL) was added methoxymethyl chloride (1.3 mL, 14.0 mmol). The reaction mixture was heated to reflux temperature for 5 h and was stirred overnight at rt. TLC (EtOAc) analysis indicated that the reaction was not complete and therefore an additional portion of methoxymethyl chloride (1.3 mL, 14.0 mmol) was added. The reaction was quenched with MeOH and the solvent was evaporated under reduced pressure. The remaining syrup was put in a glass filter filled with silica gel and washed with EtOAc. The purification by MPLC (cyclohexane:EtOAc = 8:1) yielded the 3,4-di-*O*-methoxymethyl derivative **12** (1.99 g, 4.6 mmol, 72%) as a colorless syrup. $[\alpha]_D^{20} = +3.9^\circ$ (c = 1.00, MeOH).

^{1}H NMR (C_6D_6, 300 MHz): δ 5.95 (d, $J = 9.6$ Hz, 1H, NHC = O), 4.89 (dd, $J = 9.6$ Hz, $J = 9.0$ Hz, 1H, H-2), 4.71 (dd, $J = 13.6$ Hz, $J = 6.4$ Hz, 2H, OCH_2O), 4.68 (dd, $J = 19.1$ Hz, $J = 6.6$ Hz, 2H, OCH_2O), 4.50 (d, $J = 6.4$ Hz, 1H, H-3), 4.35 (dd, $J = 12.9$ Hz, $J = 6.4$ Hz, 1H, H-4), 4.10–4.04 (m, 2H), 4.01–3.95 (m, 2H), 3.18 (s, 3H, OCH_3), 3.17 (s, 3H, OCH_3), 3.02 (ddd, $J = 13.6$ Hz, $J = 9.5$ Hz, $J = 2.9$ Hz, 1H, dithian-SCH_{ax}-a), 2.72 (ddd, $J = 13.6$ Hz, $J = 9.5$ Hz, $J = 2.7$ Hz, 1H, dithian-SCH_{ax}-b), 2.26 (ddd, $J = 14.1$ Hz, $J = 6.9$ Hz, $J = 2.9$ Hz, 1H, dithian-SCH_{eq}-a), 2.16 (ddd, $J = 14.0$ Hz, $J = 7.0$ Hz, $J = 2.7$ Hz, 1H, dithian-SCH_{eq}-b), 1.70 (s, 3H, Me-NAc), 1.65–1.49 (m, 2H, dithian-$SCCH_2CS$), 1.46 (s, 3H, CH_3-*i*-pr), 1.30 (s, 3H, CH_3-*i*-pr).

^{13}C NMR (C_6D_6, 75 MHz): δ 170.0 (NC=O), 109.9 (C_q-*i*-pr), 199.3 (OC=O), 198.3 (OC=O), 78.9 (OCH_3), 78.4 (OCH_3), 76.9 (C-4), 67.6 (C-3), 60.6 (C-5), 56.7 (C-6), 51.6 (C-2), 48.2 (C-1), 30.0 (dithian-S$\underline{C}H_2$C), 28.5 (dithian-S$\underline{C}H_2$C), 27.3 (dithian-SC$\underline{C}H_2$CS), 26.4 (CH_3-*i*-pr), 26.1 (CH_3-*i*-pr), 23.4 (Me-NAc).

MS-ESI (+): $m/z = 440.3$ $[M + H]^+$, 462.3 $[M + Na]^+$.

HRMS-ESI (+): m/z found $[M + Na]^+$ 462.1550. $C_{18}H_{33}NNaO_7S_2$ requires 462.1591.

Anal. calcd. for $C_{18}H_{33}NO_7S_2$: C, 49.18; H, 7.57; N, 3.19. Found: C, 49.01; H, 7.65; N, 3.05.

2-Acetamido-2-deoxy-5,6-di-*O*-acetyl-3,4-di-*O*-methoxy-methyl-D-glucose Pro-pane-1,3-diyldithioacetal (13a)

To a solution of 5,6-*O*-isopropylidene derivative **12** (2.05 g, 4.7 mmol) in acetone (20 mL) was added 0.7 N hydrochloric acid (31 mL). The reaction mixture was stirred at rt and followed by TLC (EtOAc). After the complete conversion the reaction was quenched with sat. $NaHCO_3$ solution (40 mL) and the

reaction mixture was extracted with CH_2Cl_2 five times. The combined organic phase was evaporated under reduced pressure and the remaining syrup as crude compound **13** was *O*-acetylated according to the general procedure. The purification by MPLC (cyclohexane:EtOAc = 1:2) yielded the 5,6-di-*O*-acetyl derivative **13a** (801 mg, 2.0 mmol, 43%) as colorless syrup. $[\alpha]_D^{20} = +33^\circ$ (c = 1.00, MeOH).

^{1}H NMR (C_6D_6, 400 MHz) δ 6.17 (d, J = 10.0 Hz, 1H, NHC═O), 5.48 (ddd, J = 7.8 Hz, J = 3.3 Hz, J = 3.2 Hz, 1H, H-5), 4.85 (dd, J = 10.0 Hz, J = 9.4 Hz, 1H, H-2), 4.68 (d, J = 6.1 Hz, 1H, 3-OCH_2O), 4.65 (d, J = 6.7 Hz, 1H, 4-OCH_2O), 4.65 (d, J = 6.1 Hz, 1H, 3-OCH_2O), 4.55 (d, J = 6.7 Hz, 1H, 4-OCH_2O), 4.53 (d, J = 7.5 Hz, 1H, H-3), 4.60 (dd, J = 12.1 Hz, J = 3.4 Hz, 1H, H-6a), 4.31 (dd, J = 12.1 Hz, J = 7.9 Hz, 1H, H-6b), 4.11 (dd, J = 7.5 Hz, J = 3.3 Hz, 1H, H-4), 3.94 (d, J = 9.5 Hz, 1H, H-1), 3.22 (s, 3H, 4-OCH_3), 3.18 (s, 3H, 3-OCH_3), 3.12–3.08 (m, 1H, dithian-SCH_{ax}-a), 3.01–2.93 (m, 1H, dithian-SCH_{ax}-b), 2.30–2.24 (m, 2H, dithian-SCH_{eq}), 1.88 (s, 3H, Me-NAc), 1.81 (s, 3H, Me-5-OAc), 1.77 (s, 3H, Me-6-OAc), 1.72–1.57 (m, 2H, dithian-$SCCH_2CS$).

^{13}C NMR (C_6D_6, 100 MHz) δ 170.6 (NC═O), 170.6 (6-OC═O), 170.1 (5-OC═O), 99.3 (3-OCH_2O), 98.1 (4-OCH_2O), 78.6 (C-4), 78.1 (C-3), 72.3 (C-5), 62.8 (C-6), 56.6 (3-OCH_3), 56.3 (4-OCH_3), 51.3 (C-2), 47.0 (C-1), 27.7 (dithian-S<u>C</u>H_2C), 26.8 (dithian-S<u>C</u>H_2C), 26.1 (dithian-SC<u>C</u>H_2CS), 23.3 (Me-NAc), 21.1 (Me-OAc), 20.8 (Me-OAc).

MS-ESI (+) m/z = 484.2 [M + H]+, 506.2 $[M + Na]^+$, 989.3 $[2M + Na]^+$.

HRMS-ESI (+): m/z found $[M + Na]^+$ 506.1458. $C_{19}H_{33}NNaO_9S_2$ requires 506.1489.

2-Acetamido-2-deoxy-3,4-*O*-(3′,4′-dimethoxy butane-3′,4′-diyl)-5,6-*O*-isopropy-lidene-D-glucose Propane-1,3-diyldithioacetal (14)

To a solution of the 5,6-*O*-isopropylidene derivative **11** (354.8 mg, 1.0 mmol), 2,3-butadione (0.10 mL, 1.1 mmol), and trimethoxy orthoformiate (0.44 mL, 4.0 mmol) in dry MeOH (3 mL) was added $BF_3 \cdot Et_2O$ (0.3 l, 0.1 mmol). After stirring at rt overnight, the yellow solution disappeared and the solvent was evaporated under reduced pressure. The purification by MPLC (cyclohexane:EtOAc = 3:1) yielded the 3,4-*O*-BDA derivative **14** (201 mg, 0.43 mmol, 43%) as a colorless syrup. $[\alpha]_D^{20} = -13.6^\circ$ (c = 1.00, MeOH).

^{1}H NMR (C_6D_6, 300 MHz): δ 5.82 (d, J = 9.9 Hz, 1H, NHC═O), 4.97 (dd, J = 9.9 Hz, J = 9.3 Hz, 1H, H-2), 4.92 (d, J = 10.1 Hz, 1H, H-3), 4.16 (ddd, J = 10.1 Hz, J = 7.4 Hz, J = 3.9 Hz, 1H, H-5), 3.91 (d, J = 9.3 Hz, 1H, H-1), 3.86–3.73 (m, 3H, H-4/6), 3.28 (s, 3H, OCH_3), 3.05 (s, 3H, OCH_3), 3.01–2.92 (m, 1H, dithian-SCH_{ax}-a), 2.80–2.71 (m, 1H, dithian-SCH_{ax}-b), 2.30–2.14

(m, 2H, dithian-SCH_{eq}), 1.69 (s, 3H, Me-NAc), 1.66–1.52 (m, 2H, dithian-$SCCH_2CS$), 1.35 (s, 3H, CH_3-*i*-pr), 1.31 (s, 3H, CH_3-*i*-pr), 1.31 (s, 3H, CH_3-*i*-pr), 1.29 (s, 3H, CH_3-*i*-pr).

^{13}C NMR (C_6D_6, 75 MHz): δ 169.8 (NC=O), 110.2 (C_q-*i*-pr), 99.8 (C_q-BDA), 98.8 (C_q-BDA), 78.8 (C-4), 78.1 (C-3), 70.0 (C-5), 62.0 (C-6), 51.1 (C-1), 48.4 (C-2), 48.3 (OMe), 48.0 (OMe), 28.1 (dithian-S$\underline{C}H_2$C), 27.6 (dithian-S$\underline{C}H_2$C), 27.4 (CH_3-*i*-pr), 27.3 (dithian-SC$\underline{C}H_2$CS), 26.1 (CH_3-*i*-pr), 23.1 (Me-NAc), 18.3 (CCH_3-BDA), 18.2 (CCH_3-BDA).

MS-MALDI (+): $m/z = 488.1$ $[M + Na]^+$.

HRMS-ESI (+): m/z found $[M + Na]^+$ 488.1737. $C_{20}H_{35}NNaO_7S_2$ requires 488.1747.

2-Acetamido-6-*O*-acetyl-2-deoxy-D-glucose Propane-1,3-diyldithioacetal (15)

A solution of the acetamido derivative **6** (311 mg, 1.0 mmol) in dry pyridine (5 mL) was cooled to -10°C. Then acetic anhydride (0.2 mL, 2.1 mmol) was added slowly to the reaction mixture and after 1.5 h of stirring the reaction was quenched with EtOH. The solvent was evaporated under reduced pressure and coevaporated with toluene several times. Purification by MPLC (toluene:EtOH = 4:1) yielded the 6-*O*-acetyl derivative **15** (240 mg, 0.68 mmol, 68%) as a colorless syrup. $[\alpha]_D^{20} = -2.7^\circ$ (c = 1.00, MeOH).

^1H NMR ($CDCl_3/CD_3OD$, 400 MHz): δ 6.77 (d, $J = 9.6$ Hz, 1H, NHC=O), 4.56 (ddd, $J = 9.6$ Hz, $J = 7.7$ Hz, $J = 3.3$ Hz, 1H, H-2), 4.26 (dd, $J = 11.6$ Hz, $J = 2.8$ Hz, 1H, H-6a), 4.21 (dd, $J = 4.1$ Hz, $J = 3.3$ Hz, 1H, H-3), 4.12 (dd, $J = 11.6$ Hz, $J = 6.6$ Hz, 1H, H-6b), 4.10 (d, $J = 7.7$ Hz, 1H, H-1), 3.81 (ddd, $J = 6.6$ Hz, $J = 6.6$ Hz, $J = 2.8$ Hz, 1H, H-5), 3.51 (dd, $J = 6.2$ Hz, $J = 4.8$ Hz, 1H, H-4), 3.32 (broad s, 3H, OH), 2.89–2.84 (m, 2H, dithian-SCH_{ax}), 2.73–2.64 (m, 2H, dithian-SCH_{eq}), 2.04 (s, 3H, Me-NAc), 2.04–1.94 (m, 1H, dithian-$SCCH_2CS$), 1.98 (s, 3H, Me-OAc), 1.89–1.81 (m, 1H, dithian-$SCCH_2CS$).

^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.3 (NC=O), 172.0 (OC=O), 72.5 (C-4), 70.5 (C-5), 69.5 (C-3), 66.0 (C-6), 53.8 (C-2), 48.1 (C-1), 28.6 (dithian-S$\underline{C}H_2$C), 28.5 (dithian-S$\underline{C}H_2$C), 25.7 (dithian-SC$\underline{C}H_2$CS), 23.0 (Me-NAc), 21.0 (Me-OAc).

MS-ESI (+): $m/z = 376.2$ $[M + Na]^+$, 729.3 $[2M + Na]^+$.

HRMS-ESI (+): m/z found $[M + H]^+$ 376.0847. $C_{13}H_{23}NNaO_6S_2$ requires 376.0859.

2-Acetamido-6-*O*-benzoyl-2-deoxy-D-glucose Propane-1,3-diyldithioacetal (16)

The acetamido compound **6** (12.64 g, 40.6 mmol) was dissolved in dry pyridine (200 mL) and the solution was cooled to -15°C. Then a solution of

benzoyl chloride (4.7 mL, 40.6 mmol) in dry pyridine (20 mL) was added slowly over a period of 45 min. After 2.5 h the reaction was quenched with 100 mL MeOH and the solvent was evaporated under reduced pressure. The purification by MPLC (toluene: EtOH = 9:1) yielded the 6-*O*-benzoate product **16** (8.11 g, 19.5 mmol, 48%) as a white solid. mp: 155−156°C; $[\alpha]_D^{20} = +1.1^\circ$ (c = 1.00, MeOH).

^{1}H NMR ($CDCl_3/CD_3OD$, 400 MHz): δ 7.99 (d, $J = 8.3$ Hz, 2H, H_{ortho}-Bz), 7.48 (m, 1H, H_{para}-Bz), 7.35 (dd, $J = 7.7$ Hz, 2H, H_{meta}-Bz), 6.74 (weak d, $J = 9.5$ Hz, 1H, NHC = O), 4.48 (dd, $J = 11.7$ Hz, $J = 2.7$ Hz, 1H, H-6a), 4.43 (dd, $J = 7.9$ Hz, $J = 3.1$ Hz, 1H, H-2), 4.40 (dd, $J = 11.6$ Hz, $J = 6.2$ Hz, 1H, H-6b), 4.26 (dd, $J = 4.6$ Hz, $J = 3.1$ Hz, 1H, H-3), 4.07 (d, $J = 7.9$ Hz, 1H, H-1), 3.89 (ddd, $J = 6.4$ Hz, $J = 6.4$ Hz, $J = 3.2$ Hz, 1H, H-5), 3.56 (dd, $J = 6.8$ Hz, $J = 4.6$ Hz, 1H, H-4), 2.86−2.81 (m, 2H, dithian-SCH_{ax}), 2.68−2.58 (m, 2H, dithian-SCH_{eq}), 2.02−1.90 (m, 1H, dithian-$SCCH_2CS$), 1.95 (s, 3H, Me-NAc), 1.87−1.77 (m, 1H, dithian-$SCCH_2CS$). ^{1}H-Signals from the amide and hydroxy protons are weakened due to a fast proton exchange with CD_3OD.

^{13}C NMR ($CDCl_3/CD_3OD$, 100 MHz): δ 172.3 (NC═O), 167.3 (OC═O), 133.2 (C_{para}-Bz), 129.8 (2C, C_{ortho}-Bz), 128.4 (2C, C_{meta}-Bz), 72.1 (C-4), 70.9 (C-5), 69.6 (C-3), 66.5 (C-6), 53.8 (C-2), 47.9 (C-1), 28.4 (dithian-S<u>C</u>H$_2$C), 28.3 (dithian-S<u>C</u>H$_2$C), 25.6 (dithian-SC<u>C</u>H$_2$CS), 22.9 (Me-NAc).

MS-ESI (+): $m/z = 438.2$ $[M + Na]^+$.

HRMS-ESI (+): m/z found $[M + Na]^+$ 438.1058. $C_{18}H_{25}NO_6S_2Na$ requires 438.1016.

Anal. calcd. for $C_{18}H_{25}NO_6S_2$: C, 52.03; H, 6.06; N, 3.37. Found: C, 51.86; H, 6.05; N, 3.29.

2-Acetamido-6-*O*-pivaloyl-2-deoxy-D-glucose Propane-1,3-diyldithioacetal (17)

The acetamido compound **6** (1.50 g, 4.8 mmol) was dissolved in 20 mL pyridine and 5 mL DMF and cooled to −50°C; a solution of pivaloyl chloride (0.6 mL, 4.9 mmol) in 5 mL DMF was added dropwise during a period of 2 h. The reaction mixture was kept stirring at this temperature for another 1 h before methanol was added to quench the reaction and the mixture was warmed to rt. All volatile components were then removed under reduced pressure and a small amount of ethanol was added to the residue. The product precipitated out by seeding. A small amount of water was added to this slurry. The mixture was stirred and filtered. The resulted white solid was collected, dried, and weighed to yield 1.35 g (71%) compound **17**. mp: 95.1−96.2°C. $[\alpha]_D^{20} = -6.4^\circ$ ($c = 1.00$, methanol).

^{1}H NMR ($CDCl_3/CD_3OD$, 400 MHz): δ 6.72 (d, $J = 9.3$ Hz, 1H, NH), 4.72 (ddd, $J = 3.1$ Hz, $J = 7.9$ Hz, $J = 9.3$ Hz, 1H, H-2), 4.44 (m, 3H, H-3, H-6),

4.33 (d, $J = 7.9$ Hz, 1H, H-1), 4.02–3.96 (m, 1H, H-5), 3.70 (dd, $J = 4.6$ Hz, 1H, $J = 7.2$ Hz, H-4), 3.13–3.05 (m, 2H, dithian), 2.94–2.82 (m, 2H, dithian), 2.20 (s, 3H, Me-NAc), 2.13–2.02 (m, 2H, dithian), 1.36 (s, 9H, Me-Pv).

^{13}C NMR (CD_3Cl, 100 MHz): δ 178.6 (CO-Pv), 171.3 (CO-Ac), 71.5 (C-5), 71.0 (C-4), 69.7 (C-3), 65.7 (C-6), 53.5 (C-2), 47.5 (C-1), 38.5 ($Me_3\underline{C}$-Pv), 28.0 (dithian), 27.8 (dithian), 26.8 (3C, Me-Pv), 25.2 (dithian), 22.8 (Me-NAc).

MS-ESI (+) $m/z = 418.1385$ $[M + Na]^+$.

Anal. calcd. for $C_{16}H_{29}NO_6S_2$: C, 48.59; H, 7.39; N, 3.54. Found: C, 48.65; H, 7.79; N, 3.09.

2-Acetamido-2-deoxy-6-*O*-trityl-D-glucose Propane-1,3-diyldithioacetal (18)

To a solution of the acetamido derivative **6** (1.56 g, 5.0 mmol) and DMAP (cat. amount) in dry pyridine (20 mL) was added trityl chloride (2.11 g, 7.5 mmol) in portions. The reaction mixture was stirred overnight at rt and after TLC (toluene: EtOH = 4:1) analysis indicated the complete conversion, the reaction was quenched with water. Extraction with CH_2Cl_2 (3 × 20 mL), evaporation of the solvent under reduced pressure, and purification by MPLC (toluene:EtOH = 1:19) yielded the 6-*O*-trityl derivative **18** (2.52 g, 4.6 mmol, 91%) as a colorless syrup. $[\alpha]_D^{20} = -2.4^\circ$ (c = 1.00, MeOH).

NMR spectroscopic data were recorded from the *O*-acetylated compound, which was produced by the general *O*-acetylation protocol.

^{1}H NMR (CD_3Cl, 400 MHz): δ 7.34 (broad m, 6H, H_{arom}), 7.21 (broad m, 6H, H_{arom}), 7.15 (broad m, 3H, H_{arom}), 5.68 (d, $J = 10.0$ Hz, 1H, NHC = O), 5.57 (dd, $J = 8.5$ Hz, $J = 3.4$ Hz, 1H, H-4), 5.39 (dd, $J = 6.9$ Hz, $J = 3.4$ Hz, 1H, H-3), 5.07 (ddd, $J = 8.4$ Hz, $J = 4.6$ Hz, $J = 2.6$ Hz, 1H, H-5), 4.48 (ddd, $J = 10.1$ Hz, $J = 6.6$ Hz, $J = 5.2$ Hz, 1H, H-2), 4.25 (d, $J = 5.0$ Hz, 1H, H-1), 3.20 (dd, $J = 10.6$ Hz, $J = 2.6$ Hz, 1H, H-6a), 2.97 (dd, $J = 10.6$ Hz, $J = 4.6$ Hz, 1H, H-6b), 2.92–2.85 (m, 2H, dithian-SCH_{ax}), 2.77–2.72 (m, 2H, dithian-SCH_{eq}), 2.05 (s, 3H, $OCOCH_3$), 2.04–1.98 (m, 1H, dithian-$SCCH_2CS$-a), 1.94 (s, 3H, $OCOCH_3$), 1.93 (s, 3H, $NCOCH_3$), 1.86–1.79 (m, 1H, dithian-$SCCH_2CS$-b), 1.75 (s, 3H, $OCOCH_3$).

^{13}C NMR (CD_3Cl, 100 MHz): δ 170.6 (OC═O), 170.1 (NC═O), 170.0 (OC═O), 169.9 (OC═O), 143.5 (3C, $C_{q,arom}$-Tr), 128.8 (6C, CH_{arom}-Tr), 127.9 (6C, CH_{arom}-Tr), 127.2 (3C, CH_{arom}-Tr), 86.8 ($OCPh_3$), 70.4 (C-3), 70.2 (C-5), 68.9 (C-4), 61.8 (C-6), 51.9 (C-2), 49.3 (C-1), 29.8 (dithian-$S\underline{C}H_2C$), 29.7 (dithian-$S\underline{C}H_2C$), 25.8 (dithian-$SC\underline{C}H_2CS$), 23.3 (Me-NAc), 21.1 (Me-OAc), 20.8 (Me-OAc), 20.7 (Me-OAc).

MS-ESI (+): $m/z = 576.4$ $[M + Na]^+$, 1129.7 $[2M + Na]^+$.

HRMS-ESI (+): m/z found $[M + Na]^+$ 576.1802. $C_{30}H_{35}NNaO_5S_2$ requires 576.1849.

2-Acetamido-6-*O*-acetyl-2-deoxy-3,4,5-tri-*O*-methoxymethyl-D-glucose Propane-1,3-diyldithioacetal (19)

To a mixture of diphosphopentoxide (31 g, 0.22 mol) in dry dimethoxymethane (300 mL) was added dropwise a solution of 6-*O*-acetate **15** (11.63 g, 32.9 mmol) in dry dioxane (40.0 mL) at reflux temperature. After 1 h of stirring at reflux temperature a TLC analysis showed the complete conversion and the reaction was quenched with a saturated $NaHCO_3$ solution until pH >7. The phases were separated and the aqueous phase was extracted with CH_2Cl_2 three times. The combined organic phases were washed with water, dried over $MgSO_4$, and filtrated. The solvent was evaporated under reduced pressure and purification by MPLC (cyclohexane:EtOAc = 5:3) yielded the 3,4,5-tri-*O*-methoxy-methyl derivative **19** (5.29 g, 10.9 mmol, 33%) and the 5-*O*-methoxymethyl-3,4-*O*-methylene derivative **20** (860 mg, 2.1 mmol, 6%) both as colorless syrup.

Compound **19**: $[\alpha]_D^{20} = +27.2^\circ$ ($c = 1.00$, MeOH).

^{1}H NMR (C_6D_6, 400 MHz): δ 5.86 (d, $J = 10.1$ Hz, 1H, NHC=O), 4.68 (d, $J = 6.2$ Hz, 1H, 3-OCH_2O), 4.64 (d, $J = 6.1$ Hz, 1H, 3-OCH_2O), 4.63 (d, $J = 6.6$ Hz, 1H, 4-OCH_2O), 4.61 (d, $J = 6.6$ Hz, 1H, 4-OCH_2O), 4.61 (d, $J = 6.7$ Hz, 1H, 5-OCH_2O), 4.54 (d, $J = 6.7$ Hz, 1H, 5-OCH_2O), 4.43 (dd, $J = 10.1$ Hz, $J = 10.1$ Hz, 1H, H-2), 4.24 (d, $J = 8.1$ Hz, 1H, H-3), 4.21 (dd, $J = 11.9$ Hz, $J = 4.2$ Hz, 1H, H-6a), 4.11 (dd, $J = 11.8$ Hz, $J = 7.3$ Hz, 1H, H-6b), 3.92 (ddd, $J = 7.3$ Hz, $J = 4.1$ Hz, $J = 2.8$ Hz, 1H, H-5), 3.74 (dd, $J = 8.1$ Hz, $J = 2.4$ Hz, 1H, H-4), 3.72 (d, $J = 9.6$ Hz, 1H, H-1), 3.30 (s, 6H, OCH_3), 3.29 (s, 3H, OCH_3), 3.03–2.91 (m, 2H, dithian-SCH_{ax}), 2.53–2.42 (m, 2H, dithian-SCH_{eq}), 1.98 (s, 3H, Me-OAc), 1.94 (s, 3H, Me-NAc), 1.92–1.87 (m, 2H, dithian-$SCCH_2CS$).

^{13}C NMR (C_6D_6, 100 MHz): δ 170.7 (OC=O), 170.1 (NC=O), 98.8 (3-OCH_2O), 97.5 (4-OCH_2O), 96.3 (5-OCH_2O), 78.8 (C-4), 76.8 (C-3), 75.6 (C-5), 63.5 (C-6), 56.5 (OCH_3), 56.0 (OCH_3), 55.7 (OCH_3), 50.9 (C-2), 46.0 (C-1), 27.0 (dithian-SCH_2C), 26.2 (dithian-SCH_2C), 25.4 (dithian-$SCCH_2CS$), 23.1 (Me-NAc), 20.9 (Me-OAc).

MS-ESI (+) $m/z = 486.2$ $[M + H]^+$, 508.2 $[M + Na]^+$, 993.3 $[2M + Na]^+$.

HRMS-ESI (+): m/z found $[M + Na]^+$ 508.1682. $C_{19}H_{35}NNaO_9S_2$ requires 508.1645.

2-Acetamido-6-*O*-acetyl-2-deoxy-5-*O*-methoxymethyl-3,4-*O*-methylene-D-glucose Propane-1,3-diyldithioacetal (20)

See procedure for the synthesis of **19**.

$[\alpha]_D^{20} = +20.9^\circ$ ($c = 1.00$, MeOH).

^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.91 (d, $J = 9.8$ Hz, 1H, NHC═O), 5.03 (s, 1H, 3-OCH_2O-4), 4.88 (s, 1H, 3-OCH_2O-4), 4.71 (d, $J = 6.8$ Hz, 1H, 5-OCH_2OMe), 4.65 (d, $J = 6.8$ Hz, 1H, 5-OCH_2OMe), 4.62 (d, $J = 6.2$ Hz, $J = 0.9$ Hz, 1H, H-3), 4.52 (ddd, $J = 9.8$ Hz, $J = 8.6$ Hz, $J = 1.0$ Hz, 1H, H-2), 4.38 (dd, $J = 12.0$ Hz, $J = 4.1$ Hz, 1H, H-6a), 4.07 (dd, $J = 12.0$ Hz, $J = 4.8$ Hz, 1H, H-6b), 3.98 (d, $J = 8.6$ Hz, 1H, H-1), 3.90 (ddd, $J = 6.2$ Hz, $J = 4.8$ Hz, $J = 4.1$ Hz, 1H, H-5), 3.79 (dd, $J = 6.2$ Hz, $J = 6.2$ Hz, 1H, H-4), 3.35 (s, 3H, OCH_3), 2.98–2.87 (m, 2H, dithian-SCH_{ax}), 2.70–2.62 (m, 2H, dithian-SCH_{eq}), 2.06 (s, 3H, Me-OAc), 2.04–1.90 (m, 2H, dithian-$SCCH_2CS$), 2.01 (s, 3H, Me-NAc).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 170.9 (OC═O), 170.5 (NC═O), 96.4 (5-OCH_2OMe), 95.7 (3-OCH_2O-4), 77.1 (C-4), 76.9 (C-3), 75.0 (C-5), 63.1 (C-6), 56.2 (OCH_3), 51.7 (C-2), 48.4 (C-1), 28.5 (dithian-$S\underline{C}H_2C$), 28.1 (dithian-$S\underline{C}H_2C$), 25.6 (dithian-$SC\underline{C}H_2CS$), 23.3 (Me-NAc), 21.0 (Me-OAc).

MS-ESI (+) $m/z = 410.1$ $[M + H]^+$, 432.1 $[M + Na]^+$, 841.2 $[2M + Na]^+$.

HRMS-ESI (+): m/z found $[M + Na]^+$ 432.1101. $C_{16}H_{27}NNaO_7S_2$ requires 432.1121.

2-Acetamido-6-*O*-benzoyl-2-deoxy-3,4,5-tri-*O*-methoxymethyl-D-glucose Propane-1,3-diyldithioacetal (21)

An experiment similar to the preparation of **21** and **22** was carried out on compound **16**, with the cosolvent as DMF instead of dioxane. After purification, it yielded compound **21** (41%) and **22** (13%).

Compound **21**: $[\alpha]_D^{20} = +28.8^\circ$ ($c = 1.00$, MeOH).

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.03 (dd, $J = 8.1$ Hz, $J = 1.4$ Hz, 2H, H_{ortho}-Bz), 7.51 (dddd, $J = 8.1$ Hz, $J = 7.5$ Hz, $J = 1.4$ Hz, $J = 1.4$ Hz, 1H, H_{para}-Bz), 7.39 (dd, $J = 7.5$ Hz, $J = 1.4$ Hz, 2H, H_{meta}-Bz), 5.88 (d, $J = 10.2$ Hz, 1H, NHC = O), 4.77 (d, $J = 6.2$ Hz, 1H, OCH_2O), 4.74 (d, $J = 6.5$ Hz, 1H, OCH_2O), 4.73 (d, $J = 6.7$ Hz, 1H, OCH_2O), 4.72 (d, $J = 6.1$ Hz, 1H, OCH_2O), 4.71 (d, $J = 6.5$ Hz, 1H, OCH_2O), 4.67 (d, $J = 6.7$ Hz, 1H, OCH_2O), 4.95 (ddd, $J = 10.2$ Hz, $J = 9.8$ Hz, $J = 0.8$ Hz, 1H, H-2), 4.53 (dd, $J = 12.1$ Hz, $J = 3.5$ Hz, 1H, H-6a), 4.46 (dd, $J = 12.1$ Hz, $J = 7.1$ Hz, 1H, H-6b), 4.37 (dd, $J = 8.1$ Hz, $J = 0.8$ Hz, 1H, H-3), 4.12 (ddd, $J = 7.1$ Hz, $J = 3.5$ Hz, $J = 2.9$ Hz, 1H, H-5), 3.90 (dd, $J = 8.1$ Hz, $J = 2.9$ Hz, 1H, H-4), 3.80 (d, $J = 9.8$ Hz, 1H, H-1), 3.37 (s, 3H, OCH_3), 3.36 (s, 3H, OCH_3), 3.32 (s, 3H, OCH_3), 3.11–2.97 (m, 2H, dithian-SCH_{ax}), 2.55–2.48 (m, 2H, dithian-SCH_{eq}), 2.00 (s, 3H, Me-NAc), 1.98–1.92 (m, 2H, dithian-$SCCH_2CS$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 170.1 (NC═O), 166.4 (OC═O), 133.1 (C_{para}-Bz), 129.8 (C_q-Bz), 130.2 (2C, C_{ortho}-Bz), 128.4 (2C, C_{meta}-Bz), 98.9 (OCH_2O), 97.6 (OCH_2O), 96.5 (OCH_2O), 78.6 (OCH_3), 77.1 (OCH_3), 76.2 (OCH_3), 64.5 (C-4), 56.6 (C-3), 56.2 (C-5), 55.9 (C-6), 51.1 (C-2), 46.2 (C-1), 27.2 (dithian-$S\underline{C}H_2C$), 26.4 (dithian-$S\underline{C}H_2C$), 25.6 (dithian-$SC\underline{C}H_2CS$), 23.3 (Me-NAc).

MS-ESI (+): $m/z = 548.2$ $[M + H]^+$, 570.2 $[M + Na]^+$, 1117.4 $[2M + Na]^+$.

HRMS-ESI (+): m/z found $[M + Na]^+$ 570.1786. $C_{24}H_{37}NNaO_9S_2$ requires 570.1802.

2-Acetamido-6-*O*-benzoyl-2-deoxy-5-*O*-methoxymethyl-3,4-*O*-methylene-D-glucose Propane-1,3-diyldithioacetal (22)

Method A: See the preparation of compound **21**.

Method B: To a mixture of 6-*O*-benzoate **16** (121 mg, 0.29 mmol) in dimethoxymethane (3.0 mL) was added dropwise $BF_3{\cdot}Et_2O$ at rt (0.16 mL, 1.3 mmol). The solid immediately dissolved and the solution was stirred overnight at rt. The reaction was quenched with a saturated $NaHCO_3$ solution. The mixture was extracted with Et_2O (3 × 4 mL) and the combined organic phases were washed with water. Evaporation of the solvent under reduced pressure yielded the 5-*O*-methoxymethyl-3,4-*O*-methylene derivative **22** (95 mg, 0.20 mmol, 69%) as a colorless syrup. $[\alpha]_D^{20} = +22.4^\circ$ ($c = 1.00$, MeOH).

^{1}H NMR (C_6D_6, 400 MHz): δ 8.27–8.25 (m, 2H, H_{ortho}-benzoyl), 7.19–7.16 (m, 3H, H-benzoyl), 5.84 (d, $J = 10.0$ Hz, 1H, NHC = O), 4.97 (dd, $J = 10.0$ Hz, $J = 9.7$ Hz, $J = 0.9$ Hz, 1H, H-2), 4.94 (d, $J = 6.5$ Hz, $J = 0.9$ Hz, 1H, H-3), 4.89 (s, 1H, 3-OCH_2O-4), 4.76 (dd, $J = 12.0$ Hz, $J = 3.4$ Hz, 1H, H-6a), 4.75 (s, 1H, 3-OCH_2O-4), 4.70 (d, $J = 6.7$ Hz, 1H, 5-OCH_2OCH_3), 4.61 (d, $J = 6.7$ Hz, 1H, 5-OCH_2OCH_3), 4.51 (dd, $J = 12.0$ Hz, $J = 4.8$ Hz, 1H, H-6b), 4.18 (dd, $J = 6.9$ Hz, $J = 6.5$ Hz, 1H, H-4), 3.98 (ddd, $J = 6.9$ Hz, $J = 4.8$ Hz, $J = 3.4$ Hz, 1H, H-5), 3.94 (d, $J = 9.7$ Hz, 1H, H-1), 3.20 (s, 3H, OCH_3), 2.91 (ddd, $J = 14.0$ Hz, $J = 9.4$ Hz, $J = 2.7$ Hz, 1H, dithian-SCH_{ax}-a), 2.70 (ddd, $J = 13.9$ Hz, $J = 9.4$ Hz, $J = 2.7$ Hz, 1H, dithian-SCH_{ax}-b), 2.24 (ddd, $J = 14.1$ Hz, $J = 7.2$ Hz, $J = 2.8$ Hz, 1H, dithian-SCH_{eq}-a), 2.18 (ddd, $J = 14.1$ Hz, $J = 7.1$ Hz, $J = 2.8$ Hz, 1H, dithian-SCH_{eq}-b), 1.69 (s, 3H, Me-NAc), 1.65–1.50 (m, 2H, dithian-$SCCH_2CS$).

^{13}C NMR (C_6D_6, 100 MHz): δ 170.4 (NC═O), 166.6 (OC═O), 133.4 (C_{para}-Bz), 131.0 (C_q-Bz), 130.5 (2C, C_{ortho}-Bz), 129.0 (2C, C_{meta}-Bz), 96.9 (5-OCH_2OCH_3), 96.0 (3-OCH_2O-4), 78.2 (C-3), 77.5 (C-4), 76.1 (C-5), 64.4 (C-6), 56.2 (OCH_3), 51.8 (C-2), 47.7 (C-1), 27.7 (dithian-S<u>C</u>H_2C), 27.1 (dithian-S<u>C</u>H_2C), 26.0 (dithian-SC<u>C</u>H_2CS), 23.1 (Me-NAc).

MS-ESI (+) $m/z = 494.3$ $[M + Na]^+$, 965.5 $[2M + Na]^+$.

HRMS-ESI (+): m/z found $[M + Na]^+$ 494.1258. $C_{21}H_{29}NNaO_7S_2$ requires 494.1278.

2-Acetamido-6-*O*-pivaloyl-2-deoxy-5-*O*-methoxymethyl-3,4-*O*-methylene-D-glucose Propane-1,3-diyldithioacetal (23)

6-*O*-Pivaloyl derivative **17** (1.00 g, 2.5 mmol) was added into 20 mL dichloromethane and 8 mL dimethoxymethane, and then $BF_3{\cdot}Et_2O$ (2.0 mL,

15.8 mmol) was added. The reaction mixture was stirred at rt for 1 h. Saturated aqueous sodium bicarbonate was then added to quench the reaction. The two phases were separated and the water phase was washed with ether. The combined organic phase was washed with brine and concentrated under reduced pressure. The residue was purified by silica gel column (dichloromethane:methanol = 50:1) to yield 0.86 g (75%) product **23** as a colorless oil. $[\alpha]_D^{20} = +5.5^\circ$ ($c = 1.00$, chloroform).

^{1}H NMR (C_6D_6, 400 MHz): δ 5.80 (d, $J = 9.8$ Hz, 1H, NH), 5.03 (s, 1H, 3-OCH_2O-4), 4.85 (s, 1H, 3-OCH_2O-4), 4.74 (d, $J = 6.8$ Hz, 1H, OCH_2O-MOM), 4.62 (d, $J = 6.8$ Hz, 1H, OCH_2O-MOM), 4.58 (dd, $J = 1.3$ Hz, $J = 6.0$ Hz, 1H, H-3), 4.53 (ddd, $J = 1.3$ Hz, $J = 8.5$ Hz, $J = 9.8$ Hz, 1H, H-2), 4.36 (dd, $J = 3.5$ Hz, $J = 12.1$ Hz, 1H, H-6), 4.10 (dd, $J = 4.4$ Hz, $J = 12.1$ Hz, 1H, H-6), 3.94 (d, $J = 8.5$ Hz, 1H, H-1), 3.82 (ddd, $J = 3.5$ Hz, $J = 4.4$ Hz, $J = 7.5$ Hz, 1H, H-5), 3.76 (dd, $J = 6.0$ Hz, $J = 7.5$ Hz, 1H, H-4), 3.35 (s, 3H, CH_3-MOM), 2.99–2.87 (m, 2H, dithian), 2.67–2.60 (m, 2H, dithian), 1.98 (s, 3H, Me-NAc), 1.96–1.87 (m, 2H, dithian), 1.15 (s, 9H, Me-Pv).

^{13}C NMR (C_6D_6, 100 MHz): δ 178.0 (CO-Pv), 170.0 (CO-NAc), 96.1 (3,4-O-methylene), 95.4 (OCH_2O-MOM), 77.4 (C-3), 76.5 (C-4), 75.1 (C-5), 63.0 (C-6), 56.1 (CH_3-MOM), 51.6 (C-2), 48.1 (C-1), 38.8 ($Me_3\underline{C}$-Pv), 28.2 (dithian), 27.8 (dithian), 27.0 (3C, Me-Pv), 25.5 (dithian), 23.1 (Me-NAc).

MS-ESI (+) $m/z = 474.1615$ ($M + Na^+$).

Anal. calcd. for $C_{19}H_{33}NO_7S_2$: C, 50.53; H, 7.37; N, 3.10. Found: C, 50.58; H, 7.46; N, 3.00.

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