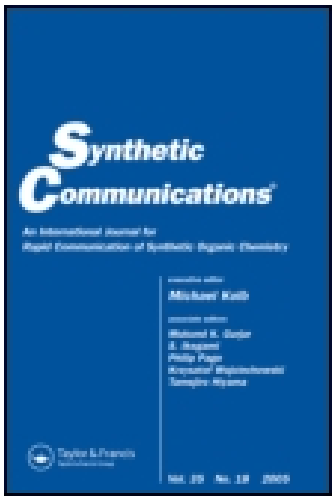

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BIS-DESULFOGLUCOSINOLATES: A NEW CLASS OF BOLAFORMS

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BIS-DESULFOGLUCOSINOLATES: A NEW CLASS OF BOLAFORMS

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ABSTRACT

Bis-desulfoglucosinolates **14–18** bearing D-*gluco*, *lacto*, *malto* and *cellobio* saccharidic moieties were synthesized in two steps from the corresponding protected 1-thio-β-D-glycopyranoses **5**, **8**, **10** and **12** and *bis*-hydroximoyl chlorides **3a** and **4a** derived from 1,8-octanedial (**1**) and 1,12-dodecanedial (**2**). Fully deprotections of the intermediate *O*-acetylated derivatives **6**, **7**, **9**, **11** and **13** were realized either using Zemplén method or methanol/triethylamine/water mixture, the choice of the conditions being dependent on the solubility in methanol of the fully and partially acetylated derivatives.

Key Words: Desulfoglucosinolates; Bolaforms; Amphiphiles

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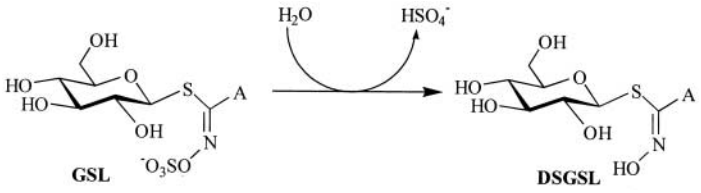
INTRODUCTION

Bolaamphiphiles are molecules in which hydrophilic groups are connected on both ends of a hydrophobic bridging chain.[1–4] The interest for these substances has increased for synthetic, biological and practical points of view.[5–7] Natural bolaamphiphilic structures are encountered in membranes of thermophilic *Archaebacteria*.[8] The structure confers a very high stability to the membrane under extreme environmental conditions.

Non-ionic bolaamphiphilic surfactants having sugars at one[9] or both[10–16] ends have been synthesized, because of: (1) their ability to from vesicles and supramolecular arrangements and (2) their potential applications in the biomedical and pharmaceutical fields. Some years ago, D-glucosaminyl bolaamphiphiles were prepared in the laboratory and their surfactant properties in water solution were described.[17]

Glucosinolates constitute a structurally homogeneous family of over 110 naturally-occurring anomeric esters—thiohydroximates—derived from 1-thio-β-D-glucose. They can undergo smooth enzymatic desulfatation by sulfatase (EC 3.1.6.1) to produce the corresponding desulfoglucosinolates, which have major analytical applications.[18]



The synthesis of natural and artificial non-sulfated glucosinolates is well-documented.[19] We herein report the synthesis and applications of bolaamphiphilic derivatives designed a *bis*-desulfoglucosinolate template.

RESULTS AND DISCUSSION

Synthetic pathway to bolaamphiphilic glucosinolates involved the preparation of the dioximes **3** and **4**, which were further condensed with 1-thiosugar derivatives. Thus, 1,8-octanedial **1** and 1,12-dodecanedial **2** were synthesized from commercially available 1,8-octanediol and 1,12-dodecanediol, respectively. In a first attempt, the corresponding ditosylates (obtained from the diols in 75% yield) were heated at 155°C in DMSO, in the presence of sodium carbonate as described by Stirling et al.[20] However, the purification of dialdehydes proved tedious due to the presence of side-products and

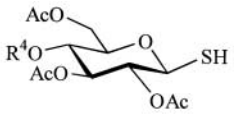
the overall yields could never exceed 40%. In contrast, when using *o*-iodoxybenzoic acid (IBX) in DMSO,[21,22] direct oxidation of the diols led to **1** and **2** in high yields. Reacting the dialdehydes with hydroxylamine hydrochloride in the presence of sodium acetate afforded the dioximes **3** and **4** in quantitative yields.

The dioximes were then transformed into the *bis*-hydroximoyl chlorides **3a** and **4a**, through chlorination with *N*-chlorosuccinimide in DMF. The key-step in the synthesis of *bis*-desulfoglucosinolates was the stereospecific 1,3-addition of the protected saccharidic thiols on the transient *bis*-nitrile oxides produced in situ by basic treatment of **3a** and **4a**. Thus, coupling reactions led to symmetrical bolaforms in the D-*gluco* **6**,**7**, *lacto* **9**, *malto* **11** and *cellobio* **13** series starting from the known β-D-glycosyl mercaptans **5**,**8**,**10** and **12**, in yields ranging from 57 to 86%. *O*-Deacetylation of these precursors was effected either using Zemplén method or the $MeOH/NEt_3/H_2O$ mixture, the choice of the conditions being dependent on the solubility in MeOH of the fully or partially acetylated derivatives.

In the case of the condensation of 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranose **5** with the C-8 *bis*-hydroximoyl chloride **3a**, the main impurity was identified as the unsymmetrical α,β-derivative **6a**; this could be due to the presence of some α-thiol in the starting material **5**. The structure of **6a** was ascertained from ^{1}H NMR spectrum (δH-1β = 5.05 ppm, δH-1α = 6.23 ppm, $J_{1,2}$ = 5.6 Hz); the large value for $J_{1,2}$ has already been observed for artificial α-glucosinolates.[23]

Evidence for the β-configuration of all the peracetylated and deprotected derivatives resulted from the chemical shifts for H-1 and the $J_{1,2}$ coupling in ^{1}H-NMR spectra.

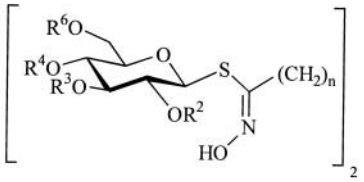
Surface tension properties of these derivatives were performed in aqueous solutions. Thus, critical micellar concentration (cmc) was carried out for water-soluble compounds above the Krafft temperature by the Lecomte du Nouÿ ring method.[24] However monosaccharidic (**14**,**15**) and disaccharidic (**16**,**18**) bolaforms were not soluble enough in water to allow measurement. In contrast, due to its high water-solubility, the *malto* derivative **17** gave 60 mmol/L for the cmc at 25°C and the area per molecule at the air–water interface was found to be 52 Å^2/molecule; the small value of the area would imply a tight packing of the disaccharidic headgroups at the air–water interface. Intermolecular hydrogen bonding can be proposed as the origin.[25] In the sugar-based bolaform surfactant series, the cmc of bolaform D-glucosaminyl surfactants were in the range 70–80 mmol/L, independent of the arm length and temperature;[17] these values for the glucosamine headgroup are close to the value measured for the *malto* derivative.



5 R^4 = Ac
8 R^4 = Ac_4-β-D-Gal
10 R^4 = Ac_4-α-D-Glc
12 R^4 = Ac_4-β-D-Glc

$[(CH_2)_n\text{-}CX{=}NOH]_2$

3 n = 3, X = H
4 n = 5, X = H
3a n = 3, X = Cl
4a n = 5, X = Cl



6 n = 3, R^2 = R^3 = R^4 = R^6 = Ac
7 n = 5, R^2 = R^3 = R^4 = R^6 = Ac
9 n = 3, R^2 = R^3 = R^6 = Ac, R^4 = Ac_4-β-D-Gal
11 n = 3, R^2 = R^3 = R^6 = Ac, R^4 = Ac_4-α-D-Glc
13 n = 3, R^2 = R^3 = R^6 = Ac, R^4 = Ac_4-β-D-Glc
14 n = 3, R^2 = R^3 = R^4 = R^6 = H
15 n = 5, R^2 = R^3 = R^4 = R^6 = H
16 n = 3, R^2 = R^3 = R^6 = H, R^4 = β-D-Gal
17 n = 3, R^2 = R^3 = R^6 = H, R^4 = α-D-Glc
18 n = 3, R^2 = R^3 = R^6 = H, R^4 = β-D-Glc

CONCLUSION

A new class of bolaamphiphilic desulfoglucosinolates has been prepared in a few steps and in good yields. However, such compounds showed low water solubilities; *O*-sulfatation of both thiohydroximate functions of compounds **14–18** certainly would help to overcome that difficulty.

EXPERIMENTAL

General methods: DMF was dried on 4 Å molecular sieves followed by distillation under reduced pressure. Methanol was refluxed over magnesium before distillation. Melting points were determined on a Büchi apparatus and were uncorrected. TLC analyses were performed

on aluminium sheets coated with silica gel 60 F 254 Merck. Compounds were visualized by spraying the TLC plates with dilute 15% aqueous sulfuric acid, followed by charring at 150°C for a few minutes. Column chromatography was performed on silica-gel Geduran Si 60 Merck. Optical rotations were recorded on a Perkin Elmer 241 polarimeter in a 1 dm cell at 21°C. ^{1}H and ^{13}C NMR spectra were recorded with Bruker AC-200 or AM-300 spectrometers operating at 200 or 300 MHz and 50 or 75.5 MHz, respectively with tetramethylsilane as internal standard. Elemental analyses were carried out by the Service Central d'Analyses du CNRS (Vernaison, France).

1,8-Octanedial (1): To a solution of *o*-iodobenzoic acid[21,22] (7.30 g, 29.43 mmol) in DMSO (30 mL), 1,8-octanediol (1.62 g, 11.08 mmol) was added and stirring was maintained for four hours. Work-up was performed by dilution with water (150 mL), filtration of the precipitate and extraction of the reaction mixture with Et_2O (3×75 mL). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure to afford the crude product which was purified by column chromatography with EtOAc/petroleum ether (1 : 1 v/v) as the eluent. Compound **1**: 1.36 g (87% yield); liquid; R_f 0.76 (EtOAc/petroleum ether 1 : 1 v/v); ^{1}H NMR ($CDCl_3$) δ 1.28 (m, 4H, 2CH_2), 1.59 (m, 4H, 2CH_2), 2.42 (dt, 4H, $J = 3.6$ Hz, $J = 1.8$ Hz, 2CH_2CHO), 9.76 (t, 2H, $J = 1.8$ Hz, 2C*H*O) was similar to the literature.[26]

1,12-Dodecanedial (2): Prepared as described above from 1,12-dodecanediol (2.02 g, 10 mmol). The crude product was purified by column chromatography with EtOAc/petroleum ether (1 : 2 v/v) as the eluent. Compound **2**: 1.83 g (92% yield); liquid; R_f 0.66 (EtOAc/petroleum ether 1 : 2 v/v); ^{1}H NMR ($CDCl_3$) δ 1.28 (m, 12H, 6CH_2), 1.59 (m, 4H, 2CH_2), 2.42 (dt, 4H, $J = 3.6$ Hz, $J = 1.8$ Hz, 2CH_2CHO), 9.76 (t, 2H, $J = 1.78$ Hz, 2C*H*O) was similar to the literature.[27]

1,8-Octanedial dioxime (3): 1,8-Octanedial (**1**) (1.35 g, 9.50 mmol) was added to a solution of hydroxylamine hydrochloride (3.96 g, 57.0 mmol) and sodium acetate trihydrate (7.76 g, 57.0 mmol) in water (42 mL). After addition of ethanol (250 mL), the solution was stirred for 3 h. Concentration of the solution to 40 mL afforded an insoluble solid which was recovered by filtration, washed with water (10 mL), then with ethanol (5 mL) and with hexane (5 mL). Compound **3**: 1.47 g (90% yield); solid, m.p. 152–153°C (lit.[28] m.p. 155–156°C); ^{1}H NMR (CD_3SOCD_3) δ 1.28–1.43 (m, 8H, 4CH_2), 2.00–2.25 (m, 4H, 2CH_2CH=NOH), 6.63 (t, 2H, $J = 5.4$ Hz, 2C*H*=NOH *Z* isomer 93%), 7.29 (t, 2H, $J = 5.9$ Hz, 2C*H*=NOH *E* isomer 7%), 10.35 (s, 2H, 2CH=NOH *E* isomer 7%), 10.72 (s, 2H, 2CH=NOH *Z* isomer 93%).

1,12-Dodecanedial dioxime (4): 1,12-Dodecanedial (**2**) (0.870 g, 4.39 mmol) was treated as described above. Compound **4**: 0.840 g (84%

yield); solid, m.p. 151°C (lit.[29] m.p. 137–139°C); ^{1}H NMR (CD_3SOCD_3) δ 1.28–1.43 (m, 16H, 8CH_2), 2.10–2.25 (m, 4H, 2CH_2CH=NOH), 6.62 (t, 2H, $J = 4.9$ Hz, 2CH=NOH *Z* isomer 93%), 7.28 (t, 2H, $J = 5.5$ Hz, 2CH=NOH *E* isomer 7%), 10.34 (s, 2H, 2CH=NOH *E* isomer 7%), 10.71 (s, 2H, 2CH=NOH *Z* isomer 93%).

General procedure for the synthesis of *bis*-[(*Z*)-1-(*S*)-β-D-glycopyranosyl] 1,*n*-alkane*bis*-thiohydroximate: The dioxime **3** or **4** (1.0 mmol) was added to a flask containing DMF (15 mL), and a few drops of pyridine; *N*-chlorosuccinimide (0.198 g, 2.0 mmol) was slowly added and the reaction mixture was stirred at r.t. for two days. After addition of the 1-thio-β-D-glycopyranose derivative (**5**, **8**, **10** or **12**) (1.0 mmol), triethylamine (418 μL, 3.0 mmol, 3 eq.) was added dropwise. The mixture was stirred 2 h more, and concentrated. The residue was extracted with CH_2Cl_2, the organic phase washed with water, dried ($MgSO_4$) and concentrated again. The residue was purified by column chromatography.

***Bis*-[2,3,4,6-tetra-*O*-acetyl-1-(*S*)-β-D-glucopyranosyl] 1,8-octane*bis*-thiohydroximate (6) and [(2,3,4,6-tetra-*O*-acetyl-1-(*S*)-β-D-glucopyranosyl) (2,3,4,6-tetra-*O*-acetyl-1-(*S*)-α-D-glucopyranosyl)] 1,8-octane*bis*thiohydroximate (6a):** Obtained as described above from 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranose (**5**) and the dioxime **3**. The product recovered after purification by column chromatography (EtOAc/petroleum ether (1 : 1 − >2 : 1 v/v) still showed the presence of a side-product which was completely eliminated by solid–liquid extraction with Et_2O; the insoluble fraction was pure **6** and the soluble fraction (mixture **6a**/**6**) was then purified again by column chromatography (Et_2O/EtOAc 13 : 1 v/v). Product **6a**: (0.027 g, 3% yield) was an amorphous solid; R_f 0.50 (EtOAc/petroleum ether 2 : 1 v/v), R_f 0.44 (EtOAc/Et_2O 1 : 13 v/v); $[\alpha]_D$ 0° (*c*, 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.42 (m, 4H, 2CH_2), 1.67 (m, 4H, 2CH_2), 2.03, 2.05, 2.06, 2.07, 2.08, 2.09, 2.12, 2.13 (8s, 24H, 8CH_3COO), 2.58 (m, 4H, 2CH_2C=NOH), 3.81 (ddd, 1H, $J_{4,5} = 10.1$ Hz $J_{5,6a} = 2.3$ Hz, $J_{5,6b} = 5.3$ Hz, H-5β), 4.09 (dd, 1H, $J_{5,6b} = 2.0$ Hz, $J_{6a,6b} = 12.2$ Hz, H-6bα), 4.18 (dd, 1H, $J_{6a,6b} = 12.3$ Hz, H-6bβ), 4.23 (dd, 1H, H-6aβ), 4.32 (dd, 1H, $J_{5,6a} = 4.2$ Hz, H-6aα), 4.45 (ddd, 1H, $J_{4,5} = 10.0$ Hz, H-5α), 5.07–5.17 (m, 5H, H-1β,2α,2β,4α,4β), 5.32 (dd, 1H, $J_{2,3} = 8.8$ Hz, $J_{3,4} = 9.2$ Hz, H-3β), 5.46 (dd, 1H, $J_{2,3} = 10.0$ Hz, $J_{3,4} = 9.6$ Hz, H-3α), 6.23 (d, 1H, $J_{1,2} = 5.9$ Hz, H-1α), 8.85 and 8.92 (s, 2H, 2C=NOH). Product **6** (0.646 g, 72% yield) was a solid; m.p. 208°C; R_f 0.50 (EtOAc/petroleum ether 2 : 1 v/v), R_f 0.37 (EtOAc/Et_2O 1/13 v/v); $[\alpha]_D - 16°$ (*c*, 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.42 (m, 4H, 2CH_2), 1.67 (m, 4H, 2CH_2), 2.03, 2.05, 2.06, 2.09 (4s, 24H, 8CH_3COO), 2.58 (m, 4H, 2 CH_2C=NOH), 3.81 (ddd, 2H, $J_{4,5} = 10.0$ Hz, $J_{5,6a} = 2.3$ Hz, $J_{5,6b} = 5.3$ Hz, 2H-5), 4.18 (dd, 2H, $J_{6a,6b} = 12.3$ Hz, 2H-6b), 4.23 (dd, 2H, 2H-6a), 5.03–5.10 (m, 4H, 2H-1,2), 5.12 (dd, 2H, $J_{3,4} = 9.5$ Hz, 2H-4), 5.26–5.34 (m, 2H, 2H-3), 8.28 (s, 2H, 2C=NOH).

Anal. Calcd. for $C_{36}H_{52}N_2O_{20}S_2$ (896.92): C, 48.20; H, 5.84; N, 3.12. Found: C, 48.48; H, 5.98; N, 3.33.

***Bis*-[2,3,4,6-tetra-*O*-acetyl-1-(*S*)-β-D-glucopyranosyl] 1,12-dodecane-*bis*thiohydroximate (7):** Obtained in 75% yield as described above from 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranose (**5**) and the dioxime **4**. The pure product was recovered after purification by column chromatography (EtOAc/petroleum ether (1 : 1 v/v). Product **7**: solid, m.p. 165°C; R_f 0.60 (EtOAc/petroleum ether 1 : 1 v/v); $[\alpha]_D -14^\circ$ (*c*, 1.0, $CHCl_3$); ^{1}H NMR was identical to the one obtained for the compound **6** except δ 1.42 (m, 12H, 6CH_2).

Anal. Calcd for $C_{40}H_{60}N_2O_{20}S_2$ (953.022): C, 50.41; H, 6.35; N, 2.94. Found: C, 50.27; H, 6.18; N, 2.83.

***Bis*-[4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-2,3,6-tri-*O*-acetyl-1-(*S*)-β-D-glucopyranosyl]1,8-octane*bis*thiohydroximate(9):** Obtained as described above from 4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-2,3,6-tri-*O*-acetyl-1-thio-β-D-glucopyranose (**8**) and the dioxime **3**. The pure product **9** was recovered after purification by column chromatography (EtOAc/petroleum ether (7 : 2 v/v). Product **9** (1.237 g, 84% yield) was a solid; m.p. 225°C, R_f 0.48 (EtOAc/petroleum ether 7 : 2 v/v); $[\alpha]_D -23^\circ$ (*c*, 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.40 (m, 2H, 2CH_2), 1.64 (m, 4H, 2CH_2), 1.99, 2.04, 2.06, 2.10, 2.10, 2.11, 2.15 (7s, 42H, 14CH_3COO), 2.49 (m, 4H, 2CH_2C=NOH), 3.69 (ddd, 2H, $J_{4,5} = 9.5$ Hz, $J_{5,6a} = 1.6$ Hz, $J_{5,6b} = 6.0$ Hz, 2H-5), 3.82 (dd, 2H, $J_{3,4} = 8.7$ Hz, 2H-4), 3.88 (ddd, 2H, $J_{4',5'} = 0.5$ Hz, $J_{5',6'a} = 6.5$ Hz, $J_{5',6'b} = 6.5$ Hz, 2H-5′), 4.03–4.14 (m, 6H, 2H-6b,6′a,6′b), 4.45 (dd, 2H, $J_{6a,6b} = 12.4$ Hz, 2H-6a), 4.48 (d, 2H, $J_{1',2'} = 7.7$ Hz, 2H-1′), 4.95 (dd, 2H, $J_{1,2} = 8.0$ Hz, $J_{2,3} = 8.5$ Hz, 2H-2), 4.96 (dd, 2H, $J_{2',3'} = 10.4$ Hz, $J_{3',4'} = 3.3$ Hz, 2H-3′), 4.97 (d, 2H, 2H-1), 5.09 (dd, 2H, 2H-2′), 5.25 (dd. 2H, 2H-3), 5.34 (dd, 2H, 2H-4′), 8.28 (s, 2H, 2C=NO*H*); ^{13}C NMR ($CDCl_3$) δ 20.90, 21.05, 21.05, 21.05, 21.08, 21.18, 21.24 (14C, 14CH_3COO), 27.09, 28.60, 32.44 (6CH_2), 61.19 (2C, 2C-6′), 62.75 (2C, 2C-6), 66.99 (2C, 2C-4′), 69.51 (2C, 2C-2′), 70.78 (2C, 2C-2), 71.13 (2C, 2C-5′), 71.31 (2C, 2C-3′), 74.22 (2C, 2C-3), 76.37 (2C, 2C-4), 76.86 (2C, 2C-5), 81.06 (2C, 2C-1), 101.53 (2C, 2C-1′), 152.55 (2*C*, 2C=NOH), 169.73, 169.6, 170.33, 170.49, 170.57, 170.81, 170.90 (14C, 14CH_3COO).

Anal. Calcd. for $C_{60}H_{84}N_2O_{36}S_2$ (1473.42): C, 48.90; H, 5.75; N, 1.90. Found: C, 48.48; H, 5.92; N, 1.88.

***Bis*-[4-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)-2,3,6-tri-*O*-acetyl-1-(*S*)-β-D-glucopyranosyl] 1,8-octane*bis*thiohydroximate (11):** Obtained as described above from 4-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)-2,3,6-tri-*O*-acetyl-1-thio-β-D-glucopyranose (**10**) and the dioxime **3**. The pure product **11** was recovered after purification by column chromatography (EtOAc/petroleum ether (7 : 2 v/v). Product **11** (86% yield): solid, m.p. 118–120°C; R_f 0.48 (EtOAc/petroleum ether 7 : 2 v/v); $[\alpha]_D +61^\circ$ (*c*, 1.0,

$CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.46 (m, 4H, 2CH_2), 1.69 (m, 4H, 2CH_2), 2.01, 2.03, 2.04, 2.04, 2.06, 2.11, 2.15 (7s, 42H, 14CH_3COO), 2.55 (m, 4H, 2CH_2C=NOH), 3.80 (ddd, 2H, $J_{4,5} = 9.8$ Hz, $J_{5,6a} = 2.4$ Hz, $J_{5,6b} = 5.1$ Hz, 2H-5), 3.99 (ddd, 2H, $J_{4',5'} = 9.6$ Hz, $J_{5',6'a} = 4.1$ Hz, $J_{5',6'b} = 2.1$ Hz, 2H-5′), 4.03 (dd, 2H, $J_{3,4} = 8.9$, $J_{4,5} = 9.8$ Hz, 2H-4), 4.07 (dd, 2H, $J_{6'a,6'b} = 12.5$ Hz, 2H-6′b), 4.24 (dd, 2H, $J_{6a,6b} = 12.1$ Hz, 2H-6b), 4.26 (dd, 2H, 2H-6′a), 4.46 (dd, 2H, 2H-6a), 4.87 (dd, 2H, $J_{1',2'} = 4.0$ Hz, $J_{2',3'} = 10.5$ Hz, 2H-2′), 4.92 (dd, 2H, $J_{1,2} = 9.8$ Hz, $J_{2,3} = 8.9$ Hz, 2H-2), 5.06 (dd, 2H, $J_{3',4'} = 9.5$ Hz, 2H-4′), 5.11 (d, 2H, 2H-1), 5.36 (dd, 2H, 2H-3′), 5.37 (dd, 2H, 2H-3), 5.42 (d, 2H, 2H-1′), 8.68 (s, 2H, 2C=NOH); ^{13}C NMR ($CDCl_3$) δ 21.00, 21.00; 21.00, 21.09, 21.10, 21.22, 21.31 (14C, 14CH_3COO), 27.09, 28.56, 32.53 (6CH$_2$), 61.94 (2C, 2C-6′), 63.47 (2C, 2C-6), 68.34 (2C, 2C-4′), 69.01 (2C, 2C-5′), 69.64 (2C, 2C-3′), 70.45 (2C, 2C-2′), 71.32 (2C, 2C-2), 73.08 (2C, 2C-4), 76.45 (2C, 2C-5), 76.66 (2C, 2C-3), 79.88 (2C, 2C-1), 96.07 (2C, 2C-1′), 152.26 (2C, 2C=NOH), 169.89, 169.89, 170.39, 170.82, 170.99, 170.99, 170.99 (14C, 14CH_3COO).

Anal. Calcd. for $C_{60}H_{84}N_2O_{36}S_2$ (1473.42): C, 48.90; H, 5.75; N, 1.90. Found: C, 48.81; H, 6.00; N, 2.05.

***Bis*-[4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-2,3,6-tri-*O*-acetyl-1-(*S*)-β-D-glucopyranosyl] 1,8-octane*bis*thiohydroximate (13)**: Obtained as described above from 4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-2,3,6-tri-*O*-acetyl-1-thio-β-D-glucopyranose (**12**) and the dioxime **3**. The pure product **13** was recovered after purification by column chromatography (EtOAc/petroleum ether (7 : 2 v/v). Product **13** (57% yield): solid, m.p. 225°C; R_f 0.48 (EtOAc/petroleum ether 7:2 v/v); $[\alpha]_D - 18^\circ$ (*c*, 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.40 (m, 4H, 2CH_2), 1.64 (m, 4H, 2CH_2), 1.98, 2.00, 2.03, 2.03, 2.04, 2.09, 2.11 (7s, 14H, 14CH_3COO), 2.50 (m, 4H, 2CH_2C=NOH), 3.67–3.72 (m, 4H, 2H-5,5′), 3.80 (dd, 2H, $J_{3,4} = 8.9$, $J_{4,5} = 10.1$ Hz, 2H-4), 4.05 (m, 2H, 2H-6b), 4.07 (m, 2H, 2H-6′b), 4.38 (dd, 2H, $J_{5',6'a} = 4.0$ Hz, $J_{6'a,6'b} = 12.5$ Hz, 2H-6′a), 4.49 (dd, 2H, $J_{5,6a} = 1.0$ Hz, $J_{6a,6b} = 12.5$ Hz, 2H-6a), 4.52 (d, 2H, $J_{1',2'} = 7.9$ Hz, 2H-1′), 4.92 (dd, 2H, $J_{2',3'} = 9.1$ Hz, 2H-2′), 5.00–5.05 (m, 4H, 2H-1,2), 5.07 (d, 2H, $J_{3',4'} = 9.4$ Hz, 2H-4′), 5.15 (dd, 2H, 2H-3′), 5.24 (d, 2H, 2H-3), 8.86 (s, 2H, 2C=NOH); ^{13}C NMR ($CDCl_3$) δ 20.94, 20.94; 20.94, 21.04, 21.06, 21.06, 21.23 (14C, 14CH_3COO), 27.09, 28.64, 32.43 (6C, 6CH$_2$), 61.86 (2C, 2C-6′), 62.63 (2C, 2C-6), 68.06 (2C, 2C-4′), 70.69 (2C, 2C-2), 71.97 (2C, 2C-2′), 72.39 (2C, 2C-5′), 73.26 (2C, 2C-3′), 73.94 (2C, 2C-3), 76.60 (2C, 2C-4), 76.70 (2C, 2C-5), 80.08 (2C, 2C-1), 101.23 (2C, 2C-1′), 152.21 (2C, 2C=NOH), 169.65, 169.75, 169.83, 170.35, 170.66, 170.85, 170.95 (14C, 14CH_3COO).

Anal. Calcd. for $C_{60}H_{84}N_2O_{36}S_2$ (1473.42): C, 48.90; H, 5.75; N, 1.90. Found: C, 48.74; H, 5.90; N, 1.99.

***Bis*-[1-(*S*)-β-D-glucopyranosyl] 1,8-octane*bis*thiohydroximate (14):** Compound **6** (1.75 g, 1.95 mmol) was added to MeOH (100 mL) containing a catalytic

amount of MeONa and the suspension was stirred till all the compound was dissolved (16 h). After addition of silica-gel (2 g), the solvent was evaporated and the solid residue was applied at the top of a column-packed with silica-gel; the product was eluted with EtOAc/EtOH/H_2O (8 : 3 : 1 v/v/v). Compound **14** was recovered as a solid (0.962 g, 88% yield): m.p. 182–183°C; R_f 0.50 (EtOAc/EtOH/H_2O 8/3/1 v/v); $[\alpha]_D$ −36° (*c*, 0.5, MeOH); ^{1}H NMR (D_2O) δ 1.44 (m, 4H, 2CH_2), 1.70 (m, 4H, 2CH_2), 2.64 (m, 4H, 2CH_2C= NOH), 3.48 (dd, 2H, $J_{1,2}$ = 9.8 Hz, $J_{2,3}$ = 9.0 Hz, 2H-2), 3.51 (dd, 2H, $J_{3,4}$ = 9.5 Hz, $J_{4,5}$ = 9.6 Hz, 2H-4), 3.58 (ddd, 2H, $J_{5,6a}$ = 2.1 Hz, $J_{5,6b}$ = 5.3 Hz, 2H-5), 3.60 (dd, 2H, 2H-3), 3.76 (dd, 2H, $J_{6a,6b}$ = 12.7 Hz, 2H-6b), 3.93 (dd, 2H, 2H-6a), 5.01 (d, 2H, 2H-1).

Anal. Calcd. for $C_{20}H_{36}N_2O_{12}S_2$ (560.63): C, 42.84; H, 6.47; N, 4.99. Found: C, 42.59; H, 6.69; N, 5.05.

***Bis*-[1-(*S*)-β-D-glucopyranosyl] 1,12-dodecane*bis*thiohydroximate (15):** Compound **7** (0.185 g, 0.20 mmol) was added to MeOH (4 mL) containing a catalytic amount of MeONa and the suspension was stirred for 16 h. After neutralization with an IR 120 (H^+) resin, the solution was concentrated to 1 mL and the product was crystallized by addition of EtOAc. Compound **15**: 0.107 g, 81% yield: amorphous hygroscopic solid: m.p. 82–83°C; R_f 0.62 (EtOAc/EtOH/H_2O 8/3/1 v/v); $[\alpha]_D$ −28° (*c*, 0.6, MeOH); the ^{1}H NMR spectrum was identical to that observed for compound **14** except δ 1.44 (m, 12H, 6CH_2).

Anal. Calcd. for $C_{24}H_{44}N_2O_{12}S_2{\cdot}2.5H_2O$ (661.774): C, 43.55; H, 7.46; N, 4.23. Found: C, 43.49; H, 7.55; N, 4.00.

***Bis*-[4-*O*-β-D-galactopyranosyl-1-(*S*)-β-D-glucopyranosyl] 1,8-octane-*bis*thiohydroximate (16):** Compound **9** (1.75 g, 1.19 mmol) was added to methanol (150 mL) containing a catalytic amount of MeONa. Dissolution occurred after a few minutes and the solution was stirred overnight, becoming like a gel. After a concentration, the residue was dissolved in water and the solution was neutralized with Amberlyst IR 120 (H^+). The pure product **16** (1.02 g, 95% yield) was obtained by concentration: solid, m.p. 225°C; $[\alpha]_D$ −13° (*c*, 0.9, H_2O); ^{1}H NMR (C_5D_5N) δ 1.32 (m, 4H, 2CH_2), 1.75 (m, 4H, 2CH_2), 2.84 (m, 4H, 2CH_2C=NOH), 3.97–4.58 (m, 24H, 2H-2,2′,3,3′,4,4′,5,5′,6a,6′a,6b,6′b), 5.13 (d, 2H, $J_{1',2'}$ = 7.7 Hz, 2H-1′), 5.46 (d, 2H, $J_{1,2}$ = 9.7 Hz, 2H-1), 13.29 (s, 2H, 2C=NO*H*); ^{13}C NMR (C_5D_5N) δ 27.91, 29.32, 32.66 (6C, 6CH_2), 61.84, 62.04 (4C, 2C-6,6′), 70.06 (2C, 2C-4′), 72.46 (2C, 2C-2′), 74.18 (2C, 2C-2), 75.12 (2C, 2C-3′), 77.22 (2C, 2C-5′), 78.24 (2C, 2C-4), 80.71 (2C, 2C-3), 81.40 (2C, 2C-5), 83.30 (2C, 2C-1), 105.70 (2C, 2C-1′), 152.48 (2C, 2*C*=N–OH).

Anal. Calcd. for $C_{32}H_{56}N_2O_{22}S_2{\cdot}H_2O$ (902.93): C, 42.56; H, 6.47; N, 3.10. Found: C, 42.70; H, 6.32; N, 3.10.

***Bis*-[4-*O*-α-D-glucopyranosyl-1-(*S*)-β-D-glucopyranosyl] 1,8-octane*bis*thiohydroximate (17):** Compound **11** (1.45 g, 0.984 mmol) was added to a $MeOH/NEt_3/H_2O$ (2 : 1 : 1 v/v/v) solution (50 mL). The mixture was stirred overnight; after evaporation of the volatiles, the residue was concentrated twice from water (2 × 30 mL) and twice from ethanol (2 × 25 mL), affording compound **17** as a solid (0.906 g, 100% yield). A sample of the product was recrystallized from EtOH. M.p. 148–150°C; $[\alpha]_D$ +60° (*c*, 0.6, H_2O); ^{1}H NMR (D_2O) δ 1.42 (m, 4H, 2CH_2), 1.68 (m, 4H, 2CH_2), 2.62 (m, 4H, 2CH_2C=NOH), 3.39–4.95 (m, 24H, 2H-2,2′,3,3′,4,4′,5,5′,6a,6′a,6b,6′b), 5.00 (d, 2H, $J_{1,2}$ = 9.8 Hz, 2H-1), 5.44 (d, 2H, $J_{1',2'}$ = 3.4 Hz, 2H-1′); ^{13}C NMR (H_2O) δ 27.48, 28.26, 32.17 (6C, 6CH_2), 61.00, 61.15 (4C, 2C-6,6′), 69.82 (2C, 2C-4′), 72.33, 72.63, 73.21, 73.37 (8C, 2C-2,2′,3′,5′), 76.83, 78.07, 79.09 (6C, 2C-3,4,5), 81.93 (2C, 2C-1), 100.21 (2C, 2C-1′), 156.50 (2C, 2*C*=N–OH).

Anal. Calcd. for $C_{32}H_{56}N_2O_{22}S_2{\cdot}2H_2O$ (920.94): C, 41.73; H, 6.57; N, 3.04. Found: C, 41.57; H, 6.73; N, 2.89.

***Bis*-[4-*O*-β-D-glucopyranosyl-1-(*S*)-β-D-glucopyranosyl] 1,8-octane*bis*thiohydroximate (18):** Compound **13** (0.390 g, 0.265 mmol) was added to a $MeOH/Et_3/H_2O$ (2 : 1 : 1 v/v/v) solution (30 mL). The mixture was stirred overnight; after evaporation of the volatiles, the residue was concentrated twice from water (2 × 10 mL) and twice from ethanol (2 × 10 mL), affording compound **18** as a solid (0.239 g), in quantitative yield. Product **18**: m.p. 108°C; $[\alpha]_D$ −18° (*c*, 0.55, MeOH); ^{1}H NMR (DMSO + D_2O) δ 1.31 (m, 4H, 2CH_2), 1.56 (m, 4H, 2CH_2), 2.51 (m, 4H, 2CH_2C=NOH), 2.97–3.63 (m, 24H, 2H-2,2′,3,3′,4,4′,5,5′,6a,6′a,6b,6′b), 4.28 (d, 2H, $J_{1',2'}$ = 7.5 Hz, 2H-1′), 4.72 (d, 2H, $J_{1,2}$ = 9.8 Hz, 2H-1); ^{13}C NMR (DMSO + D_2O) δ 27.69, 27.19, 32.15 (6C, 6CH_2), 60.80 (2C, 2C-6), 61.66 (2C, 2C-6′), 70.67 (2C, 2C-4′), 73.40, 74.01 (4C, 2C-2,2′), 76.97 (4C, 2C-3′,5′), 77.51 (2C, 2C-4), 79.75 (2C, 2C-5), 80.22 (2C, 2C-3), 82.20 (2C, 2C-1), 103.76 (2C, 2C-1′), 152.52 (2C, 2*C*=N–OH).

Anal. Calcd. for $C_{32}H_{56}N_2O_{22}S_2{\cdot}H_2O$ (902.93): C, 42.56; H, 6.47; N, 3.10. Found: C, 42.32; H, 6.53; N, 3.18.

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