195. A New Approach to 5-Thiosugars: 5-Thio-D-Gluconhydroximo-1,5-lactone, Synthesis and Evaluation as β-Glucosidase Inhibitor

by **Philipp Ermert**[1]) and **Andrea Vasella**[1])*

Organisch-Chemisches Institut der Universität Zürich, Winterthurerstrasse 190, CH–8057 Zürich

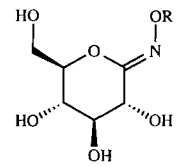
(2.VIII.93)

The thiolactone oxime **10** was synthesized in ten steps from the known tri-*O*-benzylglucose **13**, which was transformed into the oxime **14**, silylated (→**15**), and mesylated (→ **16**). Treatment of **16** with Bu_4NF yielded the L-*ido*-epoxide **17** and the hydroxylamine **18**; the isomeric D-*gluco*-configurated hydroxylamine **20** was prepared from **17**. Reaction of **17** with thiourea yielded the thiirane **19**. Ring opening was best effected with HBr (→**22**·HBr). The *N*-glycosylhydroxylamine **22** was immediately oxidized to **24**, as it reverted to **19**. Similarly, **19** was transformed into the chlorides **21** and **23**. The iodide **25** reacted with TEMPO to afford **29** besides **26** and **30**; nucleophilic substitution of **23**, **24**, or **25** gave unsatisfactory yields of **26** or **27**, and **28**. *Birch* reduction transformed **29** into **10** which was isolated *via* the pentaacetate **32**, which was also transformed into the tetraacetate **33**. The weak activity of **10** as an inhibitor of sweet-almond and *Agrobacter* β-glucosidase is in keeping with categorization of the lactone and lactam oximes **1**–**5** and the 5-thiosugars **6**–**9** as transition-state and substrate analogs, respectively.

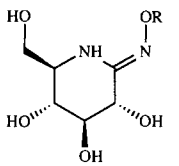
Introduction. – The lactone oxime **1** [1] and the lactam oxime **3** [2] [3] as well as the corresponding *N*-arylcarbamates **2** [1], **4**, and **5** [3] are strong competitive inhibitors of β-glucosidases. *Withers et al.* [4] confirmed the classification of **1** and **2** as (imperfect) transition-state analogs by comparing their K_I values against the wild-type and a mutant (Glu358Asp) β-glucosidase of *Agrobacterium faecalis*. The structural analogy between **1** and **3**, and between their *N*-arylcarbamate derivatives, on the one hand, and their similar behaviour as inhibitors of β-glycosidases, on the other hand, indicate that the nojirilactam derivatives **3**–**5** are also transition-state analogs. This raises the question about the inhibitory activity of the corresponding 5-thiolactone oximes.

The 5-thio-α-D-glucopyranose (**6**) [5] and 5-thio-α-L-fucose (**7**) [6] are reasonably strong inhibitors of α-glucosidase and α-fucosidase, respectively. The rather weak inhibitor 5-thio-D-glucal (**8**) [7] inhibits β-glucosidase and α-mannosidase about as well as glucal; 1-deoxy-5-thiomannose ('1-deoxythiomannojirimycin' [8]) **9** is a weak α-glucosidase inhibitor and does not inhibit sweet-almond β-glucosidase, which is inhibited by deoxymannojirimycin with a K_I of 5.3 mM [9]. The structure of these 5-thiosugars and their K_I values indicate that they act as substrate analogs. If so, replacement of the ring heteroatom in the transition-state analogs **1** and **3** by an S-atom, leading to **10**, should entail a dramatic loss of inhibitory activity. Although but a negative result, this finding would constitute evidence in favour of the classification of **1**–**5** as transition-state analogs, and of **6**–**9** as substrate analogs.

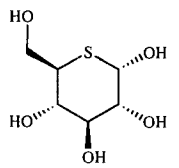
[1]) Present address: Laboratorium für Organische Chemie, ETH-Zentrum, Universitätstrasse 16, CH–8092 Zürich.



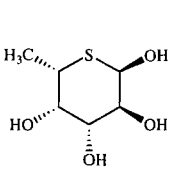
1 R = H
2 R = CONHPh



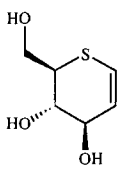
3 R = H
4 R = CONHPh
5 R = $CONHC_6H_4$-*o*-Cl



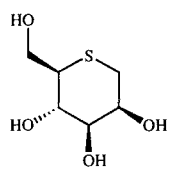
6



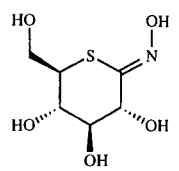
7



8



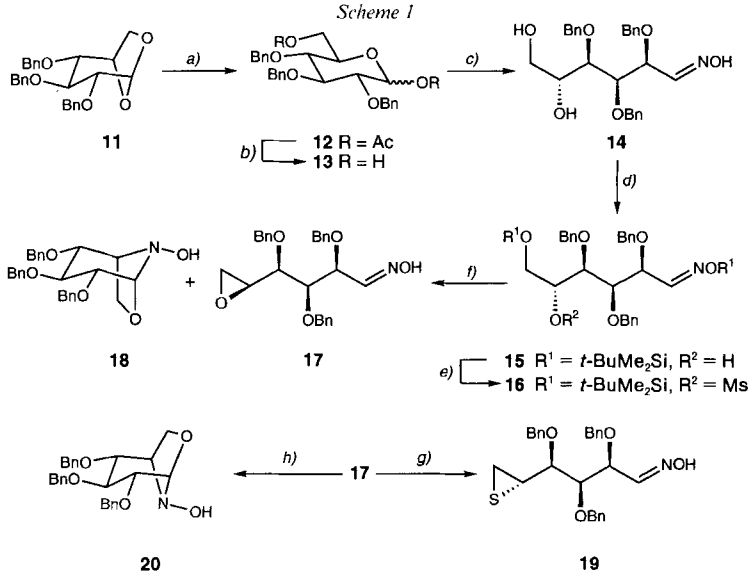
9



10

We thus prepared the 5-thiolactone oxime **10**, particularly as we required its appropriately protected precursors for the synthesis of 1-azi-5-thiopyranoses. The synthesis of **10**, as outlined in *Schemes 1* and *2*, follows an approach which further explores (*cf.* [10] [11]) the potential of inter- and intramolecular displacements at C(5) of pyranose-derived acyclic[2]) oximes, and which should constitute a general approach to the preparation of 5-thioglyconolactone derivatives.

Scheme 1



a) CF_3CO_2H, Ac_2O, 2°, 1 h. *b*) 0.5M aq. H_2SO_4, dioxane, reflux, 205 min, 77% from **11**. *c*) NH_2OH, 96% EtOH, 7.5 h. *d*) *t*-$BuMe_2SiCl$, ^1H-imidazole, DMF, molecular sieves (3 Å), r.t., 40 min, 88% from **13**. *e*) MsCl, pyridine, 0° to r.t., 14 h. *f*) $Bu_4NF \cdot 3\ H_2O$, THF, r.t., 210 min; **17** (81% from **15**) and 7% of **18**. *g*) $(NH_2)_2CS$, MeOH, r.t., 5 d, 86%. *h*) LiCl, THF, reflux, 22 h, 43%.

[2]) For examples of related approaches toward 5-thioaldose derivatives, *cf.* [12–14].

Results and Discussion. – Acid-catalyzed acetolysis of **11** afforded the diacetate **12** [15] [16], which was hydrolyzed [17] to the crystalline tri-*O*-benzylglucose **13** (77%; α-D/β-D *ca.* 1:1). The oxime **14** was obtained [18] almost quantitatively (*Scheme 1*).

Mesylation of the monoalcohol **15** (88%; (*E*)/(*Z*) *ca.* 8:2), obtained by selective di-*O*-silylation [19] of **14**, with a large excess of MsCl in pyridine proceeded smoothly, while a number of other conditions, such as MsCl and Et_3N or $(i\text{-}Pr)_2NEt$ in CH_2Cl_2 led to incomplete conversion and to further transformation of the product **16**. The mesylate **16** was desilylated with $Bu_4NF \cdot 3\ H_2O$ in THF to afford the crystalline L-*ido*-oxirane **17** (81% from **15**; (*E*)/(*Z*) *ca.* 7:3) and the hydroxylamine **18** (7% from **15**), possessing a skeleton similar to that of tropane alkaloids such as the calystegines [20] [21]. The intermediates **14**–**16** were sufficiently pure to be directly transformed in yields which compare well to those obtained from pure compounds, while the epoxide **17** was best chromatographed, direct crystallization being difficult. The hydroxylamine **18** is presumably formed by intramolecular nucleophilic substitution by the oxyimino group either of the mesylate **16** or of the oxirane **17**, leading to a nitrone which reacts further by intramolecular nucleophilic addition of the primary OH group. Inter- and intramolecular nitrone formation from epoxides and oximes [22], and from epoxyoximes [23], respectively, and ring-chain tautomerism of *N*-(β-hydroxyalkyl)aldononitrones by a formal 5-*endo*-*trig* process are well known [24]. The configuration of **18** could not be unambiguously deduced from the ^{1}H-NMR data, since similar ^3J values are expected for **18** (derived from the mesylate **16**) in a $^4C_1$ conformation and for **20** (derived from the oxirane **17**) in a $B_{N,3}$ conformation. As treatment of **17** with LiCl [23] in boiling THF produced the diastereoisomeric hydroxylamine **20** (43%), **18** must possess the L-*ido*- and **20** the D-*gluco*-configuration.

The *O*-silylaldoxime or aldoxime function of **15**–**17** and **19** is evidenced by characteristic *d*'s between 6.9 and 7.6 ppm and C(1) signals at 149–155 ppm. The configuration of the C=N bond of the major and minor diastereoisomers of these compounds is assigned on the basis of chemical-shift differences of the H–C(1) and H–C(2) signals, with H–C(1) of the major isomer resonating at lower and H–C(2) at higher field than the corresponding H of the minor isomer [25] [26].

The presence of the oxirane ring in **17** is evidenced by the shift to higher fields (as compared to the corresponding signals of **15** or **16**) of the H–C(5), H–C(6), and H′–C(6) signals, and by the small value for the geminal coupling constant (4.8 or 4.9 Hz for the (*E*)- or (*Z*)-isomer, resp.) for H–C(6) and H′–C(6). The constitution of a 1,6-anhydro-5-deoxy-5-(hydroxyamino)pyranose is assigned to **18** on the basis of signals of 3 Bn groups, 7 H of the carbohydrate skeleton and 1 CD_3OD exchangeable H (OH bands at 3580 and at 3390 cm^{-1}). In the ^{13}C-NMR spectrum, a *d* is observed at 95.87 ppm, in keeping with the presence of a O,N-substituted C-atom; the mass spectrum shows $[M + H]^+$ at *m/z* 448. Osmometric molecular-weight determination confirms the monomeric nature of **18**.

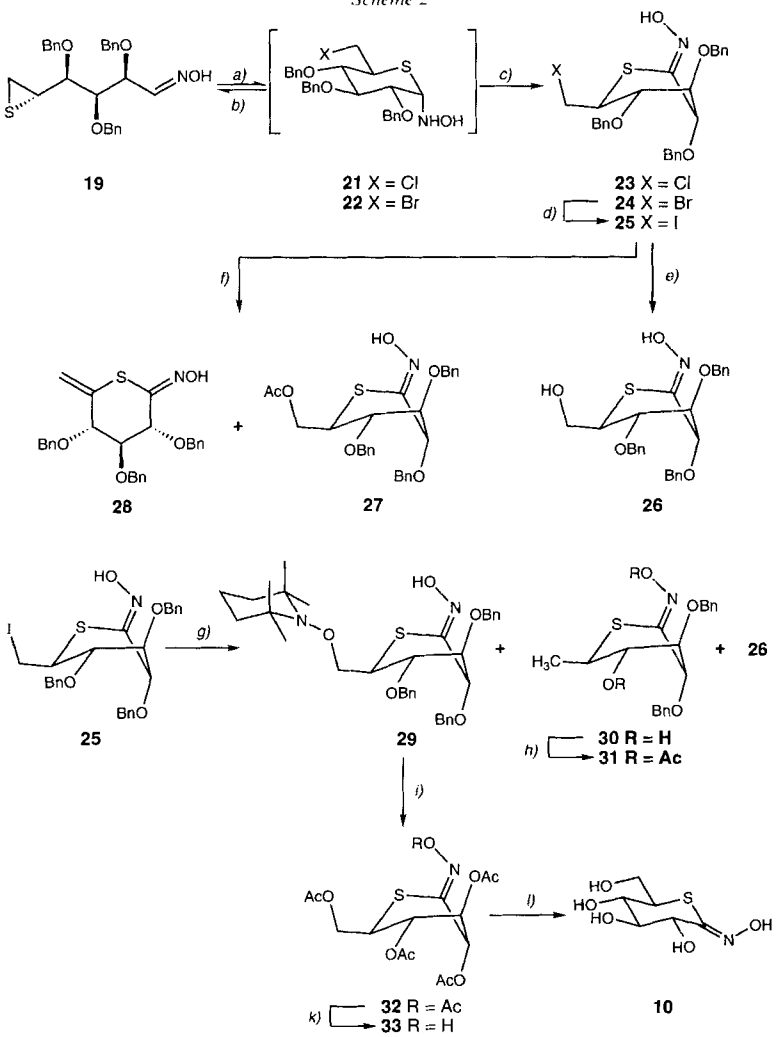
The D-*gluco*-thiirane **19** was obtained in 86% yield ((*E*)/(*Z*) *ca.* 8:2) by exposing **17** to thiourea in MeOH [27] [12]. Conversion of the oxirane **17** into the thiirane **19** causes an upfield shift for the signals of C(5) and C(6).

Acid or base-catalyzed ring opening of **19** with O-nucleophiles went along with formation of other products, among them 2,3,4-tri-*O*-benzyl-5-thio-D-glucose, or with formation of complex mixtures. Good results (*Scheme 2*) were obtained with anhydrous HCl in dioxane or HBr in MeOH, which converted **19** into the salts of the hydroxylamines **21** or **22**, respectively. After neutralisation, the hydroxylamines reverted partially back to **19**; this process occurred within hours for the bromide **22** (as detected by TLC[3]).

[3]) After 30 min, **19** became visible (5% vanillin in H_2SO_4) besides **22** as a characteristic yellow spot, which was preponderant after 40 h.

Thus, **21** and **22** were immediately oxidized by active MnO_2 [28] to give the 6-halothiolactone oximes **23** (73–81%) and **24** (65–80%), respectively[4]). The iodide **25** (86%) was obtained from the bromide **24** with NaI in boiling acetone. Conversion of the chloride **23** proceeded only very slowly under these conditions to yield, after 24 h, a 85:15 mixture of **23** and **25**.

Scheme 2



a) 15% HCl in dioxane, r.t., 75 min; or: LiBr, H_2SO_4, MeOH, 0° to r.t., 14 h. *b*) $NaHCO_3$. *c*) MnO_2, MeOH, r.t., 50 min, **23** (73–81% from **19**); or MnO_2, MeOH, AcOEt, r.t., 30 min, **24** (65–80% from **19**). *d*) NaI, acetone, reflux, 4 h, 86%. *e*) KNO_2, DMF, 110–120°, 200 min, 43%. *f*) CsOAc, [18]crown-6, DMI, 80–90°, 145 min; **27** (42% from **24**) and 35% of **28**. *g*) TEMPO, Bu_3SnH, benzene, r.t., 4 h; 56% of **29**; or 47% of **29**, 12% of **30**, and 7% of **26**. *h*) Ac_2O, pyridine, r.t., 18 h. *i*) Na, NH_3, THF; Ac_2O, pyridine; 78%. *k*) Pyridine hydrochloride, MeOH, $CHCl_3$, r.t., 2 d, 70%. *l*) NaOMe, MeOH, r.t., 1 h, 74%.

[4]) Reaction of **19** with conc. aqueous HCl solution or with 48% aqueous HBr solution in dioxane, followed by oxidation of the intermediary hydroxylamines, produced **23** and **24** in yields of *ca.* 50% only.

The displacement of the halide atom of **23**, **24**, or **25** gave unsatisfactory yields. Reaction of either **23**, **24**, or **25** with KNO_2 produced the alcohol **26** in yields of only 40–45%; **26** was also obtained in poor yields (23%) by treating **25** with KO_2 [29] [30]. The reaction of **24** with CsOAc in 1,3-dimethylimidazolidin-2-one (DMI) produced **27** in 42% yield, besides 35% of the alkene **28**; other conditions gave even less acetate. The best results were obtained by treating **25** with 2,2,6,6-tetramethylpiperidin-1-oxyl radical (TEMPO) [31] [32] in the presence of Bu_3SnH and afforded **29** (56%), the yield reflecting the laborious purification and the formation of by-products. The by-products were isolated in a preliminary experiment performed under slightly different conditions yielding 47% of **29**, 12% of **30**, and 7% of **26**.

Birch reduction of **29** gave **10**, which was isolated *via* the pentaacetate **32**. It was not possible to directly isolate **10**, as it was contaminated with an impurity, presumably 2,2,6,6-tetramethylpiperidine hydrochloride. Workup of the crude acetylation mixture and purification usually produced a 3:1 mixture of pentaacetate **32** and tetraacetate **33**; reacetylation (Ac_2O/pyridine) afforded pure **32**[5]) (78%), which was deacetylated (NaOMe/MeOH) to give **10** (74%). A pure sample of **33** was prepared by treating **32** with pyridine hydrochloride in MeOH/$CHCl_3$.

The structure of the halides **23** and **24** is evidenced by their MS which show the characteristic isotope distribution of the signals of $[M + NH_4]^+$ and $[M + H]^+$ or $[M + H]^+$, respectively. $[M + H]^+$ of **25** is found at m/z 590. In the ^{13}C-NMR spectra, the signals of C(6) are found at 6.75 (**25**), 32.82 (**24**), 43.99 (**23**), and 62.48 ppm (**26**). A CD_3OD-exchangeable t at 2.26 ppm is found in the ^{1}H-NMR spectrum of **26**, indicating the presence of a primary OH group. The signals of H–C(6) and H'–C(6) of **27** are shifted downfield by *ca.* 0.5 ppm, as compared to those of **26**. The structure of **28** is evidenced by the MS ($[M + H]^+$ at m/z 462) and the ^{1}H-NMR spectrum, which shows two d's at 5.57 and 5.71 ppm, characterized by the typical allylic coupling constant of 1.5 or 1.7 Hz, respectively.

The structure of **29** was established by X-ray analysis[6]). Notable bond lengths are S–C(1) 1.754 Å, S–C(5) 1.840 Å, and N(1)–C(1) 1.285 Å. The torsion angles S–C(1)–N(1)–O(1) and O(1)–N(1)–C(1)–C(2) are 3.3 and 177.6°, respectively, indicating these atoms to be in the same plane. The values found for C(2)–C(3)–C(4)–C(5) and C(2)–C(1)–S–C(5) and 26.3 and 13.2°, respectively, and are in keeping with the thiolactone oxime **29** adopting a distorted $B_{2,5}$ solid-state conformation as clearly visible from the ORTEP representation (*Fig. 1*). The H,H coupling constants (see *Table*) indicate a $B_{2,5}$ conformation in $CDCl_3$ solution. Similar ^3J values are observed for compounds **23**–**27**, evidencing that these compounds also adopt a $B_{2,5}$ conformation in solution. The ^{13}C-NMR chemical-shift values for C(1) of **29** and **23**–**26** are very similar to each other ($\Delta\delta$ < 1 ppm), and the (*Z*)-configuration[7]) was assigned to all these compounds, considering that chemical-shift values for the imino-C atom of (*E*)- and (*Z*)-lactone oximes or lactone-oxime phosphates differ by *ca.* 8–12 ppm [36].

---

[5]) Co-evaporation of the original acetylation mixture with toluene followed by aqueous workup and FC yielded **32**, contaminated with variable amounts of another impurity, probably acetamide.

[6]) Atomic coordinates and bond lengths and angles were deposited with the *Cambridge Crystallographic Data Center*, University Chemical Laboratory, 12 Union Road, Cambridge CB2 1EW, England.

[7]) *S*-Substituted thiohydroxamic acids are known to show a preference for the (*Z*)-form, for leading ref., see [33]; X-ray structures *e.g.* [34] [35].

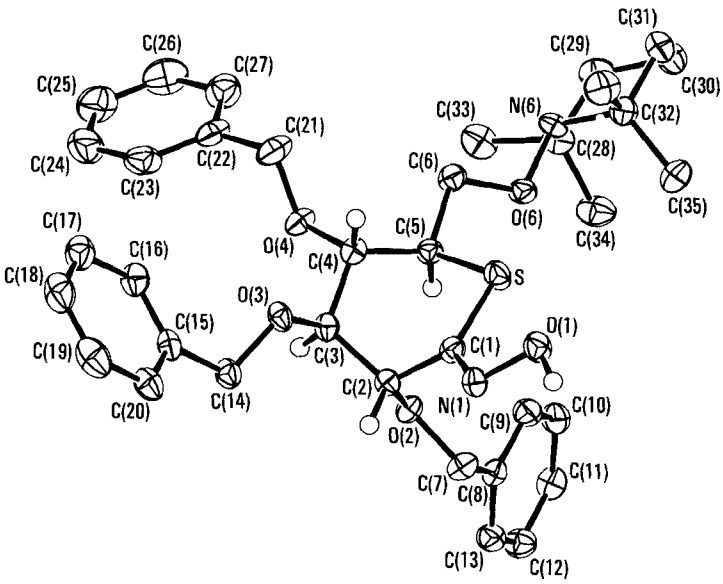


Fig. 1. *ORTEP representation of compound* **29**

Table. *H,H-Coupling Constants of Compounds* **23**–**27**, **29**, **32** *and* **10**

	$J(2,3)$	$J(3,4)$	$J(4,5)$	$J(5,6)$	$J(5,6')$	$J(6,6')$	$J(2,4)$
23	2.5	3.9	10.6	4.5	4.5		
24	2.6	3.8	10.5	5.1	3.9		
25	2.5	3.6	10.3	6.0	3.1	10.6	
26	2.1	4.5	10.8	4.6	4.6		
27	2.6	3.6	10.9	6.1	3.0	11.8	
29	2.4	3.6	10.9	8.0	3.3	9.1	
32	3.4	3.7	11.0	4.6	4.6		0.6
10	5.8	6.5	9.8	6.3	3.3	12.1	

The presence of the Me group of **30** is indicated by a *d* at 1.36 ppm in the ^{1}H-NMR spectrum, which also shows signals of 2 Bn groups. $[M + H]^+$ is found at m/z 374. Further evidence for the structure of **30** is obtained from the ^{1}H-NMR spectrum of the diacetate **31**, showing the signal of H–C(4) shifted to lower fields by *ca.* 1.4 ppm. A *qd* at 3.86 ppm is assigned to H–C(5) of **31**.

The pentaacetate **32** adopts a distorted $B_{2,5}$ conformation in $CDCl_3$, as indicated by the H,H coupling constants. The notable long-range coupling $^4J(2,4)$ (0.6 Hz) would not be expected for an ideal $B_{2,5}$ conformer. The ^{1}H-NMR spectrum of **33** indicates the presence of 4 AcO groups and of a NOH function (exchangeable H at 8.26 ppm). The signal of C(1) is shifted upfield by 9 ppm as compared to the corresponding resonance of **32**.

The structure of **10** was established by X-ray analysis[6]) (*Fig. 2*). The configuration of the thiolactone oxime is again (*Z*). There are two symmetry-independent molecules in the asymmetric unit, but there are no significant differences between their conformations. The molecules only differ in the way they are H-bonded to neighbouring molecules. In the solid state, **10** adopts a flattened $^4C_1$ conformation as indicated by the torsional angles C(2)–C(1)–S(1)–C(5) and C(2)–C(3)–C(4)–C(5) which are −34.2 (−30.9)° or 62.5

(63.1)°, respectively. The atoms O(1), N(1), C(1), and S(1) are in the same plane with C(2) slightly above it, as shown by the torsion angles S(1)–C(1)–N(1)–O(1) and O(1)–N(1)–C(1)–C(2) of −1.6 (−1.4)° and −170.9 (−172)°, respectively. These torsion angles compare well with those found for the lactam oxime **3** [3], but C(2) of **3** is in the same plane as the lactam-oxime function, indicating a more half-chair-like conformation of **3**. Notable bond lengths of **10** are S(1)–C(1) 1.760 (1.765) Å, S(1)–C(5) 1.822 (1.827) Å, and C(1)–N(1), which is 1.277 (1.279) Å. The values of the vicinal coupling constants $J(2,3)$ and $J(3,4)$ (5.8 and 6.5 Hz) of **10** suggest a mixture of conformers in D_2O solution, probably $B_{2,5}$ and $^4H_3$ or $^4C_1$.

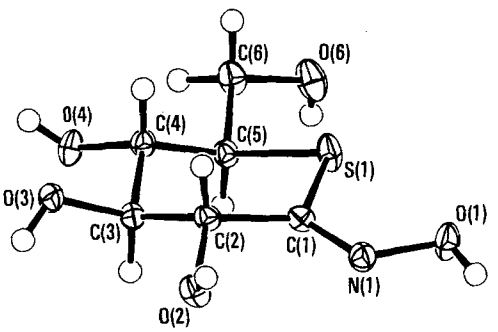


Fig. 2. *ORTEP representation of compound* **10**

The thiolactone oxime **10** is a very weak competitive inhibitor of sweet-almond β-glucosidase ($K_I \approx 50$ mM, pH 6.8) and of *Agrobacterium* β-glucosidase ($K_I = 10.8$ mM, pH 7.0); it binds to the enzymes several hundred times more weakly than the lactone oxime **1**, and several thousand times more weakly than the lactam oxime **3**, in keeping with the transition-state character of **1**, **3**, and their derivatives, and the character of substrate analogs of the 5-thiosugars **6**–**9**.

We thank Prof. Dr. *S. Withers*, University of British Columbia, Department of Chemistry, 2036 Main Mall, Vancouver, B.C., Canada V6T 1Z1, for measuring the inhibition constant against *Agrobacterium* β-glucosidase, Dr. *A. Linden*, Organisch-chemisches Institut, Universität Zürich, Winterthurerstrasse 190, CH–8057 Zürich, for the X-ray structure determinations, and the *Swiss National Science Foundation* and *F. Hoffmann-La Roche AG*, Basel, for generous support.

Experimental Part

General. Solvents were distilled before use. Active MnO_2 was prepared following a procedure by *Attenburrow* [28]. Normal workup implies distribution of the crude product between the indicated org. solvent and H_2O, drying of the org. layer ($MgSO_4$), filtration, and evaporation of the filtrate. TLC: *Merck* silica gel *60F-254* plates; detection by heating with 5% vanillin in conc. H_2SO_4 or with mostain [37] (400 ml of 10% H_2SO_4 soln., 20 g of $(NH_4)_6Mo_7O_{24}\cdot 6H_2O$, 0.4 g of $Ce(SO_4)_2$). Flash chromatography (FC): silica gel *Merck 60* (0.04–0.063 mm). M.p.: uncorrected. NMR Spectra: ^1H at 300 MHz, and ^{13}C at 50 MHz, if not indicated otherwise; chemical shifts δ in ppm and coupling constants J in Hz.

*2,3,4-Tri-*O*-benzyl-*D*-glucopyranose* [17] [38] (**13**). CF_3CO_2H (23.5 ml) was added at 2° to a soln. of **11** (20.0 g, 46.3 mmol) in Ac_2O (340 ml), and stirring was continued at 2° for 60 min. The soln. was diluted with toluene (100 ml) and evaporated (bath 40–45°). The residue was co-evaporated 4 times with toluene (150 ml each) and dried *i.v.* for 60 min. To a soln. of the remaining yellow oil (**12**) in dioxane (745 ml) was added 0.5M aq. H_2SO_4 (85 ml). The

soln. was refluxed for 205 min. Sat. aq. $NaHCO_3$ soln. (150 ml) was added (until pH 6 was reached), and 600 ml of the solvent were removed by evaporation. The resulting suspension was treated with H_2O (1 l) and cooled to 10° to give a precipitate which was collected. Recrystallisation from $EtOH/H_2O$ and then from $CHCl_3$/hexane gave **13** (13.9 g, 67%; α-D/β-D *ca.* 1:1) as a colorless solid. M.p.77–81°. FC (hexane/AcOEt 1:2) of the mother liquor gave **13** (2.09 g, 10%; α-D/β-D *ca.* 1:1) as a colorless solid. M.p. 79–81°. R_f (hexane/AcOEt 1:2) 0.21. IR ($CHCl_3$): 3600*m*, 3410*m* (br.), 3070*w*, 3010*m*, 2930*m*, 2880*m*, 1955*w*, 1875*w*, 1810*w*, 1500*m*, 1460*m*, 1400*w*, 1360*m*, 1245*w*, 1150*s*, 1080*s* (br.), 1030*s*, 915*w*, 835*w*, 700*s*. ^{1}H-NMR ($CDCl_3$): 1.88 (*t*, $J \approx 6$, 0.5 H, exchange with CD_3OD, OH–C(6)); 2.35 (br. *s*, 0.5 H, exchange with CD_3OD, OH–C(6)); 3.30–3.42 (*m*, 7 H, 6 H after addn. of CD_3OD); 4.61–4.97 (*m*, 6.5 H); 5.18 (*t*, $J \approx 3$, 0.5 H, *d* after addn. of CD_3OD, H_{eq}–C(1)); 7.25–7.37 (*m*, 15 arom. H). ^{13}C-NMR ($CDCl_3$): 61.50 (*t*); 61.83 (*t*); 70.76 (*d*); 72.63 (*t*); 74.54 (*t*); 74.79 (2*t*); 75.17 (*d*); 75.43 (2*t*); 77.59 (*d*); 77.83 (*d*); 79.89 (*d*); 81.36 (*d*); 83.05 (*d*); 84.27 (*d*); 90.55 (*d*); 97.05 (*d*); 127.19–128.39 (several *d*); 137.74–138.44 (several *s*). CI-MS (NH_3): 469 (25), 468 (100, $[M + NH_4]^+$), 450 (17, M^+).

*(E)- and (Z)-2,3,4-Tri-*O*-benzyl-6-*O*-[(*tert*-butyl)dimethylsilyl]-*D*-glucose Oxime O-[(tert-Butyl)dimethylsilyl] Ether* (**15**). $NH_2OH \cdot HCl$ (43.75 g, 630 mmol) was added at 55° to a stirred soln. of Na (7.7 g, 335 mmol) in 96% aq. EtOH (1.4 l). Stirring was continued for 5 min and was followed by addition of **13** (35 g, 78 mmol) and 96% aq. EtOH (0.5 l). The mixture was stirred for 7.5 h at 55–60° and filtered. The residue was washed with AcOEt, and the combined filtrates and washings were concentrated. Normal workup (AcOEt, H_2O) gave crude **14** (36.8 g). Yellow oil.

Molecular sieves (*Union Carbide*, type 3 Å, powder; 36 g) were dried in the reaction vessel at 130–140° *i.v.* for 18 h. After cooling to r.t., 1*H*-imidazole (26.3 g, 387 mmol) was added and drying *i.v.* continued for 30 min at r.t. A soln. of **14** (36.0 g, 77 mmol) in dry DMF (360 ml) and *t*-BuMe$_2$SiCl (29.2 g, 193 mmol) were added. The mixture was stirred for 40 min and filtered; the filtrate was poured into H_2O (1 l) and extracted with hexane. The org. layers were washed (H_2O), dried ($MgSO_4$), and evaporated to give a yellow clear oil (57 g) which was filtered through silica gel to give **15** (50.0 g, 93%; *(E)*/*(Z)* *ca.* 8:2). Colorless oil. FC (hexane/AcOEt 9:1) of crude **15** (861 mg) gave pure **15** (815 mg). R_f (hexane/AcOEt 9:1) 0.26. $[\alpha]_D^{25} = +20.2$ (*c* = 0.865, $CHCl_3$). IR ($CHCl_3$): 3550*m* (br.), 3090*w*, 3070*w*, 3000*m*, 2960*s*, 2930*s*, 2890*s*, 2860*s*, 1595*w*, 1455*m*, 1390*w*, 1360*w*, 1250*m*, 1080*s* (br.), 1030*m*, 1010*w*, 915*s*, 840*s*. ^{1}H-NMR ($CDCl_3$): 0.0–0.14 (*m*, 12 H, Me_2Si); 0.85–0.92 (*m*, 18 H, *t*-BuSi); 2.58 (*d*, $J = 5.8$, 0.8 H, exchange with CD_3OD, OH–C(5) *(E)*); 2.66 (*d*, $J = 4.6$, 0.2 H, exchange with CD_3OD, OH–C(5) *(Z)*); 3.59–3.95 (*m*, 5 H); 4.37–4.86 (*m*, 6.8 H, PhCH_2, H–C(2) *(E)*); 5.12 (*dd*, $J = 4.9$, 6.6, 0.2 H, H–C(2) *(Z)*); 7.08 (*d*, $J = 6.6$, 0.2 H, H–C(1) *(Z)*); 7.14–7.32 (*m*, 15 arom. H); 7.52 (*d*, $J = 8.1$, 0.8 H, H–C(1) *(E)*). ^{13}C-NMR ($CDCl_3$): major isomer: −5.50 to −5.16 (several *q*); 17.98–18.27 (several *s*); 25.63–26.13 (several *q*); 63.79 (*t*); 71.08 (*t*); 71.08 (*d*); 73.40 (*t*); 74.38 (*t*); 76.84 (*d*); 77.58 (*d*); 79.32 (*d*); 127.00–128.16 (several *d*); 137.44–138.40 (several *s*); 153.19 (*d*); minor isomer: 71.81 (*d*); 71.99 (*t*); 73.73 (*t*); 74.49 (*t*); 154.50 (*d*). CI-MS (NH_3): 696 (20), 695 (51), 694 (100, $[M + H]^+$), 562 (24). Anal. calc. for $C_{39}H_{59}NO_6Si_2$ (694.080): C 67.49, H 8.57, N 2.02; found: C 67.30, H 8.85, N 2.02.

*(E)- and (Z)-2,3,4-Tri-*O*-benzyl-6-*O*-[(*tert*-butyl)dimethylsilyl]-5-*O*-(methylsulfonyl)-*D*-glucose Oxime* O*-[(*tert*-Butyl)dimethylsilyl] Ether* (**16**), *(E)- and (Z)-5,6-Anhydro-2,3,4-tri-*O*-benzyl-*L*-idose Oxime* (**17**), *and 1,6-Anhydro-2,3,4-tri-*O*-benzyl-5-*N*-hydroxy-β-*L*-idopiperidinose* (**18**). MsCl (8.31 g, 73 mmol) was added to a stirred ice-cold soln. of **15** (5.03 g, 7.3 mmol) in dry pyridine (100 ml); stirring was continued for 14 h at 0°→r.t. The soln. was concentrated to about half of its volume, poured into sat. aq. $NaHCO_3$ soln., stirred for 20 min, and extracted with AcOEt. The org. layers were washed (sat. aq. $NaHCO_3$ soln., H_2O), dried ($MgSO_4$), and evaporated. The remaining oil was co-evaporated with toluene and dried *i.v.* for 30 min: crude **16** (6.05 g). Yellow oil. An anal. sample was co-evaporated with $CHCl_3$ and dried *i.v.* R_f (hexane/AcOEt 85:15) 0.30. ^{1}H-NMR ($CDCl_3$): −0.03 to 0.18 (*m*, 12 H, Me_2Si); 0.82–0.99 (*m*, 18 H, *t*-BuSi); 2.81 (*s*, 2.4 H, MsO *(E)*); 2.83 (*s*, 0.6 H, MsO *(Z)*); 3.77–3.90 (*m*, 2.2 H); 3.97 (*dd*, $J = 4.1$, 11.4, 0.8 H); 4.03 (*t*, $J = 4.1$, 0.8 H); 4.13 (*dd*, $J = 3.1$, 6.1, 0.2 H); 4.32 (*dd*, $J = 6.1$, 8.0, 0.8 H, H–C(2) *(E)*); 4.38–4.69 (*m*, 6 H, PhCH_2); 4.72–4.79 (*m*, 1 H, H–C(5) *(E/Z)*); 5.01 (*dd*, $J = 4.5$, 6.5, 0.2 H, H–C(2) *(Z)*); 7.09 (*d*, $J = 6.5$, 0.2 H, H–C(1) *(Z)*); 7.21–7.30 (*m*, 15 arom. H); 7.56 (*d*, $J = 8.0$, 0.8 H, H–C(1) *(E)*).

A soln. of $Bu_4NF \cdot 3H_2O$ (5.72 g, 18 mmol) in THF (70 ml) was added to a soln. of crude **16** (6.05 g) in THF (50 ml). The soln. was kept at r.t. for 210 min and evaporated. FC (hexane/AcOEt 3:1) of the residue gave **17** (2.63 g, 81%; *(E)*/*(Z)* *ca.* 7:3; yellowish solid) and **18** (0.24 g, 7%; colorless solid).

An anal. sample of **17** was obtained by recrystallisation in AcOEt/pentane. R_f (hexane/AcOEt 1:1) 0.43. M.p. 76–78°. $[\alpha]_D^{25} = -2.9$ (*c* = 0.86, $CHCl_3$). IR ($CHCl_3$): 3580*m*, 3340*m* (br.), 3060*m*, 3005*m*, 2870*m*, 1950*w*, 1875*w*, 1810*w*, 1495*m*, 1455*m*, 1395*m*, 1355*w*, 1250*m*, 1090*s*, 1065*s*, 1030*s*, 920*m*, 880*w*, 850*w*, 820*w*, 700*s*. ^{1}H-NMR ($CDCl_3$): 2.36 (*dd*, $J = 2.7$, 4.8, 0.7 H, H–C(6) *(E)*); 2.41 (*dd*, $J = 2.7$, 4.9, 0.3 H, H–C(6) *(Z)*); 2.49 (*t*, $J \approx 4.5$, 0.7 H, H′–C(6) *(E)*); 2.56 (*t*, $J \approx 4.6$, 0.3 H, H′–C(6) *(Z)*); 3.09–3.16 (*m*, 1 H, H–C(5) *(E/Z)*); 3.25 (*dd*, $J = 4.2$, 6.8,

0.7 H, H–C(4) (*E*)); 3.35 (*dd*, *J* = 5.6, 6.7, 0.3 H, H–C(4) (*Z*)); 3.68 (*dd*, *J* = 4.2, 5.8, 0.7 H, H–C(3) (*E*)); 3.85 (*dd*, *J* = 4.1, 5.5, 0.3 H, H–C(3) (*Z*)); 4.36 (*dd*, *J* = 5.8, 7.7, 0.7 H, H–C(2) (*E*)); 4.41–4.82 (*m*, 6 H, PhCH_2); 5.09 (*dd*, *J* = 4.0, 6.5, 0.3 H, H–C(2) (*Z*)); 6.94 (*d*, *J* = 6.5, 0.3 H, H–C(1) (*Z*)); 7.24–7.36 (*m*, 15.7 H, arom. H, NOH (*E*)); 7.43 (*d*, *J* = 7.7, 0.7 H, H–C(1) (*E*)); 7.56 (*s*, 0.3 H, NOH (*Z*)); irrad. at 7.43→change at 4.36 (*d*); irrad. at 6.94→change at 5.09 (*d*); irrad. at 3.09–3.16→change at 3.35, 3.25, 2.56, 2.49 (*d*), 2.41, 2.36 (*d*). ^{13}C-NMR ($CDCl_3$): major isomer: 42.93 (*t*); 52.78 (*d*); 71.16 (*t*); 72.20 (*t*); 74.18 (*t*); 76.37 (*d*); 79.92 (*d*); 80.19 (*d*); 127.39–128.33 (several *d*); 137.26–137.75 (several *s*); 149.28 (*d*); minor isomer: 43.36 (*t*); 52.55 (*d*); 70.70 (*d*); 71.93 (*t*); 72.49 (*t*); 74.48 (*t*); 151.10 (*d*). CI-MS (NH_3): 449 (28), 448 (100, $[M + H]^+$), 447 (42), 430 (12), 303 (10), 195 (30), 133 (12), 116 (45), 108 (26), 106 (11), 86 (10). Anal. calc. for $C_{27}H_{29}NO_5$ (447.532): C 72.46, H 6.53, N 3.13; found: C 72.34, H 6.31, N 3.04.

An anal. sample of **18** was obtained by recrystallisation in benzene/pentane. R_f (hexane/AcOEt 1:1) 0.29. M.p. 134°. $[\alpha]_D^{25} = +29.6$ (*c* = 1.13, $CHCl_3$). IR ($CHCl_3$): 3580*m*, 3390*m* (br.), 3060*w*, 3030*w*, 3005*m*, 2900*m*, 2870*m*, 1950*w*,1875*w*, 1810*w*, 1495*m*, 1455*m*, 1365*m*, 1315*w*, 1190*w*, 1110*s*, 1090*s*, 1070*s*, 1030*m*, 985*w*, 960*m*, 905*m*, 850*m*, 700*s*. ^{1}H-NMR ($CDCl_3$): 3.53 (*m*, 1 H); 3.62–3.70 (*m*, 2 H); 3.78 (*m*, 1 H); 3.98 (*dd*, *J* = 4.6, 7.8, 1 H); 4.06 (*d*, *J* = 7.7, 1 H); 4.64 (*s*, 2 H, PhCH_2); 4.64 (*d*, *J* = 11.9, PhCH_2); 4.71 (*d*, *J* = 12.0, PhCH_2); 4.80 (*s*, 2 H, PhCH_2); 5.00 (br. *s*, 1 H); 5.33 (*s*, exchange with CD_3OD, NOH); 7.24–7.37 (*m*, 15 arom. H). ^{1}H-NMR (C_6D_6): 3.53 (*t*, *J* ≈ 3.9, H–C(5)); 3.63 (*dd*, *J* = 1.4, 7.8, H–C(2)); 3.71 (*dd*, *J* = 3.7, 8.1, H–C(4)); 3.89 (*t*, *J* ≈ 8.0, H–C(3)); 4.05 (*dd*, *J* = 4.5, 7.4, H–C(6)); 4.12 (*d*, *J* = 7.5, H′–C(6)); 4.33 (*d*, *J* = 12.1, PhCH_2); 4.37 (*d*, *J* ≈ 12, PhCH_2); 4.41 (*d*, *J* = 12.1, PhCH_2); 4.51 (*d*, *J* = 12.1, PhCH_2); 4.75 (*s*, exchange with CD_3OD, NOH); 4.83 (*d*, *J* = 11.5, PhCH_2); 4.90 (*d*, *J* = 11.5, PhCH_2); 5.10 (br. *s*, H–C(1)); 7.03–7.35 (*m*, 15 arom. H); irrad. at 3.89→change at 3.71 and 3.63; irrad. at 3.71→change at 3.53 (*d*) and 3.89; irrad. at 3.53→change at 3.71 (*d*, *J* ≈ 8) and 4.05 (*d*, *J* ≈ 7.5); irrad. at 3.63→change at 3.89. ^{13}C-NMR ($CDCl_3$): 64.11 (*t*); 66.58 (*d*); 72.11 (*t*); 72.26 (*t*); 75.37 (*t*); 78.70 (*d*); 81.12 (*d*); 81.81 (*d*); 95.87 (*d*); 127.49–128.43 (several *d*); 137.79 (*s*); 137.87 (*s*); 138.44 (*s*). CI-MS (NH_3): 449 (30), 448 (100, $[M + H]^+$), 402 (11), 340 (24), 216 (15), 186 (25), 108 (13), 91 (8). Anal. calc. for $C_{27}H_{29}NO_5$ (447.532): C 72.46, H 6.53, N 3.13; found: C 72.31, H 6.38, N 3.31. Molecular-weight determination (osmometry): 481 ($CHCl_3$).

*(E)- and (Z)-2,3,4-Tri-*O*-benzyl-5,6-dideoxy-5,6-epithio-*D*-glucose Oxime* (**19**). A soln. of **17** (2.15 g, 4.8 mmol) and thiourea (1.83 g, 24 mmol) in MeOH (50 ml) was kept at r.t. for 5 d and evaporated. FC (hexane/AcOEt 3:1) of the residue gave **19** (1.91 g, 86%; (*E*)/(*Z*) *ca.* 8:2) as a yellowish solid, which was recrystallized in AcOEt/hexane. R_f (hexane/AcOEt 6:4) 0.42, 0.5. M.p. 91–93°. $[\alpha]_D^{25} = -9.1$ (*c* = 0.715, $CHCl_3$). IR ($CHCl_3$): 3580*m*, 3330*m* (br.), 3060*m*, 3000*m*, 2870*m*, 1950*w*, 1875*w*, 1810*w*, 1610*w*, 1590*w*, 1495*m*, 1455*m*, 1395*m*, 1355*m*, 1330*m*, 1305*m*, 1200*m*, 1070*s* (br.), 1045*s*, 1030*s*, 920*m* (br.), 700*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 2.18 (*dd*, *J* = 1.1, 5.5, 0.8 H, H–C(6) (*E*)); 2.20 (*dd*, *J* = 1.0, 5.5, 0.2 H, H–C(6) (*Z*)); 2.44 (*dd*, *J* = 1.0, 6.1, 0.2 H, H′–C(6) (*Z*)); 2.48 (*dd*, *J* = 1.1, 6.0, 0.8 H, H′–C(6) (*E*)); 3.07 (*dd*, *J* = 2.5, 8.1, 0.8 H, H–C(4) (*E*)); 3.10–3.19 (*m*, 1 H, H–C(5) (*E*/*Z*)); 3.23 (*dd*, *J* ≈ 3.5, 7.5, 0.2 H, H–C(4) (*Z*)); 3.87 (*dd*, *J* = 2.5, 7.4, 0.8 H, H–C(3) (*E*)); 3.89 (*dd*, *J* = 4.3, 6.9, 0.2 H, H–C(3) (*Z*)); 4.42 (*t*, *J* ≈ 7.7, 0.8 H, H–C(2) (*E*)), 4.49–4.71 (*m*, 5 H, PhCH_2); 4.83 (*d*, *J* = 11.4, 0.2 H, PhCH_2 (*Z*)); 4.88 (*d*, *J* = 11.4, 0.8 H, PhCH_2 (*E*)); 5.20 (*dd*, *J* ≈ 6, 7, 0.2 H, H–C(2) (*Z*)); 6.94 (*d*, *J* = 7.2, 0.2 H, H–C(1) (*Z*)); 7.26–7.34 (*m*, 15.8 H, arom. H, NOH (*E*)); 7.47 (*d*, *J* = 7.8, 0.8 H, H–C(1) (*E*)); 7.55 (*s*, 0.2 H, NOH (*Z*)). ^{13}C-NMR ($CDCl_3$): major isomer: 25.49 (*t*); 33.18 (*d*); 71.39 (*t*); 72.44 (*t*); 74.79 (*t*); 77.15 (*d*); 81.62 (*d*); 82.76 (*d*); 127.15–128.52 (several *d*); 137.44–137.92 (several *s*); 149.24 (*d*); minor isomer: 24.55 (*t*); 70.87 (*d*); 72.13 (*t*); 72.95 (*t*); 74.69 (*t*); 80.93 (*d*); 82.31 (*d*); 150.47 (*d*). CI-MS (NH_3): 481 (3, $[M + NH_4]^+$), 465 (19), 464 (50, $[M + H]^+$), 463 (73, M^+), 449 (29), 448 (100), 431 (13), 417 (11), 416 (38). Anal. calc. for $C_{27}H_{29}NO_4S$ (463.601): C 69.95, H 6.31, N 3.02, S 6.92; found: C 69.68, H 6.33, N 2.98, S. 6.64.

*1,6-Anhydro-2,3,4-tri-*O*-benzyl-5-*N*-hydroxy-β-*D*-glucopiperidinose* (**20**). A soln. of **17** (325 mg, 0.73 mmol) and LiCl (615 mg, 14.5 mmol) in dry THF (50 ml) was boiled under reflux for 22 h and then concentrated. Usual workup (AcOEt, H_2O) and FC (hexane/AcOEt 7:3) afforded **20** (139 mg, 43%). Colorless oil. R_f (hexane/AcOEt 6:4) 0.32. $[\alpha]_D^{25} = -4.1$ (*c* = 1.015, $CHCl_3$). IR ($CHCl_3$): 3540*m*, 3400*m* (br.), 3070*w*, 3010*m*, 2920*m*, 2870*m*, 1955*w*, 1875*w*, 1815*w*, 1500*m*, 1460*m*, 1400*w*, 1365*m*, 1330*w*, 1315*w*, 1270*w*, 1240*w*, 1195*w*, 1115*s*, 1090*s*, 1075*s*, 1055*s*, 1030*s*, 955*m*, 915*m*, 850*m*, 700*s*. ^{1}H-NMR (C_6D_6): 3.26 (*dd*, *J* = 7.1, 12.1 H–C(6)); 3.49 (*dd*, *J* ≈ 3.6, 8.4, H–C(2)); 3.52 (*dd*, *J* ≈ 4.0, 7.9, H–C(4)); 3.65 (*t*, *J* ≈ 8.2, H–C(3)); 3.80 (*d*, *J* = 12.2, H′–C(6)); 4.24 (*d*, *J* = 12.0, PhCH_2); 4.28 (*dd*, *J* = 4.1, 6.9, H–C(5)); 4.34 (*d*, *J* = 11.9, PhCH_2); 4.44 (*d*, *J* = 12.1, PhCH_2); 4.50 (*d*, *J* = 12.1, PhCH_2); 4.78 (*d*, *J* = 11.6, PhCH_2); 4.84 (*d*, *J* = 11.6, PhCH_2); 5.26 (*d*, *J* = 3.5, H–C(1)); 7.02–7.31 (*m*, 15 arom. H); 7.84 (*s*, exchange with CD_3OD, NOH); irrad. at 3.26→change at 3.80 and 4.28; irrad. at 3.65→change at 3.49 and 3.52. ^{13}C-NMR ($CDCl_3$): 59.88 (*t*); 72.83 (*t*); 72.91 (*t*); 73.01 (*d*); 75.28 (*t*); 78.93 (*d*); 79.29 (*d*); 81.89 (*d*); 97.56 (*d*); 127.49–128.39 (several *d*); 137.75 (*s*); 137.99 (*s*); 138.51 (*s*). CI-MS (NH_3): 449 (20), 448 (100, $[M + H]^+$), 433 (15), 432 (72), 430 (15). Anal. calc. for $C_{27}H_{29}NO_5$ (447.532): C 72.46, H 6.53, N 3.13; found: C 72.35, H 6.78, N 3.43. Molecular-weight determination (osmometry): 478 ($CHCl_3$).

N-(2,3,4-Tri-O-benzyl-6-chloro-6-deoxy-5-thio-α-D-glucopyranosyl)hydroxylamine (**21**) *and (Z)-2,3,4 Tri-O-benzyl-6-chloro-6-deoxy-5-thio-D-gluconhydroximo-1,5-lactone* (**23**). A soln. of **19** (250 mg, 0.54 mmol) in 15% (*w/w*) HCl in dry dioxane (12.5 ml) wa stirred at r.t. for 75 min, poured into sat. aq. $NaHCO_3$ soln. and extracted with AcOEt. Normal workup (sat. aq. $NaHCO_3$ soln., H_2O) gave crude **21** as a yellowish oil which was dried *i.v.* for 30 min, dissolved in MeOH (15 ml), and treated with MnO_2 (150 mg, 1.72 mmol). The mixture was stirred for 50 min at r.t. and filtered through *Celite*. The residue was washed with AcOEt. Filtrate and washings were evaporated. FC (hexane/AcOEt 8:2) gave **23** (218 mg, 81%). Yellowish oil.

Data of **21**: IR ($CHCl_3$): 3590*m*, 3400*w* (br.), 3290*w*, 3100*w*, 3070*w*, 3010*m*, 2930*m*, 2880*m*, 1605*w*, 1495*w*, 1455*m*, 1355*m*, 1055*s* (br., sh), 1030*s*, 930*w*, 700*m*. ^{1}H-NMR ($CDCl_3$): *ca.* 1.6 (br. *s*, NH); 3.57 (*ddd*, J = 2.6, 4.1, 9.3, H–C(5)); 3.72–3.83 (*m*, H–C(3), H–C(4), H–C(6)); 3.94 (*dd*, J = 4.3, 9.3 H–C(2)); 4.11 (*dd*, J = 4.2, 11.6, H′–C(6)); 4.31 (*d*, J = 4.2, H–C(1)); 4.72 (*s*, 2 H, PhCH_2); 4.73 (*d*, J = 10.7, PhCH_2); 4.78 (*d*, J = 11.0, PhCH_2); 4.88 (*d*, J = 10.8, PhCH_2); *ca.* 4.9 (br. *s*, OH); 4.96 (*d*, J = 10.7, PhCH_2); 7.26–7.36 (*m*, 15 arom. H).

Data of **23**: R_f (hexane/AcOEt 6:4) 0.44. $[\alpha]_D^{25}$ = +75.0 (*c* = 1.74, $CHCl_3$). IR ($CHCl_3$): 3570*m*, 3270*m* (br.), 3060*w*, 3005*m*, 2970*m*, 1950*w*, 1875*w*, 1810*w*, 1605*m*, 1500*m*, 1455*m*, 1430*w*, 1390*w*, 1355*m*, 1315*w*, 1295*w*, 1245*w*, 1180*w*, 1090*s*, 1070*s*, 1030*m*, 990*w*, 965*w*, 935*m*, 835*w*, 700*s*. ^{1}H-NMR ($CDCl_3$): 3.81 (*dd*, J = 3.9, 10.6, H–C(4)); 3.87 (*d*, J = 4.5, H–C(6), H′–C(6)); 3.93 (*dd*, J = 2.4, 3.8, H–C(3)); 4.17 (*td*, J = 4.4, 10.6, H–C(5)); 4.39 (*d*, J = 11.7, PhCH_2); 4.40 (*d*, J = 2.5, H–C(2)); 4.42 (*d*, J = 12.0, PhCH_2); 4.49 (*d*, J = 11.1, PhCH_2); 4.56–4.60 (*m*, 2 H, PhCH_2); 4.69 (*d*, J = 11.9, PhCH_2); 7.21–7.37 (*m*, 15 arom. H); 7.86 (*s*, exchange with CD_3OD, NOH). ^{13}C-NMR ($CDCl_3$): 42.11 (*d*); 43.99 (*t*); 70.62 (*t*); 71.51 (*t*); 72.92 (*t*); 76.35 (*d*); 81.90 (*d*); 82.16 (*d*); 127.72–128.40 (several *d*); 136.93 (2 *s*); 137.47 (*s*); 151.86 (*s*). CI-MS (NH_3): 517 (6, $[M + NH_4]^+$), 515 (15, $[M + NH_4]^+$), 501 (12), 500 (42, $[M + H]^+$), 499 (32), 498 (100, $[M + H]^+$), 354 (12). Anal. calc. for $C_{27}H_{28}ClNO_4S$ (498.037): C 65.11, H 5.67, N 2.81, Cl 7.12, S 6.44; found: C 65.01, H 5.87, N 2.89, Cl 7.24, S 6.25.

(Z)-2,3,4-Tri-O-benzyl-6-bromo-6-deoxy-5-thio-D-gluconhydroximo-1,5-lactone (**24**). Conc. H_2SO_4 (5.4 ml) in MeOH (20 ml) was added dropwise to an ice-cold soln. of **19** (1.229 g, 2.7 mmol) and LiBr (4.61 g, 53 mmol) in MeOH (65 ml). The soln. was stirred 14 h at 0°→r.t., poured into sat. aq. $NaHCO_3$ soln. (500 ml), and extracted twice with Et_2O (500 ml each). The combined org. layer was dried ($MgSO_4$) and evaporated and the residue (yellow oil) immediately dissolved in MeOH (75 ml)/AcOEt (12 ml) and treated with MnO_2 (1.475 g, 17 mmol). The mixture was stirred vigorously for 30 min at r.t. and filtered through *Celite*; the residue was washed with AcOEt. Filtrate and washings were concentrated. FC (hexane/Et_2O 6:4) gave **19** (impure, 0.11 g) and **24** (1.103 g, 77%). Yellow, clear oil. R_f (hexane/AcOEt 6:4) 0.48. $[\alpha]_D^{25}$ = +65.4 (*c* = 1.035, $CHCl_3$). IR ($CHCl_3$): 3570*m*, 3260*m* (br.), 3060*m*, 3005*m*, 2970*m*, 1950*w*, 1875*w*, 1810*w*, 1605*w*, 1495*m*, 1455*m*, 1420*w*, 1390*w*, 1350*m*, 1315*w*, 1265*w*, 1185*w*, 1090*s*, 1070*s*, 1030*m*, 985*m*, 945*m*, 910*m*, 830*w*, 700*s*. ^{1}H-NMR ($CDCl_3$): 3.73 (*d*, J = 5.1, H–C(6)); 3.73 (*d*, J = 3.9, H′–C(6)); 3.77 (*dd*, J = 3.7, 10.5, H–C(4)); 3.94 (*dd*, J = 2.5, 3.8, H–C(3)); 4.13 (*ddd*, J = 3.9, 5.1, 10.4, H–C(5)); 4.39 (*d*, J = 11.7, PhCH_2); 4.40 (*d*, J = 2.7, H–C(2)); 4.42 (*d*, J = 12.1, PhCH_2); 4.51 (*d*, J = 11.2, PhCH_2); 4.57 (*d*, J = 11.7, PhCH_2); 4.58 (*d*, J = 11.1, PhCH_2); 4.69 (*d*, J = 11.8, PhCH_2); 7.22–7.39 (*m*, 15 arom. H); 7.96 (*s*, exchange with CD_3OD, NOH). ^{13}C-NMR ($CDCl_3$): 32.82 (*t*); 41.72 (*d*); 70.59 (*t*); 71.56 (*t*); 73.02 (*t*); 76.42 (*d*); 82.29 (*d*); 82.81 (*d*); 127.70–128.69 (several *d*); 136.97 (2*s*); 137.53 (*s*); 151.69 (*s*). CI-MS (NH_3): 545 (31), 544 (100, $[M + H]^+$), 543 (30), 542 (96, $[M + H]^+$), 464 (14), 463 (20, $[M + H - Br]^+$), 431 (13). Anal. calc. for $C_{27}H_{28}BrNO_4S$ (542.487): C 59.78, H 5.20, Br 14.73, N 2.58, S 5.91; found: C 60.04, H 5.41, Br 15.00, N 2.58, S 5.62.

(Z)-2,3,4-Tri-O-benzyl-6-deoxy-6-iodo-5-thio-D-gluconhydroximo-1,5-lactone (**25**). A soln. of **24** (164 mg, 0.3 mmol) and NaI (907 mg, 6.0 mmol) in acetone (10 ml) was boiled under reflux for 4 h (→precipitate). Normal workup (AcOEt, sat. aq. $NaHCO_3$ soln., H_2O). FC (hexane/AcOEt 8:2) afforded **25** (154 mg, 86%). Colorless oil. R_f ($CHCl_3$/EtOH 99:1) 0.35. $[\alpha]_D^{25}$ = +51.8 (*c* = 0.73, $CHCl_3$). IR ($CHCl_3$): 3580*m*, 3280*m* (br.), 3100*w*, 3080*m*, 3010*m*, 2980*m*, 1955*w*, 1875*w*, 1815*w*, 1610*m*, 1500*m*, 1460*m*, 1420*w*, 1395*w*, 1355*m*, 1315*w*, 1095*s*, 1075*s*, 1030*m*, 990*w*, 930*m*, 700*m*. ^{1}H-NMR ($CDCl_3$): 3.50 (*dd*, J = 6.0, 10.6, H–C(6)); 3.57 (*dd*, J = 3.1, 10.6, H′–C(6)); 3.64 (*dd*, J = 3.6, 10.4, H–C(4)); 3.73 (*ddd*, J = 3.1, 6.0, 10.2, H–C(5)); 3.94 (*dd*, J = 2.5, 3.6, H–C(3)); 4.39 (*d*, J = 11.7, PhCH_2); 4.40 (*d*, $J \approx$ 2.9, H–C(2)); 4.42 (*d*, J = 12.2, PhCH_2); 4.52 (*d*, J = 11.1, PhCH_2); 4.58 (*d*, $J \approx$ 10.5, 2 H, PhCH_2); 4.69 (*d*, J = 11.8, PhCH_2); 7.22–7.40 (*m*, 15 arom. H); 7.78 (br. *s*, exchange with CD_3OD, NOH). ^{13}C-NMR ($CDCl_3$): 6.75 (*t*); 41.27 (*d*); 70.62 (*t*); 71.53 (*t*); 73.00 (*t*); 76.37 (*d*); 82.22 (*d*); 84.26 (*d*); 127.75–128.64 (several *d*); 136.94 (2 *s*); 137.53 (*s*); 151.96 (*s*). CI-MS (NH_3): 591 (30), 590 (100, $[M + H]^+$), 464 (24), 463 (20, $[M + H - I]^+$), 431 (21). Anal. calc. for $C_{27}H_{28}INO_4S$ (589.487): C 55.01, H 4.79, I 21.53, N 2.38, S 5.44; found: C 54.90, H 5.00, I 21.30, N 2.52, S 5.69.

(Z)-2,3,4-Tri-O-benzyl-5-thio-D-gluconhydroximo-1,5-lactone (**26**). A mixture of **24** (216 mg, 0.4 mmol) and KNO_2 (848 mg, 9.9 mmol) in dry DMF (10 ml) was stirred at 110–120° for 200 min. Normal workup (AcOEt, H_2O) and FC (hexane/AcOEt 6:4) of the crude gave **26** (82 mg, 43%). Yellow oil. R_f (hexane/AcOEt 6:4) 0.21.

$[\alpha]_D^{25} = +76.4$ ($c = 0.633$, $CHCl_3$). IR ($CHCl_3$): 3560*m*, 3260*m* (br.), 3060*w*, 3030*m*, 3000*m*, 2920*w*, 2870*m*, 1950*w*, 1870*w*, 1810*w*, 1605*w*, 1495*m*, 1455*m*, 1350*m*, 1180*w*, 1070*s*, 1030*m*, 945*m*, 700*s*. ^{1}H-NMR ($CDCl_3$): 2.26 (*t*, $J \approx 6.3$, exchange with CD_3OD, OH–C(6)); 3.77–3.82 (*m*, H–C(4), H–C(6), H′–C(6)); 3.92 (*td*, $J = 4.6$, 10.8, H–C(5)); 3.95 (*dd*, $J = 2.1$, 4.5, H–C(3)); 4.38 (*d*, $J = 2.1$, H–C(2)); 4.41 (*d*, $J = 11.8$, PhCH_2); 4.42 (*d*, $J = 11.7$, PhCH_2); 4.53 (*d*, $J = 11.3$, PhCH_2); 4.59 (*d*, $J = 11.6$, PhCH_2); 4.64 (*d*, $J = 11.3$, PhCH_2); 4.69 (*d*, $J = 11.8$, PhCH_2); 7.20–7.40 (*m*, 15 arom. H); 7.91 (br. *s*, exchange with CD_3OD, NOH). ^{13}C-NMR ($CDCl_3$): 41.77 (*d*); 62.48 (*t*); 70.43 (*t*); 71.49 (*t*); 72.91 (*t*); 76.36 (*d*); 82.89 (*d*); 83.34 (*d*); 127.85–128.63 (several *d*); 137.05 (2*s*); 137.41 (*s*); 151.50 (*s*). CI-MS (NH_3): 497 (10, $[M + NH_4]^+$), 481 (19), 480 (100, $[M + H]^+$), 464 (12). Anal. calc. for $C_{27}H_{29}NO_5S$ (479.592): C 67.62, H 6.10, N 2.92, S 6.68; found: C 67.56, H 6.39, N 3.16, S 6.70.

*6-*O*-Acetyl-2,3,4-tri-*O*-benzyl-5-thio-*D*-gluconhydroximo-1,5-lactone* (**27**) *and 2,3,4-Tri-*O*-benzyl-5-thio-*D*-xylo-hex-5-enonhydroximo-1,5-lactone* (**28**). A mixture of **24** (50 mg, 0.09 mmol), [18]crown-6 (6 mg), and CsOAc (177 mg, 0.9 mmol) was dried *i.v.* for 30 min, dissolved in DMI (1 ml), and stirred over 145 min at 80–90°. Normal workup (AcOEt, H_2O) and FC (hexane/AcOEt 3:1) afforded **27** (20 mg, 42%) and **28** (15 mg, 35%), both as yellow oils.

Data of **27**: R_f (hexane/AcOEt 6:4) 0.35. IR ($CHCl_3$): 3570*m*, 3270*m* (br.), 3060*m*, 3000*m*, 2930*m*, 2870*m*, 1950*w*, 1875*w*, 1810*w*, 1740*s*, 1605*m*, 1495*m*, 1455*s*, 1385*s*, 1365*s*, 1250*s*, 1190*m*, 1070*s* (br.), 1030*s*, 985*w*, 950*s*, 910*w*, 700*s*. ^{1}H-NMR ($CDCl_3$): 1.99 (*s*, AcO); 3.74 (*dd*, $J = 3.6$, 10.9, H–C(4)); 3.94 (*dd*, $J = 2.6$, 3.6, H–C(3)); 4.10 (*ddd*, $J = 3.0$, 6.1, 10.8, H–C(5)); 4.25 (*dd*, $J = 6.1$, 11.8, H–C(6)); 4.37–4.47 (*m*, 5 H, PhCH_2, H–C(2), H′–C(6)); 4.56 (*d*, $J = 11.4$, PhCH_2); 4.58 (*d*, $J = 11.7$, PhCH_2); 4.70 (*d*, $J = 11.9$, PhCH_2); 7.19–7.40 (*m*, 15 arom. H); 8.31 (*s*, NOH). CI-MS (NH_3): 540 (8), 539 (27, $[M + NH_4]^+$), 524 (16), 523 (48), 522 (100, $[M + H]^+$), 521 (14), 506 (19), 480 (12), 464 (24), 463 (67).

Data of **28**: R_f (hexane/AcOEt 6:4) 0.46. IR ($CHCl_3$): 3570*m*, 3270*m* (br.), 3060*m*, 3010*m*, 2870*m*, 1955*w*, 1875*w*, 1810*w*, 1605*m*, 1500*m*, 1455*m*, 1390*w*, 1355*m*, 1315*w*, 1185*w*, 1075*s* (br.), 1030*m*, 950*m*, 910*m*, 700*s*. ^{1}H-NMR ($CDCl_3$): 3.81 (*dd*, $J = 2.5$, 5.4, H–C(3)); 4.20 (*td*, $J = 1.6$, 5.4, H–C(4)); 4.28 (*d*, $J = 2.5$, H–C(2)); 4.35 (*d*, $J = 12.0$, PhCH_2); 4.50 (*d*, $J = 11.8$, PhCH_2); 4.51 (*d*, $J = 11.8$, PhCH_2); 4.57 (*d*, $J = 11.8$, PhCH_2); 4.65 (*d*, $J = 12.0$, PhCH_2); 4.70 (*d*, $J = 11.8$, PhCH_2); 5.57 (*d*, $J = 1.5$, H–C(6)); 5.71 (*d*, $J = 1.7$, H′–C(6)); 7.22–7.35 (*m*, 15 arom. H); 8.03 (*s*, NOH). CI-MS (NH_3): 463 (64), 462 (100, $[M + H]^+$), 308 (39).

Treatment of **25** *with 2,2,6,6-Tetramethylpiperidin-1-oxyl Radical (TEMPO): (Z)-2,3,4-Tri-*O*-benzyl-6-*O*-(2,2,6,6-tetramethylpiperidin-1-yl)-5-thio-*D*-gluconhydroximo-1,5-lactone* (**29**), *2,3-Di-*O*-benzyl-6-deoxy-5-thio-*D*-gluconhydroximo-1,5-lactone* (**30**), *and 2,3-Di-*O*-benzyl-6-deoxy-5-thio-*D*-gluconhydroximo-1,5-lactone 1-*N*,4-Diacetate* (**31**). a) TEMPO (1.75 g, 11.2 mmol) was added to a soln. of **25** (1.3 g, 2.2 mmol) in benzene (200 ml). A soln. of Bu_3SnH (6.48 g, 22.3 mmol) in benzene (7 ml) was added over 15 min at r.t. and stirring was continued for 4 h. The decolorized soln. was evaporated to a yellow oil. FC (hexane/Et_2O 65:35→Et_2O) produced *Fraction A* (R_f (hexane/Et_2O 1:1) *ca.* 0.3) and *B* (R_f *ca.* 0.15, 0.07). *Fr. A*: The material was dried *i.v.* at 70–80° for 5 h and resubjected to FC (hexane/Et_2O 65:35) to give **29** (635 mg, 47%), which was crystallized (hexane/Et_2O) to give colorless prisms. *Fr. B*: The material was resubjected to FC (hexane/Et_2O 45:55) to give **30** (98 mg, 12%; colorless oil) and **26** (73 mg, 7%; yellow oil). An anal. sample of **30** was acetylated (pyridine/Ac_2O 1:1, 2 ml) for 18 h at r.t., the soln. then diluted with toluene and evaporated, and the residue co-evaporated with toluene and dried *i.v.* to give **31**.

b) TEMPO (1.58 g, 10 mmol) was added to a soln. of **25** (1.19 g, 2 mmol) in benzene (100 ml). Bu_3SnH (5.88 g, 20 mmol) was added after 5 min and the soln. kept at r.t for 4 h (→decolorization). The soln. was evaporated to a yellow oil. FC (hexane/AcOEt 85:15) afforded a red oil which was dried *i.v.* at 60° for 90 min to give a yellow oil (1.40 g). The latter was resubjected to FC (hexane/Et_2O 65:35), dried *i.v.* at 75° for 2 h and overnight at r.t. to yield **29** (699 mg, 56%) as a yellow oil which crystallized upon standing at r.t. for several weeks.

Data of **29**: R_f (hexane/Et_2O 1:1) 0.3. M.p. 116–117°. $[\alpha]_D^{25} = +62.4$ ($c = 0.83$, $CHCl_3$). IR ($CHCl_3$): 3565*m*, 3260*m* (br.), 3000*m*, 2970*m*, 2930*m*, 2870*m*, 1950*w*, 1870*w*, 1810*w*, 1600*w*, 1495*w*, 1470*m*, 1455*m*, 1375*m*, 1360*m*, 1090*s*, 1070*s*, 1025*m*, 955*m*, 695*s*. ^{1}H-NMR ($CDCl_3$): 1.14–1.68 (*m*, 18 H); 3.72 (*dd*, $J = 3.6$, 10.9, H–C(4)); 3.89–3.96 (*m*, H–C(3), H–C(6)); 4.10 (*ddd*, $J = 3.1$, 8.0, 11.2, H–C(5)); 4.21 (*dd*, $J = 3.3$, 9.1, H′–C(6)); 4.37 (*d*, $J = 2.4$, H–C(2)); 4.38 (*d*, $J = 11.7$, PhCH_2); 4.43 (*d*, $J = 11.8$, PhCH_2); 4.44 (*d*, $J = 11.4$, PhCH_2); 4.53 (*d*, $J \approx 11$, PhCH_2); 4.57 (*d*, $J = 11.8$, PhCH_2); 4.72 (*d*, $J = 11.8$, PhCH_2); 7.18–7.85 (*m*, 15 arom. H); 7.85 (br. *s*, NOH). ^{13}C-NMR ($CDCl_3$): 16.69 (*t*); 19.90 (*q*); 20.04 (*q*); 32.42 (*q*); 32.47 (*q*); 39.12 (2 *t*); 40.24 (*d*); 59.90 (*s*); 70.10 (*t*); 71.07 (*t*); 71.99 (*t*); 74.82 (*t*); 76.02 (*d*); 81.83 (*d*); 81.93 (*d*); 127.28–128.65 (several *d*); 136.98 (*s*); 137.04 (*s*); 137.55 (*s*); 152.17 (*s*). CI-MS (NH_3): 620 (42), 619 (100, $[M + H]^+$), 513 (12), 464 (26), 374 (11), 158 (10), 142 (19). Anal. calc. for $C_{36}H_{46}N_2O_5S$ (618.833): C 69.87, H 7.49, N 4.53, S 5.18; found: C 69.65, H 7.68, N 4.28, S 5.40.

Data of **30**: R_f (hexane/Et_2O 4:6) 0.28. IR ($CHCl_3$): 3570*m*, 3290*m* (br.), 3000*m*, 2930*w*, 2870*m*, 1950*w*, 1875*w*, 1810*w*, 1715*w*, 1605*m*, 1495*m*, 1455*m*, 1350*m*, 1310*w*, 1285*w*, 1090*s*, 1075*s*, 1040*m*, 1030*m*, 950*m*, 700*s*. ^{1}H-NMR

($CDCl_3$): 1.36 (*d*, *J* = 6.3, Me); 2.27 (br. *s*, OH–C(4)); 3.52–3.65 (*m*, H–C(4), H–C(5)); 3.72 (*dd*, *J* = 2.7, 4.4, H–C(3)); 4.35 (*d*, *J* = 2.7, H–C(2)); 4.40 (*d*, *J* = 11.6, PhCH_2); 4.51 (*d*, *J* = 12.0, PhCH_2); 4.65 (*d*, *J* ≈ 11.5, PhCH_2); 4.67 (*d*, *J* ≈ 11.5, PhCH_2); 7.26–7.38 (*m*, 10 arom. H); 8.14 (br. *s*, NOH). CI-MS (NH_3): 375 (24), 374 (100, $[M + H]^+$).

Data of **31**: ^{1}H-NMR ($CDCl_3$): 1.21 (*d*, *J* = 6.9, Me); 2.01 (*s*, AcO); 2.22 (*s*, AcO); 3.75 (*dd*, *J* ≈ 2.9, 3.5, H–C(3)); 3.86 (*qd*, *J* = 6.8, 10.9, H–C(5)); 4.45 (*d*, *J* = 12.3, PhCH_2); 4.51 (*d*, *J* = 11.7, PhCH_2); 4.56 (*d*, *J* = 2.5, H–C(2)); 4.62 (*d*, *J* = 12.3, PhCH_2); 4.70 (*d*, *J* = 11.7, PhCH_2); 5.04 (*dd*, *J* = 3.6, 10.8, H–C(4)); 7.22–7.39 (*m*, 10 arom. H).

*(Z)-5-Thio-*D*-gluconhydroximo-1,5-lactone 1-*N*,2,3,4,6-Pentaacetate* (**32**). Na (100 mg) was added in portions at −70° to NH_3 (15–20 ml), and the mixture was stirred for 15 min. A soln. of **29** (162 mg, 0.26 mmol) in dry THF (5 ml) was added over 5 min to the deep-blue mixture, which was stirred for 10 min at −70° and for 60 min at reflux. After cooling to −70°, NH_4Cl (185 mg) was added. The decolorized mixture was allowed to warm to r.t. The residue was diluted with MeOH, the soln. evaporated, and the residue suspended in pyridine (10 ml). After addition of Ac_2O (10 ml), the mixture was kept at r.t. for 20 h, diluted with toluene, and evaporated. The residue was co-evaporated with toluene. FC (hexane/AcOEt 1:1) of the crude afforded a yellowish oil (82 mg), which was reacetylated (pyridine/Ac_2O 1:1, 4 ml). Co-evaporation with toluene gave **32** (86 mg, 78%). R_f (hexane/AcOEt 4:6) 0.29. IR ($CHCl_3$): 3050*w*, 2950*w*, 1750*s* (br.), 1590*m*, 1460*w*, 1435*w*, 1370*s*, 1245*s*, 1175*s*, 1145*m*, 1070*m*, 1040*s*, 1000*m*, 930*m*, 900*m*. ^{1}H-NMR ($CDCl_3$): 2.09 (*s*, AcO); 2.10 (*s*, AcO); 2.12 (*s*, AcO); 2.17 (*s*, AcO); 2.23 (*s*, AcO); 4.03 (*td*, *J* = 4.6, 11.0, H–C(5)); 4.29 (*d*, *J* = 4.6, H–C(6), H′–C(6)); 5.16 (*ddd*, *J* = 0.6, 3.7, 10.9, H–C(4)); 5.24 (*t*, *J* ≈ 3.5, H–C(3)); 5.78 (*dd*, *J* = 0.6, 3.4, H–C(2)). ^{13}C-NMR ($CDCl_3$): 19.02–20.61 (several *q*); 39.99 (*d*); 61.06 (*t*); 70.87 (*d*); 72.41 (*d*); 72.45 (*d*); 155.93 (*s*); 166.83 (*s*); 167.64 (*s*); 168.68 (*s*); 169.19 (*s*); 170.12 (*s*). CI-MS (NH_3): 438 (18), 437 (100, $[M + NH_4]^+$).

*(Z)-5-Thio-*D*-gluconhydroximo-1,5-lactone 2,3,4,6-Tetraacetate* (**33**). A soln. of **32** (116 mg, 0.28 mmol) in $CHCl_3$ (5 ml)/MeOH (15 ml) was treated with pyridine hydrochloride (320 mg, 2.76 mmol) and kept at r.t. for 2 d. Normal workup (AcOEt, sat. aq. $NaHCO_3$ soln., H_2O), co-evaporation (toluene), and FC (hexane/AcOEt 1:1) afforded **33** (73 mg, 70%). Colorless oil. R_f ($CHCl_3$/EtOH 19:1) 0.51. IR ($CHCl_3$): 3564*w*, 3258*w* (br.), 3042*w*, 3007*w*, 1750*s*, 1608*w*, 1430*w*, 1370*s*, 1252*s*, 1072*m*, 1036*s*, 981*w*, 948*w*, 909*m*. ^{1}H-NMR ($CDCl_3$): 2.09 (*s*, AcO); 2.10 (*s*, AcO); 2.10 (*s*, AcO); 2.16 (*s*, AcO); 3.96 (*m*, H–C(5)); 4.30 (*dd*, *J* = 3.9, 12.1, H–C(6)); 4.31 (*dd*, *J* = 5.4, 12.1, H′–C(6)); 5.17–5.22 (*m*, H–C(3), H–C(4)); 5.66 (*m*, H–C(2)); 8.26 (br. *s*, exchange with CD_3OD, NOH). ^{13}C-NMR (75 MHz, $CDCl_3$): 20.60–20.81 (several *q*); 39.32 (*d*); 61.57 (*t*); 71.02 (*d*); 72.81 (*d*); 73.29 (*d*); 146.93 (*s*); 168.39 (*s*); 169.26 (*s*); 169.55 (*s*); 170.62 (*s*). FAB-MS (3-nitrobenzyl alcohol): 400 (6, $[M + Na]^+$), 378 (10, $[M + H]^+$), 318 (18).

*(Z)-5-Thio-*D*-gluconhydroximo-1,5-lactone* (**10**). NaOMe (1M, 0.6 ml) was added to a soln. of **32** (245 mg, 0.58 mmol) in MeOH (30 ml). The soln. was stirred at r.t. over 60 min, and neutralized by addition of *Dowex 50* × *8* (H^+). The mixture was filtered and the residue thoroughly washed with MeOH. The filtrate and the washings were evaporated to give a turbid oil (109 mg, 89%). FC (AcOEt/MeOH 17:3) afforded **10** (90 mg, 74%). Yellow oil. For analysis, a sample was crystallized (Et_2O, MeOH). R_f (AcOEt/MeOH 8:2) 0.38. M.p. > 155° (dec.). $[\alpha]_D^{25}$ = +145.2 (*c* = 0.635, H_2O). IR (KBr): 3370*vs* (br.), 2870*w*, 1600*m*, 1555*w*, 1535*w*, 1455*m*, 1380*w*, 1355*m*, 1295*w*, 1255*w*, 1230*w*, 1140*w*, 1105*m*, 1070*s*, 1055*m*, 995*s*, 960*s*, 805*m*, 745*m*. ^{1}H-NMR (500 MHz, D_2O): 3.55 (*ddd*, *J* = 3.4, 6.4, 9.8, H–C(5)); 3.72 (*dd*, *J* = 6.5, 9.9, H–C(4)); 3.76 (*dd*, *J* = 5.9, 6.4, H–C(3)); 3.87 (*dd*, *J* = 6.3, 12.1, H–C(6)); 3.96 (*dd*, *J* = 3.3, 12.1, H′–C(6)); 4.39 (*dd*, *J* = 0.3, 5.8, H–C(2)). ^{13}C-NMR (125 MHz, D_2O): 48.00 (*d*); 63.26 (*t*); 75.59 (*d*); 76.17 (*d*); 79.13 (*d*); 156.09 (*s*). FAB-MS (glycerol): 302 (5, $[M + H + glycerol]^+$), 210 (11, $[M + H]^+$). Anal. calc. for $C_6H_{11}NO_5S$ (209.22): C 34.44, H 5.30, N 6.69; found: C 34.32, H 5.45, N 6.46.

Enzymology. Emulsin (from almonds, *E.C. 3.2.1.21*; *Fluka Biochemica*; used without any further purification) and *Agrobacter* β-glucosidase (purified as described previously [39]) were assayed using 4-nitrophenyl β-D-glucopyranoside and 80 mM potassium-phosphate buffer (pH 6.8) or 50 mM sodium-phosphate buffer, 0.1% BSA (pH 7.0), respectively. Release of nitrophenolate was monitored at 37° by UV/VIS spectroscopy through measurements at 400 nm. The K_I values were determined by measurement of rates of a series of 5 substrate concentrations which bracket K_M value in the presence of 3 different concentrations of inhibitor. Data were analysed as described elsewhere [3].

REFERENCES

[1] D. Beer, A. Vasella, *Helv. Chim. Acta* **1986,** *69,* 267.
[2] B. Ganem, G. Papandreou, *J. Am. Chem. Soc.* **1991,** *113,* 8984.
[3] R. Hoos, A. B. Naughton, W. Thiel, A. Vasella, W. Weber, K. Rupitz, S. G. Withers, *Helv. Chim. Acta* **1993,** *76,* 2666.
[4] S. G. Withers, K. Rupitz, D. Trimbur, R. A. J. Warren, *Biochemistry* **1992,** *31,* 9979.
[5] T. Kajimoto, K. K.-C. Liu, R. L. Pederson, Z. Zhong, Y. Ichikawa, J. A. Porco, C.-H. Wong, *J. Am. Chem. Soc.* **1991,** *113,* 6187.
[6] H. Hashimoto, T. Fujimori, H. Yuasa, *J. Carbohydr. Chem.* **1990,** *9,* 683.
[7] W. Korytnyk, N. Angelino, O. Dodson-Simmons, M. Hanchak, M. Madson, S. Valentekovic-Horvath, *Carbohydr. Res.* **1983,** *113,* 166.
[8] I. I. Cubero, M. T. Plaza Lopez-Espinosa, A. C. Richardson, M. D. Suarez Ortega, *Carbohydr. Res.* **1993,** *242,* 109.
[9] G. Legler, E. Jülich, *Carbohydr. Res.* **1984,** *128,* 61.
[10] P. Ermert, A. Vasella, *Helv. Chim. Acta* **1991,** *74,* 2043.
[11] P. Ermert, A. Vasella, M. Weber. K. Rupitz, S. G. Withers, *Carbohydr. Res.*, in press.
[12] E. Tanahashi, M. Kiso, A. Hasegawa, *Carbohydr. Res.* **1983,** *117,* 304.
[13] H. Hashimoto, M. Kawanishi, H. Yuasa, *Tetrahedron Lett.* **1991,** *32,* 7087.
[14] K. Blumberg, A. Fuccello, T. van Es, *Carbohydr. Res.* **1979,** *70,* 217.
[15] B. Helpap, Dissertation, Universität Hamburg, 1988.
[16] A. Chaperon, Diplomarbeit, Universität Zürich, 1991.
[17] R. Eby, S. J. Sondheimer, C. Schuerch, *Carbohydr. Res.* **1979,** *73,* 273.
[18] B. M. Aebischer, H. W. Hanssen, A. T. Vasella, W. B. Schweizer, *J. Chem. Soc., Perkin Trans. 1* **1982,** 2139.
[19] M. Salunkhe, M. Hartmann, W. Schmid, E. Zbiral, *Liebigs Ann. Chem.* **1988,** 187.
[20] O. Duclos, A. Dureault, J. D. Depezay, *Tetrahedron Lett.* **1992,** *33,* 1059.
[21] O. Duclos, M. Mondange, A. Dureault, J. C. Depezay, *Tetrahedron Lett.* **1992,** *33,* 8061.
[22] W. Kliegel, *Liebigs Ann. Chem.* **1970,** *733,* 192.
[23] R. Grigg, J. Markandu, *Tetrahedron Lett.* **1989,** *30,* 5489.
[24] W. Kliegel, H. Becker, *Chem. Ber.* **1977,** *110,* 2090.
[25] G. J. Karabatsos, R. A. Taller, *Tetrahedron* **1968,** *24,* 3347.
[26] J. M. J. Tronchet, F. Barbalat-Rey, N. Le-Hong, *Helv. Chim. Acta* **1971,** *54,* 2615.
[27] A. M. Creighton, L. N. Owen, *J. Chem. Soc.* **1960,** 1024.
[28] J. Attenburrow, *J. Chem. Soc.* **1952,** 1094.
[29] M. A. Brimble, G. M. Williams, R. Baker, *J. Chem. Soc., Perkin Trans. 1* **1991,** 2221.
[30] E. J. Corey, K. C. Nicolaou, M. Shibasaki, Y. Machida, C. S. Shiner, *Tetrahedron Lett.* **1975,** 3183.
[31] R. J. Kinney, W. D. Jones, R. C. Bergman, *J. Am. Chem. Soc.* **1978,** *100,* 7902.
[32] A. G. M. Barrett, L. M. Melcher, B. C. B. Bezuidenhoudt, *Carbohydr. Res.* **1992,** *232,* 259.
[33] W. Walter, E. Schaumann, *Synthesis* **1971,** 111.
[34] J. Waser, W. H. Watson, *Nature (London)* **1963,** *198,* 1297.
[35] M. E. Jung, D. D. Grove, S. I. Khan, *J. Org. Chem.* **1987,** *52,* 4570.
[36] D. Beer, A. Vasella, *Helv. Chim. Acta* **1985,** *68,* 2254.
[37] T. Storz, Diplomarbeit, Universität Konstanz, 1989.
[38] P. Kovac, H. J. C. Yeh, G. L. Jung, *J. Carbohydr. Chem.* **1987,** *6,* 423.
[39] J. B. Kempton, S. G. Withers, *Biochemistry* **1992,** *31,* 9961.