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Isothiocyanates and cyclic thiocarbamates of α,α'-trehalose, sucrose, and cyclomaltooligosaccharides ☆

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Abstract

6,6′-Dideoxy-6,6′-diisothiocyanato-α,α'-trehalose (**4**), 6-deoxy-6-isothiocyanato-α-D-fructofuranose β-D-fructopyranose 1,2′ : 2,1′-dianhydride (**11**), 6,6′-dideoxy-6,6′-diisothiocyanatosucrose (**16**), and per(6-deoxy-6-isothiocyanato)-cyclomaltohexaose (**23**), -cycloheptaose (**27**), and -cyclomaltooctaose (**31**) have been prepared in high yield by reaction of the corresponding amino sugars with thiophosgene. In the absence of base, all isothiocyanates were stable and could be stored and acetylated without decomposition. In the presence of triethylamine, 6,6′-dideoxy-6,6′-diisothiocyanato-α,α'-trehalose underwent intramolecular cyclisation involving HO-4 to give the corresponding bis(cyclic thiocarbamate). The product of cyclisation at a single glucopyranosyl unit was obtained in the treatment of the above diisothiocyanate with mixed (H^+, HO^-) ion-exchange resin. Under identical reaction conditions, 6,6′-dideoxy-6,6′-diisothiocyanatosucrose yielded exclusively the product of intramolecular cyclisation at the D-glucopyranosyl moiety, while derivatives of α-D-fructofuranose β-D-fructopyranose 1,2′ : 2,1′-dianhydride and cyclomaltooligosaccharides remained unchanged.

Keywords: Sugar isothiocyanates; Trehalose; Difructose dianhydrides; Sucrose; Cyclomaltooligosaccharides

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1. Introduction

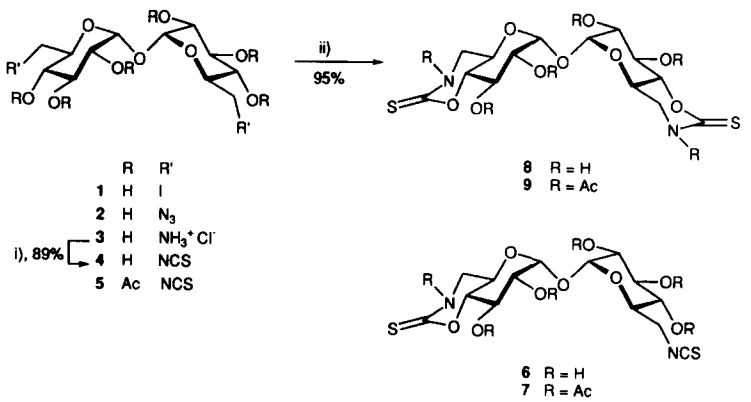
Sugar isothiocyanates [1] have proved to be useful synthons in the preparation of a variety of N- and *neo*-N-glycoconjugates [2] such as nucleosides [1,3], *N*-glycosyl compounds [1,4], or N-glycopeptides [5–7]. In addition, the high reactivity of the isothiocyanate functionality [8,9] towards nucleophiles and its ability to undergo reductive or oxidative transformations allow an easy access to other functional groups including amide, thiourea, thiocarbamate, dithiocarbamate, thioformamide [10], isonitrile [11], dichloroisonitrile [12], and isocyanate derivatives [12], which may be used for further transformations. However, to avoid undesired side-reactions, protection of the hydroxyl groups is normally required. This limitation has also been an important drawback in the use of sugar isothiocyanates in enzymology [13].

In previous papers [14–17], we have studied the synthesis and reactivity of unprotected monosaccharides bearing an isothiocyanate group at a non-anomeric position. A main conclusion of this work is that, whereas reducing derivatives from 6-deoxy-6-isothiocyanatoaldoses undergo spontaneous cyclisation through the furanose form to give five-membered cyclic thiocarbamates, nonreducing derivatives having the pyranose form anchored, e.g., alkyl 6-deoxy-6-isothiocyanatoglycopyranosides, are stable compounds. It was then expected that nonreducing oligosaccharide isothiocyanates might also be stable, thus allowing them to be used in the functionalisation of compounds of biological and economic significance such as α,α'-trehalose, sucrose, and cyclomaltooligosaccharides.

2. Results and discussion

Reaction of either 6,6′-diamino-6,6′-dideoxy-α,α'-trehalose hydrochloride (**3**) [18], 6-amino-6-deoxy-α-D-fructofuranose β-D-fructopyranose 1,2′ : 2,1′-dianhydride (**10**) [19], 6,6′-diamino-6,6′-dideoxysucrose (**15**) [20], or the hexakis(6-amino-6-deoxy)cyclomaltohexaose (**22**) [21], heptakis(6-amino-6-deoxy)cyclomaltoheptaose (**26**) [22], and octakis(6-amino-6-deoxy)cyclomaltooctaose (**30**) hydrochlorides with thiophosgene, in the presence of calcium carbonate, afforded the unprotected deoxyisothiocyanates **4**, **11**, **16**, **23**, **27**, and **31** in 78–97% yield. In order to improve the availability of amine **3**, and by analogy with the preparation of **10**, a three-step synthesis was devised involving direct iodination of α,α'-trehalose with iodine–triphenylphosphine in *N*,*N*-dimethylformamide ($\rightarrow$ **1**) [23] followed by nucleophilic displacement with azide anion ($\rightarrow$ **2**) and Staudinger reduction [24] of the resulting azide ($\rightarrow$ **3**). The latter amination process was also used for the preparation of **15** from 6,6′-dideoxy-6,6′-diiodosucrose (**13**) [19]. Per(6-amino-6-deoxy)cyclomaltooligosaccharides **22**, **26**, and **30** were similarly prepared from the corresponding per(6-deoxy-6-iodo) derivatives **20** and **24**, and the unknown octakis(6-deoxy-6-iodo)cyclomaltooctaose (**28**), which was obtained from cyclomaltooctaose using the iodine–triphenylphosphine–*N*,*N*-dimethylformamide reagent.

Attempts to isolate 6,6′-dideoxy-6,6′-diisothiocyanato-α,α'-trehalose (**4**) from the mixture of **3** with thiophosgene, by treatment with mixed (H^+, HO^-) ion-exchange resin, resulted in a concomitant partial intramolecular cyclisation involving HO-4 to give



i) $CSCl_2$, $CaCO_3$, r.t. ii) Et_3N, DMF, 80°C.

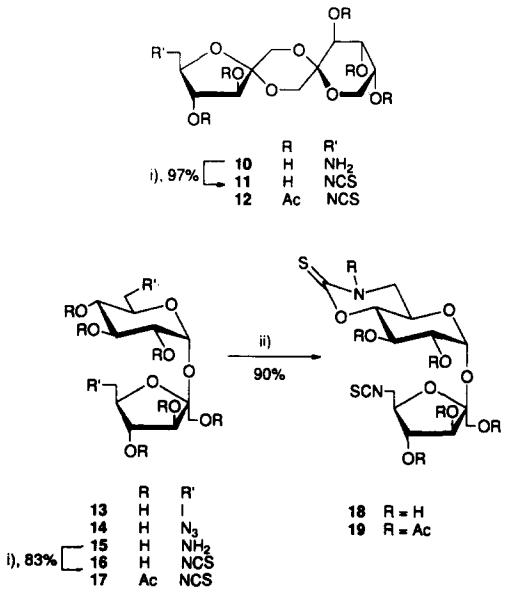
Scheme 1.

the unsymmetrical 6-amino-6,6′-dideoxy-6′-isothiocyanato-α,α'-trehalose 6,4-(cyclic thiocarbamate) (**6**) in 10% yield. Base-catalysed formation of bicyclic tetrahydrooxazine-2-thiones from methyl 6-deoxy-6-isothiocyanato-D-glycopyranosides has been recently reported [14,15], and a similar reaction seems to occur to some extent in contact with the resin. The diisothiocyanate **4** could, however, be isolated as the sole product in 89% yield after gel-permeation chromatography (GPC) of the crude mixture (Scheme 1).

It is noteworthy that no formation of intermolecular polymeric or cyclic thioureas, or other intramolecular reaction compound, was observed during the reaction of **3** with thiophosgene, whereas such side-reactions frequently take place during the synthesis of α,ω-diisothiocyanatoalkanes from the corresponding diamines [25]. This selectivity is probably related to the rigid conformational bias of the sugar molecule, and the results obtained from sucrose and cyclodextrin derivatives as reported below provide further examples.

In the absence of base, the diisothiocyanate **4** was a stable compound which could be transformed quantitatively into the corresponding hexaacetate **5** by treatment with acetic anhydride in pyridine. In the presence of triethylamine in *N*,*N*-dimethylformamide solution, **4** was converted quantitatively into the bis(cyclic thiocarbamate) **8** (Scheme 1). On treatment of **8** with acetic anhydride in pyridine, the corresponding peracetate **9** was obtained. No difference of reactivity towards acetylation between the NH and OH groups was observed, in agreement with reported results for methyl glycopyranoside derivatives [15].

6-Deoxy-6-isothiocyanato-α-D-fructofuranose β-D-fructopyranose 1,2′ : 2,1′-dianhydride (**11**), obtained in 97% yield from the corresponding amine **10**, proved to be more stable towards intramolecular thiocarbamate formation as compared to methyl 6-deoxy-6-isothiocyanatoglycopyranosides [15] and the corresponding α,α'-trehalose derivative **4**. Thus, **11** was recovered unchanged after heating in *N*,*N*-dimethylformamide at 80°C for 1 h in the presence of an excess of triethylamine (Scheme 2). The stability of an isothiocyanate group at C-6 of a fructofuranosyl unit was confirmed by

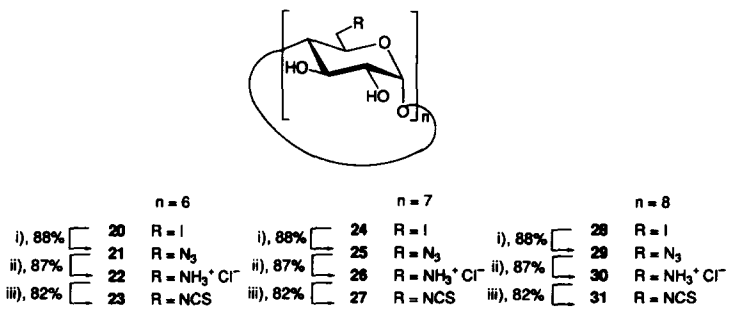


i) $CSCl_2$, $CaCO_3$, r.t. ii) Et_3N, DMF, 80°C.

Scheme 2.

comparing the reactivity of the two isothiocyanato groups in 6,6′-dideoxy-6,6′-diisothiocyanatosucrose (**16**). Upon triethylamine treatment, only the NCS group of the glucopyranosyl moiety underwent intramolecular cyclisation to give the 6,4-(cyclic thiocarbamate) **18** in 90% yield (Scheme 2).

Per(6-deoxy-6-isothiocyanato)cyclomaltooligosaccharides **23**, **27**, and **31** were found to be stable under similar basic conditions, and formation of per[6,3-(cyclic thiocarbamate)] derivatives did not occur even after prolonged heating with triethylamine in *N*,*N*-dimethylformamide (Scheme 3).



i) NaN_3, Me_2SO, 80 °C ii) (n-$Bu)_3P$, dioxane, MeOH, r.t./ NH_4OH iii) $CSCl_2$, $CaCO_3$.

Scheme 3.

The structures of the new sugar isothiocyanates **4**, **11**, **16**, **23**, **27**, and **31** and of the cyclic thiocarbamate derivatives **6**, **8**, and **18** were confirmed by analytical and spectroscopic data as well as by data for the peracetylated derivatives. Thus, compounds **4**, **5**, **11**, **12**, **16**, **17**, **23**, **27**, and **31** showed the characteristic IR absorption at $\sim 2100\ cm^{-1}$ and ^{13}C NMR signals at δ 129.0–137.0 for the isothiocyanate groups [15]. Both absorptions were absent in the corresponding spectra of the bis(cyclic thiocarbamate) derivatives **8** and **9**, which instead showed a signal at 185–187 ppm in their ^{13}C NMR spectra for the thiocarbonyl carbon atom and the expected UV $\pi \rightarrow \pi^*$ absorption at 250–280 nm for 2-thioxotetrahydro-1,3-O,N-heterocycles [15,26]. Both spectroscopic features were found in the mixed isothiocyanate–cyclic thiocarbamate derivatives **6**, **7**, **18**, and **19**.

The ^{1}H (Table 1) and ^{13}C NMR spectra (Table 2) of the α,α'-trehalose derivatives **4**, **5**, **8**, and **9** showed signals for equivalent D-glucopyranosyl moieties, in agreement with the proposed structures. The $^{3}J_{H,H}$ coupling constants around the pyranose rings indicated that they adopt the expected $^{4}C_{1}$(D) conformation in both diisothiocyanate (**4**,**5**) and bis(cyclic thiocarbamate) derivatives (**8**,**9**). No deshielding effect was observed for the resonance of H-4 in the peracetate **9** as compared to the unprotected derivative **8**, in agreement with the involvement of O-4 in the tetrahydrooxazine ring. In the case of compound **6**, and its peracetate **7**, the ^{1}H (Table 1) and ^{13}C (Table 2) NMR spectra showed two different sets of signals which could be correlated with those for the corresponding diisothiocyanate (**4** or **5**) and bis(cyclic thiocarbamate) derivatives (**8** or **9**), supporting the presence of both functionalities in the molecule.

The structure of the 6-deoxy-6-isothiocyanato-α-D-fructofuranose β-D-fructopyranose dianhydride (**11**) and its peracetate **12** was confirmed by comparison of their NMR spectra (Tables 1 and 2) with data for the parent difructose dianhydride [27] and related derivatives [19]. The values for the resonances of the anomeric carbon atoms C-2,2′ (103.2, 96.7 and 101.7, 94.6 ppm, respectively) can be considered as a fingerprint of the α-D-fructofuranose β-D-fructopyranose 1,2′ : 2,1′-dianhydride structure, while the resonances for C-6 (47.1 and 46.2 ppm, respectively) appear at higher field as compared to the unsubstituted or acetylated dianhydride [27], in agreement with the presence of the isothiocyanate group at the primary position.

The ^{13}C NMR data for the sucrose derivatives **16–19** are given in Table 2. A strong deshielding effect was observed for the resonance of C-4 in compounds **18** and **19** as compared to the corresponding diisothiocyanates **16** and **17** ($\Delta\delta$ 9.1 and 7.6, respectively), in agreement with the presence of the C-6–NH–C(= S)–O-4 bridge at the D-glucopyranosyl moiety. On the other hand, virtually no changes were observed in the resonances of the D-fructofuranosyl carbon atoms. The ^{1}H NMR spectra (Table 1) for the peracetates **17** and **19** fully agreed with the proposed structures.

The cyclomaltooligosaccharide derivates **23**, **27**, and **31** showed signals in their ^{1}H (Table 1) and ^{13}C NMR spectra (Table 2) for a single type of α-D-glucopyranosyl subunit, according to the six-, seven-, and eight-fold symmetry expected for the respective per(6-deoxy-6-isothiocyanato) derivatives. The signal at δ 129.9–129.7 in their ^{13}C NMR spectra confirmed the presence of the isothiocyanate functionality, and the highfield shift of the resonance of C-6 as compared to the parent cyclomaltooligosaccharides [28,29] was indicative of the substitution at the primary positions.

Table 1
^{1}H NMR data for compounds **4–9**, **12**, **17** and **19**

Compound	Chemical shifts (δ)													
	H-1	H-2	H-3	H-4	H-5	H-6a	H-6b	H-1′	H-2′	H-3′	H-4′	H-5′	H-6′a	H-6′b
4 [a,d]	5.25d	3.68dd	3.81t	3.42t	3.98ddd	3.90dd	3.82dd							
5 [b,d]	5.42d	5.18dd	5.52t	5.03t	4.17ddd	3.69dd	3.55dd							
6 [a,d]	5.21d	3.57dd	←-4.09m--→		4.27ddd	3.56t	3.28dd	5.28d	3.77dd	3.81t	3.42t	3.99ddd	3.90dd	3.82dd
7 [b,e]	5.34d	5.02dd	5.65t	4.14t	4.24ddd	3.88dd	3.56dd	5.36d	5.14dd	5.46t	4.96t	4.14ddd	3.65dd	3.51dd
8 [c,d]	4.93d	3.38dd	3.78t	3.83t	4.25ddd	3.10t	3.23dd							
9 [b,d]	5.32d	5.03dd	5.65dd	4.14dd	4.23ddd	3.89dd	3.57dd							
12 [b,d]	3.99d		5.28d	4.75dd	3.53m	←-3.24d--→		3.76d		5.55d	5.73dd	5.42ddd	3.43dd	3.30dd
	3.66d							3.71d						
17 [b,e]	5.74d	4.79dd	5.51t	4.96t	4.32ddd	3.73dd	3.68dd	4.40d		5.38d	4.16t	4.19dt	3.97dd	3.93dd
								4.31d						
19 [b,e]	5.68d	4.82dd	5.65t	4.08t	4.40dt	4.08dd	3.54dd	4.21s (2 H)		5.41d	5.16dd	4.16m	←-3.83m--→	

	Coupling constants (Hz)													
	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6a}$	$J_{5,6b}$	$J_{6a,6b}$	$J_{1',2'}$	$J_{2',3'}$	$J_{3',4'}$	$J_{4',5'}$	$J_{5',6'a}$	$J_{5',6'b}$	$J_{6'a,6'b}$
4 [a,d]	3.8	9.9	9.8	9.8	3.5	5.7	15.2							
5 [b,d]	3.9	10.0	10.0	10.0	6.8	3.4	14.8							
6 [a,d]	3.8	9.5		9.4	6.3	10.1	11.9	3.8	9.3	9.3	9.3	2.8	5.4	13.2
7 [b,e]	3.7	10.2	9.7	9.4	7.5	5.7	12.5	3.8	10.0	9.7	9.4	7.2	3.0	14.8
8 [c,d]	3.6	9.4	9.3	9.3	10.7	6.7	11.2							
9 [b,d]	3.8	10.1	9.4	10.1	7.5	8.9	12.4							
	$J_{1a,1b}$							$J_{1'a,1'b}$						
12 [b,d]	11.6		1.1	4.8	3.7	3.7		13.4		10.6	3.4	1.8	1.3	13.1
	$J_{1,2}$													
17 [b,e]	3.7	10.2	10.2	10.2	3.1	5.9	14.9	12.7		3.8	3.8	4.2	4.2	14.7
19 [b,e]	3.6	10.0	10.0	10.0	7.1	9.5	12.3			4.5	4.8			

[a] In D_2O. [b] In $CDCl_3$. [c] In Me_2SO-d_6. [d] At 300 MHz. [e] At 500 MHz

Table 2
^{13}C NMR chemical shifts for compounds **4–9**, **11**, **12**, **16–19**, **23**, **27**, and **31**

Compound	Carbon											
	C-1	C-2	C-3	C-4	C-5	C-6	C-1′	C-2′	C-3′	C-4′	C-5′	C-6′
4 [a,e]	93.9	72.3 [h]	74.0	72.7 [h]	71.6	47.0						
5 [b,e]	93.1	69.2	69.7	69.7	68.6	45.9						
6 [c,f]	94.1	69.9 [i]	68.4	79.1	59.6	43.5	93.6	70.0 [i]	71.7	70.2 [i]	69.9 [i]	45.1
7 [b,e]	93.9	69.5	67.8	76.8	62.9	47.3	92.8	69.4	69.3	69.2	68.5	45.7
8 [d,g]	95.6	71.3	68.8	79.7	60.2	44.2						
9 [b,e]	94.4	69.8	67.7	76.9	63.2	47.5						
11 [a,e]	62.8	103.2	81.2	79.9	84.0	47.1	63.5	96.7	70.1	70.8	70.8	62.8
12 [b,e]	60.6	101.7	80.6	78.7	80.9	46.2	61.2	94.6	66.9	68.6	67.2	61.2
16 [a,e]	93.7	72.2 [j]	74.0	72.1 [j]	72.9	48.9	63.4	105.9	78.9	77.6	81.3	47.2
17 [b,f]	90.4	70.3	68.7	69.1	68.5	45.6	61.2	105.0	75.8	76.3	79.9	47.0
18 [a,e]	94.0	70.9	72.9	81.2	61.7	49.0	63.6	106.1	78.5	77.7	81.5	47.1
19 [b,e]	90.9	70.2	66.9	76.7	63.1	47.7	61.8	104.6	75.5	76.0	79.7	47.1
23 [d,f]	101.9	71.4	72.4	83.5	68.9	46.2						
27 [d,g]	102.3	72.3	72.4	83.1	69.3	46.2						
31 [d,f]	102.2	72.3	72.3	82.6	69.4	46.2						

[a] In CD_3OD. [b] In $CDCl_3$. [c] In D_2O. [d] In Me_2SO-d_6. [e] At 75.5 MHz. [f] At 125.5 MHz. [g] At 50.3 MHz. [h,i,j] Assignments may be interchanged.

3. Experimental

General methods. — Melting points were determined with a Gallenkamp apparatus and are uncorrected. Optical rotations were measured with a Perkin–Elmer 141 polarimeter using 10-mm cells. UV spectra were recorded with a Philips PU 8710 spectrophotometer. IR spectra were recorded on a Bomen Michelson MB-120 FTIR spectrophotometer. The ^{1}H (300 and 500 MHz) and ^{13}C NMR spectra (50.3, 75.5, and 125.7 MHz) were obtained on Bruker AC-200 and Bruker 300 and 500 AMX spectrometers. Tetramethylsilane was used as internal standard. Assignments of ^{1}H signals were confirmed by COSY experiments. Gated decoupling and 2D HETCOR spectra were used for carbon signal assignments. Mass spectra were taken on a Kratos MS-80 RFA instrument. In the EI mode, operating conditions were: ionising energy, 35 eV; ionising current, 100 μA; accelerating voltage, 4 kV; resolution, 1000 (10% valley definition). In the FAB mode, the primary beam consisted of Xe atoms with a maximum energy of 8 keV. The samples were dissolved in glycerol, thioglycerol, or *m*-nitrobenzyl alcohol, and the positive ions were separated and accelerated over a potential of 7 kV. Except when otherwise stated, NaI was added as cationising agent. TLC was performed on Silica Gel 30 F_{254} (E. Merck) plates with visualisation by UV light and by charring with 10% H_2SO_4. Column chromatography was carried out on Silica Gel 60 (E. Merck, 230–400 mesh). Gel-permeation chromatography (GPC) was performed on a column (29.5 × 3.0 cm) of Bio-Gel P-2 by elution with H_2O–MeOH. The eluate was monitored by TLC (1 : 1 : 1 *n*-BuOH–AcOH–H_2O; detection with orcinol–H_2SO_4). Microanalyses were performed by the "Instituto de Química Orgánica General" (CSIC) in Madrid and by the "Service Central de Microanalyse du CNRS" (Solaize). For unprotected derivatives, the analyses were run under Ar for samples prepared in sealed tubes after drying over P_4O_{10}. The term "conventional acetylation" means treatment with 1 : 1 Ac_2O–pyridine (10 mL for 1 g of sample) overnight. The mixture was then poured into ice–water and extracted with CH_2Cl_2, and the organic layer washed with 1 M H_2SO_4 and satd aq $NaHCO_3$, dried ($MgSO_4$), filtered, and concentrated.

6,6'-Dideoxy-6,6'-diiodo-α,α'-trehalose (**1**). — To a solution of anhydrous α,α'-trehalose [30] (8 g, 23.4 mmol) in dry DMF (200 mL) were added Ph_3P (30.65 g, 117 mmol) and I_2 (23.75 g, 93.6 mmol). The mixture was heated at 80°C for 1.5 h and then concentrated to ~ 1/3 of the starting volume. Methanol (300 mL) was added and the solution was adjusted to pH 9 by addition of solid NaOMe, stirred at room temperature for 30 min, and neutralised with Amberlite IR-120 (H^+) resin. The resin was filtered off and washed with MeOH, and the combined filtrates were filtered through charcoal and concentrated to a residue which was triturated with water (250 mL). The residual Ph_3P and Ph_3PO were then removed by filtration. Evaporation of water yielded **1** (10 g, 77%) as an amorphous solid, $[\alpha]_D^{20}$ +108.1° (*c* 0.9, H_2O); FABMS (thioglycerol): *m/z* 585 ($[M + Na]^+$); lit. [31] $[\alpha]_D^{25}$ +109° (*c* 0.39, H_2O).

6,6'-Diazido-6,6'-dideoxy-α,α'-trehalose (**2**).—To a solution of **1** (4.17 g, 7.43 mmol) in dry DMF (80 mL) was added NaN_3 (2.89 g, 44.58 mmol). The mixture was heated at 80°C for 16 h, then concentrated, and the residue acetylated (1 : 1 Ac_2O–pyridine, 50 mL, 5 h). The peracetylated product (4.78 g), which showed a single spot on TLC (1 : 1 EtOAc–petroleum ether), was deacylated (Zemplén) to give **2** (2.70 g, 93%);

mp 209–210°C (from MeOH); $[\alpha]_D^{20}$ +156.0° (*c* 1, H_2O); lit. [32] mp 209–211°C, $[\alpha]_D^{20}$ +158.0° (*c* 0.7, H_2O).

6,6'-Diamino-6,6'-dideoxy-α,α'-trehalose dihydrochloride (**3**).—To a stirred solution of the diazide **2** (3.07 g, 8.76 mmol) in a mixture of dioxane (90 mL) and MeOH (18 mL) was gradually added Ph_3P (16 g, 61.3 mmol) under N_2 at room temperature. After 1 h, concentrated NH_4OH (30%, 14 mL) was added and the solution was stirred for 16 h. The solvent was evaporated, the residue was triturated with water (100 mL), and the resulting suspension was adjusted to pH 4 by addition of 1 M and 0.1 M HCl. The residual Ph_3P and Ph_3PO were then filtered off and washed with H_2O (2 × 50 mL), and the combined aqueous filtrates were washed with toluene (2 × 50 mL) and freeze-dried to give **3** (3.20 g, 89%); mp 81–83°C (from MeOH–acetone); $[\alpha]_D^{20}$ +164° (*c* 1, H_2O); lit. [18] mp 82–83°C, $[\alpha]_D^{12}$ +167° (*c* 1, H_2O).

6,6'-Dideoxy-6,6'-diisothiocyanato-α,α'-trehalose (**4**).—To a mixture of the diamine **3** (3.39 g, 8.23 mmol) in 1:1 H_2O–acetone (50 mL) and $CaCO_3$ (4.94 g, 49.4 mmol) was added $CSCl_2$ (2.84 g, 1.9 mL, 24.7 mmol). The mixture was vigorously stirred for 4 h at room temperature, then filtered, and the filtrate concentrated to dryness. The residue, which showed a single spot on TLC (45:5:3 EtOAc–EtOH–H_2O), was dissolved in MeOH and passed through an IWT TMD-8 (H^+, OH^-) resin column (3 × 20 cm). TLC of the eluate then showed the presence of **8** as a minor compound having higher R_f (see later). Column chromatography using the above eluent yielded amorphous **4** (2.72 g, 78%) as the main reaction product; $[\alpha]_D^{20}$ +100.7° (*c* 1.4, MeOH); ν_{max}^{KBr} 3335 (OH) and 2099 cm^{-1} (NCS); ^1H NMR (300 MHz, D_2O): Table 1; ^{13}C NMR (75.5 MHz, D_2O): Table 2 and δ 185.1 (C=S) and 131.3 (NCS); FABMS (*m*-nitrobenzyl alcohol): *m/z* 447 (25%, $[M + Na]^+$), 425 (40, $[M + H]^+$). Anal. Calcd for $C_{14}H_{20}N_2O_9S_2$: C, 39.62; H, 4.75; N, 6.60; S, 15.11. Found: C, 39.41; H, 4.49; N, 6.24; S, 14.69.

In another experiment, the mixture arising from the treatment of **3** (0.6 g, 1.47 mmol) with $CSCl_2$ (0.49 g, 0.33 mL, 4.41 mmol), as described above, was filtered, concentrated, and purified by GPC to give the diisothiocyanate **4** (0.55 g, 89%) as the only reaction product.

2,3,4,2',3',4'-Hexa-O-acetyl-6,6'-dideoxy-6,6'-diisothiocyanato-α,α'-trehalose (**5**).—Acetylation of **4** (0.3 g, 0.7 mmol) yielded the corresponding hexaacetate **5** (0.43 g, 90%); mp 75–77°C (from $CHCl_3$–petroleum ether); $[\alpha]_D^{20}$ +113.8° (*c* 1.1, $CHCl_3$); ν_{max}^{KBr} 2099 (NCS), 1755 (CO), and 1217 cm^{-1} (C–O–C); ^1H NMR (300 MHz, $CDCl_3$): Table 1 and δ 2.17, 2.14, and 2.07 (3 s, each 3 H, 3 OAc); ^{13}C NMR (75.5 MHz, $CDCl_3$): Table 2 and δ 169.9, 169.5, 169.2 (C=O), and 136.1 (NCS); EIMS: *m/z* 676 (1%, $M^{+\cdot}$), 617 (1, $M^+ - AcO^\cdot$), 616 (1, $M^+ - AcOH$), 330 [15, $(C_{13}H_{16}NO_7S)^+$]. Anal. Calcd for $C_{26}H_{32}N_2O_{15}S_2$: C, 46.15; H, 4.77; N, 4.14. Found: C, 46.12; H, 4.77; N, 4.24.

6-Amino-6,6'-dideoxy-6'-isothiocyanato-α,α'-trehalose 6,4-(cyclic thiocarbamate) (**6**).—Column chromatography of the mixture arising from the reaction of **3** with $CSCl_2$ and subsequent treatment with mixed (H^+, HO^-) ion-exchange resin (see above) afforded amorphous **6** (0.34 g, 10%) as the minor reaction product; $[\alpha]_D^{20}$ +10.0° (*c* 0.8, MeOH); λ_{max}^{MeOH} 254 nm (ε_{mM} 3.3); ν_{max}^{KBr} 3430, 3260 (OH, NH), 2112 (NCS), and 1559 cm^{-1} (NH); ^1H NMR (300 MHz, D_2O): Table 1; ^{13}C NMR (125.5 MHz, CD_3OD):

Table 2 and δ 185.1 (C=S) and 131.3 (NCS); FABMS (thioglycerol): m/z 447 ($[M + Na]^+$). Anal. Calcd for $C_{14}H_{20}N_2O_9S_2$: C, 39.62; H, 4.75; N, 6.60; S, 15.11. Found: C, 39.50; H, 4.42; N, 6.54; S, 14.95.

N-Acetyl-2,3,2',3',4'-penta-O-acetyl-6-amino-6,6'-dideoxy-6'-isothiocyanato-α,α'-trehalose 6,4-(cyclic thiocarbamate) (**7**).—Conventional acetylation of **6** (0.2 g, 0.47 mmol) yielded the corresponding peracetate **7** (0.29 g, 93%) as an amorphous solid; $[\alpha]_D^{20}$ +12.0° (*c* 0.7, CH_2Cl_2); $\lambda_{max}^{CH_2Cl_2}$ 280 nm (ε_{mM} 18.4); ν_{max}^{KBr} 2087 (NCS), 1750 (CO ester), 1715 (CO amide), and 1215 cm^{-1} (C–O–C); ^1H NMR (500 MHz, $CDCl_3$): Table 1 and δ 2.68 (s, 3 H, NAc), 2.17, 2.14, 2.09, 2.05, and 2.03 (5 s, each 3 H, 5 OAc); ^{13}C NMR (75.5 MHz, $CDCl_3$): Table 2 and δ 186.9 (C=S), 173.4 (C=O amide), 169.5 (2 C), 169.2 (2 C), 169.1 (5 C=O ester), 135.7 (NCS), 25.8 ($NCOCH_3$), 20.5 (2 C), 20.3 (2 C), and 20.2 (5 $OCOCH_3$); FABMS (*m*-nitrobenzyl alcohol): m/z 699 (100%, $[M + Na]^+$), 677 (15, $[M + H]^+$). Anal. Calcd for $C_{26}H_{32}N_2O_{15}S_2$: C, 46.15; H, 4.77; N, 4.14; S, 9.47. Found: C, 45.87; H, 4.79; N, 4.08; S, 9.71.

6,6'-Diamino-6,6'-dideoxy-α,α'-trehalose 6,4:6',4'-bis(cyclic thiocarbamate) (**8**).—To a stirred solution of the diisothiocyanate **4** (0.5 g, 1.17 mmol) in dry DMF (50 mL) was added Et_3N (0.1 mL, 0.7 mmol), and the mixture was heated at 80°C for 30 min. TLC (3:1 $CHCl_3$–MeOH) showed the clean conversion of **4** into a single product. Evaporation of the solvent yielded **8** (0.47 g, 95%); mp > 240°C (dec, from MeOH); $[\alpha]_D^{20}$ −67.9° (*c* 0.5, Me_2SO); $\lambda_{max}^{Me_2SO}$ 259 nm (ε_{mM} 14.2); ν_{max}^{KBr} 3390, 3277 (OH, NH), and 1557 cm^{-1} (NH); ^1H NMR (300 MHz, Me_2SO-d_6): Table 1; ^{13}C NMR (50.3 MHz, Me_2SO-d_6): Table 2 and δ 185.2 (C=S); FABMS (*m*-nitrobenzyl alcohol): m/z 447 (80%, $[M + Na]^+$), 425 (100, $[M + H]^+$). Anal. Calcd for $C_{14}H_{20}N_2O_9S_2$: C, 39.62; H, 4.75; N, 6.60; S, 15.11. Found: C, 39.27; H, 4.41; N, 6.40; S, 14.61.

N,N'-Diacetyl-2,3,2',3'-tetra-O-acetyl-6,6'-diamino-6,6'-dideoxy-α,α'-trehalose 6,4:6',4'-bis(cyclic thiocarbamate) (**9**).—Conventional acetylation of **8** (0.2 g, 0.47 mmol) yielded the peracetate **9** (0.29 g, 92%); mp 197–199°C (from EtOH); $[\alpha]_D^{20}$ −92.0° (*c* 0.9, $CHCl_3$); $\lambda_{max}^{CH_2Cl_2}$ 279 nm (ε_{mM} 20.8); ν_{max}^{KBr} 1755 (CO ester), 1710 (CO amide), and 1213 cm^{-1} (C–O–C); ^1H NMR (300 MHz, $CDCl_3$): Table 1 and δ 2.70 (s, 3 H, NAc), 2.13, and 2.07 (2 s, 6 H, 2 OAc); ^{13}C NMR (75.5 MHz, $CDCl_3$): Table 2 and δ 187.2 (C=S), 173.6 (C=O amide), 169.6, 169.2 (2 C=O ester), 26.0 ($NCOCH_3$), 20.7, and 20.6 (2 $OCOCH_3$); FABMS (*m*-nitrobenzyl alcohol): m/z 699 (100%, $[M + Na]^+$), 677 (80, $[M + H]^+$). Anal. Calcd for $C_{26}H_{32}N_2O_{15}S_2$: C, 46.15; H, 4.77; N, 4.14. Found: C, 46.13; H, 4.98; N, 3.99.

6-Deoxy-6-isothiocyanato-α-D-fructofuranose β-D-fructopyranose 1,2' : 2,1'-dianhydride (**11**).—To a mixture of 6-amino-6-deoxy-α-D-fructofuranose β-D-fructopyranose 1,2' : 2,1'-dianhydride [19] (**10**; 0.45 g, 1.39 mmol) in 2:1 H_2O–acetone (5 mL) and $CaCO_3$ (0.42 g, 4.18 mmol) was added $CSCl_2$ (0.24 g, 0.165 mL, 2.09 mmol). The mixture was vigorously stirred for 2 h at room temperature, then filtered, and the filtrate concentrated to dryness. The residue, which showed a single spot on TLC (2:1 $CHCl_3$–MeOH), was subjected to column chromatography with the above eluent to give **11** (0.49 g, 97%) as an amorphous solid; $[\alpha]_D^{20}$ −16.0° (*c* 1, MeOH); ν_{max}^{KBr} 3381 (OH) and 2108 cm^{-1} (NCS); ^{13}C NMR (75.5 MHz, CD_3OD): Table 2 and δ 133.2 (NCS). Anal. Calcd for $C_{13}H_{19}NO_9S$: C, 42.74; H, 5.24; N, 3.83; S, 8.78. Found: C, 42.42; H, 5.13; N, 3.71; S, 8.62.

3,4-Di-O-acetyl-6-deoxy-6-isothiocyanato-α-D-fructofuranose 3,4,5-tri-O-acetyl-β-D-fructopyranose 1,2′ : 2,1′-dianhydride (**12**).—Conventional acetylation of **11** (0.2 g, 0.54 mmol) yielded **12** (0.29 g, 94%) as an amorphous solid; $[\alpha]_D^{20}$ −34.0° (*c* 1, $CHCl_3$); ν_{max}^{KBr} 2106 (NCS), 1751 (CO), and 1223 cm^{-1} (C–O–C); ^1H NMR (300 MHz, $CDCl_3$): Table 1 and δ 1.82, 1.73, 1.72, 1.66, and 1.52 (5 s, each 3 H, 5 Me); ^{13}C NMR (75.5 MHz, $CDCl_3$): Table 2 and δ 170.2, 170.1, 169.6, 169.5, 168.9 (5 C=O), 132.6 (NCS), 20.6, 20.5 (2 C), 20.3, and 20.2 (5 Me); FABMS (*m*-nitrobenzyl alcohol): *m/z* 599 (100%, $[M + Na]^+$), 577 (15, $[M + H]^+$). Anal. Calcd for $C_{23}H_{29}NO_{14}S$: C, 48.00; H, 5.08; N, 2.43; S, 5.57. Found: C, 48.07; H, 5.04; N, 2.44; S, 5.13.

6,6′-Diazido-6,6′-dideoxysucrose (**14**).—To a solution of 6,6′-dideoxy-6,6′-diiodosucrose [19] (**13**; 4.17 g, 7.43 mmol) in dry DMF (80 mL) was added NaN_3 (2.89 g, 44.58 mmol). The mixture was heated at 80°C for 16 h, then concentrated, and the residue acetylated (1 : 1 Ac_2O–pyridine, 50 mL, 5 h). The peracetylated product (4.78 g), which showed one single spot on TLC (1 : 1 EtOAc–petroleum ether), was deacylated (Zemplén) to give the diazide **14** (2.70 g, 93%); $[\alpha]_D^{20}$ +78° (*c* 1, H_2O); lit. [20] $[\alpha]_D$ +78.8° (*c* 1, H_2O).

6,6′-Diamino-6,6′-dideoxysucrose (**15**).—Reduction of the diazide **14** (2.98 g, 8.76 mmol) with Ph_3P (16 g, 61.3 mmol), subsequent treatment with NH_4OH (30%, 14 mL), and concentration, following the procedure described above for the preparation of **2**, gave a solid residue which was extracted with water (3 × 50 mL). The water phase was washed with toluene (2 × 50 mL) and freeze-dried to yield **15** (2.65 g, 89%) as an amorphous solid; $[\alpha]_D^{20}$ +49.0° (*c* 1, H_2O); lit. [20] $[\alpha]_D^{20}$ +51.6° (*c* 1.5, H_2O).

6,6′-Dideoxy-6,6′-diisothiocyanatosucrose (**16**).—To a mixture of the diamine **15** (0.63 g, 1.86 mmol) in 3 : 2 H_2O–acetone (8 mL) and $CaCO_3$ (1.11 g, 11.16 mmol) was added $CSCl_2$ (0.64 g, 0.44 mL, 5.58 mmol). The mixture was vigorously stirred for 20 min and then concentrated. The residue, which showed a single spot on TLC (45 : 5 : 3 EtOAc–EtOH–H_2O), was dissolved in MeOH (30 mL) and passed through an IWT TMD-8 (H^+, OH^-) resin column (1.5 × 12 cm). Evaporation of MeOH gave **16** (0.67 g, 83%) as a syrup; $[\alpha]_D^{20}$ +74.3° (*c* 1, MeOH); ν_{max}^{film} 3380 (OH) and 2122 cm^{-1} (NCS); ^{13}C NMR (75.5 MHz, CD_3OD): Table 2 and δ 133.3 and 133.2 (2 NCS); FABMS (thioglycerol): *m/z* 447 (15%, $[M + Na]^+$). Anal. Calcd for $C_{14}H_{20}N_2O_9S_2$: C, 39.62; H, 4.75; N, 6.60; S, 15.11. Found: C, 39.34; H, 4.70; N, 6.51; S, 14.95.

2,3,4,1′,3′,4′-Hexa-O-acetyl-6,6′-dideoxy-6,6′-diisothiocyanatosucrose (**17**).—Conventional acetylation of **16** (0.2 g, 0.46 mmol) yielded the corresponding hexaacetate **17** (0.28 g, 93%) as a syrup; $[\alpha]_D^{20}$ +72.7° (*c* 1.2, $CHCl_3$); ν_{max}^{film} 2114 (NCS), 1751 (CO), and 1221 cm^{-1} (C–O–C); ^1H NMR (500 MHz, $CDCl_3$): Table 1 and δ 2.22, 2.15, 2.14, 2.13, 2.12, and 2.03 (6 s, each 3 H, 6 Me); ^{13}C NMR (125.5 MHz, $CDCl_3$): Table 2 and δ 169.9, 169.8, 169.7 (2 C), 169.4, 169.1 (6 C=O ester), 133.3, 133.1 (2 NCS), 20.5, 20.4 (2 C), 20.3 (2 C), and 20.2 (6 Me). Anal. Calcd for $C_{26}H_{32}N_2O_{15}S_2$: C, 46.15; H, 4.77; N, 4.14; S, 9.48. Found: C, 46.35; H, 4.75; N, 4.04; S, 9.71.

6-Amino-6,6′-dideoxy-6′-isothiocyanatosucrose 6,4-(cyclic thiocarbamate) (**18**).—To a stirred solution of the diisothiocyanate **16** (0.9 g, 2.12 mmol) in dry DMF (10 mL) was added Et_3N (0.2 mL, 1.4 mmol). The mixture was heated at 80°C for 30 min and then concentrated to give **18** (0.80 g, 90%) as a syrup; $[\alpha]_D^{20}$ +150.1° (*c* 1, MeOH); λ_{max}^{MeOH} 250 nm (ε_{mM} 14.2); ν_{max}^{film} 3345 (OH, NH), 2112 (NCS), 1659 and 1547 cm^{-1} (NH);

^{13}C NMR (75.5 MHz, CD_3OD): Table 2 and δ 187.9 (C=S) and 133.5 (NCS); FABMS (*m*-nitrobenzyl alcohol): *m/z* 447 (15%, $[M + Na]^+$), 425 (5, $[M + H]^+$). Anal. Calcd for $C_{14}H_{20}N_2O_9S_2$: C, 39.62; H, 4.75; N, 6.60; S, 15.11. Found: C, 39.51; H, 4.75; N, 6.85; S, 14.94.

N-Acetyl-2,3,1',3',4'-penta-O-acetyl-6-amino-6,6'-dideoxy-6'-isothiocyanatosucrose 6,4-(cyclic thiocarbamate) (**19**).—Conventional acetylation of **18** (0.15 g, 1.17 mmol) yielded the peracetate **19** (0.75 g, 95%) as a syrup; $[\alpha]_D^{20}$ −26.3° (*c* 1, $CHCl_3$); $\lambda_{max}^{CH_2Cl_2}$ 280 nm (ε_{mM} 10.4); ν_{max}^{film} 2104 (NCS), 1755 (CO), and 1223 cm^{-1} (C–O–C); ^{1}H NMR (500 MHz, $CDCl_3$): Table 1 and δ 2.70 (s, 3 H, NAc), 2.21, 2.14 (2 s, each 3 H, 2 OAc), 2.12 (s, 6 H, 2 OAc), and 2.11 (s, 3 H, OAc); ^{13}C NMR (75.5 MHz, $CDCl_3$): Table 2 and δ 187.1 (C=S), 173.5 (C=O amide), 170.0 (2 C), 169.9, 168.8, 168.6 (5 C=O ester), 133.5 (NCS), 25.7 ($NCOCH_3$) 20.4, 20.3 (2 C), and 20.2 (2 C) (6 $OCOCH_3$); FABMS (*m*-nitrobenzyl alcohol): *m/z* 699 (100%, $[M + Na]^+$), 677 (75, $[M + H]^+$). Anal. Calcd for $C_{26}H_{32}N_2O_{15}S_2$: C, 46.15; H, 4.77; N, 4.14. Found: C, 45.95; H, 4.38; N, 3.69.

Octakis(6-deoxy-6-iodo)cyclomaltooctaose (**28**).—To a stirred solution of Ph_3P (21 g, 80 mmol) in dry DMF (80 mL) was added I_2 (20.5 g, 80 mmol) in small portions. After 4 h, cyclomaltooctaose (4.32 g, 3.3 mmol) was added and the mixture was stirred for 18 h at 80°C, then concentrated to ~ half volume and cooled down to −5°C. The solution was made alkaline (pH 9–10) by addition of NaOMe (3 M, 30 mL), kept at room temperature for 30 min, and then poured into ice–water (1.5 L) under vigorous stirring. The resulting brownish precipitate was collected by filtration, washed abundantly with water, dried in the air, and suspended in CH_2Cl_2 (1 L). After vigorous stirring, the remaining insoluble material was filtered off, washed several times with CH_2Cl_2, and dissolved in DMF (100 mL). The solution was concentrated, and the product reprecipitated by addition of MeOH. After filtration and washing with additional MeOH, **28** (6.24 g, 88%) was obtained; mp 230.8–231°C (dec); $[\alpha]_D$ +72.8° (*c* 1.1, Me_2SO); ^{13}C NMR (50.3 MHz, Me_2SO-d_6): δ 102.0 (C-1), 85.3 (C-4), 72.5, 71.9, 71.2 (C-2,3,5), and 9.27 (C-6); FABMS (glycerol–thioglycerol): *m/z* 2199 (100%, $[M + Na]^+$), 2177 (21, $[M + H]^+$). Anal. Calcd for $C_{48}H_{72}I_8O_{32}$: C, 26.49; H, 3.33; I, 46.65. Found: C, 26.57; H, 3.48; I, 46.35.

Per(6-azido-6-deoxy)cyclomaltooligosaccharides (**21**, **25**, *and* **29**).—To a solution of the corresponding per(6-deoxy-6-iodo)cyclomaltooligosaccharide **20** [24,33], **24** [24,33], or **28** (2.5 g, 9.19 mequiv) in Me_2SO (25 mL), at 80°C, was added NaN_3 (2.5 g, 38.5 mmol) under stirring. After 24 h, the solvent was evaporated under low pressure, the residue was treated several times with H_2O, each time the suspension being centrifuged, and then decanted, until the aqueous phase was colourless. The azido compound was then suspended in water and freeze-dried, resulting in **21**, **25**, or **29**.

Hexakis(6-azido-6-deoxy)cyclomaltohexaose (**21**; 1.52 g, 88%); $[\alpha]_D^{20}$ +80° (*c* 1.1, Me_2SO); lit. [21] $[\alpha]_D^{20}$ +88° (*c* 1.1, Me_2SO); FABMS (thioglycerol, KI): *m/z* 2284.3 (23%, $[M_2 + K]^+$), 2246.3 (24, $[M_2 + H]^+$), 1160.9 (100, $[M + K]^+$).

Heptakis(6-azido-6-deoxy)cyclomaltoheptaose (**25**; 1.71 g, 99%); $[\alpha]_D^{20}$ +92.3° (*c* 0.52, Me_2SO); lit. [34] $[\alpha]_D^{20}$ +95.2° (*c* 0.52, Me_2SO): FABMS (thioglycerol, KI): *m/z* 2658.7 (22%, $[M_2 + K]^+$), 1348.9 (100, $[M + K]^+$).

Octakis(6-azido-6-deoxy)cyclomaltooctaose (**29**; 1.70 g, 99%); mp 220–223°C (dec);

$[\alpha]_D^{20}$ +91° (*c* 0.96, Me_2SO); ^{13}C NMR (50 MHz, Me_2SO-d_6): δ 102.2 (C-1), 82.8 (C-4), 72.5 (2 C), 70.6 (C-2,3,5), 51.3 (C-6); FABMS (thioglycerol, KI): *m/z* 1535 (100%, $[M + K]^+$), 1497 (10, $[M + H]^+$). Anal. Calcd for $C_{48}H_{72}N_{24}O_{32}$: C, 38.50; H, 4.85; N, 22.45. Found: C, 38.38; H, 4.70; N, 22.56.

Per(6-amino-6-deoxy)cyclomaltooligosaccharide hydrochlorides (**22**, **26**, *and* **30**).—To a stirred solution of the corresponding per(6-azido-6-deoxy)cyclomaltooligosaccharides **21**, **25**, or **28** (1.8 g, 9.6 mequiv) in a mixture of dioxane (150 mL) and MeOH (30 mL) was added tri-*n*-butylphosphine (7 mL, 31 mmol) under N_2 at room temperature. After 1 h, concentrated NH_4OH (28%, 77 mL) was added slowly and the solution was stirred for 12 h under N_2. The solvents were evaporated and the residue was triturated with acetone. The solid material was collected, washed with acetone (2 × 100 mL), and dispersed with stirring in a mixture of EtOAc (150 mL), MeOH (250 mL), and aq HCl (10 M, 0.9 mL). The insoluble amino compound was filtered off, dissolved in water, and freeze-dried, resulting in **22**, **26**, or **30**.

Hexakis(6-amino-6-deoxy)cyclomaltohexaose hydrochloride (**22**; 1.59 g, 87%); $[\alpha]_D^{20}$ +110° (*c* 0.53, H_2O); lit. [21] $[\alpha]_D^{20}$ +116° (*c* 0.53, H_2O).

Heptakis(6-amino-6-deoxy)cyclomaltoheptaose hydrochloride (**26**; 1.78 g, 98%); mp 182.4–182.8°C (from EtOH–H_2O); $[\alpha]_D^{20}$ +128° (*c* 1, H_2O); lit. [22] mp 182–185°C, $[\alpha]_D^{20}$ +131° (*c* 1, H_2O).

Octakis(6-amino-6-deoxy)cyclomaltooctaose hydrochloride (**30**; 1.51 g, 76%); mp 190–193°C (dec); $[\alpha]_D^{20}$ +130° (*c* 0.86, H_2O); ^{13}C NMR (125.7 MHz, D_2O): δ 100.0 (C-1), 80.4 (C-4), 71.4 (2 C), 67.2 (C-2,3,5), and 39.8 (C-6). Anal. Calcd for $C_{48}H_{93}Cl_8N_8O_{32}$: C, 36.52; H, 5.94; N, 7.13. Found: C, 36.27; H, 6.02; N, 6.89.

Per(6-deoxy-6-isothiocyanato)cyclomaltooligosaccharides (**23**, **27**, *and* **31**).—To a heterogeneous mixture of the corresponding per(6-amino-6-deoxy)cyclomaltooligosaccharide hydrochloride (0.15 g, 0.76 mequiv) in 1:1 H_2O–acetone (5 mL) and $CaCO_3$ (0.3 g, 3 mmol) was added $CSCl_2$ (0.17 g, 0.12 mL, 1.52 mmol). The mixture was vigorously stirred for 4 h at room temperature, then the acetone was evaporated and additional water (15 mL) was added. The resulting suspension was adjusted to pH 4 by addition of 1 M and 0.1 M HCl and stirred for 30 min at room temperature. The insoluble isothiocyanato compound was then filtered off, washed successively with water, cold EtOH, and Et_2O, and dried.

Hexakis(6-deoxy-6-isothiocyanato)cyclomaltohexaose (**23**; 0.12 g, 82%); amorphous solid; mp > 225°C (dec); $[\alpha]_D^{20}$ +20° (*c* 1, Me_2SO); ν_{max}^{KBr} 3383 (OH) and 2101 cm^{-1} (NCS); ^{13}C NMR (125.5 MHz, Me_2SO-d_6): Table 2 and δ 129.7 (NCS); FABMS (thioglycerol): *m/z* 1241 (100%, $[M + Na]^+$), 1219 (65, $[M + H]^+$). Anal. Calcd for $C_{42}H_{54}N_6O_{24}S_6$: C, 41.37; H, 4.46; N, 6.89; S, 15.78. Found: C, 41.27; H, 4.49; N, 6.85; S, 15.69.

Heptakis(6-deoxy-6-isothiocyanato)cyclomaltoheptaose (**27**; 0.13 g, 89%); amorphous solid; mp > 255°C (dec); $[\alpha]_D^{20}$ +46.0° (*c* 0.7, Me_2SO); ν_{max}^{KBr} 3380 (OH) and 2109 cm^{-1} (NCS); ^{13}C NMR (50.3 MHz, Me_2SO-d_6): Table 2 and δ 129.9 (NCS); FABMS (thioglycerol): KI, *m/z* 1460 (100%, $[M + K]^+$), 1422 (30, $[M + H]^+$); CsI, *m/z* 1554 (100%, $[M + Cs]^+$), 1422 (95, $[M + H]^+$). Anal. Calcd for $C_{49}H_{63}N_7O_{28}S_7$: C, 41.37; H, 4.46; N, 6.89; S, 15.78. Found: C, 41.40; H, 4.41; N, 6.51; S, 15.44.

Octakis(6-deoxy-6-isothiocyanato)cyclomaltooctaose (**31**; 0.12 g, 78%); mp > 240°C

(dec); $[\alpha]_D^{20}$ +85° (*c* 1.5, Me_2SO); ν_{max}^{KBr} 3383 (OH) and 2104 cm^{-1} (NCS); ^{13}C NMR (125.7 MHz, Me_2SO-d_6): Table 2 and δ 130.1 (NCS); FABMS (thioglycerol, KI): *m/z* 1663 (100%, $[M + K]^+$), 1625 (35, $[M + H]^+$). Anal. Calcd for $C_{56}H_{69}N_8O_{32}S_8$: C, 41.37; H, 4.46; N, 6.89; S, 15.78. Found: C, 41.16; H, 4.37; N, 6.52; S, 15.40.

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References

[1] For a review see: Z.J. Witczak, *Adv. Carbohydr. Chem. Biochem.*, 44 (1986) 91–145.
[2] N. Sharon, *Pure Appl. Chem.*, 60 (1988) 1389–1394.
[3] J. Fuentes, W. Moreda, C. Ortiz, I. Robina, and C. Welsh, *Tetrahedron*, 48 (1992) 6413–6424.
[4] J. Fuentes Mota, M.A. Pradera Adrián, C. Ortiz Mellet, and J.M. García Fernández, *Carbohydr. Res.*, 153 (1986) 318–324.
[5] A. Ya. Khorlin, S.E. Zurabyan, and R.G. Macharadze, *Carbohydr. Res*, 85 (1980) 201–208.
[6] H.G. Garg and R.W. Jeanloz, *Adv. Carbohydr. Chem. Biochem.*, 43 (1985) 135–201.
[7] W. Günther and H. Kunz, *Angew. Chem., Int. Ed. Engl.*, 29 (1990) 1050–1051.
[8] L. Drobnica, P. Kristián, and J. Augustín, in S. Patai (Ed.), *The Chemistry of Cyanates and Their Thio Derivatives*, Wiley, Chichester, 1977, Part 2, pp 1003–1221.
[9] A.K. Mukerjee and R. Ashare, *Chem. Rev.*, 91 (1991) 1–24.
[10] M. Avalos, R. Babiano, C. García-Verdugo, J.L. Jiménez, and J.C. Palacios, *Tetrahedron Lett.*, 31 (1990) 2467–2470.
[11] Z.J. Witczak, *Tetrahedron Lett.*, 27 (1986) 155–158.
[12] T. Hassel and H.P. Müller, *Angew. Chem., Int. Ed. Engl.*, 26 (1987) 359–360.
[13] W.D. Rees, J. Gliemann, and G.D. Holman, *Biochem. J.*, 241 (1987) 857–862.
[14] J.M. García Fernández, C. Ortiz Mellet, and J. Fuentes, *Tetrahedron Lett.*, 33 (1992) 3931–3934.
[15] J.M. García Fernández, C. Ortiz Mellet, and J. Fuentes, *J. Org. Chem.*, 58 (1993) 5192–5199.
[16] J. Fuentes Mota, J.L. Jiménez Blanco, C. Ortiz Mellet, and J.M. García Fernández, *Carbohydr. Res.*, 257 (1994) 127–135.
[17] J.M. García Fernández, C. Ortiz Mellet, J.L. Jiménez Blanco, and J. Fuentes, *J. Org. Chem.*, 59 (1994) 1565–1572.
[18] S. Umezawa, T. Tsuchiya, S. Nakada, and K. Tatsuta, *Bull. Chem. Soc. Jpn.*, 40 (1967) 395–401.
[19] J.M. García Fernández, A. Gadelle, and J. Defaye, *Carbohydr. Res.*, 265 (1994) 249–269.
[20] R. Khan, C.L. Bhardwaj, K.S. Mufti, and M.R. Jenner, *Carbohydr. Res.*, 78 (1980) 185–189.
[21] J. Boger, R.J. Corcorand, and J.-M. Lehn, *Helv. Chim. Acta*, 61 (1978) 2190–2218.
[22] K. Tsujihara, H. Kurita, and M. Kawazu, *Bull. Chem. Soc. Jpn.*, 50 (1977) 1567–1571.
[23] A. Gadelle and J. Defaye, *Angew. Chem., Int. Ed. Engl.*, 30 (1991) 78–80.
[24] Yu.G. Gobolobov, I.N. Zhmurova, and L.F. Kasukhin, *Tetrahedron*, 37 (1982) 437–472.
[25] H. Binder and J. Trittart, *Z. Naturforsch.*, 28 (1973) 530–532.
[26] E. Fujita and Y. Nagao, *Adv. Heterocycl. Chem.*, 45 (1989) 1–36.
[27] J. Defaye and J.M. García Fernández, *Carbohydr. Res.*, 237 (1992) 223–247.
[28] K. Bock, C. Pedersen, and H. Pedersen, *Adv. Carbohydr. Chem. Biochem.*, 42 (1984) 193–225.
[29] Y. Takahashi and T. Ogawa, *Carbohydr. Res.*, 169 (1987) 127–149.
[30] G. Birch, *J. Chem. Soc.*, (1965) 3489–3490.

[31] B. Castro, Y. Chapleur, and B. Gross, *Bull. Soc. Chim. Fr.*, 11 (1973) 3034–3039.
[32] G. Birch and A.C. Richardson, *Carbohydr. Res.*, 8 (1968) 411–415.
[33] H.H. Baer, A. Vargas Berenguel, Y.Y. Shu, J. Defaye, A. Gadelle, and F. Santoyo González, *Carbohydr. Res.*, 228 (1992) 307–314.
[34] Z. Szurmai, A. Liptak, and J. Szejtli, *Staerke*, 42 (1990) 447–449.