96. Glyconothio-*O*-lactones

Part III

Thermolysis of a 4,5-Dihydro-1,2,3- and a 2,5-Dihydro-1,3,4-thiadiazole

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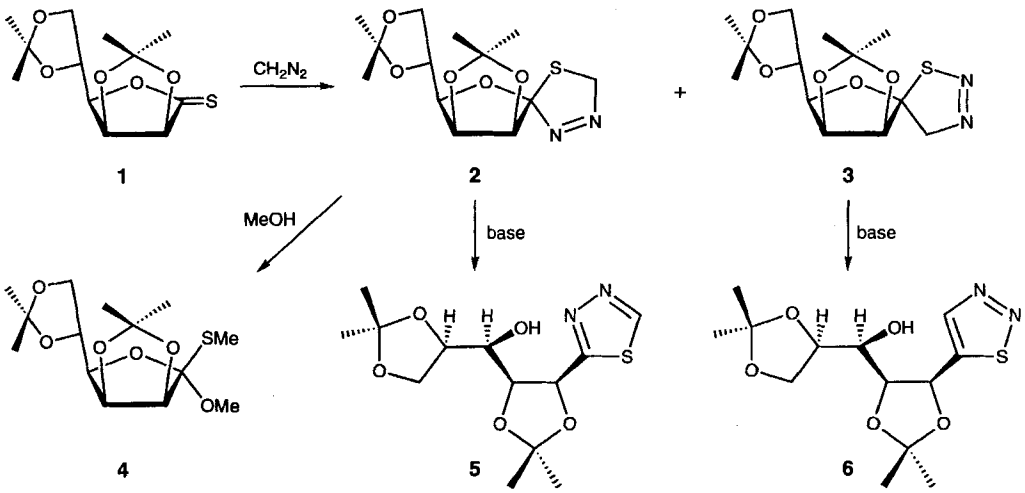
Addition of CH_2N_2 to 2,3:5,6-di-*O*-isopropylidene-1-thio-mannono-1,4-lactone (**1**) gave the 2,5-dihydro-1,3,4-thiadiazole **2** and the 4,5-dihydro-1,2,3-thiadiazole **3**. First-order kinetics were observed for the thermolysis of **3** (*Scheme 2*) at 80–110° in C_6D_5Cl solution and of **2** (*Scheme 3*) at 20–35° in $CDCl_3$, respectively. The 1,2,3-thiadiazole **3** led to mixtures of the thiirane **9**, the starting thionolactone **1**, the thiono-1,5-lactone **8**, and the enol ether **7**, while the isomeric 1,3,4-thiadiazole **2** led to mixtures of the anomeric thiiranes **9** and **12**, the *O*-hydrogen *S*,*O*,*O*-ortholactone α-D-**14**, the *S*-methyl thioester **15**, the *S*,*S*,*O*-ortholactone **13**, and the 2,3:5,6-di-*O*-isopropylidene-mannono-1,4-lactone (**16**). Pure products of the thermolysis were isolated by semipreparative supercritical fluid chromatography (SFC), whereas preparative HPLC led to partial or complete decomposition. Thus, the β-D-mannofuranosyl β-D-mannofuranoside **10**, contaminated by an unknown S species, was isolated by preparative HPLC of the crude product of thermolysis of **3** at 115–120° and partially transformed in CD_3OD solution into the symmetric di(α-D-mannofuranosyl) tetrasulfide **11**. Its structure was evidenced by X-ray analysis. Similarly, HPLC of the thermolysis product of **2** gave the enethiol **17**, the sulfide **19**, and the mercapto alcohol **18** as secondary products. Thermolysis of the thiirane **9** at 110–120° (*Scheme 4*) led to the anomeric thiirane **12** which was transformed into mixtures of the enethiol **17** and the enol ether **7**. Addition of H_2O to **17** and **7** gave the corresponding hemiacetals **18** and **20**. The mechanism of the thermolysis of the dihydrothiadiazoles **2** and **3**, and the thiiranes **9** and **12** is discussed.

Introduction. – The main primary products of the cycloaddition of thiocarbonyl compounds to CH_2N_2 are 2,5-dihydro-1,3,4-thiadiazoles and 4,5-dihydro-1,2,3-thiadiazoles. The dihydro-1,3,4-thiadiazoles are stable at low temperature only; above room temperature they cyclorevert to thiocarbonyl ylides (for leading references, see [1] [2]). The thiocarbonyl ylides either cyclize to thiiranes, or add to excess thiocarbonyl compound (*Schönberg* reaction [3]) or to other dipolarophiles. The dihydro-1,2,3-thiadiazoles are more stable; their thermolysis leads to thiiranes as the main product [4]. The cycloaddition of thio-*O*-esters to CH_2N_2 proceeds regioselectively, leading to 5-alkoxy-4,5-dihydro-1,2,3-thiadiazoles and, hence, to homologous thio-*O*-esters or enol ethers [5] [6] (see also [7] for a related case). *O*,*O*-Dimethyl dithiooxalate, however, leads preferentially to 5-alkoxy-2,5-dihydro-1,3,4-thiadiazoles and, hence, to 1,3-dithiolanes [8].

We have described a synthesis and some cycloadditions of glyconothio-*O*-lactones [9] [10]. The cycloaddition of the thio-*O*-lactone **1** to CH_2N_2 gave the 2,5-dihydro-1,3,4-thiadiazole **2** and the 4,5-dihydro-1,2,3-thiadiazole **3** in a ratio of 35:65 (*Scheme 1*). Base treatment of **2** and **3** (separated by HPLC at 5°) gave the isomeric (hydroxyalkyl)-

Scheme 1



thiadiazoles **5** and **6**, respectively. The structure of **6** has been established by X-ray analysis.

A solution of the 2,5-dihydro-1,3,4-thiadiazole **2** in $CDCl_3$ decomposed at room temperature (half-life 21.6 h) to a complex mixture. In MeOH solution, it was transformed exclusively to the *O,O,S*-ortholactone **4**. Crystalline 4,5-dihydro-1,2,3-thiadiazole **3**, however, proved stable up to 105°, while heating a solution of **3** in petrol at 100° led to a *ca.* 1:1 mixture of the spirothiirane **9** and the known enol ether **7** [11] (*Scheme 2*).

The striking difference between the thermal stability of the dihydrothiadiazoles **2** and **3** and the lack of information on the thermolytic behavior of thiadiazoles derived from thio-*O*-lactones prompted us to examine their thermal behavior more closely.

Results and Discussion. – 1. *Thermolysis of the Dihydrothiadiazoles* **2** *and* **3**. a) *Activation Energies.* The thermolysis of **2**/**3** 4:1 at 20, 25, 30, and 35° in $CDCl_3$ solution was followed by ^{1}H-NMR spectroscopy. The 1,2,3-isomer **3** is stable in $CDCl_3$ below 60° and was used for calibration. The progress of the thermolysis of **2** was followed by monitoring the signal intensity of H–C(5′) and H′–C(5′) at 5.90 and 5.67 ppm, respectively.

Purification of **3** by recrystallization was unsatisfactory, and HPLC led to samples with a purity of *ca.* 90–95% only. Semipreparative supercritical fluid chromatography (SFC), however, afforded pure samples of **3**. As decomposition of solutions of **3** started around 80°, we chose C_6D_5Cl as the solvent to determine the activation energy. Samples of 8–10 mg of crude **3** were purified by SFC, dissolved in C_6D_5Cl and a small amount of toluene for calibration, and thermolyzed at 80, 90, 100, and 110°. This sample preparation guaranteed neutral conditions avoiding base-induced aromatization (see above) but did not exclude traces of H_2O. Progress of the thermolysis was followed by monitoring the signal intensity of H–C(4′) of **3** at 5.21 ppm.

Thermolysis of both **2** and **3** followed first-order kinetics, half-lives $\tau_{1/2}$ were 2.3 h at 35° (21 h at 20°) for **2** and 0.65 h at 110° (36.7 h at 80°) for **3** (*Table 1*). The activation

Table 1. *Kinetic Parameters for the Thermolysis of* **2** *in* $CDCl_3$ *and of* **3** *in* C_6D_5Cl *Solution*

	Temperature [°C]	$\tau_{1/2}$ [h]	E_a [kcal/mol]	log A	$\Delta H^{\neq}$ [kcal/mol]	$\Delta S^{\neq}$ [cal/mol · K]
2	20	21.0				
	25	12.2				
	30	4.7	27.6	19.1	27.1	26.8
	35	2.3				
3	80	36.7				
	90	7.0				
	100	2.4	34.8	20.0	34.2	30.5
	110	0.65				

energies (E_a) were calculated using the *Arrhenius* equation [12], and the activation enthalpies ($\Delta H^{\neq}$) and entropies ($\Delta S^{\neq}$) were derived from the same data using the *Eyring* equation [12]. The log A values (19.1 and 20.0) deviate significantly from the value of 13.5 for unimolecular reactions; accordingly, larger (positive) values were determined for the activation entropies, in keeping with the formation of several primary products.

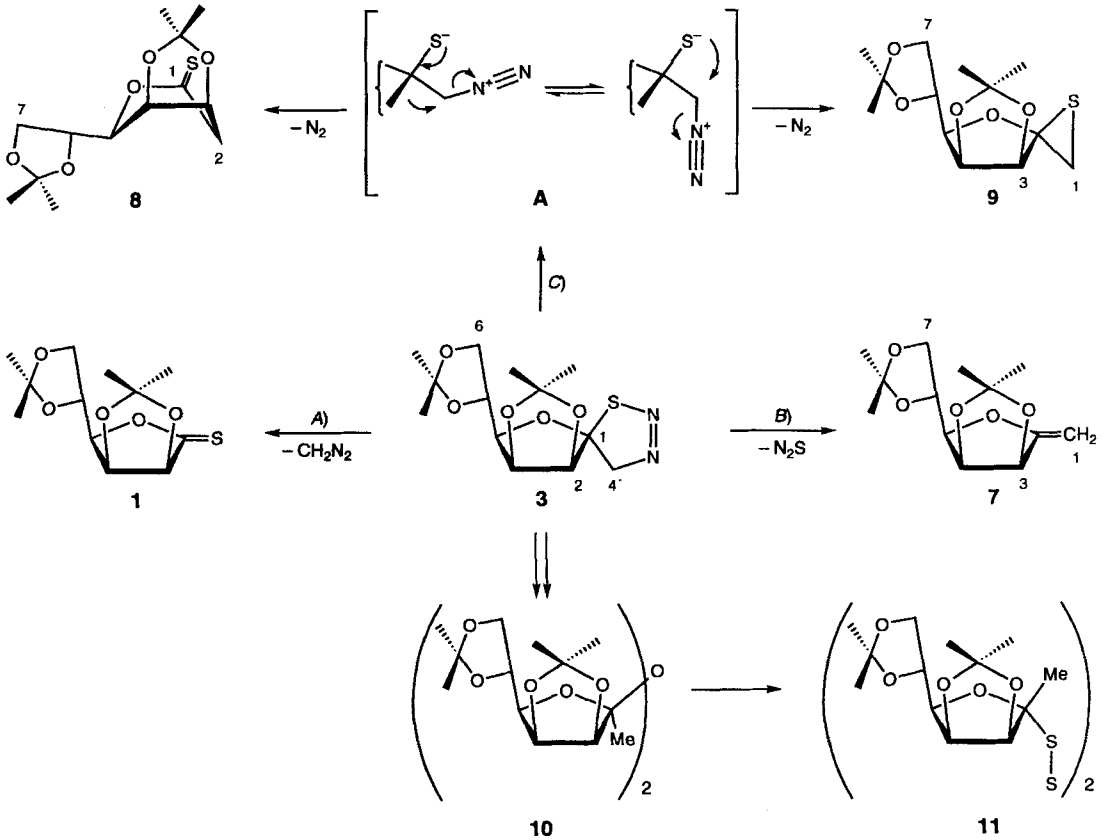
b) *Products of Thermolysis.* The thermolytic transformation of **3** in C_6D_5Cl solution was followed by ^{1}H-NMR spectroscopy. Four products of the thermolysis at 80–110° were detected: the thio-*O*-lactones **1** and **8**, the enol ether **7**, and the thiirane **9** (*Scheme 2*). The product ratio **9**/**7**/**8**/**1** of *ca.* 42:34:15:10 was determined by integration of characteristic ^{1}H-NMR signals (see *Exper. Part*). To check for additional products, 40 mg of **3** were thermolyzed at 110° and analyzed by ^{13}C-NMR spectroscopy; a nearly identical ratio **9**/**7**/**8**/**1** of 39:33:16:12 was observed. Signals for a fifth product (*ca.* 5%), were assigned to **20**, the hydrolysis product of the enol ether **7** (see below, *Scheme 4*).

Thermolysis of **3** in $C_6D_5Cl/(D_8)THF$ 1:1 or in C_6D_5Cl/CD_3OD 1:1 at 90–110° led to **9**/**7**/**8**/**1** in the slightly different ratios of 36:18:18:28 and 49:17:17:17, respectively. Thermolysis in petrol at 90°, however, gave **9**/**7**/**1** 45:40:15 and only traces of **8**. After 8 h at 90°, only 14% of **3** remained, demonstrating a lower stability of **3** in petrol ($\tau_{1/2} \approx 2.8$ h) than in C_6D_5Cl ($\tau_{1/2} = 7.0$ h). The solvent dependency of the product ratio is in agreement with the formation of several primary products.

The ratio of the products was neither affected by the temperature nor by the progress of the thermolysis, suggesting that **1** and **7**–**9** are the primary products of **3**. Cycloreversions (*Scheme 2*, paths *A* and *B*) lead to **1** and CH_2N_2, and to **7** and dinitrogen sulfide[1]). Heterolytic opening of the dihydrothiazole ring generates the intermediate **A** (path *C*) that is transformed into the thio-*O*-lactone **8** by ring expansion and into the thiirane **9** by nucleophilic substitution. The absence of the epimeric thiirane **12** supports this mechanism. The intermediate **A** is the thio analogue of the intermediate of a *Tiffeneau-Demjanov* reaction and of a ring enlargement of cyclic ketones with diazoalkanes (see [14–16] for reviews). Thermolysis of the 4,5-dihydro-1,2,3-thiadiazole derived from adamantanone has yielded analogous products: a spirothiirane (70%), a methylideneadamantane (3%), and a homoadamantane-2-thione (16%) [4].

[1]) The highly unstable dinitrogen sulfide has been generated by flash vacuum pyrolysis of 1,2,3,4-thiatriazoles [13].

Scheme 2



The separation of the products of the thermolysis of **3** was complicated by the sensitivity of **7** and **9** to silica gel, leading to their partial or complete decomposition during HPLC. Semipreparative SFC, however, gave pure samples of **7**, **8**, and **9**.

Thermolysis of 45-mg samples of **3** in C_6D_5Cl at the slightly higher temperatures of 115–120° for 14 h led to consumption both of the starting material and of the primary products **7** and **9**. The homothiolactone **8**, however, was still present in the complex reaction mixture. Apparently (according to ^{1}H-NMR) pure samples of a new product, the β-D-glycosyl β-D-glycoside **10** (5–10%), were isolated by prep. HPLC, and crystallized as fine needles[2]). In the presence of traces of acid, they were hydrolyzed to **20** (see below, *Scheme 4*). Solutions of these samples in $CDCl_3$ were stable, while their solution

[2]) The low yields of **10** and the complexity of the reaction mixture caution against more than a speculative rationalization of the formation of the presumably less stable β/β-anomer. At higher temperatures, the enol ether **7** may be hydrated by intramolecularly H-bonded H_2O, present in traces only and leading to a β-D-hemiacetal. Rapid formation of an H-bonded dimer between this hemiacetal and **7**, and intramolecular addition yields **10**. The preparative implications of this speculation have not been checked.

in CD_3OD was partially transformed into the tetrasulfide **11** (**10**/**11** 3:1) that could not be separated from **10** by preparative HPLC.

Crystallization of **10**/**11** 3:1 from AcOEt/hexane gave needles of **10** and a cube of **11**. While the crystal of **11** was suitable for X-ray analysis (*Fig. 1*), those of **10** were not. In the solid state, **11** is C_1-symmetric[3]). In keeping with the structure of all organic tetrasulfides deposited in the *Cambridge Database* [17] [18], **11** shows the all-*trans*-conformation [19] evidenced by the negative sign of the dihedral angles C(2)–S–S–S (–78.5°), S–S–S–S (–81.8°), and S–S–S–C(2′) (–87.9°). These dihedral angles, the short terminal S–S bonds (2.020 and 2.027 Å), and the long central S–S bond (2.058 Å) agree well with with the corresponding values for dialkyl and diaryl tetrasulfides. The furanose rings of **11** adopt a ^{O}E conformation with pseudoequatorial C-substituents at C(2), C(5), C(2′), and C(5′). The pseudoaxial S-substituents at C(2) and C(2′) suggest an anomeric effect. Indeed, the C(2)–O(5) and C(2′)–O(5′) bonds (1.415 and 1.419 Å) are slightly shorter than the C(5)–O(5) and C(5′)–O(5′) bonds (1.432 and 1.436 Å), and the C(2)–S and C(2′)–S bonds (1.879 and 1.885 Å) are longer than the C–S bonds of the dialkyl and diaryl tetrasulfides (1.76–1.79 Å [17] [18]). The lengthening of the C–S bonds may be enhanced by the quarternary acetal center[4]). To the best of our knowlegde, **11** is the first difuranosyl tetrasulfide to be reported (for diglucopyranosyl tetrasulfides see [20]).

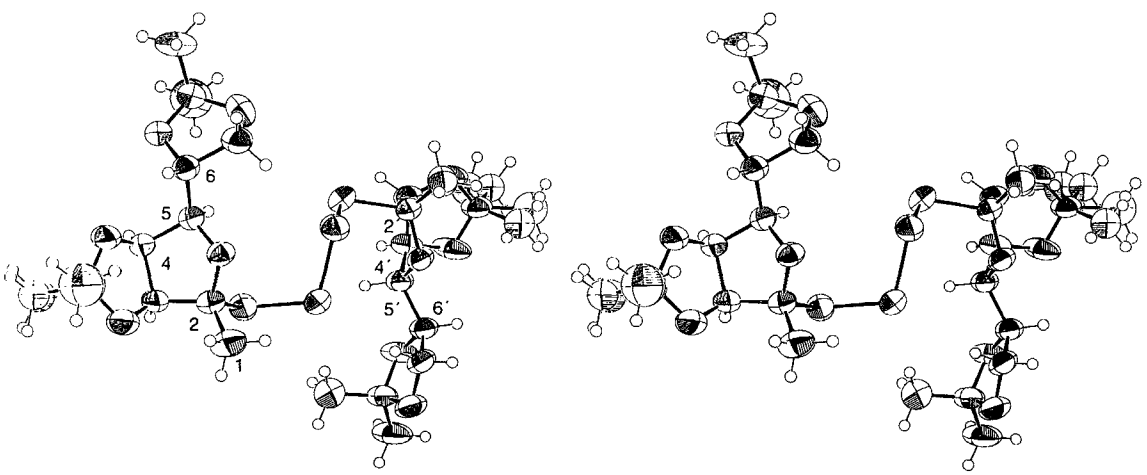


Fig. 1. *X-Ray structure of* **11**

The ^{1}H- and ^{13}C-NMR spectra of **10** and **11** reflect the C_2 symmetry; there is a single set of signals (the spectra of **8** and **9** are discussed in *Chapt. 2*). C(2) of **11** resonates at 99.7 ppm (*Table 5*). This value agrees well with a tetrasulfanyl substituent, as C(2) of methyl 3,4:6,7-di-*O*-isoproylidene-2-thio-α-D- and β-D-*manno*-hept-2-ulofuranoside res-

[3]) Coordinates and thermal parameters were deposited with the *Cambridge Crystallographic Data Center*, 12 Union Road, Cambridge CB2 1EZ, England.

[4]) According to the *Cambridge Database*, characteristic C–S bond lengths for 1-thio-β-D-aldopyranosides are 1.79–1.81 Å, for 1-thio-α-D-aldopyranosides 1.82–1.84 Å, and for monothioacetals derived from ketones 1.86–1.90 Å.

onate at 90.5 und 92.9 ppm, respectively [9], and the replacement of a MeS by a MeSS group leads to a deshielding of 5–7.5 ppm [21] [22]. C(2) and Me_2C of **10** resonate at 108.7, 109.5, and 112.3 ppm, indicating an O- rather than an S-substituent at C(2).

Combustion analysis of a sample of **10** showed the presence of 2.2% of S, too low for an equimolar amount. Thus, S must be a contamination, probably in the form of S_x or H_2S_x[5]). If this is taken into account, the values for C and H indicate a molecular formula $C_{26}H_{41.7}O_{11.1}$; *i.e.*, **10** ($C_{26}H_{42}O_{11}$) and 0.35 equiv. of S. A CI-MS shows (*m/z* 515) the signal for $[M-15]^+$, at *m/z* 257 the signal for a di-*O*-isopropylidene-heptulofuranosyl residue, and at *m/z* 275 the signal for the diprotonated di-*O*-isopropylidene-heptulofuranosyloxy residue. The assignment of the β-D-configuration to **10** is based upon irradiation of the H–C(1) *s*, leading to intensity enhancements for H–C(5) (5%) and H–C(3) (2%, see *Exper. Part*). As expected, no NOE was observed upon irradiation of the H–C(1) *s* of **11**.

Thermolysis of **2** in $CDCl_3$ (*Scheme 3*) led to a complex mixture resulting from transformations of the primary products. Minor amounts (< 20%) of the spirothiiranes **9** and **12** were detected by ^{1}H-NMR spectroscopy, but decomposed upon evaporation of the solvent. As the (isolated) spirothiirane **9** proved more stable in C_6D_5Cl than in $CDCl_3$ solution, **2** was thermolyzed in C_6D_5Cl at 23, 30, and 35°. There was no substantial difference between the half-lives of **2** in $CDCl_3$ and in C_6D_5Cl solution, but the primary products were stable in C_6D_5Cl. Characteristic ^{1}H-NMR signals evidence the formation of the epimeric spirothiiranes **9** and **12**, the *O*-hydrogen *O,O,S*-ortholactone α-D-**14**, the thio-*S*-ester **15**, and the *O,S,S*-ortholactone **13**. No signals of **1** were detected[6]). The additional MeS group of **13** must derive from MeSH, which is formed in the lactonization of **15** (or α-D-**14**) to **16**. Unfortunately, signal overlapping prevented the detection of **16** by ^{1}H-NMR spectroscopy; its presence was subsequently (see below) evidenced by ^{13}C-NMR spectroscopy, and the proportion in which it is formed (necessarily at the least equimolar to **13**) was then determined as **13**/**16** *ca.* 1:2.

The ratio of the thermolysis products of **2** did not significantly depend on the temperature between 23 and 35° (*Entries 1–3* in *Table 2*); about one third was transformed into the thiirane **9**, one sixth into the thiirane **12** (paths *C* and *D*), and one half reacted with H_2O or MeSH to α-D-**14**/**15**/**16** and **13** (paths *E* and *F*). Most probably, these products are formed *via* the alkoxythiocarbonyl ylide **B** (*Scheme 3*). The ^{13}C- and a ^{1}H-NMR spectrum at 500 MHz[7]) of the products obtained by thermolyzing a larger sample of **2** at 35° until disappearance of **2** showed the formation of a 39:20:18:16:7 mixture **9**/**12**/α-D-**14**/**16**/**13** besides traces of **15** and additional compounds (< 5%),

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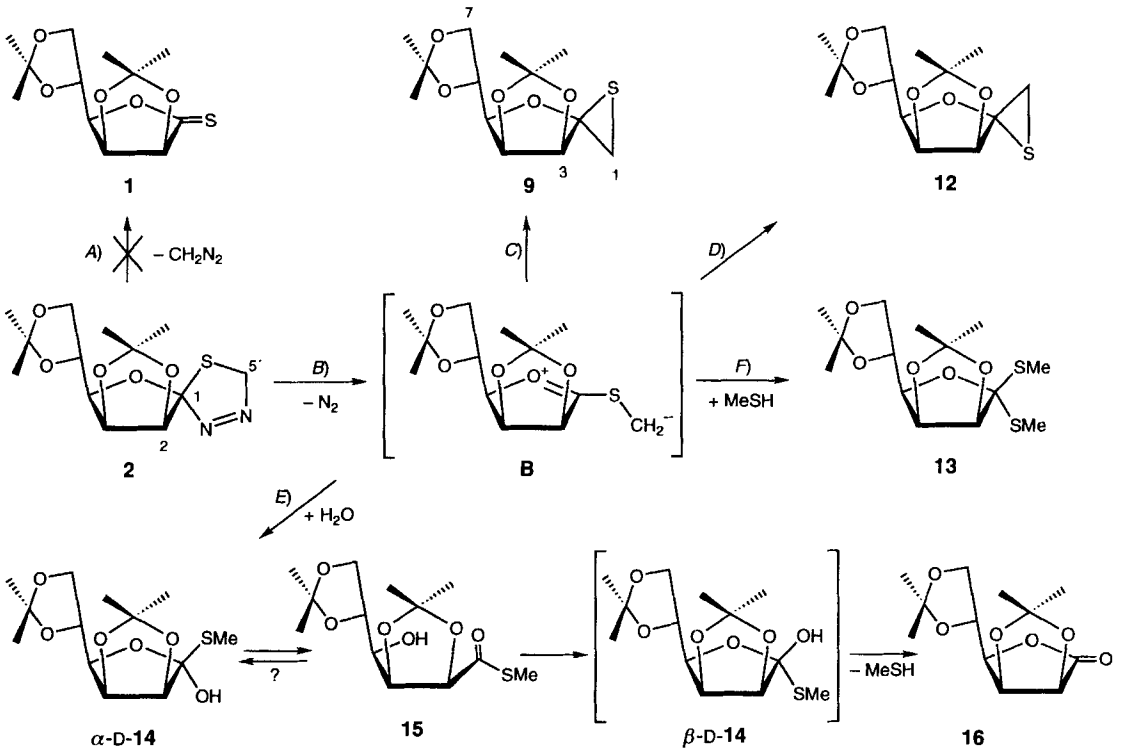
[5]) The stoichiometric transformation of **10** into **11** requires 2 mol-equiv. of S, corresponding to 19.5% in weight. As only 25% of **10** was transformed into **11**, the sample of **10** must have contained at least 4.9% of 'active sulfur', *i.e.*, a sulfur species which must derive from N_2S and possess a similar HPLC t_R value as **10**. The constitution of this S species is unknown; no hints for hydrooligosulfides could be found in the IR spectra (hydrodi- [23], hydrotri-, and hydrotetratetrasulfides [24] absorb at 2480–2540 cm^{-1}). A sample of **10** used for combustion analysis and containing 2.2% of S should lead to a maximum 9% of **11**. No **11** was, however, detected by ^{1}H-NMR spectroscopy in this sample. Presumably, the samples transformed into **10**/**11** 3:1 contained considerably more than the minimum 4.9% of such S species.

[6]) Thus, cycloreversion to **1** (path *A*, *Scheme 3*) did not occur below 35°, while 2,2,5,5-tetrasubstituted 2,5-dihydro-1,3,4-thiadiazoles undergo cycloreversion at room temperature [25].

[7]) In this NMR spectrum, the proportion of **16** was determined by integration of the *ddd* at 4.35 ppm (H–C(5)).

Scheme 3



but no trace of MeSH (*q* expected at *ca.* 7 ppm [26]; *Entry 4* in *Table 2*). The moderate influence of the H_2O content on the product ratio was evidenced by thermolyses in C_6D_5Cl, containing smaller (*Entry 5*) or larger amounts of H_2O (*Entry 6*); the ratio of the thiiranes **9**/**12** to the H_2O and MeSH addition products α-D-**14**/**15**/**16** and **13** was larger in the former than in the latter experiment (1.11 *vs.* 0.74).

Attempts to separate the thermolysis product of **2** by HPLC led to partial decomposition and to the formation of products that were subsequently also detected in the product of the thermolysis of **9** and **12** (*cf.* below, *Scheme 4*). Thus, HPLC separation of the crude product of the thermolysis of **2** led to a mixture **12**/**13**, traces of the enethiol **17** (*Scheme 4*), the thio-*S*-ester **15**, the mercapto alcohol **18**, the dimer **19**, and, as the main component, the lactone **16**. Compounds **17**–**19** were only formed during chromatography. The hydrogen ortholactone α-D-**14** was completely consumed during HPLC. The stability of α-D-**14** in solution is surprising at first sight, but less so when compared to the one of an (isolated) pentacyclic hemi-orthothiol ester [27][8]) and a 2-ethoxy-2*H*-thiopyran-2-ol that was detected by ^{1}H-NMR spectroscopy [29]. According

[8]) The structure of a postulated, monosaccharide-derived hydrogen-orthothioester [28] cannot be correct, as the ^{1}H-NMR data require the presence of a secondary OH group (J = 7 Hz) instead of the (postulated) tertiary one.

Table 2. *Thermolysis of* **2** (7 mg) *in* C_6D_5Cl *Solution* (0.7 ml); *Ratio of Products*

Entry	Temp. [°C]	Time [h]	Ratio of starting material and products[a])						
			2 :	**9** :	**12** :	**14** :	**15** :	**13** :	**16**[b])
1	23	4	53	13	7	10	5	4	8
		8	30	23	12	12	6	6	11
		10.5	24	24	12	16	6	6	12
		16.5	10	33	17	19	6	5	10
2	30	1	59	12	6	9	5	3	6
		3	30	23	11	17	4	5	10
		5	16	26	13	20	5	7	13
		7	11	28	14	21	5	7	14
3	35	0.5	62	11	6	7	5	3	6
		1	43	18	10	11	6	4	8
		2	26	26	13	16	5	5	9
		3	trace	37	18	22	6	6	11
4[c])	35	12	0	39	20	18	trace	7	16
5[d])	23	24	3	31	20	19	trace	9	18
6[e])	35	3	4	27	14	27	4	8	16

[a]) Determined by ^{1}H-NMR spectroscopy. [b]) As determined for *Entry 4*, a ratio **13**/**16** *ca.* 1:2 is assumed for the other entries. [c]) 40 mg of **2** in 0.7 ml of C_6D_5Cl; ratio determined by ^{1}H-NMR (500 MHz) and ^{13}C-NMR spectroscopy. [d]) To remove H_2O as completely as possible, dried solvents were used for HPLC, the evaporation of the fraction containing **2** was performed under inert gas, and **2** was dissolved in dried C_6D_5Cl. [e]) In the presence of 4 equiv. of H_2O, leading to an emulsion.

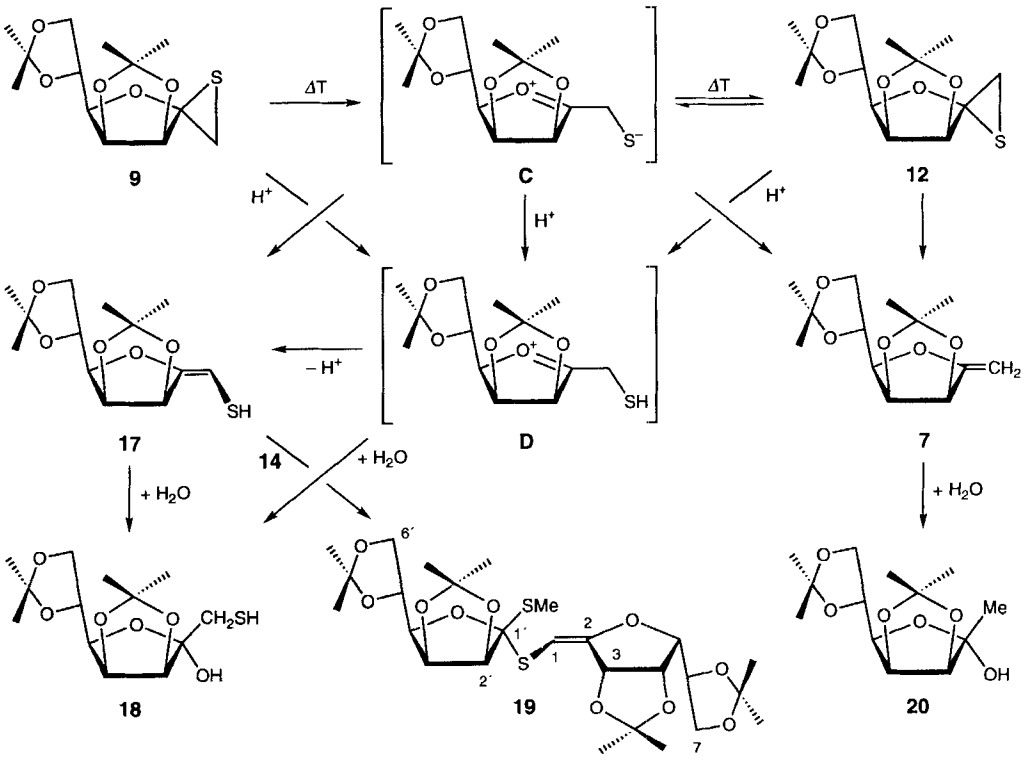
to *Deslongchamps'* rules [30], the ^OE conformer of α-D-**14** will not directly react to **16**, but rather to the thio-*S*-ester **15**. That **15** is stable to the conditions of chromatography is not surprising in view of the known stability of some γ-hydroxy-*S*-alkyl thioesters (see *e.g.* [31]). The low reactivity of **15** is also correlated with an intramolecular H-bond OH · · · O(5) possibly reducing the availability of the internal nucleophile. Conceivably, **15** may prefer to cyclize to α-D-**14** rather than to the anomer β-D-**14**, the expected intermediate on the way to **16**.

2. *Thermolysis of the Thiiranes* **9** *and* **12**. We wondered if the epimeric thiiranes **9** and **12** are transformed into each other under thermal conditions, and if the enol ether **7** is also formed *via* **9** and/or **12**, and not only by a cycloreversion of **3**.

The episulfide **9** was heated in C_6D_5Cl in the presence or absence of *Hünig*'s base. The experiments in the presence of *Hünig*'s base were performed after we discovered a strong influence of *bona fide* traces of acid and H_2O on the course of the thermolysis above 100° (see below); no reaction was observed below 90°. In the presence of *Hünig*'s base (*Entry 1*), thermolysis started at *ca.* 100°, slowly leading to **12**[9]). Above 115°, **7** was formed (br. *t* for H'–C(1) at 4.20 ppm) and remained stable even at 140°. Although the episulfide **9** was first transformed into its isomer **12**, the ratio of **12** never exceeded 18%, while the one of **7** reached 85% after 3 h at 140°, 15% of **9** and a trace of **12** remaining.

[9]) Formation of **12** was readily evidenced by the *AB* signal of H–C(1) and H'–C(1) at 2.81 and 2.65 ppm (*Table 4*).

Scheme 4



Thermolysis of **12** at 110 and 120° (*Table 3, Entries 5* and *6*) led exclusively to **7**, **17**, and **18**. No trace of **9** could be detected by ^{1}H-NMR spectroscopy.

Thermolysis for 1 h at 100° in the absence of *Hünig*'s base led to a 6:4 mixture of the thiiranes **9** and **12** (*Table 3, Entry 2*). After 3 h at 100° – similarly to the thermolysis in the presence of *Hünig*'s base – the ratio **9**/**12** had changed to 46:54, and traces of the enol ether **7** appeared. After 8 h at 100°, thermolysis resulted in a 27:58:15 mixture of **9**/**12**/**7**. Thermolysis at 120° was difficult to reproduce, as illustrated by two extreme results. In one run (*Entry 3*), the ratio **9**/**12**/**7** changed from 17:70:13 after 1 h to 6:57:37 after 3 h; after 5 h, these compounds had disappeared in favor of the enethiol **17** (55%) and the α-D-heptulofuranose **20** (3:7). In another run (*Entry 4*), thermolysis led to **17**/**18**/**7** 70:28:2. Also in the absence of *Hünig*'s base, no isomerization of **12** to **9** was observed (*Entry 7*).

Independently of the presence or absence of *Hünig*'s base, thermolysis of **9** at 100° is characterized by the initial appearance of **12**, more rapidly in the absence of *Hünig*'s base. The enol ether **7** was only formed once substantial amounts of **12** had accumulated, as illustrated by *Fig. 2*, suggesting that **12** – and not **9** – is the precursor of **7**. Thermolysis of **9** and **12** is in keeping with the conclusion that thermolysis of the dihydro-1,2,3-thiadiazole **3** leads to **7** by cycloreversion, as this takes place at 80°, while the transformation of **9** into **7** (*via* **12**) requires temperatures of 100°.

Table 3. *Thermolysis of the Thiiranes* **9** *and* **12** *in* C_6D_5Cl *Solution; Ratio of Products*

Entry	Starting material	Temp. [°C]	Time [h]	Ratio of starting material and products[a])					
				9 :	**12** :	**7** :	**17** :	**18** :	**20**
1	**9**[b])	100	1.5	100	trace				
			2.5	92	8	0			
		115	1	89	11	trace			
			4	76	14	10			
		120	1	60	17	23			
			2	54	18	28			
		130	1	48	16	36			
		140	0.75	37	17	52			
			1.5	28	6	66			
			3	15	trace	85			
2	**9**	100	1	60	40				
			2	50	50				
			3	46	54	trace			
			4	39	54	7			
			6	33	55	12			
			8	27	58	15	trace		
3	**9**	120	1	17	70	13			
			2	10	64	26			
			3	6	57	37	0	0	0
			5	0	0	0	30	0	70
4	**9**	120	2	14	7	3	61	15	0
			4	0	0	2	70	28	0
5	**12**[c])	110	2	0	0	10	54	36	0
6	**12**[c])	120	2.5	0	0	12	63	25	0
7	**12**[d])	120[e])	2.5	0	60	20	20	0	0
			3.5	0	39	trace	35	0	26

[a]) Determined by ^{1}H-NMR spectroscopy. [b]) In the presence of *ca.* 2 equiv. of $(i\text{-Pr})_2EtN$. [c]) In the presence of *ca.* 10 mol-% of $(i\text{-Pr})_2EtN$. [d]) **12**/**13** 1:1; **13** was stable under the reaction conditions. [e]) No reaction during 3.5 h at 100°.

Presumably **9** isomerizes to the zwitterion **C** that rapidly ring-closes to **12** (*Scheme 4*). The direction of the isomerization, from **9** to **12**, may reflect kinetic and/or thermodynamic control, as the ring closure to **9** involves unfavorable steric and charge-dipole interactions between S^- and C(3)–O that may be partially operative also for **9**. Indeed, AM1 calculations (AMPAC 5.0 program [32]) of the relative stability of **9** and **12** give an energy difference of 1.9 kcal/mol in favor of **12**. The higher temperatures required for the transformation of **9** to **7** are compatible either with formation of **7** from **12**, or by a high energy path from **C** to **7**; similarly, also **17** may be formed *via* **C**. Traces of acids appear to strongly catalyze the isomerization of **9** to **12**, presumably *via* **D** that may equilibrate with protonated **12** and with protonated **17**. Acid-catalyzed hydration transforms **17** into **18** and **7** into **20**. The formation of **7** and **17** prevents the determination of the position of the equilibrium between **9** and **12**. A solution of pure **17** in C_6D_5Cl was transformed into **17**/**18** 55:44 upon storage at −20° for 60 h, as shown by ^{13}C-NMR spectroscopy. The *O,S,S*-ortholactone **19** is a condensation product of the enethiol **17** and the *O*-hydrogen *O,O,S*-ortholactone α-D-**14**.

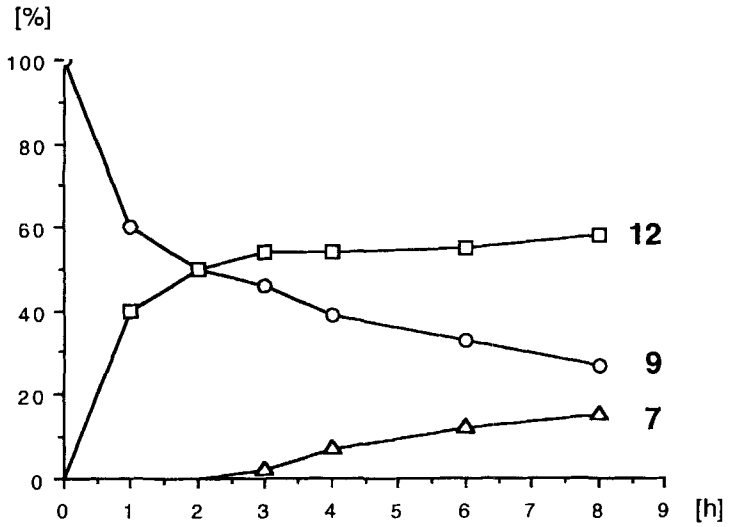


Fig. 2. *Thermolysis of* **9** *at 100° in* C_6D_5Cl*; ratio of* **9**/**12**/**7**

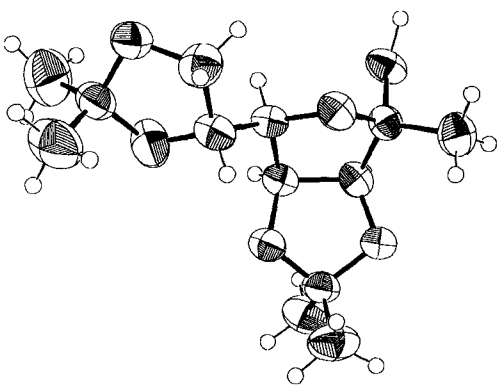


Fig. 3. *X-Ray structure of* **20**

The di-*O*-isopropylidene-furanosylidene moiety of **9**, **12**, **17**, and **18** is evidenced by the vicinal coupling constants $J(3,4) = 5.6-5.9$ and $J(4,5) = 3.4-3.7$ Hz (*Table 4*). As compared to **9**, H–C(1), H′–C(1), and H–C(3) of **12** are deshielded by *ca.* 0.5–0.6 ppm. The deshielding of H–C(3) of **12** agrees with the α-D-configuration (*cis*-arrangement of H–C(3) and S–C(2)). In the ^{13}C-NMR spectra of **9** and **12** (*Table 5*), C(2) resonates at 85.1 and 90.5 ppm and C(1) at 29.1 and 23.5 ppm (shielding by γ-effect of O–C(3)), respectively. The presence of CH_2SH and *OH* groups in **18** is indicated by weak bands at 2583 (SH), 3508 (br., associated OH) and 3605 cm^{-1} (free OH), the *dd*'s at 3.05 and 2.57 ppm (CH_2), the sharp *dd* at 1.40 ppm (SH), the br. *s* at 3.47 ppm (OH), and the *t* at 31.29 ppm (see [33–35] for IR and NMR data of related 1,1-disubstituted 2-mercaptoethanols). The vicinal coupling constants of SH (12.1 and 6.1 Hz) indicate a restricted rotation around the C(1)–S bond[10]). A single

[10]) To the best of our knowledge, no *Karplus* equation has been established for ^3J(SH, CH). ^3J(SH, CH) for freely rotating primary and secondary alkylthiols (7–8 Hz [36]) are larger than ^3J(OH, CH) of the corresponding alcohols (*ca.* 5 Hz), but smaller than ^3J(SH, CH) of 1,1-disubstituted 2-mercaptoethanols (9 Hz [33], 10 and 7.5 Hz [34]).

anomer was observed in the NMR spectra of **18**. The α-D-configuration was assigned to **18** by analogy to the higher stability of the α-D-anomer of the dethio analogue **20** (see below). The enethiol moiety of **17** is revealed by the C=C band at 1664 cm^{-1}, the SH *d* at 2.93 ppm, and the H–C(1) *dd* at 4.97 ppm with $J(1,SH) = 10.3$ and $^4J(1,3) = 1.25$ Hz. The ^{1}H-NMR values agree with those of the related diethyl 1-mercaptoprop-1-en-2-yl thiophosphate [37]. The alkenyl sulfide **19** shows two sets of ^{1}H signals for the furanosylidene residues (*Exper. Part*), a br. *s* at 5.51 ppm assigned to the vinylic H and a MeS *s* at the same field as α-D-**14** (2.24 ppm; MeS of **13** at 2.10 and 2.00 ppm). An sp^3-hybridized C(1') and an sp^2-hybridized C(2) are suggested by the $J(2',3')$ and $J(3,4)$ values of 5.9 and 5.0 ppm (similar to those of **1** and **16**) and by ^{13}C *s* at 103.92 (compare with 101.63 ppm for **13**) and 160.05 ppm. The *q* at 14.30 ppm is assigned to the MeS group (compare with 14.45 and 12.16 ppm for **13**). The enethiol group of **17** and **19** is evidenced by *s* at 154.32 and 160.05 and *d* at 88.67 and 90.74 ppm, respectively. The (*E*)-configuration is assigned to **17** and **19** for two reasons, *viz.* the characteristic downfield shift of the quaternary C-atom of (*E*)-1-alkoxy-1-alkyl-2-(methylthio)ethylenes (155–161 ppm [38] [39]; (*Z*)-isomer: 142–148 ppm [40] [41])[11]) as compared to 154.32 and 160.05 ppm for **17** and **19** and the larger allylic coupling of the (*E*)-isomer (0.9 Hz; (*Z*)-isomer: 0.65 Hz [40]) as compared to 1.25 Hz for **17**. The upfield shift of the *d* for C(1) is characteristic for 2-alkoxy-2-alkylethylenethiols (89–95 ppm [38]). A NOE of 4% was observed for H–C(3) of **19** upon irradiation of H–C(1). This enhancement is rather small for the (*Z*)-configurated isomer (H···H distance = 2.79 Å; compare with a NOE of 10% for a related enol ether with H···H distance = 2.8 Å [45]) and rather large for the (*E*)-isomer (H–H distance = 3.93 Å), but the enhancement may partially result from allylic coupling. The assignment of the (*R*)-configuration to C(1') of **19**, finally, is based on weak NOE's (1%) between H–C(1) and both H–C(2') and H–C(4') (see *Exper. Part*).

The thio-*O*-lactone structure of **8** is revealed by the low field C(1) *s* at 216.3 ppm. Small vicinal couplings between H–C(3) and both H–C(2) at 3.48 and 2.17 ppm prove that the CH_2N_2-derived CH_2 group is inserted between C(1) and C(2) of **1** (*Table 4*). These couplings, together with the large $J(3,4)$ and the small $J(4,5)$ coupling constant suggest a $B_{2,5}$ conformation. NOE Measurements corroborate the flagpole position of H–C(5) and the more shielded H'–C(2) at 2.17 ppm (see *Exper. Part*). $J(2,3)$, $J(3,4)$, $J(4,5)$, and $J(4,OH)$ of **15** (*Table 4*) are similar to the corresponding couplings of **5** and **6** showing that the conformation of the saccharide chain is only weakly influenced by the different substituents at C(1). The IR band at 3554 cm^{-1} (CH_2Cl_2) and the large $J(4,OH) = 10$ Hz agree well with an intramolecular H-bond OH···O(5). The (methylthio)carbonyl group gives rise to an IR band at 1681 cm^{-1}, an ^{1}H-NMR signal at 2.07 ppm, and ^{13}C-NMR signals at 11.05 and 201.21 ppm.

There has been some controversy about the anomeric configuration of **20**. *Tam* and *Fraser-Reid* [46] obtained **20** as a single, crystalline isomer (m.p. 102°, $[\alpha]_D^{23} = +8.33$). On the basis of an intramolecular H-bond, the β-D-configuration was assigned to this compound. Unfortunately, no spectroscopic data were published. Later on, *Csuk* and *Glänzer* obtained the same anomer (m.p. 102–104°, $[\alpha]_D^{25} = +10.5$ ($c = 0.9$, $CHCl_3$)). They either did not specify the anomeric configuration [47] (their ^{1}H- and ^{13}C-NMR data agree well with ours), or assigned the α-D-configuration to it [11]. As a rule, the α-D-anomers of ulofuranoses derived from 2,3:5,6-di-*O*-isopropylidene-D-mannose are more stable than their anomers, that in some instances are not even observed [48–50]. Similarly, 1-deoxy-3,4:6,7-di-*O*-isopropylidene-L-*gulo*-heptulofuranose, the C(6)-epimer of **20**, crystallizes as the β-L-anomer; this anomer dominates also in $CDCl_3$ and (D_6)DMSO solution [51][12]). We have now established the α-D-configuration of **20** by X-ray analysis[3]) (*Fig. 3*). In the solid state, the furanose ring of **20** adopts a ^OE conformation with pseudoequatorial Me and C(4)-dioxolanyl groups. HO–C(2) is pseudoaxial and involved in an intermolecular, bifurcated H-bond to O(4) (distance H···O(4): 2.228 Å, bond angle O(2)–H···O(4): 135.95°) and O(6) (distance H···O(6): 2.62 Å, bond angle O(2)–H···O(4): 137.65°). The α-D-configuration of **20** was ascertained by

[11]) Analogous chemical shift differences have been observed for the (*E*/*Z*)-isomers of lactone oximes [42], imines [43], and hydrazones [44].

[12]) We thank Prof. *G. Fleet* for submitting the experimental and spectroscopic data of this compound.

Table 4. *^{1}H-NMR Chemical Shifts* [ppm] *and Coupling Constants* [Hz] *of* **1**–**4**, **7**–**18**, *and* **20** *in C_6D_5Cl Solution*

	1	**2**	**3**	**4**	**13**	**14**[a])	**15**	**16**
H–C(2)	4.61	4.80	4.35	4.53	4.41	5.24	4.43	4.50
H–C(3)	4.57	4.92	4.51	4.67	4.59		4.72	4.54
H–C(4)	4.42–4.36	4.55–4.40	3.57	3.89	4.15		3.89[b])	4.08
H–C(5)	4.42–4.36	4.55–4.40	4.41	4.48	4.51		4.05–3.94	4.35
H–C(6)	4.00–3.92	4.04–3.90	3.93	4.04	4.08		4.05–3.94	3.99
H′–C(6)	4.00–3.92	4.04–3.90	3.88	4.04	4.06		4.05–3.94	3.92
CHS	–	5.47	5.21	–	–	–	–	–
CH′S	–	5.20	3.81	–	–	–	–	–
MeX	–	–	–	3.25, 1.98	2.16, 2.00	2.24	2.07	–
OH	–	–	–	–	–		2.09[b])	–
Me	1.40, 1.34, 1.25, 1.18	1.44, 1.37, 1.26, 1.19	1.40, 1.32, 1.25, 1.10	1.46, 1.42, 1.29, 1.19	1.43, 1.40, 1.31, 1.10		1.59, 1.35, 1.26, 1.18	1.39, 1.32, 1.25, 1.17
J(2,3)	5.0	5.8	5.8	5.8	5.9	5.8	8.2	5.1
J(3,4)	2.9	2.6	3.6	3.6	3.8		0.8	3.2
J(4,5)	[c])	[c])	7.2	7.0	6.3		8.2	7.4
J(5,6)	[c])	[c])	6.0	5.9	6.2		[c])	5.8
J(5,6′)	[c])	[c])	5.4	5.9	6.0		[c])	5.0
J(6,6′)	[c])	[c])	8.6	[c])	8.5		[c])	9.0
J(H,H′)	–	17.5	17.7	–	–	–	–	–

	7	**8**	**9**	**12**	**10**[d])	**11**[d])	**17**	**18**	**20**
H–C(1)	4.465[e])	3.48[f])	2.33	2.81[g])	1.72	1.77	4.97[h])	3.05[i])	1.48[j])
H′–C(1)	4.20[e])	2.17[f])	2.10	2.65	–	–	–	2.57[i])	–
H–C(3)	4.78[e])	4.17	4.20	4.79[g])	4.28	4.54	4.78[h])	4.47	4.41
H–C(4)	4.455	4.41	4.66	4.69	4.65	4.66	4.51	4.67	4.685
H–C(5)	3.89	3.78	3.72	3.92	4.08	4.23	3.90	4.17	4.21
H–C(6)	4.43	4.42	4.53	4.51	4.47	4.51	4.47	4.44	4.50
H–C(7)	4.02	4.01	4.02	4.01	4.07	4.17	4.09	4.05	4.17–4.04
H′–C(7)	4.02	3.97	4.02	3.96	4.05	4.09–4.03	4.06	4.05	4.17–4.04
OH	–	–	–	–	–	–	–	3.47	2.31
SH	–	–	–	–	–	–	2.93[g])	1.40[h])	–
Me	1.38, 1.36, 1.25, 1.18	1.42, 1.33, 1.24, 1.11	1.46, 1.41, 1.28, 1.20	1.39, 1.39, 1.28, 1.15	1.42, 1.37, 1.31, 1.16	1.425, 1.36, 1.27, 1.13	1.44, 1.34, 1.31, 1.20	1.43, 1.32, 1.31, 1.11	1.46, 1.39, 1.33, 1.16
J(1,1′)	1.2	16.1[e])	1.2	2.9	–	–	–	14.1	–
J(3,4)	5.7	8.1	5.8	5.9	5.8	5.9	5.6	5.9	5.9
J(4,5)	3.6	1.5	3.7	3.4	3.7	3.7	3.7	3.6	3.6
J(5,6)	7.0	8.0	7.0	7.0	6.4	7.3	6.8	6.9	6.6
J(6,7)	5.9	4.7	5.9	6.3	6.3	5.5	5.3	5.9	6.2
J(6,7′)	5.9	6.2	5.9	5.6	6.3	[c])	6.2	5.9	6.2
J(7,7′)	[c])	9.1	[c])	8.8	8.4	8.6	8.7	[c])	[c])

[a]) Data from the crude mixture of the thermolysis. [b]) J(4,OH) ≈ 10.0 Hz. [c]) Not determined. [d]) At 500 MHz; data from **10**/**11** 3:1. [e]) J(1,3) ≈ J(1′,3) ≈ 1.3 Hz. [f]) H–C(2), H–C(2′), and J(2,2′), respectively. J(2,3) = 2.1, J(2′,3) = 3.8 Hz. [g]) ^4J(1,3) = 0.4 Hz. [h]) J(1,SH) = 10.3, ^4J(1,3) = 1.25 Hz. [i]) J(1,SH) = 6.1, J(1′,SH) = 12.1 Hz. [j]) Sharper signal; Me_2C signals broadened by long-range coupling [9].

NOE measurements. Irradiation of HO–C(2) of **20** led to intensity enhancements for H–C(5) (2%) and H–C(3) (1–2%, see *Exper. Part*). Mutarotation was observed in $CDCl_3$ ($[\alpha]_D^{22} = +6.5 \rightarrow +4.5$ (constant after 3 h)) but not in C_6D_5Cl solution ($[\alpha]_D^{22} = +42.4$). The presence of the β-D-anomer of **20** (10% after 1 h and 13% after 3 h)

Table 5. *^{13}C-NMR Chemical Shifts* [ppm] *of* **1–4**, **7–18**, *and* **21** *in* C_6D_5Cl *Solution*

	1	**2**	**3**	**4**	**13**	**14**[a])	**15**	**16**
C(1)	219.46	141.47	104.20	118.16	101.63	117.73	201.21	173.08
C(2)	87.25[b])	85.09	85.80	86.74	88.76	87.32	80.82	76.34[b])
C(3)	77.48	80.93	80.26[b])	81.12	80.39[b])	81.47	78.03	78.29
C(4)	86.92[b])	83.43	80.19[b])	80.18	80.34[b])	79.76	69.06	76.23[b])
C(5)	72.93	73.49	72.95	73.35	73.36	73.78	76.18	73.11
C(6)	66.56	67.10	66.83	67.13	67.20	66.25	67.56	66.50
CH_2S	–	81.91	88.17	–	–	–	–	–
MeX	–	–	–	48.98, 12.28	14.45, 12.16	13.36	11.05	–
Me_2C	114.60, 109.88	113.48, 109.31	113.58, 109.12	113.25, 109.18	112.87, 109.07	113.06, 108.70	110.81, 109.75	114.06, 109.63
Me_2C	27.60, 27.19, 26.22, 25.48	27.07, 26.43, 25.55, 24.92	26.98, 26.06, 25.27, 24.30	27.08, 26.36, 25.63, 25.16	26.93, 25.66, 25.53, 24.20		26.96, 26.13, 25.40, 24.51	26.99, 26.84, 25.73, 25.30

	7	**8**	**9**	**12**	**10**[c])	**11**[c])	**17**	**18**	**20**
C(1)	82.70	45.57	29.14	23.52	19.41	23.03	88.67	31.29	22.89
C(2)	162.44	216.31	85.11	90.52	108.74[b])	99.71	154.32	103.86	105.62
C(3)	86.04	73.21	84.11	87.98	87.39	86.01	83.26	85.42	85.90
C(4)	80.28	71.61	82.42	84.49	80.41	81.34[b])	80.18	81.02	81.04
C(5)	78.89	80.47	80.79	80.18	79.93	81.16[b])	79.50	79.63	79.73
C(6)	73.67	71.37	73.32	72.94	73.52	73.11	73.79	73.39	73.71
C(7)	66.74	66.77	66.89	67.01	66.81	67.13	66.81	66.86	67.08
Me_2C	113.33, 109.16	109.81, 109.78	113.15, 109.01	113.13, 109.26	112.30, 109.47[b])	112.66, 109.10	113.57, 109.52	112.56, 108.85	112.45, 108.88
Me_2C	27.11, 27.02, 25.95, 25.52	27.10, 26.00, 25.17, 24.02	27.00, 26.22, 25.39, 25.15	27.01, 26.09, 25.68, 24.93	26.86, 26.00, 25.63, 24.59	26.96, 25.81, 25.52, 24.44	27.13, 27.02, 25.95, 25.70	26.95, 25.85, 25.59, 24.21	27.10, 26.18, 25.68, 24.56

[a]) Data from the crude mixture of the thermolysis; Me_2C not assigned. [b]) Assignment may be interchanged. [c]) Data from **10**/**11** 3:1.

is indicated in the ^{1}H-NMR spectrum ($CDCl_3$) by the appearance of signals for H–C(3), H–C(4), and H–C(5) at higher field than the corresponding signals of **20** ($\Delta\delta$ = 0.16, 0.04, and 0.09 ppm, resp.).

We thank Dr. *B. Schweizer* for the X-ray analyses and the *Swiss National Science Foundation* and *F. Hoffmann-La Roche AG*, Basel, for generous support.

Experimental Part

1. *General.* See [52]. THF *LiChrosolv*® (*Merck*) was used for HPLC. Anal. and semiprep. SFC (7–10 mg in 150 µl of Et_2O, additional loop capacity: 10 ml) were performed on a modified *Gilson* SFC apparatus (*Fig. 4*): 250 × 8 mm column (*Bischoff*) with silica gel *Spherisorb SW* (5 µm); pressure at r.t. 80 bar; flow: CO_2 with 5% of i-PrOH as modifier, flow rate 2 ml/min; UV detection (210 nm, if not indicated otherwise). Prep. HPLC: 250 × 20 mm column (*Bischoff*) with silica gel *Spherisorb SW* (5 µm); flow rate 10 ml/min; UV detection (220 nm, if not indicated otherwise); t_R in min.

2. *Separation of* **2** *and* **3**. *a*) Separation by semiprep. SFC gave pure fractions of **2** (t_R 10.5) and **3** (t_R 27.6). The fractions were used for the kinetic measurements.

b) Separation by prep. HPLC (hexane/AcOEt 4:1 (until **2** eluted) → 3:1, UV detection at 250 nm) gave less pure **2** (> 95% pure, t_R 13) and **3** (> 95% pure, t_R 40). Batches of 50 mg were ideal (decomposition of **2** *vs.* separation). The fractions were used for the preparation of larger amounts of the products of the thermolyses.

3. *Thermolysis of* **3**. *a*) In NMR tubes, solns. of **3** (15 mg, 47 µmol) and toluene (2 µl, 16 µmol) in C_6D_5Cl (0.7 ml) were held at 80, 90, 100, and 110°, resp. ^{1}H-NMR Spectra were recorded at regular intervals (*ca.* 2 h at 80 and 90°, 1 h at 100°, and 0.5 h at 110°). The decrease of the intensity of the *d* of H–C(4′) at 5.54 was monitored (calibration with the *s* of toluene at 2.17 ppm). The composition of the mixture was determined by comparison of the spectra with the spectra of the pure compounds in the same solvent (*Table 4*). The ratio **9**/**7**/**8**/**1** *ca.* 42:34:15:10 was determined by integration of characteristic signals (**3**: *d* for H–C(4′) at 5.21 ppm; **1**: *d* for H–C(2) at 4.61 ppm; **7**: *dt* for H–C(3) at 4.78 ppm; **8**: *dd* for H–C(2) at 3.48 ppm and *dd* for H′–C(2) at 2.17 ppm; **9**: *dd* for H–C(5) at 3.72 ppm, *d* for H–C(1) at 2.33 ppm, and *d* for H′–C(1) at 2.10 ppm). A larger batch of **3** (40 mg) was thermolyzed for 8 h at 110° and analyzed by ^{13}C-NMR spectroscopy: **9**/**7**/**8**/**1**/**20** 37:31.5:15:11.5:5 (comparison of this spectrum with the spectra of the pure compounds (*Table 5*): $\Delta\delta$ < 0.3 ppm; ratio determined by the mean height of the signals between 87 and 66 ppm).

b) Similarly, a soln. of **3** (15 mg, 47 µmol) in $C_6D_5Cl/(D_8)$THF 1:1 (0.7 ml) was kept for 1 h at 80°, 1 h at 90° (> 98% of **3**), 1 h at 100° (*ca.* 80% of **3**), and 5 h at 110° when **3** had completely disappeared. The ratio **9**/**7**/**8**/**1** of 36:18:18:28 was constant.

c) Similarly, a soln. of **3** (15 mg, 47 µmol) in C_6D_5Cl/CD_3OD 1:1 (0.7 ml) was kept for 1 h at 80° (> 98% of **3**), 1 h at 90° (*ca.* 70% of **3**), 1 h at 100° (*ca.* 25% of **3**), and 1 h at 110° when **3** had completely disappeared. The ratio **9**/**7**/**8**/**1** 49:17:17:17 remained constant.

d) A soln. of **3** (15 mg, 47 µmol) in petrol (*Fluka*, b.p. 80–110°) was kept for 8 h at 90°, cooled to r.t., and evaporated at $T < 25°$ (at higher temp., decomposition). According to the ^{1}H-NMR spectrum in C_6D_5Cl, the ratio **3**/**9**/**7**/**1** was 14:38:34:14. Only traces of **8** were present.

4. *Separation of the Thermolysis Products of* **3**. *a*) Separation by semiprep. SFC gave pure fractions of **7** (t_R 6.8), **9** (t_R 14.1), **8** (t_R 20.2), and **3** (t_R 29.5). The fractions were used for NMR spectroscopy.

b) Separation by prep. HPLC (hexane/THF 4:1) gave less pure fractions of **7** (> 90% pure, t_R 6.8), **9** (> 90% pure, t_R 11.0), and **8** (t_R 16.5). Batches of 40–50 mg were ideal (decomposition of **7** and **9** *vs.* separation). The fractions were used for the preparation of larger amounts of the products.

*2-Deoxy-3,4:6,7-di-*O*-isopropylidene-1-thio-*D-manno*-heptono-1,5-lactone* (**8**): IR (CH_2Cl_2): 2992*m*, 2937*w*, 1456*w*, 1428*w*, 1417*w*, 1384*m*, 1374*m*, 1322*m*, 1314*m*, 1232*s*, 1214*s*, 1173*s*, 1141*s*, 1115*w*, 1073*s*, 1042*s*, 1012*w*, 978*w*, 952*w*, 916*w*, 844*m*. ^{1}H-NMR (500 MHz, C_6D_5Cl): *Table 4*; NOE irrad. at 3.48 (H–C(2) in bow-sprit position) → 4.17 (3%, H–C(3)), 2.17 (31%, H′–C(2)); irrad. at 2.17 (H′–C(2) in flag pole position) → 4.17 (5%, H–C(3)), 3.78 (10%, H–C(5)), 3.48 (28%, H–C(2)). ^{13}C-NMR (125 MHz, C_6D_5Cl): *Table 5*. CI-MS: 306 (6, $[M + NH_4]^+$), 289 (100, $[M + 1]^+$), 273 (68, $[M - Me]^+$), 231 (18), 215 (12), 199 (11), 131 (15), 101 (38), 49 (30), 43 (18).

5. *3,4:6,7-Di-*O*-isopropylidene-β-*D-manno*-heptulofuranosyl 3,4:6,7-Di-*O*-isopropylidene-β-*D-manno*-heptulofuranoside* (**10**). Thermolysis of **3** (45 mg, 0.142 mmol) for 14 h at 115°, evaporation, and HPLC gave **10** (4 mg, *ca.* 8%; pure according ^{1}H- and ^{13}C-NMR, but containing an unknown amount of an unknown S species[5]). M.p.

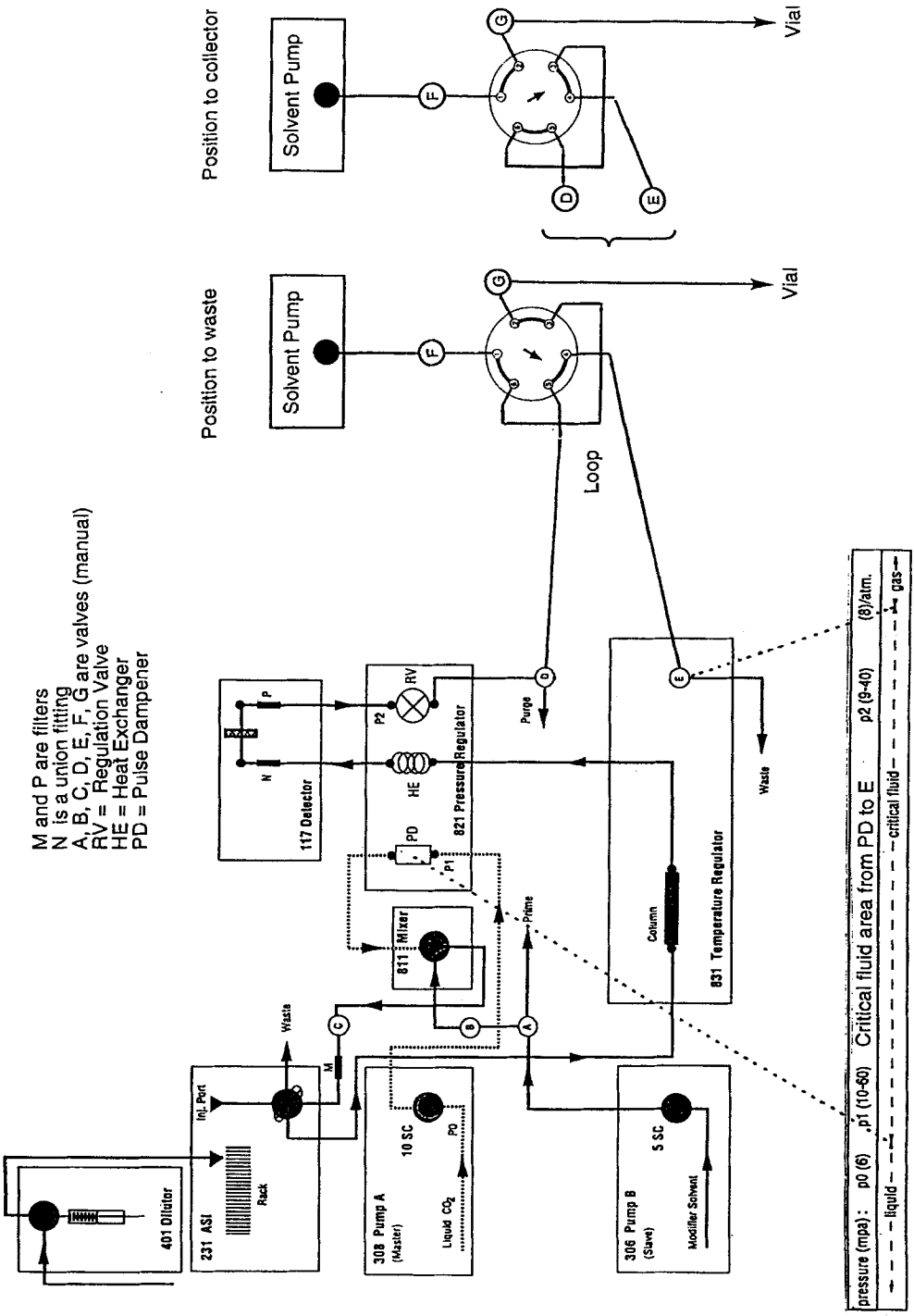


Fig. 4. *Modified* Gilson *semipreparative SF3 system: Modules and fluid paths*

117–119° (sintering at 106–107° and decomposition after melting). Prep. HPLC (hexane/THF 4:1): t_R 7.0. $[\alpha]_D^{22} = +34.1$ ($c = 0.71$, $CDCl_3$), +76.6 ($c = 1.08$, C_6D_5Cl). IR (CH_2Cl_2): 3068*w*, 2988*m*, 2939*m*, 2895*w*, 1456*w*, 1438*w*, 1422*m*, 1383*s*, 1374*s*, 1212*s*, 1170*s*, 1105*m* (sh), 1087*s*, 1067*s*, 1031*m*, 977*m*, 939*m*, 876*s*, 864*m*, 845*m*, 821*w*. ^{1}H-NMR (500 MHz, C_6D_5Cl): *Table 4*; irrad. at 1.72 (3 H–C(1)) → 4.08 (5%, H–C(5)), 4.28 (2%, H–C(3)). ^{1}H-NMR (200 MHz, $CDCl_3$): 4.77 (*dd*, $J = 5.8, 4.1$, H–C(4)); 4.37 (*ddd*, $J = 7.9, 6.2, 5.0$, H–C(6)); 4.32 (*d*, $J = 5.8$, H–C(3)); 4.09 (*dd*, $J = 8.7, 6.2$, H–C(7)); 3.93 (*dd*, $J = 8.7, 5.0$, H′–C(7)); 3.89 (*dd*, $J = 7.9, 3.8$, H–C(5)); 1.61 (*s*, 3 H–C(1)); 1.47, 1.45, 1.38, 1.33 (4*s*, 4 Me). ^{13}C-NMR (125 MHz, C_6D_5Cl): *Table 5*. ^{13}C-NMR (from **10**/**11** 3:1; 125 MHz, $CDCl_3$): 112.61 (*s*, Me_2C); 109.18, 109.09 (2*s*, Me_2C, C(2)); 87.02 (*d*, C(3)); 80.05 (*d*, C(4)); 79.56 (*d*, C(5)); 73.06 (*d*, C(6)); 66.89 (*t*, C(7)); 26.90, 25.94, 25.24, 24.66 (4*q*, 2 Me_2C); 18.69 (*d*, C(1)). CI-MS: 515 (0.7, $[M - Me]^+$), 321 (0.3, 0.5 M^+), 291 (0.6), 275 (3), 259 (14), 258 (6), 257 (39), 241 (48), 200 (11), 199 (100), 183 (23), 141 (31), 123 (12), 101 (52). Anal. calc. for $C_{26}H_{42}O_{11} \cdot 0.3S$ (542.47): C 57.57, H 7.80, S 2.19; found: C 57.40, H 7.74, S 2.19.

6. *Bis(3,4:6,7-di*-O-*isopropylidene*-α-D-manno-*heptulofuranosyl) Tetrasulfide* (**11**). A soln. of **10** in CD_3OD was left for 12 h and evaporated leading to **10**/**11** 3:1. $[\alpha]_D^{22}$ (**10**/**11** 3:1) = −88.9 ($c = 0.45$, C_6D_5Cl). ^{1}H-NMR (500 MHz, C_6D_5Cl): *Table 4*. ^{13}C-NMR (125 MHz, C_6D_5Cl): *Table 5*. ^{13}C-NMR (from **10**/**11** 3:1; 125 MHz, $CDCl_3$): 113.00, 109.43 (2*s*, 2 Me_2C); 99.36 (*s*, C(2)); 85.78 (*d*, C(3)); 80.82, 80.77 (2*d*, C(4), C(5)); 72.80 (*d*, C(6)); 67.02 (*t*, C(7)); 26.97, 25.84, 25.30, 24.66 (4*q*, 2 Me_2C); 22.62 (*d*, C(1)).

7. *X-Ray Analysis of* **11**. A crystal of the size $0.45 \times 0.4 \times 0.3$ mm was obtained from AcOEt by azeotropic condensation of hexane. $C_{26}H_{42}O_{10}S_4$ (642.84); orthorhombic $P2_12_12_1$; $a = 11.994(4)$ Å, $b = 14.809(10)$ Å, $c = 18.476(10)$ Å; $V = 3282(3)$ Å^3; $D_x = 1.301$ Mg/m^3; $Z = 4$. Intensities were measured in the ω-scan mode on an *Enraf Nonius CAD-4* diffractometer (graphite monochromator, MoK_α, $\lambda = 0.71073$ Å) at 293 K. Of the 3237 total collected reflections, 3237 independent reflections were observed. $R = 0.0548$, $R_w = 0.1219$. Part of the structure was solved by direct methods, the remaining non-H-atoms were found from a difference *Fourier* map with SHELX86 [53]. The non-H atoms were refined anisotropically with SHELXL-92 [54]. H-Atoms were calculated at idealized positions and included in the structure factor calculation with fixed isotropic displacement parameters.

8. *Thermolysis of* **2**. *a*) In NMR tubes, solns. of **2**/**3** *ca.* 4:1 (15 mg, 47 μmol) in $CDCl_3$ (0.7 ml) were kept at 20, 25, 30, and 35°, resp. ^{1}H-NMR Spectra were recorded at regular intervals (*ca.* 3 h at 20°, 2 h at 25°, and 1 h at 30 and 35°). The decrease of the *d*s of H–C(5′) at 5.90 and 5.67 ppm was monitored (calibration with the *d* of H–C(4′) of **3** at 5.54 ppm).

b) In NMR tubes, solns. of **2** (15 mg, 47 μmol) in C_6D_5Cl (0.7 ml) were kept at 23, 30, and 35°, respectively. ^{1}H-NMR Spectra were recorded at regular intervals. The ratio of the products (*Table 2*) was determined by integration of characteristic signals (**2**: *d* for H–C(5′) at 5.47 ppm and *d* for H′–C(5′) at 5.20 ppm; **9**: *d* for H–C(1) at 2.33 ppm and *d* for H′–C(1) at 2.10 ppm; **12**: *dd* for H–C(1) at 2.81 and *d* for H′–C(1) at 2.65 ppm; **13**: *s*s for MeS at 2.16 and 2.00 ppm; **14**: *d* for H–C(3) at 5.24 and *s* for MeS at 2.24 ppm; **15**: *s* for MeS at 2.07 ppm; **16**: all signal overlapped by signals of other products).

9. *Separation of the Thermolysis Products of* **2**. Separation by prep. HPLC (hexane/Et_2O 3:2) gave mixtures **12**/**13** (> 90% pure, t_R 8.6) and **15**/**18** (*ca.* 90% pure, t_R 14.6–17.4) and fractions **19** (> 90% pure, t_R 19.6) and **16** (> 95% pure, t_R 33.2) besides minor amounts of additional decomposition products. Batches of 40–50 mg were ideal (decomposition *vs.* separation). The mixture **12**/**13** (t_R 22.8) was purified by a second prep. HPLC (hexane/Et_2O 7:3), but could not be separated. Prep. HPLC (hexane/Et_2O 7:3, UV detection at 200 nm) of **15**/**18** gave **18** (> 90% pure, t_R 20) and **15**/**18** 2:1 (t_R 22). An additional HPLC afforded **15**/**18** 10:1.

1,2-Anhydro-3,4:6,7-di-O-*isopropylidene-1-thio*-α-D-manno-*hept-2-ulofuranose* (**12**) *and 1,4-Anhydro-2,3:5,6-di*-O-*isopropylidene-1,1-bis(methylthio)*-D-*mannitol* (**13**): ^{1}H-NMR (500 MHz, C_6D_5Cl, **12**/**13** 3:2): *Table 4*. ^{13}C-NMR (75 MHz, C_6D_5Cl, **12**/**13** 3:2): *Table 5*.

S-*Methyl 2,3:5,6-Di*-O-*isopropylidene-1-thio*-D-*mannonate* (**15**): IR (CH_2Cl_2): 3554*w*, 2978*s*, 2934*m*, 2873*m*, 1681*m*, 1489*w*, 1455*w*, 1446*w*, 1383*s*, 1351*w*, 1215*m*, 1151*m*, 1113*s*, 1072*m*, 1042*w*, 982*w*, 845*w*. ^{1}H-NMR (400 MHz, C_6D_5Cl): *Table 4*. ^{13}C-NMR (100 MHz, C_6D_5Cl): *Table 5*. CI-MS: 291 (0.5, $[M - Me]^+$), 276 (4), 259 (48, $[M - MeS]^+$), 243 (100, $[M - MeSH - Me]^+$), 201 (20), 101 (38), 49 (16), 43 (14).

3,4:6,7-Di-O-*isopropylidene-1-thio*-D-manno-*hept-2-ulofuranose* (**18**): IR (CH_2Cl_2): 3605*w*, 3508*w* (br.), 2993*m*, 2939*m*, 2900*w*, 2583*w*, 1480*w*, 1456*w*, 1428*w*, 1417*w*, 1383*s*, 1374*s*, 1338*w*, 1322*w*, 1211*s*, 1180*m*, 1163*s*, 1112*s*, 1102*s*, 1068*s*, 1031*s*, 972*m*, 924*w*, 910*w*, 890*m*, 867*m*, 845*s*, 822*w*. ^{1}H-NMR (300 MHz, C_6D_5Cl): *Table 4*. ^{13}C-NMR (100 MHz, C_6D_5Cl): *Table 5*. CI-MS: 324 (15, $[M + NH_4]^+$), 307 (51, $[M + 1]^+$), 291 (49, $[M - Me]^+$), 289 (70, $[M - OH]^+$), 275 (23), 259 (41), 257 (68), 249 (28), 233 (40), 231 (42), 217 (20), 199 (100), 141 (27), 101 (47).

(E)-2,5-Anhydro-1-S-*[(1R)-1,4-anhydro-2,3:5,6-di*-O-*isopropylidene-1-(methylthio)*-D-*mannitol-1-yl]-3,4:6,7-di*-O-*isopropylidene-1-thio*-D-manno-*hept-1-enitol* (**19**): IR (CH_2Cl_2): 2992*m*, 2938*m*, 2875*w*, 1649*w* (br.), 1456*w*, 1383*s*, 1374*s*, 1344*m*, 1319*w*, 1211*s*, 1162*s*, 1150*s*, 1119*s*, 1105*m*, 1069*s*, 1040*s*, 1030*s*, 1000*m*, 973*m*, 956*m*, 921*w*,

903*w*, 887*m*, 867*m*, 844*s*. ^{1}H-NMR (300 MHz, C_6D_5Cl): 5.51 (br. *s*, irrad. at 2.24 → NOE < 0.5%, H–C(1)); 4.86 (br. *d*, *J* = 5.0, irrad. at 5.51 → NOE of 4%, H–C(3)); 4.86 (*dd*, *J* = 5.9, 3.7, irrad. at 5.51 → NOE of 1%, H–C(3')); 4.60 (*d*, *J* = 5.8, H–C(2')); 4.56–4.45 (*m*, H–C(4), H–C(6), H–C(5')); 4.31 (*dd*, *J* = 6.7, 3.7, irrad. at 5.51 → NOE of 1%, H–C(4')); 4.20–4.08 (*m*, H–C(5), 2 H–C(7), 2 H–C(6')); 2.24 (*s*, irrad. at 5.51 → NOE of < 0.5%, MeS); 1.47, 1.45, 1.44, 1.42 (4*s*, 4 Me); 1.37 (*s*, 2 Me); 1.21, 1.14 (2*s*, 2 Me). ^{13}C-NMR (75 MHz, C_6D_5Cl): 160.05 (*s*, C(2)); 113.68, 113.08, 109.36, 109.16 (4*s*, 4 Me_2C); 103.92 (*s*, C(1')); 90.74 (*d*, C(1)); 88.74, 83.43 (2*d*, C(3), C(2')); 81.08, 80.52, 80.47, 78.84 (4*d*, C(4), C(5), C(3'), C(4')); 73.74, 73.32 (2*d*, C(6), C(5')); 67.15, 66.63 (2*t*, C(7), C(6')); 27.11, 27.07, 27.03, 25.93, 25.76, 25.66, 25.59, 24.42 (8*q*, 8 Me); 14.30 (*q*, MeS). CI-MS: 594 (0.7, $[M + NH_4]^+$), 576 (0.5, M^+), 561 (2, $[M - Me]^+$), 542(2), 529 (8, $[M - MeS]^+$), 290(16), 289 (100, $C_{13}H_{21}O_5S^+$), 275(12), 259(20), 231(13), 173(11), 155(14), 101(32).

10. *Thermolysis of* **9**. In NMR tubes, solns. of **9** (7 mg, 24 μmol) in C_6D_5Cl (0.7 ml) were kept at the indicated temp. (*Table 3*). ^{1}H-NMR Spectra were recorded at regular intervals. The ratio of the products was determined by integration of characteristic signals (**9**: *d* for H–C(1) at 2.33 and *d* for H'–C(1) at 2.10 ppm; **12**: *dd* for H–C(1) at 2.81 and *d* for H'–C(1) at 2.65 ppm; **7**: *t* for H'–C(1) at 4.20 ppm; **17**: *d* for SH at 2.93 and *dd* for H–C(1) at 4.97 ppm; **18**: *dd* for H–C(1) at 3.05 and *dd* for H'–C(1) at 2.57 ppm; **20**: *dd* for H–C(5) at 4.21 ppm).

11. *Thermolysis of* **12**. *a*) In a NMR tube, a soln. of **12**/**13** 1:1 (7 mg) in C_6D_5Cl (0.7 ml) was kept for 3.5 h at 120°. ^{1}H-NMR Spectra were recorded after 2.5 (**13**/**9**/**12**/**7**/**17** 50:0:30:20:20) and 3.5 h (**13**/**9**/**12**/**7**/**17**/**20** 50:0:19.5:trace:17.5:13).

b) Similarly, solns. of **12** (7 mg) and *ca.* 10 mol-% of (*i*-Pr)$_2$EtN in C_6D_5Cl (0.7 ml) were thermolysed at 110 and 120° (*Table 3*).

*(E)-2,5-Anhydro-3,4:6,7-di-*O*-isopropylidene-1-thio-*D-manno-*hept-1-enitol* (**17**): IR (CH_2Cl_2): 2988*m*, 2957*s*, 2929*s*, 2872*m*, 1664*w*, 1564*s*, 1544*s*, 1538*s*, 1456*m*, 1381*m*, 1372*m*, 1348*s*, 1338*s*, 1150*m*, 1120*m*, 1070*s*, 1046*s*, 1042*s*, 1032*s*, 1026*s*, 974*w*, 938*w*, 894*w*, 849*w*. Prep. HPLC (THF/hexane 15:85) of the thermolysis products of **9** or **12** led to complete decomposition of **17**, which was, however, obtained from the thermolysis of 50 mg-samples of **3** (12 h at 110°) immediately followed by prep. HPLC. Pure **17** decomposed at −20° within 2 d to **18**. Prep. HPLC: t_R (hexane/THF 85:15) 10.5. ^{1}H-NMR (200 MHz, C_6D_5Cl): *Table 4*. ^{13}C-NMR (75 MHz, C_6D_5Cl): *Table 5*.

*1-Deoxy-3,4:6,7-di-*O*-isopropylidene-α-*D-manno-*hept-2-ulofuranose* (**20**): M.p. 102° ([45]: 102°; [46]: 102–104°). Prep. HPLC: t_R (hexane/THF 4:1) 10.8. $[\alpha]_D^{22} = +6.5$ (10 min) → +4.5 (24 h; *c* = 1.75, $CDCl_3$); [45]: $[\alpha]_D^{23} = +8.33$ ($CHCl_3$), [46]: $[\alpha]_D^{25} = +10.5$ (*c* = 0.9, $CHCl_3$); +42.4 (*c* = 1.09, C_6D_5Cl). IR (0.05M, CH_2Cl_2): 3581*m*, 3422*w* (br.). ^{1}H-NMR (200 MHz, C_6D_5Cl): *Table 4*; NOE: irrad. at 2.31 (OH) → 4.41 (1%, H–C(3)), 4.21 (2%, H–C(5)), 1.48 (1%, 3 H–C(1)). ^{1}H-NMR (200 MHz, $CDCl_3$): identical to [46]. ^{13}C-NMR (75 MHz, C_6D_5Cl): *Table 5*. ^{13}C-NMR (75 MHz, $CDCl_3$): identical to [46]; 85.32 (*d*, C(3)).

12. *X-Ray Analysis of* **20**. $C_{13}H_{22}O_6$ (274.31); *a* = 11.814(3) Å, *b* = 12.097(2) Å, *c* = 13.327(5)° Å, α = 66.14(2)°, β = 67.37(2)°, γ = 63.24(2)°; *V* = 1506.5(7) Å^3; D_x = 1.209 Mg/m^3; *Z* = 4. Intensities were measured in the ω-scan mode on an *Enraf Nonius CAD-4* diffractometer (graphite monochromator, MoK_α, λ = 0.71073 Å) at 293 K. Of the 4452 total collected reflections, 3502 independent reflections were observed. *R* = 0.0547, R_w = 0.1334. The structure was solved with the direct-methods routine of SHELXS-86 [53], and the refinement was performed with SHELXL-92 [54].

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