ELSEVIER

www.elsevier.com/locate/carres

Carbohydrate Research 335 (2001) 55–61

CARBOHYDRATE RESEARCH

Note

Efficient syntheses of 1-*S*-alkyl-1-thio-L-ribitols, D-lyxitols and L-xylitols from D-pentono-1,4-lactones

Jérôme Lalot, Gaëtane Manier, Imane Stasik,* Gilles Demailly, Daniel Beaupère

Laboratoire des Glucides, Université de Picardie Jules Verne, 33 rue Saint-Leu, F-80039 Amiens, France

Received 1 June 2001; accepted 11 July 2001

Abstract

The thioalkylation of unprotected 5-bromo-5-deoxy-D-ribono, D-arabinono, and D-xylono-1,4-lactone was performed with the alkylthiol-sodium hydride reagent. The corresponding 5-*S*-alkyl-5-thio-D-pentono-1,4-lactones were isolated in good yields (82–95%). Reduction with $NaBH_4$ of these derivatives gave the 1-*S*-alkyl-1-thio-L-ribitols, D-lyxitols and L-xylitols in 85–96% yields.

Keywords: Unprotected bromolactones; *S*-Alkylthiopentonolactones; *S*-Alkylthiopentitols

1. Introduction

Amphiphilic carbohydrate derivatives display a number of interesting biological and physiological activities.[1–5] It is now well established that such derivatives can form liquid crystals and also find practical uses as surfactants and non-ionic detergents.[6] *S*-Alkylthiopolyols are a new group of amphiphilic carbohydrates.

The literature records a number of methods for the preparation of alkyl 1-thioglycosides,[7] which can be converted into 1-*S*-alkyl-1-thiohexitols.[8] These syntheses require tedious protection–deprotection steps and lead to substantially lower yields.

S-Alkylthiopentitols are obtained from the corresponding itols by protection followed by activation, thioetherification, and deprotection. Hence, starting from 2,3:4,5-di-*O*-isopropylidene-xylitol, 1-*S*-alkyl-1-thio-xylitols were obtained in 34–63% overall yield in a mixture with 1-*S*-alkyl-1-thio-2,3-*O*-isopropylidene-xylitols.[9]

2. Results and discussion

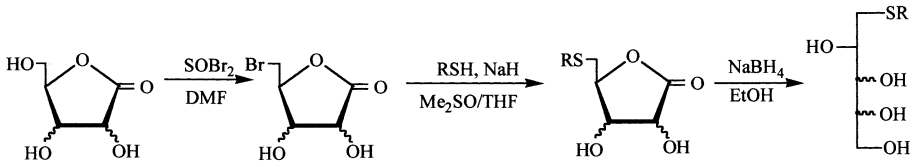
We now report an efficient transformation of unprotected D-pentono-1,4-lactones (D-ribono, D-arabinono, and D-xylono) into 1-*S*-alkyl-1-thiopentitols, in a three-step transformation via the 5-bromo-5-deoxy-D-pentono-1,4-lactones as key intermediate (Scheme 1). We have prepared these 1-*S*-alkyl-1-thiopentitol derivatives in order to study the relationship between structure and tensioactive properties as well as modification in the phase transition temperature.

We have previously described the preparation of 5-bromo-5-deoxy-D-pentono-1,4-lac-

* Corresponding author. Tel.: +33-3-22827566; fax: +33-3-22827561.

E-mail address: imane.stasik@sc.u-picardie.fr (I. Stasik).

0008-6215/01/$ - see front matter
PII: S0008-6215(01)00204-X



Scheme 1.

tones from D-pentono-1,4-lactones in good yields (75–95%) with the reagent thionyl bromide in DMF.[10]

Thioetherification could be performed by using commercially available alkylthiolate salt or the alkylthiol/base reagent to prepare the alkylthiolate in situ.[11]

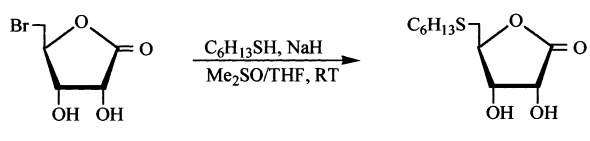
In a first approach, to a solution of a commercially available hexanethiolate salt (1.2 equiv) in 1:1 Me_2SO–THF, 5-bromo-5-deoxy-D-ribono-1,4-lactone (**1**) was added and the mixture was stirred at room temperature. The reaction was controlled by TLC. After 2 h, the reaction was stopped and a NMR analysis of the crude reaction product showed the presence of **1** and 5-*S*-hexyl-5-thio-D-ribono-1,4-lactone (**4**) in a 3:7 ratio. This ratio remained unchanged by using an excess of thiolate (2 equiv) and longer reaction times. GC analysis of the commercial thiolates pointed to the presence of the corresponding disulfides, with amounts up to 50%. For this reason, we decided to prepare the thiolate in situ.

In thioetherification reactions, MeONa or NaH are the commonly used bases. It has been reported that yields of thioetherification of 3-deoxy-3-iodo-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose are improved with MeONa compared to NaH.[12] In our study, use of MeONa is to be avoided due to the presence of the lactone functionality.[13] To hexanethiol (1.2 equiv) was added sodium hydride (1.2 equiv), at room temperature, in 1:1 Me_2SO–THF. The mixture was vigorously stirred for 1 h and the 5-bromo-5-deoxy-D-ribono-1,4-lactone (**1**) was added. After 5 min, **1** was completely consumed and the 5-*S*-hexyl-5-thio-D-ribono-1,4-lactone (**4**) was obtained in 95% isolated yield (Scheme 2). When the stirring was not vigorous enough or when the reaction was performed with an excess of sodium hydride, epimerisation at C-2 took place and 5-*S*-hexyl-5-thio-D-arabinono-1,4-lactone (**8**) (90%), contaminated with a small amount of **4** (10%), was obtained. We have previously reported such epimerisation when **1** was treated with sodium azide.[14] The configuration of the new lactone formed **8**, was identical with the one obtained from thioetherification of 5-bromo-5-deoxy-D-arabinono-1,4-lactone (**2**).

Using this method, 5-*S*-octyl, decyl, and dodecyl-5-thio-D-ribono-1,4-lactones (**5**, **6** and **7**) were obtained in good yields. When 5-bromo-5-deoxy-D-arabinono- (**2**) and D-xylono-1,4-lactones (**3**) were treated in the same conditions, no epimerisation could be observed and the 5-*S*-alkyl-5-thio-D-arabinono- and D-xylono-1,4-lactones (**8**–**15**) were obtained as the only products, in rather good yields (82–95%) (Table 1). In all cases, the thioetherification occurred in less than 5 min.

The reduction of the 5-*S*-alkyl-5-thio-D-pentono-1,4-lactones was then investigated to access to 1-*S*-alkyl-1-thiopentitols. When 5-*S*-hexyl-5-thio-D-ribono-1,4-lactone (**4**) was treated with $NaBH_4$ in EtOH at room temperature for 1 h, the 1-*S*-hexyl-1-thio-L-ribitol (**16**) was obtained in 90% yield (Scheme 3).

The method was extended to others 5-*S*-alkyl-5-thio-D-ribono-, D-arabinono-, and D-xylono-1,4-lactones, which efficiently yielded 1-*S*-alkyl-1-thio-L-ribitols (**17**, **18**, **19**), D-lyxitols (**20**, **21**, **22**, **23**), and L-xylitols (**24**, **25**, **26**, **27**) in good yields (85–96%), as shown in Table 2.



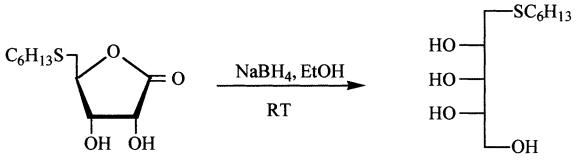
1 **4** (95%)

Scheme 2.

Table 1
Yields and physical data of 5-*S*-alkyl-5-thio-D-pentono-1,4-lactones

Substrate	Product [isolated yields (%)]	mp (°C)	$[\alpha]_D^{24}$ (°)	R_f [a]
1	**4** (95)	89–91	+25 (*c* 0.62, CH_2Cl_2)	0.34
	5 (92)	95–96	+38 (*c* 1.15, CH_2Cl_2)	0.46
	6 (93)	104–105	+15 (*c* 1.00, MeOH)	0.58
	7 (91)	99–100	+32 (*c* 0.85, CH_2Cl_2)	0.63
2	**8** (95)	69–70	+52 (*c* 1.00, MeOH)	0.32
	9 (82)	72–73	+70 (*c* 1.00, MeOH)	0.41
	10 (92)	67–68	+67 (*c* 1.00, MeOH)	0.52
	11 (90)	75–76	+58 (*c* 1.00, MeOH)	0.61
3	**12**(89)	sirup	+51 (*c* 1.00, MeOH)	0.33
	13 (92)	sirup	+64 (*c* 1.00, MeOH)	0.40
	14 (88)	49–50	+54 (*c* 1.00, MeOH)	0.54
	15 (91)	57–58	+50 (*c* 1.00, MeOH)	0.61

[a] 3:2 EtOAc–hexane.



4 **16** (90%)

Scheme 3.

3. Experimental

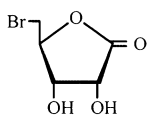
General methods.—^{1}H and ^{13}C NMR spectra were recorded in C_5D_5N with Me_4Si as internal standard on a Bruker 300 MHz spectrometer. Measurement of $[\alpha]_D$ values was effected with a JASCO DIP-370 digital polarimeter, using a sodium lamp ($\lambda = 589$ nm). Column chromatography was performed on Silica Gel (E. Merck 230–400 mesh) using EtOAc–petroleum ether or EtOAc–MeOH. Analytical TLC was performed on E. Merck glass backed Silica Gel sheets (Silica Gel F_{254}).

*General procedure for thioalkylation of 5-bromo-5-deoxy-*D*-pentono-1,4-lactones.*—To a solution of alkanethiol (2.8 mmol) in 1:1 Me_2SO–THF (8 mL) was added sodium hydride (1.2 equiv). The mixture was vigorously stirred at rt for 1 h. 5-Bromo-5-deoxy-D-pentono-1,4-lactone (0.5 g; 2.37 mmol) was then added and stirring was continued. After 5 min, MeOH (3 mL) was added and the solution was concentrated and co-concentrated with water, at 50 °C, under diminished pressure. The crude product was chromatographed on silica gel (4:1 EtOAc–petroleum ether).

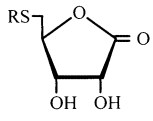
5-S-*Hexyl-5-thio*-D-*ribono-1,4-lactone* (**4**). 0.558 g; ^{1}H NMR: δ 5.10 (d, 1 H, $J_{2,3}$ 5.2 Hz, H-2), 4.70 (m, 1 H, H-3), 5.11 (m, $J_{4,5a} = J_{4,5b}$ 6.5 Hz, 1 H, H-4), 3.00 (m, 2 H, H-5a, H-5b), 2.5 (t, 2 H, H-α), 1.50–1.10 (m, 8 H, H-β–Hω–1), 0.80 (t, 3 H, H-ω); ^{13}C NMR: δ 176 (C-1), 70.8 (C-2), 68.8 (C-3), 84 (C-4), 32.8 (C-5), 32 (C-α), 30.5–21.6 (C-β–C-ω–1), 13.0 (C-ω). Anal. Calcd for $C_{11}H_{20}O_4S$: C, 53.22; H, 8.06; S, 12.9. Found: C, 53.32; H, 8.18; S, 13.4.

5-S-*Octyl-5-thio*-D-*ribono-1,4-lactone* (**5**). 0.602 g; ^{1}H NMR: δ 5.20 (d, 1 H, $J_{2,3}$ 5.2 Hz, H-2), 4.80 (m, 1 H, H-3), 5.00 (m, 1 H, $J_{4,5a} = J_{4,5b}$ 6.6 Hz, H-4), 3.10 (m, 2 H, H-5a, H-5b), 2.60 (t, 2 H, H-α), 1.50–1.20 (m, 12 H, H-β–Hω–1), 0.80 (t, 3 H, H-ω); ^{13}C NMR: δ 177.3 (C-1), 72.3 (C-2), 70.3 (C-3), 85.5 (C-4), 34.3 (C-5), 33.5 (C-α), 32.3–23.3. (C-β–C-ω–1), 14.6 (C-ω). Anal. Calcd for $C_{13}H_{24}O_4S$: C, 56.52; H, 8.69; S, 11.59. Found: C, 56.61; H, 8.71; S, 13.1.

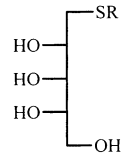
5-S-*Decyl-5-thio*-D-*ribono-1,4-lactone* (**6**). 0.673 g; ^{1}H NMR: δ 5.25 (d, 1 H, $J_{2,3}$ 5.2 Hz, H-2), 4.75 (d, 1 H, H-3), 5.10 (m, $J_{4,5a} = J_{4,5b}$ 6.6 Hz, 1 H, H-4), 3.10 (m, 2 H, H-5a, H-5b), 2.6 (t, 2H, H-α), 1.55–1.25 (m, 16 H, H-β–Hω–1), 0.80 (t, 3 H, H-ω); ^{13}C NMR: δ 176.8 (C-1), 70.2 (C-2), 68.8 (C-3), 83.9 (C-4), 32.8 (C-5), 32 (C-α), 30.7–21.7. (C-β–C-ω–1), 13.1 (C-ω). Anal. Calcd for $C_{15}H_{28}O_4S$: C, 59.21; H, 9.21; S, 10.52. Found: C, 59.22; H, 9.32; S, 11.10.



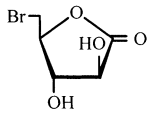
1



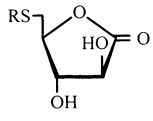
4 R=C_6H_{13}
5R=C_8H_{17}
6 R=$C_{10}H_{21}$
7R=$C_{12}H_{25}$



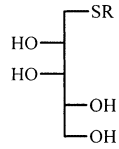
16 R=C_6H_{13}
17 R=C_8H_{17}
18 R=$C_{10}H_{21}$
19 R=$C_{12}H_{25}$



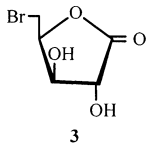
2



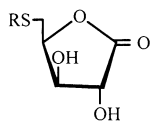
8 R=C_6H_{13}
9 R=C_8H_{17}
10 R=$C_{10}H_{21}$
11 R=$C_{12}H_{25}$



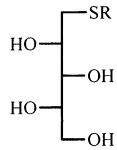
20 R=C_6H_{13}
21 R=C_8H_{17}
22 R=$C_{10}H_{21}$
23 R=$C_{12}H_{25}$



3



12 R=C_6H_{13}
13 R=C_8H_{17}
14 R=$C_{10}H_{21}$
15 R=$C_{12}H_{25}$



24 R=C_6H_{13}
25 R=C_8H_{17}
26 R=$C_{10}H_{21}$
27 R=$C_{12}H_{25}$

5-S-*Dodecyl*-*5*-*thio*-D-*ribono*-*1,4*-*lactone* (**7**). 0.715 g; ^{1}H NMR: δ 5.20 (d, 1 H, $J_{2,3}$ 5.2 Hz, H-2), 4.70 (d, 1 H, H-3), 5.00 (m, $J_{4,5a} = J_{4,5b}$ 6.6 Hz, 1 H, H-4), 3.10 (m, 2 H, H-5a, H-5b), 2.60 (t, 2 H, H-α), 1.50–1.20 (m, 20 H, H-β–Hω–1), 0.80 (t, 3 H, H-ω); ^{13}C NMR: δ 175.7 (C-1), 70.2 (C-2), 68 (C-3), 83.8 (C-4), 33.3 (C-5), 31.7 (C-α), 31.2–24.5. (C-β–C-ω–1), 14.0 (C-ω). Anal. Calcd for $C_{17}H_{32}O_4S$: C, 61.44; H, 9.64; S, 9.64. Found: C, 61.52; H, 9.51; S, 10.11.

5-S-*Hexyl*-*5*-*thio*-D-*arabinono*-*1,4*-*lactone* (**8**). 0.562 g; ^{1}H NMR: δ 4.60 (d, 1 H, $J_{2,3}$ 8.0 Hz, H-2), 4.40 (t, 1 H, $J_{3,4}$ 8.2 Hz, H-3), 4.35 (ddd, $J_{4,5a}$ 3.4, $J_{4,5b}$ 6.1 Hz, 1 H, H-4), 2.90 (dd, $J_{5a,5b}$ 14.6 Hz, 1 H, H-5a), 2.70 (dd, 1 H, H-5b), 2.30 (t, 2 H, H-α), 1.30–1.0 (m, 8 H, H-β–Hω–1), 0.60 (t, 3 H, H-ω); ^{13}C NMR: δ 175.8 (C-1), 75.6 (C-2), 73.6 (C-3), 80.7 (C-4), 34.2 (C-5), 32.7 (C-α), 31.3–21.3. (C-β–C-ω–1), 14.0 (C-ω). Anal. Calcd for $C_{11}H_{20}O_4S$: C, 53.22; H, 8.06; S, 12.9. Found: C, 53.12; H, 8.15; S, 13.2.

5-S-*Octyl*-*5*-*thio*-D-*arabinono*-*1,4*-*lactone* (**9**). 0.533 g; ^{1}H NMR: δ 4.95 (d, 1 H, $J_{2,3}$ 8.0 Hz, H-2), 4.75 (t, 1 H, $J_{3,4}$ 8.2 Hz, H-3), 4.65

Table 2
Yields and physical data of 1-*S*-alkyl-1-thiopentitols

Substrate	Product [isolated yields (%)]	mp (°C)	$[\alpha]_D^{24}$ (°) (*c* 1.00, MeOH)	R_f [a]
4	**16** (90)	78–79	+38	0.69
5	**17** (94)	81–82	+33	0.62
6	**18** (90)	83–84	+30	0.67
7	**19** (96)	86–87	+22	0.73
8	**20** (91)	62–63	+18	0.72
9	**21** (87)	85–86	+7	0.63
10	**22** (90)	81–82	+16	0.58
11	**23** (90)	89–90	−49	0.63
12	**24** (88)	56–57	−25	0.77
13	**25** (90)	49–50	−20	0.76
14	**26** (85)	58–59	−32	0.78
15	**27** (92)	66–67	−17	0.82

[a] 9:1 EtOAc–MeOH.

(ddd, $J_{4,5a}$ 3.4, $J_{4,5b}$ 6.1 Hz, 1 H, H-4), 3.25 (dd, $J_{5a,5b}$ 14.6 Hz, 1 H, H-5a), 3.0 (dd, 1 H, H-5b), 2.60 (t, 2 H, H-α), 1.50–1.10 (m, 12 H, H-β–Hω–1), 0.80 (t, 3 H, H-ω); ^{13}C NMR: δ 175.8 (C-1), 77.6 (C-2), 75.7 (C-3), 81.9 (C-4), 34.5 (C-5), 33.8 (C-α), 32.3–23.2. (C-β–C-ω–1), 14.6 (C-ω). Anal. Calcd for $C_{13}H_{24}O_4S$: C, 56.52; H, 8.69; S, 11.59. Found: C, 56.63; H, 8.58; S, 12.10.

5-S-*Decyl-5-thio*-D-*arabinono-1,4-lactone* (**10**). 0.662 g; ^{1}H NMR: δ 4.80 (d, 1 H, $J_{2,3}$ 8.0 Hz, H-2), 4.60 (t, 1 H, $J_{3,4}$ 8.2 Hz, H-3), 4.45 (ddd, $J_{4,5a}$ 3.3, $J_{4,5b}$ 6.0 Hz, 1 H, H-4), 2.90 (dd, $J_{5a,5b}$ 14.5 Hz, 1 H, H-5a), 3.10 (dd, 1 H, H-5b), 2.40 (t, 2 H, H-α), 1.30–0.95 (m, 16 H, H-β–Hω–1), 0.70 (t, 3 H, H-ω); ^{13}C NMR: δ 175.5 (C-1), 77.5 (C-2), 75.6 (C-3), 82.0 (C-4), 34.7 (C-5), 33.9 (C-α), 32.4–23.5. (C-β–C-ω–1), 14.7 (C-ω). Anal. Calcd for $C_{15}H_{28}O_4S$: C, 59.21; H, 9.21; S, 10.52. Found: C, 59.60; H, 9.32; S, 10.98.

5-S-*Dodecyl-5-thio*-D-*arabinono-1,4-lactone* (**11**). 0.713 g; ^{1}H NMR: δ 4.65 (d, 1 H, $J_{2,3}$ 8.0 Hz, H-2), 4.45 (t, 1 H, $J_{3,4}$ 8.1 Hz, H-3), 4.30 (ddd, $J_{4,5a}$ 3.4, $J_{4,5b}$ 6.1 Hz, 1 H, H-4), 2.85 (dd, $J_{5a,5b}$ 14.6 Hz, 1 H, H-5a), 2.95 (dd, 1 H, H-5b), 2.30 (t, 2 H, H-α), 1.20–0.85 (m, 20 H, H-β–Hω–1), 0.60 (t, 3 H, H-ω); ^{13}C NMR: δ 175.3 (C-1), 77.4 (C-2), 75.5 (C-3), 82.1 (C-4), 34.9 (C-5), 34.1 (C-α), 32.5–23.8. (C-β–C-ω–1), 14.8 (C-ω). Anal. Calcd for $C_{17}H_{32}O_4S$: C, 61.44; H, 9.64; S, 9.64. Found: C, 61.00; H, 9.71; S, 10.22.

5-S-*Hexyl-5-thio*-D-*xylono-1,4-lactone* (**12**). 0.524 g; ^{1}H NMR: δ 5.01 (d, 1 H, $J_{2,3}$ 5.0 Hz, H-2), 4.96 (m, 1 H, H-3), 5.16 (m, $J_{4,5a}$ 5.7, $J_{4,5b}$ 6.9 Hz, 1 H, H-4), 3.36 (dd, $J_{5a,5b}$ 14.1 Hz, 1 H, H-5a), 3.25 (dd, 1 H, H-5b), 2.65 (t, 2 H, H-α), 1.56–1.12 (m, 8 H, H-β–Hω–1), 0.80 (t, 3 H, H-ω); ^{13}C NMR: δ 176.7 (C-1), 74.7 (C-2), 74.5 (C-3), 82.4 (C-4), 31.7 (C-5), 33.4 (C-α), 33.2–24.4. (C-β–C-ω–1), 15.8 (C-ω). Anal. Calcd for $C_{11}H_{20}O_4S$: C, 53.22; H, 8.06; S, 12.9. Found: C, 53.56; H, 8.01; S, 12.41.

5-S-*Octyl-5-thio*-D-*xylono-1,4-lactone* (**13**). 0.603 g; ^{1}H NMR: δ 5.0. (d, 1 H, $J_{2,3}$ 5.0 Hz, H-2), 4.96 (m, 1 H, H-3), 5.15 (m, $J_{4,5a}$ 5.7, $J_{4,5b}$ 6.9 Hz, 1 H, H-4), 3.36 (dd, $J_{5a,5b}$ 14.1 Hz, 1 H, H-5a), 3.25 (dd, 1 H, H-5b), 3.1 (t, 2 H, H-α), 1.55–1.14 (m, 12 H, H-β–Hω–1), 0.81 (t, 3 H, H-ω); ^{13}C NMR: δ 176.7 (C-1), 74.7 (C-2), 74.5 (C-3), 82.3 (C-4), 32.1 (C-5), 33.5 (C-α), 31.7–23.0 (C-β–C-ω–1), 14.4 (C-ω). Anal. Calcd for $C_{13}H_{24}O_4S$: C, 56.52; H, 8.69; S, 11.59. Found: C, 56.75; H, 8.56; S, 10.90.

5-S-*Decyl-5-thio*-D-*xylono-1,4-lactone* (**14**). 0.632 g; ^{1}H NMR: δ 5.00 (d, 1 H, $J_{2,3}$ 4.8 Hz, H-2), 4.92 (m, 1 H, H-3), 5.15 (m, $J_{4,5a}$ 5.7, $J_{4,5b}$ 6.9 Hz, 1 H, H-4), 3.36 (dd, $J_{5a,5b}$ 14.6 Hz, 1 H, H-5a), 3.25 (dd, 1 H, H-5b), 2.7 (t, 2 H, H-α), 1.52–1.26 (m, 16 H, H-β–Hω–1), 0.85 (t, 3 H, H-ω); ^{13}C NMR: δ 176.7 (C-1), 74.7 (C-2), 74.5 (C-3), 82.3 (C-4), 32.3 (C-5), 33.4 (C-α), 32.7–23.1 (C-β–C-ω–1), 14.4 (C-

ω). Anal. Calcd for $C_{15}H_{28}O_4S$: C, 59.21; H, 9.21; S, 10.52. Found: C, 59.56; H, 9.01; S, 10.91.

5-S-*Dodecyl*-*5*-*thio*-D-*xylono*-*1,4*-*lactone* (**15**). 0.711 g; ^{1}H NMR: δ 5.02 (d, 1 H, $J_{2,3}$ 4.8 Hz, H-2), 4.92 (m, 1 H, H-3), 5.16 (m, $J_{4,5a}$ 5.7, $J_{4,5b}$ 6.9 Hz, 1 H, H-4), 3.37 (dd, $J_{5a,5b}$ 14.1 Hz, 1 H, H-5a), 3.26 (dd, 1 H, H-5b), 2.7 (t, 2 H, H-α), 1.57–1.23 (m, 20 H, H-β–Hω–1), 0.83 (t, 3 H, H-ω); ^{13}C NMR: δ 176.7 (C-1), 74.7 (C-2), 74.5 (C-3), 82.3 (C-4), 32.2 (C-5), 33.4 (C-α), 31.7–23.1 (C-β–C-ω–1), 14.4 (C-ω). Anal. Calcd for $C_{17}H_{32}O_4S$: C, 61.44; H, 9.64; S, 9.64. Found: C, 61.66; H, 9.45; S, 9.23.

General procedure for reduction of 5-S-*alkyl*-*5*-*thio*-D-*pentono*-*1,4*-*lactones*.—To a solution of 5-*S*-alkyl-5-thio-D-pentono-1,4-lactones (200 mg, 0.91 mmol) in EtOH (20 mL) was added $NaBH_4$ (1.6 equiv, 350 mg) at such a rate that the pH was maintained below 7. Then a further amount of $NaBH_4$ (1.9 equiv, 415 mg) was added to increase the pH to 9. Stirring was continued at rt for 1 h, before adding more ion-exchange resin (Dowex 50 × 8–100 ion) to decrease the pH to 3. The resin was then removed by filtration. The filtrate was concentrated and co-concentrated with MeOH (3 × 18 mL) to give the crude mixture which was chromatographed on Silica Gel (95:5 EtOAc–MeOH).

1-S-*Hexyl*-*1*-*thio*-L-*ribitol* (**16**). 0.183 g; ^{1}H NMR: δ 4.63–4.32 (m, 4 H, H-5a, H-5b, H-4, H-3), 4.62 (m, $J_{1a,2}$ 2.8, $J_{1b,2}$ 8.5, 1 H, H-2), 3.47 (dd, $J_{1a,1b}$ 13.4 Hz, 1 H, H-1a), 3.23 (dd, 1 H, H-1b), 2.70 (t, 2 H, H-α), 1.70–1.06 (m, 8 H, H-β–Hω–1), 0.76 (t, 3 H, H-ω); ^{13}C NMR: δ 37.2 (C-1), 74.1 (C-2), 75.6 (C-3), 74.9 (C-4), 65.1 (C-5), 33.3 (C-α), 31.8–22.9 (C-β–C-ω–1), 14.3 (C-ω). Anal. Calcd for $C_{11}H_{24}O_4S$: C, 52.38; H, 9.52; S, 12.70. Found: C, 52.47; H, 9.96; S, 12.11.

1-S-*Octyl*-*1*-*thio*-L-*ribitol* (**17**). 0.190 g; ^{1}H NMR: δ 4.60–4.30 (m, 5 H, H-5a, H-5b, H-4, H-3, H-2), 3.25 (dd, $J_{1a,2}$ 2.8, $J_{1a,1b}$ 13.4 Hz, 1 H, H-1a), 3.52 (dd, $J_{1b,2}$ 8.5 Hz, 1 H, H-1b), 2.60 (t, 2 H, H-α), 1.60–1.10 (m, 12 H, H-β–Hω–1), 0.81 (t, 3 H, H-ω); ^{13}C NMR: δ 37.5 (C-1), 74.2 (C-2), 75.8 (C-3), 75 (C-4), 65.2 (C-5), 33.5 (C-α), 32.5–23.2 (C-β–C-ω–1), 14.6 (C-ω). Anal. Calcd for $C_{13}H_{28}O_4S$: C, 55.71; H, 10; S, 11.43. Found: C, 55.78; H, 10.19; S, 11.8.

1-S-*Decyl*-*1*-*thio*-L-*ribitol* (**18**). 0.181 g,; ^{1}H NMR: δ 4.55–4.30 (m, 5 H, H-5a, H-5b, H-4, H-3, H-2), 3.25 (dd, $J_{1a,2}$ 2.9, $J_{1a,1b}$ 13.3 Hz, 1 H, H-1a), 3.50 (dd, $J_{1b,2}$ 8.3 Hz, 1 H, H-1b), 2.75 (t, 2 H, H-α), 1.65–1.10 (m, 16 H, H-β–Hω–1), 0.85 (t, 3 H, H-ω); ^{13}C NMR: δ 36 (C-1), 73 (C-2), 74.2 (C-3), 73.8 (C-4), 64 (C-5), 32 (C-α), 31–21.8 (C-β–C-ω–1), 15.2 (C-ω). Anal. Calcd for $C_{15}H_{32}O_4S$: C, 58.44; H, 10.38; S, 10.38. Found: C, 58.39; H, 10.80; S, 11.10.

1-S-*Dodecyl*-*1*-*thio*-L-*ribitol* (**19**). 0.191 g; ^{1}H NMR: δ 4.61–4.29 (m, 5 H, H-5a, H-5b, H-4, H-3, H-2), 3.75 (dd, $J_{1a,2}$ 2.7, $J_{1a,1b}$ 13.4 Hz, 1 H, H-1a), 3.50 (dd, $J_{1b,2}$ 8.4 Hz, 1 H, H-1b), 2.70 (t, 2 H, H-α), 1.60–1.15 (m, 20 H, H-β–Hω–1), 0.80 (t, 3 H, H-ω); ^{13}C NMR: δ 37 (C-1), 74.1 (C-2), 75.6 (C-3), 74.8 (C-4), 65 (C-5), 33.2 (C-α), 32.1–23 (C-β–C-ω–1), 14.4 (C-ω). Anal. Calcd for $C_{17}H_{36}O_4S$: C, 60.71; H, 10.71; S, 9.52. Found: C, 60.67; H, 11.11; S, 9.92.

1-S-*Hexyl*-*1*-*thio*-D-*lyxitol* (**20**). 0.182 g; ^{1}H NMR: δ 4.78 (m, 1 H, H-4), 4.56 (m, H-2), 4.31 (m, H-3, H-5a, H-5b), 3.51 (m, $J_{1a,1b}$ 12.9 Hz, 1 H, H-1a), 3.15 (dd, $J_{1b,2}$ 8.2 Hz, 1 H, H-1b), 2.66 (t, 2 H, H-α), 1.60–1.10 (m, 8 H, H-β–Hω–1), 0.80 (t, 3 H, H-ω); ^{13}C NMR: δ 38.4 (C-1), 72 (C-2), 74.5 (C-3), 72.5 (C-4), 65.2 (C-5), 33.3 (C-α), 31.8–22.9 (C-β–C-ω–1), 14.3 (C-ω). Anal. Calcd for $C_{11}H_{24}O_4S$: C, 52.38; H, 9.52; S, 12.70. Found: C, 52.17; H, 9.12; S, 12.11.

1-S-*Octyl*-*1*-*thio*-D-*lyxitol* (**21**). 0.170 g; ^{1}H NMR: δ 4.8–4.2 (m, 5 H, H-5a, H-5b, H-4, H-3, H-2), 3.45 (m, $J_{1a,1b}$ 13.4 Hz, 1 H, H-1a), 3.65 (dd, $J_{1b,2}$ 8.0 Hz, 1 H, H-1b), 3.10 (t, 2 H, H-α), 1.60–1.30 (m, 12 H, H-β–Hω–1), 1.20 (t, 3 H, H-ω); ^{13}C NMR: δ 35.8 (C-1), 70.8 (C-2), 73.3 (C-3), 71.3 (C-4), 63.9 (C-5), 32.0 (C-α), 30.8–21.7 (C-β–C-ω–1), 13.1 (C-ω). Anal. Calcd for $C_{13}H_{28}O_4S$: C, 55.71; H, 10; S, 11.43. Found: C, 55.45; H, 10.23; S, 10.98.

1-S-*Decyl*-*1*-*thio*-D-*lyxitol l* (**22**). 0.181 g; ^{1}H NMR: δ 4.8–4.2 (m, 5 H, H-5a, H-5b, H-4, H-3, H-2), 3.09 (m, $J_{1a,1b}$ 13.4 Hz, 1 H, H-1a), 3.55 (dd, $J_{1b,2}$ 8.0 Hz, 1 H, H-1b), 2.67

(t, 2 H, H-α), 1.62–1.20 (m, 16 H, H-β–Hω–1), 0.85 (t, 3 H, H-ω); ^{13}C NMR: δ 37.1 (C-1), 70.7 (C-2), 73.2 (C-3), 71.2 (C-4), 63.9 (C-5), 32.0 (C-α), 30.9–21.7 (C-β–C-ω–1), 13.1 (C-ω). Anal. Calcd for $C_{15}H_{32}O_4S$: C, 58.44; H, 10.38; S, 10.38. Found: C, 58.21; H, 10.14; S, 10.83.

1-S-*Dodecyl-1-thio*-D-*lyxitol* (**23**). 0.182 g; ^{1}H NMR: δ 4.8–4.20 (m, 5 H, H-5a, H-5b, H-4, H-3, H-2), 3.40 (m, $J_{1a,1b}$ 13.4 Hz, 1 H, H-1a), 3.62 (dd, $J_{1b,2}$ 8.0 Hz, 1 H, H-1b), 2.78 (t, 2 H, H-α), 1.50–1.20 (m, 20 H, H-β–Hω–1), 1.10 (t, 3 H, H-ω); ^{13}C NMR: δ 37.2 (C-1), 70.8 (C-2), 73.3 (C-3), 71.3 (C-4), 64 (C-5), 32.0 (C-α), 30.9–21.8 (C-β–C-ω–1), 13.1 (C-ω). Anal. Calcd for $C_{17}H_{36}O_4S$: C, 60.71; H, 10.71; S, 9.52. Found: C, 60.52; H, 10.21; S, 9.02.

1-S-*Hexyl-1-thio*-L-*xylitol* (**24**). 0.185 g; ^{1}H NMR: δ 4.52–4.32 (m, 5 H, H-5a, H-5b H-4, H-3, H-2), 3.32 (m, $J_{1a,1b}$ 13.2 Hz, 1 H, H-1a), 3.21 (m, $J_{1b,2}$ 5.9 Hz, 1 H, H-1b), 2.62 (t, 2 H, H-α), 1.56–1.09 (m, 8 H, H-β–Hω–1), 0.79 (t, 3 H, H-ω); ^{13}C NMR: δ 37.1 (C-1), 73.6 (C-2), 75 (C-3), 73.4 (C-4), 64.9 (C-5), 33.3 (C-α), 32–23.1 (C-β–C-ω–1), 14.5 (C-ω). Anal. Calcd for $C_{11}H_{24}O_4S$: C, 52.38; H, 9.52; S, 12.70. Found: C, 52.50; H, 9.68, S, 13.10.

1-S-*Octyl-1-thio*-L-*xylitol* (**25**). 0.183 g; ^{1}H NMR: δ 4.53–4.33 (m, 5 H, H-5a, H-5b H-4, H-3, H-2), 3.33 (m, $J_{1a,1b}$ 13.2 Hz, 1 H, H-1a), 3.22 (m, $J_{1b,2}$ 5.8 Hz, 1 H, H-1b), 2.68 (t, 2 H, H-α), 1.58–1.14 (m, 12 H, H-β–Hω–1), 0.84 (t, 3 H, H-ω); ^{13}C NMR: δ 37.2 (C-1), 73.6 (C-2), 74.9 (C-3), 73.4 (C-4), 64.9 (C-5), 33.4 (C-α), 32.5–23.1 (C-β–C-ω–1), 14.5 (C-ω). Anal. Calcd for $C_{13}H_{28}O_4S$: C, 55.71; H, 10; S, 11.43. Found: C, 55.78; H, 10.19; S, 11.90.

1-S-*Decyl-1-thio*-L-*xylitol* (**26**). 0.172 g; ^{1}H NMR: δ 4,54–4.38 (m, 5 H, H-5a, H-5b H-4, H-3, H-2), 3.33 (m, $J_{1a,1b}$ 13.2 Hz, 1 H, H-1a), 3.22 (m, $J_{1b,2}$ 5.9 Hz, 1 H, H-1b), 2.68 (t, 2 H, H-α), 1.61–1.19 (m, 16 H, H-β–Hω–1), 0.86 (t, 3 H, H-ω); ^{13}C NMR: δ 37.1 (C-1), 73.6 (C-2), 75 (C-3), 73.4 (C-4), 64.9 (C-5), 33.3 (C-α), 32.5–23.1 (C-β–C-ω–1), 14.6 (C-ω). Anal. Calcd for $C_{15}H_{32}O_4S$: C, 58.44; H, 10.38; S, 10.38. Found: C, 58.39; H, 1080; S, 10.90.

1-S-*Dodecyl-1-thio*-L-*xylitol* (**27**). 0.186 g; ^{1}H NMR: δ 4.53–4.32 (m, 5 H, H-5a, H-5b H-4, H-3, H-2), 3.33 (m, $J_{1a,1b}$ 13.2 Hz, 1 H, H-1a), 3.22 (m, $J_{1b,2}$ 5.8 Hz, 1 H, H-1b), 2.71 (t, 2 H, H-α), 1.63–1.24 (m, 20 H, H-β–Hω–1), 0.89 (t, 3 H, H-ω); ^{13}C NMR: δ 37.1 (C-1), 73.5 (C-2), 74.8 (C-3), 73.3 (C-4), 64.8 (C-5), 33.3 (C-α), 32.4–23.2 (C-β–C-ω–1), 14.5 (C-ω). Anal. Calcd for $C_{17}H_{36}O_4S$: C, 60.71; H, 10.71; S, 9.52. Found: C, 60.73; H, 11.11; S, 9.9.

References

1. Deisenhofer, J.; Michel, H. *Angew. Chem.* **1989**, *101*, 872–892.
2. Ahlers, M.; Müller, W.; Reichert, A.; Ringsdorf, H.; Venzmer, J. *Angew. Chem.* **1990**, *102*, 1310–1327.
3. Ikekawa, T.; Irinoda, K.; Saze, K.; Katori, T.; Matsuda, H.; Ohkawa, M.; Kosik, M. *Chem. Pharm. Bull.* **1987**, *35*, 2894–2899.
4. Nihra, Y.; Sogawa, S.; Izumi, A.; Sasamori, A.; Sudo, T.; Miki, T.; Matsumoto, H.; Satoh, T. *J. Med. Chem.* **1992**, *35*, 1618–1623.
5. Kato, K.; Terao, S.; Shimamoto, N.; Hirata, M. *J. Med. Chem.* **1988**, *31*, 793–798.
6. (a) Jeffrey, G. A.; Wingert, L. M. *Liq. Cryst.* **1992**, *12*, 179–202;
   (b) Koll, P.; Oelting, M. *Tetrahedron Lett.* **1986**, *27*, 2837–2838.
7. Collins, P.; Ferrier, R. *Monosaccharides. Their Chemistry and Their Roles in Natural Products*; Wiley: Chichester, 1995; pp. 97–106.
8. Dahlhoff, W. V. *Liebigs Ann. Chem.* **1990**, 1025–1027.
9. (a) Goodby, J. W.; Haley, J. A.; Watson, M. J.; Mackenzie, G.; Kelly, S. M.; Letellier, P.; Douillet, O.; Godé, P.; Goethals, G.; Ronco, G.; Villa, P. *Liq. Cryst.* **1997**, *22*, 367–378;
   (b) Douillet, O. Thesis, University of Amiens, France, 1999.
10. Bouchez, V.; Stasik, I.; Beaupère, D.; Uzan, R. *Carbohydr. Res.* **1997**, *300*, 139–142.
11. Wadouachi, A.; Stasik, I. B.; Demailly, G.; Uzan, R.; Beaupère, D. *Nat. Prod. Lett.* **1993**, *2*, 277–282.
12. (a) Postel, D. Thesis, University of Amiens, France, 1990; (b) Postel, D.; Vanlemmens, P.; Godé, P.; Ronco, G.; Villa, P. *Carbohydr. Res.* **1995**, *271*, 227–233.
13. Choquet-Farnier, C. Thesis, University of Amiens, France, 1996.
14. Bouchez, V.; Stasik, I.; Beaupère, D.; Uzan, R. *Tetrahedron Lett.* **1997**, *38*, 7733–7736.