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Synthesis of optically active chalcogran from L-sorbose †

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Abstract

The synthesis of (2*S*,5*RS*)-2-ethyl-1,6-dioxaspiro[4.4]nonane (chalcogran) (**1**) from 2,3:4,6-di-*O*-isopropylidene-α-L-sorbofuranose (**2**) through elongation of the carbon chain at C-1 and C-6 by the Wittig and Corey methodologies, respectively, spiroacetalation, and deoxygenation at C-3,4 of the appropriately protected derivatives by the Barton method has been accomplished.

Key words: Pheromones; Spiroacetals; Chalcogran; Stereoselective synthesis; L-Sorbose

1. Introduction

The spiroacetal chalcogran (2-ethyl-1,6-dioxaspiro[4.4]nonane) (**1**) is the major component of the aggregation pheromone of the six-spined spruce bark beetle [*Pityogenes chalcographus* (L.)] and was isolated and identified by Francke et al. in 1977 [2]. There are four stereoisomers of **1**, but only the diastereomeric (2*S*,5*RS*)-**1** mixture is present in the beetle [3], the most active isomer being that with the (2*S*,5*R*) configuration [4].

Several racemic and stereoselective syntheses of **1** have appeared in the literature [5], and only one where D-glucose is used as the chiral source in the synthesis of optically active **1** [6].

As a part of our continuing efforts to synthesise optically active pheromones, we report herein the stereoselective synthesis of (2*S*,5*RS*)-**1**, using 2,3:4,6-di-*O*-isopropylidene-α-L-sorbofuranose (**2**) [7] as the chiral starting material.

† Enantiospecific Synthesis of Spiroacetals, Part VI. For Part V, see ref. 1.

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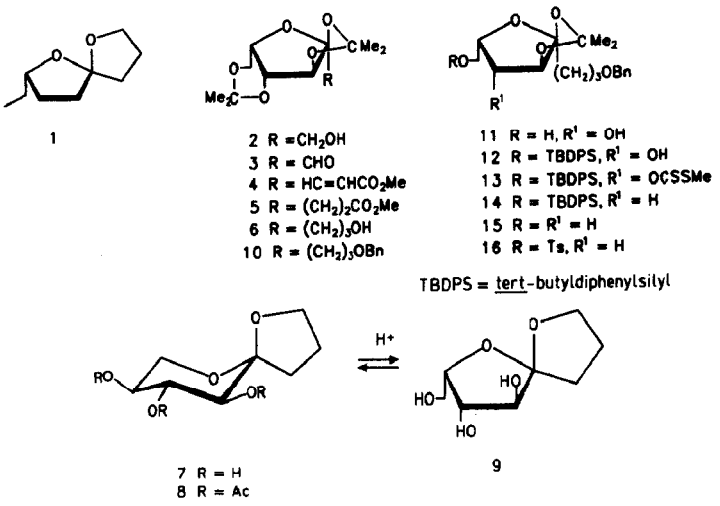
2. Results and discussion

Oxidation of **2** with pyridinium chlorochromate yielded 2,3:4,6-di-*O*-isopropylidene-α-L-*xylo*-hexos-2-ulofuranose (**3**) which reacted in situ with (methoxycarbonylmethylene)triphenylphosphorane in dichloromethane to afford methyl (*E*)-2,3-dideoxy-4,5:6,8-di-*O*-isopropylidene-α-L-*xylo*-oct-2-en-4-ulofuranosonate (**4**). The configuration at C-2,3 was shown to be *E* from the $J_{2,3}$ value (15.5 Hz). Hydrogenation (10% Pd–C) of **4** gave the saturated ester **5** that was subsequently reduced with lithium aluminium hydride to afford 2,3-dideoxy-4,5:6,8-di-*O*-isopropylidene-α-L-*xylo*-oct-4-ulofuranose (**6**).



Scheme 1.

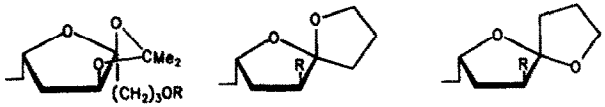
In order to shorten the synthetic route to **1**, **6** was treated with aqueous trifluoroacetic acid to promote the removal of the protecting groups and the subsequent spiroglycosidation. As a result of this process, (5*R*,8*S*,9*R*,10*S*)-8,9,10-trihydroxy-1,6-dioxaspiro [4.5]decane (**7**) was obtained. The structure of **7** was confirmed on the basis of its spectroscopic data as well as that of its tri-*O*-acetyl derivative **8**. Attempts to produce the 1,6-dioxaspiro[4.4]nonane skeleton through the isomerisation of **7** to **9** in acid medium (see Scheme 1) and acetonation of **9** at the 3,5-positions * under thermodynamic conditions, on the basis of the preferential formation of such a *cis*-fused 1,3-dioxane ring in related compounds with the *xylo* configuration [8], was unsuccessful, resulting in a complex mixture.

Treatment of **6** with benzyl bromide and potassium *tert*-butoxide gave the 1-*O*-benzyl derivative **10**. Partial deacetonation of **10** to afford **11** could be readily achieved due to the different stability [8] shown by the two isopropylidene groups present in **10**. The chemoselective protection of the primary hydroxyl group at C-8 as the *tert*-butyldiphenylsilyl ether (**12**) allowed deoxygenation at C-6 by the Barton

* Xylose numbering.

methodology [9] to yield 1-*O*-benzyl-2,3,6-trideoxy-4,5-*O*-isopropylidene-8-*O*-*tert*-butyldiphenylsilyl-α-L-*erythro*-oct-4-ulofuranose (**14**). Treatment of **14** with tetrabutylammonium fluoride caused desilylation at C-8 to afford **15**, which was transformed into the corresponding 8-*O*-*p*-toluenesulfonyl derivative **16**.

Elongation by one carbon atom at C-8, to produce **17**, was carried out by reaction of **16** with lithium dimethylcuprate. Hydrogenolysis of the benzyl group at C-1 in **17**, followed by treatment of the resulting **18** with trifluoroacetic acid, gave a mixture of (2*S*,4*S*,5*R*)-2-ethyl-4-hydroxy-1,6-dioxaspiro[4.4]nonane (**19**) and its epimer at C-5 (**20**) in a 3:1 ratio, as was shown by GLC analysis (see Experimental). Compounds **19** and **20** were found to be unstable, through epimerisation at the spiroketal linkage. This behaviour was in accordance with that reported for chalcogran itself where, even in such relatively nonpolar solvents as benzene and chloroform, a facile epimerisation took place [10,11b]. Nevertheless, we were able to measure the specific rotations of freshly isolated samples of **19** and **20**, $[\alpha]_D$ −39° and +46°, respectively, values which were in agreement with those shown by analogous compounds with 5*R* and 5*S* configurations, respectively, at the spiro centre [10b]. The ^{13}C NMR spectrum of **19**, slightly contaminated with **20**, showed a good correlation with that reported [11] for the related chalcogran. Thus, the resonance signals for C-2,10,11 in **20** (see Experimental) suffer a deshielding effect with respect to those in **19**, because of its *Z* configuration [1].



17 R = Bn
18 R = H

19 R = OH
21 R = OCSSMe

20 R = OH
22 R = OCSSMe

Compounds **19** and **20**, freshly isolated, were transformed into the corresponding 4-xanthates **21** and **22**, respectively, which appeared to be stable since no changes were observed in their NMR spectra and optical rotations.

Finally, deoxygenation of **22** by the Barton method [9] gave (2*S*,5*RS*)-**1** as an unresolvable mixture (GLC). The value of $[\alpha]_D$ −18.3° was in good accordance with that previously reported for a similar diastereomeric mixture [12]. Only Högberg et al. [10b] have reported on the resolution of such a mixture after tedious chromatography, finding $[\alpha]_D$ −100° (*c* 0.3, hexane) and +96° (*c* 1, hexane) for (2*S*,5*R*)- and (2*S*,5*S*)-**1**, respectively. The ^{13}C NMR spectrum of the mixture contained signals for both diastereomers, those of the (2*S*,5*R*)-**1** isomer [11] being of higher intensity. In addition, the mass spectrum (EI) was in good accordance to that reported by Mori et al. [12a]. We must conclude that the epimerisation occurred during the deoxygenation reaction, since **22** was a pure diastereomer.

3. Experimental

General methods.—Melting points were determined with a Gallenkamp apparatus and are uncorrected. Solutions were dried over $MgSO_4$ before concentration

under diminished pressure. ^1H and ^{13}C NMR spectra were recorded with Bruker AM-300 and WP-80 WC spectrometers for solutions in $CDCl_3$ (internal Me_4Si). IR spectra were recorded with a Perkin–Elmer 782 instrument and mass spectra with a Hewlett–Packard HP-5988-A mass spectrometer. Optical rotations were measured for solutions in $CHCl_3$ (1-dm tube) with a Jasco DIP-370 polarimeter. GLC was performed on a Perkin–Elmer 8410 gas chromatograph equipped with a flame-ionisation detector and a steel column (2 m × 0.125 in. i.d.) packed with 5% OV-17 on Chromosorb W (100–120 mesh): (*A*) 3 min at 200°C, program to 230°C, 10°C/min; (*B*) 230°C; (*C*) 180°C; and (*D*) 115°C. The N_2 flow rate was 30 mL/min; the injection port and the zone-detector temperatures were (*A*) and (*B*) 270°C; (*C*) 230°C; and (*D*) 200°C. TLC was performed on Silica Gel G (Merck) with detection by charring with H_2SO_4. Column chromatography was performed on silica gel (Merck, 7734). The noncrystalline compounds, for which elemental analyses were not obtained, were shown to be homogeneous by chromatography and characterised by NMR and mass spectrometry.

*Methyl (*E*)-2,3-dideoxy-4,5 : 6,8-di-*O*-isopropylidene-α-*L*-xylo-oct-2-en-4-ulofuranosonate* (**4**).—To a stirred solution of **2** (10.32 g, 40 mmol) [7] in dry CH_2Cl_2 (150 mL) were added pyridinium chlorochromate (13 g, 60 mmol) and 4A molecular sieve (13 g). Stirring was continued for 12 h at room temperature. In a separate experiment, GLC (*A*) showed that **2** (t_R 2.81 min) had almost disappeared and that a new compound, presumably the aldehyde **3** (t_R 1.96 min), was present. (Methoxycarbonylmethylene)triphenylphosphorane (13.7 g, 41 mmol) was added and the mixture stirred for 24 h at room temperature. GLC (*A*) then showed the presence of a product (t_R 6.54 min). The mixture was diluted with ether (300 mL), filtered through Silica Gel G, and concentrated. Chromatography (1:3 ether–hexane) of the residue gave **4** (11.2 g, 89% from **2**); mp 112–115°C (from ether–hexane); $[\alpha]_D$ +23° (*c* 1.2); ν_{max}^{KBr} 2997, 2960, and 2941 (C–H), 1725 (ester, C=O), 1670 (C=C, conjugated), 1391 and 1367 (CMe_2), 1306, 1287, 1198, 1173, 1118, 1075, and 998 cm^{-1} (C–O–C); NMR data: ^1H, δ 6.94 (d, 1 H, $J_{2,3}$ 15.5 Hz, H-3), 6.39 (d, 1 H, H-2), 4.31 (s, 1 H, H-5), 4.30 (d, 1 H, $J_{6,7}$ 2 Hz, H-6), 4.12–4.08 (m, 1 H, H-7), 4.05 (d, 2 H, $J_{7,8}$ 1.8 Hz, H-8,8), 3.72 (s, 3 H, OMe), 1.49 and 1.39 (2 s, 6 H, CMe_2, 1,3-dioxane ring), and 1.33 (s, 6 H, CMe_2, 1,3-dioxane ring); ^{13}C, δ 166.58 (C-1), 144.29 (C-3), 123.24 (C-2), 112.56 (C-4), 111.90 (CMe_2, 1,3-dioxolane ring), 97.52 (CMe_2, 1,3-dioxolane ring), 87.91 (C-7), 73.41 and 73.07 (C-5,6), 60.22 (C-8), 51.76 (OMe), 28.96 and 18.68 (CMe_2, 1,3-dioxane ring), 27.06 and 26.20 (CMe_2, 1,3-dioxolane ring). Mass spectrum: *m/z* 314 (0.04%, M^+), 300 (3.62, $M^+ + 1 - Me$), 299 (22.01, $M^+ - Me$), 256 (4.04, $M^+ - Me_2CO$), 241 (5.79, $M^+ - Me - Me_2CO$), 213 (10.06), 211 (10.19), 184 (12.66), 169 (20.49), 126 (29.11), 113 (100, $C_6H_9O_2^+$), 101 (18.94), 85 (24.50), 59 (35.79, Me_2COH^+), and 43 (71.52, Ac^+). Anal. Calcd for $C_{15}H_{22}O_7$: C, 57.32; H, 7.05. Found: C, 56.96; H, 7.08.

*Methyl 2,3-dideoxy-4,5:6,8-di-*O*-isopropylidene-α-*L*-xylo-oct-4-ulofuranosonate* (**5**). —A solution of **4** (1.8 g, 5.7 mmol) in MeOH (30 mL) was hydrogenated at 4 atm over 10% Pd–C (0.2 g). GLC (*B*) after 4 h revealed that **4** had disappeared and that a new compound (t_R 2.38 min) was present. The catalyst was collected and washed with methanol, and the combined filtrate and washings were concentrated.

Chromatography (1:1 ether–hexane) of the residue gave **5** (1.5 g, 83%) as a syrup; $[\alpha]_D$ +3° (*c* 1.7); ν_{max}^{film} 2994 and 2941 (C–H), 1741 (ester, C=O), 1385 and 1375 (CMe_2), 1288, 1241, 1201, 1194, 1172, 1124, 1080, and 946 cm^{-1} (C–O–C); NMR data: ^1H, δ 4.26 (s, 1 H, H-5), 4.21 (bd, 1 H, $J_{6,7}$ 1.8 Hz, H-6), 4.06–3.94 (m, 3 H, H-7,8a,8b), 3.64 (s, 3 H, OMe), 2.72–2.58 (m, 2 H, H-2a,2b), 2.29–2.23 (m, 2 H, H-3a,3b), 1.44, 1.39, 1.34, and 1.32 (4 s, 12 H, 2 CMe_2); ^{13}C, δ 174.08 (C-1), 114.62 (C-4), 110.92 (CMe_2, 1,3-dioxolane ring), 97.41 (CMe_2, 1,3-dioxane ring), 88.58 (C-7), 75.70 (C-6), 71.98 (C-5), 60.37 (C-8), 51.58 (OMe), 32.93 (C-2), 29.02 (C-3), 28.79 and 18.75 (CMe_2, 1,3-dioxane ring), 27.32 and 26.46 (CMe_2, 1,3-dioxolane ring). Mass spectrum: *m/z* 317 (0.19%, $M^+ + 1$), 316 (1.00, M^+), 302 (4.28, $M^+ + 1 - Me$), 301 (25.21, $M^+ - Me$), 215 (15.74), 213 (6.75), 186 (18.42), 183 (27.42), 171 (37.38), 115 (59.01), 113 (20.46), 101 (25.79), 59 (52.10), 55 (41.69), and 43 (100, Ac^+). Anal. Calcd for $C_{15}H_{24}O_7$: C, 56.95; H, 7.65. Found: C, 57.02; H, 7.83.

2,3-Dideoxy-4,5:6,8-di-O-*isopropylidene*-α-L-xylo-*oct-4-ulofuranose* (**6**).—To a stirred suspension of $LiAlH_4$ (1.17 g, 30.7 mmol) in dry THF (15 mL) was added dropwise a solution of **5** (10.4 g, 33 mmol) in the same solvent (30 mL). The mixture was heated under reflux for 7 h. TLC (4:1 ether–hexane) then showed that **5** had disappeared and a new product of lower mobility was present. The excess of reagent was decomposed by cautious addition of sat aq ammonium chloride, the mixture was filtered through a Celite pad, the filtrate extracted with ether (3 × 50 mL), and the combined extracts washed with brine and concentrated. Chromatography (1:3 ether–hexane) of the residue gave **6** (8 g, 85%) as a colourless syrup which crystallised on standing; mp 116–117°C; $[\alpha]_D$ + 4° (*c* 1); ν_{max}^{film} 3467 (OH), 2994, 2938, and 2876 (C–H), 1384 and 1375 (CMe_2), 1240, 1198, 1124, 1083, and 993 cm^{-1} (C–O–C); NMR data: ^1H, δ 4.23 (s, 2 H, H-5,6), 4.04 (dd, 1 H, $J_{7,8a}$ 2, $J_{8a,8b}$ 14 Hz, H-8a), 4.02 (t, 1 H, H-7), 3.97 (dd, 1 H, $J_{7,8b}$ 2.3 Hz, H-8b), 3.71 (dt, 1 H, $J_{1a,1b}$ 10.6, $J_{1a,2a} = J_{1a,2b} = 6.4$ Hz, H-1a), 3.65 (dt, 1 H, $J_{1b,2a} = J_{1b,2b} = 6$ Hz, H-1b), 2.24 (s, 1 H, OH), 2.14–1.92 (m, 2 H, H-2a,2b), 1.87–1.77 (m, 2 H, H-3a,3b), 1.44, 1.39, 1.33, and 1.32 (4 s, 12 H, 2 CMe_2); ^{13}C, δ 115.46 (C-4), 111.07 (CMe_2, 1,3-dioxolane ring), 97.39 (CMe_2, 1,3-dioxane ring), 88.80 (C-7), 73.62 (C-6), 72.04 (C-5), 62.78, (C-1), 60.45 (C-8), 34.32 (C-3), 28.89 and 18.76 (CMe_2, 1,3-dioxane ring), 27.45 and 26.67 (CMe_2, 1,3-dioxolane ring), 27.15 (C-2). Anal. Calcd for $C_{14}H_{24}O_6$: C, 58.32; H, 8.39. Found: C, 58.53; H, 8.43.

(5R,8S,9R,10S)-8,9,10-Trihydroxy-1,6-dioxaspiro[4.5]decane (**7**).—A solution of **6** (4.6 g, 16 mmol) in aq 70% CF_3CO_2H (20 mL) was kept at room temperature overnight. TLC (5:1 $CHCl_3$–MeOH) then showed no **6** but a new compound of lower mobility. The mixture was concentrated, and water and then CH_2Cl_2 were distilled repeatedly from the residue. Chromatography (10:1 $CHCl_3$–MeOH) of the residue gave **7** (2.94 g, 97%) as a colourless syrup that crystallised on standing; mp 110–112°C; $[\alpha]_D$ −87° (*c* 1.6); ν_{max}^{film} 3439, 3422, and 3396 (OH), 2973, 2928, 2887, and 2874 (C–H), 1132, 1109, 1093, 1055, 1028, 1007, 990, and 952 cm^{-1} (C–O–C); NMR data: ^1H, δ 4.72 (bs, 3 H, HO-8,9,10), 3.94 (bsex, 2 H, H-2a,2b), 3.73–3.42 (m, 5 H, H-7*eq*, 7*ax*, 8,9,10), 2.24–2.12, 2.07–1.94, and 1.94–1.57 (3 m, 4 H, H-3a,3b,4a,4b); ^{13}C, δ 107.88 (C-5), 76.05 (C-10), 72.75 (C-9), 70.25 (C-8), 68.82

(C-2), 62.65 (C-7), 33.65 (C-4), and 23.80 (C-3). CI-Mass spectrum (CH_4): *m/z* 192 (9%, $M^+ + 2$), 191 (84, $M^+ + 1$), 189 (7, $M^+ - 1$), 174 (10, $M^+ + 2 - H_2O$), 173 (100, $M^+ + 1 - H_2O$), 156 (4, $M^+ + 2 - 2H_2O$), 155 (38, $M^+ + 1 - 2H_2O$), 143 (10), 113 (5), 101 (15, $C_5H_9O_2^+$), 87 (33), and 51 (12). Anal. Calcd for $C_8H_{14}O_5$: C, 50.52; H, 7.42. Found: C, 50.29; H, 7.11.

Acetylation of **7** (143 mg, 0.75 mmol), in dry pyridine (2 mL) and Ac_2O (1 mL) as usual, gave, after column chromatography (1:2 ether–hexane), the corresponding 8,9,10-tri-*O*-acetyl derivative **8** (140 mg, 60%) as a syrup that crystallised on standing; mp 73–74°C; $[\alpha]_D$ – 62° (*c* 0.6); ν_{max}^{film} 2963 and 2895 (C–H), 1757 (C = O, acetate), 1372, 1248, 1228, 1100, 1058, 1032, 982, and 955 cm^{-1} (C–O–C); NMR data: ^1H, δ 5.40 (t, 1 H, $J_{8,9} = J_{9,10} = 10$ Hz, H-9), 5.08 (d, 1 H, H-10), 4.95 (ddd, 1 H, H-8), 4.02–3.87 (m, 2 H, H-2a,2b), 3.74 (dd, 1 H, $J_{7eq,7ax}$ 11, $J_{7eq,8}$ 6.2 Hz, H-7*eq*), 3.64 (t, 1 H, $J_{7ax,8}$ 11 Hz, H-7*ax*), 2.04, 1.99, and 1.97 (3 s, 9 H, 3 Ac), 2.05–1.75 (m, 4 H, H-3a,3b,4a,4b); ^{13}C, δ 170.24, 170.09, and 170.03 (Me*C*O), 106.16 (C-5), 71.69, 70.76, and 69.65 (C-8,9,10), 68.79 (C-2), 59.42 (C-7), 33.68 (C-4), 23.72 (C-3), and 20.75 (*Me*CO). Mass spectrum: *m/z* 317 (0.04%, $M^+ + 1$), 171 (5.52), 170 (26.48), 129 (15.28), 128 (39.67), 115 (13.09), 100 (28.54), 87 (71.59), 86 (24.25), 85 (23.15), 71 (23.22), 69 (64.04), and 43 (100, Ac^+). Anal. Calcd for $C_{14}H_{20}O_8$: C, 53.16; H, 6.37. Found: C, 52.75; H, 6.35.

1-O-*Benzyl-2,3-dideoxy-4,5:6,8-di*-O-*isopropylidene-α*-L-xylo-*oct-4-ulofuranose* (**10**).—To a stirred suspension of potassium *tert*-butoxide (1.8 g, 16 mmol) in dry THF (15 mL) was added dropwise a solution of **6** (2.47 g, 8.6 mmol) in the same solvent (25 mL) under Ar. The mixture was stirred for 0.5 h at room temperature and then benzyl bromide (2 mL, 16 mmol) was added dropwise. The mixture was maintained at room temperature for 1 h with stirring. TLC (4:1 ether–hexane) then revealed the absence of **6** and the presence of a new compound of higher mobility. The mixture was diluted with ether, washed with brine, and concentrated. Chromatography (1:4 ether–hexane) of the residue gave syrupy **10** (3.1 g, quantitative); $[\alpha]_D$ + 4° (*c* 1); ν_{max}^{film} 3091, 3066, and 3034 (C–H, aromatic), 2993, 2966, 2939, and 2863 (C–H), 1384 and 1374 (CMe_2), 1240, 1200, 1173, 1125, 1099, 1084, and 975 (C–O–C), 737 and 698 cm^{-1} (aromatic); NMR data: ^1H, δ 7.37–7.23 (m, 5 H, CH_2*Ph*), 4.50 (s, 2 H, C*H*$_2$Ph), 4.25 (s, 1 H, H-5), 4.23 (d, 1 H, $J_{6,7}$ 1.5 Hz, H-6), 4.08–3.96 (m, 3 H, H-7,8a,8b), 3.54 (t, 2 H, $J_{1,2}$ 6.5 Hz, H-1,1), 2.09–1.81 (m, 4 H, H-2a,2b,3a,3b), 1.46, 1.41, 1.35, and 1.33 (4 s, 12 H, 2 CMe_2); ^{13}C, δ 139.79, 128.36, 127.65, and 127.48 (Ph), 115.90 (C-4), 110.89 (*C*Me_2, 1,3-dioxolane ring), 97.35 (*C*Me_2, 1,3-dioxane ring), 86.39 (C-7), 73.80 (C-6), 72.80 (*C*H_2Ph), 71.91 (C-5), 70.50 (C-1), 60.49 (C-8), 34.50 (C-3), 24.55 (C-2), 28.88 and 18.83 (C*Me*$_2$, 1,3-dioxane ring), 27.55 and 26.79 (C*Me*$_2$, 1,3-dioxolane ring). Mass spectrum: *m/z* 378 (0.53%, M^+), 277 (1.54), 248 (1.34), 215 (1.62), 171 (1.72), 158 (1.29), 113 (14.77), 104 (16.46), 91 (100, $C_7H_7^+$), 87 (32.19), 59 (24.01) and 43 (62.39, Ac^+).

1-O-*Benzyl-2,3-dideoxy-4,5*-O-*isopropylidene-α*-L-xylo-*oct-4-ulofuranose* (**11**).—A solution of **10** (3 g, 7.9 mmol) in aq 50% AcOH (16 mL) was heated for 1 h at 50°C. TLC (4:1 ether–hexane) then revealed the presence of a new compound of lower mobility. The mixture was concentrated and dissolved in abs EtOH, and the solution neutralised (K_2CO_3), filtered, and concentrated. Chromatography (4:1

ether–hexane) of the residue gave **11** (2.6 g, quantitative); $[\alpha]_D$ +5° (*c* 1); ν_{max}^{film} 3426 (OH), 3091, 3067, and 3034 (C–H, aromatic), 2989, 2936, and 2868 (C–H), 1383 and 1373 (CMe_2), 1251, 1239, 1214, 1183, 1173, 1168, 1102, 1075, 1049, 1046, 1030, and 989 (C–O–C), 740 and 698 cm^{-1} (aromatic); NMR data: ^1H, δ 7.37–7.23 (m, 5 H, CH_2*Ph*), 4.50 (s, 2 H, C*H*$_2$Ph), 4.26 (d, 1 H, $J_{6,7}$ 3 Hz, H-6), 4.24 (s, 1 H, H-5), 4.18 (bq, 1 H, H-7), 4.10–3.60 (bs, 1 H, OH), 4.04 (dd, 1 H, $J_{7,8a}$ 2, $J_{8a,8b}$ 13 Hz, H-8a), 3.94 (dd, 1 H, $J_{7,8b}$ 2.7 Hz, H-8b), 3.62–3.46 (m, 2 H, H-1a,1b), 2.11–1.78 (m, 4 H, H-2a,2b,3a,3b), 1.45 and 1.31 (2 s, 6 H, CMe_2); ^{13}C, δ 138.23, 128.46, 127.85, and 127.74 (Ph), 115.15 (C-4), 110.98 (*C*Me$_2$), 87.59 (C-7), 79.07 (C-6), 77.61 (C-5), 72.99 (*C*H$_2$Ph), 70.25 (C-1), 61.40 (C-8), 34.69 (C-3), 27.49 and 26.65 (C*Me*$_2$), and 24.33 (C-2). Mass spectrum: *m/z* 338 (0.36%, M^+), 277 (0.73), 262 (0.37), 248 (0.67), 215 (0.45), 155 (1.35), 149 (1.69), 141 (1.86), 125 (2.07), 113 (7.54), 107 (7.52), 105 (24.56), 91 (100, $C_7H_7^+$), 77 (17.66), 71 (12.79), 59 (17.29), and 43 (47.09, Ac^+). Anal. Calcd for $C_{18}H_{26}O_6$: C, 63.89; H, 7.74. Found: C, 64.12; H, 7.37.

1-O-*Benzyl-8*-O-tert-*butyldiphenylsilyl-2,3-dideoxy-4,5*-O-*isopropylidene-α*-L-xylo-*oct-4-ulofuranose* (**12**).—To a stirred solution of **11** (5.88 g, 17.4 mmol) in dry CH_2Cl_2 (60 mL) under Ar was added 4-dimethylaminopyridine (140 mg), Et_3N (2.6 mL), and *tert*-butylchlorodiphenylsilane (5.5 mL, 21 mmol), and the mixture was maintained for 16 h at room temperature. TLC (ether) then showed the absence of **11** and the presence of a faster-running product. The mixture was washed with aq 10% HCl, water, sat aq $NaHCO_3$, and water, then concentrated. Chromatography (1:5 ether–hexane) of the residue gave **12** (10 g, quantitative); $[\alpha]_D$ −14° (*c* 1); ν_{max}^{film} 3462 (OH), 3074, 3053, and 3033 (C–H, aromatic), 2989, 2960, 2934, and 2861 (C–H), 1382 and 1373 (CMe_2), 1256, 1214, 1185, 1170, 1114, 1078, 1062, 1029, and 988 (C–O–C), 736 and 702 cm^{-1} (aromatic); NMR data: ^1H, δ 7.75–7.63 and 7.46–7.22 (2 m, 15 H, relative intensity 4:11, 3 Ph), 4.49 (s, 2 H, C*H*$_2$Ph), 4.35 (d, 1 H, $J_{6,7}$ 2.3 Hz, H-6), 4.30 (s, 1 H, H-5), 4.18–4.06 (m, 3 H, H-7,8,8), 3.53 (t, 2 H, *J* 6 Hz, H-1,1), 2.12–1.89 (m, 4 H, H-2a,2b,3a,3b), 1.45 and 1.35 (2 s, 6 H, CMe_2), and 1.04 (s, 9 H, *C*Me$_3$): ^{13}C, δ 138.78, 132.49, 131.93, 135.76, 135.58, 130.15, 130.10, 128.36, 128.01, 127.99, 127.63, and 127.48 (Ph), 115.27 (C-4), 110.72 (*C*Me$_2$), 87.46 (C-7), 78.55 (C-6), 77.89 (C-5), 72.78 (*C*H$_2$Ph), 70.45 (C-1), 63.30 (C-8), 35.14 (C-3), 27.53 and 26.73 (C*Me*$_2$ and C*Me*$_3$), 24.47 (C-2), and 19.09 (*C*Me$_3$). Mass spectrum: *m/z* 576 (0.23%, M^+), 501 (0.25), 443 (0.52), 411 (0.38), 353 (4.16), 293 (3.68), 275 (3.90), 241 (9.03), 199 (19.63), 163 (17.04), and 91 (100, $C_7H_7^+$).

1-O-*Benzyl-8*-O-tert-*butyldiphenylsilyl-2,3-dideoxy-4,5*-O-*isopropylidene-6*-O-*[(methylthio)thiocarbonyl)]-α*-L-xylo-*oct-4-ulofuranose* (**13**).—To an ice–water-cooled and stirred solution of NaH (600 mg, 25 mmol) (80% oil dispersion) and imidazole (50 mg) in anhyd THF (30 mL) were added a solution of **12** (10 g, 17.4 mmol) in the same solvent (40 mL), CS_2 (2.8 mL), and MeI (2 mL), under Ar. The stirring was continued for 75 min at room temperature. TLC (1:2 ether–hexane) revealed the presence of a faster-running compound. The mixture was neutralised with AcOH (0.1 mL) and concentrated. The residue was dissolved in ether, and the solution was washed with brine and water, then concentrated. Chromatography

(1:7 ether–hexane) of the residue gave **13** (10.4 g, 90%) as a pale-yellow syrup; $[\alpha]_D + 41°$ (*c* 0.5); ν_{max}^{film} 3074, 3052, 3034, and 3016 (C–H, aromatic), 2961, 2934, 2892, and 2860 (C–H), 1384 and 1374 (CMe_2), 1204 (C=S), 1113, 1077, 1049, 1030, 1007, and 999 (C–O–C, and C–S), 739 and 702 cm^{-1} (aromatic); NMR data: ^1H, δ 7.74–7.61 and 7.45–7.22 (2 m, 15 H, 3Ph), 6.05 (d, 1 H, $J_{6,7}$ 3 Hz, H-6), 4.59 (ddd, 1 H, $J_{7,8a}$ 6, $J_{7,8b}$ 8.4 Hz, H-7), 4.48 (s, 2 H, CH_2Ph), 4.42 (s, 1 H, H-5), 3.92 (dd, 1 H, $J_{8a,8b}$ 10 Hz, H-8a), 3.87 (dd, 1 H, H-8b), 3.50 (bt, 2 H, *J* 6 Hz, H-1,1), 2.49 (s, 3 H, SMe), 2.08–1.60 (2 m, 4 H, H-2a,2b,3a,3b), 1.51 and 1.35 (2 s, 6 H, CMe_2) and 1.08 (s, 9 H, CMe_3); ^{13}C, δ 138.74, 135.74, 134.99, 133.29, 130.16, 129.94, 128.50, 127.92, 127.90, 127.80, and 127.75 (Ph), 115.43 (C-4), 111.90 (CMe_2), 84.71, and 84.62 (C-6,7), 79.50 (C-5), 72.93 (CH_2Ph), 70.28 (C-1), 60.41 (C-8), 34.94 (C-3), 27.61, 26.91, and 26.75 (CMe_2 and CMe_3), 24.43 (C-2), 19.39 (CMe_3), and 19.19 (SMe). CI-Mass spectrum (CH_4): *m/z* 669 (18%, $M^+ + 3$), 668 (31, $M^+ + 2$), 667 (73, $M^+ + 1$), 665 (5, $M^+ - 1$), 611 (21, $M^+ + 3 - HCMe_3$), 610 (40, $M^+ + 2 - HCMe_3$), 609 (100, $M^+ + 1 - HCMe_3$), 590 (10, $M^+ + 2 - PhH$), 589 (28, $M^+ + 1 - PhH$), 501 (59, $M^+ + 1 - HCMe_3 - MeSH - SCO$), 481 (44, $M^+ + 1 - PhH - MeSH - SCO$), 423 (27), 411 (29), 333 (30), 91 (43, $C_7H_7^+$), and 79 (62). Anal. Calcd for $C_{36}H_{46}O_6S_2Si$: C, 64.83; H, 6.95. Found: C, 64.58; H, 7.33.

1-O-*Benzyl*-*8*-O-tert-*butyldiphenylsilyl*-*2,3,6*-*trideoxy*-*4,5*-O-*isopropylidene*-α-L-erythro-*oct*-*4*-*ulofuranose* (**14**).—To a stirred boiling solution of **13** (10.35 g, 15.6 mmol) in dry toluene (35 mL) was added dropwise under Ar a solution of tributyltin hydride (8.5 mL, 30 mmol) and azobis(isobutyronitrile) (100 mg) in the same solvent (10 mL). Refluxing was continued overnight. TLC (1:4 ether-hexane) then revealed no **13** but a new compound of slightly lower mobility. The mixture was concentrated and the residue was chromatographed (1:7 ether–hexane) to afford **14** (7.5 g, 86%); $[\alpha]_{435} + 5°$ (*c* 1); ν_{max}^{film} 3074, 3052, 3034, and 3017 (C–H, aromatic), 2960, 2934, 2890, and 2860 (C–H), 1382 and 1372 (CMe_2), 1259, 1214, 1192, 1168, 1114, 1030, 1009, and 999 (C–O–C), 740 and 702 cm^{-1} (aromatic); NMR data: ^1H, δ 7.68–7.55 and 7.38–7.23 (2 m, 15 H, 3 Ph), 4.49 (d, 1 H, $J_{5,6exo}$ 3.5 Hz, H-5), 4.47 (s, 2 H, CH_2Ph), 4.41–4.32 (m, 1 H, H-7), 3.85 (dd, 1 H, $J_{7,8a}$ 4, $J_{8a,8b}$ 11 Hz, H-8a), 3.70 (dd, 1 H, $J_{7,8b}$ 3.7 Hz, H-8b), 3.47 (t, 2 H, *J* 6 Hz, H-1,1), 2.80–1.70 (m, 6 H, H-2a,2b,3a,3b,6*endo*,6*exo*), 1.43 and 1.28 (2 s, 6 H, CMe_2), and 0.98 (s, 9 H, CMe_3); ^{13}C, δ 138.52, 135.55, 135.52, 134.73, 133.39, 133.29, 129.60, 129.55, 128.26, 127.64, 127.60, 127.42, and 127.40 (Ph), 115.19 (C-4), 110.30 (CMe_2), 82.92 (C-7), 78.61 (C-5), 72.74 (CH_2Ph), 70.20 (C-1), 64.28 (C-8), 34.79 and 34.61 (C-3,6), 27.37, 26.74, and 26.50 (CMe_2 and CMe_3), 24.60 (C-2), and 19.18 (CMe_3). CI-Mass spectrum (CH_4): *m/z* 562 (6%, $M^+ + 2$), 561 (15, $M^+ + 1$), 560 (4, M^+), 559 (6, $M^+ - 1$), 504 (31, $M^+ + 2 - HCMe_3$), 503 (78, $M^+ + 1 - HCMe_3$), 426 (12, $M^+ + 2 - HCMe_3 - PhH$), 425 (36, $M^+ + 1 - HCMe_3 - PhH$), 319 (47, $M^+ + 2 - HCMe_3 - PhH - PhCH_2O$), 317 (68, $M^+ + 1 - HCMe_3 - PhH - PhCH_2OH$), 257 (100, *t*-$BuPh_2SiOH_2^+$), 229 (54), 221 (29), 139 (49), and 91 (69, $C_7H_7^+$).

1-O-*Benzyl*-*2,3,6*-*trideoxy*-*4,5*-O-*isopropylidene*-α-L-erythro-*oct*-*4*-*ulofuranose* (**15**).—To a stirred solution of **14** (7.5 g, 13.4 mmol) in dry THF (30 mL) was added a solution of tetrabutylammonium fluoride trihydrate (4.42 g, 14 mmol) in the same

solvent (15 mL) under Ar. The mixture was stirred at room temperature overnight. TLC (3:2 ether–hexane) then revealed a new compound of lower mobility. The solvent was evaporated, and a solution of the residue in ether was washed with brine and water, then concentrated. Chromatography (3:2 ether–hexane) of the residue yielded **15** (2.4 g, 56%); $[\alpha]_D + 1.6°$, $[\alpha]_{435} + 6°$ (*c* 1); ν_{max}^{film} 3460 (OH), 3090 and 3067 (C–H, aromatic), 2991, 2936, and 2866 (C–H), 1382 and 1372 (CMe_2), 1214, 1103, 1028, 1017, and 995 (C–O–C), 754 and 698 cm^{-1} (aromatic); NMR data: ^1H, δ 7.47–7.18 (m, 5 H, CH_2*Ph*), 4.48 (s, 2 H, CH_2Ph), 4.45 (d, 1 H, $J_{5,6exo}$ 4 Hz, H-5), 4.36 (ddt, 1 H, $J_{6endo,7} = J_{7,8b} = 4.4$, $J_{7,8a}$ 3, $J_{6exo,7}$ 11 Hz, H-7), 3.81 (dd, 1 H, $J_{8a,8b}$ 12 Hz, H-8a), 3.53 (dt, 1 H, *J* 6.2, *J* 9.2 Hz, H-1a), 3.49 (dd, 1 H, H-8b), 3.47 (dt, 1 H, *J* 6.2, *J* 9.2 Hz, H-1b), 2.19 (bs, 1 H, HO), 1.96 (dd, 1 H, $J_{6endo,6exo}$ 13.4 Hz, H-6*endo*), 1.92–1.69 (m, 5 H, H-2a,2b,3a,3b,6*exo*), 1.35 and 1.20 (2 s, 6 H, CMe_2); ^{13}C, δ 138.33, 128.35, 127.65, and 127.57 (Ph), 115.17 (C-4), 110.63 (CMe_2), 83.13 (C-7), 78.74 (C-5), 72.90 (CH_2Ph), 70.00 (C-1), 63.26 (C-8), 34.33 and 34.08 (C-3,6), 27.36 and 26.51 (CMe_2), and 24.55 (C-2). CI-Mass spectrum (CH_4): *m/z* 323 (40%, $M^+ + 1$), 322 (18, M^+), 265 (49, $M^+ + 1 - Me_2CO$), 247 (100, $M^+ + 1 - Me_2CO - H_2O$), 157 (59, $M^+ + 1 - Me_2CO - PhCH_2OH$), 141 (15), and 91 (28, $C_7H_7^+$). Anal. Calcd for $C_{18}H_{26}O_5$: C, 67.06; H, 8.13. Found: C, 66.87; H, 8.27.

1-O-*Benzyl-2,3,6-trideoxy-4,5*-O-*isopropylidene-8*-O-(p-*toluenesulfonyl*)-α-L-erythro-*oct-4-ulofuranose* (**16**).—To an ice-cooled and stirred solution of **15** (2.22 g, 6.9 mmol) in dry pyridine (13 mL) was added stepwise *p*-toluenesulfonyl chloride (1.7 g, 9 mmol), and the mixture was left at room temperature overnight. TLC (ether) showed the absence of **15** and the presence of a new compound of higher mobility. Work-up of the mixture as usual gave a residue that, after chromatography (1:2 ether–hexane), yielded **16** (2.47 g, 75%) as a colourless thick syrup; $[\alpha]_D - 3°$, $[\alpha]_{435} - 5°$ (*c* 1); ν_{max}^{film} 3091, 3066, and 3034 (C–H, aromatic), 2989, 2937, and 2864 (C–H), 1382 and 1367 (CMe_2), 1191, 1178, 1098, 1028, 1020, and 976 (C–O–C), 698 and 665 cm^{-1} (aromatic); NMR data: ^1H, δ 7.75 and 7.25 (2 d, 4 H, *J* 8 Hz, TsO), 7.30 (bs, 5 H, CH_2*Ph*), 4.48 (s, 2 H, CH_2Ph), 4.42 (d, 1 H, $J_{5,6exo}$ 4.2 Hz, H-5), 4.38 (dq, 1 H, $J_{6exo,7}$ 10.7 Hz, H-7), 4.13 (dd, 1 H, $J_{7,8a}$ 3.8, $J_{8a,8b}$ 10.7 Hz, H-8a), 4.04 (dd, 1 H, $J_{7,8b}$ 4.2 Hz, H-8b), 3.46 (t, 2 H, *J* 6 Hz, H-1,1), 2.37 (s, 3 H, Me tosyl group), 2.03 (dd, 1 H, $J_{6endo,6exo}$ 13.4, $J_{6endo,7}$ 4.6 Hz, H-6*endo*), 1.92-1.58 (m, 5 H, H-2a,2b,3a,3b,6*exo*), 1.37 and 1.22 (2 s, 6 H, CMe_2); ^{13}C, δ 145.07, 138.70, 132.93, 130.03, 128.57, 128.18, 127.84, and 127.75 (Ph), 115.56 (C-4), 110.96 (CMe_2), 82.66 (C-7), 75.41 (C-5), 73.08 (CH_2Ph), 70.26 and 70.06 (C-1,8), 35.14 and 34.45 (C-3,6), 27.51 and 26.63 (CMe_2), 24.68 (C-2), and 21.80 (Me tosyl group). Mass spectrum: *m/z* 477 (1.25%, $M^+ + 1$), 476 (4.45, M^+), 461 (0.81, $M^+ - Me$), 401 (0.25, $M^+ - Me - AcOH$), 370 (0.40, $M^+ - Me - C_7H_7$), 353 (0.89, $M^+ - Me - PhCH_2OH$), 291 (0.88), 213 (0.90), 155 (14, Ts^+), 97 (46.92), 91 (100, $C_7H_7^+$), and 43 (30.83, Ac^+). Anal. Calcd for $C_{25}H_{32}O_7S$: C, 63.01; H, 6.77. Found: C, 62.57; H, 6.56.

1-O-*Benzyl-2,3,6,8,9-pentadeoxy-4,5*-O-*isopropylidene*-α-L-erythro-*non-4-ulofuranose* (**17**).—To a solution of Me_2SCuBr (920 mg, 4.5 mmol) in a mixture of anhyd Me_2S (6 mL) and anhyd ether (6 mL) under Ar was added, dropwise and

with stirring while maintaining the temperature at 20–25°C, a 1.6 M solution of ethereal MeLi (5.6 mL). The addition of MeLi was stopped at the point when the last of the initially formed yellow precipitate of $(MeCu)_n$ just dissolved to form a pale-yellow solution. To this solution, cooled at −10°C, **16** (710 mg, 1.5 mmol) in anhyd ether (10 mL) was added and the mixture allowed to reach room temperature and left for 1.25 h. TLC (1:1 ether–hexane) then showed a new compound with higher mobility. Saturated aq NH_4Cl (20 mL) was added, the mixture stirred for further 20 min, the organic phase separated, and the aqueous phase extracted with ether (3 × 10 mL). The combined extracts were washed with brine and water, then concentrated to a residue that was chromatographed (1:2 ether–hexane) to afford **17** (370 mg, 77%) as a colourless mobile oil; $[\alpha]_D$ + 11° (*c* 1); ν_{max}^{film} 3091, 3066, and 3032 (C–H, aromatic), 2967, 2936, and 2880 (C–H), 1381 and 1371 (CMe_2), 1214, 1101, 1044, 1011, and 994 (C–O–C), 736 and 697 cm^{-1} (aromatic); NMR data: ^1H, δ 7.30 (bs, 5 H, CH_2*Ph*), 4.45 (s, 2 H, C*H*$_2$Ph), 4.43 (d, 1 H, $J_{5,6exo}$ 4.3 Hz, H-5), 4.17 (ddt, 1 H, H-7), 3.54–3.47 (m, 2 H, H-1a,1b), 2.05 (dd, 1 H, $J_{6endo,6exo}$ 13.2, $J_{6endo,7}$ 4.2 Hz, H-6*endo*), 1.99-1.20 (m, 7 H, H-2a,2b,3a,3b, 6*exo*,8,8), 1.45 and 1.27 (2 s, 6 H, C*Me*$_2$), and 0.85 (t, 3 H, $J_{8,9}$ 7 Hz, H-9,9,9); ^{13}C, δ 138.50, 128.31, 127.31, and 127.48 (Ph), 114.80 (C-4), 110.04 (*C*Me$_2$), 82.95 (C-7), 79.38 (C-5), 72.85 (*C*H$_2$Ph), 70.26 (C-1), 38.80 (C-6), 34.77 (C-3), 27.29 and 26.51 (C*Me*$_2$), 27.27 (C-8), 24.62 (C-2), and 9.96 (C-9). Mass spectrum: *m/z* 320 (3.37%, M^+), 305 (3.09, M^+ − Me), 262 (2.59, M^+ − Me_2CO), 199 (2.11), 171 (5.49, M^+ − Me_2CO − C_7H_7), 153 (5.48), 97 (15.56), 91 (100, $C_7H_7^+$), and 43 (32.64, Ac^+). Anal. Calcd for $C_{19}H_{28}O_4$: C, 71.22; H, 8.81. Found: C, 70.74; H, 8.28.

*2,3,6,8,9-Pentadeoxy-4,5-*O*-isopropyliden-α-*L*-*erythro*-non-4-ulofuranose* (**18**).—A solution of **17** (1.1 g, 3.4 mmol) in anhyd MeOH (30 mL) that contained Raney nickel (0.5 g) was hydrogenated at 4 atm for 3 days. TLC (ether) then revealed a compound of lower mobility. The catalyst was collected and washed with MeOH, and the filtrate was concentrated. Chromatography (2:1 ether–hexane) of the residue afforded **18** (780 mg, quantitative) as a colourless syrup that decomposed on storage; $[\alpha]_D$ + 5°, $[\alpha]_{435}$ + 13° (*c* 1.1, MeOH); ν_{max}^{film} 3440 (OH), 2966, 2936, and 2881 (C–H), 1382 and 1372 (CMe_2), 1214, 1176, 1044, 1011, and 995 cm^{-1} (C–O–C); ^1H NMR data (80 MHz): δ 4.38 (d, 1 H, $J_{5,6exo}$ 4 Hz, H-5), 4.19 (ddt, 1 H, H-7), 3.80–3.00 (m, 3 H, H-1a,1b,OH), 2.02 (dd, 1 H, $J_{6endo,6exo}$ 13, $J_{6endo,7}$ 4 Hz, H-6*endo*), 1.87–1.05 (m, 7 H, H-2a,2b,3a,3b,6*exo*,8,8), 1.45 and 1.27 (2 s, 6 H, CMe_2), and 0.85 (t, 3 H, $J_{8,9}$ 7 Hz, H-9,9,9). Mass spectrum: *m/z* 217 (2.12%, M^+ + 2 − Me), 216 (11.99, M^+ + 1 − Me), 215 (100, M^+ − Me), 197 (1.69, M^+ − Me − H_2O), 155 (61.01, M^+ − Me − AcOH), 143 (37.79), 125 (98.80), 97 (90.61), 87 (37.62), 71 (29.71) and 43 (81.76, Ac^+).

(2S,4S,5R)- (**19**) *and (2S,4S,5S)-2-Ethyl-4-hydroxy-1,6-dioxaspiro[4.4]nonane* (**20**).—A solution of **18** (780 mg, 3.4 mmol) in aq 75% CF_3CO_2H (6.5 mL) was kept at room temperature for 7 h. GLC (*C*) then revealed no **18** (t_R 2.88 min) and the presence of two new products (t_R 1.50 and 1.76 min) in a 3:1 ratio. The mixture was concentrated, and water and then CH_2Cl_2 were distilled repeatedly from the residue. Chromatography (1:4 ether–hexane) gave, first, **19**; $[\alpha]_D$ − 39° (*c* 0.8); ν_{max}^{film} 3471 (OH), 2964, 2930, and 2880 (C–H), 1111, 1051, 1031, 1008, and 973

cm^{-1} (C–O–C); ^{13}C NMR data: δ 112.74 (C-5), 77.29 (C-2), 73.98 (C-4), 68.51 (C-7), 37.91 (C-9), 33.35 (C-3), 29.01 (C-10), 25.24 (C-8), and 9.60 (C-11). Mass spectrum: *m/z* 144 (1.49%, $M^+ + 1 - Et$), 143 (22.24, $M^+ - Et$), 125 (11.73, $M^+ - Et - H_2O$), 113 (4.62), 97 (8.80), 87 (100), 71 (39.90), 57 (30.07), and 43 (37.96). Anal. Calcd for $C_9H_{16}O_3$: C, 62.77; H, 9.36. Found: C, 62.57; H, 8.81.

Eluted second was **20**; $[\alpha]_D + 46°$ (*c* 0.7); ^{13}C NMR data: δ 112.74 (C-5), 79.60 (C-2), 76.87 (C-4), 67.64 (C-7), 39.01 (C-9), 33.35 (C-3), 30.42 (C-10), 24.43 (C-8), and 10.03 (C-11). Mass spectrum: *m/z* 144 (1.90%, $M^+ + 1 - Et$), 143 (22.37, $M^+ - Et$), 125 (11.18, $M^+ - Et - H_2O$), 113 (4.02), 97 (8.89), 87 (100), 71 (41.81), 57 (31.14), and 43 (37.26). Anal. Calcd for $C_9H_{16}O_3$: C, 62.77; H, 9.36. Found: C, 62.86; H, 9.45.

(2S,4S,5R)-2-Ethyl-4-[(methylthio)thiocarbonyloxy]-1,6-dioxaspiro[4.4]nonane (**21**).—To an ice–water-cooled and stirred solution of NaH (30 mg, 1.2 mmol; 80% oil dispersion) and imidazole (20 mg) in anhyd THF (3 mL) was added under Ar a solution of **19** (94 mg, 0.54 mmol) in the same solvent (6 mL), CS_2 (0.1 mL), and MeI (0.1 mL). The mixture was allowed to reach room temperature and the stirring was continued for 0.5 h. TLC (1 : 1 ether–hexane) revealed only a spot with higher mobility. The excess of hydride was destroyed by cautious addition of water and the mixture extracted with ether. The combined extracts were washed with brine and water, then concentrated. Chromatography (1 : 4 ether–hexane) of the residue yielded **21** (100 mg, 71%) as a pale-yellow syrup; $[\alpha]_D - 42°$ (*c* 1); ν_{max}^{film} 2966, 2935, and 2888 (C–H), 1227, 1200 (C=S), 1159, 1088, 1023, 1002, and 966 cm^{-1} (C–O–C and C–S); NMR data: ^1H, δ 5.76 (t, 1 H, H-4), 4.17 (bquin, 1 H, H-2), 4.07–3.98 and 3.91–3.82 (2 m, 2 H, H-7a,7b), 2.53 (s, 3 H, SMe), 2.13 (dd, 1 H, $J_{2,3a}$ 6.4, $J_{3a,4}$ 8 Hz, H-3a), 2.12 (t, 1 H, $J_{2,3b} = J_{3b,4} = 7.4$ Hz, H-3b), 2.10–1.80 and 1.64–1.41 (2 m, 6 H, H-8a,8b,9a,9b,10,10), and 0.88 (t, 3 H, $J_{10,11}$ 7.4 Hz, H-11,11,11); ^{13}C, δ 215.92 (C=S), 111.84 (C-5), 82.61 (C-4), 77.17 (C-2), 68.53 (C-7), 34.02 and 33.76 (C-3,9), 28.76 (C-10), 24.74 (C-8), 19.10 (SMe), and 9.44 (C-11). Mass spectrum: *m/z* 262 (0.63%, M^+), 233 (4.17, $M^+ - Et$), 176 (10.35), 155 (20.71, $M^+ - MeSSCO$), 154 (42.56, $M^+ - MeSH - SCO$), 125 (15.01), 99 (22.53), 97 (85.66), 91 (100, $MeSCS^+$), 87 (30.85), 71 (39.18), and 55 (60.62). Anal. Calcd for $C_{11}H_{18}O_3S_2$: C, 50.35; H, 6.91. Found: C, 50.47; H, 6.65.

(2S,4S,5S)-2-Ethyl-4-[(methylthio)thiocarbonyloxy]-1,6-dioxaspiro[4.4]nonane (**22**).—Compound **20** (140 mg, 0.81 mmol) was treated in anhyd THF (7 mL) with imidazole (20 mg), NaH (47 mg, 1.9 mmol; 80% oil dispersion), CS_2 (0.1 ml), and MeI (0.1 mL) as above, to afford syrupy **22** (170 mg, 80%); $[\alpha]_D + 46°$ (*c* 1); ν_{max}^{film} 2964, 2940, and 2880 (C–H), 1228, 1200 (C=S), 1150, 1121, 1106, 1055, 1021, 966, and 940 cm^{-1} (C–O–C and C–S); NMR data: ^1H, δ 5.86 (d, 1 H, $J_{3cis,4}$ 4.5 Hz, H-4), 4.14 (dq, 1 H, $J_{2,10}$ 6.4, $J_{2,3cis}$ 9.2 Hz, H-2), 4.06–3.98 and 3.86–3.78 (2 m, 2 H, H-7a,7b), 2.55 (s, 3 H, SMe), 2.27 (dd, 1 H, $J_{2,3trans}$ 6.2, $J_{3cis,3trans}$ 14 Hz, H-3*trans* *), 2.05 (ddd, 1 H, H-3*cis*), 2.06–1.81, 1.79–1.64, and 1.61–1.45 (3 m, 6 H, H-8a,8b,9a,9b,10,10), and 0.91 (t, 3 H, $J_{10,11}$ 7.5 Hz, H-11,11,11); ^{13}C, δ 215.02

* $^+$H-3 *trans* refers to its *trans* disposition with respect to H-4.

(C=S), 115.02 (C-5), 87.47 (C-4), 80.17 (C-2), 67.97 (C-7), 36.52 (C-9), 31.33 (C-3), 30.15 (C-10), 24.58 (C-8), 19.10 (SMe), and 10.16 (C-11). Mass spectrum: *m/z* 262 (0.27%, M^+), 233 (2.18, $M^+ - Et$), 176 (4.55), 155 (9.76, $M^+ - MeSSCO$), 154 (54.86, $M^+ - MeSH - SCO$), 125 (9.44), 97 (100), 91 (95.93, $MSCS^+$), 87 (23.57), 71 (33.47), and 55 (49.51). Anal Calcd for $C_{11}H_{18}O_3S_2$: C, 50.35; H, 6.91. Found: C, 50.19; H, 6.58.

(*2S,5RS*)-*2-Ehtyl-1,6-dioxaspiro[4.4]nonane* (**1**).—To a solution of **22** (160 mg, 0.6 mmol) in dry toluene (0.5 mL) were added tributyltin hydride (0.3 mL, 1.1 mmol) and azobis(isobutyronitrile) (5 mg) under Ar, and the mixture was refluxed for 0.5 h. TLC (1:3 ether–pentane) then revealed no **22** but a new compound of lower mobility. Chromatography (pentane → 10:1 pentane–ether) of the mixture afforded **1** (20 mg, 21.5%); t_R (*D*) 3.16 min; $[\alpha]_D$ −18.3° (*c* 1, pentane); lit. [12b] $[\alpha]_D$ −18.5° (hexane); lit [12c] $[\alpha]_D$ −14.9° (neat); ^{13}C NMR data (C_6D_6) for (*2S,5R*) − **1**: δ 114.61 (C-5), 79.22 (C-2), 66.75 (C-7), 35.31 (C-9), 34.42 (C-4), 30.71 (C-3), 30.19 (C-10), 24.93 (C-8), and 10.28 (C-11); for (*2S,5S*)-**1**: δ 112.37 (C-5), 81.44 (C-2), 66.64 (C-7), 35.18 (C-9), 34.79 (C-4), 30.90 (C-3), 29.00 (C-10), 24.81 (C-8), and 10.60 (C-11). Mass spectra: CI (CH_4): *m/z* 158 (13%, $M^+ + 2$), 157 (96, $M^+ + 1$), 155 (52, $M^+ - 1$), 139 (29, $M^+ + 1 - H_2O$), 127 (9, $M^+ + 1 - C_2H_6$), 125 (7, $M^+ - 1 - C_2H_6$), 113 (16), 111 (15), 97 (10), 85 (94, $C_4H_5O_2^+$), and 57 (100, $C_3H_5O^+$); EI (cf. lit. [12a]): *m/z* 156 (2.2%, M^+), 127 (100, $M^+ - Et$), 98 (37.8, $C_6H_{10}O^+$), 97 (30.2, $C_6H_9O^+$), 87 (48.3, $C_4H_7O_2^+$), 85 (46.3, $C_4H_5O_2^+$), 69 (19.3, $C_5H_9^+$), 57 (29.8, $C_3H_5O^+$), 56 (32.5, $C_3H_4O^+$), 55 (40.5, $C_4H_7^+$), 43 (26.3, $C_2H_3O^+$), 42 (27.0, $C_3H_6^+$), and 41 (32.9, $C_3H_5^+$).

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