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An Expedient Route to New Spiroheterocycles: Synthesis and Structural Studies

Marlène Goubert,[a] Isabelle Canet,*[a] and Marie-Eve Sinibaldi*[a]

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We have developed a short, efficient and enantioselective synthesis of 1,4,7,10-tetraoxa- and 1,7-dioxa-4,10-dithiaspiro[5.5]undecanes. The method involved the reaction of solketal **5** or thiol derivative **6** with 1,3-dichloropropanone *O*-benzyloxime (**4**) which affords the conveniently protected symmetrical ketones **7** and **8**. Elaboration of the required 4,10-disubstituted-1,7-dioxaspiro[5.5]undecane systems **1** and **2** entailed a final "one-pot" deprotection–spirocyclization process in an acidic medium. The structures and configurations of the spiroketals were established unambiguously by NMR spectroscopy.

Introduction

Significant attention has been focused on the synthesis of the 1,7-dioxaspiro[5.5]undecane moiety which is the prevalent underlying motif in several groups of bioactive natural products, from the simple spiroketals used as pheromones[1] by a large number of insect species, to more complex molecules such as polyether antibiotics[2] and antitumour compounds.[3] This diversity has led to interest in the development of original methods for the preparation of this framework and a number of strategies have been investigated.[4] Moreover, new spiroketal compounds with a supplementary heteroatom at the position β to the spiranic carbon atom have been reported that possess interesting biological activities, such as the NK1 antagonists[5] or anthelmintic agents[6] (Figure 1).

We recently described an efficient diastereoselective approach to spiroketals[7] and spiroaminoketals[8] based upon an acidic deprotection–cyclization key step of a linear α,ω-dihydroxy- or an α-amino-ω-hydroxy ketone, protected as its dimethylhydrazone, respectively.

As a continuation of our research program devoted to the synthesis and biological evaluation of various spiroketal analogues, we have explored the viability of incorporating heteroatoms into the skeleton of spiroketals. We describe here a new and expedient route towards 4,10-disubstituted-1,7-dioxaspiro[5.5]undecanes **1** and **2** as well as full conformational and structural studies on these spiroketals based on various NMR experiments.

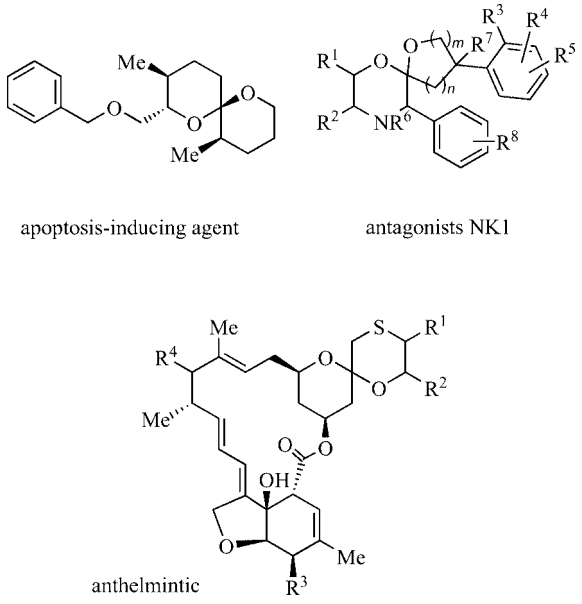


Figure 1. New spiroketal compounds with interesting biological properties.

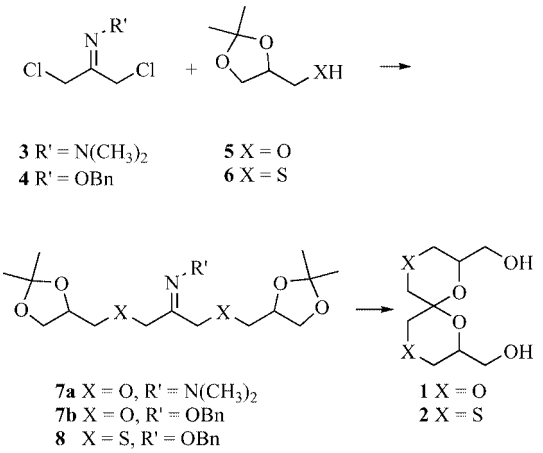
Results and Discussion

Chemistry

We first tried to introduce heteroatoms into the 4- and 10-positions of the spiroketal framework using a strategy similar to the one we reported for simple spiroketals.[7] In this way, we envisioned constructing the target skeleton by substitution of the hydrazone **3** with commercially available solketal **5** or its thiol derivative **6**. In situ acidic deprotection of the bis-alkylated intermediates **7** or **8** would lead to a nonisolated symmetrical keto-tetraol, which should spontaneously undergo spirocyclization into the required spirohet-

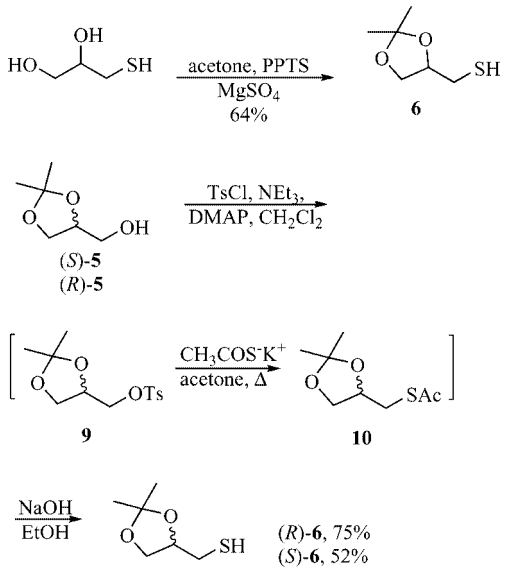
[a] Laboratoire de Synthèse et d'Etude de Systèmes à Intérêt Biologique, UMR CNRS 6504, Université Blaise Pascal, 63177 Aubière Cedex, France
E-mail: isabelle.canet@univ-bpclermont.fr
m-eve.sinibaldi-troin@univ-bpclermont.fr

erocyclic compounds **1** or **2** (Scheme 1). However, in spite of numerous attempts, we unfortunately never obtained hydrazone **7a**. Therefore, we focused on a new approach to scaffold **1** and **2**, modifying the nature of the protective group on **3**, namely by using the benzyloxime **4** (Scheme 1).



Scheme 1. Preparative routes to 4,10-disubstituted-1,7-dioxaspiro[5.5]undecanes.

The starting point was the synthesis of precursors **4** and **6**. Condensation of 1,3-dichloropropanone in EtOH with benzylhydroxylamine hydrochloride[9] led quantitatively to oxime **4**. Racemic thiol **6** (Scheme 2) was obtained from commercially available 3-mercapto-1,2-propanediol by simple treatment with acetone using a catalytic amount of PPTS in the presence of $MgSO_4$[10] and was isolated in 64% yield. Enantiopure (*R*)- and (*S*)-**6** were obtained from (*S*)- and (*R*)-solketal **5** in 75 and 52% overall yields, respectively, in three steps. Compounds (*S*)- or (*R*)-**5** were first converted to tosylate **9** using *p*-toluenesulfonyl chloride and a mixture of NEt_3/DMAP in dry CH_2Cl_2. The tosyl ether was then displaced with potassium thioacetate in boiling acetone.[11a] Cleavage of the crude thioacetate **10** with a 5 M aqueous solution of NaOH in EtOH furnished the expected thiols.[11b]



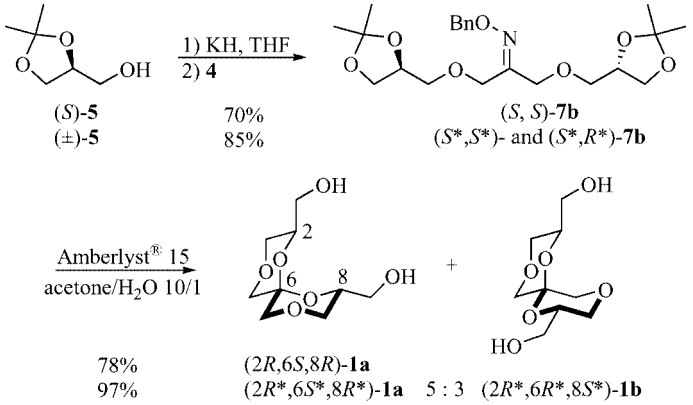
Scheme 2. Preparation of thiols **6**.

Having the precursors in hand, we then studied their condensation reactions with oxime **4** under basic conditions. The double substitution[9] of **4** (Scheme 3) by the sodium or the potassium salt of **5** in DMF or THF afforded the expected oxime **7b** in good yields (see Table 1). The best results were obtained with KH in THF. Consequently, these reaction conditions were applied to the condensation of **4** with **6** and led as expected to **8** in 80–90% yields (Scheme 4).

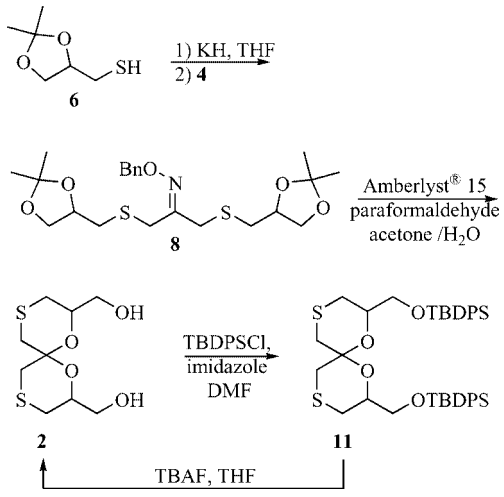
Table 1. Substitution of oxime **4** with solketal **5**.

Entry	Compound **7b**	Solvent	Base	Isolated yield [%]
1	(*R**,*S**)- and (*S**,*S**)-**7b**	DMF	NaH	79
		THF	KH	85
2	(*S*,*S*)-**7b**	DMF	NaH	28[a]
		THF	KH	70
3	(*R*,*R*)-**7b**	DMF	NaH	61
		THF	KH	87

[a] Sodium alcoholate of (*S*)-solketal led surprisingly to a gelled solution, which showed poor reactivity.



Scheme 3. Synthesis of 1,4,7,10-tetraoxaspiro[5.5]undecane **1**.



Scheme 4. Synthesis of 1,7-dioxa-4,10-dithiaspiro[5.5]undecanes **2** and **11**.

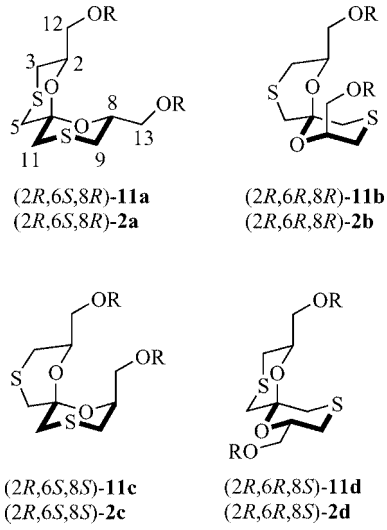


Figure 2. Structures of the isomers of the spiroketals **11** (R = TBDPS) and **2** (R = H).

The second step involved concomitant deprotection of the diol and the keto functions of **7b** and **8** and spirocyclization into **1** and **2**. For this purpose, we first treated **7b** with Amberlyst® 15 in a 10:1 mixture of acetone/water. In this way, spiroketals (2*R*,6*S*,8*R*)- and (2*S*,6*R*,8*S*)-**1a** were cleanly obtained from (*S*)- and (*R*)-**5** in 55 and 52% overall yields, respectively (Scheme 3). Spiroketal **1a** presents, as expected, a double anomeric effect and has C_2 symmetry with both cycles adopting a chair conformation.[12] Compound (±)-**5** led, in an 82% overall yield, to a mixture of (2*R**,6*S**,8*R**)-**1a** and (2*R**,6*R**,8*S**)-**1b** (5:3 ratio determined by quantitative ^{13}C NMR spectroscopy), which were easily separated by purification on silica gel and fully characterized.[12]

Applying the same conditions to oxime **8** led unfortunately to the sole deprotection of the diol function. The deprotection–spirocyclization sequence was finally achieved by adding paraformaldehyde to the acidic medium (Scheme 4).[13] Enantiopure (*R*,*R*)-**8** furnished, in a 75% yield, an inseparable mixture of C-6 epimers (2*R*,6*S*,8*R*)-**2a** and (2*R*,6*R*,8*R*)-**2b** in a 10:7 ratio (Figure 2). Their enantiomers were obtained efficiently starting from enantiopure (*S*,*S*)-**8** (71% yield). The cyclization step proceeded with a lower stereoselectivity than was the case for the tetraoxa series; the importance of the anomeric effect in the cyclization process was reduced by the presence of the less electron-withdrawing atoms in the molecule.

In order to isolate **2a** and **2b**, we prepared their TBDPS derivatives **11a**,**b** (Scheme 4) using TBDPSCl/imidazole in DMF. Flash column chromatography on SiO_2 allowed the clean separation of **11a** of **11b**. Alcohols **2a** and **2b** were then recovered by classical treatment with TBAF in THF.

Starting from (±)-**6**, oximes (*R**,*R**)- and (*R**,*S**)-**8** furnished four diastereomers, (2*R**,6*S**,8*R**)-**2a**, [(2*R**,6*R**,8*R**)-**2b** + (2*R**,6*S**,8*S**)-**2c**] and (2*R**,6*R**,8*S**)-**2d**, in a 78% yield and a 5:7:1 ratio, as determined by quantitative ^{13}C NMR spectroscopy. Isomer **2d** could be separated at this stage from the three others. A TBDPS protection–chromatography–deprotection sequence allowed us to obtain **2a** cleanly, but **2b** and **2c** remained inseparable. In order to characterize (2*R**,6*S**,8*S**)-**2c**, we therefore conducted the reaction on (*R*,*S*)-**8**. We isolated the two C-6 epimers (2*R*,6*S*,8*S*)-**2c** and (2*R*,6*R*,8*S*)-**2d** in 44% yield, with **2d**, as before, the minor compound (Figure 2).

Structural and Conformational Studies of Spiroketals 2

Analysis of the ^{1}H and ^{13}C NMR spectra of isomers (2*R*,6*S*,8*R*)-**2a**, (2*R*,6*R*,8*R*)-**2b**, (2*R*,6*S*,8*S*)-**2c** and (2*R*,6*R*,8*S*)-**2d** with the help of COSY, HETCOR and in particular NOESY experiments permitted us to assign all the ^{1}H and ^{13}C resonances (Figure 2, Table 2).

Compound **2a** presented a simplified ^{1}H NMR spectrum and only five peaks were detected in its ^{13}C NMR spectrum, which is in good agreement with a C_2 symmetrical structure. As the deprotection–spirocyclization sequence was conducted under thermodynamic control, we concluded that the configuration was unambiguously (2*R*,6*S*,8*R*). As for **1a**, 2-H and 8-H are in an axial position on the cycles adopting a chair conformation, as illustrated by the large coupling constants (11.5 Hz) measured between 2-H and 3-H^{ax}, 8-H and 9-H^{ax}, and the small ones (not measurable in the ^{1}H NMR spectrum, crosspeak on COSY) between 2-H/3-H^{eq} and 8-H/9-H^{eq}, respectively.

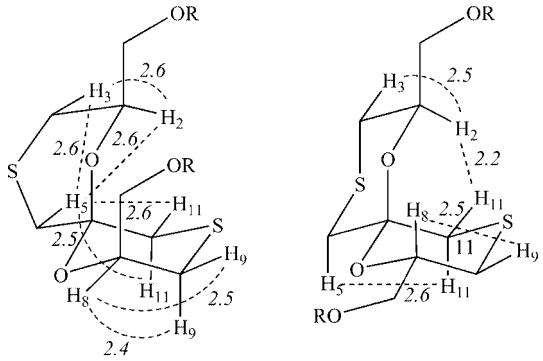
As compound **2b** is the C-6 epimer of **2a**, we assumed its configuration was (2*R*,6*R*,8*R*). The small coupling constants (less than 2.0 Hz, not measurable in the ^{1}H NMR spectrum) for 8-H (br. d, δ = 4.77 ppm) with both 9-H atoms (d, δ = 2.19 pm and δ = 3.11 pm) and the distances between 8-H and 9-H (obtained from NOESY of **11b**, see Figure 3) indicated an equatorial position of 8-H on the cycle that adopted a chair conformation. The coupling constants of 7.0 and 5.0 Hz observed between 2-H (dq, δ = 3.71 ppm) and 3-H^a (δ = 2.77 ppm) and 3-H^b (δ = 2.64 ppm) led to the assignment of a "boat" deformation for the upper cycle, and thus a pseudoaxial position for 2-

Table 2. ^{1}H and ^{13}C NMR spectroscopic data of isomers of **2**.

	(2*R*,6*S*,8*R*)-**2a**		(2*R*,6*R*,8*R*)-**2b**		(2*R*,6*S*,8*S*)-**2c**		(2*R*,6*R*,8*S*)-**2d**	
	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H
2	72.4	3.97 (dt) (*J* 11.5; 5.0)	72.9	3.71 (dq) (*J* 7.0; 5.0)	72.9	3.69 (dq) (*J* 7.0; 5.0)	72.1	3.81 (dddd) (*J* 10.5; 6.0; 5.0; 2.0)
3	27.8	2.37 (d) (*J* 11.5) 2.54 (t) (*J* 11.5)	37.8	2.64 (ddd) (*J* 13.5; 7.0; 2.0) 2.77 (dd) (*J* 13.5; 5.5)	37.8	2.63 (dd) (*J* 13.5; 7.0) 2.75 (dd) (*J* 13.5; 5.0)	29.7	2.42 (br. d) (*J* 13.5) 2.54 (dd) (*J* 13.5; 10.5)
5	35.2	2.40 (d) (*J* 13.5) 2.76 (d) (*J* 13.5)	40.6	2.83 (d) (*J* 14.0) 2.84 (d) (*J* 14.0)	40.6	2.80 (d) (*J* 15.0) 2.83 (d) (*J* 15.0)	28.7	2.42 (d) (*J* 13.5) 2.69 (d) (*J* 13.5)
6	91.9		108.3		108.3		94.7	
8	72.4	3.97 (dt) (*J* 11.5; 5.0)	76.3	4.77 (br. d) (*J* 6.0)	76.3	4.75 (br. d) (*J* 6.0)	76.3	4.36 (dtd) (*J* 11.0; 5.0; 2.0)
9	27.8	2.37 (d) (*J* 11.5) 2.54 (t) (*J* 11.5)	29.7	2.19 (d) (*J* 13.0) 3.11 (d) (*J* 13.0)	29.7	2.18 (br. d) (*J* 13.0) 3.09 (br. d) (*J* 13.0)	28.3	2.37 (dt) (*J* 13.0; 2.0) 2.55 (dd) (*J* 13.0; 11.0)
11	35.2	2.40 (d) (*J* 13.5) 2.76 (d) (*J* 13.5)	33.9	2.44 (d) (*J* 13.0) 3.01 (d) (*J* 13.0)	33.9	2.42 (d) (*J* 13.0) 2.99 (d) (*J* 13.0)	35.9	2.64 (d) (*J* 14.5) 3.58 (dd) (*J* 14.5; 2.0)
12	65.9	3.48 (dd) (*J* 11.5; 5.0) 3.56 (dd) (*J* 11.5; 5.0)	66.0	3.49 (dd) (*J* 11.0; 5.5) 3.54 (dd) (*J* 11.0; 5.0)	66.0	3.47 (dd) (*J* 11.0; 5.0) 3.52 (dd) (*J* 11.0; 5.5)	65.9	3.53 (dd) (*J* 11.0; 6.0) 3.61 (dd) (*J* 11.0; 5.0)
13	65.9	3.48 (dd) (*J* 11.5; 5.0) 3.56 (dd) (*J* 11.5; 5.0)	70.8	3.94 (t) (*J* 6.0) 4.33 (d) (*J* 6.5)	70.8	3.93 (t) (*J* 6.0) 4.31 (d) (*J* 6.0)	66.0	3.41 (dd) (*J* 11.0; 5.0) 3.47 (dd) (*J* 11.0; 5.0)

H. This conformation was also confirmed by the NOE contacts determined for **11b** between 2-H (δ = 3.71 ppm) and 3-H^b (δ = 2.64 ppm), 2-H and 5-H^a (δ = 2.83 ppm), and 5-H^a (δ = 2.83 ppm) and 3-H^b (δ = 2.64 ppm) (Figure 3). The deshielding of 5-H (δ = 2.83 and 2.84 ppm in **2b** and δ = 2.40 and 2.76 ppm in **2a**) and of C-5 (δ = 40.6 ppm in **2b** and δ = 35.2 ppm in **2a**) favour an (*R*) configuration for C-6. Moreover, the deshielding of C-13 (δ = 70.8 ppm in **2b** and δ = 65.9 ppm in **2a**) and 13-H (δ = 4.33 and 3.94 ppm in **2b** vs. δ = 3.56 and 3.48 ppm in **2a**) implied a 1,3-diaxial position for C-13 and O-1, which is in agreement with the conformation depicted in Figure 2 for **2b**.

The determination of the C-6 configuration for the other isomers **2c** and **2d** did not appear so trivial. In the minor isomer **2d**, 2-H and 8-H appeared in an axial position: indeed, we observed for 2-H (δ = 3.81 ppm) a coupling constant of 10.5 Hz with 3-H^{ax} and of 2.0 Hz with 3-H^{eq}. In the same manner, 8-H presented coupling constants of 11.0 and 2.0 Hz with 9-H^{ax} and 9-H^{eq}, respectively. Moreover, we detected in this isomer a deshielding of 11-H^{eq} (δ = 3.58 ppm) and a shielding of C-5 which is in complete agreement with an equatorial position of the C-6–O-7 bond. These results were corroborated by the NOE contacts determined for **11d** between 11-H^{ax} and 5-H^{ax} and between



(2*R*,6*R*,8*R*)-**11b** (2*R*,6*R*,8*S*)-**11d**

Figure 3. Selected NOE interactions in **11b** and **11d**. The relative distances (in Å) calculated from the NOEs are indicated.

2-H and 11-H^{eq} (Figure 3). All these data are in good agreement with a (2*R*,6*R*,8*S*) configuration for **2d**.

Isomer **2c**, whose R_f is identical to that of isomer **2b**, presented a ^{13}C NMR spectrum identical to that of isomer **2b**. In the ^1H NMR spectrum only slight differences could be detected: indeed, only three protons exhibited "dedoubled" signals. These spectroscopic data indicate a structure for **2c** similar to that of **2b**. As compound **2c** is the C-6 epimer of **2d**, all these observations are in agreement with a "boat" conformation for the O-1 cycle and an (*S*) configuration for C-6. Therefore we concluded that the configuration of **2c** should be (2*R*,6*S*,8*S*).

Conclusions

In summary, we have developed a concise and original method for the synthesis of new spiroketals with supplementary heteroatoms in the 4- and 10-positions of the cycles. The key step involved the condensation of 1,3-disubstituted-propanone *O*-benzyloxime **4** with alcohol **5** or thiol **6**. The versatility and the efficiency of our approach have been demonstrated by the synthesis, in a few steps with good yields, of symmetrical elaborated molecules of the 1,4,7,10-tetraoxa- and 1,7-dioxa-4,10-dithiaspiro[5.5]-undecane series from commercially available solketal and 1,3-dichloropropanone.

Experimental Section

General Remarks: NMR spectra were recorded with a Bruker AC 400 spectrometer operating at 400 MHz. ^1H and ^{13}C NMR were recorded in $CDCl_3$ or CD_3OD; chemical shifts are calibrated to the residual proton and carbon resonances of the solvent ($CDCl_3$: δ_H = 7.26, δ_C = 77.0 ppm; CD_3OD: δ_H = 3.34, δ_C = 49.0 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintuplet, m = multiplet, br. d = broad doublet; when coupling constants ^2J and ^3J are identical, the multiplicity "t" is attributed, a doublet when ^2J is different of ^3J), coupling constants (Hz), integration and assignment. Mass spectra were recorded with a Hewlett–Packard 5989B instrument. High-resolution mass spectra were performed with a Q-TOF micromass spectrometer. Optical rotations were measured at the sodium D line (589 nm) using a 1-dm quartz cell with a JASCO DIP-370 apparatus. Infrared spectra were recorded with a Perkin–Elmer spectrometer. Melting points were determined with a hot-stage Reichert apparatus and are uncorrected. Flash column chromatography was performed using silica gel 60 (Macherey–Nagel, 0.04–0.063 mm). Dry tetrahydrofuran was distilled from potassium and benzophenone, whereas dry dichloromethane was distilled from CaH_2. Reactions were generally run under argon. All commercially available compounds (Acros, Aldrich) were used as received. TLC analysis was conducted using the spray reagent molybdic acid and by further heating until development of colour. Compound **4** was synthesized according to ref.[9].

1,3-Bis[(4*S*)-(2,2-dimethyl-1,3-dioxolan-4-yl)methoxy]propanone *O*-Benzyloxime (7b): Solketal (*S*)-**5** (630 mg, 4.76 mmol) in THF (4 mL) was slowly added to a stirred suspension of potassium hydride (25–35% in mineral oil, 870 mg, 6.50 mmol) in anhydrous THF (9 mL) under argon at 20 °C. When bubbling had ceased (ca. 30 min), 1,3-dichloropropanone *O*-benzyloxime **4** (500 mg, 2.16 mmol) in THF (3 mL) was added in one portion. The reaction mixture was stirred at room temperature for 2 h. Additional KH could be added if starting material was left. The reaction was quenched by the addition of H_2O (7 mL) followed by CH_2Cl_2 (30 mL). The aqueous phase was extracted with CH_2Cl_2 (2 × 15 mL) and the combined organic layers were washed with brine (15 mL) and dried with $MgSO_4$. After filtration, the solvent was removed. The residue was purified by flash column chromatography (cyclohexane/ethyl acetate, 4:1) to afford **7b** as a colourless oil.

(*S*,*S*)-7b: Yield 70% (640 mg). R_f = 0.51 (cyclohexane/EtOAc, 7:3). $[\alpha]_D^{25}$ = +13.9 (*c* = 1.2, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 1680 (C=N) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.37–7.28 (m, 5 H, Ar-H), 5.10 (s, 2 H, CH_2-Ar), 4.40 (d, ^2J = 14.5 Hz, 1 H, N=C-CH_2-O), 4.38 (d, ^2J = 14.5 Hz, 1 H, N=C-CH_2-O), 4.24 (quint, ^3J = 6.0 Hz, 2 H, CH-O), 4.17 (s, 2 H, N=C-CH_2-O), 4.02 (t, ^2J = ^3J = 6.5 Hz, 2 H, CH_2-O), 3.71 (t, ^2J = ^3J = 6.5 Hz, 1 H, CH_2-O), 3.69 (t, ^2J = ^3J = 6.5 Hz, 1 H, CH_2-O), 3.51 (dd, ^2J = 10.0, ^3J = 5.5 Hz, 1 H, OC*H*-CH_2-O), 3.48 (m, 2 H, OCH-CH_2-O), 3.44 (dd, ^2J = 10.0, ^3J = 6.0 Hz, 1 H, OCH-CH_2-O), 1.40 (s, 6 H, CH_3), 1.35 (s, 6 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.4 (C=N), 137.4 (C-Ar), 128.4 (C-Ar), 128.1 (C-Ar), 127.9 (C-Ar), 109.4 (O-C-O), 76.3 (CH_2-Ar), 74.5 (CH-O), 72.3 (CH_2-O), 71.4 (CH_2-O), 68.7 (CH_2-O), 66.7 (CH_2-O), 66.6 (CH_2-O), 64.4 (CH_2-O), 26.7 (CH_3), 25.4 (CH_3) ppm. $C_{22}H_{34}NO_7$ (423.50): calcd. C 62.39, H 7.85, N 3.31; found C 62.58, H 8.03, N 3.24.

(*R*,*R*)-7b: Yield 87% (795 mg). $[\alpha]_D^{25}$ = –11.6 (*c* = 1.5, $CHCl_3$).

(*S,*S**)- and (*S**,*R**)-7b:** Yield 85% (780 mg).

2,8-Dihydroxymethyl-1,4,7,10-tetraoxaspiro[5.5]undecane (1): Amberlyst® 15 (1.15 g, 250 mg/mmol) was added to a solution of oxime **7b** (1.94 g, 4.59 mmol) in a mixture of acetone and water (10:1 v/v, 33 mL). The resulting solution was refluxed for 2 d. After filtration of the insoluble material through a Celite® pad, the solvent was eliminated and the residue purified by SiO_2 column chromatography (EtOAc/MeOH, 49:1) to give **1a** as a white powder. The racemic product was obtained in 97% yield (1.08 g) as a 5:3 mixture of two isomers, (±)-(2*R**,6*S**,8*R**)-**1a** and (±)-(2*R**,6*R**,8*S**)-**1b**, which could be separated by flash column chromatography (EtOAc/MeOH, 1:0→49:1).

(2*R*,6*S*,8*R*)-1a: Yield 78% (791 mg). R_f = 0.35 (EtOAc/MeOH, 9:1). M.p. 146 °C (EtOAc). $[\alpha]_D^{25}$ = +3.1 (*c* = 1.6, MeOH). IR (KBr): $\tilde{\nu}$ = 3430 (OH) cm^{-1}. ^1H NMR (400 MHz, CD_3OD): δ = 4.03 (dtd, ^3J = 11.0, ^3J = 5.0, ^3J = 3.0 Hz, 2 H, 2-H^{ax} and 8-H^{ax}), 3.80 (dd,

^2J = 11.0, ^3J = 3.0 Hz, 2 H, 3-H^{eq} and 9-H^{eq}), 3.55 (d, ^2J = 11.5 Hz, 2 H, 5-H^{eq} and 11-H^{eq}), 3.55 (dd, ^2J = 12.0, ^3J = 5.0 Hz, 2 H, CH_2OH), 3.51 (dd, ^2J = 12.0, ^3J = 5.0 Hz, 2 H, CH_2OH), 3.37 (t, ^2J = ^3J = 11.0 Hz, 2 H, 3-H^{ax} and 9-H^{ax}), 3.24 (d, ^2J = 11.5 Hz, 2 H, 5-H^{ax} and 11-H^{ax}) ppm. ^{13}C NMR (100 MHz, CD_3OD): δ = 93.0 (C-6), 70.2 (C-2 and C-8), 69.6 (C-5 and C-11), 68.8 (C-3 and C-9), 62.9 (C-12 and C-13) ppm. HRMS (ESI): calcd. for $C_9H_{16}O_6Na$: 243.0845; found 243.0855 $[M + Na]^+$.

(2*S*,6*R*,8*S*)-1a: Yield 60% (600 mg). $[\alpha]_D^{25}$ = –5.8 (*c* = 1.5, MeOH).

(2*R,6*R**,8*S**)-1b:** Yield 36% (401 mg). R_f = 0.45 (EtOAc/MeOH, 9:1). M.p. 118 °C (EtOAc). ^{1}H NMR (400 MHz, CD_3OD): δ = 4.22 (dtd, ^3J = 11.5, ^3J = 5.0, ^3J = 3.0 Hz, 1 H, 8-H^{ax}), 3.99 (d, ^2J = 12.0 Hz, 1 H, 11-H^{eq}), 3.80 (dd, ^2J = 11.5, ^3J = 3.0 Hz, 1 H, 9-H^{eq}), 3.78 (m, 1 H, 2-H), 3.77 (m, 1 H, CH_2OH), 3.74 (dd, ^2J = 11.5, ^3J = 3.0 Hz, 1 H, 3-H^{eq}), 3.69 (m, 1 H, CH_2OH), 3.57 (dd, ^2J = 11.5, ^3J = 6.0 Hz, 1 H, 3-H^{ax}), 3.50 (dd, ^2J = 11.5, ^3J = 5.0 Hz, 1 H, CH_2OH), 3.48 (d, ^2J = 11.5 Hz, 1 H, 5-H^{eq}), 3.47 (dd, ^2J = 11.5, ^3J = 5.0 Hz, 1 H, CH_2OH), 3.37 (t, ^2J = ^3J = 11.5 Hz, 1 H, 9-H^{ax}), 3.35 (d, ^2J = 11.5 Hz, 1 H, 5-H^{ax}), 3.23 (d, ^2J = 12.0 Hz, 1 H, 11-H^{ax}) ppm. ^{13}C NMR (100 MHz, CD_3OD): δ = 92.7 (C-6), 73.5 (C-2), 71.3 (C-5), 70.4 (C-8), 69.0 (C-9), 68.5 (C-11), 68.2 (C-3), 62.9 (C-12), 62.8 (C-13) ppm.

(±)-(2,2-Dimethyl-1,3-dioxolan-4-yl)methanethiol (6): 3-Mercapto-1,2-propanediol (3 g, 27.7 mmol) was dissolved in acetone (40 mL). Pyridinium *p*-toluenesulfonate (700 mg, 2.77 mmol) and $MgSO_4$ (5 g) were added. The mixture was stirred for 3 d at 20 °C before being filtered through a Celite® pad. After elimination of the solvent, the residue was purified by flash column chromatography (pentane/Et_2O, 24:1) to afford the thiol **6** (2.6 g, 17.7 mmol, 64%) as a colourless liquid.

[(4*R*)- or (4*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]methanethiol (6): A solution of toluene-*p*-sulfonyl chloride (5.2 g, 27.2 mmol) in dry CH_2Cl_2 (30 mL) was added to a solution of (*S*)- or (*R*)-solketal **5** (3 g, 22.7 mmol), DMAP (0.01 equiv., 28 mg, 0.23 mmol) and triethylamine (7.3 mL, 52.2 mmol) in dry CH_2Cl_2 (50 mL) at 0 °C. The flask was kept in a fridge for 2 d. After dilution with CH_2Cl_2 (225 mL), the solution was washed twice with water (45 mL). After evaporation of the solvent, the residue was dissolved in diethyl ether (75 mL) and the organic layer was dried with $MgSO_4$, filtered and concentrated under reduced pressure. The crude tosylate **9** was dissolved in acetone (120 mL) and potassium thioacetate (2.95 g, 25.8 mmol) was added. The resulting solution was refluxed for 24 h. After filtration and concentration, the residue was treated with water (20 mL) and extracted with diethyl ether (2 × 100 mL). The organic layer was dried with $MgSO_4$, filtered and concentrated to give the thioacetate **10**. This was dissolved in EtOH (3 mL) and 5 N NaOH (5.5 mL, 27.7 mmol) was added. The resulting solution was stirred for 9 h at 20 °C. The reaction was carefully neutralized with acetic acid and the EtOH was evaporated. After extraction with ether (3 × 10 mL), the combined organic layers were washed with a saturated solution of $NaHCO_3$, dried with $MgSO_4$ and concentrated. The residue was finally purified by flash column chromatography (C_5H_{12}/Et_2O, 24:1) to afford (*R*)- or (*S*)-**6** as a colourless liquid:

(*R*)-6: Yield 75% (2.52 g). $[\alpha]_D^{25}$ = +35.6 (*c* = 1.4, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.18 (q, ^3J = 6.0 Hz, 1 H, CH-O), 4.08 (dd, ^2J = 8.0, ^3J = 6.0 Hz, 1 H, CH_2-O), 3.74 (dd, ^2J = 8.0, ^3J = 6.0 Hz, 1 H, CH_2-O), 2.72 (ddd, ^2J = 13.5, ^3J = 8.0, ^3J = 6.0 Hz, 1 H, CH_2-S), 2.58 (ddd, ^2J = 13.5, ^3J = 9.0, ^3J = 6.0 Hz, 1 H, CH_2-S), 1.45 (t, ^3J = 8.5 Hz, 1 H, SH), 1.41 (s, 3 H, CH_3), 1.34 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 109.6 (O-C-O), 76.9 (CH-O), 68.2 (CH_2O), 27.6 (CH_2S), 26.8 (CH_3), 25.4 (CH_3) ppm.

(*S*)-6: Yield 52% (1.78 g). $[\alpha]_D^{25}$ = –31.1 (*c* = 1.4, $CHCl_3$).

1,3-Bis[(4*R*)-2,2-dimethyl-1,3-dioxolan-4-ylmethylthio]propanone *O*-Benzyloxime (8): According to the procedure described for the preparation of **7b**, starting from thiol **6** (1.21 g, 8.17 mmol) and oxime **4** (860 mg, 3.72 mmol), oxime **8** was obtained after purification by SiO_2 column chromatography (cyclohexane/EtOAc, 9:1) as a colourless oil.

(*R*,*R*)-8: Yield 91% (1.55 g). $[\alpha]_D^{25}$ = +22.6 (*c* = 1.4, $CHCl_3$). IR (NaCl): $\tilde{\nu}$ = 2985, 2933, 2876, 1373, 1253, 1216, 1153, 1059, 858, 753, 700 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37–7.28 (m, 5 H, Ar-H), 5.08 (s, 2 H, Ar-H), 4.22 (quint, ^3J = 6.0 Hz, 1 H, CH-O), 4.18 (quint, ^3J = 6.0 Hz, 1 H, CH-O), 4.00 (dd, ^2J = 6.0, ^3J = 2.0 Hz, 1 H, CH_2-O), 3.97 (dd, ^2J = 6.0, ^3J = 2.0 Hz, 1 H, CH_2-O), 3.63–3.52 (m, 4 H, N=C-CH_2-S, CH_2-O), 3.37 (s, 2 H, N=C-CH_2-S), 2.69 (dd, ^2J = 13.5, ^3J = 6.0 Hz, 1 H, S-CH_2), 2.58 (dd, ^2J = 13.5, ^3J = 6.5 Hz, 1 H, S-CH_2), 2.57 (dd, ^2J = 13.5, ^3J = 6.5 Hz, 1 H, S-CH_2), 2.46 (dd, ^2J = 13.5, ^3J = 6.5 Hz, 1 H, S-CH_2), 1.42 (s, 3 H, CH_3), 1.41 (s, 3 H, CH_3), 1.35 (s, 3 H, CH_3), 1.33 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.1 (CN), 137.4 (C-Ar), 128.4 (C-Ar), 128.3 (C-Ar), 128.0 (C-Ar), 109.6 (O-C-O), 76.2 (CH_2-Ar), 74.9 (CH-O), 68.7 (CH_2-O), 35.2 (CH_2-S), 34.1 (CH_2-S), 33.1 (S-CH_2), 26.9 (CH_3), 25.5 (CH_3), 25.1 (S-CH_2) ppm. $C_{22}H_{33}NO_5S_2$ (455.63): calcd. C 57.99, H 7.30, N 3.07, S 14.08; found C 58.30, H 7.47, N 3.11, S 13.93.

(*S*,*S*)-8: Yield 90% (1.52 g). $[\alpha]_D^{25}$ = –25.8 (*c* = 1.5, $CHCl_3$).

(*R,*R**)- and (*R**,*S**)-8:** Yield 83% (1.41 g).

General Procedure for the Cyclization of 8: Amberlyst® 15 (250 mg) and paraformaldehyde (10 mmol) were added to a solution of oxime **8** (1 mmol) in acetone (10 mL) and water (1 mL). The resulting mixture was refluxed for 2 d. After removing insoluble material by filtration through a Celite® pad, the solvent was evaporated. The residue was purified by SiO_2 column chromatography (EtOAc/cyclohexane, 9:1).

General Procedure for TBDPS Protection of 2: Imidazole (4.4 mmol) followed by *tert*-butylchlorodiphenylsilane (2.2 mmol) were added at 0 °C to a mixture of **2** (1 mmol) in DMF (5 mL). The resulting solution was stirred overnight and then taken up in diethyl ether (100 mL) and the organic layer was washed with water (15 mL) followed by a saturated aqueous NH_4Cl solution (15 mL). Filtration and evaporation of the dried ($MgSO_4$) organic layer afforded derivatives **11** which could be separated by two consecutive flash column chromatography (cyclohexane/EtOAc, 49:1 then cyclohexane/Et_2O, 100:1 → 50:1).

General Procedure for TPDPS Cleavage of 11: Tetrabutylammonium fluoride (1.0 M in THF, 2.4 mmol) was added to a solution of TBDPS-protected spirocompound **11** (1 mmol) in anhydrous THF (5 mL). After stirring at 20 °C overnight, the reaction mixture was diluted with ethyl acetate (100 mL) and then washed with water (10 mL) followed by brine (10 mL). The organic layer was dried with $MgSO_4$. The solvent was evaporated and the residue was purified by SiO_2 column chromatography (EtOAc/cyclohexane, 4:1).

(2*R*,6*S*,8*R*)- and (2*R*,6*R*,8*R*)-2,8-Dihydroxymethyl-1,7-dioxa-4,10-dithiaspiro[5.5]undecane (2a) and (2b): According to the general procedure of cyclization, starting from (*R*,*R*)-oxime **8**, an inseparable mixture of (2*R*,6*S*,8*R*)-**2a** and (2*R*,6*R*,8*R*)-**2b** was obtained in a 10:7 ratio and 75% yield. The isomers were separated by preparing their TBDPS derivatives **11a** and **11b** using the general procedure of protection followed by deprotection under the conditions described in the general procedure.

(2*R*,6*S*,8*R*)-11a: Viscous oil. R_f = 0.74 (cyclohexane/EtOAc, 9:1). $[\alpha]_D^{25}$ = –76.0 (*c* = 1.2, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ =

7.73 (m, 8 H, Ar-H), 7.39 (m, 12 H, Ar-H), 4.16 (dtd, ^3J = 11.0, ^3J = 5.5, ^3J = 2.0 Hz, 2 H, 2-H^{ax} and 8-H^{ax}), 3.76 (dd, ^2J = 10.5, ^3J = 5.5 Hz, 2 H, CH_2OSi), 3.60 (dd, ^2J = 10.5, ^3J = 5.5 Hz, 2 H, CH_2OSi), 2.76 (d, ^2J = 13.5 Hz, 2 H, 5-H and 11-H), 2.58 (dd, ^2J = 13.0, ^3J = 11.0 Hz, 2 H, 3-H^{ax} and 9-H^{ax}), 2.44 (d, ^2J = 13.0 Hz, 2 H, 3-H^{eq} and 9-H^{eq}), 2.40 (d, ^2J = 13.5 Hz, 2 H, 5-H and 11-H), 1.07 (s, 18 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.7 (C-Ar), 133.2 (C-Ar), 129.7 (C-Ar), 127.7 (C-Ar), 127.6 (C-Ar), 90.4 (C-6), 70.6 (C-2 and C-8), 66.5 (CH_2OSi), 34.6 (C-5 and C-11), 27.3 (C-3 and C-9), 26.8 (CH_3), 19.2 [$C(CH_3)_3$] ppm. MS (ESI): *m*/*z* (%) = 767 (53) $[M + K]^+$, 751 (100) $[M + Na]^+$, 288 (22).

(2*R*,6*R*,8*R*)-11b: Viscous oil. R_f = 0.48 (cyclohexane/EtOAc, 9:1). $[\alpha]_D^{25}$ = –2.2 (*c* = 3.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26–7.68 (m, 20 H, Ar), 4.65 (br. d, ^3J = 5.0 Hz, 1 H, 8-H), 4.30 (d, ^2J = 6.0 Hz, 1 H, CH_2OSi), 3.93 (qd, ^3J = 5.0, ^3J = 7.0 Hz, 2 H, 2-H), 3.87 (dd, ^2J = 6.0 Hz, ^3J = 7.0 Hz, 1 H, CH_2OSi), 3.74 (dd, ^2J = 10.5, ^3J = 5.0 Hz, 1 H, CH_2OSi), 3.71 (dd, ^2J = 10.5, ^3J = 5.0 Hz, 1 H, CH_2OSi), 3.14 (br. d, ^2J = 13.0 Hz, 1 H, 9-H^{ax}), 2.98 (dd, ^2J = 13.5, ^3J = 7.0 Hz, 1 H, 3-H^a), 2.91 (d, ^2J = 13.0 Hz, 1 H, 11-H), 2.66 (dd, ^2J = 13.5, ^3J = 5.0 Hz, 1 H, 3-H^{eq}), 2.55 (d, ^2J = 14.0 Hz, 1 H, 5-H), 2.50 (d, ^2J = 14.0 Hz, 1 H, 5-H), 2.33 (d, ^2J = 13.0 Hz, 1 H, 11-H), 2.11 (dd, ^2J = 13.0, ^3J = 2.0 Hz, 1 H, 9-H^{eq}), 1.04 (s, 9 H, CH_3), 1.01 (s, 9 H, CH_3) ppm.^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.0 (C-Ar), 135.8 (C-Ar), 135.6 (C-Ar), 135.5 (C-Ar), 133.9 (C-Ar), 133.8 (C-Ar), 133.5 (C-Ar), 133.4 (C-Ar), 129.6 (C-Ar), 129.5 (C-Ar), 127.6 (C-Ar), 127.5 (C-Ar), 106.8 (C-6), 74.6 (C-8), 73.1 (C-2), 69.5 (CH_2OSi), 65.4 (CH_2OSi), 39.7 (C-5), 36.5 (C-3), 33.1 (C-11), 28.9 (C-9), 26.9 (CH_3), 26.8 (CH_3), 19.2 [$C(CH_3)_3$] ppm. MS (ESI): *m*/*z* (%) = 767 (13) $[M + K]^+$, 751 (18) $[M + Na]^+$, 288 (100).

(2*R*,6*S*,8*R*)-2a: White solid. R_f = 0.37 (EtOAc). $[\alpha]_D^{25}$ = –137.5 (*c* = 0.6, CH_3OH). M.p. 98 °C (EtOAc). ^{1}H NMR (400 MHz, CD_3OD): δ = 3.97 (dt, ^3J = 11.5, ^3J = 5.0 Hz, 2 H, 2-H^{ax} and 8-H^{ax}), 3.56 (dd, ^2J = 11.5, ^3J = 5.0 Hz, 2 H, CH_2OH), 3.48 (dd, ^2J = 11.5, ^3J = 5.0 Hz, 2 H, CH_2OH), 2.76 (d, ^2J = 13.5 Hz, 2 H, 5-H and 11-H), 2.54 (t, ^2J = ^3J = 11.5 Hz, 2 H, 3-H^{ax} and 9-H^{ax}), 2.40 (d, ^2J = 13.5 Hz, 2 H, 5-H and 11-H), 2.37 (d, ^2J = 11.5 Hz, 2 H, 3-H^{eq} and 9-H^{eq}) ppm.^{13}C NMR (100 MHz, CD_3OD): δ = 91.9 (C-6), 72.4 (C-2 and C-8), 65.9 (CH_2OH), 35.2 (C-5 and C-11), 27.8 (C-3 and C-9) ppm. $C_9H_{16}O_4S_2$ (252.35): calcd. C 42.84, H 6.39, S 25.41; found C 42.67, H 6.36, S 25.54.

(2*R*,6*R*,8*R*)-2b: Colourless oil. R_f = 0.37 (EtOAc). ^{1}H NMR (400 MHz, CD_3OD): δ = 4.77 (br. d, ^3J = 6.0 Hz, 1 H, 8-H^{eq}), 4.33 (d, ^2J = 6.5 Hz, 1 H, CH_2OH), 3.94 (t, ^2J = ^3J = 6.0 Hz, 1 H, CH_2OH), 3.71 (dq, ^3J = 7.0, ^3J = $^3J_{2,3b}$ = 5.0 Hz, 1 H, 2-H), 3.54 (dd, ^2J = 11.0, ^3J = 5.0 Hz, 1 H, CH_2OH), 3.49 (dd, ^2J = 11.0, ^3J = 5.5 Hz, 1 H, CH_2OH), 3.11 (d, ^2J = 13.0 Hz, 1 H, 9-H^{ax}), 3.01 (d, ^2J = 13.0 Hz, 1 H, 11-H^{ax}), 2.84 (d, ^2J = 14.0 Hz, 1 H, 5-H^a), 2.83 (d, ^2J = 14.0 Hz, 1 H, 5-H^b), 2.77 (dd, ^2J = 13.5, ^3J = 5.5 Hz, 1 H, 3-H^a), 2.64 (ddd, ^2J = 13.5, $^3J_{3,2}$ = 7.0, ^4J = 2.0 Hz, 1 H, 3-H^b), 2.44 (d, ^2J = 13.0 Hz, 1 H, 11-H^{eq}), 2.19 (d, ^2J = 13.0 Hz, 1 H, 9-H^{eq}) ppm. ^{13}C NMR (100 MHz, CD_3OD): δ = 108.3 (C-6), 76.3 (C-8), 72.9 (C-2), 70.8 (CH_2OH), 66.0 (CH_2OH), 40.6 (C-5), 37.8 (C-3), 33.9 (C-11), 29.7 (C-9) ppm.

(2*S*,6*R*,8*S*)- and (2*S*,6*S*,8*S*)-2,8-Dihydroxymethyl-1,7-dioxa-4,10-dithia-spiro[5.5]undecane (2a) and (2b): The general procedure applied to (*S*,*S*)-oxime **8** led to the isomers (2*S*,6*R*,8*S*)-**2a** and (2*S*,6*S*,8*S*)-**2b** in a 10:7 ratio.

(2*S*,6*R*,8*S*)-11a: $[\alpha]_D^{25}$ = +62.8 (*c* = 1.1, $CHCl_3$).

(2*S*,6*S*,8*S*)-11b: $[\alpha]_D^{25}$ = +2.7 (*c* = 0.3, $CHCl_3$).

(2*S*,6*R*,8*S*)-2a: $[\alpha]_D^{25}$ = +137.2 (*c* = 0.8, CH_3OH), m.p. 95 °C (EtOAc).

(2*S*,6*S*,8*S*)-2b: $[\alpha]_D^{25}$ = +33.3 (*c* = 1.0, CH_3OH).

(2*R,6*S**,8*R**)-, (2*R**,6*R**,8*R**)-, (2*R**,6*S**,8*S**)- and (2*R**,6*R**,8*S**)-2,8-Dihydroxymethyl-1,7-dioxa-4,10-dithiaspiro-[5.5]undecane (2):** The general cyclization conditions applied to (*R**,*R**)- and (*R**,*S**)-**8** gave a mixture of four diastereoisomers: (2*R**,6*S**,8*R**)-**2a**, [(2*R**,6*R**,8*R**)-**2b** + (2*R**,6*S**,8*S**)-**2c**] and (2*R**,6*R**,8*S**)-**2d** in a 5:7:1 ratio. Isomer (2*R**,6*R**,8*S**)-**2d** was directly isolated from the others by SiO_2 column chromatography (EtOAc/cyclohexane, 9:1). Isomer **2a** was obtained after TBDPS protection followed by cleavage. (2*R**,6*R**,8*R**)-**2b** and (2*R**,6*S**,8*S**)-**2c** could not be separated even with TBDPS protection.

(2*R,6*R**,8*S**)-2d:** Colourless oil. R_f = 0.46 (EtOAc). ^{1}H NMR (400 MHz, CD_3OD): δ = 4.36 (dtd, ^3J = 5.0, ^3J = 11.0, ^3J = 2.0 Hz 1 H, 8-H), 3.81 (dddd, ^3J = 5.0, ^3J = 6.0, ^3J = 10.5, ^3J = 2.0 Hz, 1 H, 2-H), 3.61 (dd, ^2J = 11.0, ^3J = 5.0 Hz, 1 H, CH_2OH), 3.58 (dd, ^2J = 14.5, ^4J = 2.0 Hz, 1 H, 11-H^{eq}), 3.53 (dd, ^2J = 11.0, ^3J = 6.0 Hz, 1 H, CH_2OH), 3.47 (dd, ^2J = 11.0, ^3J = 5.0 Hz, 1 H, CH_2OH), 3.41 (dd, ^2J = 11.0, ^3J = 5.0 Hz, 1 H, CH_2OH), 2.69 (d, ^2J = 13.5 Hz, 1 H, 5-H^{eq}), 2.64 (d, ^2J = 14.5 Hz, 1 H, 11-H^{ax}), 2.55 (dd, ^2J = 13.0, ^3J = 11.0 Hz 1 H, 9-H^{ax}), 2.54 (dd, ^2J = 13.5, ^3J = 10.5 Hz, 1 H, 3-H^{ax}), 2.42 (br. d, ^2J = 13.5 Hz, 2 H, 3-H^{eq}), 2.42 (d, ^2J = 13.5 Hz, 1 H, 5-H^{ax}), 2.37 (dt, ^2J = 13.0, ^3J = 2.0, ^4J = 2.0 Hz, 1 H, 9-H^{eq}) ppm. ^{13}C NMR (100 MHz, CD_3OD): δ = 94.7 (C-6), 76.3 (C-8), 72.1 (C-2), 66.0 (CH_2OH), 65.9 (CH_2OH), 35.9 (C-11), 29.7 (C-3), 28.7 (C-5), 28.3 (C-9) ppm.

(2*R*,6*S*,8*S*)- and (2*R*,6*R*,8*S*)-2,8-Dihydroxymethyl-1,7-dioxa-4,10-dithiaspiro[5.5]undecane (2c and 2d): The general procedure of cyclization applied to (*R*,*S*)-**8** led to isomers (2*R*,6*S*,8*S*)-**2c** and (2*R*,6*R*,8*S*)-**2d** with isomer **2c** as the major compound.

(2*R*,6*S*,8*S*)-2c: Colourless oil. R_f = 0.37 (EtOAc). $[\alpha]_D^{25}$ = +10.0 (*c* = 0.1, CH_3OH). ^{1}H NMR (400 MHz, CD_3OD): δ = 4.75 (br. d, ^3J = 6.0 Hz, 1 H, 8-H^{eq}), 4.31 (d, ^2J = 6.5 Hz, 1 H, CH_2OH), 3.93 (t, ^2J = ^3J = 6.0 Hz, 1 H, CH_2OH), 3.69 (dq, ^3J = 7.0, ^3J = 5.0 Hz, 1 H, 2-H), 3.52 (dd, ^2J = 11.0, ^3J = 5.5 Hz, 1 H, CH_2OH), 3.47 (dd, ^2J = 11.0, ^3J = 5.0 Hz, 1 H, CH_2OH), 3.09 (br. d, ^2J = 13.0 Hz, 1 H, 9-H^{ax}), 2.99 (d, ^2J = 13.0 Hz, 1 H, 11-H^{ax}), 2.83 (d, ^2J = 15.0 Hz, 1 H, 5-H^a), 2.80 (d, ^2J = 15.0 Hz, 1 H, 5-H^b), 2.75 (dd, ^2J = 13.5, ^3J = 5.0 Hz, 1 H, 3-H^a), 2.63 (dd, ^2J = 13.5, ^3J = 7.0 Hz, 1 H, 3-H^b), 2.42 (d, ^2J = 13.0 Hz, 1 H, 11-H^{eq}), 2.18 (br. d, ^2J = 13.0 Hz, 1 H, 9-H^{eq}) ppm. ^{13}C NMR (100 MHz, CD_3OD): δ = 108.3 (C-6), 76.3 (C-8), 72.9 (C-2), 70.8 (CH_2OH), 66.0 (CH_2OH), 40.6 (C-5), 37.8 (C-3), 33.9 (C-11), 29.7 (C-9) ppm.

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