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Molecular Rods Based on Oligo-spiro-thioketals

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Supporting Information

ABSTRACT: We report on an extension of the previously established concept of oligospiroketal (OSK) rods by replacing a part or all ketal moieties by thioketals leading to oligospirothioketal (OSTK) rods. In this way, some crucial problems arising from the reversible formation of ketals are circumvented. Furthermore, the stability of the rods toward hydrolysis is considerably improved. To successfully implement this concept, we first developed a number of new oligothiol building blocks and improved the synthetic accessibility of known oligothiols, respectively. Another advantage of thioacetals is that terephthalaldehyde (TAA) sleeves, which are too flexible in the case of acetals can be used in OSTK rods. The viability of the OSTK approach was demonstrated by the successful preparation of some OSTK rods with a length of some nanometers.

INTRODUCTION

The term molecular rods generally refer to relatively rigid molecules with a large aspect ratio (i.e., the ratio between length and width). During the last decades, this substance class has enjoyed constantly growing interest, and meanwhile, a wide range of applications in material science, nanoelectronics, and biosciences has been developed.[1] In this context, an efficient synthetic accessibility is the crucial prerequisite. The nanoscopic scale of the molecular rods often requires many repetitive synthetic steps, thus diminishing the overall yield. Furthermore, the drastically decreasing solubility with increasing length is a substantial challenge.

Some years ago, we developed a new type of molecular rods, which are composed of spirocyclically connected saturated six-membered rings. Because the construction of these rods is based on the formation of ketals, we called these compounds oligospiroketal (OSK) rods.[2] Simple rods of this type with more than six ring elements exhibit scarce solubility, and therefore, longer rods are only accessible by introducing solubility enhancing groups (SEG) in terminal positions (Figure 1, **A**). These groups impede the introduction of other functional groups and thus limit the application of those rods. This problem could be circumvented by the development of building blocks bearing lateral SEGs. Because these units merge two shorter rods we have called them *sleeves* in analogy to construction.[3] A typical OSK rod with a solubility enhancing sleeve is depicted in Figure 1 (**B**).

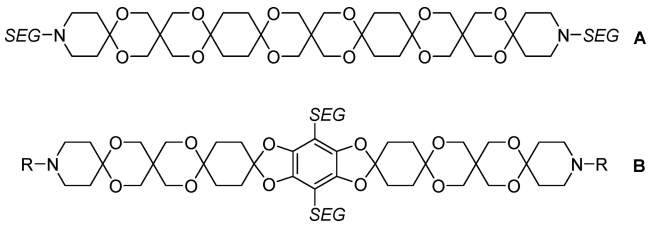

Figure 1. Typical OSK rods with terminal (A) and lateral (B) solubility enhancing groups (SEG).

OSK rods of type **B** allow for the implementation of functional groups in terminal positions leading to a number of interesting applications. Thus, the integration in biological membranes[4,5,7] as well as the usage as rigid spacer in FRET systems[8] were investigated. Recently, we used OSK rods as building blocks in porous materials[9] and dendrimers.[10] It should be noted that the solubility is also improved by incorporating a flexible joint, leading to articulated rods.[11]

Despite the considerable success with OSK rods of types **A** and **B** a serious problem should not be disregarded. The formation of acetals from diols and ketones catalyzed by acids is an equilibrium reaction. Beyond a certain number of ketal groups per molecule this leads unavoidably to drastically decreasing yields and very complex product mixtures. In our experience, this limit is exceeded with more than six ketal structures, i.e., it should be very difficult to prepare OSK rods longer than **A** and **B** with the same building blocks.

On the other hand, thioacetals are very stable toward both acidic and basic conditions, however, relatively sensitive toward oxidants.[12] Cyclic thioacetals (e.g., 1,3-dithianes) gained particular importance in organic synthetis, e.g., in the Corey–Seebach reaction.[13] The formation of cyclic thioacetals from dithiols and aldehydes or ketones is, in contrast to the oxygen counterpart, no equilibrium reaction, and therefore, the above-mentioned problems with the synthesis of longer OSK rods should not occur with thioacetals. Herein, we describe a powerful approach to circumvent the "equilibrium problem", the partial or complete replacement of acetals by thioacetals leading to oligo-spiro-thioketal (OSTK) rods. Herein, the term OSTK rod denotes an OSK rod where at least one ketal moiety is replaced by a thioketal (but not necessarily all ketals).

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RESULTS AND DISCUSSION

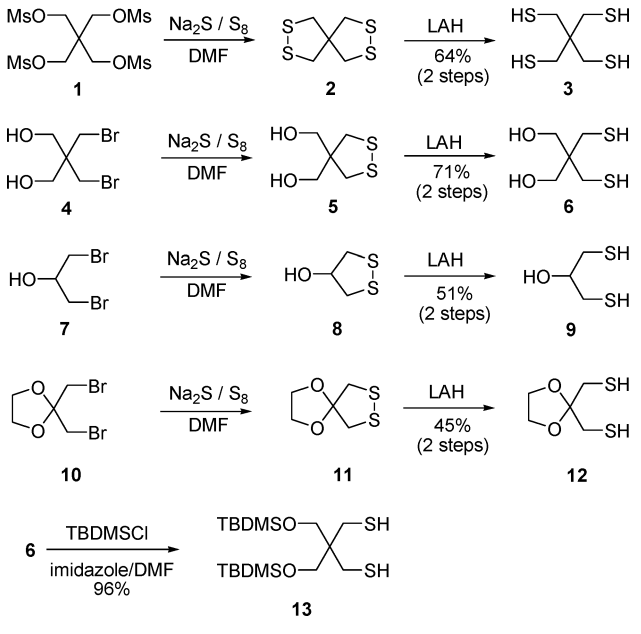
Building Blocks. Pentaerythritol is one of the central building blocks of the OSK rod backbone, and it was evident to use its tetrathia analogue 2,2-bis(mercaptomethyl)-1,3-propanedithiol **3** en route toward OSTK rods. A literature survey on the preparation and usage of **3** revealed surprisingly few references. Essentially all syntheses of **3** are based on S_N reactions between tetraelectrophiles derived from pentaerythritol and different sulfur nucleophiles.[14] Already in 1937, Backer and Evenhuis[14a] reported on the synthesis of **3** from 2,3,7,8-tetrathiaspiro[4.4]nonane **2**[15] by reduction with Na/NH_3. Some years later, a preparation of **3** by the reaction of 1,3-dibromo-2,2-bis(bromomethyl)propane and sodium tetrasulfide, followed by catalytic reduction of the resulting polysulfide mixture, has been described.[14b] In 1970, Fujihara et al. reported on the synthesis of **3** from the same tetrabromide by reaction with Na_2S_2 to give **2** and subsequent reduction with $LiAlH_4$.[14c] Wade et al. used the tetracetyl derivative of **3** directly in the synthesis of thioketals.[14d] This tetracetate was also prepared by Gaz et al.[14e] (no yields given) and converted to **3** by treatment with $LiAlH_4$.

According to our experience, all methods described up to now are difficult to reproduce and provide **3** only with low yields and/or contaminated with other sulfur-containing compounds. This is probably one of the reasons why **3** was so rarely used. After numerous attempts, we succeeded in developing an optimized procedure. Starting from tetramesylate **1**[16] (the above-mentioned and commercially available but relatively expensive tetrabromide can also be used), we obtained 2,3,7,8-tetrathiaspiro[4.4]nonane **2** by treatment of **1** with a Na_2S_x solution in DMF, prepared from Na_2S (2 equiv) and S_8 (4 equiv), by stirring for 2 h at 80 °C. The crude compound **2** was reduced without purification with $LiAlH_4$ and gave the target compound **3** reproducible with 64% yield (Scheme 1).

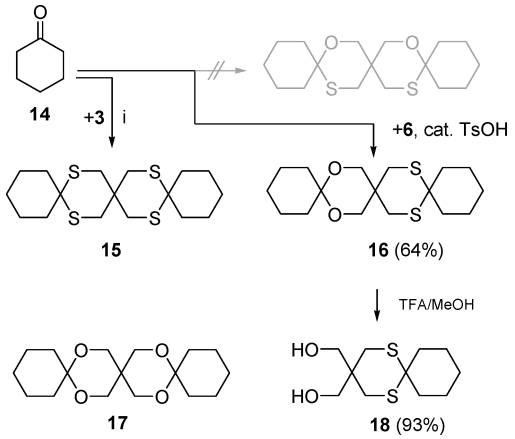
As we will demonstrate below, it is not necessary to replace all ketals by thioketals to avoid the problems mentioned above. Bearing in mind the complementary formation and reactivity of ketals and thioketals, we were, therefore, also interested in 2,2-bis(sulfanylmethyl)-1,3-propanediol **6**, which has also rarely been mentioned in literature.[17] Using the optimized conditions for **3**, we obtained **6** with 71% yield based on the commercially available 2,2-bis(bromomethyl)propane-1,3-diol **4**. Similarly, we prepared the third fundamental building block **9**[18] from 1,3-dibromopropan-2-ol **7**. With **9** it should be possible to construct OSTK rods by repetitive formation of thioketals with ketones and subsequent oxidation of the secondary alcohol to the next ketone. However, we will show that the selective oxidation of alcohols in the presence of thioacetals is certainly not an easy task. Therefore, we also prepared 2,2-bis(sulfanylmethyl)-1,3-dioxolane **12** from the known 2,2-bis(bromomethyl)-1,3-dioxolane **10**, which is prepared from commercially available 1,3-dibromoacetone.[19] Compound **12** could be used in a similar way as **9**, but the restoration of the ketone moiety should occur by removal of the dioxolane protecting group. We are also interested in OSTK rods with different functional groups in the terminal positions. This could be achieved by a stepwise formation of thioketal and ketal function from building block **6**. However, we found that an exclusive reaction of the thiols in **6** is difficult to accomplish (see next section). Therefore, we prepared compound **13** by selective protection of the hydroxyl groups with TBDMS groups in nearly quantitative yield.

Trispiranes. Equipped with the building blocks **3**, **6**, **9**, **12**, and **13**, we next investigated the synthesis and properties of simple trispiranes starting with cyclohexanone **14** (Scheme 2).

Scheme 1. Synthesis of Building Blocks 3, 6, 9, 12, and 13



Scheme 2. Synthesis of Trispiranes 15 and 16 and Spirane 18



[i]Method A: 3 equiv of BF_3Et_2O, 94%. Method B: cat. TsOH, 88%. Method C: cat. I_2, 86%.

The tetrathiatrispirane **15**, which could be regarded as the parent compound of OSTK rods, was prepared for the first time by Backer and Evenhuis[14a] and later mentioned only once.[20] A substituted trispirane was reported by Grosu et al.,[14e] whereas spiranes such as **16** with both ketal and thioketal moieties are hitherto unknown. We applied three different methods for the synthesis of **15** (BF_3·Et_2O, cat. TsOH, cat. I_2) and obtained the target compound always with very good yields. Because the formation of thioketals takes place under much milder conditions than the ketal formation, we hypothesized that the dithiapentaerythritol **6** primarily reacts only with the thiol groups to give **18**. The reaction between **14** and **6** afforded, however, the trispirane **16**. Compound **18** could

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be obtained by selective hydrolytic removal of the 1,3-dioxane ring in **16**.

From compound **15**, we obtained crystals suitable for X-ray crystal structure analysis. Compound **15** shows C_2 symmetry and axial chirality. C1 is located on the 2-fold axis. For both cyclohexane rings a torsion angle (C9−C4−C4′−C9′) of −21.303(4)° can be observed. Both dithiane rings are almost orthogonal to each other, characterized by an angle of 89.68° around the C1 atom formed by the C1/C2/C3 and C1/C2′/C3′ planes. The bond angles around C1 range from 108.99(8) to 113.02(2)°. The bond lengths are as expected (C−C: 1.518(2)−1.536(2) Å; C−S: 1.806(1)−1.827(1)°) (Figures 2 and 3, for details see Supporting Information).

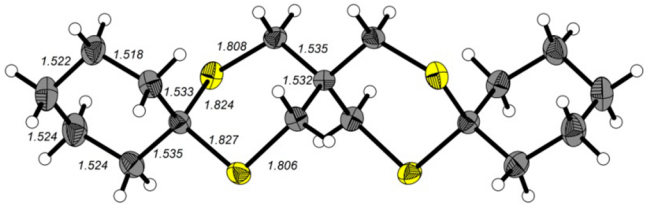

Figure 2. X-ray crystal structure analysis of compound **15** (molecular structure with thermal ellipsoids drawn at the 50% probability level).

As already mentioned, a low solubility is a serious problem for the synthesis and application of molecular rods. To evaluate the influence of exchanging oxygen atoms by sulfur atoms on the solubility of OS(T)K rods, we compared trispiranes **15** and **16** and the known compound **17**[21] concerning its solubility in various solvents (Figure 4). All three compounds have a low solubility in MeOH underlining the rather hydrophobic character of the backbone of OS(T)K rods, but whereas **17** is highly soluble in DCM and THF, the solubility is nearly halved by replacement of one ketal by a thioketal (**16**) and drops below one-tenth in the case of dithioketal **15**. This effect results from considerably reduced electronegativity of sulfur (χ = 2.58, which is nearly the same value as for carbon, χ = 2.55) compared with oxygen (χ = 3.44). Consequently, C−S bonds are essentially nonpolar in contrast to highly polarized C−O bonds. It must therefore be assumed that decreasing solubility with increasing length is an even greater problem for OSTK rods.

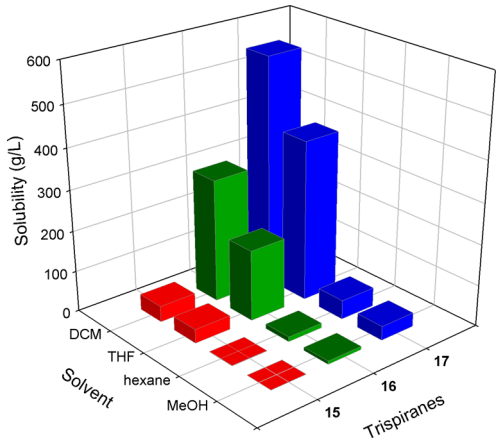

Figure 4. Solubility of trispiranes **15**−**17**.

To verify the high stability of thioketal moieties toward hydrolysis, we treated a solution of trispirane **15** in dichloromethane for a longer time with concentrated hydrochloric acid. Even after 18 days we could not detect any decomposion in the ^{1}H NMR spectrum.

Then, we prepared a variety of trispiranes to demonstrate the compatibility of the OSTK skeleton with different reaction conditions and functional groups. Thus, 4-pivaloyloxy-cyclohexanone **19**[2] reacted smoothly with **3** to give the trispirane **20a** with good yields (Scheme 3). After removal of the Piv group with DIBALH, we succeeded with the Swern oxidation to diketone **21**, whereas the conversion to the corresponding ditosylate failed. N-Protected piperidine-4-ones such as **22**[3] and **24**[2] are also suitable reactants and gave the trispiranes **23** and **25** with good to excellent yields. The reaction of N-Cbz-protected piperidin-4-one **24** with **6** afforded the trispirane **26**, containing both a ketal and a thioketal moiety by analogy with the reaction with cyclohexanone described above. Furthermore, it was possible to remove the Cbz protecting groups in **25** with HBr/HOAc giving the free diamine **27**, albeit with moderate yield.

Sleeves. As discussed in the preceding section, sleeves bearing solubility enhancing groups (SEG) are of pivotal importance for longer OSK rods and all the more for OSTK rods. Until now, we have developed four different sleeves **C**−**F**, whose structures are summarized in Figure 5.[3,6] The DBD sleeve **C** was repeatedly used in OSK rods, whereas the

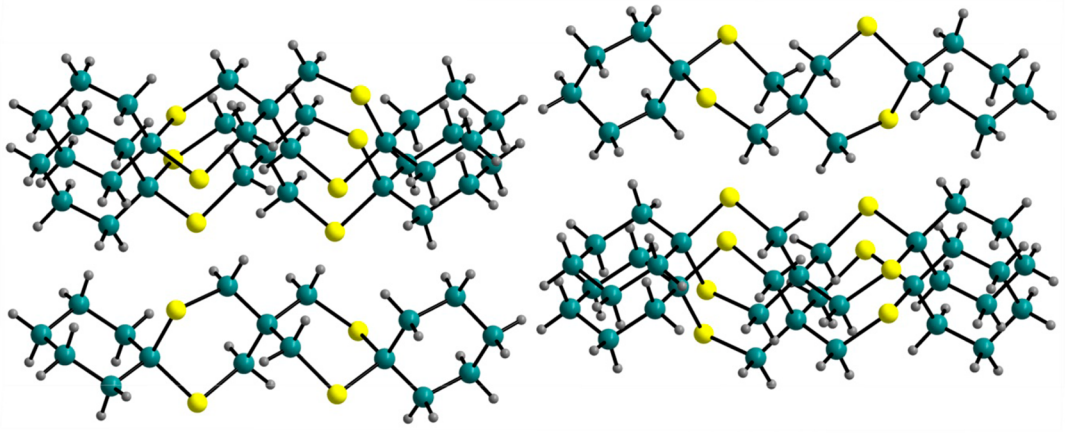

Figure 3. Crystal packing of compound **15**.

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Scheme 3. Synthesis of Various Trispiranes

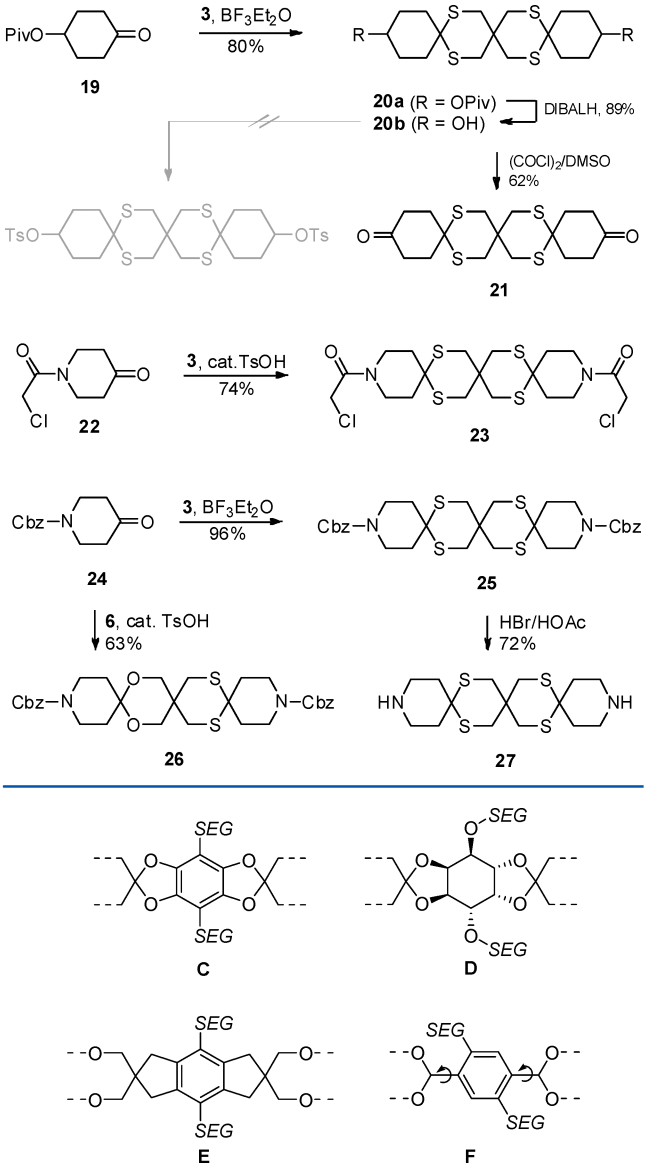
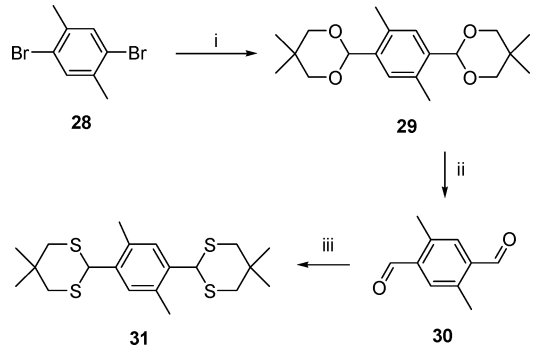


Figure 5. Sleeves C–F with solubility enhancing groups (SEG).

synthesis of sleeves **D** and **E** is rather expensive. However, the most readily accessible sleeves are acetals of 2,5-disubstituted terephtalaldehyde (**F**, TAA sleeve). Unfortunately, OSK rods with this sleeve are relatively flexible due to less hindered rotation around the C–C bonds between aromatic ring and acetal C atoms (see arrows in Figure 5), indicated by a large Levy–Martin parameter (OSK rod with **C**: LM = 23; OSK rod with **F**: LM = 44).[6]

Bearing in mind the 30% larger covalent radius and the 20% larger van der Waals radius of sulfur compared with oxygen, we hypothesized that TAA sleeves with thioacetals instead of acetals could be considerably more rigid. To prove this assumption, we prepared two model compounds **29** and **31** commencing with commercially available 2,3-dibromo-*p*-xylene **28** (Scheme 4). The synthesis of **29** comprised lithiation, formylation with DMF, and acetalization with 2,2-dimethylpropane-1,3-diol. Hydrolysis of **29** afforded 2,5-dimethylterephthalaldehyde **30**,[22] which was subsequently converted to the

Scheme 4. Synthesis of Model Compounds 29 and 31[a]



[a]Key: (i) (1) BuLi, (2) DMF, (3) 2,2-dimethyl-1,3-propanediol, (4) BuLi, (5) DMF, (6) 2,2-dimethyl-1,3-propanediol, 42%; (ii) TFA, 64%; (iii) 2,2-dimethyl-1,3-propanedithiol, I_2, 75%.

dithioacetal **31** by reaction with 2,2-dimethylpropane-1,3-dithiol.[23]

Regarding the suitability of TAA sleeves for molecular rods, three preferred conformations **T1**, **T2**, and **C** have to be discussed (Figure 6). For this we defined a pseudodihedral

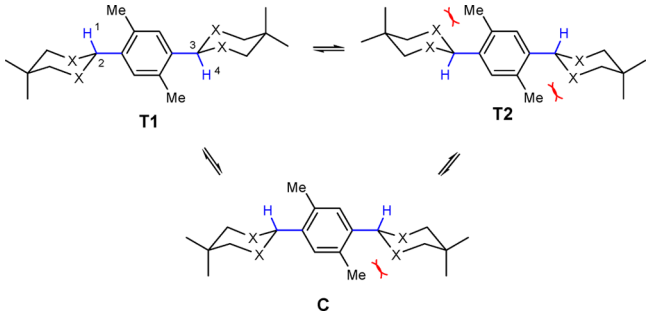


Figure 6. Preferred conformations **T1**, **T2**, and **C** of TAA sleeves.

angle α, which is given by the atoms 1–4. For conformers **T1** and **T2** α is nearly 180°, whereas for **C** the angle α is 0°. Furthermore, the distances between heteroatoms X and the substituent in the ortho position of the aromatic ring (Me in this case) have to be considered. This distance is large for both saturated rings in **T1** but small for one (**C**) or both rings (**T2**) in the remaining two conformers.

Due to the larger space requirement of atoms X compared with the hydrogen atom at the acetal carbon atom, **T1** should be the most favored conformer. At first, we compared **29** and **31** by molecular modeling. For this purpose, a conformational analysis was performed using the MMFF94x force field,[24] and all conformers within an energy window of 5 kcal/mol above the global minimum were collected. We obtained four geometries for **31** and seven geometries for **29**. These 11 structures were then optimized at DFT level (B3LYP/6-31G*). In the case of **31**, the conformation **31-A**, corresponding to T1, clearly dominates (97% based on Boltzmann distribution at 298 K). A second conformer **31-B**, which corresponds to **C** (Figure 7), was found to have a markedly higher energy (+2.1 kcal/mol, 2.8%). For the oxygen counterpart **29** we found two clearly different conformations **29-A** (46.4%) and **29-B** (44.1%) with nearly the same energy. A third conformer **29-C** with a slightly higher energy (+ 1.0 kcal/mol) contributes with 8%. These results, which are also substantiated by NOESY measurements (see the Supporting Information), confirm the assumption that

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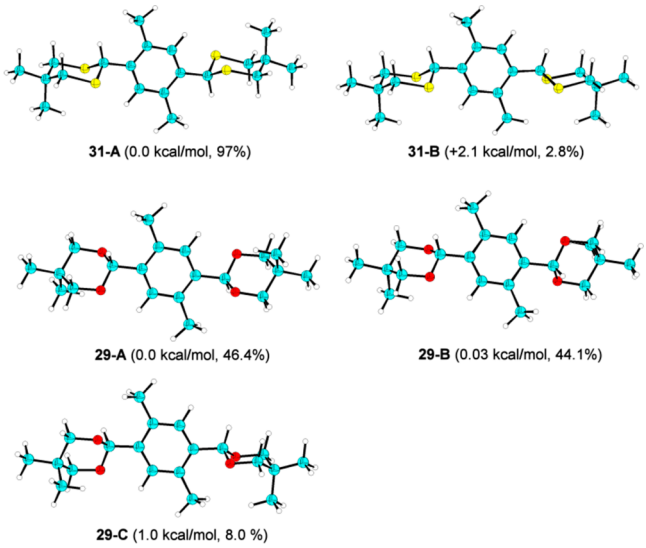
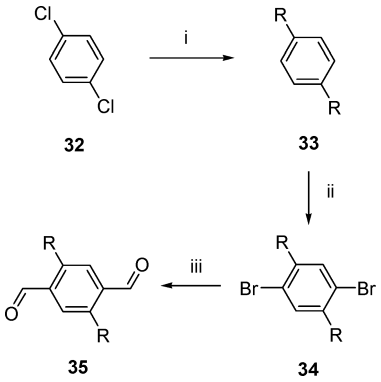


Figure 7. Dominating conformations for **29** and **31** (B3LYP/6-31G*).

the replacement of oxygen by sulfur results in considerably more rigid TAA sleeves.

Encouraged by these findings, we next prepared some terephthalaldehydes **35** bearing solubility-enhancing groups. The synthetic strategy is outlined in Scheme 5 and is known

Scheme 5. Synthesis of Terephthalaldehydes 35[a]



[a]Key: (i) RMgX, cat. Ni(dppp)Cl_2; (ii) Br_2; (iii) (1) BuLi, (2) DMF, (3) 2,2-dimethyl-1,3-propanediol, (4) BuLi, (5) DMF, (6) 2,2-dimethyl-1,3-propanediol, (7) TFA.

from the literature for **35a** (R = Bu).[6,25] Starting with 1,4-dichlorobenzene **32**, the residues R were introduced by a Kumada coupling followed by the same approach as already used for the preparation of **30** (Scheme 4). Furthermore, we prepared two further terephthaldehydes with longer (**35b**, R = Pent) and branched (**35c**, R = iOct) residues (Scheme 5, Table 1).

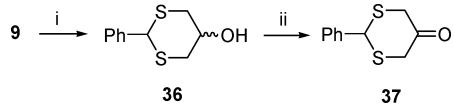
Table 1. Yields and References for Compounds 33−35

	R	33	34	35
a	Bu	ref25	ref28	ref6
b	Pent	63%	77%	47%
c	iOct[a]	ref26	ref27	32%

[a]iOct = 2-ethylhexyl.

OSTK Rods. After having established the synthesis of fundamental building blocks (**3**, **6**, **9**, **12**, and **13**) and sleeves (**35**) we turned our attention to the synthesis of longer OSTK rods. Basically, the construction of OSTK can be performed by two ways: (1) by repeated acetalization steps, either based on the different reactivity of diols and dithiols (e.g., with **6**; but we have already demonstrated that implementation of this approach is rather difficult), or by intermediate deprotection (e.g., with **12** or **13**) and (2) by alternate oxidation and acetalization steps (e.g., with **9**). Bearing in mind the variety of oxidation methods for secondary alcohols, we first explored the latter approach. For this we prepared the model compound **36** from **9** and benzaldehyde and investigated their oxidation to ketone **37** (Scheme 6).[29] The very often used Dess−Martin

Scheme 6. Synthesis of Dithiane 35[a]



[a]Key: (i) I_2, PhCHO, 98%; (ii) oxidation conditions, see Table 2.

periodinane[30] was ruled out right from the start because it is known that hypervalent iodine reagents are able to cleave thioacetals.[31,32] To our great surprise, nearly all other established methods either failed or gave the target compound in very low yields (methods 1−7 exhibited low conversion and in the case of method 8 cleavage of the thioketal was observed). The Albright−Goldman oxidation[33] using DMSO and acetic anhydride was the only successful method, which provided the ketone **37** with 52% yield (Table 2).

Table 2. Optimization of the Oxidation of 36

entry	oxidant	conditions	yield (%)
1	PCC	rt, 72 h	
2	CrO_3/pyridine	rt, 72 h	
3	Jones reagent	rt, 48 h	
4	$Al(iPr)_3$/acetone, toluene	rfx, 20 h	2
5	$Pb(OAc)_4$/benzene	rfx, 48 h	
6	$RuC_{62}H_{42}O_6$[34]/acetone	rfx, 48 h	5
7	TEMPO, NaOCl, NaBr, $NaHCO_3$	0 °C to rt, 2 h	
8	$(COCl)_2$/DMSO	−78 °C, 2 h	
9	Ac_2O/DMSO	rt, 20 h	52

Based on these findings we next compared building blocks **9** and **12** regarding their suitability to prepare diketone **40c** with iOct-TAA sleeve. We found that both routes are practicable and the overall yields range from 40 to 50%. However, 1,3-dibromoacetone, which is the parent substance for the preparation of **12**, is considerably more expensive than 1,3-dibromopropan-2-ol **7**, which is used for the preparation of **9** (cf. Scheme 1). Therefore, we prefer building block **9** and prepared compounds **40a,b** in this way. The best overall yield (64%) was observed with **40b** (Scheme 7, Table 3). To illustrate the influence of alkyl residues R, we determined the solubility of compounds **40** in dichloromethane. Whereas **40a,b** show nearly the same values, the isooctyl group in **40c** drastically increases the solubility (Table 3).

Diketone **40b** smoothly reacts with dithiol **13**, whereby the silyl protecting groups are simultaneously removed during workup giving the tetrol **41**. The suitability of building block **41**

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Scheme 7. Synthesis of Diketone 40

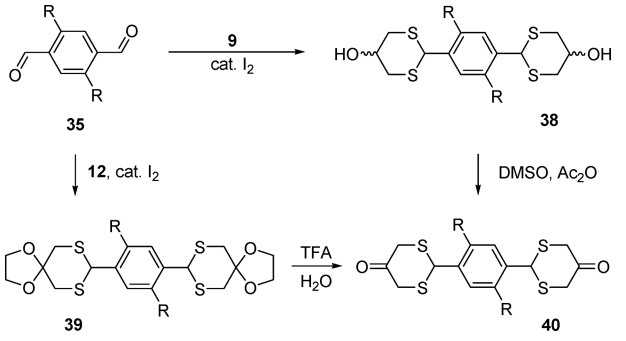


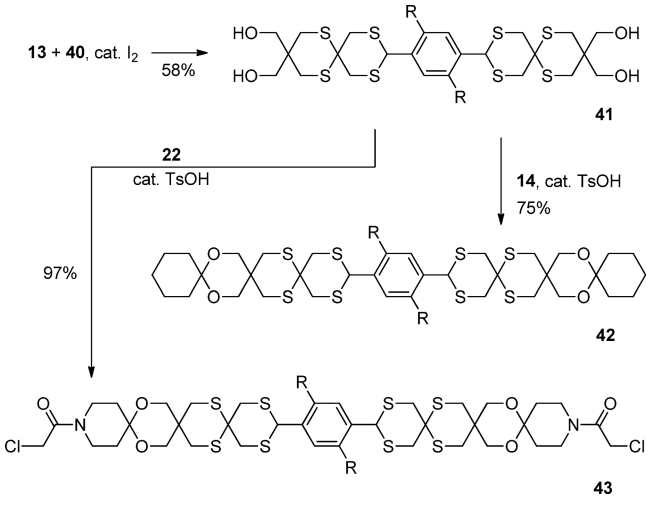
Table 3. Yields of Compounds 38−40 and Solubility of 40

	R	38[b]	39	40[b,c]	40[b,d]	S [40][e]
a	Bu	94		44		18.6
b	Pent	91		70		19.2
c	iOct[a]	>99	56	42	80	286.0

[a]iOct = 2-ethylhexyl. [b]Yield (%). [c]From **38**. [d]From **39**. [e]Solubility in DCM in g/l.

to prepare longer OSTK rods could be convincingly proven by the reaction with cyclohexanone **14** and *N*-chloroacetylpiperidin-4-one **22**, giving rods **42** and **43** in good to excellent yields (Scheme 8). It should be noted that OSK rods with TAA sleeves and a similar length than rod **43** were hitherto not accessible.

Scheme 8. Synthesis of OSTK Rods 42 and 43 (R = Pent)



Finally, we prepared tetrols **44** from sleeves **35** and dithiol **13** and explored the acetalization with ketones. The reaction of **44b** with cyclohexanone **14** gave the OSTK rod **45** with moderate yield, whereas **44a,c** provided by reaction with **22** nearly quantitatively OSTK rods **46a,c** (Scheme 9, Table 4).

CONCLUSION

The previously developed oligospiroketal (OSK) rods proved to be versatile molecular rods.[2−11] However, the length of these rods is limited due to the lability of acetals during the synthesis and the reversibility of the formation reaction. On the other hand, it is well known that thioacetals are much more stable, and the formation reaction is not reversible. Herein we have

Scheme 9. Synthesis of OSTK Rods 45 and 46

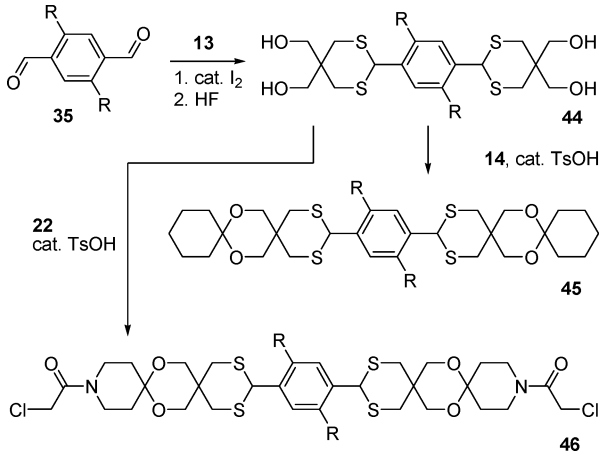


Table 4. Yields of Compounds 44−46

	R	44[b]	45[b]	46[b]
a	Bu	63		>99
b	Pent	>99	60	
c	iOct[a]	>99		>99

[a]iOct = 2-ethylhexyl. [b]Yield (%).

presented a powerful extension of our OSK rod concept by replacement of one or more acetals by thioacetals and named these constructs oligospirothioketal (OSTK) rods. The underlying building blocks, the tetrathiol **3** and the dithiols **6**, **9**, **12**, and **13** were hitherto not readily accessible. After numerous attempts we succeeded in the development of a reliable synthetic route to these thiols. Subsequently we prepared some trispiranes using building blocks **6** and **9**. This showed that the solubility is appreciably diminished if ketals are replaced by thioketals, which is not surprising in view of the low polarity of the C−S bond. Consequently, solubility enhancing building blocks (sleeves) are of great importance. We demonstrated that sleeves based on 2,5-disubstitued terephthalaldehydes (TAA), which are relatively straightforward to prepare, are suitable for this purpose. After having solved the basic problems, we prepared several OSTK rods some of them with a length of more than 3 nm (based on molecular modeling), proving the capability of the OSTK rod concept.

Equipped with a reliable access to thiol-containing building blocks and solubility enhancing sleeves we are currently investigating the scope of the OSTK concept concerning the rod length. Particular attention will be paid to mediate the solubility of rods in aqueous environment in view of biochemical and biological applications.

EXPERIMENTAL SECTION

General Information. All reactions were carried out under a nitrogen atmosphere unless otherwise noted. NMR spectra were recorded on an NMR spectrometer with the specified measurement frequency and solvents. The residual solvent signals were used as reference. Multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublets (dd), triplet (t), quadruplet (q), and multiplet (m). Column chromatography was performed on silica gel with a particle size of 40−63 μm. IR spectra were recorded as KBr pellets on an IR spectrometer with a monochromator. High-resolution mass spectra (HRMS) were recorded on a Mass spectrometer equipped with a quadropol.

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2,2-Bis(((methylsulfonyl)oxy)methyl)propane-1,3-diyl Dimethanesulfonate (1). To an ice-cooled suspension of pyridine (60 mL) and pentaerythritol (10 g, 73.45 mmol) was added dropwise a solution of methanesulfonyl chloride (23.88 mL, 308.49 mmol) in pyridine (20 mL). After being stirred overnight, a mixture of ice and HCl was added, and the precipitate was filtered off and washed with water, DCM, and Et_2O to yield **1** (32.4 g, 98%) as a white solid. Mp: 208−209 °C. ^{1}H NMR (300 MHz, DMSO-d_6, ppm): 3.27 (s, 12 H), 4.29 (s, 8 H). ^{13}C NMR (75 MHz, DMSO-d_6, ppm): 37.1, 43.0, 66.9. IR (cm^{-1}): 3025, 1471, 1387, 1348, 1412, 988, 972, 925, 750, 867, 835.

2,3,7,8-Tetrathiaspiro[4.4]nonane (2). To DMF (100 mL) were added sulfur (4.29 g, 133.87 mmol) and Na_2S (60%, 8.70 g, 66.89 mmol). The resulting mixture turned deep blue and was stirred for 2 h at 100 °C. After addition of **1** (15 g, 33.44 mmol) and additional stirring for 40 h at the same temperature, ice was added to the mixture. After extraction with DCM four times, the combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The obtained crude brown oil was used immediately in the next step without further purification. HRMS (EI): calcd for $C_5H_8S_4$ $[M]^+$ 195.9509, found 195.9503.

2,2-Bis(mercaptomethyl)propane-1,3-dithiol (3). Method A. $NaBH_4$ (5.06 g, 133.84 mmol) was dissolved in water (50 mL) and added dropwise to an ice-cooled solution of **2** (crude product) in THF (60 mL). After being stirred for 4 h at room temperature, the mixture was quenched with HCl (1 M) and the aqueous layer was extracted with DCM three times. The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude product was crystallized from EtOH to yield **3** (3.86 g, 60% over two steps) as a white solid (mp 71 °C). **Method B.** A solution of the crude product from **2** (500 mg) in THF (8 mL) was added dropwise to an ice-cooled suspension of $LiAlH_4$ (298 mg, 7.64 mmol) and dry THF (15 mL). After 4 h of stirring at room temperature, water and HCl (6 M) was carefully added to the mixture, and the resulting solution was extracted with DCM three times. The collected organic layers were dried over $MgSO_4$ and concentrated in vacuo. After crystallization with EtOH, **3** (310 mg, 64% over two steps) was obtained as a white solid. Mp: 71 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 1.27 (t, J = 8.8 Hz, 4 H), 2.66 (d, J = 8.8 Hz, 8 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 27.9, 43.0. HRMS (EI): calcd for $C_5H_{12}S_4$ $[M]^+$ 199.9822, found 199.9812. IR (cm^{-1}): 1420, 1363, 1279, 1178, 974, 911, 809, 665, 605.

(1,2-Dithiolane-4,4-diyl)dimethanol (5). To DMF (100 mL) were added sulfur (2.45 g, 76.35 mmol) and Na_2S (60%, 4.97 g, 38.18 mmol). The reaction mixture was stirred for 2 h at 80 °C and turned deep blue. After addition of bis(bromomethyl)propane-1,3-diol **4** (10 g, 38,18 mmol), the mixture was heated to 120 °C overnight. To the mixture was added ice, and the water layer was extracted with DCM three times. The combined organic phases were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by column chromatography (DCM/MeOH) to yield **5** (5.4 g, 60%) as a yellow solid. Mp: 84 °C. ^{1}H NMR (300 MHz, MeOD-d_4, ppm): 2.93 (s, 4 H), 3.59 (s, 4 H). ^{13}C NMR (75 MHz, MeOD-d_4, ppm): 44.9, 59.3, 65.0. HRMS (EI): calcd for $C_5H_{10}O_2S_2$ $[M]^+$ 166.0120, found 166.0128. IR (cm^{-1}): 3288, 2933, 2715, 1457, 1420, 1372, 1231, 1191, 1086, 843, 697, 605.

2,2-Bis(mercaptomethyl)propane-1,3-diol (6). $LiAlH_4$ (1.03 g, 27.07 mmol) was suspended in ice-cooled, dry THF (25 mL), and **5** (3 g, 18.04 mmol) in dry THF (25 mL) was slowly added. After the mixture was refluxed for 2 h and cooled to room temperature, water and HCl (concd) were added. The resulting mixture was extracted with DCM four times, and the combined organic layers were dried over $MgSO_4$. After concentration in vacuo, the crude product was purified by column chromatography (DCM/MeOH) to yield **6** (2.17 g, 71% over two steps) as a white solid. The reduction can also be carried out with $NaBH_4$ (4 equiv) with similar yields. Mp: 123 °C. ^{1}H NMR (300 MHz, DMSO-d_6, ppm): 1.96 (t, J = 8.9 Hz, 2 H), 2.43 (d, J = 8.9 Hz, 4 H), 3.29 (s, 4 H), 4.48 (bs, 2 H). ^{13}C NMR (75 MHz, DMSO-d_6, ppm): 25.8, 44.5, 60.9. HRMS (EI): calcd for $C_5H_{12}O_2S_2$ $[M]^+$ 168.0279, found 168.0274. IR (cm^{-1}): 3288, 2938, 2880, 2562, 1458, 1417, 1373, 1231, 1296, 1024, 689.

1,2-Dithiolan-4-ol (8). To DMF (100 mL) were added sulfur (1.47 g, 45.90 mmol) and Na_2S (60%, 5.97 g, 45.90 mmol). The reaction mixture was stirred for 2 h at 80 °C and turned deep blue. After addition of 1,3-dibromopropan-2-ol **7** (10 g, 45.90 mmol), the mixture was heated to 120 °C and stirred overnight. To the mixture was added ice, and the water layer was extracted with DCM four times. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was used immediately in the next step without further purification.

1,3-Dimercaptopropan-2-ol (9). In an ice-cooled Flask, $LiAlH_4$ (3.49 g, 92.06 mmol) was suspended in dry THF (100 mL), and **8** (crude product) in dry THF (40 mL) was slowly added. After the mixture was refluxed for 2 h and cooled to room temperature, water and concentrated HCl were added. The resulting mixture was extracted with DCM four times, and the combined organic layers were dried over $MgSO_4$. After concentration in vacuo, the crude product was purified by column chromatography (DCM/MeOH) to yield **9** (2.9 g, 51%) as a yellow oil. The reduction can also be carried out with $NaBH_4$ (4 equiv) with similar yields. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 1.49 (t, J = 8.7 Hz, 2 H), 2.63−2.81 (m, 4 H), 3.67−3.75 (m, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 29.8, 72.9. HRMS (EI): calcd for $C_3H_8OS_2$ $[M]^+$ 124.0017, found 124.0016.

1,4-Dioxa-7,8-dithiaspiro[4.4]nonane (11). To DMF (10 mL) were added sulfur (123 mg, 3.85 mmol) and Na_2S (60%, 300 mg, 3.85 mmol). The reaction mixture was stirred for 2 h at 100 °C and became deep blue. After addition of **10** (1 g, 3.85 mmol), the mixture was heated to 120 °C for 24 h. To the mixture was added ice, and the water layer was extracted with DCM three times. The combined organic phases were dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was used immediately in the next step without further purification. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 3.18 (s, 4 H) 4.02 (s, 4 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 45.8, 65.4. HRMS (EI): calcd for $C_5H_8O_2S_2$ $[M]^+$ 163.9966, found 163.9958.

(1,3-Dioxolane-2,2-diyl)dimethanethiol (12). $NaBH_4$ (728 mg, 19.28 mmol) was dissolved in NaOH solution (5%, 15 mL) and added dropwise to an ice-cooled solution of **11** (crude product) in THF (15 mL). After being stirred overnight at room temperature, the mixture was washed with DCM three times. The aqueous layer was carefully acidified with HCl (1 M) to pH 3−4 and was extracted with DCM three times. The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude product was purified by column chromatography (DCM) to yield **12** (291 mg, 45% over two steps) as a yellowish oil. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 1.56 (t, J = 8.7 Hz, 2 H), 2.86 (d, J = 8.6 Hz, 4 H), 4.07 (s, 4 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 30.0, 66.2, 109.7. HRMS (ESI): calcd for $C_5H_{11}O_2S_2$ $[M + H^+]$ 167.0201, found 167.0195. IR (cm^{-1}): 2973, 2888, 1412, 1271, 1196, 1115, 1115, 1027, 948, 601.

2,2-Bis(((*tert*-butyldimethylsilyl)oxy)methyl)propane-1,3-dithiol (13). To **6** (1g, 5.94 mmol), *tert*-butylchlorodimethylsilane (1.97 g, 13.07 mmol) and imidazole (2.02 g, 29.71 mmol) were added dry DMF (3 mL). After 2 h of stirring at room temperature, ice was added, and the mixture was extracted with *n*-hexane three times. The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. Purification by column chromatography (DCM) yields **13** (2.26 g, 96%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 0.07 (s, 12 H), 0.91 (s, 18 H), 1.19 (t, ^3J = 9.0 Hz, 2 H), 2.53 (d, ^3J = 9.3 Hz, 4 H), 3.48 (s, 4 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): −5.6, 18.2, 25.4, 25.9, 45.2, 61.6. HRMS (EI): calcd for $C_{17}H_{41}O_2S_2Si_2$ $[M + H]^+$ 397.2081, found 397.2083. IR (cm^{-1}): 2956, 2930, 2850, 1468, 1356, 1250, 1077, 833, 770, 668.

7,11,18,21-Tetrathiatrispiro[5.2.2.512.29.26]henicosane (15). Method A. To **3** (500 mg, 2.49 mmol) and cyclohexanone **14** (0.54 mL, 5.23) in dry chloroform (15 mL) was added dropwise BF_3·Et_2O (0.92 mL, 7.48 mmol). After being stirred for 20 min at room temperature, the mixture was charged with NaOH solution (5%) and the separated aqueous layer was extracted with DCM two times. The combined organic layers were washed with brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was washed with *n*-hexane to yield **15** (820 mg, 94%) as a white solid. **Method B.** To **3** (245 mg,

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1.22 mmol) and cyclohexanone **14** (0.26 mL, 2.57 mmol) in dry chloroform (10 mL) was added a catalyticly amount of *p*-TsOH. The mixture was refluxed for 1.5 h and, after cooling to room temperature, washed two times with saturated $NaHCO_3$ solution, water, and brine. The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residue was washed with cold *n*-hexane to yield **15** (380 mg, 88%) as a white solid. **Method C.** To **3** (300 mg, 1.5 mmol) and cyclohexanone **14** (0.33 mL, 3.16 mmol) in dry chloroform (10 mL) was added I_2 (95 mg, 374 μmol). After being stirred for 1.5 h at room temperature, the mixture was charged with $Na_2S_2O_3$ solution, and the separated organic layer was washed with water and brine and dried over $MgSO_4$. Concentration in vacuo and charging the residue with cold *n*-hexane, yields **15** (450 mg, 1.25 mmol, 86%) as a white solid. Mp: 209 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 1.44−1.49 (m, 4 H), 1.59−1.67 (m, 8 H), 1.95−1.99 (m, 8 H), 2.89 (s, 8H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 22.3, 25.8, 25.92, 34.5, 37.6, 51.5. HRMS (EI): calcd for $C_{17}H_{28}S_4$ $[M]^+$: 360.1074, found 360.106. IR (cm^{-1}): 2928, 2848, 1444, 1430, 857, 822, 776, 758, 700.

7,21-Dioxa-11,18-dithiatrispiro[5.2.2.512.29.26]henicosane (16). To **6** (500 mg, 2.97 mmol), cyclohexanone (0.64 mL, 6.24 mmol), and a catalyticly amount of *p*-TsOH was added toluene (40 mL). After the mixture was refluxed for 4 h, the solvent was removed in vacuo. To the residue was added DCM, and the mixture was washed with saturated $NaHCO_3$ solution, water, and brine. The organic layer was dried with $MgSO_4$ and concentrated under reduced pressure. Purification by column chromatography (*n*-hexane/EtOAc) yielded **16** (620 mg, 64%) as a white solid. Mp: 130 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 1.36−1.47 (m, 4 H), 1.49−1.56 (m, 4 H), 1.60−1.64 (m, 4 H), 1.68−1.74 (m, 4 H), 1.90−1.95 (m, 4 H), 2.69 (s, 4 H), 3.81 (s, 4 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 22.2, 22.4, 25.6, 25.7, 29.0, 31.0, 32.3, 37.6, 51.5, 65.9, 98.5. HRMS (EI): calcd for $C_{17}H_{28}S_2O_2$ $[M]^+$ 328.1531, found 328.1541. IR (cm^{-1}): 2935, 2863, 1108, 2846, 1443, 1269, 1256, 1156, 1130, 1087, 1068, 1037, 961, 917, 822.

(1,5-Dithiaspiro[5.5]undecane-3,3-diyl)dimethanol (18). To **16** (50 mg, 152 μmol) were added MeOH (5 mL) and TFA (1 mL). The mixture was stirred at 60 °C for 48 h and concentrated under reduced pressure. The residue was purified by column chromatography (DCM/MeOH) to yield **18** (35 mg, 93%) as a white solid. Mp: 188 °C. ^{1}H NMR (300 MHz, DMSO-d_6, ppm): 1.35−1.44 (m, 2 H), 1.47−1.59 (m, 4 H), 1.79−1.94 (m, 4 H), 2.58 (s, 4 H), 3.46 (s, 4 H). ^{13}C NMR (75 MHz, DMSO-d_6, ppm): 22.4, 25.8, 29.0, 35.8, 38.0, 51.1, 63.0. HRMS (EI): calcd for $C_{11}H_{20}S_2O_2$ $[M]^+$ 248.0905, found 248.0902.

7,11,18,21-Tetrathiatrispiro[5.2.2.512.29.26]henicosane-3,15-diylbis(2,2-dimethylpropanoate) (20a). To **3** (242 mg, 1.21 mmol) and **19** (502 mg, 2.54 mmol) in dry chloroform (15 mL) were added dropwise $BF_3{\cdot}Et_2O$ (0.46 mL, 3.62 mmol). After being stirred for 20 min at room temperature, the mixture was charged with NaOH solution (5%), and the separated aqueous layer was extracted with DCM two times. The combined organic layers were washed with brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was purified by column chromatography (DCM/MeOH) to yield **20a** (540 mg, 80%) as a white solid. Mp: 263−264 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 1.21 (s, 18 H), 1.73−1.83 (m, 4 H), 1.85−2.03 (m, 8 H), 2.08−2.19 (m, 4 H), 2.9 (d, 8 H), 4.81−4.89 (m, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 26.0, 26.7, 27.2, 33.7, 34.5, 34.7, 38.8, 50.4, 69.6, 177.8. HRMS (EI): calcd for $C_{27}H_{44}O_4S_4$ $[M]^+$ 560.2122, found 560.2138. IR (cm^{-1}): 2975, 2954, 2940, 1727, 1478, 1424, 1401, 1279, 1220, 1157, 895.

7,11,18,21-Tetrathiatrispiro[5.2.2.512.29.26]henicosane-3,15-diol (20b). Compound **20a** (500 mg, 891 μmol) was dissolved in dry DCM (50 mL) and cooled to −78 °C. DIBALH (1 M in *n*-hexane, 4.46 mL, 4.46 mmol) was added, and the mixture was stirred 2 h at this temperature. After the mixtur was warmed to room temperature, MeOH (0.4 mL) was added, and the resulting slurry was treated with 20% tartaric acid. The precipitate was filtered, washed with 20% tartaric acid, water, DCM, and Et_2O, and dried in vacuo to yield **20b** (320 mg, 92%) as a white solid. Mp: 260−261 °C. ^{1}H NMR (300 MHz, Pyridine-d_5, ppm): 1.96−2.22 (m, 12 H), 2.40−2.60 (m, 4 H), 3.04 (s, 4 H), 3.12 (s, 4 H), 3.90−4.05 (m, 2 H); insufficient solubility for ^{13}C spectrum. HRMS (EI): calcd for $C_{17}H_{28}O_2S_4$ $[M]^+$ 392.0972, found 392.0973. IR (cm^{-1}): 3359, 2858, 1697, 1432, 1405, 1276, 1223, 1067, 957, 697.

7,11,18,21-Tetrathiatrispiro[5.2.2.512.29.26]henicosane-3,15-dione (21). Oxalyl chloride (0.09 mL, 1.03 mmol) in dry DCM (15 mL) was cooled to −78 °C. DMSO (0.1 mL, 1.36 mmol) in dry DCM (5 mL) was added dropwise, and the mixture was stirred at this temperature for 30 min. Compound **20b** (130 mg, 331 μmol) in dry DMSO (15 mL) was added dropwise, and the mixture was additionally stirred for 30 min. After addition of dry triethylamine (0.45 mL, 3.31 mmol), the reaction was allowed to warm to room temperature and stirred overnight. The reaction mixture was washed with HCl (1 M) and brine and dried with $MgSO_4$. After concentration in vacuo, the residue was purified by column chromatography (DCM/MeOH) to yield **21** (80 mg, 62%) as a white solid. Mp: 275−276 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 2.29−2.41 (m, 8 H), 2.50−2.59 (m, 8 H), 2.92−3.02 (s, 8 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 34.9, 36.9, 37.7, 49.3, 209.2. HRMS (EI): calcd for $C_{17}H_{24}O_2S_4$ $[M]^+$ 388.0659, found 388.0648. IR (cm^{-1}): 2900, 1717, 1438, 1403, 1335, 1184, 801, 765, 735, 698, 651.

1,1′-(7,11,18,21-Tetrathia-3,15-diazatrispiro-[5.2.2.512.29.26]henicosane-3,15-diyl)bis(2-chloroethan-1-one) (23). Compounds **3** (50 mg, 249 μmol), **22** (96 mg, 548 μmol), and a catalyticly amount of *p*-TsOH were refluxed in chloroform (5 mL) in a Dean−Stark apparatus for 4 h. The mixture was washed with saturated $NaHCO_3$ solution, water, and brine. The organic layer was dried with $MgSO_4$ and the solvent was removed in vacuo. The crude product was purified by column chromatography (DCM/MeOH) to yield **23** (95 mg, 74%) as a white solid. Mp: 214−219 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 2.03−2.16 (m, 8 H), 2.91−2.99 (m, 8 H), 3.58−3.66 (m, 4 H), 3.69−3.79 (m, 4 H), 4.07 (s, 4 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 24.7, 34.3, 35.4, 36.2, 37.4, 38.7, 40.9, 42.8, 46.0, 49.0, 164.9. HRMS (EI): calcd for $C_{19}H_{28}N_2O_2Cl_2S_4$ $[M]^+$ 514.0411, found 514.0421.

Dibenzyl 7,11,18,21-Tetrathia-3,15-diazatrispiro[5.2.2.512.29.26]henicosane-3,15-dicarboxylate (25). To **3** (457 mg, 2.28 mmol) and **24** (1.12 g, 4.79 mmol) in dry chloroform (15 mL) was added dropwise $BF_3.Et_2O$ (0.72 mL, 5.7 mmol). After being stirred for 20 min at room temperature, the mixture was charged with NaOH solution (5%), and the separated aqueous layer was extracted with DCM two times. The combined organic layers were washed with brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was purified by column chromatography (DCM/MeOH) to yield **25** (1.4 g, 2.22 mmol, 97%) as a white solid. Mp: 147 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 1.99−2.07 (m, 8 H), 2.92 (s, 8 H), 3.58−3.69 (m, 8 H), 5.14 (s, 4 H), 7.29−7.42 (m, 10 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 25.9, 34.3, 36.8, 40.5, 49.3, 67.2, 127.9, 128.1, 128.5, 136.7, 155.1. HRMS (EI): calcd for $C_{31}H_{38}N_2O_4S_4$ $[M]^+$ 630.1714, found 630.1701. IR (cm^{-1}): 2940, 1462, 1418, 1273, 1223, 1194, 1127, 1055, 1010, 751, 764, 696.

Dibenzyl 7,21-Dioxa-11,18-dithia-3,15-diazatrispiro[5.2.2.512.29.26]henicosane-3,15-dicarboxylate (26). Compound **6** (800 mg, 4.75 mmol), **24** (2.33 mL, 9.98 mmol), and a catalyticly amount of *p*-TsOH were refluxed with toluene (20 mL) in a Dean−Stark apparatus for 4 h. The slurry was concentrated in vacuo, and DCM was added. The mixture was washed with saturated $NaHCO_3$ solution, water, and brine. The organic layer was dried with $MgSO_4$, and the solvent was removed in vacuo. The crude product was purified by column chromatography (DCM/MeOH) to yield **26** (1.82 g, 64%) as a white solid. Mp: 108 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 1.80−1.89 (m, 4 H), 1.99−2.06 (m, 4 H), 2.74 (s, 4 H), 3.48−3.56 (m, 4 H), 3.57−3.64 (m, 4 H), 3.86 (s, 4 H), 5.14 (s, 4 H), 7.32−7.40 (m, 10 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 29.0, 30.8, 40.2, 40.7, 49.3, 66.0, 67.2, 97.0, 127.8, 128.0, 128.5, 136.7, 155.0. HRMS (EI): calcd for $C_{31}H_{38}N_2O_6S_2$ $[M]^+$ 598.2171, found 598.2193. IR (cm^{-1}): 3288, 2933, 1457, 1420, 1372, 1231, 1086, 843, 697, 605.

7,11,18,21-Tetrathia-3,15-diazatrispiro[5.2.2.512.29.26]-henicosane (27). Compound **25** (250 mg, 396 μmol) in HBr (33% in acetic acid, 20 mL) was heated to 60 °C for 2 h. After the mixture

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was cooled to room temperature, water was added and the resulting solution was carefully treated with NaOH solution to pH 10 under ice cooling. The precipitate was collected washed two times with petroleum ether, DCM, and water and dried in vacuo to yield **27** (103 mg, 72%) as a white solid. Mp: >280 °C dec. ^{1}H NMR (300 MHz, DMSO-d_6, ppm): 2.21 (bs, 8 H), 3.03 (bs, 8 H), 3.11 (bs, 8 H). ^{13}C NMR (151 MHz, DMSO-d_6, ppm): 21.7, 24.1, 33.7, 40.4, 47.2. HRMS (EI): calcd for $C_{15}H_{26}N_2S_4$ $[M]^+$ 362.0979, found 362.0973. IR (cm^{-1}): 3389, 2938, 2813, 1615, 1430, 1283, 1148, 1029, 862, 779.

2,2′-(2,5-Dimethyl-1,4-phenylene)bis(5,5-dimethyl-1,3-dioxane) (29). Compound **28** (18 g, 68.19 mmol) was dissolved in dry THF (200 mL) and cooled to −60 °C. BuLi solution (1.6 M in *n*-hexane, 46.88 mL, 75.01 mmol) was added slowly, and after for 15 min of stirring dry DMF (10.52 mL, 136.39 mmol) was added. The reaction was warmed to room temperature, stirred for 2 h, and charged with HCl (concd). The mixture was extracted with Et_2O two times, and the combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was used without further purification and refluxed overnight in a Dean−Stark apparatus with toluene (130 mL), neopentyl glycol (14.2 g, 136.39 mmol), and a catalytic amount of *p*-TsOH. The mixture was washed with saturated $NaHCO_3$ solution, water, and brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was treated a second time as described above the starting compound, and the obtained crude product was crystallized in *n*-hexane to yield **29** (9.74 g, 42%) as yellowish needles. Mp: 180−182 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 0.81 (s, 6 H), 1.33 (s, 6 H), 2.38 (s, 6 H), 3.64−3.80 (m, 8 H), 5.48 (s, 2 H), 7.42 (s, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 18.3, 21.9, 23.2, 30.2, 77.8, 100.0, 127.8, 133.0, 136.4. HRMS (EI): calcd for $C_{20}H_{31}O_4$ $[M + H]^+$ 335.2211, found 335.2190. IR (cm^{-1}): 2980, 2860, 2106, 1700, 1655, 1467, 1467, 1412, 1357, 1231, 1214, 1189, 1095.

2,5-Dimethylterephthalaldehyde (30). Compound **29** (4.5 g 13.45 mmol) was refluxed in water (2.6 mL) and TFA (20 mL) for 15 min. The mixture was concentrated in vacuo, and the residue was charged with DCM. The mixture was washed with saturated $NaHCO_3$ solution and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was crystallized in *n*-hexane to yield **30** (1.4 g, 64%) as yellow crystals. Mp: 98−100 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 2.68 (s, 6 H), 7.67 (s, 2 H), 10.31 (s, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 18.7, 134.6, 136.8, 138.0, 192.1. HRMS (EI): calcd for $C_{10}H_{10}O_2$ $[M]^+$ 162.0681, found 162.0681. IR (cm^{-1}): 2979, 2931, 1690, 1459, 1439, 1417, 1395, 1288, 1163, 997, 893.

2,2′-(2,5-Dimethyl-1,4-phenylene)bis(5,5-dimethyl-1,3-dithiane) (31). To dry chloroform (20 mL) were added **30** (100 mg, 616.58 mmol), 2,2-dimethylpropane-1,3-dithiol, and I_2 (39 mg, 0.15 mmol), and the solution was stirred overnight at room temperature. The mixture was charged with $Na_2S_2O_3$ solution, and the aqueous layer was extracted with DCM two times. The combined organic layers were washed with brine, dried with $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by column chromatography (*n*-hexane/DCM, 2:1) to yield **31** (185 mg, 75%) as yellow needles. Mp: 261−266 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 1.13 (s, 6 H), 1.40 (s, 6 H), 2.41 (s, 6 H), 2.50 (d, J = 14.1 Hz, 4 H), 3.02 (d, J = 14.1, 4 H), 5.13 (s, 2 H), 7.44 (s, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 18.6, 23.2, 25.8, 31.3, 44.7, 48.2, 129.8, 133.4, 136.4. HRMS (EI): calcd for $C_{20}H_{30}S_4$ $[M]^+$ 398.1230, found 398.1217. IR (cm^{-1}): 2975, 2957, 2923, 1500, 1461, 1445, 1378, 1359, 1262, 1191, 1174, 992.

1,4-Dibutylbenzene (33a). To magnesium (25.3 g, 1 mol) and a catalyticly amount of I_2, was added 5 mL of a solution of 1-brombutane (95 mL, 887 mmol) in dry Et_2O (400 mL). After the start of the reaction, the rest of the solution was added dropwise, and the mixture was refluxed for 1 h. After cooling to 0 °C, $[Ni(dppp)Cl_2$ (250 mg, 0.46 mmol, 0.1 mol %) and a solution of 1,4-dichlorbenzene (59 g, 401 mmol) in dry Et_2O (300 mL) and dry THF (50 mL) was added, followed by refluxing for 48 h. To the mixture were added ice, water, and HCl (3 M). The water layer was extracted with Et_2O two times, and the combined organic layers were washed with EDTA solution and brine and dried over $MgSO_4$. Concentration in vacuo yielded **33a** (61.40 g, 81%) as colorless oil, which was immediately used in the next step. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 0.97 (t, J = 7.3 Hz, 6 H), 1.32−1.47 (m, 4 H), 1.57−1.69 (m, 4 H), 2.62 (t, J = 7.7 Hz, 4 H), 7.13 (s, 4 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 18.6, 23.2, 25.8, 31.3, 44.7, 48.2, 129.8, 133.4, 136.4 (**33a** was already described in ref 25, ^{1}H NMR data are essentially identical to our data).

1,4-Dipentylbenzene (33b). Prepared like **33a**, yielding **33b** (63%) as a colorless liquid, which was used in the next step without further purification. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 0.95 (t, J = 6.7 Hz, 6 H), 1.34−1.42 (m, 8 H), 1.61−171 (m, 4 H), 2.62 (t, J = 7.6 Hz, 8 H), 7.14 (s, 4 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 14.0, 22.6, 31.3, 31.6, 35.5, 128.2, 140.1.

1,4-Bis(2-ethylhexyl)benzene (33c). Prepared like **33a** with additional fractionated distillation in vacuo, yielding **33c** as a yellow oil (67%). Bp (6×10^{-3} mbar): 120−125 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 0.89 (t, J = 7.50 Hz, 12 H) 1.22−1.34 (m, 16 H) 1.53−1.61 (m, 4 H), 2.52 (d, J = 7.2 Hz, 4 H), 7.07 (s, 4 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 10.8, 14.1, 23.0, 25.5, 28.9, 32.4, 39.7, 41.0, 128.9, 138.9. HRMS (EI): calcd for $C_{22}H_{38}$ $[M]^+$ 302.2979, found 302.2977 (**33c** was already described in ref 26 without any analytical data).

1,4-Dibromo-2,5-dibutylbenzene (34a). To ice-cooled **33a** (61.40 g, 324 mmol) and I_2 (819 mg, 3.23 mmol, 0.5 mol %) was added dropwise bromine (33.05 mL, 645 mmol) under stirring with rigorous exclusion of light. Afterward, the mixture was stirred at room temperature for 48 h. NaOH solution (20%) was added, and the aqueous layer was extracted with Et_2O three times. The combined organic layers were washed with water, dried over $MgSO_4$, and concentrated in vacuo. The crude product **34a** (99 g, 88%) was obtained as a white solid and was used in the next step without further purification. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 0.98 (t, J = 7.3 Hz, 6 H), 1.36−1.49 (m, 4 H), 1.54−1.66 (m, 4 H), 2.68 (t, J = 7.6 Hz, 4 H), 7.39 (s, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 13.9, 22.4, 31.9, 35.2, 123.1, 133.8, 141.3 (**34a** was already reported in ref 33; NMR data are essentially identical to our data).

1,4-Dibromo-2,5-dipentylbenzene (34b). Prepared like **34a** yielding **34b** (77%) as a colorless liquid, which was used in the next step without further purification. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 0.94 (t, J = 6.9 Hz, 6 H), 1.33−1.41 (m, 8 H), 1.55−1.67 (m, 4 H), 2.66 (t, J = 7.7 Hz, 4 H), 7.38 (s, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 14.0, 22.5, 29.5, 31.5, 35.5, 123.1, 129.8, 133.8, 141.4.

1,4-Dibromo-2,5-bis(2-ethylhexyl)benzene (34c). Prepared like **34a**, though 2.3 equiv of bromine was used. Compound **34b** (87%) was obtained as yellow oil, which was used in the next step without further purification. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 0.88−0.94 (m, 12 H), 1.27−1.37 (m, 16 H), 1.66−1.73 (m, 2 H), 2.60 (d, J = 7.2 Hz, 4 H), 7.34 (s, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 10.7, 14.1, 23.0, 25.5, 28.6, 32.3, 39.2, 39.8, 123.3, 134.9, 140.4; MS(EI): calcd for $C_{22}H_{36}Br_2$ (M^+) 458.1184, found 458.1188 (**34c** was already reported in ref 27 without any analytical data).

2,5-Dibutylterephthalaldehyde (35a). Compound **34a** (100.2 g, 287.83 mmol) was dissolved in dry THF (1000 mL) and cooled to −60 °C. BuLi solution (1.6 M in *n*-hexane, 198 mL, 316.6 mmol) was added slowly, and after stirring for 15 min dry DMF (46.5 mL, 604.4 mmol) was added to mixture. The reaction was warmed to room temperature, stirred for 2 h, and charged with HCl (concd). The mixture was concentrated in vacuo, and the residue was extracted with Et_2O two times. The combined organic layers were washed with water, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was used without further purification and refluxed overnight in a Dean−Stark apparatus with toluene (700 mL), neopentyl glycol (45 g, 431.75 mmol), and a catalytic amount of *p*-TsOH. The mixture was washed with saturated $NaHCO_3$ solution, dried over $MgSO_4$, and concentrated in vacuo. The residue was treated a second time as described above, and the obtained crude product was crystallized in *n*-hexane. The obtained intermediate was refluxed with TFA (200 mL) and water (30 mL) for 30 min. After being cooled to room temperature, the mixture was concentrated under reduced pressure and residue was charged with DCM. The organic layer was neutralized with saturated $NaHCO_3$ solution, washed with water, and dried over

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$MgSO_4$, and the solvent was removed in vacuo. Purification with column chromatography (*n*-hexane/EtOAc) yields **35a** (10.64 g, 15%) as a waxy white solid. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 0.95 (t, J = 7.3 Hz, 6 H), 1.35−1.49 (m, 4 H), 1.56−1.69 (m, 4 H), 3.05 (t, J = 7.8 Hz, 4 H), 7.73 (s, 2 H), 10.36 (s, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 13.8, 22.5, 31.5, 34.4, 133.1, 136.8, 143.3, 191.6. HRMS (EI): calcd for $C_{16}H_{22}O_2$ $[M]^+$ 246.1620, found 246.1624. IR (cm^{-1}): 3354, 2939, 2874, 1681, 1454, 1402, 1306, 1159, 868, 723 (**35a** was already reported in ref 6 with essentially the same analytical data).

2,5-Dipentylterephthalaldehyde (35b). Prepared like **35a** yielding **35b** (22%) as a waxy white solid. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 0.87−0.94 (m, 6 H), 1.31−1.41 (m, 8 H), 1.59−1.69 (m, 4 H), 3.04 (t, J = 7.8 Hz, 4 H), 7.74 (s, 2 H), 10.37 (s, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 13.9, 22.4, 31.6, 31.8, 32.0, 133.1, 136.7, 143.4, 191.7. HRMS (EI): calcd for $C_{18}H_{26}O_2$ $[M]^+$ 274.1933, found 274.1927. IR (cm^{-1}): 3347, 2961 2919, 2853, 1674, 1457, 1401, 1312, 1155, 865.

2,5-Bis(2-ethylhexyl)terephthalaldehyde (35c). Prepared like **35a** yielding **35b** (32%) as a brown oil. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 0.82−0.94 (m, 12 H), 1.21−1.39 (m, 16 H), 1.51−1.60 (m, 2 H), 2.98 (d, J = 7.2 Hz, 4 H), 7.72 (s, 2 H), 10.40 (s, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 10.7, 14.0, 22.9, 25.5, 28.7, 32.2, 35.9, 42.1, 133.5, 136.9, 142.5, 191.6. HRMS (EI): calcd for $C_{24}H_{38}O_2$ $[M]^+$ 358.2866, found 358.2869. IR (cm^{-1}): 3375, 2958, 2928, 2857, 1688, 1461, 1377, 1172, 1106, 783.

2-Phenyl-1,3-dithian-5-ol (36). To benzaldehyde (39 mg, 366 μmol) and **9** (50 mg, 403 μmol) in dry chloroform (5 mL) was added I_2 (5 mg, 19 μmol, 5 mol %). The mixture was stirred at room temperature for 1 h, and $Na_2S_2O_3$ solution was added. The organic layer was dried with $MgSO_4$ and concentrated in vacuo. After purification with column chromatography (DCM), the two diastereomers of **36** (75 mg, 97%) were obtained as a white solid. **85 K1**. Mp: 99.5 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 2.97 (dd, J = 13.9 Hz, J = 4.2 Hz, 2 H), 3.32 (d, J = 13.9 Hz, 2 H), 3.99 (bs, 1 H), 5.08 (s, 1 H), 7.32−7.41 (m, 3 H), 7.46−7.51 (m, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 39.0, 50.7, 55.4, 127.7, 128.8, 128.8. **85 K2**. Mp: 139 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 2.94 (d, ^3J = 6.5 Hz, 4 H,), 4.11 (dt, ^3J = 12.9 Hz, ^3J = 6.5 Hz, 1 H), 5.07 (s, 1 H), 7.30−7.41 (m, 3 H), 7.54−7.58 (m, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 37.2, 49.7, 65.8, 127.8, 128.5, 128.7, 137.1. HRMS (EI): calcd for $C_{10}H_{12}OS_2$ $[M]^+$ 212.0330, found 212.0328.

2-Phenyl-1,3-dithian-5-one (37). To dry DMSO (5 mL) and **36** (25 mg, 118 μmol) was added acetic anhydride (56 μL, 589 μmol), and the mixture was stirred at room temperature for 20 h. Afterward, the mixture was concentrated under reduced pressure and purified with column chromatography (DCM) to yield **37** (13 mg, 52%) as a yellow oily solid. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 3.46 (d, ^3J = 14.6 Hz, 2 H), 3.72 (d, ^3J = 14.6 Hz, 2 H), 5.63 (s, 1 H), 7.33−7.42 (m, 3 H), 7.54−7.57 (m, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 35.5, 38.2, 48.9, 127.6, 128.9. HRMS (EI): calcd for $C_{10}H_{10}OS_2$ $[M]^+$ 210.0168, found 210.0170.

4,4′-(2,5-Dibutyl-1,4-phenylene)bis(cyclohexan-1-ol) (38a). To **35a** (150 mg, 609 μmol) and **9** (159 mg, 1.28 mmol) in dry chloroform (35 mL) was added I_2 (15 mg, 61 μmol, 10 mol %). After the mixture was stirred for 1 h at room temperature, $Na_2S_2O_3$ solution was added. The organic layer was dried with $MgSO_4$ and concentrated in vacuo. The crude product was purified by column chromatography (DCM/MeOH) to yield the two diastereomers of **38a** (262 mg, 94%) as a beige solid. Mp: 201 °C. ^{1}H NMR (300 MHz, DMSO-d_6, ppm): 0.89−0.96 (m, 6 H), 1.28−1.42 (m, 4 H), 1.45−1.58 (m, 4 H), 2.59−2.73 (m, 4 H), 2.77 (dd, ^3J = 14.0 Hz, ^3J = 3.5 Hz, 4 H), 3.38 (d, ^3J = 14 Hz, 4 H), 3.85 (bs, 2 H), 4.72 (bs, 2 H), 5.39 (s, 2 H), 7.29 (s, 0.5 H), 7.37 (s, 1.5 H). ^{13}C NMR (75 MHz, DMSO-d_6, ppm): 14.4, 22.4, 31.9, 33.8, 37.8, 38.1, 46.0, 55.5, 66.8, 129.3, 129.8, 135.7, 137.5, 137.8, 138.2. HRMS (EI): calcd for $C_{22}H_{34}O_2S_4$ $[M]^+$ 458.1436, found 458.1433. IR (cm^{-1}): 3291, 2911, 2866, 1453, 1385, 1183, 1048, 901, 769, 641.

4,4′-(2,5-Dipentyl-1,4-phenylene)bis(cyclohexan-1-ol) (38b). Prepared like **38a** yielding **38b** (91%) as a beige solid. Mp: 180−182 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 0.93−0.97 (m, 6 H), 1.39−1.43 (m, 8 H), 1.63−1.68 (m, 4 H), 2.66−2.71 (m, 4 H), 2.92−3.00 (m, 4 H), 3.33 (d, ^3J = 14.1 Hz, 4 H), 3.99 (bs, 2 H), 5.19 (s, 2 H), 7.44 (s, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 14.0, 22.5, 31.0, 31.7, 32.5, 39.4, 46.7, 55.3, 129.6, 136.1, 138.1: HRMS (EI): calcd for $C_{24}H_{38}O_2S_4$ $[M]^+$ 486.1749, found 486.1751. IR (cm^{-1}): 3276, 2937, 2844, 1461, 1397, 1175, 1044, 747, 635.

4,4′-(2,5-Bis(2-ethylhexyl)-1,4-phenylene)bis(cyclohexan-1-ol) (38c). Prepared like **38a** yielding **38c** (99%) as an orange oil. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 0.90−0.98 (m, 12 H), 1.33−1.59 (m, 16 H), 1.50−1.59 (m, 2 H), 2.57−2.62 (m, 4 H), 2.93−2.99 (m, 4 H), 3.30 (d, ^3J = 14.1 Hz, 4 H), 3.98 (bs, 2 H), 5.18 (s, 2 H), 7.41 (s, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 11.1, 14.13, 23.0, 26.0, 29.0, 32.6, 37.1, 39.4, 40.8, 46.8, 55.3, 130.9, 136.1, 137.0. HRMS (EI): calcd for $C_{30}H_{50}O_2S_4$ $[M]^+$ 570.2688, found 570.2687. IR (cm^{-1}): 3288, 2933, 2858, 1490, 1465, 1378, 1318, 1172, 1040, 750.

8,8′-(2,5-Bis(2-ethylhexyl)-1,4-phenylene)bis(1,4-dioxa-7,9-dithiaspiro[4.5]decane) (39c). To **35c** (54 mg, 150 μmol) and **12** (50 mg, 301 μmol) in dry chloroform (5 mL) was added I_2 (4 mg, 15 μmol, 10 mol %). After the mixture was stirred for 1.5 h at room temperature, $Na_2S_2O_3$ solution was added. The organic layer was washed with NaOH solution (5%), dried with $MgSO_4$, and concentrated in vacuo. The crude product was purified by column chromatography (DCM) to yield **39c** (55 mg, 56%) as a beige solid. Mp: 155−158 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 0.84−1.01 (m, 12 H), 1.19−1.37 (m, 16 H), 1.52−1.57 (m, 2 H), 2.49−2.61 (m, 4 H), 2.65−2.80 (m, 4 H), 3.13−3.23 (m, 4 H), 4.07 (dd, J = 5.3, 1.00 Hz, 8 H), 5.31 (s, 2H), 7.46 (m, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 11.2, 14.0, 23.0, 25.9, 29.1, 32.7, 37.3, 38.7, 40.9, 47.4, 64.9, 65.6, 99.8, 130.5, 134.8, 137.2. HRMS (EI): calcd for $C_{34}H_{54}O_4S_4$ $[M]^+$ 654.2899, found 654.2898. IR (cm^{-1}): 3454, 2955, 1461, 1305, 1248, 1098, 1020, 979, 740, 681.

2,2′-(2,5-Dibutyl-1,4-phenylene)bis(1,3-dithian-5-one) (40a). To **38a** (75 mg, 164 μmol) in dry DMSO (5 mL) was added acetic anhydride (155 μL, 1.63 mmol), and the reaction was stirred at room temperature for 20 h. The mixture was concentrated in vacuo, and the residue was purified with column chromatography (DCM), to yield **40a** (33 mg, 44%) as a yellowish waxy solid. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 0.95−1.05 (m, 6 H), 1.40−1.50 (m, 4 H), 1.58−1.70 (m, 4 H), 2.70−2.79 (m, 4 H), 3.40 (d, ^3J = 14.2 Hz, 4 H), 3.80 (d, ^3J = 14.2 Hz, 4 H), 5.85 (s, 2 H), 7.54 (s, 2 H); insufficient solubility for ^{13}C spectrum. HRMS (EI): calcd for $C_{22}H_{30}O_2S_4$ $[M]^+$: 454.1123, found 454.1124. IR (cm^{-1}): 3392, 2956, 2922, 2851, 1703, 1465, 1399, 1247, 1181, 773.

2,2′-(2,5-Dipentyl-1,4-phenylene)bis(1,3-dithian-5-one) (40b). Prepared like **40a** yielding **40b** (70%) as a yellowish waxy solid. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 0.91−1.01 (m, 6 H), 1.38−1.50 (m, 8 H), 1.60−1.73 (m, 4 H), 2.65−2.78 (m, 4 H), 3.40 (d, ^3J = 14.2 Hz, 2 H), 3.81 (d, ^3J = 14.2 Hz, 4 H), 5.85 (s, 4 H), 7.54 (s, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 14.0, 22.5, 31.0, 31.7, 32.5, 39.0, 45.6, 104.45, 129.8, 135.3, 138.7. HRMS (EI): calcd for $C_{24}H_{34}O_2S_4$[$M]^+$ 482.1436, found 482.1430. IR (cm^{-1}): 3417, 2954, 2925, 2853, 1713, 1462, 1400, 1246, 1176, 786.

2,2′-(2,5-Bis(2-ethylhexyl)-1,4-phenylene)bis(1,3-dithian-5-one) (40c). Prepared like **40a** yielding **40b** (42%) as an orange waxy solid. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 0.87−0.99 (m, 12 H), 1.20−1.38 (m, 16 H), 1.57−1.68 (m, 2 H), 2.62−2.69(m, 4 H), 3.37 (d, ^3J = 14.2 Hz, 4 H), 3.79 (d, ^3J = 14.2 Hz, 4 H), 5.85 (s, 2 H), 7.51 (s, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 11.0, 14.1, 23.0, 25.9, 28.9, 32.6, 37.1, 39.1, 40.8, 45.9, 130.7, 135.0, 137.4, 201.6. HRMS (EI): calcd for $C_{30}H_{46}O_2S_4$ $[M]^+$ 566.2375, found 566.2367. IR (cm^{-1}): 3399, 2956, 2926, 2859, 1708, 1459, 1374, 1244, 1175, 1019.

((2,5-Dipentyl-1,4-phenylene)bis(1,5,8,10-tetrathiaspiro-[5.5]undecane-9,3,3-triyl))tetramethanol (41). To **40b** (100 mg, 207 μmol) and **13** (181 mg, 456 μmol) in dry chloroform (15 mL) was added I_2 (5 mg, 21 μmol, 10 mol %). After the mixture was stirred for 2 h at room temperature, HF (35 μL, 830 μmol, 50%) was added. Stirring was continued for 2 h, and the precipitate was collected, washed with saturated $NaHCO_3$ solution and DCM, and dried in vacuo. Compound **41** (95 mg, 58%) was obtained as a yellowish solid,

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which was used immediately in the next step without further purification. Insufficient solubility for NMR spectroscopy.

3,3′-(2,5-Dipentyl-1,4-phenylene)bis(11,18-dioxa-2,4,7,21-tetrathiatrispiro[5.2.2.512.29.26]henicosane) (42). Compound **41** (50 mg, 63.8 μmol), cyclohexanone **14** (14 mg, 140 μmol), benzene (15 mL), and a catalytic amount of *p*-TsOH was refluxed in a Dean−Stark apparatus for 20 h. After the reaction has finished, the mixture was concentrated in vacuo, charged with DCM, washed with $NaHCO_3$ solution, and dried over $MgSO_4$. After removal of the solvent in vacuo, the crude product was purified with column chromatography (DCM/MeOH) to yield **42** (45 mg, 75%) as a beige solid. Mp: 193 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 0.930 (bs, 6 H), 1.24−1.90 (m, 32 H), 2.57−2.61 (m, 8 H), 2.88 (bs, 4 H), 3.21 3.49 (m, 8 H), 3.53−4.41 (m, 8 H), 5.22 (bs, 2 H) 7.41 (bs, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 14.0, 22.4, 30.9, 31.9, 32.7, 43.4, 48.8, 65.7, 98.7, 129.6, 136.0, 138.9. HRMS (ESI): calcd for $C_{46}H_{71}O_4S_8$ $[M + H]^+$ 943.3113, found 943.3149. IR (cm^{-1}): 3316, 2925, 2861, 1455, 1298, 1160, 1112, 1037, 916, 796.

1,1′-((2,5-Dipentyl-1,4-phenylene)bis(11,18-dioxa-2,4,7,21-tetrathia-15-azatrispiro[5.2.2.512.29.26]henicosane-3,15-diyl))bis(2-chloroethan-1-one) (43). Prepared like **42** though 1-(2-chloroacetyl)piperidin-4-one **22** was used as reactant, yielding **43** (97%) as a white solid. Mp: >285 °C dec. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 0.91−0.99 (m, 6 H), 1.36−1.42 (m, 8 H), 1.51−1.64 (m, 4 H), 1.86−2.00 (m, 8 H), 2.49−2.68 (m, 12 H), 3.28−3.45 (m, 8 H), 3.54 (bs, 4 H), 3.66 (bs, 4 H), 3.80−3.92 (m, 8 H), 4.10 (s, 3 H), 4.17 (s, 1 H), 5.26 (s, 2 H), 7.44 (s, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 14.1, 22.5, 31.0, 31.3, 31.9, 32.7, 40.9, 41.0, 43.4, 44.8, 48.3, 48.9, 66.0, 96.8, 129.8, 135.3, 138.6, 165.0. HRMS (ESI): calcd for $C_{48}H_{71}Cl_2N_2O_6S_8$ $[M + H]^+$ 1097.2449, found 1097.2473. IR (cm^{-1}): 2933, 2870, 1724, 1649, 1469, 1284, 1168, 1123, 894, 730.

((2,5-Dibutyl-1,4-phenylene)bis(1,3-dithiane-2,5,5-triyl))-tetramethanol (44a). Prepared like **41** though **35a** was used as reactant, yielding **44a** (48%) as a yellow solid. Mp: >292 °C dec. ^{1}H NMR (300 MHz, DMSO-d_6, ppm): 0.92 (t, ^3J = 7.2 Hz, 6 H), 1.31−1.43 (m, 4 H), 1.45−1.56 (m, 4 H), 2.61−2.67 (m, 8 H), 3.07 (d, ^3J = 14.0 Hz, 4 H), 3.32 (s, 4 H), 3.89 (s, 4 H), 4.25 (bs, 4 H), 5.30 (s, 2 H), 7.33 (s, 2 H). ^{13}C NMR (75 MHz, DMSO-d_6, ppm): 14.8, 22.8, 32.3, 34.2, 35.8, 47.7, 60.3, 67.2, 130.1, 137.4, 138.5. HRMS (EI): calcd for $C_{26}H_{42}O_4S_4$ $[M]^+$ 546.1960, found 546.1976. IR (cm^{-1}): 3306, 2930, 2877, 1499, 1465, 1427, 1295, 1089, 1032, 724.

((2,5-Dipentyl-1,4-phenylene)bis(1,3-dithiane-2,5,5-triyl))-tetramethanol (44b). Prepared like **41** though **35b** was used as reactant, yielding **44b** (99%) as a yellow solid. Mp: >288 °C dec. Insufficient solubility for NMR spectroscopy. HRMS (ESI): calcd for $C_{28}H_{47}O_4S_4$ $[M + H]^+$ 575.2352, found 575.2351. IR (cm^{-1}): 3343, 2926, 2855, 1915, 1610, 1397, 1292, 1021, 836, 697.

((2,5-Bis(2-ethylhexyl)-1,4-phenylene)bis(1,3-dithiane-2,5,5-triyl))tetramethanol (44c). Prepared like **41** though **35c** was used as reactant, yielding **44c** (99%) as a white solid. Mp: > 197 °C dec. ^{1}H NMR (300 MHz, DMSO-d_6, ppm): 0.80−0.91 (m, 12 H), 1.18−1.34 (m, 16 H), 1.47−1.56 (m, 2 H), 2.52−2.54 (m, 4 H), 2.67 (d, ^3J = 14.1 Hz, 4 H), 3.00 (d, ^3J = 14.1 Hz, 4 H), 3.31 (s, 4 H), 3.88 (s, 4 H), 4.12 (bs, 4 H), 5.19 (s, 2 H), 7.32 (s, 2 H). ^{13}C NMR (75 MHz, DMSO-d_6, ppm): 11.9, 14.9, 23.4, 26.4, 29.3, 32.8, 34.2, 36.1, 37.2, 41.1, 47.9, 60.3, 67.3, 131.2, 137.3, 137.3. HRMS (ESI): calcd for $C_{34}H_{59}O_4S_4$ $[M + H]^+$ 659.3291, found 659.3292. IR (cm^{-1}): 3279, 2922, 2866, 1466, 1420, 1242, 1088, 1025, 900, 720.

3,3′-(2,5-Dipentyl-1,4-phenylene)bis(8,15-dioxa-2,4-dithiadispiro[5.2.59.26]hexadecane (45b). Prepared like **42** though **44b** was used as reactant, yielding **45c** (60%) as a beige solid. Mp: 212 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 0.94 (bs, 6 H), 1.37−1.89 (m, 38 H), 2.63−2.71 (m, 4 H), 2.80−2.90 (m, 4 H), 2.97−3.09 (m, 4 H), 3.62 (s, 4 H), 4.33 (bs, 4 H), 5.19 (s, 2 H) 7.43 (s, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 14.1, 22.5, 22.5, 25.6, 27.4, 31.0, 31.8, 32.5, 37.5, 48.3, 62.8, 69.1, 98.9, 129.7, 135.9, 138.1. HRMS (EI): calcd for $C_{40}H_{62}O_4S_4$ $[M]^+$ 734.3525, found 734.3514. IR (cm^{-1}): 3316, 2929, 2854, 1442, 1302, 1111, 1036, 912, 780, 500.

1,1′-((2,5-Dibutyl-1,4-phenylene)bis(8,15-dioxa-2,4-dithia-12-azadispiro[5.2.59.26]hexadecane-3,12-diyl))bis(2-chloroethan-1-one) (46a). Prepared like **42** though 1-(2-chloroacetyl)-piperidin-4-one **22** and **44a** were used as reactants, yielding **46a** (99%) as a beige solid. Mp: > 260 °C dec. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 0.96−1.03 (m, 6 H), 1.37−1.44 (m, 4 H), 1.56−1.61 (m, 4 H), 1.90−2.04 (m, 8 H), 2.62−2.67 (m, 4 H), 2.84−3.11 (m, 8 H), 3.46−3.81 (m, 12 H,), 4.10 (s, 4 H), 4.23−4.45 (m, 4 H), 5.21 (s, 2 H), 7.42 (s, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 14.0, 22.6, 27.6, 32.2, 33.4, 37.3, 39.1, 41.0, 48.3, 63.3, 69.3, 96.9, 129.6, 135.7, 138.1, 164.9. HRMS (ESI): calcd for $C_{40}H_{59}Cl_2N_2O_6S_4$ $[M + H]^+$ 861.2628, found 861.2609. IR (cm^{-1}): 2918, 2876, 1667, 1445, 1358, 1112, 1025, 885, 727, 660.

1,1′-((2,5-Bis(2-ethylhexyl)-1,4-phenylene)bis(8,15-dioxa-2,4-dithia-12-azadispiro[5.2.59.26]hexadecane-3,12-diyl))bis-(2-chloroethan-1-one) (46c). Prepared like **42** though 1-(2-chloroacetyl)piperidin-4-one **22** and **44c** were used as reactants, yielding **46c** (99%) as a beige solid. Mp: >290 °C dec. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 0.88−0.99 (m, 12 H), 1.20−1.39 (m, 16 H), 1.58 (bs, 2 H), 1.87−2.06 (m, 8 H) 2.42−2.61 (m, 8 H), 2.80−2.89 (m, 4 H), 2.90−3.25 (m, 4 H), 3.52−3.69 (m, 8 H), 3.70−3.93 (m, 4 H), 4.09 (s, 2 H), 4.21−4.51 (m, 4 H), 5.21 (s, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 11.0, 14.1, 22.9, 25.8, 27.4, 28.9, 37.3, 40.6, 40.8, 48.3, 63.2, 69.2, 96.7, 130.8, 135.7, 136.9, 164.9. HRMS (ESI): calcd for $C_{48}H_{75}Cl_2N_2O_6S_4$ $[M + H]^+$ 973.3880, found 973.3887. IR (cm^{-1}): 2929, 2866, 1641, 1445, 1359, 1265, 1112, 1025, 897, 724.

■ ASSOCIATED CONTENT

Supporting Information

NMR spectra, NOESY spectra, solubility of **15**−**17**, details of X-ray crystal structure analysis of **15**. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02670.

NMR spectra, NOESY spectra, solubility of **15**−**17**, details of X-ray crystal structure analysis of **15** (PDF)

X-ray data for **15** (CIF)

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Notes

The authors declare no competing financial interest.

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