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Oligospiroketals as Novel Molecular Rods

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Abstract: A modular approach for the synthesis of molecular rods based on oligospiroketals has been developed. The strategy relies on different terminal and intermediate segments, which are joined by ketal formation between ketones and diols. For this purpose it was necessary to develop a new ketalization method to circumvent some problems related with the established methods. The terminal segments are either derived from 4-piperidinone or from 4-oxocyclohexane carboxylic acid whereas the intermediate segments rest on pentaerythritol and cyclohexane-1,4-dione. A series of trispiro (**14**–**18**), hexaspiro (**19**) and nonaspiro (**20**) compounds have been prepared and characterized. From these we realized that it is imperative to use solubility enhancing groups if more than seven rings are joined.

Keywords: cyclization · ketalization · molecular rods · solubility · spiro compounds

Introduction

Molecular rods, that is, long molecules with a relatively rigid conformation, claim a continuously growing interest in chemistry, materials science, and biochemistry. Based on their unique properties numerous applications were developed, such as building blocks in supramolecular assemblies,[1] in investigations of long-range interactions (charge and energy transfer),[2] as model systems for polymers with special optical and electronic properties.[3] The various types of molecular rods, their synthesis and utilization were recently summarized in two excellent reviews.[4]

A large part of previously developed molecular rods bear extended π-systems, such as polyarenes,[3–5] polyacetylenes,[6] and combinations of these structural elements.[7] The consequence of this are relatively small HOMO–LUMO gaps and low oxidation potentials. Whereas these properties are desired for many applications, they are disturbing in other areas, especially in biochemistry.

There are surprisingly few examples for molecular rods with a saturated backbone. To mention are oligobicyclo-[2.2.2]octanes and oligocubanes,[8a–d] oligopiperidines,[8e] polycarboranes[4] and, above all, [*n*]staffanes.[9] [*n*]Staffanes, the oligomers of [1.1.1]propellanes have been functionalized with various substituents[10] and have, owing to their outstanding properties,[9d,11] been applied in supramolecular structures,[9c] as liquid crystals,[12] in self-assembled monolayers[13] and in the development of medicines.[14]

The architecture of molecular rods with a saturated molecular skeleton may base on three different principles: a) the building blocks are connected by one bond (e.g. the above-mentioned [*n*]staffanes), b) by two or more bonds[4] or c) the building blocks are joined by a spiro atom, that is, the molecular rods are oligospiranes. The latter approach was hitherto realized for carbocyclic rings with different size, but, naturally, only oligospiranes consisting of rings with an even number of atoms can form an overall straight molecular shape and therefore be considered as molecular rods. Already in 1966 Buchta[15a] reported on the synthesis of oligospirocyclobutanes, which were developed further 27 years later.[15b] Recently, Schafmeister and co-workers developed spiroladder oligomers based on a peptidic backbone.[16]

Especially oligospirohexanes seem to have promising preconditions as molecular rods due to relatively rigid conformation of the cyclohexane ring. Some efforts were undertaken in this area,[17] but the cumbersome synthesis of these compounds seems to have prevented broader application. The synthetic hurdles may be at least partly circumvented by the introduction of heteroatoms in the oligospirohexane skeleton. In this connection, Rice and co-workers prepared some azaspiro-, azadispiro- and azastrispirocyclohexanes.[18]

If two carbon atoms of a cyclohexane ring of oligospirohexanes adjacent to the spiro atom are replaced by oxygen atoms, ketals are obtained. The synthesis of the correspond-

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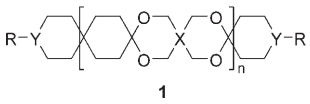
ing oligospiranes, such as **1**, should be reduced to a ketalization reaction as the key step.



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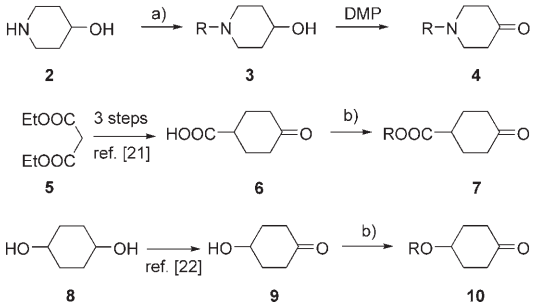
The first synthesis of oligospiroketals of type **1** was already reported in 1928 by Pfeiffer et al., who prepared trispiranes from pentaerythritol (X = C) and derivatives of 4-oxocyclohexane carboxylic acid (Y-R = CHCOOR′).[19] It is credited to the group of Grosu that many oligospiroketals of type **1** with up to seven spirocyclic joined rings (hexaspiranes) were prepared and their properties systematically investigated.[20] Based on this knowledge we planned to develop a new modular architecture of molecular rods with a backbone of type **1** and additional terminal and lateral functional groups to adapt the rods to various applications. Initial attempts using Grosu's synthetic methodology revealed two fundamental problems. On the one hand, classic methods for the preparation of ketals are unsuitable for the selective construction of longer oligospiroketals. On the other hand, due to the very scarce solubility of longer oligospiroketals the installation of solubility enhancing groups is essential.

Herein we report on a novel modular synthetic strategy for the preparation of molecular rods of type **1**, its application on the synthesis of various functionalized oligospiranes as well as on the development of new solubility enhancing groups.

Results and Discussion

The building blocks: The construction of oligospiranes of type **1** requires tetrols and diketones (cyclohexane-1,4-dione in the simplest case) as intermediate segments and monoketones as terminal segments. It is a decisive prerequisite for the versatile applicability of molecular rods that their ends can be selectively equipped with a variety of functional groups and, moreover, that these groups can be removed separately if necessary. For this purpose we developed three different types of terminal segments based on commercially available 4-hydroxypiperidine (**2**), on 4-oxocyclohexane carboxylic acid (**6**), readily available from diethyl malonate (**5**) in three steps,[21] and on 4-hydroxycyclohexanone (**9**), which can be obtained by selective oxidation of 1,4-dihydroxycyclohexane (**8**) according to the method described by Ayres.[22] The synthesis of these terminal segments as well as the introduction of functional groups, giving **4**, **7** and **10**, is summarized in Scheme 1 and Tables 1 and 2.

As mentioned above, the decreasing solubility of molecular rods with increasing chain length requires the introduction of special protective groups. To investigate the influence of such groups on the solubility of oligospiranes we



2 **3** **4** **5** **6** **7** **8** **9** **10**

Scheme 1. Synthesis of terminal segments **4**, **7** and **10**: a) For reagents and yields see Table 1; b) for reagents and yields see Table 2, DMP = Dess–Martin periodinane).

Table 1. Synthesis of compounds **4**.

Compound	R	Reagent (**2**→**3**)[a]	Yield **3** [%]	Yield **4** [%]
4a	Cbz	BnOC(O)Cl	96	99
4b	Fmoc	Fmoc-OSu	99	94
4c	Dtb-Fmoc[b]	Dtb-Fmoc-Cl	71	88
4d	MIO-Fmoc[c]	MIO-Fmoc-Cl	85	94
4e	DIO-Fmoc[d]	DIO-Fmoc-Cl	81	99
4f	OS[e]	OS-Cl	64	99
4g	TDOC[f]	TDOC-Cl [h]	48	50
4h	EHOC[g]	EHOC-Cl	94	90

[a] In the presence of *N*-ethyldiisopropylamine (1 equiv) in CH_2Cl_2. [b] 2,7-Di-*tert*-butyl-9*H*-fluorene-9-methoxycarbonyl. [c] 2-(2-Ethylhexyl)-9*H*-fluorene-9-methoxycarbonyl.[23] [d] 2,7-Bis-(2-ethylhexyl)-9*H*-fluorene-9-methoxycarbonyl.[23] [e] Octane-1-sulfonyl. [f] Tridec-7-yloxycarbonyl. [g] 2-Ethylhex-1-yloxycarbonyl. [h] See Experimental Section.

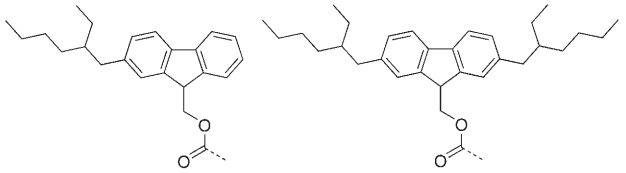
Table 2. Synthesis of compounds **7** and **10**.

Compound	R	Method	Yield [%]
7a	Al[a]	$AlBr/K_2CO_3$/DMF	95
7b	TME[b]	1) $(COCl)_2$ 2) TME-OH	67
7c	ONBn[c]	1) $(COCl)_2$ 2) 2-nitrobenzyl alcohol	68
10a	TFA	TFA_2O/Et_3N	71
10b	Piv	PivCl/pyridine	64
10c	PMB	PMB-TCAA[d]/PPTS	50
10d	Ac	Ac_2O/pyridine	49

[a] Allyl. [b] 2-Trimethylsilylethyl. [c] 2-Nitrobenzyl. [d] 4-Methoxybenzyl 2,2,2-trichloroacetimidate.

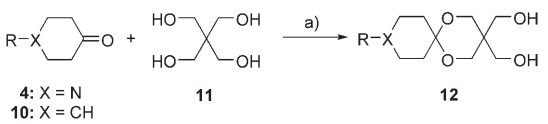
prepared 4-piperidinones **4** bearing both established protective groups (**4a**,**b**) and those supplied with alkyl chains of different length and different extent of branching (**4c**–**h**). The Fmoc group (as in **4b**) has gained great importance especially in solid-phase peptide synthesis.[24] Admittedly, Fmoc-protected amines are often poorly soluble and therefore two modified Fmoc groups were reported bearing *tert*-butyl[25] and trimethylsilyl[26] groups to enhance solubility. The former 2,7-di-*tert*-butyl-Fmoc group (Dtb-Fmoc) was used in 4-piperidinone (**4c**) but we found that the effect of this group is not sufficient for our purposes. Therefore we recently developed two new Fmoc groups (MIO-Fmoc and DIO-Fmoc) equipped with 2-ethylhexyl (isooctyl) groups, which give rise to dramatically enhanced solubility[23] and

used these groups for the preparation of **4d**,**e**. Furthermore, the octane-1-sulfonyl (OS) group,[27] the 2-ethylhexyloxycarbonyl (EHOC) group[28] as well as the newly developed tridec-7-yloxycarbonyl (TDOC) group were used (**4f–h**).



The choice of the protective groups for terminal segments **7** and **10** took place with the aim to establish a variety of cleaving conditions in the course of the construction of the molecular rods. Accordingly, we prepared terminal segments with protective groups cleavable by Pd catalysis (allyl ester, **7a**), fluoride ions (2-trimethylsilylethyl ester, **7b**), photochemically (2-nitrobenzyl ester, **7c**), bases (trifluoroacetyl, **10a**), reductive with DIBAH (pivaloyl, **10b**), oxidative with DDQ (4-methoxybenzyl, **10c**) and by classic saponification (acetyl, **10d**). As intermediate segments we used on the one hand pentaerythritol (**11**) and on the other hand synthetic equivalents of cyclohexan-1,4-dione. Cyclohexane-1,4-dione itself is less suited for our synthetic strategy because it is difficult to selectively convert only one of two keto groups. The protected 4-hydroxycyclohexanones **10**, already defined as terminal segments above, proved to be versatile building blocks for the selective construction of oligospiranes **1**.

Acetalization methods: The classic methods for the preparation of cyclic acetals rely on the reaction between a diol and a ketone in the presence of a Brønsted or a Lewis acid catalyst. In most cases, one of the reactants must be employed in large excess, which is a critical drawback if both reactants are valuable, as in our case. As catalysts were used hydrochloric acid,[29a] 4-toluenesulfonic acid (TsOH),[29b] $TiCl_4$,[29c] $ZrCl_3$,[29d] montmorillonite modified with Ce^{3+},[29e] $BF_3{\cdot}Et_2O$,[29f] Dowex 50,[29g] *N*-bromosuccinimide (NBS)[29h] and iodine.[29i] One of these methods (TsOH, DMF/benzene, reflux, azeotropic removal of water, using a Dean–Stark trap, referred to Method I in the following) could be successfully applied on the synthesis of some monospiranes **12** using the terminal segments **4** and **10** and pentaerythritol (**11**) (Scheme 2, Table 3). The method failed with Fmoc-protected 4-piperidinone **4b** owing to cleavage of the Fmoc group under these conditions.



Scheme 2. Synthesis of monospiranes **12**: a) cat. TsOH, DMF, benzene.

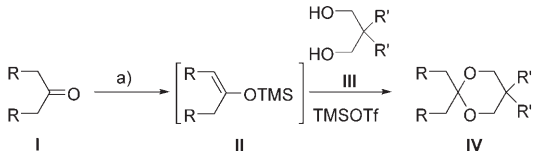
Table 3. Synthesis of monospiranes **12**.

Reactant	X	R[a]	Product	Yield [%]
4a	N	Cbz	**12a**	58
4f	N	OS	**12b**	58
4g	N	TDOC	**12c**	71
4h	N	EHOC	**12d**	72
10b	CH	OPiv	**12e**	59
10c	CH	OPMB	**12f**	45
4b	N	Fmoc	**12g**	–[b]

[a] See Tables 1, 2. [b] Cleavage of Fmoc group.

Whereas monospiranes **12** are thus easily accessible the method turned out to be completely unsuitable to gain access to longer oligospiranes. Searching for an alternative we became aware of a publication of Noyori et al.[30] who used instead of diols their bis(trimethylsilyl) ethers in the presence of a catalytic amount of trimethylsilyl triflate (TMSOTf). This method, which has been used regularly by others,[31] permits very mild reaction conditions (−78 °C) and the reactants can be employed in equimolar amounts. Despite these merits Noyori's method (referred to as Method II herein) has a decisive disadvantage. If reactants are used having already one or more acetal moieties, reacetalization reactions take place even at low temperatures and either mixtures of different oligospiranes (see Scheme 4) or the most scarcely soluble oligospirane (escaping from equilibrium) are obtained. Consequently, Method II is well suitable for the preparation of symmetric oligospiranes but mostly fails with unsymmetric target molecules.

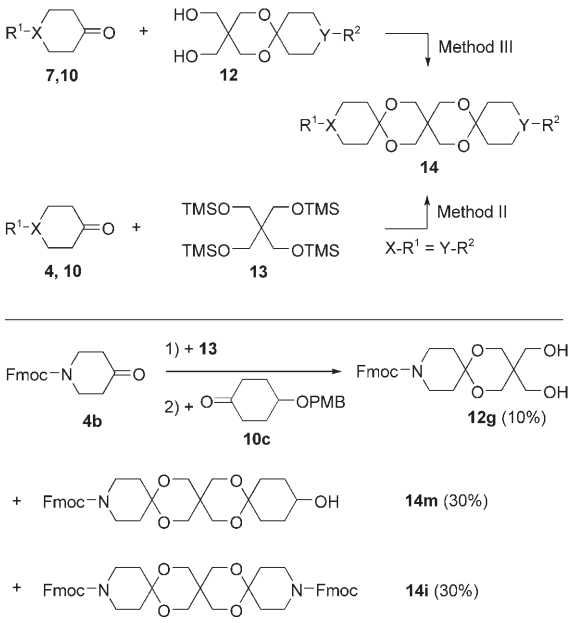
In summary, we felt that we would not reach our goal of a modular synthetic route to longer unsymmetrical oligospiranes of type **1** based on the established acetalization methods. To our delight we found, after extensive variations of the reaction conditions, a new versatile acetalization method, which we called double-activation method (called Method III herein). The principle of this method is depicted in Scheme 3. First ketone **I** is converted into the trimethylsilylenol ether **II** by treatment with NaH/TMSCl in Et_2O (the choice of this solvent is crucial); then diol **III** is added together with 0.05 equiv TMSOTf.



Scheme 3. The double-activation method (Method III): a) NaH, TMSCl, Et_2O, 0 °C.

Synthesis of oligospiranes: With terminal segments **4**, **7** and **10**, diols **12** and acetalization Methods I–III in hand, we turned to the synthesis of various oligospiranes. Trispiranes **14** (Scheme 4), which play a key role as advanced building blocks, were prepared by two different ways.

Unsymmetric compounds **14a–e** were accessible from ketones **7** (including the commercially available ethyl 4-oxocy-



Scheme 4. Synthesis of oligospiranes **14**.

clohexanecarboxylate, yielded **14e**), **10** and monospiranes **12** in good yields utilizing our new double-activation method (Method III). For compound **14a** we applied both the classic Method I and our new Method III and found dramatically improved yields in the latter case (99 vs 31%, see Table 4), impressively demonstrating the advantage of the method. The symmetric trispiranes **14f–l** were prepared from ketones **4**, **10** and the tetrakis(trimethylsilyl) ether of pentaerythritol (**13**) according to Noyoris's method (Method II). The very mild conditions of this method brought us to investigate whether unsymmetric trispiranes **14** could be prepared by stepwise treatment of **13** with two different ketones. We hoped that such an approach, besides saving synthetic steps, could circumvent the problems with Fmoc-protected ketone **4b**, the conversion of which into diol **12g** failed. To this end we treated **4b** at first with **13** and then with PMB-protected ketone **10c**. Unfortunately, we obtained instead of the desired trispirane compound **14m**, arising from a cleavage of the PMB group, in low yields the symmetric trispirane **14i** along with diol **12g**. Obviously, reacetalization reactions have taken place as mentioned above. The straight conformation of the spirocyclic backbone of compounds **14** is clearly discernable in the crystal structure of **14a** as depicted in Figure 1.[38]

Our main intention to prepare trispiranes **14i–l** was to investigate the influence of modified Fmoc groups on the solubility of these compounds. As expected the parent compound **14i** is very poorly soluble both in protic (MeOH) and in aprotic solvents (Et_2O). The introduction of two *tert*-butyl groups in Stiger's Dtb-Fmoc group improved this situation only marginally. To our delight, one (MIO-Fmoc) or two (DIO-Fmoc) isooctyl groups tethered onto 9*H*-fluorene moiety of Fmoc give rise to dramatically enhanced solubility, as seen by the values summarized in Table 5.

On our way to longer oligospiranes selected compounds **14** were converted into monoketones **16** or diketone **18** in two steps (Scheme 5). Thus, owing to the orthogonality of the protective groups in **14a–e** the PMB group could be selectively cleaved with DDQ followed by oxidation of the secondary alcohols **15a–e** with Dess–Martin periodinane (DMP) yielded the ketones **16a–e**. Alternatively, the cleavage of the Piv group in **14a** with DIBAH gave the PMB-protected ketone **16f** after oxidation with DMP. Suitable starting compounds for the diketone **18** are the symmetrically substituted trispiranes **14f–h**. Whereas attempts to deprotect diacetate **14h** resulted in degradation of the oligospirane skeleton and treatment of dipivalate **14g** with an excess DIBAH produced diol **17** only in low yields (36%), bis(trifluoroacetate) **14f** proved to be the suitable reactant. The cleavage of the TFA protective groups proceeded to diol **17**

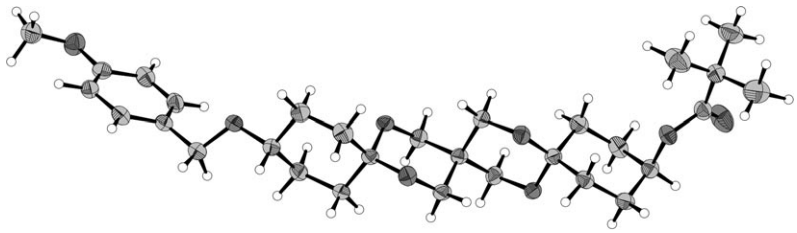


Figure 1. Crystal structure of trispirane **14a**.

Table 4. Synthesis of trispiranes **14**.

Reactant	R^1	R^2	X	Y	Product[a]	Method[b]	Yield [%]
10b, 12f	OPiv	OPMB	CH	CH	**14a**	I	31
10b, 12f	OPiv	OPMB	CH	CH	**14a**	III	99
10c, 12e	OPMB	OPiv	CH	CH	**14a**	III	53
7a, 12f	COOAl	OPMB	CH	CH	**14b**	III	89
7b, 12f	COO-TME	OPMB	CH	CH	**14c**	III	69
7c, 12f	COO-NBn	OPMB	CH	CH	**14d**	III	89
[c], **12f**	COOEt	OPMB	CH	CH	**14e**	III	99
10a, 13	OTFA	OTFA	CH	CH	**14f**	II	99
10b, 13	OPiv	OPiv	CH	CH	**14g**	II	95
10d, 13	OAc	OAc	CH	CH	**14h**	II	91
4b, 13	Fmoc	Fmoc	N	N	**14i**	II	82
4c, 13	Dtb-Fmoc	Dtb-Fmoc	N	N	**14j**	II	57
4d, 13	MIO-Fmoc	MIO-Fmoc	N	N	**14k**	II	59
4e, 13	DIO-Fmoc	DIO-Fmoc	N	N	**14l**	II	84

[a] **14a–h** are racemic mixtures due to atropisomerism. [b] Methods: I) DMF/benzene/TsOH(cat.)/Δ, II) TMSOTf (cat.),[30] III) 1) ketone/NaH/TMSCl in Et_2O, 2) diol/TMSOTf (0.1 equiv). [c] Reaction of **12f** with commercially available ethyl 4-oxocyclohexanecarboxylate.

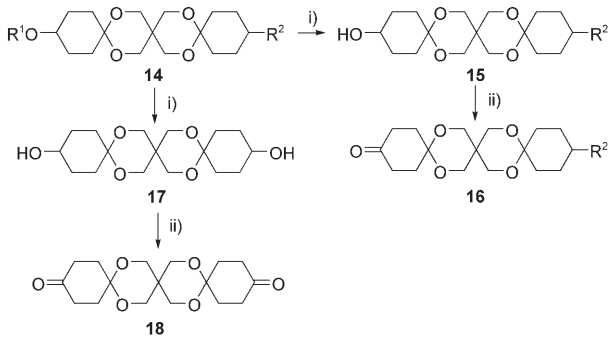
Table 5. Solubility of trispiranes **14i–l**.

Compound	PG[a]	L_{MeOH}[b]	L_{Et_2O}[b]
14i	Fmoc	<0.1	0.5 ± 0.3
14j	Dtb-Fmoc	0.4 ± 0.3	2.3 ± 0.6
14k	MIO-Fmoc	13.5 ± 1.3	>100[c]
14l	DIO-Fmoc	3.2 ± 1.3	>100[c]

[a] Protective group. [b] Solubility in $g\,L^{-1}$. [c] No saturation is observed but highly viscous mixtures are obtained with increasing amounts of the solute.

smoothly (66% yield) and, after oxidation with DMP, diketone **18** could be successfully obtained (Scheme 5, Table 6).

Equipped with a versatile "construction kit", containing



Scheme 5. Synthesis of ketones **16** and diketone **18**: i) deprotection; ii) oxidation with DMP.

Table 6. Synthesis of ketones **16** and ketone **18**.

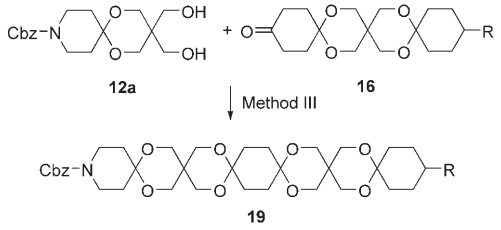
Reactant	R^1	R^2	Product	Yield [%][a]
14a	PMB	OPiv	**16a**	56/98
14b	PMB	COOAl	**16b**	53/59
14c	PMB	COOTME	**16c**	99/81
14d	PMB	COONBn	**16d**	46/97
14e	PMB	COOEt	**16e**	54/99
14a	Piv	OPMB	**16f**	95/75
14f	TFA	OTFA	**18**	66/81
14g	Piv	OPiv	**18**	36/81

[a] Deprotection/oxidation.

monocyclic compounds **4**, **7** and **10**, monospirodiols **12**, trispiroketones **16** and trispirodiketone **18**, we tackled the synthesis of longer oligospiranes to prove the efficiency of our modular approach. The first target molecules were hexaspiranes **19**.

We obtained these compounds, which already deserve the term "molecular rods", by reaction of Cbz-protected diol **12a** with various ketones **16** using Method III in good yields (Scheme 6, Table 7). It should be noted that hexaspiranes **19a–d** are derivatives of an amino acid suggesting very interesting applications. The incorporation of rod-like peptidomimetics such as **19** into peptides is one of our ongoing research projects.

Despite the promising synthesis of compounds **19**, once more the crucial problem of poor solubility became obvious. Though these compounds could still be fully characterized



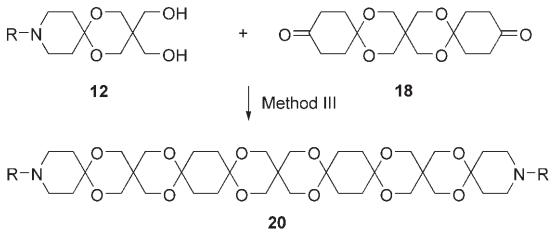
Scheme 6. Synthesis of hexaspiranes **19**.

Table 7. Synthesis of hexaspiranes **19**.

Reactants	R	Product	Yield [%]
12a/16b	COOAl	**19a**	64
12a/16c	COOTME	**19b**	65
12a/16d	COONBn	**19c**	63
12a/16e	COOEt	**19d**	72
12a/16f	OPMB	**19e**	34

by NMR spectroscopy, they mark the maximum length of oligospiranes accessible without using solubility enhancing groups.

That this problem is certainly soluble was impressively demonstrated with the successful synthesis of nonaspiranes **20** employing Method III. Whereas the reaction of diketone **18** with **12a,b** bearing a Cbz and an Fmoc group only furnished scarcely soluble hexaspiranes eluding further reaction by precipitation, diols **12c–e** with the solubility enhancing groups OS, TDOC and EHOC react smoothly with **19** to nonaspiranes **20** (Scheme 7). In this connection, the TDOC and the EHOC groups are superior to the OS group due to better yields and higher solubilities. The results are summarized in Table 8.



Scheme 7. Synthesis of nonaspiranes **20**.

Table 8. Yields and solubilities of nonaspiranes **20**.

Reactants	R	Product	Yield [%]	L_{Et_2O}[a]	$L_{CH_2Cl_2}$[a]
12c/19	OS	**20a**	14	5.7 ± 0.8	6.9 ± 2.2
12d/19	TDOC	**20b**	62	9.1 ± 1.5	62.0 ± 4.7
12e/19	EHOC	**20c**	72	6.3 ± 1.8	99.5 ± 5.1

[a] Solubility in $g\,L^{-1}$.

An unambiguous proof for the structure of compounds **20** was received by MALDI TOF mass spectroscopy. Exemplarily the appropriate spectra of **20a** and **b** are depicted in Figure 2.

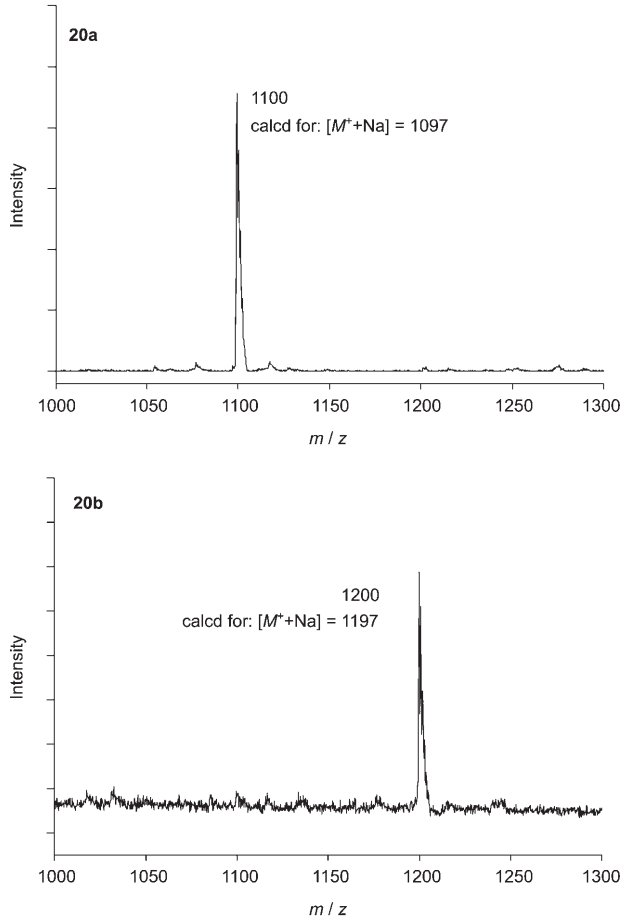


Figure 2. MALDI TOF mass spectra of **20a** (top) and **20b** (bottom).

Conclusion

In summary, we reported herein on a modular approach for the synthesis of molecular rods based on oligospiroketals with general structure **1**. For this purpose we developed a versatile construction kit containing several terminal and intermediate segments. An assortment of different protective groups, which are partly orthogonal to each other, allows flexible functionalization of these building blocks. Connecting of segments relies on three different acetalization methods at which our newly developed method of double-activation (Method III) is particularly efficient. For the preparation of oligospiroketals with more than seven joined rings the utilization of solubility mediating groups is mandatory. To this end we developed two new Fmoc derived protective groups (MIO- and DIO-Fmoc) as well as the TDOC group. With the partly dramatically improved solubility of some oligospiroketals these protective groups (together with the formerly established EHOC group) impressively demonstrate their suitability for this problem. Currently intensive research into the properties and applications of oligospiroketals is under way and we will report on this work in due course.

Experimental Section

General: All reactions using dry solvents were performed under argon in flame-dried flasks. The solvents were dried and distilled prior to use by means of usual laboratory methods. PE refers to petroleum ether b.p. 40–60 °C. All reagents obtained from commercial sources were used without further purification. Thin-layer chromatography (TLC) was performed on silica gel plates (Merck, silica gel 60 F_{254}), and silica gel (Sigma Aldrich, grade 9385, 230–400 mesh) was used for flash chromatography. IR spectra were recorded as KBr pellets or as films on a Perkin Elmer IR-881 spectrometer. ^{1}H and ^{13}C NMR spectra (selected ^{13}C NMR spectra are given in the Supporting Information) were recorded with a Bruker DPX-300, solid state NMR spectra with a Bruker AVANCE 400 spectrometer. Chemical shifts are reported in ppm using tetramethylsilane as internal standard. Mass spectra were measured on a Hewlett-Packard GCMS 5995A (EI), Thermo Finnigan LTQ-FT (ESI) or Voyager-DETM Pro Biospectrometry Workstation (MALDI) instrument. Melting points were measured by a Elektrothermal 9100 and are uncorrected.

General Procedures

Dess–Martin oxidation without buffer (GP 1a): The corresponding alcohol was dissolved in anhydrous CH_2Cl_2, treated with Dess–Martin periodinane (DMP) (1.1 equiv) and stirred at room temperature until complete conversion controlled by TLC. The organic layer was washed with an aq solution of $NaHCO_3/Na_2S_2O_3$ (3×), dried and evaporated. The resulting residue was purified by flash chromatography.

Dess–Martin oxidation with buffer (GP 1b): The corresponding alcohol was dissolved in anhydrous CH_2Cl_2, treated with 1.1 equiv DMP, 2.0 equiv $NaHCO_3$ and stirred at room temperature until complete conversion controlled by TLC. The organic layer was washed with an aq solution of $NaHCO_3/Na_2S_2O_3$ (3×), dried and evaporated. The resulting residue was purified by flash chromatography.

Acetalisation of pentaerythritol (11) with 4-oxopiperidines (4) and cyclohexanones (10) to [3-(hydroxymethyl)-1,5-dioxaspiro[5.5]undec-3-yl]methanols (12) (GP 2): A solution of the corresponding ketone, pentaerythritol (1.1 equiv) and *p*-toluenesulfonic acid (0.02 equiv) in DMF/benzene 3:2 was heated under reflux for 2 h. The water formed during the acetalisation was collected in a Dean–Stark trap. Aq $NaHCO_3$ solution was added and the reaction mixture was extracted several times with CH_2Cl_2. The combined organic layers were dried, evaporated and the resulting residue was purified by flash chromatography.

Acetalisation of [3-(hydroxymethyl)-1,5-dioxaspiro[5.5]undec-3-yl]methanols (12) with 4-oxocyclohexanecarboxylic acids (7) cyclohexanones (10) to 7,11,18,21-tetraoxatrispiro[5.2.2.5.2.2]henicosanes (14a–e) (GP 3): An ice-cooled solution of the corresponding ketone in anhydrous Et_2O was treated with NaH (1.0 equiv) and TMSCl (1.0 equiv) and stirred for 1 h. The corresponding [3-(hydroxymethyl)-1,5-dioxaspiro[5.5]undec-3-yl]methanol (1.0 equiv) and TMSOTf (0.05 equiv) were added and the reaction mixture was stirred at RT until complete conversion controlled by TLC. The organic layer was washed with aq $NaHCO_3$ solution, dried and evaporated. The resulting residue was purified by flash chromatography.

Acetalisation of tetrakis[(trimethylsilyloxy)methyl]methane (13) with 4-oxopiperidines (4) and cyclohexanones (10) to 7,11,18,21-tetraoxatrispiro[5.2.2.5.2.2]henicosanes (14f–l) (GP 4): An ice-cooled solution of tetrakis[(trimethylsilyloxy)methyl]methane and the corresponding ketone (2.0 equiv) in anhydrous Et_2O were treated with TMSOTf (0.1 equiv). The reaction mixture was stirred at RT until complete conversion controlled by TLC. The organic layer was washed with aq $NaHCO_3$ solution, dried and evaporated. The resulting residue was purified by flash chromatography.

Removal of PMB protecting group with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (GP 5): A solution of protected alcohol and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (1.1 equiv) in CH_2Cl_2/water 19:1 was stirred at RT. After 15–45 min the reaction mixture was washed with aq $NaHCO_3$ solution. The organic layer was dried, evaporated and the resulting residue purified by flash chromatography.

Characterization

Benzyl 4-hydroxy-1-piperidinecarboxylate (3a):[32] Benzyl chloroformate (6.80 mL, 47.63 mmol) was added to an ice cooled solution of 4-hydroxypiperidine (4.65 g, 45.97 mmol) and *N*-ethyldiisopropylamine (8.4 mL, 48.22 mmol) in anhydrous CH_2Cl_2 (100 mL) and stirred at RT over night. The reaction mixture was washed with diluted hydrochloric acid and aq solution of $NaHCO_3$. The organic layer was dried, evaporated and the resulting residue purified by flash chromatography (CH_2Cl_2) yielded **3a** as a colorless oil (10.33 g, 43.91 mmol, 96%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.42–1.53 (m, 2H), 1.62–1.95 (m, 3H), 3.09–3.18 (m, 2H), 3.83–3.93 (m, 3H), 5.12 (s, 2H), 7.26–7.36 ppm (m, 5H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 34.0, 41.3, 67.1, 67.3, 127.8, 128.0, 128.4, 136.7, 155.2 ppm.

Benzyl 4-oxo-1-piperidinecarboxylate (4a):[32] According to GP 1a alcohol **3a** (5.17 g, 21.97 mmol) was treated with DMP (10.27 g, 24.17 mmol) yielded **4a** as a yellow solid (5.05 g, 21.65 mmol, 99%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.45 (t, ^3J = 6 Hz, 4H), 3.79 (t, J = 6 Hz, 4H), 5.18 (s, 2H), 7.34–7.38 ppm (m, 5H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 41.0, 43.1, 67.6, 128.0, 128.2, 128.6, 136.3, 155.1, 207.2 ppm.

9*H*-Fluoren-9-ylmethyl 4-hydroxy-1-piperidinecarboxylate (3b):[33] Fmoc-OSu (6.67 g, 19.77 mmol) was added to a solution of 4-hydroxypiperidine (2.00 g, 19.77 mmol) in dioxane/water 10:1 (72 mL) and stirred over night. Brine (30 mL) was added and the mixture was extracted with Et_2O (150 mL). The organic layer was dried and evaporated yielded **3b** as a white solid (6.33 g, 19.6 mmol, 99%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.44 (brs, 2H), 1.80 (brs, 2H), 2.59 (s, 1H), 3.06–3.15 (m, 2H), 3.79–3.87 (m, 2H + 1H), 4.23 (t, ^3J = 6.8 Hz, 1H), 4.41 (d, ^3J = 6.3 Hz, 2H), 7.30 (dt, ^3J = 7.4, ^4J = 1.2 Hz, 2H), 7.38 (dt, ^3J = 7.5, ^4J = 0.6 Hz, 2H), 7.56 (dd, ^3J = 7.5, ^4J = 0.6 Hz, 2H), 7.75 ppm (d, ^3J = 7.4 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 33.9, 41.3, 47.3, 67.2, 67.2, 119.9, 124.9, 127.0, 127.6, 141.3, 143.9, 155.2 ppm.

9*H*-Fluoren-9-ylmethyl 4-oxo-1-piperidinecarboxylate (4b):[34] According to GP 1a alcohol **3b** (6.44 g, 19.9 mmol) was treated with DMP (10.58 g, 24.9 mmol) yielded **3b** (1.85 g, 5.7 mmol) and **4b** as a white solid (4.43 g, 13.8 mmol, 97%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.25–2.32 (m, 4H), 3.60–3.67 (m, 4H), 4.23 (t, ^3J = 6.0 Hz, 1H), 4.56 (d, ^3J = 6.1 Hz, 2H), 7.30 (dt, ^3J = 7.4, ^4J = 1.3 Hz, 2H), 7.38 (dt, ^3J = 7.5, ^4J = 0.6 Hz, 2H), 7.56 (dd, ^3J = 7.6, ^4J = 0.8 Hz, 2H), 7.74 ppm (d, ^3J = 7.3 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 40.8, 43.0, 47.4, 67.1, 119.9, 124.7, 127.0, 127.7, 141.3, 143.7, 154.9, 207.0 ppm.

[2,7-Di(*tert*-butyl)-9*H*-fluoren-9-yl]methyl 4-hydroxy-1-piperidinecarboxylate (3c): A solution of [2,7-di(*tert*-butyl)-9*H*-fluoren-9-yl]methanol (3.00 g, 9.73 mmol) and phosgene (15.4 mL, 29.32 mmol, 20% in toluene) was stirred in a sealed flask over night. The solvent was removed in vacuo and the residue was dissolved in NEt_3 (1.35 mL, 9.71 mmol) and treated with 4-hydroxypiperidine (0.98 g, 9.69 mmol). After stirring 2 h water was added and the mixture was extracted with CH_2Cl_2 (2×). The organic layer was dried, evaporated and the resulting residue purified by flash chromatography (CH_2Cl_2/MeOH 10:1) yielded **3c** as a white solid (3.01 g, 6.91 mmol, 71%). M.p. 173–175 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.36 (s, 18H), 1.45–1.57 (m, 2H), 1.85–1.91 (m, 2H,), 3.14 (brs, 2H), 3.62 (m, 1H + 2H), 4.18 (t, ^3J = 7.3 Hz, 1H), 4.38 (d, ^3J = 7.3 Hz, 2H,), 7.40 (dd, ^3J = 8.0, ^4J = 1.6 Hz, 2H), 7.60 (s, 2H), 7.63 ppm (d, ^3J = 8.0 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 31.6, 34.0, 34.8, 41.3, 47.3, 67.2, 67.8, 119.2, 121.8, 124.7, 138.6, 144.0, 149.7, 155.3 ppm; IR: $\tilde{\nu}$ = 3471, 2957, 1677, 1475, 1224, 1090, 817 cm^{-1}; HRMS: m/z: calcd for $C_{28}H_{37}NO_3$: 435.2773, found: 435.2772 $[M]^+$.

[2,7-Di(*tert*-butyl)-9*H*-fluoren-9-yl]methyl 4-oxo-1-piperidinecarboxylate (4c): According to GP 1a alcohol **3c** (307 mg, 0.70 mmol) was treated with DMP (331 mg, 0.78 mmol) yielded **4c** as a white solid (270 mg, 0.62 mmol, 88%). ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 1.31 (s, 18H), 2.25 (brs, 4H), 3.62 (t, ^3J = 6.3 Hz, 4H), 4.22 (t, ^3J = 6.4 Hz, 1H), 4.43 (d, ^3J = 6.6 Hz, 2H), 7.42 (dd, ^3J = 8.0, ^4J = 1.7 Hz, 2H), 7.64 (s, 2H), 7.72 ppm (d, ^3J = 8.0 Hz, 2H); ^{13}C NMR (75.5 MHz, [D$_6$]DMSO): δ = 31.3, 34.6, 40.2, 42.2, 46.9, 66.9, 119.4, 121.6, 124.7, 138.2, 143.8, 149.4, 154.5, 206.8 ppm; IR: $\tilde{\nu}$ = 3020, 1709, 1361, 1214, 755, 667 cm^{-1}; HRMS: m/z: calcd for $C_{28}H_{35}NO_3$: 433.2617, found: 433.2617 $[M]^+$.

[2-(2-Ethylhexyl)-9*H*-fluoren-9-yl]methyl 4-hydroxy-1-piperidinecarboxylate (3d): MIO-Fmoc-Cl[23] (1.07 g, 2.88 mmol) was added to a suspension of 4-hydroxypiperidine (292 mg, 2.89 mmol) and $NaHCO_3$ (292 mg, 3.48 mmol) in dioxane/water 7:1 (28.5 mL) and stirred over night. The solvents were evaporated and the resulting residue purified by flash chromatography (CH_2Cl_2) yielded **3d** as a green oil (1.07 g, 2.46 mmol, 85%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.79–0.84 (m, 6H, C*H*$_3$), 1.13–1.30 (m, 8H), 1.40–1.51 (m, 2H), 1.53–1.61 (m, 1H), 1.72 (s, 1H), 1.83 (brs, 2H), 2.52–2.64 (m, 2H), 3.09–3.18 (m, 2H), 3.71–3.89 (m, 1H + 2H), 4.19 (t, ^3J = 6.8 Hz, 1H), 4.33–4.46 (m, 2H), 7.16 (dd, ^3J = 7.8, ^4J = 1.1 Hz, 1H), 7.26 (dt, ^3J = 7.4, ^4J = 1.2 Hz, 1H), 7.35 (s, 1H), 7.36 (t, ^3J = 7.2 Hz, 1H), 7.54 (d, ^3J = 7.6 Hz, 1H), 7.64 (d, ^3J = 7.7 Hz, 1H), 7.70 ppm (d, ^3J = 7.5 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 10.8, 14.1, 23.0, 25.4, 28.8, 32.3, 34.0, 40.3, 41.3, 41.3, 47.2, 67.2, 67.4, 119.5, 119.6, 124.9, 125.7, 126.5, 127.6, 128.7, 138.8, 141.1, 141.5, 144.0, 155.2 ppm; IR: $\tilde{\nu}$ = 3020, 2401, 1691, 1427, 1213, 928, 745, 667 cm^{-1}; HRMS: m/z: calcd for $C_{28}H_{37}NNaO_3$: 458.2669, found: 458.2666 $[M+Na]^+$.

[2-(2-Ethylhexyl)-9*H*-fluoren-9-yl]methyl 4-oxo-1-piperidinecarboxylate (4d): According to GP 1a alcohol **3d** (416 mg, 0.96 mmol) was treated with DMP (450 mg, 1.06 mmol) yielded **4d** as a yellow oil (393 mg, 0.91 mmol, 94%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.88–0.93 (m, 6H), 1.23–1.38 (m, 8H), 1.59–1.62 (m, 1H), 2.35 (brs, 4H), 2.56–2.68 (m, 2H), 3.68 (brs, 4H), 4.24 (t, ^3J = 6.1 Hz, 1H), 4.50–4.66 (m, 2H), 7.21 (dd, ^3J = 7.8, ^4J = 1.1 Hz, 1H), 7.30 (dt, ^3J = 7.4, ^4J = 1.2 Hz, 1H), 7.39 (s, 1H), 7.40 (t, ^3J = 7.5 Hz, 1H), 7.58 (d, ^3J = 7.6 Hz, 1H), 7.67 (d, ^3J = 7.7 Hz, 1H), 7.74 ppm (d, ^3J = 7.4 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 10.8, 14.1, 23.0, 25.4, 28.8, 32.3, 40.3, 40.9, 41.3, 43.1, 47.3, 67.4, 119.5, 119.6, 124.7, 125.5, 126.5, 127.7, 128.8, 138.9, 141.1, 141.5, 143.7, 155.0, 207.0 ppm; IR: $\tilde{\nu}$ = 2957, 2925, 1701, 1426, 1308, 1270, 1229, 1121, 989, 760 cm^{-1}; HRMS: m/z: calcd for $C_{28}H_{35}NO_3$: 433.2617, found: 433.2617 $[M]^+$; elemental analysis calcd (%) for $C_{28}H_{35}NO_3$ (433.6): C 77.56, H 8.14, N 3.23, found: C 76.28, H 8.14, N 3.11.

[2,7-Bis(2-ethylhexyl)-9*H*-fluoren-9-yl]methyl 4-hydroxy-1-piperidinecarboxylate (3e): DIO-Fmoc-Cl[23] (1.84 g, 3.81 mmol) was added to a suspension of 4-hydroxypiperidine (390 mg, 3.86 mmol) and $NaHCO_3$ (1.05 g, 7.60 mmol) in dioxane/water 7:1 (45 mL) and stirred over night. The solvents were evaporated and the resulting residue purified by flash chromatography (CH_2Cl_2/MeOH 100:3) yielded **3e** as a yellow oil (1.70 g, 3.10 mmol, 81%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.84–0.89 (m, 12H), 1.25–1.34 (m, 16H), 1.42–1.50 (m, 2H), 1.52–1.59 (m, 2H), 1.70 (s, 1H), 1.83–1.87 (m, 2H), 2.51–2.63 (m, 4H), 3.12–3.20 (m, 2H), 3.83–3.93 (m, 1H+2H), 4.16 (t, ^3J = 7.0 Hz, 1H), 4.37 (d, ^3J = 7.1 Hz, 2H), 7.14 (dd, ^3J = 7.8, ^4J = 1.1 Hz, 2H), 7.33 (s, 2H), 7.59 ppm (d, ^3J = 7.7 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 10.8, 14.1, 23.0, 25.4, 28.8, 32.3, 34.0, 40.3, 41.2, 41.3, 47.0, 67.3, 67.6, 119.1, 125.7, 128.6, 139.0, 140.5, 144.0, 155.2 ppm; IR: $\tilde{\nu}$ = 3439, 2930, 2851, 1682, 1467, 1435, 1224, 906, 733 cm^{-1}; HRMS: m/z: calcd for $C_{36}H_{53}NNaO_3$: 570.3918, found: 570.3926 $[M+Na]^+$.

[2,7-Bis(2-ethylhexyl)-9*H*-fluoren-9-yl]methyl 4-oxo-1-piperidinecarboxylate (4e): According to GP 1a alcohol **3e** (1.63 g, 2.98 mmol) was treated with DMP (2.53 g, 5.97 mmol). Purification by flash chromatography (PE/EtOAc 5:1) yielded **4e** as a yellow oil (1.63 g, 2.97 mmol, 99%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.83–0.88 (m, 12H), 1.19–1.33 (m, 16H), 1.54–1.58 (m, 2H), 2.33 (brs, 4H), 2.50–2.62 (m, 4H), 3.67 (brs, 4H), 4.16 (t, ^3J = 6.2 Hz, 1H), 4.52 (d, ^3J = 6.3 Hz, 2H), 7.14 (dd, ^3J = 7.8, ^4J = 1.1 Hz, 2H), 7.31 (s, 2H), 7.59 ppm (d, ^3J = 7.7 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 10.8, 14.1, 23.0, 25.4, 28.8, 32.3, 40.3, 41.0, 41.4, 43.1, 47.1, 67.6, 119.2, 125.6, 128.7, 139.1, 140.6, 143.7, 155.0, 207.1 ppm; IR: $\tilde{\nu}$ = 2925, 2856, 1696, 1469, 1427, 1232, 733 cm^{-1}; HRMS: m/z: calcd for $C_{36}H_{51}NNaO_3$: 545.3869, found: 545.3869 $[M+Na]^+$.

Octan-1-sulfonyl-4-piperidinol (3f): Octan-1-sulfonyl chloride (10.1 mL, 51.61 mmol) was added dropwise to an ice-cooled solution of 4-hydroxypiperidine (5.00 g, 49.43 mmol) and NEt_3 (7.20 mL, 51.80 mmol) in anhydrous CH_2Cl_2 (150 mL). After stirring over night brine was added and the aqueous layer was extracted with CH_2Cl_2 (2×). The organic layer was dried and evaporated yielded **3f** as a white solid (8.75 g, 31.54 mmol, 64%). M.p. 72–74 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.85–0.90 (m, 3H), 1.27–1.44 (m, 10H), 1.59–1.70 (m, 2H), 1.73–1.84 (m, 2H), 1.89–1.98 (m, 2H), 2.05 (s, 1H), 2.86–2.91 (m, 2H), 3.08–3.16 (m, 2H), 3.49–3.56 (m, 2H), 3.85–3.93 ppm (m, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ =

14.0, 22.5, 23.0, 28.4, 28.9, 29.0, 31.6, 33.7, 42.7, 49.4, 66.0 ppm; IR: $\tilde{\nu}$ = 3370, 2925, 2856, 1465, 1330, 1168, 1143, 1038, 973 cm^{-1}; HRMS: *m/z*: calcd for $C_{13}H_{27}NNaO_3S$: 300.1604, found: 300.1605 $[M+Na]^+$.

Octan-1-sulfonyl-4-piperidinone (4f): According to GP 1a alcohol **3f** (8.70 g, 31.36 mmol) was treated with DMP (13.97 g, 32.94 mmol) yielded **4f** as a white solid (8.55 g, 31.04 mmol, 99%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.83 (t, ^3J = 6.9 Hz, 3H), 1.19–1.29 (m, 8H), 1.34–1.41 (m, 2H), 1.72–1.80 (m, 2H), 2.52 (t, ^3J = 6.2 Hz, 4H), 2.93–2.97 (m, 2H), 3.58 ppm (t, ^3J = 6.2 Hz, 4H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 14.0, 22.5, 23.1, 28.3, 28.8, 28.9, 31.6, 41.6, 45.5, 51.1, 205.9 ppm; HRMS: *m/z*: calcd for $C_{13}H_{25}NO_3S$: 275.1555, found: 275.1555 $[M]^+$.

1-Hexylheptyl 4-hydroxy-1-piperidinecarboxylate (3g): A solution of tridecan-7-ol (3.00 g, 14.97 mmol) and phosgene (23.6 mL, 44.85 mmol, 20% in toluene) was stirred in a sealed flask over night. The solvent was removed in vacuo and the residue was dissolved in iPr$_2$NEt (2.60 mL, 15.19 mmol) and treated with 4-hydroxypiperidine (1.51 g, 14.93 mmol). After stirring 2 h water was added and the mixture was extracted with CH_2Cl_2 (2×). The organic layer was dried, evaporated and the resulting residue purified by flash chromatography (CH_2Cl_2/MeOH 100:2) yielded **3g** as a colorless oil (2.35 g, 7.18 mmol, 48%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.81–0.86 (m, 6H), 1.23 (brs, 16H), 1.37–1.49 (m, 6H), 1.79–1.85 (m, 2H), 1.91 (brs, 1H), 3.00–3.09 (m, 2H), 3.77–3.88 (m, 1H + 2H), 4.65–4.73 ppm (m, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 14.0, 22.5, 25.2, 29.2, 31.7, 34.1, 34.2, 41.2, 67.5, 76.2, 155.5 ppm; IR: $\tilde{\nu}$ = 3439, 2930, 2856, 1693, 1667, 1434, 1224, 1076 cm^{-1}; HRMS: *m/z*: calcd for $C_{19}H_{37}NNaO_3$: 350.2666, found: 350.2669 $[M+Na]^+$.

1-Hexylheptyl 4-oxo-1-piperidinecarboxylate (4g): According to GP 1a alcohol **3g** (2.30 g, 7.02 mmol) was treated with DMP (3.13 g, 7.38 mmol) yielded **4g** as a colorless oil (1.14 g, 3.50 mmol, 50%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.81–0.85 (m, 6H), 1.22 (brs, 16H), 1.50 (brs, 4H), 2.40 (t, ^3J = 6.1 Hz, 4H), 3.72 (t, ^3J = 6.2 Hz, 4H), 4.72–4.80 ppm (m, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 14.0, 22.5, 25.2, 29.2, 31.7, 34.2, 41.1, 43.0, 76.2, 155.3, 207.4 ppm; IR: $\tilde{\nu}$ = 2920, 2856, 1698, 1467, 1427, 1225, 1119, 984, 766 cm^{-1}; HRMS: *m/z*: calcd for $C_{19}H_{36}NO_3$: 326.2695, found: 326.2760 $[M]^+$.

2-Ethylhexyl 4-hydroxy-1-piperidinecarboxylate (3h): 2-Ethylhexyl chloroformate (4.2 mL, 21.36 mmol) was added dropwise to an ice-cooled solution of 4-hydroxypiperidine (2.00 g, 19.77 mmol) and iPr$_2$NEt (3.30 mL, 19.97 mmol) in anhydrous CH_2Cl_2 (40 mL). After stirring 1 h diluted HCl was added and the organic layer was dried and evaporated yielded **3h** as a colorless oil (4.78 g, 18.57 mmol, 94%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.83–0.88 (m, 6H), 1.24–1.34 (m, 8H), 1.36–1.55 (m, 1H + 2H), 1.78–1.86 (m, 2H), 2.08 (s, 1H), 3.01–3.10 (m, 2H), 3.77–3.87 (m, 3H), 3.89–3.99 ppm (m, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 11.0, 14.0, 22.9, 23.9, 28.9, 30.5, 34.0, 38.9, 41.2, 67.4, 67.8, 155.7 ppm; IR: $\tilde{\nu}$ = 3439, 2957, 2930, 2862, 1699, 1678, 1434, 1224, 1076 cm^{-1}; HRMS: *m/z*: calcd for $C_{14}H_{27}NNaO_3$: 280.1883, found: 280.1884 $[M+Na]^+$.

2-Ethylhexyl 4-oxo-1-piperidinecarboxylate (4h): According to GP 1a alcohol **3h** (4.70 g, 18.26 mmol) was treated with DMP (8.14 g, 19.19 mmol) yielded **4h** as a colorless oil (4.20 g, 16.45 mmol, 90%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.81–0.88 (m, 6H), 1.24–1.36 (m, 8H), 1.51–1.58 (m, 1H), 2.39 (t, ^3J = 6.2 Hz, 4H), 3.71 (t, ^3J = 6.2 Hz, 4H), 3.94–4.04 ppm (m, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 11.0, 13.9, 22.9, 23.8, 28.8, 30.4, 38.9, 41.0, 42.9, 68.2, 155.4, 207.2 ppm; IR: $\tilde{\nu}$ = 3492, 2962, 2930, 2872, 1699, 1427, 1230, 1121, 1098, 766 cm^{-1}; HRMS: *m/z*: calcd for $C_{14}H_{25}NO_3$: 255.1834, found: 255.1835 $[M]^+$.

Allyl 4-oxocyclohexanecarboxylate (7a): A solution of 4-oxocyclohexanecarboxylic acid (6.30 g, 44.32 mmol), allyl bromide (5.85 g, 48.36 mmol) and K_2CO_3 (6.75 g, 48.84 mmol) in anhydrous DMF (90 mL) was stirred 1.5 h at RT. Water was added and the mixture was extracted several times with PE. The combined organic layers were dried, evaporated and purified by flash chromatography (PE/EtOAc 5:1) yielded **7a** as a yellow oil (7.68 g, 42.15 mmol, 95%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.06 (m, 2H), 2.26 (m, 2H), 2.39 (m, 2H), 2.52 (m, 2H), 2.75 (tt, ^3J = 9.4, 4.4 Hz, 1H), 4.58 (d, ^3J = 5.6 Hz, 2H), 5.21 (dd, ^2J = 1.3, ^3J = 10.4 Hz, 1H), 5.29 (dd, ^2J = 1.3, ^3J = 17.1 Hz, 1H), 5.88 ppm (ddt, ^3J = 17.1, 10.4, 5.6 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 28.4, 39.6, 40.6, 65.3, 118.4, 131.9, 173.7, 209.9 ppm; IR: $\tilde{\nu}$ = 3437, 3017, 2955, 1725, 1647, 1448, 1422, 1381, 1339, 1325, 1304, 1267, 1212, 1177, 1111, 1067, 1029, 994, 934, 751 cm^{-1}; HRMS: *m/z*: calcd for $C_{10}H_{14}O_3$: 182.0943, found: 182.0945 $[M]^+$.

2-(Trimethylsilyl)ethyl 4-oxocyclohexanecarboxylate (7b): A solution of 4-oxocyclohexanecarboxylic acid (1.00 g, 7.03 mmol) and oxalyl dichloride (0.90 mL, 10.48 mmol) in anhydrous CH_2Cl_2 (50 mL) was heated under reflux for 1.5 h. The solvent was removed in vacuo and the residue was added to a solution of NEt_3 (1.20 mL, 8.61 mmol) and (2-hydroxyethyl)trimethylsilane (1.00 mL, 6.98 mmol) in anhydrous CH_2Cl_2 (30 mL). The reaction mixture was stirred 1 h and washed with an aq solution of tartaric acid and aq solution of $NaHCO_3$. The organic layer was dried, evaporated and the resulting residue purified by flash chromatography (CH_2Cl_2) yielded **7b** as a colorless oil (1.14 g, 4.70 mmol, 67%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.18 (brs, 9H), 0.97 (t, ^3J = 8.3 Hz, 2H), 2.00 (m, 2H), 2.16 (m, 2H), 2.31 (m, 2H), 2.44 (m, 2H), 2.67 (tt, ^3J = 9.5, 3.9 Hz, 1H), 4.17 ppm (t, ^3J = 8.2 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = −1.5, 17.3, 28.5, 39.7, 40.8, 63.0, 174.3, 210.2 ppm; IR: $\tilde{\nu}$ = 3427, 3112, 2954, 2899, 1727, 1451, 1384, 1362, 1325, 1305, 1247, 1214, 1176, 1110, 1000, 959, 941, 862, 838, 695 cm^{-1}; HRMS: *m/z*: calcd for $C_{12}H_{22}O_3Si$: 242.1338, found: 242.1337 $[M]^+$.

2-Nitrobenzyl 4-oxocyclohexanecarboxylate (7c): A solution of 4-oxocyclohexanecarboxylic acid (1.00 g, 7.03 mmol) and oxalyl dichloride (0.90 mL, 10.48 mmol) in anhydrous CH_2Cl_2 (50 mL) was heated under reflux for 1.5 h. The solvent was removed in vacuo and the residue was added to a solution of NEt_3 (1.20 mL, 8.61 mmol) and (2-nitrophenyl)methanol (1.08 g, 7.05 mmol) in anhydrous CH_2Cl_2 (30 mL). The reaction mixture was stirred 1 h and washed with an aq solution of tartaric acid and aq solution of $NaHCO_3$. The organic layer was dried, evaporated and the resulting residue purified by flash chromatography (CH_2Cl_2/MeOH 100:1) yielded **7c** as a white solid (1.33 g, 4.80 mmol, 68%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.00 (m, 2H), 2.16 (m, 2H), 2.31 (m, 2H), 2.46 (m, 2H), 2.83 (tt, ^3J = 9.7, 3.9 Hz, 1H), 5.50 (s, 2H), 7.48 (m, 1H), 7.54 (m, 1H), 7.64 (dt, ^3J = 7.5, ^4J = 1.1 Hz, 1H), 8.07 ppm (dd, ^3J = 7.9, ^4J = 1.1 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 28.4, 39.6, 40.6, 63.4, 125.1, 129.1, 129.4, 131.5, 133.7, 134.1, 173.4, 209.7 ppm; IR: $\tilde{\nu}$ = 3438, 2968, 1725, 1701, 1608, 1524, 1432, 1365, 1335, 1298, 1276, 1573, 1253, 1213, 1169, 1033, 1011, 857, 795, 732 cm^{-1}; HRMS: *m/z*: calcd for $C_{14}H_{15}NO_5$: 277.0950, found: 277.0948 $[M]^+$.

4-Oxocyclohexyl 2,2,2-trifluoroacetate (10a): Trifluoroacetic anhydrid (16.40 mL, 117.90 mmol) was added dropwise to an ice cooled solution of 4-hydroxycyclohexanone (6.70 g, 58.70 mmol) and NEt_3 (17.90 mL, 118.30 mmol) in anhydrous CH_2Cl_2 (200 mL) and stirred over night. The reaction mixture was washed with phosphate buffer (3×50 mL; pH 7, 4.54 g KH_2PO_4, 3.79 g Na_2HPO_4, 820 mL H_2O) and the organic layer was dried, evaporated and the resulting residue purified by distillation yielded **10a** as a colorless oil (8.74 g, 41.90 mmol, 71%). B.p. 44 °C (1×10^{-6} bar); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.07–2.26 (m, 4H), 2.32–2.41 (m, 2H), 2.49–2.59 (m, 2H), 5.32–5.39 ppm (m, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 36.4, 73.4, 114.3 (q, ^1J = 286 Hz), 156.7 (q, ^2J = 43 Hz), 207.9 ppm; IR: $\tilde{\nu}$ = 2962, 1782, 1721, 1221, 1159 cm^{-1}.

4-Oxocyclohexyl pivalate (10b):[35] Pivaloyl chloride (6.60 mL, 53.60 mmol) was added dropwise to a cooled solution (−20 °C) of 4-hydroxycyclohexanone (3.64 g, 31.90 mmol) and pyridine (4.40 mL, 54.40 mmol) in anhydrous CH_2Cl_2 (50 mL) and stirred over night. The reaction mixture was washed with an aq solution of potassium sodium tartrate and aq solution of $NaHCO_3$. The organic layer was dried, evaporated and the resulting residue purified by flash chromatography (CH_2Cl_2/MeOH 100:2) yielded **10b** as a white solid (4.07 g, 20.50 mmol, 64%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.20 (s, 9H), 1.94–2.13 (m, 4H), 2.29–2.38 (m, 2H), 2.46–2.57 (m, 2H), 5.09–5.15 ppm (m, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 27.1, 30.3, 37.1, 38.9, 67.9, 177.8, 210.1 ppm.

4-(4-Methoxybenzyloxy)-cyclohexanone (10c):[36] (4-Methoxyphenyl)methanol (8.70 g, 62.67 mmol) and 2,2,2-trichloroacetonitrile (6.40 mL, 63.65 mmol) in anhydrous Et_2O (20 mL) was added to an ice cooled suspension of NaH (60% in mineral oil, 510 mg, 12.75 mmol) in anhydrous Et_2O (250 mL) and stirred for 30 min at 0 °C. After stirring 2 h at RT, aq $NaHCO_3$ solution was added and the organic layer was washed with brine, dried and evaporated. The resulting yellow oil was added to a solution of 4-hydroxycyclohexanone (7.10 g, 62.20 mmol) in CH_2Cl_2 (150 mL)

and treated with pyridinium *p*-toluenesulfonate (150 mg, 0.60 mmol). After stirring over night the reaction mixture was washed with water. The organic layer was dried, evaporated and the resulting residue purified by flash chromatography (PE/EtOAc 3:1) yielded **10c** as a white solid (7.37 g, 31.46 mmol, 50%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.90 (m, 2H), 2.07 (m, 2H), 2.32 (m, 2H), 2.56 (m, 2H), 3.75 (s, 3H), 3.72–3.78 (m, 1H), 4.47 (s, 2H), 6.84 (d, ^3J = 8.5 Hz, 2H), 7.23 ppm (d, ^3J = 8.5 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 30.5, 37.2, 55.3, 69.9, 71.9, 113.8, 129.0, 130.5, 159.1, 211.5 ppm.

4-Oxocyclohexyl acetate (10d):[37] Acetic anhydride (7.00 mL, 74.05 mmol) was added dropwise to an ice cooled solution of 4-hydroxycyclohexanone (7.13 g, 62.47 mmol) and pyridine (6.00 mL, 74.18 mmol) in anhydrous CH_2Cl_2 (150 mL) and stirred over night at RT. The reaction mixture was washed with an aq solution of potassium sodium tartrate and aq solution of $NaHCO_3$. The organic layer was dried, evaporated and the resulting residue purified by flash chromatography (CH_2Cl_2/MeOH 100:1) yielded **10d** as a white solid (4.73 g, 30.29 mmol, 49%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.98–2.05 (m, 4H), 2.04 (s, 3H), 2.30 (m, 2H), 2.48 (m, 2H), 5.10 ppm (m, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.2, 30.3, 37.2, 68.6, 170.4, 209.8 ppm.

Benzyl 3,3-bis(hydroxymethyl)-1,5-dioxa-9-azaspiro[5.5]undecane-9-carboxylate (12a): According to GP 2 ketone **4a** (5.90 g, 25.08 mmol) was treated with pentaerythritol (3.45 g, 25.34 mmol) and *p*-toluenesulfonic acid (81 mg, 0.43 mmol) yielded **12a** as a white solid (5.13 g, 14.60 mmol, 58%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.80 (brs, 4H), 2.82 (brs, 2H), 3.48 (t, ^3J = 6.0 Hz, 4H), 3.70 (s, 8H), 5.09 (s, 2H), 7.32 ppm (m, 5H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 31.8, 32.6, 39.2, 40.6, 62.0, 64.4, 67.2, 96.7, 127.8, 128.0, 128.5, 136.6, 155.2 ppm; IR: $\tilde{\nu}$ = 2961, 2938, 2883, 1688, 1468, 1452, 1425, 1359, 1330, 1273, 1233, 1170, 1147, 1107, 1054, 1037, 999, 951, 734, 698 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{18}H_{25}NO_6$: 351.1682, found: 351.1682 $[M]^+$.

[3-(Hydroxymethyl)-9-(octan-1-sulfonyl)-1,5-dioxa-9-azaspiro[5.5]undec-3-yl]methanol (12b): According to GP 2 ketone **4f** (2.91 g, 10.57 mmol) was treated with pentaerythritol (1.55 g, 11.39 mmol) and *p*-toluenesulfonic acid (36 mg, 0.19 mmol). Purification by flash chromatography (CH_2Cl_2/MeOH 10:1) yielded **12b** as a white solid (2.43 g, 6.18 mmol, 58%). M.p. 141–142 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.84 (t, ^3J = 6.9 Hz, 3H), 1.22–1.28 (m, 8H), 1.32–1.39 (m, 2H), 1.71–1.78 (m, 2H), 1.89–1.92 (m, 4H), 2.75 (s, 2H), 2.83–2.87 (m, 2H), 3.25–3.28 (m, 4H), 3.67 (s, 4H), 3.69 ppm (s, 4H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 14.0, 22.5, 23.0, 28.4, 28.9, 29.0, 31.6, 32.3, 39.2, 42.7, 49.5, 62.0, 64.2, 96.1 ppm; IR: $\tilde{\nu}$ = 3328, 3280, 2962, 2920, 2872, 2856, 1329, 1316, 1149, 1130, 1047 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{18}H_{35}NaO_6S$: 416.2077, found: 416.2078 $[M+Na]^+$.

1-Hexylheptyl 3,3-bis(hydroxymethyl)-1,5-dioxa-9-azaspiro[5.5]undecane-9-carboxylate (12c): According to GP 2 ketone **4g** (1.00 g, 3.07 mmol) was treated with pentaerythritol (0.43 g, 3.16 mmol) and *p*-toluenesulfonic acid (10 mg, 0.05 mmol). Purification by flash chromatography (CH_2Cl_2/MeOH 10:1) yielded **12c** as a white solid (1.00 g, 2.25 mmol, 71%). M.p. 47–50 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.81–0.86 (m, 6H), 1.23 (brs, 16H), 1.48 (brs, 4H), 1.78 (brs, 4H), 2.88 (s, 2H), 3.42–3.46 (m, 4H), 3.71 (brs, 8H), 4.65–4.73 ppm (m, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 14.0, 22.5, 25.1, 29.2, 31.7, 39.2, 34.2, 40.5, 62.1, 64.6, 75.7, 96.8, 155.5 ppm; IR: $\tilde{\nu}$ = 3428, 2930, 2856, 1671, 1467, 1438, 1235, 1109, 1055 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{24}H_{45}NNaO_6$: 466.3139, found: 466.3139 $[M+Na]^+$.

2-Ethylhexyl 3,3-bis(hydroxymethyl)-1,5-dioxa-9-azaspiro[5.5]undecane-9-carboxylate (12d): According to GP 2 ketone **4h** (2.79 g, 10.93 mmol) was treated with pentaerythritol (1.62 g, 11.90 mmol) and *p*-toluenesulfonic acid (38 mg, 0.20 mmol) yielded **12d** as a white solid (2.93 g, 7.85 mmol, 72%). M.p. 59–62 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.83–0.88 (m, 6H), 1.22–1.36 (m, 8H), 1.47–1.55 (m, 1H), 1.76–1.80 (m, 4H), 3.01 (s, 2H), 3.41–3.45 (m, 4H), 3.67–3.69 (m, 8H), 3.89–3.98 ppm (m, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 11.0, 14.0, 22.9, 23.9, 28.9, 30.4, 32.2, 38.9, 39.2, 40.5, 62.0, 64.3, 68.0, 96.7, 155.7 ppm; IR: $\tilde{\nu}$ = 3349, 2962, 1688, 1430, 1281, 1230, 1106, 1024, 696 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{19}H_{35}NO_6$: 373.2464, found: 373.2464 $[M]^+$.

3,3-Bis(hydroxymethyl)-1,5-dioxaspiro[5.5]undec-9-yl pivalate (12e): According to GP 2 ketone **10b** (6.53 g, 32.94 mmol) was treated with pentaerythritol (4.93 g, 36.21 mmol) and *p*-toluenesulfonic acid (180 mg, 0.95 mmol). Purification by recrystallization (toluene) yielded **12e** as a white solid (6.15 g, 19.44 mmol, 59%). ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 1.19 (s, 9H), 1.58–1.81 (m, 8H), 3.42 (d, ^3J = 5.3 Hz, 5H), 3.68 (d, ^3J = 7.2 Hz, 3H), 4.80 ppm (m, 1H); ^{13}C NMR (75.5 MHz, [D$_6$]DMSO): δ = 26.5, 26.8, 28.2, 38.3, 39.0, 60.5, 61.0, 61.1, 61.3, 69.5, 96.3, 176.8 ppm; IR: $\tilde{\nu}$ = 3402, 3336, 2962, 2877, 1377, 1171, 1713, 1476, 1441, 1395, 1283, 1260, 1242, 1142, 1096, 1049, 1032, 1001, 931, 896 cm^{-1}; MS (70 eV, EI): *m*/*z* (%): 259.1 (5) $[M-CMe_3]^+$, 301.2 (2) $[M-CH_3]^+$.

{3-(Hydroxymethyl)-9-[(4-methoxybenzyl)oxy]-1,5-dioxaspiro[5.5]undec-3-yl}methanol (12f): According to GP 2 ketone **10c** (8.49 g, 36.24 mmol) was treated with pentaerythritol (5.43 g, 39.88 mmol) and *p*-toluenesulfonic acid (120 mg, 0.63 mmol). Purification by flash chromatography (CH_2Cl_2/MeOH 100:8) yielded **12f** as a white solid (5.75 g, 16.32 mmol, 45%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.61–1.78 (m, 6H), 1.97–2.05 (m, 2H), 2.64 (brs, 2H), 3.46 (brs, 1H), 3.69 (brs, 8H), 3.77 (s, 3H), 4.42 (s, 2H), 6.84 (d, ^3J = 8.7 Hz), 7.23 ppm (d, ^3J = 8.7 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 27.1, 28.6, 39.0, 55.2, 61.9, 62.3, 64.8, 69.6, 74.2, 98.1, 113.7, 129.0, 130.9, 159.0 ppm; IR: $\tilde{\nu}$ = 3314, 2939, 2871, 2856, 1611, 1512, 1440, 1371, 1348, 1301, 1245, 1170, 1142, 1100, 1061, 1000, 930, 916, 823, 809 cm^{-1}; HRMS: *m*/*z*. calcd for $C_{19}H_{29}O_6$: 353.1959, found: 353.1959 $[M]^+$.

9*H*-Fluoren-9-ylmethyl 3,3-bis(hydroxymethyl)-1,5-dioxa-9-azaspiro-[5.5]undecane-9-carboxylate (12g): Compound **12g** was obtained as by-product by preparation of **14m**. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.78 (brs, 4H), 2.70 (brs, 2H), 3.46 (brs, 4H), 3.72 (s, 8H), 4.22 (t, ^3J = 6.8 Hz, 1H), 4.40 (d, ^3J = 6.8 Hz, 2H), 7.35 (dt, ^3J = 7.4, ^4J = 1.1 Hz, 2H), 7.38 (t, ^3J = 7.4 Hz, 2H), 7.55 (d, ^3J = 7.4 Hz, 2H), 7.75 ppm (d, ^3J = 7.4 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 31.8, 32.4, 39.2, 40.6, 47.2, 62.0, 64.5, 67.3, 96.7, 120.0, 124.8, 127.0, 127.7, 141.3, 143.9, 155.1 ppm; HRMS: *m*/*z*. calcd for $C_{25}H_{29}NO_6$: 440.2073, found: 440.2068 $[M]^+$.

15-[(4-Methoxybenzyl)oxy]-7,11,18,21-tetraoxatrispiro[5.2.2.5.2.2]henicos-3-yl pivalate (14a):[38] ***Method A***: According to GP 2 ketone **10b** (1.27 g, 6.42 mmol) was treated with diol **12f** (2.27 g, 6.43 mmol) and *p*-toluenesulfonic acid (120 mg, 0.63 mmol). Purification by flash chromatography (PE/EtOAc 10:2) yielded **14a** as a white solid (1.06 g, 1.99 mmol, 31%).

Method B: According to GP 3 ketone **10b** (0.68 g, 3.43 mmol) was treated with diol **12f** (1.22 g, 3.46 mmol) yielded **14a** as a white solid (1.81 g, 3.40 mmol, 99%).

Method C: According to GP 3 ketone **10c** (1.35 g, 5.77 mmol) was treated with diol **12e** (1.83 g, 5.79 mmol) yielded **14a** as a white solid (1.63 g, 3.06 mmol, 53%). M.p. 84–86 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.19 (s, 9H), 1.59–2.00 (m, 16H), 3.48 (m, 1H), 3.71–3.75 (m, 8H), 3.80 (s, 3H), 4.44 (s, 2H), 4.85 (m, 1H), 6.86 (d, ^3J = 8.7 Hz, 2H), 7.25 ppm (d, ^3J = 8.7 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 26.7, 27.1, 28.5, 30.4, 32.8, 37.1, 38.8, 55.2, 63.2, 63.3, 63.6, 69.5, 69.6, 74.2, 97.7, 98.1, 113.7, 129.0, 130.9, 159.0, 177.9 pppm; IR: $\tilde{\nu}$ = 2953, 2932, 2867, 1719, 1610, 1511, 1478, 1440, 1369, 1280, 1200, 1164, 1143, 1109, 1091, 1056, 1036, 1011, 929, 910 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{30}H_{44}O_8$: 532.3037, found: 532.3036 $[M]^+$.

Allyl 15-[(4-methoxybenzyl)oxy]-7,11,18,21-tetraoxatrispiro[5.2.2.5.2.2]-henicosane-3-carboxylate (14b): According to GP 3 cyclohexanone **7a** (1.38 g, 7.57 mmol) was treated with **12f** (2.56 g, 7.26 mmol). Purification by flash chromatography (PE/EtOAc 3:1) yielded **14b** as a white solid (3.33 g, 6.44 mmol, 89%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.45 (dt, ^3J = 12.5, 3.9 Hz, 2H), 1.63–1.89 (m, 10H), 1.97–2.04 (m, 2H), 2.16–2.19 (m, 2H), 2.37 (tt, ^3J = 10.36, 4.0 Hz, 1H), 3.48 (m, 1H), 3.72 (dd, ^3J = 9.6, 7.7 Hz, 8H), 3.80 (s, 3H), 4.44 (s, 2H), 4.57 (dt, ^3J = 5.6, = 1.5 Hz, 2H), 5.22 (tdd, ^{2}J = 1.3, ^3J = 10.4, ^4J = 1.5 Hz, 1H), 5.30 (tdd, ^2J = 1.3, ^3J = 17.2, ^4J = 1.5 Hz, 1H), 5.88 (ddt, ^3J = 17.2, ^3J = 10.4, 5.6 Hz, 1H), 6.86 (d, ^3J = 8.6 Hz, 2H), 7.25 ppm (d, ^3J = 8.6 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 24.7, 27.1, 28.4, 28.7, 30.7, 31.2, 32.8, 41.9, 55.2, 63.2, 63.5, 63.6, 64.9, 69.5, 74.2, 97.7, 98.1, 113.7, 118.0, 129.0, 131.0, 132.2, 159.0, 174.8 ppm; IR: $\tilde{\nu}$ = 3394, 2873, 1727, 1609, 1511, 1479, 1443, 1370, 1343, 1315, 1300,

1246, 1206, 1184, 1161, 1095, 1055, 1031, 1004, 914 cm^{-1}; HRMS: *m/z*: calcd for $C_{29}H_{41}O_8$: 517.2796, found: 517.2796 $[M]^+$.

2-(Trimethylsilyl)ethyl 15-[(4-methoxybenzyl)oxy]-7,11,18,21-tetraoxatrispiro[5.2.2.5.2.2]henicosane-3-carboxylate (14c): According to GP 3 cyclohexanone **7b** (1.00 g, 4.13 mmol) was treated with **12f** (1.40 g, 3.97 mmol). Purification by flash chromatography (PE/EtOAc 5:1) yielded **14c** as a white solid (1.57 g, 2.72 mmol, 69%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.00 (s, 9H), 0.93 (t, ^3J = 8.5 Hz, 2H), 1.42 (dt, ^3J = 12.3, 3.6 Hz, 2H), 1.61–1.82 (m, 10H), 1.93–2.00 (m, 2H), 2.07–2.13 (m, 2H), 2.26 (tt, ^3J = 10.3, 2.6 Hz, 1H), 3.43 (m, 1H), 3.68 (dd, ^3J = 9.6, 7.4 Hz, 8H), 3.76 (s, 3H), 4.11 (t, ^3J = 8.5 Hz, 2H), 4.41 (s, 2H), 6.83 (d, ^3J = 8.7 Hz, 2H), 7.22 ppm (d, ^3J = 8.7 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = −1.5, 17.2, 24.7, 27.1, 28.4, 28.7, 30.7, 31.2, 32.8, 42.0, 55.2, 62.5, 63.2, 63.5, 63.6, 69.5, 74.2, 97.7, 98.1, 113.7, 129.0, 131.0, 159.0, 175.3 ppm; IR: $\tilde{\nu}$ = 2952, 2896, 2865, 1725, 1613, 1513, 1444, 1369, 1307, 1250, 1203, 1188, 1165, 1091, 1058, 1035, 989, 855, 837, 760 cm^{-1}; HRMS: *m/z*: calcd for $C_{31}H_{48}NaO_8Si$: 599.3016, found: 599.3019 $[M+Na]^+$.

2-Nitrobenzyl 15-[(4-methoxybenzyl)oxy]-7,11,18,21-tetraoxatrispiro[5.2.2.5.2.2]henicosane-3-carboxylate (14d): According to GP 3 cyclohexanone **7c** (2.24 g, 8.08 mmol) was treated with **12f** (2.84 g, 8.06 mmol). Purification by flash chromatography (CH_2Cl_2/MeOH 100:4) yielded **14d** as a white solid (4.38 g, 7.16 mmol, 89%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.42 (dt, ^3J = 12.8, 3.8 Hz, 2H), 1.50–1.60 (m, 4H), 1.70–1.78 (m, 4H), 1.84–1.90 (m, 2H), 2.00–2.05 (m, 2H), 2.10–2.18 (m, 2H), 2.41 (tt, ^3J = 12.8, 3.3 Hz, 1H), 3.51 (m, 1H), 3.75 (dd, ^3J = 9.6, 7.7 Hz, 8H), 3.82 (s, 3H), 4.47 (s, 2H), 5.52 (s, 2H), 6.89 (d, ^3J = 8.7 Hz, 2H), 7.28 (d, ^3J = 8.7 Hz, 2H), 7.51–7.6 (m, 2H), 7.67 (dt, ^3J = 8.0, ^4J = 1.1 Hz, 1H), 8.11 ppm (dd, ^3J = 8.0, ^4J = 1.1 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 24.7, 27.1, 28.4, 28.6, 30.7, 31.1, 32.7, 41.9, 55.2, 62.9, 63.1, 63.2, 63.4, 63.6, 69.5, 74.2, 97.6, 98.1, 113.6, 125.0, 128.7, 128.9, 129.0, 131.0, 132.0, 133.6, 147.5, 159.0, 174.4 ppm; IR: $\tilde{\nu}$ = 3454, 3392, 3220, 2862, 1732, 1696, 1610, 1441, 1343, 1317, 1278, 1249, 1204, 1166, 1097, 1031, 978, 912, 815, 726 cm^{-1}; HRMS: *m/z*: calcd for $C_{33}H_{41}NNaO_{10}$: 634.2623, found: 634.2623 $[M+Na]^+$.

Ethyl 15-[(4-methoxybenzyl)oxy]-7,11,18,21-tetraoxatrispiro[5.2.2.5.2.2]-henicosane-3-carboxylate (14e): According to GP 3 ethyl-4-oxocyclohexanecarboxylate (0.87 g, 5.11 mmol) was treated with **12f** (1.80 g, 5.11 mmol) yielded **14e** as a white solid (2.56 g, 5.07 mmol, 99%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.18 (t, ^3J = 7.2 Hz, 3H), 1.33–1.42 (m, 2H), 1.59–1.80 (m, 10H), 1.91–1.94 (m, 2H), 2.05–2.11 (m, 2H), 2.25 (tt, ^3J = 10.4, 3.9 Hz, 1H), 3.65 (dd, ^3J = 9.2, 7.0 Hz, 8H), 3.73 (s, 3H), 3.74 (m, 1H), 4.05 (q, ^3J = 7.2 Hz, 2H), 4.38 (s, 2H), 6.80 (d, ^3J = 8.7 Hz, 2H), 7.19 ppm (d, ^3J = 8.7 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 14.2, 24.7, 27.1, 28.4, 28.7, 30.7, 31.2, 32.8, 41.9, 55.2, 60.2, 63.2, 63.5, 63.6, 69.5, 74.2, 97.7, 98.1, 113.7, 129.0, 131.0, 159.0, 175.2 ppm; IR: $\tilde{\nu}$ = 3432, 2928, 1723, 1611, 1511, 1478, 1444, 1370, 1343, 1317, 1300, 1247, 1189, 1161, 1056, 1029, 959, 929, 913, 814 cm^{-1}; HRMS: *m/z*: calcd for $C_{28}H_{41}O_8$: 505.2796, found: 505.2799 $[M]^+$.

15-[(2,2,2-Trifluoroacetyl)oxy]-7,11,18,21-tetraoxatrispiro[5.2.2.5.2.2]henicos-3-yl 2,2,2-trifluoroacetate (14f): According to GP 4 silane **13** (2.02 g, 4.76 mmol) and ketone **10a** (2.02 g, 9.61 mmol) was treated with TMSOTf (45 µL, 0.25 mmol) in anhydrous Et_2O (40 mL) yielded **14f** as a tawny oil (2.58 g, >99%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.82–1.96 (m, 16H), 3.75–3.76 (m, 8H), 5.10 ppm (s, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 26.4, 27.8, 28.1, 32.9, 63.3, 63.6, 75.4, 97.3, 114.5 (q, ^1J = 286 Hz), 156.9 ppm (q, ^2J = 42 Hz); IR: $\tilde{\nu}$ = 3020, 1777, 1214, 1168, 771, 667 cm^{-1}; HRMS: *m/z*: calcd for $C_{21}H_{26}ClF_6O_8$: 555.1229, found: 555.1215 $[M]^+$.

15-[(2,2-Dimethylpropanoyl)oxy]-7,11,18,21-tetraoxatrispiro[5.2.2.5.2.2]-henicos-3-yl pivalate (14g): According to GP 4 silane **13** (0.21 g, 0.49 mmol) and ketone **10b** (0.20 g, 1.01 mmol) was treated with TMSOTf (10 µL, 0.06 mmol). Purification by flash chromatography (CH_2Cl_2/MeOH 100:2) yielded **14g** as a white solid (0.23 g, 0.46 mmol, 95%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.15 (s, 18H), 1.59–1.89 (m, 16H), 3.70 (d, ^3J = 11.3 Hz, 8H), 4.81 ppm (m, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 26.7, 27.1, 28.2, 28.3, 32.9, 38.8, 63.3, 63.6, 69.6, 97.8, 178.0 ppm; IR: $\tilde{\nu}$ = 3269, 2964, 2868, 1714, 1477, 1443, 1395, 1378, 1364, 1283, 1254, 1229, 1199, 1168, 1090, 1074, 1032, 948, 935, 904 cm^{-1}; HRMS: *m/z*: calcd for $C_{27}H_{45}O_8$: 497.3109, found: 497.3110 $[M]^+$.

15-(Acetyloxy)-7,11,18,21-tetraoxatrispiro[5.2.2.5.2.2]henicos-3-yl acetate (14h): According to GP 4 silane **13** (0.75 g, 1.77 mmol) and ketone **10d** (0.54 g, 3.46 mmol) was treated with TMSOTf (30 µL, 0.17 mmol). Purification by flash chromatography (CH_2Cl_2/MeOH 100:4) yielded **14h** as a white solid (0.65 g, 1.58 mmol, 91%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.59–1.74 (m, 12H), 1.82–1.90 (m, 4H), 1.96 (s, 6H), 3.66 (d, ^3J = 10.6 Hz, 8H), 4.75–4.77 ppm (m, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 21.3, 26.9, 28.3, 28.6, 32.8, 63.3, 63.6, 70.4, 97.7, 170.6 ppm; HRMS: *m/z*: calcd for $C_{21}H_{33}O_8$: 413.2175, found: 413.2179 $[M]^+$.

Bis-(9*H*-fluoren-9-ylmethyl) 7,11,18,21-tetraoxa-3,15-diazatrispiro-[5.2.2.5.2.2]henicosane-3,15-dicarboxylate (14i): According to GP 4 silane **13** (0.30 g, 0.71 mmol) and ketone **4b** (0.46 g, 1.43 mmol) was treated with TMSOTf (15 µL, 0.12 mmol). Purification by flash chromatography (CH_2Cl_2/MeOH 100:4) yielded **14i** as a white solid (0.43 g, 0.58 mmol, 82%). ^{1}H NMR (300 MHz, CD_2Cl_2/CD_3OD): δ = 1.72 (brs, 8H), 3.39 (brs, 8H), 3.71 (s, 8H), 4.21 (t, ^3J = 6.5 Hz, 2H), 4.38 (d, ^3J = 6.5 Hz, 4H), 7.29 (dt, ^3J = 7.4, ^4J = 1.2 Hz, 4H), 7.37 (dt, ^3J = 7.5, ^4J = 0.6 Hz, 4H), 7.55 (d, ^3J = 7.4 Hz, 4H), 7.75 ppm (d, ^3J = 7.3 Hz, 4H); ^{13}C NMR (75.5 MHz, CD_2Cl_2/CD_3OD): δ = 32.2, 32.7, 33.3, 41.1, 47.8, 63.7, 67.8, 97.4, 120.4, 125.3, 127.5, 128.1, 141.8, 144.5, 155.9 ppm; HRMS: *m/z*: calcd for $C_{45}H_{47}N_2O_8$: 743.3332, found: 743.3327 $[M]^+$.

Bis{[2,7-di(tert-butyl)-9*H*-fluoren-9-yl]methyl} 7,11,18,21-tetraoxa-3,15-diazatri-spiro[5.2.2.5.2.2]henicosane-3,15-dicarboxylate (14j): According to GP 4 silane **13** (131 mg, 0.31 mmol) and ketone **4c** (265 mg, 0.61 mmol) was treated with TMSOTf (5 µL, 0.03 mmol). Purification by flash chromatography (CH_2Cl_2/MeOH 100:4) yielded **14j** as a white solid (170 mg, 0.18 mmol, 57%). M.p. 171–172 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.36 (s, 36H), 1.83 (brs, 8H), 3.56 (brs, 8H), 3.75–3.80 (m, 8H), 4.17 (t, ^3J = 7.2 Hz, 2H), 4.38 (d, ^3J = 7.2 Hz, 4H), 7.40 (dd, ^3J = 8.0, ^4J = 1.6 Hz, 4H), 7.58 (s, 4H), 7.63 ppm (d, ^3J = 8.0 Hz, 4H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 31.6, 33.1, 33.1, 34.9, 40.7, 47.4, 63.4, 67.9, 97.0, 119.2, 121.8, 124.8, 138.7, 144.0, 149.7, 155.2 ppm; IR: $\tilde{\nu}$ = 3455, 1698, 1446, 1232, 1100, 756, 737 cm^{-1}; MS (MALDI): *m/z*: calcd for $C_{61}H_{78}N_2NaO_8$: 989.6, found: 990.2 $[M+Na]^+$.

Bis{[2-(2-ethylhexyl)-9*H*-fluoren-9-yl]methyl} 7,11,18,21-tetraoxa-3,15-diazatri-spiro[5.2.2.5.2.2]henicosane-3,15-dicarboxylate (14k): According to GP 4 silane **13** (119 mg, 0.28 mmol) and ketone **4d** (241 mg, 0.56 mmol) was treated with TMSOTf (5 µL, 0.03 mmol). Purification by flash chromatography (PE/EtOAc 2:1) yielded **14k** as a yellow oil (160 mg, 0.17 mmol, 59%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.85–0.90 (m, 12H), 1.20–1.35 (m, 16H), 1.56–1.60 (m, 2H), 1.80 (brs, 4H), 2.52–2.64 (m, 4H), 3.49 (brs, 8H), 3.74 (brs, 8H), 4.19 (t, ^3J = 6.8 Hz, 2H), 4.32–4.48 (m, 4H), 7.17 (d, ^3J = 7.8 Hz, 2H), 7.26 (dt, ^3J = 7.4, ^4J = 1.0 Hz, 2H), 7.34 (s, 2H), 7.36 (t, ^3J = 7.5 Hz, 2H), 7.53 (d, ^3J = 7.3 Hz, 2H), 7.64 (d, ^3J = 7.7 Hz, 2H), 7.70 ppm (d, ^3J = 7.4 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 10.8, 14.1, 23.0, 25.4, 28.8, 31.5, 32.3, 32.5, 33.0, 40.3, 40.6, 41.3, 47.2, 63.3, 67.4, 96.9, 119.5, 119.6, 124.9, 125.7, 126.5, 127.6, 128.7, 138.8, 141.1, 141.5, 144.0, 155.1 ppm; IR: $\tilde{\nu}$ = 3386, 2930, 1698, 1435, 1361, 1264, 1232, 1097, 737 cm^{-1}; HRMS: *m/z*: calcd for $C_{61}H_{78}N_2NaO_8$: 989.5648, found: 989.5650 $[M+Na]^+$; elemental analysis calcd (%) for $C_{61}H_{78}N_2O_8$ (967.3): C 75.74, H 8.13, N 2.90, found: C 74.93, H 8.28, N 2.86.

Bis{[2,7-bis(2-ethylhexyl)-9*H*-fluoren-9-yl]methyl} 7,11,18,21-tetraoxa-3,15-diazatrispiro[5.2.2.5.2.2]henicosane-3,15-dicarboxylate (14l): According to GP 4 silane **13** (178 mg, 0.42 mmol) and ketone **4e** (459 mg, 0.84 mmol) was treated with TMSOTf (10 µL, 0.06 mmol). Purification by flash chromatography (PE/EtOAc 3:1) yielded **14l** as a green oil (420 mg, 0.35 mmol, 84%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.89–0.93 (m, 24H), 1.26–1.38 (m, 32H), 1.59–1.63 (m, 4H), 1.85 (brs, 8H), 2.55–2.67 (m, 8H), 3.54–3.57 (m, 8H), 3.78 (brs, 8H), 4.20 (t, ^3J = 6.9 Hz, 2H), 4.42 (d, ^3J = 7.0 Hz, 4H), 7.18 (d, ^3J = 7.8 Hz, 4H), 7.36 (s, 4H), 7.63 ppm (d, ^3J = 7.7 Hz, 4H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 10.8, 14.1, 23.0, 25.4, 28.8, 31.6, 32.3, 32.8, 33.0, 40.3, 40.6, 41.4, 47.0, 63.3, 67.6, 96.9, 119.2, 125.7, 128.6, 139.0, 140.5, 144.0, 155.1 ppm; IR: $\tilde{\nu}$ = 3439, 2930, 2856, 1699, 1465, 1434, 1230, 1098, 758 cm^{-1}; HRMS: *m/z*: calcd for $C_{77}H_{111}N_2O_8$: 1191.8334, found: 1191.8335 $[M]^+$.

9*H*-Fluoren-9-ylmethyl 15-hydroxy-7,11,18,21-tetraoxa-3-azatrispiro-[5.2.2.5.2.2]henicosane-3-carboxylate (14m): TMSOTf (15 μL, 0.08 mmol) was added to an ice cooled solution of ketone **4b** (0.76 g, 2.36 mmol) and **13** (1.00 g, 2.35 mmol) in anhydrous Et_2O and stirred at 0 °C until complete conversion of **4b** controlled by TLC. Ketone **10c** (0.55 g, 2.35 mmol) was added and the mixture was stirred at 0 °C until complete conversion of **4b** controlled by TLC. The solvent was removed in vacuo and the resulting residue was purified by flash chromatography (CH_2Cl_2/MeOH 100:4) yielded **14m** as a yellow solid (0.38 g, 0.71 mmol, 30 %), **14i** as a white solid (0.52 g, 0.70 mmol) and **12g** as a white solid (0.10 g, 0.23, 10 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.57 (m, 2H), 1.71–1.77 (m, 1H + 4H), 1.97 (m, 1H), 1.99–2.08 (m, 2H), 2.24 (ddd, ^2J = 14.6, ^3J = 7.2, 6.1 Hz, 1H), 2.58 (ddd, ^2J = 14.6, ^3J = 8.6, 6.1 Hz, 1H), 3.46 (br s, 4H), 3.72 (br s, 8H), 4.17 (m, 1H), 4.22 (t, ^3J = 6.9 Hz, 1H), 4.40 (d, ^3J = 6.8 Hz, 2H), 7.29 (dt, ^3J = 7.4, ^4J = 1.3 Hz, 2H), 7.38 (t, ^3J = 7.4 Hz, 2H), 7.54 (d, ^3J = 7.5 Hz, 2H), 7.74 ppm (d, ^3J = 7.5 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 28.6, 30.3, 31.6, 32.3, 32.8, 33.6, 37.1, 40.5, 47.2, 63.0, 63.3, 63.4, 67.1, 68.1, 96.7, 97.9, 119.8, 124.8, 126.9, 127.5, 141.2, 143.8, 155.0 ppm; HRMS: *m*/*z*: calcd for $C_{31}H_{38}NO_7$: 536.2648, found: 536.2657 $[M]^+$.

15-Hydroxy-7,11,18,21-tetraoxatrispiro[5.2.2.5.2.2]henicos-3-yl pivalate (15a): According to GP 5 trispirane **14a** (1.81 g, 3.40 mmol) was treated with DDQ (0.85 g, 3.74 mmol) yielded **15a** as a white solid (0.79 g, 1.92 mmol, 56 %). M.p. 132–134 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.15 (s, 9H), 1.50–2.06 (m, 16H), 3.68–3.72 (m, 8H), 3.75 (m, 1H), 4.85 ppm (m, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 26.7, 27.1, 28.1, 28.3, 28.6, 28.7, 30.4, 32.8, 38.8, 63.2, 63.3, 63.5, 63.6, 68.4, 69.6, 97.8, 98.0, 177.9 ppm; IR: $\tilde{\nu}$ = 2959, 2868, 1726, 1478, 1460, 1442, 1373, 1337, 1249, 1232, 1200, 1163, 1141, 1282, 1096, 1058, 971, 950, 932, 911 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{22}H_{36}O_7$: 412.2461, found: 412.2460 $[M]^+$.

15-Oxo-7,11,18,21-tetraoxatrispiro[5.2.2.5.2.2]henicos-3-yl pivalate (16a): According to GP 1a alcohol **15a** (1.16 g, 2.81 mmol) was treated with DMP (1.31 g, 3.09 mmol). Purification by flash chromatography (CH_2Cl_2/MeOH 100:4) yielded **16a** as a pale yellow solid (1.13 g, 2.75 mmol, 98 %). M.p. 141–148 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.15 (s, 9H), 1.70 (m, 4H), 1.82 (m, 4H), 2.10 (dd, ^3J = 7.0, 7.0 Hz, 4H), 2.37 (dd, ^3J = 7.0, 7.0 Hz, 4H), 3.76–3.77 (m, 8H), 4.82 ppm (m, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 26.7, 27.1, 28.2, 30.9, 32.8, 36.8, 38.8, 63.2, 63.4, 63.9, 69.5, 97.0, 97.9, 177.9, 210.4 ppm; IR: $\tilde{\nu}$ = 2963, 2937, 2867, 1709, 1478, 1441, 1426, 1378, 1321, 1283, 1254, 1231, 1197, 1170, 1145, 1121, 1086, 1033, 931, 901 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{22}H_{34}O_7$: 410.2305, found: 410.2303 $[M]^+$.

Allyl 15-hydroxy-7,11,18,21-tetraoxatrispiro[5.2.2.5.2.2]henicosane-3-carboxylate (15b): According to GP 5 trispirane **14b** (4.15 g, 8.03 mmol) was treated with DDQ (2.01 g, 8.85 mmol). Purification by flash chromatography (CH_2Cl_2/MeOH 100:4) yielded **15b** as a white solid (1.68 g, 4.24 mmol, 53 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.41 (dt, ^3J = 12.8, 3.6 Hz, 2H), 1.49–1.85 (m, 10H), 2.01–2.15 (m, 4H), 2.37 (tt, ^3J = 10.5, 4.5 Hz, 1H), 3.66–3.72 (m, 8H), 3.76 (m, 1H), 4.53 (dt, ^3J = 5.6, 1.5 Hz, 2H), 5.22 (tdd, ^2J = 1.3, ^3J = 10.5, ^4J = 1.5 Hz, 1H), 5.26 (tdd, ^2J = 1.3, ^3J = 17.2, ^4J = 1.5 Hz, 1H), 5.88 ppm (ddt, ^3J = 17.2, 10.5, 5.6 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 24.7, 28.5, 28.8, 30.5, 30.8, 31.1, 32.8, 41.9, 63.2, 63.4, 63.6, 64.9, 68.3, 97.7, 97.9, 118.0, 132.2, 174.8 ppm; IR: $\tilde{\nu}$ = 3353, 3325, 3291, 3278, 2869, 1725, 1445, 1377, 1340, 1311, 1255, 1205, 1191, 1166, 1095, 1039, 1014, 910, 982, 929 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{21}H_{32}O_7$: 396.2148, found: 396.2148 $[M]^+$.

Allyl 15-oxo-7,11,18,21-tetraoxatrispiro[5.2.2.5.2.2]henicosane-3-carboxylate (16b): According to GP 1a alcohol **15b** (1.63 g, 4.11 mmol) was treated with DMP (1.92 g, 4.53 mmol). Purification by flash chromatography (CH_2Cl_2/MeOH 100:2) yielded **16b** as a white solid (0.95 g, 2.41 mmol, 59 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.42 (dt, ^3J = 12.7, 3.6 Hz, 2H), 1.64–1.74 (m, 2H), 1.77–1.85 (m, 2H), 2.08–2.15 (m, 6H), 2.33 (tt, ^3J = 10.4, 4.6 Hz, 1H), 2.34–2.37 (m, 4H), 3.69 (s, 2H), 3.75 (m, 6H), 4.53 (dt, ^3J = 5.7, 1.5 Hz, 2H), 5.18 (tdd, ^2J = 1.3, ^3J = 10.5, ^4J = 1.5 Hz, 1H), 5.26 (tdd, ^2J = 1.3, ^3J = 17.1, ^4J = 1.5 Hz, 1H), 5.86 ppm (ddt, ^3J = 17.1, 10.5, 5.7 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 24.7, 30.8, 30.9, 31.0, 32.8, 36.8, 41.8, 63.0, 63.2, 63.9, 64.9, 97.0, 97.8, 118.0, 132.1, 174.7, 210.3 ppm; IR: $\tilde{\nu}$ = 3439, 2955, 2937, 2879, 1726, 1440, 1412, 1342, 1318, 1276, 1257, 1122, 1108, 1082, 1054, 1034, 971, 920, 907, 895 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{21}H_{30}O_7$: 394.1992, found: 394.1991 $[M]^+$.

2-(Trimethylsilyl)ethyl 15-hydroxy-7,11,18,21-tetraoxatrispiro[5.2.2.5.2.2]-henicosane-3-carboxylate (15c): According to GP 5 trispirane **14c** (1.52 g, 2.64 mmol) was treated with DDQ (0.70 g, 3.08 mmol) yielded **15c** without further purification as a yellow solid (1.20 g, 2.63 mmol, 99 %, calculated by ^{1}H NMR). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.00 (s, 9H), 0.94 (t, ^3J = 8.5 Hz, 2H), 1.42 (dt, ^3J = 12.6, 4.1 Hz, 2H), 1.50–1.83 (m, 10H), 2.02–2.14 (m, 4H), 2.26 (tt, ^3J = 10.6, 4.0 Hz, 1H), 3.69 (dd, ^3J = 8.6, 7.7 Hz, 8H), 3.76 (m, 1H), 4.11 ppm (t, ^3J = 8.5 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = −1.5, 17.2, 24.7, 28.6, 28.8, 30.5, 30.8, 31.1, 32.8, 42.0, 62.5, 63.2, 63.3, 63.4, 63.7, 68.4, 97.7, 97.9, 175.4 ppm; IR: $\tilde{\nu}$ = 3356, 3295, 2867, 1721, 1599, 11576, 458, 1443, 1380, 1340, 1312, 1249, 1204, 1162, 1127, 1092, 1037, 911, 860, 832 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{23}H_{41}O_7Si$: 457.2616, found: 457.2617 $[M]^+$.

2-(Trimethylsilyl)ethyl 15-oxo-7,11,18,21-tetraoxatrispiro[5.2.2.5.2.2]henicosane-3-carboxylate (16c): According to GP 1a alcohol **15c** (1.15 g, 2.52 mmol) was treated with DMP (1.17 g, 2.76 mmol). Purification by flash chromatography (CH_2Cl_2/MeOH 100:2) yielded **16c** as a white solid (0.93 g, 2.05 mmol, 81 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.00 (s, 9H), 0.93 (t, ^3J = 8.5 Hz, 2H), 1.42 (dt, ^3J = 12.5, 4.3 Hz, 2H), 1.61–1.74 (m, 2H), 1.77–1.83 (m, 2H), 2.06–2.14 (m, 6H), 2.26 (tt, ^3J = 10.7, 4.3 Hz, 1H), 2.34–2.38 (m, 4H), 3.70 (m, 8H), 4.11 ppm (t, ^3J = 8.5 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = −1.5, 17.2, 24.7, 30.8, 30.9, 31.0, 32.8, 36.8, 42.0, 62.5, 63.1, 63.3, 64.0, 97.0, 97.8, 175.2, 210.3 ppm; IR: $\tilde{\nu}$ = 2956, 2902, 2866, 1444, 1418, 1362, 1342, 1312, 1184, 1164, 1125, 1088, 1066, 1036, 934, 896, 834, 861, 979, 966 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{23}H_{38}NaO_7Si$: 477.2285, found: 477.2285 $[M+Na]^+$.

2-Nitrobenzyl 15-hydroxy-7,11,18,21-tetraoxatrispiro[5.2.2.5.2.2]henicosane-3-carboxylate (15d): According to GP 5 trispirane **14d** (4.30 g, 7.03 mmol) was treated with DDQ (1.75 g, 7.71 mmol). Purification by Flash Chromatography (CH_2Cl_2/MeOH 10:1) yielded **15d** as a white solid (1.60 g, 3.26 mmol, 46 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.49 (dt, ^3J = 12.4, 3.3 Hz, 2H), 1.66–1.83 (m, 8H), 1.90–2.07 (m, 4H), 2.17–2.24 (m, 2H), 2.47 (tt, ^3J = 10.6, 4.1 Hz, 1H), 3.70 (dd, ^3J = 8.5, 8.5 Hz, 8H), 3.76 (m, 1H), 5.46 (s, 2H), 7.43–7.54 (m, 2H), 7.62 (dt, ^3J = 7.7, ^4J = 1.1 Hz, 1H), 8.06 ppm (dd, ^3J = 8.0, ^4J = 1.1 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 24.7, 28.6, 28.8, 30.5, 30.8, 31.0, 32.8, 41.9, 62.9, 63.2, 63.4, 63.6, 68.4, 97.6, 97.9, 125.0, 128.9, 129.0, 132.1, 133.6, 147.6, 174.4 ppm; IR: $\tilde{\nu}$ = 3261, 2936, 2868, 1724, 1531, 1445, 1376, 1353, 1340, 1316, 1252, 1038, 1204, 1166, 1094, 1014, 982, 930, 911, 726 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{25}H_{34}NO_9$: 492.2234, found: 492.2233 $[M]^+$.

2-Nitrobenzyl 15-oxo-7,11,18,21-tetraoxatrispiro[5.2.2.5.2.2]henicosane-3-carboxylate (16d): According to GP 1a alcohol **15d** (1.55 g, 3.15 mmol) was treated with DMP (1.47 g, 3.47 mmol). Purification by flash chromatography (CH_2Cl_2/MeOH 10:1) yielded **16d** as a white solid (1.50 g, 3.06 mmol, 97 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.49 (dt, ^3J = 12.6, 4.1 Hz, 2H), 1.67–1.80 (m, 2H), 1.85–1.91 (m, 2H), 2.07–2.19 (m, 6H), 2.34–2.40 (m, 4H), 2.47 (tt, ^3J = 12.4, 4.1 Hz, 1H), 3.71 (s, 2H), 3.76 (s, 6H), 5.47 (s, 2H), 7.43–7.54 (m, 2H), 7.62 (dt, ^3J = 7.7, ^4J = 1.1 Hz, 1H), 8.06 ppm (dd, ^3J = 8.0, ^4J = 1.1 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 24.7, 30.8, 30.9, 31.0, 32.9, 36.8, 41.9, 62.9, 63.1, 63.3, 63.9, 97.0, 97.7, 125.0, 128.8, 129.1, 132.0, 133.6, 147.6, 174.3, 210.4 ppm; IR: $\tilde{\nu}$ = 2958, 2921, 2894, 2854, 1709, 1439, 1382, 1367, 1340, 1318, 1275, 1257, 1180, 1167, 1108, 1001, 918, 896, 795, 731 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{25}H_{31}NO_9$: 489.1999, found: 489.1995 $[M]^+$.

Ethyl 15-hydroxy-7,11,18,21-tetraoxatrispiro[5.2.2.5.2.2]henicosane-3-carboxylate (15e): According to GP 5 trispirane **14e** (2.50 g, 4.95 mmol) was treated with DDQ (1.27 g, 5.59 mmol). Purification by Flash Chromatography (CH_2Cl_2/MeOH 100:5) yielded **15e** as a white solid (1.02 g, 2.65 mmol, 54 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.21 (t, ^3J = 7.2 Hz, 3H), 1.36–1.45 (m, 2H), 1.48–1.83 (m, 10H), 2.00–2.14 (m, 4H), 2.28 (tt, ^3J = 10.5, 4.1 Hz, 1H), 3.69 (dd, ^3J = 8.3, 8.3 Hz, 8H), 3.74 (m, 1H), 4.08 ppm (q, ^3J = 7.2 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 14.2, 24.7, 28.6, 28.8, 30.5, 30.8, 31.1, 32.8, 41.9, 60.2, 63.2, 63.4, 63.6, 68.4, 97.7, 97.9, 175.2 ppm; IR: $\tilde{\nu}$ = 3261, 2939, 2870, 1445, 1377, 1340, 1311, 1254, 1231, 1204, 1166, 1140, 1096, 1040, 1014, 983, 931, 909, 879, 827 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{20}H_{33}O_7$: 385.2221, found: 385.2222 $[M]^+$.

Ethyl 15-oxo-7,11,18,21-tetraoxatrispiro[5.2.2.5.2.2]henicosane-3-carboxylate (16e): According to GP 1a alcohol **15e** (0.97 g, 2.52 mmol) was treated with DMP (1.18 g, 2.78 mmol). Purification by flash chromatography (CH_2Cl_2/MeOH 100:4) yielded **16e** as a white solid (0.95 g, 2.48 mmol, 99%). ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.20 (t, ^3J=7.2 Hz, 3H), 1.42 (dt, ^3J=12.6, 4.3 Hz, 2H), 1.61–1.74 (m, 2H), 1.81 (m, 2H), 2.01–2.15 (m, 6H), 2.29 (tt, ^3J=10.7, 4.1 Hz, 1H), 2.29–2.38 (m, 4H), 3.69 (m, 8H), 4.08 ppm (q, ^3J=7.2 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=14.2, 24.7, 30.8, 30.9, 31.0, 32.8, 36.8, 41.9, 60.2, 63.1, 63.3, 63.9, 97.0, 97.8, 175.1, 210.3 ppm; IR: $\tilde{\nu}$=3433, 2956, 2936, 2871, 1721, 1444, 1368, 1338, 1318, 1277, 1256, 1187, 1160, 1123, 1082, 1055, 1034, 973, 910, 897 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{20}H_{31}O_7$: 383.2064, found: 383.2067 $[M]^+$.

15-[(4-Methoxybenzyl)oxy]-7,11,18,21-tetraoxatrispiro[5.2.2.5.2.2]henicosan-3-ol (15f): A cooled solution (−78°C) of trispirane **14a** (0.61 g, 1.15 mmol) in anhydrous CH_2Cl_2 (25 mL) was treated with diisobutylaluminium hydride (1M in hexane, 2.8 mL, 2.80 mmol) and stirred for 1 h. Methanol (0.1 mL) and EtOAc were added and the mixture was washed with an aq solution of potassium sodium tartrate. The organic layers were dried and evaporated yielded **15f** as a white solid (0.49 g, 1.09 mmol, 95%). M.p. 121–123°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ= 1.50–1.79 (m, 12H), 2.06 (m, 4H), 3.48 (m, 1H), 3.73 (brs, 8H), 3.80 (s, 3H), 4.44 (s, 2H), 6.86 (d, ^3J=8.7 Hz, 2H), 7.25 ppm (d, ^3J=8.7 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=27.1, 28.4, 28.5, 28.7, 29.0, 30.5, 32.8, 55.2, 63.2, 63.3, 63.6, 63.7, 68.4, 69.5, 74.2, 97.9, 98.1, 113.7, 129.0, 131.0, 159.0 ppm; IR: $\tilde{\nu}$=3316, 2935, 2867, 1610, 1513, 1443, 1377, 1347, 1301, 1247, 1204, 1168, 1141, 1096, 982, 929, 910, 879, 813, 649 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{25}H_{36}O_7$: 448.2461, found: 448.2462 $[M]^+$.

15-[(4-Methoxybenzyl)oxy]-7,11,18,21-tetraoxatrispiro[5.2.2.5.2.2]henicosan-3-one (16f): According to GP 1a alcohol **15f** (0.39 g, 0.87 mmol) was treated with DMP (0.41 g, 0.97 mmol). Purification by flash chromatography (CH_2Cl_2/MeOH 100:4) yielded **16f** as a white solid (0.29 g, 0.65 mmol, 75%). ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.48 (m, 2H), 1.58–1.82 (m, 8H), 2.00 (m, 2H), 2.10 (m, 2H), 2.38 (m, 2H), 3.46 (m, 1H), 3.67 (brs, 8H), 3.80 (s, 3H), 4.42 (s, 2H), 6.84 (d, ^3J=8.7 Hz, 2H), 7.23 ppm (d, ^3J=8.7 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=27.1, 28.4, 28.5, 30.5, 30.7, 31.2, 31.3, 32.9, 36.8, 55.2, 63.1, 63.5, 64.0, 69.5, 74.1, 97.0, 98.3, 113.7, 128.9, 131.0, 159.0, 210.3 ppm; HRMS: *m*/*z*: calcd for $C_{25}H_{34}O_7$: 446.2305, found: 446.2305 $[M]^+$.

7,11,18,21-Tetraoxatrispiro[5.2.2.5.2.2]henicosane-3,15-diol (17): ***Method A***: A cooled solution (−78°C) of trispirane **14g** (0.90 g, 1.81 mmol) in anhydrous CH_2Cl_2 (30 mL) was treated with diisobutylaluminium hydride (1M in hexane, 9.0 mL, 9.00 mmol) and stirred for 1 h. Methanol (0.1 mL) and EtOAc were added and the mixture was washed with an aq solution of potassium sodium tartrate. The organic layer was dried, evaporated and the resulting residue purified by flash chromatography (CH_2Cl_2/MeOH 10:1) yielded **17** as a white solid (0.43 g, 1.31 mmol, 36%).

Method B: A solution of trispirane **14f** (2.58 g) in anhydrous MeOH (25 mL) was treated with sodium (220 mg, 9.57 mmol), dissolved in anhydrous MeOH (60 mL), and stirred 1.5 h. Brine was added and the mixture was extracted several times with CH_2Cl_2. The combined organic layers were dried, evaporated and purified by flash chromatography (CH_2Cl_2/MeOH 10:1) yielded **17** as a white solid (1.03 g, 3.14 mmol, 66% vs **13** (**14f**)). ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ=1.29–1.48 (m, 8H), 1.53–1.59 (m, 4H), 1.90–1.95 (m, 4H), 3.49–3.56 (m, 2H), 3.62 (s, 4H), 3.63 (s, 4H), 4.39 (s, 1H), 4.4 ppm (s, 1H); ^{13}C NMR (75.5 MHz, [D$_6$]DMSO): δ=28.5, 30.2, 32.0, 62.2, 62.6, 66.5, 97.4 ppm; IR: $\tilde{\nu}$=3330, 3297, 2967, 2940, 2870, 1444, 1375, 1291, 1253, 1233, 1203, 1164, 1138, 1092, 1038, 1013, 999, 981, 930, 911 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{17}H_{29}O_6$: 329.1959, found: 329.1959 $[M]^+$.

7,11,18,21-Tetraoxatrispiro[5.2.2.5.2.2]henicosane-3,15-dione (18): According to GP 1b alcohol **17** (1.06 g, 3.23 mmol) was treated with DMP (3.01 g, 7.10 mmol) and $NaHCO_3$ (1.09 g, 12.98 mmol). Purification by flash chromatography (CH_2Cl_2/MeOH 100:4) yielded **18** as a white solid (0.85 g, 2.62 mmol, 81%). ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ=2.06–2.10 (m, 8H), 2.23–2.27 (m, 8H), 3.79 ppm (s, 8H); ^{13}C NMR (75.5 MHz, [D$_6$]DMSO): δ=30.4, 32.1, 36.5, 72.7, 96.7, 209.5 ppm; IR: $\tilde{\nu}$=2959, 2905, 2866, 1709, 1455, 1440, 1418, 1367, 1315, 1277, 1257, 1197, 1145, 1165, 1118, 1083, 1031, 969, 927, 898 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{17}H_{24}NaO_6$: 347.1467, found: 347.1465 $[M+Na]^+$.

24-Allyl 3-benzyl 7,11,16,20,27,30,33,36-octaoxa-3-azahexaspiro[5.2.2.2.2.2.5.2.2.2.2.2]hexatriacontane-3,24-dicarboxylate (19a): According to GP 3 ketone **16b** (0.90 g, 2.28 mmol) was treated with diol **12a** (0.80 g, 2.28 mmol). Purification by flash chromatography (CH_2Cl_2/MeOH 100:2) yielded **19a** as a white solid (1.07 g, 1.48 mmol, 65%). ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.42 (dt, ^3J=12.4, 4.0 Hz, 2H), 1.62–1.86 (m, 16H), 2.10–2.14 (m, 2H), 2.34 (tt, ^3J=10.7, 3.8 Hz, 1H), 3.48 (m, 4H), 3.66–3.71 (m, 16H), 4.53 (dt, ^3J=5.7, 1.5 Hz, 2H), 5.08 (s, 2H), 5.19 (tdd, ^2J=1.3, ^3J=10.5, ^4J=1.5 Hz, 1H), 5.27 (tdd, ^2J=1.3, ^3J=17.1, ^4J= 1.5 Hz, 1H), 5.86 (ddt, ^3J=17.1, 10.5, 5.7 Hz, 1H), 7.25–7.36 ppm (m, 5H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=24.7, 27.9, 28.0, 28.1, 28.2, 30.9, 32.7, 32.9, 40.6, 41.8, 63.2, 63.3, 63.5, 63.6, 64.9, 67.1, 96.8, 97.7, 98.0, 98.2, 118.0, 127.8, 127.9, 128.4, 132.2, 136.7, 155.1, 174.7 ppm; IR: $\tilde{\nu}$=2966, 2931, 2873, 1727, 1443, 1381, 1360, 1234, 1276, 1204, 1166, 1143, 1101, 1060, 1038, 982, 961, 939, 908, 695 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{39}H_{54}NO_{12}$: 728.3646, found: 728.3662 $[M]^+$.

3-Benzyl 24-[2-(trimethylsilyl)ethyl] 7,11,16,20,27,30,33,36-octaoxa-3-azahexaspiro[5.2.2.2.2.2.5.2.2.2.2.2]hexatriacontane-3,24-dicarboxylate (19b): According to GP 3 ketone **16c** (0.85 g, 1.87 mmol) was treated with diol **12a** (0.67 g, 1.91 mmol). Purification by flash chromatography (CH_2Cl_2/MeOH 100:2) yielded **19b** as a white solid (0.96 g, 1.22 mmol, 65%). ^{1}H NMR (300 MHz, $CDCl_3$): δ=0.00 (s, 9H), 0.94 (t, ^3J=8.5 Hz, 2H), 1.41 (dt, ^3J=12.4, 4.0 Hz, 2H), 1.61–1.78 (m, 16H), 2.09–2.14 (m, 2H), 2.27 (tt, ^3J=10.7, 3.8 Hz, 1H), 3.48 (m, 4H), 3.66–3.71 (m, 16H), 4.12 (t, ^3J=8.3 Hz, 2H), 5.09 (s, 2H), 7.25–7.36 ppm (m, 5H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=−1.5, 17.2, 24.7, 27.9, 28.0, 28.1, 28.2, 30.9, 32.7, 32.9, 40.6, 42.0, 62.5, 63.2, 63.3, 63.5, 63.6, 67.1, 96.8, 97.7, 98.0, 98.2, 127.8, 128.0, 128.4, 136.7, 155.1, 175.3 ppm; HRMS: *m*/*z*: calcd for $C_{41}H_{61}NNaO_{12}Si$: 810.3855, found: 810.3859 $[M+Na]^+$.

3-Benzyl 24-(2-nitrobenzyl) 7,11,16,20,27,30,33,36-octaoxa-3-azahexaspiro[5.2.2.2.2.2.5.2.2.2.2.2]hexatriacontane-3,24-dicarboxylate (19c): According to GP 3 ketone **16d** (1.45 g, 2.96 mmol) was treated with diol **12a** (1.04 g, 2.96 mmol). Purification by flash chromatography (CH_2Cl_2/MeOH 100:4) yielded **19c** as a white solid (1.54 g, 1.87 mmol, 63%). ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.43 (dt, ^3J=12.4, 4.0 Hz, 2H), 1.66–1.90 (m, 16H), 2.12–2.17 (m, 2H), 2.41 (tt, ^3J=10.4, 4.0 Hz, 1H), 3.48 (m, 4H), 3.66–3.71 (m, 16H), 5.09 (s, 2H), 5.46 (s, 2H), 7.27–7.36 (m, 5H), 7.46 (m, 1H), 7.52 (m, 1H), 7.61 (dt, ^3J=7.5, ^4J=1.1 Hz, 1H), 8.05 ppm (dd, ^3J=7.9, ^4J=1.1 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=24.7, 27.9, 28.0, 28.1, 28.2, 30.9, 32.7, 32.9, 40.6, 41.8, 62.9, 63.2, 63.3, 63.4, 63.5, 67.1, 96.8, 97.6, 98.0, 98.1, 125.0, 127.7, 127.9, 128.4, 128.7, 129.0, 132.1, 133.6, 136.7, 147.5, 155.0, 174.3 ppm; HRMS: *m*/*z*: calcd for $C_{43}H_{54}N_2NaO_{14}$: 845.3473, found: 845.3474 $[M+Na]^+$.

3-Benzyl 24-ethyl 7,11,16,20,27,30,33,36-octaoxa-3-azahexaspiro[5.2.2.2.2.2.5.2.2.2.2.2]hexatriacontane-3,24-dicarboxylate (19d): According to GP 3 ketone **16e** (0.85 g, 2.22 mmol) was treated with diol **12a** (0.78 g, 2.22 mmol). Purification by flash chromatography (CH_2Cl_2/MeOH 100:4) yielded **19d** as a white solid (1.14 g, 1.59 mmol, 72%). ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.21 (t, ^3J=7.2 Hz, 3H), 1.41 (dt, ^3J= 12.4, 4.0 Hz, 2H), 1.61–1.78 (m, 16H), 2.09–2.14 (m, 2H), 2.29 (tt, ^3J= 10.4, 4.1 Hz, 1H), 3.48 (m, 4H), 3.66–3.71 (m, 16H), 4.08 (q, ^3J=7.2 Hz, 2H), 5.09 (s, 2H), 7.28–7.33 ppm (m, 5H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=14.2, 24.7, 27.9, 28.0, 28.1, 28.2, 30.9, 32.7, 32.9, 40.6, 41.9, 60.2, 63.2, 63.3, 63.5, 63.6, 67.1, 96.8, 97.7, 98.1, 98.2, 127.8, 128.0, 128.4, 136.7, 155.1, 175.1 ppm; IR: $\tilde{\nu}$=2968, 2932, 2873, 1725, 1697, 1443, 1428, 1407, 1381, 1365, 1278, 1235, 1204, 1188, 1166, 1102, 1060, 1039, 942, 909 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{38}H_{54}NO_{12}$: 716.3641, found: 716.3641 $[M]^+$.

Benzyl 24-[(4-methoxybenzyl)oxy]-7,11,16,20,27,30,33,36-octaoxa-3-azahexaspiro[5.2.2.2.2.2.5.2.2.2.2.2]hexatriacontane-3-carboxylate (19e): According to GP 3 ketone **16f** (0.51 g, 1.14 mmol) was treated with diol **12a** (0.40 g, 1.14 mmol). Purification by flash chromatography (CH_2Cl_2/MeOH 100:4) yielded **19e** as a pale yellow solid (0.30 g, 0.38 mmol, 34%). ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.74–2.15 (m, 20H), 3.63 (m, 4H), 3.84 (brs, 16H), 3.91 (s, 3H), 3.92 (m, 1H), 4.56 (s, 2H), 5.24 (s, 2H), 6.99 (d, ^3J=8.7 Hz, 2H), 7.37 (d, ^3J=8.7 Hz, 2H), 7.45–7.48 ppm (m, 5H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=27.1, 27.8, 28.0, 28.1, 28.3,

28.5, 32.8, 32.9, 40.6, 55.2, 63.2, 63.3, 63.5, 63.6, 67.1, 69.5, 74.2, 96.8, 96.9, 98.1, 98.2, 113.7, 127.8, 128.0, 128.5, 128.9, 131.0, 136.7, 155.1, 159.0 ppm; IR: $\tilde{\nu}$ = 3433, 2967, 2934, 2872, 1610, 1511, 1476, 1440, 1380, 1277, 1203, 1167, 1143, 1102, 1060, 1038, 981, 941, 910, 728 cm^{-1}; HRMS: *m*/*z*: calcd for $C_{43}H_{57}NNaO_{12}$: 802.3773, found: 802.3772 $[M+Na]^+$.

3,33-Bis(octylsulfonyl) 7,11,16,20,25,29,36,39,42,45,48,51-dodecaoxa-3,33-diazanonaspiro[5.2.2.2.2.2.2.2.2.5.2.2.2.2.2.2.2.2]henpentacontane (20a): According to GP 3 diketone **18** (130 mg, 0.40 mmol) was treated with diol **12b** (310 mg, 0.79 mmol) yielded **20a** as a white solid (60 mg, 0.06 mmol, 14%). M.p. >260 °C; ^{13}C NMR (CP-MAS, 10 kHz): δ = 14.0, 23.1, 23.6, 29.6, 30.7, 32.6, 34.0, 40.3, 50.8, 64.0, 96.9, 98.2 ppm; IR: $\tilde{\nu}$ = 3328, 3291, 2957, 2920, 2851, 1327, 1316, 1149, 1130, 1047 cm^{-1}; MS (MALDI): *m*/*z*: calcd for $C_{53}H_{90}N_2NaO_{16}S_2$: 1100.0, found: 1097.6 $[M+Na]^+$.

Bis(1-hexylheptyl) 7,11,16,20,25,29,36,39,42,45,48,51-dodecaoxa-3,33-diazanonaspiro[5.2.2.2.2.2.2.2.2.5.2.2.2.2.2.2.2.2]henpentacontane-3,33-dicarboxylate (20b): According to GP 3 diketone **18** (114 mg, 0.35 mmol) was treated with diol **12c** (310 mg, 0.69 mmol). Purification by flash chromatography (CH_2Cl_2/MeOH 100:4) yielded **20b** as a white solid (260 mg, 0.22 mmol, 62%). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.93–0.97 (m, 12H), 1.19 (brs, 32H), 1.44 (brs, 8H), 1.75 (brs, 8H + 16H), 3.40 (brs, 8H), 3.65–3.77 (m, 24H), 4.64–4.68 ppm (m, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 14.1, 22.6, 25.2, 28.1, 29.2, 31.7, 32.9, 34.3, 40.5, 63.4, 63.5, 75.6, 97.1, 98.1, 98.2, 155.4 ppm; IR: $\tilde{\nu}$ = 3455, 2930, 2856, 1696, 1438, 1233, 1101, 907, 801 cm^{-1}; MS (MALDI): *m*/*z*: calcd for $C_{65}H_{110}N_2NaO_{16}$: 1197.8, found: 1200.0 $[M+Na]^+$.

Bis(2-ethylhexyl) 7,11,16,20,25,29,36,39,42,45,48,51-dodecaoxa-3,33-diazanonaspiro[5.2.2.2.2.2.2.2.2.5.2.2.2.2.2.2.2.2]henpentacontane-3,33-dicarboxylate (20c): According to GP 3 diketone **18** (198 mg, 0.61 mmol) was treated with diol **12d** (458 mg, 1.23 mmol). Purification by flash chromatography (CH_2Cl_2/MeOH 10:1) yielded **20c** as a white solid (453 mg, 0.44 mmol, 72%). M.p. >300 °C (decomp); ^1H NMR (300 MHz, $CDCl_3$): δ = 0.83–0.88 (m, 12H), 1.22–1.36 (m, 16H), 1.50–1.55 (m, 2H), 1.78 (brs, 8H + 16H), 3.44 (brs, 8H), 3.68–3.71 (m, 24H), 3.94–3.96 ppm (m, 4H); ^{13}C NMR (75.5 MHz, $CDCl_3$, quantitative): δ = 11.0 (2C), 14.0 (2C), 22.9 (2C), 23.9 (2C), 28.1 (8C), 28.9 (2C), 30.5 (2C), 31.5 (2C), 32.6 (1C), 32.8 (2C), 32.9 (2C), 39.0 (2C), 40.5 (4C), 63.5 (12C), 67.9 (2C), 97.0 (2C), 98.2 (4C), 155.6 ppm (2C); IR: $\tilde{\nu}$ = 3444, 2962, 1694, 1432, 1230, 1101 cm^{-1}; elemental analysis calcd (%) for $C_{55}H_{90}N_2O_{16}$ (1035.3): C 63.81, H 8.76, N 2.71, found: C 63.67, H 8.65, N 2.68

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[38] Crystal data for **14a**: $C_{30}H_{44}O_8$, $M=532.65$, monoclinic, *Cc*, $a=42.185(7)$, $b=5.9379(15)$, $c=11.2199(19)$ Å, $\alpha=90.0$, $\beta=89.71(2)$, $\gamma=90.0°$, $V=2810.4(10)$ Å^3, $T=180(2)$ K, graphite monochromatized $Mo_{K\alpha}$ radiation, $\lambda=0.71073$ Å, $Z=2$, $\rho_{calcd}=1.259$ Mg m^{-3}, crystal size $0.40\times0.32\times0.12$ mm^3. Data collected on a STOE Ipds diffractometer, 2472 unique reflections, $R_{int}=0.0750$, Refinement on F^2, final residuals $R1=0.0340$ for 1870 reflections with $I>2\sigma I$), $wR2=0.0668$ for all data. CCDC-636085 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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