JOC The Journal of Organic Chemistry

Article

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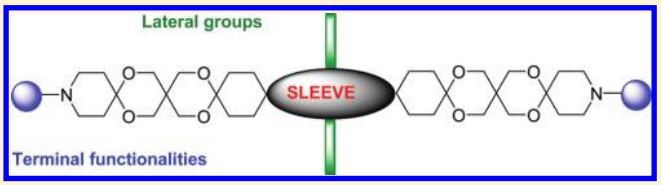
Building Blocks for Oligospiroketal (OSK) Rods and Evaluation of Their Influence on Rod Rigidity

Pablo Wessig* and Kristian Möllnitz

Universität Potsdam, Institut für Chemie, Karl-Liebknecht-Str. 24-25, D-14476 Potsdam, Germany

Supporting Information

ABSTRACT: We report on the synthesis of three new sleeves and their incorporation in OSK rods. The structures of these sleeves are based on *neo*-inositol, terephthalaldehyde diacetals, and indacene. To quantify the influence of the sleeves on rod rigidity, we applied the worm-like chain (WLC) model on the new rods and found that this approach is rather disappointing. As the chief cause of this result, we assume that the rigidity of typical molecular rods largely exceeds the rigidity of polymers, which were successfully described by the WLC model. Alternatively, we suggest quantifying the rigidity of molecular rods by fitting an empirical function on the end-to-end distance distribution curve obtained by MD simulations. After checking various function types, the Levy−Martin function proved to be most suitable for this purpose. On the basis of this function, we defined the Levy−Martin parameter and suggest using this parameter for the characterization of the rigidity of molecular rods.



INTRODUCTION

Molecular rods, that is, relatively rigid molecules with a large aspect ratio, have gained constantly increasing interest in the past decades. High rigidity of molecules is related to dimensional stability and is a substantial requirement for applications, which are based on the well-defined shape of the molecules. Because of their unique properties, molecular rods have proved useful in a broad range of applications, especially in the field of modern biosciences, nanoscience, and nanotechnology.[1] In this connection, efficient and modular methods for the synthesis of molecular rods are indispensable. Recently, we developed a new class of molecular rods based on oligospiroketals (OSK) **A** (Figure 1).[2] The molecular structures of OSK rods resemble, at first glance, marine polyethers, and one could expect a fairly good solubility of these compounds in polar solvents, including water. However, a closer look brings to light that the oxygen atoms in OSK rods are effectively shielded by the hydrogen atoms of the methylene groups, and therefore, the backbone of OSK rods is rather hydrophobic. This property causes a dramatically decreasing solubility with increasing rod length, which strongly complicates many applications. The problem of scarce solubility can be effectively surmounted by the introduction of solubility-enhancing groups (SEGs) consisting of flexible and often branched alkyl chains in the case of organic solvents, whereas charged functional groups or polyethyleneglycol chains should be suitable for aqueous systems. The SEGs can be tethered at the ends (terminal SEGs)[2] or at the sides (lateral SEGs) of the rod. The former approach is easier to realize but usually prevents the attachment of additional functional groups necessary for the application of a certain rod. On the other side, the attachment of lateral SEGs at backbone **A** of the OSK rods is too difficult from a synthetic point of view but requires the development of special building blocks bearing the SEGs. In analogy to the technical connection of pipes, we called these building blocks "sleeves". Recently, we developed the first type of solubility-enhancing sleeves for OSK rods that is based on a [1,3]dioxolo[4,5-*f*][1,3]benzodioxole (DBD) moiety (see **B** in Figure 1).[3] Although the DBD sleeve **B** is very effective and easy to make and was already used in some biophysical applications,[4] it has also some disadvantages. Because of the electron-rich aromatic core, the DBD sleeve has a low oxidation potential that could be detrimental for applications with an oxidative environment. Furthermore, the DBD sleeve is slightly fluorescent and, therefore, only limitedly

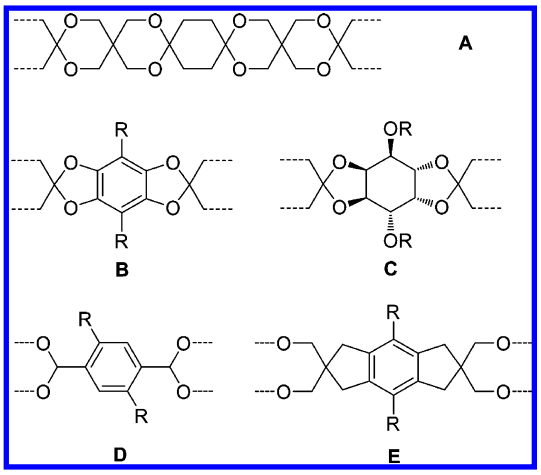


Figure 1. Oligospiroketals **A** and "sleeves" **B**−**E**.

Received: February 9, 2012
Published: April 2, 2012

suited for applications using fluorescent dyes.[5] On the basis of this situation, we were interested in the development of new sleeves, which overcome the disadvantages of the DBD sleeves. Herein, we wish to report on the development of three new sleeves **C**–**E** whose structure is based on *neo*-inositol (**C**), terephthalaldehyde diacetals (**D**), and *s*-indacene (**E**).

A substantial requirement of solubility-enhancing sleeves in OSK rods is that they, at best, marginally decrease the rigidity of the rods. In this connection, we realized that no systematic quantitative investigation of the rigidity of molecular rods has been published so far. Therefore, we herein also present a new approach to estimate the rigidity of molecular rods and propose a new parameter for the characterization of rigidity.

RESULTS AND DISCUSSION

Inositol Sleeves C. From the perspective of practical applications of molecular rods, the perfect sleeve is based on a saturated skeleton, because, in this case, interfering effects caused by a π system (oxidation sensitivity, strong UV/vis absorption or fluorescence) are avoided. Therefore 1,2,3,4,5,6-hexahydroxy-cyclohexanes (inositols) should be ideally suited as sleeves for molecular rods. The inositols occur as nine different stereoisomers, which differ in the relative arrangement of the hydroxyl groups with respect to the cyclohexane ring. Only one of these isomers is commercially available at an acceptable price, namely, the *myo*-inositol. The connection of the inositol sleeve with the rod backbone should be performed as ketals with two opposing diol moieties of the inositol. Bearing in mind that ketals of *vic*-dihydroxycyclohexanes are only smoothly formed if the two hydroxyl groups are in a cis arrangement (see gray boxes in Figure 2) and that the two pairs

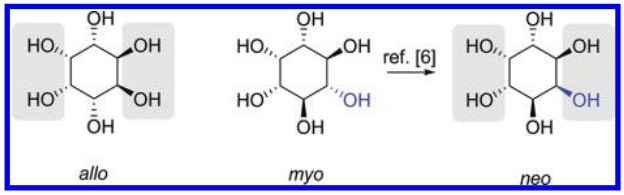


Figure 2. *allo*-, *myo*-, and *neo*-inositol.

of these *cis*-diol moieties at opposing sides of the cyclohexane ring should be positioned trans to each other to avoid a kink in the OSK rod backbone, only *allo*- and *neo*-inositol come into question. *myo*- and *neo*-inositol differ only by one chirality center (cf. blue OH group in Figure 2), and therefore, an efficient method for the conversion of *myo*- into *neo*-inositol was necessary to pursue this approach. Recently, we published a powerful procedure for the preparation of *neo*-inositol (Figure 2).[6]

Because *neo*-inositol can form diketals not only from the opposite pair of diol moieties but also from an adjacent pair, we first examined the ketalization with cyclohexanone as a simple model reactant. For this purpose, hexakis-trimethylsilyl-*neo*-inositol **1**[7] was treated with cyclohexanone in the presence of catalytic amounts of trimethylsilyl triflate (TMSOf) in different solvents (Scheme 1). At first, we employed the previously established[2] conditions using diethylether as solvent and obtained nearly equal amounts of linear diketal **2a** and angular diketal **3a**. For an unambiguous assignment of the structure, the mixture of **2a** and **3a** was converted into the corresponding allyl ethers **2b** and **3b**, which could be separated by flash chromatography (for NMR proof of the structures, see the Supporting Information). Considerably better results could be obtained in the solvents DCM, MTBE, and THF, but the best yields of the desired product **2a** (92%) were achieved in diisopropylether (see Table 1). The solvent dependence of

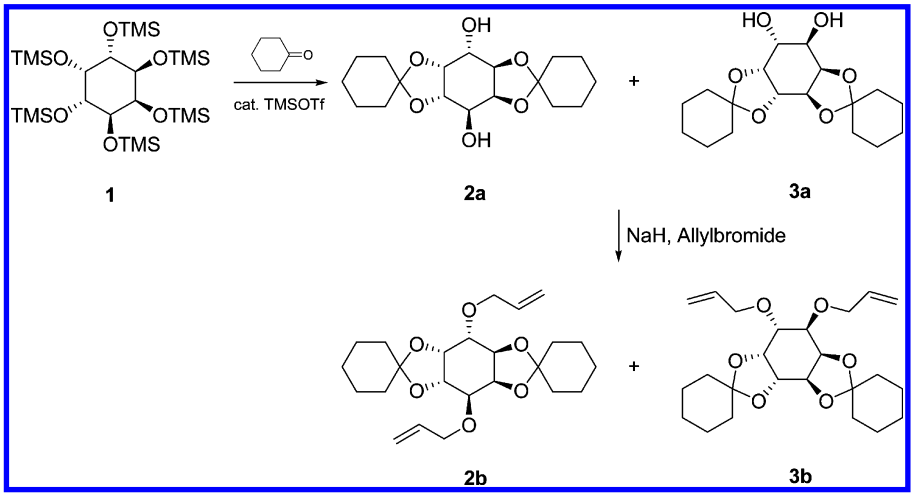
Table 1. Optimization of the Ketalization Conditions

entry	solvent	yield **2a** [%]	yield **3a** [%]
1	Et_2O	33	35
2	DCM	61	14
3	MTBE	60	4
4	THF	71	3
5	iPr_2O	92	2

regioselectivity in this reaction is surprising, and the reasons for this behavior are still unclear.

With the optimal ketalization conditions in hand, we tackled the synthesis of the inositol sleeve. Commencing with 4-pivaloyloxy-cyclohexanone **4**,[2,8] we obtained the dispirane **5** with 62% yield. The introduction of solubility-enhancing groups was performed in two steps, consisting of diallylation to **5** and catalytic hydrogenation of the double bonds to provide the dipropylether **7**. In the last two steps, the pivaloyl

Scheme 1. Ketalization of Hexakis-trimethylsilyl-*neo*-inositol 1



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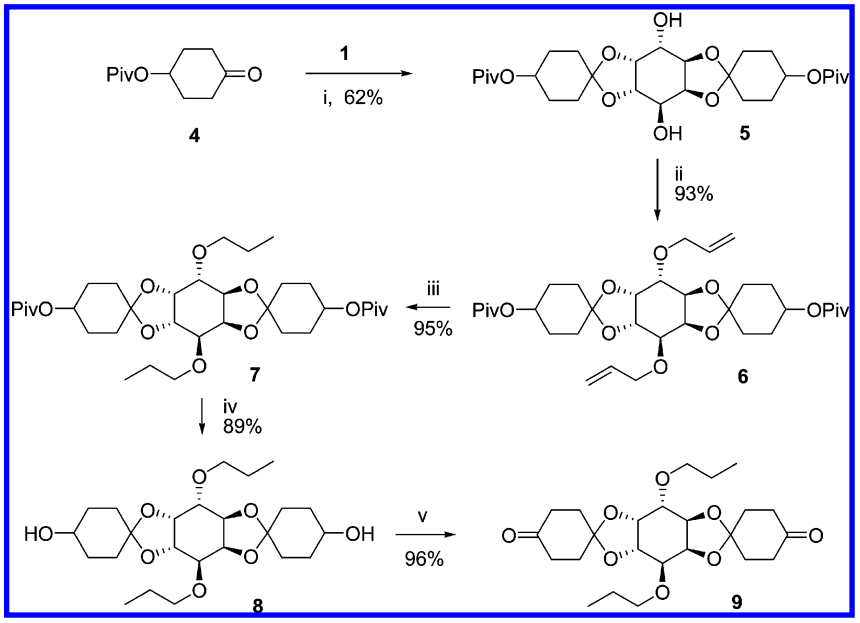
Scheme 2. Synthesis of the *neo*-Inositol Sleeve 9[a]



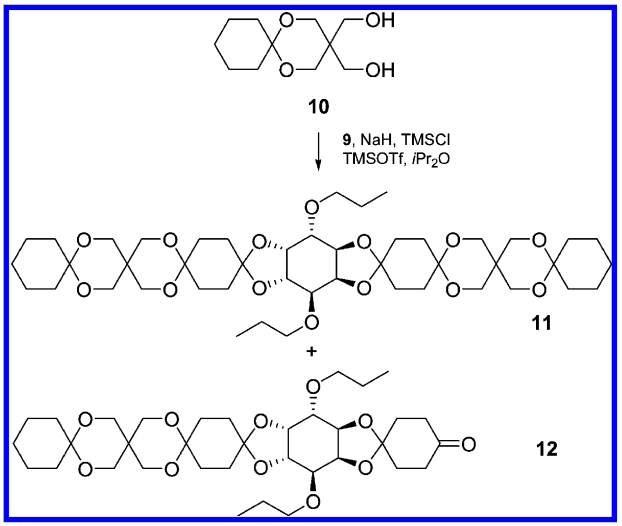
[a] i: TMSOTf, iPr$_2$O; ii: NaH, allyl bromide, DMF; iii: H_2, Pd(OH)$_2$, EtOH; iv: DIBAL, DCM; v: Dess–Martin periodinane, DCM.

protecting groups were removed with DIBAH and the resulting diol **8** was oxidized to the diketone **9** with Dess–Martin periodinane (Scheme 2).[9]

To explore the synthetic suitability of building block **9** as a sleeve in OSK rod synthesis, we investigated the reaction of **9** with the spirodiol **10**[10] using modified standard conditions (iPr$_2$O was used instead of Et$_2$O).[2] Unfortunately, the results are rather sobering. The reaction proceeded less selectively with the formation of many byproducts, and the desired OSK rod **11** was obtained only as an inseparable mixture with the monoketalization product **12** and with a yield below 8% (Scheme 3). Obviously, the strained 1,3-dioxolane moieties in **11** are too sensitive toward transketalization reactions.

Terephthalaldehyde Diacetal Sleeves D. One of the most important demands on solubility-enhancing sleeves for OSK rods is that they should reduce the rigidity of the rods at most marginally. From this point of view, diacetals of terephthalaldehyde **D** (cf. Figure 1, R = H) should be rather inappropriate due to the less hindered rotation around the bond between the acetal carbon atoms and the aromatic ring. On the other side, more or less bulky substituents R (which are already necessary to improve solubility) could considerably reduce the conformational flexibility. To verify this assumption, we defined model compounds **13a–13c** (Figure 3) and investigated their overall geometry as a function of residues R by means of molecular dynamics (MD) calculations.

Scheme 3. OSK Rod Synthesis with Sleeve 9



For this purpose, we performed MD simulations (for details, see the Supporting Information) of molecules **13a–13c** over a period of 20 ns and saved snapshots every 10 ps. For the resulting 2000 snapshot geometries, we determined the pseudo dihedral angle α, which is defined by the atoms a, b, c, and d (see Figure 3) and classified these values in 72 channels with a channel width of 5° (= full 360° rotation). The partitions of angle α over these channels are shown in Figure 4. The plot for **13a** clearly shows an equal distribution of α over the entire range, indicating the absence of a preferred conformation. The introduction of residues R in **13b** and **13c** dramatically change this situation. In the plots for these molecules, one can see a clear preference of angles α of around 180°. An examination of the corresponding geometries revealed that these values for α mainly correspond to the conformation *anti-I* (Figure 3). Obviously, the steric repulsion between residues R and the acetal oxygen atoms causes a conformational stiffening of molecules **13b** and **13c**.

On the basis of these findings, we searched for a synthetic route to terephthalaldehyde diacetal sleeves **D** bearing butyl groups. Starting from 1,4-dibutylbenzene **14**, which is easily accessible from 1,4-dichlorobenzene,[11] 1,4-dibromo-2,5-dibutylbenzene **15** was prepared.[12] The replacement of the bromine atoms for 5,5-dimethyl-1,3-dioxane moieties succeeded in four steps, in analogy to a previously reported procedure giving the diacetal **16**.[13] It should be noted that a direct conversion of **15** to **17** is not possible due to incomplete 2-fold bromine–lithium exchange. Therefore, the first formyl group was protected as acetal before the second formylation step was performed.

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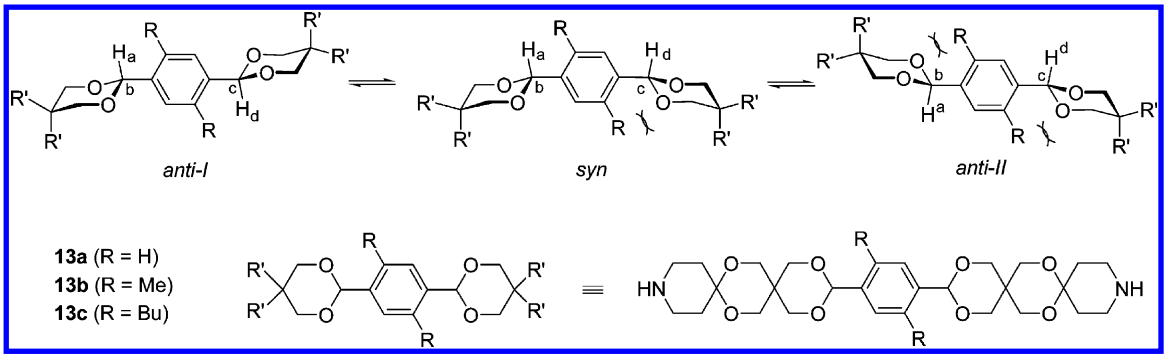


Figure 3. Conformations of terephthalaldehyde diacetals **13**.

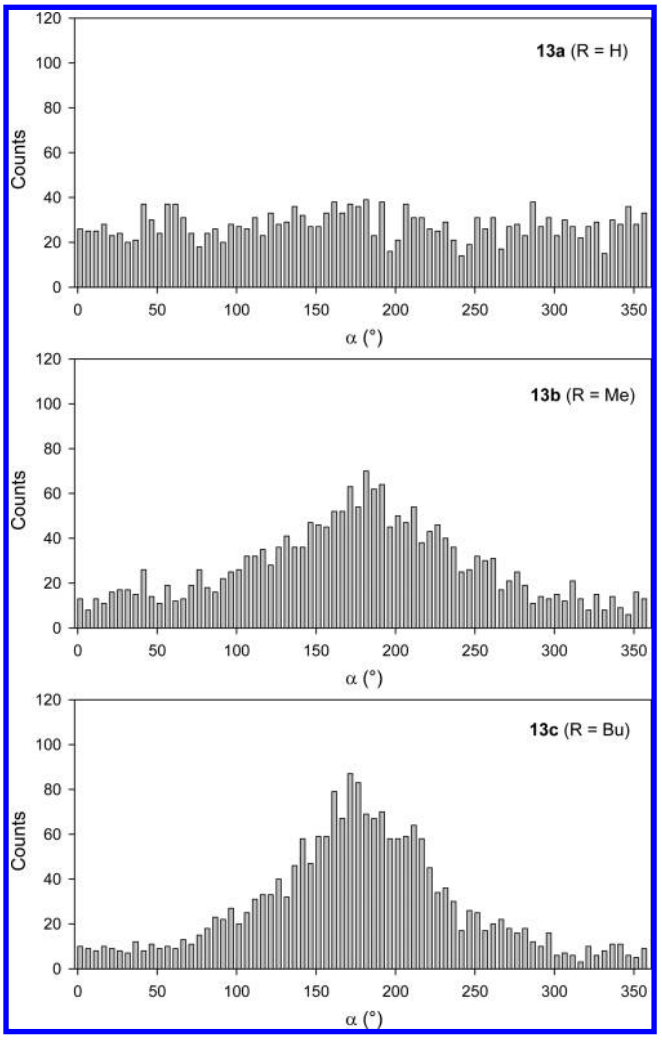
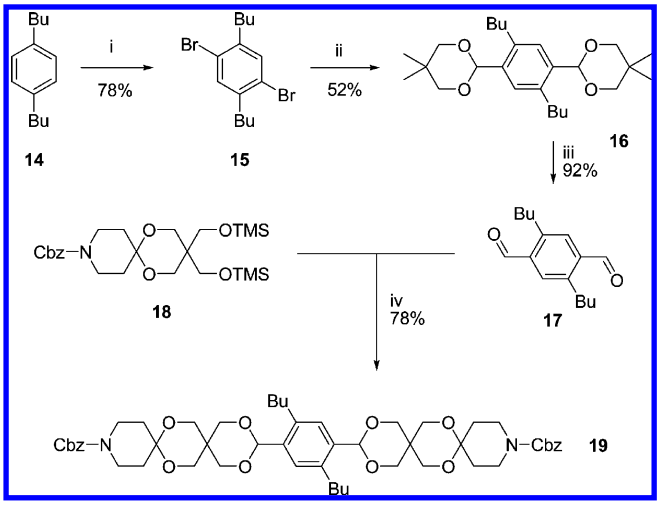


Figure 4. Partition of the pseudo dihedral angle α for **13a**–**13c**.

Furthermore, the second formyl group was also protected to facilitate the purification. After hydrolytic cleavage of the diacetal moieties,[13] we obtained the 2,5-dibutylterephthalaldehyde **17** as a building block for the introduction of sleeve **D**. Upon treatment of **17** with bistrimethylsilylether **18**, prepared from the corresponding diol,[2] we obtained the OSK rod **19** with good yields (Scheme 4).

Indacene Sleeves E. The DBD sleeve **B** has proven successful in numerous applications, but the low oxidation potential is still a significant disadvantage. The inositol sleeve **C** overcomes this drawback, but the reduced stability of the 1,3-

Scheme 4. Synthesis of OSK Rod 19 with Sleeve D[a]



[a] i: Br_2, cat. I_2; ii: 1.1. *n*BuLi, THF, 1.2. DMF, 2. neopentylglycol, *p*TsOH, 3.1. *n*BuLi, THF, 3.2. DMF, 4. neopentylglycol, *p*TsOH; iii: TFA/H_2O; iv: TMSOTf, Et_2O.

dioxolane moieties should be a serious problem if this sleeve is used for longer rods. The terephthalaldehyde diacetal sleeve **D** is most easily accessible, but the conformational flexibility is considerably higher than that of sleeves **B** and **C** (cf. the next section) and the corresponding rods are relatively sensitive to hydrolysis. This experience with the sleeves **B**–**D** prompted us to develop a fourth sleeve with a pure carbon skeleton based on a 1,2,3,5,6,7-hexahydro-*s*-indacene. We hypothesized that such hexasubstituted benzene derivatives should be accessible from 2,5-dibutyl-terephthalaldehyde **17** (Figure 5).

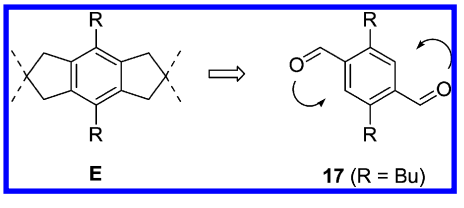


Figure 5. Retrosynthesis of 1,2,3,5,6,7-hexahydro-*s*-indacene sleeves **E**.

The synthesis commenced with a Knoevenagel–Doebner condensation of **17** with malonic acid, followed by a catalytic reduction of the C–C double bonds in the thus obtained biscinnamic acid **20** to give the dicarboxylic acid **21**. After conversion of **21** into the bisacid chloride, a 2-fold intramolecular Friedel–Crafts acylation could be achieved by

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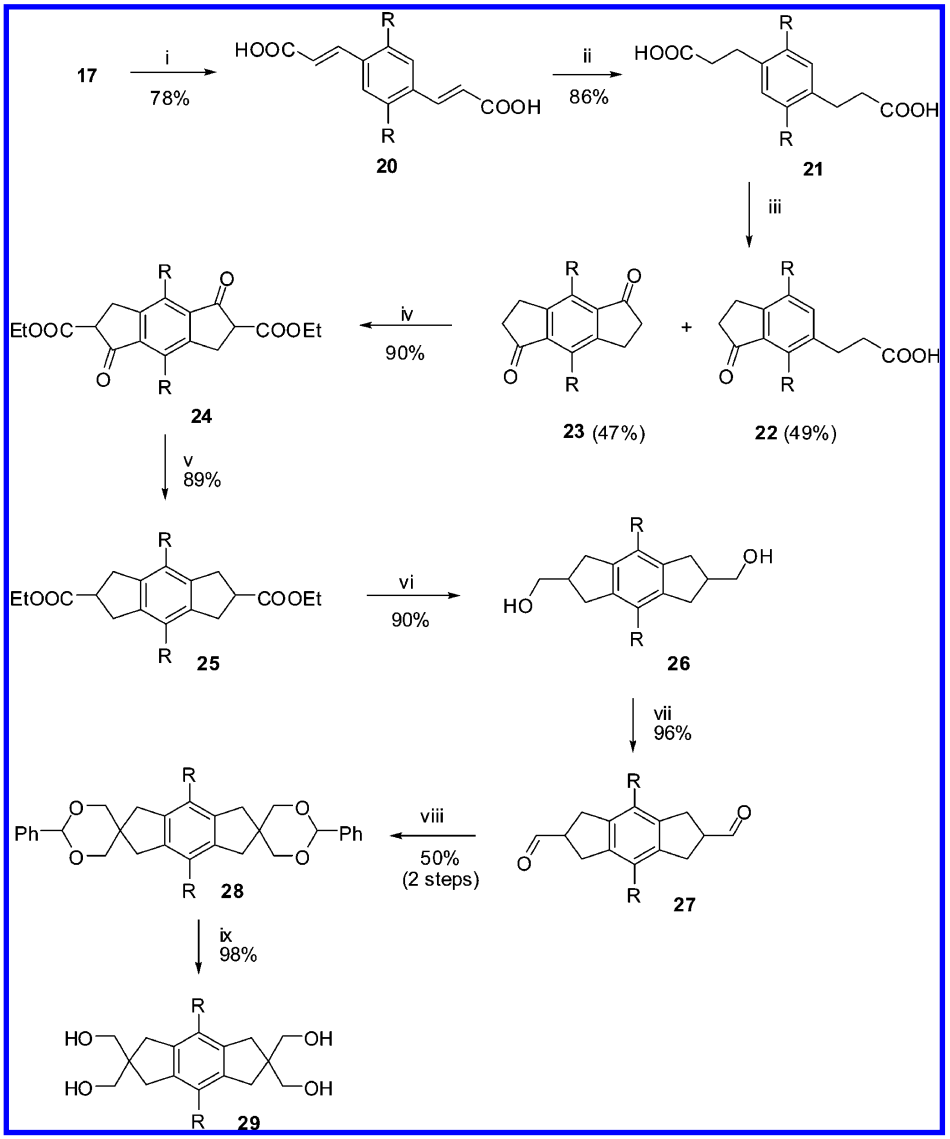
Scheme 5. Synthesis of Tetrol 29 (R = Bu)[a]



[a]i: malonic acid, piperidin, pyridine; ii: H_2, Pd/C, EtOH/HOAc, 60°; iii: 1. $(COCl)_2$, DMF, DCM, 2. $AlCl_3$, CS_2; iv: NaH, toluene, diethyl carbonate, rfx.; v: H_2, Pd/C, H_2SO_4, THF; vi: $LiAlH_4$, Et_2O; vii: $(COCl)_2$, DMSO, Et_3N; viii: 1. HCHO, NaOH, H_2O, dioxane, 2. PhCHO, *p*TsOH, toluene; ix: H_2, Pd/C, EtOH.

treatment with $AlCl_3$ in CS_2. Unfortunately, a 1:1 mixture of the desired indacen-1,5-dione **23** and the carboxylic acid **22** was obtained, but these products are easy to separate. In the remaining steps, the functionalities must be shifted from positions 1,5 to positions 2,6 (the usage of **23** as a sleeve would cause a kink in the overall rod geometry). For this purpose, the diketone **23** was first subjected to a Claisen condensation with diethyl carbonate to give compound **24** and subsequent reductive removal of the keto groups. The resulting bisester **25** was converted in two steps (reduction with $LiAlH_4$, Swern oxidation) into the dialdehyde **27**. In the final steps, **27** is converted with formaldehyde into the tetrol **29** in a sequence consisting of an aldol addition, followed by a crossed Cannizzaro reaction (the crude product was temporarily converted in the bisbenzylidene acetal **28** for the sake of purification, Scheme 5).

To evaluate the applicability of tetrol **29** in the construction of OSK rods, we prepared tetrakis-trimethylsilyl ether **30** and coupled this compound with 4-pivaloyloxy-cyclohexanone, yielding rod **31** with good yield. To perform further extension, the pivaloyloxy groups **31** were converted in two steps into keto groups, and the resulting diketone **33** was subjected to ketalization conditions in the presence of the previously reported diol **34**.[3] We obtained the remarkably long rod **35**, accompanied by rod **36**, which originated from trans-ketalization reactions, in nearly the same amounts (Scheme 6).

Characterization of the Rigidity of Molecular Rods. The outstanding feature of molecular rods compared with other large molecules is their rigidity. The term *rigidity* defines the, over a longer period of time, averaged deviation of the molecular shape from the ideally stretched geometry of a rod. Because every molecular structure is, to a certain extent, prone to stretching, compressing, buckling, and twisting, there is no perfect rigidity (similar to macroscopic bodies). Josef Michl has aptly pointed out in one of his excellent review articles that "*...truly long rods many nanometers in length should be thought of as boiled rather than raw spaghetti.*"[1b] Therefore, a method to quantify the rigidity of a molecular rod is urgently needed.

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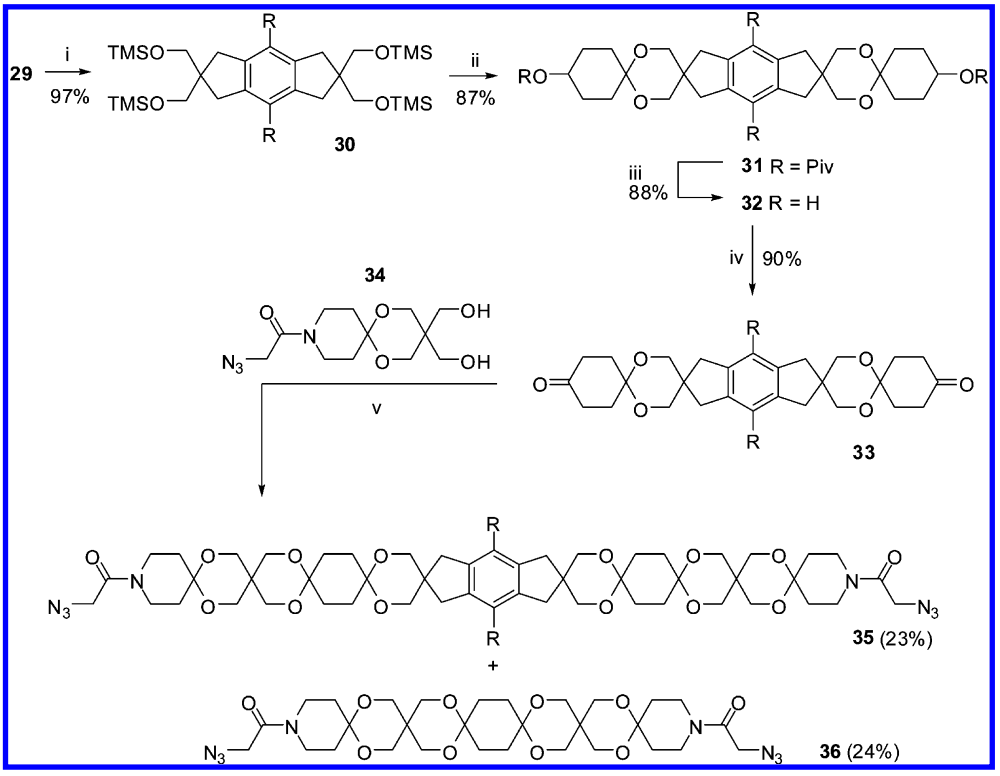
Scheme 6. Synthesis of Rods 35 and 36 with Indacene Sleeve E[a]



[a]i: TMSCl, NEt_3, toluene; ii: 4-pivaloyloxycyclohexanone, TMSOTf, iPr_2O; iii: DIBAL, DCM; iv: Dess–Martin periodinane, $NaHCO_3$, DCM; v: TMSOTf, NaH, Et_2O/DCM/iPr_2O.

Information about the rigidity of a molecule can be obtained both by theoretical calculations (molecular modeling) and by physicochemical measurements. Most of the theoretical calculations are based on molecular dynamics (MD) using an appropriately parametrized force field,[14] whereas static molecules were considered only very seldomly. Very recently, Hoz and co-workers published a realization of the latter approach.[15]

Considering the structural similarity between semiflexible polymers and molecular rods, it is appropriate to treat rod flexibility in the context of the worm-like chain model (WLC), which was originally introduced by Kratky and Porod more than 60 years ago.[16] The pivotal quantity within the framework of the WLC model is the persistence length l_p, which is defined by the sum of the projections of the vectors of all chain segments onto a given segment and is a measure for the rigidity of the polymer. The persistence length can be experimentally determined by light-scattering experiments,[17] small-angle X-ray scattering (SAXS),[18] small-angle neutron scattering (SANS),[19] and other techniques.[20] Furthermore, l_p values are accessible by analyzing the end-to-end distance distribution of molecular rods. This distribution function can be obtained experimentally[21] as well as from MD simulation data.[14]

Because we were interested both in quantifying the rigidity of our OSK rods and in a comparison with various previously reported molecular rods (which are only partly accessible), we decided to determine the persistence length from the end-to-end distance distribution, derived from MD simulations. In Figure 6, the eight investigated rod structures without sleeves are summarized. In concrete terms, we have taken alkanes (**ALK**), oligoalkynes (**OYN**), oligoparaphenylenes (**OPP**), staffanes (**STA**), oligo-bicyclo[2.2.2]octanylidens (**OBC**),

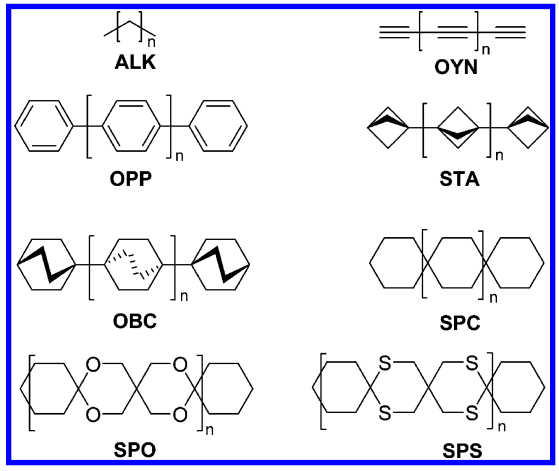


Figure 6. Rod structures without sleeves.

spiroalkanes (**SPC**), oligospiroketals (**SPO**), and oligospirothioketals (**SPS**) into consideration.

In addition, we considered four OSK rods containing the DBD sleeve (**DBD**) and the newly developed inositol (**INO**), terephthalaldehyde diacetal (**TER**), and indacene (**IND**) sleeves (Figure 7). For the sake of comparability, similar lengths of these four rods were chosen and the side chains were replaced by methyl groups to save computing time.

In a typical MD run using the force field MMFF94x[22] with a simulation time of 20 ns, snapshots were taken every 10 ps, providing 2000 saved structures. To ensure that relatively slow conformational processes (e.g., the ring inversion of cyclohexane and 1,3-dioxane rings) are also regarded, all simulations were performed at 600 K (for details regarding the optimization

dx.doi.org/10.1021/jo300266b | J. Org. Chem. 2012, 77, 3907–3920

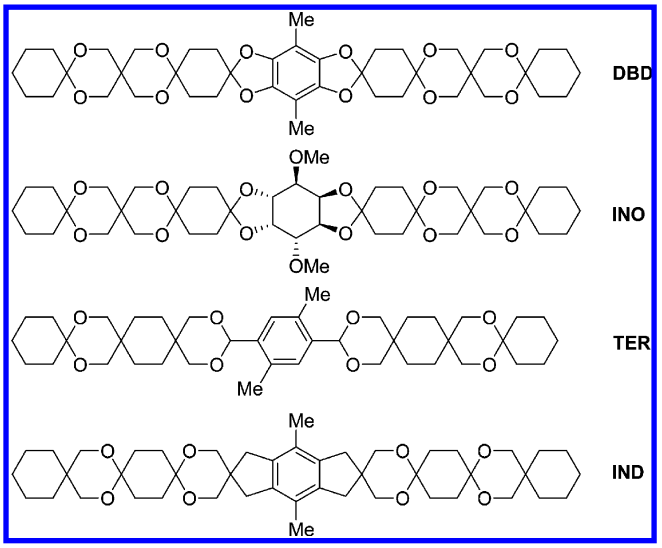


Figure 7. Structures of sleeves containing OSK rods.

of MD parameters, see the Supporting Information). From the saved structures, the end-to-end distances (=distance between the terminal carbon atoms of the rods) were extracted and statistically evaluated. In Figure 8a, a representative trace of the end-to-end distance r of OSK rod **SPO** (n = 3) is depicted. To obtain the distance distribution function, the distance range from 0 to 30 Å was subdivided into 150 channels with a width of Δr = 0.2 Å and the hits in the individual channels were counted. Figure 8b shows the so obtained distance distribution as a bar diagram.

For the determination of the persistence length in terms of the worm-like chain (WLC) model, we used eq 1[23] and obtained the parameters l_c and l_p by nonlinear regression for the rods depicted in Figure 6 for three different lengths in each case.[24] The results are summarized in Table 2.

$$f(r) = \frac{4\pi N r^2}{l_c^2\left[1-\left(\frac{r}{l_c}\right)^2\right]^{9/2}} \exp\left\{\frac{3l_c}{4l_p\left[1-\left(\frac{r}{l_c}\right)^2\right]}\right\} \quad (1)$$

It should be noted that the persistence length must not depend on the length of the respective rod or polymer molecule, and therefore, the applicability of the WLC model on molecular rods essentially depends on the congruence of the l_p values for different rod lengths.

Whereas the three l_p values for oligoalkynes **OYN** (n = 8, 11, 14) and alkanes **ALK** (n = 17, 20, 23) are sufficiently well in agreement (the value for **ALK** [l_p = 6.43−6.71 Å] is in excellent agreement with the published value for linear polyethylene [l_p = 6.5 ± 0.8 Å][20]), in all other cases, the l_p values largely increase with increasing rod length (Table 2). It is notable that, in these cases, l_p is much greater than the contour length l_c, in contrast to the values obtained for **OYN** and **ALK**. Obviously, it is not possible to extrapolate the correct persistence length l_p from MD simulations with relatively short rigid rods with a length of

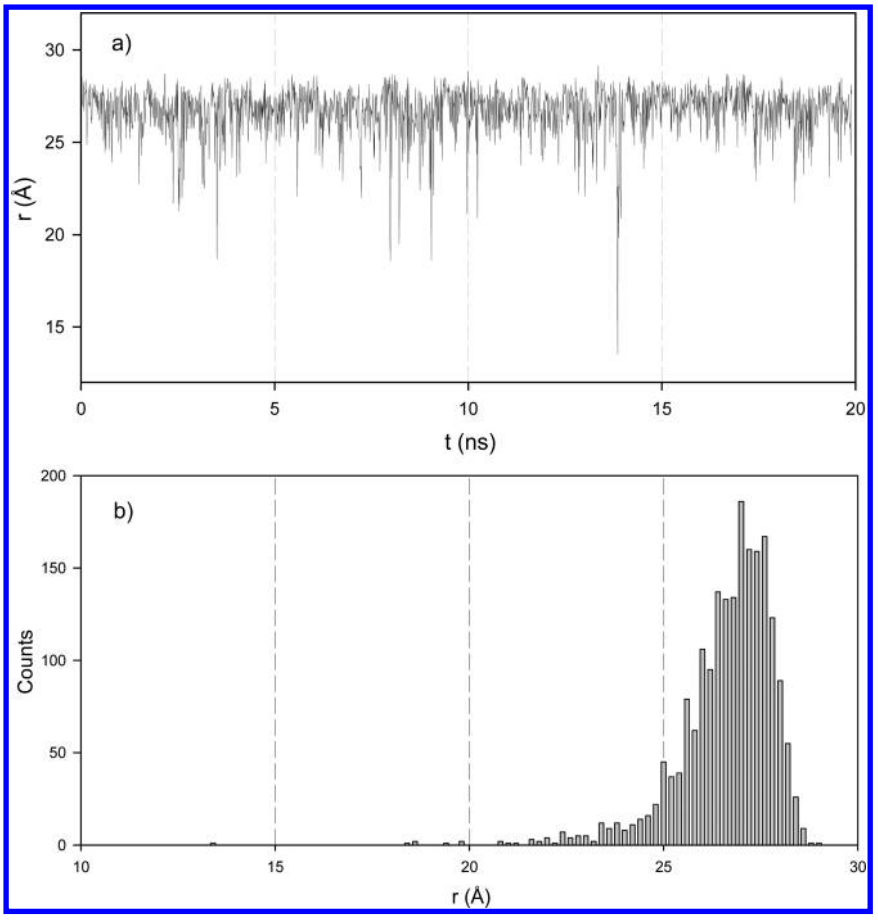


Figure 8. (a) Trace of the end-to-end distance and (b) distance distribution function for **SPO** (n = 3).

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Table 2. WLC and Levy–Martin (LM) Parameters Obtained from MD Simulations

rod	n	l_c (Å)[a]	l_p (Å)[a]	r_0 (Å)[b]	w[c]	z[c]	w/r_0	w/r_0*1000
OBC	5	20.19	**125.18**	19.78	0.1503	19.85	**0.008**	**8**
	7	28.87	**202.58**	28.36	0.1954	28.44	**0.007**	**7**
	9	37.53	**283.79**	36.95	0.2333	37.03	**0.006**	**6**
STA	6	18.65	**81.01**	18.43	0.1809	18.22	**0.010**	**10**
	9	28.57	**118.75**	28.31	0.2965	27.95	**0.010**	**10**
	12	37.53	**136.15**	38.19	0.4372	37.51	**0.011**	**11**
OPP	5	20.43	**79.92**	20.09	0.2391	19.90	**0.012**	**12**
	7	29.13	**113.88**	28.75	0.3357	28.40	**0.012**	**12**
	9	37.78	**148.28**	37.41	0.4326	36.85	**0.012**	**12**
SPC	7	21.12	**55.21**	20.80	0.3555	20.35	**0.017**	**17**
	10	29.92	**86.18**	29.74	0.4866	28.95	**0.016**	**16**
	13	38.86	**99.68**	38.20	0.6616	37.44	**0.017**	**17**
SPS	2	22.14	**52.54**	21.61	0.4240	21.24	**0.020**	**20**
	3	31.61	**73.84**	30.99	0.6098	30.15	**0.020**	**20**
	4	41.40	**93.75**	39.35	0.7671	39.35	**0.019**	**19**
SPO	2	20.38	**35.21**	19.87	0.5310	19.26	**0.027**	**27**
	3	28.73	**43.38**	28.36	0.8366	27.04	**0.029**	**29**
	4	37.36	**51.29**	36.72	1.1444	34.93	**0.031**	**31**
OYN	8	19.70	**31.38**	19.63	0.5089	18.60	**0.026**	**26**
	11	27.83	**29.36**	27.52	1.0875	25.49	**0.040**	**40**
	14	35.93	**29.24**	35.42	1.7176	32.15	**0.048**	**48**
ALK	17	21.07	**6.43**	20.12	2.4440	15.29	**0.121**	**121**
	20	24.88	**6.71**	24.00	2.9097	17.63	**0.121**	**121**
	23	29.76	**6.45**	27.77	3.9888	19.33	**0.144**	**144**
DBD		29.60	**58.75**	29.05	0.6640	28.19	**0.023**	**23**
IND		30.25	**42.26**	28.91	0.8870	28.35	**0.031**	**31**
INO		29.85	**37.78**	28.83	1.0604	27.57	**0.037**	**37**
TER		29.01	**29.75**	26.65	1.1646	26.38	**0.044**	**44**

[a]WLC parameters: l_c, contour length; l_p, persistence length. [b]r_0: end-to-end distance of the rod in the global minimum. [c]Levy–Martin (LM) parameters w and z.

20–40 Å. We assume that the WLC model is also applicable to rigid molecular rods, but the required length of the simulated molecules is far too large for manageable MD simulations.

After these rather sobering experiences with the WLC model, we looked for an alternate mathematical treatment of the end-to-end distance distribution function with the aim of obtaining rigidity parameters, which are largely independent from the rod length. In 2001, Di Marco and Bombi published 86 different equations for the description of chromatographic peaks.[25]

From this collection, we choose eight equation types considering the following four aspects: (i) the function should be valid over the entire range of values, (ii) the equation should not contain more than four parameters, (iii) the function should be able to characterize both symmetrical and asymmetrical peaks, and (iv) the function should not contain sum or integral expressions (for details, see the Supporting Information). Furthermore, it would be desirable if the parameters are interpretable in terms of the peak shape (peak width, peak asymmetry, and location of the peak maximum).

After fitting these eight equation types on various distance distribution functions of molecular rods by nonlinear regression, four types revealed very good fit results based on the regression coefficients: Simplified EMG,[26] Levy–Martin,[27] Asymmetric Logistic,[28] and Losev-A.[29] Taking into account the simplicity of the equations and, especially, the interpretability of the parameters, the Levy–Martin function proved to be best suited (eq 2; for details, see the Supporting Information).

$$f(r) = h\cdot\exp\left\{-\frac{(r-z)^2}{2[w+s(r-z)]^2}\right\} \quad (2)$$

In this equation, h corresponds to the height of the curve, z to the location of the peak maximum, w to the peak width, and s to the peak asymmetry. Because the width of the distance distribution function, in relation to the length r_0 of the rods, should be a measure of the rod rigidity, it seems reasonable to consider the quotient w/r_0. In remembrance of the inventors of eq 2, we propose to name this expression the Levy–Martin parameter LM (eq 3; for better manageability, the quotient w/r_0 should be multiplied by 1000).

$$\mathrm{LM}=\frac{w}{r_0}\cdot 1000 \quad (3)$$

In Table 2, the LM parameters of the eight rods depicted in Figure 6 as well as of the four OSK rods with different sleeves (Figure 7) are summarized. In contrast to the persistence length l_p, the LM parameters of rigid rods (**OBC**, **STA**, **OPP**, **SPC**, **SPS**, **SPO**) only marginally depend on the length of the rods. On the other hand, this model seems to be rather less suitable for the floppy chains of **OYN** and **ALK**. According to this formalism, very rigid rods, such as **OBC**, **STA**, or **OPP**, have LM values between 6 and 12, whereas spiranes **SPC**, **SPO**, and **SPS** give LM values between 17 and 30. The rigidity is decreasing from pure carbon spirane (**SPC**, LM = 17) over spirothioketals (**SPS**, LM = 20) to spiroketals (**SPO**, LM = 29). On the basis of these results, we are now able to assess the influence of the four sleeves **B**–**E** (cf. Figure 1) on the rod

dx.doi.org/10.1021/jo300266b | J. Org. Chem. 2012, 77, 3907–3920

rigidity. Surprisingly, the DBD sleeve **B** considerably enhances the rigidity compared with a pure OSK rod (**DBD**, LM = 23). The indacene sleeve **E** hardly at all influences the rigidity (**IND**, LM = 31), whereas the inositol sleeve **C** and the terephthalaldehyde diacetyl sleeve **D** clearly decrease the rigidity (**INO**, LM = 37; **TER**, LM = 44).

CONCLUSION

In extension to the previously reported[3] DBD sleeve **B**, we have herein presented the synthesis of three new sleeves and their incorporation in OSK rods. The structures of these sleeves are based on *neo*-inositol (**C**), terephthalaldehyde diacetals (**D**), and indacene (**E**). Each of the new sleeves has specific advantages and disadvantages with respect to its synthesis, use as a building block in OSK rods, and influence on the rod rigidity. To quantify this influence, we applied the worm-like chain (WLC) model, developed for the description of semiflexible polymers, on the new rods and found that this approach is rather disappointing. As the chief cause of this result, we assume that the rigidity of typical molecular rods largely exceeds the rigidity of polymers, which were successfully described by the WLC model. Alternatively, we suggest quantifying the rigidity of molecular rods by fitting an empirical function on the end-to-end distance distribution curve obtained by MD simulations. After checking various function types, the Levy−Martin function proved to be most suitable for this purpose. We demonstrated that the quotient between the parameter w (which is a measure of the width of the distance distribution) and the contour length r_0 of a certain rod (multiplied by 1000) is largely independent of the rod length, and we have named this term the Levy−Martin (LM) parameter. In the future, this parameter should be very helpful to compare molecular rods with respect to their rigidity.

EXPERIMENTAL SECTION

[(1*R*,2*R*,3*S*,4*S*,5*S*,6*S*)-Cyclohexane-1,2,3,4,5,6-hexaylhexakis(oxy)]hexakis(trimethylsilane) (1). *neo*-inositole[6] (998 mg, 5.54 mmol) was suspended in anhyd NEt_3 (250 mL), and TMSCl (14 mL, 110 mmol, 20 equiv) was added. The resulting mixture was heated to reflux for 24 h. The mixture was allowed to reach room temperature. TMSCl (3 mL, 23.6 mmol, 4 equiv) was added, and the mixture was stirred overnight. The resulting suspension was cooled at 0 °C, then filtered, and the solvent was evaporated. The residue was suspended in hexanes and filtered. The solvent was evaporated, yielding **1** (2.88 g, 4.70 mmol, 85%) as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.85−1.15 (m, 54H, CH_3), 3.73 (s, 6H, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 0.2 (CH_3), 0.5 (CH_3), 70.7 (CH), 76.3 (CH).

(3a′*R*,4a′*R*,7a′*S*,8a′*S*)-Hexahydrodispiro[cyclohexane-1,2′-benzo[1,2-*d*:4,5-*d*′]bis[1,3]dioxole-6′,1″-cyclohexane]-4′,8′-diol (2a). Variant A: **1** (362 mg, 594 μmol) and cyclohexanone (127 mg, 1.29 mmol, 2.2 equiv) were dissolved in anhyd iPr_2O (20 mL), and TMSOTf (two drops) was added. The resulting mixture was stirred overnight. A spatula tip of K_2CO_3 and MeOH were added, and the solvents were evaporated. CH_2Cl_2 was added and the mixture washed with 0.1 N HCl and brine. The organic layer was dried over $MgSO_4$, evaporated, and purified by flash chromatography ($CHCl_3$/EtOAc 10:1 > $CHCl_3$/EtOAc 5:1), yielding **2a** (186 mg, 546 μmol, 92%) as a white solid. Variant B: **1** (356 mg, 581 μmol) and cyclohexanone (193 mg, 1.97 mmol, 3.4 equiv) were dissolved in anhyd Et_2O (20 mL), and TMSOTf (two drops) was added. The resulting mixture was stirred for 48 h. A spatula tip of K_2CO_3 and MeOH were added, and the solvents were evaporated. CH_2Cl_2 was added and the mixture washed with 0.1 N HCl and brine. The organic layer was dried over $MgSO_4$, evaporated, and purified by flash chromatography ($CHCl_3$ > $CHCl_3$/EtOAc 5:1), yielding a mixture of **2a** (65 mg, 192 μmol, 33%) and **3a** (69 mg, 201 μmol, 35%) as a white solid. The molar ratios were determined by ^{1}H NMR. R_f ($CHCl_3$/EtOAc 3:1) = 0.3; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 1.26− 1.28 (m, 4H, CH_2), 1.39−1.52 (m, 16H, CH_2), 2.50 (d, ^3J = 4.3 Hz, 2H, OH), 4.03−4.07 (m, 2H, CH), 4.26−4.35 (m, 4H, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 23.4 (CH_2), 23.8 (CH_2), 25.1 (CH_2), 32.8 (CH_2), 35.9 (CH_2), 69.0 (CH), 74.2 (CH), 75.5 (CH), 109.5 (C); mp = 189−190 °C; IR 3407, 2929, 2849, 1450, 1372, 1162, 1117, 1054, 952, 869 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{28}O_6Na$ [M + Na]$^+$, 363.1784; found, 363.1765.

***rac*-Hexahydrodispiro[cyclohexane-1,2′-benzo[1,2-*d*:3,4-*d*′]bis[1,3]dioxole-7′,1″-cyclohexane]-4′,5′-diol (3a).** R_f ($CHCl_3$/EtOAc 3:1) = 0.2; ^{1}H NMR (600 MHz, $CDCl_3$) δ_H 1.31−1.73 (m, 20H, CH_2), 2.59 (s, 2H, OH), 3.78−3.86 (m, 2H, CH), 4.50−4.60 (m, 4H, CH); ^{13}C NMR (150 MHz, $CDCl_3$) δ_C 23.4 (CH_2), 23.9 (CH_2), 25.0 (CH_2), 32.9 (CH_2), 35.6 (CH_2), 67.2 (CH), 73.8 (CH), 73.9 (CH), 109.5 (C).

(3a′*R*,4a′*R*,7a′*S*,8a′*S*)-4′,8′-Bis(prop-2-en-1-yloxy)-hexahydrodispiro[cyclohexane-1,2′-benzo[1,2-*d*:4,5-*d*′]bis-[1,3]dioxole-6′,1″-cyclohexane] (2b). Variant A: **2a** (97 mg, 285 μmol) was dissolved in dry DMF (5 mL), and NaH (60% in mineral oil, 42 mg, 1.05 mmol, 3.7 equiv) and allyl bromide (100 μL, 1.16 mmol, 4.1 equiv) were added. The resulting mixture was stirred overnight. CH_2Cl_2 was added, and the mixture was washed with 1N HCl, aqueous saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$, evaporated, and purified by flash chromatography ($CHCl_3$/EtOAc 40:1), yielding **2b** (113 mg, 269 μmol, 94%) as a colorless oil. Variant B: A mixture of **2a** (38 mg, 111 μmol) and **3a** (39 mg, 116 μmol) was dissolved in dry DMF (5 mL), and NaH (60% in mineral oil, 45 mg, 1.13 mmol, 5.0 equiv) and allyl bromide (105 mg, 868 μmol, 3.8 equiv) were added. The resulting mixture was stirred overnight. CH_2Cl_2 was added, and the mixture was washed with 1N HCl, aqueous saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$, evaporated, and purified by flash chromatography ($CHCl_3$), yielding **2b** (40 mg, 95 μmol, 42%) as a colorless oil and **3b** (47 mg, 111 μmol, 49%) as a colorless oil. R_f ($CHCl_3$/EtOAc 40:1) = 0.5; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 1.30−1.75 (m, 20H, CH_2), 3.89 (dd, ^3J = 4.7 Hz, ^3J = 2.9 Hz, 2H, CH), 4.21 (dt, dt, ^3J = 5.5 Hz, ^4J = 1.3 Hz, 4H, CH_2), 4.38 (dd, ^3J = 7.6 Hz, ^3J = 4.8 Hz, 2H, CH), 4.49 (dd, ^3J = 7.6 Hz, ^3J = 2.9 Hz, 2H, CH), 5.16 (ddd, ^3J = 10.4 Hz, ^2J = 2.9 Hz, ^4J = 1.3 Hz, 2H, CH_2), 5.28 (ddd, ^3J = 17.2 Hz, ^2J = 3.3 Hz, ^4J = 1.6 Hz, 2H, CH_2), 5.92 (ddt, ^3J = 17.1 Hz, ^3J = 10.8 Hz, ^3J = 5.4 Hz, 2H, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 23.6 (CH_2), 24.0 (CH_2), 25.2 (CH_2), 33.4 (CH_2), 35.9 (CH_2), 72.0 (CH_2), 73.9 (CH), 75.3 (CH), 76.1 (CH), 109.6 (C), 116.7 (CH_2), 135.0 (CH); IR 2936, 2856, 1724, 1447, 1369, 1161, 1104, 947, 754 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{36}O_6Na$ [M + Na]$^+$, 443.2410; found, 443.2404.

***rac*-4′,5′-Bis(prop-2-en-1-yloxy)hexahydrodispiro-[cyclohexane-1,2′-benzo[1,2-*d*:3,4-*d*′]bis[1,3]dioxole-7′,1″-cyclohexane] (3b).** R_f ($CHCl_3$/EtOH 20:1) = 0.55; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ_H 1.19−1.82 (m, 20H, CH_2), 3.78−3.86 (m, 2H, CH), 4.18−4.35 (m, 4H, CH_2), 4.42−4.48 (m, 2H, CH), 4.50−4.58 (m, 2H, CH), 5.13−5.36 (m, 4H, CH_2), 5.88−6.04 (m, 2H, CH); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ_C 23.5 (CH_2), 23.9 (CH_2), 25.1 (CH_2), 33.0 (CH_2), 35.7 (CH_2), 72.5 (CH_2), 72.8 (CH), 74.6 (CH), 74.7 (CH), 109.1 (C), 116.9 (CH_2), 135.5 (CH); HRMS (ESI) calcd for $C_{24}H_{36}O_6Na$ [M + Na]$^+$, 443.2410; found, 443.2406.

(For structural assignment of **2b** and **3b**, see the Supporting Information.)

(3a′*R*,4a′*R*,7a′*S*,8a′*S*)-4′,8′-Dihydroxyhexahydrodispiro-[cyclohexane-1,2′-benzo[1,2-*d*:4,5-*d*′]bis[1,3]dioxole-6′,1″-cyclohexane]-4,4″-diyl Bis(2,2-dimethyl-propanoate) (5). **1** (2.88 g, 4.69 mmol) and **4**[30] (1.91 g, 9.61 mmol, 2.05 equiv) were dissolved in anhyd MTBE (250 mL), and TMSOTf (50 μL, 0.28 mmol, 0.06 equiv) was added. The resulting mixture was stirred overnight. A spatula tip of K_2CO_3 and MeOH were added, and the solvents were evaporated. CH_2Cl_2 was added and the mixture washed with 0.1 N HCl and brine. The organic layer was dried over $MgSO_4$, evaporated, and purified by flash chromatography ($CHCl_3$ > $CHCl_3$/EtOAc 5:2), yielding **5** (2.00 g, 3.70 mmol, 79%) as a white solid. R_f ($CHCl_3$/EtOAc 3:1) = 0.3; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 1.18 (s, 18H, CH_3), 1.65−1.92 (m, 16H, CH_2), 2.41 (s, 2H, OH), 4.20−4.23 (m,

dx.doi.org/10.1021/jo300266b | J. Org. Chem. 2012, 77, 3907−3920

2H, CH), 4.41−4.51 (m, 4H, CH), 4.82−4.92 (m, 2H, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 27.1 (CH_3), 27.6 (CH_2), 28.0 (CH_2), 28.7 (CH_2), 31.9 (CH_2), 38.8 (C), 69.0 (CH), 69.0 (CH), 74.4 (CH), 75.6 (CH), 108.7 (C), 177.8 (C); mp = 211−212 °C; IR 3470, 2959, 1720, 1639, 1479, 1378, 1282, 1170, 1101, 1045, 951 cm^{-1}; HRMS (ESI) calcd for $C_{28}H_{45}O_{10}$ [M + H]$^+$, 541.3013; found, 541.2965.

Note: The letters ***a*****−****d** *in the context of compounds* ***6*****−****8** *refer to different diastereomers. After oxidation, all diastereomers of* ***8*** *(****8a*****−****8d****) provide the same compound* ***9****.*

(3a′*R*,4a′*R*,7a′*S*,8a′*S*)-4′,8′-Bis(prop-2-en-1-yloxy)-hexahydrodispiro[cyclohexane-1,2′-benzo[1,2-*d*:4,5-*d*′]bis-[1,3]dioxole-6′,1″-cyclohexane]-4,4″-diyl Bis(2,2-dimethylpropanoate) (6a−6d). **5** (1315 mg, 2.43 mmol) was dissolved in anhyd DMF (40 mL), and NaH (60% in mineral oil, 330 mg, 8.25 mmol, 3.4 equiv) was added and the mixture stirred for 30 min at room temperature. Allyl bromide (700 μL, 8.10 mmol, 3.3 equiv) was added, and the resulting mixture was stirred overnight. CH_2Cl_2 was added, and the mixture was washed with 1N HCl and brine. The organic layer was dried over $MgSO_4$, evaporated, and purified by flash chromatography ($CHCl_3$ > $CHCl_3$/EtOAc 10:1), yielding four diastereomers **6a**−**6d** (1403 mg, 2.26 mmol, 93%). Diastereomers **6a** and **6b** could be separated by flash chromatography. Diastereomers **6c** and **6d** could be obtained only as a mixture. **6a**: colorless crystals; R_f ($CHCl_3$/EtOAc 20:1) = 0.4; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 1.18 (s, 18H, CH_3), 1.57−2.02 (m, 16H, CH_2), 3.90 (dd, ^3J = 4.4 Hz, ^3J = 2.9 Hz, 2H, CH), 4.21 (dt, ^3J = 5.6 Hz, ^4J = 1.2 Hz, 4H, CH_2), 4.40 (dd, ^3J = 7.6 Hz, ^3J = 4.8 Hz, 2H, CH), 4.52 (dd, ^3J = 7.6 Hz, ^3J = 2.9 Hz, 2H, CH), 4.83−4.94 (m, 2H, CH), 5.18 (ddd, ^3J = 10.4 Hz, ^2J = 2.8 Hz, ^4J = 1.2 Hz, 2H, CH_2), 5.29 (ddd, ^3J = 17.2 Hz, ^2J = 3.3 Hz, ^4J = 1.6 Hz, 2H, CH_2), 5.92 (ddt, ^3J = 17.2 Hz, ^3J = 10.6 Hz, ^3J = 5.4 Hz, 2H, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 27.1 (CH_3), 27.7 (CH_2), 28.1 (CH_2), 29.0 (CH_2), 31.5 (CH_2), 38.8 (C), 68.9 (CH), 72.1 (CH_2), 74.1 (CH), 75.4 (CH), 76.0 (CH), 108.9 (C), 117.0 (CH_2), 134.8 (CH), 177.8 (C); mp = 120−122 °C; IR 2957, 1723, 1478, 1376, 1281, 1166, 1106, 952 cm^{-1}; HRMS (ESI) calcd for $C_{34}H_{52}O_{10}$ [M]$^+$, 620.3560; found, 620.3618. **6b**: colorless crystals; R_f ($CHCl_3$/EtOAc 20:1) = 0.3; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 1.18 (s, 18H, CH_3), 1.52−1.99 (m, 16H, CH_2), 3.90 (dd, ^3J = 4.5 Hz, ^3J = 2.8 Hz, 2H, CH), 4.21 (dt, ^3J = 5.5 Hz, ^4J = 1.3 Hz, 4H, CH_2), 4.40 (dd, ^3J = 7.6 Hz, ^3J = 4.7 Hz, 2H, CH), 4.49 (dd, ^3J = 7.6 Hz, ^3J = 2.8 Hz, 2H, CH), 4.77−4.88 (m, 2H, CH), 5.17 (ddd, ^3J = 10.4 Hz, ^2J = 2.9 Hz, ^4J = 1.2 Hz, 2H, CH_2), 5.29 (ddd, ^3J = 17.2 Hz, ^2J = 3.3 Hz, ^4J = 1.6 Hz, 2H, CH_2), 5.91 (ddt, ^3J = 17.2 Hz, ^3J = 10.6 Hz, ^3J = 5.4 Hz, 2H, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 27.1 (CH_3), 27.9 (CH_2), 28.2 (CH_2), 29.5 (CH_2), 32.0 (CH_2), 38.7 (C), 69.5 (CH), 72.0 (CH_2), 74.0 (CH), 75.4 (CH), 76.0 (CH), 108.8 (C), 116.9 (CH_2), 134.8 (CH), 177.8 (C); mp = 130−131 °C; IR 2954, 1721, 1478, 1377, 1281, 1167, 1109, 933 cm^{-1}; HRMS (ESI) calcd for $C_{34}H_{52}O_{10}$ [M]$^+$, 620.3560; found, 620.3613. **6c**−**6d**: colorless oil; R_f ($CHCl_3$/EtOAc 20:1) = 0.2; ^{1}H NMR (600 MHz, $CDCl_3$) δ_H 1.18 (s, 18H, CH_3), 1.18 (s, 18H, CH_3), 1.54−2.00 (m, 16H + 16H, CH_2), 3.84−3.95 (m, 2H + 2H, CH), 4.19 (dt, ^3J = 5.6 Hz, ^4J = 1.4 Hz, 4H, CH_2), 4.23 (dt, ^3J = 5.6 Hz, ^4J = 1.4 Hz, 4H, CH_2), 4.38 (dd, ^3J = 7.6 Hz, ^3J = 4.7 Hz, 2H, CH), 4.41 (dd, ^3J = 7.7 Hz, ^3J = 4.7 Hz, 2H, CH), 4.48 (dd, ^3J = 7.7 Hz, ^3J = 2.7 Hz, 2H, CH), 4.52 (dd, ^3J = 7.6 Hz, ^3J = 2.9 Hz, 2H, CH), 4.77−4.93 (m, 2H + 2H, CH), 5.13−5.21 (m, 2H + 2H, CH_2), 5.23−5.35 (m, 2H + 2H, CH_2), 5.82−6.00 (m, 2H + 2H, CH); ^{13}C NMR (300 MHz, $CDCl_3$) δ_C 27.1 (CH_3), 27.7 (CH_2), 27.9 (CH_2), 28.1 (CH_2), 28.2 (CH_2), 29.0 (CH_2), 29.5 (CH_2), 31.5 (CH_2), 32.0 (CH_2), 38.7 (C), 38.8 (C), 68.9 (CH), 69.5 (CH), 72.1 (CH_2), 74.0 (CH), 74.1 (CH), 75.4 (CH), 76.0 (CH), 76.0 (CH), 108.7 (C), 108.9 (C), 116.8 (CH_2), 117.0 (CH_2), 134.8 (CH), 134.8 (CH), 177.8 (C), 177.8 (C); IR 2954, 1721, 1477, 1377, 1281, 1166, 1106, 951, 934 cm^{-1}; HRMS (ESI) calcd for $C_{34}H_{52}O_{10}$ [M]$^+$, 620.3560; found, 620.3567.

(3a′*R*,4a′*R*,7a′*S*,8a′*S*)-4′,8′-Dipropoxyhexahydrodispiro-[cyclohexane-1,2′-benzo[1,2-*d*:4,5-*d*′]bis[1,3]dioxole-6′,1″-cyclohexane]-4,4″-diyl Bis(2,2-dimethyl-propanoate) (7a). **6a** (231 mg, 372 μmol) was dissolved in EtOH (25 mL), and $Pd(OH)_2$ on charcoal (20%, spatula tip) was added. The resulting mixture was stirred under a hydrogen atmosphere (1 bar). After complete conversion monitored by TLC, the reaction mixture was filtered over Celite, evaporated, and purified by flash chromatography ($CHCl_3$/EtOAc 20:1), yielding **7a** (219 mg, 351 μmol, 94%) as white foam. R_f ($CHCl_3$/EtOAc 20:1) = 0.5; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.92 (t, ^3J = 7.4 Hz, 6H, CH_3), 1.19 (s, 18H, CH_3), 1.53−1.96 (m, 4H, CH_2, 16H, CH_2), 3.60 (t, ^3J = 6.8 Hz, 4H, CH_2), 3.80 (dd, ^3J = 4.5 Hz, ^3J = 2.9 Hz, 2H, CH), 4.38 (dd, ^3J = 7.6 Hz, ^3J = 4.7 Hz, 2H, CH), 4.48 (dd, ^3J = 7.6 Hz, ^3J = 2.9 Hz, 2H, CH), 4.76−4.88 (m, 2H, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 10.5 (CH_3), 23.1 (CH_2), 27.1 (CH_3), 27.8 (CH_2), 28.1 (CH_2), 29.0 (CH_2), 31.5 (CH_2), 38.8 (C), 68.9 (CH), 73.2 (CH_2), 74.0 (CH), 75.3 (CH), 77.0 (CH), 108.7 (C), 177.9 (C); IR 2961, 1723, 1478, 1377, 1281, 1165, 1107, 951 cm^{-1}; HRMS (ESI) calcd for $C_{34}H_{56}O_{10}Na$ [M + Na]$^+$, 647.3771; found, 647.3797.

(3a′*R*,4a′*R*,7a′*S*,8a′*S*)-4′,8′-Dipropoxyhexahydrodispiro-[cyclohexane-1,2′-benzo[1,2-*d*:4,5-*d*′]bis[1,3]dioxole-6′,1″-cyclohexane]-4,4″-diyl Bis(2,2-dimethyl-propanoate) (7b). **6b** (139 mg, 224 μmol) was prepared according to **7a**, yielding **7b** (135 mg, 216 μmol, 97%) as white foam. R_f ($CHCl_3$/EtOAc 20:1) = 0.4; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.92 (t, ^3J = 7.4 Hz, 6H, CH_3), 1.19 (s, 18H, CH_3), 1.55−1.93 (m, 4H, CH_2, 16H, CH_2), 3.60 (t, ^3J = 6.8 Hz, 4H, CH_2), 3.80 (dd, ^3J = 2.9 Hz, ^3J = 4.8 Hz, 2H, CH), 4.38 (dd, ^3J = 4.7 Hz, ^3J = 7.6 Hz, 2H, CH), 4.48 (dd, ^3J = 2.9 Hz, ^3J = 7.6 Hz, 2H, CH), 4.77−4.87 (m, 2H, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 10.5 (CH_3), 23.1 (CH_2), 27.1 (CH_3), 27.9 (CH_2), 28.3 (CH_2), 29.6 (CH_2), 32.0 (CH_2), 38.8 (C), 68.6 (CH), 73.0 (CH_2), 73.8 (CH), 75.2 (CH), 76.9 (CH), 108.6 (C), 177.9 (C); IR 2961, 1723, 1477, 1377, 1280, 1165, 1109, 950 cm^{-1}; HRMS (ESI) calcd for $C_{34}H_{56}O_{10}Na$ [M + Na]$^+$, 647.3771; found, 647.3784.

(3a′*R*,4a′*R*,7a′*S*,8a′*S*)-4′,8′-Dipropoxyhexahydrodispiro-[cyclohexane-1,2′-benzo[1,2-*d*:4,5-*d*′]bis[1,3]dioxole-6′,1″-cyclohexane]-4,4″-diyl Bis(2,2-dimethyl-propanoate) (7c−7d). **6c**−**6d** (270 mg, 757 μmol) was prepared according to **7a**, yielding **7c**−**7d** (227 mg, 715 μmol, 95%) as white foam. R_f ($CHCl_3$/EtOAc 20:1) = 0.3; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.92 (t, ^3J = 7.4 Hz, 6H, CH_3), 0.93 (t, ^3J = 7.4 Hz, 6H, CH_3), 1.19 (s, 18H, CH_3), 1.19 (s, 18H, CH_3), 1.51−2.06 (m, 4H + 4H, CH_2, 16H + 16H, CH_2), 3.60 (t, ^3J = 6.9 Hz, 4H, CH_2), 3.62 (t, ^3J = 6.9 Hz, 4H, CH_2), 3.76−3.84 (m, 2H + 2H, CH), 4.36 (dd, ^3J = 7.6 Hz, ^3J = 4.8 Hz, 2H, CH), 4.39 (dd, ^3J = 7.6 Hz, ^3J = 4.7 Hz, 2H, CH), 4.47 (dd, ^3J = 7.6 Hz, ^3J = 2.8 Hz, 2H, CH), 4.51 (dd, ^3J = 7.6 Hz, ^3J = 2.9 Hz, 2H, CH), 4.76−4.95 (m, 2H + 2H, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 10.5 (CH_3), 10.5 (CH_3), 23.1 (CH_2), 27.1 (CH_3), 27.7 (CH_2), 27.9 (CH_2), 28.1 (CH_2), 28.3 (CH_2), 29.0 (CH_2), 29.6 (CH_2), 31.4 (CH_2), 32.1 (CH_2), 38.8 (C), 38.8 (C), 68.9 (CH), 69.6 (CH), 73.1 (CH_2), 73.1 (CH_2), 73.9 (CH), 74.0 (CH), 75.2 (CH), 75.2 (CH), 76.9 (CH), 77.0 (CH), 108.6 (C), 108.7 (C), 177.9 (C), 177.9 (C); IR: 2957, 1723, 1478, 1377, 1281, 1166, 1108, 951 cm^{-1}; HRMS (ESI) calcd for $C_{34}H_{56}O_{10}Na$ [M + Na]$^+$, 647.3771; found, 647.3792.

(3a′*R*,4a′*R*,7a′*S*,8a′*S*)-4′,8′-Dipropoxyhexahydrodispiro-[cyclohexane-1,2′-benzo[1,2-*d*:4,5-*d*′]bis[1,3]dioxole-6′,1″-cyclohexane]-4,4″-diol (8a). **7a** (204 mg, 327 μmol) was dissolved in anhyd CH_2Cl_2 (20 mL) and cooled to −78 °C. DIBAL (1 M in hexanes, 1.80 mL, 1.80 mmol, 5.5 equiv) was added, and the reaction was stirred for 1 h. CH_2Cl_2 was added, and resulting mixture was washed with 1N HCl, aqueous saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$, evaporated, and purified by flash chromatography (CH_2Cl_2/MeOH 100:3), yielding **8a** (132 mg, 290 μmol, 89%) as a ductile colorless oil. R_f (CH_2Cl_2/MeOH 100:4) = 0.1; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.91 (t, ^3J = 7.4 Hz, 6H, CH_3), 1.44−1.97 (m, 2H, OH, 4H, CH_2, 16H, CH_2), 3.52−3.64 (m, 4H, CH_2), 3.78 (dd, ^3J = 4.7 Hz, ^3J = 2.9 Hz, 2H, CH), 3.74−3.87 (m, 2H, CH), 4.35 (dd, ^3J = 7.6 Hz, ^3J = 4.8 Hz, 2H, CH), 4.48 (dd, ^3J = 7.6 Hz, ^3J = 2.9 Hz, 2H, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 10.5 (CH_3), 23.1 (CH_2), 29.4 (CH_2), 31.4 (CH_2), 31.8 (CH_2), 31.9 (CH_2), 67.6 (CH), 72.9 (CH_2), 73.7 (CH), 75.2 (CH), 76.9 (CH), 108.8 (C); IR 3386, 2933, 1372, 1103, 1074, 1039, 939, 752 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{40}O_8Na$ [M + Na]$^+$, 479.2621; found, 479.2622.

(3a′*R*,4a′*R*,7a′*S*,8a′*S*)-4′,8′-Dipropoxyhexahydrodispiro-[cyclohexane-1,2′-benzo[1,2-*d*:4,5-*d*′]bis[1,3]dioxole-6′,1″-cy-

clohexane]-4,4″-diol (8b). **7b** (130 mg, 209 μmol) was treated according to **8a**, yielding **8b** (84 mg, 181 μmol, 87%) as a ductile colorless oil. R_f (CH_2Cl_2/MeOH 100:4) = 0.1; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.92 (t, ^3J = 7.4 Hz, 6H, CH_3), 1.40−1.96 (m, 2H, OH, 4H, CH_2, 16H, CH_2), 3.61 (t, ^3J = 6.8 Hz, 4H, CH_2), 3.69−3.81 (m, 2H, CH), 3.79 (dd, ^3J = 4.6 Hz, ^3J = 2.9 Hz, 2H, CH), 4.36 (dd, ^3J = 7.6 Hz, ^3J = 4.8 Hz, 2H, CH), 4.47 (dd, ^3J = 7.6 Hz, ^3J = 2.9 Hz, 2H, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 10.5 (CH_3), 23.1 (CH_2), 30.0 (CH_2), 31.8 (CH_2), 32.2 (CH_2), 32.7 (CH_2), 68.6 (CH), 73.1 (CH_2), 74.0 (CH), 75.2 (CH), 76.9 (CH), 108.7 (C); IR 3386, 2933, 1371, 1105, 1074, 1039, 937, 753 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{40}O_8Na$ [M + Na]$^+$, 479.2621; found, 479.2607.

(3a′*R*,4a′*R*,7a′*S*,8a′*S*)-4′,8′-Dipropoxyhexahydrodispiro-[cyclohexane-1,2′-benzo[1,2-*d*:4,5-*d*′]bis[1,3]dioxole-6′,1″-cyclohexane]-4,4″-diol (8c−8d). **7c−7d** (232 mg, 695 μmol) was treated according to **8a**, yielding **8c−8d** (319 mg, 626 μmol, 90%) as a ductile colorless oil. R_f (CH_2Cl_2/MeOH 100:4) = 0.1; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.87−0.94 (m, 6H + 6H, CH_3), 1.42−1.95 (m, 2H + 2H, OH, 4H + 4H, CH_2, 16H + 16H, CH_2), 3.53−3.66 (m, 4H + 4H, CH_2), 3.67−3.85 (m, 2H + 2H, CH, 2H + 2H, CH), 4.30−4.40 (m, 2H + 2H, CH), 4.42−4.45 (m, 2H + 2H, CH); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ_C 10.4 (CH_3), 10.5 (CH_3), 23.0 (CH_2), 23.1 (CH_2), 29.6 (CH_2), 30.0 (CH_2), 31.4 (CH_2), 31.8 (CH_2), 31.8 (CH_2), 32.0 (CH_2), 32.1 (CH_2), 32.7 (CH_2), 67.7 (CH), 68.5 (CH), 72.9 (CH_2), 73.1 (CH_2), 73.8 (CH), 73.9 (CH), 75.1 (CH), 75.3 (CH), 76.7 (CH), 77.1 (CH), 108.7 (C), 108.7 (C); IR 3389, 2933, 1445, 1371, 1232, 1107, 1075, 1037, 938, 754, 732 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{40}O_8Na$ [M + Na]$^+$, 479.2621; found, 479.2608.

(3a′*R*,4a′*R*,7a′*S*,8a′*S*)-4′,8′-Dipropoxyhexahydro-4*H*,4″*H*-dispiro[cyclohexane-1,2′-benzo[1,2-*d*:4,5-*d*′]bis[1,3]dioxole-6′,1″-cyclohexane]-4,4″-dione (9). **8a** (129 mg, 282 μmol) and $NaHCO_3$ (147 mg, 1.75 mmol, 6.2 equiv) were suspended in anhyd CH_2Cl_2 (12 mL). Dess−Martin periodinane (285 mg, 672 μmol, 2.4 equiv) was added, and the resulting suspension was stirred for 1 h at room temperature. The mixture was washed three times with saturated aqueous $NaHCO_3$/$Na_2S_2O_3$ (250 g/L) and brine. The organic layer was dried over $MgSO_4$, evaporated, and purified by flash chromatography (CH_2Cl_2/MeOH 100:2), yielding **9** (120 mg, 266 μmol, 94%) as a ductile colorless oil. R_f (CH_2Cl_2/MeOH 100:4) = 0.4; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.92 (t, ^3J = 7.4 Hz, 6H, CH_3), 1.54−1.68 (m, 4H, CH_2), 1.90−2.19 (m, 8H, CH_2), 2.37−2.60 (m, 8H, CH_2), 3.61 (t, ^3J = 6.7 Hz, 4H, CH_2), 3.86 (t, ^3J = 2.9 Hz, ^3J = 4.6 Hz, 2H, CH), 4.46 (t, ^3J = 4.7 Hz, ^3J = 7.6 Hz, 2H, CH), 4.57 (t, ^3J = 2.9 Hz, ^3J = 7.6 Hz, 2H, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 10.4 (CH_3), 23.1 (CH_2), 32.0 (CH_2), 34.6 (CH_2), 37.7 (CH_2), 38.2 (CH_2), 73.2 (CH_2), 74.3 (CH), 75.6 (CH), 76.8 (CH), 107.8 (C), 209.7 (C); IR 2961, 2936, 1714, 1436, 1367, 1270, 1124, 1102, 965, 755 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{36}O_8Na$ [M + Na]$^+$, 475.2308; found, 475.2262. **8b** (79 mg, 173 μmol) was treated according to **8a**, yielding **9** (74 mg, 164 μmol, 95%). The analytical data are consistent with those of **9** prepared from **8a**. **8c−8d** (281 mg, 615 μmol) was treated according to **8a**, yielding **9** (270 mg, 597 μmol, 97%). The analytical data are consistent with those of **9** prepared from **8a**.

2,2′-(2,5-Dibutylbenzene-1,4-diyl)bis(5,5-dimethyl-1,3-dioxane) (16). The preparation of **16** was performed accroding to Krebs et al.[13] **15** (52.2 g, 0.150 mol,) was dissolved in anhyd THF (500 mL), then cooled to −60 °C, and *n*-butyllithium (1.6 M in hexanes, 110 mL, 0.176 mol, 1.17 equiv) was added dropwise. The reaction was stirred for 15 min, and anhyd DMF (27 mL, 0.351 mol, 2.3 equiv) was added and the mixture allowed to reach room temperature. After 1 h, aqueous HCl (37%, 100 mL) was added and the mixture evaporated until the THF had been removed. The aqueous layer was extracted three times with Et_2O, and the combined organic layers were washed with water. Drying over $MgSO_4$ and evaporation gave a yellow oil that was used in the next step without further purification. The crude product was refluxed in toluene (400 mL) containing neopentyl glycol (24 g, 0.23 mol, excess) and *p*-toluenesulfonic acid (80 mg) with a water separator. After 5 h, the mixture was cooled and washed with aqueous $NaHCO_3$ and water. Drying with $MgSO_4$ and evaporation gave a brown oil that was used in the next step without further purification. The crude product was dissolved in anhyd THF (450 mL), then cooled to −60 °C, and *n*-butyllithium (1.6 M in hexanes, 110 mL, 0.176 mol) was added dropwise. The reaction was stirred for 15 min, and anhyd DMF (27 mL, 0.351 mol) was added and the mixture allowed to reach room temperature. After 1 h, aqueous HCl (37%, 100 mL) was added and the organic layer was separated and washed with water. Evaporation gave a yellow oil that was used in the next step without further purification. The crude product was refluxed in toluene (400 mL) containing neopentyl glycol (24 g, 0.23 mol, excess) and *p*-toluenesulfonic acid (80 mg) with a water separator. After 3 h, the mixture was cooled and washed with saturated aqueous $NaHCO_3$ and water. The organic layer was dried over $MgSO_4$ and evaporated. The resulting residue was recrystallized from hexanes (45 °C), yielding **16** (32.65 g, 0.078 mol, 52%) as white crystals. R_f (hexanes/EtOAc 20:1) = 0.2; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.82 (s, 6H, CH_3), 0.98 (t, ^3J = 7.3 Hz, 6H, CH_3), 1.35 (s, 6H, CH_3), 1.37−1.49 (m, 4H, CH_2), 1.57−1.67 (m, 4H, CH_2), 2.67−2.73 (m, 4H, CH_2), 3.65 (d, ^2J = 10.8 Hz, 4H, H-6), 3.79 (d, ^2J = 11.1 Hz, 4H, H-6), 5.29 (s, 2H, CH), 7.46 (s, 2H, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 14.0 (CH_3), 21.9 (CH_3), 22.8 (CH_2), 23.2 (CH_3), 30.1 (C), 31.8 (CH_2), 33.8 (CH_2), 77.8 (CH_2), 99.9 (CH), 127.1 (CH), 136.1 (C), 137.9 (C); IR 2954, 2931, 2867, 2838, 1466, 1388, 1192, 1098, 1038, 1016, 991, 968, 912 cm^{-1}; mp = 131−132 °C; HRMS (ESI) calcd for $C_{26}H_{42}O_4$ [M + H]$^+$, 419.3161; found, 419.3153.

2,5-Dibutylbenzene-1,4-dicarbaldehyde (17). The preparation of **17** was applied in accordance to Krebs et al.[13] **16** (39.92 g, 95.36 mmol) was dissolved in trifluoroacetic acid (155 mL) and water (20 mL). The reaction mixture was heated to reflux for 15 min and allowed to reach room temperature. The solvents were removed at a rotary evaporator, and residual volatile compounds were evaporated at 1 × 10^{-3} mbar. The residue was dissolved in CH_2Cl_2, and the mixture was washed with saturated aqueous $NaHCO_3$ and brine. The organic layer was dried over $MgSO_4$, evaporated, and purified by flash chromatography (hexanes > hexanes/EtOAc 10:1), yielding **17** (21.62 g, 87.78 mmol, 92%) as a white solid. R_f (hexanes/EtOAc 10:1) = 0.4; ^{1}H NMR (300 MHz, CD_2Cl_2) δ_H 0.94 (t, ^3J = 7.3 Hz, 6H, CH_3), 1.35−1.47 (m, 4H, CH_2), 1.56−1.66 (m, 4H, CH_2), 3.01−3.07 (m, 4H, CH_2), 7.73 (s, 2H, CH), 10.35 (s, 2H, CH); ^{13}C NMR (75 MHz, CD_2Cl_2) δ_C 13.3 (CH_3), 22.2 (CH_2), 31.1 (CH_2), 34.1 (CH_2), 132.7 (CH), 136.5 (C), 143.0 (C), 191.3 (CH); IR 3356, 2957, 2937, 2871, 2856, 1686, 1465, 1403, 1173, 1159, 1104, 867, 720 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{23}O_2$ [M + H]$^+$, 247.1698; found, 247.1705.

(2*E*,2′*E*)-3,3′-(2,5-Dibutylbenzene-1,4-diyl)bisprop-2-enoic Acid (20). A solution of **17** (20.72 g, 84.11 mmol), malonic acid (26.50 g, 254.7 mmol, 3.0 equiv), and piperidine (2.5 mL, 25.25 mmol, 0.3 equiv) in anhyd pyridine (130 mL) was stirred for 94 h at 50 °C. The resulting suspension was acidified with 6N HCl (330 mL) and filtered. The precipitate was washed several times with 1N HCl and water. The residue was dissolved in aqueous NaOH (2.5%, 600 mL) and extracted three times with Et_2O/EtOAc (v/v 1:1). The aqueous layer was acidified with 6N HCl. The resulting precipitate was collected by filtration, washed with water, and dried, yielding **20** (21.62 g, 65.44 mmol, 78%) as a white solid. R_f (CH_2Cl_2/MeOH 10:1) = 0.3; ^{1}H NMR (300 MHz, C_5D_5N) δ_H 0.84 (t, ^3J = 7.3 Hz, 6H, CH_3), 1.25−1.37 (m, 4H, CH_2), 1.51−1.61 (m, 4H, CH_2), 2.74−2.80 (m, 4H, CH_2), 7.00 (d, ^3J = 15.8 Hz, 2H, CH), 7.70 (s, 2H, CH), 8.40 (d, ^3J = 15.8 Hz, 2H, CH); ^{13}C NMR (75 MHz, C_5D_5N) δ_C 14.1 (CH_3), 22.8 (CH_2), 32.9 (CH_2), 34.2 (CH_2), 122.4 (CH), 128.7 (CH), 135.1 (C), 140.7 (C), 141.0 (CH), 169.3 (C); mp = 306−307 °C; IR 3441, 2931, 1688, 1622, 1418, 1328, 1310, 1222, 945, 860, 679 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{27}O_4$ [M + H]$^+$, 331.1909; found, 331.1898.

3,3′-(2,5-Dibutylbenzene-1,4-diyl)dipropanoic Acid (21). **20** (13.95 g, 42.23 mmol) was suspended in EtOH (480 mL) and CH_3COOH (60 mL), and palladium on charcoal (10%, 610 mg) was added. The reaction was stirred at 60 °C under a hydrogen atmosphere (60 bar). After complete conversion monitored by TLC, the reaction mixture was filtered over Celite and the solvents were evaporated. The residue was suspended in THF (100 mL) and aqueous NaOH (5%, 150 mL) and heated under reflux for 3 h. THF

dx.doi.org/10.1021/jo300266b | *J. Org. Chem.* 2012, 77, 3907−3920

was removed at a rotary evaporator, and the resulting solution was extracted twice with Et_2O/EtOAc (v/v 1:1). The aqueous layer was acidified with 3N HCl, and the resulting precipitate was collected by filtration, washed with water, and recrystallized from EtOH/water (v/v 1:1), yielding **21** (12.09 g, 36.15 mmol, 86%) as white crystals. R_f (CH_2Cl_2/MeOH 10:1) = 0.3; ^{1}H NMR (300 MHz, C_5D_5N) δ_H 0.84 (t, ^3J = 7.3 Hz, 6H, CH_3), 1.25−1.40 (m, 4H, CH_2), 1.50−1.62 (m, 4H, CH_2), 2.60−2.70 (m, 4H, CH_2), 2.85−2.93 (m, 4H, CH_2), 3.17−3.26 (m, 4H, CH_2), 7.20 (s, 2H, CH); ^{13}C NMR (75 MHz, C_5D_5N) δ_C 14.2 (CH_3), 23.1 (CH_2), 28.2 (CH_2), 32.4 (CH_2), 34.0 (CH_2), 36.6 (CH_2), 130.4 (CH), 137.1 (C), 138.5 (C), 175.5 (C); mp = 191−192 °C; IR 3445, 2929, 2855, 1710, 1429, 1290, 1220, 936, 661 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{30}O_4Na$ $[M + Na]^+$, 357.2042; found, 357.2065.

4,8-Dibutyl-2,3,6,7-tetrahydro-*s*-indacene-1,5-dione (23) and 3-(4,7-Dibutyl-3-oxo-2,3-dihydro-1*H*-inden-5-yl)-propanoic Acid (22). **21** was suspended in anhyd CH_2Cl_2 (300 mL) and oxalyl chloride (15 mL, 175 mmol, 5.1 equiv), and five drops of anhyd DMF were added. The resulting mixture was heated to reflux for 4 h. The volatile compounds were evaporated at 1×10^{-3} mbar, yielding 3,3′-(2,5-dibutylbenzene-1,4-diyl)dipropanoyl chloride as a tawny solid, which was used without further purification. The acid chloride was dissolved in anhyd CS_2 (400 mL), and under intensive stirring, $AlCl_3$ (9.25 g, 69.37 mmol, 3.1 equiv) was added. The resulting mixture was heated to reflux for 18 h, then cooled at 0 °C, and ice and 6N HCl (30 mL) were added. The aqueous layer was extracted three times with Et_2O. The combined organic layer was washed with brine and decolorized with charcoal. The resulting solution was dried over $MgSO_4$, evaporated, and purified by flash chromatography (hexanes/EtOAc 20:1 > 3:1), yielding **23** (4.83 g, 16.19 mmol, 47%) as white crystals and **22** (5.38 g, 17.00 mmol, 49%) as a brown solid. **23**: R_f (CH_2Cl_2/hexanes 5:1) = 0.5; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ_H 0.94 (t, ^3J = 7.0 Hz, 6H, CH_3), 1.37−1.55 (m, 8H, CH_2), 2.70−2.74 (m, 4H, CH_2), 3.02−3.07 (m, 8H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ_C 13.9 (CH_3), 23.0 (CH_2), 23.1 (CH_2), 26.8 (CH_2), 32.1 (CH_2), 37.4 (CH_2), 137.2 (C), 138.2 (C), 153.7 (C), 207.9 (C); mp = 136−137 °C; IR 2953, 2926, 2854, 1693, 1450, 1340, 1275, 1261, 1245, 1113, 1056, 756 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{27}O_2$ $[M + H]^+$, 299.2011; found, 299.2028. **22**: R_f (CH_2Cl_2/MeOH 25:1) = 0.2; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.97 (t, ^3J = 7.2 Hz, 6H, CH_3), 1.35−1.66 (m, 8H, CH_2), 2.59−2.71 (m, 6H, CH_2), 2.95−3.11 (m, 6H, CH_2), 7.22 (s, 1H, CH), 10.74 (bs, 1H, COOH); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 13.9 (CH_3), 13.9 (CH_3), 22.6 (CH_2), 23.1 (CH_2), 23.3 (CH_2), 26.6 (CH_2), 26.6 (CH_2), 31.3 (CH_2), 32.0 (CH_2), 33.4 (CH_2), 35.8 (CH_2), 37.0 (CH_2), 134.1 (C), 134.9 (CH), 137.5 (C), 137.6 (C), 139.3 (C), 153.4 (C), 178.5 (C), 208.1 (C); mp = 72−73 °C; IR 2956, 2926, 2859, 1704, 1572, 1269, 1210, 640 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{29}O_3$ $[M + H]^+$, 317.2117; found, 317.2092.

Diethyl 4,8-Dibutyl-1,5-dioxo-1,2,3,5,6,7-hexahydro-*s*-indacene-2,6-dicarboxylate (24). NaH (60% in mineral oil, 2.63 g, 65.76 mmol, 6.1 equiv) was washed three times with anhyd hexanes. The residue was suspended in anhyd toluene (120 mL), and diethyl carbonate (11 mL, 90.32 mmol, 8.2 equiv) was added. A solution of **23** (3.20 g, 10.73 mmol) in anhyd toluene (70 mL) was added dropwise and heated to reflux for 5 h. The reaction mixture was cooled to 0 °C, and acetic acid (4 mL) was added. 1N HCl and brine were added, and the aqueous layer was extracted with EtOAc. The combined organic layers were dried over $MgSO_4$, evaporated, and purified by flash chromatography (CH_2Cl_2), yielding **24** (4.26 g, 9.62 mmol, 90%) as a pale yellow solid. R_f ($CHCl_3$/EtOAc 50:1) = 0.5; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.92−1.00 (m, 6H, CH_3), 1.30−1.69 (m, 6H, CH_2, 8H, CH_2), 2.95−3.16 (m, 4H, CH_2), 3.26−3.38 (m, 1.2H, CH_2), 3.41−3.53 (m, 2.8H, CH_2), 3.72−3.81 (m, 1.1H, CH), 4.22−4.41 (m, 4H, CH_2), 10.79 (bs, 0.9H, OH); mp = 152−153 °C; IR 3440, 3296, 2954, 2930, 1729, 1702, 1655, 1593, 1570, 1461, 1402, 1377, 1347, 1311, 1218, 1127, 1029, 776 cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{34}O_6$ $[M]^+$, 442.2355; found, 442.2359.

Diethyl 4,8-Dibutyl-1,2,3,5,6,7-hexahydro-*s*-indacene-2,6-dicarboxylate (25). **24** (424 mg, 0.96 mmol) and palladium on charcoal (10%, spatula tip) were suspended in anhyd THF (25 mL). The reaction mixture was stirred at 40 °C under a hydrogen atmosphere (15 bar). After complete conversion monitored by TLC, the reaction mixture was filtered over Celite and washed with brine. The resulting solution was dried over $MgSO_4$, evaporated, and purified by flash chromatography (hexanes/EtOAc 50:1 > 15:1), yielding **25** (356 mg, 0.859 mol, 89%) as white crystals. R_f (hexanes/EtOAc 10:1) = 0.5; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.96 (t, ^3J = 7.1 Hz, 6H, CH_3), 1.33 (t, ^3J = 7.1 Hz, 6H, CH_3), 1.33−1.55 (m, 8H, CH_2), 2.50−2.56 (m, 4H, CH_2), 3.17−3.25 (m, 8H, CH_2), 3.25−3.39 (m, 2H, CH), 4.22 (q, ^3J = 7.1 Hz, 4H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 13.9 (CH_3), 14.2 (CH_3), 23.0 (CH_2), 30.8 (CH_2), 31.7 (CH_2), 34.5 (CH_2), 43.7 (CH), 60.5 (CH_2), 131.9 (C), 138.8 (C), 175.4 (C); mp = 72−73 °C; IR 2929, 2855, 1727, 1367, 1344, 1211, 1179, 1035 cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{38}O_4$ $[M]^+$, 414.2770; found, 414.2770.

(4,8-Dibutyl-1,2,3,5,6,7-hexahydro-*s*-indacene-2,6-diyl)-dimethanol (26). **25** (1.73 g, 4.17 mmol) was dissolved in anhyd Et_2O (150 mL), and $LiAlH_4$ (700 mg, 18.44 mmol, 4.4 equiv) was added. The resulting mixture was stirred for 1 h at room temperature, and EtOAc (2 mL) was added. 1N HCl was added, and the aqueous layer was extracted twice with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, evaporated, and purified by flash chromatography (CH_2Cl_2/MeOH 100:3), yielding **26** (1.25 g, 3.77 mmol, 90%) as white crystals. R_f (hexanes/EtOAc 2:1) = 0.3; ^{1}H NMR (300 MHz, DMSO-D_6) δ_H 0.92 (t, ^3J = 7.0 Hz, 6H, CH_3), 1.28−1.45 (m, 8H, CH_2), 2.40−2.60 (m, 2H, CH, 8H, CH_2), 2.82−2.90 (m, 4H, CH_2), 3.37−3.42 (m, 4H, CH_2), 4.61 (t, ^3J = 5.2 Hz, 2H, OH); ^{13}C NMR (75 MHz, DMSO-D_6, ppm) δ_C 13.8 (CH_3), 22.4 (CH_2), 30.2 (CH_2), 31.3 (CH_2), 33.7 (CH_2), 41.1 (CH), 64.8 (CH_2), 131.1 (C), 139.0 (C); mp = 161−162 °C; IR 3407, 2926, 2857, 1466, 1104, 1035, 1008 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{34}O_2$ $[M]^+$, 330.2559; found, 330.2541.

4,8-Dibutyl-1,2,3,5,6,7-hexahydro-*s*-indacene-2,6-dicarbaldehyde (27). Anhyd DMSO (1.1 mL, 15.49 mmol, 4.1 equiv) was dissolved in anhyd CH_2Cl_2 (125 mL) at −70 °C. Oxalyl chloride (1.0 mL, 12.83 mmol, 3.4 equiv) was added dropwise. After 30 min, **26** (1.25 g, 3.77 mmol) dissolved in anhyd CH_2Cl_2 (30 mL) and anhyd DMSO (5 mL) was added dropwise. After 30 min, anhyd NEt_3 (5.3 mL, 38.13 mmol, 10.1 equiv) was added, and the mixture was stirred for 30 min, allowing to reach room temperature. CH_2Cl_2 was added, and the mixture was washed with 1N HCl and brine. The resulting organic solution was dried over $MgSO_4$, evaporated, and purified by flash chromatography (hexanes/EtOAc 20:1 > 10:1), yielding **27** (1.18 g, 3.61 mmol, 96%) as white crystals. R_f (hexanes/EtOAc 20:1) = 0.2; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.97 (t, ^3J = 7.1 Hz, 6H, CH_3), 1.36−1.56 (m, 8H, CH_2), 2.53−2.56 (m, 4H, CH_2), 3.10−3.35 (m, 2H, CH, 8H, CH_2), 9.81 (s, 1H, CH), 9.81 (s, 1H, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 13.9 (CH_3), 23.0 (CH_2), 30.9 (CH_2), 31.4 (CH_2), 31.6 (CH_2), 50.7 (CH), 132.4 (C), 138.7 (C), 203.0 (CH); mp = 85−86 °C; IR 2954, 2931, 2855, 1719, 1466, 1103, 1091 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{30}O_2$ $[M]^+$, 326.2246; found, 326.2244.

4′,8′-Dibutyl-2,2″-diphenyl-5′,7′-dihydro-1′*H*,3′*H*-dispiro-[1,3-dioxane-5,2′-[*s*]indacene-6′,5″-[1,3]dioxane] (28). **27** (1.18 g, 3.61 mmol) was dissolved in 60 mL of 1,4-dioxane. Aqueous HCHO (37%, 10% MeOH stabilized, 20 mL, 266 mmol, 74 equiv) was added and the mixture cooled to 0 °C. Aqueous NaOH (2 M, 50 mL, 100 mmol, 28 equiv) was added dropwise and the mixture stirred at room temperature overnight. HCl (37%, 10 mL) was added, and the solvents were evaporated. The resulting residue was suspended with benzaldehyde (10 mL, 99 mmol, 27 equiv) and *p*-toluenesulfonic acid (spatula tip) in toluene (100 mL) and heated to reflux with a water separator. After 2 h, the mixture was cooled to room temperature and was washed with saturated aqueous $NaHCO_3$ and brine. The resulting solution was dried over $MgSO_4$, and the solvents were evaporated. The resulting residue was purified by recrystallization (hexanes/EtOAc 1:1), yielding **28** (1.02 g, 1.80 mmol, 50%) as a white solid. R_f ($CHCl_3$) = 0.4; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 1.02 (t, ^3J = 7.1 Hz, 6H, CH_3), 1.45−1.55 (m, 8H, CH_2), 2.55−2.58 (m, 4H, CH_2), 2.62 (bs, 4H, CH_2), 3.33 (bs, 4H, CH_2), 3.96 (d, ^2J = 10.8 Hz, 4H, CH_2), 4.12 (d, ^2J = 10.8 Hz, 4H, CH_2), 5.62 (s, 2H, CH), 7.41−7.49 (m, 6H,

dx.doi.org/10.1021/jo300266b | J. Org. Chem. 2012, 77, 3907−3920

CH), 7.63 (d, ^3J = 7.3 Hz, 4H, CH); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 14.0 (CH_3), 23.1 (CH_2), 30.7 (CH_2), 31.7 (CH_2), 37.0 (CH_2), 40.0 (CH_2), 41.5 (C), 76.2 (CH_2), 101.7 (CH), 126.1 (CH), 128.3 (CH), 128.9 (CH), 132.2 (C), 133.0 (C), 133.7 (C), 137.4 (C), 138.3 (C), 138.9 (C), 139.2 (C); mp = 235−237 °C; IR 2927, 2847, 1450, 1384, 1304, 1179, 1095, 1066, 1026, 992, 961, 741, 696 cm^{-1}; HRMS (ESI) calcd for $C_{38}H_{46}O_4$ $[M]^+$, 566.3396; found, 566.3368.

(4,8-Dibutyl-1,2,3,5,6,7-hexahydro-*s*-indacene-2,2,6,6-tetrayl)tetramethanol (29). **28** (992 mg, 1.75 mmol) was dissolved in EtOH (80 mL), and palladium on charcoal (10%, spatula tip) was added. The resulting mixture was stirred at 60 °C under a hydrogen atmosphere (20 bar). After complete conversion monitored by TLC, the reaction mixture was filtered over Celite and the solvent was evaporated, yielding **29** (668 mg, 1.71 mmol, 98%) as a white solid. R_f (CH_2Cl_2/MeOH 10:1) = 0.4; ^{1}H NMR (300 MHz, DMSO-D_6) δ_H 0.90 (t, ^3J = 6.9 Hz, 6H, CH_3), 1.28−1.40 (m, 8H, CH_2), 2.35−2.40 (m, 4H, CH_2), 2.59 (s, 8H, CH_2), 3.35−3.37 (m, 8H, CH_2), 4.56 (s, 4H, OH); ^{13}C NMR (75 MHz, DMSO-D_6) δ_C 13.7 (CH_3), 22.3 (CH_2), 30.1 (CH_2), 31.1 (CH_2), 35.8 (CH_2), 49.0 (C), 64.8 (CH_2), 131.5 (C), 138.5 (C); mp = 215−216 °C; IR 3417, 2957, 1655, 1381, 1045, 1027, 1002, 823, 763 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{38}O_4$ $[M]^+$, 390.2770; found, 390.2763.

[(4,8-Dibutyl-1,2,3,5,6,7-hexahydro-*s*-indacene-2,2,6,6-tetrayl)tetrakis(methane-diyloxy)]tetrakis(trimethylsilane) (30). **29** (311 mg, 0.796 μmol) was suspended in anhyd toluene (20 mL) and anhyd NEt_3 (20 mL). TMSCl (2.0 mL, 15.65 mmol, 19.7 equiv) was added, and the reaction was stirred overnight at room temperature. The resulting suspension was cooled at 0 °C, then filtered, and the solvents were evaporated. The residue was suspended in hexanes and filtered. The solvent was evaporated, yielding **30** (527 mg, 776 μmol, 97%) as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.12 (s, 36H, CH_3), 0.95 (t, ^3J = 7.0 Hz, 6H, CH_3), 1.34−1.51 (m, 8H, CH_2), 2.43−2.48 (m, 4H, CH_2), 2.67 (s, 8H, CH_2), 3.54 (s, 8H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C −0.47 (CH_3), 14.0 (CH_3), 23.1 (CH_2), 30.8 (CH_2), 31.8 (CH_2), 36.6 (CH_2), 49.3 (C), 65.2 (CH_2), 132.6 (C), 139.0 (C).

4″,8″-Dibutyl-5″,7″-dihydro-1″*H*,3″*H*-tetraspiro-[cyclohexane-1,2′-[1,3]dioxane-5′,2″-[*s*]indacene-6″,5‴-[1,3]-dioxane-2‴,1‴′-cyclohexane]-4,4‴′-diyl Bis(2,2-dimethylpropanoate) (31). **30** (500 mg, 736 μmol) and **4**[4] (292 mg, 1.47 mmol, 2.0 equiv) were dissolved in anhyd iPr_2O (20 mL), and TMSOTf (20 μL, 110 μmol, 0.15 equiv) was added. The resulting mixture was stirred overnight, evaporated, and purified by flash chromatography ($CHCl_3$ > $CHCl_3$/EE 20:1), yielding **31** (418 mg, 640 μmol, 87%) as a white solid. R_f ($CHCl_3$/EE 20:1) = 0.6 and 0.3; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.95 (t, ^3J = 7.0 Hz, 6H, CH_3), 1.22 (s, 18H, CH_3), 1.33−1.50 (m, 8H, CH_2), 1.69−2.06 (m, 16H, CH_2), 2.45−2.50 (m, 4H, CH_2), 2.84 (s, 8H, CH_2), 3.66−3.89 (m, 8H, CH_2) 4.89−4.91 (m, 2H, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 14.0 (CH_3), 23.1 (CH_2), 26.9 (CH_2), 27.1 (CH_3), 28.5 (CH_2), 30.7 (CH_2), 31.6 (CH_2), 38.7 (CH_2), 38.8 (C), 41.5 (C), 68.6 (CH_2), 68.9 (CH_2), 69.8 (CH), 97.1 (C), 132.9 (C), 138.3 (C), 177.9 (C); mp = 227−229 °C; IR 2951, 2859, 1720, 1477, 1377, 1281, 1168, 1094, 1032, 937 cm^{-1}; HRMS (ESI) calcd for $C_{37}H_{57}O_6$ $[M + H]^+$, 597.4155; found, 597.4144.

4″,8″-Dibutyl-5″,7″-dihydro-1″*H*,3″*H*-tetraspiro-[cyclohexane-1,2′-[1,3]dioxane-5′,2″-[*s*]indacene-6″,5‴-[1,3]-dioxane-2‴,1‴′-cyclohexane]-4,4‴′-diol (32). **31** (419 mg, 558 μmol) was dissolved in anhyd CH_2Cl_2 (20 mL) and cooled to −78 °C. DIBAL (1 M in hexanes, 3.0 mL, 3.0 mmol, 4.9 equiv) was added dropwise and was stirred until complete conversion monitored by TLC. The reaction mixture was allowed to reach room temperature, and MeOH (200 μL) was added. The resulting solution was washed with aqueous tartaric acid (20%) and brine. The organic layer was dried over $MgSO_4$, evaporated, and purified by flash chromatography (CH_2Cl_2/MeOH 100:3 > 100:4), yielding **32** (285 mg, 489 μmol, 88%) as a white solid. R_f (CH_2Cl_2/MeOH 50:1) = 0.2; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.95 (t, ^3J = 6.9 Hz, 6H, CH_3), 1.33−1.92 (m, 2H, OH, 20H, CH_2), 2.17−2.22 (m, 4H, CH_2), 2.45−2.49 (m, 4H, CH_2), 2.83 (s, 8H, CH_2), 3.76−3.85 (m, 8H, CH_2, 2H, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 14.0 (CH_3), 23.1 (CH_2), 29.0 (CH_2), 30.7 (CH_2), 31.7 (CH_2), 38.8 (CH_2), 41.5 (C), 68.6 (CH_2), 68.6 (CH), 69.0 (CH_2), 97.3 (C), 132.9 (C), 138.3 (C); mp = 237−239 °C; IR 3441, 2919, 2851, 1644, 1466, 1095, 982, 931, 747 cm^{-1}; HRMS (ESI) calcd for $C_{36}H_{55}O_6$ $[M + H]^+$, 583.3999; found, 583.3987.

4″,8″-Dibutyl-5″,7″-dihydro-1″*H*,3″*H*,4*H*,4‴′*H*-tetraspiro-[cyclohexane-1,2′-[1,3]dioxane-5′,2″-[*s*]indacene-6″,5‴-[1,3]-dioxane-2‴,1‴′-cyclohexane]-4,4‴′-dione (33). **32** (265 mg, 455 μmol) was dissolved in anhyd CH_2Cl_2 (25 mL). $NaHCO_3$ (92 mg, 1.1 mmol, 2.4 equiv) and Dess−Martin periodinane (430 mg, 1.01 mmol, 2.2 equiv) were added. The resulting mixture was stirred for 1 h at room temperature. Et_2O was added, and the mixture was washed three times with saturated aqueous $NaHCO_3$/$Na_2S_2O_3$ (250 g/L) and brine. The organic layer was dried over $MgSO_4$, evaporated, and purified by flash chromatography (CH_2Cl_2/MeOH 100:2), yielding **33** (237 mg, 410 μmol, 90%) as a white solid. R_f (CH_2Cl_2/MeOH 25:1) = 0.6; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.97 (t, ^3J = 7.0 Hz, 6H, CH_3), 1.37−1.50 (m, 8H, CH_2), 2.22−2.26 (m, 8H, CH_2), 2.45−2.52 (m, 4H + 8H, CH_2), 2.87 (s, 8H, CH_2), 3.83 (s, 8H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 14.0 (CH_3), 23.1 (CH_2), 30.7 (CH_2), 31.2 (CH_2), 31.7 (CH_2), 37.0 (CH_2), 38.6 (CH_2), 41.6 (C), 69.2 (CH_2), 96.4 (C), 133.0 (C), 138.2 (C), 210.5 (C); mp = 272−273 °C; IR 2936, 2855, 1709, 1276, 1121, 1089, 1076, 1023, 903 cm^{-1}; HRMS (ESI) calcd for $C_{36}H_{51}O_6$ $[M + H]^+$, 579.3686; found, 579.3710.

1,1′-(4‴″,8‴″-Dibutyl-5‴″,7‴″-dihydro-1*H*,1‴″*H*,1‴″″′*H*,3‴″*H*-decaspiro-[piperidine-4,2′-[1,3]-dioxane-5′,5″-[1,3]dioxane-2″,1‴-cyclohexane-4‴,2‴′-[1,3]-dioxane-5‴′,2‴″-[*s*]indacene-6‴″,5‴″-[1,3]dioxane-2‴″,1‴″′-cyclo-hexane-4‴″′,2‴″″-[1,3]dioxane-5‴″″,5‴″″-[1,3]-dioxane-2‴″″,4‴″″′-piperidine]-1,1‴″″′-diyl)bis(2-azidoethanone) (35) and 1,1′-(7,11,16,20,27,30,33,36-Octaoxa-3,24-diazahexa-spiro[5.2.2.2.2.2.5.^{21}2.^{18}2.^{15}2.^{12}2.^{9}2^{6}]-hexatriacontane-3,24-diyl)bis(2-azidoethanone) (36). **33** (58 mg, 100 μmol) was suspended in anhyd Et_2O (20 mL) and anhyd CH_2Cl_2 (5 mL) and cooled at 0 °C. NaH (60% in mineral oil, 10 mg, 250 μmol, 2.5 equiv) and TMSCl (25 mg, 230 μmol, 2.3 equiv) were added. After stirring for 1 h, **34**[8] (61 mg, 203 μmol, 2.0 equiv) and TMSOTf (one drop) were added. After 20 and 28 h, respectively, iPr_2O (5 mL) was added. After 48 h, anhyd pyridine (5 drops) was added, the solvents evaporated, and the resulting residue purified by flash chromatography (CH_2Cl_2/MeOH 100:2 > 100:3), yielding **35** (26 mg, 23 μmol, 23%) as a white solid and **36** (21 mg, 24 μmol, 24%) as a white solid. **35**: R_f (CH_2Cl_2/MeOH 25:1) = 0.2; ^{1}H NMR (300 MHz, CD_2Cl_2) δ_H 0.94 (t, ^3J = 6.9 Hz, 6H, CH_3), 1.29−1.51 (m, 8H, CH_2), 1.74−1.97 (m, 24H, CH_2), 2.43−2.48 (m, 4H, CH_2), 2.78 (s, 8H, CH_2), 3.30−3.34 (m, 4H, CH_2) 3.59−3.62 (m, 4H, CH_2), 3.67−3.78 (m, 24H, CH_2), 3.92 (s, 4H, CH_2); ^{13}C NMR (75 MHz, CD_2Cl_2) δ_C 14.2 (CH_3), 23.4 (CH_2), 28.7 (CH_2), 28.8 (CH_2), 31.0 (CH_2), 31.7 (CH_2), 32.2 (CH_2), 33.5 (C), 33.7 (CH_2), 39.0 (CH_2), 39.3 (CH_2), 42.0 (C), 42.1 (CH_2), 51.0 (CH_2), 63.8 (CH_2), 63.9 (CH_2), 69.1 (CH_2), 97.0 (C), 97.8 (C), 98.8 (C), 133.3 (C), 138.7 (C), 165.7 (C); mp > 350 °C; IR 2935, 2855, 2103, 1651, 1442, 1377, 1096, 1033, 910 cm^{-1}; HRMS (ESI) calcd for $C_{60}H_{87}N_8O_{14}$ $[M + H]^+$, 1143.6342; found, 1143.6412. **36**: R_f (CH_2Cl_2/MeOH 25:1) = 0.1; ^{1}H NMR (300 MHz, $CDCl_3$/CD_3OD/DMSO-D_6) δ_H 1.19 (s, 8H, CH_2), 1.24−1.29 (m, 8H, CH_2), 2.75−2.76 (m, 4H, CH_2), 2.96−3.00 (m, 4H, CH_2), 3.10−3.16 (m, 16H, CH_2), 3.46 (s, 4H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$/CD_3OD/DMSO-D_6) δ_C 26.8 (CH_2), 30.3 (CH_2), 31.3 (C), 31.5 (CH_2), 37.5 (CH_2), 40.1 (CH_2), 48.9 (CH_2), 61.8 (CH_2), 95.2 (C), 96.7 (C), 164.4 (C); mp > 350 °C; IR 2959, 2871, 2103, 1655, 1444, 1381, 1149, 1099, 908 cm^{-1}; HRMS (ESI) calcd for $C_{30}H_{45}N_8O_{10}$ $[M + H]^+$, 677.3259; found, 677.3284.

Benzyl 3,3-Bis{[(trimethylsilyl)oxy]methyl}-1,5-dioxa-9-azaspiro[5.5]undecane-9-carboxylate (18). Benzyl 3,3-bis-(hydroxymethyl)-1,5-dioxa-9-azaspiro[5.5]undecane-9-carboxylate[2] (1.41 g, 4.02 mmol) was suspended in anhyd toluene (100 mL) and anhyd NEt_3 (2.8 mL, 20.20 mmol, 5.0 equiv). TMSCl (2.55 mL, 19.95 mmol, 5.0 equiv) was added, and the reaction was stirred overnight at room temperature. The resulting suspension was cooled at 0 °C, then filtered, and the solvents were evaporated. The residue was suspended in hexanes and filtered. The solvent was evaporated, yielding **18** (1.98

dx.doi.org/10.1021/jo300266b | J. Org. Chem. 2012, 77, 3907−3920

g, 3.99 mmol, 99%) as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.11 (s, 18H, CH_3), 1.84 (bs, 4H, CH_2), 3.53−3.56 (m, 8H, CH_2), 3.71 (s, 4H, CH_2), 5.15 (s, 2H, CH_2), 7.30−7.38 (m, 5H, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C −0.71 (CH_3), 32.1 (CH_2), 32.6 (CH_2), 39.6 (C), 40.8 (CH_2), 61.6 (CH_2), 67.0 (CH_2), 96.1 (C), 127.8 (CH), 127.9 (CH), 128.4 (CH), 136.8 (C), 155.2 (C).

Dibenzyl 3,3′-(2,5-Dibutylbenzene-1,4-diyl)bis(2,4,8,15-tetraoxa-12-azadi-spiro[5.2.5.2]hexadecane-12-carboxylate) (19). **17** (210 mg, 852 μmol) and **18** (825 mg, 1.66 mmol, 2.05 equiv) were dissolved in anhyd Et_2O (40 mL). TMSOTf (two drops) was added, and the reaction was stirred overnight. The solvent was evaporated, and the resulting residue was purified by flash chromatography (CH_2Cl_2/MeOH 100:1), yielding **19** (580 mg, 635 μmol, 78%) as a white solid. R_f (CH_2Cl_2/MeOH 100:2) = 0.3; ^{1}H NMR (300 MHz, CD_2Cl_2) δ_H 0.97 (t, ^3J = 7.2 Hz, 6H, CH_3), 1.34−1.47 (m, 4H, CH_2), 1.51−1.61 (m, 4H, CH_2), 1.83−1.88 (m, 8H, CH_2), 2.61−2.67 (m, 4H, CH_2), 3.50−3.55 (m, 4H + 8H, CH_2), 3.65 (d, ^2J = 11.7 Hz, 4H, CH_2), 4.17 (s, 4H, CH_2), 4.25 (d, ^2J = 11.1 Hz, 4H, CH_2), 5.12 (s, 4H, CH_2), 5.53 (s, 2H, CH), 7.30−7.41 (m, 2H + 10H, CH); ^{13}C NMR (75 MHz, CD_2Cl_2) δ_C 13.5 (CH_3), 22.5 (CH_2), 31.4 (CH_2), 31.4 (CH_2), 32.3 (C), 32.3 (CH_2), 33.6 (CH_2), 40.4 (CH_2), 62.6 (CH_2), 63.1 (CH_2), 66.5 (CH_2), 70.8 (CH_2), 96.7 (C), 99.9 (CH), 126.9 (CH), 127.4 (CH), 127.5 (CH), 128.1 (CH), 135.7 (C), 136.9 (C), 137.7 (C), 154.7 (C); mp = 227−229 °C; IR 2955, 2871, 1699, 1430, 1362, 1232, 1082, 697 cm^{-1}; HRMS (ESI) calcd for $C_{52}H_{69}N_2O_{12}$ $[M + H]^+$, 913.4851; found, 913.4854.

■ ASSOCIATED CONTENT

Supporting Information

Structural assignment of **2b** and **3b**, details of theoretical calculations, and NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: wessig@uni-potsdam.de.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The financial support of this work by the Deutsche Forschungsgemeinschaft (We1850-7/1-2 and Heisenberg fellowship of P.W.) is gratefully acknowledged.

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