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Pseudohelical and Helical Primary Structures of 1,2-Spiroannelated Four- and Five-Membered Rings: Syntheses and Chiroptical Properties†

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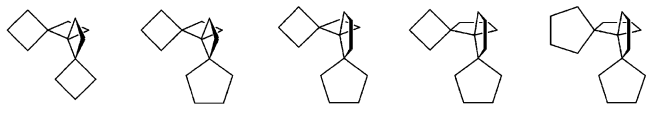

	(*P*)-**4**	(*R*)-**6**	(*S*)-**7**	(*R*)-**8**	(*P*)-**9**
$[\alpha]_D^{20}$ =	+63.3	-4.1	-0.9	-30.7	-62.6

The pseudohelical hydrocarbons (*R*)-**6**, (*S*)-**7**, and (*R*)-**8** and the helical hydrocarbon (*P*)-**9**, formally derived from the helical hydrocarbon (*P*)-**4** by stepwise replacement of each of the four-membered rings by a five-membered ring, have been prepared. Their optical rotations vary systematically, both in magnitude and sign. Of the extremes, (*P*)-**4** represents the usual case of a right-handed dextrorotatory helix, while (*P*)-**9** represents the unusual case of a right-handed levorotatory helix. To rationalize these facts, DFT calculations of the rotatory power of (*P*)-helices of three-, four-, and five-membered rings have been performed. The results show a very good agreement with the experimental data for the rigid helices of three-membered rings and always show the correct sign and order of magnitude for the flexible helices of four- and five-membered rings for which Boltzmann-averaged optical rotations of up to six conformers had to be used. Within the conformers of the latter, a set of large dihedral angles for the bonds of the inner sphere correspond to a high specific rotation, and a set of small dihedral angles correspond to a low specific rotation. As a consequence, the Boltzmann-averaged values markedly depend on the geometry and weight of the conformers involved.

Introduction

Helical primary structures of spiroannelated rings are unknown in nature but have been artificially produced, both in racemic and enantiomerically pure form.[2] However, it was only in 1999[3] that the first enantiomerically pure helical hydrocarbon was reported. Today, five examples[3−6] for helices of three-membered rings are known, among them trispiro[2.0.0.2.1.1]-nonane (**1**),[3,4] tetraspiro[2.0.0.0.2.1.1.1]undecane (**2**),[4] and octaspiro[2.0.0.0.0.0.0.0.2.1.1.1.1.1.1.1.1]nonadecane (**3**).[5,6] In comparison, only two examples of helices of four-membered

† Polyspiranes, Part 29. For Part 28, see ref 1.

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(1) Fitjer, L.; Kanschik, A.; Gerke, R. *Tetrahedron* **2004**, *60*, 1205−1213.

(2) (a) Gange, D.; Magnus, P.; Bass, L.; Arnold, E. V.; Clardy, J. *J. Am. Chem. Soc.* **1980**, *120*, 317−328. (b) Trost, B. M.; Shi, Y. *J. Am. Chem. Soc.* **1991**, *113*, 701−703. (c) Trost, B. M.; Shi, Y. *J. Am. Chem. Soc.* **1993**, *115*, 9421−9438. (d) Hormuth, S.; Schade, W.; Reiβig, H.-U. *Liebigs Ann.* **1996**, 2001−2006.

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(6) de Meijere, A.; Khlebnikov, A. F.; Kozhushkov, S. I.; Yufit, D. S.; Chetina, O. V.; Howard, J. A. K.; Kurahashi, T.; Mijazawa, K.; Frank, D.; Schreiner, P. R.; Rinderspacher, B. C.; Fujisawa, M.; Yamamoto, C.; Okamoto, Y. *Chem. Eur. J.* **2006**, 5697−5721.

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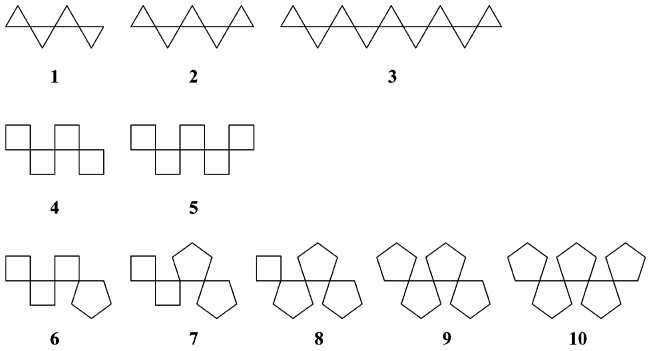


rings have been reported: trispiro[3.0.0.3.2.2]tridecane (**4**)[7] and tetraspiro[3.0.0.0.3.2.2.2]hexadecane (**5**).[1] Of the systems cited, **1**−**3** are rigid and exist as single minimum structures,[3−6] while **4** and **5** are flexible and adopt different conformations.[7] These peculiarities translate to a high specific rotation of (*M*)-**1** ($[\alpha]_D^{20} = -192.7$, $c = 1.2$, $CHCl_3$),[3,4] which doubles in (*M*)-**2** ($[\alpha]_D^{20} = -381.2$, $c = 1.2$, $CHCl_3$)[4] and again in (*M*)-**3** ($[\alpha]_D^{20} = -890.5$, $c = 1.01$, $CHCl_3$),[5,6] and to a low specific rotation of (*M*)-**4** ($[\alpha]_D^{20} = -63.3$, $c = 1.1$, $CHCl_3$)[7] which is further diminished in (*M*)-**5** ($[\alpha]_D^{20} = -24.2$, $c = 1.2$, $CHCl_3$).[1] The latter observation is especially surprising.

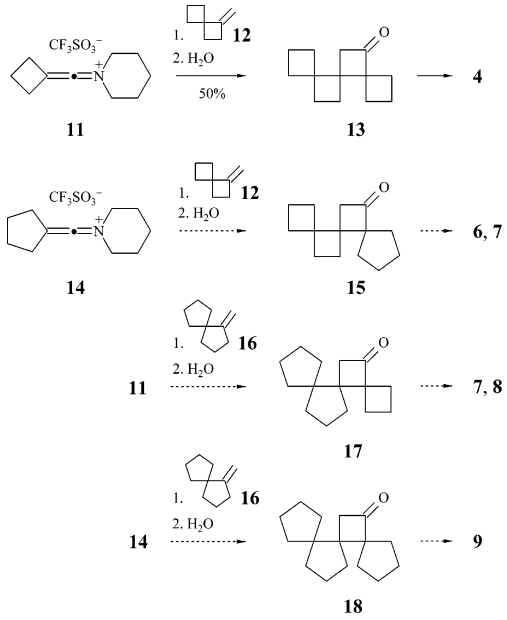
As pointed out elsewhere,[7] striking differences in the overall geometry (identity period, diameter, and length of the helix) of helices of three- (**1**, **2**, **3**) and four-membered rings (**4**, **5**) exist. However, it is only with the rigid helices **1**, **2**, and **3** that a single geometry determines the observed optical rotations. With **4** and **5**, the observed optical rotations are Boltzmann averages over different conformations. Experimentally, these conformations can neither be distinguished nor be weighted.

The same problem exists with the hitherto unknown pseudohelical trispiranes **6**, **7**, and **8** and the helical trispirane **9**, formally derived from **4** by stepwise replacement of each of the four-membered rings by a five-membered ring. Our objective in studying their chiroptical properties was twofold: first, to investigate whether the systematic variation of the structure within the series **4**, **6**, **7**, **8**, and **9** would also provoke a systematic variation of the specific rotations, and second, to establish an understanding of the experimental data by means of an adequate theoretical treatment. Accordingly, we developed syntheses for the pseudo-*P*-helical trispiranes (*R*)-**6**, (*S*)-**7**, and (*R*)-**8** as well as for the helical trispirane (*P*)-**9**, determined their optical rotations, and finally performed quantum chemical calculations of structures, relative energies, and specific rotations. As the number of potential low-energy conformations of the pseudohelical trispiranes **6**, **7**, and **8** was found to be too high as to allow an in-depth theoretical treatment, the calculations were restricted to the helical trispiranes (*P*)-**4**, (*P*)-**5**, and (*P*)-**9** but included the as yet unknown tetraspirane (*P*)-**10** as a higher analogue of (*P*)-**9**. In fact, the collective data show that the specific rotations systematically depend on the conformations involved.

Results

Synthetic Aspects. For the synthesis of the trispiranes **6**−**9**, we thought to benefit from the fact[1] that the keteniminium salt **11**, as generated from the corresponding carboxylic acid amide by successive treatment with trifluoromethanesulfonic acid anhydride and 2,4,6-collidine,[8] adds to 1-methylenespiro[3.3]-heptane (**12**) to yield, after hydrolysis, ketone **13** as a direct precursor of **4**. Likewise, the keteniminium salt **14** could add to **12** with the formation of ketone **15**, and both **11** and **14** could react with 1-methylenespiro[4.4]nonane (**16**) to yield the ketones **17** and **18**, respectively. A final deoxygenation could then lead from **15** and **17** to **6** and **7**, respectively, and after ring enlargement, from **15**, **17**, and **18** to **7**, **8**, and **9**, respectively (Scheme 1). With a successful resolution at the stage of the ketones given, a synthesis of optically active samples seemed feasible.

SCHEME 1



Synthesis of (*R*)-6 and (*S*)-7. The amide **20**, needed for the generation of **14**, was obtained by reaction of the acid chloride **19** with piperidine, and the olefin **16**, needed for cycloaddition reactions, was obtained by cyclobutylidenation of cyclopentanone (**21**), followed by an epoxidation, an oxaspirohexane to cyclopentanone rearrangement,[9] and a methylenation (**21**−**22**−**23**−**16**) (Scheme 2). This sequence compares favorably with the known syntheses of **23**[10] and **16**.[11]

For the synthesis of trispiroketone **15**, we followed the same protocol[1] as for the synthesis of **13**: to a solution of **20** in dichloromethane were added trifluoromethanesulfonic acid anhydride and a solution of 2,4,6-collidine in **12**, and, after 20 h of reflux, **15** was isolated in 21% yield (Scheme 3). This compound was easily recognized by an AB system for the protons neighboring the carbonyl group ($\delta = 2.87$, $\Delta\nu_{AB} = 300$ Hz, $J_{AB} = 16.5$ Hz, 2H). To complete the synthesis of **6** and **7**, we subjected **15** both directly and after ring enlargement with diazomethane[12] to a Wolff−Kishner reduction. In the first case,

(7) Fitjer, L.; Gerke, R.; Weiser, J.; Bunkoczi, G.; Debreczeni, J. E. *Tetrahedron* **2003**, *59*, 4443−4449.

(8) Schmit, C.; Falmagne, J. B.; Escudero, J. Vanlierde, H.; Ghosez, L. *Org. Synth.* **1990**, *69*, 199−205.

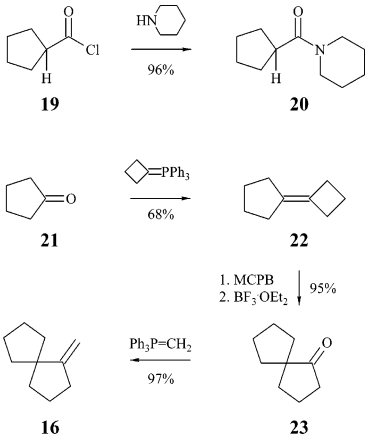
(9) (a) Leriverend, M. L.; Leriverend, P. *C. R. Acad. Sci. Ser. C* **1975**, *280*, 791−792. (b) Trost, B. M.; Latimer, L. H. *J. Org. Chem.* **1978**, *43*, 1031−1040. (c) Halazy, S.; Krief, A. *J. Chem. Soc., Chem. Commun*. **1982**, 1200−1201.

(10) (a) Mayer, R.; Wenschuh, G.; Töpelmann, W. *Chem. Ber*. **1958**, *91*, 1616−1620. (b) Krieger, H.; Ruotsalainen, H.; Montin, J. *Chem. Ber*. **1966**, *99*, 3715−1717.

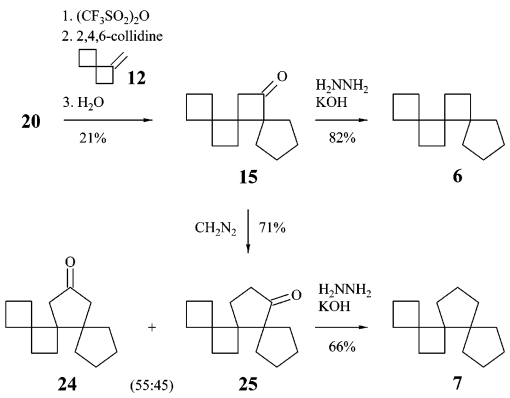
(11) (a) Christol, H.; Vanel, R. *Bull. Soc. Chim. France* **1968**, 1398−1402. (b) Rieke, R. D.; Xiong, H. *J. Org. Chem*. **1992**, *57*, 6560−6565.

(12) Review: Gutsche, C. D. *Org. React*. **1954**, *8*, 365−429.

SCHEME 2



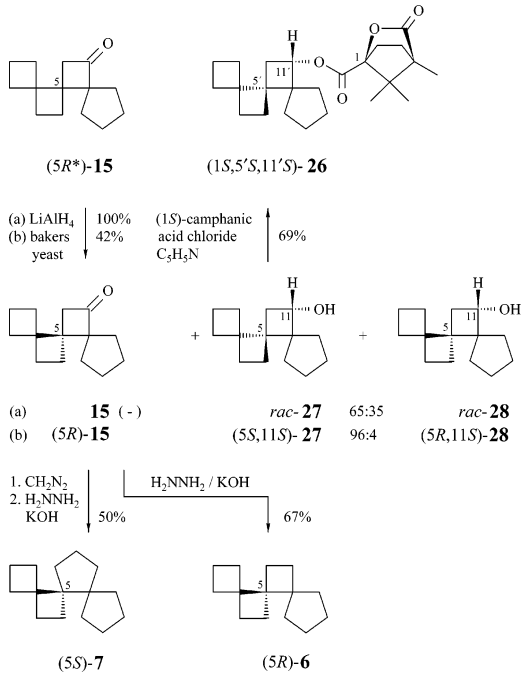
SCHEME 3



we obtained the trispirane **6**, and in the second case, with intermediate formation of a 55:45 mixture of the ketones **24** and **25**, we obtained the trispirane **7**.

For the resolution of the ketone **15**, we hoped for a dia- and enantioselective reduction with bakers' yeast.[7,13] Indeed, after 22 h of exposure, 42% conversion to a 96:4 mixture of two diastereoisomeric alcohols was observed (Scheme 4). The major alcohol was identical with the major alcohol formed by reduction with lithium aluminum hydride and enantiomerically pure according to capillary gas chromatography on a chiral phase. Unfortunately, the enantiomers of the minor alcohol could not be resolved. For the determination of the relative and absolute configuration of the major alcohol formed by reduction with bakers' yeast, we reacted the 96:4 mixture of alcohols with (−)-(1*S*)-camphanic acid chloride,[14] eliminated the minor ester by fractional crystallization, and subjected the major ester (mp 109−110 °C, yield 69%, $[\alpha]_D^{20} = +29.5$, *c* 1.28, acetone) to an X-ray structure analysis. This disclosed its identity as (1*S*,5′*S*,-11′*S*)-**26** and hence that of the corresponding alcohol as (5*S*,-

SCHEME 4



11*S*)-**27**. The observed *S*-selective reduction had already been met with **13**[7] and is in accord with Prelog's rule.[15] The assignment of the minor diastereoisomer as (5*R*,11*S*)-**28** is tentative and implies an *S*-selective reduction too.[16]

At this stage we had to decide whether to oxidize the 96:4 mixture of the alcohols (5*S*,11*S*)-**27** and (5*R*,11*S*)-**28** and to accept a diminished optical purity of the ketone (5*S*)-**15** or to eliminate the minor enantiomer from the 83:17 mixture of (5*R*)- and (5*S*)-**15** of the recovered ketones by further reductions. In view of the fact that the alcohols could not be separated on a preparative scale, we subjected the recovered ketones to further reductions. Four days of a second exposure to bakers' yeast resulted in 28% conversion to a 58:42 mixture of (5*S*,11*S*)-**27** and (5*R*,11*S*)-**28**, and hence in a 99:1 mixture of (5*R*)- and (5*S*)-**15** as remaining ketones, and two days of a third exposure resulted in 12% conversion to a 5:95 mixture of (5*S*,11*S*)-**27** and (5*R*,11*S*)-**28**, and hence in enantiopure (5*R*)-**15** (>99% ee, $[\alpha]_D^{20} = -0.6°$, $c = 1.13$, acetone).

The reactions which followed were identical to those applied for the synthesis of racemic **6** and **7**: direct Wolff−Kishner reduction delivered (*R*)-trispiro[3.0.0.4.2.2]tetradecane [(*R*)-**6**] (>99% ee, $[\alpha]_D^{20} = -4.5°$, $c = 1.13$, $CHCl_3$), and ring enlargement with diazomethane followed by Wolff−Kishner reduction (*S*)-trispiro[3.0.0.4.3.2]pentadecane [(*S*)-**7**] (>99% ee, $[\alpha]_D^{20} = -1.1°$, $c = 1.09$, $CHCl_3$).

Synthesis of (*R*)-8 and (*P*)-9. Much to our disappointment, all efforts to achieve cycloadditions between the keteniminium salts **11** and **14**, respectively, and the olefin **16** failed. Occasionally extensive polymerization was observed, but usually no reaction occurred, neither in refluxing dichloromethane nor in refluxing 1,2-dichloroethane.[8] Therefore, other routes for a synthesis of **8** and **9** had to be explored.

At first glance, the spiroanellation of a four- and a five-membered ring, respectively, to dispiroketone **32** seemed most

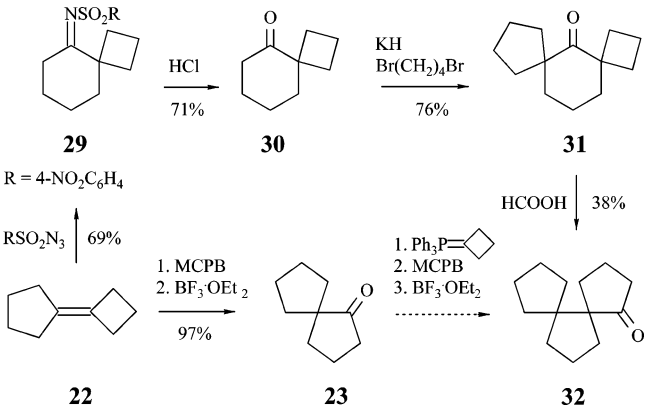
(13) For bakers' yeast reductions of cyclobutanones in bicyclic systems, see: (a) Newton, R. F.; Paton, J.; Reynolds, D. P.; Young, S.; Roberts, S. M. *J. Chem. Soc. Chem. Commun.* **1979**, 908−909. (b) Dawson, M. J.; Lawrence, G. C.; Lilley, G.; Todd, M.; Noble, D.; Green, S. M.; Roberts, S. M.; Wallace, T. W.; Newton, R. F.; Carter, M. C.; Hallet, P.; Paten, J.; Reynolds, D. P.; Young, S. *J. Chem. Soc. Perkin Trans. 1* **1983**, 2119−2125. (c) Lowe, G.; Swain, S. *J. Chem. Soc. Perkin Trans. 1* **1985**, 391−398. (d) Kertesz, D. J.; Kluge, A. F. *J. Org. Chem.* **1988**, *53*, 4962−4968.

(14) (a) Gerlach, H.; *Helv. Chim. Acta* **1968**, *51*, 1587−1593. (b) Gerlach, H.; Müller, W. *Helv. Chim. Acta* **1972**, *55*, 2277−2286. (c) Gerlach, H.; Oertle, K.; Thalmann, A. *Helv. Chim. Acta* **1976**, *59*, 755−760. (d) Gerlach, H. *Helv. Chim. Acta* **1978**, *61*, 2773−2776. (e) Gerlach, H. *Helv. Chim. Acta* **1985**, *68*, 1815−1821.

(15) Prelog, V. *Pure Appl. Chem.* **1964**, *9*, 119−130.

(16) Bakers' yeast reductions of cyclobutanones are *S*-selective.[7,13] Exceptions exist for fluorinated derivatives.

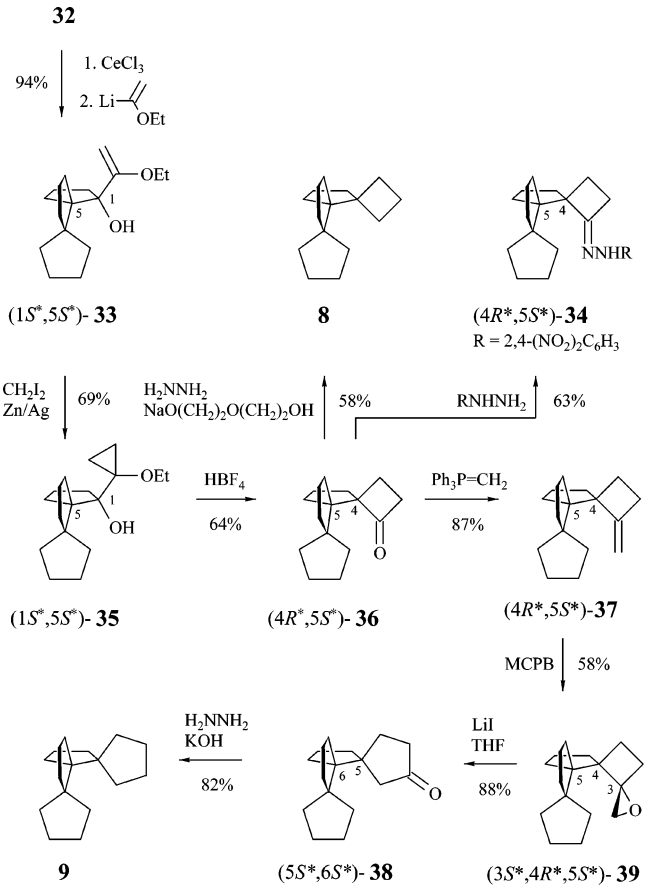
SCHEME 5



promising.[17] In contrast to the only existing synthesis,[18] this compound was prepared as follows: 4-nitrobenzenesulfonic acid azide[19] reacted with cyclobutylidene-cyclopentane (**22**) to yield the sulfonimide **29**,[20,21] which was hydrolyzed to spiroketone **30**,[20] then spiroalkylated to dispiroketone **31**,[22] and finally rearranged to dispiroketone **32**[23] by treatment with acid. Albeit extensive polymerization during the last step occurred, multigram quantities of **32** could be prepared. A cyclobutylidenation of ketone **23** as requisite for an alternative synthesis via an epoxidation and oxaspirohexane to cyclopentanone rearrangement[9] failed (Scheme 5).

It soon turned out that enolization and/or steric hindrance were the main problems in reactions with **32**. Thus, cyclopropylidenetriphenylphosphorane,[24] diphenylsulfoniumcyclopropylide,[25] and 1-lithio-cyclopropylphenylsulfide,[26] which may act as nucleophile and base, did not react at all. Therefore, we were pleased to learn that, catalyzed by anhydrous cerium trichloride,[27] 1-ethoxyvinyllithium[28] added to **32** yields a single allylic alcohol **33** as the first intermediate of an annelation sequence first described by Baldwin et al.[29] The next two steps proceeded

SCHEME 6



smoothly: cyclopropanation using a modified Simmons−Smith procedure[30] yielded the ethoxycyclopropane **35**,[31] and acid catalyzed rearrangement of **35** delivered a single cyclobutanone, recognized as **36** by an X-ray structure analysis of its 2,4-dinitrophenylhydrazone **34** (Scheme 6). Interestingly, the formation of **34** was extremely slow and took 7 days at room temperature to go to completeness. This indicated that other carbonyl reactions of **36** could also be difficult to achieve. Indeed, the Wolff−Kishner reduction using a variant of Barton et al.[32] for sterically hindered ketones required 66 h at 180 °C for the formation of the hydrazone and 72 h at 205 °C for the liberation of trispirane **8**.

Disappointingly, all attempts of a direct ring enlargement of **36** with diazomethane failed. Therefore, a sequential ring enlargement via a high-temperature methylenation,[33] an epoxidation, and a lithium iodide-induced rearrangement[9] proved necessary. This sequence led to a single cyclopentanone **38** (**36**−**37**−**39**−**38**), and a subsequent Wolff−Kishner reduction then yielded the desired trispirane **9** (symmetry C_2), easily recognized by the appearance of only nine resonance lines in the ^{13}C NMR spectrum [δ = 19.6 (t), 23.4 (t), 24.3 (t), 32.5 (t), 35.2 (t), 35.8 (t), 40.9 (t), 55.9 (s), 56.7 (s)]. However, in view

(17) For a compilation of methods, see: (a) Krapcho, A. P. *Synthesis* **1974**, 383−419. (b) Krapcho, A. *Synthesis* **1976**, 425−444. (c) Krapcho, A. *Synthesis* **1978**, 77−126.

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(21) For other ring enlargements via Δ^2-triazolines, see: (a) Wohl, R. A. *J. Org. Chem*. **1973**, *38*, 3862−3864. (b) McManus, S. P.; Ortiz, M.; Abramovitch, R. A. *J. Org. Chem*. **1981**, *46*, 336−342. (c) Fitjer, L. *Chem. Ber*. **1982**, *115*, 1047−1060.

(22) For spiroalkylations of cycloalkanones, see: (a) Mousseron, M.; Jacquier, R.; Christol, H. *Bull. Soc. Chim. Fr*. **1957**, 346−356. (b) Brugidou, J.; Christol, H. *Bull. Soc. Chim. Fr*. **1968**, 1141−1144.

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(24) Utimoto, K.; Tamura, M.; Sisido, K. *Tetrahedron* **1973**, *29*, 1169−1171.

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(30) Denis, J. M.; Girard, C.; Conia, J. M. *Synthesis* **1972**, 549−551.

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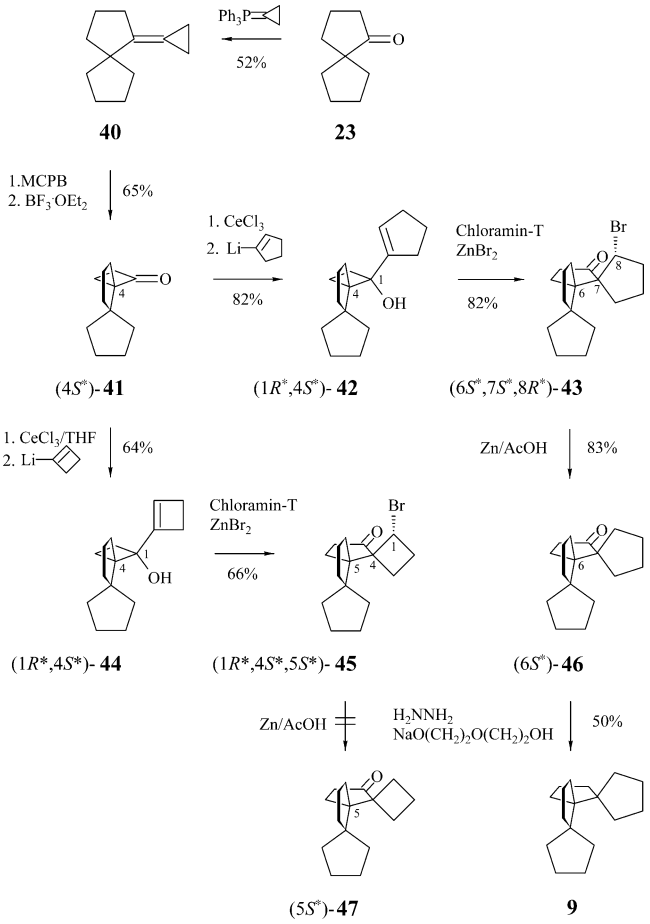
(32) Barton, D. H. R.; Ives, D. A. J.; Thomas, B. R. *J. Chem. Soc. (London)* **1955**, 2056.

(33) Fitjer, L.; Quabeck, U. *Synth. Commun*. **1985**, *15*, 855−864.

SCHEME 7

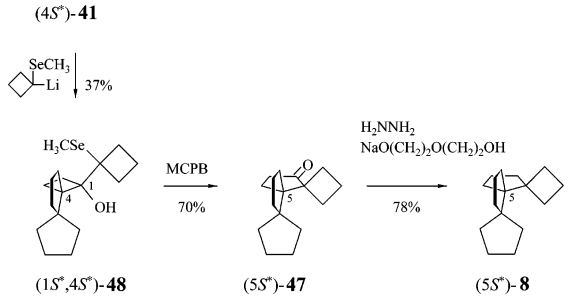


of an enantioselective synthesis, the need to combine a sequential annelation with a sequential ring enlargement seemed inconvenient. Therefore, a more direct approach to **8** and **9** was searched for.

At this stage, we became aware of a study of a halogen cation-induced rearrangement of allylic alcohols to β-haloketones,[34] indicating that an addition of 1-lithiocyclobutene[35] and 1-lithiocyclopentene,[36] respectively, to the hitherto unknown dispiroketone **41** could lead to the allylic alcohols **42** and **44**, and hence to two further potential precursors of **8** and **9** (Scheme 7). For the experimental realization, we reacted spiroketone **23** with cyclopropylidene-triphenylphosphorane,[24] subjected the resulting olefin **40** to an epoxidation and oxaspiropentane to cyclobutanone rearrangement,[9] and added the vinyllithium reagents, catalyzed by anhydrous cerium trichloride,[27] to the dispiroketone **41** formed. A single allylic alcohol resulted in both cases, and a regio- and stereoselective rearrangement then yielded the bromoketones **43** (**42**−**43**) and **45** (**44**−**45**), respectively. Of these, the structure and relative configuration of **43** was secured by an X-ray structure analysis.

Nothing was known about the reductive debromination of α-tertiary β-bromoketones. With **43**, lithium aluminum hydride led to ring opening, tri-*n*-butyltin hydride led to ring enlargement, and only zinc in acetic acid provided the desired ketone **46**. The subsequent Wolff−Kishner reduction in the variant of Barton et al.[32] proved even more difficult than that of **36**. It required 2 days at 180 °C for the formation of the hydrazone and 10 days at 205 °C for the liberation of trispirane **9**.

SCHEME 8



In contrast to that of **43**, a reductive debromination of **45** with zinc in acetic acid failed. Therefore, an alternative approach to **47** via a β-hydroxyselenide[37] was envisaged. Accordingly, we treated **41** with 1-lithio-1-methylselenocyclobutane,[38] rearranged the β-hydroxyselenide **48** obtained with a large excess of 3-chloroperbenzoic acid, and deoxygenated the resulting ketone **47** to trispirane **8** (Scheme 8).

Clearly, the syntheses of **8** and **9** from **21** via **41** were much more effective than those from **21** via **32**. Therefore, the necessary resolution was performed with **41**. Two methods were employed: (a) an addition of (+)-(*S*)-*N*,*S*-dimethyl-*S*-phenylsulfoximine with subsequent fragmentation,[39] and (b) a reduction with (−)-diisopinocampheyl chloroborane [(−)-DIP-Cl][40] with subsequent oxidation (Scheme 9).

In the first case, two diastereoisomeric β-hydroxy-sulfoximines were formed. Their separation was achieved by column chromatography and their identity disclosed as (*SS*,1*R*,4*R*)-**50** (mp 61−63 °C; >99% ee, $[\alpha]_D^{20} = +61.3$, *c* 1.07, $CHCl_3$) and (*SS*,1*S*,4*S*)-**52** (mp 70 °C; >99% ee, $[\alpha]_D^{20} = +42.0$, *c* 1.06, $CHCl_3$) by X-ray analyses. Subsequent thermal fragmentations delivered the enantiopure ketones (4*R*)-**41** (>99% ee, $[\alpha]_D^{20} = +145$, *c* 1.21, acetone) and (4*S*)-**41** (>99% ee, $[\alpha]_D^{20} = -145$, *c* 1.14, acetone), respectively. As could have been expected,[41] (4*R*)-**41** showed a strong positive Cotton effect ($\theta_{307} = +6328$, CH_3OH), and (4*S*)-**41** showed a strong negative Cotton effect ($\theta_{307} = -6538$, CH_3OH).

In the second case, two diastereoisomeric alcohols resulted. Upon oxidation with pyridinium chlorochromate,[42] the major alcohol ($[\alpha]_D^{20} = +1.2$, *c* 1.24, acetone) yielded (4*S*)-**41** ($[\alpha]_D^{20} = -84.4$, *c* 1.24, acetone) with diminished optical purity (69% ee), but the minor alcohol ($[\alpha]_D^{20} = +22.1$, *c* 1.20,

(34) Wang, B. M.; Song, Z. L.; Fan, C. A.; Tu, Y. Q.; Chen, W. M. *Synlett* **2003**, 1497−1499.

(35) Synthesis of 1-bromo-cyclobutene: (a) Willstätter, R.; von Schmädel, W. *Ber. Dtsch. Chem. Ges.* **1905**, *38*, 1992−1999. The reductive lithiation was performed as described or 1-bromo-cyclopentene.[36b]

(36) Synthesis of 1-bromo-cyclopentene: (a) Abell, P. I.; Chiao, C. *J. Am. Chem. Soc*. **1960**, *82*, 3610−3613. Reductive lithiation: (b) Neumann, H.; Seebach, D. *Chem. Ber*. **1978**, *111*, 2785−2812.

(37) For ring enlargements of β-hydroxyselenides with insertion of a cyclobutane ring, see: Fitjer, L.; Steeneck, C.; Gaini-Rahimi, S.; Schroeder, U.; Justus, K.; Puder, P.; Dittmer, M.; Hassler, C.; Weiser, J.; Noltemeyer, M.; Teichert, M. *J. Am. Chem. Soc*. **1998**, *120*, 317−328.

(38) Synthesis of selenoketals: (a) Krief, A.; Clarembeau, M.; Cravador, A.; Dumont, W.; Hevesi, L.; Luchetti, J.; van Ende, D. *Tetrahedron* **1985**, *41*, 4793−4812. Reductive lithiations: (b) Krief, A. *Tetrahedron* **1980**, *36*, 2531−2540.

(39) (a) Johnson, C. R.; Zeller, J. R. *J. Am. Chem. Soc*. **1982**, *104*, 4021−4023. (b) Johnson, C. R.; Zeller, J. R. *Tetrahedron* **1984**, *40*, 1225−1233.

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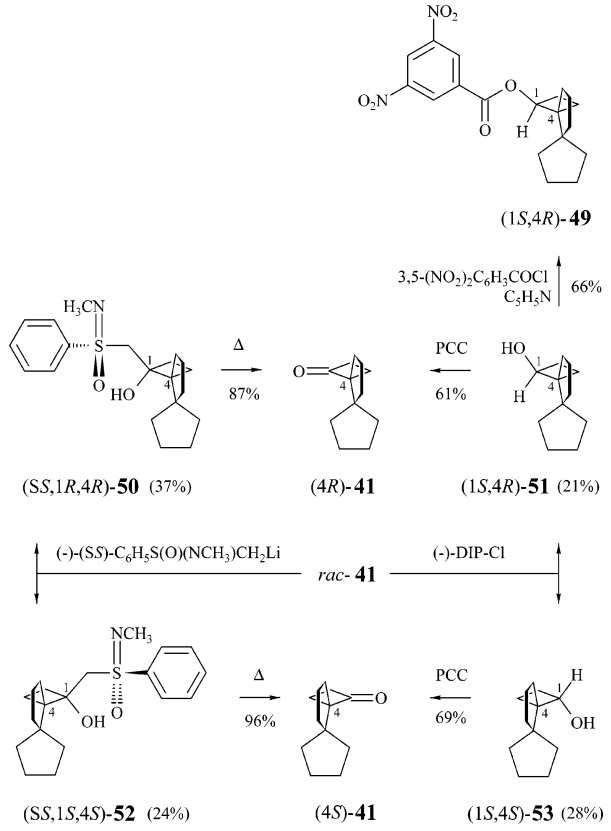
SCHEME 9

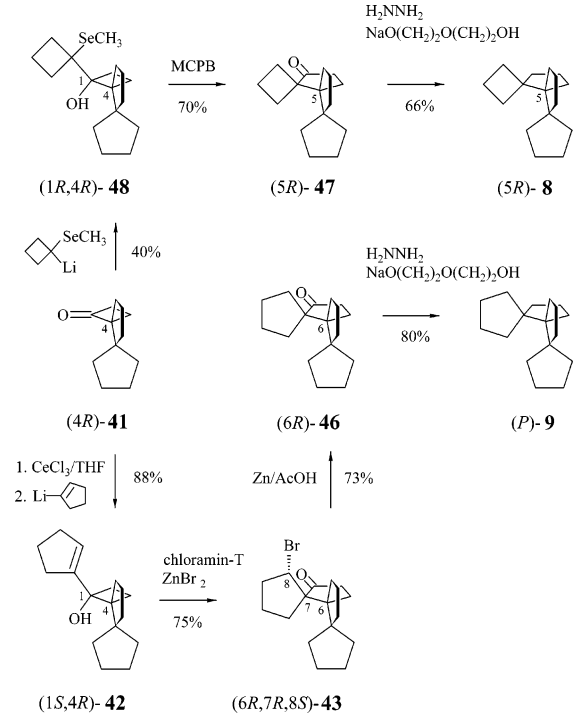


acetone) yielded (4*R*)-**41** ($[\alpha]_D^{20} = +145$, *c* 1.21, acetone) optically pure (>99% ee). The minor alcohol was recognized as (1*S*,4*R*)-**51** by an X-ray analysis of its 3,5-dinitrobenzoate (1*S*,4*R*)-**49**, and accordingly, the major alcohol was (1*S*,4*S*)-**53**. For the syntheses of optically pure samples of **8** and **9**, (4*R*)-**41** was used throughout.

For the syntheses of (5*R*)-**8** and (*P*)-**9**, we applied the same reactions as for the synthesis of the racemic specimen (Scheme 10). For the synthesis of (5*R*)-**8**, we reacted (4*R*)-**41** with 1-lithio-1-methylselenocyclobutane, rearranged the β-hydroxyselenide (1*R*,4*R*)-**48** obtained with 3-chloroperbenzoic acid, and deoxygenated the resulting dispiroketone (5*R*)-**47** (>99% ee, $[\alpha]_D^{20} = -12.7$, *c* 1.23, acetone) to trispirane (5*R*)-**8** (>99% ee, $[\alpha]_D^{20} = -30.7$, *c* 1.15, $CHCl_3$). For the synthesis of (*P*)-**9**, we reacted (4*R*)-**41** with 1-lithio-cyclopentene, rearranged the resulting allyl alcohol (1*S*,4*R*)-**42** (>99% ee, $[\alpha]_D^{20} = -46.1$, *c* 1.30, acetone) to the β-bromoketone (6*R*,7*R*,8*S*)-**43** (>99% ee, $[\alpha]_D^{20} = -46.3$, *c* 1.24, acetone), debrominated this compound to (6*R*)-**46** (>99% ee, $[\alpha]_D^{20} = -127$, *c* 1.21, acetone), and deoxygenated the latter to trispirane (*P*)-**9** (>99% ee, $[\alpha]_D^{20} = -62.6$, *c* 1.10, $CHCl_3$). This completed the series of optically pure nonregular [(*R*)-**6**, (*S*)-**7**, (*R*)-**8**)] and regular helices [(*P*)-**9**] of spiroannelated four- and five-membered rings.

Chiroptical Properties. As may be seen from the specific rotations of (*P*)-**1**, (*P*)-**4**, (*P*)-**5**, (*R*)-**6**, (*S*)-**7**, (*R*)-**8**, and (*P*)-**9**, interesting regularities exist (Table 1). On going from (*P*)-**1** to (*P*)-**4**, a distinct decrease of the specific rotation is observed, which continues with (*P*)-**5**, (*R*)-**6**, and (*S*)-**7**, until with (*R*)-**8** and (*P*)-**9** the sign of rotation changes and the amount increases again. Of the extremes, (*P*)-**1** represents the usual case of a right-handed, dextrorotatory helix, while (*P*)-**9** represents the unusual

SCHEME 10



case of a right-handed, levorotatory helix. With respect to their rotatory powers, all other cases fall in between.

As already pointed out, it is only with (*P*)-**1** that a single geometry determines the observed optical rotation. In all other cases, the observed optical rotations should be interpreted as Boltzmann averages over different conformations. Therefore, the unusual but systematic changes in the specific rotations on going from (*P*)-**1** via (*P*)-**4**, (*P*)-**5**, (*R*)-**6**, (*S*)-**7**, and (*R*)-**8** to (*P*)-**9** could only be explored computationally by a quantum chemical study of all energetically low-lying conformers. Given the fact that a preliminary conformational search using our search routine HUNTER[43] in connection with MM3[44] produced by far more low-lying minima for the nonregular helices (*R*)-**6**, (*S*)-**7**, and (*R*)-**8** than for the regular helices (*P*)-**4**, (*P*)-**5**, and (*P*)-**9**, we restricted our study to the latter but included (*P*)-**1**, (*P*)-**2**, and (*P*)-**3** as rigid helices and the as yet unknown (*P*)-**10** as a higher analogue of (*P*)-**9**.

Calculations. All quantum chemical calculations were carried out with the TURBOMOLE[45] program package. The geometries were optimized at the B97-D DFT level of theory[45] using triple-ζ valence basis sets on all atoms [TZV(d,p)].[46] This approach includes intramolecular dispersion effects that are important in larger, sterically overcrowded organic molecules. The optical rotations were obtained from time-dependent density functional theory (TDDFT[47]) calculations using the BH-LYP functional[48] and a split valence basis set [SV(d,p)][49] augmented by a set of

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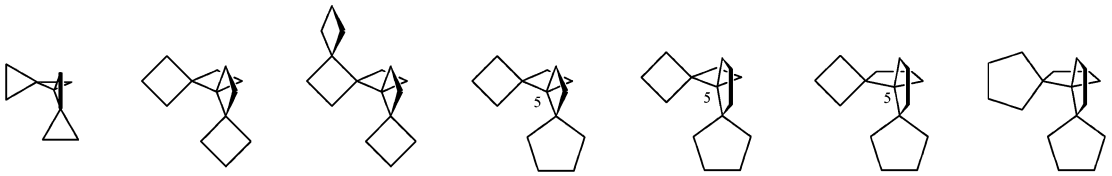
TABLE 1. Experimental Optical Rotations (in $CHCl_3$) of Pseudohelical and Helical Hydrocarbons of Three-, Four-, and Five-Membered Rings



(*P*)-**1**[a] (*P*)-**4**[b] (*P*)-**5**[c] (5*R*)-**6**[d] (*pseudo-P*) (5*S*)-**7**[d] (*pseudo-P*) (5*R*)-**8**[d] (*pseudo-P*) (*P*)-**9**[d]

λ [nm]	c 1.20 $[\alpha]_{nm}^{20}$	c 1.09 $[\alpha]_{nm}^{20}$	c 1.18 $[\alpha]_{nm}^{20}$	c 1.19 $[\alpha]_{nm}^{20}$	c 1.22 $[\alpha]_{nm}^{20}$	c 1.15 $[\alpha]_{nm}^{20}$	1.10 $[\alpha]_{nm}^{20}$
589	+192.7	+63.3	+26.0	–4.1	–0.9	–30.7	–62.6
578	–	+65.9	+27.5	–4.5	–0.9	–31.9	–65.2
546	+229.7	+74.9	+31.3	–4.7	–1.1	–36.1	–74.0
436	+400.2	+126.9	+55.1	–6.2	–1.2	–60.0	–124.3
365	+648.2	+199.1	+89.1	–6.3	–0.7	–92.8	–192.6

[a]Derived from *(M)*-**1**, see ref 4. [b]Derived from (*M*)-**4**, see ref 7. [c]From ref 1. [d]This work.

diffuse functions (s,p,d) taken from the Dunning's aug-cc-pVDZ basis set[50] (hereafter called aug-SVP). For a general overview about chiroptical calculations, see ref 51; for the particular application of TDDFT methods for computations of optical rotations, see ref 52; and for examples that include several conformers, see ref 53. For **1** the basis set effect on the optical rotation has been studied by comparing the aug-SVP derived value with one obtained by an accordingly composed aug-TZV-(p,d) basis set. The difference of about 8° (4%) is very small compared to other sources of error inherent to the TDDFT method. Similar differences were obtained in test calculations employing optimized geometries from other sources (e. g. DFT-B3LYP).[54] Due to technical reasons, the TDDFT/BHLYP calculations of the optical rotations could be performed only in the coordinate origin-dependent dipole-length representation for the rotatory strengths. Test calculations employing nonhybrid density functionals and the origin-independent velocity gauge representation show, however, that the differences between the two forms with the aug-SVP basis set are only about 1%. Note that our TDDFT/BHLYP results for **1** agree better with the experiment than those reported recently using the B3LYP functional[55] (see below).

Except for **1**, **2**, and **3**, the correct determination of the optical rotation of the investigated compounds required a careful analysis of their respective conformational flexibility. With **4** and **5**, this analysis was done by systematically generating all different combinations arising by ring flippings, and with **9** and **10** the analysis was done by using the GMMX routine as implemented in PC-Model 7.0.[56] Subsequent optimization at the DFT-B-97-D/TZVP level yielded six relevant conformers each for **4** and **5**, four conformers for **9**, and two conformers for **10**. For all compounds, the Boltzmann weighting for the calculation of the total optical rotations was done on the basis of SCS-MP2/TZVPP[58] and, for the sake of comparison, also with DFT-B-97-D/TZVPP relative energies. All conformers with populations above 3% at room temperature were taken into account.

Results and Discussion. A comparison of the computed and experimental optical rotations for the (*P*)-helices of **1**−**5**, **9**, and **10** is given in Table 2, and a list of contributions of the individual conformers of **4**, **5**, **9**, and **10** together with views along and perpendicular to their helical axis is given in Tables 3−5. Perusing Table 2, one finds in general a good agreement between theory and experiment for the optical rotations, i.e., a correct sign, and always the right order of magnitude. In particular, the agreement for the rigid systems **1**−**3** is excellent.

For the flexible systems **4**, **5**, **9**, and **10**, the specific rotations refer to Boltzmann-averaged values of different conformations.

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(54) (a) Grimme, S.; Bahlmann, A.; Haufe, G. *Chirality* **2002**, *14*, 793−797. (b) Pecul, M.; Ruud, K.; Rizzo, A.; Helgaker, T. *J. Phys. Chem. A* **2004**, *108*, 4269−4276. (c) Lattanzi, A.; Viglione, R. G.; Scettri, A.; Zanasi, R. *J. Phys. Chem. A* **2004**, *108*, 10749−10753. (d) Marchesan, D.; Coriani, S.; Forzato, C.; Nitti, P.; Pitacco, G.; Ruud, K. *J. Phys. Chem. A* **2005**, *109*, 1449−1453. (e) Wiberg, K. B.; Wang, Y. G.; Vaccaro, P. H.; Cheeseman, J. R.; Luderer, M. R. *J. Phys. Chem. A* **2005**, *109*, 3405−3410. (f) Giorgio, E.; Roje, M.; Tanaka, K.; Hamersak, Z.; Sunjic, V.; Nakanishi, K.; Rosini, C.; Berova, N. *J. Org. Chem.* **2005**, *70*, 6557−6563.
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TABLE 2. Experimental and Computed Specific Rotations for (*P*)-Helices of Three-, Four-, and Five-Membered Rings

molecule	calc.[a]	exp.[b]
(*P*)-**1**	+184.1	+192.7[c]
(*P*)-**2**	+388.3	+373.0[d]
(*P*)-**3**	+827.8	+909.9[e]
(*P*)-**4**[f]	+82.7 (+79.5)	+63.3[g]
(*P*)-**5**[f]	+61.7 (+83.8)	+26.0[h]
(*P*)-**9**[f]	−50.9 (−54.1)	−62.6
(*P*)-**10**[f]	−36.2 (−35.4)	

[a] TDDFT/aug-SVP//B-97-D/TZVP level. [b] In $CHCl_3$, $c = 0.96-1.20$. [c] Derived from (*M*)-**1**; see ref 4. [d] From ref 4. [e] From ref 6. [f] Boltzmann weighted average of two (**10**), four (**9**), and six conformations (**4**, **5**), respectively, at 298 K based on SCS-MP2/TZVPP//B-97-D/TZVP relative energies. Specific rotations based on B-97-D/TZVPP//B-97-D/TZVP relative energies are given in parentheses. [g] Derived from (*M*)-**4**; see ref 7. [h] From ref 1.

TABLE 3. Conformers of (*P*)-4: Views along and Perpendicular to the Helical Axis, Dihedral Angles of the Bonds Forming the Inner Helix, Relative Energies (in kcal/mol), Populations (at 298 K), and Specific Rotations

conformer	type	dihedral angles $\Theta_{1456}\Theta_{4567}$	ΔE	population	$[\alpha]_D$
4-1	**A**	+138 +138	0.000	0.369	+117.0
4-2	**C**	+85 +146	0.417	0.183	+79.0
4-3	**B**	+80 +80	0.475	0.165	−8.5
4-4	**A**	+139 +139	0.624	0.129	+118.9
4-5	**A**	+139 +139	0.748	0.104	+116.4
4-6	**B**	+82 +83	1.185	0.050	−6.4

Therefore, in these cases each conformer had to be analyzed separately. In a search for a simple but reliable relation between the geometry of a conformer and its specific rotation we found that the dihedral angles of the bonds of the inner spheres and the specific rotations correlated best.

In (*P*)-**4** (Table 3) and (*P*)-**5** (Table 4), three types of conformers may be distinguished: in conformers of type **A** (**4**−**1**, **4**−**4**, **4**−**5**, **5**−**2**, **5**−**4**, **5**−**6**), a set of large dihedral angles generates inner helices of five bonds within two helical turns; in conformers of type **B** (**4**−**3**, **4**−**6**, **5**−**1**, **5**−**3**), a set of small dihedral angles generates inner helices of four bonds within one helical turn; and in conformers of type **C** (**4**−**2**, **5**−**5**), a combination of large and small dihedral angles leads to cases which fall in between. Within a given type, the calculated specific rotations vary only slightly. They are consistently high for conformers of type **A**, consistently low for conformers of type **B**, and lie in between for conformers of type **C**. Especially the large differences between the calculated specific rotations

TABLE 4. Conformers of (*P*)-5: Views along and Perpendicular to the Helical Axis, Dihedral Angles of the Bonds Forming the Inner Helix, Relative Energies (in kcal/mol), Populations (at 298 K), and Specific Rotations

conformer	type	dihedral angles $\Theta_{1456}\Theta_{4567}\Theta_{5678}$	ΔE	population	$[\alpha]_D$
5-1	**B**	+80 +83 +80	0.000	0.563	+30.5
5-2	**A**	+139 +140 +139	0.886	0.126	+133.7
5-3	**B**	+81 +85 +80	1.059	0.094	+14.3
5-4	**A**	+139 +140 +139	1.102	0.088	+134.6
5-5	**C**	+138 +88 +79	1.244	0.069	+94.9
5-6	**A**	+139 +140 +139	1.327	0.060	+135.8

of conformers of type **A** and **B** (>100) render the averaged values extremely sensitive toward any change in the population of individual conformers. This means that even small errors for ΔE in the order of 0.1 kcal/mol can lead to large errors in the averaged specific rotations. It is therefore no surprise that both the SCS-MP2 and DFT energy based Boltzmann-weighted values for the specific rotation of (*P*)-**4** and (*P*)-**5** do not exactly match the experimental values (Table 2). Especially for (*P*)-**5**, the theoretical values are distinctly too high. This indicates that at least in this case the contribution of conformers of type **A** (**5**−**2** and/or **5**−**4** and/or **5**−**6**) is overestimated. Note, however, that the theoretical data derived from the more sophisticated quantum chemical model (i.e., SCS-MP2) agree in this critical case better with experiment.

In (*P*)-**9** and (*P*)-**10**, the number of relevant conformers is reduced to four and two, respectively, and all conformers belong to type **B** (Table 5). Consequently, only small, but, surprisingly, positive rotations result. These vary to a considerably larger extent than those of type **B** in (*P*)-**4** and (*P*)-**5**. Tentatively, this may be attributed to a greater conformational mobility of five- as compared to four-membered rings, but no simple explanation can be given for the sign change of the optical rotation in going from (*P*)-**4** to (*P*)-**9** and from (*P*)-**5** to (*P*)-**10**. In any case, the calculated Boltzmann-averaged values for the specific rotation of (*P*)-**9** match the experimental value closely, while for the still unknown (*P*)-**10** these values remain to be verified.

An interesting quest concerns the relation between the specific rotation and the length of a helix. In helices of three-membered rings, the specific rotation increases as the length of the helix increases. It is already high in (*P*)-**1**, and doubles in (*P*)-**2**, and again in (*P*)-**3**. Obviously, the electronic structure of helices of three-membered rings allows some conjugation, and, due to their

TABLE 5. Conformers of (*P*)-9 and (*P*)-10: Views along and Perpendicular to the Helical Axis, Dihedral Angles of the Bonds Forming the Inner Helix, Relative Energies (in kcal/mol), Populations (at 298 K), and Specific Rotations

conformer	type	dihedral angles Θ_{1567} Θ_{5678}	ΔE	population	$[\alpha]_D$
9-1	**B**	+74 +74	0.000	0.444	−75.0
9-2	**B**	+71 +84	0.184	0.325	−30.9
9-3	**B**	+71 +81	0.716	0.132	−39.5
9-4	**B**	+76 +76	0.889	0.099	−23.9

conformer	type	dihedral angles Θ_{1567} Θ_{5678} Θ_{6789}	ΔE	population	$[\alpha]_D$
10-1	**B**	+69 +96 +69	0.000	0.848	−33.5
10-2	**B**	+69 +93 +68	1.020	0.152	−48.0

rigid structures, an increase of the spatial dimension of their chromophore with the length of the helix results.

In helices of four- and five-membered rings the situation is different. In these cases several conformers exist, but only the rotations of pairs with identical or closely related geometries are meaningful and may be compared. Within helices of four-membered rings, such pairs are **4**−**3** and **5**−**1**, and **4**−**5** and **5**−**6**, and in both cases the specific rotation increases as the length of the helix increases. This means that no principal differences between helices of three- and four-membered rings exist, albeit the rotatory power of the latter is strongly diminished.

Due to pronounced differences within the geometry of the outer spheres, no closely related pairs of conformers could be found for helices of five-membered rings. Therefore, in this case no conclusive answer concerning a possible relation between the specific rotation and the length of the helix can be given. All in all, with the exception of **4**−**5** and **5**−**6**, the conformers of the flexible systems (*P*)-**4**, (*P*)-**5**, (*P*)-**9**, and (*P*)-**10** seem to behave more like a collection of mutually independent and electronically isolated rings, which in the large system limit could well lead to cryptochirality. However, this hypothesis remains to be verified.

In summary, the optical rotations of the considered molecules are very well reproduced by TDDFT-BH-LYP/aug-SV(d,p) computations. Density functionals with a smaller fraction of Hartree−Fock exchange (like, e.g., B3-LYP) or nonhybrid functionals perform significantly worse. For example, a test calculation for (*P*)-**2** with TDDFT-B3-LYP/aug-SVP yielded $[\alpha]_D = 436.1$, corresponding to an error of ∼15%, which has to be compared to the almost perfect agreement with the experiment that is obtained at the TDDFT-BH-LYP/aug-SVP level. To this end this work impressively confirms the suitability of BH-LYP calculations to reproduce the optical rotations of saturated systems. We therefore strongly recommend the use of this functional for comparable applications in the future.

Conclusion

In conclusion, we developed syntheses for the pseudohelical hydrocarbons **6**−**8** and the helical hydrocarbon **9**, formally derived from the helical hydrocarbon **4** by stepwise replacement of each of the four-membered rings by a five-membered ring. Optically active specimens were obtained via enzymatic [(*R*)-**6**, (*S*)-**7**] or chemical resolution [(*R*)-**8**, (*P*)-**9**] of appropriate precursor ketones. In going from (*P*)-**1** via (*P*)-**4**, (*P*)-**5**, and (*R*)-**6** to (*S*)-**7**, a distinct decrease in the specific rotation is observed, until, with (*R*)-**8** and (*P*)-**9**, the sign of rotation changes and the amount increases again. To account for this finding, a quantum chemical study on the rotatory power of helical hydrocarbons of three- [(*P*)-**1**, (*P*)-**2**, (*P*)-**3**], four- [(*P*)-**4**, (*P*)-**5**], and five-membered rings [(*P*)-**9**, (*P*)-**10**] has been performed. We have shown that for the rigid helices of three-membered rings the agreement between theory and experiment is excellent, while for the flexible helices of four- and five-membered rings the results strongly depend on the geometry and weight of the conformers involved. However, even in these cases, the sign and the order of magnitude of the specific rotation were reproduced correctly. With regard to the fact that up to six conformers with very different specific rotations had to be analyzed and weighted, this result is remarkable.

Experimental Section

(5*R)-Trispiro[3.0.0.4.2.2]tetradecan-11-one (15).** To a solution of **20** (15.1 g, 83.5 mmol) in dichloromethane (80 mL) was added at −15 °C under argon with stirring trifluoromethanesulfonic acid anhydride (28.3 g, 100 mmol). Then, within 15 min, a solution of 2,4,6-collidine (13.1 g, 108 mmol) in 1-methylenespiro[3.3]heptane (**12**) was also added.[1] The mixture was heated for 20 h to reflux and then concentrated on a rotary evaporator (bath temperature 40 °C/20 Torr). The residue was extracted with anhydrous ether (6 × 40 mL), and the remaining brown oil was hydrolyzed in a two-phase system of dichloromethane (170 mL) and water (170 mL). After 2 h of reflux the phases were separated, the aqueous phase was extracted with dichloromethane (6 × 60 mL), and the combined organic phases were washed with saturated ammonium chloride (60 mL) and dried (K_2CO_3/$MgSO_4$). The solvent was distilled off (bath temperature 40 °C/20 Torr), the residue (26.1 g) was extracted with pentane/ether (1:1, 3 × 50 mL), and the combined extracts were washed with 2 N HCl (30 mL) and dried ($MgSO_4$). The solvent was evaporated (bath temperature 40 °C/20 Torr) and the remaining material (9.4 g) chromatographed on silica gel (0.05−0.20 mm) in pentane/ether [9:1, column 75 × 5 cm, $R_f = 0.45$ (**15**)] to yield 3.63 g (21%) of **15** as a colorless liquid [purity 83% GC, column A, 230 °C, retention time (min): 5.11 (**15**)]. For the reduction with bakers' yeast, the material was used as such. For other preparations, the material was chromatographed twice (purity 95%). An analytically pure sample was obtained by preparative GC. IR (neat): 1770 cm^{-1} (C═O). ^1H NMR (600 MHz, $CDCl_3$, $CHCl_3$ int): $\delta = 1.54-1.78$ (m, 9H), 1.78−1.93 (m, 5H), 1.97−2.04 (m, 2H), 2.10 (m_c, 1H), 2.28 (m_c, 1H), 2.62 (d, $J = 16.5$ Hz, 1H), 3.12 (d, $J = 16.5$ Hz, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$,

$CDCl_3$ int): δ = 15.4 (t), 25.2 (t), 26.0 (t), 26.3 (t), 30.0 (t), 31.0 (t), 31.3 (t), 32.5 (t), 44.6 (s), 48.7 (s), 51.7 (t), 71.8 (s), 214.1 (s). MS (EI): *m*/*e* = 204 (<1, M^+), 134 (100). $C_{14}H_{22}O$ requires C, 82.30; H, 9.87. Found: C, 81.99, H, 9.72.

(5*R)-Trispiro[3.0.0.4.2.2]tetradecane (6).** To a solution of hydrazine hydrate (150 mg, 3.0 mmol) and powdered potassium hydroxide (225 mg, 4.0 mmol) in diethylene glycol (2.0 mL) was added under argon with stirring **15** (102 mg, 0.50 mmol). The mixture was heated for 1.5 h to 160 °C, until it was diluted with water (20 mL) and extracted with pentane (3 × 15 mL). The combined extracts were washed with water (15 mL), dried ($MgSO_4$), and concentrated using a 20 cm vigreux column. The last traces of solvent were evaporized under reduced pressure yielding 88 mg (82%) of **6** as a colorless oil [purity 99% GC, column A, 180 °C, retention time (min): 3.69]. The enantiomers could be resolved by capillary gas chromatography on a chiral phase [column D, 90 °C, retention times (min): 32.85/33.42]. An analytically pure sample was obtained by preparative GC. ^{1}H NMR (600 MHz, $CDCl_3$, $CHCl_3$ int): δ = 1.35−1.40 (m, 1H), 1.40−1.65 (m, 11H), 1.68−1.87 (m, 6H), 1.93 (m_c, 1H), 1.99 (m_c, 1H), 2.09 (m_c, 1H), 2.23−2.30 (m, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$, $CDCl_3$ int): δ = 15.8 (t), 23.1 (t), 24.3 (t), 26.6 (t), 27.1 (t), 30.4 (t), 31.1 (t), 32.1 (t), 32.2 (t), 33.4 (t), 36.1 (t), 49.0 (s), 51.9 (s), 52.1 (s). MS (EI): *m*/*e* = 190 (<1, M^+), 162 (38, $M^+ - C_2H_4$), 79 (100). $C_{14}H_{22}$ requires C, 88.35; H, 11.65. Found: C, 88.01; H, 11.45.

(5*R)-Trispiro[3.0.0.4.3.2]pentadecan-12-one (24) and (5*R**)-Trispiro[3.0.0.4.3.2]pentadecan-11-one (25).** To a stirred solution of powdered potassium hydroxide (1.94 g, 34.7 mmol) in methanol (4.4 mL) and water (0.7 mL) containing **15** (592 mg, 2.90 mmol) was added within 25 min *N*-methyl-*N*-nitroso-4-toluenesulfonic acid amide (Diazald) (806 mg, 3.76 mmol) in small portions. Afterward, the mixture was diluted with methanol (3.0 mL), and, after 45 min, more Diazald (820 mg, 3.83 mmol) followed by more methanol (3.0 mL) was added. After additional 1 h, GC analysis [column A, 230 °C, retention times (min): 4.88 (**15**), 7.86 (**25**), 10.13 (**24**)] indicated the presence of a 55:45 mixture of **24** and **25**. The heterogeneous reaction mixture was diluted with water (8 mL) and the resulting clear solution extracted with pentane (7 × 10 mL). The extracts were washed with saturated ammonium chloride (15 mL) and water (15 mL) and were dried ($MgSO_4$) until the solvent was distilled off on a rotary evaporator (bath temperature 40 °C/15 Torr) yielding 449 mg (71%) of a 55:45 mixture of **24** and **25** as a colorless liquid (purity 93% GC). This mixture was used for the preparation of **7**. Analytically pure samples of **24** and **25** were obtained by preparative GC as colorless liquids. **24**: IR (neat): 1750 cm^{-1} (C═O). ^{1}H NMR (600 MHz, $CDCl_3$, $CHCl_3$ int): δ = 1.35−1.40 (m, 1H), 1.41−1.46 (m, 1H), 1.50−1.89 (m, 12H), 1.92−2.08 (m, 3H), 1.95 (d, *J* = 18 Hz, 1H), 2.16 (d, *J* = 18 Hz, 1H), 2.18 (d, *J* = 18 Hz, 1H), 2.31−2.38 (m, 1H), 2.37 (d, *J* = 18 Hz, 1H). ^{13}C NMR (150.8 MHz, $CDCl_3$, $CDCl_3$ int): δ = 15.7 (t), 24.5 (t), 25.1 (t), 25.2 (t), 32.0 (t), 32.3 (t), 32.9 (t), 33.2 (t), 34.9 (t), 47.8 (t), 48.3 (s), 51.6 (s), 52.5 (t), 53.0 (s), 218.9 (s). MS (EI): *m*/*e* = 218 (29, M^+), 122 (100). HRMS: *m*/*e* (M^+) calcd 218.1671, obsd 218.1671. **25**: IR (neat): 1740 cm^{-1} (C═O). ^{1}H NMR (600 MHz, $CDCl_3$, $CHCl_3$ int): δ = 1.50−1.55 (m, 2H), 1.57−1.74 (m, 12H), 1.76−1.85 (m, 2H), 1.91−2.00 (m, 2H), 2.01−2.09 (m, 2H), 2.21 (pseudo t, *J* = 7.5 Hz, 2H). ^{13}C NMR (75.5 MHz, $CDCl_3$, $CDCl_3$ int): δ = 15.8 (t), 24.2 (t), 25.8 (t), 26.5 (t), 28.5 (t), 29.5 (t), 31.5 (t), 32.2 (t), 32.8 (t), 33.1 (t), 33.9 (t), 48.1 (s), 52.4 (s), 62.3 (s), 221.4 (s). MS (EI): *m*/*e* = 218 (6, M^+), 41 (100). $C_{15}H_{22}O$ requires C, 82.52; H, 10.16. Found: C, 82.42; H, 9.82.

(5*R)-Trispiro[3.0.0.4.3.2]pentadecane (7).** To a solution of hydrazine hydrate (446 mg, 8.9 mmol) and powdered potassium hydroxide (670 mg, 11.9 mmol) in diethylene glycol (7.0 mL) was added under argon with stirring a 55:45 mixture of **24** and **25** (325 mg, 1.49 mmol). The mixture was heated for 2 h to 120° and 5 h to 195 °C, until it was diluted with water (10 mL) and extracted with pentane (6 × 10 mL). The combined extracts were washed with saturated ammonium chloride (15 mL) and water (15 mL) and dried ($MgSO_4$). The solvent was distilled off over a 20 cm vigreux column and the remaining material chromatographed on silica gel (0.05−0.20 mm) in pentane [column 45 × 3 cm, R_f = 0.77 (**7**)] yielding 187 mg (66%) of **7** as a colorless liquid (purity 87% GC). An analytically pure sample was obtained by preparative GC [column A, 180 °C, retention time (min): 6.64 (**7**)]. The enantiomers of the racemic material could not be resolved [column E, 110 °C, retention time (min): 21.09 (5*R*)-**7**/(5*S*)-**7**]. ^{1}H NMR (600 MHz, $CDCl_3$, $CHCl_3$ int): δ = 1.19−1.26 (m, 1H), 1.28−1.37 (m, 2H), 1.39−1.64 (m, 13H), 1.67−1.81 (m, 4H), 1.88−1.96 (m, 2H), 1.99 (m_c, 1H), 2.28 (m_c, 1H). ^{13}C NMR (150.8 MHz, $CDCl_3$, $CDCl_3$ int): δ = 16.0 (t), 19.4 (t), 24.9 (t), 25.2 (t), 25.6 (t), 32.21 (t), 32.22 (t), 32.8 (t), 33.4 (t), 33.6 (t), 34.7 (t), 38.2 (t), 48.8 (s), 54.0 (s), 55.1 (s). MS (EI): *m*/*e* = 204 (5, M^+), 121 (100). $C_{15}H_{24}$ requires C, 88.16; H, 11.84. Found: C, 88.02; H, 11.79.

Reduction of 15 with Lithium Aluminum Hydride: (5*S,11*S**)-Trispiro[3.0.0.4.2.2]tetradecan-11-ol (27) and (5*R**,11*S**)-Trispiro[3.0.0.4.2.2]tetradecan-11-ol (28).** To a suspension of lithium aluminum hydride (114 mg, 3.0 mmol) in anhydrous ether (8.0 mL) was added at room temperature under argon with stirring a solution of **15** (204 mg, 1.0 mmol) in ether (1.5 mL). After 30 min the reduction was complete according to GC [column A, 230 °C, retention times (min): 5.11 (15), 7.22 (27), 7.62 (28)]. Water (114 μL), 15% aqueous potassium hydroxide (114 μL), and water (442 μL) were added, the liquid phase was decanted, and the residue was extracted with ether (3 × 10 mL). The combined organic phases were dried ($MgSO_4$) and concentrated on a rotary evaporator (bath temperature 45 °C/20 Torr) to yield 200 mg of a 65:35 mixture of **27** and **28**. Unfortunately, the two alcohols could not be separated by preparative GC, but the enantiomers of **27** could be resolved [column C, 130 °C, retention times (min): 27.02 (5*R*,-11*R*)-**27**, 27.45 (5*S*,11*S*)-**27**, 30.07 (5*R*,11*S*)- and (5*S*,11*R*)-**28**]. All assignments are based on the results of the reduction with bakers' yeast (see below). The ^{1}H and ^{13}C NMR spectra of the mixture were in accord with the spectra of the pure alcohols. The analysis counts for the mixture. $C_{14}H_{22}O$ requires C, 81.50; H, 10.75. Found: C, 81.38; H, 10.81.

Reduction of 15 with Bakers Yeast: (5*S*,11*S*)-(+)-Trispiro[3.0.0.4.2.2]tetradecan-11-ol [(5*S*,11*S*)-(+)-27], (5*R*,11*S*)-(+)-Trispiro[3.0.0.4.2.2]tetradecan-11-ol [(5*R*,11*S*)-(+)-28], and (5*R*)-(−)-Trispiro[3.0.0.4.2.2]tetradecan-11-one [(5*R*)-(−)-15]. To a stirred mixture of fresh bakers' yeast (40 g), sucrose (40 g), and water (400 mL), maintained at 37 °C, was added a solution of **15** (3.25 g, purity 83%, 13.3 mmol) in ethanol (13.5 mL). The reaction progress was monitored by GC [column A, 230 °C, retention times (min): 5.11 (15), 7.22 (27), 7.62 (28)], and, after 8 h, more yeast (40 g), sucrose (40 g), and water (200 mL) were added. After 22 h, the mixture was diluted with water (4.5 l) and continuously extracted with ether (1.0 L, 6 h, control by GC). The extract was concentrated to 150 mL, washed with saturated sodium bicarbonate (2 × 30 mL), dried ($MgSO_4$), and evaporated to dryness (bath temperature 50 °C/20 Torr). According to GC, the residual oil (3.46 g) contained **15**, (5*S*,11*S*)-**27**, and (5*R*,11*S*)-**28** in proportions of 58:40:2—hence **15** as 83:17 mixture of (5*R*)- and (5*S*)-**15**. This material was chromatographed on silica gel (0.05−0.20 mm) in pentane/ether [7:3, column 80 × 5 cm, R_f = 0.65 (15), 0.35 (27/28)] yielding 1.44 g (53%) of **15** as a colorless oil (purity 90%) and 919 mg (34%) of a 96:4 mixture of (5*S*,11*S*)-**27** and (5*R*,11*S*)-**28** as a colorless solid, mp 47−52 °C (purity 98%). $\alpha[\alpha]_D^{20}$ = +33.6, *c* = 1.13, acetone). According to GC on a chiral phase [column C, 130 °C, retention times (min): 27.45] (5*S*,11*S*)-**27** was enantiomerically pure (>99% ee). The reduction of the 83:17 mixture of (5*R*)- and (5S)-**15** (1.44 g, purity 90%, 6.35 mmol) in a mixture of yeast (19 g), sucrose (19 g), and water (190 mL) was performed analogously. After 7, 24, 31, 48, and 72 h more yeast (19 g), sucrose (19 g), and water (95 mL) were added, and after 96 h the extract (1.26 g) contained **15**, (5*S*,11*S*)-**27**, and (5*R*,11*S*)-**28** in proportions of 78:16:12—hence **15** as 99:1 mixture of (5*R*)- and (5*S*)-**15**. A total of 810 mg (62%) of **15** was isolated by chroma-

tography on silica gel. Of this, 786 mg (purity 92%, 3.54 mmol) was subjected to a third reduction with yeast (11 g), sucrose (11 g), and water (110 mL). After 6, 23, and 30 h, more yeast (11 g), sucrose (11 g), and water (55 mL) were added, and after 48 h the extract (811 mg) contained **15**, (5*S*,11*S*)-**27**, and (5*R*,11S)-**28** in proportions of 88:0.5:11.5—hence **15** as enantiomerically pure (5*R*)-**15**. Chromatography on silica gel yielded 564 mg (78%) of (5*R*)-**15** as a colorless liquid (purity 92%) and 73 mg (10%) of a 95:5 mixture of (5*R*,11*S*)-**28** and (5*S*,11*S*)-**27** as a colorless solid, mp 78−82 °C (purity 96%). Analytically pure samples of (5*R*)-**15** ($[\alpha]_D^{20} = -0.5$, $c = 1.13$, acetone) and the 95:5 mixture of (5*R*,-11*S*)-**28** and (5*S*,11*S*)-**27** ($[\alpha]_D^{20} = +62.5$, $c = 1.13$, acetone) were obtained by preparative GC. The ^{1}H and ^{13}C NMR data of (5*R*)-**15** were identical with those of racemic **15**. The spectral data for the alcohols was as follows. (5*S*,11*S*)-**27**: ^{1}H NMR (600 MHz, $CDCl_3$, $CHCl_3$ int): $\delta = 1.41-1.49$ (m, 3H), 1.49−1.68 (m, 6 H), 1.68−1,90 (m, 8H), 1.92−2.06 (m, 3H), 2.28 (m_c, 1H), 3.74 (dd, $J = 8$ Hz, 7 Hz, 1H). ^{13}C NMR (150.8 MHz, $CDCl_3$, $CDCl_3$ int): $\delta =$ 15.5 (t), 24.2 (t), 24.8 (t), 26.1 (t), 27.1 (t), 30.1 (t), 30.5 (t), 32.5 (t), 35.9 (t), 38.0 (t), 44.9 (s), 48.4 (s), 57.6 (s), 72.1 (d). (5*R*,-11*S*)-**28**: ^{1}H NMR (600 MHz, $CDCl_3$, $CHCl_3$ int): $\delta = 1.440-$ 1.46 (m, 2H), 1.47−1.59 (m, 6H), 1.59−1.65 (m, 1H), 1.59−1.65 (m, 2H), 1.65 − 1.72 (m., 1H), 1.74−1.88 (m, 6H), 2.07 (m_c, 1H), 2.18 (m_c, 1H), 2.34 (dd, $J = 9$ Hz, 7.5 Hz, 1H), 3.85 (dd, $J = 7.5$ Hz, 7.5 Hz, 1H). ^{13}C NMR (150.8 MHz, $CDCl_3$, $CDCl_3$ int): $\delta =$ 16.0 (t), 24.4 (t), 25.1 (t), 25.3 (t), 28.1 (t), 32.0 (t), 32.2 (t), 32.2 (t), 34.3 (t), 37.7 (t), 46.8 (s), 49.3 (s), 57.8 (s), 72.8 (d).

(1*S,5*S**)-1-(1-Ethoxy-vinyl)-dispiro[4.0.4.3]tridecan-1-ol [(1*S**, 5*S**)-33].** To a solution of methyl-vinylether (7.22 g, 100 mmol) in anhydrous THF (85 mL) was added within 50 min at −78 °C under argon with stirring a 1.5 M solution of *tert*-butyllithium in hexane (40 mL, 60 mmol). After an additional 15 min at −78 °C, the mixture was allowed to warm to room temperature. The resulting pale yellow solution of 1-ethoxy-vinyllithium was used in the next step. A suspension of finely powdered dry $CeCl_3$ (9.60 g, 39.0 mol) in anhydrous THF (145 mL) was stirred at room temperature under argon for 2 h. After addition of **32** (3.10 g, 16.1 mmol), stirring was continued for 2 h until the mixture was cooled to 0 °C, and the freshly prepared solution of 1-ethoxy-vinyllithium was added within 45 min. After an additional 45 min at room temperature, GC analysis [column B, 210 °C; retention times (min): 2.81 (**32**), 4.32 (**33**)] indicated no further rise in the concentration of **33** (89%). The mixture was diluted with pentane (100 mL) and hydrolyzed with saturated aqueous ammonium chloride (40 mL). The mixture was suction filtered and the residue washed with pentane (4 × 50 mL). The combined filtrates were washed with water (2 × 250 mL), the phases were separated, the aqueous phase was extracted with pentane (250 mL), and the combined organic phases were dried ($MgSO_4$) and concentrated (bath temperature 50 °C/15 Torr) to yield 3.88 g (94%) of crude **33** as a slightly yellow liquid (purity 81% GC). This material was used in the next step. An analytically pure sample was obtained by preparative GC. IR (neat): 3600−3300 cm^{-1} ($OH_{ass.}$). ^{1}H NMR (600 MHz, C_6D_6, C_6D_5H int): $\delta = 0.97$ (t, $J = 7$ Hz, 3H), 1.39−1.86 (m, 16H), 1.92−1.99 (m, 1H), 2.13−2.22 (m, 3H), 2.41 (m_c, 1H), 3.32 (q, $J = 7$ Hz, 2H), 3.93 (d, $J =$ 2 Hz, 1H), 4.40 (d, $J = 2$ Hz, 1H). ^{13}C NMR (150.8 MHz, C_6D_6, C_6D_6 int): $\delta = 14.3$ (q), 20.1 (t), 20.3 (t), 24.3 (t), 25.5 (t), 33.6 (t), 35.6 (t), 35.8 (t), 36.5 (t), 39.3 (t), 41.5 (t), 56.6 (s), 60.9 (s), 62.9 (t), 82.1 (t), 85.8 (s), 166.3 (s). MS (EI): $m/e = 264$ (22, M^+), 97 (100). HRMS m/e (M^+) calcd 264.2089, obsd 264.2089.

(1S*,5S*)-1-(1-Ethoxy-cyclopropyl)-dispiro[4.0.4.3]tridecane-1-ol [(1S*,5S*)-35]. To a suspension of freshly prepared zinc/silver couple[30] (9.2 g) in anhydrous ether (50 mL) was added under argon with stirring diiodomethane (20.7 g, 77.4 mmol) causing an exothermic effect and a gentle to strong reflux. After 20 min, **33** (3.65 g, 13.8 mmol, purity 81%) was added, and after an additional 1.5 h of reflux, the reaction was complete according to GC [column B, 210 °C; retention times (min): 4.32 (**33**), 6.41 (**35**)]. The mixture was diluted with pentane (130 mL) and hydrolyzed with saturated aqueous ammonium chloride (1.6 mL, 15 min stirring). The liquid phase was decanted, and the residue was extracted with ether (3 × 50 mL). The combined organic phases were washed with saturated aqueous ammonium chloride (80 mL) and water (2 × 80 mL), dried ($MgSO_4$), and concentrated (bath temperature 50 °C/15 Torr) to yield 2.65 g (69%%) of crude **35** as a slightly yellow liquid (purity 80% GC). This material was directly used in the next step. An analytically pure sample was obtained by preparative GC. IR (neat): 3600−3400 cm^{-1} ($OH_{ass.}$). ^{1}H NMR (600 MHz, C_6D_6, C_6D_5H int): $\delta = 0.62-0.68$ (m, 1H), 0.68−0.76 (m, 3H), 0.98 (dd, $J = 7$, 7 Hz, 3H), 1.20−1.28 (m, 2H), 1.32 (m_c, 1H), 1.42−1.83 (m, 13H), 1.87 (ddd, $J = 12$, 10, 5 Hz, 1H), 2.02−2.10 (m, 2H), 2.18−2.24 (m, 1H), 2.30 (ddd, $J = 13$, 10, 7 Hz, 1H), 3.13 (dq, $J = 9$, 7 Hz, 1H), 3.35 (dq, $J = 9$, 7 Hz, 1H). ^{13}C NMR (150.8 MHz, C_6D_6, C_6D_6 int): $\delta = 8.9$ (t), 10.4 (t), 16.1 (t), 20.2 (q), 20.7 (t), 24.3 (t), 25.3 (t), 34.6 (t), 35.6 (t), 36.4 (t), 38.3 (t), 39.1 (t), 40.3 (t), 56.7 (s), 61.4 (s), 63.4 (t), 65.2 (s), 87.0 (s). MS (EI): $m/e = 278$ (8, M^+), 108 (100). HRMS m/e (M^+) calcd 278.2246, obsd 278.2246.

(4*R,5*S**)-Trispiro[3.0.0.4.3.3]hexadecane-1-one [4*R**,5*S**)-36]:** A mixture of **35** (2.42 g, 8.68 mmol, purity 80%) and 8 M aqueous tetrafluoroboric acid (4.40 mL, 35.2 mmol) in ether (85 mL) was stirred at room temperature. According to ^{1}H NMR, after 2 h the reaction was complete. The mixture was treated with saturated aqueous sodium bicarbonate (3 × 50 mL), then washed with water (2 × 50 mL), and dried ($MgSO_4$). The solvent was evaporated (bath temperature (45 °C/15 Torr) and the residue (2.12 g) chromatographed on silica gel (0.05−0.20 mm) in pentane/ether 9:1 [column 75 × 5.5 cm, $R_f = 0.42$ (**36**)] to yield 1.09 g (64%) of **35** as a colorless liquid. According to GC [column B, 210 °C; retention time (min): 5.88 (**36**)], the material was 94% pure. IR (neat): 1770 cm^{-1} (C=O). ^{1}H NMR (600 MHz, $CDCl_3$, $CHCl_3$ int): $\delta = 1.20$ (m_c, 1H), 1.27 (m_c, 1H), 1.35−1.80 (m, 16H), 1.86 (ddd, $J = 12.5$, 9, 9 Hz, 1H), 1.95 (m_c, 1H), 2.03 (ddd, $J = 10.5$, 8, 4 Hz, 1H), 2.25 (ddd, $J = 10.5$, 10, 7 Hz, 1H), 2.77 (ddd, $J =$ 18, 10.5, 5.5 Hz, 1H), 2.88 (ddd, $J = 18$, 10, 7 Hz, 1H). ^{13}C NMR (150.8 MHz, $CDCl_3$, $CDCl_3$ int): $\delta = 19.9$ (t), 20.7 (t), 21.4 (t), 22.7 (t), 23.8 (t), 34.7 (t), 34.8 (t), 35.4 (t), 35.6 (t), 38.8 (t), 38.9 (t), 40.4 (t), 55.9 (s), 59.0 (s), 76.1 (s), 216.4 (s). MS (EI): $m/e =$ 232 (23, M^+), 108 (100). $C_{16}H_{24}O$ requires C, 82.70; H, 10.41. Found: C, 82.54; H, 10.56.

(5*S)-Trispiro[3.0.0.4.3.3]hexadecane (5*S**-8).** To a solution of sodium (276 mg, 12.0 mmol) in diethylene glycol (16 mL) were added **36** (232 mg, 1.0 mmol) and anhydrous hydrazine (2.60 g, 81 mmol), and the mixture was heated under argon with stirring to 180 °C until GC analysis [column A, 230 °C; retention times (min): 3.75 (**8**), 10.09 (**36**), 25.80 (hydrazone)] indicated that **36** had been consumed (66 h). Most of the surplus hydrazine and most of the water formed were distilled off under a stream of argon while the temperature was gradually raised to 200−205 °C. According to GC, after additional 72 h at this temperature the reduction was complete. The apparatus was rinsed with pentane (20 mL), and the reaction mixture was poured into water (60 mL) and extracted with pentane (2 × 60 mL). The combined organic phases were washed with water (3 × 60 mL), dried ($MgSO_4$), and concentrated (bath temperature 35 °C/15 Torr), and the residue was filtered over a short path of silica gel (0.05−0.20 mm, column 15 × 1 cm) and eluted with pentane [$R_f = 0.77$ (**8**)]. The solvent was evaporated (bath temperature 50 °C/15 Torr) to yield 140 mg (58%) of crude **8** as a colorless liquid (purity 90% GC). An analytically pure sample was obtained by preparative GC. ^{1}H NMR (600 MHz, $CDCl_3$, $CHCl_3$ int): $\delta = 1.24-1.29$ (m, 1H), 1.30−1.38 (m, 4H), 1.43−1.74 (m, 16H), 1.78−1.90 (m, 2H), 1.93 (ddd, $J = 12$, 8, 4 Hz, 1H), 2.25 (ddd, $J = 10$, 10, 10 Hz, 1H), 2.31 (ddd, $J = 10$, 10, 10 Hz, 1H). ^{13}C NMR (150.8 MHz, $CDCl_3$, $CDCl_3$ int): $\delta = 15.9$ (t), 19.6 (t), 20.6 (t), 23.7 (t), 24.7 (t), 30.3 (t), 32.0 (t), 32.6 (t), 34.1 (t), 35.1 (t), 35.8 (t), 40.4 (t), 41.4 (t), 52.1 (s), 55.7 (s), 56.5 (s).

MS (EI): m/e = 218 (1, M^+), 79 (100). $C_{16}H_{26}$ requires C, 88.00; H, 12.00. Found: C, 87.87; H, 11.83.

(4*R,5*S**)-1-Methylen-trispiro[3.0.0.4.3.3]hexadecane [(4*R**, 5*S**)-37].** To a suspension of methyltriphenylphosphonium bromide (3.97 g, 11.1 mmol) in dry benzene (20 mL) was added under argon with stirring potassium *t*-butoxide (1.12 g, 10.0 mmol), and the mixture was heated to reflux. After 2.5 h, most of the benzene was distilled off (bath temperature up to 120 °C) until **36** (700 mg, 2.92 mmol) was added. According to GC [column B, 200 °C; retention times (min): 3.73 (**37**), 7.56 (**36**)] after 1.5 h at 120 °C the reaction was complete. The mixture was diluted with pentane (40 mL) and hydrolyzed with water (0.8 mL). The organic phase was decanted, the residue was extracted with pentane (3 × 8 mL), and the combined organic phases were concentrated over a 30 cm vigreux column (bath temperature up to 90 °C). Precipitated triphenylphosphine oxide was filtered off, and the filtrate was chromatograped on silica gel (0.05−0.20 mm) in pentane [column 30 × 2.5 cm, R_f = 0.66 (**37**)] yielding 582 mg (87%) of **37** as a colorless glassy solid, mp 27−33 °C (purity >99% GC). IR (neat): 1660 cm^{-1} (C=C). ^1H NMR (600 MHz, C_6D_6, C_6D_5H int): δ = 1.30−1.42 (m, 3H), 1.43−1.48 (m, 1H), 1.50−1.80 (m, 14H), 1.87 (m_c, 1H), 1.96−2.01 (m, 1H), 2.15−2.26 (m, 2H), 2.46−2.56 (m, 2H), 4.83 (dd, J = 2.25, 2.25 Hz, 1H), 4.85 (dd, J = 2.75, 2.75 Hz, 1H). ^{13}C NMR (150.8 MHz, C_6D_6, C_6D_6 int): δ = 19.6 (t), 19.8 (t), 23.2 (t), 24.1 (t), 25.5 (t), 26.2 (t), 33.2 (t), 34.9 (t), 35.2 (t), 36.0 (t), 39.6 (t), 43.7 (t), 56.4 (s), 57.3 (s), 60.2 (s), 106.2 (t), 158.6 (s). MS (EI): m/e = 230 (28, M^+), 121 (100). $C_{17}H_{26}$ requires C, 88.63; H, 11.37. Found: C, 88.53; H, 11.09.

(3*S,4*R**,5*S**)-1-Oxa-tetraspiro[2.0.0.0.4.3.3.2]octadecane [(3*S**, 4*R**,5*S**)-39].** To a solution of **37** (582 mg, 2.53 mmol) in dichloromethane (8.0 mL) was added 3-chloroperoxybenzoic acid (940 mg, 70% w/w, 3.80 mmol), and the mixture was stirred at room temperature. According to TLC [pentane/ether 9:1, R_f = 0.72 (**37**), 0.30 (**39**)] after 1.5 h the reaction was complete. The mixture was washed with 1 N KOH (6 mL), the aqueous phase was extracted with dichloromethane (3 × 8 mL), and the combined organic phases were washed with water (2 × 15 mL) and dried ($MgSO_4$). The solvent was distilled off (bath temperature 40 °C/ 15 Torr) and the solid residue (650 mg) chromatographed on silica gel (0.05−0.20 mm) in pentane/ether 9:1 (column 65 × 4.5 cm) to yield 360 mg (58%) of pure **39** as a colorless glassy solid, mp 78 °C. ^1H NMR (600 MHz, C_6D_6, C_6D_5H int): δ = 1.20−1.82 (m, 20H), 1.90−1.99 (m, 1H), 2.08−2.19 (m, 2H), 2.43 (d, J = 4.5 Hz, 1H), 2.54−2.68 (m, 1H), 2.83 (d, J = 4.5 Hz, 1H). ^{13}C NMR (150.8 MHz, C_6D_6, C_6D_6 int): δ = 20.3 (t), 21.3 (t), 22.9 (t), 23.7 (t), 23.9 (t), 26.1 (t), 33.8 (t), 35.2 (t), 36.7 (t), 37.17 (t), 37.19 (t), 40.8 (t), 54.0 (t), 55.3 (s), 58.1 (s), 58.7 (s), 65.5 (s). MS (EI): m/e = 246 (3, M^+), 108 (100). $C_{17}H_{26}O$ requires C, 82.87; H, 10.64. Found: C, 82.61; H, 10.48.

(5*S,6*S**)-Trispiro[4.0.0.4.3.3]heptadecan-2-one [(5*S**,6*S**)-38].** Lithium iodide (1.98 g, 14.8 mmol) was dried for 1.5 h at 120 °C/0.1 Torr and dissolved in anhydrous THF (14.8 mL, exothermic effect) yielding a 1 M stock solution. A total of 0.98 mL (0.98 mmol) of this solution was added to a solution of **39** (242 mg, 0.98 mmol) in anhydrous THF. After 6 h at 60−70 °C, TLC [pentane/ether 8:2, R_f = 0.67 (**39**), 0.42 (**38**)] indicated that the rearrangement was complete. The mixture was diluted with pentane (4 mL) and washed with water (4 mL). The aqueous phase was extracted with pentane (3 × 5 mL), and the combined organic phases were washed with water (2 × 8 mL) and dried ($MgSO_4$). The solvents were evaporated (bath temperature 45 °C/15 Torr), and the liquid residue was chromatographed on silica gel (0.05−0.20 mm) in pentane/ether 8:2 (column 95 × 2.5 cm, R_f = 0.42) yielding 213 mg (88%) of **38** as a colorless liquid. According to GC [column B, 230 °C; retention time (min): 9.58 (**38**)] the material was >99% pure. IR (neat):1745 cm^{-1} (C=O). ^1H NMR (600 MHz, C_6D_6, C_6D_5H int): δ = 1.08−1.13 (m, 1H), 1.15−1.27 (m, 4H), 1.28−1.58 (m, 16H), 1.80−1.94 (m, 2H), 1.94−2.01 (m, 2H), 2.17 (d, J = 17 Hz, 1H). ^{13}C NMR (150.8 MHz, C_6D_6, C_6D_6 int): δ = 19.3 (t), 19.7 (t), 23.7 (t), 24.6 (t), 33.3 (t), 33.4 (t), 33.5 (t), 35.4 (t), 35.5 (t), 36.6 (t), 40.1 (t), 40.8 (t), 46.9 (t), 51.9 (s), 56.2 (s), 56.5 (s), 216.8 (s). MS (EI): m/e = 246 (3, M^+), 67 (100). $C_{17}H_{26}O$ requires C, 82.87; H, 10.64. Found: C, 82.67; H, 10.42.

***rac*-Trispiro[4.0.0.4.3.3]heptadecane (*rac*-9).** To finely ground potassium hydroxide (224 mg, 4.0 mmol) and hydrazine hydrate (150 mg, 3.0 mmol) in diethylene glycol (2.5 mL) was added **38** (123 mg, 0.50 mmol), and the mixture was heated under argon with stirring to 180 °C. After 2 h, GC analysis [column B, 200 °C; retention times (min): 4.13 (**9**), 25.59 (**38**)] indicated that the reaction was complete. The apparatus was rinsed with pentane (15 mL), and the reaction mixture was poured into water (8 mL) and extracted with pentane (3 × 8 mL). The combined organic phases were washed with water (2 × 8 mL), dried ($MgSO_4$), and concentrated over a 30 cm vigreux column (bath temperature 60 °C). The residue was chromatographed over a short path of silica gel (0.05−0.20 mm, column 15 × 1 cm) and eluted with pentane (R_f = 0.74). The solvent was evaporated (bath temperature 40 °C/ 15 Torr) to yield 94 mg (82%) of pure **9** as a colorless liquid. ^1H NMR (600 MHz, $CDCl_3$, $CHCl_3$ int): δ = 1.28−1.36 (m, 6H), 1.45−1.67 (m, 18H), 1.67−1.73 (m, 2H), 1.82−1.88 (m, 2H). ^{13}C NMR (150.8 MHz, $CDCl_3$, $CDCl_3$ int): δ = 19.6 (t), 23.4 (t), 24.3 (t), 32.5 (t), 35.2 (t), 35.8 (t), 40.9 (t), 55.9 (s), 56.7 (s). MS (EI): m/e = 232 (14, M^+), 43 (100). $C_{17}H_{28}$ requires C, 87.86; H, 12.14. Found: C, 88.06; H 11.92.

(1*R,4*S**)-1-Cyclopent-1-enyl-dispiro[3.0.4.3]dodecan-1-ol [(1*R**, 4*S**)-42].** To a solution of 1-bromo-cyclopentene[36a] (10.6 g, 72 mmol) in anhydrous THF (240 mL) was added within 1 h at −78 °C under argon with stirring a 1.5 M solution of *tert*-butyllithium in pentane (96 mL, 144 mmol). After an additional 45 min at −78 °C, the mixture was allowed to warm to 0 °C. The resulting 0.21 M solution of 1-lithio-cyclopentene (340 mL) was used in the next step. A suspension of finely powdered dry $CeCl_3$ (14.8 g, 60 mmol) in anhydrous THF (220 mL) was stirred at room temperature under argon for 2 h. After addition of **41** (5.34 g, 30 mmol, purity 87%), stirring was continued for 2 h until the mixture was cooled to 0 °C, and 230 mL (48 mmol) of the 0.21 M solution of 1-lithio-cyclopentene was added. Afterward, the mixture was stirred at room temperature, and the reaction progress was monitored by GC [column B, 200 °C; retention time (min): 2.56 (**41**), 5.90 (**42**)]. After 16 h, 28% of unreacted ketone was still present. Therefore, the remaining 110 mL (23 mmol) of the 0.21 M solution of 1-lithio-cyclopentene was added, and, after an additional 30 min, the reaction was complete. The mixture was diluted with pentane (300 mL) and hydrolyzed with saturated aqueous ammonium chloride (60 mL). The liquid phase was decanted, the residue was extracted with pentane (2 × 150 mL), and the combined organic phases were washed with water (2 × 300 mL) and dried ($MgSO_4$). The solvents were distilled off (bath temperature 40 °C/15 Torr), and the residual brown liquid (8.8 g) was chromatographed on silica gel (0.05−0.20 mm) in pentane/ether 9:1 [column 100 × 7 cm, R_f = 0.46 (**42**)] yielding 5.49 g (82%) of **42** as a colorless liquid (purity 96% GC). IR (neat): 3600 (OH), 3580−3350 cm^{-1} ($OH_{ass.}$). ^1H NMR (600 MHz, C_6D_6, C_6D_5H int): δ = 0.94−0.97 (m, 1H), 1.32−1.60 (m, 8H), 1.61−1.72 (m, 4H), 1.73−1.84 (m, 4H), 1.89−1.95 (m, 1H), 2.15 (m_c, 1H), 2.22−2.28 (m, 3H), 2.31 (m_c, 1H), 2.35−2.45 (m, 2H), 5.43 (dddd, J = 2, 2, 2, 2 Hz, 1H). ^{13}C NMR (150.8 MHz, C_6D_6, C_6D_6 int): δ = 19.5 (t), 24.4 (t), 25.1 (t), 25.6 (t), 26.7 (t), 31.9 (t), 32.6 (t), 33.4 (t), 34.2 (t), 35.5 (t), 36.3 (t), 38.9 (t), 55.2 (s), 58.2 (s), 81.2 (s), 125.4 (d), 149.4 (s). MS (EI): m/e = 246 (1, M^+), 110 (100). HRMS m/e (M^+) calcd 246.1984, obsd 246.1984. $C_{17}H_{26}O$ requires C, 82.87; H, 10.64. Found: C, 81.64: H, 10.33.

(6*S,7*S**,8*R**)-8-Bromo-trispiro[4.0.0.4.3.3]heptadecan-12-one [(6*S**,7*S**,8*R**)-43].** To dry zinc bromide (1.08 g, 4.8 mmol) in dry acetonitrile (22 mL) was added dry *N*-chloro-toluene-4-sulfonamide (1.09 g, 4.8 mmol), and the mixture was stirred under argon until a nearly clear yellow solution was formed (10 min). This solution was added under argon with stirring to neat **42** (984

mg, 4.0 mmol). A precipitate formed, and the mixture went colorless. After 15 min, TLC [pentane/ether 8:2; R_f = 0.62 (**42**), 0.45 (**43**)] indicated that the reaction was complete. The mixture was filtered over a short path of silica gel (colum 8 × 4.5 cm) and eluted with ether. The solvents were evaporated (bath temperature 40 °C/15 Torr), and the heterogeneous residue was extracted with pentane (2 × 25 mL). The extracts were concentrated (bath temperature 40 °C/15 Torr), and the residue (1.34 g) was chromatographed on silica gel (0.05−0.20 mm) in pentane/ether 8:2 (column 70 × 4.5 cm) to yield 1.07 g (82%) of pure **43** as a slightly beige-colored solid, mp 76 °C. IR (KBr): 1730 cm^{-1} (C═O). ^{1}H NMR (600 MHz, C_6D_6, C_6D_5H int): δ = 1.03−1.15 (m, 3H), 1.18−1.27 (m, 2H), 1.30−1.51 (m, 10H), 1.52−1.67 (m, 3H), 1.85 (m_c, 1H), 1.89−2.07 (m, 3H), 2.15 (ddd, J = 18.5, 10, 10 Hz, 1H), 2.47−2.56 (m, 1H), 4.11 (ddd, J = 8, 8, 2.5 Hz, 1H). ^{13}C NMR (150.8 MHz, C_6D_6, C_6D_6 int): δ = 19.9 (t), 23.2 (t), 23.7 (t), 24.3 (t), 28.8 (t), 31.4 (t), 33.9 (t), 34.7 (t), 35.7 (t), 35.8 (t), 37.4 (t), 40.1 (t), 53.6 (d), 56.6 (s), 56.7 (s), 65.1 (s), 215.8 (s). MS (EI): m/e = 326, 324 (9, 9, M^+), 108 (100). $C_{17}H_{25}BrO$ requires C, 62.77; H, 7.75. Found: C, 62.85; H, 7.64.

(6*S)-Trispiro[4.0.0.4.3.3]heptadecan-12-one [(6*S**)-46].** A mixture of **43** (976 mg, 3.00 mmol) and zinc powder (1.11 g, 17 mmol) in acetic acid (3.0 mL) was heated under argon with stirring to 60 °C. According to GC [column B, 230 °C; retention times (min): 6.63 (**46**), 11.89 (**43**)], after 1.5 h the reaction was complete. The mixture was diluted with water (40 mL) and extracted with pentane (40 mL). The aqueous phase was extracted with pentane (3 × 30 mL), and the combined organic phases were washed with saturated aqueous sodium bicarbonate (80 mL) and water (2 × 80 mL) and dried ($MgSO_4$). The solvent was evaporated (bath temperature 40 °C/15 Torr), and the remaining **46** (mp 61 °C, purity 94% GC) was used in the next step. Crystallization from acetone by diffusion of water yielded an analytically pure sample of colorless crystals, mp 67−68 °C. IR (KBr): 1730 cm^{-1} (C═O). ^{1}H NMR (600 MHz, C_6D_6, C_6D_5H int): δ = 1.10−1.16 (m, 1H), 1.20−1.35 (m, 5H), 1.37−1.63 (m, 14H), 1.64−1.74 (m, 2H), 1.89−1.99 (m, 2H), 2.02 (m_c, 1H), 2.14 (ddd, J = 19, 10, 2 Hz, 1H). ^{13}C NMR (150.8 MHz, C_6D_6, C_6D_6 int): δ = 20.3 (t), 23.3 (t), 24.0 (t), 25.2 (t), 25.5 (t), 28.7 (t), 29.7 (t), 31.1 (t), 32.8 (t), 33.1 (t), 34.7 (t), 36.4 (t), 40.1 (t), 55.0 (s), 56.1 (s), 63.3 (s), 219.0 (s). MS (EI): m/e = 246 (100, M^+). $C_{17}H_{26}O$ requires C, 82.87; H, 10.64. Found: C, 82.68; H, 10.65.

***rac*-Trispiro[4.0.0.4.3.3]heptadecane (*rac*-9):** To a solution of sodium (276 mg, 12.0 mmol) in diethylene glycol (16 mL) were added **46** (246 mg, 1.0 mmol) and anhydrous hydrazine (2.60 g, 81 mmol), and the mixture was heated under argon with stirring to 180 °C until GC analysis [column A, 230 °C; retention times (min): 2.06 (**9**), 5.93 (**46**), 51.85 (hydrazone)] indicated that **46** had been consumed (48 h). Most of the surplus hydrazine and of the water formed was distilled off under a stream of argon while the temperature was gradually raised to 200−205 °C. After 10 days at this temperature the reduction was complete. The apparatus was rinsed with pentane (20 mL), and the reaction mixture was poured into water (50 mL) and extracted with pentane (2 × 50 mL). The combined organic phases were washed with water (3 × 50 mL) and dried ($MgSO_4$). The solvent was evaporated (bath temperature 35 °C/15 Torr), and the residue (150 mg) was filtered over a short path of silica gel (0.05−0.20 mm, column 18 × 1 cm) and eluted with pentane [R_f = 0.74 (*rac*-**9**)] to yield 119 mg (50%) of *rac*-**9** as a colorless liquid (purity 96% GC). The ^{1}H and ^{13}C NMR data were identical with those of an authentic sample prepared from **37**.

(1*S,4*S**)-1-[(1′-Methylselanyl)cyclobutyl)]dispiro[3.0.4.3]-dodecan-1-ol [(1*S**,4*S**)-48].** To a solution of 1,1-bis(methylselanyl)-cyclobutane[38a] (2.70 g, 11.0 mmol) in anhydrous ether (11 mL) was added at −78 °C under argon with stirring a 1.5 M solution of *tert*-butyllithium in pentane (7.9 mL, 11.8 mmol) such that the internal temperature did not exceed 60 °C (1 h). After an additional 1 h at −78 °C, **41** (1.60 g, 9.0 mmol) was added, and stirring at −78 °C continued until TLC [pentane/ether 9:1, R_f = 0.52 (**48**), 0.43 (**41**)] indicated that no further reaction occurred (1 h). The still cold mixture was hydrolyzed with saturated aqueous ammonium chloride (5 mL), and the organic phase was separated and dried ($MgSO_4$). The solvents were evaporated (bath temperature 60 °C/20 Torr), and the remaining liquid (3.60 g) was chromatographed on silica gel (0.05−0.20 mm) in pentane/ether 9:1 (column 65 × 4.5 cm) to yield 1.26 g (37%) of a 85:15 mixture of **48** and **41** as a vile-smelling colorless liquid. This material was used in the next step. **48**: ^{1}H NMR (600 MHz, $CDCl_3$, $CHCl_3$ int): δ = 1.24−1.35 (m, 3H), 1.36−1.48 (m, 4H), 1.49−1.69 (m, 6H), 1.77−1.99 (m, 4H), 2.02−2.18 (m, 3H), 2.12 (s, 3H), 2.21−2.34 (m, 3H), 2.47 (m_c, 1H), 2.67−2.74 (m, 1H). ^{13}C NMR (150.8 MHz, $CDCl_3$, $CDCl_3$ int): δ = 4.9 (q), 16.6 (t), 19.1 (t), 25.7 (t), 25.8 (t), 27.3 (t), 28.5 (t), 29.0 (t), 34.1 (t), 34.2 (t), 34.8 (t), 35.1 (t), 38.1 (t), 55.2 (s), 56.9 (s), 58.5 (s), 83.8 (s).

(5*S)-Trispiro[3.0.0.4.3.3]hexadecan-16-one [(5*S**)-47].** To a solution of 4-chloroperoxybenzoic acid (2.94 g, 70% w/w, 12.0 mmol) in dichloromethane (30 mL) was added under argon with stirring **48** (556 mg, 1.70 mmol), causing a slightly exothermic effect. After 45 min, the reaction was complete according to TLC [pentane/ether 9:1, R_f = 0.52 (**48**), 0.43 (**41**), 0.27 (**47**)]. The mixture was washed with 1 N NaOH (3 × 20 mL) and water (30 mL) and dried ($MgSO_4$). The solvent was evaporated (bath temperature 30 °C/15 Torr) and the residue (520 mg) chromatographed on silica gel in pentane/ether 9:1 (colum 45 × 2.5 cm) to yield 236 mg (70%) of **47** as a colorless liquid. According to GC [column B, 230 °C; retention time (min): 3.78 (**47**)], the material was >99% pure. IR (neat): 1735 cm^{-1} (C═O). ^{1}H NMR (600 MHz, $CDCl_3$, $CHCl_3$ int): δ = 1.32−1.38 (m, 3H), 1.46−1.67 (m, 11H), 1.67−1.77 (m, 2H), 1.84−1.98 (m, 3H), 2.04 (m_c, 1H), 2.17−2.25 (m, 3H), 2.29 (m_c, 1H). ^{13}C NMR (150.8 MHz, $CDCl_3$, $CDCl_3$ int): δ = 14.8 (t), 19.7 (t), 22.6 (t), 23.3 (t), 25.5 (t), 28.2 (t), 28.3 (t), 33.05 (t), 33.09 (t), 33.4 (t), 35.1 (t), 38.4 (t), 54.2 (s), 56.4 (s), 58.4 (s), 221.1 (s). MS (EI): m/e = 232 (30, M^+), 123 (100). $C_{16}H_{24}O$ requires C, 82.70; H, 10.41. Found: C, 82.76; H, 10.12.

(5*S)-Trispiro[3.0.0.4.3.3]hexadecane [(5*S**)-8]**: The reduction of **47** was performed as described for **36**. A total of 116 mg (0.5 mmol) of **47** yielded 87 mg (78%) of (5***S****)-**8**. According to GC [column A, 230 °C; retention times (min): 3.86 (**8**), 13.54 (**47**), 34.31 (hydrazone)], the formation of the hydrazone occurred at 16 h at 180 °C, and the subsequent liberation of **8** occurred at 72 h at 200−205 °C. The ^{1}H and ^{13}C NMR data were identical with those of an authentic sample.

(S*S*,1*R*,4*R*)-(+)-[(*N*-Methyl-*S*-phenylsulfonimidoyl)methyl]-dispiro[3.0.4.3]dodecan-1-ol [(S*S*,1*R*,4*R*)-(+)-50] and (S*S*,1*S*,4*S*)-(+)-[(*N*-Methyl-*S*-phenylsulfonimidoyl)methyl]-dispiro[3.0.4.3]-dodecan-1-ol [(S*S*,1*S*,4*S*)-(+)-52]. To a solution of (*S*)-(+)-*N*,*S*-dimethyl-*S*-phenylsulfonimid[39] (8.80 g, 50 mmol) in anhydrous THF (150 mL) was added at 0 °C under argon with stirring a 1.6 M solution of *n*-butyllithium in hexane (31.2 mL, 50 mmol). The mixture was stirred for 1 h at 0 °C and then used in the next step. A suspension of finely powdered dry $CeCl_3$ (4.94 g, 20 mmol) in anhydrous THF (75 mL) was stirred at room temperature under argon for 2 h. After addition of *rac*-**41** (1.78 g, 10 mmol), stirring was continued for 2 h until the mixture was cooled to −78 °C; then the solution of the lithiated *N*,*S*-dimethyl-*S*-phenylsulfonimid was added within 15 min. According to TLC (pentane/ether 7:3; R_f = 0.58 (**41**), 0.33 [(S*S*,1*R*,4*R*)-**50**], 0.25 [(S*S*,1*S*,4*S*)-**52**]), after 1 h at −78 °C and 1 h at room temperature, the reaction had ceased. The mixture was diluted with ether (300 mL) and hydrolyzed with water (10 mL). The liquid phase was decanted, the residue was extracted with ether (100 mL), and the combined organic phases were dried ($MgSO_4$) and concentrated (20 °C/15 Torr). The residue (6.10 g) was chromatographed on silica gel (0.05−0.20 mm) in pentane/ether 7:3 (column 70 × 5 cm) to yield 0.26 g (15%) of unreacted **41** as a colorless liquid, 1.28 g (37%) of (S*S*,1*R*,4*R*)-**50** as a colorless solid, mp 61−63 °C, (purity 99% ^{1}H NMR, 99% ee, $[\alpha]_D^{20}$ = +61.3, c = 1.07, $CHCl_3$), and 0.84 g (24%) of (S*S*,1*S*,4*S*)-

52 as a colorless solid, mp 70 °C, (purity 99% ^{1}H NMR, 99% ee, $[\alpha]_D^{20} = +42.0$, $c = 1.06$, $CHCl_3$). Both sulfonimides were crystallized from ethanol by diffusion of water. (*SS*,1*R*,4*R*)-(+)-**50**: IR (KBr): 3600−3200 cm^{-1} ($OH_{ass.}$). ^{1}H NMR (600 MHz, CD_2Cl_2, $CDHCl_2$ int, −50 °C): $\delta = 1.05-1.10$ (br s, 1H), 1.13−1.24 (m, 2H), 1.37−1.50 (m, 10H), 1.51−1.59 (m, 2H), 2.04 (m_c, 1H), 2.14 (m_c, 1H), 2.25−2.32 (m, 1H), 2.48 (s, 3H), 2.55 (m_c, 1H), 3.22 (AB, $\Delta\nu_{AB} = 45$ Hz, $J_{AB} = 13$ Hz, 2H), 7.58 (t, $J = 7.5$ Hz, 2H), 7.64 (t, $J = 7.5$ Hz, 1H), 7.84 (d, $J = 7.5$ Hz, 2H). ^{13}C NMR (150.8 MHz, $CDCl_3$, $CDCl_3$ int): $\delta = 18.60$ (t), 24.75 (t), 24.91 (t), 27.77 (t), 28.69 (q), 31.34 (t), 33.75 (t), 34.68 (t), 34.72 (t), 38.02 (t), 54.72 (s), 58.26 (s), 62.32 (t), 78.52 (s), 128.95 (d), 129.65 (d), 133.29 (d), 138.38 (s). MS (EI): $m/e = 348$ (<1, M^+), 125 (100). $C_{20}H_{29}NO_2S$ requires C, 69.12; H, 8.41. Found: C, 68.99: H, 8.66. (*SS*,1*S*,4*S*)-(+)-**52**: IR (KBr): 3350−3100 cm^{-1} ($OH_{ass.}$). ^{1}H NMR (600 MHz, CD_2Cl_2, $CDHCl_2$ int, −50 °C): $\delta = 1.06-1.24$ (m, 5H), 1.27−1.33 (m, 1H), 1.35−1.48 (m, 5H), 1.49−1.61 (m, 5H), 1.96 (m_c, 1H), 2.24 (m_c, 2H), 2.63 (s, 3H), 3.33 (AB, $\Delta\nu_{AB} = 29$ Hz, $J_{AB} = 14$ Hz, 2H), 7.55 (t, $J = 7.5$ Hz, 2H), 7.63 (t, $J = 7.5$ Hz, 1H), 7.78 (d, $J = 7.5$ Hz, 2H). ^{13}C NMR (150.8 MHz, $CDCl_3$, $CDCl_3$ int): $\delta = 18.7$ (t), 24.7 (t), 24.9 (t), 27.1 (t), 28.8 (q), 32.4 (t), 33.5 (t), 34.5 (t), 34.8 (t), 37.9 (t), 54.8 (s), 58.0 (s), 63.2 (t), 76.7 (s), 129.47 (d), 129.54 (d), 133.4 (d), 138.3 (s). MS (EI): $m/e = 348$ (1, M^+), 211 (100). $C_{20}H_{29}NO_2S$ requires C, 69.12; H, 8.41. Found: C, 69.24; H, 8.50.

(4*R*)-(+)-Dispiro[3.0.4.3]dodecan-1-one [(4*R*)-(+)-41]. (*SS*,1*R*,4*R*)-(+)-**50** (1.10 g, 3.16 mmol) was heated under argon to 110 °C. According to TLC (pentane/ether 7:3; $R_f = 0.52$ [(4*R*)-(+)-**41**], 0.30 [(*SS*,1*R*,4*R*)-(+)-**50**]), after 14 h the reaction was complete. The mixture was dissolved in ether, the solution was concentrated (20 °C/15 Torr), and the residue was chromatographed on silica gel (0.05−0.20 mm) in pentane/ether 7:3 (column 45 × 2.5 cm) yielding 495 mg (87%) of (4*R*)-(+)-**41** as a colorless liquid (purity 99%, >99% ee, $[\alpha]_D^{20} = +145$, $c = 1.21$, acetone; $\theta_{307} = +6328$, CH_3OH). The chemical purity was determined by GC [column A, 230 °C; retention time (min): 3.71 (4*R*)-(+)-**41**]. The ^{1}H and ^{13}C NMR data were identical with those of *rac*-**41**.

(4*S*)-(−)-Dispiro[3.0.4.3]dodecan-1-one [(4*S*)-(−)-41]. (*SS*,1*S*,4*S*)-(+)-**52** (675 mg, 1.94 mmol) was thermolyzed and the reaction mixture purified as described for (*SS*,1*R*,4*R*)-(+)-**50**, yielding 331 mg (96%) of (4*S*)-(−)-**41** as a colorless liquid (purity 99%, >99% ee, $[\alpha]_D^{20} = -145$, $c = 1.14$, acetone; $\theta_{307} = -6538$, CH_3OH). The ^{1}H and ^{13}C NMR data were identical with those of *rac*-**41**.

X-ray Analyses of 26, 34, 43, 49, 50, and 52. The data were collected at 140 K on a Stoe IPDS 2 diffractometer with Mo Kα radiation (71.073 pm) (**26**, **34**, **43**) and at 100 K on a Bruker-Smart 6000 diffractometer with Cu Kα radiation (154.178 pm) (**49**, **50**, **52**), respectively. The structures were solved by direct methods and refined anisotropically against F^2 using SHELXL-97.[59] The crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publications number CCDC 652397 (**26**), 652398 (**34**), 652399 (**43**), 652400 (**49**), 652401 (**50**), and 652402 (**52**). Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. (fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk).

Supporting Information Available: Experimental procedures for all compounds not covered in the Experimental Section, ^{1}H and ^{13}C NMR spectra, data of the X-ray analyses including ORTEP-plots of **26**, **34**, **43**, **49**, **50**, and **52**, and computational data of the (*P*)-helices of **1**, **2**, **3**, **4**, **5**, **9**, and **10**. This material is available free of charge via the Internet at http://pubs.acs.org.

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