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Helical primary structures of 1,2-spiroannelated five-membered rings: attempted synthesis of (±)-tetraspiro[4.0.0.0.4.3.3.3]heneicosane☆

Tien Widjaja [a], Lutz Fitjer [a,*], Kathrin Meindl [b], Regine Herbst-Irmer [b]

[a] Institut für Organische und Biomolekulare Chemie der Universität Göttingen, Tammannstrasse 2, D-37077 Göttingen, Germany
[b] Institut für Anorganische Chemie der Universität Göttingen, Tammannstrasse 4, D-37077 Göttingen, Germany

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Abstract

A β-hydroxy ketone with a helical carbon skeleton of five 1,2-spiroannelated cyclopentane rings is the main product of a Lewis acid catalyzed rearrangement of suitable sized α-hydroxy epoxides followed by an in situ equilibration via retro aldol reactions. Various attempts of a conversion to the title hydrocarbon failed.

Keywords: Helicenes; Spiro compounds; α-Hydroxy epoxides; Rearrangements

1. Introduction

During the past decade, helical primary structures of spiroannelated hydrocarbon rings have been the focus of considerable interest.[1–8] Representative examples are the trispiranes **1**,[2,3] **2**,[4] and **3**,[8] and the tetraspiranes **4**[3] and **5**[5] (Fig. 1). With regard to their specific rotations, interesting observations have been made: the specific rotation of (*P*)-**1** is high ($[\alpha]_D^{20}$ +192.7 (*c* 1.20, $CHCl_3$))[2,3] and doubles in (*P*)-**4** ($[\alpha]_D^{20}$ +373.0 (*c* 1.0, $CHCl_3$)),[3] while the specific rotation of (*P*)-**2** is low ($[\alpha]_D^{20}$ +63.3 (*c* 1.09, $CHCl_3$))[4] and diminishes in (*P*)-**5** ($[\alpha]_D^{20}$ +26.0, (*c* 1.18, $CHCl_3$)).[5] Surprisingly, with (*P*)-**3** ($[\alpha]_D^{20}$ −62.6 (*c* 1.10, $CHCl_3$))[8] the sign of rotation changes, and the magnitude increases again. It is therefore tempting to speculate that the specific rotation of (*P*)-**6** could further increase. However, quantum chemical computations predict the contrary ($[\alpha]_D^{20}$ −36.2).[8] To clarify the matter, a synthesis of (*P*)-**6** seems highly desirable. We hereby report on an attempted synthesis of (±)-**6**.

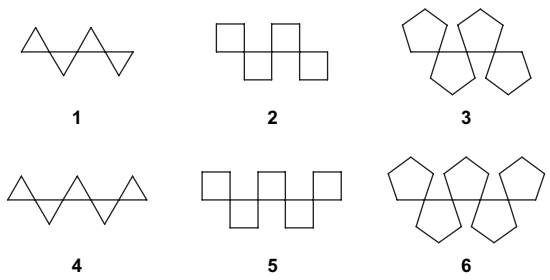

Figure 1.

2. Results

Our first approach to a synthesis of **6** was based on the successful synthesis of **3** (Scheme 1).[8] The key step of this synthesis was a regio- and stereoselective brominative rearrangement[9] of the vinylcyclobutanol **9**, itself obtained by a stereoselective addition of 1-lithio-cyclopentene (**8**) to dispiroketone **7**. Debromination and deoxygenation of the β-bromo ketone **10** then yielded **3**.

For an analogous synthesis of **6** we needed 1-lithio-spiro-[4.4]non-1-ene (**14**). This reagent was generated by treatment of the tosylhydrazone **12** of spiroketone **13** with *n*-butyllithium, but not used as such,[10] but first brominated to 1-bromo-spiro[4.4]non-1-ene (**11**) and then regenerated by

☆ Polyspiranes: Part 29. For Part 28, see Ref. 8.

* Corresponding author. Tel.: +49 551 393278.
E-mail address: lfitjer@gwdg.de (L. Fitjer).

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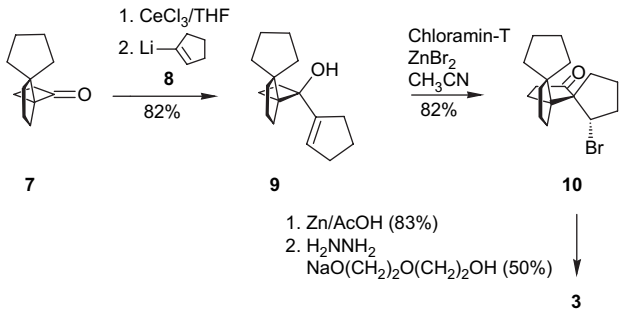
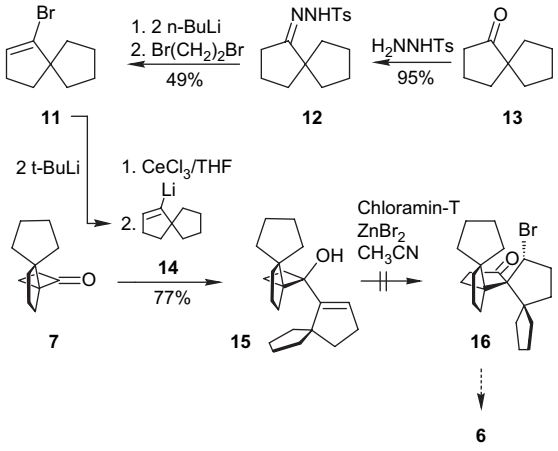


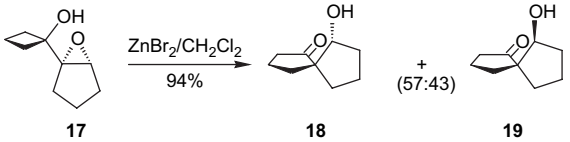
Scheme 1.

treatment with *tert*-butyllithium (Scheme 2).[11] Catalyzed by anhydrous cerium trichloride,[12] **14** added to dispiroketone **7**, yields a single vinylcyclobutanol, thought to be formed by an attack of the reagent from the less hindered side of **7** and deduced to be **15**. Albeit we recognized that a regioselective ring enlargement of **15** could have led not only to the bromo ketone **16**, but also to a stereoisomer with an undesired non-helical carbon skeleton, we were disappointed by the fact that no tetraspirane was formed at all. Ring opened products and polymers were observed instead. We therefore tried to modify **15** such that the desired ring enlargement could take place.

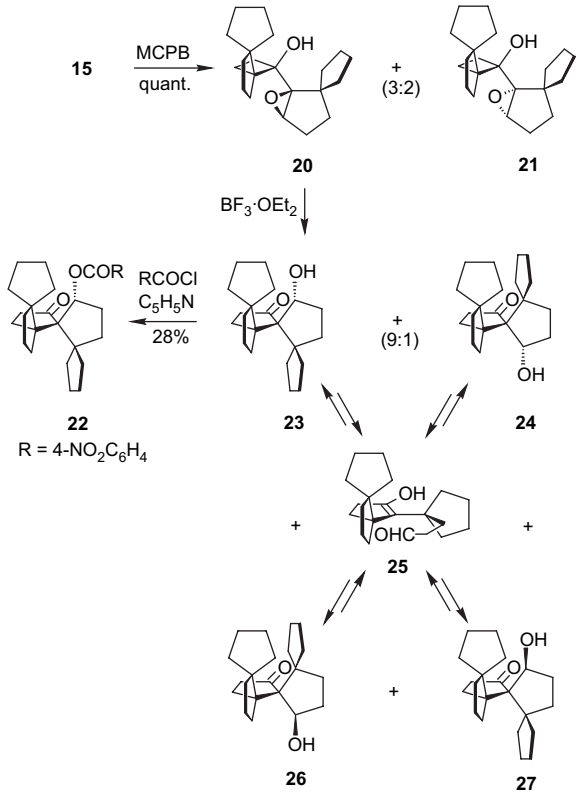


Scheme 2.

It has been reported[13] that α-hydroxy epoxides undergo Lewis acid catalyzed rearrangements to β-hydroxy ketones, including spirocyclic systems. An illustrative example is the zinc bromide catalyzed rearrangement of the α-hydroxy epoxide **17** yielding a 57:43 mixture of the β-hydroxy ketones **18** and **19** (Scheme 3). Although the poor diastereoselectivity pointed to a cationic intermediate that would eventually favor ring openings in more complex systems, we set out to implement this approach for a synthesis of **6**.



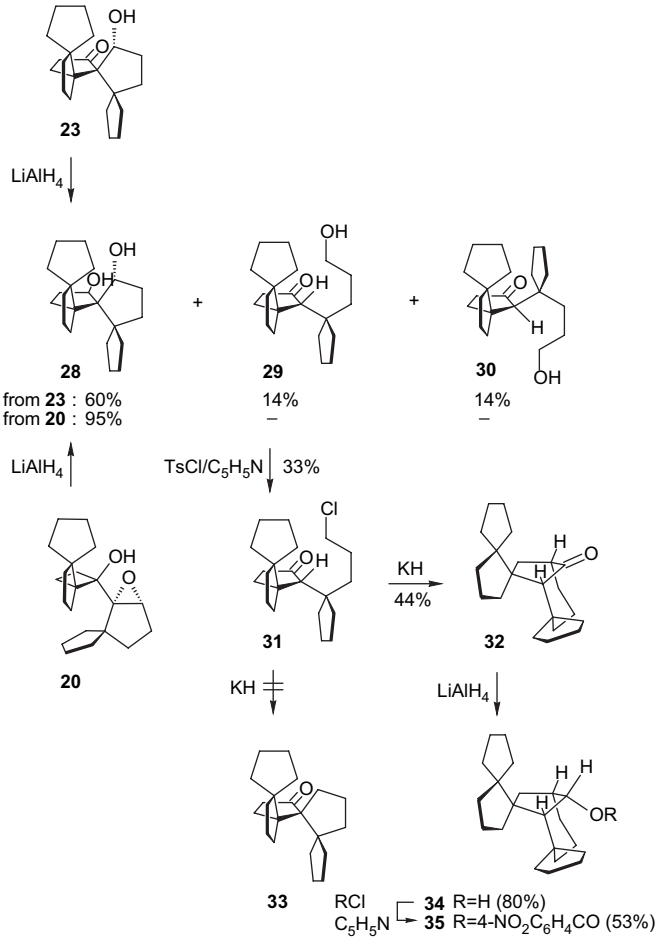
Scheme 3.



Scheme 4.

Toward this end, we subjected the vinylcyclobutanol **15** first to a buffered epoxidation and obtained a 3:2 mixture of two epoxides (^{1}H/^{13}C NMR). Upon chromatography on silica gel in pentane/ether 8:2, the minor epoxide (R_f=0.42) proved unstable and rearranged, while the major epoxide (R_f=0.55) persisted and was obtained pure. Next, we subjected both the 3:2 mixture of the two epoxides, and the major epoxide to a boron trifluoride etherate catalyzed rearrangement in dichloromethane. To our surprise, in both cases identical 9:1 mixtures of two β-hydroxy ketones were formed (^{1}H/^{13}C NMR). This indicated that in both cases the rearrangements were followed by an in situ equilibration via retro aldol reactions, i.e., via **25** as the common intermediate (Scheme 4). Chromatography on silica gel in pentane/ether 8:2 delivered the major β-hydroxy ketone (R_f=0.11) pure, while the minor β-hydroxy ketone (R_f=0.18) was isolated to a lower degree of purity (85%).

Of the products formed, the major β-hydroxy ketone could unequivocally be identified as **23** by a crystal structure analysis of its 4-nitro benzoate **22**. To identify the minor product, we calculated the heats of formation of all four β-hydroxy ketones (**23**, **24**, **26**, **27**), which could have been formed and taken part in the observed equilibration using our conformational search routine HUNTER[14] in connection with MM3.[15] The result was clear: it confirmed **23** (ΔH_f=−99.4 kcal/mol) as the most thermodynamically stable β-hydroxy ketone, followed by **24** (ΔH_f=−98.7 kcal/mol). As **26** (ΔH_f=−95.1 kcal/mol) and **27** (ΔH_f=−95.5 kcal/mol) were calculated to be considerably less stable, we deduced the minor β-hydroxy ketone to be **24**.



Scheme 5.

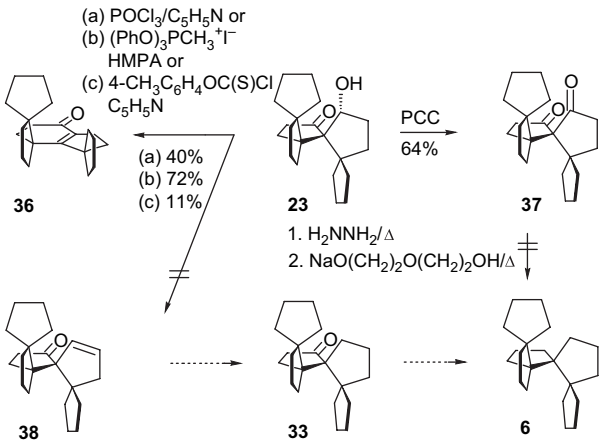
The assignment of **20** as the major and **21** as the minor epoxide was based on the results of a reduction of the β-hydroxy ketone **23** in conjunction with the results of a reductive rearrangement[16] of the major epoxide (Scheme 5). Upon treatment with lithium aluminium hydride, both compounds yielded the *cis-cis*-1,3-diol **28**.[17] This indicated that the reductive rearrangement of the major epoxide had been proceeded via **23** and that the sought structure was **20**.

Unexpectedly, the reduction of **23** yielded not only the diol **28**, but also an inseparable 1:1 mixture of the primary alcohols **29** and **30**. Obviously, these alcohols resulted from a retro aldol reaction to the lithium salt of **25** (Scheme 4) followed by a reduction of the aldehyde and a non-stereoselective protonation of the enolate during the final hydrolysis. In any case, their formation opened up the opportunity to explore the feasibility of a spiroalkylation with an eventual formation of ketone **33** as another potential precursor of **6**. For the experimental realization, we reacted the 1:1 mixture of **29** and **30** with an excess of *p*-toluenesulfonyl chloride in pyridine and were pleased to learn that after 24 h, the alcohols had disappeared and that the intermediately formed *p*-toluenesulfonates had largely been chlorinated.[18] To accelerate the chlorination, the remaining reagent was hydrolyzed with a stoichiometric amount of water, and after an additional 36 h the reaction was complete. Unfortunately, a chromatographic separation of the chlorides proved difficult, and only one of them could be obtained pure. Cyclization by treatment with potassium hydride in toluene at 110 °C proceeded smoothly, but much to our disappointment the spectral data indicated that a bridged ketone had been formed.[19] To clarify its stereochemistry, we reduced the ketone with lithium aluminum hydride, reacted the resulting alcohol with 4-nitrobenzoic acid chloride in pyridine, and subjected the 4-nitro benzoate formed to a crystal structure analysis. This analysis disclosed its structure as **35**, and hence the structures of the corresponding alcohol, ketone, and chloride as **34**, **32**, and **31**, respectively.

Faced with the fact that arrival at **33** via **31** was barred, we focused on **23** and investigated the possibility of an elimination followed by a hydrogenation (**23**–**38**–**33**) (Scheme 6). We soon discovered that all reactions carried out for this purpose were to no avail. Treatment of **23** with phosphoryl chloride in pyridine[20] or with methyltriphenoxyphosphonium iodide in hexamethylphosphoramide[21] afforded an α,β-unsaturated ketone. A crystal structure analysis confirmed its structure as **36** and thus made clear that in both cases ionization with a concomitant 1,2-acyl shift had taken place.[22] An attempted synthesis of a thiocarbonate ester as substrate for a thermal *syn*-elimination[23] failed as well. Upon treatment of **23** with 4-methylphenyl thiochloroformate in pyridine a plethora of products was formed, and the only one, which could be obtained pure was once again **36**.

In a last approach to a synthesis of **6** we explored the feasibility of an oxidation of **23** followed by a Wolff–Kishner reduction (**23**–**37**–**6**). Toward this end, we reacted **23** with pyridinium chlorochromate[24] and heated the resulting dione **37** with a large excess of neat hydrazine to reflux. However, even after prolonged reaction times, no derivatization was observed.

In summary, boron trifluoride catalyzed rearrangements of the α-hydroxy epoxides **20** and **21** yield a 9:1 mixture of the β-hydroxy ketones **23** and **24**. Of these, **23** exhibits the desired helical carbon skeleton and has been obtained pure. However, until now all attempts to remove its functionalities have failed. Due to a pronounced tendency to ring openings and rearrangements, **23** may be an unsuitable candidate for a conversion to **6**. We therefore believe that new strategies must be developed for a successful synthesis of **6**.



Scheme 6.

3. Experimental

3.1. General

IR spectra were obtained with a Perkin–Elmer 298 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Varian VXR 500 or VXR 600 spectrometer. As standards the following chemical shifts were used: δ_H ($CHCl_3$)=7.24, δ_H (C_6D_5H)=7.15, δ_H (CD_3COCD_2H)=2.04, δ_C ($CDCl_3$)=77.00, δ_C (C_6D_6)=128.00, δ_C [$(CD_3)_2CO$]=29.80. ^{13}C multiplicities were studied by HMQC measurements. Mass spectra were obtained with a Finnegan MAT 95 spectrometer (EI and HREI) operated at 70 eV. Analytical and preparative GC were carried out on a Carlo Erba 6000 Vega 2 instrument using a thermal conductivity detector and hydrogen as carrier gas. R_f values are quoted for Macherey and Nagel Polygram SIL G/UV_{254} plates. Colorless substances were detected by oxidation with 3.5% alcoholic 12-molybdophosphoric acid and subsequent warming. Melting points were observed on a Reichert microhotstage. Boiling and melting points are not corrected. Microanalytical determinations were done at the Microanalytical Laboratory of the Institute of Organic and Bioorganic Chemistry, Göttingen. For the preparation of anhydrous $CeCl_3$, finely powdered $CeCl_3 \cdot 7H_2O$ was heated at 140 °C/0.1 Torr to constant weight.

3.2. Spiro[4.4]nonan-1-one tosylhydrazone (**12**)

To a solution of **13**[8] (30.0 g, 217 mmol) in absolute methanol (375 mL) was added *p*-toluenesulfonyl hydrazine (43.5 g, 234 mmol) and the mixture was stirred under argon at room temperature. According to TLC [pentane/ether 1:1; R_f=0.67 (**13**), 0.32 (**12**)], after 94 h the reaction was complete. The mixture was concentrated (bath temperature 35 °C/15 Torr) and the residue was washed with cold methanol (2×60 mL) and dried to constant weight (4 h at 40 °C/15 Torr, 24 h at 45 °C/0.1 Torr). The combined yield of two identical experiments amounted to 122 g (95%). Colorless solid, mp 145 °C (lit.[19e] 146–147 °C). This material was used in the next step. An analytically pure sample was obtained by crystallization from methanol, mp 148 °C. IR (KBr): 3230 (N–H), 1605 cm^{-1} (C=N); ^{1}H NMR (600 MHz, CD_3COCD_3, CD_3COCD_2H int): δ=1.36–1.44 (m, 2H), 1.50–1.59 (m, 2H), 1.61 (t, J=7 Hz, 2H), 1.61–1.70 (m, 4H), 1.70 (quint, J=7 Hz, 2H), 2.32 (t, J=7 Hz, 2H), 2.39 (s, 3H), 2.85 (br s, 1H), 7.36 (AA′-part of an AA′BB′-system, 2H), 7.76 (BB′-part of an AA′BB′-system, 2H), 8.61 (s, 1H); ^{13}C NMR (125.7 MHz, CD_3COCD_3, CD_3COCD_3 int): δ=21.38 (q), 22.11 (t), 25.55 (t), 28.48 (t), 38.29 (t), 39.82 (t), 54.80 (s), 128.74 (d), 129.89 (d), 137.68 (s), 144.10 (s), 172.64 (s); MS (EI): m/z=306 (32, M^+), 121 (100). $C_{16}H_{22}N_2O_2S$ requires C, 62.72; H, 7.24. Found: C, 62.76; H, 6.95.

3.3. 1-Bromo-spiro[4.4]non-1-ene (**11**)

To a stirred solution of **12** (29.0 g, 94.5 mmol) in anhydrous THF (280 ml) was added under argon a 1.6 M solution of *n*-butyllithium in hexane (236 mL, 378 mmol) within 1.5 h at −78 °C. After an additional 30 min at −78 °C the mixture was allowed to warm up to 20 °C and held at this temperature until the nitrogen evolution had ceased (3 h). At this stage, a GC analysis [3 m×1/4″ all glass system. 15% FFAP on Chromosorb W AW/DMCS, 60/80 mesh, 140 °C; retention times (min): 1.55 (olefin), 8.49 (**11**)] of a hydrolyzed sample indicated complete conversion to spiro[4.4]non-1-ene. The mixture was cooled to −35 °C and 1,2-dibromoethane (26.6 g, 142 mmol) was added dropwise. After the addition was complete, the mixture was stirred for 30 min at room temperature until it was poured into water (1 L) and extracted with pentane (3×300 mL). The extracts were washed with water (2×300 mL) and dried ($MgSO_4$). The solvents were evaporated on a rotary evaporator (bath temperature 40 °C/15 Torr) and the residual brown liquid was filtered through silica gel (0.05–0.20 mm) in pentane [column 25×4.5 cm; R_f=0.72 (olefin), 0.61 (**11**)] to yield 14.4 g of crude **11** as slightly yellow liquid (purity 76%, GC). The material of three identical experiments (56.0 g, purity 70%, GC) was combined and distilled over a 30 cm vigreux column to yield 40.3 g (49%) of **11** as a colorless liquid, bp 95–108 °C/35 Torr (purity 94%, GC). An analytically pure sample was obtained by preparative GC. IR (neat): 1620 cm^{-1} (C=C); ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ int): δ=1.35–1.42 (m, 2H), 1.53–1.77 (m, 6H), 1.83 (t, J=7 Hz, 2H), 2.24 (dt, J=7, 2.5 Hz, 2H), 5.97 (t, J=2.5 Hz); ^{13}C NMR (125.7 MHz, $CDCl_3$, $CDCl_3$ int): δ=24.81 (t), 30.02 (t), 36.90 (t), 37.83 (t), 58.12 (s), 129.51 (d), 131.90 (s); MS (EI): m/z=200 (36, M^+), 121 (100). $C_9H_{13}Br$ requires C, 53.75; H, 6.52. Found: C, 53.92; H, 6.51.

3.4. rel-(1R,4R)-1-(Spiro[4.4]non-1-enyl)-dispiro[3.0.4.3]-dodecan-1-ol (**15**)

To a stirred solution of **11** (16.0 g, 75 mmol) in anhydrous THF (250 mL) was added under argon a 1.5 M solution of *tert*-butyllithium in pentane (100 mL, 150 mmol) within 1.75 h at −78 °C. After additional 45 min at −78 °C the mixture was allowed to warm up to 0 °C. The resulting 0.21 M solution of 1-lithio-spiro[4.4]non-1-ene (**14**) 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 **7** (5.74 g, 30 mmol), stirring was continued for 2 h until the mixture was cooled to 0 °C and the solution of 1-lithio-spiro[4.4]non-1-ene (**14**) was added dropwise. According to TLC [pentane/ether 95:5; R_f=0.35 (**15**), 0.20 (**7**)], after an additional 30 min at room temperature the reaction was complete. The mixture was diluted with pentane (300 mL) and hydrolyzed with saturated ammonium chloride (60 mL). The organic 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 on a rotary evaporator (bath temperature 40 °C/15 Torr) and the residue (15.5 g) was chromatographed on silica gel (0.05–0.20 mm) in pentane/ether 95:5 to yield 7.0 g (77%) of pure **15** as a colorless viscous oil. IR (neat): 3650–3400 cm^{-1} (OH_{ass}); ^{1}H NMR (600 MHz, C_6D_6, C_6D_5H int): δ=1.34–1.76 (m, 19H), 1.78 (ddd, J=12, 7, 2 Hz, 1H), 1.83–1.98 (m, 4H),

2.00–2.06 (m, 1H), 2.09–2.15 (m, 2H), 2.25 (dddd, J=16, 9, 7, 2 Hz, 1H), 2.34–2.40 (m, 2H), 5.52 (dd, J=2.5, 2 Hz, 1H); ^{13}C NMR (150.8 MHz, C_6D_6, C_6D_6 int): δ=19.19 (t), 24.82 (t), 25.01 (t), 25.40 (t), 25.69 (t), 27.46 (t), 29.43 (t), 34.13 (t), 35.28 (t), 35.99 (t), 36.99 (t), 37.40 (t), 37.42 (t), 38.84 (t), 42.33 (t), 55.19 (s), 58.23 (s), 60.00 (s), 81.60 (s), 125.97 (d), 153.69 (s); MS (EI): m/z=300 (11, M^+), 164 (100). $C_{21}H_{32}O$ requires C, 83.94; H, 10.73. Found: C, 83.62; H, 10.82.

3.5. *rel-(1R,1′S,2′R,4R)-1-(1′,2′-Epoxy-spiro[4.4]non-1′-yl)-dispiro[3.0.4.3]dodecan-1-ol (**20**) and rel-(1R,1′R,2′S,4R)-1-(1′,2′-epoxy-spiro[4.4]non-1′-yl)-dispiro[3.0.4.3]dodecan-1-ol (**21**)*

To a vigorously stirred solution of **15** (500 mg, 1.66 mmol) in dichloromethane (10 mL) were added a solution of sodium bicarbonate (349 mg, 4.15 mmol) in water (6.6 mL) and a solution of 3-chloro-perbenzoic acid (821 mg, 70% w/w, 3.32 mmol) in dichloromethane (11 mL). According to TLC [pentane/ether 8:2; R_f=0.68 (**15**), 0.55 (**20**), 0.42 (**21**)], after 10 min the reaction was complete. The mixture was diluted with dichloromethane (60 mL) and the organic phase was extracted with 1 M aqueous KOH (2×60 mL), washed with water (2×60 mL), and dried ($MgSO_4$). The solvent was distilled off (bath temperature 40 °C/15 Torr) to yield 530 mg of a 3:2 mixture of **20** and **21** (^{1}H and ^{13}C NMR). Attempted separation on silica gel (0.05–0.20 mm) in pentane/ether 8:2 (column 45×2.5 cm) led to complete conversion of **21** to a mixture of ketols (see below), while 145 mg (30%) **20** persisted and were obtained pure. Colorless oil. Compound **20**: IR (neat): 3650–3350 cm^{-1} (OH_{ass}); ^{1}H NMR (600 MHz, C_6D_6, C_6D_5H int): δ=1.09–1.14 (m, 1H), 1.16–1.20 (m, 1H), 1.24–1.79 (m, 21H), 1.84–1.98 (m, 3H), 2.16–2.22 (m, 1H), 2.33–2.42 (m, 2H), 2.49–2.55 (m, 1H), 2.56 (s, 1H, OH), 3.31 (s, 1H); ^{13}C NMR (125.7 MHz, C_6D_6, C_6D_6 int): δ=19.98 (t), 25.17 (t,t) (coincidence of two lines), 25.54 (t), 26.02 (t), 28.65 (t), 32.69 (t), 33.90 (t), 34.61 (t), 34.83 (t), 35.90 (t), 36.05 (t), 37.43 (t), 38.94 (t), 53.33 (s), 55.47 (s), 60.01 (s), 63.09 (d), 71.56 (s), 81.32 (s); MS (EI): m/z=316 (2, M^+), 121 (100). $C_{21}H_{32}O_2$ requires C, 79.70; H, 10.19. Found: C, 79.45; H, 9.97. Compound **21**: the ^{1}H and ^{13}C NMR data were extracted from the spectra of the 3:2 mixture of **20** and **21**. In the ^{1}H NMR spectrum only the proton of the epoxide ring could be assigned. In the ^{13}C NMR spectrum all resonances could be identified. ^{1}H NMR (600 MHz, C_6D_6, C_6D_5H int) δ=3.20 (s, 1H); ^{13}C NMR (125.7 MHz, C_6D_6, C_6D_6 int): δ=19.56 (t), 24.71 (t), 24.72 (t), 25.14 (t), 25.35 (t), 26.22 (t), 28.71 (t), 31.31 (t), 33.89 (t), 34.03 (t), 34.87 (t), 36.04 (t), 37.78 (t), 38.06 (t), 38.10 (t), 53.38 (s), 55.85 (s), 58.75 (s), 61.58 (d), 70.69 (s), 82.48 (s).

3.6. *rel-(6R,7R,15R)-15-Hydroxy-tetraspiro[4.0.0.0.4.3.3.3]-heneicosan-16-one (**23**) and rel-(6R,7S,15S)-15-hydroxy-tetraspiro[4.0.0.0.4.3.3.3]heneicosan-16-one (**24**)*

3.6.1. *From **20** and **21***

A 3:2 crude mixture of **20** and **21** (525 mg), obtained by epoxidation of **15** (500 mg, 1.66 mmol), was dissolved in dry dichloromethane (250 mL) and rearranged at 0 °C by dropwise addition of boron trifluoride etherate (90 μL). According to TLC [pentane/ether 8:2; R_f=0.55 (**20**), 0.42 (**21**), 0.18 (**24**), 0.11 (**23**)], after the last drop the rearrangement was complete. The mixture was stirred with potassium carbonate (30 g) until it was filtered and concentrated (bath temperature 40 °C/15 Torr) to yield 510 mg of a slightly impure 9:1 mixture of **23** and **24** (^{1}H and ^{13}C NMR). Chromatography on silica gel (0.05–0.20 mm) in pentane/ether 8:2 yielded 12 mg (2%) of **24** as colorless liquid (purity 85%, ^{13}C NMR) and 327 mg (62%) of **23** as colorless solid, mp 142–145 °C (purity 99%, ^{1}H NMR). An analytically pure sample was obtained by crystallization from acetone by diffusion of water, mp 146–147 °C. Compound **23**: IR (KBr): 3600–3200 (OH_{ass}), 1725 cm^{-1} (C=O); ^{1}H NMR (600 MHz, C_6D_6, C_6D_5H int) δ=1.01–1.05 (m, 1H), 1.19–1.23 (m, 1H), 1.29–1.71 (m, 22H), 1.77–1.83 (m, 1H), 1.94–2.05 (m, 2H), 2.10–2.18 (m, 2H), 2.44–2.54 (m, 2H), 4.53 (symm m, 1H); ^{13}C NMR (125.7 MHz, C_6D_6, C_6D_6 int): δ=20.13 (t), 23.53 (t), 23.70 (t), 24.67 (t), 24.71 (t), 31.16 (t), 32.80 (t), 33.50 (t), 35.58 (t), 35.93 (t), 37.34 (t), 37.47 (t), 38.02 (t), 39.43 (t), 40.21 (t), 57.13 (s), 57.94 (s), 58.56 (s), 70.58 (s), 76.49 (d), 221.84 (s); MS (EI): m/z=316 (28, M^+), 108 (100). $C_{21}H_{32}O_2$ requires C, 79.70; H, 10.19. Found: C, 79.46; H, 10.13. Compound **24**: ^{1}H NMR (600 MHz, C_6D_6, C_6D_5H int) δ=1.10–1.15 (m, 1H), 1.17–1.90 (m, 26H), 2.07 (symm m, 1H), 2.20 (symm m, 1H), 2.26 (symm m, 1H), 2.32–2.41 (br s, 1H), 3.79 (dd, J=7.5, 5.5 Hz, 1H); ^{13}C NMR (125.7 MHz, C_6D_6, C_6D_6 int): δ=20.87 (t), 22.93 (t), 23.41 (t), 23.53 (t), 24.46 (t), 29.03 (t), 31.65 (t), 31.74 (t), 33.44 (t), 35.26 (t), 35.48 (t), 35.75 (t), 36.18 (t), 36.32 (t), 37.83 (t), 56.53 (s), 56.61 (s), 62.86 (s), 82.56 (d), 224.88 (s).

3.6.2. *From **20***

A solution of analytically pure **20** (5.0 mg, 16 μmol) in C_6D_6 (160 μL) was placed in a 3 mm o.d. NMR tube. Addition of 10 μL (2.7 μmol) of a 0.27 M solution of boron trifluoride etherate in C_6D_6 induced complete conversion to a 9:1 mixture of **23** and **24** (^{1}H and ^{13}C NMR).

3.7. *4-Nitrobenzoic acid rel-(6R,7R,15R)-16-oxo-tetraspiro[4.0.0.0.4.3.3.3]heneicos-15-yl ester (**22**)*

A solution of 4-nitrobenzoic acid chloride (23 mg, 0.12 mol) and **23** (30 mg, 0.10 mmol) in dry pyridine (200 μL) was stirred under argon at 90 °C. According to TLC [pentane/ether 8:2; R_f=0.31 (**22**), 0.11 (**23**)], after 1 h the reaction was complete. The mixture was diluted with water (2 mL) and extracted with dichloromethane (4 mL). The extract was washed with 1 N aqueous HCl, water (2×3 mL) and dried (K_2CO_3). The solvent was evaporated (bath temperature 40 °C/15 Torr) and the residue (48 mg) purified by thick layer chromatography in pentane/ether 8:2 to yield 12.4 mg (28%) of **22** as a colorless solid, mp 193 °C (crystallized from ethanol). IR (KBr): 1720 cm^{-1} (C=O); ^{1}H NMR (600 MHz, C_6D_6, C_6D_5H int) δ=1.08 (symm m, 1H), 1.19–1.31 (m, 3H), 1.33–1.74 (m, 17H), 1.76–1.88 (m, 5H), 2.12 (symm m, 1H), 2.26 (dd,

J=18, 8 Hz, 1H), 2.45 (symm m, 1H), 2.71 (symm m, 1H), 5.72 (dd, J=9, 4 Hz, 1H), 7.56 (AA′-part of an AA′BB′-system, 2H), 7.75 (BB′-part of an AA′BB′-system, 2H); ^{13}C NMR (125.7 MHz, C_6D_6, C_6D_6 int): δ=20.32 (t), 23.55 (t), 23.65 (t), 24.66 (t), 25.01 (t), 30.89 (t), 31.16 (t), 32.71 (t), 36.00 (t), 36.30 (t), 37.17 (t), 37.34 (t), 37.56 (t), 39.34 (t), 40.49 (t), 57.19 (s), 57.73 (s), 58.85 (s), 68.22 (s), 81.50 (s), 123.65 (d), 130.25 (d), 135.20 (s), 150.67 (s), 163.83 (s), 217.61 (s); MS (EI): m/z=465 (2, M^+), 298 (100). $C_{28}H_{35}NO_5$ requires C, 71.92; H, 7.98. Found: C, 72.29; H, 7.78.

3.8. Reduction of *23*: rel-(6R,7R,15R,16R)-tetraspiro-[4.0.0.0.4.3.3.3]heneicosan-15,16-diol (*28*), rel-(1R,5S)-1-[1-(3-hydroxy-propyl)-cyclopentyl]-dispiro[4.0.4.3]tridecan-2-one (*29*), and rel-(1R,5R)-1-[1-(3-hydroxy-propyl)-cyclopentyl]-dispiro[4.0.4.3]tridecan-2-one (*30*)

To a stirred suspension of $LiAlH_4$ (600 mg, 15.8 mmol) in anhydrous ether (30 mL) was added under argon a solution of **23** (1.00 g, 3.16 mmol) in anhydrous ether (40 mL) and the mixture was heated to reflux. According to TLC [pentane/ether 1:1; R_f=0.42 (**23**), 0.22 (**28**), 0.13 (**29**, **30**)], after 3 h the reaction was complete. Water (0.6 mL), 15% aqueous potassium hydroxide (0.6 mL), and water (1.8 mL) were added, the liquid was decanted, and the residue was extracted with ether (3×25 mL). The combined organic phases were dried ($MgSO_4$) and concentrated (bath temperature 40 °C/15 Torr), and the heterogeneous residue (960 mg) was chromatographed on silica gel (0.05–0.20 mm) in ethyl acetate/hexane 1:1 [column 90×4.5 cm; R_f=0.52 (**28**), 0.41 (**29**, **30**)] to yield 605 mg (60%) of **28** as a colorless solid, mp 153 °C, and 276 mg (28%) of a 1:1 mixture of **29** and **30** as a colorless oil. An analytically pure sample of **28** was obtained by crystallization from ethanol by diffusion of water, mp 154–158 °C. Compound **28**: IR (KBr): 3600–3200 cm^{-1} (OH_{ass}); ^{1}H NMR (600 MHz, $CDCl_3$, $CHCl_3$ int): δ=1.22–1.69 (m, 20H), 1.70–1.77 (m, 3H), 1.83 (symm m, 2H), 1.94 (symm m, 1H), 2.09–2.25 (m, 4H), 4.56 (dd, J=9, 7 Hz, 1H), 4.61 (dd, J=6.5, 6.5 Hz, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$, $CDCl_3$ int): δ=19.23 (t), 23.47 (t), 23.91 (t), 24.08 (t), 24.72 (t), 32.20 (t), 33.48 (t), 34.29 (t), 34.40 (t), 34.67 (t), 35.69 (t), 37.04 (t), 38.95 (t), 39.08 (t), 39.50 (t), 55.88 (s), 57.67 (s), 59.99 (s), 65.68 (s), 75.62 (d), 77.36 (d); MS (DCI): m/z=336 (63, $[M+NH_4]^+$), 318 (52, $[M-H_2O+NH_4]^+$). $C_{21}H_{34}O_2$ requires C, 79.19; H, 10.76. Found: C, 78.93; H, 10.50. The data for **29** and **30** account for the 1:1 mixture: IR (neat): 3600–3200 (OH_{ass}), 1725 cm^{-1} (C=O); ^{1}H NMR (600 MHz, C_6D_6, C_6D_5H int): δ=0.92–0.97 (m, 1H), 0.98–1.04 (m, 1H), 1.04–1.10 (m, 1H), 1.17–1.93 (m, 55H), 2.01 (symm m, 2H), 2.03–2.13 (m, 3H), 2.14 (s, 1H), 3.30–3.34 (m, 2H), 3.36–3.40 (m, 2H); ^{13}C NMR (150.8 MHz, C_6D_6, C_6D_6 int, 70 °C): δ=18.53 (t), 20.02 (t), 23.78 (t), 24.07 (t), 24.80 (t), 24.83 (t), 25.04 (t), 25.11 (t), 25.17 (t), 25.85 (t), 28.71 (t), 29.08 (t), 30.07 (t), 32.30 (t), 34.32 (t), 34.40 (t), 34.59 (t,t) (coincidence of two lines), 34.62 (t), 35.41 (t), 35.87 (t), 36.31 (t), 36.46 (t,t) (coincidence of two lines), 36.92 (t), 37.02 (t), 38.35 (t), 38.44 (t), 40.09 (t), 41.80 (t), 48.45 (s), 50.16 (s), 55.44 (s), 56.04 (s), 58.69 (s), 58.71 (s), 59.88 (d), 63.58 (d,t) (coincidence of two lines), 63.80 (t), 217.48 (s), 221.56 (s); MS (EI): m/z=318 (3, M^+), 192 (100); HRMS m/z (M^+) calcd 318.2559, obsd 318.2553.

3.9. Reductive rearrangement of *20*: rel-(6R,7R,15R,16R)-tetraspiro[4.0.0.0.4.3.3.3]heneicosan-15,16-diol (*28*)

The reductive rearrangement of **20** (36.6 mg, 0.12 mmol) with $LiAlH_4$ (30.0 mg, 0.80 mmol) in anhydrous ether (3.5 mL) was performed as described for the reduction of **23** (see Section 3.8). After 1.5 h of reflux, TLC [pentane/ether 1:1; R_f=0.67 (**20**), 0.22 (**28**)] indicated that the reaction was complete. Hydrolysis and work up yielded 36.8 mg (100%) of **28** as a colorless solid (purity 95%). The ^{1}H and ^{13}C NMR data were identical with those of the product given in Section 3.8.

3.10. rel-(1R,5S)-1-[1-(3-Chloro-propyl)-cyclopentyl]-dispiro[4.0.4.3]tridecan-2-one (*31*)

To a stirred solution of a 1:1 mixture of **29** and **30** (240 mg, 0.76 mmol) in dry pyridine (6.0 mL) was added *p*-toluenesulfonic acid chloride (430 mg, 2.26 mmol) under argon at room temperature. The reaction progress was monitored by TLC [CH_2Cl_2; R_f=0.69 (**31**), 0.50 (tosylates), 0.05 (**29**, **30**)]. After 24 h the alcohols had been consumed and 70% of the initially formed tosylate(s) had been chlorinated (^{1}H NMR). To accelerate the chlorination, the remaining acid chloride was hydrolyzed with water (27 mg, 1.52 mmol), and after an additional 36 h the chlorination was complete (^{1}H NMR). The mixture was poured into water and extracted with dichloromethane (4×40 mL). The combined organic phases were washed with water (120 mL), dried ($MgSO_4$), and concentrated (bath temperature 40 °C/15 Torr) to yield 390 mg of a pyridine-containing liquid. Chromatography on silica gel (0.05–0.20 mm) in dichloromethane (column 45×2.5 cm) yielded 83 mg (33%) of **31** as a colorless oil (purity 95%). This material was cyclized without further purification. ^{1}H NMR (600 MHz, $CDCl_3$, $CHCl_3$ int): δ=1.10–1.16 (m, 1H), 1.19–1.26 (m, 2H), 1.30–1.37 (m, 1H), 1.42–1.78 (m, 21H), 1.93–2.00 (m, 1H), 2.02–2.30 (m, 5H), 3.43–3.51 (m, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$, $CDCl_3$ int): δ=19.44 (t), 22.99 (t), 24.22 (t), 24.54 (t), 25.27 (t), 28.29 (t), 31.74 (t), 33.77 (t), 33.96 (t), 34.93 (br t), 34.96 (t), 35.71 (t), 36.31 (br t), 37.88 (t), 38.13 (t), 45.96 (s), 49.46 (s), 55.49 (s), 58.04 (br d), 224.44 (s); MS (EI): m/z=300 (5, M^+–HCl), 96 (100).

3.11. rel-(6R,7S,16R)-7,16-Methano-trispiro[4.0.1.4.5.3]-eicosan-21-one (*32*)

To a stirred suspension of potassium hydride (71 mg, 1.8 mmol) in dry toluene (4.0 mL) was added **31** (75 mg, 0.22 mmol) under argon. After the hydrogen evolution had ceased, the mixture was heated to 110 °C. According to GC

[3 m×1/4″ all glass system, 15% OV 210 on Chromosorb W/AW DMCS 60/80 mesh, 230 °C; retention times (min): 13.1 (**32**), 24.3 (**31**)], after 2 h the reaction was complete. The mixture was diluted with pentane (8 mL) and hydrolyzed with water (4 mL). The phases were separated, the aqueous phase was extracted with pentane (2×8 mL), and the combined organic phases were washed with water (10 mL) and dried ($MgSO_4$). The solvent was evaporated (bath temperature 40 °C/15 Torr) and the residue (57 mg) purified by thick layer chromatography in pentane/ether 9:1 [R_f=0.36 (**32**)] to yield 29.4 mg (44%) of pure **32** as a colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$, $CHCl_3$ int): δ=1.12–1.25 (m, 3H), 1.26–1.39 (m, 2H), 1.40–1.73 (m, 21H), 1.78 (symm m, 1H), 1.88–1.98 (m, 2H), 2.02 (s, 1H), 2.40–2.48 (m, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$, $CDCl_3$ int): δ=19.21 (t), 20.99 (t), 23.12 (t), 23.92 (t), 24.65 (t,t) (coincidence of two lines), 29.65 (t), 33.41 (t), 33.47 (t), 34.04 (t), 35.90 (t), 36.48 (t), 40.46 (t), 42.62 (t), 44.95 (d), 46.43 (s), 52.73 (s), 57.56 (s), 62.93 (d), 224.44 (s); MS (EI): *m/z*=300 (100, M^+); HRMS *m/z* (M^+) calcd 300.2453, obsd 300.2453.

3.12. rel-(6R,7S,16R,21R)-7,16-Methano-trispiro-[4.0.1.4.5.3]eicosan-21-ol (34) and 4-nitrobenzoic acid rel-(6R,7S,16R,21R)-7,16-methano-trispiro[4.0.1.4.5.3]eicos-21-yl ester (35)

To a stirred suspension of $LiAlH_4$ (20 mg, 0.51 mmol) in anhydrous ether (0.7 mL) was added under argon a solution of **32** (24 mg, 0.080 mmol) in anhydrous ether (1.0 mL) and the mixture was heated to reflux. After 1.5 h, TLC [pentane/ether 8:2; R_f=0.56 (**32**), 0.40 (**34**)] indicated that the reaction was complete. The mixture was diluted with ether (4 mL) and hydrolyzed by successive addition of water (20 μL), 15% potassium hydroxide (20 μL), and water (60 μL). The liquid phase was decanted and the residue extracted with ether (3×4 mL). The combined organic phases were dried ($MgSO_4$) and concentrated (bath temperature 40 °C/15 Torr) to yield 19.3 mg (80%) of **34** as a colorless oil (purity 95%). ^{1}H NMR (600 MHz, $CDCl_3$, $CHCl_3$ int): δ=1.08 (symm m, 1H), 1.20–1.71 (m, 25H), 1.78 (symm m, 1H), 1.86–1.91 (m, 2H), 1.91–2.13 (m, 3H), 2.28 (symm m, 1H), 4.40 (dd, *J*=7.5, 7.5 Hz, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$, $CDCl_3$ int): δ=19.56 (t), 22.21 (t), 22.86 (t), 23.39 (t), 24.06 (t), 24.91 (t), 31.58 (t), 34.69 (t), 34.78 (t), 35.37 (t), 37.27 (t), 37.84 (t), 40.56 (t), 40.65 (t), 40.70 (t), 44.45 (d), 50.01 (s), 56.09 (d), 56.65 (s), 58.47 (s), 78.40 (d). To a solution of the crude **34** in dry pyridine (500 μL) was added 4-nitrobenzoic acid chloride (15.4 mg, 0.083 mmol). The resulting solution was stirred at 90 °C under argon. According to TLC [pentane/ether 8:2; R_f=0.65 (**35**), 0.40 (**34**)], after 9 h the reaction was nearly complete. The mixture was diluted with water (6 mL) and extracted with dichloromethane (4×4 mL). The combined organic phases were washed with 1 N aqueous HCl (8 mL), water (2×10 mL), and dried ($MgSO_4$). The solvent was evaporated (bath temperature 40 °C/15 Torr) and the residue (22 mg) purified by thick layer chromatography in pentane/ether 8:2 to yield 15.4 mg (53%) of **35** as a colorless solid, mp 164 °C, and 2.4 mg (10%) of recovered **34**. Compounds **35**: ^{1}H NMR (600 MHz, C_6D_6, C_6D_5H int): δ=1.05 (dd, *J*=13, 2 Hz, 1H), 1.17–1.80 (m, 24H), 1.83–1.95 (m, 4H), 2.00 (symm m, 1H), 2.33 (d, *J*=7 Hz, 1H), 2.37–2.43 (m, 1H), 5.67 (dd, *J*=7.5, 7.5 Hz, 1H), 7.63 (AA′-part of an AA′BB′-system, 2H), 7.88 (BB′-part of an AA′BB′-system, 2H); ^{13}C NMR (125.7 MHz, C_6D_6, C_6D_6 int): δ=19.95 (t), 22.45 (t), 23.29 (t), 23.67 (t), 24.50 (t), 25.28 (t), 32.36 (t), 35.25 (t), 35.32 (t), 36.14 (t), 36.16 (t), 38.39 (d), 38.48 (t), 41.06 (t), 41.21 (t), 42.00 (t), 50.28 (s), 54.18 (d), 56.85 (s), 58.51 (s), 80.08 (d), 123.66 (d), 130.40 (d), 135.88 (s), 150.52 (s), 164.62 (s); MS (EI): *m/z*=451 (2, M^+), 284 (100); HRMS *m/z* (M^+) calcd 451.2722, obsd 451.2722.

3.13. Trispiro[4.0.1.4.6.3]heneicos-7,15-en-16-one (36)

3.13.1. From 23 with phosphorous oxychloride

To a stirred solution of **23** (100 mg, 0.31 mmol) in dry pyridine (2.2 mL) was added phosphorous oxychloride (121 mg, 0.79 mmol) at 0 °C under argon. After 3 h the mixture was allowed to warm up to room temperature, and after an additional 20 h, TLC [pentane/ether 7:3, R_f=0.34 (**36**), 0.25 (**23**)] indicated that the reaction was complete. The mixture was diluted with water (8 mL) and extracted with ether (15 mL). The organic phase was washed with 1 N aqueous HCl (2×6 mL), water (3×10 mL), and dried ($MgSO_4$). The solvent was distilled off (bath temperature 40 °C/15 Torr), and the residue (46 mg) was purified by thick layer chromatography in pentane/ether 7:3 to yield 37.4 mg (40%) of **36** as a colorless solid, mp 82–84 °C. This material was recrystallized from ethanol (2.5 mL) by diffusion of water (2.5 mL) to yield 18.4 mg of pure **36**, mp 86–88 °C. IR (KBr): 1655 cm^{-1} (C=O); ^{1}H NMR (600 MHz, C_6D_6, C_6D_5H int): δ=1.05–1.12 (m, 1H), 1.13–1.55 (m, 21H), 1.61 (dd, *J*=12, 7.5 Hz, 1H), 1.82 (ddd, *J*=14, 6.5, 1 Hz, 1H), 2.05–2.11 (m, 1H), 2.18–2.26 (m, 2H), 2.36 (ddd, *J*=16.5, 10.5, 7.5 Hz, 1H), 2.54 (ddd, *J*=19, 13, 6.5 Hz, 1H), 2.84 (dd, *J*=16.5, 8.5 Hz, 1H); ^{13}C NMR (125.7 MHz, C_6D_6, C_6D_6 int): δ=21.09 (t), 21.91 (t), 22.94 (t), 23.72 (t), 25.94 (t), 26.96 (t), 35.09 (t), 35.70 (t), 35.96 (t), 36.09 (t), 36.11 (t), 36.34 (t), 37.26 (t), 38.16 (t), 38.75 (t), 49.94 (s), 60.47 (s), 62.15 (s), 139.47 (s), 169.12 (s), 196.60 (s); MS (EI): *m/z*=298 (100, M^+). $C_{21}H_{30}O$ requires C, 84.51; H, 10.13. Found: C, 84.36; H, 10.11.

3.13.2. From 23 with methyltriphenoxyphosphonium iodide

To a stirred solution of **23** (50.0 mg, 0.16 mmol) in hexamethylphosphoramide (530 μL) was added methyltriphenoxyphosphonium iodide (152 mg, 0.34 mmol) under argon and the mixture was heated to 75 °C. According to TLC [pentane/ether 8:2, R_f=0.18 (**36**), 0.12 (**23**)], after 16 h the reaction was complete. Aqueous KOH (2 N, 4 mL) was added, the mixture was extracted with ether (3×6 mL), and the combined extracts were washed with water (2×8 mL), and dried ($MgSO_4$). The solvent was evaporated (bath temperature 40 °C/15 Torr) to yield 34.4 mg (72%) of slightly impure **36** as a highly viscous oil (purity 95%). The ^{1}H and ^{13}C NMR data were identical with those of the product given in Section 3.8.

*3.13.3. From **23** with 4-methylphenyl thiochloroformate*

To a stirred solution of **23** (50 mg, 0.16 mmol) in dry pyridine (580 μL) was added at room temperature under argon a solution of 4-methylphenyl thiochloroformate (45 mg, 0.24 mmol) in anhydrous THF (75 μL). After 72 h, TLC [pentane/ether 8:2, R_f=0.60, 0.53, 0.46, 0.40, 0.30, 0.35, 0.18 (**36**), 0.12 (**23**)] indicated that at least seven products had been formed. The mixture was worked up as described in Section 3.13.1, and the residue (64 mg) was subjected to thick layer chromatography in pentane/ether 8:2. Of the products formed, only **36** (5.2 mg, 11%) could be obtained pure. Its ^{1}H and ^{13}C NMR data were identical with those of the product given in Section 3.8.

*3.14. rel-(6R,7R)-Tetraspiro[4.0.0.0.4.3.3.3]heneicosan-15,16-dione (**37**)*

To a stirred suspension of pyridinium chlorochromate (371 mg, 1.72 mmol) in dichloromethane (0.8 mL) was added under argon a solution of **23** (223 mg, 0.71 mmol) in dichloromethane (1.5 mL) causing an exothermic effect and the separation of black grease. According to TLC [pentane/ether 7:3; R_f=0.57 (**37**), 0.25 (**23**)], after 1.5 h the reaction was complete. The supernatant liquid was decanted and the residual grease extracted with ether (3×1 mL). The combined organic phases were filtered through silica gel (0.05–0.20 mm, column 14×1 cm) and concentrated (bath temperature 40 °C/15 Torr) to yield 199 mg of crude **37** as a highly viscous yellow oil. Thick layer chromatography in pentane/ether 7:3 yielded 143 mg (64%) of pure **37** as a colorless solid, mp 116–119 °C. IR (KBr): 1738, 1705 cm^{-1} (C=O); ^{1}H NMR (600 MHz, C_6D_6, C_6D_5H int): δ=1.10–1.15 (m, 1H), 1.15–1.20 (m, 1H), 1.22–1.48 (m, 12H), 1.49–1.69 (m, 8H), 1.89 (symm m, 1H), 1.96 (ddd, J=18, 13, 9.5 Hz, 1H), 2.03 (ddd, J=18, 13, 9.5 Hz, 1H), 2.200 (dd, J=18, 8.5 Hz, 1H), 2.202 (dd, J=18, 8.5 Hz, 1H), 2.32 (symm m, 1H), 2.49 (dddd, J=13, 13, 8.5, 2 Hz, 1H), 2.83 (dddd, J=13, 13, 8.5, 2 Hz, 1H); ^{13}C NMR (125.7 MHz, C_6D_6, C_6D_6 int): δ=23.06 (t), 23.64 (t), 23.97 (t), 24.24 (t), 25.31 (t), 31.24 (t), 36.00 (t), 36.26 (t), 36.88 (t), 38.23 (t,t) (coincidence of two lines), 38.46 (t), 39.08 (t), 39.47 (t), 42.90 (t), 54.93 (s), 56.06 (s), 60.44 (s), 79.06 (s), 214.22 (s), 215.36 (s); MS (EI): m/z=314 (100, M^+). $C_{21}H_{30}O_2$ requires C, 80.21; H, 9.62. Found: C, 79.95; H, 9.35.

*3.15. X-ray analyses of rel-(6R,7R,15R)-**22**, (6R,7S,16R,21R)-**35** and **36***

X-ray data were collected at 100 K on a Bruker three-circle diffractometer with mirror-monochromated Cu Kα radiation (λ=1.54178 Å) equipped with a SMART 6000 area detector. The structures were solved by using direct methods with SHELXS-97 and refined by full-matrix least-squares on F^2 for all data with SHELXL-97.[25] All non-hydrogen atoms were refined anisotropically. A riding model with idealized geometry was employed for all hydrogen atoms. Data for (6*R*,7*S*,16*R*,21*R*)-**35** were collected on a non-merohedrally twinned crystal. The fractional contribution of the second twin domain was refined to 0.1346(19). The crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC 668187 (**36**), 668188 (**35**), and 668189 (**22**). Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 (0)1223 336033 or e-mail: deposit@ccdc.cam.ac.uk).

Supplementary data

^{1}H and ^{13}C NMR spectra of **11**, **12**, **15**, **20**–**24**, **28**–**32**, and **34**–**37**, and data of the X-ray analyses including ORTEP plots of **22**, **35**, and **36**. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2008.02.073.

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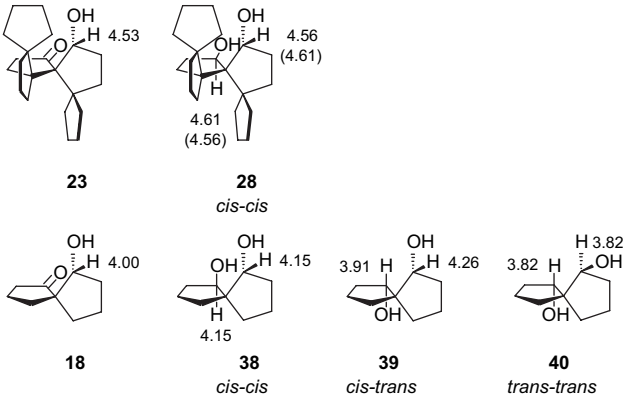

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