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Percycloalkylated cyclohexanes: attempted synthesis of a trispropellane☆

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ABSTRACT

The acid catalyzed rearrangement of two cyclohexanols of spiroannelated four-membered rings has been studied. In accordance with molecular mechanics calculations, far-reaching reorganizations with formation of unsaturated hexacyclic systems, including a fully cycloalkylated cyclohexene with a bispropellane partial structure, were observed. Attempts to convert this bispropellane to a trispropellane failed.

1. Introduction

The structure, conformation and dynamics of percycloalkylated cyclohexanes strongly depend on the degree of nonbonding interactions. These, in turn, depend on the topology, i.e., on the ring size and on the way the rings are tied up. Of a number of examples known,[2–8] [6.4]rotane **1**[7] and [6.5]coronane **2**[5] mark two extremes: the spiroannelated **1** exists at room temperature in a fixed chair conformation and its barrier of inversion ($\Delta G^{\neq}_{487}$=156.8 kJ/mol) exceeds those of other percycloalkylated cyclohexanes by far.[9] In contrast, the edge-annelated **2** adopts at room temperature a flexible chair conformation and its barrier of inversion ($\Delta G^{\neq}_{173}\leq$35.9 kJ/mol) falls even below that of cyclohexane ($\Delta G^{\neq}_{298}$=42.3 kJ/mol).[10] This illustrates the fact, that within the half-chair as transition state, the energetically most important interactions are exclusively nonbonding (C1–C6, C3–C8) and hence strong in **1**, but are to the half part of a pseudorotation of a five-membered ring (C2–C4) and hence weak in **2** (Fig. 1). As in the half-chair of the trispropellane **3**[11] two pseudorotations (C13–C15, C16–C18) are passed through, its barrier of inversion should once again lowered. We herein report on an attempted synthesis.

2. Results

Our approach was based on the fact, that on treatment with thionyl chloride in pyridine the alcohol **4** rearranges to the 1,5-diene **5**, which, after hydrozirconization and bromination may be cyclized to **2**.[5] It thus seemed obvious that the 1,5-diene **6** would be a promising candidate for a synthesis of the trispropellane **3** (Scheme 1). However, it seemed not sure, that the envisaged acid catalyzed rearrangement of **4** and/or **5** would lead to the desired bispropellane **6**. We therefore decided to use the alcohols **8**[12] and **10**[13] as a model, and to study their acid catalyzed rearrangements both by molecular mechanics using our conformational search routine HUNTER[14] in connection with MMP2,[15] and experimentally. As **8** had formerly been rearranged with thionyl chloride in pyridine to yield the hexacyclic olefin **22**,[12] we could be sure that an acid catalyzed rearrangement would at least go as far, but probably would go beyond. Therefore, the calculations on **8** and **10** were restricted to the carbenium ions **12**–**16** and **17**–**21**, respectively, and to all olefins derived from these (Scheme 2).

As it could have been expected, the differences in the calculated enthalpies of formation in going from **7** to **12**, and from **9** to **17** were large.[16] However, in going from **12** to **16**, and from **17** to **21**, these differences became small. Together with the fact, that all dihedral angles between the empty p-orbitals and the bonds to be shifted were small, an unhindered equilibration within the two sets of carbenium ions could be expected.[17] Therefore, the differences in the calculated enthalpies of formation of the corresponding olefins were thought to decide on what products would be formed. In this respect, the result was clear: in the case of **8**, the

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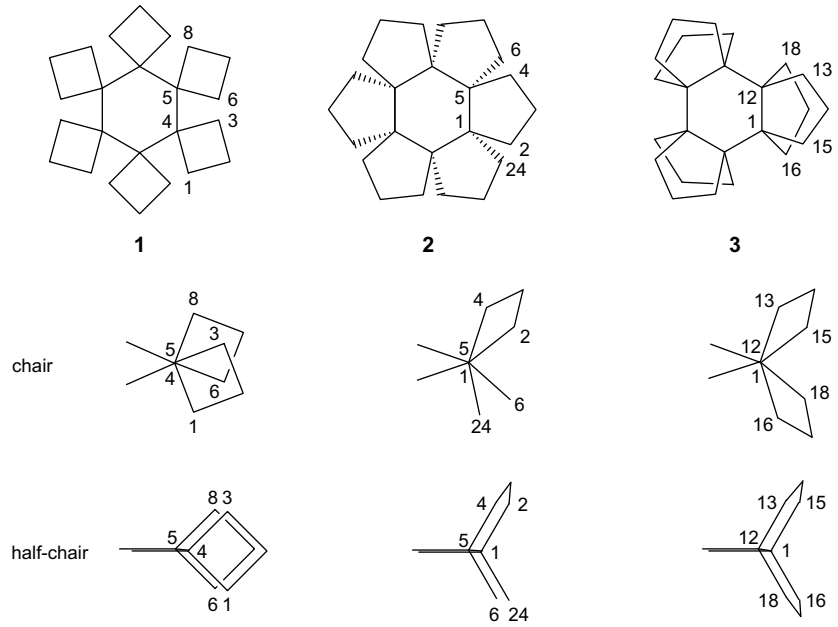


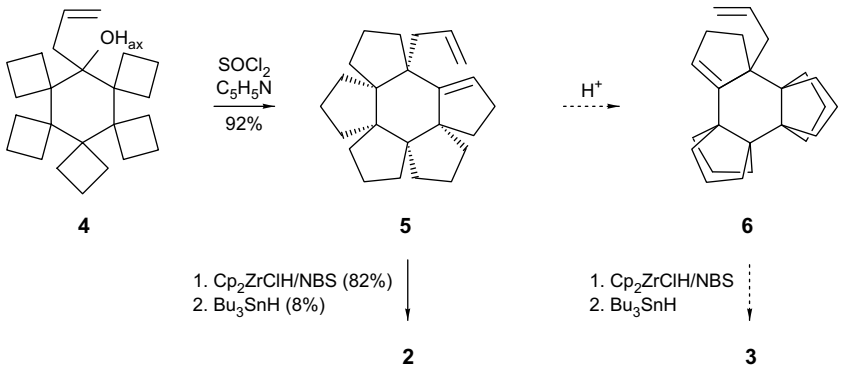
Figure 1. [6.4]Rotane **1**, [6.5]coronane **2** and trispropellane **3**: geometries of the ground state (chair) and the transition state (half-chair) in Newman projection.

favoured products were **22** and/or **24**, and in the case of **10**, the favoured product was **11**. Of these, **11** represented another potential precursor of **3**.

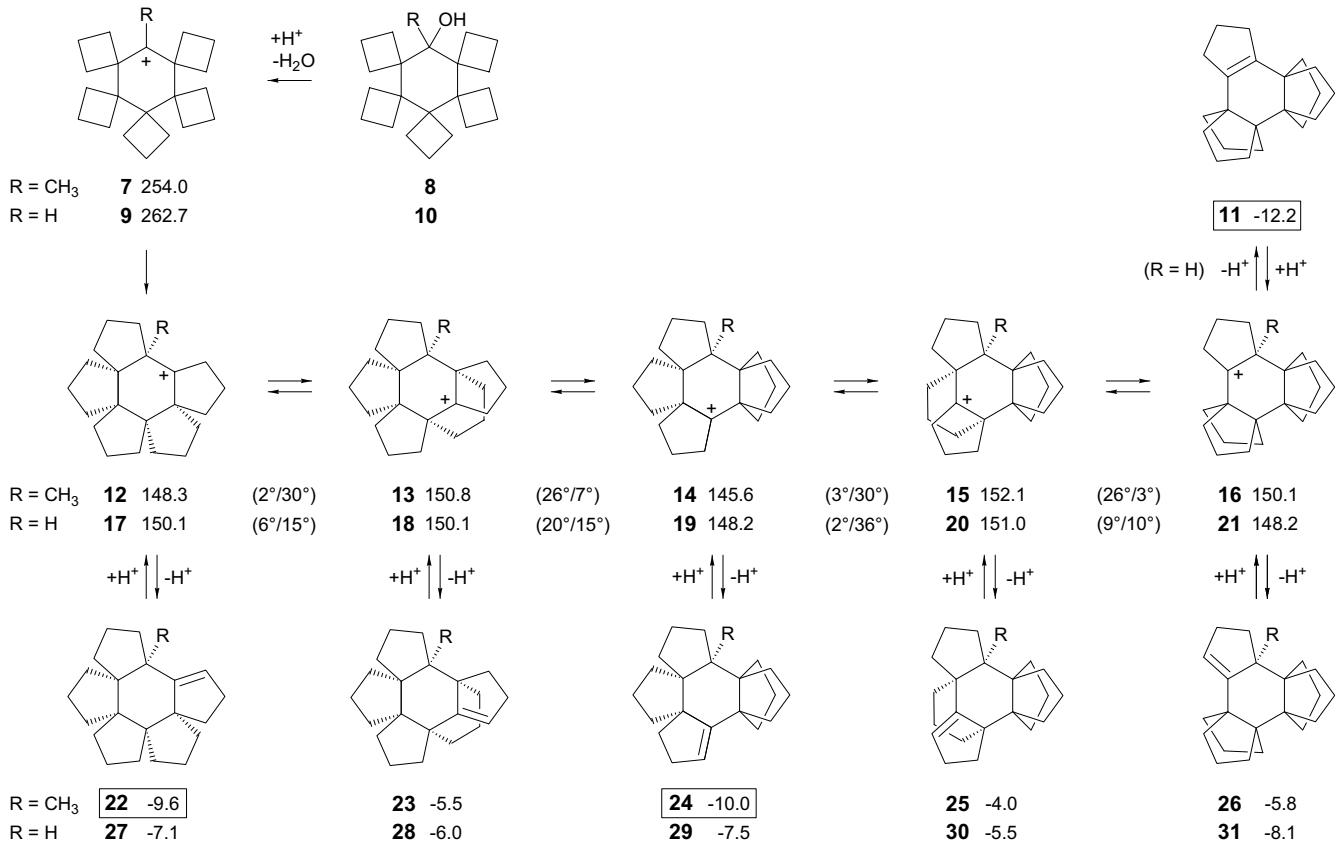
For the synthesis of the educts required, we reacted ketone **32**[7] with methyllithium and lithium aluminium hydride, respectively. The resulting alcohols **8**[12] and **10**[13] were subsequently heated with 1.1 equiv of a 0.05 molar solution of anhydrous *p*-toluenesulfonic acid in benzene to 70 °C. In accord with the calculated heats of formation, **8** rearranged within 5 min to yield a 45:55 mixture of **22** and **24**, while **10** rearranged within 40 min to yield the bispropellane **11**. Interestingly, under more forcing conditions, i.e., on use of 5.0 equiv of a 0.58 molar solution of *p*-toluenesulfonic acid in benzene under otherwise unchanged conditions, two new products were observed: the alcohol **8** and the 45:55 mixture of **22** and **24** now rearranged to **33**, while the bispropellane **11** rearranged to **36** (Scheme 3). Of the products formed, **22** was identified by its known ^{1}H and ^{13}C NMR data,[12] while the structure of **24** followed from an analysis of its ^{1}H and ^{13}C NMR spectra in connection with COSY, HMQC and HMBC measurements. Olefin **33** was identified by a 2D INADEQUATE[18] experiment, and **11** and **36** by crystal structure analyses of the epoxides **34** and **35**, respectively.

To rationalize the formation of **33** and **36**, originally not taken into account, additional molecular mechanics calculations proved necessary. This time we started with the carbenium ions **13** and **20**, which had already been identified as precursors of **24** and **11**, respectively. As may be seen from the calculated enthalpies of formation and the dihedral angles between the empty orbitals and the bonds to be shifted, the formation of **33** may be explained by three 1,2-shifts (**13**–**37**–**38**–**43**) starting with **13**, and the formation of **36** by two 1,2-shifts (**20**–**44**–**45**) starting with **20** (Scheme 4). In both cases the second 1,2-shift is associated with a large energy gain, and in both cases the observed olefin is favoured over all congeners (**40**–**42**, **47**–**50**), which may be derived from carbenium ions (**37**, **39** and **44**, **46**) formed in between.

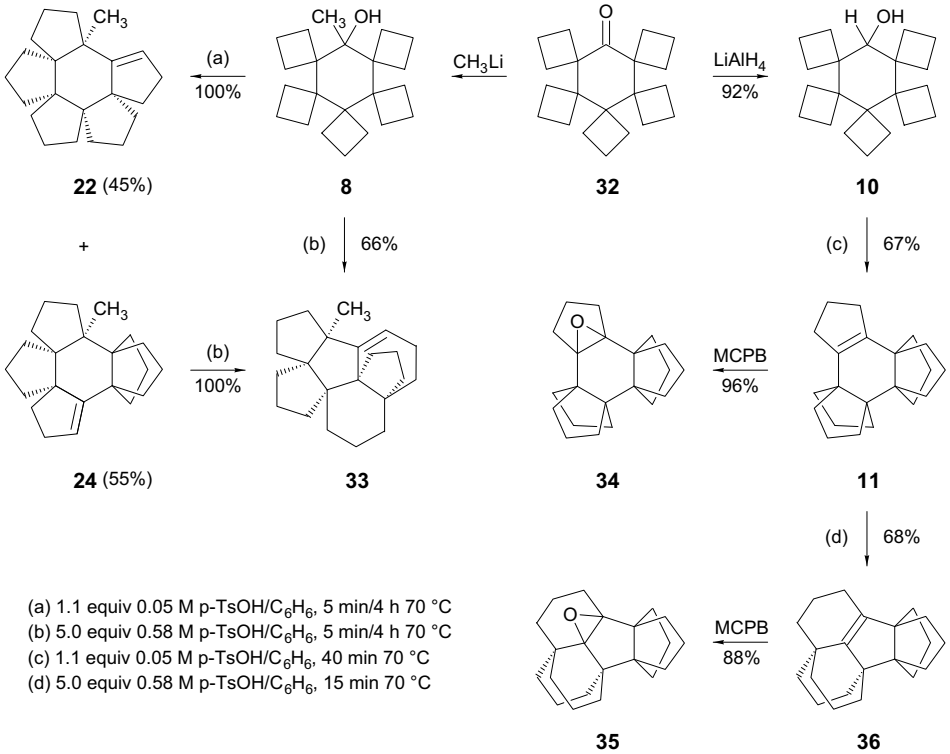
At this stage it became clear, that a rearrangement of diene **5** to diene **6** as most promising precursor of the desired trispropellane **3** would not be feasible. Therefore, we turned our attention to the bispropellane **11** and the epoxide **34** as two other potential precursors of **3** and studied several annelation procedures (Scheme 5). However, to our disappointment, the double bond of **11** proved unreactive not only in attempted [2+2]-cycloadditions with dichloroketene, as generated from trichloroacetyl chloride with zinc under sonification,[19] and with allene catalyzed by ethyl aluminium dichloride,[20] but also in attempted [2+1]-cycloadditions with chloromethylcarbene, as generated from 1,1-dichloroethane



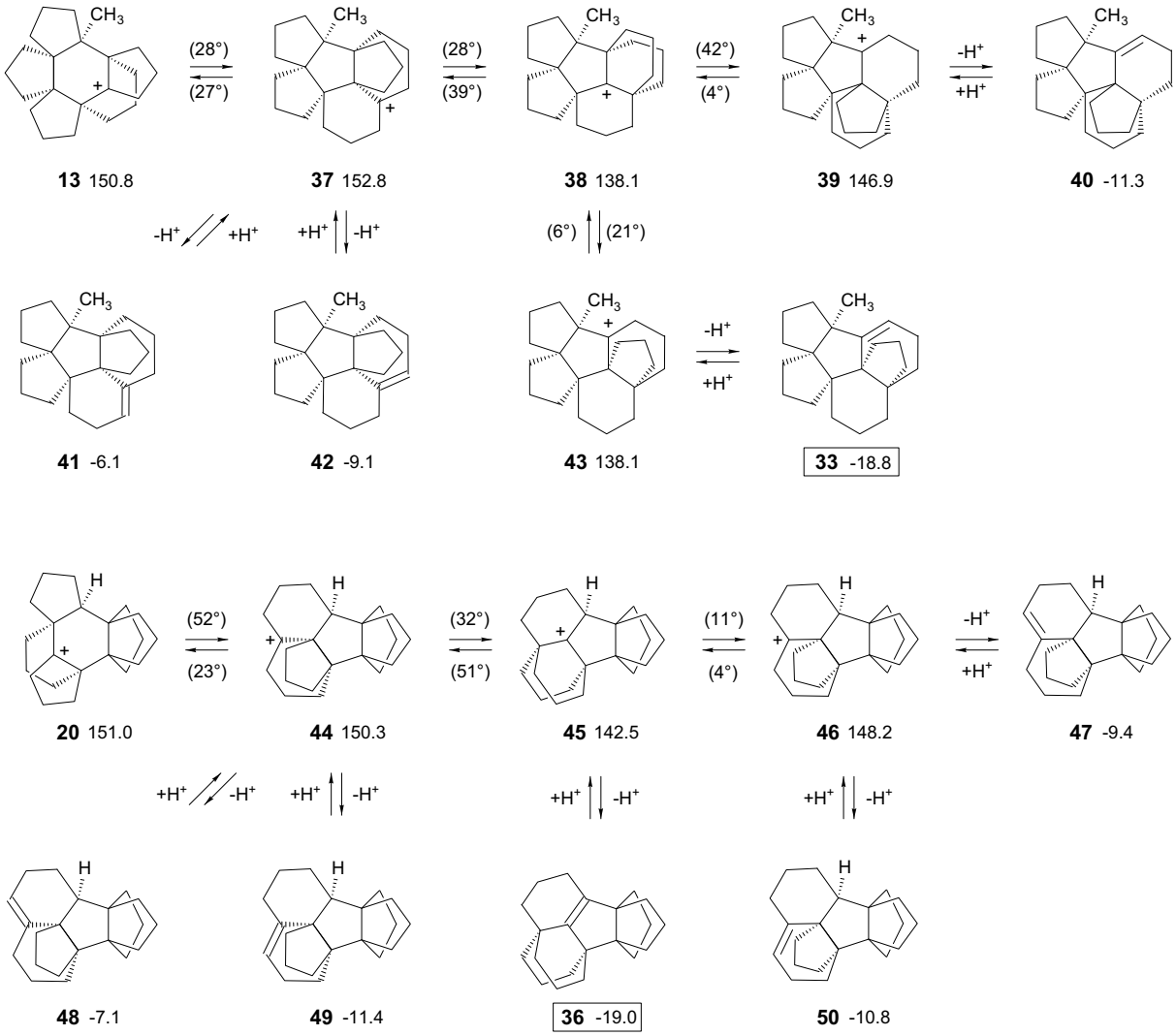
Scheme 1.



Scheme 2. Enthalpies of formation (in kcal/mol) of the global minimum structures of selected carbenium ions and olefins derived therefrom as calculated by HUNTER[14] in connection with MMP2.[15] The values for the dihedral angles between the empty p-orbitals and the bonds to be shifted are given in brackets. The first value refers to the forward, and the second to the backward reaction.



Scheme 3.



Scheme 4. Enthalpies of formation (in kcal/mol) of the global minimum structures of selected carbenium ions and olefins derived therefrom on the way from **13** to **33**, and from **20** to **36**, respectively, as calculated by HUNTER[14] in connection with MMP2.[15] The values for the dihedral angles between the empty p-orbitals and the bonds to be shifted are given in brackets.

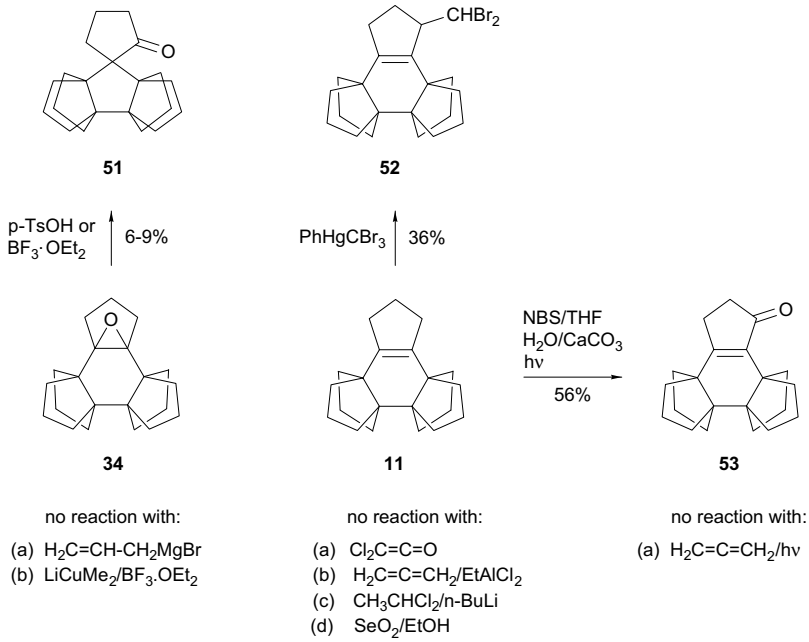
with *n*-butyllithium,[21] and with dibromocarbene, as generated from phenylmercury tribromomethane.[22] At least, in this last case, formation of **52** indicated that reactions in allylic position could occur. Indeed, albeit an oxidation of **11** with selenium dioxide in ethanol[23] failed, an oxidation with *N*-bromosuccinimide in aqueous tetrahydrofuran in the presence of calcium carbonate under irradiation with visible light[24] yielded the cyclopentenone **53**, and hence another potential precursor of **3**. Once again an atttempted [2+2]-cycloaddition with allene[25] failed, and similar observations were made with the epoxide **34**. This compound proved unreactive towards allyl magnesium bromide and lithium dimethylcuprate,[26] and gave only very low yields of spiroketone **51** on exposure to proton or lewis acids.

In summary, in an approach to trispropellane **3**, we studied the acid catalyzed rearrangements of the alcohols **8** and **10**, both by molecular mechanics, and experimentally. While the product formation from **8** rendered a rearrangement of **4** and/or **5** to **6** unfeasible, **10** yielded a bispropellane **11**, which could be transformed to the epoxide **34** and the enone **53**. Albeit a series of reactions with **11**, **34** and **53** as potential precursors of the trispropellane **3** failed, other possibilities remain to be explored. However, steric hindrance will remain a serious problem difficult to overcome.

3. Experimental

3.1. General

IR spectra were obtained with a Perkin–Elmer 298 spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on a Varian VXR 500 or VXR 600 spectrometer. For standards other than TMS the following chemical shifts were used: δ_H ($CHCl_3$)=7.24, δ_H (C_6D_5H)=7.15, δ_C ($CDCl_3$)=77.00, δ_C (C_6D_6)=128.00. The ^{13}C multiplicities followed from $^{1}J_{CH}$ correlation spectra. Mass spectra were determined with a Varian MAT 311A or Varian MAT 731 instrument (HRMS) operated at 70 eV. Analytical and preparative GC was carried out on an Intersmat IGC 16 instrument employing a thermal conductivity detector and hydrogen as carrier gas. Product ratios were not corrected for relative response. R_f values are quoted for Macherey & Nagel Polygram SIL G/UV_{254} plates. Colourless substances were detected by oxidation with 3.5% alcoholic 12-molybdophosphoric acid and subsequent warming. Melting points were observed on a Reichert microhotstage and are not corrected. Microanalytical determinations were done at Microanalytical Laboratory of the Institute of Organic and Biomolecular Chemistry, Göttingen.



Scheme 5.

3.2. Pentaspiro[3.0.3.0.3.0.3.0.3.1]heneicosan-21-ol (10)

To a suspension of lithium aluminium hydride (742 mg, 19.6 mmol) in ether (20 mL) was added within 30 min under nitrogen with stirring a solution of **32**[7] (4.88 g, 16.3 mmol) in ether (60 mL). Afterwards, the mixture was heated to reflux until DC analysis [pentane/ether 9:1; R_f: 0.56 (**32**), 0.41, 0.24 (**10**)] indicated that the reaction was complete (3 h). Water (0.7 mL), 15% sodium hydroxide (0.7 mL) and water (2.1 mL) were added, the liquid was decanted and the residue extracted with ether (2×20 mL). The combined organic layers were concentrated on a rotary evaporator (bath temperature 25 °C/20 Torr) and the residual crude **10** (4.79 g) was chromatographed on silica gel (0.05–0.20 mm) in pentane/ether (9:1; column 80×4 cm) to yield 4.52 g (92%) of pure **10** as colourless solid, mp 145–148 °C. The ^{1}H and ^{13}C NMR data were in accord with the literature data.[12b]

3.3. Rearrangement of 8, 10, 11, 22 and 24

The selected alcohol (**8**, **10**) or olefin (**11**, **22**, **24**) was heated with 1.1 equiv of a 0.050 M (method A) or 5.0 equiv of a 0.58 M (method B) solution of anhydrous *p*-toluenesulfonic acid in benzene to 70 °C. To establish comparable conditions, with olefins 1.0 equiv of water was added. After the time given the mixture was filtered through a short pad of silica gel, the product(s) were eluted with pentane, the solvents were evaporated and the residue purified as indicated.

*3.3.1. rel-(1R,5S,9R,13S,18R)-18-Methyl-hexacyclo-[16.3.0.0^{1,5}.0^{5,9}.0.^{9,13}.0.^{13,17}]heneicos-16-ene (**22**) and rel-(6R,10S,14R)-14-methyl-hexacyclo[13.3.3.0^{1,15}.0^{2,6}.0^{6,10}.0^{10,15}]-heneicos-2-ene (**24**)*

From **8**[12] (70 mg, 0.22 mmol) within 5 min (4 h) after method A. According to ^{13}C NMR, the residue contained a 1:1.3 mixture of **22** and **24**. Upon thick layer chromatography on silica gel impregnated with silver nitrate in dichloromethane (SIL G-100 UV_{254}, 20×20×0.1 cm; R_f=0.90–0.75 (**24**), 0.75–0.63 (**22**, **24**)] **22** partially isomerized to yield 30 mg (45%) of **24** as colourless solid, mp 175–185 °C, and 20 mg (30%) of a 1:1.3 mixture of **22** and **24**. **22** was identified by its known ^{13}C NMR data.[12] Compound **24**: ^{1}H NMR (600 MHz, $CDCl_3$, $CHCl_3$ int): δ=0.97 (s, 3H), 1.20–1.31 (m, 2H), 1.32–1.41 (m, 3H), 1.45–1.71 (m, 14H), 1.87–1.97 (m, 3H), 2.02–2.10 (m, 3H), 2.10–2.17 (m, 1H), 2.24–2.34 (m, 2H), 5.32 (dd, J=2.5, 1.5 Hz, 1H); ^{13}C NMR (150.8 MHz, $CDCl_3$, $CDCl_3$ int): δ=20.03 (t), 20.79 (t), 24.81 (t), 25.40 (t), 25.47 (t), 29.43 (t), 37.21 (t), 38.65 (t), 39.19 (t), 40.10 (t), 40.33 (t), 40.51 (t), 42.18 (t), 45.89 (t), 45.93 (t), 49.58 (s), 52.84 (s), 56.87 (s), 57.80 (s), 59.28 (s), 119.77 (d), 157.90 (s); MS (CI): m/e=296 (85, M^+), 235 (97), 157 (100). HRMS m/z (M^+) calcd 296.2504, obsd 296.2504.

*3.3.2. rel-(2R,6R,10S,11S,15R)-2-Methyl-hexacyclo-[9.7.0.3^{10,15}.0^{2,6}.0^{6,10}.0^{11,15}]heneicos-1-ene (**33**)*

From **8**[12] (256 mg, 0.81 mmol) within 5 min (4 h) after method B. The residue (250 mg) was crystallized from acetone/methanol to yield 159 mg (66%) of **33** as colourless solid, mp 170–175 °C. ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ int): δ=0.98–1.97 (m, 25H), 1.07 (s, 3H), 2.02–2.16 (m, 2H), 2.19–2.26 (m, 1H), 5.16 (dd, J=5, 2.5 Hz, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$, TMS int): δ=19.00 (C-20), 21.10 (C-13), 22.18 (C-17), 26.27 (C-4), 27.70 (CH_3), 28.06 (C-8), 29.24 (C-21), 32.35 (C-16), 34.00 (C-9), 35.50 (C-19), 36.32 (C-14), 38.97 (C-5), 40.08 (C-7), 40.27 (C-12), 42.49 (C-3), 43.42 (C-15), 52.62 (C-2), 56.05 (C-10), 56.99 (C-11), 66.96 (C-6), 111.56 (C-18), 158.71 (C-1); MS (CI): m/e=296 (33, M^+), 254 (100). HRMS m/z (M^+) calcd 296.2504, obsd 296.2504. For the 2D INADEQUATE spectrum of **33**, see Supplementary data given. A rearrangement of the 1:1.3 mixture of **22** and **24** (Section 3.3.1) yielded the same result.

*3.3.3. Hexacyclo[10.3.3.3^{7,11}.0^{1,12}.0^{2,6}.0^{7,11}]heneicos-2(6)-ene (**11**)*

From **10** (1.40 g, 4.66 mmol) within 40 min after method A. The residue was chromatographed on silica gel (0.05–0.20 mm) in pentane [column 120×4 cm; R_f=0.64 (**11**)] to yield 880 mg (67%) of **11** as colourless solid, mp 110 °C. ^{1}H NMR (600 MHz, $CDCl_3$, $CHCl_3$ int): δ=1.45–1.57 (m, 8H), 1.59–1.68 (m, 12H), 1.74 (quint, J=7.5 Hz, 2H), 1.84–1.91 (m, 4H), 2.24 (t, J=7.5 Hz, 4H); ^{13}C NMR (150.8 MHz, $CDCl_3$, $CDCl_3$ int): δ=22.44 (t), 23.61 (t), 32.77 (t), 38.67 (t), 39.37 (t), 55.08 (s), 59.20 (s), 137.15 (s); MS (CI): m/e=282 (75, M^+), 239 (100). $C_{21}H_{30}$ requires: C, 89.29; H, 10.70. Found: C, 89.23; H, 10.64.

*3.3.4. Hexacyclo[9.3.3.3^{2,6}.1^{2,6}.0^{1,11}.0^{10,21}]heneicos-10(21)-ene (**36**)*

From **11** (89 mg, 0.32 mmol) within 15 min after method B. The residue was crystallized from acetone/methanol to yield 61 mg

(68%) of **36** as colourless solid, mp 102 °C. ^{1}H NMR (600 MHz, $CDCl_3$, $CHCl_3$ int): δ=1.17 (ddd, J=13, 6.5, 6.5 Hz, 2H), 1.28–1.62 (m, 22H), 1.80 (t, J=6 Hz, 2H), 1.83–1.93 (m, 4H); ^{13}C NMR (150.8 MHz, $CDCl_3$, $CDCl_3$ int): δ=20.60 (t), 22.63 (t), 22.72 (t), 27.37 (t), 34.04 (s), 35.24 (t), 37.09 (t), 37.90 (t), 38.52 (t), 38.57 (t), 47.34 (s), 67.17 (s), 71.40 (s), 131.35 (s), 142.66 (s); MS (CI): m/e=282 (49, M^+), 239 (100). HRMS m/z (M^+) calcd 282.2348, obsd 282.2348.

3.4. Epoxidation of 11 and 36

To a solution of the selected olefin (1.0 mmol) in dichloromethane (10 mL) were added at room temperature with stirring a 0.5 M solution of sodium bicarbonate (5 mL) and 3-chloroperoxybenzoic acid (80% w/w, 1.5 mmol). After the reaction was complete (control by TLC in pentane/ether 95:5), the organic phase was washed with 1 N sodium hydroxide (2×5 mL), water (5 mL) and dried ($MgSO_4$). The solvent was evaporated and the residue crystallized from acetone.

*3.4.1. 22-Oxa-heptacyclo[10.3.3.3^{7,11}.1^{2,6}.0^{1,12}.0^{2,6}.0^{7,11}]-docosane (**34**)*

From **11** (502 mg, 1.78 mmol) within 2 h [R_f=0.72 (**11**), 0.40 (**34**)]. Yield 508 mg (96%). Colourless solid, mp 154–155 °C. ^{1}H NMR (600 MHz, C_6D_6, C_6D_5H int): δ=1.28–1.35 (m, 1H), 1.38–1.88 (m, 25H), 2.16 (ddd, J=12.5, 9.0, 6.0 Hz, 2H), 2.27 (ddd, J=12.5, 9.0, 5.5 Hz, 2H); ^{13}C NMR (150.8 MHz, C_6D_6, C_6D_6 int): δ=19.02 (t), 23.53 (t), 23.84 (t), 28.88 (t), 38.12 (t), 38.72 (t), 39.01 (t), 40.11 (t), 54.08 (s), 59.43 (s), 72.97 (s); MS (CI): m/e=298 (93, M^+), 280 (88), 144 (92), 134 (93), 107 (100). $C_{21}H_{30}O$ requires: C, 84.51; H, 10.13. Found: C, 84.41; H, 10.10.

*3.4.2. rel-(10R,22S)-21-Oxa-heptacyclo-[9.3.3.3^{2,6}.2^{2,10}.0^{1,11}.0^{6,22}.0^{10,22}]docosane (**35**)*

From **36** (59 mg, 0.21 mmol) within 3 h [R_f=0.72 (**36**), 0.45 (**35**)]. Yield 55 mg (88%). Colourless solid, mp 138 °C. ^{1}H NMR (600 MHz, $CDCl_3$, $CHCl_3$ int): δ=0.90 (ddd, J=13, 3.5, 3.5 Hz, 1H), 1.02 (symm m, 1H), 1.22–1.88 (m, 23H), 1.92–2.08 (m, 5H); ^{13}C NMR (150.8 MHz, $CDCl_3$, $CDCl_3$ int): δ=17.09 (t), 21.24 (t), 21.86 (t), 22.50 (t), 27.35 (t), 27.46 (t), 30.56 (t), 32.44 (s), 32.48 (t), 33.63 (t), 33.81 (t), 34.34 (t), 36.53 (t), 37.00 (t), 37.67 (t), 40.24 (t), 40.70 (s), 66.68 (s), 69.12 (s), 72.54 (s), 80.07 (s); MS (CI): m/e=298 (100, M^+). HRMS m/z (M^+) calcd 298.2297, obsd 298.2297.

3.5. 3-Dibromomethyl-hexacyclo-[10.3.3.3^{7,11}.0^{1,12}.0^{2,6}.0^{7,11}]heneicos-2(6)-ene (52)

To a stirred solution of **11** (207 mg, 0.73 mmol) in benzene (1.0 mL) was added phenylmercury tribromomethane (388 mg, 0.73 mmol) and the mixture heated to 70 °C. The reaction progress was monitored by GC [2.5 m×1/4″ all-glass system, 15% SE 30 on Chromosorb W AW/DMCS, 60–80 mesh, 250 °C; retention times (min): 3.30 (**11**), 4.96 (**52**)] and after 2 h (50% conversion) and 4 h (80% conversion), additional reagent (2×388 mg) was added. After 7 h (95% conversion) the phenylmercury bromide formed was filtered off and washed with pentane. The combined filtrates were concentrated and the residual oil chromatographed on silica gel (0.05–0.20 mm) in pentane [column 90×2 cm, control by TLC; R_f=0.64 (**11**), 0.43 (**52**)] to yield 102 mg (31%) of **52** as colourless solid. Analytically pure **52** was obtained by crystallization from acetone. Colourless solid, mp 94–95 °C. ^{1}H NMR (600 MHz, $CDCl_3$, $CHCl_3$ int): δ=1.25–1.33 (m, 1H), 1.44–1.92 (m, 21H), 1.96–2.17 (m, 5H), 2.50–2.57 (m, 1H), 3.48–3.52 (m, 1H), 6.03 (d, J=2 Hz, 1H); ^{13}C NMR (150.8 MHz, $CDCl_3$, $CDCl_3$ int): δ=22.02 (t), 23.79 (t), 24.36 (t), 24.49 (t), 25.82 (t), 32.04 (t), 37.57 (t), 37.81 (t), 37.87 (t), 38.90 (t), 39.31 (t), 39.50 (t) (coincidence of two lines), 41.11 (t), 54.80 (s), 55.18 (s), 55.35 (d), 58.36 (d), 58.70 (s), 60.70 (s), 133.41 (s), 146.80 (s); MS (CI): m/e=456, 454, 452 (5, 10, 7, M^+), 281 (100). HRMS m/z (M^+) calcd 452.0714, obsd 452.0714. $C_{22}H_{30}Br_2$ requires: C, 58.17; H, 6.66. Found: C, 59.31; H, 7.35.

3.6. Hexacyclo[10.3.3.3^{7,11}.0^{1,12}.0^{2,6}.0^{7,11}]heneicos-2(6)-en-3-one (53)

Compound **11** (407 mg, 1.44 mmol) and *N*-bromosuccinimide (641 mg, 3.60 mmol) were dissolved in tetrahydrofuran (4.0 mL) containing 5% (v/v) water. Finely ground calcium carbonate (288 mg, 2.88 mmol) was added with stirring and the resulting suspension was irradiated at room temperature with visible light (Osram Krypton, 100 W). According to TLC in pentane/ether 4:1 [R_f=0.72 (**11**), 0.40, 0.33, 0.17 (**53**)], after 10 min the reaction was complete. The mixture was diluted with ether (10 mL) and washed with water (3×5 mL). The combined aqueous phases were extracted with ether (5 mL), and the combined organic phases were dried ($MgSO_4$) and concentrated to yield 430 mg of a slightly yellow solid. Chromatography on silica gel (0.05–0.20 mm) in pentane/ether 4:1 (column 50×2 cm) yielded 241 mg (56%) of **53** as colourless solid, mp 124 °C. IR (KBr): 1690 (C=O), 1630 cm^{-1} (C=C); ^{1}H NMR (600 MHz, $CDCl_3$, $CHCl_3$ int): δ=1.43–2.01 (m, 24H), 2.33 (AA′-part of an AA′BB′-system, 2H), 2.47 (BB′-part of an AA′BB′-system, 2H); ^{13}C NMR (150.8 MHz, $CDCl_3$, $CDCl_3$ int): δ=23.52 (t), 23.75 (t), 26.12 (t), 35.11 (t), 37.77 (t), 38.57 (t), 38.62 (t), 39.70 (t), 52.74 (s), 57.05 (s), 59.39 (s), 59.77 (s), 141.30 (s), 175.64 (s), 209.61 (s); MS (CI): m/e=296 (100, M^+). $C_{21}H_{28}O$ requires: C, 85.08; H, 9.52. Found: C, 85.07; H, 9.61.

3.7. Pentacyclo[8.3.3.3^{2,6}.0^{1,8}.0^{2,6}]heptadecan-7-spiro-5′-cyclopentan-1′-one (51)

(a) From **34** with *p*-toluenesulfonic acid: **34** (100 mg, 0.34 mmol) was added to a 0.58 M solution of anhydrous *p*-toluenesulfonic acid in benzene (2.89 mL, 1.68 mmol) and the resulting mixture stirred at room temperature until TLC in pentane/ether (95:5) [R_f=0.72, 0.45 (**34**), 0.35 (**51**)] indicated that the reaction was complete (15 min). The solution was diluted with ether (10 mL), washed with saturated sodium bicarbonate (2×3 mL) and water (3 mL) and dried ($MgSO_4$). The solvents were evaporated and the residual yellow solid (101 mg) was chromatographed on silica gel (0.05–0.20 mm) in pentane/ether 95:5 (column 60×1 cm) to yield 9 mg (9%) of **51** as colourless solid, mp 108–109 °C. IR (KBr): 1760 cm^{-1} (C=O); ^{1}H NMR (600 MHz, $CDCl_3$, $CHCl_3$ int): δ=1.07–1.14 (m, 2H), 1.17–1.24 (m, 2H), 1.33–1.39 (m, 2H), 1.51–1.81 (m, 18H), 2.03 (t, J=6.5 Hz, 2H), 2.16 (t, J=7.5 Hz, 2H), 2.21–2.27 (symm m, 2H); ^{13}C NMR (150.8 MHz, $CDCl_3$, $CDCl_3$ int): δ=19.71 (t), 24.15 (t), 26.50 (t), 34.27 (t), 38.12 (t), 38.87 (t), 39.33 (t), 40.22 (t), 41.93 (t), 66.59 (s), 67.27 (s), 71.42 (s), 220.44 (s); MS (CI): m/e=298 (100, M^+). HRMS m/z (M^+) calcd 298.2297, obsd 298.2297.

(b) From **34** with borontrifluoride etherate: to a solution of **34** (114 mg, 0.38 mmol) in ether (3.5 mL) was added at room temperature under argon with stirring borontrifluoride etherate (54 mg, 0.38 mmol) and the reaction progress followed by TLC in pentane/ether 95:5 [R_f=0.72, 0.45 (**34**), 0.35 (**51**)]. After 1.5 h more borontrifluoride etherate (54 mg, 0.38 mmol) was added, and after 2.5 h the reaction was complete. Work up and chromatography as described above delivered 7 mg (6%) of **51** as colourless solid, mp 108–109 °C. The ^{13}C NMR data were identical with those of an authentic sample.

3.8. Crystal structure determinations of 34 and *rel*-(10*R*,22*S*)-35

X-ray data were collected on a Stoe IPDSII diffractometer at 133 K for **34** using graphite-monochromated Mo Kα radiation

(λ=71.073 pm) and for **35** on a Bruker Smart 6000 equipped with Incoatec multilayer optics using Cu Kα radiation (λ=154.178 pm). The structures were solved by using direct methods with SHELX-97 and refined by full-matrix least squares on F^2 for all data with SHELX-97.[27] All non-hydrogen atoms were refined anisotropically. A riding model with idealized geometry was employed for all hydrogen atoms. The crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC 274096 (**34**) and 722384 (**35**). 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

INADEQUATE spectrum of **33**, ^{1}H and ^{13}C NMR spectra of **11**, **24**, **33**–**36** and **51**–**53**, and data of the X-ray analyses including ORTEP plots of **34** and **35**. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2009.05.005.

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