Pergamon

Tetrahedron 54 (1998) 10713–10720

TETRAHEDRON

THE BICYCLOBUTYLIDENE TO BICYCLOOCTENE REARRANGEMENT: FORMAL SYNTHESES OF (±)-CERATOPICANOL AND (±)-HIRSUTENE[1]

Thorsten Anger,[a] Onno Graalmann,[a] Heike Schröder,[a] Ralf Gerke,[a] Uta Kaiser,[a] Lutz Fitjer,*[a] and Mathias Noltemeyer[b]

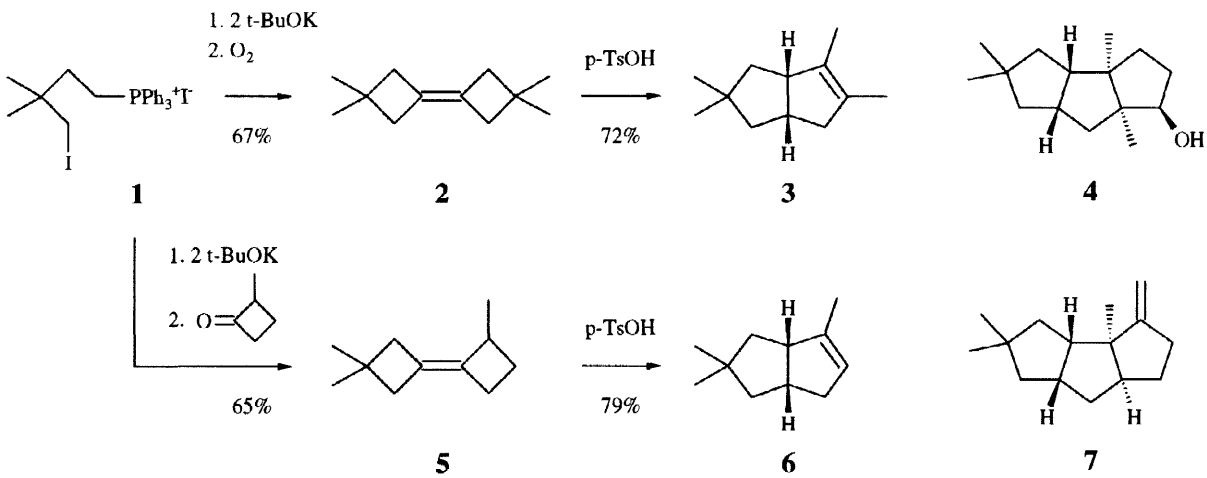
Institut für Organische Chemie der Universität Göttingen,[a] Tammannstr. 2, D-37077 Göttingen, Germany

Institut für Anorganische Chemie der Universität Göttingen,[b] Tammannstr.4, D-37077 Göttingen, Germany

Received 28 May 1998; accepted 23 June 1998

Abstract: The bicyclobutylidenes **2** and **5** have been rearranged to the bicyclooctenes **3** and **6**, respectively, and further transformed to the tricyclic ketones **16** and **21**, respectively, as known precursors of (±)-ceratopicanol (**4**) and (±)-hirsutene (**7**). For the cyclopentane annelation, a [3+2]cycloaddition with cyclopropane-1,1-dicarboxylic acid ester, followed by an alkaline hydrolysis and an oxidative decarboxylation of the diacids formed was used (**3-8-14-16**, **6-18-20-21**). The structures of the cycloadduct **9**, the diacid **15** and the ketone **17** followed from an X ray analysis of the ditosylate **13**, itself obtained by reduction and tosylation (**9-12-13**). The new syntheses of **16** and **21** represent short entries to **4** and **7**.

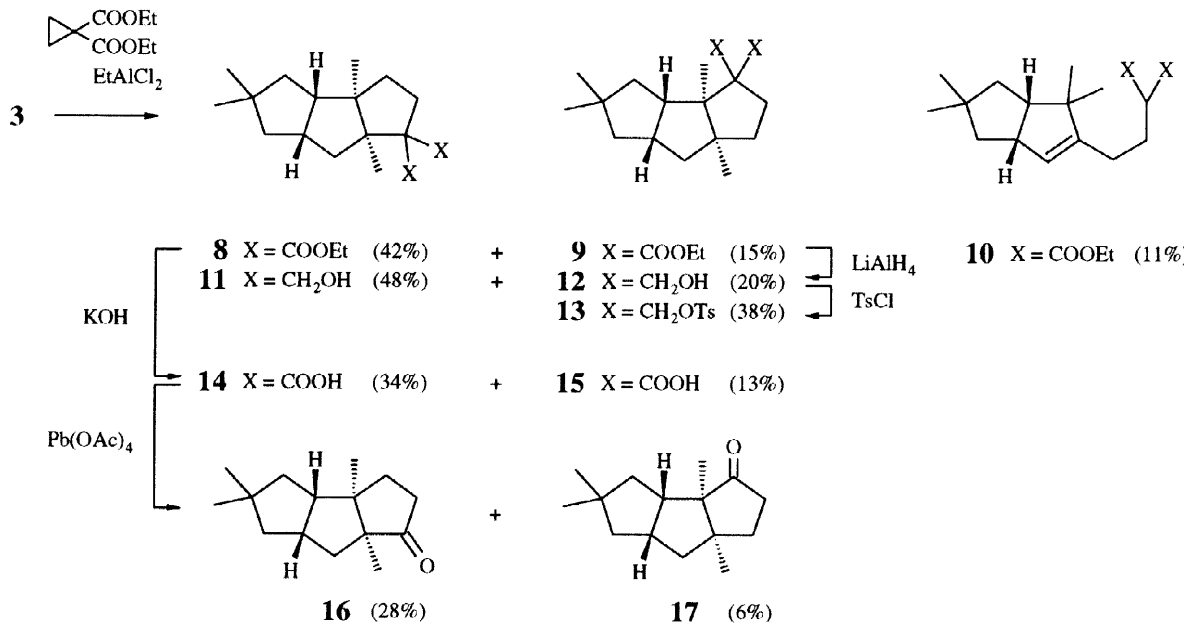
The bicyclobutylidene to bicyclooctene rearrangement is a potentially useful method for the construction of diquinanes. However, except with the parent bicyclobutylidene[2] and two dibenzoannelated derivatives,[3] no such rearrangements have become known. In order to demonstrate the utility of bicyclobutylidenes in natural product synthesis, we reported[4] on the synthesis and rearrangement of bicyclobutylidene **2** to bicyclooctene **3** as potential precursor of (±)-ceratopicanol (**4**).[5] In extension and completion of this work, we now describe the rearrangement of bicyclobutylidene **5** to bicyclooctene **6** as a known[6] precursor of (±)-hirsutene (**7**),[7] and report on new syntheses for both **4** and **7**.



0040-4020/98/$ - see front matter
PII: S0040-4020(98)00635-8

For the synthesis of bicyclooctene **6**, the phosphonium iodide **1**[4] was first treated with two equivalents of potassium tert-butoxide in benzene and then reacted with 2-methyl-cyclobutanone,[8] until the resulting bicyclobutylidene **5** was rearranged with 0.25 equivalents of a 0.089 M solution of anhydrous p-toluenesulfonic acid in benzene. After 30 min at room temperature the formation of **6** as stabilomer of a series of twelve conceivable rearrangement products[9] was complete.

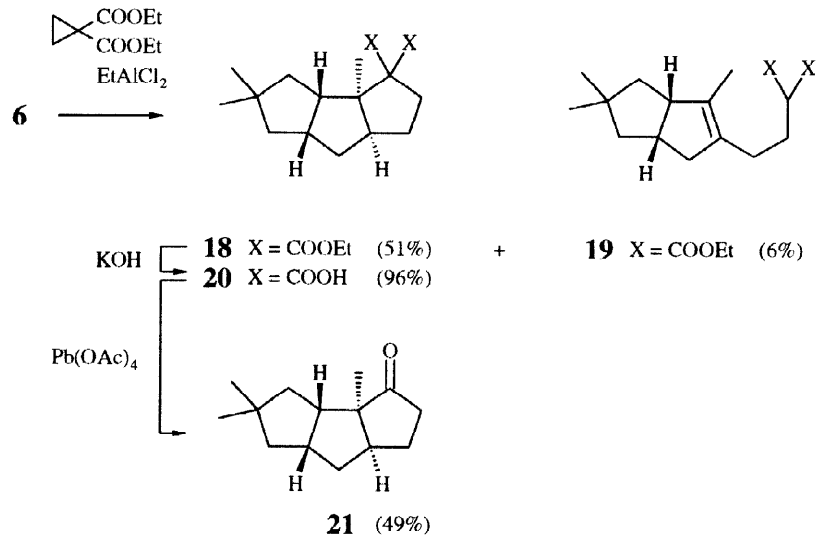
For the annelation of the missing cyclopentane rings, we followed the protocol of Snider[10] for the $EtAlCl_2$ promoted [3+2]cycloaddition of diethyl cyclopropane-1,1-carboxylate to alkenes and first applied it to **3**. In this case, an *exo*-attack of the reagent could be expected, but no predictions concerning the regiochemistry could be made. Experimentally, the reaction led within 6 days at room temperature to an inseparable 8:3-mixture of two cycloadducts (57%) accompanied by a small amount (11%) of an open chain compound, easily recognized as **10**. Direct evidence for the identity of the minor cycloadduct emerged from the fact, that reduction of the two cycloadducts yielded two separable diols, and tosylation of the minor diol a ditosylate suitable for an X-ray analysis.[11] It thus turned out, that the ditosylate was the *cis-anti-cis*-configurated triquinane **13** derived from the diester **9** via the diol **12**.



Anticipating, that the major cycloadduct was the regioisomer **8**, the mixture of diesters was saponified with potassium hydroxide in methanol-water, and the 8:2-mixture of diacids obtained subjected to an oxidative decarboxylation[12] with lead tetraacetate in benzene-pyridine. This time, the 8:2-mixture of the ketones formed could be separated, and the spectral data of the major isomer disclosed its identity as **16**,[5c] the desired direct precursor of (±)-ceratopicanol (**4**).[5c]

For the synthesis of (±)-hirsutene (**7**), we followed the same protocol as for the synthesis of **4**. As was to be expected, the $EtAlCl_2$ promoted [3+2]cycloaddition of diethyl cyclopropane-1,1-dicarboxylate to diquinane **6** proceeded regio- and stereoselectively, and within 23 h at room temperature, a 8:1-mixture of a single cyclo-

adduct **18** (51%) and an open chain isomer **19** (6%) was formed. As with **8** and **9**, this mixture was saponified with potassium hydroxide in methanol-water, and the dicarboxylic acid **20** obtained (96%) oxidized with lead tetraacetate to ketone **21** (47%) as direct precursor of (±)-hirsutene (**7**).[13]



In summary, the rearrangement of bicyclobutylidenes **2** and **5** to bicyclooctenes **3** and **6** enables new and very short syntheses of **16** and **21** as direct precursors of (±)-ceratopicanol (**4**) and (±)-hirsutene (**7**), respectively. While the overall yield from **3** to **16** (4%) is unsatisfactory, the overall yield from **6** to **21** (24%) is acceptable. More direct approaches to **4** and **7** via rearrangements of preassembled skeletons containing a bicyclobutyl subunit are under active investigation.

EXPERIMENTAL

^1H and ^{13}C NMR spectra were recorded on a Varian VXR 200, VXR 500 or a Bruker AMX 300 spectrometer. For standards other than TMS the following chemical shifts were used: $\delta_H(CHCl_3)$ = 7.24, $\delta_H(CD_2HOD)$ = 3.30, $\delta_C(CDCl_3)$ = 77.00, $\delta_C((CD_3)_2SO)$ = 39.50. Mass spectra were obtained with a Varian MAT 311A or a Finnigan MAT 95 instrument operated at 70 eV. Analytical and preparative gas chromatography was carried out on a Carlo Erba 6000 Vega 2 instrument using a FID 40 and a thermal conductivity detector, respectively, 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 (Merck) and subsequent warming. Melting and boiling points are not corrected.

3,3,2′-Trimethyl-1,1′-bi(cyclobutylidene) (5): To a vigorously stirred suspension of 4-iodo-3,3-dimethyl-butyltriphenylphosphonium iodide **1**[4] (113.5 g, 189 mmol) in dry benzene (350 ml) under nitrogen was added potassium *tert*-butoxide (3 x 14.1 g, 378 mmol) and the mixture heated to 50°C. After 4 h, 2-methylcyclobutanone[8] (15.9 g, 189 mmol) was added, and after another 3 h at 70°C the reaction was complete. After addition of water (16 ml), the organic layer was decanted and the heterogeneous residue extracted with pentane (3 x 60 ml). The combined organic layers were concentrated by distillation through a 20 cm Vigreux column

(bath temperature up to 140°C), the residue was diluted with pentane (300 ml) and the precipitated triphenylphosphine oxide was filtered off. The filtrate was concentrated as before and the remaining material fractionated yielding 18.5 g (65%) of pure **5** as colourless liquid, bp 59°C/16 torr. ^{1}H NMR (300 MHz, $CDCl_3$, $CHCl_3$ int): δ = 1.07 (d, J = 7 Hz, 3H), 1.11 (s, 3H), 1.13 (s, 3 H), 1.45 (dddd, J = 11, 9, 9, 7 Hz, 1H), 2.06 (dddd, J = 11, 9, 7, 7 Hz, 1H), 2.19-2.31 (m, 3H), 2.32-2.44 (m, 3H), 2.85-3.02 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ int): δ = 19.26 (C_{prim}), 25.73, 25.79 (C_{sek}), 29.07 , 29.21 (C_{prim}), 32.28 (C_{quart}), 37.78 (C_{tert}), 41.99, 42.26 (C_{sek}), 122.98, 136.16 (C_{quart}); MS m/z 150 (M^+, 2), 41 (100). Anal. Calcd for $C_{11}H_{18}$: C, 87.93; H, 12.07. Found: C, 87.84; H, 11.94.

(3a*RS*,6a*RS*)-2,2,6-Trimethyl-1,2,3,3a,4,6a-hexahydropentalene (6): To a stirred solution of **5** (16.4 g, 109 mmol) in dry benzene (270 ml) under nitrogen was added a solution of anhydrous p-toluenesulfonic acid in dry benzene (0.74 M, 36.9 ml, 27.4 mmol) causing a slightly exothermic effect. After 30 min the reaction was complete according to glpc [30 m x 0.32 i.d. fused silica capillary column coated with 0.25 μm DB FFAP, 60°C; retention times (min): 3.14 (**5**), 4.87 (**13**)]. The mixture was washed with water (3 x 50 ml), saturated sodium bicarbonate (3 x 50 ml), saturated sodium chloride (3 x 50 ml), and dried ($MgSO_4$). The solvent was distilled off, and the residue was fractionated in vacuo yielding 13.0 g (79%) of pure **6** as colourless liquid, bp 68°C/16 torr. The ^{1}H NMR data were in accord with literature data.[6] The ^{13}C NMR data (75 MHz, $CDCl_3$, $CDCl_3$ int) have not yet been reported and were as follows: δ = 15.08, 27.27, 28.95 (C_{prim}), 38.70 (C_{sek}), 41.07 (C_{tert}), 41.11 (C_{quart}), 45.87, 49.84 (C_{sek}), 53.64, 121.52 (C_{tert}), 143.40 (C_{quart}).

(3a*SR*,3b*RS*,6a*RS*,7a*SR*)-3a,5,5,7a-Tetramethyl-decahydro-cyclopenta[a]pentalene-1,1-dicarboxylic acid diethyl ester (8), (3a*SR*,3b*RS*,6a*RS*,7a*SR*)-3a,5,5,7a-tetramethyl-decahydro-cyclopenta[a]pentalene-3,3-dicarboxylic acid diethyl ester (9) and (3a*SR*,6a*RS*)-2-[2-(1,1,5,5-tetramethyl-1,3a,4,5,6,6a-hexahydropentalen-2-yl)-ethyl]-malonic acid diethyl ester (10): To a solution of **3** (5.00 g, 30.5 mmol) and cyclopropane-1,1-dicarboxylic acid diethyl ester (5.66 g (30.5 mmol) in 1,2-dichloroethane (90 ml) was added at 0°C under nitrogen with stirring within 40 min a solution of ethyl aluminium dichloride in hexane (1.0 M, 70.0 ml, 70.0 mmol). After the addition was complete, the mixture was stirred at room temperature and the reaction progress monitored by tlc in pentane/ether [95:5; R_f = 0.75 (**3**), 0.23 (**8**, **9**), 0.17 (**10**)]. After 6 days, dichloromethane (60 ml), water (50 ml), and hydrochloric acid (2N, 50 ml) were added. The phases were separated, the aqueous phase was extracted with dichloromethane (3 x 80 ml), and the combined organic phases were washed with saturated sodium chloride (100 ml) and dried ($MgSO_4$). The solvents were evaporated (bath temperature 20°C/20 torr) and the residue chromatographed on silica gel (70-130 mesh) in pentane/ether (95:5, column 80 x 5 cm, control by tlc) to yield 0.50 g (7%) of unreacted **3**, 6.11 g (57%) of a 8:3-mixture of **8** and **9**, and 1.22 g (11%) of **10** as colourless liquids. **8** and **9**: ^{1}H NMR (300 MHz, $CDCl_3$, $CHCl_3$ int): Only the uncoupled methyl groups could be assigned: **8**: δ = 0.86, 1.04, 1.07, 1.34 (4 s, 4 CH_3); **9**: δ = 0.85, 1.01, 1.01, 1.08 (4 s, 4 CH_3). The coupled methyl groups showed overlapping triplets at δ = 1.16-1.28, and the remaining protons a series of multiplets at δ = 1.30-2.60 and 4.00-4.20. ^{13}C NMR (125 MHz, C_6D_6, C_6D_6 int): All resonances could be assigned. **8**: δ = 13.71, 13.82, 20.64, 22.50, 28.33, 30.35 (C_{prim}), 32.33 (C_{sek}), 40.37 (C_{quart}), 40.76 (C_{tert}), 41.76, 44.54, 48.95, 49.03 (C_{sek}), 54.56, 58.03 (C_{quart}), 58.84 (C_{tert}), 60.28, 60.36 (C_{sek}), 70.26, 170.98, 171.71 (C_{quart}); **9**: δ = 13.71, 13.89, 16.88, 24.99, 27.68, 29.75 (C_{prim}), 32.63, 38.03 (C_{sek}), 40.79 (C_{tert}), 42.15 (C_{quart}), 42.98, 47.29, 50.20 (C_{sek}), 55.55 (C_{tert}), 56.40, 56.63 (C_{quart}), 60.17, 60.28 (C_{sek}), 70.62, 171.09, 171.69 (C_{quart}); MS m/z 350 (M^+, 2), 163 (100). Anal. Calcd for $C_{21}H_{34}O_4$: C, 71.96; H, 9.78. Found: C, 71.76; H, 9.80. **10**: ^{1}H NMR (300 MHz, $CDCl_3$, $CHCl_3$ int): δ = 0.87 (s, 3H), 0.88 (s, 3H), 0.95 (s, 3H), 0.98 (s, 3H), 0.96-1.04 (m, 1H), 1.24 (t, J = 7 Hz, 6H), 1.20-1.28 (m, 2H), 1.62 (mc, 1H), 1.80-1.92 (m, 2H), 1.91-2.12 (m, 2H), 2.38 (mc, 1H), 3.06 (mc, 1H), 3.35 (t, J = 7 Hz, 1H), 4.17 (q, J = 7 Hz, 4H), 5.10 (mc, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ int): δ = 14.07, 21.60 (C_{prim}), 24.12, 27.19 (C_{sek}), 27.86, 29.45, 29.70 (C_{prim}), 40.45 (C_{quart}), 42.74, 46.08 (C_{sek}), 46.12 (C_{tert}), 46.91 (C_{quart}), 51.67, 54.75 (C_{tert}), 61.20 (C_{sek}), 127.29 (C_{tert}), 146.63, 169.47 (C_{quart}); MS m/z 350 (M^+, 16), 190 (100). Anal. Calcd for $C_{21}H_{34}O_4$: C, 71.96; H, 9.78. Found: C, 71.83; H, 9.90.

(3a*SR*,3b*RS*,6a*SR*,7a*SR*)-(1-Hydroxymethyl-3a,5,5,7a-tetramethyl-decahydro-cyclopenta[a]pentalen-1-yl)-methanol (11) and (3a*SR*,3b*RS*,6a*SR*,7a*SR*)-(3-hydroxymethyl-3a,5,5,7a-tetramethyl-decahydro-cyclopenta[a]pentalen-3-yl)-methanol (12): To a suspension of lithium aluminium hydride (304 mg, 8.00 mmol) in anhydrous ether (10 ml) under nitrogen was added a 8:3-mixture of **8** and **9** (351 mg, 1.00 mmol)

and the mixture heated to reflux. After 2 h, the mixture was diluted with ether (10 ml) and hydrolyzed by successive addition of water (288 µl), 15% aqueous sodium hydroxide (288 µl) and water (846 µl). The organic layer was decanted, the residue was extracted with ether (10 ml), the combined organic phases were concentrated on a rotary evaporator (bath temperature 20°C/20 torr), and the residue (260 mg colourless oil) was chromatographed on silica gel (70-130 mesh) in ether [column 45 x 3 cm, control by tlc; R_f = 0.50 (**12**), 0.42 (**11**)] to yield 128 mg (48%) of **11** as colourless liquid and 52 mg (20%) of **12** as colourless solid, mp 112-114°C. **11**: ^{1}H NMR (300 MHz, $CDCl_3$, $CHCl_3$ int): δ = 0.86 (s, 3H), 0.98 (s, 3H), 1.01 (s, 3H), 1.02 (s, 3H), 1.12-1.26 (m, 3H), 1.30-1.42 (m, 2H), 1.50-1.82 (m, 4H), 2.17 (mc, 1H), 2.37 (mc, 1H), 2.42-2.56 (m, 1H), 2.61 (br s, 2H), 3.55-3.65 (m, 1H), 3.70-3.90 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ int): δ = 20.34, 20.41, 27.37 (C_{prim}), 28.83 (C_{sek}), 29.36 (C_{prim}), 39.67 (C_{quart}), 40.19 (C_{tert}), 40.65, 43.47, 44.01, 47.71 (C_{sek}), 52.15, 53.41, 55.32 (C_{quart}), 56.85 (C_{tert}), 66.75, 68.71 (C_{sek}); MS m/z 266 (M^+, 2), 78 (100). Calculated for $C_{17}H_{30}O_2$: 266.2245. Found: 266.2245 (MS). **12**: ^{1}H NMR (300 MHz, $CDCl_3$, $CHCl_3$ int): δ = 0.79 (s, 3H), 0.90 (s, 3H), 0.95 (mc, 1H), 1.00 (s, 3H), 1.01 (s, 1H), 1.12-1.24 (m, 2H), 1.36 (mc, 1H), 1.45-1.58 (m, 3H), 1.65-1.78 (m, 2H), 1.80-1.90 (m, 1H), 2.40-2.60 (m, 1H), 2.43 (br s, 1H), 2.72 (mc, 1H), 3.64-3.72 (m, 1H), 3.76-3.90 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ int): δ = 15.24, 25.56, 28.02 (C_{prim}), 29.40 (C_{sek}), 29.67 (C_{prim}), 37.24 (C_{quart}), 40.87 (C_{tert}), 42.37, 42.93, 43.47, 48.57 (C_{sek}), 51.04 (C_{tert}), 53.62, 54.93, 57.38 (C_{quart}), 67.71, 70.40 (C_{sek}); MS m/z 248 (M^+-H_2O, 5), 163 (100). Anal. Calcd for $C_{17}H_{30}O_2$: C, 76.64; H, 11.35. Found: C, 76.76; H, 11.37.

Toluene-4-sulfonic acid (3a*SR*,3b*RS*,6a*SR*,7a*SR*)-3a,5,5,7a-tetramethyl-3-(4-tolylsulfonyloxymethyl)-decahydro-cyclopenta[a]pentalen-3-yl-methyl ester (13): To a solution of **12** (40 mg, 0.15 mmol) in pyridine (300 µl) was added at 0°C under nitrogen with stirring a solution of toluene-4-sulfonic acid chloride (85 mg, 0.45 mmol) in pyridine (150 µl). After 3 h at 0°C, the mixture was diluted with ether (3 ml) and hydrolyzed with water (1 ml). The organic phase was separated, washed with sulfuric acid (2N, 1 ml), saturated sodium bicarbonate (1 ml) and water (1 ml), and dried (molecular sieves 4Å). The solvent was evaporated (bath temperature 20°C /20 torr) and the residue chromatographed on silica gel (70-130 mesh) in pentane/ether [1:1, column 30 x 2 cm, control by tlc; R_f = 0.38 (**13**), 0.10 (**12**)] to give 33 mg (38%) of pure **13** as colourless solid, mp 140-142°C. ^{1}H NMR (300 MHz, $CDCl_3$, $CHCl_3$ int): δ = 0.70 (s, 3H), 0.79 (s, 3H), 0.83 (s, 3H), 0.94 (s, 3H), 1.10-1.35 (m, 4H), 1.45-1.75 (m, 6H), 2.30-2.60 (m, 2H), 2.43 (s, 6H), 3.80-4.06 (m, 4H), 7.33 (mc, 4H), 7.72 (mc, 4H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ int): δ = 15.77, 21.70, 25.46, 27.90 (C_{prim}), 28.97 (C_{sek}), 29.69 (C_{prim}), 36.55 (C_{quart}), 40.92 (C_{tert}), 41.77, 42.74, 47.63, 48.29 (C_{sek}), 51.14 (C_{tert}), 51.82, 55.44, 57.50 (C_{quart}), 69.78, 71.67 (C_{sek}), 127.95, 128.00, 129.96, 129.97 (C_{tert}), 132.57, 132.66, 144.88, 144.90 (C_{quart}); MS m/z 574 (M^+, 2), 162 (100). Calculated for $C_{31}H_{42}O_6S_2$: 574.2422. Found: 574.2422 (MS).

(3a*SR*,3b*RS*,6a*RS*,7a*SR*)-3a,5,5,7a-Tetramethyl-decahydro-cyclopenta[a]pentalene-1,1-dicarboxylic acid (14) and (3a*SR*,3b*RS*,6a*RS*,7a*SR*)-3a,5,5,7a-tetramethyl-decahydro-cyclopenta[a]pentalene-3,3-dicarboxylic acid (15): A a solution of potassium hydroxide in methanol (10 M, 600 ml) was diluted with water (170 ml), a 8:3-mixture of **8** and **9** (7.5 g, 21.4 mmol) was added, and the mixture was heated to reflux. After 6 days, the mixture was acidified to pH 1 (12 N HCl) and perforated with ether (4 h). The etheral phase was dried ($MgSO_4$) and concentrated on a rotary evaporator (bath temperature 20°C /20 torr), and the residue (6.5 g) was chromatographed on silica gel (70-130 mesh) in pentane/ether [3:1, column 70 x 4 cm, control by tlc; R_f = 0.12 (**14**, **15**)] yielding 3.0 g (47%) of a 8:3-mixture of **14** and **15** as colourless solid, mp 130-158°C (dec.). ^{1}H NMR (200 MHz, CD_3OD, CD_2HOD int): Only the methyl groups could be assigned: **14**: δ = 0.90, 1.06, 1.09, 1.40 (4 s, 4 CH_3); **15**: δ = 0.89, 1.03, 1.04, 1.15 (4 s, 4 CH_3). The remaining protons showed overlapping multiplets at δ = 1.20-2.60; ^{13}C NMR (50 MHz, $(CD_3)_2SO$, $(CD_3)_2SO$ int): Due to the poor solubility, only the resonances of the major isomer can be given: **14**: δ = 20.57, 22.07, 28.22, 30.26 (C_{prim}), 31.39 (C_{sek}), 39.98 (C_{tert}), 40.16 (C_{sek}), 41.28 (C_{quart}), 44.06, 48.43, 48.54 (C_{sek}), 53.64, 56.89 (C_{quart}), 58.25 (C_{tert}), 69.33, 172.56, 173.22 (C_{quart}); MS m/z 294 (M^+, 3), 163 (100). Anal. Calcd for $C_{17}H_{26}O_4$: C, 69.36; H, 8.90. Found: C, 69.43; H, 8.95.

(3a*SR*,3b*RS*,6a*RS*,7a*SR*)-3a,5,5,7a-Tetramethyl-decahydro-cyclopenta[a]pentalen-1-one (16) and (3a*SR*,3b*RS*,6a*RS*,7a*SR*)-3a,5,5,7a-tetramethyl-decahydro-cyclopenta[a]pentalen-3-one (17): To a stirred solution of a 8:3-mixture of **14** and **15** (2.0 g, 6.9 mmol) in benzene (12.5 ml) was added pyridine (1.24 g, 17.0 mmol) and 85% (w/w) lead tetraacetate in acetic acid (8.85 g, 17.0 mmol) and the mixture heated to reflux.

After 4.5 h, the mixture was diluted with ether (15 ml), filtrated, and the residue washed with ether (3 x 10 ml). The combined organic phases were washed with hydrochloric acid (2N, 4 x 7 ml), saturated sodium bicarbonate (4 x 7 ml) and dried (molecular sieves 3Å). The solvents were evaporated (bath temperature 20°C/20 torr) and the residue (1.85 g) chromatographed on silica gel (70-130 mesh) in pentane/ether [95:5, column 70 x 4 cm, control by tlc; R_f = 0.33 (**17**), 0.18 (**16**)] to yield 430 mg (28%) **16** and 85 mg (6%) **17**. The ^{1}H- and ^{13}C-NMR data of **16** were in accord with literature data.[5e] **17**: ^{1}H NMR (300 MHz, $CDCl_3$, $CHCl_3$ int.): δ = 0.82 (s, 3H), 0.87 (s, 3H), 1.04 (s, 3H), 1.08 (s, 3H), 1.08-1.18 (m, 1H), 1.30-1.40 (m, 3H), 1.50-1.75 (m, 4H), 2.52 (mc, 1H), 2.79 (q, J = 10 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ int.): δ = 13.91, 13.82, 26.79, 29.30 (C_{prim}), 31.96, 34.54 (C_{sek}), 41.09 (C_{tert}), 41.92 (C_{quart}), 42.49, 44.93, 49.32 (C_{sek}), 50.74 (C_{tert}), 52.21, 59.74, 224.20 (C_{quart}). MS m/z 220 (M^+, 22), 107 (100). Calculated for $C_{15}H_{24}O$: 220.1827. Found: 220.1827 (MS).

(3a*RS*,3b*SR*,6a*SR*,7a*RS*)-3a,5,5-Trimethyl-decahydrocyclopenta[a]pentalene-3,3-dicarboxylic acid diethyl ester (18) and (3a*RS*,6a*SR*)-2-[2-(3,5,5-trimethyl-1,3a,4,5,6,6a-hexahydropentalen-2-yl)-ethyl]-malonic acid diethyl ester (19): To a solution of **6** (2.25 g, 15 mmol) and cyclopropane-1,1-dicarboxylic acid diethyl ester (2.80 g, 15 mmol) in 1,2-dichloroethane (75 ml) was added at 0°C under nitrogen with stirring within 10 min a solution of ethyl aluminium dichloride in hexane (1.0 M, 45 mmol). After the addition was complete, the mixture was stirred at room and the reaction progress monitored by GC [3 m x 1/4″ all glass system, 15% OV 101 on Chromosorb W AW/DMCS, 60/80 mesh, 10°C/min 50-220°C, 25 min 220°C; retention times (min): 10.7 (**6**), 12.8 (cyclopropane-1,1-dicarboxylic acid diethyl ester), 30.9 (**18**), 34.8 (**19**)]. After 23 h, water (75 ml) and hydrochloric acid (2N, 75 ml) were added, the phases were separated, the aqueous phase was extracted with dichloromethane (50 ml), and the combined organic phases were washed with water (2 x 50 ml) and dried ($MgSO_4$). The solvents were evaporated (bath temperature 40°C/15 torr) and the residue (6.20 g yellow oil) chromatographed on silica gel (0.06-0.20 mm) in pentane/ether [8:2, column 4 x 70 cm; R_f = 0.53 (**18**, **19**)] to yield 3.17 (63%) of a slightly yellow oil, containing 80% **18** and 11% **19** (GC). A pure sample of **18** and a 1:1-mixture of **18** and **19** were obtained by preparative GC. Colourless liquids. **18**: ^{1}H NMR (300 MHz, $CDCl_3$, $CHCl_3$ int): δ = 0.88 (s, 3H), 1.03 (s, 3H), 1.12 (s, 3H), 1.15-1.40 (m, 10H), 1.53-1.63 (m, 2H), 1.73 (mc, 1H), 2.00-2.13 (m, 2H), 2.20-2.38 (m, 2H), 2.57 (mc, 1H), 2.70 (mc, 1H), 4.06-4.23 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ int): δ = 14.02 (coincidence of two lines), 19.93, 27.40 (C_{prim}), 28.71 (C_{sek}), 29.38 (C_{prim}), 32.70, 37.80, 42.10 (C_{sek}), 43.22 (C_{tert}), 43.91 (C_{quart}), 48.50 (C_{sek}), 51.16, 55.90 (C_{tert}), 56.44 (C_{quart}), 60.56, 60.71 (C_{sek}), 69.41, 171.75, 172.57 (C_{quart}); MS m/z 336 (M^+, 2), 176 (100). Calculated for $C_{20}H_{32}O_4$: 336.2300. Found: 336.2300 (MS). **19**: ^{1}H NMR .(300 MHz, $CDCl_3$, $CHCl_3$ int): In the 1:1-mixture with **18**, only the uncoupled methyl groups could be assigned: δ = 0.91, 1.00, 1.47 (3 s, 3 CH_3). The remaining protons showed overlapping multiplets at δ = 1.15-3.05 and 4.06-4.25. ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ int): All resonances could be assigned: δ = 12.32, 13.97 (coincidence of two lines) (C_{prim}), 25.97, 26.97 (C_{sek}), 27.25, 28.87, 38.37 (C_{prim}), 40.71 (C_{quart}), 41.39, 45.97, 49.67 (C_{sek}), 51.32, 55.15 (C_{tert}), 61.17 (coincidence of two lines) (C_{sek}), 130.19, 136.28, 169.48, 169.52 (C_{quart}).

(3a*RS*,3b*SR*,6a*SR*,7a*RS*)-3a,5,5-Trimethyl-decahydrocyclopenta[a]pentalene-3,3-dicarboxylic acid (20): A a solution of potassium hydroxide in methanol (10 M, 170 ml) was diluted with water (50 ml), crude **18** (2.02 g, content 80%, 4.80 mmol) was added, and the mixture was heated to reflux. After 3 days, the mixture was acidified with conc. HCl (150 ml) and perforated with ether (150 ml, 2 h). The etheral phase was dried ($MgSO_4$) and concentrated on a rotary evaporator (bath temperature 50°C /15 torr), and the residue (1.73 g yellowish foamy solid) purified by short path chromatography on silica gel (0.06-0.20 mm) in ether (column 4.5 x 15 cm). The forerun (20 ml) was discarded, while the main fraction (60 ml) yielded 1.29 g (96%) of nearly pure **20** as colourless solid, mp 74-80°C (dec.). ^{1}H NMR (300 MHz, $CDCl_3$, $CHCl_3$ int): δ = 0.90 (s, 3H), 1.05 (s, 3H), 1.20 (s, 3H), 1.25-1.55 (m, 5H), 1.60 (mc, 1H), 1.74 (mc, 1H), 2.04-2.24 (m, 2H), 2.30-2.52 (m, 2H), 2.62 (mc, 1H), 2.76 (mc, 1H), 10.4 (br s, 2H); ^{13}C NMR (50 MHz, $CDCl_3$, $CDCl_3$ int): δ = 19.92, 27.43 (C_{prim}), 28.76 (C_{quart}), 29.36 (C_{prim}), 32.06, 37.33 (C_{quart}), 41.80 (C_{sek}), 43.26 (C_{tert}), 44.10, 48.76 (C_{sek}), 50.94, 55.98 (C_{tert}), 57.27, 69.42 (C_{sek}), 177.37, 178.42 (C_{quart}); MS m/z 280 (M^+, 7), 149 (100). Calculated for $C_{16}H_{24}O_4$: 280.1674. Found: 280.1674 (MS).

(3a*RS*,3b*SR*,6a*SR*,7a*RS*)-3a,5,5-Trimethyl-decahydrocyclopenta[a]pentalen-3-one (21): To a solution of **20** (400 mg, 1.43 mmol) in dry benzene (2.0 ml) and pyridine (295 mg, 3.73 mmol) was added 91% (w/w) lead tetraacetate in acetic acid (1.53 g, 3.16 mmol) and the mixture heated to reflux. After 3 h, the

mixture was diluted with ether (8 ml), filtrated, and the residue washed with ether (3 x 5 ml). The combined organic phases were washed with hydrochloric acid (2N, 4 x 2 ml), saturated sodium bicarbonate (4 x 2 ml) and dried (molecular sieves 4 Å). The solvents were evaporated (bath temperature 40°C/20 torr) and the residue hydrolyzed with a solution of potassium hydroxide (0.50 g) in methanol (1.0 ml) and water (1.0 ml). After 30 min of reflux, the mixture was diluted with ether (5 ml), the aqueous phase was saturated with potassium carbonate, the layers were separated, the aqueous phase was extracted with ether (4 x 2 ml), the combined organic phases were dried (molecular sieves 4 Å), and the solvents were evaporated (bath temperature 40°C/20 torr). The residue was chromatographed on silica gel (70-130 mesh) in pentane/ether [95:5, column 10 x 2 cm, R_f = 0.24 (**21**)] to yield 144 mg (49%) of pure **21** as colourless needles, mp 45°C. The ^1H and ^{13}C NMR data were in accord with literature data.[13]

Acknowledgement: Financial support of the Fonds der Chemischen Industrie is gratefully acknowledged.

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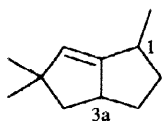
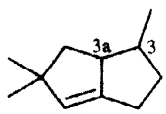
8. 2-Methyl-cyclobutanone (bp 108°C) was prepared in 30 g batches (yield 61%) from cyclopropyl phenyl sulfide as described for cyclobutanone (Trost, B. M.; Vladuchick, W. C. *Synthesis* **1978**, 821). The ^1H NMR data were in accord with literature data (Hanack, M.; Collins, C. J.; Stutz, H.; Benjamin, B. M. *J. Am. Chem. Soc.* **1981**, *103*, 2356-2360). The ^{13}C NMR data (75 MHz, $CDCl_3$, $CHCl_3$ int) have not yet been reported and were as follows: δ = 13.71 (C_{prim}), 18.37, 44.37 (C_{sek}), 54.61 (C_{tert}), 211.87 (C_{quart}). For an alternative synthesis, see: Van Leusen, D.; van Leusen, A. M. *Synthesis* **1980**, 325-326.

9. Only products derived from tertiary carbenium ions have been taken into account: 1,5,5-trimethyl-1,2,3,3a,4,5-hexahydropentalene (**22**), 3,5,5-trimethyl-1,2,3,3a,4,5-hexahydropentalene (**23**), 2,2,4-trimethyl-1,2,3,3a,4,5-hexahydropentalene (**24**), 5,5-dimethyl-1-methylene-octahydropentalene (**25**), 2,2,6-trimethyl-1,2,3,3a,4,5-hexahydropentalene (**26**), 1,5,5-trimethyl-1,2,3,4,5,6-hexahydropentalene (**27**) and 2,2,6-trimethyl-1,2,3,3a,4,6a-hexahydropentalene (**6**). The heats of formation (kcal/mol) were calculated using the conformational search routine HUNTER (Weiser, J.; Holthausen, M. C.; Fitjer, L. *J. Comput. Chem.* **1997**, *18*, 1264-1281) in connection with MMP2 (Sprague, J. T.; Tai, J. C.; Yuh, Y. H.; Allinger, N. L. *J Comput. Chem.* **1987**, *8*, 581-603) and MM3(92) (Allinger, N. L.; Yuh, Y. H.; Lii, J.-H. *J. Am. Chem. Soc.* **1989**, *111*, 8551-8566). The values of MM3(92) are given in brackets. Interestingly, only MMP2 would have been predicted the exclusive formation of (3a*RS*,6a*RS*)-**6**.



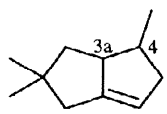
22

-14.7 (-15.9) (1*RS*,3a*RS*)
-14.8 (-15.4) (1*RS*,3a*SR*)



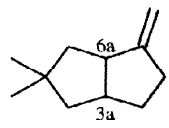
23

-13.2 (-14.0) (3*RS*,3a*RS*)
-15.0 (-16.1) (3*RS*,3a*SR*)



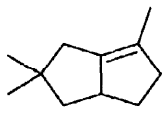
24

-13.2 (-12.4) (3a*RS*,4*RS*)
-15.1 (-14.5) (3a*RS*,4*SR*)



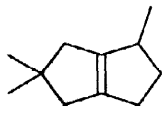
25

-8.5 (-8.9) (3a*RS*,6a*RS*)
-15.5 (-15.1) (3a*RS*,6a*SR*)



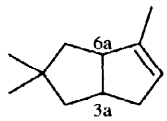
26

-17.4 (-18.0)



27

-19.1 (-18.2)



6

-10.0 (-8.4) (3a*RS*,6a*SR*)
-20.3 (-18.1) (3a*RS*,6a*RS*)

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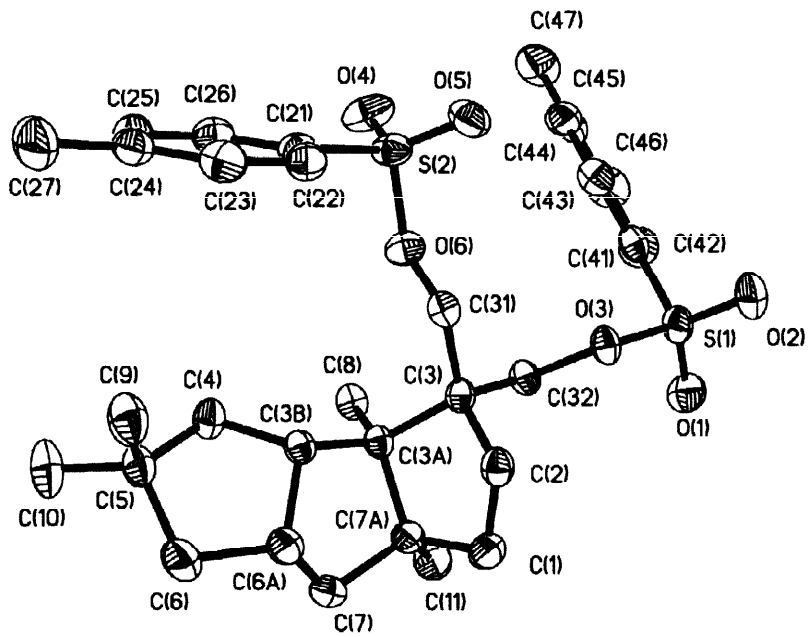
11. **13** ($C_{31}H_{42}O_6S_2$, M 574.2, mp 140-142°C) formed colourless crystals from ether, space group *P1*, a = 1078(4), b = 1300.5(4), c = 1324.2(4) pm, α = 112.55(2), β = 98.560(10), γ = 111.970(10)°, V = 1.4947(9) nm^3. 4001 reflections with 3.5 < Θ < 22.5° were measured on a Stoe four-circle diffractometer using graphite monochromated radiation Mo K_α. Of these, 3886 with $|F| > 3\sigma(F)$ were used for the structure determination and refinement. The structure was solved by direct methods. The anisotropic refinement with geometrically positioned H atoms (riding model: C-H = 96 pm, ∠HCH = 109.5°) converged at R_1 = 0.0379 (wR_2 = 0.0996). All calculations were performed with the program SHELX TL. All relevant crystallographic data have been deposited with the Cambridge Crystallographic Data Centre.



Molecular structure of **13** (hydrogen atoms omitted)

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