237. Consecutive Application of the α-Alkynone Cyclization: Total Synthesis of (±)-$\Delta^{9(12)}$-Capnellene[1])

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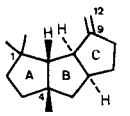
Summary

The synthesis of the (±)-form of the marine sesquiterpene (–)-$\Delta^{9(12)}$-capnellene (**1**) by double application of the α-alkynone cyclization is described. Starting with 2,2,5-trimethylcyclopentanone (**2**), the elaboration of the tricyclo[6.3.0.$0^{2,6}$]undecane C-skeleton of **1** proceeded through the α-alkynone **3**, which was cyclized thermally to the bicyclo[3.3.0]octenone **4**. For the anellation of the third five-membered ring, **4** was transformed into the α-alkynone **5** and the latter cyclized thermally to a mixture of the angular triquinenone **6** and the linear triquinenone **7**. The last steps in the synthesis of (±)-$\Delta^{9(12)}$-capnellene (**1**) were then accomplished from **7** by known methods.

1. Introduction. – (–)-$\Delta^{9(12)}$-Capnellene ((–)-**1**), a marine sesquiterpene isolated in 1978 by *Djerassi et al.* [1], represents a parent hydrocarbon and presumed biosynthetic intermediate of the capnellanes, a class of oxygenated derivatives of **1**, isolated from the soft coral *Capnella imbricata* [2]. The three rings of the tricyclo[6.3.0.$0^{2,6}$]undecane (a triquinane [3]) skeleton of **1** are fused in a *cis-transoid-cis* arrangement.



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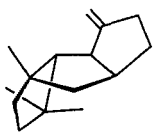
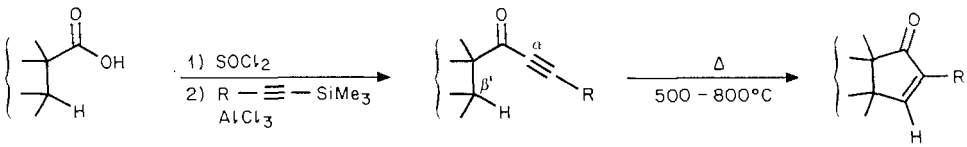


Two syntheses of **1** have recently published [4] [5]. We were interested in testing the synthetic usefulness of the reaction sequence **A** → **B** → **C**, which includes the



A R = H, CH_3, $SiMe_3$ **B** **C**

[1]) Presented by *J. Huguet* at the meeting of the Swiss Chemical Society in Berne, October 15, 1982.

[2]) Postdoctoral fellow, University of Zürich, 1980–1982.

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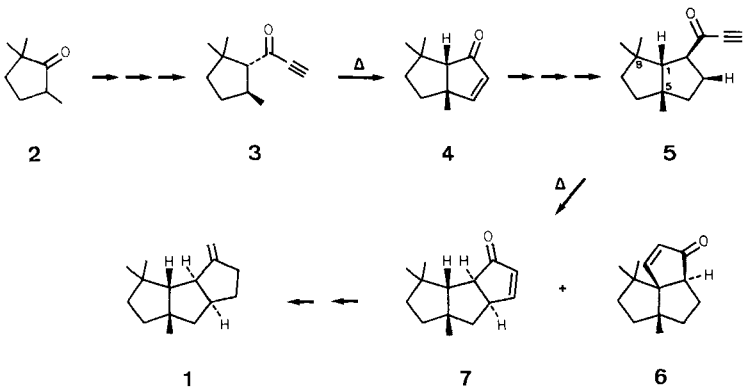
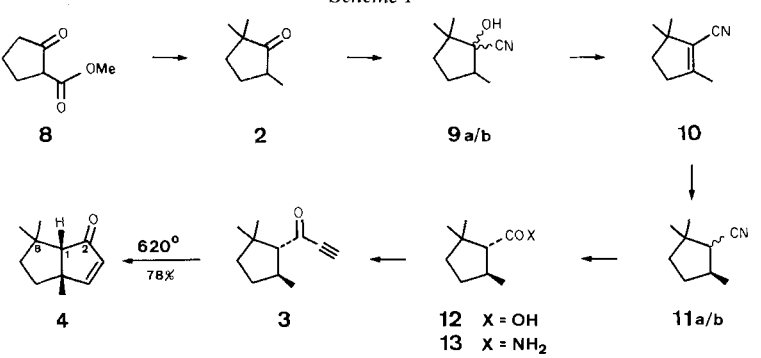
α-alkynone cyclization [6] in the same way as it was done in the synthesis of modhephene [7] and of albene [8].

Thus our approach to **1** was based on two key intermediates, the 2-cyclopentenones **4** and **7**, to be obtained by gas-phase thermolysis from the α-alkynones **3** and **5**. While **4** was expected [9] to be the only product in the cyclization of **3** with only one H_β-atom *cis* to the propioloyl group, the same reaction with **5** (two *cis* H_β-atoms) could lead to two products, namely the linear triquinenone **7** and the angular triquinenone **6**. Our previous experience [9] would actually predict **6** to be preferred by a factor of 2, except that steric hindrance at H–C(1) of **5** might suppress the formation of **6** in favor of the desired **7**. All chiral compounds in *Chapters 2* to *4* are racemic mixtures.



2. Synthesis and thermolysis of ethynyl *trans*-2,2,5-trimethyl-1-cyclopentyl ketone (*3*). – The synthesis of the first key intermediate, 5,8,8-trimethylbicyclo[3.3.0]-oct-3-en-2-on (**4**), is outlined in *Scheme 1*. Exhaustive methylation of methyl 2-oxocyclopentanecarboxylate (**8**) with methyl iodide in THF solution using NaH, followed by hydrolysis and decarboxylation of the crude product, yielded 49% of 2,2,5-trimethylcyclopentanone (**2**) [10]. Reaction of **2** with trimethylsilyl cyanide, catalyzed by zinc iodide and subsequent cleavage of the trimethylsilyl group according to [11] afforded 95% of a *ca.* 5:1 mixture of the diastereomeric cyanohydrines **9a** and **9b**. These isomers were separable by column chromatography,

Scheme 1



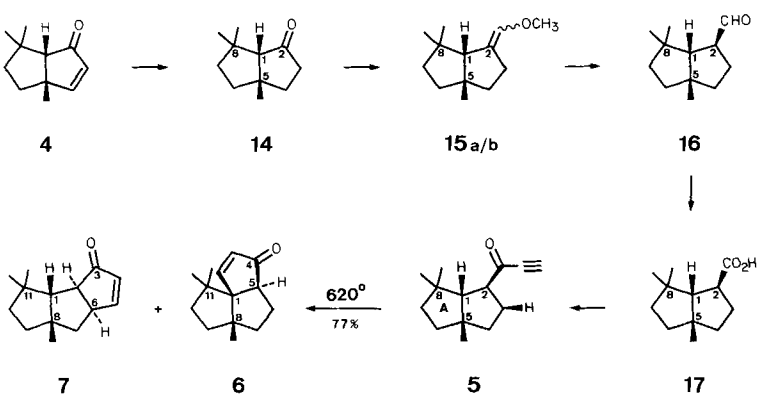
but their spectral data did not offer an evident argument for their relative configurations.

The α,β-unsaturated nitrile **10** (64%) was obtained by dehydration of the mixture **9a/b** with phosphorus oxychloride in pyridine. On treatment with 'copper hydride complex' by the procedure described by *Paquette et al.* [12], **10** was reduced to a *ca.* 1:1 mixture of the epimeric nitriles **11a/b** (69%). The hydrolysis of the latter required a large excess of KOH in refluxing diethyleneglycol to give 2,2,5-trimethylcyclopentanecarboxylic acid (**12**) (50%), along with 4% of the corresponding amide **13**. Since the more stable stereoisomer is expected to be formed under these drastic conditions, the *trans*-configuration is assigned to **12**. This was later confirmed by the thermolysis of the α-alkynone **3** (see below).

The α-alkynone **3** was prepared without isolation of the intermediates in 87% overall yield by acylation of bis(trimethylsilyl)acetylene with the acyl chloride of **12** (*cf.* [6]) and by hydro-de-silylation[3]) of the crude β-trimethylsilyl-alkynone under the conditions given in [7]. The α-alkynone cyclization to the bicyclic enone **4** was achieved in 78% yield by passing gaseous **3** in a stream of nitrogen at reduced pressure through a hot quartz tube filled with quartz chips at 620° (*cf.* [6]). Since such a cyclization occurs only when the propioloyl side chain and the H–C(β') bond to be inserted are located on the same ring side of the five-membered ring [9], this result confirms the *trans*-configuration of **12**.

3. Synthesis and thermolysis of the α-alkynone *5*. – The conversion of the bicyclic enone **4** to the second key intermediate (1*R**,2*R**,6*S**,8*R**)-8,11,11-trimethyltricyclo[6.3.0.0^{2,6}]undec-4-en-3-one (**7**), is outlined in *Scheme 2*. Catalytic hydrogenation of the double bond in **4** led to the saturated ketone **14**, which was shown to be identical with the intermediate of *Paquette*'s synthesis[4]) of **1** [5]. A modified

Scheme 2



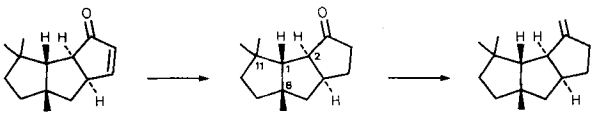
[3]) *Cf.* IUPAC Provisional Nomenclature for Straightforward Transformations in Pure Appl. Chem. *53*, 305 (1981).

[4]) We thank Prof. *L. A. Paquette* for kindly providing us with copies of the IR. and ^{1}H-NMR. spectra of the intermediates **14** and **7** of his synthesis of **1** [5].

Wittig-Horner methoxyolefination (without isolation of the diphenylphosphinoyl intermediate [13]) with **14** led to a *ca.* 1:1 mixture of the stereoisomeric enol ethers **15a** and **15b** (51% yield, but 68% when based on unrecovered starting ketone **14**), which were separated by column chromatography. The spectral data of **15a** and **15b** offered no immediately evident argument for their configuration at the double bond.

Acid hydrolysis of a **15a/b** mixture gave the aldehyde **16** (95%) as a single stereoisomer which on oxidation with *Jones* reagent [14] was converted to the acid **17** (89%). The bicyclic α-alkynone **5** was then obtained from the acyl chloride of **17** by the method described above for the conversion **12** → **3** (without isolation of the intermediate β-trimethylsilyl alkynone) in an overall yield of 76%. Since the coupling constant between H–C(1) and H–C(2) in **16**, **17** and **5** was about the same, all three compounds may be taken to have the same configuration at C(2). Although the size of this coupling constant ($J = 8$–9 Hz) does not allow the assignment of the relative configuration at this center, we write the substituent at C(2) in *cis*-position relative to H–C(1) on the basis of a preliminary steric argument, which assumes that the *exo*-position is favored over the *endo*-position in bicyclo[3.3.0]octane systems [3] and that the conditions of formation of these (in all cases enolizable) substituents in **16**, **17** and **5** lead to the thermodynamically more stable isomer. The thermolysis of **5**, under the same conditions as mentioned above for **3**, led to a mixture of the isomeric tricyclic compounds **6** and **7** in a ratio of 55:45. The configurations at C(2) of **5** and **7** show the correspondance expected from the known stereospecificity [9] of this reaction. After chromatographic separation, the two isomers **6**, m.p. 147–150°, and the previously known [5] **7**[3]), were obtained in 44 and 33% yield, respectively. The specificity of this α-alkynone cyclization, expressed by the ratio **6**/**7** of 55:45, deviates significantly from the 2:1 ratio predicted by our previous work [9]. This may be explained by a crowding due to two of the methyl groups, one at C(5) and the other at C(8), both pointing towards the same side of ring A in **5** as the tertiary H–C(1), which impedes insertion at C(1) and therefore disfavors the formation of **6**.

4. Synthesis of (±)-$\Delta^{9(12)}$-capnellene (*1*). – The synthesis of (±)-**1** from the tricyclic enone **7** was completed by using the two steps which have already been worked out in [5] and partially in [4]: catalytic hydrogenation of the α,β-double bond produced the tricyclic ketone **18**, and *Wittig* olefination (*cf.* [15]) introduced the methylidlene group. The synthetic (±)-$\Delta^{9(12)}$-capnellene (**1**), obtained in 84% yield from **7**, showed the same IR., ^{1}H- and ^{13}C-NMR. spectra as the natural product [1][5]).



7 **18** **1**

This work was supported by the *Schweizerischer Nationalfonds zur Förderung der wissenschaftlichen Forschung* and by the *Sandoz AG*, Basel.

[5]) We thank Prof. *C. Djerassi* for kindly providing us with copies of the IR., ^{1}H- and ^{13}C-NMR. spectra of natural (–)-**1** [1].

Experimental Part

1. *General.* See [9].

2. *Preparation of 2,2,5-trimethylcyclopentanone* (**2**). To a stirred suspension of 14.4 g (0.6 mol) of NaH in 500 ml of dry THF at −10°, a mixture of 28.4 g (0.2 mol) of methyl 2-oxocyclopentanecarboxylate (**8**) and 75 ml (1.2 mol) of methyl iodide was added within 1 h, the temp. being kept between −10 and −5°. The mixture was then allowed to warm up to RT., stirred overnight, poured onto 400 g ice, acidified to pH 1 with *ca.* 20 g of conc. sulfuric acid and saturated with solid NaCl. After separation of the org. phase, the aq. phase was extracted 3 times with 100 ml of ether, the combined org. phases were washed twice with 200 ml of water, and once with 100 ml of 1M $Na_2S_2O_3$ (to reduce the I_2 present), 200 ml of water and 200 ml of sat. NaCl-solution. After drying over anh. $MgSO_4$ and evaporation, the remaining yellow oil was dissolved in 25 ml of methanol and stirred for 1 h with 35 ml of 40% KOH-solution. After acidification to pH 1 by addition of *ca.* 25 ml of conc. hydrochloric acid and heating to reflux for 1.5 h, the mixture was cooled to RT., the org. layer separated and the aq. phase extracted 3 times with 50 ml of pentane. The combined org. extracts were washed with water, and sat. NaCl-solution, dried over anh. $MgSO_4$, and distilled at atmospheric pressure through a 10-cm-*Vigreux* column, collecting at 142–147° ([10]: b.p. 70°/50 Torr) 12.36 g (49%) of **2** as a colorless liquid (purity: 98% by anal. GC. (*SE-52*, 100°) containing at most 2% of 2,2,5,5-tetramethylcyclopentanone). – IR. ($CHCl_3$): 2960*s*, 2930*m*, 2870*m*, 1730*s* (C=O), 1460*m*, 1380*w*, 1005*w*, 895*w*. – ^{1}H-NMR. (200 MHz, $CDCl_3$): 2.40–2.00 (*m*, 2 H); 1.95–1.35 (*m*, 3 H); 1.12 (*d*, J = 7.5, 3 H, H_3C–C(5)); 1.08 (*s*, 3 H, H_3C–C(2)); 0.98 (*s*, 3 H, H_3C–C(2)). – MS. (70 eV): 126 (55, M^+), 111 (29), 93 (16), 83 (18), 69 (72), 56 (82), 41 (100).

3. *Preparation of 1-hydroxy-2,2,5-trimethylcyclopentane-1-carbonitrile* (**9a/b**). Using the procedure of [11], 1.26 g (10 mmol) of **2** was transformed into 1.45 g (95%) of **9**, a yellow solid containing **9a** and **9b** in a ratio of *ca.* 5:1 (purity: 97% by anal. GC. (*SE-52*, 100°)) For analysis, the isomers were separated by column chromatography (silica gel, hexane/ethyl acetate 95:5), **9a** being eluted before **9b**.

Properties of **9a**. White solid, m.p. 42–46°. – IR. ($CHCl_3$): 3590*m*, 3600–3100*m* br., 2960*s*, 2870*m*, 2230*w* (C≡N), 1460*m*, 1370*m*, 1130*m*, 1000*m*, 990*m*. – ^{1}H-NMR. (200 MHz, $CDCl_3$): 2.70–2.30 (*m*, 2 H, H–C(5) and HO, about half of it is exchangeable with D_2O); 2.10–1.30 (*m*, 4 H); 1.17 (*s*, 6 H, 2 H_3C–C(2)); 1.15 (*d*, J = 7.5, 3 H, H_3C–C(5)). – MS. (70 eV): 138 (9, $M^+ - 15$), 126 (17), 111 (11), 97 (10), 83 (6), 70 (22), 56 (100).

$C_9H_{15}NO$ (153.23) Calc. C 70.55 H 9.87 N 9.14% Found C 70.20 H 9.60 N 9.10%

Properties of **9b**. White solid, m.p. 56.5–58.0°. – IR. ($CHCl_3$): 3590*m*, 3600–3100*m* br., 2970*s*, 2880*m*, 2240*w* (C≡N), 1465*m*, 1390*m*, 1160*m*, 1080*s*. – ^{1}H-NMR. (200 MHz, $CDCl_3$): 2.57 (br. *s*, 1 H, HO, exchangeable with D_2O); 2.40–2.15 (*m*, 1 H); 2.10–1.84 (*m*, 1 H); 1.78–1.50 (*m*, 2 H); 1.48–1.27 (*m*, 1 H); 1.23 (*d*, J = 7.5, 3 H, H_3C–C(5)); 1.22 (*s*, 3 H, H_3C–C(2)); 1.03 (*s*, 3 H, H_3C–C(2)). – MS. (70 eV): 138 (9, $M^+ - 15$), 126 (18), 111 (11), 97 (10), 83 (8), 70 (22), 56 (100).

$C_9H_{15}NO$ (153.23) Calc. C 70.55 H 9.87 N 9.14% Found C 70.53 H 9.80 N 9.01%

4. *Preparation of 2,5,5-trimethyl-1-cyclopentene-1-carbonitrile* (**10**). A stirred solution of 11.84 g (77.3 mmol) of **9a/b** in 100 ml of pyridine was treated with 25 ml (*ca.* 280 mmol) of $POCl_3$ and heated to reflux for 45 min. The cooled mixture was poured onto 400 g of ice and 90 ml of conc. hydrochloric acid. After separation of the org. layer, the aq. phase was extracted 6 times with 50 ml of ether. The combined org. extracts were washed twice with 200 ml water and with 200 ml of sat. NaCl-solution, dried over anh. $MgSO_4$, and evaporated to give 9.17 g of a brown oil which, after bulb-to-bulb distillation, afforded at 120°/35 Torr 6.68 g (64%) of **10** as a yellow oil (purity: 92% by anal. GC. (*SE-52*, 93°)). An analytical sample of **10** was obtained by prep. GC. (*Carbowax*, 120°) followed by bulb-to-bulb distillation. – IR. (film): 2950*s*, 2860*m*, 2210*s* (C≡N), 1645*m* (C=C), 1445*s*, 1380*m*, 1365*m*, 1325*w*. – ^{1}H-NMR. (90 MHz, $CDCl_3$): 2.45 (br. *t*, J = 7, 2 H, 2 H–C(3)); 1.93 (*d*, J = 1, H_3C–C(2)); 1.78 (br. *t*, J = 7, 2 H, 2 H–C(4)); 1.13 (*s*, 6 H, 2 H_3C–C(5)). – MS. (70 eV): 135 (10, M^+), 120 (100), 103 (7), 93 (53), 77 (16).

$C_9H_{13}N$ (135.21) Calc. C 79.95 H 9.69 N 10.36% Found C 79.92 H 9.90 N 10.32%

5. *Preparation of 2,2,5-trimethylcyclopentane-1-carbonitrile* (**11a/b**). A solution of 6.68 g (49.4 mmol) of **10** in 100 ml of dry THF was added at −78° to a stirred suspension of 385 mmol of 'copper hydride

complex' in 350 ml of THF, prepared according to the procedure of [12]. After removing the cooling bath, the mixture was stirred for 24 h at RT., cooled to 10° and treated with 100 ml of 10% $NaHCO_3$-solution and 200 ml of 20% NaOH-solution. The mixture was stirred for 30 min, the org. phase decanted and the residual black thick paste stirred vigorously with 3 portions of 100 ml of ether and decanted. The combined org. phases were washed 3 times with 100 ml of water, once with 200 ml of sat. NaCl-solution, dried over anh. $MgSO_4$, and evaporated to a volume of *ca.* 50 ml. The remaining solvent was then distilled through a 10-cm-*Vigreux*-column until the temp. reached 85° at 100 Torr. Bulb-to-bulb distillation of the residue at 115°/14 Torr yielded 4.68 g (69%) of **11a/b** (*ca.* 1:1 mixture) as a colorless oil (purity: 98% by anal. GC. (*SE-52*, 90°)). A better overall yield of **11a/b** (65%) from **9a/b** was obtained by using undistilled **10** for this reaction. An analytical sample of **11a/b** was obtained by column chromatography (silica gel, hexane/ethyl acetate 9:1). – IR. (film): 2970*s*, 2880*s*, 2240*m* (C≡N), 1465*s*, 1390*m*, 1380*m*, 1375*m*. – ^{1}H-NMR. (200 MHz, $CDCl_3$): 2.66–2.20 (*m*); 2.10–1.86 (*m*); 1.76–1.38 (*m*); 1.23 (*s*); 1.21 (*d*, J = 6.8); 1.16 (*d*, J = 6.6); 1.15 (*s*); 1.13 (*s*); 1.11 (*s*); all doublet lines being of about half the intensity of singlet lines, which show similar intensities. – MS. (70 eV): 122 (32, $M^+ - 15$), 105 (15), 95 (43), 82 (88), 70 (77), 55 (90), 41 (100).

$C_9H_{15}N$ (137.23) Calc. C 78.77 H 11.02 N 10.21% Found C 78.89 H 10.79 N 9.98%

6. *Preparation of* trans-*2,2,5-trimethylcyclopentane-1-carboxylic acid* (**12**) *and* trans-*2,2,5-trimethylcyclopentane-1-carboxamide* (**13**). A solution of 4.68 g (34.1 mmol) of **11a/b** and 19.1 g (342 mmol) of KOH in 40 ml of diethyleneglycol was heated to reflux in an oil bath at 200° for 16 h. After cooling and addition of 120 ml of water, the mixture was extracted 3 times with 50 ml of ether. The combined extracts were washed with water and sat. NaCl-solution, dried over anh. $MgSO_4$, and evaporated to yield a waxy solid which, after recrystallization from hexane/acetone/ether afforded 220 mg (4%) of **13** as white needles, m.p. 153–155°. – IR. ($CHCl_3$): 3530*m*, 3410*m*, 2950*s*, 2870*m*, 1680*s* (C=O), 1590*s*, 1460*m*, 1400*m*, 1370*m*. – ^{1}H-NMR. (200 MHz, $CDCl_3$): 5.60 (br. *s*, 1 H, HN); 5.40 (br. *s*, 1 H, HN); 2.54–2.30 (*m*, 1 H); 2.00–1.80 (*m*, 1 H); 1.78 (*d*, J = 10.3, 1 H, H–C(1)); 1.60–1.46 (*m*, 2 H); 1.32–1.06 (*m*, 4 H) including at 1.15 (*s*, 3 H, H_3C–C(2)); 1.01 (*d*, J = 6.6, 3 H, H_3C–C(5)); 0.96 (*s*, 3 H, H_3C–C(2)). – MS. (70 eV): 155 (6, M^+), 140 (7), 133 (6), 122 (21), 109 (10), 99 (42), 96 (50), 86 (100), 81 (65), 69 (65), 55 (70), 41 (75).

$C_9H_{17}NO$ (155.24) Calc. C 69.63 H 11.04 N 9.02% Found C 69.69 H 10.80 N 9.09%

The aq. phase was acidified at 0° with 30 ml of conc. hydrochloric acid and extracted 4 times with 50 ml of ether. The combined extracts were washed with water and sat. NaCl-solution, dried over anh. $MgSO_4$, and evaporated to yield 2.63 g (50%) of **12** as a yellow oil (purity: 100% by anal. GC. (*SE-52*, 120°)). An analytical sample of **12** was obtained by bulb-to-bulb distillation at 130°/14 Torr. – IR. (film): 3500–2200*s* br., 1705*s* (C=O), 1465*m*, 1425*m*, 1390*w*, 1380*w*, 1370*m*, 1295*m*, 1230*m*, 940*m* br., 725*m*. – ^{1}H-NMR. (200 MHz, $CDCl_3$): 8.30 (br. *s*, 1 H, HO); 2.54–2.28 (*m*, 1 H, H–C(5)); 2.04 (*d*, J = 10.5, 1 H, H–C(1)); 2.00–1.80 (*m*, 1 H); 1.70–1.42 (*m*, 2 H); 1.36–1.08 (*m*, 4 H) including at 1.20 (*s*, 3 H, H_3C–C(2)); 1.04 (*d*, J = 6.5, 3 H, H_3C–C(5)); 0.98 (*s*, 3 H, H_3C–C(2)). – MS. (70 eV): 141 (3, $M^+ - 15$), 123 (10), 100 (11), 95 (22), 87 (90), 70 (100), 55 (37).

$C_9H_{16}O_2$ (156.23) Calc. C 69.19 H 10.32% Found C 69.40 H 10.49%

7. *Preparation of ethynyl* trans-*2,2,5-trimethyl-1-cyclopentyl ketone* (**3**). From 2.63 g (16.9 mmol) of **12** and $SOCl_2$ (*cf.* [9]), 2.61 g (89%) of the acyl chloride of **12** was obtained as a colorless oil after bulb-to-bulb distillation at 85°/14 Torr. Treatment of 1.75 g (10 mmol) of the latter with bis(trimethylsilyl)acetylene according to [6] gave 2.44 g of crude (trimethylsilyl)alkynone (not isolated), which was treated according to [7] to yield, after bulb-to-bulb distillation at 115°/14 Torr, 1.42 g (87%) of **3** as a slightly yellowish oil (purity: 98% by anal. GC. (*SE-52*, 120°)). An analytical sample of **3** was obtained by column chromatography (silica gel, hexane/ethyl acetate 98.5:1.5) followed by bulb-to-bulb distillation. – UV. (ethanol): 212 (5600), 219 *S* (4300). – IR. (film): 3260*m* (H–C≡), 2960*s*, 2870*m*, 2090*s* (C≡C), 1665*s* (C=O), 1460*m*, 1390*w*, 1370*m*, 1130*m*, 1085*m*. – ^{1}H-NMR. (200 MHz, $CDCl_3$): 3.27 (*s*, 1 H, H–C≡); 2.76–2.48 (*m*, 1 H, H–C(5)); 2.28 (*d*, J = 10.2, 1 H, H–C(1)); 2.02–1.78 (*m*, 1 H); 1.74–1.42 (*m*, 2 H); 1.34–1.04 (*m*, 4 H) including at 1.26 (*s*, 3 H, H_3C–C(2)); 0.98 (*d*, J = 6.6, 3 H, H_3C–C(5)); 0.94 (*s*, 3 H, H_3C–C(2)). – MS. (70 eV): 149 (15, $M^+ - 15$), 107 (11), 95 (100), 77 (20), 69 (35), 55 (33).

$C_{11}H_{16}O$ (164.25) Calc. C 80.44 H 9.82% Found C 80.53 H 10.02%

8. *Preparation of* cis-*5,8,8-trimethylbicyclo[3.3.0]oct-3-en-2-one* (**4**). The thermolysis of 4.61 g (28.1 mmol) of **3** at 620°/14 Torr for 12 h was carried out in the apparatus described in [16]. The crude oil from the cooling trap was dissolved in ether, and the solution dried over anh. $MgSO_4$ and evaporated to give 3.96 g of a yellow oil which, after bulb-to-bulb distillation at 110°/14 Torr, afforded 3.60 g (78%) of **4** as a yellow oil (purity: 97% by anal. GC. (*SE-52*, 120°)). An analytical sample of **4** was obtained by column chromatography (silica gel, hexane/ethyl acetate 95:5). – UV. (ethanol): 222 (8600). – IR. (film): 3080*w* (H–C=), 3040*w* (H–C=), 2960*s*, 2870*s*, 1705*s* (C=O), 1590*m* (C=C), 1465*m*, 1390*w*, 1380*w*, 1370*m*, 1345*m*, 1285*m*, 1160*m*, 805*m*. – ^{1}H-NMR. (200 MHz, $CDCl_3$): 7.32 (*d*, J = 5.5, 1 H, H–C(4)); 5.98 (*d*, J = 5.5, 1 H, H–C(3)); 1.87 (*s*, 1 H, H–C(1)); 1.84–1.60 (*m*, 2 H); 1.54–1.36 (*m*, 2 H); 1.32, 1.11 and 1.02 (3*s*, 9 H, H_3C–C(5) and 2 H_3C–C(8)). – MS. (70 eV): 164 (20, M^+), 149 (75), 131 (21), 121 (22), 109 (47), 96 (100), 79 (32), 67 (30), 55 (21).

$C_{11}H_{16}O$ (164.25) Calc. C 80.44 H 9.82% Found C 80.19 H 9.70%

9. *Preparation of* cis-*5,8,8-trimethylbicyclo[3.3.0]octan-2-one* (**14**). A solution of 3.46 g (2.1 mmol) of **4** in 30 ml of 95% ethanol was hydrogenated at atmospheric pressure and RT. over 300 mg of 10% Pd/C for 2 h. Filtration through *Celite* and evaporation yielded 3.20 g (91%) of **14** [5][3]) (purity: 97% by anal. GC. (*SE-52*, 120°)) as a yellowish oil.

10. *Preparation of* cis-*2-methoxymethylidene-5,8,8-trimethyl-bicyclo[3.3.0]octane* (**15a/b**). A solution of 1.84 g (11.1 mmol) of **14** in 5 ml of THF was added at – 78° to a stirred solution containing 27.7 mmol of the lithium ylide of methoxymethyldiphenylphosphine oxide in 200 ml of THF, prepared according to [13]. The mixture was warmed to RT., stirred for 24 h and poured into 500 ml of sat. NH_4Cl-solution. After separation of the org. layer, the aq. phase was extracted 3 times with 50 ml of ether, the combined extracts washed with sat. NaCl-solution, dried over anh. $MgSO_4$, and evaporated to yield 5.5 g of a brown oil. The latter was adsorbed on 10 g of silica gel and placed on top of 25 g of silica gel in a chromatography column. Elution with 1000 ml of hexane afforded 1.1 g (51%) of **15a/b** as a *ca.* 1:1 mixture (purity: 91% by anal. GC. (*SE-52*, 120°)). Further elution with 250 ml of hexane/ethyl acetate 99:1 and then with 200 ml of hexane/ethyl acetate 95:5 gave 597 mg (32%) of unreacted **14**; thus the yield of **15a/b** based on unrecovered **14** was 68%. The two isomers were separated by column chromatography (silica gel, hexane), **15a** being eluted before **15b**.

Properties of **15a**. – IR. (film): 2950*s*, 2860*s*, 2830*m*, 1730*s*, 1690*m*, 1460*s*, 1385*w*, 1375*m*, 1365*m*, 1220*m*, 1120*s*. – ^{1}H-NMR. (200 MHz, $CDCl_3$): 5.90 (*m*, 1 H, H–C=C); 3.50 (*s*, 3 H, CH_3O); 2.32 (br. *s*, 1 H, H–C(1)); 2.24–2.00 (*m*, 2 H, 2 H–C(3)); 1.70–1.20 (*m*, 6 H); 1.12, 0.85 (2*s*, 6 and 3 H, H_3C–C(5) and 2 H_3C–C(8)). – MS. (70 eV): 194 (14, M^+), 179 (4), 165 (17), 137 (10), 123 (100), 109 (42), 93 (43), 81 (56), 75 (83), 67 (26), 55 (33).

$C_{13}H_{22}O$ (194.32) Calc. C 80.35 H 11.41% Found C 80.06 H 11.39%

Properties of **15b**. – IR. (film): 2950*s*, 2860*s*, 2830*m*, 1725*m*, 1690*m*, 1460*m*, 1385*w*, 1375*w*, 1365*m*, 1230*m*, 1120*s*. – ^{1}H-NMR. (200 MHz, $CDCl_3$); 5.74 (br. *s*, 1 H, H–C=C); 3.56 (*s*, 3 H, CH_3O); 2.60–2.38 (*m*, 1 H, H–C(3)); 2.30–2.04 (*m*, 1 H, H–C(3)); 1.93 (*s*, 1 H, H–C(1)); 1.72–1.20 (*m*, 6 H); 1.10, 0.99 and 0.82 (3*s*, 9 H, H_3C–C(5) and 2 H_3C–C(8)). – MS. (70 eV): 194 (18, M^+), 179 (4), 165 (4), 137 (10), 123 (99), 109 (21), 93 (33), 81 (24), 75 (100), 67 (16), 55 (18).

11. *Preparation of (1R*,2R*,5S*)-5,8,8-trimethylbicyclo[3.3.0]octane-1-carboxaldehyde* (**16**). A mixture of 1.10 g (5.66 mmol) of **15a/b**, 10 ml of 10% hydrochloric acid and 10 ml of THF was stirred at RT. for 48 h. After separation of the org. phase, the aq. phase was extracted 5 times with 2 ml of ether, the combined org. solutions were washed with sat. NaCl-solution, dried over anh. $MgSO_4$, and evaporated to yield 0.97 g (95%) of **16** as a colorless oil (purity: 92% by anal. GC. (*SE-52*, 140°)). – IR. (film): 2950*s*, 2870*s*, 2810*w*, 2710*w* (H–C=O), 1725*s* (C=O), 1465*m*, 1390*w*, 1380*w*, 1370*w*, 1070*w*, 990*w*, 920*w*, 735*m*. – ^{1}H-NMR. (200 MHz, $CDCl_3$): 9.59 (*d*, J = 3.2, 1 H, H–C=O); 2.68–2.46 (*m*, 1 H, H–C(2)); 2.10–1.28 (*m*, 9 H) including at 1.77 (*d*, J = 8, *ca.* 1 H, H–C(1)); 1.16, 1.01 and 0.93 (3*s*, 9 H, H_3C–C(5) and 2 H_3C–C(8)); irradiation at 2.58 → 1.77 (*s*). – MS. (70 eV): 180 (5, M^+), 165 (42), 147 (17), 137 (11), 124 (26), 109 (68), 95 (84), 81 (100), 67 (42), 55 (45).

2,4-Dinitrophenylhydrazone of **16**. Yellow-orange needles, m.p. 155–156.5°.

$C_{18}H_{24}N_4O_4$ (360.42) Calc. C 59.99 H 6.71 N 15.55% Found C 60.23 H 7.00 N 15.27%

12. *Preparation of (1R*,2R*,5S*)-5,8,8-trimethylbicyclo[3.3.0]octane-1-carboxylic acid* (**17**). A solution of 972 mg (5.4 mmol) of **16** in 5 ml of acetone was treated for 10 min with 2.5 ml of 2.7M

Jones reagent according to [14], diluted with 3 ml 2-propanol, stirred for 5 min and evaporated. The residue was taken up in 5 ml of 10% hydrochloric acid and extracted with 5 ml of ether and then 5 times with 1 ml of ether. The combined org. extracts were washed with water and sat. NaCl-solution, dried over anh. $MgSO_4$, and evaporated to yield 941 mg (89%) of **17** as a white solid (purity: 92% by anal. GC. (*SE-52*, 140°)), which, for analytical purposes, was recrystallized twice from pentane at −60°, m.p. 84–86°. – IR. ($CHCl_3$): 3600–2400*s* br., 2940*s*, 2860*s*, 1700*s* (C=O), 1455*m*, 1410*w*, 1380*w*, 1370*w*, 1360*w*, 1295*m*. – ^{1}H-NMR. (200 MHz, $CDCl_3$): 2.66–2.46 (*m*, 1 H, H–C(2)); 2.06–1.26 (*m*, 9 H) including at 1.88 (*d*, J = 8.8, *ca.* 1 H, H–C(1)); 1.18, 0.99 and 0.97 (3 *s*, 9 H, H_3C–C(5) and 2 H_3C–C(8)); irradiation at 2.56 → 1.88 (*s*). – MS. (70 eV): 196 (49, M^+), 181 (13), 163 (8), 151 (7), 140 (8), 135 (18), 127 (43), 109 (63), 95 (57), 81 (100), 70 (46), 55 (43).

$C_{12}H_{20}O_2$ (196.29) Calc. C 73.43 H 10.27% Found C 73.30 H 10.36%

13. *Preparation of ethynyl (1*R*,2*R*,5*S*)-5,8,8-trimethylbicyclo[3.3.0]oct-2-yl ketone* (**5**). The acyl chloride obtained from 1.277 g (6.5 mmol) of **17** was treated with bis(trimethylsilyl)acetylene according to [6] to give 1.860 g of the crude (trimethylsilyl)alkynone (not isolated), which was treated according to [7] to yield, after bulb-to-bulb distillation at 140°/14 Torr, 1.003 g (76%) of **5** as a slightly yellowish oil (purity: 95% by anal. GC. (*SE-52*, 160°)). An analytical sample of **5** was obtained by column chromatography (silica gel, hexane/ethyl acetate 97.5:2.5) as a colorless oil. – UV. (ethanol): 211 (5200), 218 *S* (4000). – IR. (film): 3260*m* (H–C≡), 2950*s*, 2870*s*, 2100*s* (C≡C), 1680*s* (C=O), 1465*m*, 1390*w*, 1380*m*, 1360*m*, 1120*m*, 1100*m*. – ^{1}H-NMR. (200 MHz, $CDCl_3$): 3.22 (*s*, 1 H, H–C≡); 2.84–2.74 (*m*, 1 H, H–C(2)); 2.14–1.24 (*m*, 9 H) including at 2.03 (*d*, J = 8.6, *ca.* 1 H, H–C(1)); 1.19, 1.01 and 0.93 (3 *s*, 9 H, H_3C–C(5) and 2 H_3C–C(8)); irradiation at 2.79 → 2.03 (*s*). – MS. (70 eV): 204 (4, M^+), 189 (13), 161 (11), 148 (12), 135 (18), 123 (48), 109 (84), 95 (100), 81 (87), 67 (41), 55 (41).

$C_{14}H_{20}O$ (204.31) Calc. C 82.30 H 9.87% Found C 81.97 H 10.00%

14. *Thermolysis of* **5**. From the thermolysis of 843 mg (4.1 mmol) of **5** at 620°/14 Torr during 1 h [6], 751 mg of a dark yellow oil was recovered which by anal. GC. (*SE-52*, 160°) was shown to contain *(1*R*,5*R*,8*S*)-8,11,11-trimethyltricyclo[6.3.0.0^{1,5}]undec-2-en-4-one* (**6**) and *(1*R*,2*R*,6*S*,8*R*)-8,11,11-trimethyltricyclo[6.3.0.0^{2,6}]undec-4-en-3-one* (**7**) in the ratio 55:45. By column chromatography (silica gel, hexane/ethyl acetate 96:4) 380 mg (44%) of **6** and 275 mg (33%) of **7** were obtained.

Properties of **6**. White solid, m.p. 147–150° (subl.). – UV. (ethanol): 234 (8400). – IR. ($CHCl_3$): 2940*s*, 2860*m*, 1690*s* (C=O), 1580*m* (C=C), 1450*m*, 1385*w*, 1375*m*, 1360*w*, 1345*m*, 1080*w*, 980*w*. – ^{1}H-NMR. (200 MHz, $CDCl_3$): 7.56 (*d*, J = 5.8, 1 H, H–C(2)); 6.15 (*d*, J = 5.8, 1 H, H–C(3)); 2.60–2.48 (*m*, 1 H, H–C(5)); 1.94–1.18 (*m*, 8 H); 1.12 (*s*, 6 H, 2 H_3C–C(11)); 0.89 (*s*, 3 H, H_3C–C(8)). – ^{13}C-NMR. (20 MHz, $CDCl_3$): 211.6 (*s*, C(4)); 166.2 (*d*, C(2)); 133.4 (*d*, C(3)); 70.7 (*s*, C(1)); 54.6 (*d*, C(5)); 51.7 (*s*); 45.1 (*s*); 42.2 (*t*); 41.1 (*t*); 38.1 (*t*); 26.9 (*qa*); 26.5 (*t*); 24.9 (*qa*). – MS. (70 eV): 204 (56, M^+), 189 (17), 161 (22), 147 (18), 135 (100), 122 (90), 117 (35), 107 (76), 91 (89), 79 (63), 70 (42), 65 (35), 55 (66).

$C_{14}H_{20}O$ (204.31) Calc. C 82.30 H 9.87% Found C 82.14 H 10.04%

Properties of **7**. IR. and ^{1}H-NMR. agree with the ones supplied by Prof. *Paquette* [5][4]).

15. *Preparation of (±)-Δ$^{9(12)}$-capnellene* (**1**). A solution of 137 mg (0.671 mmol) of **7** in 5 ml of ethyl acetate was hydrogenated for 20 min at atmospheric pressure and RT. in the presence of 25 mg of 10% Pt/C [5]. The suspension was filtered through *Celite* and the filtrate evaporated to yield 127 mg of *(1*R*,2*R*,6*R*,8*R*)-8,11,11-trimethyltricyclo[6.3.0.0^{2,6}]undecan-3-one* (**18**) [5], which was treated with 1.5 ml of a *ca.* 0.65 M solution of methylidenetriphenylphosphorane in THF according to [15] to yield 115 mg (84%) of (±)-**1** as a colorless oil, identified by comparison of the IR., ^{1}H- and ^{13}C-NMR. with the ones of the authentic (−)-**1**[5]).

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