70. Synthetic Routes to Trace Constituents of Algal Pheromone Bouquets and Other Information-Imitating Substances

by **Wilhelm Boland*** and **Karin Mertes**

Institut für Biochemie der Universität, An der Bottmühle 2, D-5000 Köln 1

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Summary

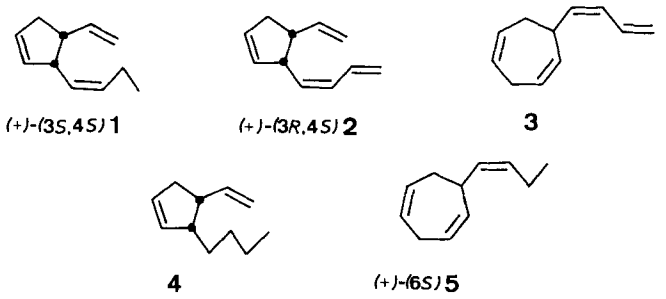
Structural modifications of multifidene (**1**), viridiene (**2**) and ectocarpene (**5**) led to the synthesis of eleven new pheromone components or imitating substances mostly by *Grignard* alkylation of cyclopentene and cycloheptadiene synthons. A new lactone α,ω-dienol conversion is reported.

The techniques of isolation and structure elucidation of volatile trace components from natural sources received substantial improvement from refined adsorptive concentration techniques such as the 'closed-loop-stripping' sampling of *Grob & Zürcher* [1]. Application and adaptation[1]) of this method to the analysis of volatiles from mature gynogametes of brown algae made possible the identification of several ethylenic hydrocarbons acting as chemical messengers between gametes of opposite polarity [2]. These substances are always secreted by gynogametes and are recognized by the sensory system of the respective androgametes at impressively low concentrations, usually in the range of 10^{-12} to 10^{-9} mol/l sea water [3][4].

Careful analyses of such messengers often revealed, apart from the specific pheromone, several other closely related ethylenic hydrocarbons. *Cutleria multifida* from the Mediterranean sea, *Syringoderma* from New Zealand and *Desmarestia aculeata* or *Desmarestia viridis* from the Atlantic may serve as examples [5]. Their respective gynogametes produce, besides the actual highly unsaturated lures multifidene (**1**), viridiene (**2**) or desmarestene (**3**), the more saturated derivatives **4** and **5**. The latter compounds *per se* proved to be ineffective, and no immediate connection with the fertilization process is apparent.

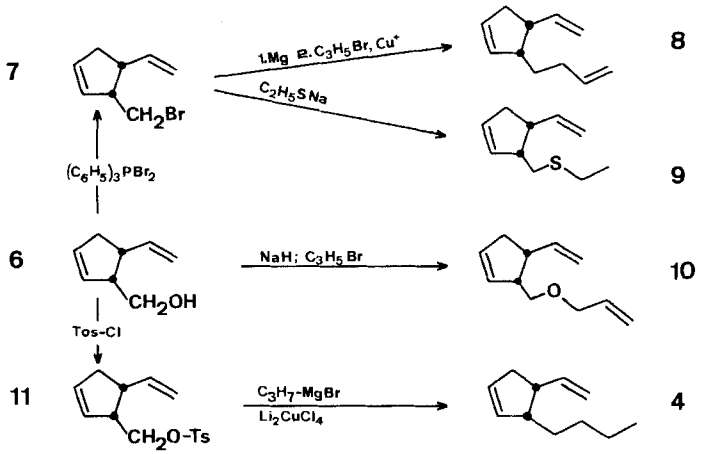
To check pheromone bouquets as complex chemical information carriers possibly exerting synergistic or antagonistic effects [6] among the species sharing a natural habitat, we need unambiguous and stereospecific syntheses of each individual compound. Their subsequent bioassay as sole components as well as in concert with all constituents of a naturally secreted mixture is a prerequisite to the understanding of mechanistic and ecological correlations. We report here on the chemical syntheses of trace components of pheromone bouquets and other imitating substances (parapheromones) for physiological purposes.

[1]) A refined equipment (according to *Gassmann*) is offered by *Normag* (*Otto Fritz GmbH*, D-6238 Hofheim/Ts.).



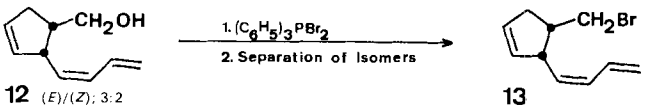
Synthetic Routes to Cyclopentene Derivatives. – *Synthesis of Multifidene-Type Hydrocarbons (Scheme 1).* An intriguing puzzle is presented by the two seaweeds *Cutleria multifida* and *Syringoderma*. Both species respond specifically to cyclopentene derivatives of essentially identical space-filling and overall geometry, namely *Cutleria* androgametes for multifidene (**1**) and *Syringoderma* spermatozoids for the more unsaturated $C_{11}H_{14}$-hydrocarbon viridiene (**2**). Notwithstanding their structural conformity both molecules are cross-distinguished by the respective receptor systems [7]. Since the additional double bond in the side chain is the only difference between the messengers, we were encouraged to synthesize the multifidene isomer **8** as well as the more saturated derivative **4.** Binding studies with their appropriate receptors should make the molecular interactions more transparent. In addition, biogenetic considerations [2] suggest all these hydrocarbons to be possible catabolites of unsaturated fatty acids which may likewise be involved in communication systems of brown algae.

Scheme 1

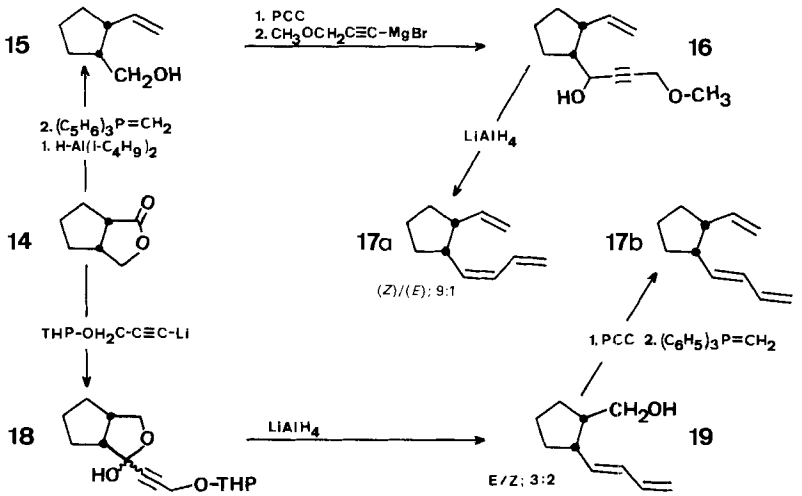


The alcohol **6,** readily available from cyclopentadiene and dibromoketene [5b], served as a versatile starting material. The alcohol **6** was converted to the bromide **7** which gave the corresponding *Grignard* reagent. Addition of 3-bromopropene in the presence of CuCN afforded the desired hydrocarbon **8** in high yield and stereochemically pure (NMR and GC). A direct nucleophilic displacement of the halide with the

Scheme 2



Scheme 3



sodium salt of ethanethiol was also possible and gave the sulfide **9** as a parapheromone for *Cutleria* androgametes [3]. Similarly, the allylic ether **10** was obtained by alkylation of the sodium alkoxide of **6** on treatment with 3-bromopropene in THF. The more saturated derivative **4** is accessible in high yield by reaction of the tosylate **11** with propylmagnesium bromide in the presence of Li_2CuCl_4 as catalyst. With this authentic reference the analysis of trace constituents of *Cutleria multifida* or *Chorda tomentosa* was facilitated, and the natural occurrence of **4** was substantiated for both species[2]) [4].

Synthesis of Viridiene-Type Molecules (Scheme 2 and *3).* Preceding studies with systematically altered multifidenes established the double bonds of this particular messenger as the points of molecular interaction [2][3]. The postulated mechanism of mutual polarization between ligand and receptor macromolecules could be further confirmed by substitution of the vinyl moiety of **1** by altered side chains with similar sterical and electronic properties such as CH_2Br, COOMe or $CH_2{-}O{-}CH_3$.

To find mechanistic analogies between the *Syringoderma* and the *Cutleria multifida* recognition system, the bromide **13** was required. Similar compounds, derived from **1,** showed full biological activity when applied as artificial signal molecules for *Cutleria* androgametes [3]. From the alcohol **12,** the desired compound **13** was easily accessible by treatment with triphenylphosphonium dibromide. Separation of the (*E*)/(*Z*)-isomers could be done with 4-phenyl-1,2,4-triazoline-3,5-dione as a selective dienophile.

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[2]) Reexamination of the *Cutleria* pheromone-bouquet [2] revealed **4** to be present as a trace constituent.

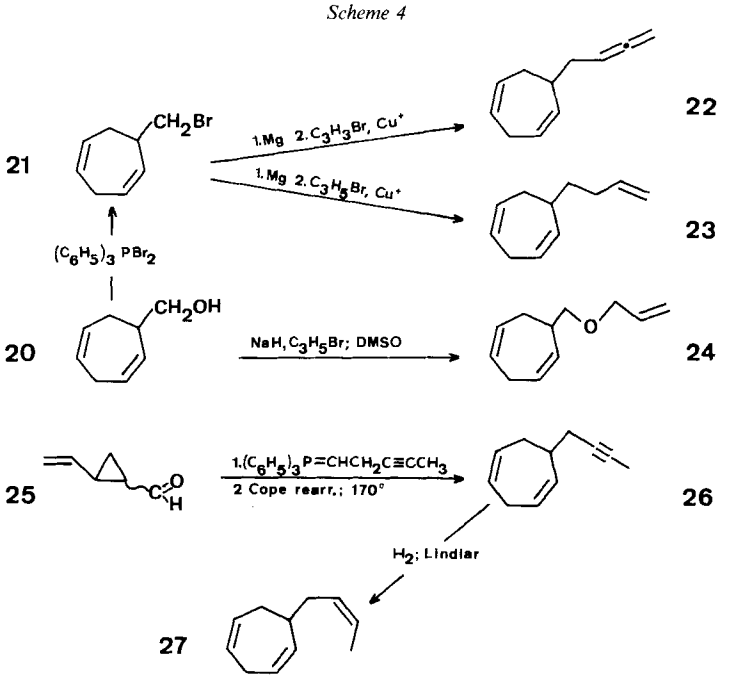
With respect to the current biogenetic concept [2], the more saturated viridiene-type hydrocarbons **17a** and **17b** were also desired as references for comparison with natural specimens.

Reductive alkenylation of the bicyclic lactone **14** with diisobutylaluminium hydride and methylidenetriphenylphosphorane gave the vinylcyclopentyl alcohol **15,** which, after oxidation to the appropriate aldehyde, was easily alkylated to the acetylenic intermediate **16.** Reduction of the latter with $LiAlH_4$ removed all oxygen substituents and led predominantly to the butadienylhydrocarbon **17a** by way of an allenic intermediate [9]. The isomer ratio was 9:1 (GC), and the pure (*Z*)-alkene **17a** was obtained as described for **13.**

Alternatively, the lactone **14** was alkylated with the lithium alt of 3-(tetrahydro-2-pyranyloxy)propyne to give, after reduction with $LiAlH_4$, the butadienyl alcohol **19;** isolation and purification of the intermediate bicyclic hydroxy-alkyne proved to be unnecessary. In contrast to the preceeding synthesis the butadienyl element consisted mainly of the (*E*)-isomer (*ca.* 65%), thus giving a stereoselective access to either of the two isomers. Finally, oxidation and subsequent *Wittig* reaction with methylidenetriphenylphosphorane led to the (*E*)-alkene **17b.**

Synthetic Routes to Cycloheptadiene Derivatives *(Scheme 4).* – A similar problem as described for the pair *Syringoderma/Cutleria multifida* was observed by testing the two seaweeds *Ectocarpus siliculosus* and *Desmarestia aculeata.* The latter species produces desmarestene (**3**) which in addition to the extra conjugated double bond in the side chain has all structural and electronic properties of the *Ectocarpus* pheromone **5.**

Scheme 4



In fact, strong interference of **3** with the *Ectocarpus* recognition system has been observed, whereas the reverse was insignificant [5a][6]. These findings clearly underline the special importance of the additional double bond in **2** or **3** as an element for differentiation of pheromones, even if the overall shape of molecules is totally preserved. To study this particular point of interaction, compounds like **22, 23, 24** and **27** were required.

Starting from the readily available alcohol **20** [10] the bromide **21** was prepared, and its *Grignard* reagent again could be very easily used to obtain the desired compounds in the same way as described for the cyclopentane family. Alkylation of the *Grignard* reagent with 3-bromopropene in the presence of Li_2CuCl_4 gave the alkene **23,** whereas addition of 3-bromopropyne formed the allene **22** as the exclusive product. The ether **24** was obtained from **20** by treating its sodium salt with 3-bromopropene in DMSO. Other solvents or elevated temperatures (*e.g.* THF; reflux) led to extensive formation of ring-conjugated by-products which, however, could be easily removed on treatment with 4-phenyl-1,2,4-triazoline-3,5-dione. Finally, compound **27** was synthesized from the aldehyde **25.** *Wittig* reaction with 3-pentynylidenetriphenylphosphorane followed by *Cope* rearrangement gave the acetylene **26,** and subsequent hydrogenation with *Lindlar's* catalyst afforded the desired hydrocarbon **27.**

Using the hydrocarbons **4, 8** and **23** as authentic references made in part possible the elucidation of the very complex pheromone bouquets of various *Laminariales* [11]. In addition, biological activity tests with the whole set of compounds described here contributed substantially to the understanding of receptor specificities and mechanisms of pheromone differentiation in the two seaweed pairs *Syringoderma/Cutleria multifida* or *Desmarestia aculeata* and *Ectocarpus siliculosus*. Detailed results will be presented elsewhere.

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Experimental Part

All melting (m.p.) and boiling (b.p.) points are uncorrected. Analytical GC: *Carlo Erba* gas chromatograph, Series *4200* equipped with *Duran* glass capillaries 50 m × 0.32 mm coated with *OV 73*. Prep. GC: stainless steel column 2 m × 4 mm filled with 15% *Apiezon L* on *Chromosorb W*, 40–60 mesh, AW, DMCS treated. Elemental analyses were performed by *I. Beetz*, Kronach. All solvents and reagents were purified prior to use. Reactions were carried out under an inert atmosphere if not stated otherwise. IR spectra (cm^{-1}) were recorded with a *Pye Unicam SP3-200* spectrophotometer. The ^{1}H-NMR spectra were obtained with a *Varian EM-390* 90-MHz spectrometer in CCl_4 with TMS as internal standard. MS (*m/z*) were run on a *Finnigan 4510* GC/MS system.

cis-*3-Bromomethyl-4-vinylcyclopentene* (**7**). To a well-stirred suspension of 12.7 g (30.0 mmol) of triphenylphosphonium dibromide in 60 ml of dry benzene was added dropwise a solution of 5.0 g (27.0 mmol) alcohol **6** in 20 ml of the same solvent. Stirring was continued at r.t. overnight, and the precipitated phosphonium salts were removed by suction. Pentane (100 ml) was added to the benzene layer, and the org. phase was carefully washed with sat. $NaHCO_3$ solution (2 × 50 ml) and H_2O (2 × 50 ml). After drying ($MgSO_4$) and evaporation of solvent *i.v.* the crude product was purified by CC on silica gel with pentane. Removal of solvent yielded 4.1 g (82%) of a colorless, fruity smelling liquid. IR (neat): 3080, 3070, 3005, 2980, 2960, 2930, 2850, 1640, 1425, 1260, 1220, 1005, 920, 705, 640. ^{1}H-NMR (CCl_4): 2.05–2.75 (*m*, 2H); 2.80–3.55 (*m*, 4H); 5.06 (*dd*, J = 10.5 and 1.5, 1H); 5.10 (*dd*, J = 18 and 1.5, 1H); 5.82 (*s*, 2H); 5.65–6.2 (*m*, 1H). MS (70 eV): 186/188(0.2, M^+), 107(53), 93(26), 91(54), 79(100), 77(43), 66(40), 51(17), 41(33). Anal. calc. for $C_8H_{11}Br$ (187.09): C 51.36, H 5.93; found: C 51.06, H 5.95.

cis-3-(Ethylthiomethyl)-4-vinylcyclopentene (**9**). Sodium ethanethiolate (3.5 mmol) and bromide **7** (0.5 g, 2.7 mmol) in 5.0 ml dry MeOH were refluxed for 5 h. After cooling, H_2O (10 ml) was added, and the sulfide was extracted with pentane (3 × 10 ml). The org. phase was washed with H_2O, dried ($MgSO_4$) and concentrated *i.v.* CC on silica gel (pentane) and removal of solvent afforded 0.35 g (77%) of the pure compound. IR (neat): 3075, 3055, 2970, 2925, 2840, 1635, 1435, 1420, 1260, 1000, 910, 785, 720. ^{1}H-NMR (CCl_4): 1.16 (*t*, 3H); 2.05–2.74 (*m*, 7H); 2.92 (*m*, 1H); 4.95 (*dd*, J = 10 and 2.5, 1H); 5.06 (*dd*, J = 17.5 and 2.5, 1H); 5.70–6.15 (*m*, 3H). MS (70 eV): 168(13, M^+), 139(43), 105(17), 93(63), 91(90), 77(78), 75(100), 65(26), 53(18), 47(56). Anal. calc. for $C_{10}H_{16}S$ (168.30): C 71.37, H 9.58; found: C 71.16, H 9.43.

cis-3-(3-Butenyl)-4-vinylcyclopentene (**8**). Magnesium turnings (0.15 g, 6.2 mmol), bromide **7** (0.5 g, 2.7 mmol) dissolved in 5 ml pentane and a few iodine crystals were placed in a flame dried glass apparatus, and formation of the *Grignard* reagent was initiated by gentle heating. When the exothermic reaction had ceased, stirring was continued for 2 h, and 50 mg of CuCN were added after cooling (0°). A solution of 3-bromopropene (0.8 g, 76.5 mmol) in 5 ml THF was added dropwise, and the reaction was allowed to complete within 2 h at r.t. The mixture was poured onto ice/NH_4Cl, and the hydrocarbon was extracted with pentane. After washing (H_2O), drying ($MgSO_4$) and evaporation of solvent, the crude product was purified by CC on silica gel (pentane). Concentration *i.v.* left 0.28 g (68%) of the stereochemically homogeneous alkene **8.** IR (neat): 3080, 3055, 3000, 2980, 2920, 2845, 1635, 1610, 1445, 1420, 995, 910, 725. ^{1}H-NMR (CCl_4): 1.00–1.65 (*m*, 2H); 1.65–2.70 (*m*, 5H); 2.90 (*quint.*, 1H); 4.80–5.12 (*m*, 4H), 5.72 (*s*, 2H); 5.5–6.28 (*m*, 2H). MS (70 eV): 148(0.6, M^+), 133(3), 119(8), 106(64), 91(87), 79(100), 77(62), 65(28), 53(26), 53(26), 51(19), 40(95). Anal. calc. for $C_{11}H_{16}$ (148.20): C 89.12, H 10.87; found: C 88.70, H 10.78.

cis-3-(2-Propenyloxymethyl)-4-vinylcyclopentene (**10**). The alcohol **6** (0.25 g, 2.0 mmol) and NaH (3.0 mmol) were suspended in 5 ml dry THF and heated to 50° with stirring. After 30 min 3-bromopropene (0.4 g, 3.3 mmol) was added, and stirring was continued under reflux for another 2 h. The cooled mixture was poured onto ice/NH_4Cl and extracted with Et_2O. Following usual workup and chromatography (silica gel, pentane) 0.105 g (32%) of a flowery smelling substance were obtained. IR (neat): 3080, 3060, 2980, 2930, 2855, 1640, 1420, 1350, 1105, 1000, 915, 790, 765. ^{1}H-NMR (CCl_4): 2.30 (*m*, 2H); 2.87 (*m*, 2H); 3.27 (*m*, 2H); 3.85 (*dd*, J = 4.5 and 1.5, 2H); 4.80–5.32 (*m*, 4H); 5.71 (*s*, 2H); 5.50–6.10 (*m*, 2H). MS (70 eV): 164(0.3, M^+), 163(0.9, M^+–1), 109(17), 106(25), 93(54), 91(77), 79(34), 77(68), 71(30), 65(18), 53(11), 41(100). Anal. calc. for $C_{11}H_{16}O$ (164.25): C 80.44, H 9.82; found: C 80.28 H 9.78.

cis-(5-Vinyl-2-cyclopenten-1-yl)methyl p-*Toluenesulfonate* (**11**). Alcohol **6** (2.0 g, 16.1 mmol) and TosCl (4.0 g, 20.2 mmol) in 30 ml dry pyridine were stirred for 24 h at r.t. Ice and 4N NCl were added to the mixture which was then extracted with CH_2Cl_2 (3 × 50 ml). The combined org. layers were washed with Na_2CO_3-solution (2 × 50 ml) and H_2O, dried ($MgSO_4$) and evaporated *i.v.* The oily residue was chromatographed on silica gel with hexane/Et_2O (80:20) to yield 3.2 g (72%) of a colorless viscous oil. IR (neat): 3070, 2980, 2960, 2930, 2860, 1595, 1375, 1365, 1190, 1175, 965, 815, 655. ^{1}H-NMR (CCl_4): 2.10–2.65 (*m*, 2H); 2.44 (*s*, 3H); 2.95 (br. *q*, 2H,), 3.85 (*m*, 2H); 4.92 (*dd*, J = 10 and 2, 1H); 4.98 (*dd*, J = 18 and 2, 1H); 5.47–6.00 (*m*, 3H); 7.3 (*d*, 2H); 7.71 (*d*, 2H). MS (70 eV): 278(0.01, M^+), 223(33), 155(25), 149(19), 106(37), 93(100), 77(50), 65(45), 40(41). Anal. calc. for $C_{15}H_{18}O_3S$ (278.37): C 64.72, H 652; found: C 64.55, H 6.52.

cis-3-Butyl-4-vinylcyclopentene (**4**). A solution of propylmagnesium bromide (20.0 mmol) in 30 ml dry THF was cooled to −78° and 200 µl Li_2CuCl_4 (1M in THF) and **11** (1.7 g, 6.0 mmol) were added successively. The mixture was allowed to come to r.t. over 3 h, and stirring was continued for another 12 h. The solution was poured onto ice/NH_4Cl, extracted with Et_2O (3 × 50 ml) and washed with 2N HCl and H_2O. After drying ($MgSO_4$) and evaporation of solvent *i.v.* the crude product was chromatographed on silica gel (pentane). Concentration *i.v.* yielded 0.6 g (67%) of the hydrocarbon **4** as a colorless liquid. IR (neat): 3080, 3055, 3000, 2960, 2930, 2850, 1635, 1450, 1000, 910, 725. ^{1}H-NMR (CCl_4): 0.85 (*t*, 3H); 1.23 (*m*, 6H); 1.70–2.45 (*m*, 2H); 2.57 (br. *m*, 1H); 2.98 (*sext.*, 1H); 4.94 (*dd*, J = 10 and 2.5, 1H); 4.98 (*dd*, J = 18 and 2.5, 1H); 5.70 (*s*, 2H); 5.55–6.10 (*m*, 1H). MS (70 eV): 150 (4, M^+), 135(1), 121(7), 107(8), 93(62), 91(47), 80(52), 79(100), 77(49), 67(27), 41(39). Anal. calc. for $C_{11}H_{18}$ (150.27): C 87.93, H 12.07; found: C 88.01, H 11.96.

cis-4-Bromomethyl-3-[(Z)-1,3-butadienyl]cyclopentene (**13**). To a suspension of triphenylphosphonium (13 mmol) dibromide in 30 ml dry benzene was added a solution of **13** (1.5 g, 10.0 mmol; mixture of (*E*)/(*Z*)-isomers [5b]) in 5 ml of the same solvent. The mixture was stirred for 5 h, and 100 ml pentane were then added to precipitate the phosphonium salts. The clear filtrate was washed with sat. $NaHCO_3$ (3 × 50 ml) and H_2O 2 × 50 ml), dried ($MgSO_4$), evaporated *i.v.* and chromatographed on silica gel (pentane). Concentration under reduced pressure gave 1.3 g (65%) of the bromide **13** as a mixture of (*E*)/(*Z*)-isomers. An attempt to purify **13** by distillation led to considerable decomposition and formation of by-products (b.p. 105–110°/14 Torr).

To obtain the pure (*Z*)-isomer an aliquot (0.5 g, 2.5 mmol) in 5 ml THF was gradually treated with 4-phenyl-1,2,4-triazoline-3,5-dione (*ca.* 0.3 g) until the red color just persisted. The solution was concentrated *i.v.* and purified by CC on silica gel (pentane). Removal of solvent left 0.22 g of a pleasant smelling liquid whose aroma strongly resembles that of the pheromone **2.** IR (neat): 3090, 3060, 3010, 2960, 2940, 2850, 1640, 1610, 1435, 1275, 1220, 1000, 910, 720, 680, 640. ^{1}H-NMR (CCl_4): 2.0–3.0 (*m*, 3H); 3.30 (*dd*, *J* = 7.5 and 3, 3H); 3.77 (br. *t*, 1H); 4.90–5.30 (*m*, 3H); 5.50–6.18 (*m*, 3H); 6.67 (*dd*, *J* = 17, 9.5 and 9.5, 1H). MS (70 eV): 212/214(1.2, M^+), 133(53), 119(30), 105(37), 91(100), 79(72), 77(35), 67(42), 55(28), 51(20), 40(62). Anal. calc. for $C_{10}H_{13}Br$ (213.12): C 56.34, H 6.11; found: C 56.24, H 6.05.

cis-*(2-Vinyl-1-cyclopentyl)methanol* (**15**). Racemic lactone **14** (2.0 g, 16.1 mmol) was converted into **15** as described previously for the preparation of the chiral compound *[12]*. *Yield: 1.3 g (64%).*

*4-Methoxy-1-[*cis-*(2-vinyl-1-cyclopentenyl)]-2-butyn-1-ol* (**16**). – a) *Oxidation.* To a suspension of pyridinium chlorochromate (5.4 g, 10 mmol) in 30 ml CH_2Cl_2 was added with stirring the alcohol **15** (1.0 g, 7.9 mmol). When CC analysis indicated complete conversion, 70 ml pentane were added and the precipitated chromium salts removed by suction. After evaporation of solvent *i.v.* the crude residue was redissolved in 50 ml pentane, dried ($MgSO_4$) and filtered. Vacuum concentration gave a crude aldehyde which was used without further purification in the alkylation step.

b) *Alkylation.* To a freshly prepared solution of 3-methoxypropynylmagnesium bromide (15.0 mmol) in 30 ml dry THF was added dropwise with stirring a solution of the above aldehyde in 5 ml of the same solvent. The solution was stirred for 1 h at 0° and then poured onto ice/NH_4Cl. The aq. phase was extracted with Et_2O (2 × 50 ml), and the combined org. phases were washed with 2N HCl (20 ml) and H_2O (20 ml). After drying ($MgSO_4$) and evaporation of solvent *i.v.* the crude alkynol was further purified by CC on silica gel (hexane/Et_2O, 80:20). Removal of solvent yielded 0.79 g (52%) **16.** IR (neat): 3410, 3080, 2960, 2880, 2820, 1640, 1100, 1005, 910, 810. ^{1}H-NMR (CCl_4): 1.00–2.45 (*m*, 6H); 2.75 (br. *m*, 3H); 3.31 (*s*, 3H); 4.05 (*s*, 2H); 4.17 (*d*, 1H); 4.85–5.25 (*m*, 2H); 5.90 (*ddd*, *J* = 18, 9 and 9, 1H). MS (70 eV): 194(0.2, M^+), 179(1), 161(5), 147(13), 133(24), *119(26), 105(32), 95(53), 91(57), 79(42), 67(97), 55(57), 45(37), 41(100).* Anal. calc. for $C_{12}H_{18}O_2$ (194.28): C 74.19, H 9.34; found: C 73.99, H 9.35.

cis*-1-[(Z)-1,3-Butadienyl]-2-vinylcyclopentane* (**17a**). To a stirred, ice cooled suspension of $LiAlH_4$ (0.50 g, 10 mmol) in 15 ml dry THF a solution of alkynol **16** (0.75 g, 3.9 mmol) in 5 ml of the same solvent was added dropwise. The mixture was stirred for 1 h at 40° followed by cooling with an ice bath and addition of $AlCl_3$ (20 mg, 0.15 mmol). The solution was refluxed for 1 h, cooled and slowly poured onto ice/dil. HCl (*ca.* 10%). After extraction with pentane (2 × 50 ml) the combined org. phases were washed with H_2O, dried ($MgSO_4$) and evaporated *i.v.* CC on silica gel (pentane) afforded 0.40 g (68%) of the two hydrocarbons **17a/b** ((*Z*)/(*E*) 9:1). A pure sample of **17a** was obtained on treatment with 4-phenyl-1,2,4-triazoline-3,5-dione as described for **13.** IR (neat): 3090, 3030, 3010, 2955, 2870, 1640, 1455, 1435, 1425, 995, 905, 795. ^{1}H-NMR (CCl_4): 1.20–2.15 (*m*, 6H); 2.60 (br. *quint.*, 1H); 3.10 (*m*, 1H); 4.85–6.30 (*m*, 7H); 6.63 (*ddd*, *J* = 17, 10.5 and 10.5, 1H). MS (70 eV): 148(12, M^+), 133(5), 119(11), 105(13), 94(52), 91(38), 79(100), 77(37), 66(17), 53(16), 41(30). Anal. calc. for $C_{11}H_{16}$ (148.20): C 89.12, H 10.87; found: C 88.85, H 10.71.

cis-*{2-[(1E,3Z)-1,3-Butadienyl]cyclopentyl}methanol* (**19**). A solution of lactone **14** (1.0 g, 7.9 mmol) in 20 ml dry THF was cooled to −78° and 8.0 ml of a 1M solution of 3-(tetrahydropyranyl-2-oxy)propynyllithium in THF was added with stirring. After additional 15 min at −78° the mixture was poured onto ice/NH_4Cl and extracted with Et_2O (2 × 50 ml). The org. phases were washed with H_2O (2 × 50 ml), dried ($MgSO_4$) and concentrated *i.v.* The crude THP-ether (1.6 g, 76% yield; its bicyclic structure is proven by IR which shows none of the typical absorptions of an α,β-unsaturated alkyne-ketone) was reduced with $LiAlH_4$ as described for **17a.** CC on silica gel (hexane/Et_2O, 80:20) gave 0.66 g of the alcohol **19** (55% overall yield from **14**). IR (neat): 3340, 3090, 3040, 3010, 2960, 2870, 1645, 1600, 1500–1300 (br.), 1035, 1005, 955, 900, 800. ^{1}H-NMR (CCl_4): 1.20–2.00 (*m*, 6H); 2.17 (*m*, 1H); 2.42 (br. *s*, 1H); 2.68 (*m*, 1H); 3.20–3.70 (*m*, *ABX*, 2H); 4.80–6.90 (*m*, 5H). MS (70 eV): 152(18, M^+), 134(8), 119(32), 105(24), 98(32), 91(88), 79(100), 77(48), 70(28), 67(70), 57(22), 55(26), 53(20), 51(11), 41(61). Anal. calc. for $C_{10}H_{16}O$ (152.23): C 78.90, H 10.60; found: C 78.61, H 10.46.

cis*-1-[(1E)-1,3-Butadienyl]-2-vinylcyclopentane* (**17b**). The alcohol **19** (0.5 g, 3.3 mmol) were oxidized with pyridinium chlorochromate (3 equiv.) as described for **16.** The crude aldehyde thus obtained was added dropwise to a solution of methylidenetriphenylphosphorane (5 mmol) in 30 ml dry THF (BuLi as base). Stirring was continued for 30 min, and the mixture was hydrolyzed with 2N HCl (20 ml). Following extraction with pentane (2 × 50 ml), washing with H_2O and drying ($MgSO_4$), the crude alkene was chromatographed on silica gel (pentane). Removal of solvent afforded 0.29 g hydrocarbons consisting of 66% **17b** and 34% **17a.** An analytically pure sample of **17b** was obtained by GC on silver-impregnated silica gel (10%) using a pentane/Et_2O

gradient. IR (neat): 3090, 3040, 3010, 2960, 2880, 1640, 1605, 1005, 955, 910, 900, 800. ^{1}H-NMR (CCl_4): 1.20–2.20 (*m*, 6H); 2.63 (br. *m*, 2H); 4.85–6.20 (*m*, 7H); 6.30 (*ddd*, *J* = 16.5, 9 and 9, 1H). MS (70 eV); identical with MS of **17a.**

6-(Bromomethyl)-1,4-cycloheptadiene (**21**). Alcohol **20** (5.0 g, 40 mmol) were converted to the bromide as described for **13.** Following usual workup and CC on silica gel (pentane) 5.5 g (78%) of the pure bromide **21** were obtained. IR (neat): 3020, 2960, 2910, 1655, 1430, 1220, 1050, 855, 825, 790, 685, 665. ^{1}H-NMR (CCl_4): 2.40 (*m*, 2H); 2.85 (br. *m*, 3H); 3.85 (*d*, *J* = 6.5, 2H); 5.45–6.00 (*m*, 4H). MS (70 eV): 186/188(3, M^+), 107(94), 93(48), 91(92), 79(100), 77(70), 65(40), 53(28), 51(41), 40(73). Anal. calc. for $C_8H_{11}Br$ (187.086): C 51.36, H 5.93; found: C 51.21, H 5.94.

6-(2,3-Butadienyl)-1,4-cycloheptadiene (**22**). Bromide **21** (0.5 g, 2.7 mmol) reacted with Mg-turnings as described for **8.** CuCN (50 mg) was then added at 0°, and after 5 min stirring 3-bromo-propyne (0.7 g), dissolved in 5 ml dry THF, was added dropwise. When the strongly exothermic reaction had ceased, stirring was continued for 1 h, and the mixture was hydrolyzed with ice/dil. HCl (10%). After usual workup and CC on silica gel (pentane) 0.19 g (49%) of the allene **22** were obtained. IR (neat): 3020, 2930, 2905, 2850, 1955, 1650, 1440, 845, 790. ^{1}H-NMR (CCl_4): 1.90–2.35 (*m*, 4H); 2.55 (br. *m*, 1H); 2.85 (*m*, 2H); 4.52–5.40 (*m*, 3H), 5.45–5.90 (*m*, 4H). MS (70 eV): 145(3, M^+–1), 131(26), 117(23), 105(24), 93(36), 92(65), 91(100), 79(37), 77(84), 65(23), 53(19), 51(17), 41(21). Anal. calc. for $C_{11}H_{14}$ (146.23): C 90.35, H 9.65; found: C 90.23, H 9.62.

6-(3-Butenyl)-1,4-cycloheptadiene (**23**). Preparation of *Grignard* reagent and alkylation with 3-bromopropene followed the procedure given for **8.** Workup and CC on silica gel (pentane) afforded 0.28 g (71%) of the hydrocarbon **23.** IR (neat): 3080, 3015, 2980, 2920, 2850, 1640, 1450(broad), 995, 910, 790, 680, 650. ^{1}H-NMR (CCl_4): 1.20–1.60 (*m*, 2H); 1.85–2.25 (*m*, 4H); 2.45 (br. *m*, 1H); 3.65–2.95 (*m*, 2H); 4.80–5.18 (*m*, 2H); 5.40–6.15 (*m*, 5H). MS (70 eV): 148(0.7, M^+), 133(9), 119(17), 106(27), 91(89), 79(100), 77(63), 65(23), 53(20), 40(65). Anal. calc. for $C_{11}H_{16}$ (148.20): C 89.12, H 10.87; found: C 88.73, H 10.67.

6-(2-Propenyloxymethyl)-1,4-cycloheptadiene (**24**). To a well-stirred solution of **20** (0.30 g, 2.42 mmol) and 3-bromopropene (0.44 g, 3.63 mmol) in 5 ml dry DMSO was added 0.1 g NaH (80%, mineral oil dispersion). A slightly exothermic reaction took place, and the suspension was stirred for another hour at r.t. Ice/dil. HCl were added and the aqueous phase was carefully extracted with pentane (3 × 50 ml). The combined org. layers were washed with water, dried and concentrated *i.v.* To remove conjugated by-products (1,3-cycloheptadienes), the crude residue was re-dissolved in THF and treated with 4-phenyl-1,2,4-triazoline-3,5-dione until the red color just persisted. Removal of solvent *i.v.* and CC on silica gel (pentane) yielded 0.18 g (49%) of a fruity smelling liquid. IR (neat): 3080, 3020, 2960, 2930, 2860, 1650, 1450, 1350, 1265, 1110, 1020, 990, 925, 805. ^{1}H-NMR (CCl_4): 2.32 (br. *m*, 2H); 2.55–3.00 (*m*, 3H); 3.32 (*d*, *J* = 7, 2H); 3.45 (*td*, *J* = 5.5 and 1.5, 2H); 5.04–6.18 (*m*, 7H). MS (70 eV): 164(0.15, M^+), 163(0.1), 133(3), 106(68), 79(63), 92(40), 91(100), 79(60), 78(82), 77(87), 71(32), 67(22), 65(32), 55(18), 53(20), 51(15), 41(98). Anal. calc. for $C_{11}H_{16}O$ (164.25): C 80.44, H 9.82; found: C 80.34, H 9.85.

6-(2-Butynyl)-1,4-cycloheptadiene (**26**). a) Wittig *Reaction.* To a well-stirred suspension of 3-pentynyltriphenylphosponium bromide (7.95 g, 20.0 mmol) in 50 ml dry THF was slowly added at 0° 20 ml of BuLi (1N in pentane). Stirring was continued for another 30 min, and aldehyde **25** (1.6 g, 15 mmol) [10], dissolved in 5 ml dry THF, was added dropwise. The reactants were allowed to stir for 1 h at r.t., and workup was as described for **17b.** CC (pentane) afforded 1.1 g acetylenic intermediate.

b) Cope *Rearrangement.* The above product (1.1 g) was enclosed in a sealed glass ampoule and heated for 4 h to 180°. Purification of the slightly yellow product was achieved by CC on silica gel (pentane) and yielded 0.85 g of the hydrocarbon **26** (39% overall yield from **25**). IR (neat): 3010, 2960, 2920, 2910, 2860, 1650, 1435, 790, 765, 690, 640. ^{1}H-NMR (CCl_4): 1.78 (*t*, *J* = 2.1, 3H); 2.00–2.40 (*m*, 4H); 2.48 (br. *m*, 1H); 2.87 (*m*, 2H); 5.40–5.85 (*m*, 4H). MS (70 eV): 146(2, M^+), 145(12), 131(86), 117(28), 105(52), 93(73), 92(60), 91(100), 77(96), 65(51), 53(37), 51(38), 41(37). Anal. calc. for $C_{11}H_{14}$ (146.23): C 90.35, H 9.65; found: C 90.27, H 9.53.

6-[(2Z)-Butenyl]-1,4-cycloheptadiene (**27**). Alkyne **26** (0.2 g, 1.37 mmol) and quinoline (0.5 μl) were dissolved in 5 ml pentane, and 0.1 g *Lindlar* catalyst was added. Uptake of H_2 proceeded instantaneously, and the course of the reaction was monitored by CC. When all of the starting material had been consumed, the catalyst was filtered off, and after CC on silica gel (pentane) and evaporation of solvent, 0.15 g (72%) of the hydrocarbon **27** was obtained. A small amount (*ca.* 5%) of saturated by-products were removed by prep. CC using DEGS (10%) as stationary phase. IR (neat): 3015, 2960, 2920, 2860, 1650, 1440, 1260, 1100, 785, 765. ^{1}H-NMR (CCl_4): 1.68 (*d*, 3H); 1.90–2.30 (*m*, 4H); 2.45 (br. *m*, 1H); 2.83 (*m*, 2H); 5.20–5.85 (*m*, 6H). MS (70 eV): 148(1.5, M^+), 133(6), 119(7), 107(10), 106(11), 105(10), 93(92), 92(82), 91(100), 79(53), 78(47), 77(98), 70(33), 65(46), 55(21), 53(27), 51(21), 41(51). Anal. calc. for $C_{11}H_{16}$ (148.20): C 89.12, H 10.87; found: C 88.98, H 10.75.

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