131. Synthesis of Enantiomerically Pure Pheromones of South-Pacific Brown Algae: Hormosirene and Dictyopterene A

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Dedicated to Prof. Dr. *Karl Dimroth* on the occasion of his 75th birthday

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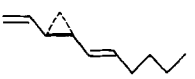
Hormosirene ((−)-**1**; (1*R*,2*R*)-1-((1*E*,3*Z*)-1,3-hexadienyl)-2-vinylcyclopropane) is the specific sex attractant of several brown algae of the Australian shelf, while dictyopterene A ((+)-**2**; (1*R*, 2*R*)-1-((1*E*)-1-hexenyl)-2-vinylcyclopropane) is found as a minor constituent of the pheromone bouquets. The asymmetric synthesis of the two hydrocarbons is performed by resolution of the amides (−)-**5** and (+)-**5a** obtained from (−)-(*R*)-2-phenylglycinol and racemic *trans*-vinylcyclopropanecarboxylic acid (*rac*-**4**) on silica gel. Both diastereoisomers are obtained optically pure. They are converted by stereoselective *Wittig* olefination into the title compounds. Compound (−)-**1** is the active mating pheromone of the reproductive system of the seaweed *Xiphophora chondrophylla* as established by biological-activity assays.

1. Introduction. – Female gametes (eggs) of the Australian seaweeds *Hormosira banksii, Durvillaea potatorum, Xiphophora chondrophylla, Scytosiphon lomentaria,* and *Colpomenia peregrina* produce ethylenic hydrocarbons to lure their conspecific male gametes (spermatozoids) in the sexual cycle [1] [2]. On average, a few μg of volatiles were collected from 4×10^6 viable eggs using the 'stripping-technique' described previously [3]. Despite this small amount, they were readily identified as hormosirene (**1**) and dictyopterene A (**2**) by GC, GC/MS, and UV comparison with authentic reference substances. Their biological activity was determined by the droplet-assay [4] [5] and revealed threshold concentrations as low as 10^{-12} mol per liter of sea water [2].

(−)-**1** (1*R*, 2*R*)



(+)-**2** (1*R*, 2*R*)

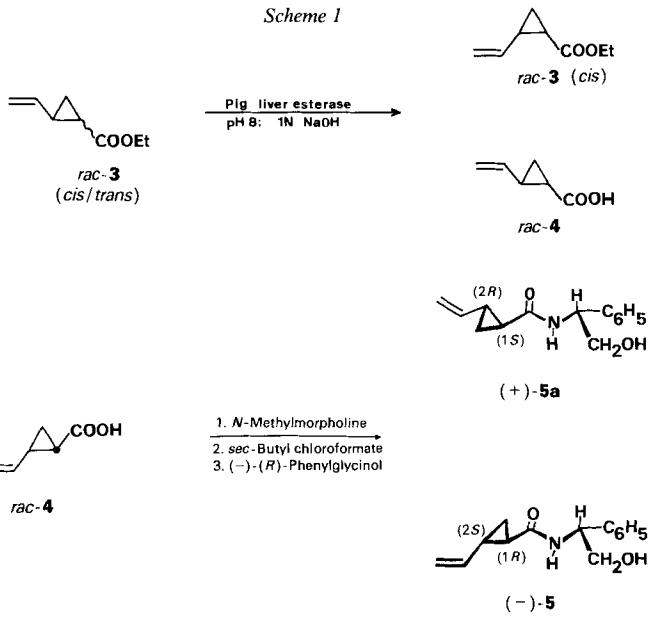
However, due to the extreme activity of the pheromones and their consequently low concentration in the 'strippates' of the female gametes, no information on the chirality of these messenger compounds was available by direct chromatographic or chiroptical methods.

We therefore synthesized the optically pure enantiomers of **1** and **2** and established the handedness of hormosirene by comparative activity tests with the synthetic (+)- and (−)-enantiomers of **1**. The asymmetric synthesis of **1** and **2** and the biological activity of hormosirene enantiomers for male gametes of *Xiphophora chondrophylla* and *Durvillaea potatorum* are reported.

2. Asymmetric Synthesis of Hormosirene and Dictyopterene A. – Racemic hormosirene ((±)-**1**) and dictyopterene A ((±)-**2**) were the subject of various synthetic attempts since *Moore et al.* [6] reported their occurrence in lipid extracts of the Hawaiian seaweeds *Dictyopteris australis* and *Dictyopteris plagiogramma*. As the starting material in most cases served ethyl *trans*-vinylcyclopropanecarboxylate (*rac*-**3**; *trans*) which is readily accessible in large quantities from butadiene and ethyl diazoacetate [7]. Our strategy also starts with a 1:1 mixture of ethyl *cis*- and *trans*-vinylcyclopropanecarboxylate, but utilizes the diastereoselective saponification of the isomers with pig-liver esterase [8]. The *trans*-ester is preferentially hydrolyzed, and the acid *rac*-**4** is obtained in 87% yield and an isomeric purity of > 98.5%. *Kajiwara et al.* had worked out an asymmetric synthesis of (−)-**1** and (+)-**2** *via* fractional crystallization of the quinine salt of *rac*-**4** [9]; they reported an enantiomeric excess of 85% which, however, is insufficient for accurate determination of enantioselective biological effects. The unnatural enantiomers of **1** and **2**, more interesting for comparative activity studies, have not been available as yet.

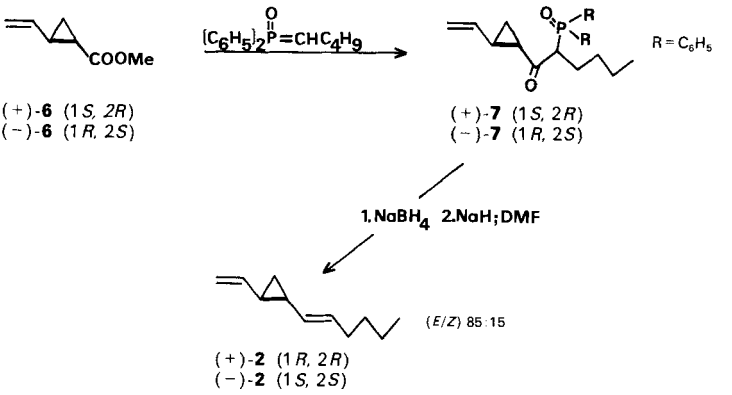
Following the procedure of *Helmchen et al.* for the separation of racemic acids *via* diastereoisomeric amides [10], *rac*-**4** is converted into the pair of diastereoisomers (−)-**5** and (+)-**5a** using (−)-(*R*)-2-phenylglycinol and the mixed-anhydride method [11] for activation of the acid *(Scheme 1)*. Chromatography of (−)-**5**/(+)-**5a** (isooctane/AcOEt) separates the diastereoisomers by a factor α of 1.6, well sufficient for baseline separation of large quantities. Due to the *'anti'* orientation of the aromatic nucleus and the cyclopropyl moiety in (−)-(1*R*, 2*S*), its diastereoselective interaction with the stationary phase is minimized [12], and this amide elutes first. After one recrystallization from AcOEt, (−)-**5** is obtained with > 99% optical purity[1]) as confirmed by chromatography on an analy-

Scheme 1



[1]) Based on the optical purity of commercially available (−)-(*R*)-2-phenylglycinol (99.2% ee, [10]).

Scheme 2

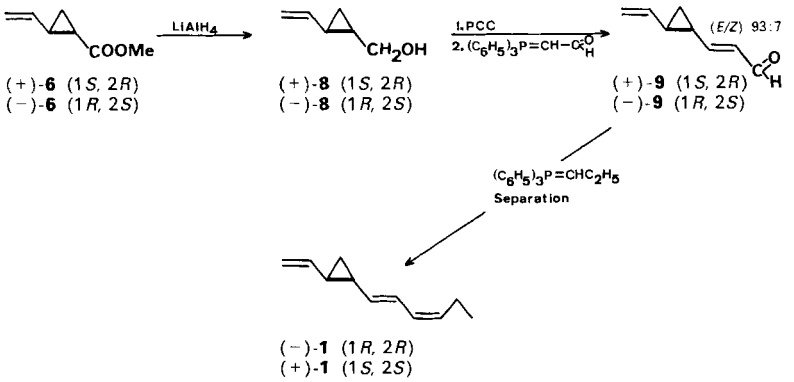


tical column. Also the more tightly bound second amide (+)-**5a** (1*S*,2*R*) is > 99% optically pure[1]) after recrystallization. Mild alkaline hydrolysis of (−)-**5** of (+)-**5a** (1.2N KOH in aq. MeOH) yields the two acids (+)- and (−)-**4**, respectively, which are esterified with excess diazomethane (→(−)- and (+)-**6**, resp.).

To introduce the hexenyl substituent of dictyopterene A, the esters (+)- and (−)-**6** are condensed with pentylidenediphenylphosphine oxide (BuLi as base) [13] to give the *β*-ketophosphine oxides (+)- and (−)-**7**, respectively, and the latter are immediately reduced with $NaBH_4$ to the corresponding hydroxy derivatives *(Scheme 2)*. Attempts, to separate the *threo-* and *erythro*-hydroxyphosphine oxides by recrystallization or chromatography remained unsuccessful. Therefore, the crude alcohols are directly converted to (+)- and (−)-dictyopterene A ((+)- and (−)-**2**), respectively, by treatment with NaH in dry DMF at 50°. The (*E*)/(*Z*) ratio is 85:15, and pure dictyopterene A is obtained after chromatography on silver-impregnated silica gel.

A different reaction sequence *(Scheme 3)* is employed to introduce the hexadienyl substituent. Reduction of the esters (+)- and (−)-**6** yields the alcohol (+)- and (−)-**8**, respectively; oxidation with pyridinium chlorochromate (PCC) gives the corresponding aldehydes, and alkylation with (formylmethylidene)triphenylphosphorane yields the (*E*)-

Scheme 3



aldehydes (+)- and (−)-**9**, respectively, each as a mixture of isomers ((*E*)/(*Z*) = 93:7), which are readily purified by MPLC on silica gel. A second *Wittig* olefination with propylidenetriphenylphosphorane (BuLi as base) gives mixtures of (1*E*,3*E*)- and (1*E*,3*Z*)-hexadienyl isomers (ratio 1:1). Final treatment with 4-phenyl-1,2,4-triazoline-3,5-dione selectively removes the unwanted (1*E*,3*E*)-isomer and leaves the pure enantiomeric hydrocarbons (−)- and (+)-**1**, respectively. The same sequence has been independently used by *Dorsch et al.* [19] to synthesize both enantiomers of hormosirene *via* a highly stereoselective $S_{CN'}$ reaction with esters derived from (+)-camphor.

3. Biological Activity of (+)- and (−)-Hormosirene ((+)- and (−)-1, resp.). – Stock solutions of 10^{-3}M (+)- and (−)-**1** in the biologically inert fluorocarbon *FC 72* are made, and graded dilutions are used for activity determination [4] [5]. As seen from the *Table*, spermatozoids of *Xiphophora chondrophylla* show a clear preference for (−)-**1** by a factor of 30 [2]. Thus, the absolute configuration of hormosirene secreted by the eggs of *Xiphophora* is 1*R*,2*R*. The same configuration was reported by *Moore et al.* for this component in the essential oils of *Dictyopteris plagiogramma* and *Dictyopteris australis* [6]. Male gametes of *Durvillaea potatorum* do not distinguish between the two enantiomers of **1**.

Table. *Biological Activity of (+)- and (−)-Hormosirene ((+)- and (−)-1)* [2]

Species	Threshold concentration [nmol/l]	
	(+)-**1**	(−)-**1**
Xiphophora chondrophylla[a])	1.80	0.06
Durvillaea potatorum[a])	0.61	0.61

[a]) Quantitative data for the natural pheromone are not available because of the very low amount of isolated compounds.

This low or even totally lacking of enantio-differentiation of the sexual communication systems of these seaweeds deviates from that of other brown algae. Sperm of *Cutleria multifida* or *Chorda tomentosa*, for example, effectively responds to their lure (+)-multifidene (= (+)-(3*S*,4*S*)-3-((*Z*)-1-butenyl)-4-vinyl-1-cyclopentene) at a 100-fold lower concentration than to the (−)-enantiomer [14] [15]. Whether or not such differences in interspecific receptor response towards a common messenger used by several members within a genus or family represents environmental adaption or a competitive strategy must, at present, remain speculative.

Recent advances in analytical methods for direct determination of the enantiomer composition of the secreted pheromones [16] promise aid in unravelling such sociobiological interactions.

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Experimental Part

General. All solvents and reagents were purified prior to use. Reactions, except the enzymatic saponification, were carried out under an inert atmosphere. Anh. $MgSO_4$ was used for all drying operations. Solns. were concentrated by rotary evaporation under reduced pressure. Pig-liver esterase *(EC 3.1.1.1)* was obtained from *Boehringer*, Mannheim, Germany. Anal. GC: *Carlo-Erba* gaschromatograph, series *4200*, equipped with *Duran* glass capillaries 50 m × 0.32 mm coated with *OV 73*; for prep. separations: stainless steel columns (1.5 m × 5 mm) filled with *Chromosorb P* (60–80 mesh) coated with 15% *Fractonitril III*. Anal. HPLC: *Altex-420* HPLC system combined with a *Kratos SF 770* variable-wavelength UV monitor. M.p. and b.p. are uncorrected. $[\alpha]_D$'s at 23°, measured with a *Carl-Zeiss*-Präzisionspolarimeter 0.005°.

trans-*2-Vinylcyclopropane-1-carboxylic Acid* (rac-**4**). Ethyl *cis/trans*-2-vinylcyclopropane-1-carboxylate (*rac*-**3**, *cis/trans*; 28.0 g, 0.2 mol) [7] was suspended by slow stirring in 100 ml of 0.1M Na_3PO_4 buffer at pH 8.0 followed by addn. of 5 mg pig-liver esterase. The pH was maintained at 8.0 by continuous titration with 1.0N NaOH from a peristaltic pump. After *ca.* 24 h, another 5 mg of esterase were added, and the titration was continued until the theor. amount of NaOH was consumed (*ca.* 3–4 days). Unreacted *cis*-ester was extracted with Et_2O (4 × 80 ml), and the aq. phase was brought to pH 2 with 2N HCl. Following extractive workup (4 × 80 ml of Et_2O), drying, and evaporation of solvent, 9.75 g (87.1%) of crude *rac*-**4** were obtained. A reesterified sample (CH_2N_2) consisted of 98.5% of *trans*- and 1.5% of *cis*-isomer (GC). Spectroscopic data: see [7].

*(1R,2S)- and (1S,2R)-*N*-(2-Hydroxy-1-phenylethyl)-2-vinylcyclopropane-1-carboxamide* ((−)-**5** and (+)-**5a**, *resp.*). To a well stirred soln. of *rac*-**4** in 250 ml of dry THF were added dropwise at −20° 5.5 ml (50 mmol) of *N*-methylmorpholine followed by 6.95 ml (52.5 mmol) of *sec*-butyl chloroformate. After 4 min, 7.2 g (52.5 mmol) of (−)-(*R*)-2-phenylglycinol (*Sigma*; Munich, FRG) was added, and stirring was continued for 15 min at −20°. The soln. was allowed to come to r.t. (30 min) and the solvent removed. The residue was taken up in 200 ml of AcOEt/CH_2Cl_2 85:15 (*v/v*), successively washed with H_2O, sat. $NaHCO_3$ soln., 2N HCl, and H_2O (100 ml each), and finally dried. Removal of solvents yielded 10.95 g (94.8%) of crystalline colourless (−)-**5**/(+)-**5a**.

The mixture (−)-**5**/(+)-**5a** was chromatographed in 1-g portions on 250 g of silica gel (column: 40 × 3 cm) using isooctane/AcOEt 3:7 (flow rate 24 ml/min (*Duramat* membrane pump), monitoring at 254 nm). Amide (−)-**5** eluted first (separation factor $\alpha = 1.6$) and yielded, after recrystallization from AcOEt, 4.13 g (71.5%) of a crystalline solid, optically pure according to HPLC (silica gel *Nucleosil 50-5*; 10 × 0.4 cm, isooctane/AcOEt 1:1). $[\alpha]_{578} = -198.1°$ ($c = 4.86$, CH_3OH). M.p. 152–153°. IR (KBr): 3310, 3090, 2960, 2880, 1630, 1540, 1400, 1240, 1060, 990, 900, 855, 765, 710. ^{1}H-NMR ((D_6)DMSO): 0.8 (*m*, 1H); 1.05 (*m*, 1H); 1.80 (*m*, 2H); 3.60 (*t*, 2H; *d* on addition of D_2O, $J = 6.3$); 4.86 (*d*, 1H; disappears on addition of D_2O); 4.88 (*m*, 1H); 5.10 (*dd*, $J = 18$, 2.5, 2H); 5.22–5.75 (*m*, 1H); 7.35 (*s*, 5H); 8.52 (*d*, $J = 9$, 1H). MS (70 eV): 232 (0.16, $M^+ + 1$), 200 (22), 130 (5), 120 (4), 106 (100), 95 (37), 91 (18), 77 (24), 67 (91), 51 (11), 41 (48). Anal. calc. for $C_{14}H_{17}NO_2$ (231.295): C 72.70, H 7.41; found: C 72.81, H 7.41.

The more polar amide (+)-**5a**, after recrystallization from AcOEt, yielded 3.88 g (67.2%) of optically pure compd. (HPLC). $[\alpha]_{578} = +11.1°$ ($c = 3.89$, CH_3OH). M.p. 182–183°. IR (KBr): 3310, 3080, 3040, 2970, 2950, 2880, 1630, 1545, 1400, 1245, 1055, 1005, 915, 900, 765, 700. ^{1}H-NMR ((D_6)DMSO): 0.85 (*m*, 1H); 1.12 (*m*, 1H); 1.78 (*m*, 2H); 3.57 (*t*, 2H; *d* on addition of D_2O, $J = 6.3$); 4.82 (*d*, 1H; exchangeable with D_2O); 4.87 (*m*, 1H); 5.08 (*dd*, $J = 18$, 2.5); 5.20–5.75 (*m*, 1H); 7.32 (*s*, 5H); 8.50 (*d*, $J = 9$, 1H). MS (70 eV): 232 (0.16, $M^+ + 1$), 213 (0.16), 200 (42), 130 (4), 120 (3), 106 (100), 95 (30), 91 (17), 77 (23), 67 (72), 51 (8), 41 (41). Anal. calc. for $C_{14}H_{17}NO_2$ (231.295): C 72.70, H 7.41; found: C 72.81, H 7.43.

(−)-(1R,2S)-Methyl 2-Vinylcyclopropane-1-carboxylate ((−)-**6**). A soln. of 4.03 g (17.4 mmol) of (−)-**5** in 100 ml of 10% KOH in CH_3OH and 50 ml H_2O was heated to 80° for 24 h and concentrated to *ca.* 40 ml after cooling. Following removal of phenylglycinol with CH_2Cl_2 (3 × 30 ml), the aq. phase was strongly acidified (pH 1) with 6N HCl, and the acid was extracted with CH_2Cl_2 (5 × 30 ml). The combined org. layers were dried and evaporated, and the remaining pale yellow oil was redissolved in Et_2O/CH_3OH 20:1. CH_2N_2 was added until the yellow colour persisted. The soln. was concentrated and chromatographed on silica gel with hexane/Et_2O 9:1: 1.89 g (86.0%) of (−)-**6**. $[\alpha]_{578} = -214.9°$ ($c = 8.635$, CH_2Cl_2). Spectroscopic data: see [7].

(+)-(1S,2R)-Methyl 2-Vinylcyclopropane-1-carboxylate ((+)-**6**). As above, 3.47 g (15.0 mmol) of (+)-**5a** were saponified to give 1.55 g (81.9%) of (+)-**6**. $[\alpha]_{578} = +218.1°$ ($c = 8.77$, CH_2Cl_2) ([9]: $[\alpha]_D = +191°$ (EtOH)).

(−)-[1-Oxo-1-((1R,2S)-2-vinyl-1-cyclopropyl)hexan-2-yl]diphenylphosphine Oxide ((−)-**7**). A suspension of 1.82 g (6.68 mmol) of pentyldiphenylphosphine oxide [17] in 40 ml of dry THF was metallated at −78° by slow addn. of 1 equiv. of BuLi (0.8M in hexane). A soln. of 0.47 g (3.34 mmol) of (−)-**6** in 10 ml of dry THF was added and stirring continued for 2 h. The soln. was allowed to come to r.t. over night, and the solvent removed. Then, 50 ml of CH_2Cl_2 were added, the org. layer was washed with H_2O (3 × 20 ml), dried, and evaporated. The crude

phosphine oxide was purified by HPLC on silica gel with AcOEt: 0.762 g (56.2%) of pure (−)-**7**. $[\alpha]_{578} = -134.1°$ ($c = 9.00$, $CHCl_3$). M.p. 141–145°. IR (KBr): 3060, 2960, 2930, 2865, 1700, 1450, 1310, 1185, 1110, 995, 915, 765, 715. ^{1}H-NMR ($CDCl_3$): 0.60–1.10 (*m*, 5H); 1.10–1.55 (*m*, 4H); 1.55–2.10 (*m*, 2H); 2.10–2.60 (*m*, 2H); 3.60 (*m*, 1H); 4.80–5.60 (*m*, 3H); 7.30–8.20 (*m*, 10H). MS (70 eV): 366 (8, M^+), 312 (6), 269 (8), 256 (10), 243 (5), 229 (28), 219 (16), 201 (100), 183 (18), 165 (10), 151 (9), 125 (13), 104 (11), 95 (15), 91 (21), 77 (82), 67 (34), 55 (32), 47 (50), 41 (58). MS (HR): 366.18049 ($C_{23}H_{27}O_2P$, calc. 366.17769).

(+)-[1-Oxo-1-((1S,2R)-2-vinyl-1-cyclopropyl)hexan-2-yl]diphenylphosphine Oxide ((−)-**7**). As above, (+)-**6** was converted to 0.50 g (36.8%) of (+)-**7**. $[\alpha]_{578} = +131.8°$ ($c = 8.67$, $CHCl_3$). M.p. 143–150°.

(+)-(1R,2R)-((1E)-1-Hexenyl)-2-vinylcyclopropane (= *(+)-Dictyopterene A*; (+)-**2**). A soln. of 0.762 mg (2.1 mmol) of (+)-**7** in 5 ml of EtOH was slowly added to a stirred suspension of 0.2 g of $NaBH_4$ in EtOH. After 4 h, the mixture was hydrolyzed by addn. of 5 ml of 2N HCl, extracted with CH_2Cl_2 (3 × 50 ml), dried, and purified by HPLC on silica gel using hexane/dioxane 1:1: 0.532 g (69.5%) of β-hydroxyphosphine oxide, which was converted immediately to (+)-dictyopterene A on treatment with 2 equiv. of NaH in 10 ml of dry DMF in a sealed tube. The mixture was kept at 50° for 2 h, cooled, and poured into 10 ml of sat. NH_4Cl soln. The olefine was extracted with pentane (3 × 30 ml), and the combined org. layers were washed with H_2O (20 ml) and dried. The (*E*)/(*Z*)-ratio was 85:15 (GC). Stereochemically homogeneous (+)-**2** was obtained by chromatography on silver-impregnated silica gel (10%) using a pentane/Et_2O gradient, followed by prep. GC on *PEG 4000* (20% on *Chromosorb P*, 60–80 mesh, *AW*, DMCS treated): 60.1 mg (19.1% overall from (+)-**7** of (+)-**2**. $[\alpha]_{578} = +80.6°$ ($c = 1.83$, CH_2Cl_2; [9]: $[\alpha]_D = +65°$ ($CHCl_3$); [6]: $[\alpha]_D = +72°$ ($CHCl_3$)). Spectroscopic data: see [6].

(−)-(1S,2S)-1-((1E)-1-Hexenyl)-2-vinylcyclopropane (= *(−)-Dictyopterene A*; (−)-**2**). As above; 0.5 g (1.4 mmol) of (−)-**7** were converted to 48.9 mg (23.3% overall from (−)-**7**) of (−)-**2**. $[\alpha]_{578} = -80.6°$ ($c = 2.01$, CH_2Cl_2).

(+)-(1S,2R)-2-Vinylcyclopropane-1-methanol ((+)-**8**). A soln. of 2.62 g (20.8 mmol) of (+)-**6** in 20 ml of dry Et_2O was slowly added with stirring to a chilled suspension of 1.0 g (26.3 mmol) of $LiAlH_4$ in 20 ml of Et_2O. After 4 h, excess $LiAlH_4$ was decomposed with H_2O, and 80 ml of 2N H_2SO_4 were added cautiously. The product was extracted with Et_2O (3 × 50 ml), the combined extract washed with H_2O (2 × 20 ml), dried, and evaporated. Distillation *i.v.* yielded 1.38 g (67.7%) of (+)-**8**, colourless oil. B.p. 66°/16 Torr. $[\alpha]_{578} = +65.4°$ ($c = 8.06$, CH_2Cl_2; [9]: $[\alpha]_D = +54°$ (EtOH). Spectroscopic data: see [7].

(−)-(1R,2S)-2-Vinylcyclopropane-1-methanol ((−)-**8**). A above, 3.12 g (24.8 mmol) of (−)-**6** yielded 1.98 g (81.6%) of (−)-**8**. $[\alpha]_{578} = -64.3°$ ($c = 8.54$, CH_2Cl_2).

(+)-(2E)-3-[(1S,2R)-2-Vinyl-1-cyclopropyl]-2-propenal ((+)-**9**). To a stirred suspension of 5.0 g (23.2 mmol) of PCC in 25 ml of CH_2Cl_2 were added 1.37 g (14.0 mmol) of (+)-**8** (monitoring by GC). After 1 h, additional PCC (1 g) was added. After complete conversion, the org. layer was decanted from the dark viscous oil and washed with H_2O (2 × 20 ml), and 50 ml of pentane were added to precipitate the chromium salts. The clear filtrate was evaporated: 0.42 g (31%) of crude aldehyde.

A soln. of 0.41 g (4.3 mmol) of the crude aldehyde and 2.28 g (7.5 mmol) of (formyl methylidene) triphenylphosphorane [18] in 50 ml of dry benzene was refluxed for 24 h. After cooling, 30 ml of 1N NH_4Cl were added and the 2 layers separated. The aq. phase was extracted with Et_2O (3 × 30 ml) and the combined org. layers dried and evaporated. HPLC on silica gel with hexane/Et_2O 2:1 removed the (*Z*)-isomer (7% according to GC) and other by-products and yielded 0.217 g (41%) of (+)-**9**, pale yellow oil. $[\alpha]_{578} = +226.9°$ ($c = 8.99$, CH_2Cl_2). IR (neat): 3090, 3010, 2980, 2820, 2740, 1680, 1630, 1180, 1120, 1050, 975, 930, 910, 850, 820, 785. ^{1}H-NMR (CCl_4): 1.00–1.40 (*m*, 2H); 1.55–2.00 (*m*, 2H); 4.90–6.55 (*m*, 5H); 9.5 (*d*, 1H). MS (70 eV): 122 (5, M^+), 107 (9), 104 (9), 93 (61), 91 (69), 81 (97), 77 (100), 68 (72), 53 (42), 41 (28), 39 (80). MS (HR): 122.07461 ($C_8H_{10}O$, calc. 122.07391).

(−)-(2E)-3-[(1R,2S)-2-Vinyl-1-cyclopropyl]-2-propenal ((−)-**9**). As above, 1.98 g (22.0 mmol) of (−)-**8** yielded 0.71 g (26.6%) of (−)-**9**. $[\alpha]_{578} = -218.9°$ ($c = 8.90$, CH_2Cl_2).

(−)-(1R,2R)-1-((1E,3Z)-1,3-Hexadienyl)-2-vinylcyclopropane (= *(−)-Hormosirene*; (−)-**1**). BuLi (4.3 ml, 0.8M in hexane) was slowly added at 0° to a stirred suspension of 1.37 g (3.55 mmol) of propyltriphenylphosphonium bromide in 10 ml of dry THF. Stirring was continued for 30 min, and 0.22 g (1.77 mmol) of (+)-**9** in 5 ml of dry THF were added dropwise. Following addn. of 10 ml of 1N HCl after 30 min and extraction with pentane (5 × 20 ml), the combined org. layers were washed with H_2O (2 × 20 ml), dried, and evaporated. The residue was purified on silica gel (pentane): 0.22 g (82.8%) of natural hormosirene as a 1:1 mixture of the (1*E*,3*Z*)- and (1*E*,3*E*)-isomers. To a soln. of 0.198 g (1.34 mmol) of this mixture in 2 ml of dry THF at −30° were added 0.12 g (0.69 mmol) of 4-phenyl-1,2,4-triazoline-3,5-dione with stirring (monitoring by GC). After complete separation of the isomers, the solvent was evaporated and the residue purified by column chromatography on silica gel (pentane). Removal of solvent yielded 82.5 mg (83% referring to the (1*E*,3*Z*)-isomer) of (−)-**1**. $[\alpha]_{578} = -48.9°$ ($c = 3.075$, CH_2Cl_2; [6]: $[\alpha]_D = -43°$ ($CHCl_3$); [9]: $[\alpha]_D = -37°$ ($CHCl_3$)). Spectroscopic data: see [6].

(+)-(1S,2S)-1-((1E,3Z)-1,3-Hexadienyl)-2-vinylcyclopropane (= (+)-Hormosirene; **(+)-1**). As above, 0.36 g (2.9 mmol) of (−)-**9** yielded 0.138 g (32.2% overall from (−)-**9**) of isomerically pure (+)-**1**. $[\alpha]_{578} = +48.2°$ ($c = 3.005$, CH_2Cl_2).

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