# Concise syntheses of cembrenes based on radical-mediated vinylcyclopropane ring-opening reactions in casbene

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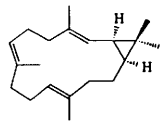
**Treatment of the bicyclo[12.1.0]pentadecatriene casbene 1 with ethanethiol radical (EtSH in $C_6H_6$, heat) results in regiospecific 1,4-addition to the vinylcyclopropane ring system, producing the cembrene sulfide 10. In similar reactions chrysanthemyl alcohol 11 and carene 13 lead exclusively to the corresponding sulfides 12 and 14, respectively, whereas irradiation of methyl chrysanthemate 15 with ethanethiol produces a 1:1 mixture of the isomeric sulfides 16 and 17. Oxidation of the cembrene sulfide 10, followed by thermolysis of the resulting sulfoxide then produces isocembrene 20, identical with natural material from *Pinus sibirica*. When a solution of casbene 1 in $CCl_4$ was heated in the presence of NBS and AIBN, it underwent smooth oxidative rearrangement, *via* 21 and 22, to cembrenene 23, identical with the natural product isolated from the soft coral *Sinularia maji*.**

The diterpene hydrocarbon casbene **1** was first isolated from seedlings of the castor bean *Ricinus communis*.[1] It has a novel bicyclo[12.1.0]pentadecane carbon framework, and the hydrocarbon is suggested to be the first distinct precursor of members of the lathyrane *e.g.* bertyadionol **2**,[2] tigliane *e.g.* phorbol **3**[3] and ingenane *e.g.* ingenol **4**,[4] families of biologically important cyclopropane ring-containing natural products. In addition, casbene is probably linked biogenetically with other families of polycyclic diterpenes, *e.g.* jatrophanes A and B,[5] crotofolane,[6] jatrofolane,[7] rhamnifolane,[8] daphnane,[9] whose carbon skeletons are derived from transannulation/rearrangement reactions accompanied by cleavage of the cyclopropane ring in casbene at one or other of the three possible bonds. It is also possible that casbene is implicated in the biosynthesis of members of the cembrane family of 14-ring containing compounds, *e.g.* **19** and **23**, and their oxygenated derivatives.[10]



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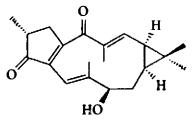

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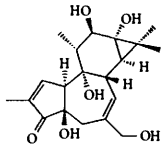

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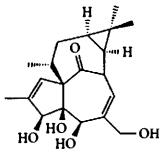

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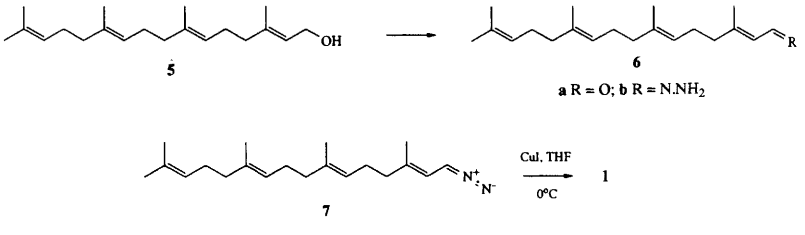
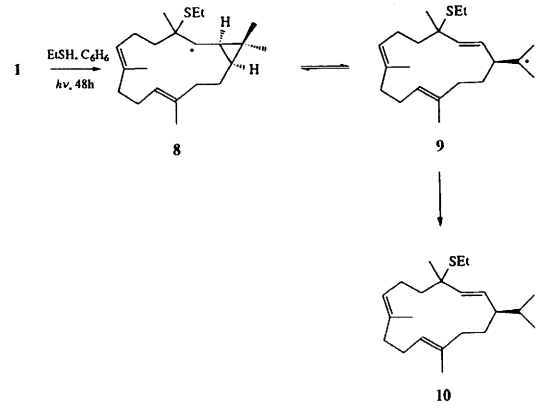
As a contribution towards an understanding of the biogenetic interrelationships between casbene **1** and the natural products referred to above, we have studied both electrophilic[11] and radical mediated transannulation/cyclopropane ring-opening reactions of casbene and some of its relatives. In this paper we describe the stereocontrolled cleavage of the cyclopropane ring in casbene **1** in the presence of radical initiating reagents resulting in smooth access to members of the natural cembranes **19**, **23**, **24** and **25**.[12]

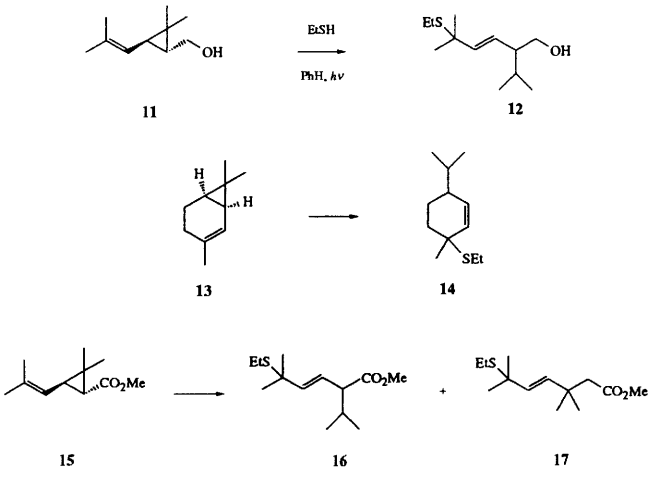
The synthesis of casbene **1** was first described by ourselves in 1976, in studies which also established the structure and stereochemistry of this intriguing secondary metabolite.[13] Later, Takahashi *et al.*[14] published a biomimetic type synthesis of (±)-casbene from geranylgeraniol using a procedure involving intramolecular carbene-alkene cyclisation. In the past few years several additional strategies towards natural (−)-casbene and its optical antipode have been described.[15–17] Although low yielding, the route to (±)-casbene from geranylgeraniol described by Takahashi *et al.* is the most convenient, especially when large quantities are required quickly. We also chose to use this route in the present studies, since we had large supplies of (all-*E*)-geranylgeraniol **5** which we had extracted from seeds of *Bixa orellana*.[18] Thus, oxidation of (all-*E*)-geranylgeraniol **5**, using manganese dioxide, first led to the aldehyde **6a**, which was next converted into the corresponding hydrazone **6b** by treatment with hydrazine hydrate in triethylamine and ethanol containing anhydrous magnesium sulfate. Without purification the hydrazone **6b** was then oxidised with manganese dioxide leading to the diazo species **7** which could be isolated as a red oil, stable below 0 °C. Addition of a solution of the diazo species **7** in tetrahydrofuran to a solution of copper(I) iodide in tetrahydrofuran at 0 °C, followed by work-up and chromatography on silica impregnated with silver nitrate, then gave (±)-casbene **1** in approximately 10% overall yield from geranylgeranial **6a**.

We began our investigations of radical-mediated reactions with casbene **1** by first examining treatment of the hydrocarbon with alkylsulfanyl radicals.[19] Thus, irradiation of a benzene solution of **1** in the presence of ethanethiol (1.2 equiv., 48 h), using light from a conventional sunlamp, resulted in

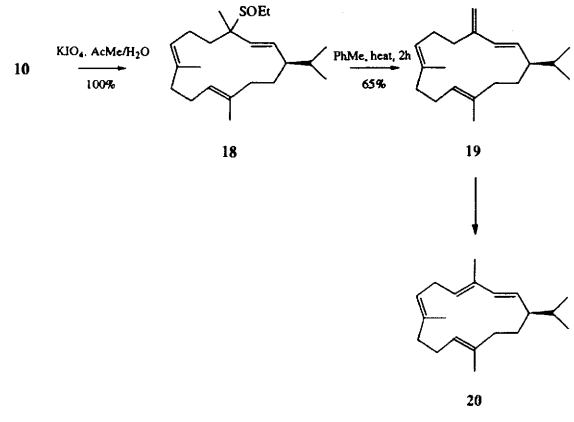





regioselective (1,4)-addition of the elements of ethanethiol to the vinylcyclopropane unit in casbene, and produced mainly one diastereoisomer of the all-*E* 14-ring sulfide **10** in 67–75% yields. It is assumed that **10** is produced from **1** *via* the radical intermediates **8** and **9**. Interestingly, we obtained no evidence from the co-formation of polycyclic structures resulting from further (transannular) interactions between the radical centres in **8**/**9**, and proximate carbon-to-carbon double bonds.[20]

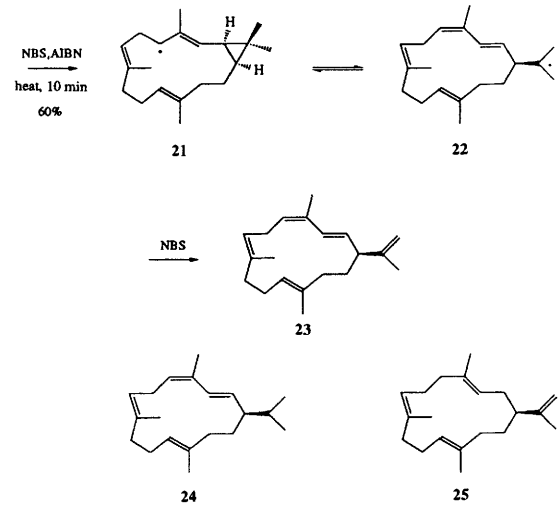



In contemporaneous studies we also examined the reactions between chrysanthemyl alcohol **11**, carene **13** and methyl chrysanthemate **15** with ethanethiol under the same irradiation conditions. Thus, whereas the cyclopropane rings in the alcohol **11** and carene suffered regiospecific ring opening, leading to the sulfides **12** and **14**, respectively, methyl chrysanthemate **15** produced a 1 : 1 mixture of the isomeric sulfides **16** and **17** on irradiation with ethanethiol in benzene solution.




Oxidation of the sulfide **10** resulting from treatment of casbene with ethanethiol, using potassium periodate, next led to a 1 : 1 mixture of the corresponding diastereoisomeric sulfoxides **18** in quantitative yield, which could be separated by chromatography. When either of the pure diastereoisomeric sulfoxides was then heated in toluene for 2 h, they underwent facile elimination of ethanesulfinic acid, producing (±)-isocembrene **19** (65%), which showed identical spectroscopic data with those reported for the natural material isolated from *Pinus sibirica*.[21] Prolonged heating of the sulfoxide **18**, or subsequent thermal isomerisation of isocembrene **19**, led to the (all-*E*)-cembrene **20**.

In a separate study we treated casbene **1** with *N*-bromosuccinimide under conditions which would be expected to promote allylic radical formation in the compound. Thus, when a solution of casbene in carbon tetrachloride was heated with freshly recrystallised dry *N*-bromosuccinimide in the presence of catalytic AIBN for 10 min, it underwent clean oxidative rearrangement, possibly *via* **21** and **22**, to (±)-cembrenene **23** in 60% yield. (*R*)-Cembrenene **23** has been isolated from the soft coral *Sinularia maji*,[22] and our synthetic material showed spectroscopic data identical with those reported for the natural product. Hydrogenation of synthetic cembrenene **23** in the presence of Wilkinson's catalyst then led to cembrene **24** whereas hydrogenation using Pd-on-charcoal proceeded in a 1,4-fashion producing neocembrene **25**. The spectroscopic data recorded for synthetic compounds **24** and **25** were identical with those reported for the natural products isolated from soft corals and terrestrial sources.[23,24]




The efficacies of the radical-mediated reactions with casbene **1** described above are encouraging, and bode well for future development in this area. The specificities of the additions of ethanethiol to the vinylcyclopropanes **11**, **13**, **15** and to casbene **1** owe a great deal to the facility with which the cyclopropylmethyl radical intermediates in these reactions undergo fragmentation rather than β-elimination of ethanethiyl radicals. Further work is now in progress to study the scope for similar radical-mediated, biogenetic type, transannulation reactions amongst cembranoids leading to polycyclic ring systems found in natural products represented by structures **2**–**4**.

## Experimental

For general experimental details see ref. 25.

### (±)-Casbene 1

Manganese dioxide (30.5 g, 0.35 mol) was added portionwise

over 5 min to a solution of geranylgeraniol (10.05 g, 35 mmol)[18] in dichloromethane (250 $cm^3$), and the mixture was then stirred at room temperature for 24 h. The mixture was filtered through Celite and the residue was washed with dichloromethane (4 × 100 $cm^3$). The filtrate was evaporated to dryness under reduced pressure and the yellow liquid was then purified by distillation to give geranylgeranial (9.63 g, 96%) as a yellow liquid; bp 156 °C/0.8 mmHg (lit.,[26] 150 °C/0.5 mmHg); $\nu_{max}$(film)/$cm^{-1}$ 2921, 2854, 2767, 1725, 1676, 1445, 1382, 1194, 1120 and 835; $\delta_H$(270 MHz; $CDCl_3$) 1.60 (3 H, s, $CH_3$), 1.61 (3 H, s, $CH_3$), 1.68 (3 H, s, $CH_3$), 1.97–2.08 (12 H, m), 2.17 (3 H, s, $CH_3$), 2.23 (3 H, s, $CH_3$), 5.09 [3 H, m, $(CH_3)C{=}CH$], 5.90 (1 H, d, *J* 7.9, *CH*CHO) and 9.99 (1 H, d, *J* 7.9, CHO); $\delta_C$(67.8 MHz; $CDCl_3$) 15.9 (q), 16.0 (q), 17.5 (q), 17.6 (q), 25.6 (q), 25.6 (t), 26.5 (t), 26.7 (t), 39.6 (t), 39.6 (t), 40.6 (t), 122.4 (d), 123.9 (d), 124.3 (d), 127.3 (d), 131.2 (s), 135.0 (s), 136.5 (s), 163.7 (s) and 191.2 (d). Hydrazine monohydrate (2.7 $cm^3$, 56.3 mmol) and triethylamine (7.92 $cm^3$, 56.3 mmol) were added dropwise over 5 min to a stirred solution of geranylgeranial (2.7 g, 9.4 mmol) in ethanol (150 $cm^3$) and then anhydrous magnesium sulfate (10 g) was added to the solution. The mixture was stirred at room temperature for 36 h, and then filtered through Celite. The residue was washed with ethanol (50 $cm^3$) and the solvent and excess of reagents were then removed under reduced pressure. The crude hydrazone was redissolved in pre-chilled dichloromethane (150 $cm^3$) and the solution was cooled to 0 °C. Manganese dioxide (12 g, 0.14 mol) was added in one portion, and the solution was then stirred at 0 °C for 3 h. The mixture was filtered through Celite whilst the solution was kept at 0 °C, and the residue was then washed with pre-chilled dichloromethane (4 × 50 $cm^3$). The solvent was removed under reduced pressure the product being kept below 0 °C to leave the corresponding diazo compound as a red oil,[14] which was then dissolved in pre-chilled tetrahydrofuran (200 $cm^3$). The solution was added dropwise over 4 h to a stirred suspension of copper(I) iodide (3.55 g, 0.1 mmol) in tetrahydrofuran (600 $cm^3$) at 0 °C. When the addition was complete, the mixture was stirred for a further 2 h at 0 °C and then filtered through Celite and evaporated under reduced pressure to leave a green oil. This was purified by column chromatography, firstly on silica using pentane as eluent, and secondly on silica impregnated with silver nitrate (10%) using pentane–ethyl acetate (15:1) as eluent to give (±)-casbene (250 mg, 9.6% based upon geranylgeranial) as a colourless oil;[13] $\nu_{max}$(film)/$cm^{-1}$ 2976, 2922, 2857, 1450, 1376, 1162 and 836; $\delta_H$(400 MHz; $CDCl_3$) 0.58 (app t, *J* ~8.9), 0.93 [3 H, s, $C(CH_3)_2$], 1.05 [3 H, s, $C(CH_3)_2$], 1.20–1.25 (2 H, m), 1.55 (3 H, s, $CH_3$), 1.58 (3 H, s, $CH_3$), 1.65 (3 H, s, $CH_3$), 1.69–2.29 (12 H, m), 4.86–4.88 [2 H, m, *CH*=C($CH_3$)] and 4.97 [1 H, app t, *J* ~6.6, *CH*=C($CH_3$)]; $\delta_C$(100 MHz; $CDCl_3$) 15.7 (2 × q), 16.2 (q), 16.5 (q), 19.8 (s), 24.0 (2 × t), 24.9 (t), 25.7 (d), 28.9 (q), 30.6 (d), 39.3 (t), 39.5 (t), 40.3 (t), 121.2 (d), 123.4 (d), 125.5 (d), 133.3 (s), 135.4 (s) and 136.0 (s); *m/z* (EI) 272.2504 ($M^+$. $C_{20}H_{32}$ requires 272.2504), 257 (6%), 229 (8%), 189 (16%), 161 (22%), 136 (93%) and 121 (100%).

### (all-*E*)-1-Ethylsulfanyl-4-isopropyl-1,7,11-trimethylcyclotetradeca-2,7,11-triene 10

Ethanethiol (0.26 $cm^3$, 3.53 mmol) was added dropwise over 2 min to a stirred solution of casbene (800 mg, 2.94 mmol) in benzene (8 $cm^3$), in a sealed tube fitted with a plastic tap. The solution was stirred and irradiated with UV light from a conventional sunlamp at room temp. for 48 h, after which it was evaporated under reduced pressure to leave a yellow oil. This was purified by column chromatography on silica using light petroleum–dichloromethane (15:1) as eluent to give the *sulfide* (676 mg, 70%) as a colourless oil; $\nu_{max}$(film)/$cm^{-1}$ 2928, 2854, 1460, 1376, 1130 and 979; $\delta_H$(400 MHz; $CDCl_3$) 0.86 and 0.89 [6 H, 2 × d, *J* 6.8, $CH(CH_3)_2$], 1.20 (3 H, t, *J* 7.5, $SCH_2CH_3$), 1.20–1.40 (4 H, m), 1.38 (3 H, s, $CH_3$), 1.40–1.76 (4 H, m), 1.62 [1 H, m, $CH(CH_3)_2$], 1.68 (3 H, s, $CH{=}CCH_3$), 1.70 (3 H, s, $CH{=}CCH_3$), 1.82 [1 H, m, $CHCH(CH_3)_2$], 1.88–2.42 (4 H, m), 2.44 (2 H, q, *J* 7.5, $SCH_2CH_3$), 5.08–5.12 [1 H, m, $CH{=}C(CH_3)$], 5.20–5.23 [1 H, m, *CH*=C($CH_3$)], 5.36 (1 H, d, *J* 15.9, *CH*=CHCH) and 5.46 (1 H, dd, *J* 15.9 and 8.04, CH=*CH*CH); $\delta_C$(100 MHz; $CDCl_3$) 14.5 (q), 19.5 (q), 20.5 (q), 22.4 (t), 23.3 (q), 24.0 (q), 24.2 (t), 26.4 (q), 27.7 (t), 30.2 (t), 31.2 (t), 33.0 (d), 33.5 (t), 42.1 (t), 48.8 (d), 49.2 (s), 123.6 (d), 124.4 (d), 132.3 (d), 135.4 (d), 135.9 (s) and 137.8 (s); *m/z* (EI) 334.2709 ($M^+$. $C_{22}H_{38}S$ requires 334.2694), 272 (19%), 257 (5%) and 229 (16%).

### (*E*)-5-Ethylsulfanyl-2-isopropyl-5-methylhex-3-en-1-ol 12

Ethanethiol (490 $mm^3$, 6.62 mmol) † was added dropwise over 2 min to a stirred solution of *trans*-chrysanthemyl alcohol[27] (1.02 g, 6.62 mmol) in benzene (30 $cm^3$) in a sealed tube, and the mixture was then irradiated at room temp. for 18 h using UV light from a conventional sunlamp. Following TLC analysis, more ethanethiol (490 $mm^3$, 6.62 mmol) was added to the solution which was then irradiated for a further 11 h. The mixture was evaporated under reduced pressure to leave a residue which was purified by column chromatography on silica using light petroleum–ethyl acetate (5:1) as eluent to give the *sulfide* (1.08 g, 76%) as a yellow liquid; $\nu_{max}$(film)/$cm^{-1}$ 3382, 2962, 2928, 2871, 1658, 1464, 1384, 1125, 976 and 758; $\delta_H$(250 MHz; $CDCl_3$) 0.81 and 0.86 [6 H, 2 × d, *J* 6.8, $CH(CH_3)_2$], 1.15 (3 H, t, *J* 7.5, $SCH_2CH_3$), 1.33 [3 H, s, $SC(CH_3)$], 1.34 [3 H, s, $SC(CH_3)$], 1.69 (1 H, m, CH=CH*CH*$CH_2OH$), 1.73 (1 H, br s, OH), 1.97 [1 H, m, $CH(CH_3)_2$], 2.37 (2 H, q, *J* 7.5, $SCH_2$), 3.41 (1 H, dd, *J* 10.5 and 8.4, $CH_2OH$), 3.61 (1 H, dd, *J* 10.5 and 5.3, $CH_2OH$), 5.15 [1 H, dd, *J* 15.6 and 9.3, $(CH_3)_2CCH{=}CH$] and 5.56 [1 H, d, *J* 15.6, $(CH_3)_2CCH{=}CH$]; $\delta_C$(67.8 MHz; $CDCl_3$) 14.4 (q), 19.1 (q), 20.7 (q), 22.8 (t), 28.1 (q), 28.2 (q), 28.4 (d), 45.9 (s), 51.8 (d), 64.0 (t), 126.1 (d) and 140.7 (d); *m/z* (EI) 216.1533 ($M^+$. $C_{12}H_{24}OS$ requires 216.1548), 155 (11%), 137 (12%), 123 (13%), 109 (11%), 95 (15%), 81 (38%) and 69 (100%).

### 3-Ethylsulfanyl-6-isopropyl-3-methylcyclohex-1-ene 14

Ethanethiol (220 $mm^3$, 3.0 mmol) was added dropwise to a stirred solution of 2-carene (204 mg, 1.5 mmol) in benzene (10 $cm^3$) in a sealed tube and the mixture was irradiated at room temp. for 3 days using UV light from a conventional sunlamp. The mixture was evaporated under reduced pressure to leave a residue which was purified by column chromatography on silica using light petroleum–dichloromethane (15:1) as eluent to give the *sulfide* (179 mg, 60%) as a yellow liquid; $\nu_{max}$(film)/$cm^{-1}$ 3017, 2958, 2870, 1668, 1447, 1367, 1262, 1102 and 738; $\delta_H$(250 MHz; $CDCl_3$) 0.87 [6 H, 2 × d, *J* 6.8, $CH(CH_3)_2$], 1.21 (3 H, t, *J* 7.6, $SCH_2CH_3$), 1.29 [3 H, s, $SC(CH_3)$], 1.3–1.5 (2 H, m), 1.5–1.7 (2 H, m), 1.7–1.95 (2 H, m), 2.50 (2 H, m, $SCH_2$) and 5.59 (2 H, m, CH=CH); $\delta_C$(67.8 MHz; $CDCl_3$) 14.7 (q), 19.2 (q), 19.5 (q), 22.3 (q), 22.8 (t), 27.9 (t), 31.8 (d), 35.8 (t), 41.2 (d), 45.8 (s), 131.2 (d) and 134.5 (d); *m/z* (EI) 198.1440 ($M^+$. $C_{12}H_{22}S$ requires 198.1442), 137 (46%), 121 (15%), 95 (19%), 93 (44%) and 81 (100%).

### (*E*)-Methyl 5-ethylsulfanyl-2-isopropyl-5-methylhex-3-enoate 16 and (*E*)-methyl 6-ethylsulfanyl-3,3,6-trimethylhept-4-enoate 17

Ethanethiol (294 $mm^3$, 3.97 mmol) was added dropwise over 2 min to a stirred solution of *trans*-methyl chrysanthemate (0.5 g, 2.75 mmol)[28] in benzene (10 $cm^3$) in a sealed tube and the mixture was then irradiated at room temp. for 48 h using

† 1 $mm^3$ = 1 μl.

UV light from a conventional sunlamp. The mixture was evaporated under reduced pressure to leave a residue which was purified by column chromatography on silica using light petroleum–dichloromethane (2:1) as eluent to give: (i) the *sulfide* **16** (242 mg, 36%) as a yellow liquid; $\nu_{max}$(film)/cm$^{-1}$ 2930, 2872, 1728, 1458, 1365, 1296, 1154, 1124 and 945; $\delta_H$(250 MHz; $CDCl_3$) 0.87 and 0.90 [6 H, 2 × d, *J* 6.8, CH(C$H_3$)$_2$], 1.16 (3 H, t, *J* 7.5, SCH$_2$C$H_3$), 1.35 [6 H, s, SC(CH$_3$)$_2$], 1.96 [1 H, m, C*H*(CH$_3$)$_2$], 2.36 (2 H, q, *J* 7.5, SCH$_2$), 2.69 (1 H, app t, *J* 8.8, C*H*CO$_2$CH$_3$), 3.66 (3 H, s, CO$_2$CH$_3$), 5.36 [1 H, dd, *J* 15.6 and 9.4, (CH$_3$)$_2$CCH=C*H*] and 5.57 [1 H, d, *J* 15.6, (CH$_3$)$_2$CH*H*=CH]; $\delta_C$(100 MHz; $CDCl_3$) 14.7 (q), 19.8 (q), 20.8 (q), 23.0 (t), 28.0 (q), 28.2 (q), 31.0 (d), 46.0 (s), 51.6 (q), 56.6 (d), 123.9 (d), 141.0 (d) and 174.7 (s); *m*/*z* (EI) 244.1496 (M$^+$. $C_{13}H_{24}O_2S$ requires 244.1497), 185 (7%), 183 (52%), 141 (27%), 129 (46%), 123 (42%) and 115 (100%); and (ii) the sulfide **17** (254 mg, 38%) as a yellow liquid; $\nu_{max}$(film)/cm$^{-1}$ 2928, 2854, 1728, 1461, 1365, 1124 and 976; $\delta_H$(270 MHz; $CDCl_3$) 1.08 [6 H, s, C(CH$_3$)$_2$], 1.12 [3 H, t, *J* 7.3, SCH$_2$C$H_3$], 1.28 [6 H, s, SC(C$H_3$)$_2$] 2.24 (2 H, s, C$H_2$CO$_2$CH$_3$), 2.29 (2 H, q, *J* 7.3, SC$H_2$CH$_3$), 3.56 (3 H, s, CO$_2$C$H_3$) and 5.37 (2 H, s, CH=CH); $\delta_C$(100 MHz; $CDCl_3$) 14.8 (q), 23.0 (t), 27.9 (2 × q), 28.3 (2 × q), 35.3 (s), 45.9 (s), 47.4 (t), 51.2 (q), 133.7 (d), 135.8 (d) and 172.2 (s); *m*/*z* (EI) 244.1484 (M$^+$. $C_{13}H_{24}O_2S$ requires 244.1497), 183 (49%), 152 (41%), 151 (27%), 140 (11%), 127 (11%), 123 (55%) and 109 (100%).

### (all-*E*) 1-Ethylsulfinyl-4-isopropyl-1,7,11-trimethylcyclotetradeca-2,7,11-triene 18

Potassium periodate (0.45 g, 1.98 mmol) was added in one portion to a stirred solution of (all-*E*)-1-ethylsulfanyl-4-isopropyl-1,7,11-trimethylcyclotetradeca-2,7,11-triene (600 mg, 1.8 mmol) in aqueous acetone (4:1; 600 cm$^3$). The solution was stirred at room temp. for 48 h, and then evaporated under reduced pressure. The residue was extracted with ether (3 × 150 cm$^3$), and the combined organic extracts were then dried and evaporated under reduced pressure. The residue was purified by column chromatography on silica using dichloromethane–ether (15:1) as eluent to give two diastereoisomeric *sulfoxide* products, each as a pale yellow oil: (i) less polar sulfoxide (310 mg, 49%); $\nu_{max}$($CHCl_3$)/cm$^{-1}$ 2961, 2929, 2868, 1460, 1377, 1216, 1074, 1013 and 757; $\delta_H$(400 MHz; $CDCl_3$) 0.84 and 0.87 [6 H, 2 × d, *J* 6.8, CH(C$H_3$)$_2$], 1.29 (3 H, s, CH$_3$), 1.35 (3 H, m, SCH$_2$C$H_3$), 1.65 (3 H, s, CH=CC$H_3$), 1.67 (3 H, s, CH=CC$H_3$), 1.55–2.3 (14 H, m), 2.55 (2 H, m, SC$H_2$CH$_3$), 5.09 [1 H, app d, *J* ~9.3, C*H*=C(CH$_3$)], 5.20 [1 H, app t, *J* ~6.8, C*H*=C(CH$_3$)], 5.56 (1 H, d, *J* 16.1, C*H*=CHCH) and 5.61 (1 H, dd, *J* 16.1 and 8.84, CHC*H*CH); $\delta_C$(100 MHz; $CDCl_3$) 8.5 (q), 19.3 (q), 19.8 (q), 20.6 (q), 22.9 (t), 23.4 (q), 24.0 (q), 27.6 (t), 29.7 (t), 30.3 (t), 31.5 (t), 32.7 (d), 33.3 (t), 33.3 (t), 49.9 (d), 60.9 (s), 123.4 (d), 123.8 (d), 128.1 (d), 136.2 (s), 137.9 (s) and 139.0 (d); *m*/*z* (FAB) 351 (M$^+$ + H, 2.1%) 257 (2.1%), 229 (3.5%): (ii) more polar sulfoxide (310 mg, 49%); $\nu_{max}$($CHCl_3$)/cm$^{-1}$ 2961, 2927, 2868, 1460, 1376, 1216, 1049, 1014 and 753; $\delta_H$(400 MHz; $CDCl_3$) 0.81 and 0.87 [6 H, 2 × d, *J* 6.7, CH(C$H_3$)$_2$], 1.31 (3 H, m, SCH$_2$C$H_3$), 1.36 (3 H, s, CH$_3$), 1.67 (3 H, s, CH=CC$H_3$), 1.69 (3 H, s, CH=CC$H_3$), 1.4–2.1 (14 H, m), 2.37 (2 H, m, SC$H_2$CH$_3$), 5.11–5.15 [1 H, m, C*H*=C(CH$_3$)], 5.22–5.24 [1 H, m, C*H*=C(CH$_3$)], 5.24 (1 H, d, *J* 16.1, C*H*CHCH) and 5.48 (1 H, dd, *J* 16.1 and 9.4, CHC*H*CH); $\delta_C$(100 MHz; $CDCl_3$) 8.6 (q), 14.9 (q), 19.4 (q), 20.7 (q), 22.6 (t), 23.3 (q), 23.9 (q), 27.6 (t), 29.6 (t), 30.0 (t), 31.9 (t), 32.4 (d), 33.2 (t), 36.3 (t), 50.5 (d), 53.3 (s), 123.3 (d), 123.7 (d), 130.1 (d), 135.9 (s), 137.6 (s) and 139.0 (d); *m*/*z* (FAB) 351 (M$^+$ + H, 1.3%), 335 (2.3%), 273 (9.5%), 257 (2.0%) and 229 (3.1%).

### (±)-Isocembrene 19

A solution of (all-*E*)-1-ethylsulfinyl-4-isopropyl-1,7,11-trimethylcyclotetradeca-2,7,11-triene (50 mg, 0.14 mmol) in toluene (25 cm$^3$) was heated at 120 °C for 2 h in a nitrogen atmosphere and then cooled and evaporated to dryness. The residue was purified by column chromatography on silica using pentane as eluent to give (±)-isocembrene (25 mg, 65%) as a colourless oil;[21] $\nu_{max}$($CHCl_3$)/cm$^{-1}$ 2929, 2855, 1460, 975 and 892; $\delta_H$(400 MHz; $CDCl_3$) 0.85 and 0.90 [6 H, 2 × d, *J* 6.8, CH(C$H_3$)$_2$], 1.69 (3 H, s, CH=CC$H_3$), 1.70 (3 H, s, CH=CC$H_3$), 1.5–2.4 (14 H, m), 4.85 (2 H, s, C=CH$_2$), 5.08 [1 H, app t, *J* ~7.0, C*H*=C(CH$_3$)], 5.21–5.2 [1 H, m, C*H*=C(CH$_3$)], 5.54 (1 H, dd, *J* 15.9 and 9.2, CH=C*H*CH) and 5.98 (1 H, d, *J* 15.9, C*H*=CHCH); $\delta_C$(100 MHz; $CDCl_3$) 19.9 (q), 20.7 (q), 23.5 (q), 23.8 (q), 28.1 (t), 28.6 (t), 29.6 (t), 32.4 (d), 32.7 (t), 33.2 (t), 34.0 (t), 49.7 (d), 113.8 (t), 123.8 (d), 124.7 (d), 132.3 (d), 134.0 (d), 135.9 (s), 137.9 (s) and 146.2 (s); *m*/*z* (EI) 272.2524 (M$^+$. $C_{20}H_{32}$ requires 272.2504), 257 (4.2%), 229 (8.0%) and 161 (9.6%).

### (all-*E*)-Cembrene 20

A solution of (all-*E*)-1-ethylsulfinyl-4-isopropyl-1,7,11-trimethylcyclotetradeca-2,7,11-triene (50 mg, 0.14 mmol) in toluene (25 cm$^3$) was heated under reflux for 12 h in a nitrogen atmosphere and then cooled and evaporated to dryness. The residue was purified by column chromatography on silica using pentane as eluent to give a mixture of (±)-isocembrene and the (all-*E*)-cembrene (27 mg, 70%) as a colourless oil; $\nu_{max}$($CHCl_3$)/cm$^{-1}$ 2929, 2855, 1460, 975 and 892; $\delta_H$(400 MHz; $CDCl_3$) (*E*)-cembrene, 0.89 and 0.90 [6 H, 2 × d, *J* 6.8, CH(C$H_3$)$_2$], 1.65 (3 H, s, CH=CC$H_3$), 1.70 (3 H, s, CH=CC$H_3$), 1.82 (3 H, s, CH=CC$H_3$), 1.5–2.4 (11 H, m), 3.21–3.29 (1 H, m, =CHC$H_2$CH=), 5.12 [1 H, app t, *J* ~6.7, C*H*=C(CH$_3$)], 5.19 [1 H, app t, *J* ~7.9, C*H*=C(CH$_3$)], 5.30–5.35 [1 H, m, C*H*=C(CH$_3$)], 5.53 (1 H, dd, *J* 15.5 and 9.1, CH=C*H*CH) and 6.46 (1 H, d, *J* 15.5, C*H*=CHCH); $\delta_C$(100 MHz; $CDCl_3$) 20.0 (q), 20.7 (q), 21.1 (q), 22.4 (q), 23.8 (q), 27.0 (t), 27.7 (t), 28.8 (t), 29.1 (t), 32.9 (d), 33.0 (t), 47.9 (d), 122.5 (d), 126.5 (d), 126.7 (d), 128.2 (d), 130.9 (s), 133.0 (d), 134.2 (s) and 135.2 (s).

### (±)-Cembrenene 23

*N*-Bromosuccinimide (131 mg, 0.74 mmol) and AIBN (10 mg) were added, each in one portion, to a stirred solution of casbene (200 mg, 0.74 mmol) in carbon tetrachloride (10 cm$^3$). The solution was heated under reflux for 10 min in a nitrogen atmosphere and then cooled, filtered and evaporated to dryness. The orange oily residue was purified by column chromatography on silica using pentane as eluent to give (±)-cembrenene (119 mg, 60%) as a colourless oil;[22] $\nu_{max}$($CHCl_3$)/cm$^{-1}$ 2927, 2854, 1603, 1459, 1379, 1125, 1099, 945 and 899; $\delta_H$(400 MHz; $CDCl_3$) 1.53 (3 H, s, CH$_3$), 1.61 (3 H, s, CH$_3$), 1.72 (3 H, s, CH$_3$), 1.79 (3 H, s, CH$_3$), 1.5–2.5 (10 H, m), 3.02–3.12 (1 H, m, =CHC$H_2$CH=), 4.70 (2 H, s, C=CH$_2$), 4.91 [1 H, br d, *J* 7.0, C*H*=C(CH$_3$)], 5.11 [1 H, br d, *J* 9.1, C*H*=C(CH$_3$)], 5.25 (1 H, dd, *J* 15.4 and 9.8, CH=C*H*CH], 5.56 [1 H, br t, *J* 15.3, C*H*=C(CH$_3$)] and 6.16 (1 H, d, *J* 15.4, C*H*=CHCH); $\delta_C$(100 MHz; $CDCl_3$) 14.4 (q), 14.4 (q), 19.8 (q), 21.5 (q), 23.5 (t), 26.3 (t), 29.1 (t), 36.4 (t), 38.9 (t), 49.0 (d), 108.7 (t), 126.2 (d), 126.3 (d), 126.7 (d), 130.3 (d), 130.5 (d), 131.4 (s), 132.3 (s), 135.0 (s) and 149.7 (s); *m*/*z* (EI) 270.2303 (M$^+$. $C_{20}H_{30}$ requires 270.2348), 255 (2.9%), 159 (6.6%), 145 (9.9%) and 133 (12.0%).

### (±)-Cembrene 24

Tris(triphenylphosphine)rhodium(I) chloride (24 mg, 0.026 mmol) was added in one portion to a stirred solution of (±)-cembrenene (70 mg, 0.26 mmol) in a mixture of ethanol and benzene (1:1; 5 cm$^3$). The solution was stirred at room temp. for 16 h in a hydrogen atmosphere, then filtered and evaporated to

dryness. The yellow oily residue was purified by column chromatography on silica using pentane as eluent to give (±)-cembrene (49 mg, 69%) as a colourless oil;[23] $\nu_{max}(CHCl_3)/cm^{-1}$ 2928, 2854, 1604, 1457, 1382, 1351, 1110 and 980; $\delta_H$(400 MHz; $CDCl_3$) 0.82 and 0.86 [6 H, 2 × d, *J* 6.8, $CH(CH_3)_2$], 1.50 (3 H, s, CH=CC$H_3$), 1.59 (3 H, s, CH=CC$H_3$), 1.79 [3 H, t, *J* 1.3, CH=C(C$H_3$)], 1.65–2.45 (11 H, m), 3.04 (1 H, m, =CH-C$H_2$CH=), 4.87 [1 H, br d, *J* 6.7, C*H*=C($CH_3$)], 5.10 [1 H, br d, *J* 10.8, C*H*=C($CH_3$)], 5.17 (1 H, dd, *J* 15.5 and 9.7, CH=C*H*CH), 5.53 [1 H, br t, *J* 7.7, C*H*=C($CH_3$)] and 6.06 (1 H, d, *J* 15.5, C*H*=CHCH); $\delta_C$(100 MHz; $CDCl_3$) 14.3 (q), 19.9 (q), 19.9 (q), 20.8 (q), 23.5 (q), 26.2 (t), 27.7 (t), 32.8 (d), 36.5 (t), 38.9 (t), 48.2 (d), 125.4 (d), 125.7 (d), 126.5 (d), 130.3 (d), 131.1 (d), 131.3 (s), 132.6 (s) and 135.2 (s); *m/z* (EI) 272.2472 ($M^+$ $C_{20}H_{32}$ requires 272.2504), 257 (3.9%) and 229 (5.5%).

### Neocembrene 25

A vessel containing a suspension of cembrenene (20 mg, 0.07 mmol) and palladium-on-charcoal (10%; 10 mg) in ethyl acetate (10 $cm^3$) was evacuated and then filled with hydrogen. The mixture was stirred under a hydrogen atmosphere at room temp. for 24 h and then filtered through Celite. The filtrate was evaporated under reduced pressure to leave a yellow oil which was purified by column chromatography on silica using pentane as eluent to give neocembrene (8 mg, 40%) as a colourless oil. The oil showed spectroscopic data which were identical with those reported in the literature.[24]

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