219. Sesquiterpenoids from Costus Root Oil (*Saussurea lappa* CLARKE)

by **Bruno Maurer** and **Alfred Grieder**

Firmenich SA, Research Laboratories, 1211 Geneva 8

(19.VII.77)

Summary

Apart from the well-known constituents (+)-β-selinene (**2**), (−)-β-elemene (**4**), (+)-β-costol (**7**), (−)-caryophyllene (**17**), and (−)-elemol (**19**) the following sesquiterpenoids have been isolated for the first time from costus root oil (*Saussurea lappa* CLARKE): (−)-α-selinene (**1**), (+)-selina-4,11-diene (**3**), (−)-α-*trans*-bergamotene (**5**), (−)-α-costol (**6**), (+)-γ-costol (**8**), (−)-elema-1,3,11(13)-trien-12-ol (**9**), (−)-α-costal (**11**), (+)-β-costal (**12**), (+)-γ-costal (**13**), (−)-elema-1,3,11(13)-trien-12-al (elemenal, **14**), (−)-(*E*)-*trans*-bergamota-2,12-dien-14-al (**15**), (−)-*ar*-curcumene (**16**), and (−)-caryophyllene oxide (**18**). Compounds **6**, **8**, **9**, and **13** are new sesquiterpenoids. IR. and NMR. spectra of 12 sesquiterpenoids are reproduced.

The essential oil obtained by steam distillation of the roots of the costus plant, *Saussurea lappa* CLARKE (*Compositae*), has found wide use in medicine and perfumery, and has, therefore, been subject to analytical investigations since 1914 [1][1]). The fact that the oil contains a number of allergy-inducing sesquiterpenoid α-methylene lactones [3] might well lead to a restriction of its use in perfumery, so a synthetic reconstitution free of potentially harmful lactones is desirable. We therefore undertook a detailed analysis of the oil and report here the identification of 18 sesquiterpenoids[2]). Apart from the well-known constituents β-selinene (**2**), β-elemene (**4**), β-costol (**7**)[3]), caryophyllene (**17**), and elemol (**19**) we have isolated for the first time the following sesquiterpenoids from costus root oil[4]): α-selinene (**1**), selina-4,11-diene (**3**), α-*trans*-bergamotene (**5**), α-costol (**6**)[3]), γ-costol (**8**)[3]), elema-1,3,11(13)-trien-12-ol (**9**), α-costal (**11**)[3]), β-costal (**12**)[3]), γ-costal (**13**)[3]), elema-

[1]) Recent publication including leading references [2].

[2]) The analysis of the sesquiterpenoid lactones and acids is not included in the present work in view of greater clarity.

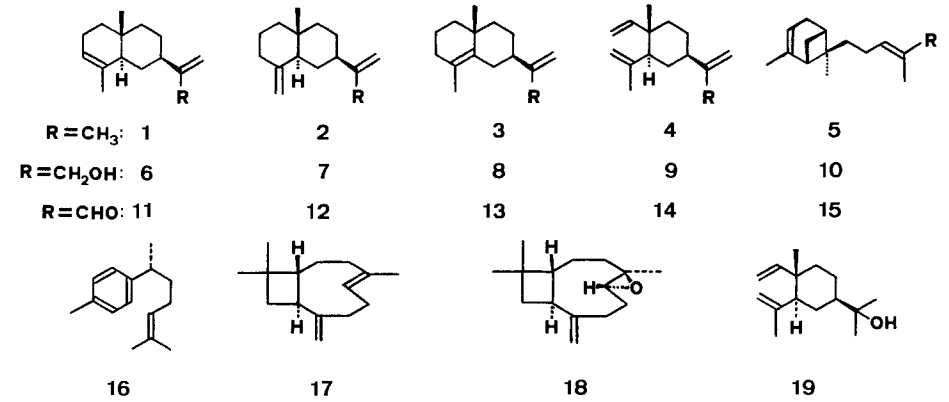
[3]) Considering the presence of three isomers of 'costol' in costus root oil we propose to name these alcohols α-(**6**), β-(**7**), and γ-costol (**8**), respectively, in analogy to the closely related and well-known α-, β-, and γ-eudesmol. The name 'costol' for β-costol should be abandoned. The corresponding aldehydes should be named accordingly α-(**11**), β-(**12**), and γ-costal (**13**), respectively. Unfortunately, a reference [4] using a misleading nomenclature (the names of α- and β-costal are interchanged) is cited by the 'Handbook of Naturally Occurring Compounds' [5] which also erroneously lists **7** as α-costol.

[4]) For details, see exper. part.

1,3,11(13)-trien-12-al (elemenal, **14**), (*E*)-*trans*-bergamota-2,12-dien-14-al (**15**)[5]), *ar*-curcumene (**16**), and caryophyllene oxide (**18**).

Pure samples of many sesquiterpenoids are often not easily available for direct comparison. Identification of many known sesquiterpenoids is achieved by comparing their spectra with spectral data (often incomplete) reported in the literature. Because it would be much safer in such cases to have the full details, we reproduce the entire NMR. and IR. spectra of 12 sesquiterpenoids.

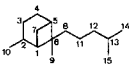
The *Table* summarizes the sesquiterpenoids identified in this work, including means of identification and literature references to spectra.



A few compounds require comment.

α-Selinene (**1**). A positive $[\alpha]_D$ value has been ascribed repeatedly to this sesquiterpene (absolute configuration as shown) [19]. *Wojtkiewicz* [20][6]) and *Andersen* [21] were the first to report negative values for **1**. To clarify this ambiguity, which arises either from the presence of impurities or erroneous configurational assignments, we carefully purified a sample of **1** by chromatography on SiO_2-$AgNO_3$ and GC. (Carbowax) thus obtaining α-selinene of >99% purity[7]). This sample, the absolute configuration of which was established by CD.[8]), showed $[\alpha]_D^{20} = -14.5°$ ($CHCl_3$, 1%), confirming the value measured by *Andersen et al.* ($[\alpha]_D = -16°$ (pentane, 0.2%)). Hydrocarbon **1** should thus be named (−)-α-selinene.

[5]) The semisystematic name is based on the bergamotane (= sesquipinane) skeleton which has been numbered as shown (using the fixed numbering of pinane).



The systematic name for this compound is 5-((1*S*,5*S*,6*R*)-2,6-dimethylbicyclo[3.1.1]hept-2-en-6-yl)-2-methyl-(*E*)-2-pentenal or 4-[(1*S*,5*S*,6*R*)-2-pinen-8-yl]-2-methyl-(*E*)-2-butenal.

[6]) We thank Dr. *C. Ganter*, ETH Zurich, for bringing this reference to our attention.

[7]) Determined by GC. on a capillary column. Another sample containing *ca.* 5% of the same impurity showed unchanged optical rotation, demonstrating that the impurity had no measurable influence on the $[\alpha]_D$ values.

[8]) We are grateful to Professor *G. Snatzke*, Bochum, for recording the CD. spectrum of **1** which is identical with that reported [21].

Table. *Sesquiterpenoids from costus root oil*

Compound	No.	%[a])	Identification	References[b])	
(−)-α-selinene	**1**	0.14	NMR., MS.	[c])	[6–8]
(+)-β-selinene	**2**	1.40	IR., NMR., MS.	[2] [9]	[6–8] [10] [11]
(+)-selina-4,11-diene	**3**	0.23	NMR.	[c])	[6]
(−)-β-elemene	**4**	1.20	[d])	[2] [9] [12]	[6–8] [13]
(−)-α-*trans*-bergamotene	**5**	0.23	[d])	[c])	[7] [8] [13–15]
(−)-α-costol[3])	**6**	3.8	IR., NMR., MS.	[e])	
(+)-β-costol[3])	**7**	6.0	IR., NMR., MS.	[16]	[2] [11]
(+)-γ-costol[3])	**8**	3.3	IR., NMR., MS.	[e])	
(−)-elema-1,3,11(13)-trien-12-ol	**9**	4.9	[d])	[e])	
(−)-α-costal[3])	**11**	0.10	[d])	[c])	[4]
(+)-β-costal[3])	**12**	0.14	[d])	[c])	[4] [11] [17]
(+)-γ-costal[3])	**13**	0.12	[d])	[e])	
(−)-elema-1,3,11(13)-trien-12-al	**14**	0.23	[d])	[c])	[4]
(−)-2,12-bergamotadien-14-al[5])	**15**	0.20	[d])	[c])	
(−)-*ar*-curcumene	**16**	0.70	IR., NMR., MS.	[c])	[8] [18]
(−)-caryophyllene	**17**	0.90	[d])	[2] [12]	[8]
(−)-caryophyllene oxide	**18**	0.80	[d])	[c])	[18]
(−)-elemol	**19**	1.00	[d])	[16]	

[a]) Approximate concentration of constituent in commercial costus root oil. The figures have been estimated from GC. and/or isolated yields.

[b]) The first and the second set of references refer to isolation from costus root oil and to spectral data of constituents, respectively.

[c]) Identified for the first time in costus root oil.

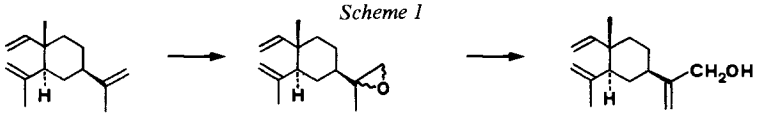
[d]) Substance identical with an authentic (or synthetic) sample spectrally and by retention time.

[e]) New compound.

α-, β-, and γ-Costol (**6**, **7**, *and* **8**)[3]). Indian workers [16] examined 'costol' isolated from costus root oil and found it to be an intimate mixture of at least three major components which they were unable to separate. One of these components was shown to be (+)-β-costol (**7**) obtained in a pure state from costic acid. Our work shows that 'costol' is a mixture of the double bond isomers **6**, **7**, and **8** (*ca.* 1:2:1), separable by combined chromatographic techniques (see exper. part). The structures of **6** and **8** follow from their spectral data, in particular the similarities in their NMR. spectra when compared with those of the known and closely related compounds **1**, **2**, **3**, and **7**.

Elema-1,3,11(13)-trien-12-ol (**9**). The structure and absolute configuration of this new sesquiterpene alcohol were established by its identity (including optical rotation) with a sample synthesized by rearrangement of (−)-β-elemene 11,12-epoxide (**20**) [22][9]) with lithium diethylamide (*Scheme 1*). Moreover, oxidation of alcohol **9** with manganese dioxide gave the known aldehyde **14** [4], also present in costus root oil.

Scheme 1



4 **20** **9**

[9]) We are grateful to Dr. *A. F. Thomas* for a gift of (−)-β-elemene.

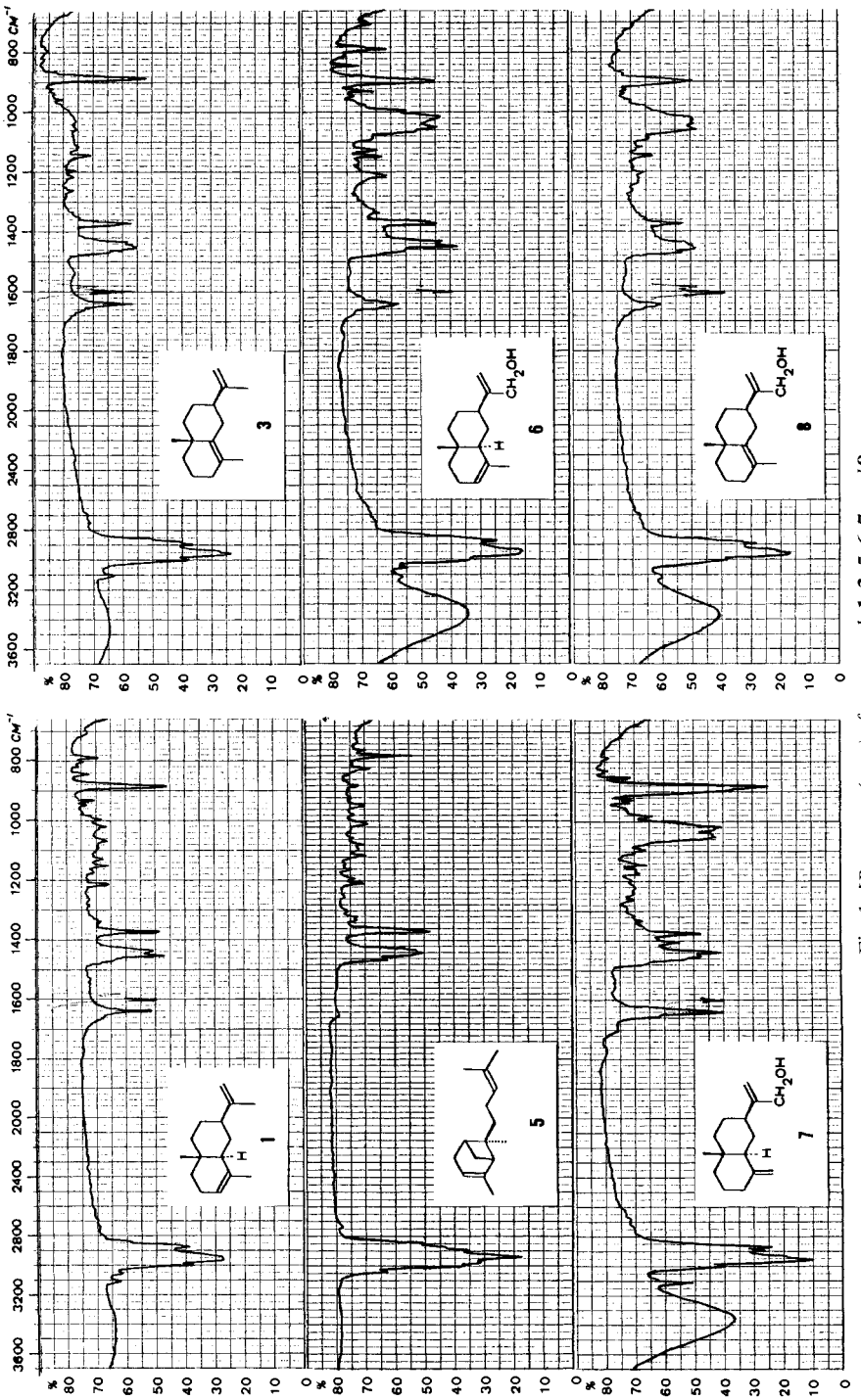


Fig. 1. *IR. spectra (neat) of compounds* **1**, **3**, **5**, **6**, **7**, *and* **8**

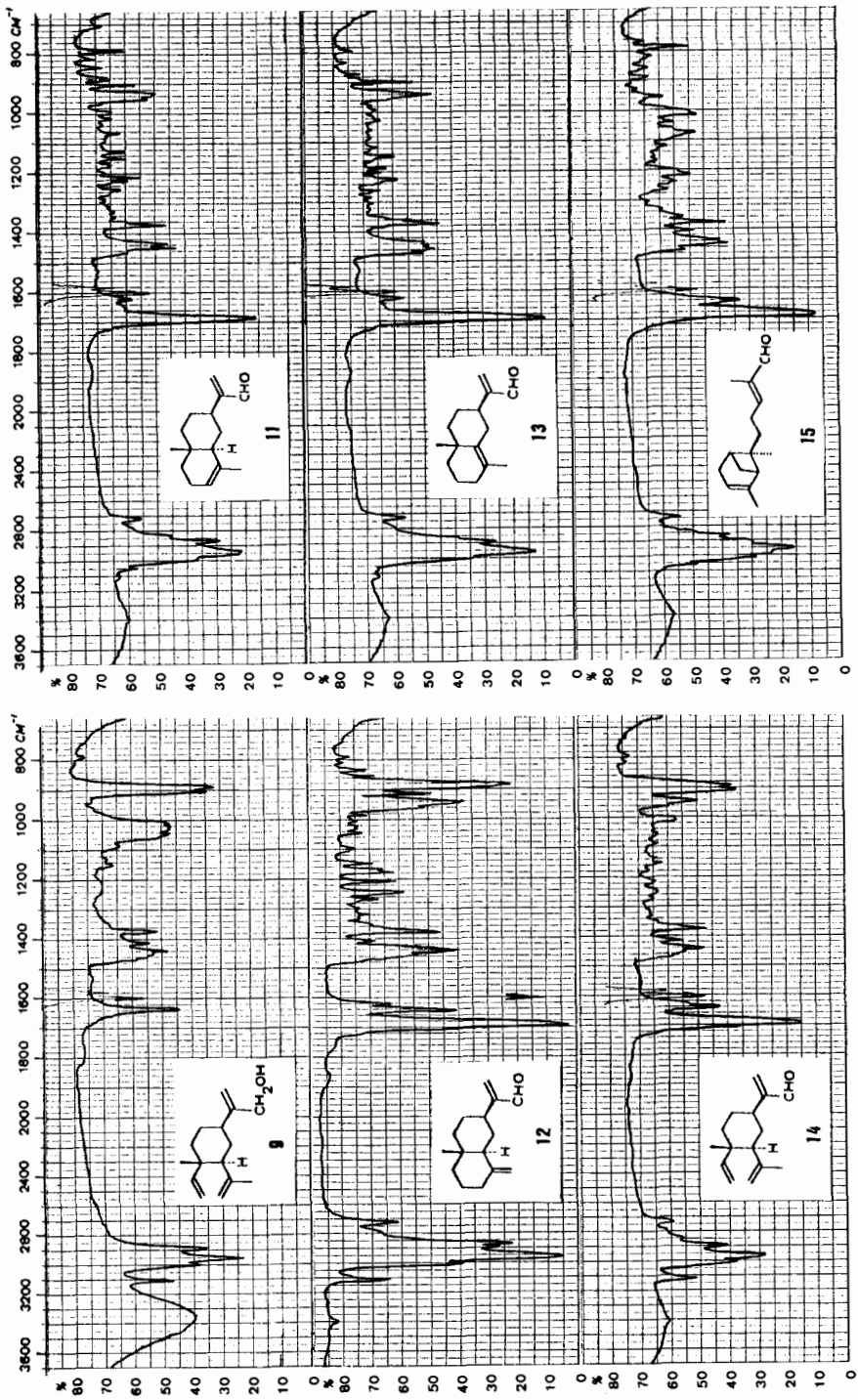


Fig. 2. *IR. spectra (neat) of compounds* **9**, **11**, **12**, **13**, **14**, *and* **15**

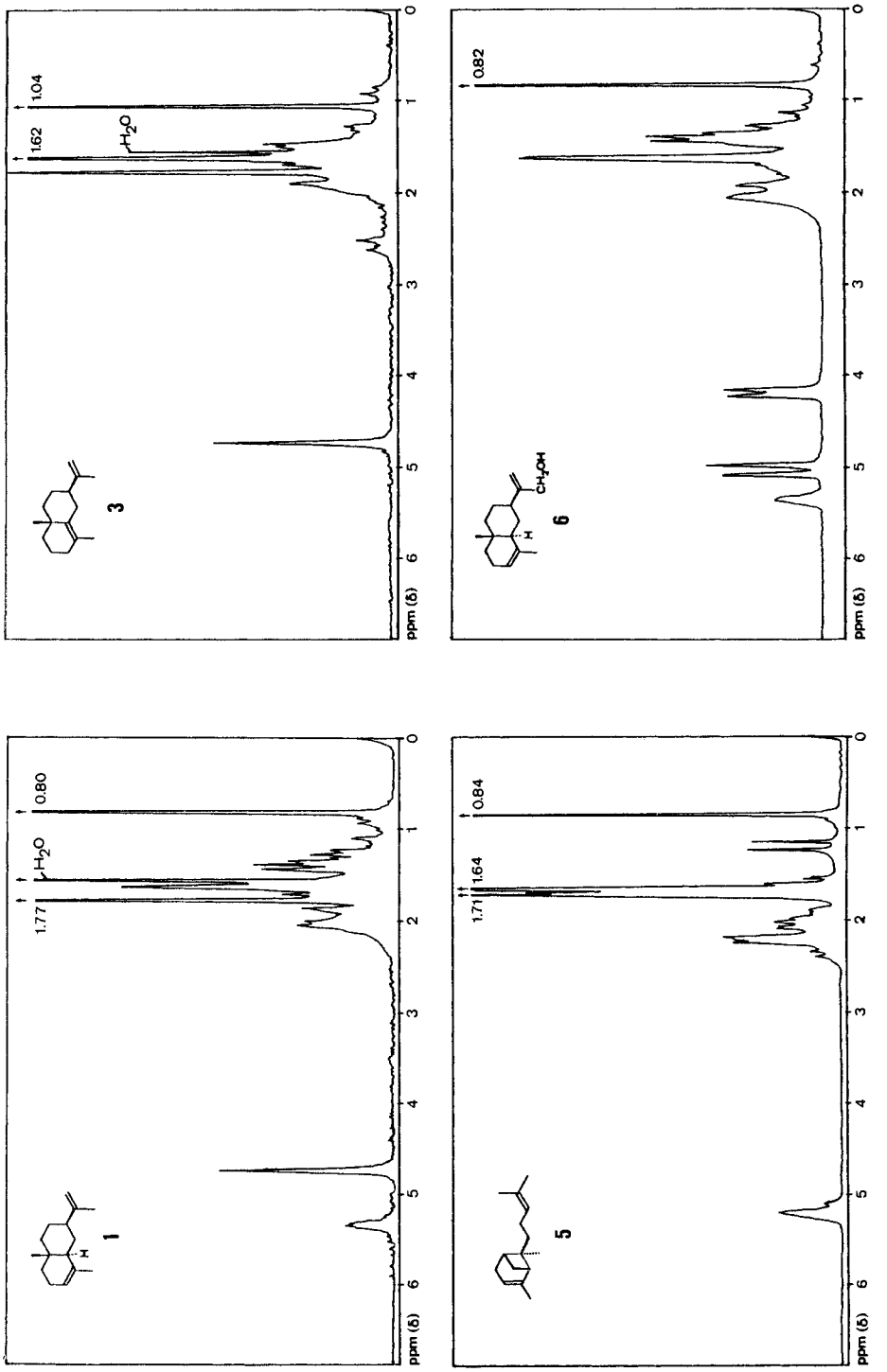


Fig. 3. *NMR. spectra (90 MHz, $CDCl_3$) of compounds* **1**, **3**, **5**, *and* **6**

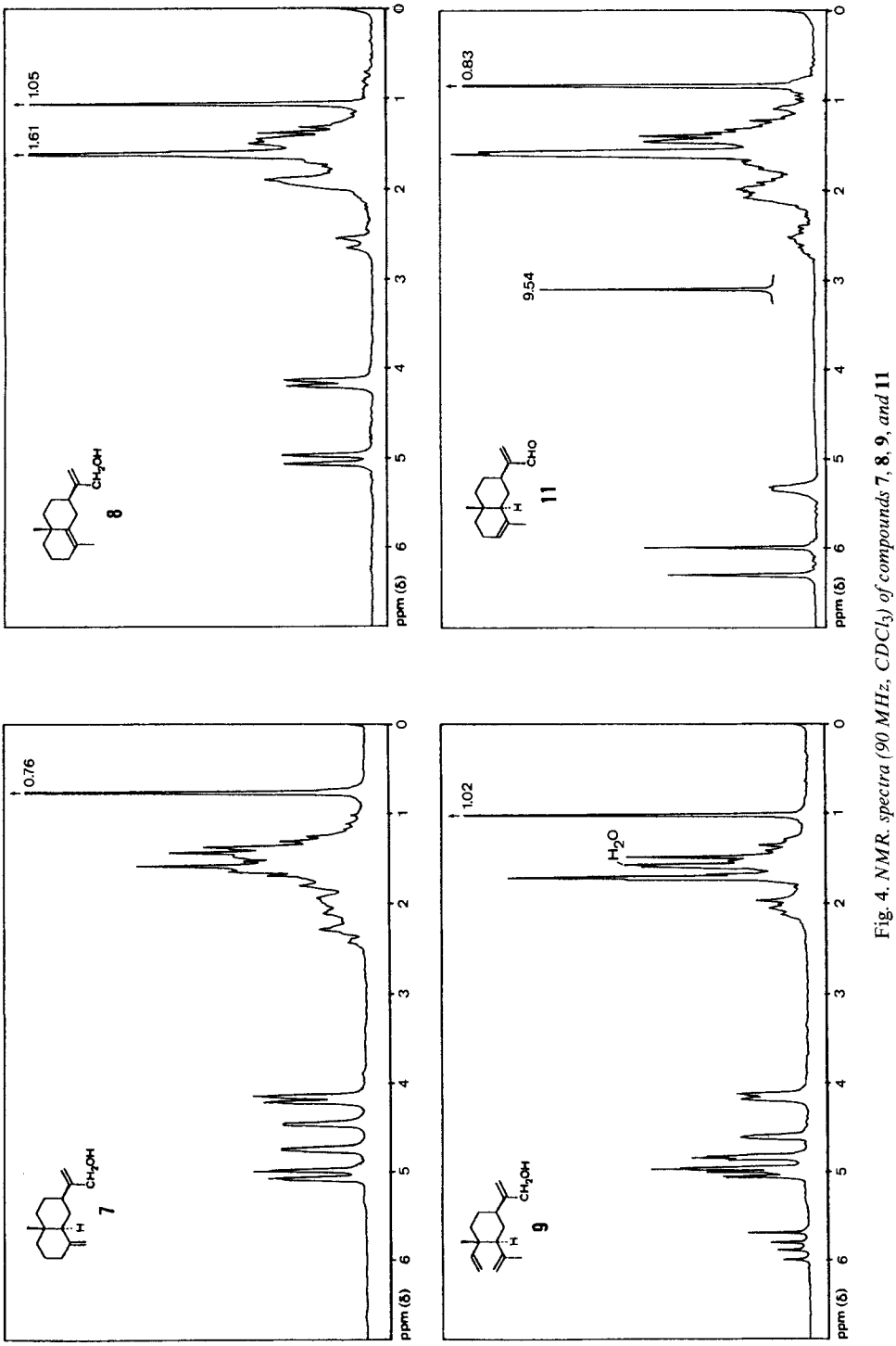


Fig. 4. *NMR. spectra (90 MHz, $CDCl_3$) of compounds* **7**, **8**, **9**, *and* **11**

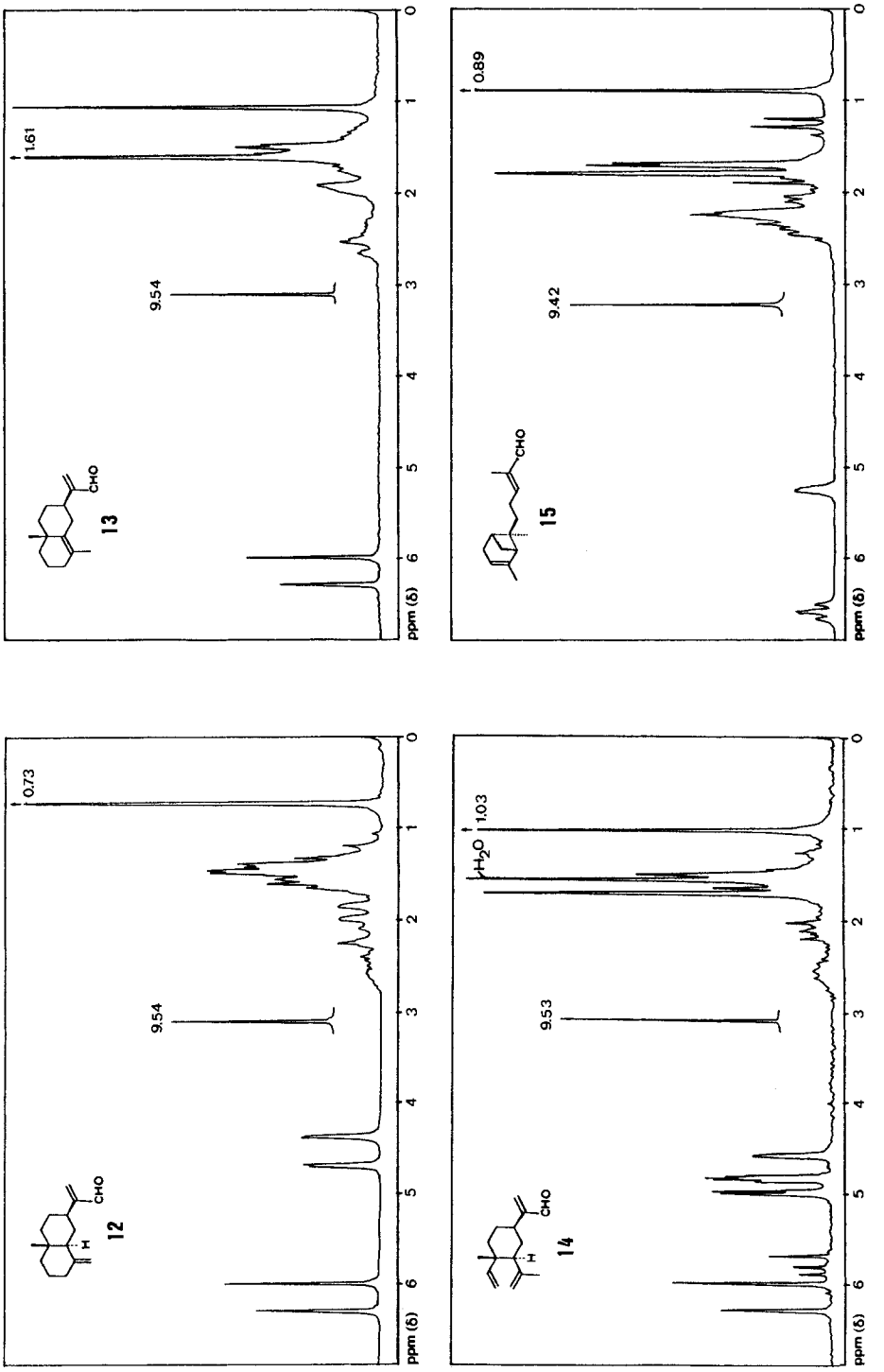
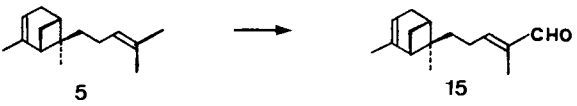


Fig. 5. *NMR. spectra (90 MHz, $CDCl_3$) of compounds* **12**, **13**, **14**, *and* **15**

α-, β-, and γ-Costal (**11**, **12**, *and* **13**)[3]) *and elema-1,3,11(13)-trien-12-al* (**14**). The structures of these aldehydes followed from their spectral data and their syntheses from the corresponding alcohols **6**, **7**, **8**, and **9** by oxidation with manganese dioxide. (−)-β-Costal (**12**) has been synthesized previously from (−)-β-costol (**7**) [11] and from (−)-β-selinene (**2**) [17]. Up to now, the only natural occurrence of the sesquiterpene aldehydes **11**, **12**, and **14** has been reported by Japanese workers who isolated an 'unseparable' mixture of α- and β-costal (**11** and **12**) as well as (−)-elema-1,3,11(13)-trien-12-al (elemenal, **14**) from *Thujopsis dolabrata* [4].

(E)-trans-*Bergamota-2,12-dien-14-al* (**15**)[5]). The structure of this followed from its synthesis from (−)-α-*trans*-bergamotene (**5**) by oxidation with selenium dioxide (*Scheme 2*). Although **15** has been obtained previously[10]) by virtually the same method, its natural occurrence has not so far been reported.

Scheme 2



5 **15**

The NMR. spectrum of **15** shows a broad triplet at $\delta = 6.58$ ppm which is the typical position for the signal of the β-proton in the *cis*-position to the carbonyl group of α,β-unsaturated carbonyl compounds (*cf.* [23]). The (*E*)-configuration of the non-cyclic double bond is further supported by the fact that oxidations of similar olefins with selenium dioxide give the (*E*)-α,β-unsaturated aldehydes exclusively (*cf.* [24]).

Experimental Part

The spectra and the GC. were performed on the instruments already mentioned [25]. NMR. spectra were measured in $CDCl_3$ with tetramethylsilane as internal standard ($\delta = 0.00$ ppm); abbreviations: *s* = singlet, *d* = doublet, *t* = triplet, *m* = multiplet, br. = broad, *J* = spin-spin coupling constant (Hz), $w_{1/2}$ = half-width (Hz). For the mass spectra, an inlet temperature of *ca.* 150° and electrons of *ca.* 70 eV energy were used; the intensity of the molecular ion (*M*) and of the 12 most intense fragment ions are given in % of the most abundant peak. - Specific rotations $[\alpha]_D$ were measured using 1.0% solutions (*w/v*) in $CHCl_3$, unless otherwise stated. The melting points were determined in open capillary tubes in an oil bath and are not corrected. - Column chromatography was performed on silica gel *Merck* (0.05–0.2 mm) or silica gel/$AgNO_3$ (prepared by mixing 500 g of silica gel *Merck* (0.05–0.2 mm) with a solution of 50 g of $AgNO_3$ in 700 ml of distilled water and subsequent drying of the slurry for 48 h at 150°).

1. Preliminary Separation of Costus Root Oil. - 1.1. *Hydrocarbons and alcohols.* In order to remove sesquiterpenoid lactones and carboxylic acids (together *ca.* 50% of the oil) commercial costus root oil (*P. Chauvet*, France) (100 g) was heated to reflux for 3 h in ethanolic-aqueous NaOH (400 ml of 5% aqueous NaOH and 300 ml of ethanol). The ethanol was removed by distillation, and the residue diluted with water (400 ml) and extracted with ether (3 × 400 ml). The combined extracts were washed to neutrality (brine), dried (Na_2SO_4) and evaporated (60°/10 Torr). GC. analysis (Carbowax and silicone) of the residue (48.6 g) showed that it contained the same constituents as the original oil[11]), except for the absence of acids and lactones, both of which could be isolated by extraction of the acidified aqueous

[10]) The reaction of (−)-α-*trans*-bergamotene (**5**) with various oxidizing reagents has been studied by Dr. *K. H. Schulte-Elte* (to be published). We thank Dr. *K. H. Schulte-Elte* for a sample of (−)-α-*trans*-bergamotene.

[11]) This result means that apart from the lactones the oil does not contain appreciable amounts of saponifiable constituents.

phase with ether[2]). Chromatography of the neutral residue (47.5 g) on silica gel (1 kg) with petroleum ether (b.p. 50–70°) → CH_2Cl_2 gave: *A*) 22.0 g (eluted with *ca.* 10 l of petroleum ether), mainly hydrocarbons; *B*) 6.5 g (petroleum ether/CH_2Cl_2 99:1 → 1:1), complex mixture of constituents of medium polarity (mainly carbonyl compounds); *C*) 17.9 g (*ca.* 4 l of CH_2Cl_2), polar constituents, mainly alcohols.

Distillation of *fraction A* (10 g) through a 'Mikro-Spaltrohr-System' (*Fischer*) allowed the separation of the sesquiterpene hydrocarbon fraction (3.1 g, b.p. 35–40°/0.001 Torr) from the higher boiling aplotaxene[12]) fraction (6.4 g, b.p. 52°/0.001 Torr). Chromatography of the lower boiling fraction (1.3 g) on silica gel/$AgNO_3$ (100 g) gave: A_1) 290 mg (eluted with 700 ml of petroleum ether/ether 9:1) containing *α-trans*-bergamotene (**5**), selina-4,11-diene (**3**), *α*-selinene (**1**), and *ar*-curcumene (**16**); A_2) 160 mg (100 ml of petroleum ether/ether 8:2) containing *β*-selinene (**2**) and caryophyllene oxide (**18**); A_3) 210 mg (400 ml of petroleum ether/ether 1:1) containing *β*-selinene (**2**) and caryophyllene (**17**); A_4) 250 mg (500 ml of ether) of *β*-elemene (**4**); A_5) 290 mg (200 ml of ether/methanol 9:1) of aplotaxene[12]).

Fraction B was not further investigated, because its main constituents (carbonyl compounds) were more conveniently isolated by extraction of the total oil with *Girard* reagent P (see below).

Chromatography of *fraction C* (2.0 g) on silica gel/$AgNO_3$ (200 g) gave: C_1) 200 mg (eluted with 200 ml petroleum ether/ether 6:4), complex mixture of compounds of medium polarity, not further examined; C_2) 280 mg (200 ml of petroleum ether/ether 1:1) containing mainly *γ*-costol (**8**); C_3) 200 mg (150 ml of petroleum ether/ether 4:6) containing *ca.* 70% of *α*-costol (**6**) and some *γ*-costol (**8**); C_4) 250 mg (250 ml of petroleum ether/ether 4:6) mixture of *α*-, *β*-, and *γ*-costol; C_5) 250 mg (400 ml of petroleum ether/ether 3:7) of *β*-costol (**7**); C_6) 200 mg (300 ml of ether) consisting of *β*-costol (**7**) and elemol (**19**); C_7) 180 mg (500 ml of ether) of elema-1,3,11(13)-trien-12-ol (**9**).

1.2. *Carbonyl compounds.* A mixture of costus root oil (100 g), ethanol (150 ml), acetic acid (15 ml) and *Girard* reagent P (30 g) (pyridinium acetohydrazide chloride) was heated to reflux for 90 min under argon. After 120 ml of ethanol had been distilled at ordinary pressure, the residue was poured into ice-water (400 g) containing 3 g of NaOH. The aqueous phase was washed with ether (4 × 300 ml)[13]), acidified with conc. HCl (100 ml), and, after 2 h at 20°, extracted with ether (4 × 200 ml). The ether extract was washed ($NaHCO_3$ solution), dried (Na_2SO_4), and the solvent distilled at 40°/10 Torr. The residue (10.2 g) contained a considerable amount of non-carbonyl compounds (due to the emulsion) by GC. and was therefore extracted a second time with *Girard* reagent P (6.0 g) by the same procedure. The carbonyl compounds (2.46 g) were obtained as an oil. Chromatography of this (1.45 g) on silica gel (150 g) afforded: *D*) 410 mg (eluted with *ca.* 800 ml of petroleum ether/CH_2Cl_2 1:1), mixture of sesquiterpene aldehydes **11**, **12**, **13**, and **14**; *E*) 140 mg (500 ml of petroleum ether/CH_2Cl_2 1:1), mainly (*E*)-*trans*-bergamota-2,12-dien-14-al (**15**); *F*) 120 mg (*ca.* 200 ml petroleum ether/CH_2Cl_2 1:1), a complex mixture containing dihydro-*α*-ionone, (*E*)-geranylacetone and (*E*)-9-isopropyl-6-methyl-5,6-decadien-2-one [27] as main constituents; *G*) 620 mg (1.2 l of CH_2Cl_2), mainly *α*-ionone[14]); *H*) 160 mg (800 ml of CH_2Cl_2), mainly *β*-ionone[14]).

Chromatography of *fraction D* (235 mg) on silica gel/$AgNO_3$ (60 g) gave: D_1) 105 mg (eluted with 80 ml of petroleum ether/ether 1:1) of *α*-costal (**11**) (40%) and *γ*-costal (**13**) (50%); D_2) 40 mg (500 ml of the same solvent mixture), *ca.* 70% *β*-costal (**12**); D_3) 50 mg (500 ml of the same solvent mixture), *ca.* 90% elema-1,3,11(13)-trien-12-al (**14**).

2. Isolation, Identification and Physical Properties of Individual Constituents. – *Fraction* A_1 was separated by prep. GC. (Carbowax, 130°) into four components (in order of elution):

2.1. (−)-*α*-trans-*Bergamotene* (**5**) (17% of the fraction), $[\alpha]_D^{20} = -42.0°$, identical with an authentic sample. – IR., Figure 1: identical with published spectrum [8] [14] [15]. – NMR., Figure 3: 0.84 (*s*, 3 H; CH_3–C(6)), 1.18 (*d*, *J* = 8.5, 1 H; H–C(7) *syn* to C(2)), 1.56–1.78 (*m*, 11 H; with peaks at 1.64 and 1.71), 1.8–2.5 (*m*, 7 H), 5.04–5.31 (*m*, 2 H; H–C(3) and H–C(12)); practically identical with published spectrum [14]. – MS.: practically identical with published spectrum [7] [15].

2.2. (+)-*Selina-4,11-diene* (**3**) (17%), $[\alpha]_D^{20} = +54.5°$ ([6]: +56.3° ($CHCl_3$, 1.95%)). – IR., Figure 1. – NMR., Figure 3: 1.04 (*s*, 3 H; CH_3–C(10)), 1.62 (*s*, 3 H; CH_3–C(4)), 1.77 (br. *s*, 3 H; CH_3–C(11)),

[12]) Aplotaxene = (8*Z*,11*Z*,14*Z*)-1,8,11,14-heptadecatetraene is a major constituent [26].

[13]) Apart from the ether and aqueous layer, a stable emulsion was formed during the washing. This third layer was treated together with the aqueous phase.

[14]) *α*- and *β*-ionone are known constituents of this oil [28].

ca. 1.22–2.22 (*m*, total 18 H), 2.57 (br. *d*, *J* = *ca.* 9, 1 H; $H_{eq.}$–C(6)), 4.73 (br. *s*, 2 H; CH_2=C(11)); *cf.* [6]. – MS.: 204 (*M*, 42), 189 (100), 133 (66), 105 (50), 41 (50), 91 (49), 93 (41), 81 (40), 107 (34), 79 (34), 147 (32), 119 (32), 55 (32).

2.3. (–)-*α-Selinene* (**1**) (10%), $[\alpha]_D^{20} = -14.5°$ (see text). – IR., Figure 1: identical with published spectrum [8]. – NMR., Figure 3: 0.80 (*s*, 3 H; CH_3–C(10)), 1.62 (br. *s*, 3 H; CH_3–C(4)), 1.77 (br. *s*, 3 H; CH_3–C(11)), *ca.* 1.06–2.33 (*m*, total 18 H), 4.73 (br. *s*, 2 H; CH_2=C(11)), 5.33 (*m*, 1 H; H–C(3)); *cf.* [6]. – MS.: 204 (*M*, 50), 189 (100), 93 (87), 107 (79), 41 (75), 81 (72), 133 (67), 105 (66), 91 (66), 79 (59), 55 (53), 161 (44), 95 (42); these values differ considerably from published data [7].

2.4. (–)-ar-*Curcumene* (**16**) (55%), $[\alpha]_D^{20} = -39.4°$ ([18]: $-45.1°$ ($CHCl_3$, 0.75%), [29]: $-40°$ ($CHCl_3$, 3.3%))[15]. – IR.: identical with published spectrum [8] [18]. – NMR. (90 MHz): 1.22 (*d*, *J* = 7, 3 H; >CH–CH_3), 1.54 and 1.69 (2× br. *s*, 6 H; >C=C(CH_3)$_2$), *ca.* 1.4–2.1 (*m*, total 10 H), 2.33 (*s*, 3 H; ar-CH_3), 2.68 (*q*, *J* = 7, 1 H; CH–CH_3), 5.11 (br. *t*, *J* = *ca.* 6, 1 H; >C=CH–), 7.11 (*s*, 4 H; ar. H); *cf.* [18]. – MS.: 202 (*M*, 29), 119 (100), 132 (78), 105 (51), 41 (42), 131 (26), 91 (26), 145 (25), 120 (25), 55 (23), 117 (17), 133 (15), 69 (14).

Fraction A_2 was separated by prep. GC. (Carbowax, 170°) into:

2.5. (+)-*β-Selinene* (**2**) (shorter retention time, 65% of the fraction), $[\alpha]_D^{20} = +54.6°$ ([6]: +43° ($CHCl_3$, 0.95%), [11]: +59.5° ($CHCl_3$, 2.05%)). – IR.: identical with published spectrum [8] [11]. – NMR. (90 MHz): 0.73 (*s*, 3 H; CH_3–C(10)), 1.77 (br. *s*, 3 H; CH_3–C(11)), 1.1–2.5 (*m*, total 17 H), 4.46 (br. *s*, 1 H; H–C(14)), 4.73 (br. *s*, 3 H; H–C(14) and CH_2=C(11)); identical with published spectrum [6] [11]. – MS.: 204 (*M*, 52), 93 (100), 41 (98), 107 (91), 105 (90), 79 (83), 81 (77), 67 (67), 121 (66), 91 (65), 55 (57), 161 (51), 108 (49); these data differ considerably from published spectra [7] [10].

2.6. (–)-*Caryophyllene oxide* (**18**) (35%), $[\alpha]_D^{20} = -71.6°$, m.p. 61–63° ([18]: $[\alpha]_D^{20} = -74.2°$ ($CHCl_3$, 4.2%), m.p. 62–63°). – IR.: identical with authentic sample; *cf.* [18]. – NMR. (90 MHz): 0.98 and 1.00 (2× *s*, 6 H; >C(CH_3)$_2$), 1.20 (*s*, 3 H; C(O)–C–CH_3), *ca.* 1.2–2.7 (*m*, 12 H), 2.89 (*d*× *d*, *J* = 11, 4, 1 H; C(O)–C–H), 4.88 and 4.99 (2× br. *s*, 2 H; >C=CH_2); *cf.* [18]. – MS.: 220 (*M*, < 1), 41 (100), 43 (90), 79 (78), 93 (68), 69 (61), 91 (51), 55 (49), 95 (45), 67 (42), 39 (41), 81 (40), 107 (38).

By prep. GC. (Carbowax, 130°) *fraction* A_3 gave:

2.7. (–)-*Caryophyllene* (**17**) (shorter retention time, *ca.* 60% of the fraction), $[\alpha]_D^{20} = -14.8°$ ([18]: $-14.02°$ ($CHCl_3$, 4.7%)). – IR.: identical with authentic sample and published spectrum [8]. – NMR. (90 MHz): 0.98 and 1.00 (2× *s*, 6 H; >C(CH_3)$_2$, 1.62 (br. *s*, 3 H; HC=C(\)–CH_3), *ca.* 1.4–2.67 (*m*, total 15 H), 4.86 and 4.96 (2× *m*, 2 H; >C=CH_2), 5.33 (*m*, $w_{1/2} = 18$, 1 H; >C=CH–). – MS.: 204 (*M*, 4), 41 (100), 93 (87), 69 (83), 133 (64), 91 (62), 79 (62), 105 (43), 55 (38), 107 (37), 81 (36), 39 (35), 67 (34); these values differ considerably from published data [7] [10].

The main component of *fraction* A_4 was purified by prep. GC. (Carbowax, 150°):

2.8. (–)-*β-Elemene* (**4**), $[\alpha]_D^{20} = -14.5°$ ([12]: $-16.4°$), identical with an authentic sample. – IR.: [8] [13]. – NMR.: identical with published spectrum [6]. – MS.: 204 (*M*, 1), 81 (100), 93 (91), 68 (76), 41 (72), 67 (58), 107 (56), 79 (51), 55 (45), 53 (42), 121 (41), 91 (36), 147 (34); these values differ considerably from published data [7].

The main constituent of *fraction* C_2 was purified by prep. GC. (Carbowax, 230°):

2.9. (+)-*γ-Costol* (**8**), $[\alpha]_D^{20} = +37.0°$. – IR., Figure 1. – NMR., Figure 4: 1.05 (*s*, 3 H; CH_3–C(10)), 1.61 (br. *s*, 3 H; CH_3–C(4)), *ca.* 1.1–2.1 (*m*, total 16 H), 2.60 (br. *d*, *J* = *ca.* 10, 1 H; $H_{eq.}$–C(6)), 4.17 (br. *d*, *J* = *ca.* 6, 2 H; $-CH_2OH$), 4.97 and 5.07 (2× br. *s*, 2 H; CH_2=C(11)). – MS.: 220 (*M*, 45), 187 (100), 91 (83), 41 (71), 105 (64), 93 (59), 79 (59), 81 (56), 107 (50), 55 (49), 145 (46), 131 (46), 147 (44).

Fraction C_3 was separated by prep. GC. (Carbowax, 230°) into γ-costol (**8**) (*ca.* 20% of the fraction, shorter retention time) and:

2.10. (–)-*α-Costol* (**6**) (*ca.* 70% of the fraction), $[\alpha]_D^{20} = -12.4°$. – IR., Figure 1. – NMR., Figure 3: 0.82 (*s*, 3 H; CH_3–C(10)), 1.62 (br. *s*, 3 H; CH_3–C(4)), *ca.* 1.0–2.3 (*m*, total 16 H), 4.19 (br. *d*, *J* = *ca.* 6, 2 H; $-CH_2OH$), 4.98 and 5.09 (2× br. *s*, 2 H; CH_2=C(11)), 5.35 (*m*, 1 H; H–C(3)). – MS.: 220 (*M*, 35), 91 (100), 105 (97), 41 (92), 79 (85), 187 (80), 93 (78), 81 (76), 55 (69), 107 (68), 147 (60), 119 (53), 95 (51).

Fraction C_5 was purified by prep. GC. (Carbowax, 230°):

[15]) Both references referred to dextrorotary **16**.

2.11. (+)-*β-Costol* (**7**) (same retention time as *α*-costol), $[\alpha]_D^{20} = +31.5°$ ([16]: $+32.8°$ ($CHCl_3$, 4.3%)). – IR., Figure 1: identical with reported spectrum [11]. – NMR., Figure 4: 0.76 (*s*, 3 H; CH_3–C(10)), *ca.* 1.0–2.5 (*m*, total 15 H), 4.18 (br. *d*, *J* = *ca.* 6, 2 H; $-CH_2OH$), 4.46 and 4.75 (2×*m*, 2 H; CH_2=C(4)), 4.99 and 5.09 (2×*m*, 2 H; CH_2=C(11)); identical with reported spectrum [11]. – MS.: 220 (*M*, 22), 41 (100), 79 (90), 93 (86), 91 (82), 105 (81), 81 (75), 121 (71), 67 (67), 55 (67), 107 (56), 95 (54), 77 (49); these values differ considerably from literature data [2].

Prep. GC. of *fraction* C_6 (Carbowax, 230°) gave:

2.12. (–)-*Elemol* (**19**) (much shorter retention time than *β*-costol also present in this fraction): $[\alpha]_D^{20} = -4.0°$, m.p. 48–50° ([16]: $[\alpha]_D^{20} = -4.13°$ ($CHCl_3$, 2.8%), m.p. 51–52°); identical with an authentic sample.

Purification of *fraction* C_7 by prep. GC. (Carbowax, 230°) gave:

2.13. (–)-*Elema-1,3,11(13)-trien-12-ol* (**9**), $[\alpha]_D^{20} = -30.9°$; identical with a synthetic sample. – IR., Figure 2. – NMR., Figure 4: 1.02 (*s*, 3 H; CH_3–C(10)), 1.71 (br. *s*, 3 H; CH_3–C(4)), *ca.* 1.22–1.87 (*m*, total 10 H), 1.87–2.22 (*m*, 2 H; H–C(5) and H–C(7)), 4.16 (br. *d*, *J* = *ca.* 5, 2 H; $-CH_2OH$), 4.61 (*br. s*, 1 H; H–C(3)), 4.78–5.11 (*m*, 5 H; CH_2=C(1), CH_2=C(11), and H–C(3)), 5.84 (*d*×*d*, *J* = 18, 10, 1 H; H–C(1)). – MS.: 220 (*M*, 1), 41 (100), 81 (94), 79 (86), 93 (79), 91 (74), 55 (69), 67 (68), 105 (58), 53 (58), 68 (53), 119 (50), 77 (48).

By prep. GC. (Carbowax 200°), *fraction* D_1 gave (in order of elution):

2.14. (+)-*γ-Costal* (**13**), $[\alpha]_D^{20} = +71.5°$, identical with a sample synthesized from *γ*-costol (**8**). – IR., Figure 2. – NMR., Figure 5: 1.06 (*s*, 3 H; CH_3–C(10)), 1.61 (*s*, 3 H; CH_3–C(4)), *ca.* 1.2–2.1 (*m*, total 14 H), 2.2–2.7 (*m*, 2 H; $H_{eq.}$–C(6) and H–C(7)), 6.00 and 6.29 (2×*s*, 2 H; CH_2=C(11)), 9.54 (*s*, 1 H; –CHO). – MS.: 218 (*M*, 38), 91 (100), 41 (97), 43 (76), 93 (72), 79 (68), 105 (63), 55 (61), 203 (59), 77 (54), 39 (52), 29 (52), 107 (49).

2.15. (–)-*α-Costal* (**11**), $[\alpha]_D^{20} = -7.2°$, identical with a sample synthesized from *α*-costol (**6**). – IR., Figure 2. – NMR., Figure 4: 0.83 (*s*, 3 H; CH_3–C(10)), 1.58 (*m*, 3 H; CH_3–C(4)), *ca.* 1.1–2.2 (*m*, total 14 H), *ca.* 2.4–2.78 (*m*, 1 H; H–C(7)), 5.33 (*m*, 1 H; H–C(3)), 6.00 and 6.30 (2×*s*, 2 H; CH_2=C(11)), 9.54 (*s*, 1 H; –CHO). – MS.: 218 (*M*, 57), 41 (100), 91 (93), 203 (79), 79 (71), 93 (69), 107 (67), 105 (67), 81 (63), 55 (59), 43 (57), 77 (55), 185 (53).

The main constituent of *fraction* D_2 was isolated by prep. GC. (Carbowax, 200°):

2.16. (+)-*β-Costal* (**12**), $[\alpha]_D^{20} = +29.5°$ ([17]: $+40.6°$ ($CHCl_3$)); identical with a sample prepared from *β*-costol (**7**). – IR., Figure 2: identical with reported spectrum [17]. – NMR., Figure 5: 0.73 (*s*, 3 H; CH_3–C(10)), 1.13–2.78 (*m*, 14 H), 4.38 and 4.70 (2×*m*, 2 H; CH_2=C(4)), 6.00 and 6.30 (2×*s*, 2 H; CH_2=C(11)), 9.54 (*s*, 1 H; –CHO); identical with reported spectrum [17]. – MS.: 218 (*M*, 37), 121 (100), 41 (84), 93 (80), 79 (79), 91 (75), 105 (59), 81 (59), 67 (58), 95 (56), 107 (55), 55 (51), 77 (45).

Fraction D_3 was purified by prep. GC. (Carbowax, 200°):

2.17. (–)-*Elema-1,3,11(13)-trien-12-al* (**14**), $[\alpha]_D^{20} = -33.5°$ ([4]: $[\alpha]_{600} = -11°$ ($CHCl_3$)), identical with a sample ($[\alpha]_D^{20} = -36.6°$) prepared from (–)-*β*-elemene (**4**). – IR., Figure 2. – NMR., Figure 5: 1.03 (*s*, 3 H; CH_3–C(10)), 1.71 (br. *s*, 3 H; CH_3–C(4)), *ca.* 1.2–2.0 (*m*, total 9 H), 2.00–2.22 (*m*, 1 H; H–C(5)), *ca.* 2.38–2.78 (*m*, 1 H; H–C(7)), 4.59 (br. *s*, 1 H; H–C(3)), 4.78–5.06 (2×*m*, 3 H; H–C(3) and CH_2=C(1)), 5.86 (*d*×*d*, *J* = 18, 10, 1 H, partly covered; H–C(1)), 6.00 and 6.31 (2×*s*, 2 H; CH_2=C(11)), 9.53 (*s*, 1 H; –CHO); *cf.* reported spectrum [4]. – MS.: 218 (*M*, 1), 81 (100), 41 (53), 79 (47), 67 (46), 93 (43), 91 (38), 95 (36), 68 (36), 107 (32), 55 (32), 53 (31), 105 (27).

Purification of *fraction E* by prep. GC. (Carbowax 200°) gave:

2.18 (–)-(E)-trans-*Bergamota-2,12-dien-14-al* (**15**) as a homogeneous oil, $[\alpha]_D^{20} = -44.9°$, identical with a sample synthesized from (–)-*α-trans*-bergamotene (**5**). – IR., Figure 2. – NMR., Figure 5: 0.89 (*s*, 3 H; CH_3–C(6)), 1.23 (*d*, *J* = 8.5, 1 H; H–C(7) *syn* to C(2)), 1.69 (*m*, 3 H; CH_3–C(2)), 1.79 (br. *s*, 3 H; CH_3–C(13)), 1.5–2.5 (*m*, total 15 H), 5.26 (*m*, 1 H; H–C(3)), 6.58 (br. *t*, *J* = *ca.* 7, 1 H; H–C(12)), 9.42 (*s*, 1 H; –CHO). – MS.: 218 (*M*, 1), 93 (100), 119 (71), 91 (40), 55 (38), 79 (33), 41 (31), 77 (30), 107 (27), 121 (26), 105 (23), 135 (19), 134 (17).

3. Synthesis of Some Constituents. – 3.1. *Elemanes* **9** *and* **14** *from* (–)-*β-elemene* (**4**). A solution of 660 mg (3.0 mmol) of (–)-*β*-elemene 11,12-epoxide (**20**) (obtained by epoxidation of (–)-*β*-elemene with peracetic acid [22]) in 5 ml of dry ether was added dropwise at 20° and under argon to a stirred solution of 18 mmol of lithium diethylamide in 12 ml of dry ether. After 30 h at 20°, the mixture was hydrolyzed and the product extracted with pentane. Chromatography of the product (650 mg) through

silica gel/$AgNO_3$ (100 g) with petroleum ether/ether 8:2 gave two compounds: *alcohol* **I**[16]) (eluted first, *ca.* 20% of the mixture), $[\alpha]_D^{20} = -27.0°$, IR. and mass spectrum practically identical with those of alcohol **9**. – NMR. (90 MHz): 1.02 (*s*, 3 H; CH_3–C(10)), 1.76 (br. *s*, 3 H; CH_3–C(4)), *ca.* 1.27–2.44 (*m*, total 12 H), 4.03 (br. *d*, *J* = *ca.* 6, 2 H; $-CH_2OH$), 4.74, 4.87, 5.01, and 5.18 (4 × *m*, total 6 H; CH_2=C(1), CH_2=C(4), and CH_2=C(11)), 5.81 (*d* × *d*, *J* = 18, 10, 1 H; H–C(1)). (–)-*Elema-1,3,11(13)-trien-12-ol* (**9**), *ca.* 70% of the mixture), colourless oil, $[\alpha]_D^{20} = -29.2°$; identical with the natural compound.

(–)-*Elema-1,3,11(13)-trien-12-al* (**14**). A solution of synthetic alcohol **9** (2.0 g) in petroleum ether (10 ml) was stirred with MnO_2 (20 g, *Merck*, activated at 110°) for 6 h at 20°. After filtration and evaporation of the solvent the product was purified through a column of silica gel (40 g) with petroleum ether/CH_2Cl_2 8:2. 1.35 g (67%) of pure aldehyde **14** were obtained as an oil, $[\alpha]_D^{20} = -36.6°$, identical with the natural compound.

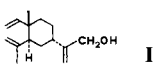
3.2. *Costals* **11**, **12**, *and* **13** *from the corresponding costols.* The three natural costols **6**, **7**, and **8** were oxidized separately with MnO_2 in petroleum ether as described for alcohol **9** → aldehyde **14**. The costals thus obtained (all oils) were identical with the natural aldehydes **11**, **12**, and **13**.

3.3. *Oxidation of* (–)-*α*-trans-*bergamotene* (**5**) *with selenium dioxide*/tert-*butyl hydroperoxide*[17]). A solution of impure (–)-*α-trans*-bergamotene (**5**)[18]) (10.2 g), selenium dioxide (555 mg, 5 mmol), and *tert*-butyl hydroperoxide (75%, 9.0 g, 75 mmol) in CH_2Cl_2 (50 ml) was heated to reflux for 30 h. The volatiles were distilled at 60°/10 Torr and the residue (14 g) was chromatographed through a column of silica gel (100 g). Apart from some starting material (1.6 g) (eluted with petroleum ether) the following fractions were obtained: (–)-(E)-trans-*bergamota-2,12-dien-14-al* (**15**) (0.9 g, eluted with petroleum ether/ether 98:2, *ca.* 85% pure). A pure sample for analysis was obtained by GC. (Carbowax, 200°) of this fraction, colourless oil, $[\alpha]_D^{20} = -46.7°$; identical with the natural compound. (–)-(E)-trans-*Bergamota-2,12-dien-14-ol* (**10**) (2.2 g, eluted with petroleum ether/ether 98:2, *ca.* 90%). This fraction (1.0 g) was purified by chromatography on silica gel/$AgNO_3$ (70 g) with petroleum ether/ether 8:2. A homogeneous oil with $[\alpha]_D^{20} = -46.1°$ was obtained. – IR. (neat): 3360*s* (br.), 3060*w*, 3020 sh., 1650*w* (br.), 1450*m*, 1375*m*, 1015*s*, 785*m* cm^{-1}. – NMR. (90 MHz): 0.84 (*s*, 3 H; CH_3–C(6)), 1.18 (*d*, *J* = 8.5, 1 H; H–C(7) *syn* to C(2)), 1.24 (br. *t*, *J* = *ca.* 5, 1 H; OH), 1.6–1.78 (*m*, 8 H), *ca.* 1.8–2.44 (*m*, 7 H), 4.03 (br. *d*, *J* = *ca.* 5, 2 H; $-CH_2OH$), 5.23 (*m*, 1 H; H–C(3)), 5.49 (br. *t*, *J* = *ca.* 7, 1 H; H–C(12)). – MS.: 220 (*M*, < 1), 93 (100), 119 (53), 41 (49), 43 (40), 55 (38), 91 (37), 79 (36), 107 (29), 77 (29), 29 (24), 105 (22), 92 (22)[19]).

REFERENCES

[1] *F. W. Semmler & J. Feldstein,* Ber. deutsch. chem. Ges. *47,* 2433, 2687 (1914).
[2] *E. Klein & F. Thömel,* Tetrahedron *32,* 163 (1976).
[3] *J. C. Mitchell,* Arch. Dermatol. *109,* 572 (1974); *Y. Asakawa, G. Ourisson & T. Aratani,* Tetrahedron Letters *1975,* 3957.
[4] *S. Itô, K. Endo, H. Honma & K. Ota,* Tetrahedron Letters *1965,* 3777.
[5] *T. K. Devon & A. I. Scott,* 'Handbook of Naturally Occurring Compounds', Vol. 2, p. 138, 144, Academic Press, New York and London 1972.

[16]) On the basis of the spectral data and the synthesis we tentatively assign structure **I** to this alcohol.



I

[17]) *cf. M. Fieser & L. Fieser,* Reagents for Organic Synthesis, Vol. 2, p. 362, Wiley-Interscience, New York 1969.

[18]) The starting material was obtained by fractional distillation of the terpenes of bergamot oil and consisted of *ca.* 60% of *α-trans*-bergamotene (**5**) and *ca.* 35% of caryophyllene (by GC. on a capillary column).

[19]) The fact that alcohol **10** could be converted to aldehyde **15** by oxidation with MnO_2 proves the structure of **10** (including the (*E*)-configuration of the non-cyclic double bond).

[6] *C. Ganter & B. Keller-Wojtkiewicz*, Helv. *54*, 183 (1971).
[7] *M. G. Moshonas & E. D. Lund*, The Flavour Industry *1*, 375 (1970).
[8] *J. A. Wenninger, R. L. Yates & M. Dolinsky*, J. Assoc. offic. anal. Chem. *50*, 1313 (1967).
[9] *R. S. Joshi, A. S. Bawdekar, G. H. Kulkarni, A. S. Rao, G. R. Kelkar & S. C. Bhattacharyya*, Perf. and Essent. Oil Rec. *52*, 773 (1961).
[10] *P. Schreier, F. Drawert & A. Junker*, J. agric. Food Chemistry *24*, 331 (1976).
[11] *A. S. Bawdekar & G. R. Kelkar*, Tetrahedron *21*, 1521 (1965).
[12] M. *Romanuk, V. Herout & F. Šorm*, Coll. Czechoslov. chem. Commun. *23*, 2188 (1958).
[13] *C. J. Muller & W. G. Jennings*, J. agric. Food Chemistry *15*, 762 (1967).
[14] *E. sz. Kováts*, Helv. *46*, 2705 (1963).
[15] *G. F. Russell, W. J. Murray, C. J. Muller & W. G. Jennings*, J. agric. Food Chemistry *16*, 1047 (1968).
[16] *A. S. Bawdekar, G. R. Kelkar & S. C. Bhattacharyya*, Tetrahedron *23*, 1993 (1967), and references cited therein.
[17] *E. Klein & W. Rojahn*, Parfums, Cosmét., Savons de France *2*, 66 (1972).
[18] *N. P. Damodaran & S. Dev*, Tetrahedron *24*, 4113 (1968).
[19] *G. L. Chetty, G. S. Krishna Rao, S. Dev & D. K. Banerjee*, Tetrahedron *22*, 2311 (1966), and references cited therein; *T. Okude & S. Hayashi*, Bull. chem. Soc. Japan *43*, 2984 (1970).
[20] *B. Wojtkiewicz*, Diss. Nr. 4361 ETH Zurich 1970.
[21] *N. H. Andersen, B. Shunk & C. R. Costin*, Experientia *29*, 645 (1973).
[22] *A. F. Thomas, C. Vial, M. Ozainne & G. Ohloff*, Helv. *56*, 2270 (1973).
[23] *G. Büchi & H. Wüest*, Helv. *50*, 2440 (1967).
[24] *J. J. Plattner, U. T. Bhalerao & H. Rapoport*, J. Amer. chem. Soc. *91*, 4933 (1969); *J. Meinwald, K. Opheim & T. Eisner*, Tetrahedron Letters *1973*, 281; *C. H. Miller, J. A. Katzenellenbogen & S. B. Bowlus*, ibid. *1973*, 285.
[25] *B. Maurer & A. Grieder*, Helv. *60*, 1155 (1977).
[26] *M. Romanuk, V. Herout & F. Šorm*, Coll. Czechoslov. chem. Commun. *24*, 2018 (1959).
[27] *B. Maurer & G. Ohloff*, Chem. Commun. *1977*, 353; Helv. *60*, 2191 (1977).
[28] *Y. R. Naves*, Helv. *32*, 1064 (1949).
[29] *V. K. Honwad & A. S. Rao*, Tetrahedron *21*, 2593 (1965).