intervall: 175–185°. Zur Analyse wurde eine Probe im Hochvakuum sublimiert (170°/0,01 Torr). – IR. (KBr): Banden u.a. bei 3230 s (breit, aufgesp.). 1635 s (aufgesp.), 1550 s, (aufgesp.), 700 m (aufgesp.) cm^{-1}. – ^1H-NMR. ($CDCl_3$): 1,18 (*d*, $J = 7$, 6H); 1,87 (*s*, 6H); 5,06 (*qi*, $J = 7$, 2H); 7,1–7,5 (*Sh*, 16H); 7,57 (*d*, $J = 8$, breit, 2H). – MS.: 476 (M^+). – DC. (zusammen mit dem Diastereomeren, XIb, vermessen): Rf 0,44.

$C_{32}H_{32}N_2O_2$ Ber. C 80,64 H 6,77 N 5,88% Gef. C 80,76 H 7,00 N 5,86%

Dieselbe Verbindung, 10 mg, erhielt man durch katalytische Hydrierung von 20,5 mg (–)-(*aR*)-Xa unter den für die Herstellung des Diastereomeren, (–)-XIb, beschriebenen Bedingungen. Der Vergleich der auf verschiedenen Wegen hergestellten Substanzen erfolgte durch DC. und MS.

Die Spektren und pK^*_{MCS}-Werte wurden in unserer Abteilung für Instrumentalanalyse (Leitung Prof. *W. Simon*, Prof. *J. F. M. Oth* und PD Dr. *J. Seibl*) aufgenommen. Die Mikroanalysen wurden in unserer mikroanalytischen Abteilung (Leitung *W. Manser*) ausgeführt.

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239. The Oxidation of the Double Bonds of β-Elemene

by **Alan F. Thomas, Christian Vial, Michel Ozainne** and **Günter Ohloff**

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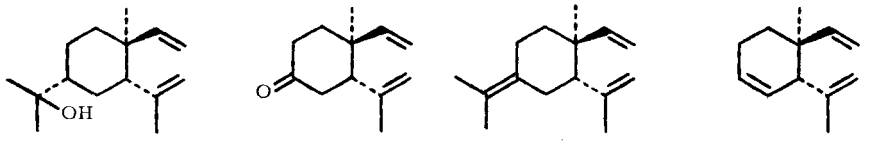
(30. VIII. 73)

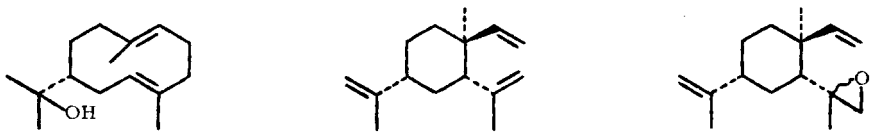
Summary. Peracid oxidation of β-elemene (**6**) occurs by attack specifically on the isolated [isopropenyl group at C(4). The structures of the epoxides thus obtained were demonstrated by [conversion to tetrahydrogeijerol **12** (R = H), which was identical with the substance obtained from geijerone (**2**) by reduction, first catalytically, then with metal hydride. Ozonolysis of β-elemene is less specific, attack occurring on the other isopropenyl group (at C(2)) in addition to the one at C(4), and subsequently on the vinyl group (at C(1)). The structures of the ozonolysis products were confirmed by a sequence of reactions from elemol.

Introduction. – The dehydration products of elemol (**1**), together with elemol itself are widely distributed in nature. (–)-Elemol was first isolated from Manila elemi oil (*Canarium luzonicum*) in 1907 [1], but the correct structure was not assigned

until 1955 [2], shortly before it was linked directly with eudesmol [3]. Synthesis of elemol (**1**) (and therefore of the elemenes) was achieved in 1969 [4]. More recently, the C_{12}-ketone, (–)-geijerone (**2**) was discovered, and synthesized from γ-elemene (**3**) [5], although geijerene (**4**) had been known for some time [6] and synthesized [7]. It has been suggested [8] that the elemene type of structure is an artefact that arises during isolation from cyclodecadiene precursors (*e.g.* hedycaryol (**5**), for elemol (**1**)), and evidence that this may not be so in the case of geijerone has also been advanced [5][1]).



1 **2** **3** **4**



5 **6** **7**

β-Elemene (**6**) presents an interesting assemblage of double bonds, and the present work was undertaken to try and determine with what specificity these react towards oxidation, particularly epoxidation and ozonolysis.

Epoxidation of (–)-β-elemene. – The reaction of peracetic acid on (–)-β-elemene (**6**), which could lead to an epoxide on either the isopropenyl group at C(2) (to **7**) or at C(4) (to **8**), occurs over 90% site-specifically, giving a mixture of the two possible epoxides on the C(4) isopropenyl group (**8a** and **8b**). The reaction was studied by oxidizing the mixture (**8a**, **8b**) directly with periodic acid to the corresponding ketones. Of the resulting mixture, 75% was a mixture of the two epimeric ketones **9a** and **9b** resulting from attack on the isopropenyl group at C(4), 6% was the alternative ketone **10** resulting from the epoxides **7**, and 10% were diketones. In order to show that the main products of the epoxidation were the epimeric mixture **8**, the principal ketone **9a** was hydrogenated over platinum oxide to the ketone **11**, and this was converted to the fully reduced cyclohexyl acetate **12** (R = $COCH_3$) by a *Bayer-Villiger* oxidation. This substance, and the corresponding alcohol **12** (R = H), were identical with those obtained by the following reaction sequence from (–)-geijerone (**2**). Hydrogenation of the latter over palladium led to specific reduction of the vinyl group (to **13**), and platinum oxide reduced the remaining double bond **14**, and metal hydride reduction of the latter compound gave a mixture of the two epimeric alcohols **12** and **15** (R = H), in which 92% proved to be the desired equatorial isomer **12** (R = H).

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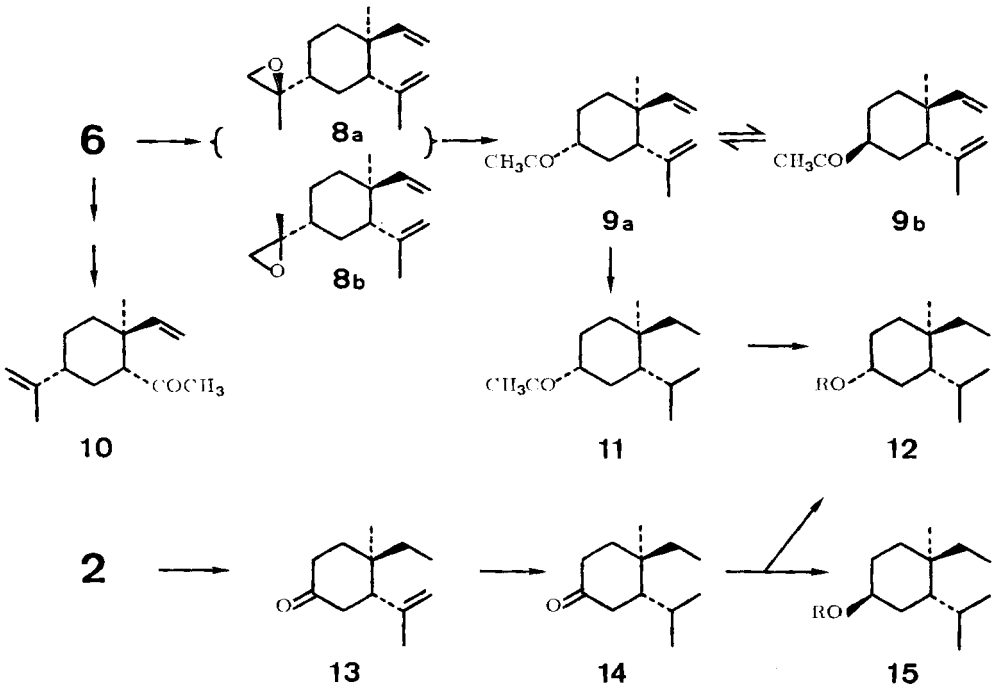
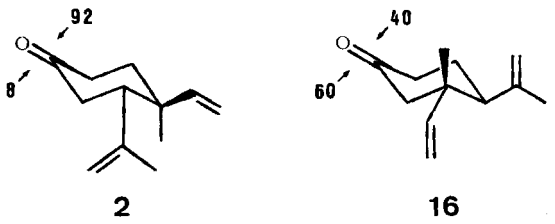
[1]) The supposition that conformational interconversions of cyclodecadienes would be more rapid than *Cope* cyclizations was the main basis for the geijerone argument [5] and has recently received some experimental support [9].

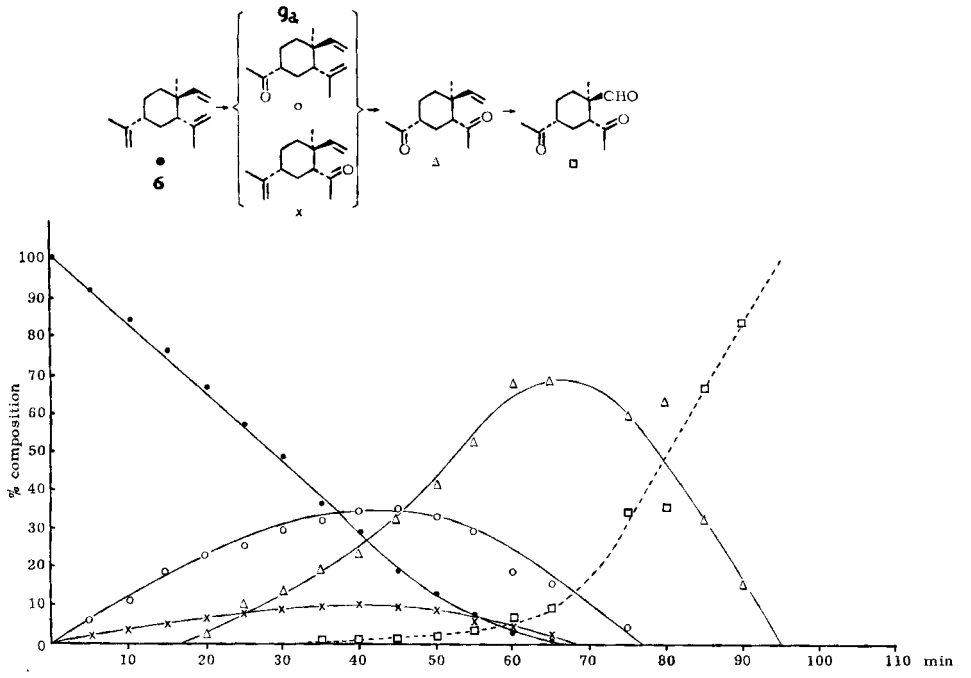


The proportion of equatorial to axial hydroxy compound obtained on reduction of (–)-geijerone (**2**) with lithium alumium hydride contrasts with the much lower amount of equatorial alcohol in the mixture obtained by lithium aluminium hydride reduction of the isomer **16** [10–11] (or its hydrogenated derivatives). This result



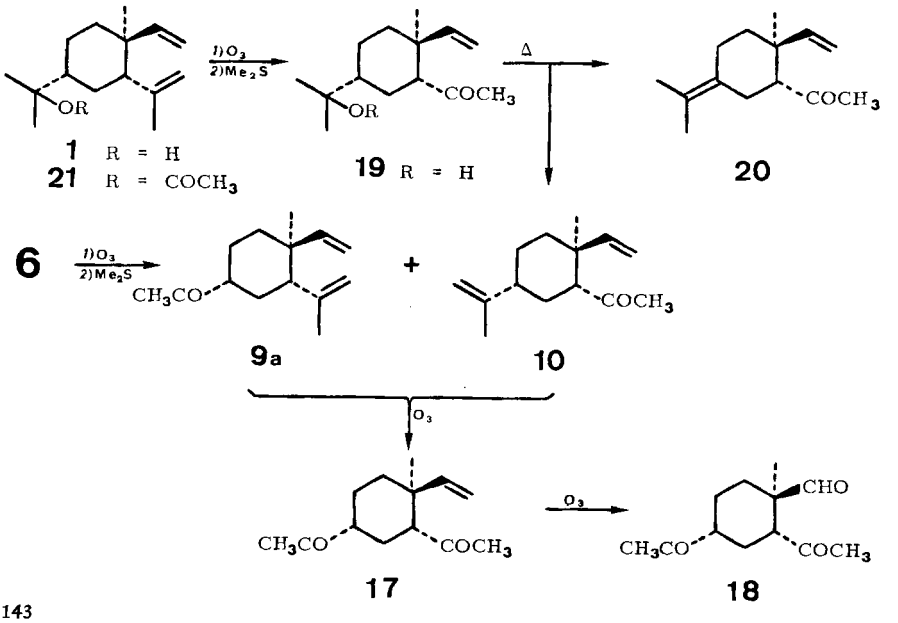
agrees qualitatively with that of *Marshall & Caroll* [12], who examined the sodium borohydride reduction of *trans*-9β- and *trans*-10β-methyl-2-decalones, where the case having an axial methyl group in the 3-position to the carbonyl group results in lowering the specificity of the reduction by hindering the approach of the reagent from the favored side.

Ozonolysis Experiments. – Reaction of (–)-β-elemene (**6**) with ozone, and decomposition of the ozonides with dimethyl sulfide led to two methyl ketones **9a** and **10** in the first instance, continued ozonolysis giving the diketone **17** as the major product. The selectivity of the reaction is illustrated in the Fig., showing that the mixture finally becomes very complex, the end product being mostly the diketo-

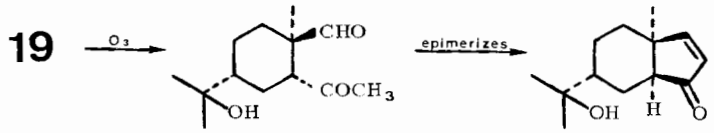


Ozonization of (−)-β-Elemene

Solvent: $CH_3COOC_2H_5/CH_3OH$ 1:1. Temp.: 0°. Reduction of ozonide with $(CH_3)_2S$

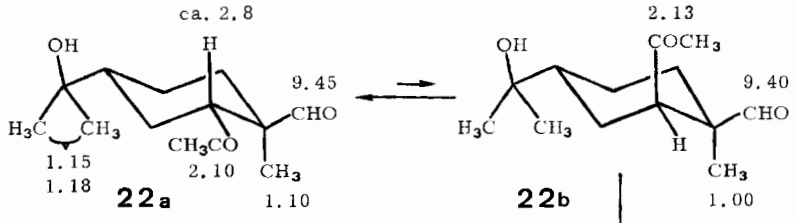


aldehyde **18**. One of the ketones (**9a**) was identical with the ketone obtained by oxidation of β-elemene epoxide (**8**), the structure of which had already been proved, and the structure of the other ketone was proved in the following way. (−)-Elemol (**1**) was treated with ozone, and decomposition of the ozonide gave a hydroxyketone **19**, dehydration of which with phosphorus oxychloride in pyridine led to the ketone **10**, together with the isomer **20** derived from γ-elemene (**3**). Ozonolysis of elemol acetate (**21**) followed by pyrolysis gave the same two ketones **10** and **20** in different proportions. Continued treatment of the reaction mixture from (−)-β-elemene with ozone led to the diketone **17**, identical with one of the diketones obtained in small amounts from the reaction of the epoxide mixture from (−)-β-elemene (**6**) with periodic acid. Ultimately, the diketoaldehyde **18** was formed. Although the latter decomposed to some extent on GLPC., an impure sample was prepared by chromatography on silica-gel, and an NMR.-spectrum of this showed clearly the presence of two methyl ketone functions and an aldehyde group.

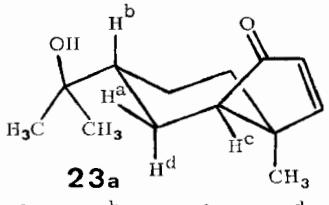


22 **23**

It was described above how the (−)-methyl ketone **9** epimerizes during the ring-opening reaction of the epoxides **8**, and it was interesting to observe that the isomeric ketone **10** did not epimerize appreciably at room temperature in the presence of alcoholic sodium hydroxide for 140 h. The C(2) position can, however, be induced to epimerize, as was shown when the hydroxy-ketoaldehyde **22**, obtained after complete ozonolysis of elemol (**1**) was treated with base at reflux. The epimer of **22** was not purified (see below), but apparently cyclized to the hexahydroindenone **23**, the sole



The figures are chemical shifts (ppm).



Shift/0.1 equiv. Eu(fod)$_3$ in ppm:	H^a	H^b	H^c	H^d
	1.13	1.08	0.76	0.33

product from this reaction. This hexahydroindenone was ascribed the *cis*-configuration on the basis of the NMR.-spectrum measured in the presence of $Eu(fod)_3$ [13]. The four protons (H^a, H^b, H^c, H^d in formula **23a**) shifted to the greatest extent exhibited characteristic coupling constants (verified by double resonance experiments). These were as follows: $J_{ad} = 14$ Hz (presumably negative), $J_{bd} = 12$ Hz, $J_{cd} = 6$ Hz, $J_{ac} = 2$ Hz, J_{bc} *ca.* 0. The couplings J_{cd} and J_{ac} are thus too low for either to be attributed to a *trans*-diaxial coupling, thus excluding the alternative *trans* ring junction. Cyclization thus involves epimerization of the acetyl group in **22a**. Indeed, the NMR.-spectrum of the substance isolated indicated the presence of two isomers, the second presumably being **22b** in the proportions of about 4:1 of **22a**:**22b**.

Experimental Part

NMR.-spectra were recorded on a *Hitachi Perkin-Elmer* R-20B instrument, and chemical shifts are given in ppm with tetramethylsilane as 0,00 ppm. IR.-spectra were measured with a *Perkin-Elmer* type 125 spectrophotometer. Mass spectra were measured on an *Atlas* CH 4 mass spectrometer, using an inlet temperature of about 150° and electrons of 70 eV. Results are quoted as *m/e* (% most important fragment), and generally, the ten most important fragments are quoted. Gas chromatography (GLPC.) was carried out on a *Carlo Erba* Fractovap P (preparative), or a *Carlo Erba* type GT instrument, using Carbowax 20M, 15% on Chromosorb W 60–80 mesh, acid-washed. All products isolated from Carbowax columns were checked for purity on silicone oil columns.

Acetylations were carried out by treating the alcohol with an excess of acetic anhydride in dry pyridine. After washing with acid and base, then with water to neutrality, the acetates were purified by GLPC.

β-Elemene epoxides (8). – The epoxidation of β-elemene ($[\alpha]_D^{20} = -21.8°$) was carried out using peracetic acid, as previously described for γ-elemene [5]. The main peak on GLPC. was characterized as being produced by a mixture of *threo*- and *erythro*-2-*cis*-isopropenyl-1-vinyl-*cis*-*p*-menth-8-ene 8,9-epoxides (**8a**, **8b**), b.p. 47°/0.001 Torr, $[\alpha]_D^{20} = -7.28°$ ($c = 6$ in CCl_4). – NMR.: 0.97 (3H, *s*, CH_3–C(–)–); 1.23 (3H, *s*, CH_3–C(O)C); 1.69 (3H, *s*, CH_3C(–)=); 2.3 to 2.6 (2H, *m*, CH_2(O)C, 2 isomers); 4.5 to 5.0, and 5.85 (the latter is 1H, $d \times d$, $J = 10$ and 18 Hz, $=CH_2$ and $-CH=CH_2$. – MS.: 41 (100), 81 (97), 107 (94), 71 and 93 (85), 55 (81), 67 (74), 43 and 68 (56), 121 (55) ... 162 (48), 189 (15), 205 (3.5), 220 (M^+, 1).

$C_{15}H_{24}O$ (220.34) Calc. C 81.76 H 10.98% Found C 81.85 H 10.78%

Periodic acid oxidation of β-elemene epoxides (7, 8a, 8b). – A solution of 5.9 g of periodic acid ($HIO_4 \cdot 2H_2O$) in 60 ml of aqueous (60%) tetrahydrofuran was stirred while 5.6 g of β-elemene epoxides in 50 ml of tetrahydrofuran were added dropwise. After 5 h, the mixture was extracted into pentane, washed (sodium thiosulfate and water), dried, and concentrated. The products were purified by GLPC., when the following were eluted in order:

1. *1-Vinyl*-cis-p-*menth-8-en-2*-cis-*yl methyl ketone* (**10**, 6%). Identified by comparison of the NMR.-spectrum with that of the authentic substance (see below).

2. *1-Vinyl*-cis-o-*menth-8-en-4*-trans-*yl methyl ketone* (**9b**, 15%). – NMR.: 0.98 (3H, *s*, CH_3–C(–)–); 1.71 (3H, *d*, $J = 1.5$ Hz, CH_3–C(–)=); 2.08 (3H, *s*, CH_3CO); 2.58 (1H, $w_{1/2}$ *ca.* 8 Hz, –C(H_{eq})–CO); 4.5 to 5.0 (4H, *m*, $=CH_2$); 5.78 (1H, $d \times d$, $J = 10$ and 17 Hz, $-CH=CH_2$). – MS.: 43 (100), 95 (48), 41 (33), 81 (31), 93 (24), 79 (22), 55, 68, 107 and 123 (21) ... 163 (15), 191 (7), 206 (M^+, 7).

3. *1-Vinyl*-cis-o-*menth-8-en-4*-cis-*yl methyl ketone* (**9a**, 60%). – NMR.: similar to the *trans*-isomer (**9b**) but with differences in the CH_2 region, in particular 2.28 (1H, $w_{1/2}$ *ca.* 16 Hz, –C(H_{ax})–CO). – MS.: 43 (100), 95 (50), 41 and 81 (33), 163 (31), 93 (28), 107 (27), 55 and 79 (23), 68 (22), 67 and 121 (21) ... 191 and 206 (M^+, 4). $[\alpha]_D^{20} = -35.6°$ ($c = 18$ in CCl_4).

$C_{14}H_{22}O$ (206.32) Calc. C 81.50 H 10.75% Found C 81.16 H 10.75%

Semicarbazone, m.p. 192° (ethanol).

$C_{15}H_{25}N_3O$ (263.37) Calc. C 68.40 H 9.57 N 15.96% Found C 68.39 H 9.55 N 16.12%

4. *3*-trans-*Acetyl-4*-trans-*methyl-4*-cis-*vinylcyclohexyl methyl ketone* (10%). – NMR.: 0.97 (3H, *s*, CH_3—C(—)—); 2.06 and 2.10 (3H each, *s*, CH_3CO); 2.3 to 2.9 (2H, *m*, —C*H*—CO, including at least one H_{eq} at lower field than the isomer **17**), 4.86 and 5.09 (2H, *m*, $CH{=}CH_2$); 5.82 (1H, $d \times d$, J = 9.5 and 18 Hz, $CH{=}CH_2$). – MS.: 43 (100), 29 (15), 41 and 165 (10), 27, 39, 55, 71, 95 and 107 (7), 193 and 208 (*ca.* 1).

5. *3*-cis-*Acetyl-4*-cis-*methyl-4*-trans-*vinylcyclohexyl methyl ketone* (**17**, 8%). – NMR.: 1.00, 2.04, 2.10, attribution as in spectrum of section 4; *ca.* 2.2 to 2.7 (2H, C*H*—CO); 4.86 and 5.09 as before; 5.92 ($d \times d$, $CH{=}CH_2$). – MS.: 43 (100), 95 (14), 71 (10), 41 (8) ... 165 (5), 193 and 208 (*ca.* 1).

1-Ethyl-*cis*-*o*-menth-4-yl methyl ketone (11). – A solution of 1-vinyl-*cis*-*o*-menth-8-en-4-*cis*-yl methyl ketone (**9a**) in alcohol was shaken with hydrogen over platinum oxide. The yield was practically quantitative. For analysis, the product was purified by GLPC. $[\alpha]_D^{20} = -43.8°$ (c = 15 in CCl_4). – NMR.: 0.7 to 1.0 (12H, CH_3) having main signal at 0.85, 2.05 (3H, *s*, CH_3CO), no vinyl protons. – MS.: 43 (100), 55 (31), 41 and 71 (26), 69 (21), 83 (20), 111 (17), 181 (15), 123 (15), 57, 81, 97, 125, and 167 (12), 70, 95, 139, and 210 (M^+, 10).

$C_{14}H_{26}O$ (210.35) Calc. C 79.93 H 12.46% Found C 80.16 H 12.36%

Semicarbazone, m.p. 178° (ethanol).

$C_{15}H_{29}N_3O$ (267.41) Calc. N 15.72% Found N 16.08%

1-Ethyl-*cis*-*o*-menth-*cis*-4-yl acetate (**12**, R = $COCH_3$). – 1-Ethyl-*cis*-*o*-menth-4-yl methyl ketone (1 g) was added dropwise at room temperature to 1.9 ml of 40% peracetic acid in acetic acid, and the mixture allowed to stand overnight. The products were isolated in pentane, washed with saturated sodium hydrogencarbonate solution, then water, and the product purified by GLPC. The NMR.-, mass-, and IR.-spectra were identical with those of the product obtained from (–)-geijerone (see below).

$C_{14}H_{26}O$ (210.35) Calc. C 74.28 H 11.58% Found C 74.14 H 11.68%

Catalytic Reduction of Geijerone (2). – A solution of 31.3 g of geijerone in 320 ml of ethanol was shaken in hydrogen in the presence of palladium on charcoal. After absorption of 3.9 l (corr. to 0° and 760 mm; theory for 1 mol 3.94 l) of hydrogen, the reduction almost stopped. Removal of half the solution, filtering, and concentrating, gave 15 g of practically pure 1-ethyl-*cis*-*o*-menth-8-en-4-one (**14**). The analytical sample was further purified by GLPC. $[\alpha]_D^{20} = -12.7°$ (c = 5 in $CHCl_3$). – NMR.: 0.88 (3H, *t*, J = 7 Hz, CH_3CH_2); 1.06 (3H, *s*, CH_3—C(—)—); 1.73 (3H, *s*, CH_3—C(=)—); 4.70 and 4.87 (2H, C=CH_2). – MS.: 55 and 69 (100), 41 (69), 97 (59), 83 (50), 70 (39), 69 (34), 43 and 139 (31), 67, 95, 111, and 151 (28) ... 180 (M^+, 15).

The catalyst in the remainder of the solution was replaced with platinum oxide, and the hydrogenation continued. A further 2.0 l of hydrogen was absorbed. Filtration, concentration, and distillation gave pure 1-ethyl-*cis*-*o*-menth-4-one (**14**), b.p. 56–58°/0.001 Torr, $[\alpha]_D^{20} = +8.60°$ (c = 20 in $CHCl_3$). – NMR.: complex methyl region (12H) with signals at 0.76, 0.85, 0.87, 0.97, and 1.06, 1.2 to 1.8 (6H); 1.9 to 2.5 (4H, CH_2—CO—CH_2); no vinyl signals. – MS.: 55 (100), 139 (93), 65 (72), 98 (59), 41 (52), 43 (48), 83 (43), 70 (33), 81 and 100 (21), 27 and 29 (19), 111 (17) ... 153 (5), 167 (7), 182 (M^+, 6).

$C_{12}H_{22}O$ (182.30) Calc. C 79.06 H 12.16% Found C 78.83 H 11.89%

1-Vinyl-*cis*-*o*-menth-8-en-4-ols. – A solution of 5 g of (–)-geijerone (**2**) in 30 ml of dry ether was reduced with 0.5 g of lithium aluminium hydride in 20 ml of ether. The excess reagent was decomposed with a few drops of water, and the products isolated by filtration and concentration. GLPC. showed the presence of two isomers, eluted from Carbowax in the following order:

1. *1-Vinyl*-cis-o-*menth-8-en-4*-trans-*ol*, 8% of mixture. – NMR.: 0.96 (3H, *s*, CH_3—C(—)—); 1.67 (3H, *s*, CH_3—C(=)—); 4.05 (1H, $w_{1/2}$ *ca.* 8 Hz, —CH_{eq}—OH); 5 protons in vinyl region. – MS.: 68 (100), 67 (95), 81 (94), 82 (91), 41 (83), 55 (74), 43 (71), 79 (62), 147 (61), 69 and 93 (46), 39, 53, and 162 (40).

2. *1-Vinyl*-cis-o-*menth-8-en-4*-cis-*ol*, 92% of mixture. – NMR.-spectrum: 1.00, 1.68, attributions as for the *trans*-isomer; 3.5 (1H, $w_{1/2}$ *ca.* 18 Hz, $-CH_{\overline{ax}}-OH$). – MS.: 68 (100), 81 (90), 67 (89), 82 (84), 41 (77), 55 (71), 43 (65), 79 (63), 93 (49), 69 (46), 147 (44), 39 and 53 (35), 162 (22).

1-Ethyl-*cis*-o-menth-8-en-4-ols were made from 1-ethyl-*cis*-o-menth-8-en-4-one (**16**) in the same way as described in the foregoing experiment. The following were separated on Carbowax:

1. *1-Ethyl*-cis-o-*menth-8-en-4*-trans-*ol*, 15% of mixture. – NMR.: 0.86 (3H, *s*, $CH_3-\overset{|}{C}-$), 0.85 (3H, *t*, $J = 7$ Hz, CH_3-CH_2); 1.72 (3H, *s*, $CH_3-\overset{|}{C}=$); 4.05 ($w_{1/2}$ *ca.* 8 Hz, $-CH_{\overline{eq}}-OH$); 4.65 and 4.80 (2H, $C=CH_2$). – MS.: 81 (100), 84 (97), 55 (83), 41 (74), 69 (70), 43 (63), 95 (59), 123 (53) ... 113 (33), 137 (30), 155 (15), 182 (M^+, 6.6).

2. *1-Ethyl*-cis-o-*menth-8-en-4*-cis-*ol*, 75% of mixture. – NMR.: 0.88, 1.28, 1.71, 4.64, 4.80, attributions as for the *trans*-isomer; 3.5 (1H, $w_{1/2}$ *ca.* 18 Hz, $-CH_{\overline{ax}}-OH$). – MS.: 84 (100), 81 (86), 55 (85), 69 (83), 41 (79), 113 (77), 95 (74), 43 (70), 70 and 79 (40), 29 and 67 (32) ... 182 (M^+, 18), 164 (5.8), 149 (3.5).

$C_{12}H_{22}O$ (182.30) Calc. C 79.06 H 12.16% Found C 78.79 H 11.95%

1-Ethyl-*cis*-o-menth-4-ols (**12**, **15**, R = H) were made from 1-ethyl-*cis*-o-menth-4-one (**11**) in the same way. Separated on Carbowax, the following were obtained:

1. *1-Ethyl*-cis-o-*menth-4*-trans-*ol* (**15**, R = H), 12% of mixture. – MS.: 137 (100), 81 (94), 55 (66), 84 (60), 41 (55), 123 (52), 43 and 69 (48), 95 (46), 67 (37), 57 (33), 83 (29) ... 155 (17), 166 (< 1).

Acetate (**15**, R = $COCH_3$). – NMR.: complex methyl region with signals at 0.71, 0.82, 0.86, 0.93; 1.95 (3H, *s*, CH_3COO); 5.0 (1H, $w_{1/2}$ *ca.* 7 Hz, $-CH_{\overline{eq}}-OAc$). – MS.: 43 (100), 81 (93), 137 (81), 96 (73), 123 (54), 67 and 95 (41), 166 (6.0).

2. *1-Ethyl*-cis-o-*menth-4*-cis-*ol* (**12**, R = H). – NMR.: complex methyl region (12H), with signals at 0.74, 0.78, 0.86, and 0.95; 3.4 ($w_{1/2}$ *ca.* 18 Hz, $-CH_{\overline{ax}}-OH$). – MS.: 81 (100), 84 (87), 55 and 123 (81), 41 (67), 43, 69, and 137 (58), 95 (52), 67 (46), 57 (40), 83 (38) ... 155 (24), 166 (1.5).

Acetate (**12**, R = $COCH_3$), $d_4^{20} = 0.9475$; $n_D^{20} = 1.4634$; $[\alpha]_D^{20} = +9.3$ (neat). – NMR.: methyl region, signals at 0.73, 0.81, 0.85, 0.87, 0.97; 1.93 (3H, *s*, CH_3COO); 4.55 (1H, $w_{1/2}$ *ca.* 18 Hz, $-CH_{\overline{ax}}-OAc$). – MS.: 43 (100), 81 (97), 96 (95), 123 (74), 137 (57), 67 (54), 55 (47), 41 and 95 (42), 166 (7.8). These spectra were identical with 1-ethyl-*cis*-o-menth-*cis*-4-yl acetate (**12**, R = $COCH_3$), prepared from β-elemene (see above).

Ozonolysis of β-Elemene (6). – A solution of 6.9 g of β-elemene ($[\alpha]_D^{20} = -15°$) in 60 ml ethyl acetate/methanol 1:1 was ozonized at 0° ($1^1/_2$ h). Every 5 min. a sample (0.1 ml) of the solution was reduced with dimethyl sulfide, and the products examined by GLPC. For analysis, a slightly larger amount was treated, and the compounds recovered by GLPC. The spectra of the two monoketones (**9a**, **10**) and the diketone (**17**) were identical with those described above.

After the reaction had been running for the full $1^1/_2$ h, the mixture was worked up as usual and then chromatographed on silica gel (*Merck*, 100 g). After washing with 500 ml ether/hexane 1:9 and 500 ml ether/hexane 2:8, further elution with 1000 ml ether/hexane 9:1 allowed 27 mg of a substance to be isolated that had the following NMR.-spectrum: 1.15 (*s*, $CH_3-\overset{|}{C}-$); 2.08, 2.12 (CH_3CO); 9.48 (*s*, $-CHO$); no vinyl protons, and which was attributed the structure of 2-*trans*,4-*trans*-diacetyl-1-methylcyclohexanal (**18**), although there is no proof for the stereochemistry, and there is in any case about 25% of another epimer present (having a methyl signal at 1.05 ppm).

Ozonolysis of Elemol (1). – A solution of 111 g of (–)-elemol in 900 ml of methanol was treated with ozone at 0° until a solution of potassium iodide placed at the exit was colored. The solution of the ozonides was reduced at –30° with zinc in acetic acid (50% aqueous) and the products isolated in ether. After washing and concentrating, the residue was destilled, b.p. 110–140°/0.07 Torr, 85 g of a mixture of two products being obtained. These were separated by chromatography on silica gel using solvents from hexane/ethanol 17:3 and increasing the proportion of ethanol.

1. *2*-cis-*Acetyl-1-vinyl*-cis-p-*menth-8-ol* (**19**, R = H), $d_4^{20} = 0.9940$; $n_D^{20} = 1.4932$; $[\alpha]_D^{20} = -59°$ (neat). – NMR.: 0.97 (3H, *s*, CH_3—C(—)); 1.13 (6H, *s*, $2CH_3$—C(—)); 2.02 (3H, *s*, CH_3CO); 2.3 to 2.65 (1H, $w_{1/2}$ *ca.* 20 Hz, —$\underline{CH}_{ax}$—$COCH_3$); 3H in vinyl region. MS.: 43 (100), 111 (86), 59 (61), 123 (57), 81 (29), 93 (26), 41 (23), 55 (22), 107 (21) ... 163 (14), 224 (M^+, *ca.* 1).

$C_{14}H_{22}O_2$ (222.32) Calc. C 74.95 H 10.75% Found C 74.67 H 10.78%

2. *2*-cis-*Acetyl-1-formyl*-cis-p-*menth-8-ol* (**22**). Viscosity prevented accurate density measurement; $n_D^{20} = 1.4930$; $[\alpha]_D^{20} = +8°$ ($c = 8.9$ in $CHCl_3$). – For NMR. see theorectical section. – MS.: 43 (100), 71 (57), 59 (52), 85 (32), 44 (30), 28 (29), 41 (24), 81 (21), 109 (20), 137 and 55 (17) ... 165 (3), 180 (6), 226 (M^+, 0).

$C_{13}H_{22}O_3$ (226.31) Calc. C 68.99 H 9.80% Found C 68.74 H 10.01%

3a-Methyl-6-(2-hydroxyprop-2-yl)-3a,4,5,6,7,7a-hexahydroinden-1-one (23). – A solution of 10 g of *2-cis*-acetyl-1-formyl-*cis-p*-menth-8-ol (**22**) in 100 ml of methanol and 10 ml of 5% aqueous sodium hydroxide was heated under reflux for 1 h. After dilution, extraction into ether and the usual washings, the product was distilled, b.p. 120–130°/0.1 Torr, to yield 9 g (97%) of material that crystallized from acetone, m.p. 95–96°, $[\alpha]_D^{20} = -15.7°$ ($c = 10.1$ in $CHCl_3$). – NMR.: 1.13 (6H, *s*, $2CH_3$—C(—)); 1.25 (3H, *s*, CH_3—C(—)); 6.00 and 7.40 (each 1H, *d*, $J = 5.8$ Hz, CH=CH). – MS.: 43 (100), 59 (67), 150 (66), 109 (43), 96 (42), 58 (29), 44 (23), 28 (22), 135 and 108 (18) ... 175 (7), 190 (5), 208 (M^+, *ca.* 1).

$C_{13}H_{20}O_2$ (208.29) Calc. C 74.96 H 9.68% Found C 74.95 H 9.92%

Dehydration of 2-*cis*-acetyl-1-vinyl-*cis*-*p*-menth-8-ol (19). – A mixture of 44.8 g of the alcohol (**19**, R = H), 31.7 g of phosphorus oxychloride, and 200 ml of dry pyridine was allowed to stand at room temperature for 50 h. The mixture was poured onto ice, extracted with pentane, and the pentane solution washed with hydrochloric acid, then water, sodium hydrogencarbonate solution and finally water. Drying, concentrating, and distilling gave 30.9 g of a mixture (b.p. 60–70°/0.03 Torr) of two ketones that were separated by GLPC. In order of elution, these were:

1. *2*-cis-*Acetyl-1-vinyl*-cis-p-*menth-8-ene* (**10**), (33%), $[\alpha]_D^{20} = -67.4°$ (neat); $d_4^{20} = 0.9326$; $n_D^{20} = 1.4886$. – NMR.: 1.03 (3H, *s*, CH_3—C(—)); 1.73 (3H, *m*, CH_3—C(=)); 2.02 (3H, *s*, CH_3CO); 2.3 to 2.7 (1H, $w_{1/2}$ *ca.* 18 Hz, —$\underline{CH}_{ax}$—C(=)); 5 protons in vinyl region. – MS.: 43 (100), 107 (41), 93 (40), 41 (38), 81 (37), 55 (32), 79 (29), 163, 191, and 95 (29) ... 206 (M^+, 4).

$C_{14}H_{22}O$ (206.32) Calc. C 81.50 H 10.75% Found C 81.61 H 10.73%

2. *2*-cis-*Acetyl-1-vinyl*-p-*menth-4(8)-ene* (**20**), (64%), m.p. 31–32°, $[\alpha]_D^{20} = +9.5°$ ($c = 10$ in $CHCl_3$). – NMR.: 1.05 (3H, *s*, CH_3—C(—)); 1.65 (6H, *s*, $2CH_3$—C(=)); 2.01 (3H, *s*, CH_3CO); 3 vinyl protons. – MS.: 43 (100), 123 (66), 41 (42), 95 (35), 107 (30), 206 (M^+, 27), 163 (27), 55 (26), 93 (24), 67 (21), 79 (21), 191 (16).

$C_{14}H_{22}O$ (206.32) Calc. C 81.50 H 10.75% Found C 81.73 H 10.83%

2-*cis*-Acetyl-1-vinyl-*cis*-*p*-menth-8-yl acetate (19, R = $COCH_3$). – A solution of 262 g of elemol acetate (*ca.* 80% pure) in 1000 ml of methanol was ozonized at 0° as described above. The ozonides were reduced with dimethyl sulfide, and the ketonic products isolated through *Girard*'s 'P' reagent. After distillation, there were obtained 76 g of the title substance, b.p. 115–118°/0.2 Torr. $[\alpha]_D^{20} = -58°$ ($c = 10$ in $CHCl_3$), too viscous for accurate density measurement; $n_D^{20} = 1.4798$. – NMR.: 0.97 (3H, *s*, CH_3—C(—)); 1.40 (6H, *s*, $2CH_3$—C(—)); 1.92 (3H, *s*, CH_3OCO); 2.02 (3H, *s*, $COCH_3$); 2.30 to 2.70 (1H, $w_{1/2}$ *ca.* 18 Hz, —$\underline{CH}_{ax}$—$COCH_3$); 3H in vinyl region. – MS.: 43 (100), 93 (25), 28 (22), 41, 81, and 107 (20), 163 (19), 44 and 55 (18), 95 (15) ... 199 (9), 206 (6), 266 (M^+, *ca.* 1).

$C_{16}H_{26}O_3$ (266.37) Calc. C 72.14 H 9.84% Found C 72.16 H 10.03%

Pyrolysis of this substance (**19**, R = $COCH_3$) at 350° through a quartz column, 1 m long, and packed with broken quartz tubing, leads to the same mixture of ketones (**10** and **20**, 88:12) as described above.

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240. Ansamycine, eine neuartige Klasse von mikrobiellen Stoffwechselprodukten[1])

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(7. VIII. 73)

Summary. Isolation, structure elucidation, and biological properties of a novel class of microbial metabolites, ansamycins, are reviewed as background for the following papers. Structural similarities and differences of ansamycins (rifamycins, tolypomycin, streptovaricins, and geldanamycin) relevant to the common steps in their biogenesis are discussed.

Ende der fünfziger Jahre haben *Sensi et al.* [4] einen Komplex von Stoffwechselprodukten des *Streptomyces mediterranei n. sp.*[2]) beschrieben, die sie Rifomycine nannten. Um Verwechslungen mit anderen ähnlich benannten Antibiotica[3]) zu erschweren, wurden die Rifomycine in Rifamycine umbenannt [7].

Neben den ursprünglich isolierten Rifamycinen A bis E wurden später die Rifamycine L [8] und Y [3] isoliert und charakterisiert. Die zuerst nur auf chemischem Wege erhaltenen Umwandlungsprodukte des Rifamycins B – die Rifamycine O, S und SV – konnten später aus Kulturen von Mutanten des *Streptomyces mediterranei* [9] und von anderen *Streptomyces* bzw. *Nocardia*-Stämmen [10] [11] isoliert werden; diese Verbindungen sind also nicht nur Artefakte, sie sind auch genuine Stoffwechselprodukte. Die als Nancimycine beschriebenen Antibiotica sind offenbar mit Rifamycinen identisch [11].

[1]) 4. Mitt. über Rifamycine, 1.–3. Mitt. [1] [2] [3].
[2]) Über die Zuteilung dieses Mikroorganismus zum Genus *Nocardia* vgl. [5].
[3]) Es handelte sich insbesondere um Rufomycin [6].