179. New Carbonyl Compounds in the High-Boiling Fraction of Lavender Oil

2nd Communication1)

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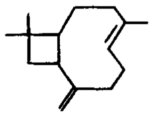
(8.VI.83)

Summary

In addition to the sesquiterpenoid compounds reported in [1] the in-depth analysis of lavender oil also led to the identification of new constituents with caryophyllane (**1**–**6**), cedrane (**7** and **8**) and other skeletons (**9**–**21**). Spectroscopic properties as well as partial syntheses of these compounds are discussed.

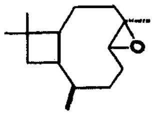
Introduction. – In addition to the new lavender constituents with santalane and cadinane skeletons described in [1] we discuss a further series of carbonyl components **1**–**21** identified in the same natural product.

A. Sesquiterpene Derivatives with Caryophyllane Skeleton. – The sesquiterpene hydrocarbon (–)-caryophyllene represents one of the main constituents (4%) of lavender oil. Therefore, it is not surprising to identify an oxygenated derivative of it as a dominating constituent in the high-boiling carbonyl fraction. This ketone, present to 1% in the total carbonyl fraction, was eluted with hexane/ether 2:1 and could be purified by crystallization (m.p. 60–60.5°). It proved to be the (–)-kobusone (**1**)2) already known as a constituent of *Cyperus rotundus* [2]. The ketone **1**



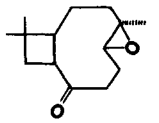
(–)-Caryophyllene

$[\alpha]_D$ *ex* clove oil –11.8°
$[\alpha]_D$ *ex* lavender oil –11.5°



(–)-Caryophyllene epoxide

ex (–)-caryophyllene –69.3°
ex lavender oil –67.5°



(–)-Kobusone **1** (1%)

–136.1°
–134.3°

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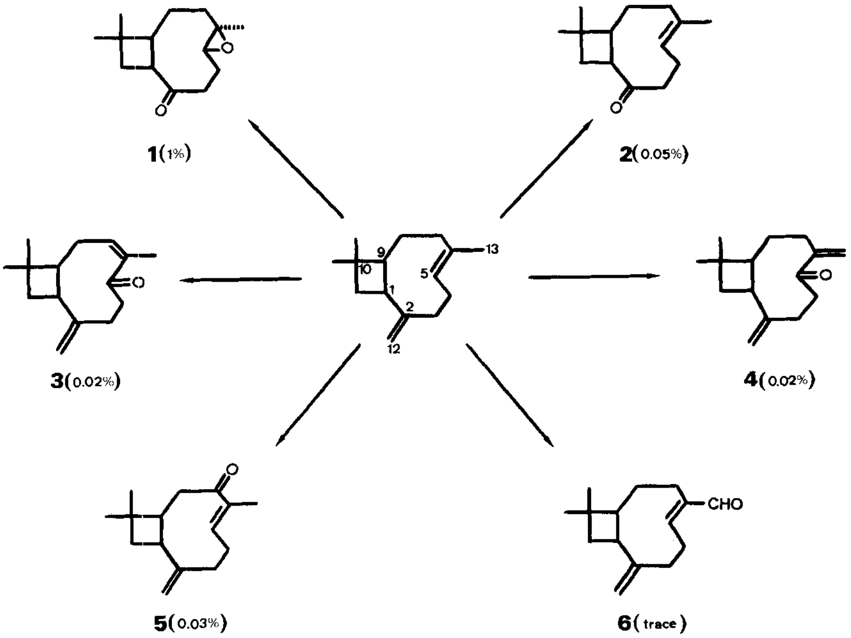
1) Partially presented at the '13th International Workshop on Essential Oils, Würzburg/Germany', September 7–11, 1982.

2) The percentages in parentheses given beneath the corresponding formula are approximate values based on the total carbonyl fraction of lavender oil.

is easily accessible by ozonolysis [2] or oxidation with $KMnO_4$ [3] of (–)-caryophyllene epoxyde also present in lavender oil to 0.3%.

As a further derivative of (–)-caryophyllene we isolated (–)-12-norcaryophyllen-2-one (**2**, $[\alpha]_D^{20} = -77.5°$) *(Scheme 1)*. We synthesized compound **2** several years ago in connection with the structural elucidation of the caryophyllan 2,6-*β*-oxide [4] by reductive elimination of the epoxy group in **14** with Zn/Cu-couple.

Scheme 1



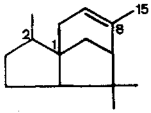
Furthermore, GC/MS measurements of appropriate fractions followed by co-injections with authentic samples also allowed the identification of the trace constituents **3**–**6**.

The dienones **3** and **4** were synthesized by oxidation of the corresponding caryophylladienols which are easily accessible by rearrangement of caryophyllene epoxide with aluminium isopropoxide [5] in a suitable solvent or by photooxygenation of (–)-caryophyllene [6].

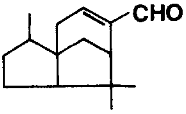
The dienone **5** with original position of the double bonds has recently become known under the name buddledin C as a constituent of *Buddleja davidii* [7]. It was obtained by epoxidation of **3** in alkaline medium followed by a *Wharton* rearrangement [8] of the epoxy ketone to the corresponding allylic alcohol and subsequent oxidation.

The application of the same reaction sequence to **4** led to the caryophyllen-13-al (**6**) (*α*-betulenal in [9]) which is also accessible by direct oxidation of caryophyllene with SeO_2.

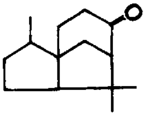
B. Sesquiterpene Derivatives with Cedrane Skeleton. – GC/MS measurements allowed us to identify similar oxidation products of α-cedrene (**7** and **8**) as trace constituents.



α-Cedrene



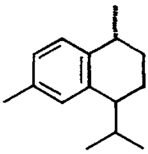
7 (trace)



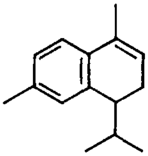
8 (trace)

Cedrenal (**7**) was obtained by SeO_2-oxidation of α-cedrene. Hydrogenation of **7** and subsequent Cu-catalyzed oxidation of the saturated aldehyde using the conditions of *Van Rheenen* [10] furnished the 15-norcedran-8-one (**8**).

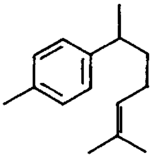
C. Derivatives of Partially Aromatized Sesquiterpene Hydrocarbons. – A series of further constituents identified in the high-boiling carbonyl fraction of lavender oil can be considered as oxidation products of calamenene, α-calacorene and ar-curcumene all present in this oil.



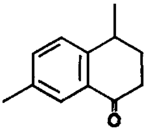
Calamenene



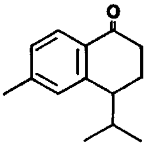
α-Calacorene



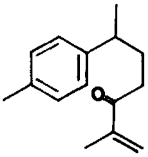
ar-Curcumene



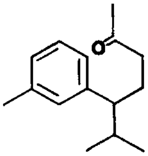
9 (0.2%)



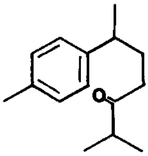
10 (0.1%)



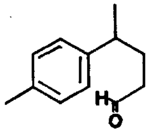
12 (trace)



11 (0.4%)



13 (trace)



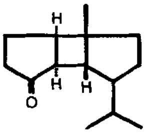
14 (trace)

4,7-Dimethyl-1-tetralone (**9**) is already known as a constituent of lavandin oil [11] whereas the 4-isopropyl-6-methyl-1-tetralone (**10**)[3] and the 6-methyl-5-(3-methylphenyl)-2-heptanone (**11**) are not yet mentioned as natural products. Compound **10** showed the same spectral data as the synthetic product described as intermediate in the synthesis of α-calacorene [12]. The structure of **11** was established by interpretation of the spectral data.

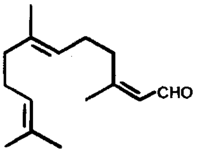
The ar-curcumene derivatives **12** and **13**, present as trace constituents, may be formed in analogy to the previously discussed santalene derivatives (**3** and **4** in [1]) *via* photooxygenation of ar-curcumene, subsequent oxidation of the corresponding allylic alcohols and partial hydrogenation. The synthetic samples of **12** and **13** have been prepared following this sequence.

The ketones **12** and **13** have recently been published as constituents of *Cinnamomum cassia* [13] and the 4-(4-methylphenyl)pentanal (**14**) as trace constituent of sandalwood oil [14].

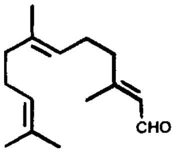
D. Other Skeletons. – The elution with hexane/ether 30:1 furnished fractions containing 11-norbourbonan-1-one (**15**) already known as ingredient of geranium oil [15] as well as the (2*Z*,6*E*)- and (2*E*,6*E*)-farnesal (**16** and **17**, resp.). The last carbonyl constituents in this communication are the well-known natural products β-ionone (**18**), methyl jasmonate (**19**) and 6,10,14-trimethylpentadecan-2-one (**20**), the latter representing 0.5% of the total carbonyl fraction.



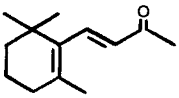
15 (0.2%)



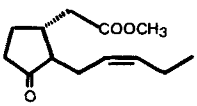
16 (0.01%)



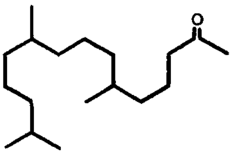
17 (0.04%)



18 (0.05%)



19 (0.02%)



20 (0.5%)

Finally, we would like to mention the cyclohexene derivative **21** which was recently discussed by *Giraudi et al.* [16] as a new 'nor-sesquiterpene ketone' of lavender oil. The structure of **21** was established by spectral comparison with the synthetic sample obtained by *Diels-Alder* reaction of ocimene and methyl vinyl ketone *(Scheme 2)*.

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[3] Compound **10** as well as **11** were independently identified in the same substrate by *Ch. Ehret, Roure-Bertrand-Dupont* (private communication).

Scheme 2

21 (0.7%)

We also isolated and identified compound **21** together with a whole series of related components which can be considered as *Diels-Alder* adducts of dienes and dienophiles also occurring in lavender oil. The identification and synthesis of these products will be discussed in the third communication on new carbonyl compounds in the high-boiling fraction of lavender oil.

Experimental Part

(With the valuable collaboration of *E. Schwendener* and *E. Stocker*)

General. See [1].

A. Sesquiterpene Derivatives with Caryophyllane Skeleton. – *(–)-Kobusone* (**1**). For synthesis, IR and NMR see [2]. MS: 222 (1, M^+), 194 (3), 165 (10), 137 (11), 123 (9), 109 (20), 107 (23), 96 (80), 95 (31), 81 (50), 67 (42), 55 (78), 43 (100), 41 (79).

(–)-12-Norcaryophyllen-2-one (**2**). For synthesis, IR, NMR and MS see [4].

Caryophylla-2(12),6-dien-5-one (**3**) *and Caryophylla-2(12),6(13)-dien-5-on* (**4**). (–)-Caryophyllene epoxide (94.3 g, 0.43 mol) was dissolved together with 46.9 g (0.23 mol) aluminum isopropoxide in 300 ml 2-propanol; the vessel was placed in an oil bath at 160° and nine-tenths of 2-propanol used were distilled off over a 20-cm *Vigreux* column in such a manner that the internal temperature of the mixture rose to 130°. The residual viscous mass was subsequently stirred for 2 h at an oil bath temperature of 145°, then cautiously treated with the removed portion of 2-propanol, the resulting mixture was cooled to r.t. and extracted with Et_2O. Usual workup and subsequent distillation gave 24.4 g (85%) of a mixture consisting of the 4 possible caryophylladien-5-ols (see [6]), b.p. 100-102°/0.04 Torr. This mixture (50.0 g, 0.23 mol) was oxidized with pyridinium chlorochromate following the procedure in [17] to obtain 36.6 g (79.9%) of a 3:1 mixture of **3** and **4**, b.p. 90-98°/0.05 Torr. Pure **3** and **4** were obtained by CC and subsequent prep. GC.

3: IR ($CHCl_3$): 1685, 1630, 1117, 1073, 928, 902, 892. ^{1}H-NMR (400 MHz): 0.97 and 0.99 (2 *s*, 2 CH_3–C(10)); 1.61 (*ddd*, J = 11, 9, 1, H–C(9)); 1.68 (*t*, J = 11, 1 H–C(11)); 1.78 (*dd*, J = 8, 10, 1 H–C(11)); 1.84 (*s*, CH_3–C(6)); 1.95 (*ddd*, J = 14, 8, 1, 1 H–C(8)); 2.31 (*ddd*, J = 14, 11, 8, 1 H–C(8)); 2.40-2.70 (*m*, 5 H); 4.66 and 4.83 (2 *s*, 2 H–C(12)); 5.72 (*tq*, J = 8, 1, H–C(7)). MS: 218 (9, M^+), 203 (6), 175 (13), 161 (13), 150 (21), 147 (26), 135 (46), 119 (37), 109 (35), 107 (36), 105 (54), 93 (43), 91 (61), 79 (44), 67 (31), 55 (41), 43 (44), 41 (100).

4: IR: 1680, 1635, 1112, 1075, 920, 870. ^{1}H-NMR (400 MHz): 0.94 and 0.96 (2 *s*, 2 CH_3–C(10)); 1.40-1.50 (*m*, 2 H); 1.55-1.70 (*m*, 3 H); 2.19-2.29 (*m*, 2 H); 2.30-2.47 (*m*, 2 H); 2.56 (*m*, 1 H); 2.69 (*m*, 1 H); 2.83 (*m*, 1 H); 4.92 and 4.98 (2 *s*, 2 H–C(12)); 5.55 and 5.61 (2 *s*, 2 H–C(13)). MS: 218 (8, M^+), 175 (7), 147 (15), 134 (65), 119 (21), 107 (28), 105 (27), 93 (40), 91 (52), 79 (57), 69 (65), 53 (37), 41 (100).

Caryophylla-2(12),5-dien-7-one (**5**, *buddledin C*) *and Caryophylla-2(12),5-dien-13-al* (**6**, *a-betulenal*). From the 3:1 mixture of **3** and **4** 19.8 g (0.09 mol) were epoxidized with H_2O_2 in alkaline medium [18] to give a 3:1 mixture of the corresponding epoxy ketones in good yield. They were isolated as pure products by CC on silica gel using hexane/Et_2O 5:1.

6(7)-Epoxycaryophyll-2(12)-en-5-one. IR ($CHCl_3$): 1712, 1635, 1110, 1098, 1072, 965, 908, 900, 867. ^{1}H-NMR (60 MHz): 0.95 and 0.98 (2 *s*, 6 H); 1.62 (*s*, 3 H); 1.10–3.10 (*m*, 11 H); 4.63 and 4.85 (2 br. *s*, 2 H). MS: 234 (< 1, M^+), 178 (3), 135 (8), 125 (36), 107 (23), 98 (19), 93 (23), 91 (24), 79 (26), 67 (20), 55 (23), 43 (100), 41 (45).

6(13)-Epoxycaryophyll-2(12)-en-5-one. IR (neat): 1708, 1638, 1108, 1065, 955, 900, 890. ^{1}H-NMR (60 MHz): 0.98 (2 *s*, 6 H); 1.00–2.85 (*m*, 14 H); 4.97 (br. *s*, 2 H). MS: 234 (1, M^+), 203 (9), 161 (11), 134 (47), 121 (20), 107 (32), 93 (42), 91 (46), 79 (65), 69 (39), 67 (39), 55 (50), 41 (100).

6(7)-Epoxycaryophyll-2(12)-en-5-one (5.0 g, 0.02 mol) was subjected to a *Wharton* rearrangement [8] and the crude product oxidized with pyridinium chlorochromate [17]. CC of the product using hexane/Et_2O 10:1 gave 3.5 g of pure **5**. For IR and NMR see [7]. MS: 218 (3, M^+), 190 (8), 175 (12), 149 (50), 121 (64), 107 (50), 105 (45), 93 (93), 91 (48), 79 (81), 69 (60), 55 (40), 41 (100).

The same reaction sequence with 0.60 g (2.5 mmol) 6(13)-epoxycaryophyll-2(12)-en-5-one gave 0.32 g **6** (purity *ca.* 80%). For analysis the material was purified by prep. GC. IR: 2710, 1685, 1640, 1132, 1094, 885. ^{1}H-NMR (60 MHz): 0.94 and 0.98 (2 *s*, 6 H); 1.40–2.80 (*m*, 12 H); 4.85 (*m*, 2 H); 6.55 (*t*, *J* = 8, 1 H); 9.40 (*s*, 1 H). MS: 218 (2, M^+), 203 (5), 175 (8), 161 (9), 150 (11), 147 (13), 133 (28), 119 (18), 105 (30), 93 (37), 91 (54), 79 (43), 69 (97), 55 (27), 41 (100). The direct oxidation of (–)-caryophyllene with SeO_2 in EtOH and subsequent oxidation of the allylic alcohol obtained with pyridinium chlorochromate proved to be a more convenient method.

B. Sesquiterpene Derivatives with Cedrane Skeleton. – *a-Cedrenal* (**7**). A solution of 20.4 g (0.10 mol) (–)-*a*-cedrene (obtained by dehydration of natural cedrol [19]) and 5.40 g (0.05 mol) SeO_2 in 80 ml EtOH was heated under reflux for 3 h. The product obtained (18.5 g) after usual workup (containing *ca.* 70% 8-cedren-15-ol) was oxidized with pyridinium chlorochromate to give 16.2 g of crude **7** (purity *ca.* 50%). For analysis the material was purified by CC and prep. GC. IR: 2705, 1685, 1632, 1182, 982, 968, 918, 820, 805, 797. ^{1}H-NMR (60 MHz): 0.88 and 1.06 (2 *s*, 6 H); 0.95 (*d*, *J* = 6.5, 3 H); 1.20–2.10 (*m*, 8 H); 2.39 (*m*, 2 H); 2.69 (*m*, 1 H); 6.72 (*t*, *J* = 3.5, 1 H); 9.53 (*s*, 1 H). MS: 218 (40, M^+), 175 (29), 162 (15), 147 (30), 134 (49), 133 (100), 105 (71), 91 (62), 79 (45), 69 (90), 55 (49), 41 (90).

15-Norcedran-8-one (**8**). The aldehyde **7** (2.18 g, 0.01 mol) in 10 ml EtOH was hydrogenated in the presence of 0.10 g of 10% Pd/C. After 20 min, the theoretical amount of H_2 had been absorbed. The catalyst was removed by filtration, the solvent distilled off and the residue oxidized with air in the presence of diazabicyclo[2.2.2]octane (DABCO), cupric acetate and 2,2′-bipyridyl according to [10]. Usual workup resulted in 1.5 g product containing 75% **8**. For analysis the material was purified by prep. GC. IR: 1705, 1298, 1240, 1188, 992, 954. ^{1}H-NMR. (400 MHz): 0.90 (*d*, *J* = 7, CH_3–C(1)); 1.01 (2 *s*, 2 CH_3–C(6)); 1.42 (*m*, 1 H); 1.52 (*m*, 1 H); 1.56–1.78 (*m*, 4 H); 1.86 (*m*, H–C(2)); 1.90–2.02 (*m*, 3 H); 2.28–2.37 (*m*, 2 H); 2.49 (*m*, 1 H). MS: 206 (27, M^+), 188 (13), 163 (27), 147 (29), 136 (21), 123 (33), 121 (52), 107 (39), 95 (47), 93 (54), 79 (41), 69 (45), 55 (63), 41 (100).

C. Derivatives of Partially Aromatized Sesquiterpene Hydrocarbons. – *4,7-Dimethyl-1,2,3,4-tetrahydronaphthalen-1-one* (**9**). For IR and NMR see [11]. MS: 174 (92, M^+), 159 (100), 146 (23), 132 (39), 131 (36), 118 (30), 117 (26), 115 (18), 91 (19), 77 (5).

4-Isopropyl-6-methyl-1,2,3,4-tetrahydronaphthalen-1-one (**10**). For synthesis see [12]. $[\alpha]_D^{20} = +51.0°$ (*c* = 0.220, $CHCl_3$). IR ($CHCl_3$): 1675, 1610, 1285, 1134, 1030, 875, 828, 809. ^{1}H-NMR (400 MHz): 0.96 and 0.98 (2 *d*, *J* = 7, 6 H); 2.05 (*m*, *J* = 7, 1 H); 2.15 (*m*, 2 H); 2.39 (*s*, 3 H); 2.52 (*dt*, *J* = 5.5, 18, 1 H); 2.55 (*m*, 1 H); 2.73 (*ddd*, *J* = 6, 10, 18, 1 H); 7.06 (*s*, 1 H); 7.12 (*d*, *J* = 8, 1 H); 7.92 (*d*, *J* = 8, 1 H). MS: 202 (29, M^+), 160 (62), 159 (100), 145 (26), 131 (64), 115 (27), 91 (27), 77 (8), 51 (7).

6-Methyl-5-(3-methylphenyl)-2-heptanone (**11**). IR ($CHCl_3$): 1712, 1608, 1590, 1165, 1090, 1040. ^{1}H-NMR (400 MHz): 0.70 and 0.96 (2 *d*, *J* = 6.5, 6 H); 1.78 (*m*, 2 H); 2.00 (*s*, 3 H); 2.08 (*m*, 1 H); 2.10–2.22 (*m*, 3 H); 2.32 (*s*, 3 H); 6.88 (*d*, *J* = 7, 1 H); 6.89 (*s*, 1 H); 7.00 (*d*, *J* = 7, 1 H); 7.16 (*dd*, *J* = 7, 1 H). MS: 218 (5, M^+), 175 (11), 160 (33), 157 (9), 145 (18), 131 (3), 117 (5), 105 (13), 91 (5), 43 (100).

2-Methyl-6-(4-methylphenyl)-1-hepten-3-one (**12**) *and 2-methyl-6-(4-methylphenyl)-3-heptanone* (**13**). For synthesis and spectral data see [13].

4-(4-Methylphenyl)pentanal (**14**). For synthesis and spectral data see [14].

D. Other Skeletons. – *11-Norbourbonan-1-one* (**15**). For IR and NMR see [15]. MS: 206 (1, M^+), 164 (4), 124 (10), 123 (14), 107 (5), 93 (7), 81 (100), 80 (26), 79 (14), 67 (7), 55 (13), 41 (20).

(2Z, 6E)-3, 7, 11-Trimethyl-2, 6, 10-dodecatrienal (**16**). MS: 220 (4, M^+), 159 (5), 123 (6), 109 (10), 107 (10), 95 (9), 84 (57), 81 (30), 69 (100), 55 (10), 41 (10).

(2E, 6E)-3, 7, 11-Trimethyl-2, 6, 10-dodecatrienal (**17**). MS practical identical with that of **16**.

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