170. Two New Sesquiterpenoid Ketones from Cassia Oil

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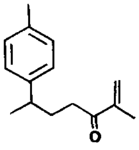
Summary

The synthesis of 2-methyl-6-(4′-methylphenyl)-1-hepten-3-one (**1**) and 2-methyl-6-(4′-methylphenyl)-3-heptanone (**2**), constituents of the oil of *Cinnamomum cassia,* is described.

Cassia, or Chinese cinnamon oil is a steam distillate of the bark, leaves, and twigs of the tree *Cinnamomum cassia*. The most recent study of the constituents is that of *ter Heide* [1]. We have examined a sample of the commercial oil from the People's Republic of China, and in this paper we report the synthesis of the two sesquiterpene components **1** and **2** which we identified uniquely from their mass spectra[1].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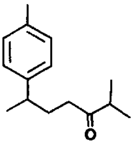
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The fraction containing the heavier ketones was isolated from the crude oil by distillation and column chromatography. The fraction with b.p. 115–128°/0.001 Torr (15% of the oil) consisted mainly of (*E*)-2-methoxycinnamaldehyde, a well known constituent; this crystallized, and the mother liquors were then chromatographed on silica gel when a fraction weighing 1.0 g was eluted just after the hydrocarbons. This was a very complex mixture, but gas chromatographic (GLC.) separation of various zones, followed by ^{1}H-NMR.- and GLC./mass spectrometry (MS.) enabled a number of components to be identified. In zone A (with shortest retention time) issuing from an *SP 1000* GLC. column, tetradecanal and very probably 4,8,12-trimethyltridecanal were identified[2]. Shortly after, a

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[1] Cassia oil has a reputation for being regularly adulterated [2]. Our sample contained a fairly high amount of (Z)-cinnamaldehyde, and the sesquiterpenes copaene, epiaromadendrene, and spathulenol. These seem unlikely materials for adulteration.

[2] Chemical Abstracts reports the presence of 4,8,12-trimethyltridecanal in cold-pressed lemon oil [3], but the original paper to which this refers [4] does not mention it. The same aldehyde, together with the ketone 6,10,14-trimethylpentadecan-2-one, is reported to arise during a chemical degradation of α-tocopherol [5], and the ketone has also been found in sediments [6].

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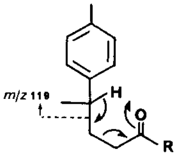
complex zone B contained ketone **2**, together with 1-phenylheptanone. A zone C followed, which contained ketone **1**, followed by a somewhat larger amount of a ketone probably identified as 6,10,14-trimethylpentadecan-2-one[2]).

The ketones **1** and **2** were identified on the basis of their molecular ions, and the fact that both had their most important fragment at *m/z* 132, corresponding to a *McLafferty* γ-hydrogen shift (**3**). Furthermore, loss of the side chain from the C-atom *a* to the benzene ring leaves the characteristic fragment at *m/z* 119, the second most important in the MS. of both **1** and **2**.



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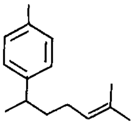

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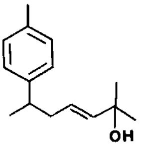
Ketone **2** has already been prepared in 40% yield by *Watanabe et al.* [7] by a *Friedel-Crafts* reaction between toluene and 2-methyl-6-hepten-3-one, but neither **1** nor **2** has been reported to be naturally occurring.

Our synthesis of **1** and **2** started from (±)-*a*-curcumene (**4**), prepared from 4-methylphenylmagnesium bromide and 6-methyl-5-hepten-2-one followed by reduction with sodium in liquid ammonia [8]. Sensitized photooxygenation of **4** yielded the tertiary alcohol (±)-**5**, and a mixture of the *threo-* and *erythro-*alcohols **6**. Chromatography on silica gel enabled the separation of **5** and **6**, although we found no conditions that separated the two isomers of **6**. The mixture **6** was oxidized with manganese dioxide, and the resulting ketone was identical (MS. and retention time on capillary GLC.) with ketone **1**. Catalytic hydrogenation of **1** gave a ketone identical (MS. and capillary GLC.) with **2**.



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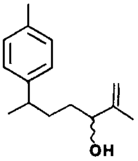

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It is not often that substances can be identified only by mass spectra, but this work shows that in simple cases it is possible.

Thanks are extended to Mr. *Christian Starkemann* for the workup of the natural oil, and to *Roberto Di Giorgio* for assistance with the synthesis.

Experimental Part

General remarks. NMR. spectra were recorded in $CDCl_3$ on a *Hitachi-Perkin-Elmer* R 20B (60 MHz), a *Bruker* HX-90 (90 MHz), or a *Bruker* VH-360 (360 MHz) instrument. Chemical shifts are given in ppm downfield from tetramethylsilane (=0 ppm), coupling constants *J* in Hz. Mass spectra were measured either on an *Atlas* CH-4 mass spectrometer using an inlet temperature of *ca.* 150°, or on a *MAT* 112 instrument coupled with a capillary gas chromatograph, both spectrometers using electrons of 70 eV. Results are quoted as m/z (% most important fragment), and generally the ten most important fragments are given. Column chromatography was carried out on *Merck* H (Type 60) silica gel using a *Jobin-Yvon* medium pressure preparative chromatograph.

Workup of the oil of Cinnamomum cassia. The commercial oil (2.025 kg) was distilled, first at 0.01 Torr up to 110° through a 20-cm *Vigreux* column, thereby obtaining 1.675 kg of distillate. Further distillation with a 10-cm *Vigreux* column yielded 312 g (15%) of material with b.p. 115-128°/0.001 Torr. A large proportion of this fraction crystallized as *(*E*)-2-methoxycinnamaldehyde.* The mother liquors (115 g) were chromatographed on 800 g of silica gel in hexane/ether 7:3, thereby separating 28 g of less polar constituents from more 2-methoxycinnamaldehyde eluted just after. Rechromatography of these less polar constituents on 500 g silica gel in hexane/ether 95:5 gave the following fractions: (1) 1.5 g of hydrocarbons, principally *s-guaiazulene, rimuene,* and other *diterpenes* $C_{20}H_{32}$; (2) 1.2 g of a complex mixture of *ketones* and *esters;* (3) 11.6 g of *(*E*)-cinnamyl acetate;* (4) 5.0 g of *(*E*)-2-methoxycinnamyl acetate;* (5) 5.2 g of a mixture of *cinnamaldehyde* and *(Z)-2-methoxycinnamaldehyde* [the latter was identified by means of its ^{1}H-NMR. (90 MHz): 3.88 (*s*, 3 H, CH_3O); 6.16 ($d \times d$, $J=8$ and 11, 1 H, CH=C*H*CHO, (*Z*)); 7.76 (*d*, $J=11$, 1 H, C*H*=CHCHO, (*Z*)); 9.85 (*d*, $J=8$, 1 H, CHO); an (*E*)-configuration of the double bond implies a coupling constant of 16 Hz, and the aldehyde proton signal at higher field [9]]; (6) 2.5 g of *(*E*)-2-methoxycinnamaldehyde.*

Fraction (2) was separated into zones by GLC. on an *SP 1000* column, each zone being subsequently rechromatographed on an *OV 17* column. From the first zone (from the *SP 1000* column) were thus identified *tetradecanal* (MS. and ^{1}H-NMR.), and *4,8,12-trimethyltridecanal.* - ^{1}H-NMR. (360 MHz): 0.84 (*d*, $J=6$, 3 H), 0.86 (*d*, $J=6$, 6 H), and 0.88 (*d*, $J=6$, 3 H, together 4 CH_3); 1.0-1.6 (*m*, 15 H); 1.66 (*m*, 2 H); 2.42 (*m*, 2 H) and 9.78 (*t*, $J=2$, 1 H, CH_2CH_2CHO). Addition of $Eu(fod)_3$ shifted the *d* at 0.88, and double irradiation clearly established the presence of the $>CHCH_2CH_2CHO$ group. - MS.: 240 (M^+, trace), 196 ($M^+ - 44$, 5), 85 (48), 81 (40), 71 (73), 57 (100), 69 (60), 56 (70), 55 (58), 43 (98), 41 (58).

The next, highly complex zone from the *SP 1000* column contained *1-phenylheptanone* (identified by MS. and retention time of an authentic sample), and ketone **2**.

The third zone from the *SP 1000* column contained ketone **1** and many other substances, the main component of the mixture being *6,10,14-trimethylpentadecan-2-one.* - ^{1}H-NMR. (90 MHz): 0.87 (*d*, $J=6$, 12 H, 4 CH_3); 1.0-1.8 (*m* of very similar shape to that in the ^{1}H-NMR. of 4,8,12-trimethyltridecanal, *ca.* 17 H); 2.13 (*s*, 3 H, 3 H-C(1)); 2.42 (*t*, $J=7$, 2 H, 2 H-C(3)). - MS.: 250 ($M^+ - 18$, 5), 85 (22), 71 (47), 69 (25), 59 (43), 58 (90), 57 (43), 55 (30), 43 (100), 41 (25).

The main constituent of fraction (2) was eluted in a later zone from the *SP 1000* column, and was identified as *benzyl benzoate* (^{1}H-NMR., MS.).

Sensitized photooxygenation of α-curcumene. A solution of 35 g of α-curcumene (**4**) [8] in 400 ml of methanol containing rose bengale was irradiated while oxygen was bubbled through. After 7 h, 4.4 l of O_2 had been absorbed (theory: 4.33 l at 20°/730 Torr), and the solution was added dropwise to 2 l of ice-cooled aqueous (15%) Na_2SO_3-solution. After the addition was completed, the mixture was stirred for 15 h, then extracted with pentane. Usual workup gave 35.8 g of crude material, showing approximately equal amounts of two components by GLC. *(Apiezon L).* Of this, 30.2 g were chromatographed in ether/hexane 2:3 over 1 kg of silica gel. There were thus obtained, first, 14.7 g of *(±)-(3*E*)-2-methyl-6-(4′-methylphenyl)-3-hepten-2-ol* (**5**) which was practically pure. For analysis it was collected by GLC. - ^{1}H-NMR. (60 MHz): 1.20 (*s* and *d*, $J=6.5$, 9 H); 2.29 (*s*, superimposed on *m*, 3 H and 2 H); 2.68 (5 bands, 1 H, H-C(arom.)); 5.52 (*s*, superimposed on *m*, 2 H); 7.04 (*s*, 4 H). - MS.: 203 (2), 200 (4), 188 (16), 131 (29), 119 (100), 118 (21), 105 (12), 91 (15).

$C_{15}H_{22}O$ (218.36) Calc. C 82.51 H 10.16% Found C 82.38 H 10.20%

The next substance eluted from the silica gel was a mixture of threo- *and* erythro-*(±)-2-methyl-6-(4′-methylphenyl)-1-hepten-3-ol* (**6**) which was collected from GLC. *(Apiezon L).* - ^{1}H-NMR. (60 MHz): 1.22 (*d*, $J=7$, 3 H); 1.63 (br.) superimposed on 1.3-1.8 (*m*, 7 H in all); 2.29 (*s*, 3 H); 2.64 (1 H); 4.00 (br., 1 H, H-C(3)); 4.75-4.95 (2 H, 2 H-C(1)); 7.04 (*s*, 4 H). - MS.: 218 (M^+, 0.5), 200 (9), 132 (85), 120 (11), 119 (100), 117 (11), 105 (13), 91 (15), 41 (11).

$C_{15}H_{22}O$ (218.36) Calc. C 82.51 H 10.16% Found C 82.40 H 10.15%

Synthesis of (±)-2-methyl-6-(4′-methylphenyl)-1-hepten-3-one (**1**). A suspension of manganese dioxide (*Merck*, activated 2 h at 120°), was shaken with 9.3 g of **6** in 500 ml of petroleum ether (b.p. 50-70°) for 3 h. After filtration, the solution was concentrated and the residue distilled to obtain 6.2 g (68%) of **1**, b.p. 71-74°/0.01 Torr. For analysis the material was purified by GLC. *(Apiezon L)*. - ^{1}H-NMR. (60 MHz): 1.24 (*d*, $J=6.5$, 3 H); 1.83 (*d*, $J=1$, 3 H); 2.30 (*s*, 3 H); 5.67 and 5.78 (each 1 H, 2 H–C(1)); 7.04 (*s*, 4 H). - MS.: 216 (M^+, 12), 133 (12), 132 (100), 131 (8), 119 (60), 117 (15), 105 (8), 91 (12), 41 (14). The pure substance polymerized within a few h at room temp.

Synthesis of (±)-2-methyl-6-(4'-methylphenyl)-3-heptanone (**2**). The preceding ketone (**1**, 1.5 g) in 150 ml of ethanol was hydrogenated in the presence of 0.2 g of 10% Pd/C. After 35 min, the theoretical amount of hydrogen had been absorbed. The catalyst was removed by filtration, and the residue was distilled in a bulb tube, bath temp. 90°/0.01 Torr, yield 1.3 g. For analysis, the substance was collected by GLC. *(Apiezon L)*. - ^{1}H-NMR. (60 MHz): 1.00 (*d*, $J=6$, 6 H); 1.22 (*d*, $J=6.5$, 3 H); 2.30 (*s*, 3 H); 7.04 (*s*, 4 H). - MS.: 218 (M^+, 9), 133 (13), 132 (100), 119 (38), 117 (8), 105 (9), 43 (9).

$C_{15}H_{22}O$ (218.36) Calc. C 82.51 H 10.16% Found C 82.76 H 10.11%

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