220. (*E*)-9-Isopropyl-6-methyl-5,9-decadien-2-one, a Terpenoid C_{14}-Ketone with a Novel Skeleton[1])

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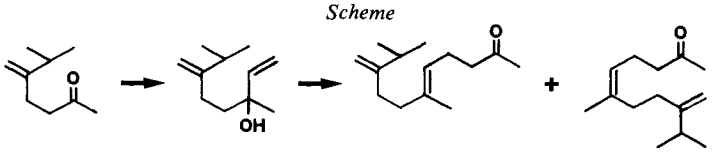
Summary

(*E*)-9-Isopropyl-6-methyl-5,9-decadien-2-one (**1a**), a terpenoid C_{14}-ketone with a novel skeleton, was isolated from costus root oil (*Saussurea lappa* CLARKE) and its structure established by a two-step synthesis from thuja ketone (**2**). The possible role of the new compound as an intermediate in the biosynthesis of the irones is discussed.

An earlier publication [2] has described the isolation and identification of some new sesquiterpenoids from costus root oil (*Saussurea lappa* CLARKE). We now wish to report the isolation and synthesis of another constituent, (*E*)-9-isopropyl-6-methyl-5,9-decadien-2-one (**1a**), a terpenoid C_{14}-ketone with a novel skeleton.

The title compound (*ca.* 0.03% in the commercial oil) was isolated from the carbonyl fraction (extracted with *Girard* reagent P) by chromatography on silica gel [2] and prep. GC. The structure **1a** was attributed to the new substance on the basis of the spectral data. The MS. and the NMR. integration curve indicated the empirical formula $C_{14}H_{24}O$. The NMR. spectrum (Fig.) suggested the presence of an isopropyl group, a methyl group on a trisubstituted double bond, a methyl ketone, and a methylene group (see exper. part). The presence of a non-conjugated ketone (1715 cm^{-1}) and of a methylene group (3110, 1640, and 885 cm^{-1}) was also indicated by the IR. spectrum (Fig.). The biogenetically satisfying structure **1a** accounts for all of these units and is in good agreement with the NMR. spectrum, which exhibits the same characteristic fine structure between 2.20 and 2.62 ppm as (*E*)-geranylacetone. Finally, the compound was shown to be **1a** by synthesis.

Scheme



2 **3** **1a** **1b**

[1]) Preliminary report [1].

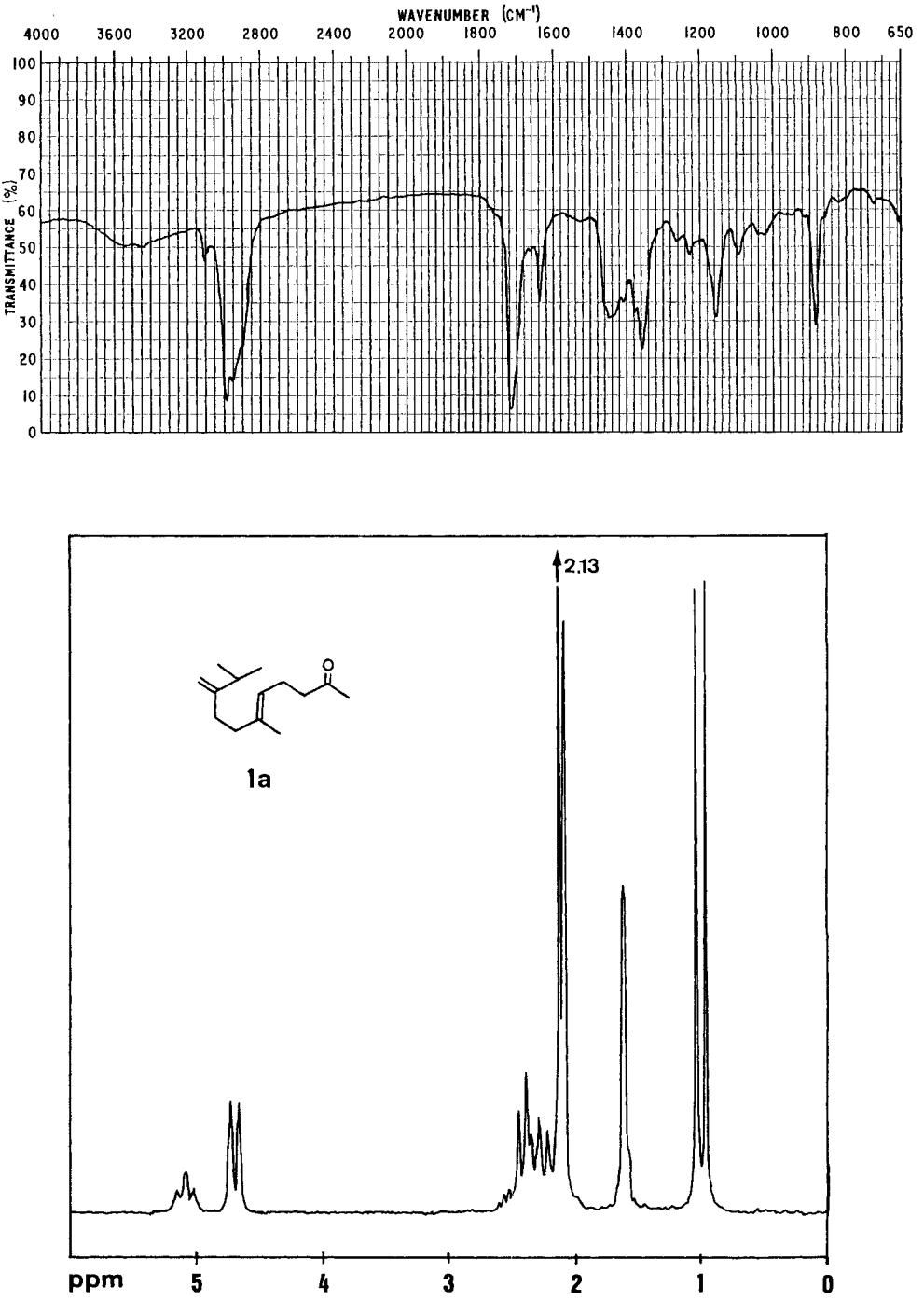


Fig. *IR. (liquid film) and NMR. (90 MHz, $CDCl_3$) spectra of* (E)*-9-isopropyl-6-methyl-5,9-decadien-2-one* (**1a**)

Addition of vinyl magnesium bromide (in tetrahydrofuran) to thuja ketone (**2**) [3] gave the known alcohol **3** which, with ethyl acetoacetate in the presence of sodium acetate (*Carroll* reaction [4]), gave a mixture (70% yield) of the geometric isomers **1a** and **1b** (*ca.* 2:1) which were separated by prep. GC. The more abundant isomer (with longer retention time on both polar and apolar columns) proved identical with the natural product. It was unambiguously assigned the (*E*)-configuration by comparing the NMR. spectra of both isomers **1a** and **1b** with those of authentic samples of (*E*)- and (*Z*)-geranylacetone, *cf.* [5].

The fact that the new ketone **1a** is encountered together with (*E*)-geranylacetone[2]), α- and β-ionone, and dihydro-α-ionone in the same oil [2] could mean that **1a** is formed *via* one of the following biosynthetic routes. 1) Oxidative degradation of the corresponding carotenoids or higher isoprenoids, analogous to routes proposed for geranylacetone and the ionones, *cf.* [6]. 2) Methylation of (*E*)-geranylacetone. Such methylations are known to occur in the biogenesis of certain steroids and fatty acids [7]. A few examples of terpenoids with additional methyl or methylene groups are known [8].

As long as 2- or 2'-methyl substituted carotenoids remain unknown in nature [9], we prefer route 2. The close structural relationship between the ketone **1a** and the irones suggests that **1a** might be an intermediate in the biosynthesis of the irones[3]).

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Experimental part

Details of apparatus and techniques have already been described [2].

*Isolation of (*E*)-9-Isopropyl-6-methyl-5,9-decadien-2-one* (**1a**). – The separation on silica gel of the carbonyl fraction of costus root oil into fractions D–H has been described [2]. Fraction F containing the title compound **1a** (20%), dihydro-α-ionone (20%), and (*E*)-geranylacetone (50%) as the main constituents, was separated by prep. GC. (Carbowax 130°). Dihydro-α-ionone and (*E*)-geranylacetone (in order of elution) were identical (spectra and retention times) with authentic samples. Spectra of ketone **1a** (eluted last), which has a similar odour to geranylacetone, are shown in the figure.

6-Isopropyl-3-methyl-1,6-heptadien-3-ol (**3**). – The known alcohol **3** was prepared by a shorter route than described [3]. To a *Grignard* reagent (70 mmol) in dry THF (40 ml) from 1.70 g of magnesium and 7.50 g of vinyl bromide was added dropwise under argon at 20°, a solution of 4.81 g (34.3 mmol) of 5-isopropyl-5-hexen-2-one (thuja ketone **2**, prepared from thujone [3]) in 20 ml of dry THF.

After stirring for 1 h at 60°, the mixture was poured onto ice, and the product isolated in ether. Distillation of the residue at *ca.* 90°/10 Torr gave 3.5 g (60%) of the alcohol **3** (95% by GC.) as a colourless oil. – IR. (neat): 3450*s* (br.), 3120*m*, 1640*m*, 920*s*, 890*s* cm^{-1}. – NMR. (60 MHz): 1.03 (*d*, J=6.5, 6 H, $-CH(CH_3)_2$); 1.30 (*s*, 3 H, $CH_3-C(3)$); 1.45–2.5 (*m*, 6 H); 4.7 (*m*, $w^1/_2$=*ca.* 6, 2 H, CH_2=C(6)); 5.05 (*d*×*d*, J=10, *ca.* 2, 1 H, H–C(1)); 5.17 (*d*×*d*, J=17, *ca.* 2, 1 H, H–C(1)); 5.93 (*d*×*d*, J=17, 10, 1 H, H–C(2)). – MS.: 168 (M, <1), 71 (100), 43 (53), 55 (40), 41 (32), 107 (29), 83 (19), 69 (16), 125 (12), 79 (12), 70 (11), 67 (11), 39 (11).

Carroll *Reaction of Alcohol* **3** *with Ethyl Acetoacetate.* – In a simple distillation apparatus a mixture of 3.36 g (20.8 mmol) of alcohol **3**, 2.6 g (20 mmol) of ethyl acetoacetate, and 20 mg of anhydrous sodium acetate was heated to 200° for 4 h with stirring. Some ethanol distilled and CO_2 was

[2]) (*E*)-Geranylacetone is a major constituent of the ketone fraction, *ca.* 0.07% of the commercial oil.

[3]) α-Irone has been obtained *in vitro* by acid-catalysed cyclisation of 9-isopropyl-6-methyl-3,5,9-decatrien-2-one (the 3,4-didehydro derivative of **1a**) [3].

evolved. The residue was dissolved in ether, washed with 10% NaOH and saturated NaCl solution, and distilled in a bulb tube at 0.005 Torr (oven temp. 80°). The distillate (2.91 g, 70%), consisting of a mixture (*ca.* 2:1) of (*E*)- and (*Z*)-isomers, was separated by prep. GC. (Carbowax, 180°).

(E)-9-Isopropyl-6-methyl-5,9-decadien-2-one (**1a**) (with longer retention time): IR. (neat), Fig.: 3110*w*, 1715*s*, 1660*w*, 1640*m*, 1360*s*, 1155*m*, 885*s* cm^{-1}. – NMR. (90 MHz), Fig.: 1.01 (*d*, $J=6.5$, 6 H, $-CH(CH_3)_2$); 1.62 (br.*s*, 3 H, $CH_3-C(6)$); 2.09 (br.*s*, *ca.* 4 H, C(6) $-CH_2-CH_2-C(9)$); 2.13 (*s*, 3 H, $-COCH_3$); 2.16–2.62 (*m*, *ca.* 5 H); 4.67 and 4.73 (2× br. *s*, 2 H, $CH_2=C(9)$); 5.09 (br.*t*, $J=6$, 1 H, H–C(5)). – MS.: 208 (*M*, < 1), 190 (< 1), 175 (< 1), 165 (< 1), 150 (14), 147 (2), 135 (7), 123 (7), 107 (23), 105 (2), 95 (6), 93 (4), 91 (3), 83 (7), 82 (4), 81 (9), 79 (5), 69 (2), 67 (8), 55 (15), 53 (5), 43 (100), 41 (22), 39 (7). The spectral data and the retention time were identical with those of the natural compound.

(Z)-9-Isopropyl-6-methyl-5,9-decadien-2-one (**1b**): IR. and MS. are practically identical with those of the (*E*)-isomer **1a**. – NMR. (90 MHz): 1.02 (*d*, $J=6.5$, 6 H, $-CH(CH_3)_2$); 1.69 (*d*, $J=ca.$ 1, 3 H, $CH_3-C(6)$); 2.0–2.6 (*m*, 9 H); 2.13 (*s*, 3 H, $-COCH_3$), 4.71 and 4.77 (2× br.*s*, 2 H, $CH_2=C(9)$); 5.09 (br.*t*, $J=6$, 1 H, H–C(5)).

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