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STRUCTURE AND STEREOCHEMISTRY OF CHILOSCYPHONE

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Abstract—A new α,β-unsaturated sesquiterpene ketone, chiloscyphone, was isolated as a major component from the essential oil of the liverwort, *Chiloscyphus polyanthus*. This paper deals with the structure and stereochemistry of the ketone.

THE liverworts (Hepaticae) phyllogenetically between the vascular plants and the algae, form a unique group and together with the mosses (Musci); their haploid plant bodies (gametophytes), which contain characteristic oil bodies in each cell, are grown from the spores as well as the pollen of higher plants. From the essential oil of *Chiloscyphus polyanthus* (L.) Corda a novel α,β-unsaturated sesquiterpene ketone, chiloscyphone, was isolated and the structure given in a preliminary report.[1,2]

Chiloscyphus polyanthus, belonging to the Lophocoleaceae family of Jungermanniales, contains 2–3 pieces of ovoid oil bodies (6–9 × 5 μ) in each cell. Chiloscyphone, $C_{15}H_{22}O$, was isolated in an oily homogeneous state on GLC and TLC from the essential oil of the liverwort by a combination of fractional distillation and elution chromatography. This compound afforded a 2,4-DNP, m.p. 174–175°, and its IR (Fig 1) and UV spectra exhibit characteristic absorption bands and a maximum at $\nu_{C=O}$ 1670 and $\nu_{C=C}$ 1629 cm^{-1}, and λ_{max}^{EtOH} 220 nm (ε 8960) respectively, whose values indicate the compound to be an α,β-unsaturated ketone.

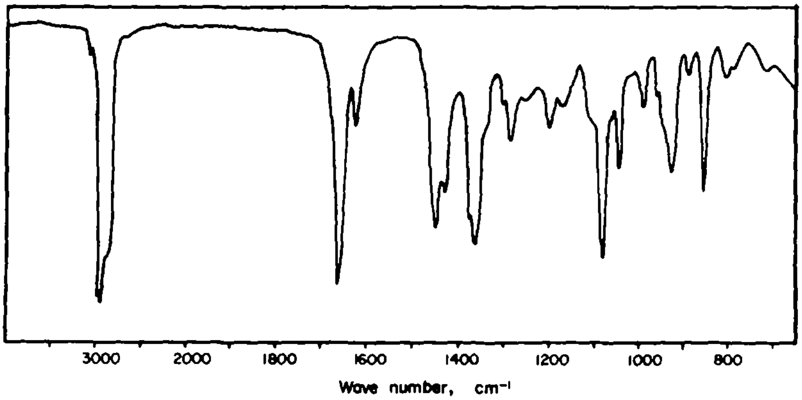


FIG 1. IR spectrum of chiloscyphone

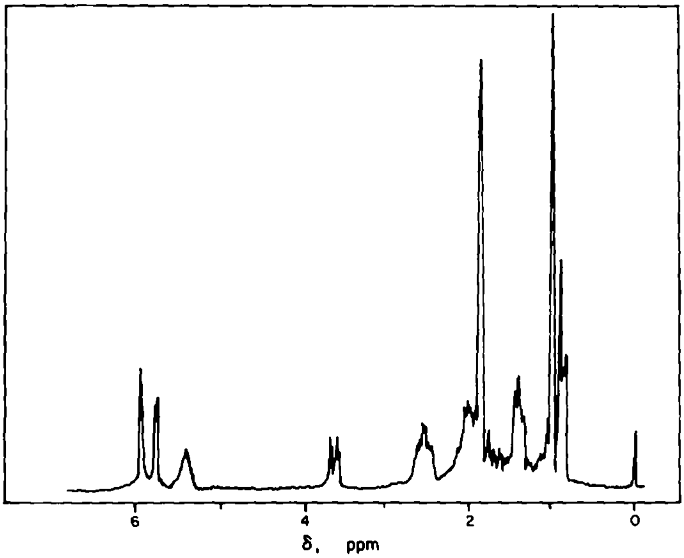


FIG 2. NMR spectrum of chiloscyphone

The IR, NMR (Fig 2) and mass (Fig 3) spectra also reveal that the compound contains an isopropyl group (1380 and 1370 cm^{-1}; δ 0·85, 3H, d, J = 5·5 Hz and 0·96, 3H, s; *m/e* 175·113 [M −43]$^+$), an *exo*-methylene group (935 cm^{-1}; δ 5·75, 1H, d, 1·2 Hz and 5·96, 1H, s) and a trisubstituted double bond bearing a Me group (857 cm^{-1}; δ 1·83, 3H, d, J = 1·2 Hz and 5·42, 1H, m).

In fact, when chiloscyphone was catalytically hydrogenated with Adams catalyst, it took up two molar equivalents of hydrogen, and produced a saturated ketone without an active methylene group ($C_{15}H_{26}O$; $\nu_{C=O}$ 1702 cm^{-1}).

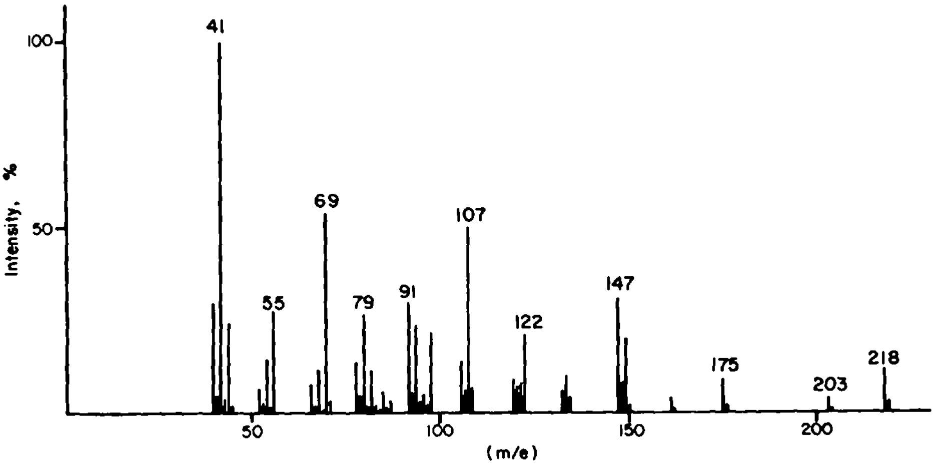
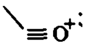
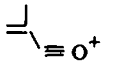
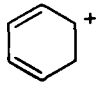
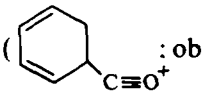


FIG 3. Mass spectrum of chiloscyphone

On the other hand, the ketone, on dehydrogenation, produced cadalene in a good yield, which was identified by IR and mass spectrometry.[3] Chiloscyphone is a cadinene-type α,β-unsaturated ketone which contains an *exo*-methylene group and a trisubstituted double bond bearing a Me group.

Catalytic hydrogenation of chiloscyphone using Pd-C in EtOH produced a non-conjugated dihydro ketone ($C_{15}H_{24}O$: $\nu_{C=O}$ 1703 and $\nu_{C=C}$ 850 cm^{-1}) leaving the trisubstituted double bond unattacked. Therefore the CO group of the original ketone is conjugated with the *exo*-methylene group, and this is in agreement with the NMR spectra of the original ketone: the proton signals of the *exo*-methylene group appear, in $CDCl_3$, at δ 5·75 (1H, d, J = 1·2 Hz) and δ 5·96 (1H, s), the values of which are lower by about one ppm as compared to the normal position, and they shift to δ 5·33 and 5·58 in the C_6D_6. The absorption maximum (λ 220 nm) of chiloscyphone, also supports the fact that the CO group is in conjugation with the *exo*-methylene group (calcd 225 nm as α-substituted α,β-unsaturated ketone).

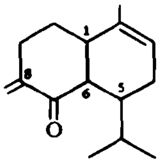
In tetrahydro-chiloscyphone, the active methylene group, which was recognized at ν 1433 cm^{-1} in the original ketone, has disappeared, and a methyne proton adjacent to a CO group appears at δ 3·59 (1H, q, J = 5·9 and 2·0 Hz). The only structure which is in accordance with these facts is structure I.

This is also supported by the mass spectrum of the original ketone: Chiloscyphone, as shown in Fig 3, produces a set of ions at *m/e* 55 ( ; obsd 55·019), 69 ( : obsd 69·034), 79 ( ; obsd 79·054) and 107 ( : obsd 107·051) which can be explained as characteristic for the α-decalone derivatives.[4]

The structure of chiloscyphone was, thus, elucidated as 2-methyl-5-isopropyl-8-methylene bicyclo[4.4.0]dec-2-en-7-one.

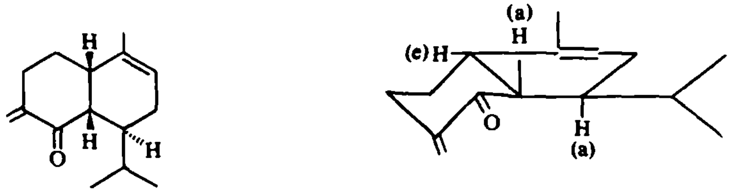
Stereochemistry

For the plane formula (I), which contains three asymmetric centers, eight stereoisomers consisting of four *cis*- and four *trans*-decaline types are possible. As for each of the four *cis*-decaline types, both steroidal and nonsteroidal conformers should be considered, the total possible conformers for structure I amount to twelve.



I

The NMR spectrum of chiloscyphone exhibits a sharp quartet (J = 6·9 and 2·0 Hz) attributable to the C_6-methyne proton adjacent to the CO group at δ 3·59. This splitting pattern, by application of Karplus equation, is an indication that three neighboring methyne protons on C_1, C_6 and C_5 are axial–axial–equatorial or equatorial–axial–axial.[5] The possible conformers with such a relationship are II, III, IV and V.



II

The ORD and CD curves of this ketone exhibit a negative Cotton effect: $[\phi]_{323}$ $+3100$, $[\phi]_{377}$ -1590, a = $-46{\cdot}9$; $[\theta]_{350}$ -2540 (in dioxane); $[\phi]_{323}$ $+3170$, $[\phi]_{380}$ -2780, a = $-59{\cdot}5$; $[\theta]_{362}$ -2810 (in isooctane) as shown in Fig 4. Regarding to the R-band ($n \rightarrow \pi^*$ transition) Cotton effect of α,β-unsaturated ketones, the cisoidal ones obey the normal octant rule.[6] Molecular models of the four conformers confirmed that both II and III give a negative sign and their antipodes, IV and V, a positive sign for ORD and CD curves. Accordingly chiloscyphone should be represented by either II or III.

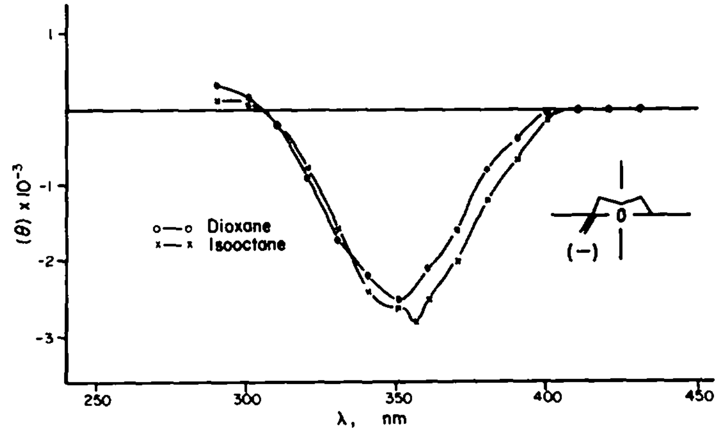
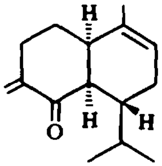


FIG 4. CD curves of chiloscyphone

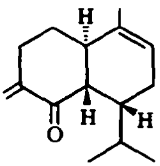
Tetrahydro-chiloscyphone inversely exhibits a positive Cotton effect: $[\phi]_{322}$ $+910$, $[\phi]_{275}$ -870, $a = +15{\cdot}8$; $[\theta]_{298}$ $+9300$ (in dioxane); $[\phi]_{313}$ $+1140$, $[\phi]_{270}$ $+30$, $a = +11{\cdot}1$. $[\theta]_{299}$ $+8010$ (in isooctane), and the model of the fully saturated ketones indicate that all saturated ones derived from II should show a positive sign, whereas all those from III, a negative sign. Accordingly, chiloscyphone should be the nonsteroidal *cis*-decaline type II.

III



IV

The above conclusion is supported by the ORD and CD curves of the K-band ($\pi \rightarrow \pi^*$ transition) of chiloscyphone which show a negative Cotton effect: $[\phi]_{228}$ $-13{,}080$, $[\phi]_{205}$ $+91{,}560$, $a = -1050$; $[\theta]_{222}$ $-46{,}040$ (in isooctane). This result is in agreement with that obtained from structure II according to the normal octant rule, which can be applied to the K-band Cotton effect of α,β-unsaturated ketones.[7]



V

Secondly, the molecular ions of chiloscyphone (12%) and its derivatives (dihydrochiloscyphone, 4%; tetrahydro-chiloscyphone, 23%) show a relatively lower intensity in the mass spectra. These facts suggest the compounds to be *cis*-junction types.[4] Thirdly, the R-band CD-curve of chiloscyphone, show very little solvent dependence ($[\theta]_{350}$ -2540 in dioxane, $[\theta]_{356}$ -2810 in isooctane) or temperature dependence ($[\theta]_{350}$ -2990 at $+24°$, $[\theta]_{350}$ -3550 at $-74°$ in EPA*). This indicates that chiloscyphone is a stable conformer and the isopropyl group is in equatorial conformation.

EXPERIMENTAL

M.ps and b.ps are uncorrected. Gas chromatography was carried out on a flame ionization-type apparatus with two kinds of stainless steel columns (each 2 mm × 2 m), DEGS (10%) and NGS (10%) on Diasolid L (60–80 mesh) respectively, under a 20 ml/min flow rate of N_2. The IR spectra were measured with liquid film, and the NMR spectra were obtained in $CDCl_3$ on a 60 MHz or 100 MHz spectrometer using TMS as an internal reference. The low-resolution mass spectra were measured by a Hitachi-RMU 6D spectrometer at 80 eV ionization chamber voltage, 80 μA total emission, 1800 eV ion accelerating voltage and 200° ionization chamber temp, and the high-resolution mass spectra by a Hitachi-7L spectrometer operating in the same condition as in the low-resolution spectrometer. ORD and CD curves were obtained by a Japan Spectroscopic-Model ORD/UV-5. an automatically recording spectropolarimeter equipped the CD attachment.

Collection of the essential oil. Chiloscyphus polyanthus, was collected at the Yabakei in S.W. Japan. After being dried in the shade for several days, the plant (1200 g) was steam-distilled to obtain the essential oil (14·4 g, yield 1·2%, $[\alpha]_D^{25}$ $+34·4°$, n_D^{25} 1·5118, d_4^{25} 1·0098) together with ether extract from the distillated water.

Isolation of chiloscyphone. The essential oil (13·0 g) was fractionated through a small-size distillation column (15 cm in length) packed with single turn helixes, and the main fraction (b.p. 121–122°/2 mm Hg) rich in the ketone was then chromatographed over silica gel with C_6H_6–$CHCl_3$ (1 : 1) to isolate the ketone in a homogeneous state on GLC (DEGS and NGS) and TLC (C_6H_6-$CHCl_3$, 1 : 1, R_f = 0·85): yield 26·8% for the total oil, b.p. 121–122°/2 mm Hg, $[\alpha]_D^{25}$ $-45·7°$ (1·0% dioxane), n_D^{25} 1·4983, $C_{15}H_{22}O$ (M^+, obsd

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* EPA solvent is composed of ether–isopentane–ethanol in ratio 5 : 5 : 2 by volume.

218·167, calcd 218·167). It afforded 2,4-DNP, m.p. 152–153°, R_f = 0·70 (hexane-EtOAc, 1:1), λ_{max}^{EtOH} 373 nm (ε 13,000). Chemical composition of the predominant ions of chiloscyphone were determined in the high-resolution mass spectrometry as follows.

m/e	Composition	Found	Calcd
41	C_3H_5	41·040	41·039
55	C_3H_3O	55·019	55·018
	C_4H_7	55·055	55·055
69	C_4H_5O	69·034	69·034
	C_5H_9	69·070	69·070
79	C_6H_7	79·054	79·055
91	C_7H_7	91·054	91·055
107	C_7H_7O	107·051	107·050
	C_8H_{11}	107·086	107·086
122	$C_8H_{10}O$	122·070	122·073
	C_9H_{14}	122·112	122·110
147	$C_{10}H_{11}O$	147·084	147·081
	$C_{11}H_{15}$	147·116	147·117
175	$C_{12}H_{15}O$	175·113	175·112
203	$C_{14}H_{19}O$	203·143	203·143
218	$C_{15}H_{22}O$	218·167	218·167

Preparation of tetrahydro-chiloscyphone. Chiloscyphone (200 mg) was hydrogenated over Adams catalyst (20 mg) in glacial AcOH (6 ml) at room temp. When about 2 molar equivs of H_2 was taken up, the reaction ceased. The mixture was then filtered, and the filtrate, after being diluted with water, was extracted with ether. The ether soln was washed with 5% $NaHCO_3$ aq and with H_2O, dried over Na_2SO_4 and distilled to remove the solvent. The hydrogenated product thus obtained ($[\alpha]_D^{25}$ +109·0°, 1·2% in $CHCl_3$; n_D^{25} 1·4719) showed only one peak or spot on GLC (DEGS and NGS) or TLC (C_6H_6–$CHCl_3$, 1:1, R_f = 0·47): $C_{15}H_{26}O$ (M^+, obsd 222·201, calcd 222·198), ν 1702, 1454, 1374, 1364, 1298, 1209, 1116, 1092, 1047, 1023 and 989 cm^{-1}. δ 0·56 (3H, d, J = 7·0 Hz), 1·10–1·20 (3H × 3, complex), 2·73 (1H, q, J = 14·5 and 7·5 Hz). m/e 41 (37%), 55 (12), 69 (28), 81 (36), 95 (92), 109 (95), 121 (16), 136 (base ion), 151 (40), 161 (18), 179 (27), 204 (14) and 222 (M^+, 23).

Preparation of dihydro-chiloscyphone. The ketone (100 mg) was hydrogenated with 10% Pd-C catalyst (25 mg) in EtOH (6 ml). When one equiv of H_2 was absorbed, the dihydro product was separated as oily matter according to the procedure mentioned: R_f = 0·50 (C_6H_6–$CHCl_3$, 1:1). ν 1703, 1461, 1366, 1298, 1200, 1116, 1101, 1066, 1043, 991 and 850 cm^{-1}. m/e 43 (base ion), 55 (28), 71 (26), 81 (27), 93 (29), 107 (38), 123 (27), 149 (31), 163 (14), 177 (10), 202 (2), 205 (2) and 220 (M^+, 4).

Dehydrogenation of chiloscyphone. Chiloscyphone (150 mg) was heated with 10% Pd-C (300 mg) in a sealed tube at 300° for 30 min. The product was taken up in hexane, and eluted over silica gel with the same solvent. The eluate was subjected to preparative GLC using PEG 6000 (10%), cadalene being isolated as a major product. The IR and mass spectra, ν 1630, 1605, 1517, 1464, 1443, 1387, 1365, 1165, 1105, 1062, 833, 808 and 778 cm^{-1}; m/e 141 (8%), 153 (19), 168 (25), 183 (base ion) and 198 (M^+, 53), were identical with those of cadalene.[3]

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