

Absolute Configurations of the Liverwort Sesquiterpenoids, (–)-Chiloscyphone and (+)-Chiloscypholone: Total Synthesis of Optically Active Compounds

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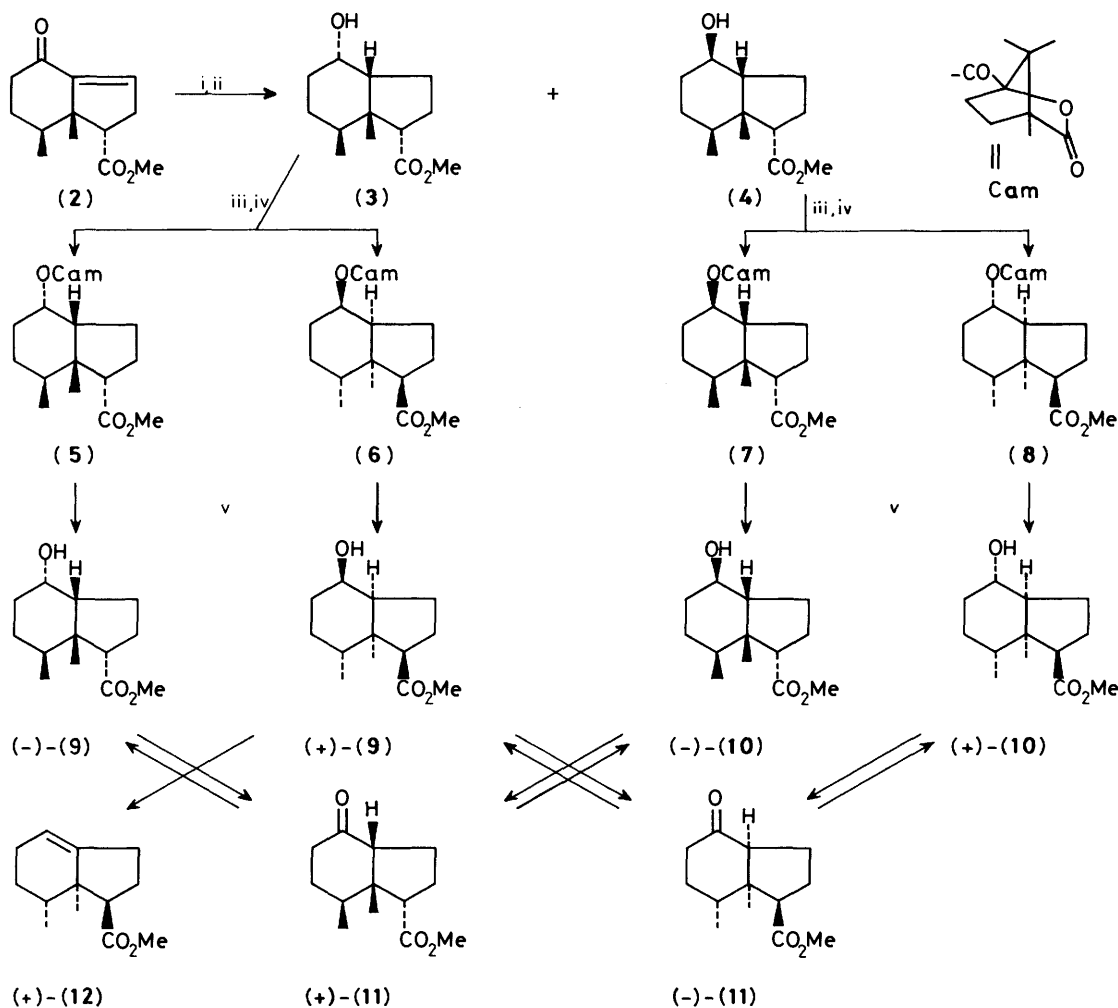
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The absolute configurations of (–)-chiloscyphone and (+)-chiloscypholone isolated from the liverworts *Chiloscyphus polyanthos* and *C. pallescens* have been determined by the total synthesis of the optically active compounds. The key intermediate alcohol has been resolved by the use of (1*S*)-(–)-camphanic chloride.

Since some of the terpenoids and/or aromatic compounds produced by liverwort have optical rotations of opposite sign to that commonly found in higher plants, it is both interesting and important to determine their absolute configurations. The structure of (–)-chiloscyphone (1), first isolated from the liverwort *Chiloscyphus polyanthos* by Matsuo,² was revised by Connolly and his associates³ who, at the same time, also found (+)-chiloscypholone in *C. pallescens*.³ Since, however, the absolute configurations of these compounds remained unknown, we planned the total synthesis of the optically active isomers *via* resolution of the key intermediate alcohol by

esterification with (*S*)-(–)-camphanic chloride. We now report the preliminary results of our investigations.

The enone (2), prepared from 3,4-dimethylcyclohex-2-enone by intramolecular aldol condensation,⁴ was hydrogenated and reduced to afford two isomeric alcohols (3) and (4). Each alcohol was esterified with (1*S*)-(–)-camphanic chloride (*N,N*-dimethylaminopyridine–CH₂Cl₂–pyridine) to form a mixture of diastereoisomers (5)–(8) (see Scheme 1). Separation of these isomers was achieved by h.p.l.c. [JASCO TRI ROTAR-V, KNAUER RI detector, NUCLEOSIL 50-5 10X250; hexane–EtOAc (9:1)] to give (5) (95 mg), (6) (96 mg), (7) (85 mg), and (8)



Scheme 1. Reagents: i, H₂/Pd-C; ii, NaBH₄; iii, (1*S*)-(–)-camphanic chloride; iv, h.p.l.c.; v, KOH, MeOH

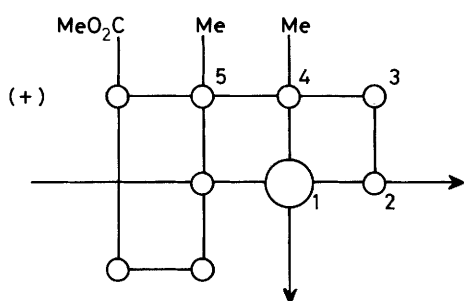
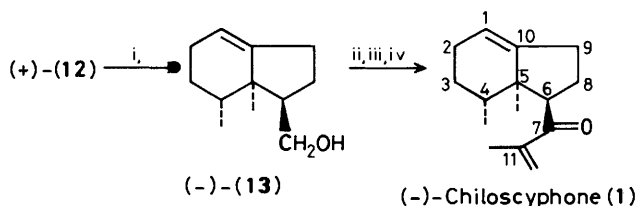


Figure. Back octant for (+)-(11)

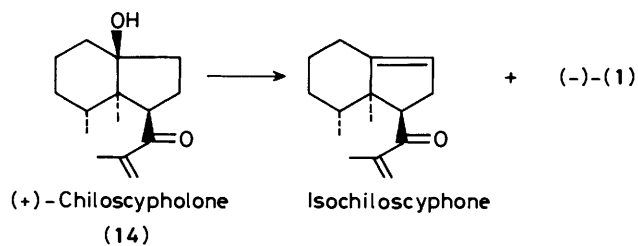


Scheme 2. Reagents: i, LiAlH₄; ii, Swern oxidation; iii, CH₂=C(Me)-MgBr, THF, 0 °C; iv, Jones oxidation

* All the new compounds show satisfactory spectral and analytical data.

† (+)-(11): $[\alpha]_D^{25} +29.8^\circ$ (*c* 1.9 in CHCl₃); ν_{\max} (film) 1720 and 1700; δ_H (CDCl₃) 3.66 (3 H, s, OMe), 1.15 (3 H, s, Me), and 0.80 (3 H, d, *J* 6.2 Hz, 4-Me); *m/z* 224 (*M*⁺), 192, 164, and 147 (base); $[\theta]_{289\text{nm}}^{25} = +1984$ ($\Delta\epsilon +0.60$). (-)-(11): $[\alpha]_D^{25} -25.0^\circ$ (*c* 2.3 in CHCl₃); ν_{\max} (film) 1720 and 1700 cm⁻¹; δ_H (CDCl₃) 3.66 (3 H, s, OMe), 1.15 (3 H, s, Me), and 0.80 (3 H, d, *J* 6.2 Hz, 4-Me); *m/z* 224 (*M*⁺), 192, 164, and 147 (base); $[\theta]_{289\text{nm}}^{25} = -2176$ ($\Delta\epsilon -0.66$).

‡ The synthetic material showed spectral data identical with those reported in the literature,² including the c.d. spectrum.



(101 mg).^{*} These camphanic esters were hydrolysed (KOH-MeOH, at room temp. for 5 h) to afford (-)-(9), (+)-(9), (-)-(10), and (+)-(10).[†] Ketones (11)[‡] derived from these alcohols showed antipodal c.d. curves, from which the absolute configuration was determined as depicted in the Figure by application of the back octant for (+)-(11).

Compound (+)-(9) was dehydrated (POCl₃-pyridine at 100 °C) to give a trisubstituted olefin (+)-(12), which was converted into (-)-(1) [$\alpha]_D^{25} -15.1^\circ$ (*c* 0.4 in CHCl₃)][‡] [*lit.*,³ -24.4° (*c* 0.76 in CHCl₃)] in four steps (see Scheme 2).

Since (+)-chiloscypholone (14) was converted into (-)-(1),³ the absolute configuration of (14) was also determined as depicted in the Figure.

References

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