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Revised Structure of a Brasilane-Type Sesquiterpene Isolated from the Red Alga *Laurencia implicata* and its Absolute Configuration

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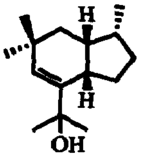
***Abstract*:**. The structure of a brasilane-type sesquiterpene, isolated from the red alga *Laurencia implicata*, has been revised by total synthesis of three kinds of isomers, one of which with the correct stereostructure has been synthesized as an optically active form to establish the absolute configuration.

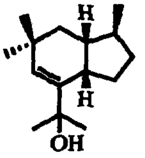
The absolute configuration of terpenoids isolated from liverworts is very complicated and interesting.[1] We have synthesized conocephalenol [(-)-**4**], with a brasilane-type, to establish the relative and absolute structure.[2] Since the structure of a brasilane-type sesquiterpene (-)-**1** reported by the Swiss group[3] is very similar to that of conocephalenol [(-)-**4**][2] or tamariscol [(-)-**5**][4] and its absolute configuration has not been determined, we have been interested in the synthesis of compound **1**. We now report our preliminary results concerning revision of the structure for **1** into **3** including its absolute configuration.

In order to prepare the isomeric compounds due to the sec-methyl group at the five-membered ring, we started from 5,5-dimethyl-2-cyclohexen-1-one (**6**) and used 1,4-addition and intramolecular aldol cyclization as shown in the Scheme. Alkylation of the cis-hydrindanones, **10** and **11**, afforded predominantly α-alkyl compounds in each case. Four steps conversion of these alcohols gave the desired compounds, **1** [δ_H (C_6D_6) 5.48 (br s, H-4), 1.26, 1.24, 1.04, 0.96 (each s, Me), 0.98 (d, J=6.4, Me); δ_C ($CDCl_3$) 15.4, 28.8, 30.2, 30.5, 31.0, 31.9, 32.25, 32.33, 32.6, 37.1, 40.3, 40.9, 73.1, 129.7, 145.2] and **2** [δ_H (C_6D_6) 5.53 (br s, H-4), 1.27, 1.27, 1.01, 0.97 (each s, Me), 1.00 (d, J=7.3, Me); δ_C ($CDCl_3$) 22.5, 28.6, 30.7, 31.1, 31.7, 32.8, 33.3, 33.3, 38.3, 39.6, 41.3, 44.0, 72.7, 130.1, 145.2] respectively. However, neither **1** nor **2** was identical with the natural one. Thus we thought that the compound must have a **trans** junction.

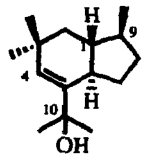
As we used the methyl ester **13** on the way to synthesize conocephalenol [(-)-**4**],[2] compound **13** was converted into the **trans** product **3** [δ_H ($CDCl_3$) 5.36 (br s, H-4), 1.36, 1.33, 1.02, 0.98 (each s, Me), 0.99 (d, J=6.3, Me); δ_H (C_6D_6) 5.45 (br s, H-4), 1.29, 1.27, 1.05, 1.03 (each s, Me), 1.01 (d, J=6.9, Me); δ_C ($CDCl_3$) 19.0, 29.2, 29.78, 29.83, 29.9, 31.9, 32.3, 34.5, 36.4, 40.8, 45.8, 49.4, 73.3, 130.9, 143.6]. The spectral data of **3** are in very good agreement with those of the natural one.[3] Thus, the structure should be revised to have a trans junction with a cis methyl group to the proton at the C-1 position. Synthesis of the optically active compound was carried out by optical resolution of an alcohol **14** as its camphanoyl ester.[1] The absolute configuration of the ketone (+)-**15** was determined by the CD spectrum (Δε298nm +2.6). Compound **3** derived from (+)-**15** showed the specific rotation $[\alpha]_D$ -11.5° (c=4.2, $CHCl_3$),[3] thus establishing the absolute configuration of (-)-**3** as in the formula.



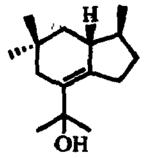
1



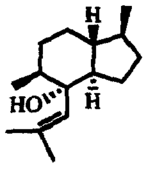
2



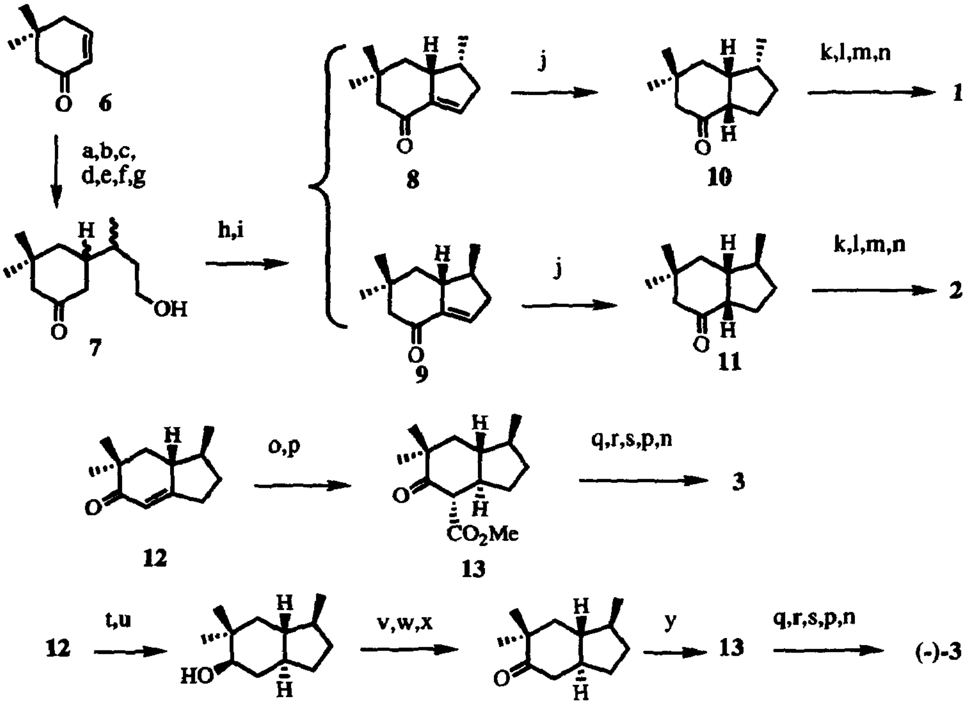
(-)-**3**



(-)-**4**



(-)-**5**



Scheme

a) CH_2=CHMgBr/CuBr/Me_2S; b) $HOCH_2CH_2OH$/TsOH; c) $PdCl_2/CuCl_2$/DMF-H_2O; d) $(MeO)_2P(O)CH_2CO_2Me$/NaH; e) H_2/Pd-C; f) $LiAlH_4$; g) TsOH/THF-H_2O; h) Swern oxid. i) TsOH/PhH/reflux; j) H_2/PtO_2/hexane; k) CH_2=C(Me)MgBr; l) O_3; Me_2S; m) $SOCl_2$; n) MeLi o) Li/NH_3; CO_2; p) CH_2N_2; q) L-Selectride; r) BzCl; s) tBuOK; t) Li/NH_3; u) $NaBH_4$ v) 1(S)-(-)-camphanyl chloride/DMAP/Et_3N; HPLC; w) KOH; x) Jones; y) LDA/$NCCO_2Me$

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