# X-Ray Structure and Absolute Stereochemistry of Stemarin, a Diterpene with a New Skeleton

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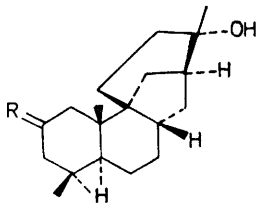
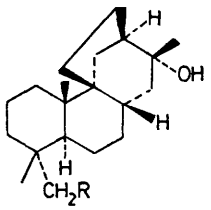
*Summary* The structure and absolute stereochemistry of stemarin, a novel tetracyclic diterpene isolated from *Stemodia maritima* L. and shown to possess a new skeleton, were determined with the aid of spectral and *X*-ray crystallographic analyses.

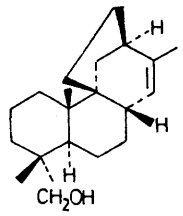
RECENTLY we reported[1] the isolation from *Stemodia maritima* L. (Scrophulariaceae)[2] of stemodin (**1**) and stemodinone (**2**) which, with aphidicolin,[3] represent a new class of diterpenoids. Further examination of *S. maritima* has now resulted in the isolation of a novel tetracyclic diterpene,



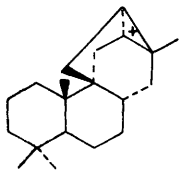
(1) R = α-OH, β-H
(2) R = O
(3) R = $H_2$



(4) R = OH
(5) R = $OSO_2C_6H_4Me$-*p*
(6) R = H



(7)



(8)

stemarin (**4**), whose structure has revealed it to possess a new skeleton, for which we propose the name stemarane.

Stemarin (**4**), $C_{20}H_{34}O_2$, ($M^+$ 306), m.p. 183—184 °C, $[\alpha]_D^{25}$ + 17·8 (MeOH, c 1·01), showed OH (3300 $cm^{-1}$) but no C=O i.r. absorptions ($CHCl_3$). The $^1H$ n.m.r.

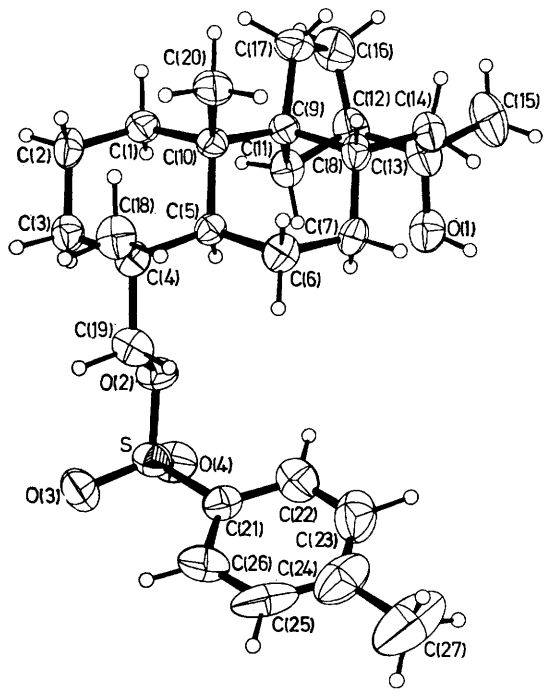



FIGURE. A perspective view of the *X*-ray diffraction structure of stemarin tosylate (**5**).

spectrum [$(CD_3)_2SO$] displayed signals at δ 0·66 (3H, s, Me), 0·90 (3H, s, Me), 1·00 (3H, s, Me), 3·01 (2H, d of q, *J* 11 and 5 Hz, $CH_2OH$, collapsing into an AB quartet on $D_2O$

addition, $J$ 11 Hz),[4] 3·80 (1H, s, OH), and 4·40 (1H, t, $J$ 5 Hz, OH).

Mild dehydration of (**4**) with $HClO_4$ ($Me_2CO$, molecular sieves, 2 h, 25 °C) gave (**7**), $[\alpha]_D^{25}$ + 72·8 ($CHCl_3$, c 0·84), δ 5·00 (1H, d of q, $J$ 5 and 1 Hz). Dehydration of (**1**) and (**2**) gave products[1] showing a broad singlet at δ 5·00. Treatment of stemarin with toluene-*p*-sulphonyl chloride (pyridine, 25 °C, 16 h) gave the tosylate (**5**), m.p. 126—127 °C, $[\alpha]_D^{25}$ + 29·4 ($CHCl_3$, c 1·02), which on reduction ($NaBH_4$–$Me_2SO$, 90 °C, 24 h) gave (**6**) rather than deoxystemodinone (**3**), which was also isolated from *S. maritima*. The preceding evidence suggests that stemarin does not belong to the stemodin group of diterpenoids.

The structure and absolute stereochemistry of stemarin (**4**) were determined through *X*-ray crystallographic analysis of the tosylate (**5**). Crystals of (**5**), $C_{27}H_{40}O_4S.\frac{1}{2}H_2O$, are orthorhombic, space group $P2_12_12_1$, with $a$ = 7·053(4), $b$ = 22·080(6), $c$ = 32·922(10) Å, and $Z$ = 8. The data were collected on a computer-controlled four-circle diffractometer ($\theta$–$2\theta$ scans, Ni-filtered Cu-$K_\alpha$ radiation). The structure was solved by a multiple solution procedure[5] and was refined by block diagonal least squares in which the matrix was partitioned into three blocks.

The absolute stereochemistry was established by refining each antipode separately and was taken as the one corresponding to the lower weighted $R$ value (0·0900 *vs.* 0·0935). This difference is significant at the 0·995 confidence level.[6] The final discrepancy index is $R$ = 0·071 for 4392 observed reflections (non-hydrogen atoms anisotropic, hydrogens isotropic). The conformation and absolute stereochemistry of (**5**) are shown in the Figure.

Pimaradiene and, by conjecture, 13-*epi*-pimaradiene have been implicated[7] recently in the biogenesis of aphidicolin and stemodin respectively. Although stemarin may also be derived from a pimaradiene precursor *via* the carbocation (**8**),[8] neither the stereoelectronic requirements for cyclisation of a pimaradiene precursor to a tetracyclic system[9] nor the involvement of other skeletal types (*e.g.*, a strobane precursor[10]) should be ignored.

(*Received, 28th August*, 1975; *Com.* 986.)

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