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NEW TERPENE HYDROCARBONS FROM THE  
SPONGE *HIGGINZIA* SP.

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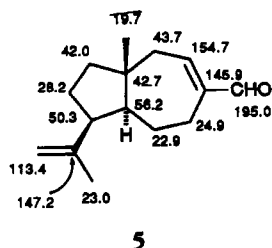
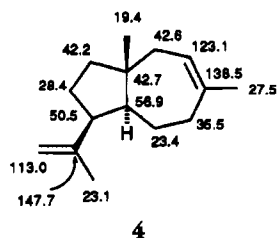
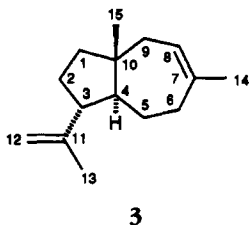
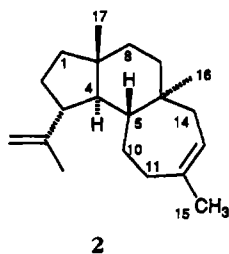
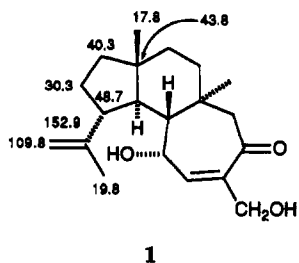
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ABSTRACT.—The isolation and structures of a new tricyclic diterpene **2** and a new daucadiene sesquiterpene hydrocarbon **3** from the sponge *Higginsia* sp. are described. Revision of the relative stereochemistry of a previously reported daucadiene hydrocarbon is suggested.

In a previous report, we described the isolation and structures of three oxygenated tricyclic diterpenes from an unclassified rare sponge *Higginsia* sp. (order Axinellidae, family Desmoxiidae) (1). The structures of these diterpenes were determined by spectroscopic analysis and secured by an X-ray crystallography study on the dihydroxy ketone **1**. This paper reports the structure of a diterpene **2** and a sesquiterpene hydrocarbon **3** from the nonpolar fraction of the lipophilic extract from this sponge.

The sponge was diced and extracted

with MeOH-CH<sub>2</sub>Cl<sub>2</sub> (1:1), and the CH<sub>2</sub>Cl<sub>2</sub>-soluble extract was filtered through Si gel. Elution with petroleum ether yielded a fraction containing two hydrocarbons (gc-ms) which could be separated by preparative gc. The less volatile compound **2** showed an [M]<sup>+</sup> at *m/z* 272, corresponding to C<sub>20</sub>H<sub>32</sub>. The <sup>1</sup>H-nmr spectrum showed signals for two tertiary methyl (δ<sub>H</sub> 0.79 and 0.85) and a vinylic methyl group (δ<sub>H</sub> 1.68) coupled (*J*=1 Hz) to two mutually coupled vinylic protons (δ<sub>H</sub> 4.56 and 4.66, *J*=2.0 Hz), indicating an isopropenyl group. A



second vinylic methyl ( $\delta_{\text{H}}$  1.52) showed long-range coupling to a vinylic proton ( $\delta_{\text{H}}$  5.33, br t,  $J=6$  Hz). Irradiation of this proton showed it to be coupled to a methylene which appeared as an AB quartet ( $\delta_{\text{A}}$  2.0 and  $\delta_{\text{B}}$  1.7). The ms showed major ions arising from fragmentations similar to those observed for the oxygenated counterpart **1** and its congeners (1). The position of the double bond in **2** leads to the suggestion that the nuclear oxygenation pattern present in the cometabolites (e.g., **1**) arises from **2** via a 10,12-diene which can interact with oxygen in a [4+2] cycloaddition reaction.

From ms ( $[\text{M}]^+$  204) and the  $^{13}\text{C}$ -nmr spectrum, the sesquiterpene hydrocarbon was assigned the formula  $\text{C}_{15}\text{H}_{24}$ . An analysis of its  $^1\text{H}$ -nmr spectrum and decoupling experiments revealed the presence of an isopropenyl group and a trisubstituted double bond carrying a methyl, similar to those observed in **2**. This analysis resulted in structure **3**. Furthermore, the ms showed a major ion at  $m/z$  121, attributed to the cleavage of C-9-C-10 and C-4-C-5. This ion is dominant in the ms of **1** and **2**.

The  $^{13}\text{C}$ -nmr spectrum (Figure 1) was critical in the assignment of the relative stereochemistry to **3**. Of the three quartets observed, that resonating at  $\delta_{\text{C}}$  27.4 was assigned to the vinylic methyl in the cycloheptene ring. The corresponding methyl in 1-methylcycloheptene occurs at  $\delta_{\text{C}}$  26.4, significantly different from that of the same group in 1-methylcyclohexene ( $\delta_{\text{C}}$  23.4) (2). The other two methyls, resonating at  $\delta_{\text{C}}$  18.4 and 19.9, were assigned to C-15 and C-13, respectively. These values are in good

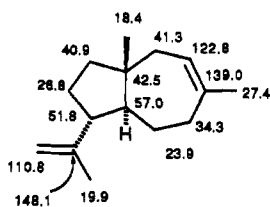


FIGURE 1.  $^{13}\text{C}$ -nmr data of compound **3**.

agreement with those observed for the corresponding carbons in **1**, as is the value for C-12. The trans ring junction follows from the chemical shift ( $\delta_{\text{C}}$  18.4) of the methyl at C-10. For a cis arrangement, values of ca. 25 are expected (3). These observations allow the structure and relative stereochemistry of the sesquiterpene hydrocarbon to be depicted as shown in **3**.

A compound corresponding to **3** has been reported as a metabolite of *Vernonia galpinii* (4). Although its ms had identical fragment ions, its optical rotation and spectroscopic parameters were significantly different to those obtained for **3**. Furthermore, the  $^{13}\text{C}$ -nmr spectral assignments for the *V. galpinii* metabolite seemed to be incorrect. In particular, C-14 was assigned a chemical shift of 23.1 which, as mentioned above, does not correspond to a methyl on a cycloheptene ring. In fact, the carbon chemical shifts observed seemed to be better accommodated if, in this compound, the methyl and the isopropenyl groups were trans-arranged as shown in **4**. To obtain support for this reassignment, we searched for a suitable model system. One such system is the carotane (daucane) aldehyde **5**, which co-occurs with related compounds, including the corresponding acid, in the leaves of *Rosa rugosa* (5). The structure of **5** was assigned by spectroscopic techniques, including CH-COSY, and the stereochemistry was indicated from nOe experiments. The assignments of the carbon chemical shift were therefore soundly based with the exception of C-7 and C-11, which had been assigned the values of 147.2 and 145.9, respectively. The acid corresponding to **5** shows these two carbons at 134.0 and 147.4. Consequently, the original assignments have to be reversed. This change has been made in the values shown in structure **5**. Comparison of the carbon chemical shifts obtained for **4**, after reassignment, with those of **5** shows remarkable agreement for all by C-7-C-9 and C-14, sites ex-

pected to be influenced by the oxygenation present in **5**. Thus, it would appear that the relative stereochemistry ( $3S^*,4S^*,10R^*$ ) originally assigned to the sesquiterpene hydrocarbon from *V. galpinii* (**4**) has to be changed to  $3R^*,4S^*,10R^*$ .

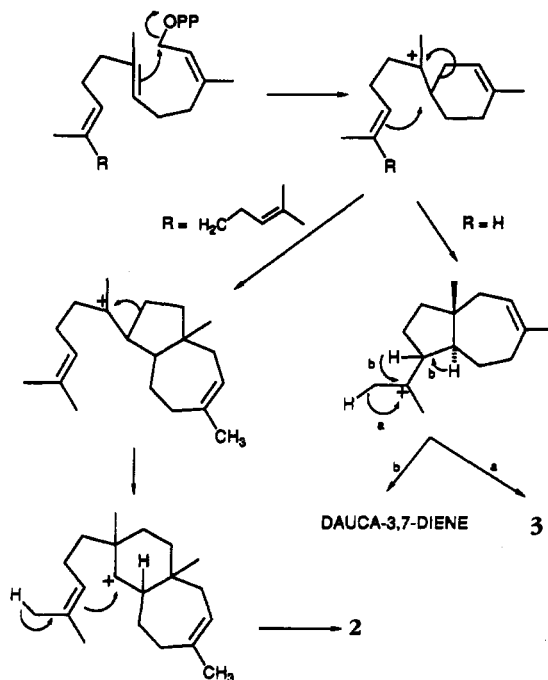
Although most daucane sesquiterpenes seem to arise from a hydrocarbon with a 3,4-ene, metabolites **3**, **4**, and **5** appear to reflect an alternative, and simpler, termination of the cyclization process (Scheme 1). The hydrocarbons **2** and **3** share the same relative stereochemistry which is interesting from the biosynthetic point of view. In essence, initial cyclization in the elaboration of both the sesquiterpene and diterpene nucleus (**6**) can be considered to be similar (Scheme 1). For the sesquiterpene pathway, migration of the other  $\sigma$  bond in the first proposed intermediate allows the formation of the isodaucane skeleton to be rationalized.

## EXPERIMENTAL

**GENERAL EXPERIMENTAL PROCEDURES.**—Experimental details have been recorded previously (7). A specimen of *Higginsia* sp. (WAM-145-82) has been deposited with the Western Australian Museum.

**EXTRACTION AND ISOLATION.**—A detailed description of the extraction of the sponge (72 g) has been given (1). The crude dried extract (780 mg, oil) was added to Si gel and eluted successively with petroleum ether,  $\text{CH}_2\text{Cl}_2$ , and EtOAc. The fraction eluted with petroleum ether contained two compounds as determined by gc-ms. These were separated by preparative gc (3% OV-17 on Chromasorb W, 60-80 mesh; Varian Aerograph 1800) to give the diterpene hydrocarbon **2** (5 mg, Rt 22 min) and the sesquiterpene hydrocarbon **3** (20 mg, Rt 8 min).

**Diterpene hydrocarbon 2.**—Colorless oil:  $[\alpha]_D^{25} -28^\circ$  ( $c=0.4$ ;  $\text{CHCl}_3$ );  $\nu_{\text{max}}$  ( $\text{CCl}_4$ ) 3075 (w), 2915 (s), 1640 (w)  $\text{cm}^{-1}$ ;  $^1\text{H}$  nmr (80 MHz,  $\text{CDCl}_3$ )  $\delta$  0.79 and 0.85 (each s, 3H,  $\text{H}_3$ -16 and  $\text{H}_3$ -17), 1.52 (br s, 3H,  $\text{H}_3$ -15), 1.68 (br s, 3H,  $\text{H}_3$ -20), 4.56 (br d, 1H,  $J=2$  Hz,  $\text{H}_1$ -19), 4.66 (br d, 1H,  $J=2$  Hz,  $\text{H}_2$ -19), 5.33 (br t, 1H,  $J=6$  Hz,  $\text{H}_1$ -13); ms  $m/z$  (% rel. int.)  $[\text{M}]^+$  272 (24), 257 (36), 229 (11), 203 (22), 191 (84), 189 (96), 149 (18),



SCHEME 1. Hypothetical sequence for the biosynthesis of the *Higginsia* terpene hydrocarbons.

147 (61), 135 (35), 133 (50), 121 (100), 107 (85), 93 (56), 91 (52), 69 (29).

*Sesquiterpene hydrocarbon 3*.—Colorless oil:  $[\alpha]_D -7.0^\circ$  ( $c=1.1$ ,  $\text{CHCl}_3$ );  $\nu_{\text{max}}$  ( $\text{CCl}_4$ ) 3075 (w), 2915 (s), 1640 (w), 1450 (m), 1375 (m)  $\text{cm}^{-1}$ ;  $^1\text{H}$  nmr (90 MHz,  $\text{CDCl}_3$ )  $\delta$  0.74 (s, 3H,  $\text{H}_3$ -15), 1.67 (t, 3H,  $J=1$  Hz,  $\text{H}_3$ -13), 1.74 (br s,  $\text{H}_3$ -14), 4.66 (br d, 1H,  $J=2$  Hz,  $\text{H}_4$ -12), 4.67 (br d, 1H,  $J=2$  Hz,  $\text{H}_5$ -12), 5.38 (br t, 1H,  $J=6.5$  Hz, H-6);  $^{13}\text{C}$  nmr see Figure 1; ms  $m/z$  (% rel. int.)  $[\text{M}]^+$  204 (23), 189 (29), 175 (11), 163 (2), 161 (23), 147 (25), 134 (19), 121 (88), 119 (35), 107 (67), 93 (100), 91 (34).

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