Phytochemistry, Vol. 28, No. 5, pp. 1425-1426, 1989.
Printed in Great Britain.

0031-9422/89 \$3.00 + 0.00

SESQUITERPENES FROM *EREMOPHILA* SPECIES

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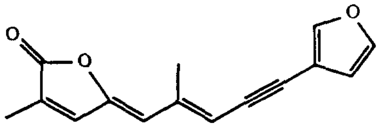
(Received 29 September 1988)

Key Word Index—*Eremophila*; Myoporaceae; sesquiterpene butenolide; (+)-oplopanone.

Abstract-The structure of a new bis-butenolide sesquiterpene, a likely precursor of the acetylenic sesquiterpene freelingyne, from *Eremophila* spp. is described. The isolation of (+)-oplopanone from ***E.** miniata* is reported.

Several classes of sesquiterpenes have been isolated from *Eremophila* species (family Myoporaceae) and these can be divided into two groups. On the one hand the carbocyclic group contains examples of cadinane [1], eremophilane [2, 3], eudesmane [4], aromadendrane [5], and zizane [6] types, and on the other hand one finds a large group of furanosesquiterpenes [7–10] of which freelingyne (1) the first acetylenic sesquiterpene described [9], is perhaps the more remarkable. In our work on the phytochemistry of *Eremophila we* have investigated the sesquiterpenes of *Eremophila* sp. nov and ***E.** miniata.* We report on the structure of a new sesquiterpene from *Eremophila* sp. nov and the isolation of (+)-oplopanone from ***E.** miniata.*

Extraction of a sample of ***Eremophila*** sp. nov with ether afforded an extract which appeared to consist of fatty material and flavones. Further extraction of the plant material with methanol yielded an extract, the dichloromethane soluble portion of which appeared to contain mainly one compound. Purification by column chromatography provided the bis-butenolide (**2**), $C_{15}H_{18}O_4$, as a semi-solid oil, whose structure was assigned as follows. The ^{13}C NMR spectrum contained resonances for two carboxylate carbons (singlets at δ 174.14, 170.24), three trisubstituted double bonds (6 131.79, 129.96, 126.51, *s*; 148.85, 126.51, 115.49, d) and two carbons attached to oxygen atoms (679.70, *d*; 73.19, t). The IR spectrum showed absorption at 1750 cm^{-1} which, with the absence of absorption due to carboxylic acid or hydroxyl group, indicated the presence of two α,β-unsaturated y-lactones. The ^{1}H NMR spectrum included signals for a β-proton of one of these lactone units at δ 6.98 *(dq)* which was shown to have coupling (*J* 1.6 Hz) to a vinylic methyl (6 1.83) and (*J* 1.6 Hz) to an allylic oxymethine (6 4.91) which in turn showed coupling (*J* 7.6 Hz) to an allylic methylene group (6 2.28). These results define the connectivity C-8-C-13 in structure 2 which is supported by the correspondence between the chemical shifts of hydrogens at C-9, C-10 and C-12 with the comparable ones in freelingnite (3) [11]. The C-l to C-8 portion of 2 was deduced from extensive ^{1}H–^{1}H decoupling experiments. Thus an a-proton of an α,β-unsaturated carbonyl system at δ 5.78 was found to have long-range coupling to an allylic oxymethylene group (6 4.69, ***d***, *J* = 1.7 Hz) and to an allylic methylene (6 2.40) which in turn was strongly coupled to a second methylene (6 2.18) itself coupled (*J* = 7.0 Hz) to a vinylic proton (δ 5.18). This proton showed coupling to a second vinyl methyl (6 1.64). Thus the gross structure of the new sesquiterpene from *Eremophila* sp. nov is represented by 2.



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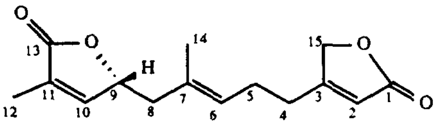

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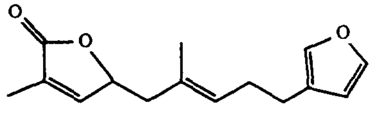

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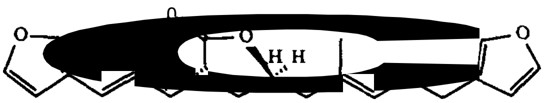

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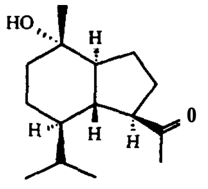

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The E-configuration of the double bond at C-6 is assigned from the chemical shift of C-14 (6 16.82). The remaining point of configuration at C-9 is tentatively assumed as ***R*** by comparison of the optical rotations of 2 ($[\alpha]_D + 21.5°$) with that of the marine furanoterpene (4) ($[\alpha]_D -$ 16.8') of known (S) absolute configuration [12]. In this context it is worth noting that freelingnite **(3)**, of unknown absolute configuration, has the same sign for the optical rotation ($[\alpha]_D +$ **11.5")**) [11] as 2, a probable precursor.

Extraction of a sample of *E.* ***miniata*** and separation of the neutral lipophilic metabolites yielded myoporone, a furanosesquiterpene diketone, previously isolated from ***Myoporum*** *deserti* [13] and another sesquiterpene whose structure, as deduced from spectroscopic data, corresponded to that of oplopanone. This compound has been isolated from the Japanese shrub ***Oplopanax japonicus,*** and the absolute configuration of the (-)-enantiomer has been assigned [14]. The sample from *E.* ***miniata*** was shown to be the (+)-enantiomer and must be represented by structure 5. (A literature search revealed that (+)-oplopanone (5) may have been isolated previously, but not recognised as such, from the marine alga ***Laurencia subopposita*** [15]. In this paper the authors state "that the melting point (93-94") was undepressed on admixture with an authentic sample [of (-)-oplopanone]", represent their compound with the stereochemistry of (−)-oplopanone but quote an $[\alpha]_D + 13°$.} The isolation of (+)-oplopanone from *E.* ***miniata*** extends the number of cases, already observed for the calamenene [1] and zizaene [6] sesquiterpenes, where ***Eremophila*** species elaborate the opposite enantiomer to that obtained from other terrestrial sources.

EXPERIMENTAL

General experimental details have been described **[16]**. A voucher specimen of the plant has been deposited in the State Herbarium, Adelaide, Australia (No. 4011).

Extraction of Eremophila *sp. nov.* Leaves and terminal branches of the plant (10.2 g), collected I.6 km north of Cue in Western Australia, were washed with Et_2O and then soaked in **MeOH** overnight. The Et_2O extract, which from 'HNMR appeared to consist mainly of fat with a trace of **flavones**, was not investigated further. The **MeOH** soluble residue (2.1 g) was extracted with CH_2Cl_2 and the soluble portion (0.8 g) was adsorbed on a column of silicic acid (30 g). Elution with CH_2Cl_2 and CH_2Cl_2–30% EtOAc gave fractions (280 mg) of the **bis-butenolide (2)**, amorphous solid, $[\alpha]_D + 21.5°$, ($CHCl_3$; *c* 3.0), $[\alpha]_{578} + 22.7°$, $[\alpha]_{546} + 26.8°$, $[\alpha]_{436} + 57.4°$, $[\alpha]_{365} + 57.1°$. $\nu_{max}^{CHCl_3}$ 1750 cm^{-1}; 'HNMR (300 MHz, $CDCl_3$) 66.98 (1H, dq, $J_{9,10} = J_{10,12} = 1.6$ Hz, H-10), 5.78 (1H, app. quintet, $J_{2,4} = J_{2,15} = 1.7$ Hz, H-2), 5.18 (1H, *dq*, $J_{5,6} = 7.0$ Hz, $J_{6,14} = 1.3$ Hz, H-6), 4.91 (1H, *dtq*, $J_{9,10} = 1.6$ Hz, $J_{8,9} = 7.6$ Hz, $J_{9,12} = 1.8$ Hz, H-9), 4.69 (2H, ***d,*** $J_{2,15}$ = 1.7 Hz, H_2-15), 2.40 (2H, *m*, H_2-4), 2.28 (4H, *m*, H_2-5, H_2-8), 1.83 (3H, dd, $J_{9,12}$ = 1.8 Hz, $J_{10,12}$ = 1.6 Hz, H_3-12), 1.64 (3H, ***d,*** $J_{6,14}$ = 1.3 Hz, H_3-14); ^{13}C NMR (75.5 MHz, CDCI,) δ 10.61 (*q*, C-12), 16.82 (*q*, C-14). 25.87 and 28.34 (c, C-4 and C-5), 43.27 (*t*, C-8), 73.19 (*t*, C-8), 73.19 (*t*, C-IS), 79.70 (*d*, C-9), 115.49 ***(d,*** C-2), 126.51 (*d*, C-6), 126.51 and 129.96 (s, C-3, C-11), 131.79 (*s*, C-7), 148.85 (*d*, C-10), 170.24(s), 174.14(s). **EIMS,** m/z (rel. int.) 262 [M]' (I), 244 (1), 165 (100), 151 (16), 150 (27), 147 (16), 119 (15), 105 (15), 98 (69), 97 (83), GC/MS (X-linked Me silicone gum, 0.31 mm × 25 m WCOT capillary 100–260° at 20°/min) (CI_{Me}): R_t 12.1 min, m/z (rel. int.) 263 $[M + 1]^+$ (41) 245 (10), 165 (28). 107 (21), 98 (22). 97 (23), 71 (23), 69 (32), 57 (100).

Extraction of E. miniata. A sample of the flowering plant (169 g), collected 23 km north of Kalgoorlie in Western Australia, was extracted with Et_2O (1.5 1) and the extract was partitioned into neutral (7.03 g). 8% aq. $NaHCO_3$ soluble (2.7 g) and 5% aq. **NaOH** soluble (2.58 g) fractions. A portion (4.07 g) of the neutral fraction was adsorbed onto a column of alumina (Act III; 140 g). Elution with petrol–CH_2Cl_2 (gradient) gave fractions of fat (820 mg), myoporone (115 mg) with identical spectroscopic properties with those reported [13], and (+)-oplopanone (115 mg), which crystallized from Et_2O as needles. mp 85–86°, $[\alpha]_D$ i-20" (CHCI,; *c* 0.4) {lit [4] for the enantiomer, **mp 96–97°**, $[\alpha]_D$ -20" ($CHCl_3$)}. ^1H NMR (300 MHz, $CDCl_3$) δ 0.68 (3H. ***d,*** ***J*** **=** 6.8 Hz) and 0.89 (3H, ***d, J*** **=** 6.9 Hz) (isopropyl methyls). 1.20 (3H, s, tertiary methyl), 2.19 (3H, *s*, MeCO–) 2.66 (1H, m), ^{13}C **NMR** (75.5 MHz, CDCI,) δ 15.5 ***(q),*** 20.2 ***(q).*** 21.9 (2 ***q).*** 22.9 (*t*), 25.2 (*t*), 28.5 (*t*), 29.4 ***(d),*** 41.9 (*t*), 46.6 ***(d),*** 49.3 ***(d),*** 55.8 ***(d),*** 56.9 ***(d),*** 72.9 (s), 211.6 (*s*).

Acknowledgements— We are grateful to Dr R. Chinnock (State Herbarium, Adelaide, South Australia), for providing the sample of ***Eremophila*** sp. nov. and for taxonomic information.

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