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GERIN, A EUDESMANE METHYL ESTER IN TRICHOME EXUDATES OF *GERAEA VISCIDA*

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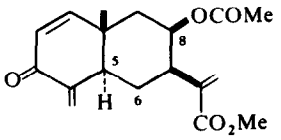
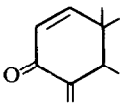
Key Word Index—*Geraea viscida*; Compositae; trichome exudate; gerin; sesquiterpene methyl ester.

Our continuing phytochemical investigations of California plants which are reported to exhibit cytotoxic activity and cause allergic contact dermatitis in humans, prompts us to report the structure elucidation of gerin (**1**), a sesquiterpene methyl ester from *Geraea viscida* (Gray) Blake. This naturally occurring plant constituent, present in copious amounts in the leaf trichomes, belongs to the eudesmane skeletal class of sesquiterpenes, and is similar to arbusculin-E methyl ester, a known eudesmane from *Artemisia arbuscula* var. *arbuscula* [1].

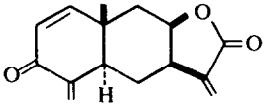


1

Gerin (mp 140.0–141.5°), isolated in 0.12% yield from *Geraea viscida*, had the composition $C_{18}H_{22}O_5$ and its MS exhibited a molecular ion peak at *m/e* 318, along with peaks at *m/e* 275 (M − 43), 258 (M − 60), 247 (M − 75), 232 (M − 86) and a base peak at *m/e* 43. The IR spectrum of **1** contained a very strong band (broad) at 1727 cm^{-1} (ester) and sharp bands at 1670 and 1625 cm^{-1}, indicative of a cross-conjugated dienone system. In addition, gerin showed ultraviolet absorption at 239 nm (ε 11 029) indicating the presence of an α,β-unsaturated ketone unit, and end absorption at 202 nm (ε 11 348). The 250 MHz ^{1}H NMR spectrum of gerin revealed a pair of sharp doublets located at δ 6.86 and 5.99 (1 proton each, J = 10 Hz) having the characteristic AB pattern of a γ,γ-disubstituted cyclohexenone. The presence of a sharp three-proton singlet at δ 1.15 (tertiary methyl) and a pair of signals at δ 6.15 (*q*) and 5.29 (*t*) lead to the conclusion that gerin possessed the partial structure **i**. The spectral characteristics were in very close agreement with the NMR, IR and UV spectra recorded for encelin (**2**), a eudesmanolide isolated from *Encelia farinosa* (Compositae) which also possesses a ring A cross-conjugated dienone system [2].

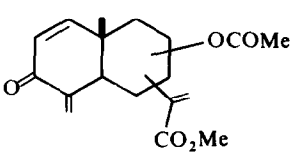


i



2

The presence of a sharp three-proton singlet at δ 1.98 and a one-proton quartet at δ 5.36 suggested the presence of an acetate. In addition, the ^{1}H NMR spectrum revealed a pair of singlets (6.34 and 5.68, one proton each) characteristic of a methylene group conjugated with a carbonyl group. These data, coupled with a three-proton singlet located at 3.78, clearly established the presence of a methyl α-substituted acrylate moiety. These observations lead to the conclusion that gerin possessed the partial structure **ii**.



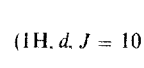
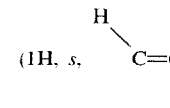
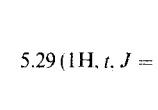
ii

That gerin possessed the structure shown in formula **1** was unambiguously deduced by detailed examination of its expanded 250 MHz ^{1}H NMR spectrum and from spin-decoupling experiments. A doublet of quartets located at δ 2.76 with J = 11.5 and 2.5 Hz was assigned to the axial proton at C-5. The doublet of triplets centered at δ 3.01 with J = 12.0 and 3.0 Hz was attributed to the axial proton situated on C-7. The downfield quartet at δ 5.36 (J = 2.5 Hz) was assigned to the equatorial proton at C-8. Irradiation of the C-8 equatorial proton at δ 5.36 collapsed the doublet of triplets at 3.01 to a doublet of doublets (J = 12.0 and 3.0 Hz) and the complex pattern for the C-9 protons into a simple AB quartet pattern (J = 14.5 Hz). Irradiation at δ 3.01 collapsed, among other things, the quartet centered at 5.36 into a triplet. Irradiation of the C-5 proton (δ 2.76) collapsed the two C-4 exocyclic olefinic protons into doublets, the C-6 axial proton into a doublet of doublets and the C-6 equatorial proton into a doublet of doublets.

Preliminary dermatological testing of gerin indicates that this terpene is a potent contact allergen, particularly to individuals sensitized to sesquiterpene lactones (Rodriguez and Epstein, unpublished results). Further biological studies are in progress for testing the cytotoxic and allergenic potential of gerin.

EXPERIMENTAL

Mps were determined on a Fisher–Johns hot stage apparatus and are uncorr. ^{1}H NMR spectra were recorded at 250 MHz; chemical shifts are reported in ppm (δ) relative to TMS as an internal standard. Micro-analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn.

Gerin (**1**). *Isolation from* Geraea viscida (*Gray*) *Blake* (*Compositae*). *Geraea viscida* was collected on 12 May, 1978, 5 miles south of Highway 8, Campo Exit, San Diego County, California (Rodriguez and Sanchez s.n.). Voucher specimens are deposited in the University of California Irvine Herbarium. Leaves were stripped from the plant, air-dried, ground and extracted with $CHCl_3$. The extract was processed as previously described [3]. The crude $CHCl_3$ extract, obtained from 82.7 g of dry plant material, provided a crude syrup (2.5 g). The crude material was chromatographed on Si gel packed in $CHCl_3$ and eluted with $CHCl_3$–Me_2CO (15:1). Fractions containing gerin, as evidenced by TLC analysis, were combined. Evapn of the solvent *in vacuo* gave 100 mg of crude crystalline material. Analysis of the trichome exudates by TLC also showed the presence of gerin as the major constituent. Recrystallization of the crude crystalline gerin from $CHCl_3$–isopropyl ether yielded 92 mg gerin, mp 126–133°. Further recrystallization from Et_2O provided analytically pure gerin as colourless prisms: mp 140.0–141.5°; $[\alpha]_D^{24}$ −243° (c 0.50 $CHCl_3$); UV λ_{max}^{EtOH} nm: 202 (ε 11348), 239 (ε 11029); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3025, 3005, 2950, 2910, 2850, 1727, 1670, 1625, 1440, 1409, 1380, 1312, 1275, 1250, 1210, 1180, 1155, 1135, 1110, 1080, 1022, 980, 955, 845, 820; NMR (250 MHz) ($CDCl_3$): δ 6.86 (1H, *d*, J = 10 Hz, C-1H), 6.34 (1H, *s*, ) 6.15 (1H, *q*, J = 2.5 and 1.2 Hz) 5.99 (1H, *d*, J = 10 Hz, C-2H), 5.68 (1H, *s*, ), 5.36 (1H, *q*, J = 2.5 Hz, C-8H), 5.29 (1H, *t*, J = 1.2 Hz, ), 3.78 (3H, *s*, $-CO_2Me$), 3.01 (1H, *dt*, J = 12.0, 3.0 Hz, C-7H), 2.76 (1H, *dq*, J = 11.5, 2.5 Hz, C-5H), 2.05 (1H, *dd*, J = 14.5, 2.5 Hz, C-9 equatorial H), 1.98 (3H, *s*, MeCO), 1.95 (1H, *dt*, J = 13.0, 12.0 Hz, C-6 axial H), 1.85 (1H, *dd*, J = 14.5, 2.5 Hz, C-9 axial H), 1.73 (1H, *dt*, J = 13.0 Hz, 2.5 Hz, C-6 equatorial H), 1.15 (3H, *s*, C-10 Me). (Found: C, 68.02; H, 6.95. $C_{18}H_{22}O_5$ requires: C, 67.91; H, 6.97%.)

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