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# AN ACYCLIC DITERPENE FROM *VIGUIERA DELTOIDEA*

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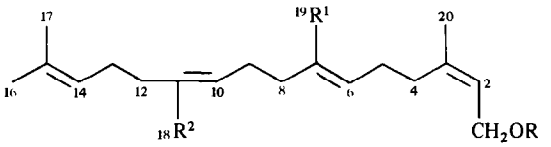
**Key Word Index**—*Viguiera deltoidea*; Heliantheae; Asteraceae; diterpene; viguieric acid.

**Abstract**—A new geranylgeraniol type diterpene, named viguieric acid, was isolated from the dichloromethane extracts of *V. deltoidea*. Its structure was assigned to be (2*Z*,6*Z*,10*E*)-3,15-dimethyl-7-carboxy-11-formyl-2,6,10,14-hexadecatetraen-1-ol.

The dichloromethane extract of leaves of *V. deltoidea* afforded as one major component an acyclic diterpene (**1**) in a yield of 0.13% of the dried leaves.

Spectral data for compound **1** indicated that it was an acyclic diterpene related to geranylgeraniol [1, 2], and also confirmed the presence of a hydroxyl group (IR: 3440 $cm^{-1}$; $^1H$ NMR: two-proton doublet at $\delta$4.14, $J$ = 7 Hz), one carboxylic acid group (IR: 3200–2500, 1690 $cm^{-1}$; $^{13}C$ NMR: $\delta$171.6) and an $\alpha,\beta$-unsaturated aldehyde function ($^1H$ NMR: one-proton singlet at $\delta$9.36; IR: 2720 $cm^{-1}$ and the broadened nature of the 1690 $cm^{-1}$ adsorption; $^{13}C$ NMR: $\delta$195.6 doublet and UV adsorption: $\lambda$231 nm, $\varepsilon$ = 13000). $^{13}C$ NMR showed the molecular formula was $C_{20}H_{30}O_4$ (a molecular ion was not detected in the electron impact mass spectrum). In accordance with **1** being an acyclic diterpene, $^1H$ NMR (Table 1) indicated four isolated double bonds, i.e. four vinylic one-proton triplets at $\delta$5.0–6.5; moreover, $^{13}C$ NMR signals for eight $sp^2$ carbon atoms were observed between $\delta$100–160 (Table 2). When the $^1H$ NMR spectrum was recorded at 500 MHz (see **1***), all signals were cleanly separated. 2D-FT homonuclear $J$-correlation experiments indicated the coupling relationship between signals (Fig. 1) including the long-range coupling between H-14 and H-17, H-16. In the mass spectrum of **1**, the ion of $m/z$ 69 $[C_5H_9]^+$ (100%) indicated the partial structure, $Me_2C{=}CHCH_2{-}$ [3]. In the $^1H$ NMR spectrum, the signal at $\delta$5.47 (1H, $t$ (*br*), $J$ = 7 Hz) provided the partial structure $C(Me){=}CHCH_2OH$. Thus, positions C-18 and C-19 were available for the aldehyde and the carboxyl groups. The 2D-COSY experiments as well as the irradiation experiments led to the assignment of the aldehydic group to C-18 and the carboxylic group to C-19. For example, the 2D-COSY experiments allowed detection of the signals for protons at 12, 13 and 14; moreover, irradiation of the signal for H-12 dramatically increased the sharpness of the aldehyde signal at $\delta$9.36. This assignment was also confirmed by spectral data for the reduction products **4** and **5**: the reduction of the aldehyde function (in **4**) affected not only protons at positions C-10, C-12, C-13, C-9 and C-8, it also affected H-14 (from multiplet-triplet to broadened multiplet), while the signal for H-5 was unaffected. In contrast, reduction of the carboxylic group affected H-5 and H-6 only [4].

Chan *et al.* [5] reported that chemical shifts of aldehydic protons and of $\beta$-vinylic protons of carboxylic acid can be used to distinguish *cis* and *trans* isomers. Thus, the 10*E*,6*Z* configuration was assigned on the basis of the aldehydic signal being at $\delta$9.36 and the $\beta$-vinylic proton signal being at $\delta$6.09, respectively. These assignments were also in accord with the chemical shifts of the carbinol signals ($\delta$4.02 in **4** and **5** and $\delta$4.09 in **5**, respectively) which were in agreement with the *trans* and *cis* alcoholic isomers [5]. The C-2 double bond was also assignable to be *Z* on the basis of the chemical shift of C-3 methyl at $\delta$1.75, which apparently differs from its *trans* isomer [1, 4, 6]. This was further confirmed by the comparison of the $^{13}C$ NMR chemical shift of C-20 ($\delta$23.4) with that ($\delta$16.3) of the *trans* isomers [7]. The configuration assignments at C-2 and C-6 double bonds were in full agreement with those reported by Bohlmann *et al.* [8]. Therefore, the structure of **1** was deduced to be (2*Z*,6*Z*,10*E*)-3,15-dimethyl-7-carboxy-11-formyl-2,6,10,14-hexadecatetraen-1-ol, which we named viguieric acid. Viguieric acid might be a precursor of some cyclic diterpenes.




| | R | $R^1$ | $R^2$ |
|---|---|---|---|
| **1** | H | $CO_2H$ | CHO |
| **2** | H | $CO_2Me$ | CHO |
| **3** | Ac | $CO_2Me$ | CHO |
| **4** | H | $CO_2H$ | $CH_2OH$ |
| **5** | H | $CH_2OH$ | $CH_2OH$ |

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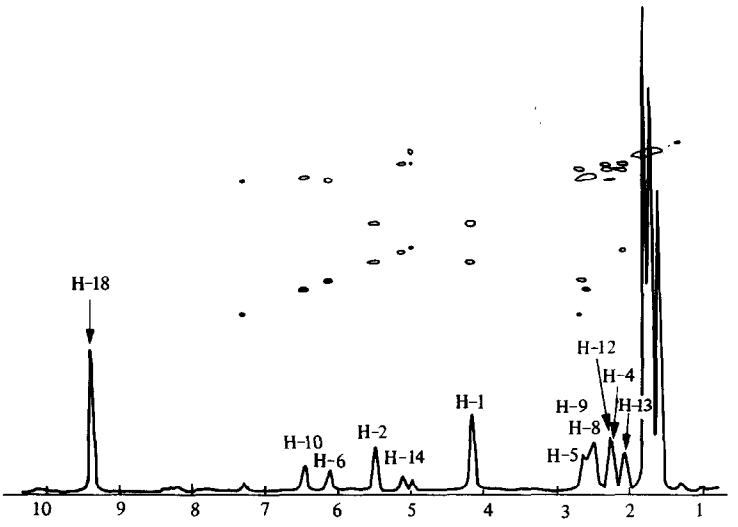


Fig. 1. 2D-COSY of compound 1 (2D-FT homonuclear *J*-correlation recorded at 360 MHz in $CDCl_3$).

## EXPERIMENTAL

*Viguiera deltoidea* Gray was collected 30 miles south of El Rosario, Baja California Norte in Mexico along Highway 1 by John Norris. A voucher specimen (JN No. 429) is deposited in the Herbarium of the University of Texas at Austin, and was determined by Alan Whittemore in the Department of Botany, the University of Texas at Austin.

The dried leaves of *V. deltoidea* (360 g) were extracted with 7 l of $CH_2Cl_2$ ( × 2). The extracts were combined and evaporated to yield a dark brown syrup which was dissolved in $Me_2CO$ and kept in a refrigerator overnight. After filtering to remove the ppt the soln was evaporated to yield 18.5 g of residue. The residue was then loaded onto a silica gel column, which was first eluted with a hexane–EtOAc gradient solvent system to yield sesquiterpene lactones [Gao, F. and Mabry, T. J., unpublished]. Next, the column was eluted with EtOAc–MeOH (7:1) to obtain polar fractions which were further purified by CC on Sephadex LH-20 column with cyclohexane–$CH_2Cl_2$–MeOH (7:4:1) as eluting solvent; yield: 480 mg of 1.

*Compound* 1. UV $\lambda_{max}^{MeOH}$ nm: 207 ($\varepsilon$ = 13 900) ($CO_2H$), 231 ($\varepsilon$

Table 1. $^1H$ NMR data of compounds 1–5 ($CDCl_3$ with TMS as int. standard. Data were recorded at 200 MHz except for 1*, which was recorded at 500 MHz)

| H | 1* | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|---|
| 1 | 4.14 *d* | 4.14 *d* | 4.12 *d* | 4.57 *d* | 4.12 *d* | 4.07 *d* |
| 2 | 5.48 *t* | 5.47 *t* | 5.47 *t* | 5.39 *t* | 5.45 *t* | 5.47 *t* |
| 4 | 2.22 *t* | 2.22 *t* | 2.21 *t* | | † | ‡ |
| 5 | 2.62 *q* | 2.63 *q* | 2.58 *q* | | 2.57 *q* | ‡ |
| 6 | 6.10 *t* | 6.09 *t* | 5.95 *t* | 5.94 *t* | 5.98 *t* | 5.31 *t* |
| 8 | 2.46 *t* | 2.50 *t* | | | † | ‡ |
| 9 | 2.55 *q* | | | | † | ‡ |
| 10 | 6.44 *t* | 6.44 *t* | 6.41 *t* | 6.43 *t* | 5.40 *t* | 5.41 *t* |
| 12 | 2.27 *t* | 2.27 *t* | 2.27 *t* | | † | ‡ |
| 13 | 2.04 *q* | 2.03 *q* | 2.03 *q* | | † | ‡ |
| 14 | 5.10 *t* | 5.09 *mt* | 5.09 *mt* | 5.09 *mt* | 5.10 *m* (*br*) | 5.12 *m* (*br*) |
| 16 | 1.67 *s* | 1.66 *s* | 1.67 *s* | 1.67 *s* | 1.67 *s* | 1.68 *s* |
| 17 | 1.57 *s* | 1.56 *s* | 1.57 *s* | 1.57 *s* | 1.59 *s* | 1.60 *s* |
| 18 | 9.36 *s* | 9.36 *s* | 9.36 *s* | 9.36 *s* | 4.02 *s* | 4.02 *s* |
| 19 | | | | | | 4.09 *s* |
| 20 | 1.76 *s* | 1.75 *s* | 1.75 *s* | 1.77 *s* | 1.74 | 1.75 *s* |
| OMe | | | 3.76 *s* | 3.76 *s* | | |
| OAc | | | | 2.05 *s* | | |

*$J$ (Hz) for compound 1: 1, 2 = 8, 9 = 9, 10 = 12, 13 = 7; 4, 5 = 5, 6 = 13, 14 = 8. $J$ for 2–5 were substantially the same as those of 1*.

†These signals overlapped each other at $\delta$2.08–2.32.

‡These signals overlapped each other at $\delta$2.09–2.12.

Table 2. $^{13}C$ NMR data of compound 1 (22.6 MHz, $CDCl_3$ with TMS as int. standard)

| C | 1 |
|---|---|
| 1 | 58.7 *t* |
| 2 | 124.9 *d* |
| 3 | 139.1 *s* |
| 4 | 33.6 *t* |
| 5 | 27.1 *t* |
| 6 | 165.0 *d* |
| 7 | 132.5 *s* |
| 8 | 31.5 *t* |
| 9 | 28.5 *t* |
| 10 | 154.3 *d* |
| 11 | 143.8 *s* |
| 12 | 38.7 *t* |
| 13 | 24.3 *t* |
| 14 | 123.6 *d* |
| 15 | 130.8 *s* |
| 16 | 25.8 *q* |
| 17 | 17.7 *q* |
| 18 | 195.6 *d* |
| 19 | 171.6 *s* |
| 20 | 23.4 *q* |

= 13 000) ($\alpha,\beta$-unsaturated aldehyde); IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3460 (OH), 3200–2500, 1690 ($CO_2H$), 2720, 1690 (CHO), 1640 (C=C); EIMS (probe) 70 eV, *m/z* (rel. int.): 316 $[M-H_2O]^+$ (2), 298 $[M-2H_2O]^+$ (8), 283 $[298-Me]^+$ (5), 69 $[C_5H_9]^+$ (100), 55 $[C_4H_7]^+$ (49), 41 $[C_3H_5]^+$ (77).

*Methylation product* **2**. Compound **1** (66 mg) was methylated with $CH_2N_2$ in the usual way. After workup and purification on TLC (hexane–EtOAc, 1:1), 54 mg **2** were yielded. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3440 (OH), 2700, 1675 (CHO), 1705 ($CO_2R$), 1630, (C=C); EIMS (probe); 70 eV, *m/z* (rel. int): 330 $[M-H_2O]^+$ (6), 298 $[330-MeOH]^+$ (22), 69 $[C_5H_9]^+$ (100), 55 $[C_4H_7]^+$ (81).

*Acetylation product* **3**. Compound **2** (10 mg) was acetylated with $AC_2O$–$C_5H_5N$ at room temp. for 2.5 hr. Workup afforded 8 mg **3**. EIMS (probe), 70 eV, *m/z* (rel. int.): 330 $[M-AcOH]^+$ (8), 315 $[330-Me]^+$ (7), 312 $[330-H_2O]^+$ (7), 298 $[330-MeOH]^+$ (24), 283 $[298-Me]^+$ (10), 269 $[298-CHO]^+$ (15), 69 $[C_5H_9]^+$ (96), 55 $[C_4H_7]^+$ (11), 41 $[C_3H_5]^+$ (100).

*Reduction products* **4** *and* **5**. Compound **1** (68 mg) in 8 ml $Et_2O$ was reacted with 25 mg $LiAlH_4$ with stirring at room temp. for 30 min. Then three drops of EtOAc were added. The reaction mixture was suspended in $H_2O$ and extracted with $Et_2O$. The $Et_2O$ extract yielded compound **5**. The water layer was acidified with 1% HCl and then extracted with $Et_2O$ to yield 50 mg compound **4** as colourless gum. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3400 (OH), 3200–2500, 1690, ($CO_2H$), 1640 (C=C); EIMS (probe) 70 eV, *m/z* (rel. int.): 251 $[M-C_5H_9O]^+$ (4), 236 $[251-Me]^+$ (6), 208 $[251-C_3H_7]^+$ (15), 86 $[C_5H_{10}O]^+$ (60), 69 $[C_5H_9]^+$ (82), 43 $[C_3H_7]^+$ (100). **5**, 10 mg of colourless gum. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3350 (OH), 1660 (C=C), 1440, 1370, 1000. No carbonyl adsorption was observed. EIMS (probe), *m/z* (rel. int.): 236 $[M-C_5H_{10}O]^+$ (6), 218 $[236-H_2O]^+$ (5), 69 $[C_5H_9]^+$ (52), 43 $[C_3H_7]^+$ (100).

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