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# ARGOPHYLLONE-B, A SESQUITERPENE LACTONE FROM *HELIANTHUS ARGOPHYLLUS*

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**Key Word Index**—*Helianthus argophyllus*; germacranolide; argophyllone-B; X-ray crystal structure; sesquiterpene lactone.

**Abstract**—The sesquiterpene lactone, 2-methyl-2-butenoic acid dodecahydro-4-(hydroxymethyl)-10a-methyl-8-methylene-3,7-dioxooxineno[5,6]cyclodeca[1,2-*b*]furan-9-yl ester [1a*R**-[1a*S**,4*R**,5a*S**,8a*R**,9*R**(*E*)]], argophyllone-B, was isolated from acetone extracts from the leaves of *Helianthus argophyllus*. Its structure has been determined by single crystal X-ray analysis. Complete $^1$H NMR and $^{13}$C NMR assignments have been made.

## INTRODUCTION

*Helianthus* species are known to be a rich source of terpenes, including diterpenes and sesquiterpene lactones (for a review see ref. [1]; [2–9]). During our investigation of natural products in sunflower, we isolated a new compound from *H. argophyllus*. Previous work on this species has been reported [2]. This paper reports the isolation and structure of the sesquiterpene lactone, argophyllone-B (**1**).

## RESULTS AND DISCUSSION

Acetone extracts from freeze-dried leaves of *H. argophyllus* yielded a sesquiterpene lactone as indicated in the $^1$H NMR spectrum by two one-proton doublets at $\delta 6.37$ ($J = 1.3$ Hz) and 5.84 ($J = 1.3$ Hz) characteristic of the vinyl protons of an α-methylene-lactone (Table 1). The compound contained an angelic acid ester as shown by $^1$H NMR peaks at $\delta 6.13$ (1H, *q* of *q*, $J = 1.4$ Hz), 1.97 (3H, *d* of *q*, $J = 7.3$ and $J = 1.5$ Hz) and 1.84 (3H, pentet, $J$

Table 1. $^1$H NMR spectral data for argophyllone-B (360 Mz, $CDCl_3$, $CDCl_3$ as internal standard)

| Proton | δ | Multiplicity (*J* in Hz) |
|---|---|---|
| 1 | 3.39 | *dd* (9.8, 5.6) |
| 2α | 2.35 | *dd* (14.4, 9.8) |
| 2β | 3.29 | *dd* (14.4, 5.6) |
| 4 | 3.21 | *m* |
| 5α | 1.53 | *ddd* (13.2; 11.4, 3.3) |
| 5β | 2.23 | *td* (13.2, 3.3) |
| 6 | 4.56 | *dd* (11.4, 3.3) |
| 7 | 3.06 | *s* (*br*) |
| 8 | 5.22 | *t* (≃ 3.5) |
| 9α | 1.45* | *dd* (15.4, 3.9) |
| 9β | 2.72* | *dd* (15.4, 3.3) |
| 13α | 5.84 | *d* (1.3) |
| 13β | 6.37 | *d* (1.3) |
| 14 | 1.40‡ | *s* |
| 15α | 3.87† | *dd* (9.7, 8.7) |
| 15β | 3.69† | *dd* (9.7, 4.9) |
| 18 | 6.13 | *qq* (7.3, 1.4) |
| 19 | 1.97‡ | *dq* (7.3, 1.5) |
| 20 | 1.84‡ | pentet (1.4) |

*·†Assignments carrying the same symbol are interchangeable.

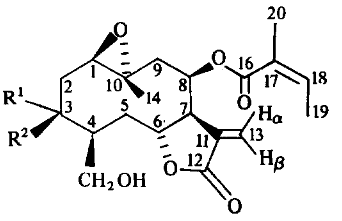
‡Three protons.

Table 2. $^{13}$C NMR spectral data for argophyllone-B (22.6 MHz)

| Carbon | δ<br>$CDCl_3$ | <br>$C_6D_6$ | Multiplicity (in coupled spectrum) |
|---|---|---|---|
| 1 | 58.7 | 58.5 | *d* |
| 2 | 45.8 | 46.2 | *t* |
| 3 | 209.4 | 208.9 | *s* |
| 4 | 46.3 | 46.2 | *d* |
| 5 | 34.8 | 35.1 | *t* |
| 6 | * | 75.5† | — |
| 7 | 47.9 | 47.5 | *d* |
| 8 | * | 76.2† | — |
| 9 | 43.5 | 43.8 | *t* |
| 10 | 57.3 | 57.0 | *s* |
| 11 | 137.3 | 138.4 | *s* |
| 12 | 168.6 | 168.3 | *s* |
| 13 | 125.4 | 124.3 | *t* |
| 14 | 18.0 | 17.9 | *q* |
| 15 | 65.0 | 65.4 | *t* |
| 16 | 165.8 | 165.8 | *s* |
| 17 | 126.3 | * | *s* |
| 18 | 141.1 | 141.2 | *d* |
| 19 | 15.6 | 15.8 | *q* |
| 20 | 20.1 | 20.4 | *q* |

*Signal obscured by solvent peak.

†These assignments are interchangeable.



**1** $R^1 = R^2 = O$

**2** $R^1 = H, R^2 = OH$

= 1.4 Hz). The $^{13}C$ NMR spectrum supported this assumption, indicating 20 carbons (Table 2).

Although other structural features were apparent from the $^1H$ NMR spectrum, complete assignments were originally complicated because the molecule did not show a parent peak in the mass spectrum (highest *m/z* at 360, $[M - H_2O]^+$). However, a single crystal X-ray study, by direct methods, clearly showed argophyllone-B to have structure **1**, which has been partially refined to $R = 9.2\%$; H atoms have been located in a difference map. (A completely refined structure with absolute configuration determination will be the subject of a separate paper.) Careful analysis of the $^1H$ NMR spectrum, using decoupling experiments, allowed the assignment of all 25 protons attached to carbons. The $-CH_2-OH$ group appeared as two doublets of doublets at $\delta 3.87$ and 3.69. These methylene protons were coupled to a methine proton (C-4) at $\delta 3.21$. The methine proton was coupled to another methylene group (C-5) which appeared as an overlapping doublet of doublets at $\delta 1.53$ and a triplet of doublets at $\delta 2.23$. The peaks at $\delta 1.53$ and 2.23 were identified as a pair of methylene protons because of their geminal coupling constant ($J = 13.2$ Hz). These methylene protons were coupled to an oxygen-substituted methine (C-6) proton at $\delta 4.56$.

Other couplings could be observed between an oxygen-substituted methine proton (C-1) at $\delta 3.39$ and the methylene protons (C-2) at $\delta 2.35$ and 3.29. Oxygen-substituted methine–methylene coupling was also observed between the methine (C-8) peaks at $\delta 5.22$ and the methylene protons (C-9) at $\delta 1.45$ and 2.72. A broadened singlet (1H) was observed at $\delta 3.06$ (C-7) and a sharp singlet (3H) at $\delta 1.40$ (C-14).

Comparison of structure **1** with that of argophyllin-B (**2**) [2], isolated from the same species, shows that argophyllone-B has a C-3 keto function rather than a C-3 alcohol. Consistent with this close similarity is the agreement between many of the chemical shifts in both the $^1H$ NMR and $^{13}C$ NMR spectra for the two compounds.

## EXPERIMENTAL

$^1H$ NMR and $^{13}C$ NMR spectra were measured at 360 and 22.5 MHz, respectively, using $CDCl_3$ as internal standard ($\delta 7.26$ for $^1H$ and $\delta 76.9$ for $^{13}C$). MS were recorded at 70 eV on a Varian CH-7 spectrometer. ORD spectra were recorded on a Cary Model 60 recording spectropolarimeter and optical rotations were determined on a Perkin–Elmer Model 241. Purifications were performed on Mallinckrodt silica gel (column: CC-4; TLC: 7GF).

*Extraction and isolation.* Freeze-dried and ground leaves (100 g) of *H. argophyllus* (collected in July 1983, along U.S. Highway 281 at Encino, TX) were extracted with $Me_2CO$ (2 l.). The soln was concd and absorbed on silica gel (15 g) and chromatographed over a silica gel (120 g) column. The column was eluted with $C_6H_6$–EtOAc–MeOH (49:49:1), and 24 ml fractions were collected. Argophyllone-B was concd in fractions 15–35. The crude material was reabsorbed on silica gel (5 g) and chromatographed over a silica gel column (50 g). The column was eluted with $CHCl_3$ (1 l.) and 22 ml fractions were collected. Argophyllone-B was concd in fractions 39–92. A small sample was purified by TLC ($C_6H_6$–EtOAc–*i*-PrOH, 24:24:1). The UV absorbing band was eluted with $Et_2O$ and concd. Argophyllone-B crystallized after standing in the cold. These crystals were used as seeds, providing 236 mg of crude argophyllone-B (mp 140–164°/$C_6H_6$).

*Argophyllone-B* (**1**). Mp 171–179° ($C_6H_6$), MS *m/z* (rel. int.): (parent ion not observed), 360 (0.8), 261 (2), 243 (7), 215 (6), 173 (6), 145 (6), 98 (6), 97 (11), 95 (12), 91 (7), 84 (8), 83 (100). IR $\nu_{max}^{CDCl_3}$ cm$^{-1}$: 3625, 2970, 1770, 1720, 1705, (sh), 1270, 1230, 1150, 1125, 1045. $[\alpha]_D^{22}$ $-158°$ (*c* 0.06; EtOH). ORD (*c* $1.6 \times 10^{-3}$; EtOH) 25°; $[\Phi]_{400}$ $+1.1° \times 10^3$; $[\Phi]_{332}$ 0.0°; $[\Phi]_{320}$ $+1.5° \times 10^3$; $[\Phi]_{317}$ $+1.4° \times 10^3$; $[\Phi]_{313}$ $+1.5° \times 10^3$; $[\Phi]_{307}$ 0.0°;$[\Phi]_{230}$ $-4.3° \times 10^4$; $[\Phi]_{220}$ $-1.8° \times 10^4$. Crystal data: (140 K) orthorhombic, $P2_12_12_1$, $Z = 4$, $a = 6.741$ (2), $b = 14.963$ (6), $c = 19.000$ (14) Å; current $R = 9.2\%$, isotropic.

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