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THREE SESQUITERPENE LACTONES FROM *HELIANTHUS NIVEUS* SUBSP. *CANESCENS* AND *H. ARGOPHYLLUS*

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Key Word Index—*Helianthus niveus*; *H. argophyllus*; Heliantheae; Compositae; germacranolide; 3-acetylchamissonin; simsiolide; argophyllin C.

Abstract—Further investigation of the minor terpenoids in *Helianthus niveus* subsp. *canescens* and *H. argophyllus* afforded two known 12,8-fused sesquiterpene lactones, 3-acetylchamissonin and simsiolide as well as one new germacranolide, argophyllin C. Identification and structure elucidation of these lactones by ^{1}H NMR and chemical transformations are described.

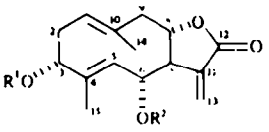
INTRODUCTION

The species in *Helianthus* investigated so far have afforded several 12,6-*trans*-lactonized germacranolides and heliangolides as the major terpenoids [1–12]. However, 12,8-*trans*-fused germacranolides with 6α-hydroxy group have been isolated from *H. pumilis* and *H. californicas* [8, 11]. On further investigation of the minor sesquiterpenoids in *H. niveus* subsp. *canescens* and *H. argophyllus* previously investigated [3, 5], two 12,8-*trans*-lactonized germacranolides were isolated and identified as 3-acetylchamissonin (**1**) and simsiolide (**5**) respectively. A new sesquiterpene lactone (**6**) with a 12,6-*trans* ring closure, namely argophyllin C, was also isolated from *H. argophyllus*.

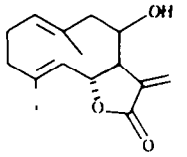
RESULTS AND DISCUSSION

Further purification of the fraction containing mainly of niveusin C which is the main sesquiterpene lactone of *H. niveus* subsp. *canescens* [3] furnished lactone **1** (mp 160–161°) as a minor component. Compound **1** was identified by comparison of its IR and ^{1}H NMR spectra and mp with those of 3-acetylchamissonin which has been isolated from *Viguiera deltoidea* by one of the authors (T. J. M.) and his co-worker [13]. The structure of **1** was also confirmed by direct comparison of its acetate with a synthetic specimen of chamissonin diacetate (**3**) derived from chamissonin (**2**) (see Experimental).

Preparative TLC purification of the fractions from *H. argophyllus*, more polar than eupatolide (**4**), which is the major constituent of the species [5], also gave a 12,8-*trans*-fused sesquiterpene lactone with an α-oriented hydroxy group at C_6. On the basis of the spectroscopic data, it was identified as simsiolide (**5**), previously isolated from *Simsia dombeyana* (Heliantheae) by Bohlmann *et al.* [14, 15]. Furthermore, preparative TLC purification of the fraction containing simsiolide (**5**) gave argophyllin C (**6**) which did not give a molecular ion peak in its EI-MS. However, on acetylation with acetic anhydride–pyridine, **6** yielded monoacetate **7** ($C_{22}H_{28}O_7$, $[M]^+$ *m/z* 398) indicating that **6** had a formula of $C_{20}H_{26}O_6$. IR (1755 and 1720 cm^{-1}) and ^{1}H NMR (δ6.33 *d*, 5.63 *d*, 3.00 *dd*, 1H, each) indicated that **6** is a sesquiterpene lactone with an unsaturated ester side chain and an epoxy ring. A detailed analysis of ^{1}H and ^{13}C NMR data for **6** has revealed the close similarity of **6** to argophyllin B (**8**) (see Tables 1 and 2). However, instead of the typical AB quartet for H_{15a} and H_{15b} in **8**, **6** exhibited the signal at δ1.20 (3H, *d*, *J* = 7.0 Hz) for C_4β-methyl group whose ^{13}C NMR signal was observed at δ22.7 (*q*). These data indicate that **6** is 15-deoxyargophyllin B. Therefore, the structure for argophyllin C must be as depicted in formula **6**.



1 R^1 = Ac R^2 = H
2 R^1 = H R^2 = H
3 R^1 = Ac R^2 = Ac



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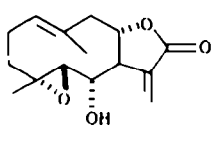

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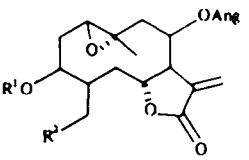

6 R^1 = H, R^2 = H
7 R^1 = Ac R^2 = H
8 R^1 = H, R^2 = OH

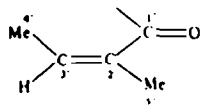

Table 1. ^{1}H NMR spectra of 6, 7 and 8*

H	6	7	8
1	3.10 *dd*†	3.00	2.98
3	3.90 *m*	5.00	4.23
6	4.87 *m*	4.88	4.88
7	2.90 *m*	2.92	2.91
8	5.23 *m*	5.26	5.28
9a	‡	2.64 *dd*	2.52 *dd*
9b	2.80 *dd*	2.77	2.75
13a	5.60 *d*	5.76	5.65
13b	6.35 *d*	6.36	6.40
14	1.43 *s*	1.54	1.47
15	1.18 *d*	1.13	3.98 *dd*
			3.90 *dd*
3'	6.13 *m*	6.12	6.09
4'	1.95 *br d*	1.95	1.95
5'	1.83 *br s*	1.85	1.86
AcO		2.06 *s*	

*Run in $CDCl_3$ with TMS as internal standard on a 90 MHz instrument.

†Multiplicities indicated by standard abbreviations. Coupling constants were virtually identical for 6, 7 and 8; *J* values in Hz for compound 6: 1,2a = 10.0; 1,2b = 5.0; 3,4 = 7.0; 7,8 = 4.0; 8,9a = 5.0; 8,8b = 3.0; 9a,9b = 15.0; 7,13a = 2.5; 7,13b = 2.0; 3',4' = 7.5.

‡Could not be observed because of overlapping of signals.

Table 2. ^{13}C NMR data for compounds 6 and 8*

Carbon	6	8
1†	59.5 *d*‡	60.0 *d*
2	36.5 *t*§	36.6 *t*§
3	72.0 *d*	70.8 *d*
4	43.3 *d*‖	43.9 *d*‖
5	36.6 *t*§	36.9 *t*§
6	74.9 *d*	74.8 *d*
7	49.7 *d*	49.1 *d*
8	75.8 *d*	75.3 *d*
9	43.1 *t*‖	43.3 *t*‖
10	58.4 *s*	58.1 *s*
11	137.1 *s*	137.1 *s*
12	169.7 *s*	169.1 *s*
13	124.7 *t*	124.9 *t*
14	19.6 *q*	19.5 *q*
15	22.7 *q*	66.0 *t*
1'	166.4 *s*	166.4 *s*
2'	126.7 *s*	127.0 *s*
3'	140.6 *d*	140.2 *d*
4'	20.3 *q*	20.2 *q*
5'	15.7 *q*	15.7 *q*

*Run in $CDCl_3$ on a 22.6 MHz instrument.

†Signals were assigned by means of partially decoupled off resonance spectra.

‡Indicate multiplicities on partially decoupled spectra.

§‖Assignments are interchangeable.

EXPERIMENTAL

^{1}H and ^{13}C NMR spectra were measured at 90 and 12.6 MHz, respectively with TMS as an internal standard. Mass spectra were recorded by direct inlet system at 70 eV ionization. Toluene–EtOAc (4:1–1:4) and $CHCl_3$–*iso*-PrOH (15:1) solvent systems were used for TLC development.

Isolation of 3-acetylchamissonin (1). The CC fractions (16–26) consisting mainly of niveusin C from the $CHCl_3$ extract of *Helianthus niveus* subsp. *canescens* (3.14 kg) [3] were combined and purified on a silica gel column ($CHCl_3$–Me_2CO, 15:1) to give a less polar fraction (350 mg) than niveusin C which was successively purified on prep. TLC plates ($CHCl_3$–*iso*-PrOH, 30:1) to yield 200 mg of 3-acetylchamissonin (1).

Isolation of simsiolide (5) *and argophyllin C* (6). The chromatographic fractions (40–50) of the previous study on *H. argophyllus* [5], which contained eupatolide (4) as a main component, were combined (1.70 g) and purified on a silica gel column (120 g) eluted with toluene–EtOAc (4:1). The material from fractions 31–50 was purified by prep. TLC (developed with toluene–EtOAc, 1:1, then with $CHCl_3$–*iso*-PrOH, 20:1) to give 12 mg of simsiolide (5) as colourless oil. The fractions eluted with toluene–EtOAc (1:1) showed several spots on TLC and the concentrate from the combined fractions weighed 1.64 g. After purification (×2) on prep. TLC (2.0 mm × 10; 0.5 mm × 8) developed with toluene–EtOAc (1:4), 320 mg of argophyllin C (6) was afforded as white needles.

3-Acetylchamissonin (1). Mp 160–161° (EtOAc); $[\alpha]_D$ – 18.0 (*c* 0.35; $CHCl_3$). IR and ^{1}H NMR spectra and mp were identical to the authentic specimen [13].

Acetylation of 3-acetylchamissonin. Compound 1 (50 mg) was acetylated with Ac_2O (2 ml) and pyridine (1 ml) for 12 hr at room temp. After prep. TLC (EtOAc) of the crude product, 48 mg of chamissonin diacetate (3) was obtained and recrystallized from MeOH, mp 174–175°. IR and ^{1}H NMR spectra and mp were identical to those of an authentic specimen prepared from chamissonin (2) under the same condition.

Simsiolide (5). Colourless oil, IR and ^{1}H NMR spectra were identical to the previously published data [14]. For the final identification, its monoacetate was prepared from 5, whose IR, ^{1}H NMR spectra and mp were identical to those of the previously published data [14].

Argophyllin C (6). Mp 84–86° (EtOAc); $[\alpha]_D$ – 47.5 (*c* 0.40; $CHCl_3$); MS (rel. int.) *m/z*: $[M]^+$ was not found, 83 (100), 55 (91). IR ν_{max}^{KBr} cm^{-1}: 3400, 2940, 1755, 1715, 1680, 1650, 1230, 1150, 1040, 1000. ^{1}H NMR: see Table 1. ^{13}C NMR: see Table 2.

Acetylation of argophyllin C. Compound 6 (60 mg) was acetylated with Ac_2O (2.0 ml) and pyridine (1.0 ml) for 12 hr at room temp. After the usual work-up, the crude product was purified on prep. TLC (0.5 mm) with toluene–EtOAc (3:1) to give 40 mg of monoacetate 7, mp 92–93°; $[\alpha]_D$ – 25.0 (*c* 0.20; $CHCl_3$); MS (rel. int.) *m/z*: 406 (0.1), 388 (0.05), 363 (0.1), 83 (100), 55 (57), 43 (50). IR ν_{max}^{KBr} cm^{-1}: 2940, 1760, 1720, 1700, 1690, 1650, 1230, 1140, 1040.

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REFERENCES

1. Ohno, N. and Mabry, T. J. (1979) *Phytochemistry* **18**, 1003.
2. Ohno, N., Mabry, T. J., Zabel, V. and Watson, W. H. (1979) *Phytochemistry* **18**, 1687.

3. Ohno, N. and Mabry, T. J. (1980) *Phytochemistry* **19**, 609.
4. Ohno, N., Gershenzon, J., Neuman, P. and Mabry, T. J. (1981) *Phytochemistry* **20**, 2393.
5. Watanabe, K., Ohno, N., Yoshioka, H., Gershenzon, J. and Mabry, T. J. (1982) *Phytochemistry* **21**, 709.
6. Gershenzon, J. and Mabry, T. J. (1984) *Phytochemistry* **23**, 1959.
7. Gershenzon, J. and Mabry, T. J. (1984) *Phytochemistry* **23**, 2557.
8. Gershenzon, J., Mabry, T. J., Korp, J. D. and Bernal, I. (1984) *Phytochemistry* **23**, 2561.
9. Melek, F. R., Ahmed, A. A., Gershenzon, J. and Mabry, T. J. (1984) *Phytochemistry* **23**, 2573.
10. Gershenzon, J., Ohno, N. and Mabry, T. J. (1981) *Rev. Latinoam. Quim.* **11**, 53.
11. Herz, W. and Kumar, N. (1981) *Phytochemistry* **20**, 1339.
12. Stipanovic, R. D., Miller, R. and Hope, H. (1985) *Phytochemistry* **24**, 358.
13. Gao, F. and Mabry, T. J. (1986) *Phytochemistry* **25**, 137.
14. Bohlmann, F. and Zdero, C. (1977) *Phytochemistry* **16**, 776.
15. Bohlmann, F., Jakupovic, J., Ahmed, M. and Schuster, A. (1983) *Phytochemistry* **22**, 1623.