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SHORT REPORTS

DITHIACYCLOHEXADIENES AND THIOPHENES FROM *AMBROSIA CHAMISSONIS*

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Key Word Index—*Ambrosia chamissonis*; Asteraceae; dithiacyclohexadiene polyynes; thiophenes.

Abstract—The roots of *Ambrosia chamissonis* gave, in addition to known 1,2-dithia-3,5-cyclohexadienes, a new epoxide, a diol and their corresponding thiophenes.

INTRODUCTION

Ambrosia chamissonis (Less.) Greene (tribe Heliantheae) is a common weed in coastal areas ranging from southern California to British Columbia, Canada. In previous work several sesquiterpene lactones have been identified from the upper parts of this species [1]. In a continuing study of the phytochemistry of the Asteraceae, we report the isolation and characterization of novel sulphur-containing polyynes, together with known compounds from root extracts. In addition to 3-(1-propynyl)-6-(5-hexen-3-yn-1-ynyl)-1,2-dithiacyclohexa-3,5-diene (**1**) and 3-(pent-3-yn-1-ynyl)-6-(3-buten-1-ynyl)-1,2-dithiacyclohexa-3,5-diene (**2**), and their thiophenes (**5** and **6**) previously identified in *Chaenactis douglasii* (Hook.) H. & A., *Rudbeckia hirta* L., *Ambrosia eliator* L. as well as other species in the Asteraceae [2–4], two new cyclic disulphides, 3-(1-propynyl)-6-(5,6-epoxyhex-3-yn-1-ynyl)-1,2-dithiacyclohexa-3,5-diene (**3**), 3-(1-propynyl)-6-(5,6-dihydroxyhex-3-yn-1-ynyl)-1,2-dithiacyclohexa-3,5-diene (**4**) and their corresponding thiophenes, 2-(1-propynyl)-5-(5,6-epoxyhex-3-yn-1-ynyl)-thiophene (**7**) and 2-(1-propynyl)-5-(5,6-dihydroxyhex-3-yn-1-ynyl)-thiophene (**8**), have been isolated and identified.

RESULTS AND DISCUSSION

Reverse-phase HPLC analysis of the methanolic extract of roots of *A. chamissonis* L. showed the presence of at least four unidentified compounds. These natural products had shorter R_ts than the acetylenic disulphides **1** and **2**, and their thiophenes **5** and **6**, suggesting an increased polarity [2].

The UV-Vis spectral data of **3** and **4** resembled very closely that of **1** and **2**. Mass spectral analyses afforded molecular ions at *m/z* 244 for **3**, strongly indicating incorporation of an oxygen atom to isomeric dithiacyclohexadienes **1** or **2** ($M^{+\cdot}$, *m/z* 228), and *m/z* 262 for **4** (18 mass units higher than that of **3**). Furthermore, elution of these compounds from an MCH-10 column, as mentioned above, showed that the disulphide **3** (R_t 13.6 min) was more polar than **1** (21.1 min) and **2** (19.8 min), and considerably less polar than **4** (6.2 min). Similar chromatographic behaviour was observed for the thiophenes **5** (17.9 min), **6** (16.7 min), **7** (11.7 min) and **8** (5.6 min).

Compound **4** also exhibited major fragments at *m/z* 231 and 199. These ions presumably arise from the α-cleavage of a carbon–carbon bond joining the two hydroxyl substituents (*m/z* 231), followed by a further loss of sulphur (*m/z* 199). The corresponding thiophene **8** with a molecular ion at *m/z* 230, revealed a major single fragment at $[M-31]^+$ (*m/z* 199), suggesting a diol functional group as well.

The 400 MHz ^{1}H NMR spectrum of **3** displayed an acetylenic methyl singlet at δ2.08 and an AB pattern at δ6.84 (H-8) and 6.62 (H-9). An ABX system at δ2.99 (H-1′), 2.95 (H-1) and 3.57 (H-2) was the only observable difference of **3** with the resonances of compounds with an end vinyl group as **1** and **2** (Table 1). Moreover, close inspection of the H-8 and H-9 signals, together with homonuclear decoupling experiments showed the latter as a doublet of quartets ($J = 7.0$, 0.6 Hz) originating in long-range coupling of H-9 and the methyl group. Thus **3** was the epoxide of **1**, the only isomer able to exhibit a coupling ($^6J = 0.6$ Hz) between the high field ring-proton signal and the nearby C-12 methyl [2]. Similar findings were observed for diol **4**, including a pronounced deshielding of the H-2 doublet of doublets and the two (one-proton) doublets of doublets (H-1 and H-1′), compared to the corresponding proton signals of the acetylenic epoxide **3**.

As shown by HPLC analysis, thiophenes **5–8** were readily identified from the cyclic disulphides after irradiation (380–700 nm; 1.5 mW/cm^2) of the crude root extract for 1 hr in methyl cyanide, a time period that invariably produces a complete conversion of all dithiacyclohexadienes to thiophenes, and incidentally proving to be a fast and reliable method for the synthesis of the latter. Bioassays are currently underway to establish whether these new compounds are also antibiotics.

Table 1. ^1H NMR spectral data of compounds **1**, **3–5**, **7** and **8** (400 MHz, TMS as int. standard, δ)

H		1	3	4	5	7	8
1	*dd*	5.90	2.95	3.75	5.90	2.94	3.74
1′	*dd*	5.78	2.99	3.82	5.78	2.98	3.81
2	*dd*	6.01	3.57	4.61	6.03	3.56	4.60
8	*d*	6.79	6.84	6.68	7.25	7.28	7.14
9	*dd*	6.62	6.62	6.52	7.05 *br d*	7.03 *br d*	6.95 *br d*
13	(Me) *br s*	2.07	2.08	2.09	2.07	2.07	2.08

J(Hz): compounds **1** and **5**: 1,1′ = 2; 1′,2 = 11; 1,2 = 17.5 compounds **3** and **7**: 1,1′ = 6; 1′,2 = 4; 1,2 = 2.5; compounds **4** and **8**: 1,1′ = 11; 1′,2 = 4; 1,2 = 6; compounds **1**, **3** and **4**: 8,9 = 7; 13,9 = 0.6; compounds **5**, **7** and **8**: 8,9 = 4; 13,9 = 0.3

Spectra were determined in $CDCl_3$ (compounds **4** and **8**), and in CD_3CN (compounds **1**, **3**, **5** and **7**).

EXPERIMENTAL

Plant material. Ambrosia chamissonis (Less.) Greene was collected near the coast of Santa Barbara, California. A voucher specimen is deposited at the Museum of Systematic Biology, University of California, Irvine.

Extraction and isolation. Freeze-dried roots (100 g) were extracted with cold MeOH and centrifuged. The crude extract was concd and chromatographed on a silica gel 60 column (230–400 mesh), packed and eluted with *n*-hexane gradually changing to *n*-hexane–EtOAc (2:3), and finally EtOAc. Compounds **3**, **4**, **7** and **8** were further purified on a Varian 5000 Liquid Chromatograph at 340 nm. Isocratic elution was carried out in a MCH-10 reverse-phase column (4 × 300 mm), using $MeCN–H_2O$ (18:7) at a flow rate of 1.0 ml/min. Improvement in the resolution of **4** and **8** was achieved with $MeCN–H_2O$ (2:3), and each compound isolated by extraction of the recovered HPLC fractions with $CHCl_3$. All procedures were performed in dim light to prevent photodegradation of the compounds. Compound **3**: UV λ_{max}^{MeCN} nm: 484, 344, 272; MS *m/z* (rel. int.): 244 $[M]^{+\cdot}$ (100), 214 (75), 182 (21), 170 (98). Compound **4** UV λ_{max}^{MeCN} nm: 482, 342, 326 (sh); MS *m/z* (rel. int.): 262 $[M]^{+\cdot}$ (100), 231 $[M-CH_2OH]^+$ (80), 199 $[M-CH_2OH-S]^+$(15). Compound 7: UV λ_{max}^{MeCN} nm: 340, 325, 252, 239; GC-MS *m/z* (rel. int.): 212 $[M]^{+\cdot}$ (42), 196 (14), 182 (100), 138 (41). Compound **8**: UV λ_{max}^{MeCN} nm: 340, 322, 248, 236; GC-MS *m/z* (rel. int.): 230 $[M]^{+\cdot}$ (39), 199 $[M-CH_2OH]^+$ (100).

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