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# ARTEANNUIN-C, A SESQUITERPENE LACTONE FROM *ARTEMISIA ANNUA*

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**Key Word Index**—*Artemisia annua;* Compositae; sesquiterpene lactone; arteannuin-C.

**Abstract**—*Artemisia annua*, a medicinal plant native to China has been introduced into India. In addition to known monoterpenoids, novel sesquiterpenoids including artemisinin, arteannuin-B and flavonoids the plant yielded a new sesquiterpene lactone now named as arteannuin-C.

In pursuing our interest in artemisinin, a constituent of *Artemisia annua* and a promising antimalarial drug, we have recently reported the cultivation of the plant in our research farms and isolation of the compound [1]. A detailed chemical investigation of the herb is now reported in this communication.

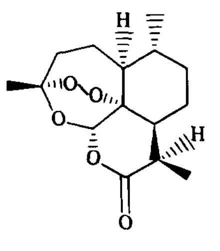
The monoterpene fraction of the extract contained almost similar compounds as reported earlier [2] with a higher percentage of borneol. The relatively polar part contained artemetin, chrysosplenol, 3′-methoxy chrysosplenol and 6,7,4′-trimethoxy-3,5,3-trihydroxyflavone [3] besides yielding stigmasterol, artemisinin (**1**), arteannuin B (**2**) and an isomer of **2**, named as arteannuin-C (**3**).

The structure of **3** was similar to that of **2** which has been elucidated by X-ray analysis [4, 5] but the striking difference in the $^1$H NMR spectrum of **3** was the upfield shift of one of the C-13 protons at $\delta$6.20. The C-1 proton at 2.05 with $J_{1,10} = 10$ Hz supported the α-orientation of Me-14 as in the case of **2**. It also coupled with H-2α and H-2β in a similar way as in **2** which showed that H-1 is also α-oriented. The H-7 had $J$ values of 12, 3 and 3 Hz also similar to that of **2**. The CD curve with a negative cotton effect and negative optical rotation suggested that the lactone ring is α-oriented. This was further supported by the large coupling of $J_{7,13}$ (3 Hz). Therefore the possibility of a difference in stereochemistry exists only for the β-orientation of the epoxide. The model of **3** also showed the possible effect of a β-epoxide on the chemical shift of H-13. The IR and mass spectra were also in agreement with the structure of **3** (see Experimental).

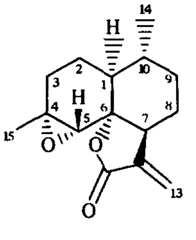
## EXPERIMENTAL

$^1$H NMR was recorded at 80 MHz in $CDCl_3$ with TMS as internal reference. The ppm values are in $\delta$ units. GC of the monoterpene fraction was on a carbowax 20 m column, detector TCD, carrier gas $H_2$ with flow rate 30 ml/min. Programming 60° (isothermal 8 min at 4°/min to 180° isothermal 16 min). CD was recorded on Dichrograph III using 1.0 and 0.5 cm path length cuvettes.

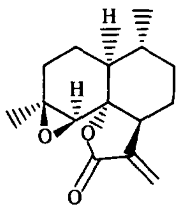
Air dried aerial part of the plant (700 g) harvested in March 1985, was extracted with a mixture of petrol (bp 60–80°)–$Et_2O$–MeOH (1:1:1) and the fatty portion was precipitated out by keeping the extract in MeOH at 0° for 2 hr. The MeOH soluble portion was chromatographed over silica gel to yield the following fractions: fractions 1 and 2 by petrol, fraction 3 by petrol–$Et_2O$ (9:1); fraction 4 by petrol–$Et_2O$ (4:1), fractions 5 and 6 by petrol–$Et_2O$ (1:1); fraction 7 by $Et_2O$, fractions 8 and 9 by $Et_2O$–MeOH (9:1). Fraction 1 on GC analysis tentatively yielded tricyclene (1.6%), α-pinene (0.1%), fenchone (1.7%), artemisia ketone (5.1%), camphor (3.3%), linalool (5.7%), isoborneol (9.5%), α-terpineol (14.4%), borneol (38.4%), and a few unidentified compounds. Fraction 2 on TLC afforded β-caryophyllene (30 mg), while fractions 3 and 4 yielded nothing of interest. Fraction 5 on repeated TLC (petrol–$Et_2O$, 7:3) yielded **1** (9 mg) and stigmasterol (28 mg). Fraction 6 after TLC (petrol–$Et_2O$, 7:3, five developments) gave a mixture which on further TLC ($CH_2Cl_2$–$C_6H_6$–$Et_2O$, 3:3:1) afforded **1** (26 mg, $R_f$ 0.6) and another mixture after exhaustive TLC ($CH_2Cl_2$–$C_6H_6$–$Et_2O$, 4:4:1) gave **2** (10 mg) and **3** (15 mg, $R_f$ 0.35). Fraction 7 on further TLC yielded artemetin (20 mg)



**1**



**2**



**3**

while fraction 8 gave 3′-OMe-chrysosplenol (8 mg) and 6,7,4′-tri-OMe-3,5,3′-trihydroxyflavone (12 mg). Fraction 9 afforded chrysosplenol (22 mg).

*Arteannuin C* (**3**). Colourless crystals, mp 128°; IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm$^{-1}$: 1770 ($\gamma$-lactone), 1250, 930, 860, (epoxide), MS $m/z$ (rel. int.): 248 $[M]^+$ (5), 230 $[M-H_2O]^+$ (7), 206 $[M-\text{ketene}]^+$ (70), 190 $[M-OCOCH_2]^+$ (67), 177 (75), 169 (100), 55 (35), 43 (58), 41 (42); $^1$H NMR (CDCl$_3$): $\delta$2.05 (*ddd*, H-1$\alpha$, $J = 12, 3, 3$ Hz), 2.65 (*s*, H-5$\alpha$), 2.66 (*dddd*, H-7, $J = 12, 6, 3, 3$ Hz), 6.20 (*d*, H-13, $J = 3$ Hz), 5.40 (*d*, H-13′, $J = 3$ Hz), 0.95 (*brd*, H-14, $J = 6$ Hz), 1.30 (*s*, H-15). $[\theta]_{270} - 1249$.

$$\alpha_{26}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 435}{-26.04 \quad -27.36 \quad -36.04 \quad -55.6} \text{ (MeOH; } c \text{ 0.53).}$$

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## REFERENCES

1. Singh, A., Kaul, V. K., Singh, A., Mahajan, V. P., Misra, L. N., Thakur, R. S. and Husain, A. (1986) *Indian J. Pharm. Sci.* (in press).
2. Tu, Y., Ni, M., Zhong, Y., Li, L., Cui, S., Zhang, M., Wang, X. and Liang, X. (1981) *Yaoxue Xuebao* **16**, 366 (Chem. Abstr. **97**, 52497q).
3. Liu, H., Li, K. and Wo, W. C. (1980) *Yao Hsueh Tung Pao*, **15**, 39 (Chem. Abstr. **95**, 121030e).
4. Tu, Y., Ni, M., Zheng, Y., Li, L., Cui, S., Zhang, M., Wang, X., Ji, Z. and Liang, X. (1982) *Planta Med.* **44**, 143.
5. Jeremic, D., Jokic, A., Behbund, A. and Stefanovic, M. (1973) *Tetrahedron Letters* **32**, 3039.

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# A *NOR*-DITERPENE AND OTHER CONSTITUENTS FROM *ISOCOMA CORONOPIFOLIA*

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**Key Word Index**—*Isocoma coronopifolia*; Astereae; grindelanes; diterpenes; *nor*-labdane; sesquiterpenes; endoperoxide; renecraviotonic acid, a cedrene derivative.

**Abstract**—The aerial parts of *Isocoma coronopifolia* afforded several known compounds including diterpenes related to grindelic acid, one of them being a new *nor*-diterpene. Furthermore a new eudesmene endoperoxide and a derivative of $\alpha$-cedrene were isolated.

The aerial parts of *Isocoma coronopifolia* Greene, tribe Astereae, afforded, in addition to the widespread compounds $\beta$-seseline, caryophyllene, $\delta$-cadinene and $\beta$-phytene (see Experimental), the diterpene grindelic acid **1** [1–6], and its analogs **2** [7], **3** [8] and **4** [9] as well as the *nor*-diterpene **5**. The structure of the latter was deduced from the molecular formula and the $^1$H NMR spectrum (see Experimental) which was in part close to that of the corresponding 6-desoxo derivative [9]. The presence of a singlet at $\delta$2.91 and the downfield shifts of H-7 and H-17 indicated the presence of 6-keto group. From a W-coupling between H-14 and H-16 the quasi-axial orientation of the 13-methyl group was deduced. Furthermore, the endoperoxide **6** and the cedrene derivative renecraviotonic acid (**7**) were present. The structure of **6** was deduced from the spectral data. The presence of an endoperoxide was indicated by the mass spectrum, which showed loss of oxygen from the molecular ion. The $^1$H NMR spectrum (see Experimental) showed that an eudesmane derivative was present. Spin decoupling allowed the assignment of most signals. The stereochemistry followed from the presence of a W-coupling between H-1$\alpha$ and H-14$\alpha$, from the NOE between H-15 and from biogenetic considerations. The necessary precursor would be eudesm-5,7-diene which should react with oxygen from the $\alpha$-side as the $\beta$-side is hindered by the methyl groups at C-4 and C-10.

The structure of renecraviotonic acid (**7**), which was transformed to the methyl ester **7a**, was deduced from the $^1$H NMR spectrum (see Experimental) which was very similar to that of $\alpha$-cedrene and the corresponding 15-aldehyde. Spin decoupling allowed the assignment of