*Chemistry of Natural Compounds, Vol. 34, No. 2, 1998*

# 3-OXOCOSTUSIC ACID FROM *Artemisia altaiensis*

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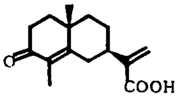
UDC 547.314+548.737

*From the epigeal part of* Artemisia altaiensis *Krash. we have isolated 3-oxocostus acid (selina-4,11(13)-dien-3-on-12-oic acid), the structure of the molecule of which has been confirmed by x-ray structural analysis, while its absolute configuration has been established from the results of circular dichroism.*

*Artemisia altaiensis* Krash. belongs to the Absinthium DC section within the subgenus *Artemisia* L. Its area is located in the south-eastern Altai and in the region of Mongolia adjacent to it [1]. This *Artemisia* species has not been studied at all chemically.

We have carried out an investigation of the air-dry epigeal part of this plant. An evaporated ethanolic extract was succesively treated with water (to eliminate ballast substances) and extracted with benzene. According to TLC, the benzene extract contained one substance predominantly, and this was isolated by chromatography on $SiO_2$, being obtained in the form of colorless crystals with mp 149-151°C, yield 0.02% on the initial raw material. According to the results of high-resolution mass spectrometry and elementary analysis, the substance isolated, (1), had the empirical formula $C_{15}H_{20}O_3$. Its molecular structure was established by x-ray structural analysis (see Fig. 1). The bond lengths are close to the statistically mean values [2]. The cyclohexane fragment of the molecule is present in the chair conformation, and the cyclohexene ring has the form of a distorted half-chair with deviations of the C(2) and (C1) atoms in different directions from the plane of the double bond by 0.162(5) and 0.550(5) Å, respectively.

The closest analog in the Cambridge Crystallographic Data Centre* [3] to the keto acid (1) that we have investigated is the structurally related lactone 1,2-dihydro-6β-santonin (2) [4].



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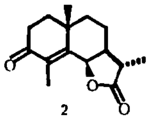

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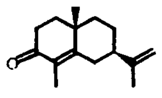

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On the whole, the geometries and conformations of these two compounds agree. We may note that in lactone (2), in contrast to the keto acid (1), in the cyclohexene fragment the C(2) and C(1) atoms deviate from the plane of the double bond in the same direction by 0.102 and 0.686 Å, respectively. There is also some discrepancy in the values of the C(3)-C(4) and C(3)-O(1) bond lengths: for (1) they are 1.505 and 1.198 Å, respectively. In the crystal, the molecules of keto acid (1) are linked into infinite chains twisted around a fourth-order $4_3$ axis with the aid of the hydrogen bonds O(3)-H...O(1) (O-H 0.89, O(3)...O(1) 2.68, H...O(1) 1.81 Å, O(3)-H...O(1) 164°).

The absolute configuration of the molecule of acid (1) was the same as that of (+)-α-cyperone (3), which was established by circular dichroism studies: for both compounds a negative Cotton effect was observed for the $n \rightarrow \pi^*$ transition and a positive one for the $\pi \rightarrow \pi^*$ transition in the α-enone system, as for 4-methyl-$\Delta^4$-cholesten-3-one [5].

A substance with mp 153°C and the presumed structure (1) (3-oxocostus acid) was isolated by Bohlman et al. [6] from the epigeal part of *Ageratina glabrata* (HBK) King. et Rob. As these authors report, the absolute configuration of the molecule

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*The authors thank RFFI (project 96–07–89 187) for the possibility of using the Cambridge Crystallographic Data Centre.

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TABLE 1. Coordinates ($\times 10^4$) and Equivalent Temperature Factors ($\times 10^3/\text{Å}^2$) of the Nonhydrogen Atoms of Compound (1)

| Atom | $x/a$ | $y/b$ | $z/c$ | $U_{eq.}$ |
|---|---|---|---|---|
| C(1) | 2720 (5) | 1823 (6) | 8010 (1) | 69 (1) |
| C(2) | 643 (5) | 1080 (6) | 8051 (1) | 73 (1) |
| C(3) | 291 (4) | 90 (4) | 8486 (1) | 55 (1) |
| C(4) | 1468 (4) | 690 (4) | 8874 (1) | 54 (1) |
| C(5) | 2783 (4) | 2159 (4) | 8839 (1) | 51 (1) |
| C(6) | 3747 (4) | 3037 (4) | 9245 (1) | 57 (1) |
| C(7) | 5985 (4) | 3204 (4) | 9203 (1) | 55 (1) |
| C(8) | 6482 (4) | 4326 (5) | 8780 (1) | 66 (1) |
| C(9) | 5580 (4) | 3307 (5) | 8379 (1) | 62 (1) |
| C(10) | 3333 (4) | 3111 (4) | 8399 (1) | 54 (1) |
| C(11) | 6866 (4) | 4073 (4) | 9621 (1) | 59 (1) |
| C(12) | 7134 (4) | 2680 (4) | 9998 (1) | 58 (1) |
| C(13) | 7328 (6) | 5950 (5) | 9670 (1) | 86 (1) |
| C(14) | 1014 (6) | −390 (6) | 9299 (1) | 79 (1) |
| C(15) | 2370 95) | 5152 (5) | 8367 (1) | 75 (1) |
| O(1) | −1042 (3) | −1110 (3) | 8527 (1) | 68 (1) |
| O(2) | 6580 (5) | 1006 (4) | 9989 (1) | 89 (1) |
| O(3H) | 8022 (3) | 3446 (3) | 10349 (1) | 71 (1) |
| H(3O) | 8213 (57) | 2476 (64) | 10544 (14) | 80 (11) |

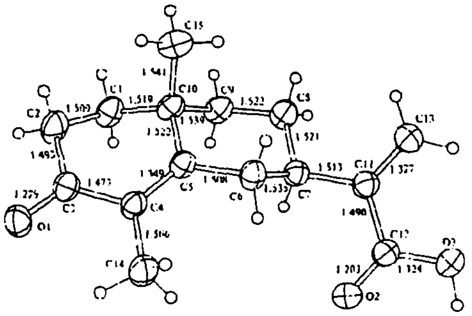

Fig. 1. Molecular structure of compound (1). The errors in the bond lengths amount to 0.003-0.005 Å.

of the acid isolated remained undetermined, and no information on its optical activity is given in the cited paper. The PMR spectrum of acid (1) (in $C_6D_6$) corresponds to that described in [6].

We have found no literature reports on the presence of acid (1) in *Artemisia* species.

## EXPERIMENTAL

The melting point was determined on a Kofler stage. The IR spectrum was obtained on a UR-20 instrument. The PMR spectrum ($\delta$ scale, TMS — 0) was recorded on a Bruker AC-200 spectrometer (working frequency for $^1$H, 200 MHz; for $^{13}$C, 50.323 MHz). A high-resolution mass spectrum (EI, 70 eV) was obtained on a Finnigan MAT 8200 instrument. Optical rotations were determined for a solution in MeOH on a Polamat A polarimeter (at 580 nm). The CD spectrum of acid (1) was recorded on a JASCO J-600 dichrograph in MeOH.

The epigeal part of *Artemisia altaiensis* gathered in 1996 in the flowering phase (beginning of August) in the environs of the village of Kosh-Agach (Kosh-Agachskii region, Altai republic) was dried in the air, the stems were separated out, and the material was comminuted.

**(7R,10S)-Selina-4,11(13)-dien-3-on-12-oic Acid (1).** The raw material (500 g) was charged into a 5-liter flask fitted with a reflux condenser, and 2.5 liters of 96% ethanol was added. The flask was heated in the water bath until the extractant began to boil and was then cooled, and the extractant was poured off. This process was repeated twice more. The combined extract (7 liters) was filtered and evaporated under vacuum to small volume (0.2 liter), and 0.4 liter of hot distilled water was added to it with stirring. After cooling, the precipitate that had deposited was filtered off and dissolved in the minimum volume of 96% ethanol, and this solution was mixed with double its volume of distilled water. After cooling, the precipitate was filtered off, and the combined aqueous ethanolic filtrates were extracted with benzene. The benzene extract was evaporated to dryness. Chromatography of the product on $SiO_2$ (eluent — petroleum ether with increasing concentrations of ethyl acetate) led to the isolation of 0.1 g of the acid (1) with mp 149-151°C (petroleum ether). $[\alpha]^{22}_{580}$ +62.3° (*c* 0.61). Mass spectrum *m/z* (*I*, %): 248 ($M^+$, 93), 233 (100), 215 (20), 206 (16). Found: 248.14060. Calculated $C_{15}H_{20}O_3$: 248.14123.

Found, %: C 72.47; H 8.29. Calculated $C_{15}H_{20}O_3$: C 72.55; H 8.12.

UV spectrum ($\lambda_{max}$EtOH (lg$\varepsilon$, nm): 248 (4.05). CD spectrum ($\lambda_{max}$MeOH ($\Delta\varepsilon$, nm): 250 (+35.4), 300 (−5.0) (*c* $3.2 \times 10^{-4}$ M). IR spectrum (in $CHCl_3$): 1690, 1655 (C=O), 1625, 1610 (C=C) $cm^{-1}$; (in KBr): 1711 (C=O), 1616 (C=C), 1550, 1518, 1423, 1385, 1140, 1005, 584 $cm^{-1}$.

$^{13}C$ NMR spectrum ($\delta$, ppm, in $CDCl_3$): singlets at 199.07, 171.49, 161.04, 143.78, 129.14, and 35.69; doublet at 39.62; triplets at 125.56, 41.69, 37.27, 33.65, 33.23, and 27.06; quartets at 22.40 and 10.83.

**The x-ray structural analysis** of compound (1) was conducted on a Syntex $P2_1$ diffractometer (Cu-$K_\alpha$ radiation with a graphite monochromator). The crystals were tetragonal: $a = b = 6.8180$ (9), $c = 30.047$ (4) Å, V = 1396.7 (3) Å$^3$, space group $P4_3$, Z = 4, $C_{15}H_{20}O_3$, $\mu = 0.651$ mm$^{-1}$, $d_{calc} = 1.181$ g/cm$^3$. The intensities of 1352 independent reflections with $2\theta < 140°$ were measured by the $\theta/2\theta$ scanning method. Corrections were made for absorption at the crystal face (transmission 0.67-0.80). The structure was interpreted by the direct method using the SHELX-86 program. The final refinement of the parameters was carried out by the method of least squares in the full-matrix anisotropic (isotropic for H atoms) approximation by the SHELX-93 program to $wR_2 = 0.1108$ for all $F^2$ (R = 0.0375 for 1242 $F_0 > 4\sigma$; 169 parameters were refined). The coordinates and equivalent temperature factors of the nonhydrogen atoms are given in Table 1.

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