Chemistry of Natural Compounds, Vol. 36, No. 2, 2000

MOLECULAR STRUCTURE OF CREPIDIOSIDE A AND ISOLIPIDIOL FROM *Crepis multicaulis*

A. S. Fazylova, K. M. Turdybekov, G. M. Kadirberlina, B. B. Rakhimova, and S. M. Adekenov

UDC 547.314:548.737

Crepidioside A, a guaian-like sesquiterpene lactone, is isolated from Crepis multicaulis *Ldb. and identified. The structure 15-glycoside-2-oxo-5,7α,6β(H)-guai-1(10),3(4),11(13)-trien-6,12-olide is found from an x-ray structure analysis. 8-Epi-isolipidiol is isolated from* Crepis tectorum *L. Its new polymorphic crystal structure is found from an x-ray structure analysis.*

Key words: *Crepis multicaulis*, 15-glycoside-2-oxo-5,7α,6β(H)-guai-1(10),3(4),11(13)-trien-6,12-olide, 8-*epi*-isolipidiol, x-ray structure analysis.

Sixteen species of the *Crepis* L. genus grow in Kazakhstan. The chemical composition of the secondary metabolites from plants of this genus are little studied. It has been reported that they contain sterols, glycosides, and terpenes [1, 2]. Therefore, we studied the phytochemistry of six species of the *Crepis* L. genus.

The above-ground part of *Crepis multicaulis* Ldb. that was collected during flowering near Leninogorsk in East Kazakhstan district was extracted with $CHCl_3$. Chromatography of the extract on a KCK silica-gel column yielded crystalline $C_{21}H_{26}O_9 \cdot H_2O$, which had spectral properties (PMR, IR) identical to those of crepidioside A (**1**), which was previously isolated from *C. keiskeanum* Nakai by Japanese researchers [1].

An x-ray structure analysis of the crystalline hydrate was performed in order to find the molecular structure of **1**. Figure 1 shows that the five-membered ring A and seven-membered ring B are *pseudotrans* fused whereas ring B and lactone ring C are *trans* fused [torsion angles C10C1C5C6 = 52.7°, C2C1C5C4 = -3.6°, and H6C6C7H7 = 111.2°).

Ring A is planar (the absolute sum of the internal torsion angles is 17°). The flattening of the ring is due to the ketone on C2 and the C3=C4 double bond. Atoms C1, C2, C3, C4, and C5 are coplanar within ±0.02 Å. The conformation of ring B is 7α,1,10β-C ($\Delta C_S^7 = 5.0°$). Such a conformation might be stabilized by the presence of the C1=C10 double bond. The lactone ring C has the conformation 6β,7α-half chair ($\Delta C_2^{6,7} = 3.8°$). The glycoside residue has a significantly distorted chair conformation ($\Delta C_2^{2',3'} = 3.2°$, $\Delta C_S^1 = 11.2°$). The intracyclic torsion angles in the main framework of **1** are listed in Table 1. The structure 15-glycoside-2-oxo-5,7α,6β(H)-guai-1(10),3(4),11(13)-trien-6,12-olide is proposed on the basis of the data above.

It was communicated earlier that a crystalline compound was isolated from *Crepis tectorum* L. It was identified as 8-*epi*-isolipidiol (**2**) from its spectral properties [3]. The crystal structure of **2** was proposed to be 3,8β-dihydroxy-1,5,7α,4,6,11β(H)-guai-10(14)-en-6,12-olide [4]. However, the crystal-lattice parameters of the compound isolated by us did not agree with those in the literature. Therefore, we performed an x-ray structure analysis of the compound. It was found that the previously studied crystalline **2a** and **2b** isolated by us are polymorphic forms of 8-*epi*-isolipidiol.

Figure 2 shows that five-membered ring A and seven-membered ring B are *cis*-fused whereas ring B and ring C are *trans*-fused (torsion angles H1C1C5H5 = 11.5°, H6C6C7H7 = -157.2°).

The conformation of ring A in **2** in crystalline polymorph **2b** is a slightly distorted 3α-envelope ($\Delta C_S^3 = 7.0°$). Atoms C1, C2, C4, and C5 are coplanar within ±0.03 Å. Atom C3 lies out of this plane by 0.61 Å to the α-side. However, ring A in **2a** is a 4β-envelope ($\Delta C_S^4 = 3.8°$) (intracyclic torsion angles in **2a** and **2b** are listed in Table 1).

Institute of Phytochemistry, Ministry of Science and Higher Education, Republic of Kazakhstan, fax (3212) 43 37 73, e-mail: arglabin@phyto.karaganda.su. Translated from Khimiya Prirodnykh Soedinenii, No. 2, pp. 139-141, March-April, 2000. Original article submitted February 14, 2000.

0009-3130/00/3602-0177$25.00

TABLE 1. Ring Torsion Angles φ (deg)

1		2a		2b	
Torsion angle	φ	Torsion angle	φ	Torsion angle	φ
		Ring A			
C1C2C3C4	2.0	C1C2C3C4	26.5	C1C2C3C4	42.4
C2C3=C4C5	-4.5	C2C3C4C5	-40.1	C2C3C4C5	-38.2
C3=C4C5C1	5.1	C3C4C5C1	37.8	C3C4C5C1	19.7
C4C5C1C2	-3.6	C4C5C1C2	-21.7	C4C5C1C2	5.6
C5C1C2C3	1.3	C5C1C2C3	-3.0	C5C1C2C3	-29.3
		Ring B			
C10=C1C5C6	52.7	C10C1C5C6	-17.4	C10C1C5C6	10.3
C1C5C6C7	-75.2	C1C5C6C7	-60.0	C1C5C6C7	-77.9
C5C6C7C8	73.5	C5C6C7C8	95.8	C5C6C7C8	88.5
C6C7C8C9	-68.9	C6C7C8C9	-65.9	C6C7C8C9	-57.3
C7C8C9C10	73.9	C7C8C9C10	53.9	C7C8C9C10	60.6
C8C9C10=C1	-59.9	C8C9C10C1	79.3	C8C9C10C1	-87.4
C9C10C1C5	4.5	C9C10C1C5	80.8	C9C10C1C5	62.2
		Ring C			
C6C7C11C12	29.0	C6C7C11C12	21.3	C6C7C11C12	22.9
C7C11C12O1	-13.7	C7C11C12O1	-15.1	C7C11C12O1	-11.4
C11C12O1C6	-8.5	C11C12O1C6	2.0	C11C12O1C6	-5.8
C12O1C6C7	26.8	C12O1C6C7	12.1	C12O1C6C7	20.7
C1C6C7C11	-33.6	C1C6C7C11	-20.5	C1C6C7C11	-26.6

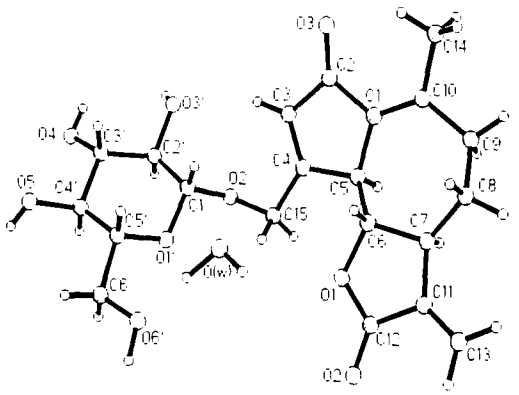

Fig. 1. Structure of **1**.

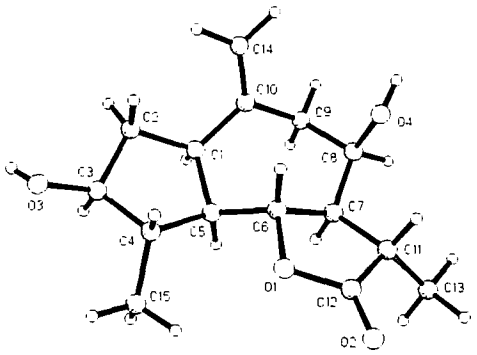

Fig. 2. Structure of **2**.

The methyl group on C4 has the α-orientation. The hydroxy group on C3 has the β-orientation. Seven-membered ring B has the 1,5α,8β-C conformation. It is noteworthy that the ring in **2a** is more distorted relative to the ideal C than in **2b** (ΔC_S^8 = 17.1 and 9.6°, respectively). The hydroxy group on C8 has the β-orientation. The conformation of the lactone ring in **2b** is 6β,7α-half chair ($\Delta C_2^{6,7}$ = 3.8°) whereas in **2a** it is almost an ideal 7α-envelope (ΔC_S^7 = 2.1°). The methyl group on C11 has the α-orientation. All differences in the conformations of **2** are due to crystal packing effects.

TABLE 2. Atomic Coordinates ($\times 10^4$; for H, $\times 10^3$) in **1**

Atom	*x*	*y*	*z*	Atom	*x*	*y*	*z*
O(1)	7204(5)	1495(2)	1700(1)	O(2′)	7562(5)	4520(2)	823(1)
O(2)	6913(5)	-244(3)	1384(1)	O(3′)	6438(5)	6791(3)	846(1)
O(3)	7075(5)	5774(3)	2851(1)	O(4′)	4211(5)	7311(3)	-145(1)
C(1)	7982(7)	3818(4)	2738(2)	O(5′)	1106(5)	5809(3)	-285(1)
C(2)	7402(7)	4957(4)	2564(2)	O(6′)	2050(5)	2476(3)	-285(1)
C(3)	7304(7)	4951(4)	1966(2)	C(1′)	5695(6)	4866(3)	714(2)
C(4)	7698(6)	3936(4)	1776(2)	C(2′)	5824(6)	6008(3)	449(2)
C(5)	8274(6)	3132(4)	2222(2)	C(3′)	3939(7)	6369(3)	204(2)
C(6)	7223(7)	2032(4)	2238(2)	C(4′)	2979(6)	5467(3)	-126(2)
C(7)	8143(7)	1160(4)	2601(2)	C(5′)	2909(6)	4390(3)	208(2)
C(8)	7918(8)	1350(4)	3213(2)	C(6′)	2074(8)	3433(4)	-110(2)
C(9)	9074(8)	2364(5)	3408(2)	O(w)	2683(8)	2618(3)	1359(2)
C(10)	8260(7)	3493(5)	3255(2)	H(O3′)	697(10)	725(5)	70(2)
C(11)	7447(8)	108(4)	2352(2)	H(O4′)	475(7)	778(5)	3(2)
C(12)	7160(8)	372(4)	1767(2)	H(O5′)	99(8)	568(5)	-64(2)
C(13)	7104(8)	-887(4)	2554(2)	H(O6′)	142(12)	183(6)	8(3)
C(14)	7848(9)	4222(5)	1767(2)	H(1)w	266(10)	196(5)	150(2)
C(15)	7703(7)	3588(3)	1187(2)	H(2)w	223(12)	252(7)	95(3)
O(1′)	4852(4)	4096(2)	345(1)				

TABLE 3. Atomic Coordinates ($\times 10^4$; for H, $\times 10^3$) in **2b**

Atom	*x*	*y*	*z*	Atom	*x*	*y*	*z*
O1	6832(3)	2629(3)	556(1)	H(O3)	1102(5)	206(5)	191(1)
O2	6019(3)	3161(3)	-81(1)	H(O4)	248(5)	275(5)	139(1)
O3	10691(3)	2427(4)	1706(1)	H(1)	702(3)	-6(4)	171(1)
O4	3224(3)	2767(3)	1214(1)	H(2)a	805(3)	272(4)	195(1)
C1	6953(5)	1001(5)	1652(1)	H(2)b	832(4)	127(5)	217(1)
C2	8211(5)	1689(6)	1890(1)	H(3)	986(4)	44(4)	161(1)
C3	9494(5)	1508(5)	1606(1)	H(4)	883(3)	291(4)	118(1)
C4	8891(5)	1874(5)	1177(1)	H(5)	741(3)	29(3)	104(1)
C5	7364(5)	1221(5)	1181(1)	H(6)	596(4)	300(4)	112(1)
C6	6229(5)	2121(5)	953(1)	H(7)	523(4)	33(4)	78(1)
C7	4864(5)	1310(5)	834(1)	H(8)	281(4)	67(4)	106(1)
C8	3694(5)	1305(5)	1168(1)	H(9)a	343(4)	67(3)	179(1)
C9	4217(5)	676(6)	1581(1)	H(9)b	445(4)	-27(4)	153(1)
C10	5453(5)	1455(5)	1783(1)	H(11)	379(4)	288(4)	48(1)
C11	4409(5)	2014(5)	423(1)	H(13)a	347(4)	156(4)	-16(1)
C12	5783(5)	2650(5)	262(1)	H(13)b	429(4)	17(4)	3(1)
C13	3689(6)	999(6)	114(2)	H(13)c	264(5)	64(4)	25(1)
C14	5222(6)	2455(6)	1071(1)	H(14)a	415(4)	264(4)	218(1)
C15	9827(5)	1391(7)	814(1)	H(14)b	609(5)	301(4)	222(1)
				H(15)a	994(4)	24(5)	81(1)
				H(15)b	1081(4)	187(4)	83(1)
				H(15)c	933(4)	155(5)	55(1)

EXPERIMENTAL

The purity of the isolated compounds was monitored by TLC on Silufol plates using ethylacetate and $KMnO_4$ in H_2SO_4. IR spectra (KBr pellets) were recorded on a UR-20 spectrometer; PMR, on a Bruker WP-200 SY (200.13 MHz, C_5D_5N, 0-TMS). Elemental analyses of the compounds agreed with those calculated.

Isolation of Crepidioside A. Leaves and flower heads of *Crepis multicaulis* were exhaustively extracted with $CHCl_3$. The solids obtained were chromatographed on a KCK silica-gel column at a 1:25 solid:silica gel ratio. Elution of the column with benzene—ethylacetate (1:1) yielded colorless crystals of $C_{21}H_{26}O_9 \cdot H_2O$, mp 132-135°C (ethanol), $[\alpha]_D^{20}$ +115° (*c* 0.3, ethanol). TLC gave one spot with $R_f = 0.37$. Yield 0.11 g of dry mass. IR spectrum (cm^{-1}): 3600-3200, 2950, 2880, 2850, 1755, 1670, 1630, 1605, 1405, 1170, 1070, 1030, 1000, 980, 955, 930, 870. PMR spectrum (δ, ppm): s, 2.30 (3H); d, 3.44 (1H, J = 10 Hz); t, 3.86 (1H, J = 10 Hz); d, 6.39 and d, 6.48 (1H, J = 3 Hz); t, 6.16 (1H, J = 1.2 Hz); s, 4.32; m, 4.5-4.9.

X-ray Structure of Crepidioside A. Cell constants and intensities of 3420 independent reflections were measured on a Syntex $P2_1$ diffractometer (Mo Kα-radiation, graphite monochromator, Θ/2Θ-scanning, $2\Theta \leq 60°$). Crystals are orthorhombic, $a = 6.978(2)$, b = 12.019(5), c = 24.492(14) Å, $V = 2054.1$ Å^3, $d_{calc} = 1.424$ g/cm^3, $Z = 4$ ($C_{21}H_{28}O_{10}$), space group $P2_12_12_1$.

A total of 1624 reflections with $I > 2\sigma$ was used. The structure was solved by direct methods using the SHELXTL (PC version) programs with anisotropic parameters for nonhydrogen atoms. H atoms of the hydroxyl and water of hydration were located in a difference electron-density map and refined isotropically. The coordinates of the remaining H atoms were assigned geometrically. The final discrepancy factors $R = 0.040$ and $R_w = 0.039$. Atomic coordinates are listed in Table 2.

Isolipidiol. Cell constants and intensities of 3367 independent reflections were measured on a Syntex $P2_1$ diffractometer (Mo Kα-radiation, graphite monochromator, Θ/2Θ-scanning, $2\Theta \leq 56°$). Crystals of **2b** are tetragonal, space group $P4_12_12_1$, $a = 9.271(2)$, c = 32.063(9) Å, $V = 2755.9$ Å^3, $d_{calc} = 1.284$ g/cm^3, $Z = 8$ ($C_{15}H_{22}O_4$). Crystals of **2a** are orthorhombic with space group $P2_12_12_1$.

A total of 1331 reflections with $I > 2\sigma$ was used. The structure was solved by direct methods using the SHELXTL (PC version) programs with anisotropic parameters for nonhydrogen atoms. H atoms were located in a difference electron-density map and refined isotropically. The final discrepancy factors $R = 0.041$ and $R_w = 0.034$. Atomic coordinates are listed in Table 3. All calculations were performed using a PC Pentium-150.

REFERENCES

1. S. Adegawa, T. Miyase, and A. Ueno, *Chem. Pharm. Bull.*, **33**, No. 11, 4906 (1985).
2. W. Kisiel and S. Kohlmunzer, *Planta Med.*, **53**, No. 4, 390 (1987).
3. S. M. Adekenov, G. M. Kadirberlina, K. M. Turdybekov, and Yu. T. Struchkov, *Khim. Prir. Soedin.*, 5 (1991).
4. U. Rychlewska and W. Kisiel, *Acta Crystallogr. Sect. C: Cryst. Struct. Commun.*, **47**, 129 (1991).