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MOLECULAR AND CRYSTAL STRUCTURES OF THE COMPLEX OF 18-DEHYDROGLYCYRRHETIC ACID WITH DIMETHYL SULFOXIDE

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The crystal structure of the complex of 18-dehydroglycyrrhetic acid (GLD) with DMSO ($C_{30}H_{41}O_4 \cdot C_2H_6OS$) has been determined by x-ray structural analysis. Syntex P21 diffractometer, CuK_α radiation, 1309 reflections, R = 0.080. A conformational analysis has been made of the GLD molecule in comparison with that of glycyrrhetic acid. The conformations of rings A *and* B *in the GLD molecule do not differ from the conformations of the corresponding rings of glycyrrhetic acid. Differences arise in rings* C, D, *and* E *because of the presence of the double bond between the C18 and C19 atoms.*

Glycyrrhetic acid, a component of the saponin of *Glycyrrhiza glabra*, and its derivatives possess fairly strong antiinflammatory properties [1]. These properties are most pronounced in 18-dehydroglycyrrhetic acid, known under the name of gliderinin, which is obtained by a dehydrogenation reaction [2-4].

The structure of the complex of glycyrrhetic acid–acetone–water has been studied [5]. In the present paper we give the results of x-ray structural analysis for the complex of 18-dehydroglycyrrhetic acid (GLD) with DMSO and those of a comparative conformational analysis.

The triterpenoid gliderinin is a pentacyclic system in which rings *A/B* and *B/C* are *trans*-linked (Fig. 1).

Ring *A* has the form of a slightly distorted chair with the asymmetry parameter [6, 7] $\Delta C_S = 4.2°$, calculated from the values of the torsional angles (Table 1) because of the repulsion of the axial methyl groups at C4 and C10 (the distance between C23 and C24 is 3.22 Å). In ring *A* the C1, C2, C4, and C5 atoms are coplanar to within 0.01 Å, and C3 and C10 depart from this plane in opposite directions by 0.68 and 0.63 Å, respectively.

The deviation from the conformation of an ideal chair of ring *B* ($\Delta C_S = 3.7°$) is caused by the repulsion of the axial methyl groups at C4 and C8 (the C24–C26 distance is 3.33 Å). In ring *B* the C6, C7, C9, and C10 atoms are coplanar to within 0.01 Å, and C5 and C8 depart from this plane by 0.73 and 0.56 Å, respectively.

Rings *C, D,* and *E* have half-chair conformations, differing from the conformations of the corresponding rings in glycyrrhetic acid. These differences are explained by the presence of the C18–C19 double bond. Ring *C* exists in the half-chair form with C_2 symmetry ($\Delta C_2 = 6.9°$) instead of the traditional sofa, and rings *D* and *E* in the half-chair form instead of the chair form. For rings *D* and *E* the asymmetry parameters ΔC_2 are 1.2 and 15.2°, respectively. The position of the carboxy group is axial in relation to ring *E*.

In the crystal structure of the complex GLD+DMSO, the DMSO molecule has two bonds: O4–H···OG, 2.59 Å long, with the basis GLD molecule, and S1···H–O2, 3.20 Å long, with another GLD molecule. These two bonds bind the GLD molecules into chains. The structure of the complex is formed by the packing of these chains extended along the *z* axis (Fig. 2). The interaction between the chains is of the van der Waals type.

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TABLE 1. Torsional Angles (degrees) for the GLD Molecule

C10	C1	C2	C3	58.9	C8	C9	C10	C1	166.7
C1	C2	C3	C4	-61.9	C8	C9	C10	C5	51.6
C1	C2	C3	O2	175.5	C8	C9	C10	C25	-75.3
C2	C3	C4	C5	56.5	C11	C9	C10	C1	-63.0
C2	C3	C4	C23	-71.4	C11	C9	C10	C5	-178.2
C2	C3	C4	C24	171.2	C11	C9	C10	C25	55.0
O2	C3	C4	C5	179.6	C8	C9	C11	C12	-41.9
O2	C3	C4	C23	51.7	C8	C9	C11	O1	137.1
O2	C3	C4	C24	-65.6	C10	C9	C11	C12	-175.9
C3	C4	C5	C6	175.2	C10	C9	C11	O1	3.2
C3	C4	C5	C10	-53.3	C9	C11	C12	C13	7.6
C23	C4	C5	C6	-58.7	O1	C11	C12	C13	-171.5
C23	C4	C5	C10	72.8	C11	C12	C13	C14	7.1
C24	C4	C5	C6	61.6	C11	C12	C13	C18	-173.1
C24	C4	C5	C10	-166.9	C7	C8	C14	C13	-170.1
C4	C5	C6	C7	-159.3	C7	C8	C14	C15	69.3
C10	C5	C6	C7	64.1	C7	C8	C14	C27	-51.6
C5	C6	C7	C8	-56.5	C9	C8	C14	C13	-48.4
C6	C7	C8	C9	44.7	C9	C8	C14	C15	-168.9
C6	C7	C8	C14	164.6	C9	C8	C14	C27	70.2
C6	C7	C8	C26	-77.4	C26	C8	C14	C13	71.4
C7	C8	C9	C10	-44.4	C26	C8	C14	C15	-49.1
C7	C8	C9	C11	-177.6	C26	C8	C14	C27	-170.0
C14	C8	C9	C10	-165.3	C12	C13	C14	C8	14.9
C14	C8	C9	C11	61.4	C12	C13	C14	C15	138.4
C26	C8	C9	C10	76.6	C12	C13	C14	C27	-108.2
C26	C8	C9	C11	-56.6	C18	C13	C14	C8	-164.9
C2	C1	C10	C5	-50.0	C18	C13	C14	C15	-41.4
C2	C1	C10	C9	-166.2	C18	C13	C14	C27	72.0
C2	C1	C10	C25	69.9	C8	C14	C15	C16	175.2
C4	C5	C10	C1	50.7	C13	C14	C15	C16	50.3
C4	C5	C10	C9	166.6	C27	C14	C15	C16	-61.0
C4	C5	C10	C25	-64.9	C14	C15	C16	C17	-60.0
C6	C5	C10	C1	-175.7	C15	C16	C17	C18	50.8
C6	C5	C10	C9	-59.9	C15	C16	C17	C22	172.1
C6	C5	C10	C25	68.7	C15	C16	C17	C28	-66.0
C12	C13	C18	C17	-141.2	C18	C19	C20	C30	122.6
C12	C13	C18	C19	39.1	C19	C20	C21	C22	-32.6
C14	C13	C18	C17	38.6	C29	C20	C21	C22	87.9
C14	C13	C18	C19	-140.8	C30	C20	C21	C22	-154.0
C16	C17	C18	C13	-39.8	C16	C17	C22	C21	-167.6
C16	C17	C18	C19	139.6	C18	C17	C22	C21	-46.8
C22	C17	C18	C13	-160.1	C28	C17	C22	C21	70.2
C22	C17	C18	C19	19.2	C20	C21	C22	C17	55.7
C28	C17	C18	C13	80.1	C19	C20	C30	O3	146.8
C28	C17	C18	C19	-100.6	C19	C20	C30	O4	-42.9
C13	C18	C19	C20	-178.3	C21	C20	C30	O3	-91.8
C17	C18	C19	C20	2.3	C21	C20	C30	O4	78.6
C18	C19	C20	C21	3.1	C29	C20	C30	O3	27.3
C18	C19	C20	C29	-118.1	C29	C20	C30	O4	-162.4

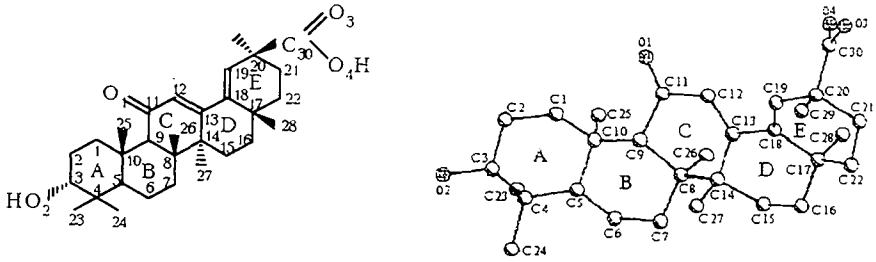

Fig. 1. Conformation of the 18-dehydroglycyrrhetic acid molecule.

EXPERIMENTAL

Single crystals of the GLD+DMSO complex were obtained by preparing a saturated solution of gliderinin (purity 83%) in DMSO at 65°C, and leaving this at room temperature. After a month, crystals of the complex suitable for x-ray structural analysis had formed.

TABLE 2. Coordinates ($\times 10^{-4}$) and Temperature Factors (Å $\times 10^{-3}$) of the Atoms of the Complex GLD−DMSO

Atom	x	y	z	U†
C1	10526(25)	9069(20)	3001(5)	48(8)
C2	10668(30)	8992(24)	3433(6)	80(11)
C3	9415(29)	8123(23)	3588(6)	65(9)
C4	7525(32)	8515(23)	3502(6)	66(10)
C5	7397(23)	8652(20)	3063(5)	44(7)
C6	5576(25)	8928(21)	2918(4)	49(8)
C7	5411(22)	8611(19)	2501(6)	52(8)
C8	6764(22)	9264(14)	2258(5)	30(6)
C9	8619(25)	9204(16)	2442(5)	42(7)
C10	8710(26)	9457(18)	2866(5)	43(7)
C11	9902(27)	9902(19)	2200(5)	47(8)
C12	9656(28)	9691(17)	1792(5)	49(7)
C13	8364(24)	9067(15)	1622(4)	34(6)
C14	6871(24)	8640(18)	1859(5)	43(7)
C15	5188(27)	8882(22)	1620(6)	66(9)
C16	5288(27)	8385(25)	1215(5)	71(10)
C17	6760(30)	8921(20)	994(6)	55(8)
C18	8476(27)	8841(18)	1218(5)	48(7)
C19	9948(30)	8561(24)	1041(6)	75(11)
C20	10225(35)	8339(24)	637(6)	68(10)
C21	8520(31)	8553(26)	415(6)	86(12)
C22	6908(32)	8253(29)	614(7)	98(13)
C23	6932(34)	9585(23)	3731(6)	97(12)
C24	6340(33)	7443(25)	3624(6)	99(13)
C25	8548(31)	10811(18)	2977(6)	71(9)
C26	6178(25)	10545(19)	2201(5)	53(9)
C27	7134(26)	7245(16)	1885(5)	58(8)
C28	6431(33)	10244(22)	923(6)	87(11)
C29	10817(37)	7054(22)	582(7)	96(13)
C30	11548(38)	9195(25)	483(7)	69(11)
O1	11002(19)	10602(16)	2317(4)	77(7)
O2	9637(24)	7983(19)	3993(4)	117(9)
O3	12542(28)	8936(18)	227(6)	126(10)
O4	11426(25)	10319(18)	596(5)	103(8)
S1	8686(13)	3067(9)	189(3)	125(4)
C1d	10279(35)	4234(24)	213(8)	131(15)
C2d	7012(35)	3857(30)	449(8)	153(18)
O1d	8073(19)	3069(11)	−205(3)	103(5)

†$U_{eq} = 1/3\ \Sigma_i\Sigma_j U_{ij} a_i^* a_j^* a_i a_j$.

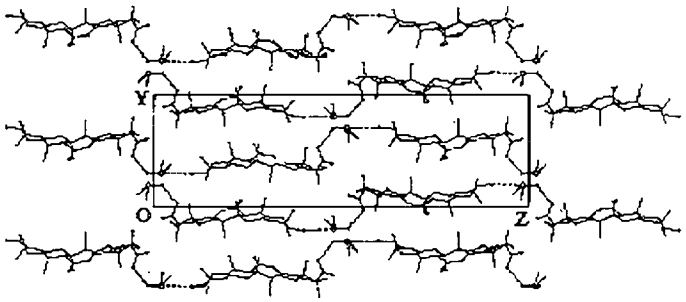

Fig. 2. Crystal structure of the complex of 18-dehydroglycyrrhetic acid with DMSO.

The crystallographic parameters of single crystals were determined and refined from 15 reflections on a Syntex P21 automatic four-circle diffractometer: $a = 7.704(2)$ Å, $b = 11.074(4)$ Å, $c = 35.517(8)$ Å. Sp. gr. $P2_12_12_1$, $V = 3030.8(5)$ Å^3.

Integral intensities (2489 reflections) were measured by the $\theta/2\theta$ scanning method using CuK_α radiation monochromatized by reflection from a graphite crystal. After allowing for Lorentz and polarization factors and eliminating weak reflections with $I < 3\sigma(I)$, the working group consisted of 1309 reflections. The structure was interpreted by the direct method with the aid of the program package SHELXS-86 adapted for an IBM AT-386 PC [8] and was refined with the aid of the SHELX-76 program [9]. The hydrogen atoms of the molecule were localized by means of difference Fourier syntheses. The

divergence factor after the final stage of refinement of the position and anisotropic thermal parameters was R = 0.080. The definitive coordinates of the atoms are given in Table 2.

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