MOLECULAR AND CRYSTAL STRUCTURE OF JURINEOLIDE — A GERMACRANE LACTONE FROM Jurinea multiflora

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By extraction with chloroform, followed by treatment of the total extractive substances with hexane and chromatography of the resulting precipitate, the epigeal part of Jurinea multiflora has yielded a sesquiterpene lactone of the germacrolide type, jurineolide. The following spatial structure is proposed for jurineolide: 8α-(4'-hydroxytigloyloxy)-6β,7α(H)-germacra-trans-1(10),trans-4(5),11(13)-trien-6, 12-olide.

The epigeal part of Jurinea multiflora (L.) B. Fedtsch gathered in the flowering phase in the Karakalinskii region of Karaganda province, Kazakh SSR, was extracted with chloroform, the total extractive substances were treated with hexane, and the resulting precipitate was chromatographed on a column of type KSK silica gel, whereupon ether—ethyl acetate fractions yielded a crystalline substance with the composition $C_{20}H_{26}O_7$, mp 170-172°C (from acetone). From its physicochemical constants and spectral characteristics (IR, mass, and PMR spectra) this substance proved to be identical with jurineolide, a sesquiterpene of the germacrane type isolated previously from Jurinea cyanoides (L.) Rchb.

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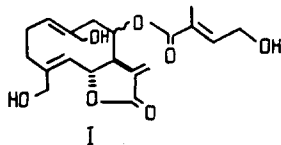
With the aim of determining the stereochemistry of the carbon skeleton, of the hydroxy groups at C14 and C15, of the endocyclic double bonds, and of the ester residue in the jurineolide molecule, we have made an x-ray structural study of it.

The general form of the molecule is shown in Fig. 1. The bond lengths (Fig. 1) and valence angles (Table 1) and are close to the usual values [2], with the exception of the ordinary C2—C3 bond, which is lengthened to 1.576(6) Å.
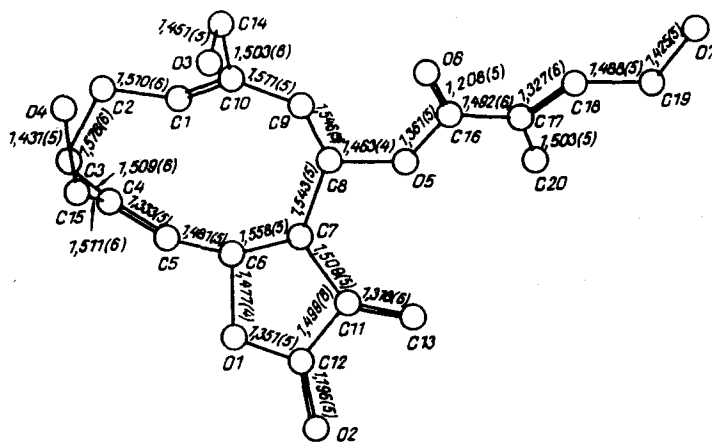

Fig. 1. Structure of the jurineolide molecule.

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TABLE 1. Valence Angles

| Angle	Degrees	Angle	Degrees
C6O1C12	111.1 (3)	C1C10C9	121.3 (3)
C8O5C16	115.7 (3)	C1C10C14	123.2 (4)
C2C1C10	126.5 (4)	C9C10C14	115.5 (3)
C1C2C3	129.0 (3)	C7C11C12	107.9 (3)
C2C3C4	109.6 (3)	C7C11C13	132.0 (4)
C3C4C5	117.8 (3)	C12C11C13	119.7 (4)
C3C4C15	118.4 (3)	O1C12O2	121.6 (4)
C5C4C15	123.7 (4)	O1C12C11	109.5 (3)
C4C5C6	126.5 (4)	O2C12C11	128.9 (4)
O1C6C5	110.3 (3)	O3C14C10	111.3 (3)
O1C6C7	105.8 (3)	O4C15C4	114.2 (3)
C5C6C7	113.8 (3)	O5C16O6	123.2 (4)
C6C7C8	111.4 (3)	O5C16C17	111.5 (3)
C6C7C11	102.4 (3)	O6C16C17	125.2 (4)
C8C7C11	118.0 (3)	C16C17C18	116.2 (4)
O5C8C7	108.3 (3)	C16C17C20	119.8 (3)
O5C8C9	105.9 (3)	C18C17C20	124.1 (4)
C7C8C9	114.4 (3)	C17C18C19	123.9 (4)
C8C9C10	113.9 (3)	O7C19C18	109.0 (3)
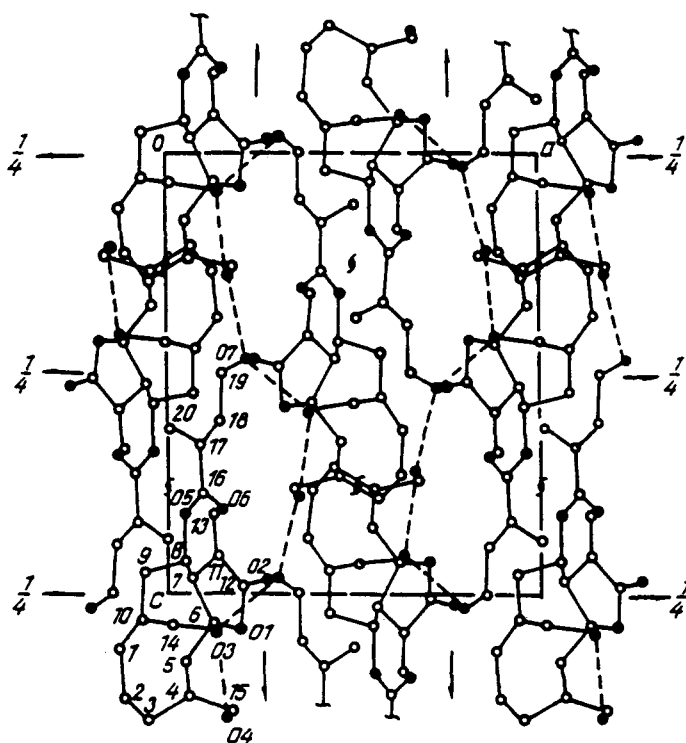
Fig. 2. Packing of the jurineolide molecules.

The lactone ring and the germacrane skeleton are trans-linked (the H6C6C7H7 torsional angle is 149(5°)). The 4-hydroxytigloyloxy group at the C8 atom has the α-orientation. The values of the C2C1C10C9 and C3C4C5C6 torsional angles relative to the endocyclic double bonds (166.6(6) and 154.2(6)°, respectively) permit jurineolide to be assigned to the trans,-trans-$\Delta^{1(10)},^4(5)$-germacranolides. As follows from Fig. 1 and the value of the C10C1C4C5 pseudotorsional angle (74.5(6)°), the germacrane ring has a chair-chair conformation of the $_1D^{14}$, $^{15}D_5$ type [3]. The intracyclic torsional angles in jurineolide (Table 2) are close to the values of the corresponding angles in eupatolide [4], alatolide [5], tamaulipin-A [6], costunolide [7], and salitenolide and hanphyllin [8]. The coordinates of the atoms are given in Table 3.

The lactone ring has the twist conformation: the C6 and C7 atoms depart from the plane of the O1, O2, C11, C12, and C13 atoms (satisfied to an accuracy of ±0.008 Å) by 0.16 and 0.14 Å in the β- and α-directions, respectively. Mention must be made of the substantially planar geometry of the C13=C11–C12=O2 grouping (torsional angle 0.1(7)°), which thereby

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TABLE 2. Intracylic Torsional Angles

Angle	Degrees	Angle	Degrees
C10C1C2C3	−106.4 (6)	C8C9C10C1	−167.3 (5)
C1C2C3C4	49.7 (4)	C9C10C1C2	166.6 (2)
C2C3C4C5	−83.9 (5)		
C3C4C5C6	154.2 (6)	C11C7C6O1	−18.0 (4)
C4C5C6C7	−133.9 (6)	C7C6O1C12	16.4 (4)
C5C6C7C8	93.6 (5)	C6O1C12C11	−7.4 (4)
C6C7C8C9	−91.6 (7)	O1C12C11C7	−5.0 (4)
C7C8C9C10	78.7 (4)	C12C11C7C6	14.1 (4)

TABLE 3. Coordinates of the Atoms ($\times 10^4$; for the H atoms, $\times 10^3$)

Atom	x	y	z	Atom	x	y	z
O1	1926 (2)	5208 (2)	10739 (2)	HO3	154 (3)	964 (3)	1069 (2)
O2	2656 (3)	3934 (2)	9702 (2)	HO4	166 (3)	898 (3)	1231 (2)
O3	1289 (3)	9228 (2)	10832 (2)	HO7	233 (3)	963 (3)	412 (2)
O4	1581 (3)	8727 (2)	12772 (2)	H1	−182 (3)	736 (3)	1113 (2)
C5	447 (2)	7329 (2)	8205 (2)	H2.1	−73 (3)	908 (3)	1255 (2)
O6	1401 (3)	8990 (2)	8113 (2)	H2.2	−200 (3)	835 (3)	1260 (2)
O7	2169 (3)	9642 (3)	4659 (2)	H3.1	−43 (3)	751 (3)	1355 (2)
C1	−1300 (3)	8059 (3)	11280 (3)	H3.2	−134 (3)	662 (3)	1289 (2)
C2	−1188 (4)	8310 (4)	12355 (3)	H5	−33 (3)	588 (3)	1147 (2)
C3	−563 (4)	7291 (4)	12873 (3)	H6	183 (3)	692 (3)	1067 (2)
C4	533 (1)	6987 (3)	12321 (3)	H7	−26 (3)	594 (3)	976 (2)
C5	427 (3)	6309 (3)	11552 (3)	H8	122 (3)	785 (3)	948 (2)
C6	1224 (3)	6250 (3)	10762 (3)	H9.1	−128 (3)	753 (3)	945 (2)
C7	582 (3)	6228 (3)	9700 (3)	H9.2	−88 (3)	866 (3)	901 (2)
C8	458 (3)	7420 (3)	9269 (2)	H13.1	176 (3)	451 (3)	802 (2)
C9	−689 (3)	8627 (3)	9548 (3)	H13.2	69 (3)	524 (3)	772 (2)
C10	−684 (3)	8520 (3)	10564 (3)	H14.1	2 (3)	1000 (3)	1016 (2)
C11	1284 (3)	5375 (3)	9133 (3)	H14.2	−16 (3)	998 (3)	1143 (2)
C12	2040 (4)	4750 (3)	9842 (3)	H15.1	203 (3)	727 (3)	1336 (2)
C13	1244 (4)	5052 (3)	8214 (3)	H15.2	243 (3)	729 (3)	1213 (2)
C14	74 (4)	9540 (3)	10702 (3)	H18	192 (3)	938 (3)	643 (2)
C15	1667 (4)	7539 (4)	12618 (3)	H19.1	64 (3)	870 (3)	473 (2)
C16	941 (3)	8202 (3)	7713 (3)	H19.2	188 (3)	790 (3)	481 (2)
C17	847 (3)	8047 (3)	6636 (3)	H20.1	−58 (3)	684 (3)	664 (2)
C18	1467 (4)	8751 (3)	6992 (3)	H20.2	51 (3)	659 (3)	611 (2)
C19	1497 (4)	8717 (4)	5007 (3)	H20.3	−49 (3)	745 (3)	560 (2)
C20	65 (4)	7147 (4)	6230 (3)				

loses chirality, this being unusual for α,β-unsaturated γ-lactones (in the molecules of eupatolide, tamaulipin-A, costunolide, salitenolide, and hanphyllin, this angle ranges from -20 to -10°). It is possible that the flattening is due to the influence of the crystal field, in a similar way to what is observed in the crystal structure of alatolide, where the C13C11C12O2 torsional angle amounts to 0.1(5)° and agrees with the value obtained by a calculation of the conformation of the free molecule by the method of molecular mechanics (MMM).

Thus, the results obtained permit us to propose for jurineolide the spatial structure of 8α-(4'-hydroxytigloyloxy)-6β,7α(H)-germacra-trans-1(10),trans-4(5),11(13)-trien-6,12-olide.

An ac projection of the crystal structure of jurineolide is shown in Fig. 2. All three H atoms of OH groups participate in H-bonds: intramolecular O4—H...O3 (x, y, z) O...O 2.75, H...O 2.09 Å, angle O—H...O 154.2°); intermolecular O3—H...O7 (0.5 + x, 2.5 − y, −z), (O...O 2.74, H...O 2.12 Å, angle O—H...O 147.8°) and O7—H...O4 (x, y, −1 + z) (O...O 2.89 Å, H...O 2.30 Å, angle O7—H...O 171.6°), forming infinite ribbons of molecules along a 2_1 axis [1/4, 0, z].

EXPERIMENTAL

The individuality of the substances isolated was checked by TLC on Silufol plates in the ethyl acetate—acetone system, with revelation by a saturated solution of $KMnO_4$ in H_2SO_4. Melting points were determined on a Boëtius instrument. IR spectra were taken on a UR-20 spectrophotometer (tablets with KBr)), PMR spectra on a Bruker WP 200 SY (200 MHz), CDCl₃, O — TMS), and mass spectra on a Finnigan MAT-8200.

The results of elementary analysis agreed with the corresponding calculated figures.

Isolation of Jurineol. The flower heads and leaves of <u>J. multiflora</u> (2.4 kg) gathered in the flowering phase in Karkaralinskii region of Karaganda province, Kazakh SSR, were exhaustively extracted with chloroform. Evaporation of the solvent yielded 115 g of a syrupy mass, which was treated with hexane (5 × 0.3 liter). The precipitate that then deposited (35.2 g) was chromatographed on a column of KSK silica gel at a ratio of substance to support of 1:24. When the column was eluted with ether—ethyl acetate (1:1) a crystalline mass deposited, and after recrystallization from acetone a colorless crystalline substance with the composition $C_{20}H_{26}O_7$, mp 170-172°C (from acetone) was obtained. TLC revealed a single spot with R_f 0.83. The yield calculated on the air-dry raw material was 0.013%.

IR spectrum: ν_{max}^{KCl} 3320, 2960, 2840, 2860, 1770, 1720, 1660, 1480, 1450, 1410, 1370, 1280-1250, 1150-1130, 1080, 1040, 1010, 960 cm^{-1}. Mass spectrum (m/z, %): 260(6.8) $M^+ - C_5H_{10}O_3$: 242(21.9) $M^+-C_5H_{10}O_3-H_2O$; 213(16.4); 169(6.84); 105(12.3); 99(95.9); 95(6.84); 91(18.5); 82(24.6); 79(14.7); 71(84.9); 53(16.4); 43(100). PMR spectrum, 1.97 (3H, s); 4.52 (2H, s); 4.59 (2H, d, J = 6 Hz); 5.19 (1H, d, J = 11 Hz); 5.37 (1H, tr, $J_1 = J_2 = 11$ Hz); 5.53 (1H, m); 5.70 (1H, d, J = 3 Hz); 6.14 (1H, d, J = 3 Hz); 6.43 (1H, tr, $J_1 = 9$ Hz, $J_2 = 8.5$); 7.56 (1H, tr. d, $J_1 = 5.5$, $J_2 = 5.0$).

X-Ray Structural Analysis. The cell parameters and the intensities of the reflections were measured on a Hilger—Watts automatic four-circle diffractometer (λMoK_α, graphite monochromator, $\theta/2\theta$ scanning, $2\theta \leq 62°$). Crystals rhombic, a = 11.4486(7), b = 11.8924(6), c = 13.709(1) Å, V = 1866.5(2) $Å^3$, M = 375.4, d_{calc} = 1.335 g/cm^3, Z = 4 ($C_{20}H_{26}O_7$), sp. gr. $P2_12_12_1$.

The calculation were made with 1511 independent reflections having I ≥ 2σ. The structure was interpreted by the direct method and was refined by block-diagonal MLS in the anisotropic approximation for the nonhydrogen atoms. The positions of the H atoms were revealed in a difference synthesis and were refined in the isotropic approximation with the fixed value B_{iso} = 4.0 $Å^2$. The final discrepancy indices were R = 0.043 and R_w = 0.032. All the calculations were performed on an Eclipse S/200 computer by the INEXTL programs [9].

LITERATURE CITED

1. M. Suchy, L. Dolejš, V. Herout, F. Šorm, G. Snatzke, and J. Himmelreich, Collect. Czech. Chem. Commun., 34, 229-239 (1969).
2. F. H. Allen, O. Kennard, D. G. Watson, L. Brammer, A. G. Orpen, and R. Taylor, J. Chem. Soc. Perkin Trans. II, S1 (1987).
3. Z. Samek and J. Harmatha, Collect. Czech. Chem. Commun., 43, 2779 (1978).
4. A. T. McPhail and K. D. Onan, J. Chem. Soc. Perkin Trans. II, 1798 (1975).
5. P. J. Cox and G. A. Sim, J. Chem. Soc. Perkin Trans. II, 255 (1977).
6. M. E. Will and S. F. Watkins, J. Chem. Soc. Perkin Trans. II, 204 (1978).
7. M. J. Bovill, P. J. Cox, P. D. Cradwick, M. H. P. Guy, G. A. Sim, and D. N. J. Whill, Acta Crustallogr., B 32, 3203 (1976).
8. K. M. Turdybekov, S. M. Adekenov, T. V. Timofeev, S. V. Lindeman, and Yu. T. Struchkov, Khim. Prir. Soedin., 781-785 (1989).
9. R. G. Gerr, A. N. Yanovskii, and Yu. T. Struchkov, Kristallografiya, 28, 1029 (1983).