Loganin

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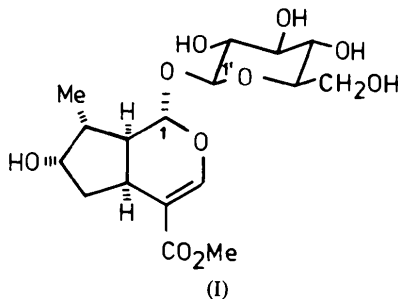
and Karl-Heinz Glüsenkamp and Lutz F. Tietze

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Abstract. $C_{17}H_{26}O_{10}$, $M_r = 390 \cdot 39$, orthorhombic, $P2_12_12_1$, $a = 8 \cdot 187$ (3), $b = 14 \cdot 277$ (8), $c = 15 \cdot 693$ (6) Å, $U = 1834$ Å^2, $Z = 4$, $D_x = 1 \cdot 413$ Mg m^{-3}, μ(Mo $K\alpha) = 0 \cdot 08$ mm^{-1}. The structure refined to $R = 0 \cdot 041$ for 3165 independent reflexions. The absolute configuration confirms that deduced by chemical means. The dihydropyran ring is in a sofa conformation.

Introduction. The monoterpene glucoside loganin (I) is a key intermediate in the biosynthesis of *Corynanthe, Aspidosperma, Iboga, Cinchona, Ipecacuanha* and *Pyrrolochinolin* alkaloids (Cordell, 1974) and of simple monoterpene alkaloids (Gross, 1970; Leete, 1969). It was first isolated from *Strychnos nux vomica* (Dunstan & Short, 1884). Its chemically deduced structure (Battersby, Hall & Southgate, 1969; Inouye, Yoshida & Tobita, 1968; Brechbühler-Bader, Coscia, Loew, von Szczepanski & Arigoni, 1968) has been confirmed by total synthesis (Büchi, Carlson, Powell & Tietze, 1973) and by X-ray structure determination of a bromo derivative (Lentz & Rossmann, 1969).

(I)

The absolute conformation of loganin is of interest because of its biological importance. We, and others, have already investigated the conformation by ^{1}H and ^{13}C NMR (Heckendorf, Mattes & Hutchinson, 1976; Tietze, Niemeyer, Marx & Glüsenkamp, 1979) and circular dichroism (CD) spectroscopy (Tietze, Niemeyer, Marx, Glüsenkamp & Schwenen, 1979). In this paper we describe the X-ray crystal structure.

Crystals in the form of flattened colourless prisms were obtained from ethanol. Data in the range $3 < 2\theta < 55°$ were collected on a Stoe Stadi-2 diffractometer (monochromated Mo $K\alpha$ radiation) with two crystals: $0 \cdot 6 \times 0 \cdot 35 \times 0 \cdot 15$ mm mounted about a (layers 0–9, 2094 reflexions), and $0 \cdot 75 \times 0 \cdot 25 \times 0 \cdot 25$ mm mounted about b (layers 0–15, 3358 reflexions). Systematic absences $h00$, h odd; $0k0$, k odd; $00l$, l odd indicated space group $P2_12_12_1$. Interlayer scale factors were obtained by least squares from common reflexions, and cell constants were determined by least squares from ω values from various layers. After application of Lp corrections, averaging unique reflexions gave 3498 unique reflexions, 3165 with $F > 4\sigma(F)$.

Attempts to solve the structure with the program *SHELXTL* were unsuccessful until the method of Boeyens (1977) was employed. The $0kl$ projection was solved; 11 reflexions having the same phases for the six best two-dimensional solutions were then included in the three-dimensional starting set. One resulting E map (merit figures NQEST $-0 \cdot 126$, $R\alpha$ $0 \cdot 137$) showed all non-hydrogen atoms.

Refinement proceeded to $R = 0 \cdot 11$ (isotropic), $0 \cdot 08$ (anisotropic), at which stage all H atoms were revealed by a difference synthesis. In the final stages C—H distances and H—C—H angles were fixed at $0 \cdot 96$ Å and $109 \cdot 5°$ respectively; hydroxyl H atoms were allowed to refine freely, and overall isotropic temperature factors were used for H atoms bonded to C and O. Slow and incomplete refinement of the ester methyl group may indicate rotational disorder. The final $R' = \sum w^{1/2} \Delta / \sum w^{1/2} |F_o|$ was $0 \cdot 048$, with a corresponding unweighted R of $0 \cdot 041$. The weighting scheme was $w = 1/[\sigma^2(F) + 0 \cdot 001F^2]$. A final difference map showed no peaks $> 0 \cdot 3$ e Å^{-3}. Final atomic coordinates are given in Table 1,* bond lengths, bond angles and

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* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 34846 (21 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. *Atom coordinates* ($\times 10^4$) *and isotropic temperature factors* ($\text{Å}^2 \times 10^3$)

	x	y	z	U
C(1')	11175 (2)	−556 (1)	−97 (1)	25 (1)*
H(1)	11433	−869	428	45 (2)
C(2')	10091 (2)	−1183 (1)	−629 (1)	27 (1)*
H(2)	9792	−863	−1144	45 (2)
C(3')	11018 (3)	−2076 (1)	−824 (1)	31 (1)*
H(3)	11229	−2399	−299	45 (2)
C(4')	12673 (2)	−1861 (1)	−1231 (1)	28 (1)*
H(4)	12488	−1570	−1774	45 (2)
C(5')	13634 (2)	−1163 (1)	−686 (1)	28 (1)*
H(5)	13910	−1471	−162	45 (2)
C(6')	15182 (2)	−844 (2)	−1117 (2)	39 (1)*
H(6)	14897	−484	−1612	45 (2)
H(7)	15796	−1385	−1287	45 (2)
O(1')	10362 (2)	286 (1)	57 (1)	28 (1)*
O(2')	8665 (2)	−1414 (1)	−160 (1)	38 (1)*
H(8)	8082 (31)	−973 (22)	−218 (19)	58 (3)
O(3')	10061 (2)	−2654 (1)	−1359 (1)	55 (1)*
H(9)	10643 (35)	−3071 (21)	−1567 (19)	58 (3)
O(4')	13564 (2)	−2694 (1)	−1384 (1)	40 (1)*
H(10)	13553 (37)	−2966 (21)	−915 (20)	58 (3)
O(6')	16174 (2)	−283 (1)	−579 (1)	54 (1)*
H(11)	15779 (34)	272 (21)	−564 (19)	58 (3)
O(10)	12642 (2)	−341 (1)	−553 (1)	28 (1)*
C(1)	10841 (2)	755 (1)	819 (1)	25 (1)*
H(12)	11991	883	842	45 (2)
O(2)	10495 (2)	171 (1)	1539 (1)	30 (1)*
C(3)	8885 (3)	71 (1)	1724 (1)	30 (1)*
H(13)	8568	−453	2070	45 (2)
C(4)	7718 (2)	656 (1)	1466 (1)	28 (1)*
C(41)	5984 (3)	451 (1)	1663 (1)	36 (1)*
O(42)	5783 (2)	−307 (1)	2155 (1)	51 (1)*
C(42)	4112 (3)	−516 (2)	2393 (2)	54 (1)*
H(24)	4293	−959	2844	45 (2)
H(25)	3490	−807	1947	45 (2)
H(26)	3521	13	2611	45 (2)
O(43)	4866 (2)	906 (1)	1396 (2)	67 (1)*
C(4a)	8062 (2)	1543 (1)	973 (1)	28 (1)*
H(14)	7467	1480	449	45 (2)
C(5)	7532 (3)	2435 (1)	1467 (2)	39 (1)*
H(15)	7127	2269	2021	45 (2)
H(16)	6698	2764	1158	45 (2)
C(6)	9052 (3)	3042 (1)	1550 (1)	37 (1)*
H(17)	8986	3435	2044	45 (2)
O(61)	9279 (2)	3634 (1)	817 (1)	49 (1)*
H(18)	8705 (32)	4053 (19)	844 (18)	58 (3)
C(7)	10450 (2)	2339 (1)	1551 (1)	29 (1)*
H(19)	10600	2037	2092	45 (2)
C(71)	12159 (3)	2758 (2)	1461 (1)	38 (1)*
H(20)	13004	2294	1502	45 (2)
H(21)	12277	3097	936	45 (2)
H(22)	12244	3185	1932	45 (2)
C(7a)	9922 (2)	1671 (1)	835 (1)	26 (1)*
H(23)	10176	1931	287	45 (2)

* Equivalent isotropic U calculated from anisotropic U.

torsion angles in Tables 2–4. A diagram of the loganin molecule is given in Fig. 1.

Discussion. The dihydropyran ring is in a sofa conformation with C(1) out of the plane of the other atoms (Table 5); the torsion angles in the ring (Table 4) show

Table 2. *Bond lengths* (Å)

C(1')—C(2')	1·511 (4)	C(1')—O(1')	1·396 (3)
C(1')—O(10)	1·433 (3)	C(2')—C(3')	1·515 (4)
C(2')—O(2')	1·419 (4)	C(3')—C(4')	1·529 (4)
C(3')—O(3')	1·414 (4)	C(4')—C(5')	1·530 (4)
C(4')—O(4')	1·415 (4)	C(5')—C(6')	1·507 (4)
C(5')—O(10)	1·442 (3)	C(6')—O(6')	1·418 (4)
C(1)—O(1')	1·426 (3)	C(1)—O(2)	1·432 (3)
C(1)—C(7a)	1·509 (4)	C(3)—O(2)	1·357 (4)
C(3)—C(4)	1·333 (4)	C(4)—C(41)	1·482 (4)
C(4)—C(4a)	1·510 (4)	C(41)—O(42)	1·341 (4)
C(41)—O(43)	1·197 (4)	C(42)—O(42)	1·449 (4)
C(4a)—C(5)	1·553 (4)	C(4a)—C(7a)	1·549 (4)
C(5)—C(6)	1·522 (4)	C(6)—O(61)	1·439 (4)
C(6)—C(7)	1·522 (4)	C(7)—C(71)	1·528 (4)
C(7)—C(7a)	1·535 (4)		

Table 3. *Bond angles* (°)

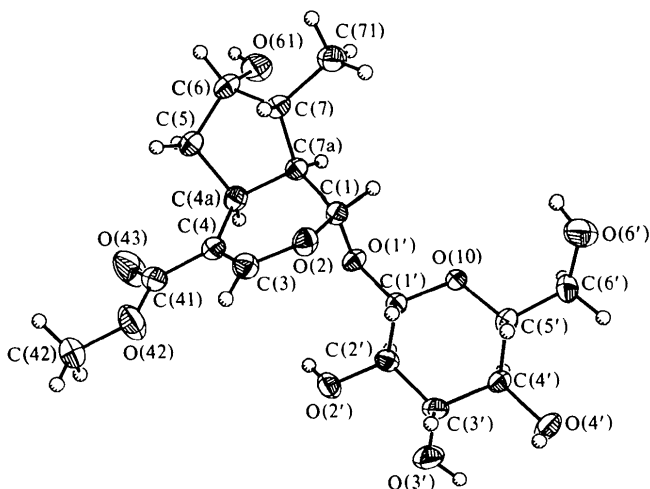|			
C(2')—C(1')—O(1')	109·0 (3)	C(2')—C(1')—O(10)	110·1 (3)
O(1')—C(1')—O(10)	107·5 (2)	C(1')—C(2')—C(3')	108·4 (3)
C(1')—C(2')—O(2')	109·5 (3)	C(3')—C(2')—O(2')	108·7 (3)
C(2')—C(3')—C(4')	111·1 (3)	C(2')—C(3')—O(3')	109·5 (3)
C(4')—C(3')—O(3')	111·1 (3)	C(3')—C(4')—C(5')	110·7 (3)
C(3')—C(4')—O(4')	111·0 (3)	C(5')—C(4')—O(4')	112·1 (3)
C(4')—C(5')—C(6')	112·3 (3)	C(4')—C(5')—O(10)	108·8 (3)
C(6')—C(5')—O(10)	107·0 (3)	C(5')—C(6')—O(6')	112·7 (3)
C(1')—O(1')—C(1)	114·7 (2)	C(1')—O(10)—C(5')	111·7 (2)
O(1')—C(1)—O(2)	109·6 (2)	O(1')—C(1)—C(7a)	106·5 (2)
O(2)—C(1)—C(7a)	113·1 (3)	C(1)—O(2)—C(3)	115·0 (2)
O(2)—C(3)—C(4)	124·4 (3)	C(3)—C(4)—C(41)	120·0 (3)
C(3)—C(4)—C(4a)	123·2 (3)	C(41)—C(4)—C(4a)	116·8 (3)
C(4)—C(41)—O(42)	113·4 (3)	C(4)—C(41)—O(43)	123·5 (3)
O(42)—C(41)—O(43)	123·1 (3)	C(41)—O(42)—C(42)	115·5 (3)
C(4)—C(4a)—C(5)	112·3 (3)	C(4)—C(4a)—C(7a)	110·7 (3)
C(5)—C(4a)—C(7a)	104·4 (3)	C(4a)—C(5)—C(6)	106·3 (3)
C(5)—C(6)—O(61)	111·9 (3)	C(5)—C(6)—C(7)	103·9 (3)
O(61)—C(6)—C(7)	106·9 (3)	C(6)—C(7)—C(71)	115·5 (3)
C(6)—C(7)—C(7a)	101·3 (3)	C(71)—C(7)—C(7a)	115·7 (3)
C(1)—C(7a)—C(4a)	113·0 (3)	C(1)—C(7a)—C(7)	114·2 (3)
C(4a)—C(7a)—C(7)	104·4 (3)		

Fig. 1. The loganin molecule.

Table 4. Torsion angles (°)

The sign convention is as defined by Klyne & Prelog (1960).

O(1')–C(1')–C(2')–C(3')	177·4 (3)	C(41)–C(4)–C(4a)–C(7a)	178·7 (3)	O(10)–C(5')–C(6')–O(6')	67·6 (3)
O(10)–C(1')–C(2')–C(3')	59·8 (3)	O(43)–C(41)–O(42)–C(42)	−3·7 (5)	C(6')–C(5')–O(10)–C(1')	−176·3 (3)
C(2')–C(1')–O(1')–C(1)	153·2 (3)	C(7a)–C(4a)–C(5)–C(6)	2·7 (3)	C(1')–O(1')–C(1)–C(7a)	176·0 (2)
C(2')–C(1')–O(10)–C(5')	−65·8 (3)	C(4)–C(4a)–C(7a)–C(7)	−97·0 (3)	C(7a)–C(1)–O(2)–C(3)	47·6 (3)
C(1')–C(2')–C(3')–C(4')	−53·9 (3)	C(5)–C(4a)–C(7a)–C(7)	24·0 (3)	O(1')–C(1)–C(7a)–C(7)	−172·1 (2)
O(2')–C(2')–C(3')–C(4')	−172·9 (3)	C(4a)–C(5)–C(6)–C(7)	−28·7 (3)	O(2)–C(1)–C(7a)–C(7)	67·5 (3)
C(2')–C(3')–C(4')–C(5')	52·5 (3)	C(5)–C(6)–C(7)–C(7a)	43·2 (3)	O(2)–C(3)–C(4)–C(41)	176·5 (3)
O(3')–C(3')–C(4')–C(5')	174·8 (3)	O(61)–C(6)–C(7)–C(7a)	−75·2 (3)	C(3)–C(4)–C(41)–O(42)	4·5 (4)
C(3')–C(4')–C(5')–C(6')	−173·1 (3)	C(6)–C(7)–C(7a)–C(4a)	−41·6 (3)	C(4a)–C(4)–C(41)–O(42)	−175·3 (3)
O(4')–C(4')–C(5')–C(6')	62·3 (3)	C(71)–C(7)–C(7a)–C(4a)	−167·3 (3)	C(3)–C(4)–C(4a)–C(5)	−117·3 (3)
C(4')–C(5')–C(6')–O(6')	−173·1 (3)	O(1')–C(1')–C(2')–O(2')	−64·0 (3)	C(41)–C(4)–C(4a)–C(5)	62·5 (3)
C(4')–C(5')–O(10)–C(1')	62·2 (3)	O(10)–C(1')–C(2')–O(2')	178·3 (2)	C(4)–C(41)–O(42)–C(42)	177·7 (3)
C(1')–O(1')–C(1)–O(2)	−61·3 (3)	O(10)–C(1')–O(1')–C(1)	−87·5 (3)	C(4)–C(4a)–C(5)–C(6)	122·7 (3)
O(1')–C(1)–O(2)–C(3)	−71·0 (3)	O(1')–C(1')–O(10)–C(5')	175·6 (2)	C(4)–C(4a)–C(7a)–C(1)	27·6 (3)
O(1')–C(1)–C(7a)–C(4a)	68·8 (3)	C(1')–C(2')–C(3')–O(3')	−177·0 (3)	C(5)–C(4a)–C(7a)–C(1)	148·6 (3)
O(2)–C(1)–C(7a)–C(4a)	−51·6 (3)	O(2')–C(2')–C(3')–O(3')	64·0 (3)	C(4a)–C(5)–C(6)–O(61)	86·3 (3)
C(1)–O(2)–C(3)–C(4)	−20·2 (4)	C(2')–C(3')–C(4')–O(4')	177·7 (3)	C(5)–C(6)–C(7)–C(71)	169·1 (3)
O(2)–C(3)–C(4)–C(4a)	−3·7 (4)	O(3')–C(3')–C(4')–O(4')	−60·0 (3)	O(61)–C(6)–C(7)–C(71)	50·6 (3)
C(3)–C(4)–C(41)–O(43)	−174·1 (3)	C(3')–C(4')–C(5')–O(10)	−54·9 (3)	C(6)–C(7)–C(7a)–C(1)	−165·4 (3)
C(4a)–C(4)–C(41)–O(43)	6·1 (4)	O(4')–C(4')–C(5')–O(10)	−179·5 (3)	C(71)–C(7)–C(7a)–C(1)	68·9 (3)
C(3)–C(4)–C(4a)–C(7a)	−1·1 (4)				

Table 5. Deviations (Å) of atoms from the plane of the dihydropyran ring

All e.s.d.'s are ±0·02 Å. Equation of mean plane:
$$0·7706x + 7·0207y + 13·5844z = 3·0486.$$

C(1)	−0·57	C(4)*	0·00
O(2)*	−0·03	C(4a)*	−0·02
C(3)*	+0·03	C(7a)*	+0·02

* Atoms used to calculate mean plane. R.m.s. deviation of starred atoms from mean plane = 0·023 Å.

Table 6. Intermolecular hydrogen bonds

	O···O (Å)*	O···H (Å)†	Second O atom at
O(6')···H(8)–O(2')	2·68	1·93	$1 + x, y, z$
O(2')···H(10)–O(4')	2·74	1·91	$−0·5 + x, −0·5 − y, −z$
O(61)···H(11)–O(6')	2·84	2·03	$−0·5 + x, 0·5 − y, −z$
O(10)···H(18)–O(61)	2·81	2·08	$0·5 + x, 0·5 − y, −z$

* E.s.d.'s < 0·01 Å.
† E.s.d.'s = 0·03 Å.

a mean absolute deviation of 4° from those of the ideal sofa (0, 0, 28, −56, 54, −27° cyclically, starting from the double bond; Bucourt & Hainaut, 1965). The torsion angle C(1)–O(2)–C(3)–C(4) is negative and the glucosyloxy group is in the quasiaxial position. Qualitative MO theory (Snatzke, 1979) predicts a negative CD effect for the inherently chiral enolether chromophore; this is confirmed experimentally (Tietze, Niemeyer, Marx, Glüsenkamp & Schwenen, 1979) and hence loganin has similar conformations in the solid state and in solution. We are now investigating the influence on the conformation of β-alkoxy, rather than glucosyloxy, groups at C(1).

The molecules are linked by a series of hydrogen bonds (Table 6). There are no other unusually short non-bonded distances.

The absolute configuration was not determined directly, but was inferred from the known natural configuration of the glucose moiety.

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