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STRUCTURE OF BREYNOLIDE

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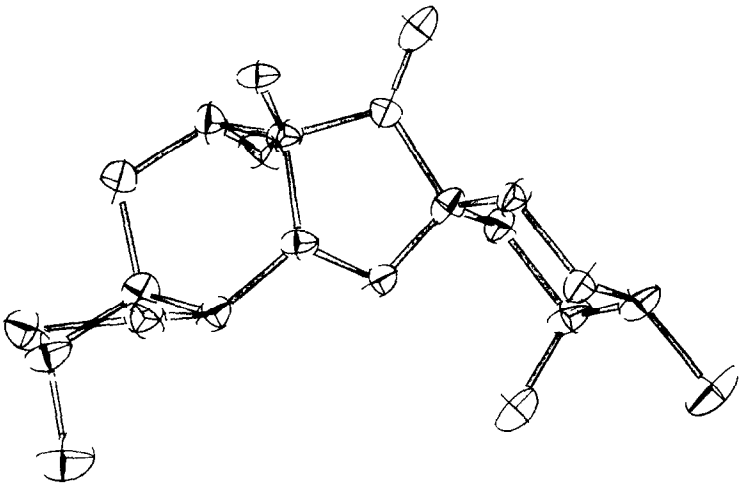
Extraction of Breynia officinalis Hemsl has yielded a bioactive sulfur-containing glycoside, breynin A,[1] $C_{40}H_{56}O_{23}S$, m p 142-144°

Hydrolysis of breynin A with hydrochloric acid (3N) gave an aglycone, breynogenin[1] ($C_{22}H_{26}O_9S$, m p 260-262°), which was further hydrolyzed to p-hydroxybenzoic acid and breynolide[1] (1), $C_{15}H_{22}O_7S$, m p 241-243°, ν_{max} (KBr) 1780 (C=O) cm^{-1} The n m r spectrum (δ, 60 MHz, DMSO-d_6) of (1) showed signals for CH_3-CH (0 83, d, J=11 Hz), O-CH (4 10, s), C-OH (5 55,s), and three CH-OH (4 88, 4 80, 4 05) The difficulty in clarifying the structure of (1) by chemical methods stimulated us to the present X-ray crystallographical study We have established the crystal structure of breynolide by direct phase determination

Recrystallization from ethylacetate afforded colorless monoclinic crystals elongated along the c-axis giving the unit cell dimensions of a=13 434 Å, b=8 628 Å, c=6 652 Å, β=91 08° and space group $P2_1$, D_c 1 492 g cm^{-3}, D_m 1 485 g cm^{-3} (in n-hexane and CCl_4) with two molecules in the unit cell

Lattice constants and intensities were measured on a Hilger & Watts four-circle automatic diffractometer Y-290 with Cu-Kα radiation A total of 1614 independent non-zero intensities were collected in the range, $\theta<78°$, and then the structure was solved by the symbolic addition procedure [2] Refinement of the structural parameters were carried out by the block-diagonal least-squares calculations with anisotropic thermal parameters, and the final R-factor was 7 07% The hydrogen atoms were given constant anisotropic thermal factors equal to those of the heavier atoms to which they were attached The molecular shape of breynolide is shown in Fig 1

The ring system of breynolide is novel one and the most interesting feature in the



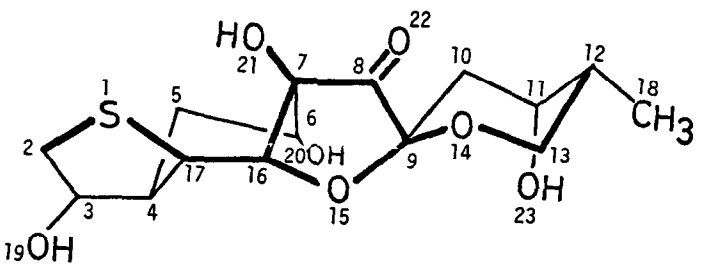


Fig 1 Structure of breynolide

chemical structure is the five- and the six-membered ketal rings formed from a ketone group at C-9 and two hydroxyl groups at C-13 and C-16 The unique sesquiterpene skeleton could be constructed biogenetically by the cyclization of farnesyl pyrophosphate followed by the rearrangement from 8 — 16 bond to 7 — 16

The absolute configuration of breynolide was determined by Bijvoet's method,[3] based on the sulfur ($\Delta f''=0.6$) and the oxygen ($\Delta f''=0.1$) The differences between Friedel pairs were measured on a Hilger & Watts diffractometer with Cu-$K\alpha$ radiation In Table 1, the square root of counted intensity, G, is reported for Friedel pairs The G values have not been

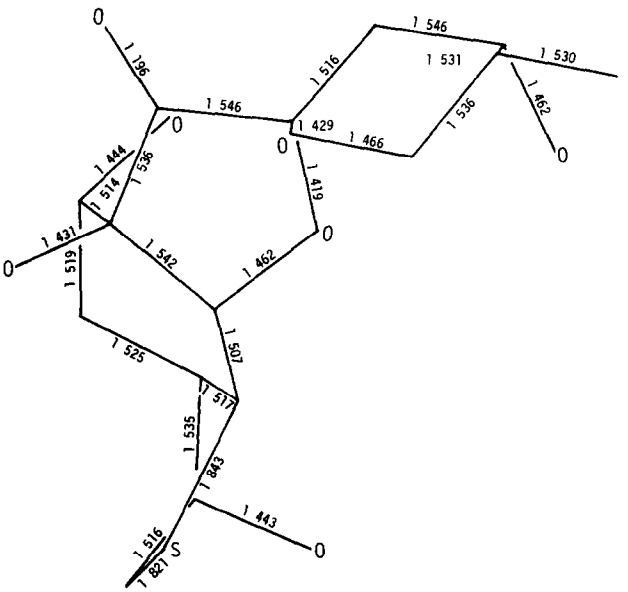


Fig 2 Bond lengths (Å) of breynolide The range of their e s d 's is 0 009 - 0 014 Å

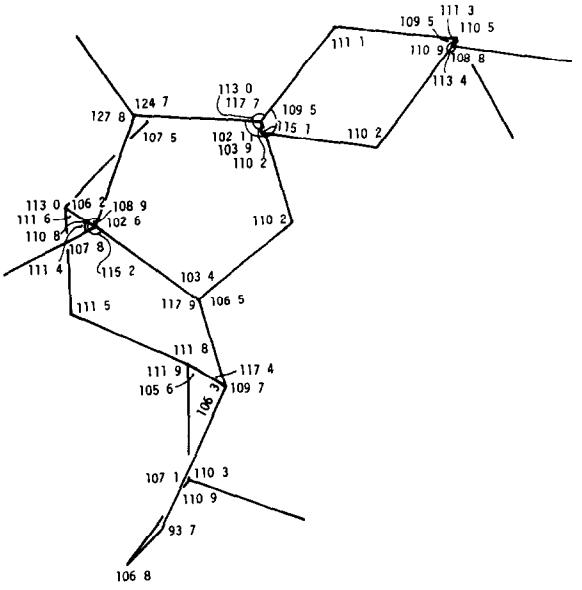


Fig 3 Bond angles (°) of breynolide The range of their e s d 's is 0 5 - 0 8°

placed on an absolute scale or corrected for Lp factors These corrections will not affect the calculation of the percentage deviation from Friedel's law, as expressed by the parameter, Δ

$$\Delta = \frac{100[\ |F(\bar{h}\bar{k}\bar{\ell})| - |F(hk\ell)|\ ]}{[\ \frac{|F(\bar{h}\bar{k}\bar{\ell})| + |F(hk\ell)|}{2}\ ]}$$

The values of Δ_{obs} are listed in Table 1, along with values of Δ_{calc} for the proper enantiomorph The structure in Fig 1 shows the correct absolute configuration of breynolide

Table 1 Observed and calculated Bijvoet differences (percentages) for breynolide

h	k	ℓ	|G(hkℓ)|	|G(h̄k̄ℓ̄)|	Δ(obs)	Δ(calc)	h	k	ℓ	|G(hkℓ)|	|G(h̄k̄ℓ̄)|	Δ(obs)	Δ(calc)
1	2	1	187	172	-8 4	-6 1	7	2	1	96	92	-4 3	-5 8
1	3	2	157	152	-3 2	-4 6	-1	2	2	122	117	-4.2	-4 9
2	1	2	140	135	-3 6	-6 5	-1	4	1	198	186	-6 3	-7 0
2	1	3	168	178	5 8	4 2	-2	2	1	210	219	4.2	4 6
2	3	2	95	100	5.1	4 0	-2	2	2	165	160	-3 1	-5 1
2	4	3	103	97	-6 0	-7 0	-4	4	2	80	86	7 2	4 7
3	1	2	143	135	-5 8	-4 2	-6	2	4	89	95	6 5	7 5
3	4	1	196	206	5 0	5 3	-7	2	1	149	155	3 9	6 2
4	3	2	96	90	-6 5	-8 0	-7	2	2	81	77	-5 1	-6 5
4	4	1	141	147	4 2	7 1	-8	3	1	84	80	-4 9	-4 7
6	3	2	101	93	-8 2	-6.8	-10	2	1	105	101	-3 9	-4 6

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REFERENCES AND FOOTNOTE

1 The full detail of breynins, breynogenin and breynolide will be reported elsewhere from Bristol-Banyu Research Institute

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(b) K Sasaki and Y Hirata, Acta Cryst , B29, 547 (1973)

3 J M Bijvoet, A F Peerdeman, and A J van Bommel, Nature, 168, 271 (1951)