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THE STRUCTURAL STUDIES OF HERQUEINONE AND ITS DERIVATIVES. THE ABSOLUTE CONFIGURATION OF DIHYDROHERQUEINONE MONOMETHYL ETHER

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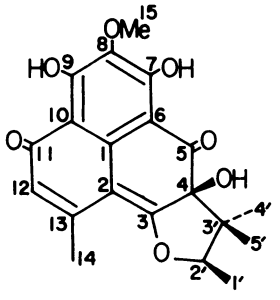
The absolute configurations at C-3 and C-4 of dihydroherqueinone monomethyl ether were determined to be *R* and *S*, respectively, by the X-ray crystallography, with relation to the previously established 2'*R*-configuration of herqueinone. Also, the recently proposed configuration at C-4 of herqueinone was confirmed by relating it to dihydroherqueinone monomethyl ether.

In the structural studies of herqueinone (1)† and its derivatives, the configuration at C-2' of 1 had been established to be *R* by relating 1 to atrovenetin (2).[1,2] On the basis of the NOE and the anisotropic effect of the carbonyl group at the 5-position to the geminal dimethyl groups, we have recently proposed that the configuration at C-4 of 1 is *S* and the configuration at C-3 and C-4 of its dihydro monomethyl derivative (3) are *R* and *S*, respectively.[3] However, the configuration at C-3 of 3 is still unsettled, since the NOE was too small to explain unambiguously the 3*R*-configuration of 3. On the other hand, Morrison has described that glycol A derived from 3 is represented in 4 with the 3*S*-configuration on the basis of the long-range



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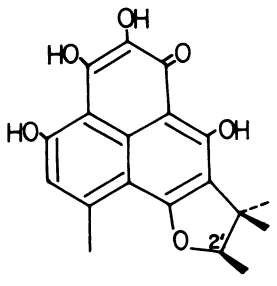

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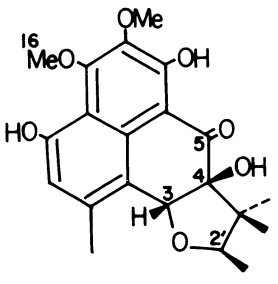

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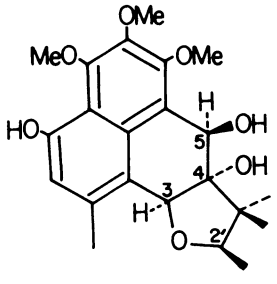

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† Herqueinone (1) was isolated from the mycelia of *Penicillium herquei*.[4]

coupling between the 3-H and 5-H.[2] We have now examined the structure of dihydroherqueinone monomethyl ether (3) by the X-ray crystallography to establish the structures of dihydroherqueinone-type derivatives, and here communicate the result promptly.

Hydrogenation of herqueinone (1) with 10% Pd-C followed by methylation with CH_2N_2 at 0°C gave dihydroherqueinone monomethyl ether (3): mp 173-174°C; $[\alpha]_D^{25}$ +39° (*c* 7.28, EtOH); ^{1}H NMR ($CDCl_3$) δ=4.30 (3H, s, OCH_3), 5.45 (1H, s, -CH-O-); Found: C, 64.65; H, 6.33%. Calcd for $C_{21}H_{24}O_7$: C, 64.93; H, 6.23%. All the physical and spectral data of 3 are in fair agreement with the data described in Ref. 2, though $[\alpha]_D$ has not been given in the literature, and these informations satisfy perfectly the structure of 3. This monomethyl ether (3) was crystallized from EtOH to give the single-crystals for the X-ray analysis. Crystal data are: $C_{21}H_{24}O_7$; *M*=388.45; monoclinic (space group $P2_1$); *Z*=2 per unit cell with dimensions *a*=11.214(4), *b*=6.229(3), *c*=14.252(5) Å, β=110.21(3)°; *U*=934.3 Å^3; *Dc*=1.38 g·cm^{-3}; *Dm*=1.40 g·cm^{-3}; μ(Mo-Kα)=0.8 cm^{-1}. A total of 1811 reflections were collected by ω-scan ($2\theta_{max}$=58.0°) on a Syntex R3 diffractometer using graphite-monochromated Mo-Kα radiation; 283 reflections were smaller than 1.96 times of the standard deviations in intensities and were recorded as "unobserved." The phases of 244 reflections with |E|>1.40 were determined by MULTAN.[5] An E map for the best solution yielded positions for all the atoms except hydrogens, followed by a difference map to find the positions for all the hydrogen atoms. Three cycles of anisotropic block-diagonal least-squares refinement for carbon and oxygen atoms and isotropic refinement for hydrogen atoms reduced the R index to 0.058. The final atomic coordinates of the carbon and oxygen atoms and the hydrogen atoms of hydroxyl groups are given in Table 1. The molecular structure is shown in Fig. 1. This result unambiguously demonstrates that the configuration at C-3 and C-4 of dihydroherqueinone monomethyl ether (3) are *R* and *S*, respectively, with relation to the *R*-configuration at C-2'. The molecular arrangement and the hydrogen bond networks in the crystal are shown in Fig. 2. The molecules are packed along the *c*-axis, and are linked by long intermolecular hydrogen bonding between O(6)-H and O(7')[6] (furan ring) along the *b* direction. On the other hand, three intramolecular hydrogen bondings between O(1)-H and O(2) (methoxyl group), O(4)-H and O(5) (carbonyl group), and O(6)-H and O(5) (carbonyl group) are formed.

The absolute configuration of dihydroherqueinone monomethyl ether (3) was thus demonstrated to be 3-*R*, 4-*S*, and 2'-*R*, in contrast to Morrison's proposal[2] for the absolute configuration of 4 derived from 3. This demonstration leads to the establishment of the absolute configuration of all the dihydroherqueinone-type compounds. During the course of establishing of the absolute configuration of 3, the recently proposed 4*S*-congiguration of herqueinone (1)[3] was incidentally confirmed by relating the configuration of it to that of 3.

Table 1. Atomic parameters ($\times 10^4$) of dihydroherqueinone monomethyl ether (3).

atom	x	y	z	atom	x	y	z
C(1)	4166(5)*	8057(11)	6823(4)	C(1')	9115(7)	7972(20)	9452(7)
C(2)	5377(5)	8780(10)	6857(4)	C(2')	7791(6)	8609(14)	9238(5)
C(3)	6564(5)	7775(11)	7573(5)	C(3')	6832(5)	6915(12)	9289(4)
C(4)	6419(5)	5913(11)	8212(4)	C(4')	5745(6)	8128(13)	9457(5)
C(5)	5097(5)	4963(10)	7934(4)	C(5')	7367(6)	5246(13)	10096(5)
C(6)	4026(5)	6179(10)	7347(4)	O(1)	2195(5)	12002(12)	4993(5)
C(7)	2819(5)	5433(11)	7254(4)	O(2)	803(4)	9557(10)	5667(3)
C(8)	1727(5)	6644(12)	6729(4)	O(3)	540(4)	5900(9)	6623(3)
C(9)	1857(5)	8432(13)	6233(4)	O(4)	2638(4)	3577(8)	7655(3)
C(10)	3063(5)	9165(12)	6220(4)	O(5)	5011(4)	3159(8)	8259(3)
C(11)	3192(6)	10886(13)	5630(5)	O(6)	7273(4)	4270(8)	8156(3)
C(12)	4379(6)	11484(12)	5641(5)	O(7)	7256(4)	9448(9)	8240(3)
C(13)	5471(5)	10447(11)	6246(4)	H[O(1)]	1583(49)	11510(99)	4950(39)
C(14)	6731(6)	11151(13)	6173(4)	H[O(4)]	3349(49)	2720(99)	7909(38)
C(15)	252(6)	5776(19)	7535(6)	H[O(6)]	7049(48)	3151(99)	8451(38)
C(16)	42(6)	10488(14)	6177(6)				

* E.s.d.,s are in parentheses ($\times 10^4$).

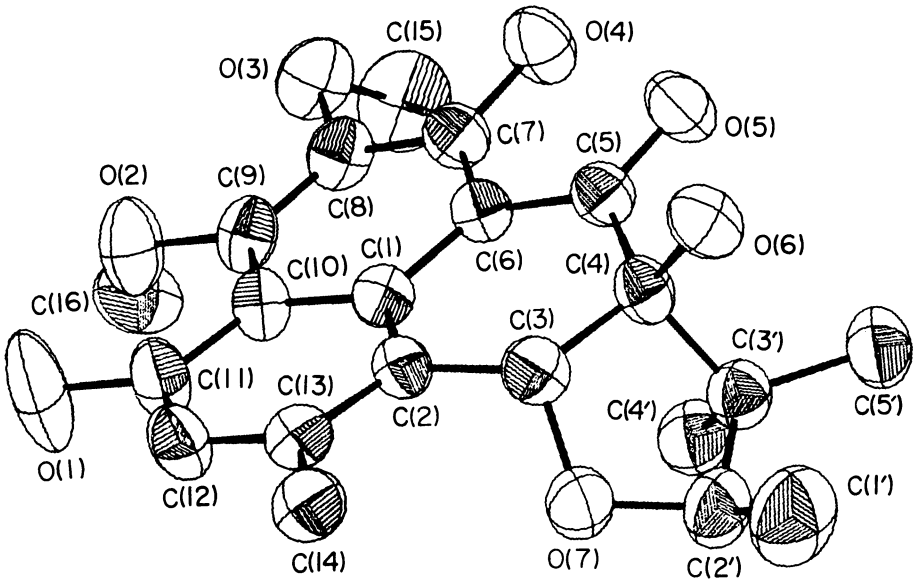

Fig. 1. ORTEP drawing[7] of the molecular structure of dihydroherqueinone monomethyl ether (3).

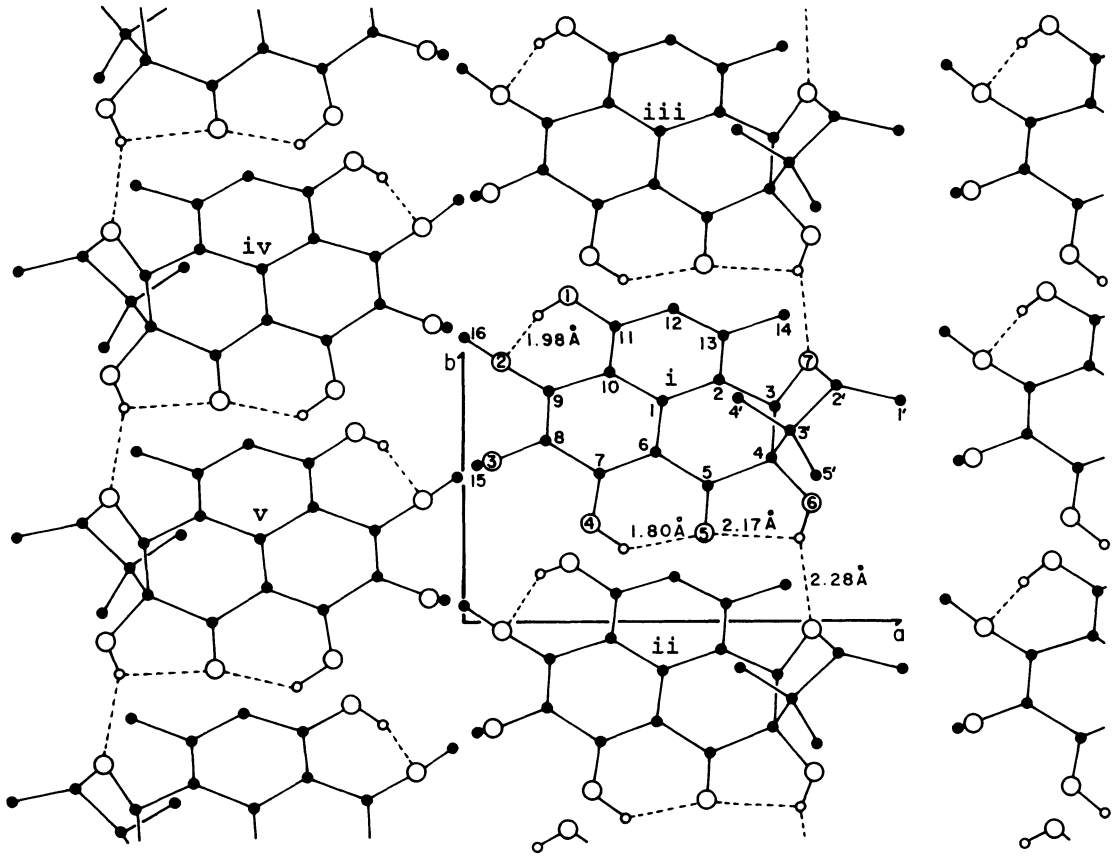

Fig. 2. The projection of dihydroherqueinone monomethyl ether (3) along the the *c*-axis. The atoms indicated with ●, ○, and o denote carbon, oxygen, and hydrogen atoms, respectively. The hydrogen bondings are shown by a broken line. Symmetry code: (i) *x*, *y*, *z*; (ii) *x*, -1+*y*, *z*; (iii) *x*, 1+*y*, *z*; (iv) -*x*, 1/2+*y*, -*z*; (v) -*x*, -1/2+*y*, -*z*. The other molecules related by a 2_1 axis are omitted in order to avoid overlapping.

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6) The O(7') denotes the O(7) of the molecule translated by the symmetry code: *x*, -1+*y*, *z*.
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