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THE C-4 CONFIGURATION AND ^{13}C NMR SIGNALS OF HERQUEINONE FROM *PENICILLIUM HERQUEI*

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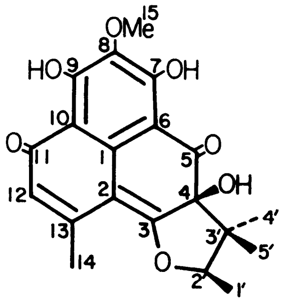
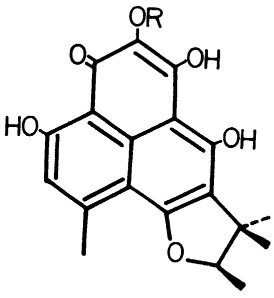
The C-4 configuration of herqueinone was determined to be *S* on the basis of the anisotropic effect of the carbonyl group at the 5-position on the geminal dimethyl groups in the ^{1}H NMR spectra. Also, the full assignment of the ^{13}C NMR signals of herqueinone was established by the selective ^{1}H decoupling and the ^{13}C-labeling techniques.

Herqueinone (I), $C_{20}H_{20}O_7$, is a red pigment isolated from the mycelia of *Penicillium herquei*.[1)] The configuration at C-2' of I has been established to be *R* by relating I to atrovenetin (II).[2,3)] However, the C-4 configuration of I has not been clarified yet. In connection with studies of the biosynthetic mechanism, especially the prenylation at C-4, of this kind of compounds, we have completed the determination of the C-4 configuration of I and the full assignment of its ^{13}C NMR signals, and here communicate the results promptly.

The carbon atom at the 3'-position of herqueinone (I) has the geminal dimethyl groups which are composed of the C-4' methyl group occupying the *pro-R* position and the C-5' methyl group doing the *pro-S* position. The assignment of ^{1}H NMR signals due to the geminal dimethyl groups were performed by measuring the nuclear Overhauser effect (NOE).[4)] The result shown in I of Scheme 1 indicates that the proton signal at δ_H 1.00 is assigned to the C-4' methyl and the signal at δ_H 1.40 to the C-5' methyl groups.[5)]

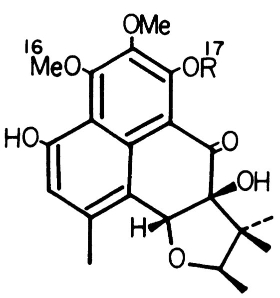


I



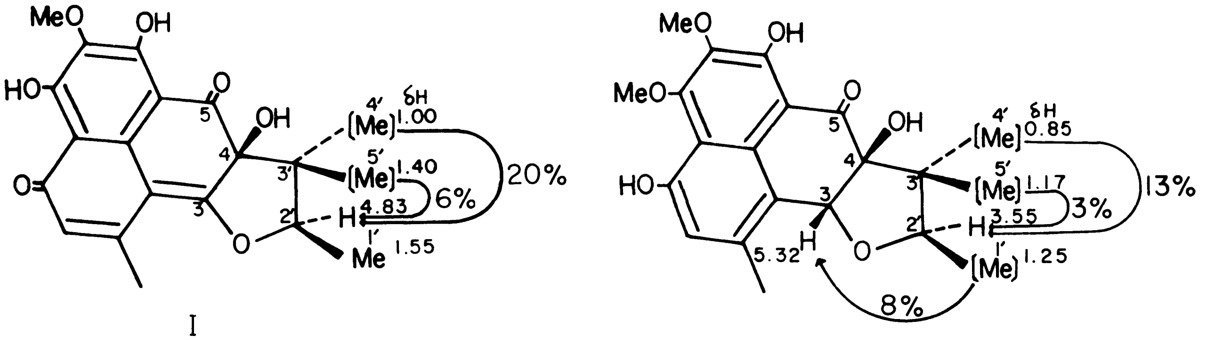
II: R=H

IV: R=Me



III: R=H

V : R=Me



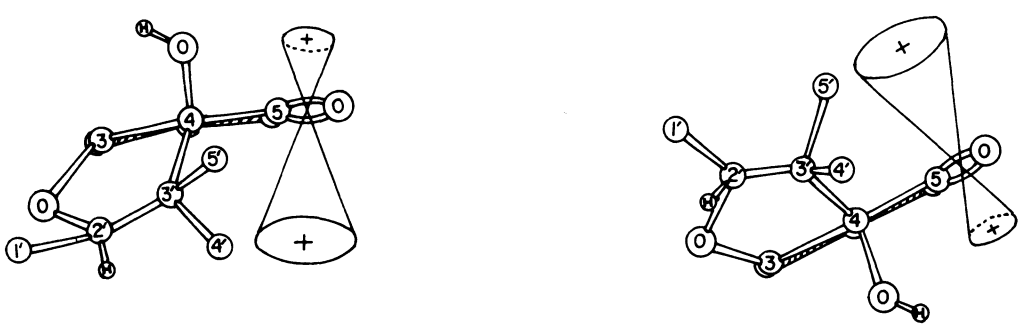
I

III

Scheme 1. Nuclear Overhauser effect observed for I and III.

Owing to the anisotropic effect[6,7] of the carbonyl group at the 5-position, an upfield shift would be expected for the C-4' methyl group in Ia with the *S*-configuration at C-4, whereas a downfield one for the C-4' methyl group in Ib with the *R*-configuration at C-4, as shown in Fig. 1. Appearance of the C-4' methyl signal in a higher field than the C-5' methyl signal as described above showed unambiguously the configuration at C-4 of herqueinone to be *S* as in Ia This was further supported by measurement of the NOE of dihydroherqueinone monomethyl ether (III) derived from I, as shown in III of Scheme 1. Thus, it was established that the configuration at C-4 of herqueinone is *S*. Incidentally, the NOE measurement of III showed also that the C-2' hydrogen atom and the C-4' methyl group are *cis*, and the hydrogen atoms at C-2' and C-3 are *trans*. This indicates that the configurations at C-3 and C-4 of dihydroherqueinone monomethyl ether (III) are *R* and *S*, respectively.

The assignment of ^{13}C signals of I was performed on the ground of proton noise decoupling and single-frequency off-resonance decoupling (SFORD) techniques,[8,9] the chemical shift rule,[8,9] and comparisons with the ^{13}C signals of dihydro derivatives, III and V and previously-documented deoxyherqueinone (IV).[10] The chemical shifts of I, III, and V are listed in Table 1. The assignment for the



Ia: 2'*R*,4*S*

Ib: 2'*R*,4*R*

Fig. 1. Anisotropic effect of the carbonyl group at the 5-position of I.

Table 1. ^{13}C chemical shifts of I, III, and V, ^{13}C,^{13}C spin coupling in the spectrum of I,[a)] and ^{1}H chemical shifts of I[b)]

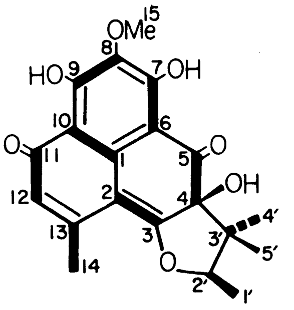
carbon	I δ_C	I $^{1}J_{CC}$[c)]	I δ_H	III δ_C	V δ_C
1	109.2	68		109.2	112.7
2	131.3	75		129.1	130.8
3	178.6	75		81.5	82.2
4	78.9	51		82.0	84.3
5	197.0	51		202.9	199.0
6	102.7	61		105.9	118.6
7	162.0	61		162.0	153.2
8	150.7	42		140.2	142.4
9	163.0	44		153.9	153.2
10	103.2	70		117.8	119.3
11	186.4	56		156.5	154.9
12	122.8	58	6.27	113.5	113.6
13	138.8	35		136.5	138.5
14	23.8	35	2.50	24.6	23.2
15	59.9	0	3.80	60.9	61.1
16				62.4	62.4
17					61.8
1'	18.6	38	1.55	17.6	18.1
2'	95.9	38	4.83	81.5	82.2
3'	60.3[d)]	36[d)]		50.1	50.2
4'	15.9	37[d)]	1.00	16.3	15.6
5'	23.8	0	1.40	19.9	19.4

a) Taken on a Hitachi R-42 FT NMR spectrometer at 22.631 MHz at 35°C in [^{2}H]DMSO containing TMS as an internal standard (δ_C=0) in a 8 mm spinning tube; precisions of δ_C are about ±0.1. FT measurement conditions were as follows: spectral width, 250 ppm; filtering, 6 KHz; pulse width, 25 micro sec; pulse interval, 1.800 sec; number of data points, 8000.

b) Taken on a Hitachi R-22 ^{1}H NMR spectrometer at 90.0 MHz at 35°C in [^{2}H]DMSO.

c) The ^{13}C,^{13}C spin coupling constants (Hz) in the ^{13}C NMR of I biosynthesized from sodium [1,2-^{13}C$_2$]acetate.

d) Taken in [^{2}H]pyridine.



I

Fig. 2. The ^{13}C incorporation pattern of nine acetate units (▬) in I.

protonated carbon atoms could be confirmed by the selective ^{1}H decoupling technique.[8,9,11] Distinction between pairs of the C-5 and C-11, the C-6 and C-10, and the C-7 and C-9 signals of I was difficult, because of the symmetry of its phenalenone skeleton. Accordingly, precise assignment for these ^{13}C signals was performed by diagnosis of the $^{13}C,^{13}C$ spin coupling in I biosynthesized from sodium $[1,2\text{-}^{13}C_2]$acetate (92% enriched) on feeding of the acetate to *P. herquei*. The feeding gave a sample of ^{13}C-labeled herqueinone (I) with *ca*. 31% ^{13}C-abundance at each labeled position. The ^{13}C NMR spectrum of the ^{13}C-labeled sample showed nine pairs of $^{13}C,^{13}C$ spin couplings, as shown in Table 1. Since a study on the ^{13}C labeling of deoxyherqueinone (IV) biosynthesized from the $[1,2\text{-}^{13}C_2]$acetate by *P. herquei* has established the incorporation pattern of acetate units in the phenalenone skeleton,[10] the $^{13}C,^{13}C$ spin coupling pairs in I biosynthesized from $[1,2\text{-}^{13}C_2]$acetate should be expected as shown in Fig. 2. Observed pairs of the $^{13}C,^{13}C$ spin coupling shown in Table 1 were in full agreement with these expected coupling pairs. The above-described results fully supported the assignment of all the carbon signals in ^{13}C NMR spectrum of I. Thus, the full assignment of the ^{13}C signals of herqueinone (I) and its related compounds, III and V, have been completed.

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