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THE STRUCTURE OF PENTALENOLACTONE (PA-132)

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An acidic lipophylic antibiotic was isolated from the fermented broth of the Streptomyces sp. No. 8403-MC$_1$ in the course of our screening program for the inhibitory substances against nucleic acid synthesis in the bacterial cells (1), and was confirmed to be identical with PA-132 by the direct comparison (2,3).

The antibiotic has an unique pentalene skeleton with a seven membered glycidic lactone based on the chemical and spectroscopic evidences to assign the structure as shown in Fig. 1, and is named pentalenolactone (I). I was obtained as white hygroscopic powder of $C_{15}H_{16}O_5$* (m/e 276); mp. 61-62°; $[\alpha]_D^{23}$=-172° (c=1, MeOH) pKmcs 5.8; UV λ_{max}^{MeOH} 218.5 mμ (ε 8625); IR $\nu_{max}^{CHCl_3}$ 1765 (γ-lactone or strained lactone), 1695 (carboxyl) and 1635 cm^{-1} (double bond). I gave positive reaction of the thiosulfate test for epoxide (4).

Catalytic reduction of I with PtO_2 in ethanol containing 20 % acetic acid yielded corresponding tetrahydropentalenolactone (II) as crystals of $C_{15}H_{20}O_5$ (m/e 280); mp. 107-108.5°; $[\alpha]_D^{25}$=+74° (c=1, MeOH); pKmcs 6.15; IR $\nu_{max}^{CHCl_3}$ 1765 (lactone) and 1705 cm^{-1} (carboxyl). In comparison of those properties and spectral data of I and II, it reveals that two double bonds in I are separated from each other and one of them is conjugated with a carboxyl group.

Crystalline bromohydrin of II ($C_{15}H_{21}O_5Br$, mp. 123-124°) was formed with dry HBr in benzene at room temperature. A band due to the lactone shifted to 1735 cm^{-1} in the IR spectrum of bromohydrin of II, while it was observed at

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* The molecular formula of $C_{16}H_{18-20}O_5$ for PA-132 presented by Koe and others was corrected to be $C_{15}H_{16}O_5$ by the molecular ion peak of masspectrometory.

1765 cm^{-1} in I or II. In addition, the hydrolysis of II or I by refluxing in aqueous $Ba(OH)_2$ solution afforded about one mole of $BaCO_3$. These results suggested the presence of glycidic lactone in I (5).

The NMR spectrum of methyl ester of I (colorless oil, $C_{16}H_{18}O_5$, m/e 290) is shown in Fig. 2, and the details of assignments providing evidences for the structural elucidation are summerized in Table 1.

Fig. 1

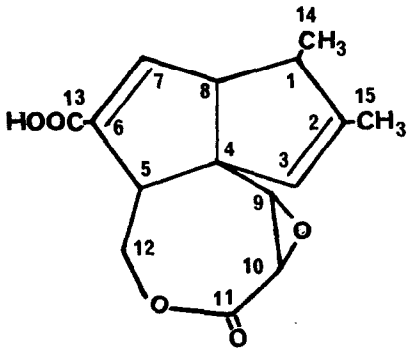
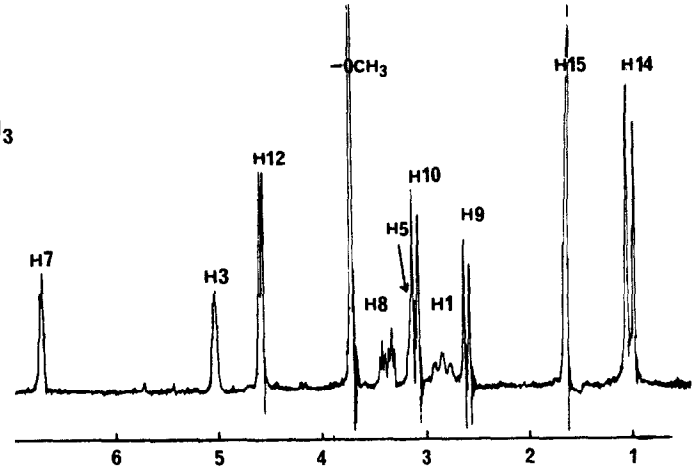


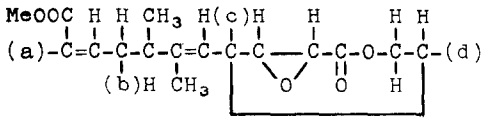
Fig. 2

NMR of Pentalenolactone methyl ester
100MC, $CDCl_3$ (ppm)



In particularly, the signals of H9 and H10 assigned to epoxide methines are observed as distinct doublets in the NMR of I and II, indicating that these protons are independent from other protons.

From the evidences described above, the partial structures of I shown in Table 1 could be expanded as follows. The two possibilities of cases A and B remain to construct the whole structure of I.

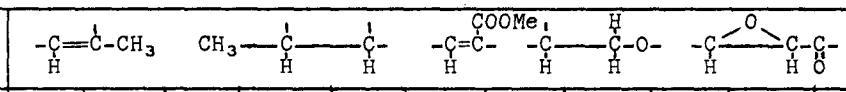
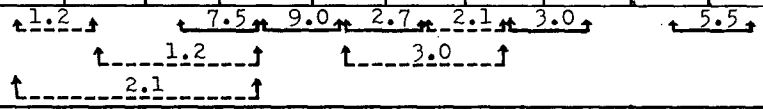


case A, (a)-(d), (b)-(c)

case B, (b)-(d), (a)-(c)

Table 1

NMR Experiments of Pentalenolactone methyl ester

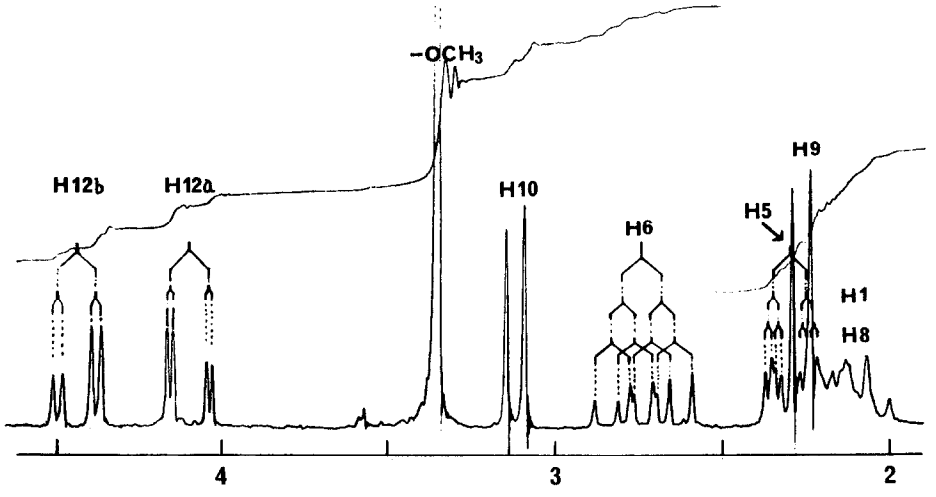
partial structures											
protons	H3	H15	H14	H1	H8	H7	H5	H12	H9	H10	-OMe
couplings (c/s)											
chem. shifts (ppm)	5.05	1.65	1.05	2.80	3.35	6.65	3.10	4.55	2.60	3.10	3.70
split.	q	t	d	sex(br)	q,d	t	?	d	d	d	s
spin-decoup.	d←irr irr→d		s←irr→q irr→d(br)		d,d←irr irr→d		irr→s		irr→s s←irr		
double spin-decoup.	s←irr		irr		irr→s←irr						
NOE	obs←irr 110%			irr→obs 105%							
			irr→obs 115%								

abbreviations; ⌐—¬ = coupling, ⌐- -¬ = long range coupling
s=singlet, d=doublet, t=triplet, q=quartet, sex=sextet,
br=broard, ?=overlaped, NOE=intramolecular Overhauser effect,
obs=observed, %=increased signal

It is difficult to explain the correlation of H5 and H8 from their coupling constant of 3.0 cps whether they are interacted by allylic or neighboring coupling. The important derivative of dihydropentalenolactone (III), $C_{15}H_{18}O_5$ (m/e 278), was prepared by catalytic hydrogenation of I in ethanol with PtO_2. In the NMR of methyl ester of III (colorless needles, $C_{16}H_{20}O_5$, m/e 292), the signals at 2.74 (H6) and 1.60 ppm (H7) were observed by the saturation of the double bond. The partly enlarged NMR spectrum of methyl ester of III is given in Fig. 3. From the coupling of the octet signal at 2.74 ppm due to the H6 methine with H5 at 2.30 ppm (J_{5-6}=10.5 cps), it is suggested that C5 must attach to C6 as in the case A.

Fig. 3

NMR of dihydropentalenolactone methyl ester 100MC, C_6D_6 (ppm)



The results of intramolecular Overhauser effect(NOE) shown in Table 1 indicate that H3 is located spatialy close to H5 and similarly H7 is close to H14, coinciding with the pentalene structure of I.

Thus, the authors propose the structure I for pentalenolactone from the evidences described above.

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