STRUCTURES OF JIETACINES: UNIQUE α,β-UNSATURATED AZOXY ANTIBIOTICS

Sir:

Jietacins A (**1**) and B (**2**) were isolated from the culture broth of a strain of *Streptomyces* and exhibited 10 times higher activities against the pine wood nematode, *Bursaphelenchus lignicolus*, than did avermectin B_{1a} as reported in the previous paper[1]. This communication describes the structure elucidation of these antibiotics.

The UV ($\lambda_{max}^{C_6H_{12}}$ nm (ε) 228 (3,650), 250 (sh)) and IR (ν_{max}^{KBr} cm^{-1} 2950, 2870, 1705, 1475, 1415, 1380, 1270) spectra of **1** and **2** were superimposable, and suggested the presence of an azoxy group in these compounds[2]. The molecular formula of **1** was established as $C_{18}H_{34}N_2O_2$ by field desorption mass spectrum (FD-MS) (*m/z* 311 $(M+H)^+$) and high-resolution electron impact mass spectrum (HREI-MS) (found *m/z* 293.2592; calcd for $C_{18}H_{33}N_2O$ (M−OH) *m/z* 293.2592) data. The M+H ion peak at *m/z* 325 in FD-MS spectrum of **2** indicated the formula to be $C_{19}H_{36}N_2O_2$ and it was confirmed by HREI-MS data (found *m/z* 307.2739; calcd for $C_{19}H_{35}N_2O$ (M−OH) *m/z* 307.2749). Unambiguously, the structural difference between the two compounds is a methylene group.

In the ^{13}C NMR spectrum of **1**, two equivalent methyls (δ_C 22.6 (2×C)), twelve methylenes (δ_C 23.8~29.5 (8×C), 38.8, 42.8, 42.9, 52.5), and a methine (δ_C 27.9) were observed as sp^3 carbons, while a vinyl group (methylene; δ_C 115.3 and methine; δ_C 143.5) and a ketone carbonyl (δ_C 211.6) were shown in the sp^2 area. The ^1H NMR spectrum of **1** clearly demonstrated two overlapping methyl doublets (δ_H 0.86 (6H, d)), three triplets of methylenes (δ_H 3.53, 2.39 and 2.38) being adjacent to deshielding functional groups and a terminal vinyl group (δ_H 7.09, 6.42 and 5.49). The remaining protons (19H) were observed at 1~2 ppm. The ^1H-^1H homonuclear chemical shift correlated (HOMCOR) spectrum of **1** (Fig. 1) revealed the presence of an isopropyl group, a trimethylene and two almost equivalent trimethylene moieties in connection with above mentioned methyl and methylene protons. An ethylene moiety (δ_H 1.15 and 1.26) and the terminal vinyl group were also indicated, but the relationship of other protons were not made plain because these signals gathered at 1.25~1.40 ppm. Since the standard chemical shift of methylene in linear alkane is around at 1.30

Fig. 1. The ^1H-^1H homonuclear chemical shift correlated spectrum of **1** (400 MHz, $CDCl_3$).

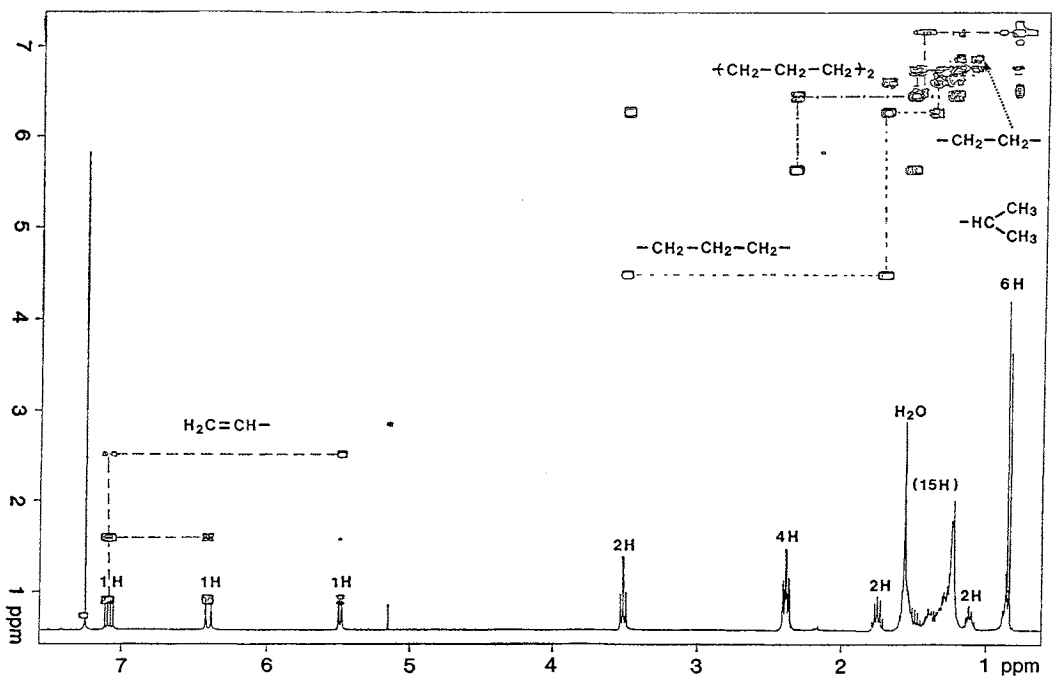
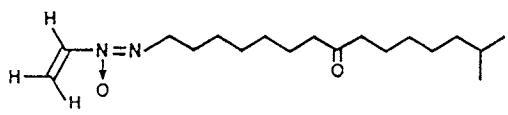


Fig. 2. The structures of jietacins A (1) and B (2).



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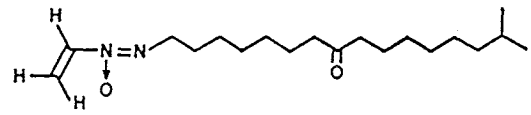

2

ppm[3], it was suggested that **1** contained linear aliphatic chains. It was confirmed by ^{1}H-^{13}C heteronuclear correlated (HETCOR) spectral data that the methylene protons at δ_H 1.15, 2.38, 2.39 and 3.53 were bound to carbons at δ_C 38.8, 42.9, 42.8 and 52.5, respectively. The first and middle two chemical shifts were attributable to those of a methylene carbon of an isobutyl moiety and of the α-carbons of ketone carbonyl[4] respectively. This suggests the presence of an oxoalkyl group which consists of 16 carbon atoms and contains an isopropyl moiety as a terminal. Thus, the structure of **1** was expected to be one in which a vinyl group was bound to the oxoalkyl group through an azoxy moiety.

To decide the position of the ketone carbonyl group in the alkyl chain, hydrogenolysis of **1** was carried out by H_2 - PtO_2 in acetic acid[5]. Under these conditions the azoxy linkage of **1** was cleaved to an amine. The EI-MS of the amine showed characteristic fragment ion peaks at *m/z* 239 $(M-H_2O)^+$, 144, 58, 44 and 30. The last three were typical fragment ion peaks of a primary aliphatic amine. The ion at *m/z* 144 was attributable to a fragment ion formed by cleavage of the bond between the α- and β-carbons to a hydroxyl group and it was confirmed by HREI-MS data (found *m/z* 144.1385; calcd for $C_8H_{18}NO$ *m/z* 144.1387). These data revealed the structure of this amine to be 14-methyl-8-hydroxydecylamine. The position of the ketone carbonyl was also supported by the observation of a large fragment ion peak at *m/z* 195 in the EI-MS of **1**. Since azoxy compounds have been reported to show the ion peak corresponding to loss of an oxygen and a hydrogen atom from the molecular ion[6], and alkanone compounds are known to fragment readily at the α,β-bound of a ketone carbonyl by McLAFFERTY rearrangement, the peak at *m/z* 195 might correspond to the fragment ion peak formed by cleavage of the α,β-bond of the ketone carbonyl and loss an oxygen atom. It was confirmed by HREI-MS data (found *m/z* 195.1479; calcd for $C_{11}H_{19}N_2O$ 195.1496). The position of the oxygen atom in the azoxy group was revealed to be on the vinyl group side by the proton chemical shift of the methylene (δ_H 3.53) adjacent to the azoxy group[6]. The structure of **1** was determined as demonstrated in Fig. 2. That of **2** was also established as shown, based on the large fragment ion peak at *m/z* 195 and the overlapping two methyl doublets were observed in the EI-MS and ^{1}H NMR spectra of **2**, respectively.

Only three antibiotics, elaiomycin[5], LL-BH 872α[7], and valanimycin[8] have been reported to contain an azoxy moiety. All of these compounds are produced by *Streptomyces* sp. and contain an α,β-unsaturated azoxy chromophore. Jietacins are new compounds of this class, whose structures are unusual in light of the terminal vinyl and long oxoalkyl groups.

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