STRACTIONS OF JIETACINES: UNIQUE \( \alpha,\beta \)-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 B1a as reported in the previous paper\(^1\). This communication describes the structure elucidation of these antibiotics.

The UV \( \lambda_{\text{max}}^\text{nm} (\epsilon) 228 (3,650), 250 (sh) \) and IR \( \nu_{\text{max}}^\text{cm}^{-1} 2950, 2870, 1705, 1475, 1415, 1380, 1270 \) 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 \( \text{C}_{18}\text{H}_{34}\text{N}_{2}\text{O}_{2} \) by field desorption mass spectrum (FD-MS) \( m/z 311 (M+H)^+ \) and high-resolution electron impact mass spectrum (HREI-MS) \( \text{found} m/z 293.2592; \text{calcd for} \text{C}_{18}\text{H}_{33}\text{N}_{2}\text{O} (M-OH) m/z 293.2592 \) data. The \( M+H \) ion peak at \( m/z 325 \) in FD-MS spectrum of 2 indicated the formula to be \( \text{C}_{19}\text{H}_{36}\text{N}_{2}\text{O}_{2} \) and it was confirmed by HREI-MS data \( \text{found} m/z 307.2739; \text{calcd for} \text{C}_{19}\text{H}_{35}\text{N}_{2}\text{O} (M-OH) m/z 307.2749 \). Unambiguously, the structural difference between the two compounds is a methylene group.

In the \( ^{13}\text{C} \) NMR spectrum of 1, two equivalent methyls \( (\delta_c 22.6 (2 \times C)) \), twelve methylenes \( (\delta_c 23.8 \sim 29.5 (8 \times C), 38.8, 42.8, 42.9, 52.5) \), and a methine \( (\delta_c 27.9) \) were observed as \( sp^3 \) carbons, while a vinyl group \( (\text{methylene}; \delta_c 115.3 \) and methine; \( \delta_c 143.5 \) and a ketone carbonyl \( (\delta_c 211.6) \) were shown in the \( sp^2 \) area. The \( ^1\text{H} \) NMR spectrum of 1 clearly demonstrated two overlapping methyl doublets \( (\delta_c 0.86 (6\text{H}, d)) \), three triplets of methylenes \( (\delta_c 3.53, 2.39 \) and 2.38) being adjacent to deshielding functional groups and a terminal vinyl group \( (\delta_c 7.09, 6.42 \) and 5.49) \). The remaining protons \( (19\text{H}) \) were observed at 1 \( \sim \) 2 ppm. The \( ^1\text{H}-^1\text{H} \) homonuclear chemical shift correlated (HOMCOR) spectrum of 1 \( (\text{Fig. 1}) \) 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 \( (\delta_c 1.15 \) 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 \( \sim \) 1.40 ppm. Since the standard chemical shift of methylene in linear alkane is around at 1.30 ppm.

![Fig. 1. The \(^1\text{H}-^1\text{H} \) homonuclear chemical shift correlated spectrum of 1 (400 MHz, CDC\(_3\)).](attachment:image.png)
Fig. 2. The structures of jietacins A (1) and B (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 $\delta_H$ 1.15, 2.38, 2.39 and 3.53 were bound to carbons at $\delta_C$ 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 $\alpha$-carbons of ketone carbonyl$^6$ 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 $\alpha$- and $\beta$-carbons to a hydroxyl group and it was confirmed by HREI-MS data (found $m/z$ 144.1385; calcd for $C_{15}H_{35}NO$ $m/z$ 144.1387). These data revealed the structure of this amine to be 14-methyl-8-hydroxydecalylamine. 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 $\alpha,\beta$-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 $\alpha,\beta$-bond of the ketone carbonyl and loss an oxygen atom. It was confirmed by HREI-MS data (found $m/z$ 195.1479; calcd for $C_{11}H_{15}N_2O$ 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 ($\delta_H$ 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 872$^6$, and valanimycin$^8$ have been reported to contain an azoxy moiety. All of these compounds are produced by Streptomyces sp. and contain an $\alpha,\beta$-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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