STRUCTURE OF ANTITUMOR ALKALOID AM-6201

Sir:

In the course of our studies on alkaloids from microorganisms, alkaloid AM-6201 was isolated from culture broth of *Streptomyces xanthochromogenus* strain No. AM-6201, and was found to have antitumor activity against Ehrlich ascites carcinoma in mice. In this paper we report the structure of the alkaloid AM-6201.

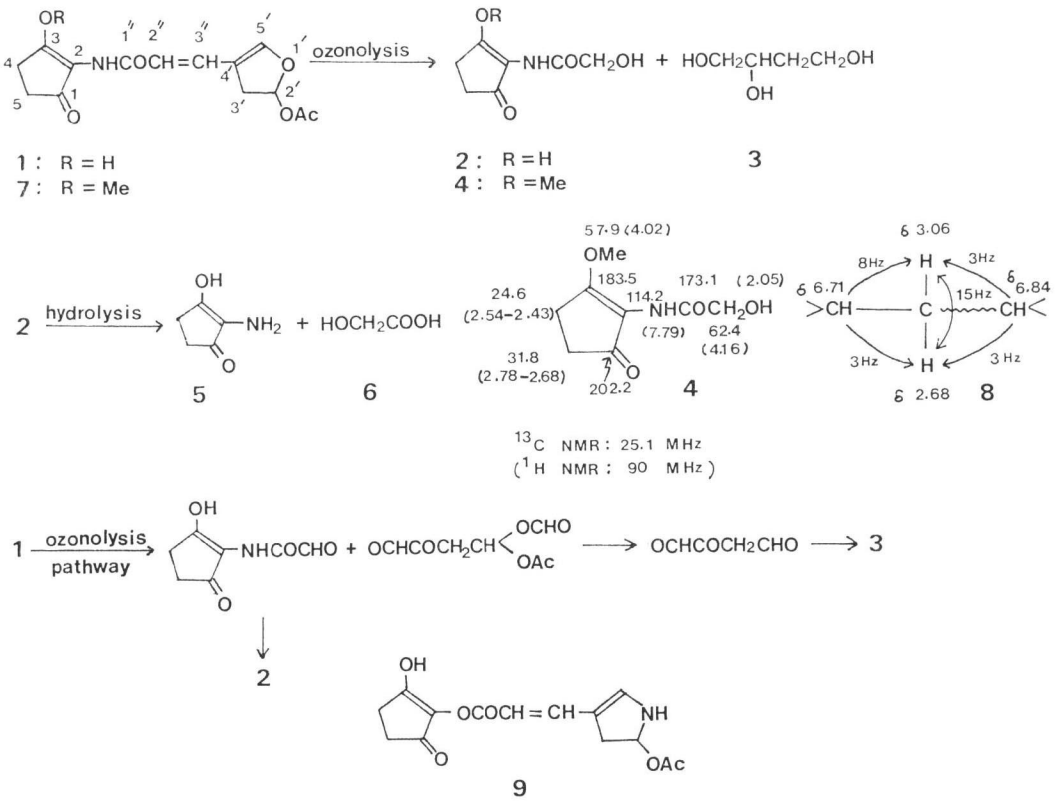
Characterization of Alkaloid AM-6201

Pale yellow needles of mp. 232~233°C (from benzene). IR ν_{max} (chloroform) cm^{-1}: 3380, 3270, 1762, 1750, 1630. $[\alpha]_D^{25}+306°$ (c 0.26, acetone). UV λ_{max} (methanol): 282 nm (ε= 26300); λ_{max} (0.1 N HCl-methanol): 290 nm (ε= 25995). ^1H NMR (100 MHz)* δ: 13.71 (1H, s, 3-OH)**, 7.84 (1H, s, NH)**, 7.48 (1H, d, J= 15 Hz, 3''-H), 6.84 (1H, t, J=3 Hz, 5'-H), 6.71 (1H, dd, J=8 and 3 Hz, 2'-H), 5.86 (1H, d, J= 15 Hz, 2''-H), 3.06 (1H, ddd, J=15, 8 and 3 Hz, 3'-H), 2.68 (1H, dt, J=15 and 3 Hz, 3'-H), 2.68~2.45 (4H, m, 4- and 5-H_2), 2.10 (3H, s, 2'-$OCOCH_3$). ^{13}C NMR (25.1 MHz) δ: 197.2 (s, C-1), 173.9 (s, 2'-$OCOCH_3$), 169.4 (s, C-1''), 165.9 (s, C-3), 150.6 (d, C-5'), 135.6 (d, C-3''), 115.5 (d, C-2''), 115.2 (s, C-4')***, 114.8 (s, C-2)***, 98.6 (d, C-2'), 34.4 (t, C-3'), 32.3 (t, C-5), 25.7 (t, C-4), 20.9 (q, 2'-$OCOCH_3$). *Anal.* Calcd. for $C_{14}H_{15}NO_6$: C, 57.33; H, 5.16; N, 4.78. Found: C, 57.12; H, 4.99; N, 4.60. Mass m/z: M^+, 293.090 (M, 293.089).

Structure Elucidation

On ozonization and reductive degradation, AM-6201 (**1**) afforded the cyclopentenone (**2**), $C_7H_9NO_4$, and the triol (**3**), $C_4H_{10}O_3$. The ^1H NMR spectrum (90 MHz, acetone-d_6) of **2**

Chart 1.



* The ^1H and ^{13}C NMR spectra were taken in deuteriochloroform unless otherwise noted.

** On addition of deuterium oxide, this signal disappeared.

*** These assignments may be reversed.

showed two two-proton triplets for an ethylene group at δ 2.58 (J=6 Hz) and 2.53 (J=6 Hz), and a two-proton triplet for a methylene group coupled with a hydroxyl group at δ 4.25 (J=5 Hz). Treatment of **2** with diazomethane gave the enol ether (**4**) [^{1}H NMR (90 MHz): δ 4.02 (s) for OMe]. Its ^{13}C NMR spectrum (25.1 MHz) showed signals for four quaternary, three methylene and one methyl carbons. Thus, the structure of **4** is deduced to be 2-glycolamido-3-methoxy-2-cyclopenten-1-one on the basis of the ^{1}H and ^{13}C NMR data. As expected, hydrolysis of **2** with hydrochloric acid yielded 2-amino-3-hydroxy-2-cyclopenten-1-one (**5**) and glycolic acid (**6**) which were identified with authentic samples, respectively. The triol (**3**) was identified with an authentic sample of 1,2,4-trihydroxybutane. Treatment of **1** with diazomethane gave the enol ether (**7**) [^{1}H NMR (100 MHz): δ 4.06 (s) for OMe], suggesting the presence of an enol function. It is clear, at this stage, that the 2-acrylamido-3-hydroxy-2-cyclopenten-1-one moiety is present in the framework of **1**.

The ^{1}H NMR spectrum (100 MHz) of **1** provided two one-proton doublets for an (*E*)-acrylamide group at δ 7.48 (J=15 Hz) and 5.86 (J=15 Hz), and a three-proton singlet for an acetoxy group at δ 2.10. Decoupling experiments showed the presence of a system (**8**) consisted of a methylene group coupled with a proton vicinally and a proton in the long range mode.

Taking into account that ozonolysis of **1** was accompanied by loss of three carbon atoms, the rest of the framework of **1** can be determined to be 2-acetoxy-2,3-dihydrofuran-4-yl moiety. The structure of **1** shown in Chart 1 is in accord with the ^{1}H and ^{13}C NMR data observed (*vide supra*), and ozonolysis pathway can be reasonably explained. Recently, SHIMIZU *et al.* reported the structure of reductiomycin (**9**) isolated from *Streptomyces griseorubiginosus* nov. sp., in which the positions of the nitrogen and oxygen atoms are reversed to those in **1**[1,2]. Since the physicochemical, spectral properties and mass fragmentation of **1** are quite similar to those of **9**[3], both compounds are thought to be the same.

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(Received June 25, 1981)

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