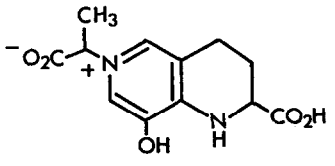
Tetrahedron Letters No. 9, pp 735 - 736, 1977. Pergamon Press. Printed in Great Britain.

ACID HYDROLYSIS PRODUCTS OF SULFOMYCIN I

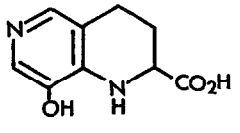
Hiroshi Abe, Masaharu Ikeda, Tetsuo Takaishi, Yukio Ito and Tomoharu Okuda
Microbial Chemistry Research Laboratory
Tanabe Seiyaku Co., Ltd. Toda, Saitama, Japan

(Received in Japan 10 January 1977; received in UK for publication 19 January 1977)

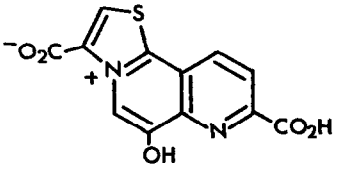
Sulfomycin I (1)[1], $C_{55-57}H_{56-64}N_{15-17}O_{20-22}S_2$, a sulfur-containing peptide antibiotic, was hydrolyzed for 6 hours at 110° in conc.-HCl in a sealed tube. Yellow needles which deposited out after cooling were recrystallized from conc.-HCl to give an amphoteric compound (2) as hydrochloride: $C_{12}H_6N_2O_5S \cdot HCl \cdot H_2O$; m.p. > 220° (dec.); uv (MeOH): 232 (log ε 4.27) and 277 nm (4.29); ir (KBr): 3400, 3100, 3000-2400 and 1720 cm^{-1}. Hydrogenolysis of 2 with Raney nickel catalyst in alkaline aqueous solution gave two novel products assigned 3 and 4. The compounds 3 and 4 were characterized as a methyl and ethyl ester, respectively. Dimethyl ester of 3: $C_{14}H_{18}N_2O_5$; m.p. 166-167° (dec.); uv (MeOH): 240 (sh., log ε 4.19), 245 (4.21) and 326 nm (4.40); ir (KBr): 1740 cm^{-1}; nmr ($CDCl_3$): 1.76 (3H,d,J=7), 2.18 (2H,q,J=6), 2.72 (2H,t,J=6), 3.78 (6H,s), 4.32 (1H,t,J=6), 4.72 (1H,q,J=7) and 7.05 (2H,br.s); ms: *m/e* 294 (M^+), 236 and 177. Ethyl ester of 4: $C_{11}H_{14}N_2O_3$; uv (MeOH): 229 and 293 nm; ir (KBr): 1735 cm^{-1}; ms: *m/e* 222 (M^+) and 149. Thanks to Prof. R.L. Rinehart,Jr., University of Illinois, 2 was identified in his laboratory as berninamycinic acid (5)[2], a degradation product of berninamycins. Derivation of 3 and 4 from 2 is reasonable to expect.



3



4

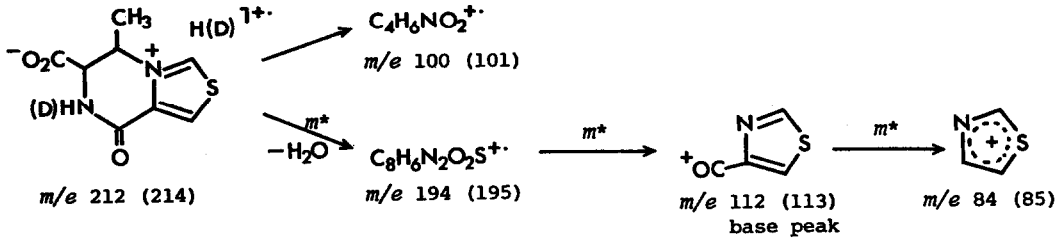


2,5 Berninamycinic acid

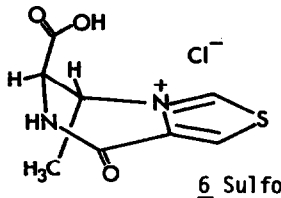
From the filtrate of the above reaction, pyruvic acid, threonine and aminoacetone were recovered. In addition, another new degradation product named sulfomycinine (6) was isolated as hydrochloride: colorless needles; $C_8H_8N_2O_3S \cdot HCl$; m.p. 205-207° (dec.); uv (MeOH): 230 nm (log ε 3.85), uv (alkaline MeOH): 230 (3.97) and 326 nm (4.20); ir (KBr): 3100, 2900-2500, 1740 and 1695 cm^{-1}. The compound 6 was esterified with HCl/EtOH and gave a crystalline ethylester chloride, $C_{10}H_{13}N_2O_3S \cdot Cl$; m.p. 178-180° (dec.); ir (KBr): 3090, 1740 and 1690 cm^{-1}; ms: *m/e* 240 (M^+-1), 128, 112 (base peak) and 84. In the nmr spectrum of 6 in freshly prepared D_2O solution, the signals corresponding to CH_3-CH-CH- system [1.83 (3H,d,J=7), 5.73 (1H,dq,J=2 and 7) and 4.72 (1H,d,J=2)] and aromatic ring protons [8.71 (1H,d,J=2) and 10.25 (1H,d,J=2)] were observed. The latest signal which disappeared on standing in D_2O solution would be assigned to a proton at C_2-position of a thiazolium ring. From nmr spectra and high resol-

ution mass spectra of 6 and its deuterized derivative (scheme I), 6 was assumed to be 6-carboxy-5-methyl-8-oxo-5,6,7,8-tetrahydro-thiazolo[3,4-a]pyrazinium chloride. The proposed structure was supported by X-ray crystallography, which further showed that 6 is in DL-form and the conformation is as depicted.

Scheme I



The compound 6 was finally confirmed by synthesis starting from the condensation of 4-thiazolecarboxylic acid with DL-threonine ethylester followed by bromination, cyclization and de-esterification[3].



6 Sulfomycinine hydrochloride

Similarly to thiostrepton[4], siomycin[5] and thiopeptin[6], presence of dehydroalanine residue(s) in 1 was suggested by 1) liberation of pyruvic acid, 2) reduction of 1 with sodium borohydride followed by acid hydrolysis to give alanine and 3) reaction of 1 with thioglycolic acid followed by acid hydrolysis to give S-carboxymethylcysteine[7]. However, 4-(α-hydroxyethyl)-8-hydroxyquinaldic acid and thiostreptine found in alike antibiotics were not detected in the acid hydrolyzate of 1.

References

1) Y. Egawa, K. Umino, Y. Tamura, Y. Shimizu, K. Kaneko, M. Sakurazawa, S. Awataguchi and T. Okuda, J. Antibiotics, 22, 12 (1969).

2) J.M. Liesch, J.A. McMillan, R.C. Pandey, I.C. Paul, K.L. Rinehart, Jr., and F. Reusser, J. Amer. Chem. Soc., 98, 299 (1976).

3) To be published.

4) B. Anderson, D.C. Hodgkin and M.A. Viswamitra, Nature, 225, 233 (1969).

5) M. Ebata, K. Miyazaki and H. Otuka, J. Antibiotics, 22, 434 (1969).

6) I. Muramatsu, A. Hagitani, Y. Motoki, Y. Kitamura, H. Imanaka and H. Miyairi, Abstracts Papers of the 32nd Annual Meeting of Chemical Society of Japan, No. 1F26 , Tokyo, April 1-4, 1975.

6) M. Ebata, K. Miyazaki and H. Otuka, J. Antibiotics, 22, 451 (1969).