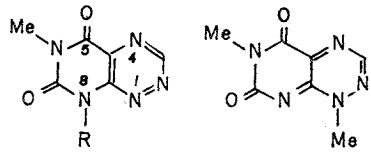
Communications to the editor

THE STRUCTURE OF REUMYCIN

Sir:

In 1967 S. M. NAVASHIN *et al.*[1] reported on the antitumor activity of a crude antibiotic preparation from a strain of *Actinomyces* originally isolated from Kazakhstan soil. We have found the antibiotic, reumycin, to be 6-methyl-pyrimido-[5,4-e]-*as*-triazine-5,7(6H,8H)-dione (**1**).



1 : R = H
2 : R = Me

3

Reumycin, $C_6H_5N_5O_2$,* yellow crystals, m.p. 244~245°C (from EtOH); R_f 0.50 (TLC on silica gel in EtOAc-C_6H_6 3 : 2); UV (EtOH): λ_{max} 235, 265 sh, 340, 400 nm ($\lg\varepsilon$ 4.25, 3.49, 3.72, 2.87), UV (0.05 N NaOH in EtOH) λ_{max} 258, 400 nm ($\lg\varepsilon$ 4.18, 3.42); IR (KBr): ν_{max} 1738, 1700, 1690, 1685, 1590 cm^{-1}; NMR (d_5-Py): δ 3.39 (3H, s), 9.84 (1H, s), 10.94 (1H, bs).

The molecular formula and spectral characteristics of reumycin, in particular the resemblance of its UV absorption to that of the antibiotic fervenulin (**2**),[2] indicated it to probably be a demethyl analog of the latter. In fact, it was found that reumycin reacts with CH_2N_2 to yield three isomeric methyl derivatives, $C_7H_7N_5O_2$,* R_f 0.67, 0.33 and 0.09 (under the above conditions). One of them was proved to be reumycin 7-methyl ether [m.p. 157~158°C (from EtOH); R_f 0.33; UV (EtOH): λ_{max} 243, 263 sh, 343 nm ($\lg\varepsilon$ 4.11, 3.80, 3.55); IR (KBr): ν_{max} 1712, 1594, 1550 cm^{-1}; NMR ($CDCl_3$): δ 3.61 (3H, s), 4.33 (3H, s), 9.89 (1H, s)]. The other two were fervenulin (**2**) [m.p. 175~176°C (from EtOH); R_f 0.67; UV (EtOH): λ_{max} 239, 277, 345 nm ($\lg\varepsilon$ 4.24, 3.27, 3.66); IR (KBr): ν_{max} 1725, 1680, 1580, 1540 cm^{-1}; NMR ($CDCl_3$): δ 3.58 (3H, s), 3.91 (3H, s), 9.84 (1H, s). Lit.[3], m.p. 178~179°C, UV (EtOH): λ_{max} 238, 275, 340 nm (ε 18,500; 1,600; 4,200)] and toxoflavin[4] (known also as the antibiotic xanthothricin[5]) (**3**) [m.p. 172~173°C (from EtOAc); R_f 0.09; UV (EtOH): λ_{max} 261, 330 sh, 400 nm ($\lg\varepsilon$ 4.18, 3.29, 3.59); IR (KBr): λ_{max} 1706, 1680, 1615, 1540 cm^{-1}; NMR ($CDCl_3$): δ 3.50 (3H, s), 4.16 (3H, s), 8.79 (1H, s). Lit.[3], m.p. 172~173°C, UV (pH 7): λ_{max} 257.5, 394 nm (ε 16,400; 2,500)].

The formation of **2** and **3** established the position of the only methyl group present in the parent antibiotic, thus proving structure **1** for reumycin. An independent proof for this structure was achieved by a facile synthesis of reumycin from 4-chloro-1-methyl-uracil according to the method of T. K. LIAO *et al.*[6]

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* Microanalyses and mass spectral data agree with the molecular formula shown.

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