CHEMICAL MODIFICATION OF OXANOSINE I. SYNTHESIS AND BIOLOGICAL PROPERTIES OF 2′-DEOXYOXANOSINE

Sir:

Oxanosine (**1**)[1,2] is a novel nucleoside antibiotic isolated from the culture filtrate of *Streptomyces capreolus* MG265-CF3. The total synthesis of **1** was recently reported by us.[3] In this paper we wish to describe the synthesis and biological properties of 2′-deoxyoxanosine (**2**).

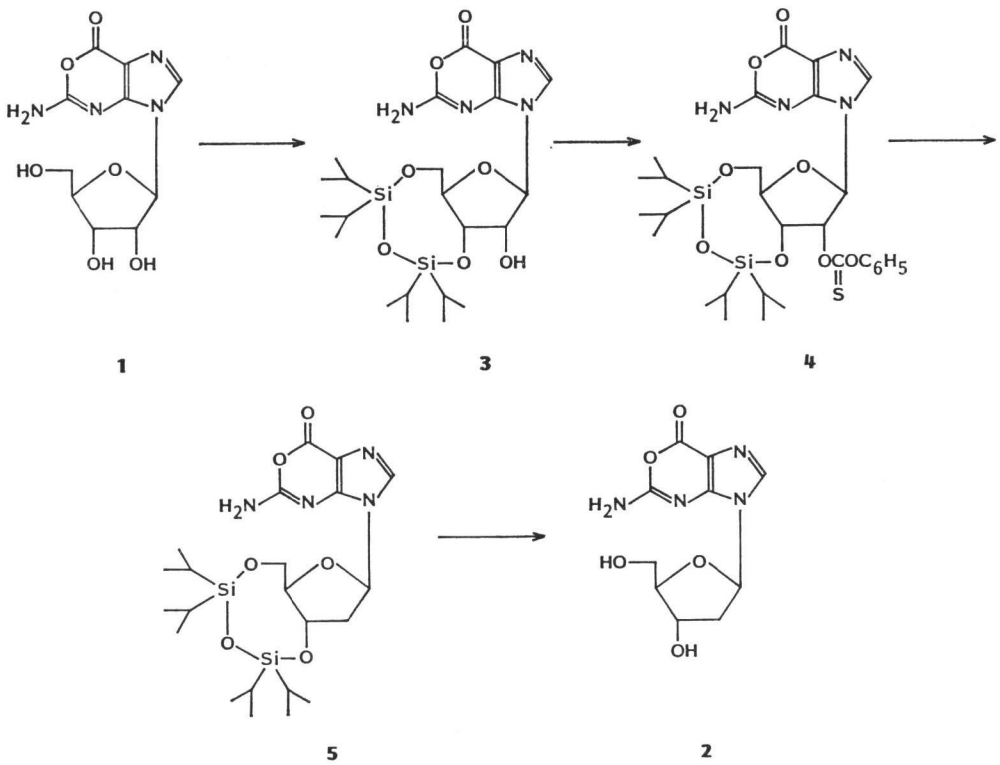
The synthesis of **2** was performed according to the deoxygenation procedure developed by ROBINS and WILSON[4] (Scheme 1).

Treatment of **1** with 1,3-dichloro 1,1,3,3-tetraisopropyl disiloxane (in pyridine, room temp, 4 hours) afforded 3′,5′-*O*-(1,1,3,3-tetraisopropyl disilox-1,3-diyl)oxanosine (**3**) [76%, mp 199~202°C, SIMS: *m/z* 527 $(M+H)^+$]. **3** was coupled with phenoxythiocarbonyl chloride by means of 4-dimethylaminopyridine (in CH_3CN, room temp, 1 hour) to give 2′-*O*-phenoxythiocarbonyl-3′,5′-*O*-(1,1,3,3-tetraiso-

Table 1. Antimicrobial spectra of oxanosine and 2′-deoxyoxanosine (peptone agar).

Test organism	MIC (μg/ml)	
	Oxanosine	2′-Deoxy-oxanosine
Staphylococcus aureus FDA 209P	>100	>100
Micrococcus flavus FDA 16	>100	>100
M. luteus PCI 1001	>100	>100
Bacillus subtilis PCI 219	>100	>100
Corynebacterium bovis 1810	>100	>100
Escherichia coli NIHJ	>100	12.5
E. coli K-12	>100	0.78
E. coli ML 1629	>100	3.12
Shigella dysenteriae JS 11910	>100	1.56
S. flexneri 4b JS 11811	>100	1.56
S. sonnei JS 11746	>100	0.78
Salmonella typhi T-63	>100	>100
Proteus vulgaris OX-19	<0.2	<0.2
P. mirabilis IFM OM-9	1.56	6.25
P. rettgeri GN 466	>100	>100
Serratia marcescens	>100	>100
Klebsiella pneumoniae PCI 602	>100	>100
Pseudomonas aeruginosa A3	>100	>100
Mycobacterium smegmatis ATCC 607	>100	>100
Candida albicans 3147	>100	>100

Scheme 1. Synthesis of 2′-deoxyoxanosine.



propyl disilox-1,3-diyl)oxanosine (**4**) [53%, mp 185~187°C, SIMS: *m/z* 663 $(M+H)^+$]. Then, homolytic deoxygenation of **4** with tri-*n*-butyltinhydride in the presence of α,α'-azobisisobutyronitrile (in toluene, 75°C, 2 hours) gave 2′-deoxy-3′,5′-*O*-(1,1,3,3-tetraisopropyl disilox-1,3-diyl)-oxanosine (**5**) [82%, mp 205~207°C, SIMS: *m/z* 511 $(M+H)^+$, NMR ($CDCl_3$) δ 6.05 (1H, t, $J=6$ Hz)]. Finally deprotection of **5** was readily accomplished by using tetra-*n*-butyl ammonium fluoride (in THF, room temp, 10 minutes) to afford 2′-deoxyoxanosine (**2**) [82%; mp 193~196°C; FDMS *m/z* 268 (M^+); IR ν_{max}^{Nujol} 3300, 3225, 3175, 3125, 1770, 1635, 1045, 1000, 945 cm^{-1}; UV λ_{max}^{MeOH} nm (log ε) 286 (3.91) and 247 (4.07); NMR (CD_3OD) δ 6.22 (1H, t, $J=7$ Hz); $[\alpha]_D^{20}$ −7.0° (*c* 0.4, MeOH)].

MIC of **1** and **2** against selected microorganisms was measured in peptone medium (Table 1).

As shown in Table 1, the activities of **2** against *E. coli* NIHJ, *E. coli* K-12, *Shigella dysenteriae* JS11910, *S. sonnei* JS11746 and *Proteus vulgaris* OX19 were enhanced remarkably in comparison with those of **1**. 2′-Deoxyoxanosine had also a stronger activity in inhibiting the growth of L-1210 *in vitro* (IC_{50} 0.15 μg/ml) than oxanosine (IC_{50} 0.53 μg/ml).

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