Sir:

A large number of aminocyclitol antibiotics contain 2-deoxystreptamine or its derivatives as the cyclitol unit. The cyclitol moiety N,N′-dimethyl-2-epi-streptamine appearing to be unique to spectinomycin. In the neamine1 and sisomicin2 antibiotics, an overall decrease in antibacterial activity was observed when the 2-deoxystreptamine unit was replaced by either streptamine or 2-epi-streptamine. Thus, it was of interest to prepare 7-deoxyspectinomycin** (7) in order to compare its activity with that of spectinomycin. In this paper we describe the preparation of 7-deoxyspectinomycin (7) and 7-deoxy-8-epi-4(R)-dihydrospectinomycin (10), as outlined in Scheme 1.

Many of the experimental methods employed in this work have been described in our earlier papers.1,3,4 The route we employed for the preparation of 7-deoxy-N,N′-dicarbobenzoxy-spectinomycin (6) was similar to that recently reported*** except for the use of 7-O-acetyl-N,N′-dicarbobenzoxy-4(R)-dihydrospectinomycin-4,4a-acetonide (1)5 as the starting material. Oxidation of 1 using the chromium trioxide-pyridine complex in methylene chloride afforded the unsaturated ketone 2 directly. Reduc-

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* Paper number IV in a series on Spectinomycin Chemistry.

** In the spectinomycin numbering system, the 7-position of spectinomycin corresponds to the 2-position of streptamine.

*** Following the completion of this work the preparation of 5 and 6 was reported by W. ROSENbrook, et al.5
of the unsaturated cyclic carbamate 4,* IR
(KBr) 1788, 1698 cm⁻¹; Calcd. for C₂₆H₃₂N₂O₉:
C 60.46, H 6.24, N 5.42; Found: C 60.38,
H 6.23, N 5.41.

The triol 5, obtained on acid hydrolysis of 3,
was oxidized using dimethylsulfoxide-acetic an-
hydride to yield the protected 7-deoxyspectinomycin
6. Despite the earlier reported failure¹,²,
hydrogenolysis of 6 (purified by preparative
TLC using n-hexane - ethyl acetate - acetone,
5: 5: 3) using the palladium black-isopropanol-
water conditions¹,² proceeded without difficulty
to afford crystalline 7-deoxyspectinomycin dihy-
drochloride (7), mp 195 - 199°C (dec), high resolu-
tion MS on the free base Calcd. for C₁₄H₂₄N₂O₆:
(M⁺) 316.1633; Found: (M⁺) 316.1655.

The unsaturated cyclic carbamate 4 was sub-
jected to catalytic hydrogenation-hydrogenolysis
using 5% palladium on carbon to yield the 7-
deoxy-8-epi-4(R)-dihydrospectinomycin cyclic
 carbamate 8, PMR (CDCl₃) 4.42 (t, J₈,₉=7.0
Hz, J₉,₁₀a=7.5 Hz, H-9), 4.58 (s, H-10a). The
7 Hz coupling between H-8 and H-9 indicated a
cis fused cyclic carbamate ring, since the coupl-
ings reported for a trans fused cyclic carbamate
are 9~12 Hz.² The formation of a cis fused cyclic carbamate ring between C-8 and C-9 re-
quired that epimerization had occurred at one of
these centers, and the 7.5 Hz coupling between
H-9 and H-9a was only consistent with an
equatorial hydroxyl group at C-9 (natural con-
figuration). Hydrolysis of the cyclic carbamate
ring in 8 (excess Ba(OH)₂ in refluxing methanol-
water, 1: 1) gave the dihydrospectinomycin acet-
one 9, PMR (CD₂OD) 3.63 (t and dd, J₈,₉a=J₉,₉a=9.5 Hz, H-5a; J₉,₁₀a=4.5 Hz, J₁₀a,a=9.5
Hz, H-9), 4.62 (s, H-10a), MS 358 (M⁺). The
observed coupling constants were in com-
plete accord with the assignment of the epi
configuration at C-8.** The acetone protecting
group in 9 was removed by acidic hydroly-
sis to afford crystalline 7-deoxy-8-epi-4(R)-dihy-
drospectinomycin dihydrochloride (10), mp 248°C
decl.); Calcd. for C₁₄H₂₄N₂O₆·2HCl: C 42.97,
H 7.21, N 7.16, Cl 18.12. Found: C 43.03,
H 7.22, N 7.07, Cl 18.04.

The 7-deoxyspectinomycin (7) and 7-deoxy-8-
epi-4(R)-dihydrospectinomycin (10) were found
to be inactive when tested in vitro against 12
spectinomycin sensitive Gram-positive and Gram-
negative organisms. Similarly, in agreement with
the report of ROSENBROOK et al.¹,² the 7-deoxy
dihydrospectinomycin 5 (R = H) was found to
be inactive when tested in vitro.

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