SPECTINOMYCIN CHEMISTRY. III[1]

9-*EPI*-4(*R*)-DIHYDROSPECTINOMYCIN AND 9-*EPI*-SPECTINOMYCIN

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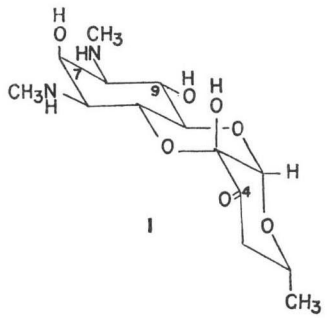
(Received for publication July 28, 1978)

The preparation of 9-*epi*-4(*R*)-dihydrospectinomycin (**8**) and of 9-*epi*-spectinomycin (**11**) is described.

It has been reported that the R-factor-mediated resistance of certain strains of *Escherichia coli* to spectinomycin (**1**) is due to enzymic adenylylation of the C-9 hydroxyl group[2]. Streptomycin is also inactivated by the same enzyme, which apparently recognizes the D-*threo* methylamino alcohol moieties present in both spectinomycin and streptomycin[2]. The removal or epimerization of the C-9 hydroxyl group of spectinomycin would be expected to generate a molecule which no longer can serve as a substrate for this inactivating enzyme and thus give an antibiotic active against these resistant strains.

We have previously described the preparation of 9-deoxyspectinomycin and its lack of antibacterial activity[1]. We now report the preparation of 9-*epi*-4(*R*)-dihydrospectinomycin (**8**) and 9-*epi*-spectinomycin (**11**), as outlined in Scheme 1.



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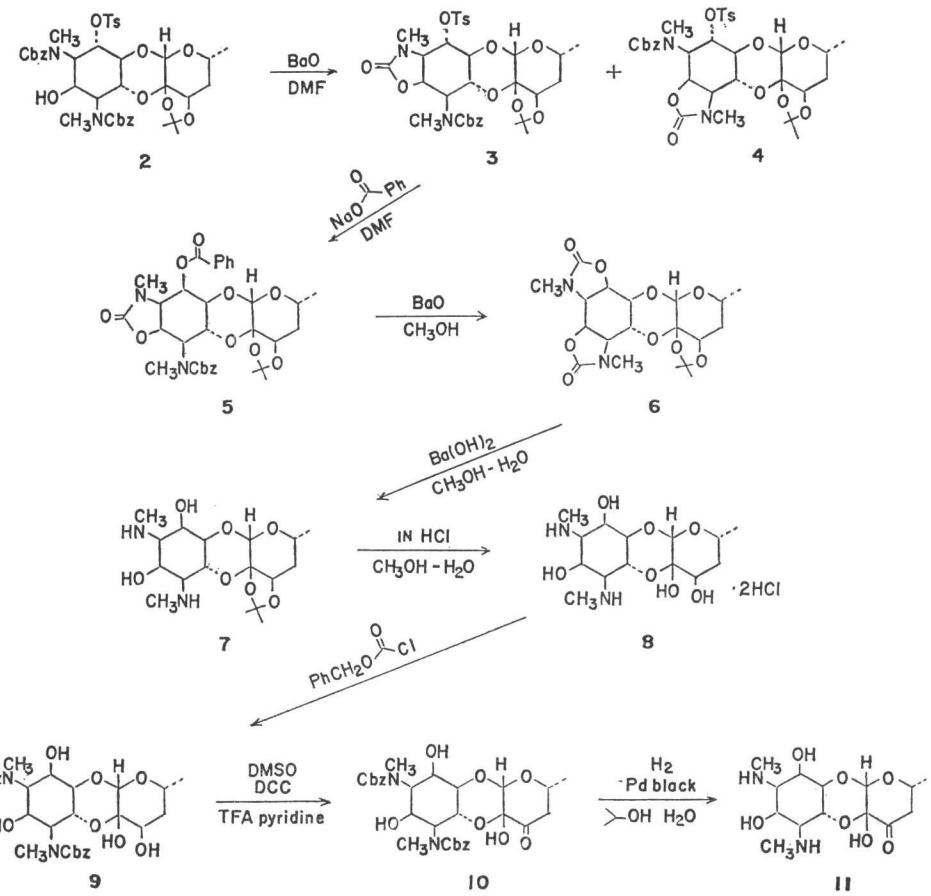
The direct nucleophilic displacement reactions carried out on the tosylate **2*** resulted in complex mixtures of products. This complication could be overcome by first reacting **2** at 35°C with barium oxide in DMF to give a readily separable mixture of the cyclic carbamates **3** and **4****. The 7,8-cyclic carbamate **3**, isolated in 61% yield, on reaction with sodium benzoate in DMF at 140°C afforded the 9-*epi*-benzoate **5** (79%). The mono-cyclic carbamate **5** underwent a facile rearrangement in methanol containing barium oxide, at room temperature or on heating, to give the crystalline 9-*epi*-6,7-8,9-bis cyclic carbamate **6**. An X-ray analysis carried out on **6** confirmed its structure. (J. F. BLOUNT, unpublished results.) Basic hydrolysis of both carbamate rings was accomplished by reaction of **6** with barium hydroxide in refluxing methanol - water (1 : 1) to afford the crystalline 9-*epi*-dihydrospectinomycin acetonide **7**. Hydrolysis of the acetonide protecting group using 1 N hydrochloric acid solution in refluxing methanol yielded 9-*epi*-4(*R*)-dihydrospectinomycin dihydrochloride (**8**).

Oxidation of the dicarbobenzoxy dihydrospectinomycin derivative **9** using the DMSO-acetic anhydride oxidation conditions resulted in a complex mixture of products. We have previously found

* Following the completion of this work, a preparation of the tosylate **2** identical to our own was reported: CARNEY, R. E. & W. ROSENBROOK, Jr.: Spectinomycin modification. III. Chloro-deoxy analogs. J. Antibiotics 30: 960~964, 1977

** Although not described here, the 6,7-cyclic carbamate **4** has also been converted to the bis-cyclic carbamate **6**.

Scheme 1.



that under the DMSO-trifluoroacetic acid-pyridine-dicyclohexylcarbodiimide[8] conditions, *N,N'*-dicarbobenzoxy-4(*R*)-dihydrospectinomycin was oxidized to give a 2 : 1 mixture of the 9-oxo-*N,N'*-dicarbobenzoxy-4(*R*)-dihydrospectinomycin and 9-oxo-*N,N'*-dicarbobenzoxyspectinomycin. (J. T. S. LIN, unpublished results). These oxidation conditions appear to show some specificity for the equatorial C-9 hydroxy group, rather than the more accessible axial C-4 hydroxyl function*. It therefore seemed reasonable that under these conditions, the 9-*epi* derivative **9**, with all hydroxyl groups axial, might be selectively oxidized at C-4. Indeed, by quenching the reaction before complete consumption of the tetrol **9****, the desired 9-*epi*-spectinomycin derivative **10** was isolated in 40% yield (based on unrecovered **9**). Hydrogenolysis of the carbobenzoxy groups, employing the conditions previously reported[1], afforded 9-*epi*-spectinomycin (**11**).

All new compounds described here were found to be inactive when tested *in vitro* against a selection of 12 spectinomycin-sensitive Gram-positive and Gram-negative bacteria.

* A preference in the case of hindered alcohols for the oxidation of equatorial over axial has been reported for several steroid alcohols[8].

** Allowing the reaction to proceed for longer times resulted in further oxidation of the 9-*epi*-spectinomycin derivative **10** yielding only 9-oxo-*N,N'*-dicarbobenzoxy spectinomycin.

Experimental Section

Melting points were taken on a Kofler hot stage melting point apparatus (Reichert) and are uncorrected. Infrared (IR) spectra were recorded on a Digilab FTS 14 spectrometer. PMR spectra measured at 100 MHz were obtained with Varian XL-100 and HA-100 instruments, 220 MHz spectra were measured on a Varian HR-220 instrument and 60 MHz spectra were measured on a Varian T-60 instrument. Chemical shifts are reported in parts per million downfield from internal tetramethylsilane. Mass spectra (MS) were obtained on a CEC-110 mass spectrometer.

Silica gel 60 (0.063~0.200 mm), silica gel PF-254 and plates precoated with silica gel 60 F-254 (all from E. Merck) were used for column, preparative thin-layer and thin-layer chromatography (TLC), respectively.

Dimethylformamide (DMF) and pyridine were dried by prolonged storage over Davidson 4A Molecular Sieves and filtered just prior to use.

Dimethylsulfoxide (DMSO) was distilled and then stored under argon over Davidson 4A Molecular Sieves. Benzene was distilled and then stored under argon.

6-*N*-Carbobenzoxy-9-*O*-tosyl-4(*R*)-dihydrospectinomycin-4,4a-acetonide-7,8-cyclic carbamate (**3**) and 8-*N*-Carbobenzoxyl-9-*O*-tosyl-4(*R*)-dihydrospectinomycin-4,4a-acetonide-6,7-cyclic carbamate (**4**).

The tosylate **2*** (3.3 g, 4.14 mmole) in dry DMF (50 ml) containing BaO (3.06 g, 20 mmole) was stirred at 35°C for 2 days. The solids were then removed by filtration through Celite and washed with dry DMF. The combined filtrates were evaporated *in vacuo* to leave 3.3 g of an oil. Purification by column chromatography on silica gel (350 g) using *n*-hexane - EtOAc (1 : 1) afforded first the 7,8-cyclic carbamate **3** (1.73 g, 61%) as a glass: Rf 0.50; IR (KBr) 1775, 1695 cm^{-1}; PMR ($CDCl_3$, 100 MHz), rotomers present, δ 1.10 (d, 3H, C-2 C$\underline{H}_3$), 1.39 and 1.42 [2 broad s, 6H, C(C$\underline{H}_3$)$_2$], 1.40~2.00 (m, 2H, *H*-3), 2.41 (s, 3H, tosyl C$\underline{H}_3$), 2.97, 3.00 and 3.11 (3s, 6H, NC$\underline{H}_3$), 3.40~3.70 (m, 1H, *H*-2), 3.78 (t, 1H, $J_{9,9a}=J_{5a,9a}=9$ Hz, *H*-9a), 3.80 (m, 1H), 3.90 (m, 1H), 4.01 (s, 1H, *H*-10a), 4.16 (dd, 1H, $J_{5a,9a}=9$ Hz, $J_{5a,6}=11.5$ Hz, *H*-5a), 4.39 (dd, 1H, $J_{5a,6}=11.5$ Hz, $J_{6,7}=4$ Hz, *H*-6), 4.74 (dd, 1H, $J_{6,7}=4$ Hz, $J_{7,8}=6$ Hz, *H*-7), 4.80 (dd, 1H, $J_{8,9}=7.5$ Hz, $J_{9,9a}=9$ Hz, *H*-9), 5.15 (s, 2H, C$\underline{H}_2$Ph), 7.20~7.40 (m, 7H, arom.), 7.80 (d, 2H, arom.); MS *m/e* 688 (M^+), 673 ($M-CH_3$), 524 ($M-CH_3NCbz$), 516 ($M-HOTs$).

Further elution with *n*-hexane - EtOAc (1 : 1) gave 0.93 g (33%) of the 6,7-cyclic carbamate **4** as a glass: Rf 0.24; IR (KBr) 1775, 1705 cm^{-1}; PMR ($CDCl_3$, 100 MHz), rotomers present, δ 1.18 (d, 3H, C-2 C$\underline{H}_3$), 1.46 [broad s, 6H, C(C$\underline{H}_3$)$_2$], 1.50~2.10 (m, 2H, *H*-3), 2.35 and 2.40 (2s, 3H, tosyl C$\underline{H}_3$), 2.98 and 3.00 (2s, 6H, NC$\underline{H}_3$), 3.52 (dd, 1H, $J_{5a,6}=7.5$ Hz, $J_{6,7}=6$ Hz, *H*-6), 3.50~3.80 (m, 1H, *H*-2), 3.88 (t, 1H, $J_{5a,9a}=J_{9,9a}=11$ Hz, *H*-9a), 4.07 (dd, 1H, $J_{5a,6}=7.5$ Hz, $J_{5a,9a}=11$ Hz, *H*-5a), 4.29 and 4.34 (2s, 1H, *H*-10a), 4.63 (dd, 1H, $J_{6,7}=6$ Hz, $J_{7,8}=4$ Hz, *H*-7), 4.78 (dd, 1H, $J_{7,8}=4$ Hz, $J_{8,9}=10$ Hz, *H*-8), 5.07 (dd, 1H, $J_{8,9}=10$ Hz, $J_{9,9a}=11$ Hz, *H*-9), 5.10 (s, 2H, C$\underline{H}_2$Ph), 7.21 (m, 3H, arom.), 7.45 (s, 5H, arom.), 7.79 (d, 2H, arom.); MS *m/e* 426 [M-($CH_2Ph+OTs$)], 411 [M-($CH_2Ph+OTs+CH_3$)].

9-*epi*-*O*-Benzoyl-6-*N*-carbobenzoxy-4(*R*)-dihydrospectinomycin-4,4a-acetonide-7,8-cyclic carbamate (**5**).

A solution of the tosylate **3** (0.635 g, 0.92 mmole) in dry DMF (40 ml) containing sodium benzoate (0.198 g, 1.38 mmole) was stirred rapidly in a 140°C oil bath for 7 hours. After cooling to room temperature, the solids were filtered off and washed with dry DMF. The residue, obtained on concentration of the combined filtrate *in vacuo*, was dissolved in toluene and washed with saturated NaCl solution. The aqueous washings were extracted with toluene. Drying and concentration of the combined toluene solutions yielded 0.61 g of a white solid. Crystallization from CH_3OH gave 0.46 g (79%) of **5** as fine needles: m.p. 242~243°C; IR (KBr) 1773, 1728, 1700 cm^{-1}; PMR ($CDCl_3$, 220 MHz), rotomers present, δ 1.23 (d, 3H, C-2 C$\underline{H}_3$), 1.31 and 1.41 [2s, 6H, C(C$\underline{H}_3$)$_2$], 1.40~2.00 (m, 2H, *H*-3), 2.75, 3.13 and 3.17 (3s, 6H, NC$\underline{H}_3$), 3.79 (m, 1H, *H*-2), 3.84 (dd, 1H, $J_{7,8}=5.2$ Hz, $J_{8,9}=4.8$ Hz, *H*-8), 4.05 and

* See footnote * on page 985

4.10 (2dd, 1H, $J_{5a,9a}=10$ Hz, $J_{9,9a}=3$ Hz, *H*-9a), 4.07 (m, 1H, *H*-4), 4.27 and 4.50 (2dd, 1H, $J_{5a,6}=11$ Hz, $J_{6,7}=5$ Hz, *H*-6), 4.53 (s, 1H, *H*-10a), 4.66 (dd, 1H, $J_{5a,6}=11$ Hz, $J_{5a,9a}=10$ Hz, *H*-5a), 4.82 (t, 1H, $J_{6,7}=5$ Hz, $J_{7,8}=5.2$ Hz, *H*-7), 5.10 (s, 2H, CH_2Ph), 5.85 and 5.91 (2dd, 1H, $J_{8,9}=4.8$ Hz, $J_{9,9a}=3$ Hz, *H*-9), 7.20~7.60 (m, 8H, arom.), 8.00 (m, 2H, arom.); MS *m/e* 638 (M^+), 623 ($M-CH_3$).

Peaks in the PMR spectrum due to the presence of rotomers collapsed when the spectum was run at 62°C and reappeared after cooling to room temperature.

Spin decoupling: Irradiation at δ 5.86 (*H*-9) caused the d of d at 3.84 (*H*-8) to collapse to a d ($J=5.2$ Hz) and the d of d's at 4.05 and 4.10 (2 rotomers, *H*-9a) each to collapse to a d ($J=10$ Hz).

Anal. Calcd. for $C_{33}H_{38}N_2O_{11}$: C, 62.06; H, 6.00; N, 4.39.
Found: C, 62.23; H, 6.01; N, 4.20.

9-*epi*-4(*R*)-Dihydrospectinomycin-4,4a-acetonide-6,7-8,9-bis-cyclic carbamate (**6**).

A rapidly stirred mixture of the 9-*epi*-benzoate **5** (4.9 g, 7.67 mmole), CH_3OH (250 ml) and BaO (1.76 g, 11.5 mmole) was heated to reflux for 25 minutes. After cooling to room temperature, excess CO_2 was bubbled through the reaction mixture and the resulting insoluble solids were filtered off and washed with CH_3OH. Concentration of the combined filtrates gave 5.0 g of a residue which was triturated with $CHCl_3$ and the insoluble solids were again removed by filtration. Concentration of the $CHCl_3$ solution gave 4.9 g of an oil which was crystallized from CH_3OH to yield 2.9 g (88%) of pure **6** in the form of plates: m.p. 302~303°C; IR (KBr) 1768, 1755, 1745 cm^{-1}; IR ($CHCl_3$) 1767 cm^{-1}; PMR ($CDCl_3$, 100 MHz) δ 1.28 (d, 3H, C-2 CH_3), 1.47 [s, 6H, $C(CH_3)_2$], 1.71 (dq, 1H, $J_{gem}=15$ Hz, $J_{2,3ax}=11$ Hz, $J_{3ax,4}=5$ Hz, *H*-3ax), 2.00 (dq, 1H, $J_{gem}=15$ Hz, $J_{2,3eq}=3$ Hz, $J_{3eq,4}=2$ Hz, *H*-3eq), 2.92 and 2.99 (2s, 6H, NCH_3), 3.70~4.00 (broad m, 1H, *H*-2), 3.89 (dd, 1H, $J_{5a,6}=6.5$ Hz, $J_{6,7}=9.5$ Hz, *H*-6), 3.92 (dd, 1H, $J_{9,9a}=4$ Hz, $J_{5a,9a}=11.5$ Hz, *H*-9a), 4.15 (m, 1H, *H*-4), 4.23 (dd, 1H, $J_{7,8}=4.5$ Hz, $J_{8,9}=9.5$ Hz, *H*-8), 4.40 (dd, 1H, $J_{5a,9a}=11.5$ Hz, $J_{5a,6}=6.5$ Hz, *H*-5a), 4.55 (s, 1H, *H*-10a), 4.76 (dd, 1H, $J_{6,7}=9.5$ Hz, $J_{7,8}=4.5$ Hz, *H*-7), 4.87 (dd, 1H, $J_{8,9}=9.5$ Hz, $J_{9,9a}=4$ Hz, *H*-9); MS *m/e* 426 (M^+), 411 ($M-CH_3$).

Anal. Calcd. for $C_{19}H_{26}N_2O_9$: C, 53.52; H, 6.15; N, 6.57.
Found: C, 53.65; H, 6.23; N, 6.39.

9-*epi*-4(*R*)-Dihydrospectinomycin-4,4a-acetonide (**7**).

A solution of the bis-carbamate **6** (1.00 g, 2.34 mmole) and $Ba(OH)_2\cdot H_2O$ (1.40 g, 7.39 mmole) in H_2O (20 ml) and CH_3OH (20 ml) was heated to reflux for 4 hours. After the reaction solution had cooled to room temperature, excess CO_2 was bubbled into the reaction solution and the insoluble solids were filtered off and washed with CH_3OH. The combined filtrates were concentrated to give 0.98 g of a residue which was crystallized from $CHCl_3$-ligroine (b.p. 60~90°C) to yield 0.745 g (85%) of **7** as fine needles: m.p. 183~188°C; IR (KBr) 3400, 1600 cm^{-1}; PMR (CD_3OD, 100 MHz) δ 1.23 (d, 3H, C-2 CH_3), 1.44 and 1.49 [2s, 6H, $C(CH_3)_2$], 1.70 (dq, 1H, $J_{gem}=15$ Hz, $J_{2,3ax}=11$ Hz, $J_{3ax,4}=4.5$ Hz, *H*-3ax), 1.99 (dt, 1H, $J_{gem}=15$ Hz, $J_{2,3eq}=J_{3eq,4}=2.5$ Hz, *H*-3eq), 2.56 and 2.61 (2s, 6H, NCH_3), 2.84 (t, 1H, $J_{7,8}=J_{8,9}=3$ Hz, *H*-8), 2.87 (dd, 1H, $J_{5a,6}=10.5$ Hz, $J_{6,7}=3$ Hz, *H*-6), 3.79 (dd, 1H, $J_{5a,9a}=10$ Hz, $J_{9,9a}=2.5$ Hz, *H*-9a), 3.86 (m, 1H, *H*-2), 4.21 (t, 1H, $J_{8,9}=3$ Hz, $J_{9,9a}=2.5$ Hz, *H*-9), 4.25 (dd, 1H, $J_{3ax,4}=4.5$ Hz, $J_{3eq,4}=2.5$ Hz, *H*-4), 4.32 (t, 1H, $J_{6,7}=J_{7,8}=3$ Hz, *H*-7), 4.36 (t, 1H, $J_{5a,9a}=10$ Hz, $J_{5a,6}=10.5$ Hz, *H*-5a), 4.68 (s, 1H, *H*-10a); MS *m/e* 359 ($M-CH_3$), 356 ($M-H_2O$), 343 ($M-H_2NCH_3$).

Spin decoupling: Irradiation at δ 2.85 (*H*-6 and *H*-8) caused the collapse of the t at 4.36 (*H*-5a) to a d ($J=10$ Hz) and the t at 4.32 (*H*-7) to a s and the t at 4.21 (*H*-9) to a d ($J=2.5$ Hz).

Irradiation at δ 1.70 (*H*-3ax) resulted in the collapse of the dd at 4.25 (*H*-4) to a d ($J=2.5$ Hz).

Irradiation at δ 1.99 (*H*-3eq) collapsed the dd at 4.25 (*H*-4) to a d ($J=4.5$ Hz).

Irradiation at δ 3.83 (*H*-2 and *H*-9a) caused the collapse of the t at 4.21 (*H*-9) to a d ($J=3$ Hz) and the t at 4.36 (*H*-5a) to a d ($J=10.5$ Hz) and the d at 1.23 (C-2 CH_3) to a s.

Anal. Calcd. for $C_{17}H_{30}N_2O_7$: C, 54.53; H, 8.08; N, 7.48.
Found: C, 54.58; H, 8.06; N, 7.55.

9-*epi*-4(*R*)-Dihydrospectinomycin (**8**).

The 9-*epi*-dihydrospectinomycin acetonide **7** (0.60 g, 1.60 mmole) was dissolved in CH_3OH (40 ml) and 1 N aqueous HCl (40 ml) was added. The resulting milky white mixture was heated to reflux on a

steam bath for 40 minutes. After cooling to room temperature, the solvents were removed under reduced pressure to give 0.62 g of crude **8**. This product was purified by precipitation from an ethanol solution with ether to yield 0.57 g (87%) of **8** as an amorphous white powder: IR (KBr) 3400, 2860~2740, 1600 cm^{-1}; PMR (D_2O-DCl, 100 MHz) δ 1.84 (d, 3H, C-2 CH_3), 2.30~2.70 (m, 2H, *H*-3), 3.48 and 3.50 (2s, 6H, NCH_3), 4.16 (dd, 1H, $J_{5a,6}=10.5$ Hz, $J_{6,7}=3.2$ Hz, *H*-6), 4.19 (t, 1H, $J_{7,8}=3.2$ Hz, $J_{8,9}=3$ Hz, *H*-8), 4.54 (t, 1H, *H*-4), 4.71 (dd, 1H, $J_{5a,9a}=10.5$ Hz, $J_{9,9a}=2.5$ Hz, *H*-9a), 4.50~5.00 (m, 1H, *H*-2), 5.09 (t, 1H, $J_{8,9}=3$ Hz, $J_{9,9a}=2.5$ Hz, *H*-9), 5.32 (t, 1H, $J_{5a,9a}=J_{5a,6}=10.5$ Hz, *H*-5a), 5.38 (t, 1H, $J_{6,7}=J_{7,8}=3.2$ Hz, *H*-7), 5.58 (s, 1H, *H*-10a); MS *m/e* (free base) 316 ($M-H_2O$).

Spin decoupling: Irradiation at δ 4.17 (*H*-6 and *H*-8) caused the collapse of the t at 5.09 (*H*-9) to a d ($J=2.5$ Hz) and the t at 5.32 (*H*-5a) to a d ($J=10.5$ Hz) and t at 5.38 (*H*-7) to a s.

Irradiation at δ 5.35 (*H*-7 and *H*-5a) resulted in the collapse of the dd at 4.16 (*H*-6) to a s and the t at 4.19 (*H*-8) to a d ($J=3$ Hz).

Anal. Calcd. for $C_{14}H_{26}N_2O_7\cdot\frac{1}{2}H_2O$: C, 48.97; H, 7.93; N, 8.16.
Found: C, 49.05; H, 7.75; N, 8.08.

9-*epi*-*N,N'*-Dicarbobenzoxy-4(*R*)-dihydrospectinomycin (**9**).

The 9-*epi*-4(*R*)-dihydrospectinomycin dihydrochloride (**8**) (600 mg, 1.47 mmole) was dissolved in 10% $NaHCO_3$ (7.5 ml) and this solution was stirred and cooled in an ice-water bath while benzyl chloroformate (528.8 mg, 3.1 mmole) in acetone (5 ml) was added dropwise. After the addition was complete, the resulting white mixture was stirred at room temperature for 1½ hours. The reaction mixture was then concentrated *in vacuo* and the residue was dissolved in EtOAc. The resulting EtOAc solution was washed once with saturated NaCl solution. The aqueous washings were extracted twice with EtOAc. The combined EtOAc extracts were dried and evaporated *in vacuo* to afford 830 mg of a glass. Purification by preparative TLC using $CHCl_3$-CH_3OH (9 : 1) yielded 750 mg (85%) of **9** as a glass: Rf 0.5; IR (KBr) 3420, 1695 cm^{-1}; PMR (CD_3OD, 100 MHz) δ 1.19 (d, 3H, C-2 CH_3), 1.60~1.80 (m, 2H), 3.08 and 3.28 (2s, 6H, NCH_3), 3.63 (t, 1H, $J=3$ Hz, *H*-4), 3.90~4.30 (m, 6H), 4.79 (s, 1H, *H*-10a), 4.85 (dd, 1H, $J=9.5$ and 11.5 Hz, *H*-5a), 5.12 (s, 4H, CH_2Ph), 7.30 (s, 10 H, arom.).

Anal. Calcd. for $C_{30}H_{38}N_2O_{11}$: C, 59.79; H, 6.36; N, 4.65.
Found: C, 59.53; H, 6.42; N, 4.53.

9-*epi*-*N,N'*-Dicarbobenzoxyspectinomycin (**10**).

To a stirred solution of dicyclohexylcarbodiimide (308 mg, 1.49 mmole) in DMSO (4 ml), under an atmosphere of argon, was added a solution of 9-*epi*-*N,N'*-dicarbobenzoxy-4(*R*)-dihydrospectinomycin (**9**) (300 mg, 0.497 mmole) in DMSO (1 ml) and dry benzene (2 ml). To this stirred solution was then added a mixture of trifluoroacetic acid (0.0192 ml, 0.249 mmole), dry pyridine (0.0384 ml, 0.497 mmole) and DMSO (1 ml) over 10 minutes. The resulting mixture was stirred under argon at room temperature for 14 hours and then stored at −3°C for 7 hours. The partially frozen mixture was allowed to warm to room temperature and then diluted with EtOAc (10 ml). To this stirred mixture was slowly added a solution of oxalic acid monohydrate (188 mg, 1.49 mmole) in 4.5 ml of methanol. After the evolution of gas had ceased, 15 ml of saturated NaCl solution was added and the resulting mixture was stirred for 20 minutes. The insoluble dicyclohexylurea was filtered off and the EtOAc layer was separated from the filtrate and washed successively with 25 ml of saturated NaCl solution, 25 ml of saturated $NaHCO_3$ solution and 25 ml of saturated NaCl solution. The EtOAc solution was dried and concentrated to leave 350 mg of an oily solid which was dissolved in 3 ml of $CHCl_3$. The insoluble solids were filtered off and washed with $CHCl_3$. The combined filtrates were evaporated *in vacuo* to yield 320 mg of an oil. Preparative TLC using *n*-hexane - EtOAc - acetone (5 : 5 : 3) gave 110 mg of the desired 9-*epi*-*N,N'*-dicarbobenzoxyspectinomycin (**10**) (41% based on unrecovered **9**) as a glass: Rf 0.39; IR (KBr) 3400, 1740, 1695 cm^{-1}; PMR ($CDCl_3$-D_2O, 220 MHz), rotomers present, δ 2.40 (d, 3H, C-2 CH_3), 2.44 (dd, 1H, $J_{gem}=14$ Hz, $J_{2,3eq}=2$ Hz, *H*-3eq), 2.84 (dd, 1H, $J_{gem}=14$ Hz, $J_{2,3ax}=12$ Hz, *H*-3ax), 3.03 and shoulder at 3.05 (s, 3H, NCH_3), 3.26 (broad s, 3H, NCH_3), 3.74 (m, 1H, *H*-2), 3.90~4.00 (m, 1H), 4.15 (broad d, 1H, $J=12$ Hz, *H*-9a), 4.29 (dd, 1H, $J_{5a,6}=9.5$ Hz, $J_{6,7}=3$ Hz, *H*-6), 4.41 (broad m, 2H), 4.69 (s, 1H, *H*-10a), 4.91 (dd, 1H, $J_{5a,9a}=12$ Hz, $J_{5a,6}=9.5$ Hz, *H*-5a), 5.12 and 5.14 (2s, 4H, CH_2Ph), 7.26 and 7.33 (2s, 10H, arom.); MS *m/e* 600 (M^+), 509 ($M-CH_2Ph$), 492 (M−

$HOCH_2Ph$), 465 ($M-OCOCH_2Ph$).

Anal. Calcd. for $C_{30}H_{36}N_2O_{11}$: C, 59.99; H, 6.05; N, 4.66.
Found: C, 59.96; H, 5.89; N, 4.45.

In addition to **10** and 32 mg of starting tetrol **9**, 24 mg of 9-oxo-*N,N'*-dicarbobenzoxy-4(*R*)-dihydrospectinomycin was isolated as a glass: Rf 0.30; IR (KBr) 3480~3400, 1745 (sh), 1698 cm^{-1}.

9-Oxo-*N,N'*-dicarbobenzoxyspectinomycin (67 mg) was also isolated as a glass: Rf 0.45; IR (KBr) 3440, 1740, 1700 cm^{-1}; PMR ($CDCl_3$-D_2O, 60 MHz) δ 1.18 (d, 3H, C-2, CH_3), 2.20~2.80 (m, 2H), 3.02 and 3.05 (2s, 6H, NCH_3), 3.60~3.80 (m, 1H), 4.20~5.20 (m, 6H), 4.77 (s, 1H, *H*-10a), 5.13 (s, 4H, CH_2Ph), 7.33 (s, 10H, arom.); MS *m/e* 562 ($M-2H_2O$).

9-*epi*-Spectinomycin (11).

Hydrogenolysis of **10** (44 mg, 0.073 mmole) in 2-propanol (3 ml) and water (3 ml) using palladium black (22 mg) at room temperature and atmospheric pressure for 20 minutes afforded, after removal of the catalyst by filtration and concentration of the filtrate, 22 mg (90%) of **11** as a glass: IR (KBr) 3440~3320, 1740 cm^{-1}; PMR (D_2O-DCl, 100 MHz) δ 1.80 (d, 3H, C-2 CH_3), 2.15~2.30 (m, 2H, *H*-3), 3.38 and 3.40 (2s, 6H, N-CH_3), 4.00~4.20 (m, 2H, *H*-6 and *H*-8), 4.51 (m, 1H, *H*-2), 4.63 (dd, 1H, $J_{9,9a}=3$ Hz, $J_{5a,9a}=10.5$ Hz, *H*-9a), 4.94 (broad t, 1H, $J=3$ Hz, *H*-9), 5.14 (t, 1H, $J_{5a,9a}=J_{5a,6}=10.5$ Hz, *H*-5a), 5.24 (t, 1H, $J=3$ Hz, *H*-7), 5.39 (s, 1H, *H*-10a); MS *m/e* 314 ($M-H_2O$).

Spin decoupling: Irradiation at δ 4.10 (*H*-6 and *H*-8) caused the collapse of the t at 4.94 (*H*-9) to a d ($J=3$ Hz), the t at 5.14 (*H*-5a) to a d ($J=10.5$ Hz) and t at 5.24 (*H*-7) to a s.

Irradiation at δ 2.20 (*H*-3) caused the m at 4.51 (*H*-2) to collapse to a q.

Acknowledgements

We are most grateful to Dr. DAVID PRUESS of the Microbiology Department for carrying out the *in vitro* testing. The assistance of Mr. DAVID GREELEY and Mr. GINO SASSO of the NMR Laboratory (directed by T. WILLIAMS) in carrying out the decoupling experiments is gratefully acknowledged. We wish to thank Mr. Ross PITCHER for his assistance in obtaining 220 MHz PMR spectra. The 220 MHz PMR facilities, located at the Rockefeller University and operated by a consortium, are supported by NSF Grant PCM 74-12247. We also thank Dr. J. F. BLOUNT for the X-ray analysis confirming the structure of the bis carbamate **6**.

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