+46.8° (*c* 0.774, 1 *N* HCl). The ir spectrum in KBr was identical with that of polyoxin C acid.

Polyoxin C Acid (33). Polyoxin D (**1d**) (150 mg) was hydrolyzed with 6 ml of 0.5 *N* NaOH at 65° for 4 hr. The hydrolysate was passed through 10 ml of Amberlite IRC-50 (H). The effluent was evaporated to dryness and the residue was chromatographed on Dowex 50W-X8 with pyridine–acetic acid buffer (pH 3.1). From the uv and ninhydrin-positive fraction, crystals were obtained, which were pulverized and extracted with ether overnight to remove uracil-5-carboxylic acid. The residue was recrystallized from water affording 50 mg of **33**: mp 240–260° dec; $[\alpha]^{23}D$ +2.5° (*c* 0.24, H_2O); $[\alpha]^{23}D$ +14.6° (*c* 1.15, 1 *N* HCl); uv max (0.05 *N* HCl) 220 mμ (ε 10,400), 275 mμ (ε 11,700), (0.05 *N* NaOH) 270 mμ (ε 7100). A sample was dried at room temperature.

Anal. Calcd for $C_{11}H_{13}N_3O_9 \cdot 0.5H_2O$: C, 38.83; H, 4.15; N, 12.35. Found: C, 38.58; H, 4.01; N, 12.21.

A small sample was dried at 100° for 2 hr before analysis.

Anal. Calcd for $C_{11}H_{13}N_3O_9$: C, 39.88; H, 3.96; N, 12.69. Found: C, 40.13; H, 4.16; N, 12.36.

Small samples of polyoxins E and F were hydrolyzed similarly and **33** was detected on tlc.

The *N*-acetyl derivative was prepared in a similar way to *N*-acetylpolyoxin C as a homogeneous white powder: mp 150–180° dec; pmr (DMSO-d_6) δ 1.94 (s, 3, CH_3), 4.09 (m, 3, 2′, 3′, and 4′ H's), 4.72 (q, 1, 5′-H, J = 8.4 and 4.6 Hz), 5.83 (d, 1, 1′-H, $J_{1',2'}$ = 3.7 Hz), 2.34 (s, 1, 5-H), 2.36 (d, 1, AcN*H*, J = 8.4 Hz). On acid hydrolysis (3 *N* HCl, 100° 1 hr) it gave polyoxin C acid (**33**), which was identified by the ir spectrum.

Thymine-polyoxin C (34). Polyoxin H (**1h**) (100 mg) was hydrolyzed in 2 ml of 0.5 *N* NaOH at 65° for 4 hr. The hydrolysate was passed through 3 ml of Amberlite XE-64 (H) and the effluent was evaporated to dryness. The residue was purified by preparative tlc with the solvent systems A and C. From uv and ninhydrin-positive fraction, 3 mg of crystalline **34** was obtained: mp 235–240° dec; $[\alpha]^{22}D$ +7°, $[\alpha]^{22}_{365}$ +37° (*c* 0.046, H_2O). The ir spectrum was identical with that of deoxypolyoxin C.

A few milligrams of polyoxin J was hydrolyzed similarly and **34** was identified on tlc.

Uracil-polyoxin C (35). Polyoxin K (**1k**) (250 mg) was treated with 10 ml of 0.5 *N* NaOH at 65° for 4 hr. The hydrolysate was passed through a column of Amberlite XE-64 (H), the effluent was concentrated, and the residue was submitted to a cellulose chromatography with the solvent system A. The uv and ninhydrin-positive fraction was further purified by preparative tlc with the solvent system B. On crystallization from aqueous ethanol, 4.3 mg of crystalline **35** was obtained: mp 240–247° dec; $[\alpha]^{22}D$ +15.8 (*c* 0.205, H_2O); $[\phi]_{280}$ +2340 pk $[\phi]_{253}$ −5300 tr (H_2O); ux max (0.05 *N* HCl) 258 mμ (ε 9460), (0.05 *N* NaOH) 262 mμ (ε 7310).

Anal. Calcd for $C_{10}H_{13}N_3O_7$: C, 41.81; H, 4.56; N, 14.63. Found: C, 41.52; H, 4.60; N, 14.65.

Polyoxin L (**1l**) (20 mg) was hydrolyzed similarly and the hydrolysate was purified on preparative tlc with the solvent systems A and B. On crystallization, about 1 mg of crystalline **35** was obtained. The ir spectrum was identical with that of the compound obtained from polyoxin K (**1k**).

Decarboxylation of Polyoxin C Acid (33). A solution of 1 g of **33** in 4 ml of 3 *N* HCl was refluxed overnight. The reaction mixture was passed through 20 ml of Amberlite CG-4B (OH) and 3 ml of Amberlite XE-64 (H). The effluent was concentrated to a small volume and precipitated with ethanol–ether. The residue thus obtained was purified by preparative tlc with the solvent system A. The ninhydrin- and uv-positive fraction was collected. The purified material thus obtained [uv max (0.05 *N* HCl) 259 mμ, (0.05 *N* NaOH) 262 mμ] was identical with **35** on tlc. Acid elution from Amberlite CG-4B recovered 380 mg of the unreacted material.

Hydrogenolysis of Polyoxin B. Polyoxin B (**1b**) (50 mg) was hydrogenated over platinum (from 10 mg of PtO_2) in 10 ml of water at atmospheric pressure and at room temperature. Approximately 1 equiv of hydrogen was taken up in 3 hr. After the catalyst was filtered off, the filtrate was evaporated to dryness and the residue was chromatographed on cellulose with the solvent system A. Deoxypolyoxin B was obtained as a homogeneous powder from water–ethanol–ether, $[\alpha]^{23}D$ +30.6° (*c* 1.03, H_2O). It showed the same R_f value with polyoxin J (**1j**) on tlc. A small sample was dried at 110° for 4 hr before analysis.

Anal. Calcd for $C_{17}H_{25}N_5O_{12}$: C, 41.55; H, 5.13; N, 14.25. Found: C, 41.62; H, 5.19; N, 13.85.

Hydrogenation of Polyoxin H. Polyoxin H (**1h**) (40 mg) was hydrogenated over platinum (from 8 mg of PtO_2) in 10 ml of water at atmospheric pressure and at room temperature. The catalyst was filtered off and the filtrate was evaporated to dryness. The residue was chromatographed on cellulose with butanol–acetic acid–water (4:1:1), then purified on preparative tlc with 75% phenol. The homogeneous powder thus obtained showed the identical pmr spectrum in D_2O and R_f values on tlc with those of **22**.

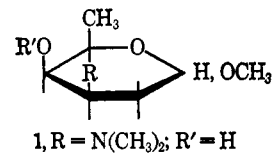
Acknowledgments. We are indebted to Dr. Y. Sumiki of this institute for his interest and Dr. S. Emoto of this institute for valuable discussion. We thank Mrs. K. Kobinata for technical assistance. The sample of the polyoxin complex was supplied by Kaken Kagaku Co., Ltd., Tokyo.

Communications to the Editor

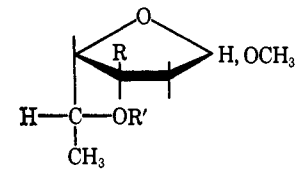
The Megalomicins. I. D-Rhodosamine, a New Dimethylamino Sugar

Sir:

D-Rhodosamine, a new dimethylamino sugar isolated from megalomicin A, B, C_1, and C_2, a new family of macrolide antibiotics elaborated by *Micromonospora megalomicea* sp. n.,[1] has been shown to be 2,3,6-trideoxy-3-dimethylamino-D-*lyxo*-hexopyranose.[2] Methanolysis of megalomicin A gave anomeric mixtures of the 1-*O*-methyl pyranoside **1** and furanoside **2** forms



1, R = $N(CH_3)_2$; R′ = H
3, R = O←$N(CH_3)_2$; R′ = H
4, R = $N(CH_3)_2$; R′ = CH_3CO
6, R = R′ = H



2, R = $N(CH_3)_2$; R′ = H
8, R = $N(CH_3)_2$; R′ = CH_3CO
9, R = O←$N(CH_3)_2$; R′ = H
11, R = R′ = H
12, R = H; R′ = CH_3

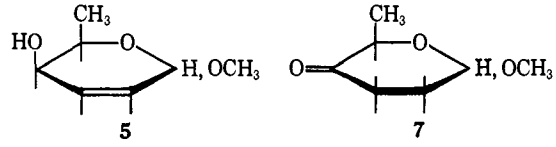
of D-rhodosamine.

(1) (a) H. Reimann, R. S. Jaret, and A. K. Mallams, paper presented at the 8th Interscience Conference on Antimicrobial Agents and Chemotherapy, American Society for Microbiology, New York, N. Y., Oct 21–23, 1968, Abstracts, p 4; (b) M. J. Weinstein, G. H. Wagman, J. Marquez, G. Luedemann, E. Oden, and J. A. Waitz, ref 1a, p 4; (c) M. J. Weinstein, G. H. Wagman, J. A. Marquez, R. T. Testa, E. Oden, and J. A. Waitz, *J. Antibiotics* (Tokyo), *Ser. A*, 22, 253 (1969); (d) J. A. Marquez, A. Murawski, G. H. Wagman, R. S. Jaret, and H. Reimann, *ibid.*, 22, 259 (1969); (e) J. A. Waitz, E. L. Moss, Jr., E. Oden, and M. J. Weinstein, *ibid.*, 22, 265 (1969).

(2) L-Rhodosamine occurs in a number of antibiotics and in particular in the rhodomycins [H. Brockmann, E. Spohler, and T. Waehneldt, *Chem. Ber.*, 96, 2925 (1963)].

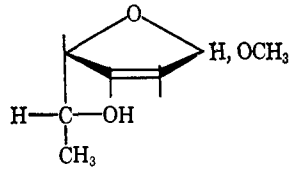
The pyranoside **1** was converted to the *N*-oxides **3** (M^+ 205), chromatography of which gave the α[3] [$C_9H_{19}NO_4$; mp 162–163°; $[\alpha]_D$ +117.3° (MeOH)] and β anomers [$C_9H_{19}NO_4$; mp 178–179°; $[\alpha]_D$ −37.2° (MeOH)]. Treatment of **3**α and **3**β with triethyl phosphite gave methyl α-D-rhodosaminide (**1**α; $[\alpha]_D$ +119.1° (MeOH); ν_{max} (liquid film) 3410, 2770, and 1045 cm^{-1}) and methyl β-D-rhodosaminide (**1**β; $[\alpha]_D$ −58.8° (MeOH); ν_{max} (liquid film) 3440, 2780, and 1070 cm^{-1}), respectively. The nmr of **1**α indicated a secondary methyl (δ 1.34, $J_{5a,6}$ = 7 Hz), a dimethylamino group (δ 2.30), a methoxyl group (δ 3.38), a triplet (H_1, δ 4.80, $J_{1e,2a} = J_{1e,2e}$ = 3 Hz), an octet (H_5, δ 4.07, $J_{5a,6}$ = 7 Hz, $J_{4e,5a}$ = 2.5 Hz), a quartet (H_4, δ 3.71, $J_{4e,5a}$ = 2.5 Hz, $J_{3a,4e}$ = 3 Hz), and an octet (H_3, δ 2.63, $J_{3a,4e}$ = 3 Hz, $J_{2a,3a}$ = 8.5 Hz, $J_{2e,3a}$ = 7.5 Hz). The nmr of **1**β showed a secondary methyl group (δ 1.29, $J_{5a,6}$ = 6.5 Hz), a dimethylamino group (δ 2.31), a methoxyl group (δ 3.39), a quartet (H_1, δ 4.66, $J_{1a,2a}$ = 8 Hz, $J_{1a,2e}$ = 5 Hz), a multiplet (H_{2a}, δ 1.55, $J_{1a,2a}$ = 8 Hz, $J_{2a,2e} = J_{2a,3a}$ = 12.5 Hz), a multiplet (H_{2e}, δ 1.99, $J_{1a,2e}$ = 5 Hz, $J_{2e,2a}$ = 12.5 Hz, $J_{2e,3a}$ = 4 Hz, $J_{2e,4e}$ = 1.5 Hz), an octet (H_5, δ 3.93, $J_{5a,6}$ = 6.5 Hz, $J_{4e,5a}$ = 4.5 Hz), a sextet (H_4, δ 3.54, $J_{4e,5a}$ = 4.5 Hz, $J_{3a,4e}$ = 4 Hz, $J_{2e,4e}$ = 1.5 Hz), and an octet (H_3, δ 2.31, $J_{3a,4e} = J_{2e,3a}$ = 4 Hz, $J_{2a,3a}$ = 12.5 Hz). The 1,3-diequatorial coupling between H_{2e} and H_{4e} lent additional support to the *lyxo* configuration. The mass spectrum of **1** gave a molecular ion at *m/e* 189 and fragment ions at *m/e* 114, 87, and 71, consistent with the proposed structure. The pK_a of 8.8 was in agreement with a β-amino alcohol grouping in **1**. Attempted acid hydrolysis of glycoside **1** caused extensive decomposition even under mild conditions. Acetylation of **1** gave the monoacetate **4** [M^+ 231; pK_a = 7.5; ν_{max} ($CHCl_3$) 1725, 1240 cm^{-1}; δ 1.12 (acetate)], which was identical with the product obtained in high yield on attempted oxidation of **1** with acetic anhydride–DMSO.[4,5] Pfitzner–Moffatt oxidation conditions gave only unreacted starting material **1**. The decrease in the pK_a on acetylation confirmed the presence of the β-amino alcohol sequence in **1**.

A Cope elimination on **3** gave a mixture of the amine **1** and the olefin **5**. When methyl D-rhodosaminide (**1**)



5

7



10

was quaternized with methyl iodide and heated with sodium hydride, the same olefin [**5**; M^+ 144; ν_{max} 3400, 1055 cm^{-1}; δ 5.83 (multiplet, olefinic protons)] was obtained. The formation of the olefin **5** in the latter reaction, rather than an epoxide, confirmed the *cis* orientation of the dimethylamino and hydroxyl groups at C_3 and C_4, respectively, in D-rhodosamine.

Reduction of the olefin **5** gave the pyranoside[6] **6**, which on oxidation with ruthenium tetroxide gave the ketone **7** [M^+ 144; ν_{max} (liquid film) 1730 cm^{-1}], the CD curve of which showed a negative Cotton effect at λ_{max} 298 mμ ($\Delta\epsilon$ = −1.07) (methanol) indicating a D configuration for sugar **1**.[7]

The nmr of the furanoside **2** [$C_9H_{19}NO_3$; M^+ 189; $[\alpha]_D$ +12.4°; pK_a = 7.9; ν_{max} ($CHCl_3$) 3400, 2770, 1035 cm^{-1}] indicated a secondary methyl group (δ 1.21, J = 6 Hz, and δ 1.24, J = 6 Hz), a dimethylamino group (δ 2.23 and 2.29), and a methoxyl group (δ 3.36 and 3.38), while the mass spectrum gave ions at *m/e* 144, 115, 114, and 100 consistent with structure **2**. Acetylation of the furanoside **2** gave a monoacetate (**8**, M^+ 231; $[\alpha]_D$ +46.6°; pK_a = 7.6; ν_{max} ($CHCl_3$) 1730, 1245 cm^{-1}) which was identical with the product obtained on attempted oxidation of **2** with acetic anhydride–DMSO.[4,5] The nmr spectrum in deuteriobenzene showed a secondary methyl group (δ 1.31, J = 6.5 Hz), an acetyl group (δ 1.78), a dimethylamino group (δ 2.03), a methoxyl group (δ 3.18), a triplet (H_1, δ 4.86, $J_{1,2'} = J_{1,2}$ = 4 Hz), a quintet (H_5, δ 5.23, $J_{5,6} = J_{4,5}$ = 6.5 Hz), a quartet (H_4, δ 3.99, $J_{4,5}$ = 6.5 Hz, $J_{3,4}$ = 4.5 Hz), and a multiplet (H_3, δ 3.19). The above assignments were confirmed by spin decoupling.

The furanoside **2** was converted to the *N*-oxides **9**, and the α anomer crystallized [**9**α; mp 129–131°; M^+ 205; $[\alpha]_D$ +94.1°; pK_a = 6.0; δ 3.12, 3.20 (dimethylamino N-oxide)]. A Cope elimination on the *N*-oxide **9**α gave a mixture of the amine **2**α and the olefin **10**α [M^+ 144; $[\alpha]_D$ +147.5°; δ 6.06 (multiplet, olefinic protons)]. Reduction of the olefin **10** gave the furanoside[6] **11** (M^+ 146; $[\alpha]_D$ +38.3°), which on methylation gave the methyl ether **12** (M^+ 160; $[\alpha]_D$ +49.2°). Mercaptolysis of the furanoside **11** with ethanethiol gave the mercaptal (M^+ 238; $[\alpha]_D$ +12.1°).

Acknowledgments. The author wishes to express his thanks to Mr. M. Yudis and his colleagues for providing analytical and spectral services.

(3) Elemental analyses were satisfactory for all new compounds. Unless otherwise stated optical rotations were recorded at 26° in ethanol; nmr spectra were run at 60 MHz in $CDCl_3$ with internal TMS standard; ir spectra were obtained in CCl_4; pK_a values were recorded coulometrically in 66% aqueous DMF; mass spectra were obtained on a Perkin-Elmer RMU-6D instrument.

(4) Y. Ali and A. C. Richardson, *J. Chem. Soc.*, *C*, 320 (1969).

(5) B. A. Dmitriev, A. A. Krost, and N. K. Kochetkov, *Bull. Acad. Sci. USSR, Chem. Ser.*, 903 (1969).

(6) C. L. Stevens, P. Blumbergs, and D. L. Wood, *J. Amer. Chem. Soc.*, **86**, 3592 (1964), reported the corresponding ethyl glycoside.

(7) The CD curve of a cuprammonium solution of methyl D-rhodosaminide (**1**α)[8a] gave a positive band at 570 mμ and a negative band at 290 mμ corresponding to the formation of a *k* chelate[8b] (*i.e.*, a negative dihedral angle between the dimethylamino and hydroxyl groups), thus confirming the D-*lyxo* configuration for **1** and demonstrating that no racemization occurred at C_5 under the mild oxidation conditions used to prepare **7**.

(8) (a) Kindly run by Dr. R. D. Guthrie and Miss S. T. K. Bukhari, University of Sussex, Brighton, England; (b) S. T. K. Bukhari, R. D. Guthrie, A. I. Scott, and A. D. Wrixon, *Chem. Commun.*, 1580 (1968).

Alan K. Mallams

Natural Products Research Department, Schering Corporation
Bloomfield, New Jersey 07003

Received July 16, 1969

The Megalomicins. II.[1] The Structure of Megalomicin A

Sir:

Megalomicin A, which may be regarded as the parent antibiotic of a new family of macrolides elaborated by

(1) Part I: A. K. Mallams, *J. Amer. Chem. Soc.*, 91, 7505 (1969).