The Megalomicins. Part IV.[1] The Structures of Megalomicins A, B, C_1, and C_2

By **Robert S. Jaret, Alan K. Mallams,*** and **Hans Reimann,** Natural Products Research Department, Schering Corporation, Bloomfield, New Jersey 07003, U.S.A.

The elucidation of the structures and absolute stereochemistry of megalomicins A, B, C_1, and C_2, a group of macrolide antibiotics elaborated by *Micromonospora megalomicea* sp. n., is described. Megalomicin A has been shown to be (2*R*,3*S*,4*S*,5*R*,6*R*,8*R*,10*R* 11*R*,12*S*,13*R*)-3-(2,6-dideoxy-3-*C*-methyl-α-L-*ribo*-hexopyranosyloxy)-6,12-dihydroxy-4,6,8,10,12-hexamethyl-9-oxo-11-(2,3,6-trideoxy-3-dimethylalmino-β-D-*lyxo*-hexopyranosyloxy)-5-(3,4,6-trideoxy-3-dimethylamino-β-D-*xylo*-hexopyranosyloxy)pentadecan-13-olide. Megalomicins B, C_1, and C_2 have been shown to be derivatives of megalomicin A acylated in the 3-glycosyl system.

THE megalomicins comprise a macrolide antibiotic complex produced by the soil micro-organism, *Micromonospora megalomicea* sp. n., first reported by Weinstein *et al.*[2] The isolation of the antibiotic complex from the fermentation medium, and preliminary chemical studies have been reported.[2,3] Like other macrolide antibiotics, the megalomicins exhibit broad spectrum activity, but are primarily active against gram-positive bacteria.[4] Preliminary communications describing the structure of

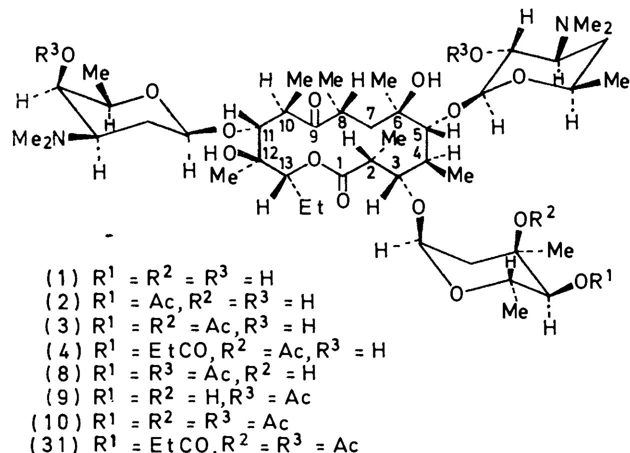
[1] Part III. A. K. Mallams, preceding paper.

[2] M. J. Weinstein, G. H. Wagman, J. A. Marquez, R. T. Testa, E. Oden, and J. A. Waitz, *J. Antibiotics*, 1969, **22**, 253.

[3] J. A. Marquez, A. Murawski, G. H. Wagman, R. S. Jaret, and H. Reimann, *J. Antibiotics*, 1969, **22**, 259.

[4] J. A. Waitz, E. L. Moss, jun., E. Oden, and M. J. Weinstein, *J. Antibiotics*, 1969, **22**, 265.

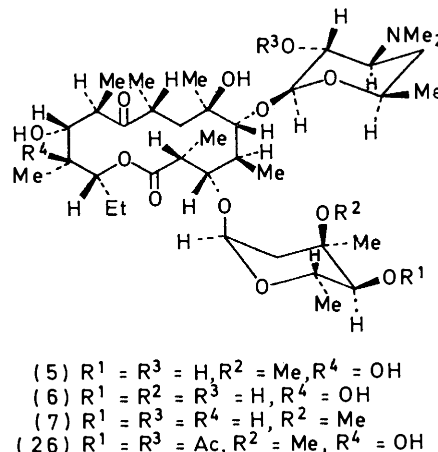
megalomicin A (1) have been published;[5,6] this substance may be regarded as the parent antibiotic of the complex, the remaining members, megalomicin B (2), megalomicin C_1 (3), and megalomicin C_2 (4), being acyl

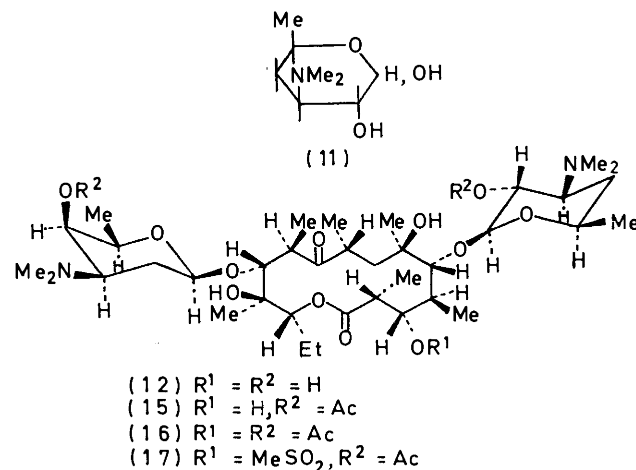


derivatives thereof. The megalomicins are structurally related to the erythromycins produced by *Streptomyces erythreus*.[7] Both erythromycin A (5) [8-11] and erythromycin C (6) [12] have the same aglycone as the megalomicins, and erythromycin B (7) [13-16] lacks the 12-hydroxy-function. These antibiotics all contain a 3,4,6-trideoxy-3-dimethylamino-D-*xylo*-hexopyranosyl (D-desosaminyl) system, and, in the case of erythromycin C (6) and the megalomicins, a common 2,6-dideoxy-3-*C*-methyl-L-*ribo*-hexopyranosyl (L-mycarosyl) system.

Megalomicin A (1) was obtained in crystalline form from acetone (m.p. 255—259°). The i.r. spectrum indicated the presence of hydroxy-groups (3510 cm^{-1}), a lactone function (1730 and 1190), a keto-group (1700), and a dimethylamino-group (2770). The pK_a value was 9·0, confirming the presence of a basic function. The n.m.r. spectrum showed the presence of two dimethylamino-groups (δ 2·27, and 2·23) and an ethyl group [δ 0·8 (t, J 7 Hz)]. A doublet of doublets at δ 5·20 was assigned to H-13, indicating that C-12 was fully substituted, and a band at δ 1·60 was attributed to the deshielded tertiary methyl group at C-6. The mass spectrum gave a molecular ion at m/e 876 ($C_{44}H_{80}N_2O_{15}$), in good agreement with the analytical data.

The mass spectrum [17] of megalomicin A (1) showed a base peak at m/e 158 (ions *a* and *b*) and a peak at m/e 145 due to the mycarosyl-derived ion *c* ($R^1 = R^2 = H$). The formation of the ions *a*—*c* suggested that megalomicin A (1) contained two dimethylamino-trideoxyhexose systems, each having the composition $C_8H_{17}NO_3$, as well as a neutral sugar system of composition $C_7H_{14}O_4$. Cleavage of the glycosidic bonds of the amino-sugar systems gave peaks at m/e 718 (M − 158), 719 (M − 157, H transfer), 702 (M − 174), and 703 (M − 173, H transfer) in the high mass region (Scheme 1). Similarly,





cleavage of the glycosidic bond of the mycarosyl system gave peaks at m/e 732 (M − 144, H transfer), and 715 (M − 161) (Scheme 2). Fragmentation of megalomicin A (1) led to the formation of the ion *d* [17] at m/e 444, arising from cleavage between C-6 and C-7 accompanied

[5] A. K. Mallams, *J. Amer. Chem. Soc.*, 1969, **91**, 7505.

[6] A. K. Mallams, R. S. Jaret, and H. Reimann, *J. Amer. Chem. Soc.*, 1969, **91**, 7506.

[7] J. M. McGuire, R. L. Bunch, R. C. Andersen, H. E. Boaz, E. H. Flynn, H. M. Powell, and J. W. Smith, *Antibiotics and Chemotherapy*, 1952, **2**, 281.

[8] E. H. Flynn, M. V. Sigal, P. F. Wiley, and K. Gerzon, *J. Amer. Chem. Soc.*, 1954, **76**, 3121.

[9] P. F. Wiley, K. Gerzon, E. H. Flynn, M. V. Sigal, and U. C. Quarck, *J. Amer. Chem. Soc.*, 1955, **77**, 3676.

[10] M. V. Sigal, P. F. Wiley, K. Gerzon, E. H. Flynn, U. C. Quarck, and O. Weaver, *J. Amer. Chem. Soc.*, 1956, **78**, 388.

[11] P. F. Wiley, K. Gerzon, E. H. Flynn, M. V. Sigal, O. Weaver, U. C. Quarck, R. C. Chauvette, and R. Monahan, *J. Amer. Chem. Soc.*, 1957, **79**, 6062.

[12] P. F. Wiley, R. Gale, C. W. Pettinga, and K. Gerzon, *J. Amer. Chem. Soc.*, 1957, **79**, 6074.

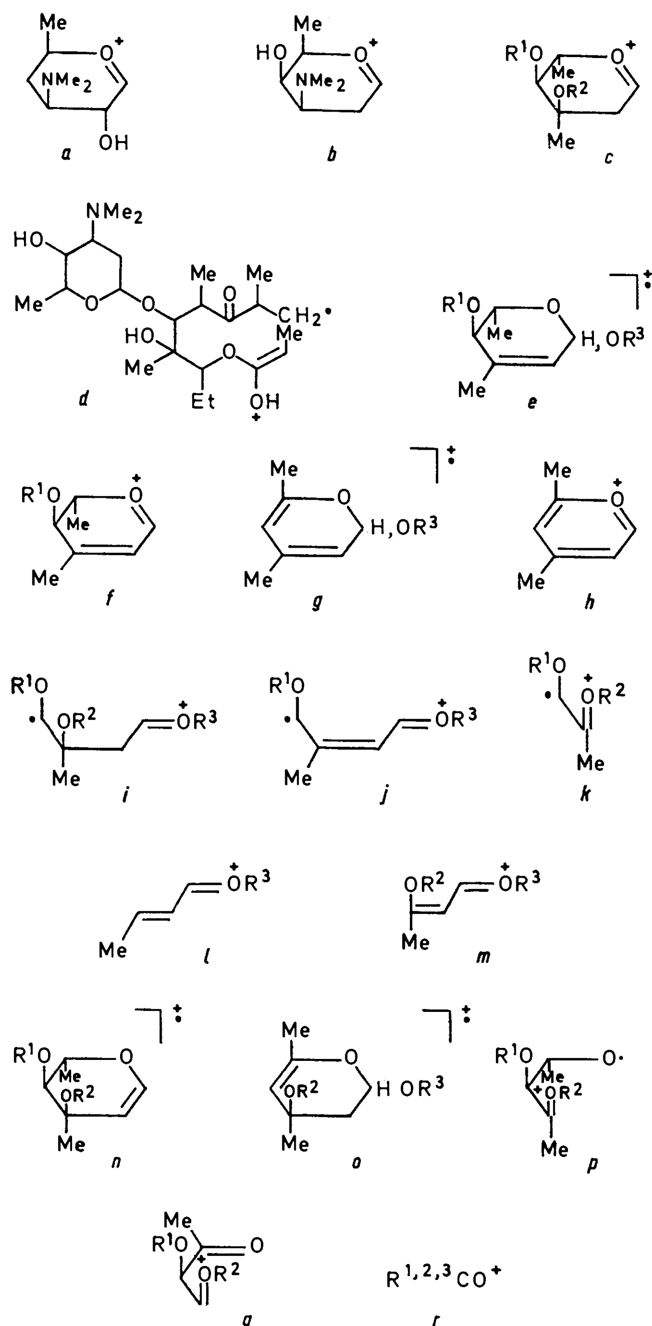
[13] C. W. Pettinga, W. M. Stark, and F. R. van Abeele, *J. Amer. Chem. Soc.*, 1954, **76**, 569.

[14] R. K. Clark and M. Taterka, *Antibiotics and Chemotherapy*, 1955, **5**, 206.

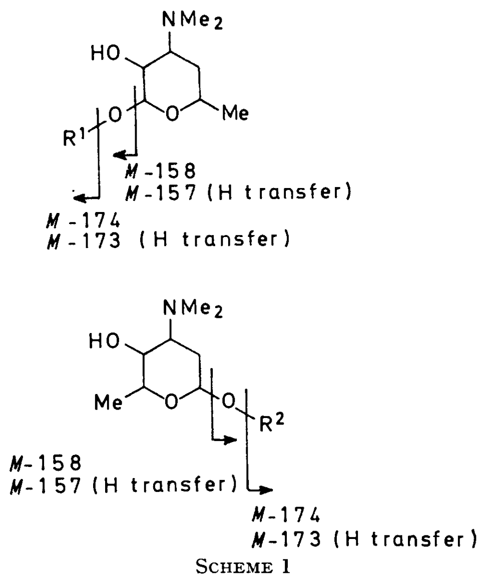
[15] K. Gerzon, R. Monahan, O. Weaver, M. V. Sigal, and P. F. Wiley, *J. Amer. Chem. Soc.*, 1956, **78**, 6412.

[16] P. F. Wiley, M. V. Sigal, O. Weaver, R. Monahan, and K. Gerzon, *J. Amer. Chem. Soc.*, 1957, **79**, 6070.

[17] A detailed interpretation of the mass spectra of the megalomicins is given in Part V, R. S. Jaret, A. K. Mallams, and H. F. Vernay, following paper.

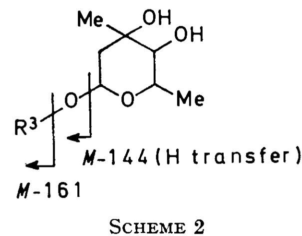


by McLafferty rearrangement at the lactone group. Another important fragmentation involved loss of the rhodosaminyl system (Scheme 3) to give a peak at *m/e* 801, followed by loss of the mycarosyl system to give a peak at *m/e* 657 (with H transfer). The formation of



SCHEME 1

the ions at *m/e* 801 and 657 suggested that one of the amino-sugars was a 2,3,6-trideoxy-3-dimethylamino-hexose, and the fragmentation to give *d* indicated that one of the amino-sugars was located between C-7 and



SCHEME 2

C-13, the remaining amino-sugar and the neutral sugar being located between C-1 and C-6 in the aglycone.

Acetylation of megalomicin A (1) under mild conditions at 25° gave 4′,2″,4‴-tri-*O*-acetylmegalomicin A (8), indicating that the molecule contained three primary or secondary hydroxy-groups. The presence of a band at 3520 cm^{-1} in the i.r. spectrum indicated that additional hydroxy-groups (tertiary or hindered secondary) were present which did not undergo acetylation under these

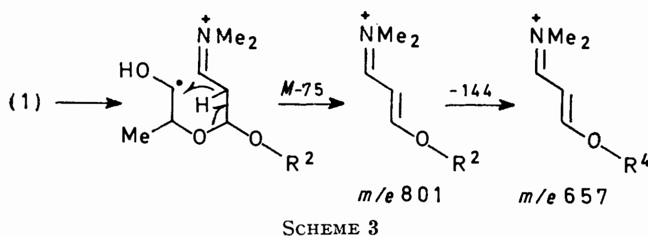
TABLE 1

N.m.r. spectra of the megalomicins (δ values; J in Hz)

Compd	R^1	R^2	R^3	13-CH_3·CH_2 [a]	Envelope of Me groups	6-Me [b]	4′-OAc [b]	3′-OAc [b]	2″-OAc [b]	4‴-OAc [b]	3″-NMe2 [c]	3‴-NMe2 [c]	H-1′ [d]	H-1′ [e]	H-13 [f]	3′-Me [g]
(1)	H	H	H	0·8 (3H, t, J 7)	1·05—1·35 (*ca.* 27H)	1·60					2·27	2·33	4·33	5·13	5·20	
(2)	Ac	H	H	0·81 (3H, t, J 7)	1·05—1·3 (*ca.* 27H)	1·54	2·09				2·28	2·35	4·33	5·25	5·19	
(3)	Ac	Ac	H	0·8 (3H, t, J 7)	1·05—1·3 (*ca.* 24H)	1·53	2·10	2·10			2·30	2·38	4·32	5·06	5·19	1·45
(4)	EtCO	Ac	H	0·81 [h] (6H, t, J 7)	1·05—1·3 (*ca.* 24H)	1·53		2·10			2·29	2·36	4·31	5·07	5·17	1·43
(8)	Ac	H	Ac	0·81 (3H, t, J 7)	1·05—1·3 (*ca.* 27H)	1·52	2·08		2·03	2·14	2·28	2·32	4·32	5·02	5·12	
(9)	H	H	Ac	0·83 (3H, t, J 7)	0·85—1·3 (*ca.* 27H)	1·54			2·02	2·14	2·24	2·30	4·32	5·02	5·12	
(10)	Ac	Ac	Ac	0·82 (3H, t, J 7)	0·9—1·3 (*ca.* 24H)	1·54	2·11	2·17	2·02	2·17	2·29	2·32	4·32	4·90	5·12	1·48
(31)	EtCO	Ac	Ac	0·82 [h] (6H, t, J 7)	0·9—1·3 (*ca.* 24H)	1·53		2·17	2·02	2·17	2·28	2·30	4·33	4·90	5·12	1·47
(22)	9,*O*(9)-Dihydromegalomicin A			0·82 (3H, t, J 7)	0·95—1·35 (*ca.* 27H)	1·61					2·24	2·30	4·35	5·02	5·22	

[a] All J 7 Hz. [b] All 3H, s. [c] All 6H, s. [d] All 1H, d, $J_{1''ax,2''ax}$ 7. [e] All 1H, t, $J_{1'eq,2'ax} = J_{1'eq,2'eq} = 2{\cdot}5$. [f] All 1H, dd, $J_{13,14}$ 10, $J_{13,14'}$ 3. [g] All 3H, s. [h] This triplet is comprised of the combined methyl signals from the 13-ethyl group and the 4′-propionyl group.

conditions. The pK_a of the triacetate (8) was 7·5, indicating that two of the acetyl groups were located β to the dimethylamino-groups.[8,10] The i.r. spectrum showed the expected acetate bands at 1736 and 1242 cm^{-1}, and bands at δ 2·03, 2·08, and 2·14 in the n.m.r. spectrum



SCHEME 3

confirmed the presence of three acetyl groups. The mass spectrum of (8) gave a molecular ion at *m/e* 1002 consistent with a triacetate, and showed a base peak at *m/e* 200 indicating that one acetyl group was located in each of the amino-sugar systems. This was further confirmed by the presence of peaks at *m/e* 802 ($M-$ 200), 786 ($M-216$), and 787 ($M-215$, H transfer) in the high mass region due to cleavages of the type illustrated in Schemes 1 and 2. Fragmentation of the rhodosaminyl system (Scheme 3) gave a peak at *m/e* 885 ($M-117$), and the formation of an ion corresponding to a monoacetyl-*d* at *m/e* 486 further supported the foregoing conclusions. The third acetyl group was shown to to be in the mycarosyl system by the presence of peaks at *m/e* 816 ($M-186$, H transfer), 815 ($M-187$), and 799 ($M-203$) due to cleavages of the type illustrated in Scheme 2, as well as the presence of a peak at *m/e* 187 due to the monoacetyl ion *c* (R^1 = Ac, R^2 = H). Peaks at *m/e* 169 and 109 due to fragments *f* (R^1 = Ac), and *h*, respectively, indicated that the acetate was located at the 4-position in the mycarose as anticipated.

When megalomicin A (1) was acetylated with acetic anhydride in acetone under carefully controlled conditions, 2″,4‴-di-*O*-acetylmegalomicin A (9) was obtained. A pK_a of 7·6 indicated that the acetates were located in the amino-sugar systems, and bands at 1739 and 1245 cm^{-1} in the i.r. spectrum, and at δ 2·02, and 2·14 in the n.m.r. spectrum, indicated the presence of only two acetyl groups. The mass spectrum showed a molecular ion at *m/e* 960 with a base peak at *m/e* 200, and fragment ions at *m/e* 760 ($M-200$), 745 ($M-215$, H transfer), 744 ($M-216$), 843 ($M-117$), 699 ($M-117-144$), 816 ($M-144$, H transfer), 486, 145, 127, and 109, all consistent with structure (9).

Acetylation of megalomicin A (1) under forcing conditions (acetic anhydride–pyridine at 80°) gave 3′,4′,2″,-4‴-tetra-*O*-acetylmegalomicin A (10). A pK_a of 7·4 indicated that two of the acetyl groups were in the amino-sugar residues. The n.m.r. spectrum revealed the presence of four acetyl groups. The base peak in the mass spectrum was at *m/e* 200, indicating the presence of acetylated amino-sugar systems. This was further confirmed by peaks at *m/e* 844 ($M-200$), 828 ($M-$ 216), and 829 ($M-215$, H transfer) in the high mass region. The mass spectrum of (10) also showed that the remaining two acetyl groups were located in the mycarose unit, from the fact that ions were present at *m e* 229, 169, and 109; and at *m/e* 815 ($M-229$) and 799 ($M-245$) in the high mass region. Acetylation of the tertiary hydroxy-group in the mycarose unit under these conditions occurred by intramolecular transacylation of the vicinal *cis*-glycol system. Proof of this will be discussed later in connection with megalomicin C_2 (4). The tetra-acetate (10) still contained free tertiary hydroxy-groups as shown by the presence of an i.r. band at 3550 cm^{-1}. The only other by-product formed during the acetylation was a pentaester which exhibited no carbonyl absorption.[18]

In order to prove the structures of the sugar units, and of the aglycone in megalomicin A (1), a series of acidic hydrolyses was performed. Vigorous acidic hydrolysis of megalomicin A (1) with 6N-hydrochloric acid on a steam-bath at 100° caused extensive decomposition of the aglycone, and led to the isolation of D-desosamine (11) [8,19-22] as an anomeric mixture, characterised both as the free base and as the hydrochloride.* The spectral and t.l.c. properties of (11) were identical with those of authentic samples prepared by vigorous acidic hydrolysis of erythromycin A (5).[8] D-Desosamine (11) has previously been found in picromycin,[23-25] narbomycin,[26] griseomycin,[26] erythromycin,[8] and methymycin.[26]

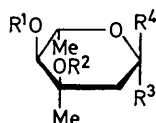
When megalomicin A (1) was subjected to mild acidic hydrolysis with 0·75N-hydrochloric acid the neutral sugar was hydrolysed, leaving the remainder of the molecule, megalalosamine (12), intact. The physical constants (m.p., $[\alpha]_D$, analysis), and the spectral properties [i.r., n.m.r. (Table 2), and mass (Table 3)] of the neutral sugar component were in excellent agreement with published data for L-mycarose (13),[26-31] which occurs in

* Preliminary degradative studies on the megalomicin complex carried out in these laboratories by G. H. Wagman *et al.*[3] had demonstrated by t.l.c., and mixed m.p. of the hydrochloride with an authentic sample, that the antibiotics contained D-desosamine.

[18] H. Reimann and R. S. Jaret, unpublished observations.
[19] R. K. Clark, *Antibiotics and Chemotherapy*, 1953, **3**, 663.
[20] H. Brockmann, H. B. König, and R. Oster, *Chem. Ber.*, 1954, **87**, 856.
[21] C. H. Bolton, A. B. Foster, M. Stacey, and J. M. Webber, *J. Chem. Soc.*, 1961, 4831.
[22] P. W. K. Woo, H. W. Dion, L. Durham, and H. S. Mosher, *Tetrahedron Letters*, 1962, 735.
[23] H. Brockmann, *Angew. Chem.*, 1957, **69**, 237.
[24] R. Anliker, D. Dvornik, K. Gubler, H. Heusser, and V. Prelog, *Helv. Chim. Acta*, 1956, **39**, 1785.
[25] H. Muxfeldt, S. Shrader, P. Hansen, and H. Brockmann, *J. Amer. Chem. Soc.*, 1968, **90**, 4748.
[26] P. P. Regna, F. A. Hochstein, R. L. Wagner, jun., and R. B. Woodward, *J. Amer. Chem. Soc.*, 1953, **75**, 4625.
[27] R. Paul and S. Tchelitcheff, *Bull. Soc. chim. France*, 1957, 443.
[28] A. B. Foster, T. D. Inch, J. Lehmann, L. F. Thomas, J. M. Webber, and J. A. Wyer, *Proc. Chem. Soc.*, 1962, 254.
[29] F. Korte, U. Claussen, and K. Göhring, *Tetrahedron*, 1962, **18**, 1257.
[30] W. Hofheinz, H. Grisebach, and H. Friebolin, *Tetrahedron*, 1962, **18**, 1265.
[31] D. M. Lemal, P. D. Pacht, and R. B. Woodward, *Tetrahedron*, 1962, **18**, 1275.

TABLE 2

N.m.r. spectra ($CDCl_3$) of L-mycarose derivatives (δ values; J in Hz)

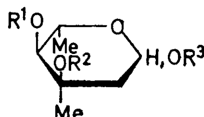


Compd	R¹	R²	R³	R⁴	H-1	H-2*eq*	H-2*ax*	H-4*ax*	H-5*ax*	3-Me	5-Me	Substituents at C-1	C-3	C-4
(13β) [a]	H	H	OH	H	5·08dd $J_{1ax,2ax}$ 9·5 $J_{1ax,2eq}$ 2·5	2·03dd $J_{1ax,2eq}$ 2·5 $J_{2eq,2ax}$ 14	1·57dd $J_{1ax,2ax}$ 9·5 $J_{2eq,2ax}$ 14	3·08d $J_{4ax,5ax}$ 9·5	3·78dq $J_{4ax,5ax}$ 9·5 $J_{5ax,6}$ 6·5	1·27s	1·26d $J_{5ax,6}$ 6·5			
(14)	Ac	H	OAc	H	6·07dd $J_{1ax,2ax}$ 9 $J_{1ax,2eq}$ 3	2·08dd $J_{1ax,2eq}$ 3 $J_{2eq,2ax}$ 13	1·70dd $J_{1ax,2ax}$ 9 $J_{2ax,2eq}$ 13	4·65d $J_{4ax,5ax}$ 10	4·01dq $J_{4ax,5ax}$ 10 $J_{5ax,6}$ 6	1·18s	1·17d $J_{5ax,6}$ 6	2·07s		2·13s
(28α)	Ac	H	H	OH	5·20dd $J_{1eq,2ax}$ 3·5 $J_{1eq,2eq}$ 1·5	2·10dd $J_{1eq,2eq}$ 1·5 $J_{2eq,2ax}$ 14	1·80dd $J_{1eq,2ax}$ 3·5 $J_{2ax,2eq}$ 14	4·67d $J_{4ax,5ax}$ 10	4·20dq $J_{4ax,5ax}$ 10 $J_{5ax,6}$ 6	1·17s	1·17d $J_{5ax,6}$ 6			2·15s
(29β)	Ac	Ac	OH	H	4·94dd $J_{1ax,2ax}$ 10 $J_{1ax,2eq}$ 2	3·12dd $J_{1ax,2eq}$ 2 $J_{2eq,2ax}$ 14	1·57dd $J_{1ax,2ax}$ 10 $J_{2ax,2eq}$ 14	4·61d $J_{4ax,5ax}$ 10	3·99dq $J_{4ax,5ax}$ 10 $J_{5ax,6}$ 6	1·50s	1·18d $J_{5ax,6}$ 6		2·09s	2·17s
(29α)	Ac	Ac	H	OH	5·27dd $J_{1eq,2ax}$ 4 $J_{1eq,2eq}$ 1	3·18dd $J_{1eq,2eq}$ 1 $J_{2eq,2ax}$ 15	1·92dd $J_{1eq,2eq}$ 4 $J_{2ax,2eq}$ 15	4·65d $J_{4ax,5ax}$ 10	3·99dq $J_{4ax,5ax}$ 10 $J_{5ax,6}$ 6	1·47s	1·14d $J_{5ax,6}$ 6		2·05s	2·15s
(30)	Ac	Ac	OAc	H	5·82dd $J_{1ax,2ax}$ 10 $J_{1ax,2eq}$ 2·5	3·05dd $J_{1ax,2eq}$ 2·5 $J_{2eq,2ax}$ 14	1·71dd $J_{1ax,2ax}$ 10 $J_{2ax,2eq}$ 14	4·62d $J_{4ax,5ax}$ 10	4·03dq $J_{4ax,5ax}$ 10 $J_{5ax,6}$ 6	1·50s	1·18d $J_{5ax,6}$ 6	2·08s	2·08s	2·13s
(32β)	EtCO	Ac	OH	H	4·93dd $J_{1ax,2ax}$ 10 $J_{1ax,2eq}$ 2	3·12dd $J_{1ax,2eq}$ 2 $J_{2eq,2ax}$ 14	1·53dd $J_{1ax,2ax}$ 10 $J_{2ax,2eq}$ 14	4·61d $J_{4ax,5ax}$ 9·5	3·98dq $J_{4ax,5ax}$ 9·5 $J_{5ax,6}$ 6	1·48s	1·17d $J_{5ax,6}$ 6		2·06s	1·17t J 7 2·42q J 7
(32α)	EtCO	Ac	H	OH	5·23dd $J_{1eq,2ax}$ 4 $J_{1eq,2eq}$ 1·5	3·17dd $J_{1eq,2eq}$ 1·5 $J_{2eq,2ax}$ 15	1·92dd $J_{1eq,2ax}$ 4 $J_{2ax,2eq}$ 15	4·63 $J_{4ax,5ax}$ 9·5	3·98dq $J_{4ax,5ax}$ 9·5 $J_{5ax,6}$ 6	1·45s	1·15d $J_{5ax,6}$ 6		2·03s	1·17t J 7 2·42q J 7
(18β)	H	H	OMe	H	4·69dd $J_{1ax,2ax}$ 9 $J_{1ax,2eq}$ 2·5	2·02dd $J_{1ax,2eq}$ 2·5 $J_{2eq,2ax}$ 14	1·51dd $J_{1ax,2ax}$ 9 $J_{2ax,2eq}$ 14	3·0d $J_{4ax,5ax}$ 9·5	3·63dq $J_{4ax,5ax}$ 9·5 $J_{5ax,6}$ 6	1·26s	1·30d $J_{5ax,6}$ 6	3·48s		
(18α)	H	H	H	OMe	4·77dd $J_{1eq,2ax}$ 3 $J_{1eq,2eq}$ 1·5	2·09dd $J_{1eq,2eq}$ 1·5 $J_{2eq,2ax}$ 15	1·74dd $J_{1eq,2ax}$ 3 $J_{2ax,2eq}$ 15	2·94d $J_{4ax,5ax}$ 10	3·63dq $J_{4ax,5ax}$ 10 $J_{5ax,6}$ 6	1·22s	1·32d $J_{5ax,6}$ 6	3·38s		
(36β)	Ac	H	OMe	H	4·73dd $J_{1ax,2ax}$ 9 $J_{1ax,2eq}$ 2·5	2·02dd $J_{1ax,2eq}$ 2·5 $J_{2eq,2ax}$ 14	1·57dd $J_{1ax,2ax}$ 9 $J_{2ax,2eq}$ 14	4·60d $J_{4ax,5ax}$ 9·5	3·87dq $J_{4ax,5ax}$ 9·5 $J_{5ax,6}$ 6·5	1·15s	1·17d $J_{5ax,6}$ 6·5	3·48s		2·12s
(36α)	Ac	H	H	OMe	4·79dd $J_{1eq,2ax}$ 3 $J_{1eq,2eq}$ 2	2·06dd $J_{1eq,2eq}$ 2 $J_{2eq,2ax}$ 14	1·79dd $J_{1eq,2ax}$ 3 $J_{2ax,2eq}$ 14	4·63d $J_{4ax,5ax}$ 10	4·01dq $J_{4ax,5ax}$ 10 $J_{5ax,6}$ 6·5	1·11s	1·16d $J_{5ax,6}$ 6·5	3·38s		2·13s
(37β)	EtCO	H	OMe	H	4·75dd $J_{1ax,2ax}$ 9 $J_{1ax,2eq}$ 2·5	2·05dd $J_{1ax,2eq}$ 2·5 $J_{2eq,2ax}$ 14	1·59dd $J_{1ax,2ax}$ 9 $J_{2ax,2eq}$ 14	4·64d $J_{4ax,5ax}$ 9·5	3·87dq $J_{4ax,5ax}$ 9·5 $J_{5ax,6}$ 6	1·14s	1·18d $J_{5ax,6}$ 6	3·49s		1·19t J 7·5 2·41q J 7·5
(37α)	EtCO	H	H	OMe	4·80dd $J_{1eq,2ax}$ 3 $J_{1eq,2eq}$ 2	2·08dd $J_{1eq,2eq}$ 2 $J_{2eq,2ax}$ 14	1·81dd $J_{1eq,2ax}$ 3 $J_{2ax,2eq}$ 14	4·66d $J_{4ax,5ax}$ 10	4·01dq $J_{4ax,5ax}$ 10 $J_{5ax,6}$ 6	1·11s	1·17d $J_{5ax,6}$ 6	3·39s		1·18t J 7 2·43q J 7
(35β)	EtCO	Ac	OMe	H	4·49dd $J_{1ax,2eq}$ 2 $J_{1ax,2ax}$ 10	3·02dd $J_{1ax,2eq}$ 2 $J_{2eq,2ax}$ 14	1·56dd $J_{1ax,2ax}$ 10 $J_{2ax,2eq}$ 14	4·60d $J_{4ax,5ax}$ 10	3·92dq $J_{4ax,5ax}$ 10 $J_{5ax,6}$ 6	1·48s	1·17d $J_{5ax,6}$ 6	3·48s	2·08s	1·17t J 7 2·42q J 7
(35α)	EtCO	Ac	H	OMe	4·68dd $J_{1eq,2ax}$ 4 $J_{1eq,2eq}$ 1	3·18dd $J_{1eq,2eq}$ 1 $J_{2eq,2ax}$ 15	1·67dd $J_{1eq,2ax}$ 4 $J_{2ax,2eq}$ 15	4·62d $J_{4ax,5ax}$ 9·5	4·19dq $J_{4ax,5ax}$ 9·5 $J_{5ax,6}$ 6	1·42s	1·12d $J_{5ax,6}$ 6	3·30s	1·99s	1·18t J 7 2·42q J 7
(38β)	Ac	EtCO	OMe	H	4·48dd $J_{1ax,2eq}$ 2 $J_{1ax,2ax}$ 10	3·01dd $J_{1ax,2eq}$ 2 $J_{2eq,2ax}$ 14	1·55dd $J_{1ax,2eq}$ 10 $J_{2ax,2ax}$ 14	4·58d $J_{4ax,5ax}$ 9·5	3·91dq $J_{4ax,5ax}$ 9·5 $J_{5ax,6}$ 6	1·47s	1·17d $J_{5ax,6}$ 6	3·45s	2·11s	1·14t J 7 2·35q J 7
(38α)	Ac	EtCO	H	OMe	4·68dd $J_{1eq,2ax}$ 4 $J_{1eq,2eq}$ 1	3·20dd $J_{1eq,2eq}$ 1 $J_{2eq,2ax}$ 15	1·68dd $J_{1eq,2ax}$ 4 $J_{2ax,2eq}$ 15	4·62d $J_{4ax,5ax}$ 10	4·19dq $J_{4ax,5ax}$ 10 $J_{5ax,6}$ 6	1·44s	1·13d $J_{5ax,6}$ 6	3·30s	2·14s	1·12t J 7 2·30q J 7

[a] In D_2O

TABLE 3

Mass spectra [m/e (%)] of the mycarose derivatives [a]

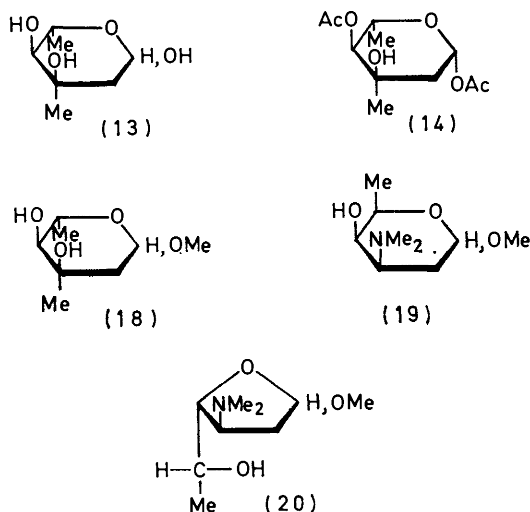


Compd	R¹	R²	R³	M^+	*c*	*e*	*f*	*g*	*h*	*i*	*j*
(13)	H	H	H	162(0·07)	145(0·25)	144(0·6)	127(0·2)	126(0·2)		118(0·4)	100(20)
(28)	Ac	H	H	203(0·1) [a]	187(0·4)	186(0·6)			109(1)	160(0·2) 118((1) [b]	142(3) 100(29) [c]
(14)	Ac	H	Ac							160(0·2) [b]	142(0·1) [c] 100(12) [f]
(29)	Ac	Ac	H			186(0·3)	169(0·2) 127(2) [g]	126(1)	109(1)		142(2) 100(19) [c]
(30)	Ac	Ac	Ac		229(0·05)	228(0·2)	169(2) 127(2) [g]	168(0·4)	109(7)		184(1·7) 142(8) [c] 100(16) [f]
(32)	EtCO	Ac	H		201(0·2)	200(0·2)	183(0·2) 127(5) [j]	126(2)	109(2)		156(2) 100(18) [k]
(18)	H	H	Me	176(0·5)	145(1·9)	158(0·5)	127(1)	140(0·3)		132(3)	114(1)
(36)	Ac	H	Me	218(0·07)	187(0·3)	200(0·1)	169(0·2) 127(1·1) [g]	140(0·4)	109(2)	174(0·2)	114(6)
(37)	EtCO	H	Me		201(2·2)	214(0·1)	183(0·1)	140(0·5)	109(3)	188(0·3)	114(17)
(35)	EtCO	Ac	Me	273(0·03) [a]	243(0·2)	214(1·1)	183(1)	140(3)	109(27)	230(0·03)	170(2) 114(56) [k]
(38)	Ac	EtCO	Me	274(0·03)	243(0·02)	200(0·17)	169(0·4)	140(5)	109(8)	230(0·02)	156(3·4) 114(42) [e]

Compd	R¹	R²	R³	*k*	*l*	*m*	*n*	*o*	*p*	*q*	*r*
(13)	H	H	H	74(53)	71(48)	87(18)	144(0·6)	144(0·6)	118(0·4)	117(0·4)	43(100)
(28)	Ac	H	H	116(9) 74(24) [d]	71(11)	87(8) [e]	186(0·6)	186(0·6)	160(0·2)		43(100)
(14)	Ac	H	Ac	116(10) 74(19) [d]		129(1) 87(4) [e]	186(0·6)	186(0·6)	160(0·2)		43(100)
(29)	Ac	Ac	H	158(0·5) 116(3) [d] 74(5) [h]	71(10)	87(3) [e]	186(0·3)	186(0·3)			43(100)
(30)	Ac	Ac	Ac	158(0·4) 116(3) [d] 74(2) [i]	71(5)	129(1) [e] 87(2) [i]	228(0·2)	228(0·2)			43(100)
(32)	EtCO	Ac	H	172(0·5) 130(1) [d] 116(2) [l] 74(5) [m]	71(9)	129(4) 87(3) [e]		186(0·5)			57(100) 43(72)
(18)	H	H	Me	74(100)	85(3)	101(4)	144(1·2)	158(0·5)	118(9)		43(53)
(36)	Ac	H	Me	116(22) 74(43) [d]	85(4)	101(5)	186(2·1)	158(0·6)	160(2·3)	159(0·2)	43(100)
(37)	EtCO	H	Me	130(3) 74(5) [l]	85(3)	101(6)	200(1·5)	158(0·5)			57(100) 43(21)
(35)	EtCO	Ac	Me	172(2) 130(7) [d] 116(7) [l] 74(8) [m]	85(10)	101(5) [e]	242(0·3)	200(0·3)		215(0·12)	57(97) 43(100)
(38)	Ac	EtCO	Me	172(1·1) 130(6) [d] 116(5) [l] 74(7) [m]	85(9)	157(3·5)	242(0·19)	214(0·28)		215(0·07)	57(100) 43(69)

[a] $M^+ - 1$. [b] $i - 42$. [c] $j - 42$. [d] $k - 42$. [e] $m - 42$. [f] $j - 42 - 42$. [g] $f - 42$. [h] $k - 42 - 42$. [i] $m - 42 - 42$. [j] $f - 56$. [k] $j - 56$. [l] $k - 56$. [m] $k - 56 - 42$.

erythromycin C,[12] the magnamycins,[32-34] the spiramycins,[33,35,36] and the leucomycins.[37-39] Acetylation of L-mycarose (13) under mild conditions gave 1,4-di-*O*-acetyl-β-L-mycarose (14).[30] The macrolide component from the hydrolysis, megalalosamine (12), showed i.r. bands due to the keto-group at 1685 cm^{-1}, indicating that no spiroacetal formation had occurred, as was observed



when erythromycin A was similarly treated.[8] The presence of two dimethylamino-groups with bands at δ 2·27 and 2·40 in the n.m.r. spectrum (Table 4) demonstrated that both amino-sugar units were still glycosidically attached to the aglycone. The mass spectrum gave a molecular ion at *m*/*e* 732 consistent with structure (12), and, as in the case of megalomicin A (1), showed a base peak at *m*/*e* 158 due to ions *a* and *b*. The typical fragment ions from the amino-sugar units at *m*/*e* 574 ($M-$ 158), 558 ($M - 174$), and 559 ($M - 173$, H transfer) were observed (Scheme 1), together with fragment ions at *m*/*e* 444 (ion *d*) and 657 ($M - 75$) due to the fragmentation outlined in Scheme 3.

When megalalosamine (12) was treated with acetic anhydride at 25°, 2′,4″-di-*O*-acetylmegalalosamine (15) was obtained which had a pK_a of 7·8 [*cf.* 8·8 for megalalosamine (12)] indicating that the acetyl groups were located in the amino-sugar units. This was confirmed by a molecular ion at *m*/*e* 816, and by the presence of a base peak at *m*/*e* 200 in the mass spectrum, with peaks at *m*/*e* 616 ($M - 200$), 600 ($M - 216$), 601 ($M - 215$, H transfer), and 699 ($M - 117$) in the high mass region. A fragment ion corresponding to a monoacetyl *d* was observed at *m*/*e* 486. It is well documented that under mild acetylation conditions such as those used here the secondary hydroxy-groups in the aglycone of the erythomycins do not undergo acetylation.[40] When megalalosamine (12) was acetylated under forcing conditions (acetic anhydride–pyridine at 90°), 3,2′,4″-tri-*O*-acetylmegalalosamine (16) was formed. The n.m.r. spectrum showed bands due to the two acetates in the amino-sugar residues at δ 2·09 and 2·20, with a third band due to the C-3 acetate at δ 2·11. The pK_a (7·6) was consistent with structure (16), as was the molecular ion at *m*/*e* 858. The mass spectrum exhibited peaks due to the expected glycosidic cleavages of the acetylated amino-sugar units as in the case of the diacetate (15), and the peak at *m*/*e* 486 due to a monoacetyl *d* showed that the third acetate was located on the aglycone between C-3 and C-6. Mesylation of 2′,4″-di-*O*-acetylmegalalosamine (15) gave 2′,4″-di-*O*-acetyl-3-*O*-methylsulphonylmegalalosamine (17), which showed the expected i.r. bands at 1335 and 1170 cm^{-1}, and an n.m.r. signal at δ 3·05 ($MeSO_2$). The formation of an ion corresponding to monoacetyl *d* at *m*/*e* 486 in the mass spectrum of (17) confirmed the fact that the mesyl group was located between C-3 and C-6 on the aglycone, a point which will be dealt with in connection with the location of the mycarose residue.

Methanolysis of megalomicin A (1) with 0·6N-hydrogen chloride in methanol gave methyl α- and β-L-mycaroside (18),[27] methyl 2,3,6-trideoxy-3-dimethylamino-α- and -β-D-*lyxo*-hexopyranoside (19),[1,5] methyl 2,3,6-trideoxy-3-dimethylamino-α- and -β-D-*lyxo*-hexofuranoside (20),[1,5] and erythralosamine (21).[8,11] The new amino-sugar

TABLE 4

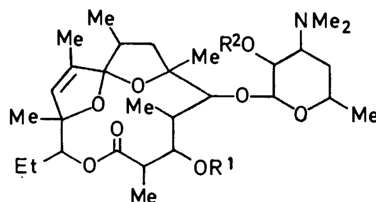
N.m.r. spectra (δ values; *J* in Hz) of the megalalosamines

Compd	R¹	R²	13-$CH_3{\cdot}CH_2$ [a]	Me envelope [b]	6-Me [c]	R¹ [c]	2′-OAc [c]	4″-OAc [c]	3′-NMe_2 [d]	3″-NMe_2 [d]	H-1′ [e]	H-13 [f]	H-3 [g]
(12)	H	H	0·81	1·08—1·32	1·49				2·27	2·40	4·42	5·27	
(15)	H	Ac	0·83	0·9—1·3	1·41		2·08	2·20	2·28	2·33	4·14	5·23	
(16)	Ac	Ac	0·83	1·0—1·3	1·38	2·11	2·09	2·20	2·28	2·33	4·12	5·22	5·51
(17)	$MeSO_2$	Ac	0·83	1·05—1·35	1·45	3·05	2·08	2·19	2·28	2·32	4·28	5·23	5·36
(23)	9,*O*(9)-Dihydromegalalosamine		0·82	0·85—1·35	1·47				2·28	2·33	4·48	5·11	

[a] All 3H, t, *J* 7. [b] All *ca.* 21H. [c] All 3H, s. [d] All 6H, s. [e] All 1H, d, $J_{1'ax,2'ax}$ 7. [f] All 1H, dd, $J_{13,14}$ 10, $J_{13,14'}$ 3. [g] All 1H, dd, $J_{2,3}$ 11, $J_{3,4}$ 1.

[32] R. B. Woodward, *Angew. Chem.*, 1957, **69**, 50.
[33] M. E. Kuehne and B. W. Benson, *J. Amer. Chem. Soc.*, 1965, **87**, 4660.
[34] R. B. Woodward, L. S. Weiler, and P. C. Dutta, *J. Amer. Chem. Soc.*, 1965, **87**, 4662.
[35] R. Paul and S. Tchelitcheff, *Bull. Soc. chim. France*, 1965, 650.
[36] S. Omura, A. Nakagawa, M. Otani, T. Hata, H. Ogura, and K. Furuhata, *J. Amer. Chem. Soc.*, 1969, **91**, 3401.
[37] S. Omura, M. Katagiri, and T. Hata, *J. Antibiotics*, 1968, **21**, 199.
[38] S. Omura, M. Katagiri, H. Ogura, and T. Hata, *Chem. and Pharm. Bull.* (*Japan*), 1968, **16**, 1181.
[39] S. Omura, M. Katagiri, and T. Hata, *J. Antibiotics*, 1968, **21**, 272.
[40] A. Banaszek, J. St. Pyrek, and A. Zamojski, *Roczniki Chem.*, 1969, **43**, 763.

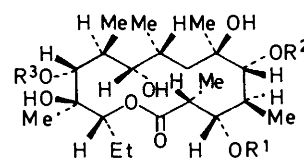
which was obtained in both pyranoside and furanoside forms was named D-rhodosamine.[1,5] The spectral data and physical constants for (18) and for (21) were in excellent agreement with published data, and a direct comparison {i.r., n.m.r. (Table 5), and mass spectra, $[\alpha]_D$, t.l.c., m.p., and mixed m.p.} of (21) with an authentic sample of erythralosamine prepared by treatment of



(21) $R^1 = R^2 = H$
(25) $R^1 = MeSO_2, R^2 = Ac$
(27) $R^1 = H, R^2 = Ac$

erythromycin A (5) with 0·75N-hydrochloric acid[8] showed that they were identical. This important finding indicated that both erythromycin A (5), and megalomicin A (1) have a common aglycone, and that in megalomicin A (1) the D-desosamine unit is glycosidically attached to the aglycone at C-5. The β-configuration of the anomeric linkage of the desosamine to the aglycone was evident from the n.m.r. spectra of megalomicin A (1), megalalosamine (12), and erythralosamine (21), each of which contained a doublet (J 7 Hz) (at δ 4·33, 4·42, and 4·26, respectively) consistent with an axial–axial coupling between H-1 and H-2 in the desosamine unit. When megalalosamine (12) was similarly methanolysed the products (19)—(21) were formed.

Reduction of the 9-oxo-group in megalomicin A (1) by sodium borohydride at 25° gave the 9(S)-hydroxy-analogue A (22), the i.r. spectrum of which showed no ketone carbonyl absorption. The mass spectrum gave a molecular ion at m/e 878. Similarly, reduction of megalalosamine (12) with sodium borohydride gave the 9-hydroxy-compound (23). Both derivatives (22) and (23) were labile towards dilute aqueous mineral acids. When megalomicin A (1) was reduced with sodium borohydride and the product was worked up under acidic conditions, (9S)-5-β-D-desosaminyloxy-9,O(9)-dihydroerythronolide (24) was formed. Under similar conditions the D-rhodosamine unit could not be hydrolysed from megalomicin A (1) or megalalosamine (12). The



(22) R^1 = α-L-mycarosyl, R^2 = β-D-desosaminyl, R^3 = β-D-rhodosaminyl,
(23) R^1 = H, R^2 = β-D-desosaminyl, R^3 = β-D-rhodosaminyl
(24) $R^1 = R^3$ = H, R^2 = β-D-desosaminyl

S-configuration was assigned to C-9 in the reduction products (22)—(24) because (24) was identical with the corresponding product prepared from erythromycin A (5), and both (22) and (23) could be converted into (24) by acidic treatment. Further proof of the S-configuration at C-9 was obtained by treating (24) with benzeneboronic acid: a mono-9,11-phenylboronate was obtained. The latter would not have been formed if the configuration at C-9 had been R.[41] The product (24) was identical with the corresponding derivative prepared from erythromycin A (5) by sodium borohydride reduction followed by mild acidic hydrolysis.[9,10] We therefore concluded that the gross structure and total absolute stereochemistry of the aglycone in megalomicin A (1) were identical with those of erythromycin A (5),[42] that the D-desosaminyl residue was at C-5 on the aglycone, and that the anomeric linkage had the β-configuration. The assignment of the β-configuration to the anomeric linkage at C-5 agreed with the n.m.r. data, and also with the application of Klyne's rule[43-45] to the molecular rotations of the appropriate derivatives (Table 6). With the desosamine located at C-5, it followed from mass spectral considerations that it was the rhodosamine residue that was located between C-7 and C-13, giving rise to ions of the type d. Since there was only one secondary hydroxy-group (at C-11) in this portion of the aglycone, and since acetylation of megalalosamine (12) under forcing conditions gave only 3,2′,4″-tri-O-acetylmegalalosamine (16) and not a tetra-acetate, it followed

TABLE 5

N.m.r. spectra (δ values; J in Hz) of the erythralosamines

Compd	R^1	R^2	13-CH_3·CH_2 [a]	Me groups *	2-Me [b]	5-Me [b]	6-Me [c]	12-Me [c]	10-Me [d]	R^1 [c]	2′-OAc [c]	3′-NMe_2 [e]	H-2′ [f]	H-5 [g]	H-1′ [g]	H-13 [f]	H-11 [h]	H-3 [f]
(21) †	H	H	0·86	0·96,[b] 1·07 [b]	1·14	1·20	1·25	1·43	1·88			2·28	3·22 [j]	3·43 [m]	4·19 [p]	4·95 [r]	5·5	4·27 [t]
(25)	$MeSO_2$	Ac	0·84	0·93,[i] 0·95—1·25 (*ca.* 9H)			1·24	1·51	1·75	3·18	2·05	2·30	4·79 [k]	3·62 [n]	4·25 [q]	4·90 [s]	5·48	5·17 [u]
(27)	H	Ac	0·85	0·98,[i] 1·0—1·27 (*ca.* 9H)			1·27	1·42	1·81		2·07	2·29	4·82 [l]	3·40 [o]	4·28 [q]	5·0 [s]	5·51	4·26 [v]

[a] All 3H, t, J 7. [b] 3H, d, J 6·5. [c] All 3H, s. [d] All 3H, d, J 1·5. [e] All 6H, s. [f] All 1H, dd. [g] All 1H, d. [h] All 1H, q, J 1·5. [i] 3H, d, J 7. [j] $J_{1'ax,2'ax}$ 7, $J_{2'ax,3'ax}$ 10. [k] $J_{1'ax,2'ax}$ 7·5, $J_{2'ax,3'ax}$ 10. [l] $J_{1'ax,2'ax}$ 7·5, $J_{2'ax,3'ax}$ 10·5. [m] $J_{4,5}$ 8. [n] $J_{4,5}$ 9. [o] $J_{4,5}$ 9·5. [p] $J_{1'ax,2'ax}$ 7. [q] $J_{1'ax,2'ax}$ 7·5. [r] $J_{13,14}$ 11, $J_{13,14'}$ 3. [s] $J_{13,14}$ 10, $J_{13,14}$ 3·5. [t] $J_{2,3}$ 5, $J_{3,4}$ 3·5. [u] $J_{2,3}$ 4·5, $J_{3,4}$ 3·5. [v] $J_{2,3}$ 6, $J_{3,4}$ 3.

* Location uncertain. † At 100 MHz.

[41] T. J. Perun, R. S. Egan, and J. R. Martin, *Tetrahedron Letters*, 1969, 4501.

[42] D. R. Harris, S. G. McGeachin, and H. H. Mills, *Tetrahedron Letters*, 1965, 679.

[43] W. Klyne, *The Royal Institute of Chemistry Lecture Series*, 1962, **4**, 13.

[44] T. Reichstein and E. Weiss, *Adv. Carbohydrate Chem.*, 1962, **17**, 99.

[45] W. D. Celmer, in 'Biogenesis of Antibiotic Substances,' eds. Z. Vanek and Z. Hostalek, Academic Press, New York, 1965, p. 119.

that the D-rhodosamine unit was glycosidically attached to the secondary hydroxy-group at C-11. This was confirmed by the formation of a monomethanesulphonate (17) on treatment of 2′,4″-di-*O*-acetylmegalalosamine (15) with methanesulphonyl chloride, under conditions which would have been expected to lead to a dimethanesulphonate had the 11-hydroxy-group been free in megalalosamine (12). Application of Klyne's rule (Table 6) to the appropriate derivatives resulted in the assignment of the β-configuration to the glycosidic linkage of the D-rhodosamine residue.

The mass spectral evidence suggested that the mycarose unit was located between C-3 and C-6, and since the desosamine was at C-5, the mycarose had to be at C-3 or C-6. When megalomicin A (1) was acetylated under forcing conditions known to acetylate any free secondary hydroxy-groups on the aglycone, no such derivative was formed. The only products isolated were 3′,4′,2″,4‴-tetra-*O*-acetylmegalomicin A (10) and the penta-ester of an intramolecular hemiacetal of megalomicin A,[18] thus indicating that the mycarose was glycosidically attached to the secondary 3-hydroxy-group. This was confirmed by methanolysis of 2′,4″-di-*O*-acetyl-3-*O*-methylsulphonylmegalalosamine (17), in which the mesyl group was located at the site of the mycarose residue in megalomicin A (1); this gave 2′-*O*-acetyl-3-*O*-methylsulphonylerythralosamine (25). The highest mass peak in the mass spectrum of (25) was at *m/e* 563 ($M - CH_3SO_3H$), and the n.m.r. spectrum clearly indicated the presence of one methylsulphonyl group (δ 3·20), together with an acetate at δ 2·07, and a dimethylamino-group at δ 2·30. An authentic sample of (25) was prepared by methanolysis of 4′,2″-di-*O*-acetylerythromycin A [8] (26) to give 2′-*O*-acetylerythralosamine (27), followed by treatment of the latter with methanesulphonyl chloride. The product was identical with (25) prepared from megalomicin A (1). The glycosidic bond at C-3 was shown to have an α-configuration by application of Klyne's rule (Table 6), and by the fact that the anomeric proton in the mycarose residue in megalomicin A (1) gave rise to a triplet at δ 5·13 with $J_{1'eq,2'ax} = J_{1'eq,2'eq} = 2{\cdot}5$ Hz in the n.m.r. spectrum, consistent with an α-L-glycoside. Hence the total structure, and absolute stereochemistry of megalomicin A, may be represented by structure (1).

Megalomacin B (2) was obtained as a crystalline solvate, m.p. 135—140°, which gave a molecular ion at *m/e* 918 ($C_{46}H_{82}N_2O_{16}$). The analytical data were in agreement with a monohydrate. The pK_a (8·8) indicated the presence of at least one basic group as in the case of megalomicin A (1). The i.r. spectrum revealed the presence of hydroxy- (3497 cm^{-1}), dimethylamino- (2786), acetate (1751 and 1245), lactone (1724 and 1190), and keto- (1695) groups. The n.m.r. spectrum showed a triplet at δ 0·81 (*J* 7 Hz) due to an ethyl group, and, in addition to the two dimethylamino-groups at C-3″, and C-3‴ (δ 2·28 and 2·35, respectively), gave a singlet due to an acetyl group at δ 2·09. Ammonolysis of megalomicin B (2) gave megalomicin A (1), demonstrating that (2) was a monoacetyl derivative of (1). The pK_a of (2) excluded the presence of the acetate in either of the amino-sugar residues. Acetylation of megalomicin B (2) with acetic anhydride in pyridine at 25° gave a diacetyl derivative identical with 4′,2″,4‴-tri-*O*-acetylmegalomicin A (8), indicating that the acetyl group in (2) was at C-4′ in the mycarose residue. The mass spectral fragmentation pattern of megalomicin B (2) also indicated that the acetate was located at C-4′. The base peak in the spectrum (ions *a* and *b*) was at *m/e* 158, and the mycarosyl unit gave rise to an ion corresponding to a monoacetyl *c* ($R^1 = Ac$, $R^2 = H$) at *m/e* 187. Cleavage of the glycosidic bonds gave peaks at *m/e* 760 ($M - 158$), 761 ($M - 157$, H transfer), 744 ($M - 174$), 745 ($M - 173$, H transfer), and 732 ($M - 186$, H transfer) in the high mass region. Peaks at *m/e* 843 (Scheme 3) and 444 due to ion *d* were also observed. The monoacetyl *c* ion (*m/e* 187) underwent further fragmentation to give ions *f* ($R^1 = Ac$) (*m/e* 169) and *h* (*m/e* 109), confirming the location of the acetyl group.

TABLE 6

Configurations of the anomeric centres

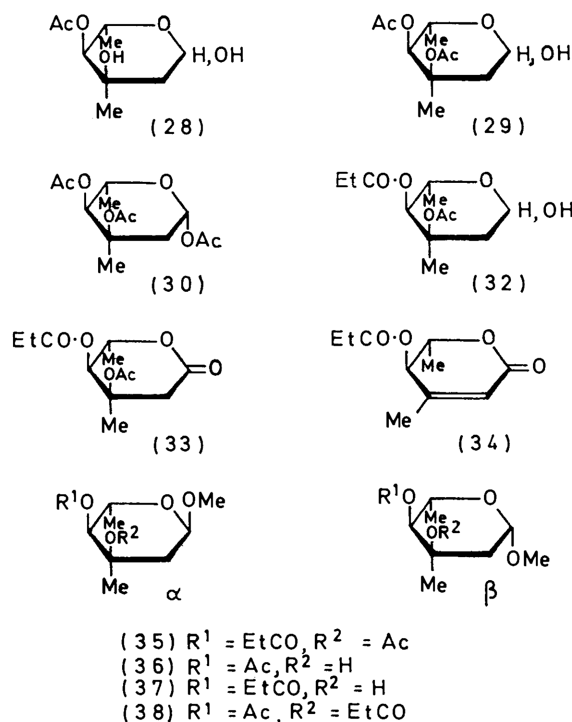
Compound	$[M]_D^{26a}$ (°)	$[M]_D^{26}$ (°)
9,*O*(9)-Dihydroerythronolide (from erythromycin A) [9,10]	+39·9 [b]	
5-β-D-Desosaminyloxy-9,*O*(9)-dihydroerythronolide (24) (from megalomicin A)	−7·5	−47·4
5-β-D-Desosaminyloxy-9,*O*(9)-dihydroerythronolide (24) (from erythromycin A) [9,10]	−11·5 [c]	−51·4
n-Butyl α-D-desosaminide [45]	+323 [45]	
n-Butyl β-D-desosaminide [45]	−11·5 [45]	
5-β-D-Desosaminyloxy-11-β-D-rhodosaminyloxy-9,*O*(9)-dihydroerythronolide (23)	−231	−223·5
Methyl α-D-rhodosaminide (19α) [1,5]	+225·1	
Methyl β-D-rhodosaminide (19β) [1,5]	−111·1	
Megalalosamine (12)	−446 [d]	
Megalomicin A (1)	−788 [d]	−342
Methyl α-L-mycaroside (18α)	−243 [d]	
Methyl β-L-mycaroside (18β)	+36·6 [d]	

[a] Recorded in methanol. [b] Based on $[\alpha]_D^{27}$ +9·5.[10] [c] Based on $[\alpha]_D^{25}$ −2.[10] [d] Recorded in ethanol.

Mild acidic hydrolysis of megalomicin B (2) by 0·75N-hydrochloric acid gave megalalosamine (12), identical with that obtained from megalomicin A (1), and 4-*O*-acetyl-α- and -β-L-mycarose (28). The physical data for the latter were in good agreement with those reported.[45] Acetylation of (28) at room temperature gave 1,4-di-*O*-acetyl-β-L-mycarose (14), identical with that prepared from L-mycarose (13).

Megalomicin C_1 (3) was obtained crystalline, m.p. 243—246°; analytical data and a molecular ion at *m/e* 960 indicated the formula $C_{48}H_{84}N_2O_{17}$. The i.r. spectrum indicated the presence of hydroxy- (3497 cm^{-1}), dimethylamino- (2786), acetate (1748, 1247, and 1232), lactone (1727 and 1163 cm^{-1}), and keto- (1698) groups. The n.m.r. spectrum revealed two dimethylamino-groups at C-3″ and C-3‴ at (δ 2·30 and 2·35, respectively), and two acetyl groups (δ 2·10). Alkaline hydrolysis of

megalomicin C_1 (3) gave megalomicin A (1), indicating that (3) was a diacetyl derivative of (1). The pK_a (8·8) showed that neither of the acetates was located on the amino-sugar residues. When megalomicin C_1 (3) was acetylated at room temperature a diacetyl derivative was obtained which was identical with 3',4',2'',4'''-tetra-*O*-acetylmegalomicin A (10), indicating that the two acetyl groups in megalomicin C_1 (3) were at C-3' and C-4' in the mycarose unit. This was further supported by the mass spectrum of (3) which showed a base peak at *m/e* 158 (ions *a* and *b*) and peaks at *m/e* 229, 169, and 109 due to diacetyl *c* ($R^1 = R^2 =$ Ac), *f* ($R^1 =$ Ac), and *h*, respectively. In the high mass region, cleavage of the



glycosidic bonds gave peaks at *m/e* 802 (*M* — 158), 786 (*M* — 174), 787 (*M* — 173, H transfer), and 731 (*M* — 229). Peaks at *m/e* 885 (Scheme 3), and at *m/e* 444 due to ion *d*, were also present.

Hydrolysis of megalomicin C_1 (3) with 0·75N-hydrochloric acid at ambient temperature gave megalalosamine (12), identical with that obtained from megalomicin A (1), and 3,4-di-*O*-acetyl-α- and -β-L-mycarose (29). Acetylation of (29) gave 1,3,4-tri-*O*-acetyl-β-L-mycarose (30). The mass spectral (Table 3) and n.m.r. (Table 2) data for the acetate (29) and (30) were in good agreement with the proposed structures. 3,4-Di-*O*-acetyl-α- and -β-L-mycarose (29) has not previously been reported.

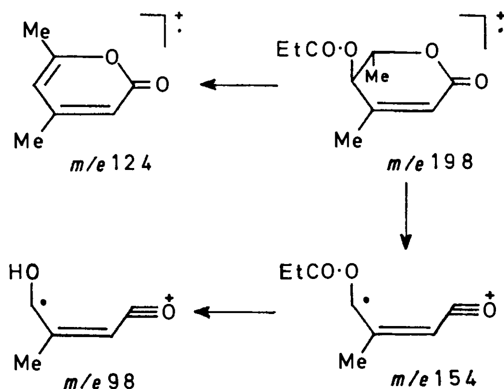
The fourth major component of the megalomicin complex, megalomicin C_2 (4), was obtained crystalline, m.p. 147—150°; the analytical data and the molecular ion (*m/e* 974) indicated the molecular formula $C_{49}H_{86}N_2O_{17}$. The i.r. spectrum revealed the presence of hydroxy- (3484 cm^{-1}), dimethylamino- (2786), acetate (1748 and 1247), propionate (1748 and 1176), lactone (1727 and 1176), and keto- (1698) groups. The n.m.r. spectrum showed peaks due to two dimethylamino-groups at C-3'' and C-3''' (δ 2·29 and 2·36, respectively) as well as a singlet at δ 2·10 due to an acetyl group. The methyl of the ethyl group at C-13 and that of the propionate gave a triplet at δ 0·81 (*J* 7 Hz). The pK_a of megalomicin C_2 (4) (8·8) indicated that neither the acetate nor the propionate was in either of the amino-sugar units. Alkaline hydrolysis of megalomicin C_2 (4) gave megalomicin A (1), showing that (4) was a monoacetyl monopropionyl derivative of (1). The mass spectrum of megalomicin C_2 (4) showed a base peak at *m/e* 158 (ions *a* and *b*) with peaks at *m/e* 816 (*M* — 158), 800 (*M* — 174), 801 (*M* — 173, H transfer), and 732 (*M* — 242, H transfer) in the high mass region due to cleavage of the glycosidic bonds. Peaks at *m/e* 899 (Scheme 3), and at *m/e* 444 due to ion *d* were also present. The presence of peaks at *m/e* 243, 183, and 109 due to monoacetyl monopropionyl *c* ($R^1 =$ EtCO, $R^2 =$ Ac), monopropionyl *f* ($R^1 =$ EtCO) and *h*, respectively (Table 3), suggested that the acetate was at C-3' and that the propionate was at C-4' in the mycarose residue. Acetylation of megalomicin C_2 (4) at ambient temperature gave 2'',4'''-di-*O*-acetylmegalomicin C_2 (31), which gave a molecular ion at *m/e* 1058 with a base peak at *m/e* 200. The pK_a (7·4) supported the fact that the two newly introduced acetyl groups were both located in the amino-sugars. The n.m.r. spectrum revealed the presence of three acetyl groups [δ 2·02 (C-2'') and 2·17 (C-3' and C-4''')].

Mild acidic hydrolysis of megalomicin C_2 (4) with 0·75N-hydrochloric acid at 25° gave megalalosamine (12), identical with that obtained from megalomicin A (1), and 3-*O*-acetyl-4-*O*-propionyl-α- and -β-L-mycarose (32), a new naturally occurring mycarose derivative. The mass spectral (Table 3) and n.m.r. (Table 2) evidence was consistent with structure (32).

Chemical evidence to support the locations of the acyl functions in (32) was obtained by oxidation with bromine water to give the lactone (33), which on treatment with toluene-*p*-sulphonic acid underwent β-elimination to give the αβ-unsaturated lactone (34). The latter gave a molecular ion at *m/e* 198 ($C_{10}H_{14}O_4$), and its u.v. spectrum was consistent with an αβ-unsaturated δ-lactone system; this was supported by the i.r. spectrum, which also revealed the presence of a propionate (1740 and 1165 cm^{-1}). The mass spectral fragmentation pattern (Scheme 4) afforded evidence for the location of the propionate at C-4' in the mycarose unit of megalomicin C_2 (4).

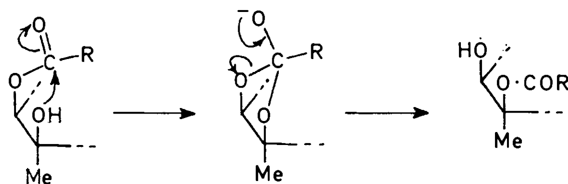
Alternatively, methanolysis of megalomicin C_2 (4) gave erythralosamine (21), methyl D-rhodosaminide [(19) and (20)], and methyl 3-*O*-acetyl-4-*O*-propionyl-α- and -β-L-mycaroside (35). The anomeric mixture of the latter gave a single spot in a number of t.l.c. systems, and could not readily be separated chromatographically. For comparison each of the anomers of (35) was synthesised separately. This was achieved by first acetylating the 4-hydroxy-group in each of the anomers of methyl

mycaroside (18) at room temperature with acetic anhydride in pyridine to give the 4-*O*-acetyl derivatives (36).[39,46] The latter on heating with propionic anhydride



SCHEME 4

in pyridine underwent intramolecular transacylation of the *cis*-glycol system to give the α- and β-anomers of methyl 3-*O*-acetyl-4-*O*-propionyl-L-mycaroside (35), identical with the anomeric mixture of products (35) obtained from the methanolysis of megalomicin C_2 (4). Initially each of the anomers of methyl mycaroside (18) had been converted into the 4-*O*-propionyl derivatives (37)[39] with propionic anhydride in pyridine at ambient temperature. However, on treatment of the latter with acetic anhydride–pyridine on a steam-bath, instead of the desired methyl 3-*O*-acetyl-4-*O*-propionyl-α- and -β-L-mycarosides (35) being formed, methyl 4-*O*-acetyl-3-*O*-propionyl-α- and -β-L-mycarosides (38) were obtained as the sole products, which indicated that intramolecular transacylation (Scheme 5) was occurring rather than



SCHEME 5

direct acylation of the tertiary hydroxy-group. The mass (Table 3) and the n.m.r. (Table 2) spectra of the foregoing mycarose derivatives supported the structural assignments.

EXPERIMENTAL

For general details see preceding paper.[1]

Isolation of the Megalomicin Antibiotics.—The antibiotic complex produced by *Micromonospora megalomicea* sp. n. was isolated, and separated into four principal components as described previously.[3] *Megalomicin A* (1) formed needles (from acetone), m.p. 255—259° (decomp.) (Found: C, 60·5; H, 9·3; N, 3·1. $C_{44}H_{80}N_2O_{15}$ requires C, 60·25; H, 9·2; N, 3·2%), *m/e* 876 (M^+), $[\alpha]_D^{25}$ −90°, pK_a 9·0, $\nu_{max.}$ (Nujol) 3510, 2770, 1730, 1700, and 1190 cm^{-1}. *Megalomicin B* (2) gave needles (from acetone–water), m.p. 135—140° (Found: C, 58·75; H, 9·0; N, 2·75. $C_{46}H_{82}N_2O_{16},H_2O$ requires C, 58·95; H, 9·05; N, 3·0%), *m/e* 918 (M^+), $[\alpha]_D^{25}$ −92°, pK_a 8·8, $\nu_{max.}$ (Nujol) 3500, 2785, 1751, 1724, 1695, 1245, and 1190 cm^{-1}. *Megalomicin C_1* (3) formed needles (from acetone–water), m.p. 243—246° (decomp.) (Found: C, 59·65; H, 8·9; N, 2·95. $C_{48}H_{84}N_2O_{17}$ requires C, 60·0; H, 8·8; N, 2·9%), *m/e* 960 (M^+), $[\alpha]_D^{25}$ −102°, pK_a 8·8, $\nu_{max.}$ (Nujol) 3500, 2785, 1748, 1727, 1698, 1247, 1232, and 1163 cm^{-1}. *Megalomicin C_2* (4) gave needles (from acetone–water), m.p. 147—150° (Found: C, 60·55; H, 8·6; N, 2·85. $C_{49}H_{86}N_2O_{17}$ requires C, 60·35; H, 8·9; N, 2·85%), *m/e* 974 (M^+), $[\alpha]_D^{25}$ −102°, pK_a 8·8, $\nu_{max.}$ (Nujol) 3484, 2786, 1748, 1727, 1698, 1247, and 1176 cm^{-1}.

4′,2″,4‴-Tri-O-acetylmegalomicin A (8).—Megalomicin A (1) (100 mg) in dry pyridine (10 ml) was treated with acetic anhydride (1 ml) kept at 25° for 18 h. The mixture was taken up in chloroform; the solution was washed with water, dried ($MgSO_4$), and evaporated to give the *acetate* (63 mg), which crystallised as needles (from ether–pentane), m.p. 203—206° (Found: C, 60·7; H, 8·9; N, 2·65. $C_{50}H_{86}N_2O_{18}$ requires C, 59·85; H, 8·65; N, 2·8%), *m/e* 1002 (M^+), $[\alpha]_D$ −86·0°, pK_a 7·5, $\nu_{max.}$ (Nujol) 3520, 2780, 1736, 1692, 1242, and 1163 cm^{-1}.

2″,4‴-Di-O-acetylmegalomicin A (9).—Megalomicin A (1) (2 g) in acetone (10 ml) was treated with acetic anhydride (0·6 ml). The mixture was stirred at 25° for 48 h, then cooled in an ice-bath, and a solution of concentrated ammonium hydroxide (0·85 ml) in water (20 ml) was slowly added to give *2″,4‴-diacetylmegalomicin A* (9) (1·63 g) as needles, m.p. 129—134° (Found: C, 58·8; H, 8·7; N, 3·25. $C_{48}H_{84}N_2O_{17},H_2O$ requires C, 58·9; H, 8·85; N, 2·9%), *m/e* 960 (M^+), $[\alpha]_D$ −81°, pK_a 7·6, $\nu_{max.}$ (Nujol) 3510, 3330, 2785, 1739, 1698, 1245, 1190, and 1163 cm^{-1}.

3′,4′,2″,4‴-Tetra-O-acetylmegalomicin A (10).—Megalomicin A (1) (1 g) in dry pyridine (25 ml) was treated with acetic anhydride (2 ml). The mixture was heated at 80° for 24 h, then concentrated *in vacuo*, and the residue was dissolved in acetone. The solution was poured into 5% ammonium hydroxide solution. Chromatography on silica gel (3% methanol in chloroform as eluant), followed by crystallisation from aqueous acetone afforded the *tetra-acetate* (305 mg) as needles, m.p. 242—245° (Found: C, 59·95; H, 8·45; N, 2·55. $C_{52}H_{88}N_2O_{19}$ requires C, 59·75; H, 8·5; N, 2·7%), *m/e* 1044 (M^+), $[\alpha]_D$ −88·8°. The i.r., n.m.r., and mass spectra matched those of 2″,4‴-di-*O*-acetylmegalomicin C_1. The only other product isolated from the chromatogram was a penta-ester which did not retain the ketone carbonyl absorption in the i.r. spectrum.[18]

Vigorous Acidic Hydrolysis of Megalomicin A (1).—Megalomicin A (1) (5 g) in ethanol (50 ml) was treated with 6N-hydrochloric acid (160 ml). The mixture was heated under reflux on a steam-bath for 4 h, cooled, filtered, and extracted with chloroform and then n-butanol after dilution with sufficient water to maintain a two-phase system. The aqueous solution was concentrated and passed through a bed of Amberlite IR45 ion-exchange resin. Evaporation of the eluate gave D-desosamine (11) (916 mg) as a pale yellow oil. Preparative t.l.c. on silica gel [methanol–ammonia–chloroform (1 : 1 : 2) as eluant] gave an anomeric mixture of D-desosamine as an oil which deposited needles, m.p. 83—85°, $[\alpha]_D$ +41·7° (mutarotated), pK_a 8·9, $\nu_{max.}$ 3330,

[46] T. Watanabe, T. Fujii, and K. Satake, *J. Biochem.*, **1961**, **50**, 197.

2770, and 1060 cm^{-1}, δ 1·12 and 1·21 (3H, d, $J_{5ax,6}$ 6·5 Hz, 5-CH_3 for both anomers), 2·31 (6H, s, 3-NMe_2), 4·55 (1H, d, $J_{1ax,2ax}$ 7 Hz, H-1*ax*), and 5·32 (1H, d, $J_{1eq,2ax}$ 3·5 Hz, H-1*eq*). The spectral data agreed with those of an authentic sample prepared in a similar manner from erythromycin A. Mixed t.l.c. with an authentic sample on silica gel [methanol–ammonia–chloroform (1 : 1 : 2) as eluant] showed only one spot.

Mild Acidic Hydrolysis of Megalomicin A (1).—Megalomicin A (1) (2 g) was dissolved in 0·75N-hydrochloric acid (100 ml). The mixture was kept at 25° for 20 h, then poured with stirring into a concentrated aqueous solution of sodium hydrogen carbonate, and extracted with chloroform. The extract was dried ($MgSO_4$) and evaporated to give *megalalosamine* (12) (1·6 g) as an amorphous solid which was precipitated from benzene–hexane; m.p. 110—125° (Found: C, 61·95; H, 9·65; N, 3·55. $C_{37}H_{68}N_2O_{12}$ requires C, 60·65; H, 9·35; N, 3·8%), *m/e* 732 (M^+), $[\alpha]_D^{25}$ −60·8°, pK_a 8·8, $\nu_{max.}$ 3450, 2740, 1730, 1685, and 1170 cm^{-1}.

Evaporation of the aqueous layer *in vacuo*, followed by extraction of the residue with boiling benzene, gave (after evaporation) a mixture of anomers of L-mycarose (13) (250 mg), which crystallised as needles from chloroform, m.p. 112—129° (Found: C, 52·35; H, 8·9. Calc. for $C_7H_{14}O_4$: C, 51·8; H, 8·6%), *m/e* 162 (M^+), $[\alpha]_D^{25}$ −71·2°, $\nu_{max.}$ (Nujol) 3400, 3150, and 1070 cm^{-1}.

2′,4″-*Di*-O-*acetylmegalalosamine* (15).—Megalalosamine (12) (1 g) in dry pyridine (30 ml) was treated with acetic anhydride (3 ml). The mixture was kept at room temperature for 16 h, then taken up in chloroform. The solution was washed with water, dried ($MgSO_4$), and evaporated. Preparative t.l.c. on silica gel (25% methanol in chloroform as eluant) gave the *acetate* as an amorphous powder (710 mg), which crystallised as prisms (from carbon tetrachloride–hexane), m.p. 132—140° (Found: C, 60·0; H, 9·0; N, 3·1. $C_{41}H_{72}N_2O_{14}$ requires C, 60·3; H, 8·9; N, 3·4%), *m/e* 816 (M^+), $[\alpha]_D$ −62·7°, pK_a 7·8, $\nu_{max.}$ 3440, 2740, 1740, 1725, 1685, 1235, and 1160 cm^{-1}.

3,2′,4″-*Tri*-O-*acetylmegalalosamine* (16).—Megalalosamine (12) (500 mg) in dry pyridine (20 ml), and acetic anhydride (2 ml) were heated under reflux on a steam-bath for 16 h. The mixture was taken up in chloroform; the solution was washed with water, dried ($MgSO_4$), and evaporated. Preparative t.l.c. on silica gel (10% methanol in chloroform as eluant) gave the *acetate* as an amorphous powder (340 mg), m.p. 115—122° (Found: C, 59·7; H, 8·7; N, 3·1. $C_{43}H_{74}N_2O_{15}$ requires C, 60·1; H, 8·6; N, 3·3%), *m/e* 858 (M^+), $[\alpha]_D$ −48·8°, pK_a 7·6, $\nu_{max.}$ 3430, 2740, 1740, 1725, 1685, 1235, and 1160 cm^{-1}.

2′,4″-*Di*-O-*acetyl*-3-O-*methylsulphonylmegalalosamine* (17).—2′,4″-Di-*O*-acetylmegalalosamine (15) (1·5 g) in dry pyridine (10 ml) was treated with methanesulphonyl chloride (1 ml). The mixture was kept at 25° for 16 h, diluted with chloroform, washed with water, dried ($MgSO_4$), and evaporated. Preparative t.l.c. on silica gel (10% methanol in chloroform as eluant) gave the *methanesulphonate*, which precipitated from benzene–hexane as an amorphous powder (918 mg), m.p. 155—168° (Found: N, 3·1; S, 3·2. $C_{42}H_{74}N_2O_{16}S$ requires N, 3·1; S, 3·6%), *m/e* 598 (M^+ − 96 − 200), $[\alpha]_D$ −44·1°, pK_a 7·5, $\nu_{max.}$ 3430, 2740, 1740, 1725, 1685, 1335, 1235, 1170, and 1160 cm^{-1}.

1,4-*Di*-O-*acetyl*-β-L-*mycarose* (14).—Mycarose (13) (40 mg) in dry pyridine (10 ml) was treated with acetic anhydride (1 ml). The mixture was kept at 25° for 16 h, then worked up as above, and the product was purified by preparative t.l.c. on silica gel (10% methanol in chloroform as eluant) to give the *acetate* as a gum that crystallised as prisms (42 mg) from hexane; m.p. 91—92° (Found: C, 52·9; H. 7·5. $C_{11}H_{18}O_6$ requires C, 53·65; H, 7·4%), $[\alpha]_D$ −55·7°, $\nu_{max.}$ 3580, 3450, 1750, 1220, and 1040 cm^{-1}.

Methanolysis of Megalomicin A (1).—Megalomicin A (1) (30 g) was dissolved in methanolic 0·6N-hydrogen chloride (750 ml). The solution was kept at 25° for 48 h, then passed through an Amberlite IR45 ion-exchange resin. The methanolic eluate was evaporated, and azeotroped with benzene to remove moisture. The crude mixture of products was obtained as a gum (30 g), which was chromatographed on silica gel (first 2%, then 10% methanol in chloroform as eluant. The following four components (in order of elution) were collected: (i) methyl α- and β-L-mycaroside (18) (7 g), identical with an authentic sample prepared from mycarose (13); (ii) erythralosamine (21) (17·9 g), needles (from benzene–hexane), m.p. and mixed m.p. 199—203° (Found: C, 64·7; H, 9·5; N, 2·7. Calc. for $C_{29}H_{49}NO_8$: C, 64·5; H, 9·15; N, 2·6%), *m/e* 539 (M^+), $[\alpha]_D$ +46·0°, pK_a 8·6, $\nu_{max.}$ 3460, 2780, 1730, and 1180 cm^{-1}, identical with an authentic sample prepared [8] from erythromycin A (5); (iii) methyl 2,3,6-trideoxy-3-dimethylamino-α- and -β-D-*lyxo*-hexofuranoside (20) (650 mg), obtained as an oil;[1,5] (iv) methyl 2,3,6-trideoxy-3-dimethylamino-α- and -β-D-*lyxo*-hexopyranoside (19) (360 mg), obtained as an oil.[1,5]

Methanolysis of Megalosamine (12).—Megalalosamine (12) (10 g) was dissolved in methanolic 0·6N-hydrogen chloride (250 ml). The solution was kept at 25° for 48 h, then worked up as above, and chromatographed on silica gel (10% methanol in chloroform as eluant) to give (in order of elution): (i) erythralosamine (21) (6·2 g); (ii) methyl 2,3,6-trideoxy-3-dimethylamino-α- and -β-D-*lyxo*-hexofuranoside (20) (75 mg); (iii) methyl 2,3,6-trideoxy-3-dimethylamino-α- and -β-D-*lyxo*-hexopyranoside (19) (70 mg).

9,O(9)-*Dihydromegalomicin A* (22).—Megalomicin A (1) (1 g) in propan-2-ol (50 ml) was treated with sodium borohydride (0·5 g). The mixture was stirred at 25° for 65 h, then diluted with water (25 ml), and most of the propanol was removed *in vacuo*. Aqueous ammonium chloride was added, the mixture was extracted with chloroform, and the extract was washed with water, dried ($MgSO_4$), and evaporated. Preparative t.l.c. on silica gel (50% methanol in chloroform as eluant) gave 9,O(9)-*dihydromegalomicin A* (22) (600 mg) as an amorphous solid, m.p. 124—143° (Found: C, 58·6; H, 9·0; N, 2·6. $C_{44}H_{82}N_2O_{15}$,H_2O requires C, 59·0; H, 9·4; N, 3·1%), *m/e* 878 (M^+), $[\alpha]_D$ −59·1° (MeOH), pK_a 9·0, $\nu_{max.}$ 3450, 2780, 1725, 1720, and 1170 cm^{-1}.

9,O(9)-*Dihydromegalalosamine* (23).—Megalalosamine (12) (1 g) in propan-2-ol (50 ml) was treated with sodium borohydride (0·5 g). The mixture was stirred at 25° for 65 h, then diluted with water (100 ml), and most of the propanol was removed *in vacuo*. The pH was adjusted to 1 with dilute hydrochloric acid, the temperature being maintained at 0°, and the mixture was set aside for 30 min. The solution was eluted through an Amberlite IR45 ion-exchange column; the eluate was evaporated to dryness and the residue was chromatographed on a silica gel column (40% methanol in chloroform as eluant) to give 9,O(9)-*dihydromegalalosamine* (23) (566 mg), which crystallised as needles (from acetone–ether–hexane), m.p. 118—128° (Found: C, 60·65; H, 9·6; N, 3·9. $C_{37}H_{70}N_2O_{12}$ requires C, 60·5; H,

9·5; N, 3·8%), *m/e* 734 (M^+), $[\alpha]_D$ −31·5° (MeOH), pK_a 8·9, $\nu_{max.}$ 3440, 3300, 2780, 1740, and 1165 cm^{-1}.

5-β-D-*Desosaminyloxy*-9,O(9)-*dihydroerythronolide* (24).—Megalomicin A (1) (1 g) in propan-2-ol (50 ml) was treated with sodium borohydride (0·5 g). The mixture was kept at 25° for 5 days, then filtered, and the filtrate was evaporated to dryness *in vacuo*. The residue was taken up in 0·75N-hydrochloric acid (50 ml), and the mixture was kept at 25° for 16 h. The pH was adjusted to 10 with concentrated ammonium hydroxide, and the mixture was extracted with chloroform. The extracts were washed with water, dried ($MgSO_4$), and evaporated to give the crude product (0·89 g), which was chromatographed on silica gel (7% methanol in chloroform as eluant) to give 5-β-D-*desosaminyloxy*-9,O(9)-*dihydroerythronolide* (24) (0·56 g) as crystals, m.p. 226—228° (partially melts at 203—205°, and then resolidifies) (Found: C, 58·95; H, 9·4; N, 2·5. $C_{29}H_{55}NO_{10}$,H_2O requires C, 58·5; H, 9·6; N, 2·35%), *m/e* 577 (M^+), $[\alpha]_D$ 0° (MeOH) and −5·6° (pyridine). pK_a 8·3, $\nu_{max.}$ (Nujol) 3400, 2750, 1730, 1170, and 1040 cm^{-1}, δ 0·89 (3H, t, *J* 7 Hz, $CH_2 \cdot CH_3$), 1·0—1·3 (*ca.* 21H, envelope of Me groups), 2·27 (6H, s, 3′-NMe_2), 4·42 (1H, d, $J_{1'ax,2'ax}$ 7·5 Hz, H-1′), and 4·59 (1H, dd, $J_{13,14}$ 9·5, $J_{13,14'}$ 2 Hz, H-13). Direct comparison with a sample prepared from erythromycin A confirmed the identity and stereochemistry of the product obtained from megalomicin A.

5-β-D-Desosaminyloxy-9,*O*(9)-dihydroerythronolide (24) (300 mg), and benzeneboronic acid (200 mg) were dissolved in dry acetone (25 ml). The solution was heated under reflux for 5 h, then evaporated to dryness. The residue was taken up in tetrahydrofuran and passed through an Amberlite IR45 resin. The eluate was evaporated to give the 9.11-phenylboronate (280 mg). Preparative t.l.c. on silica gel (25% methanol in chloroform as eluant) gave the pure *boronate* as an amorphous white powder, m.p. 200—205° (Found: C, 63·3; H, 8·9; N, 2·2. $C_{35}H_{58}BNO_{10}$ requires C, 63·4; H, 8·75; N, 2·1%), *m/e* 663 (M^+), $[\alpha]_D$ −21·4°, $\nu_{max.}$ ($CHCl_3$) 3410, 2780, 1725, 1600, 1170, and 700 cm^{-1}, δ 0·95 (3H, t, *J* 7 Hz, $CH_2 \cdot CH_3$), 1·0—1·5 (envelope of Me groups), 2·26 (6H, s, 3′-NMe_2), 4·38 (1H, d, $J_{1'ax,2'ax}$ 7·5 Hz, H-1′), 5·26 (1H, dd, $J_{13,14}$ 10, $J_{13,14'}$ 3 Hz, H-13), and 7·25—7·5 and 7·8—7·95 (5H, complex multiplets, aromatic protons).

Methanolysis of 2′,4″-*Di*-O-*acetyl*-3-O-*methylsulphonylmegalalosamine* (17).—The triester (17) (500 mg) was dissolved in methanolic 0·6N-hydrogen chloride (25 ml). The mixture was kept at room temperature for 48 h, then passed through an Amberlite IR45 ion-exchange column, The eluate was evaporated, and the residue chromatographed on silica gel plates (5% methanol in benzene as eluant) to give 2′-O-*acetyl*-3-O-*methylsulphonylerythralosamine* (25) (250 mg), which crystallised from aqueous methanol as needles, m.p. 100—104° (Found: C, 57·05; H, 8·5; N, 2·1; S, 4·3. $C_{32}H_{53}NO_{11}S$ requires C, 58·3; H, 8·0; N, 2·2; S, 4·9%), *m/e* 563 ($M - 96$), $[\alpha]_D$ +33·5°, pK_a 7·1, $\nu_{max.}$ 2780, 1740, 1235, and 1175 cm^{-1}.

Acetylation of Erythromycin A (5).—Erythromycin A (5) (2 g) in dry pyridine (20 ml) was treated with acetic anhydride (2 ml). The mixture was kept at 25° for 16 h, then poured into water and extracted with chloroform. The latter extract was dried ($MgSO_4$) and evaporated, and the residue chromatographed on silica gel plates (5% methanol in chloroform as eluant). The more polar 2″-O-*acetylerythromycin A* (459 mg) crystallised from benzene–hexane as needles, m.p. 128—138°, *m/e* 775 (M^+), $[\alpha]_D$ −62·2°, pK_a 6·5, $\nu_{max.}$ 3490, 2780, 1750, 1700, 1240, 1170, and 1060 cm^{-1}, δ 2·06 (3H, s, 2″-OAc) and 2·27 (6H, s, 3″-NMe_2). The less polar 4′,2″-*di*-O-*acetylerythromycin A* (26) (835 mg) crystallised from benzene–hexane as needles, m.p. 98—132° (solvated), *m/e* 817 (M^+), $[\alpha]_D$ −75·6°, pK_a 6·5, $\nu_{max.}$ 3470, 2780, 1740, 1710, 1235, 1170, and 1050 cm^{-1}, δ 2·06 (3H. s, 2″-OAc), 2·10 (3H, s, 4′-OAc), and 2·30 (6H, s, 3″-NMe_2).

Methanolysis of 4′,2″-*Di*-O-*acetylerythromycin A* (26).—4′,2″-Di-*O*-acetylerythromycin A (26) (600 mg) in methanolic 0·6N-hydrogen chloride (30 ml) was kept at 25° for 64 h. The mixture was passed through an Amberlite IR45 anion-exchange column, dried ($MgSO_4$), and evaporated, and the residue was chromatographed on silica gel plates (5% methanol in chloroform as eluant) to give 2′-O-*acetylerythralosamine* (27) (123 mg) as an amorphous powder after precipitation from acetone–hexane; m.p. 140—150° (decomp.) (Found: C, 62·6; H, 8·5; N, 2·4. $C_{31}H_{51}NO_9$,H_2O requires C, 62·1; H, 8·8; N, 2·3%), *m/e* 581 (M^+), $[\alpha]_D$ +30·8°, $\nu_{max.}$ 3460, 2780, 1750, 1235, 1170, and 1060 cm^{-1}; and methyl cladinoside (26 mg).

2′-O-*Acetyl*-3-O-*methylsulphonylerythralosamine* (25).—2′-*O*-Acetylerythralosamine (27) (50 mg) in dry pyridine (2 ml) was treated with methanesulphonyl chloride (0·5 ml). The mixture was kept at 25° for 16 h, poured into water, and extracted with chloroform. The extract was dried ($MgSO_4$) and evaporated, and the residue was chromatographed on silica gel plates (5% methanol in chloroform as eluant) to give 2′-*O*-acetyl-3-*O*-methylsulphonylerythralosamine (25) (18 mg), which crystallised as needles (from aqueous methanol), m.p. and mixed m.p. 100—104°. The physical constants (i.r., n.m.r., and mass spectra; $[\alpha]_D$) were identical with those of the corresponding product from the methanolysis of 2′,4″-di-*O*-acetyl-3-*O*-methylsulphonylmegalalosamine (17). Mixed t.l.c. on silica gel (5% methanol in chloroform) showed no separation.

Alkaline Hydrolysis of Megalomicin B (2).—Megalomicin B (2) (50 mg) was dissolved in methanolic N-ammonium hydroxide (1 ml) and the solution was kept at 25° for 72 h. Concentration to dryness followed by addition of acetone gave megalomicin A (1) (21 mg) as needles, m.p. and mixed m.p. 250—255°, identical (i.r., $[\alpha]_D$, and mixed t.l.c. on silica gel with 40% methanol in chloroform) with authentic material.

Acetylation of Megalomicin B (2).—Megalomicin B (2) (100 mg) in dry pyridine (1 ml) was treated with acetic anhydride (0·2 ml). The mixture was kept at 25° for 23 h, poured into water, and extracted with ethyl acetate. The extract was dried ($MgSO_4$) and evaporated, and the 2″,4‴-di-*O*-acetylmegalomicin B (8) (46 mg) crystallised from ether–pentane as needles, m.p. 198—201° (Found: C, 57·7; H, 8·4; N, 2·65. Calc. for $C_{50}H_{86}N_2O_{18}$,$2H_2O$: C, 57·8; H, 8·7; N, 2·7%), $[\alpha]_D$ −78·5°, identical (i.r. and n.m.r. spectra and mixed t.l.c. on silica with 10% methanol in chloroform) with 3′,2″,4‴-tri-*O*-acetylmegalomicin A (8).

Mild Acidic Hydrolysis of Megalomicin B (2).—Megalomicin B (2) (200 mg) was dissolved in 0·75N-hydrochloric acid (10 ml). The mixture was kept at 25° for 20 h and poured with stirring into concentrated aqueous sodium hydrogen carbonate. The solution was extracted with chloroform; the extract was dried ($MgSO_4$) and evaporated, and the residue was chromatographed on silica gel plates (20% methanol in chloroform as eluant) to give megalalosamine (12) (81 mg), identical (i.r., n.m.r., $[\alpha]_D$, pK_a, and mixed t.l.c. on silica gel with 40% methanol in

chloroform) with megalalosamine obtained by mild acidic hydrolysis of megalomicin A (1).

Evaporation of the aqueous layer followed by extraction with boiling benzene gave 4-O-acetyl-α- and β-L-mycarose (28) (5 mg), which was combined with the less polar band (19 mg) from the preparative t.l.c. to give the acetate (24 mg) as a gum, *m/e* 205 ($M^+ + 1$), $[\alpha]_D^{25}$ −69·9° (after mutarotation), $\nu_{max.}$ 3400, 1740, 1225, and 1040 cm⁻¹.

1,4-*Di-O-acetyl-β-L-mycarose* (14).—4-*O*-Acetyl-α- and -β-L-mycarose (28) (50 mg) in dry pyridine (10 ml) was treated with acetic anhydride (1 ml). The mixture was kept at 25° for 16 h, then worked up as described before to give 1,4-di-*O*-acetyl-β-L-mycarose (14) (53 mg), which crystallised as prisms from hexane, m.p. and mixed m.p. 91—92°, identical (i.r., n.m.r., $[\alpha]_D$) with the corresponding acetate prepared from L-mycarose (13).

Alkaline Hydrolysis of Megalomicin C_1 (3).—Megalomicin C_1 (3) (75 mg) was dissolved in methanolic 0·5% sodium hydroxide (1 ml) [from aqueous 50% sodium hydroxide (1 ml) and methanol (50 ml)]. The solution was kept at 25° for 24 h, diluted with water, and extracted with methylene chloride. The extract was dried ($MgSO_4$) and evaporated, and the residue was crystallised from acetone to give megalomicin A (1) (21 mg) as needles, m.p. 252—255°, identical (i.r. spectrum and mixed t.l.c. on silica gel with 33% methanol in chloroform) with authentic material.

2″,4‴-*Di-O-acetylmegalomicin C_1* (10).—Megalomicin C_1 (3) (12·5 g) in dry pyridine (68 ml) was treated with acetic anhydride (6·25 ml). The mixture was kept at 25° for 16 h, then poured into water (2·5 l), and the pH was adjusted to 8·5 with 8% ammonium hydroxide (40 ml). The 2″,4‴-*di-O-acetylmegalomicin C_1* (10) (10·2 g) was filtered off and crystallised from aqueous acetone to give needles, m.p. 240—243° (Found: C, 59·4; H, 8·3; N, 2·65. $C_{52}H_{88}N_2O_{19}$ requires C, 59·75; H, 8·5; N. 2·7%), *m/e* 1044 (M^+), $[\alpha]_D$ −89·0°, pK_a 7·4, $\nu_{max.}$ 3550, 2800, 1750, 1700, 1250, 1235, 1220, 1175, and 1050 cm⁻¹.

Mild Acidic Hydrolysis of Megalomicin C_1 (3).—Megalomicin C_1 (3) (1 g) was dissolved in 0·75N-hydrochloric acid (50 ml). The solution was kept at 25° for 20 h, neutralised with sodium hydrogen carbonate, and extracted with chloroform. The extract was dried ($MgSO_4$) and evaporated, and the residue was chromatographed on silica gel plates (20% methanol in chloroform as eluant). The more polar megalalosamine (12) (158 mg) was identical (i.r., n.m.r., $[\alpha]_D$, mixed t.l.c. on silica gel with 40% methanol in chloroform) with that obtained by acidic hydrolysis of megalomicin A (1). The less polar 3,4-di-*O*-acetyl-α- and -β-L-mycarose (29) (118 mg) was obtained as a gum (Found: C, 54·1; H, 7·65. Calc. for $C_{11}H_{18}O_6$: C, 53·65; H, 7·4%), *m/e* 186 ($M^+ - 60$), $[\alpha]_D^{25}$ −86·3° (after mutarotation), $\nu_{max.}$ 3550, 3400, 1740, 1220, and 1040 cm⁻¹.

1,3,4-*Tri-O-acetyl-β-L-mycarose* (30).—3,4-Di-*O*-acetyl-α- and -β-L-mycarose (29) (25 mg) in dry pyridine (10 ml) was treated with acetic anhydride (0·5 ml). The mixture was kept at 25° for 16 h and worked up as before to give 1,3,4-*tri-O-acetyl-β-L-mycarose* (30) (11 mg), which crystallised from benzene–hexane as needles, m.p. 133—135° (Found: C, 54·6; H, 7·2. $C_{13}H_{20}O_7$ requires C, 54·2; H, 7·0%), *m/e* 228 ($M^+ - 60$), $[\alpha]_D$ −61·3°, $\nu_{max.}$ 1750, 1225, and 1050 cm⁻¹.

Alkaline Hydrolysis of Megalomicin C_2 (4).—Megalomicin C_2 (4) (75 mg) was subjected to alkaline hydrolysis as in the case of megalomicin C_1 (3) to give megalomicin A (1) (29 mg), which crystallised as needles (from acetone), m.p. 252—255°, identical (i.r. spectrum and mixed t.l.c. on silica gel with 40% methanol in chloroform) with authentic material.

2″,4‴-*Di-O-acetylmegalomicin C_2* (31).—Megalomicin C_2 (4) (250 mg) in dry pyridine (2·5 ml) was treated with acetic anhydride (0·25 ml). The mixture was kept at 25° for 16 h, concentrated *in vacuo*, diluted with acetone (7 ml), and treated with aqueous 5% ammonium hydroxide to give 2″,4‴-*di-O-acetylmegalomicin C_2* (31) (204 mg) as a crystalline solid. Recrystallisation from aqueous acetone gave needles, m.p. 236—237° (Found: C, 59·9; H, 8·5; N, 2·7. $C_{53}H_{90}N_2O_{19}$ requires C, 60·1; H, 8·6; N, 2·65%), *m/e* 1058 (M^+), $[\alpha]_D$ −86·9°, pK_a 7·4, $\nu_{max.}$ (Nujol) 3410, 2780, 1750, 1740, 1690, 1240, 1225, 1170, 1155, and 1050 cm⁻¹.

Mild Acidic Hydrolysis of Megalomicin C_2 (4).—Megalomicin C_2 (4) (500 mg) dissolved in 0·75N-hydrochloric acid (25 ml) was kept at 25° for 20 h. The mixture was worked up as in the case of megalomicin C_1 to give the more polar megalalosamine (12) (87 mg), identical (i.r., n.m.r., $[\alpha]_D$, mixed t.l.c. on silica gel with 40% methanol in chloroform) with megalalosamine obtained by acid hydrolysis of megalomicin A (1). The less polar 3-*O*-acetyl-4-*O*-propionyl-α- and -β-L-mycarose (32) (80 mg) was obtained as a gum (Found: C, 55·0; H, 7·7. Calc. for $C_{12}H_{20}O_6$: C, 55·4; H, 7·75%), *m/e* 200 ($M - 60$), $[\alpha]_D^{25}$ −78·3 (after mutarotation), $\nu_{max.}$ 3600, 3400, 1740, 1235, and 1040 cm⁻¹.

(4S,5S)-3-*Methyl-4-propionyloxyhex-2-en-5-olide* (34).—3-*O*-Acetyl-4-*O*-propionyl-α- and -β-L-mycarose (32) (127 mg) was dissolved in water (8 ml), and tetrahydrofuran (2 ml) and barium carbonate (0·3 g) were added. Bromine water [bromine (0·14 ml) in water (10 ml)] was added in 0·5 ml portions to the stirred mixture at 25°. As soon as no starting material remained (t.l.c.) the addition of bromine water was stopped, the mixture was filtered, and the residue was washed with chloroform. The filtrate was shaken: the chloroform layer was separated, dried ($MgSO_4$), and evaporated to give the lactone (33) as an oil. The crude lactone (33) was dissolved in dry benzene (10 ml) containing toluene-*p*-sulphonic acid (1 mg), and the mixture was heated on a steam-bath for 6 h, then filtered through a short column of neutral, grade 1 alumina; the alumina was washed with chloroform. Evaporation of the eluate followed by preparative t.l.c. on silica gel (2% methanol in chloroform as eluant) gave the *unsaturated lactone* (34) (40 mg) as an oil, (Found: C, 60·7; H, 7·3. $C_{10}H_{14}O_4$ requires C, 60·6; H, 7·1%), *m/e* 198 (M^+), $[\alpha]_D$ −94·1°, $\lambda_{max.}$ (MeOH) 212 nm (ε 12,600), $\nu_{max.}$ 1740, 1690, and 1165 cm⁻¹, δ 1·19 (3H, t, *J* 7·5 Hz, Me of propionate), 1·39 (3H, d, $J_{5,6}$ 7 Hz, 5-CH_3), 1·95 (3H, d, *J* 1·5 Hz, 3-CH_3), 2·43 (2H, q, *J* 7·5 Hz, CH_2 of propionate), 4·52 (1H, dq, $J_{5,6} = J_{4,5}$ = 7 Hz, H-5), 5·38 (1H, d, $J_{4,5}$ 7 Hz with additional long range coupling of 1 Hz, H-4), and 5·93 (1H, m, *J* 1·5 and 1 Hz, H-2).

Methanolysis of Megalomicin C_2 (4).—Megalomicin C_2 (4) (500 mg) was dissolved in methanolic 0·6N-hydrogen chloride (30 ml). The mixture was kept at 25° for 48 h, then passed through an Amberlite IR45 ion-exchange column. The eluate was evaporated and the residue chromatographed on silica gel plates (10% methanol in chloroform as eluant) to give methyl 3-*O*-acetyl-4-*O*-propionyl-α- and -β-L-mycaroside (35) (50 mg) as a gum (Found: C, 57·0; H, 8·2. Calc. for $C_{13}H_{22}O_6$: C, 56·9; H, 8·1%), *m/e* 273 ($M^+ - 1$), $[\alpha]_D$ −128·9°, $\nu_{max.}$ 1740, 1240, 1175, and 1055 cm⁻¹. The erythralosamine (21), and methyl D-rhodosaminide [(19) and (20)] fractions were not separated.

Methyl α- *and* β-L-*Mycaroside* (18).—L-Mycarose (13) (500 mg) was dissolved in methanolic 0·6N-hydrogen chloride (25 ml). The mixture was kept at 25° for 16 h, then passed through an Amberlite IR45 ion-exchange column. The eluate was evaporated, and the residue chromatographed on silica gel (5% methanol in chloroform as eluant) to give *methyl* α-L-*mycaroside* (18α) (80 mg) as a gum which sublimed at 25—40° and 0·1 mmHg to give needles, m.p. 60—61° (Found: C, 52·6; H, 10·6. $C_8H_{16}O_4$ requires C, 54·5; H, 9·15%), $[\alpha]_D$ −138·1°, $\nu_{max.}$ 3500, 1060, and 1050 cm^{-1}, and *methyl* β-L-*mycaroside* (18β) (326 mg) as an oil (Found: C, 53·7; H, 9·0%), *m/e* 176 (M^+), $[\alpha]_D$ +20·8°, $\nu_{max.}$ 3400, 1080, and 1050 cm^{-1}.

Acylation of Methyl α- *and* β-L-*Mycaroside* (18).—Methyl α-L-mycaroside (18α) (3 g) in dry pyridine (25 ml) was treated with acetic anhydride (4 ml). The mixture was kept at 25° for 16 h, treated with methanol (25 ml), and set aside for 4 h. Evaporation *in vacuo* followed by preparative t.l.c. on silica gel (2% methanol in chloroform as eluant) gave *methyl* 4-O-*acetyl*-α-L-*mycaroside* (36a) (3 g) as an oil (Found: C, 54·95; H, 8·3. $C_{10}H_{18}O_5$ requires C, 55·0; H, 8·3%), *m/e* 218 (M^+), $[\alpha]_D$ −166·4°, $\nu_{max.}$ 3550, 1750, 1240, and 1050 cm^{-1}.

In a similar manner methyl β-L-mycaroside (18β) (3 g) was acetylated to give *methyl* 4-O-*acetyl*-β-L-*mycaroside* (36β) (2·9 g) as prisms (from acetone–hexane), m.p. 70—71° (Found: C, 55·0; H, 8·3%), *m/e* 218 (M^+), $[\alpha]_D$ −4·1° $\nu_{max.}$ 3600, 3480, 1750, 1225, 1050, and 1035 cm^{-1}.

Similarly methyl α-L-mycaroside (18α) (3 g) was propionylated with propionic anhydride (4 ml) to give *methyl* 4-O-*propionyl*-α-L-*mycaroside* (37α) (2·8 g) as a gum (Found: C, 56·7; H, 8·9. $C_{11}H_{20}O_5$ requires C, 56·9; H, 8·7%), *m/e* 214 (M^+ − 18), $[\alpha]_D$ −164·8°, $\nu_{max.}$ 3510, 1750, 1180, and 1050 cm^{-1}; and methyl β-L-mycaroside (18β) (3 g) gave *methyl* 4-O-*propionyl*-β-L-*mycaroside* (37β) (3·0 g) as needles (from acetone–hexane), m.p. 80—81° (Found: C, 57·0; H, 8·9%), *m/e* 201 (M^+ − 31), $[\alpha]_D$ −11·3°, $\nu_{max.}$ 3660, 3440, 1750, 1160, 1080, and 1050 cm^{-1}.

Acylation of the Methyl 4-O-*Acyl*-α- *and* -β-L-*mycarosides*.—Methyl 4-*O*-acetyl-α-L-mycaroside (36α) (1 g) in dry pyridine (25 ml) was treated with propionic anhydride (4 ml). The mixture was heated on a steam-bath for 16 h, then treated with methanol (25 ml), set aside for 4 h, and evaporated. The residue was chromatographed on silica gel plates (1% methanol in chloroform as eluant) to give *methyl* 3-O-*acetyl*-4-O-*propionyl*-α-L-*mycaroside* (35α) (0·5 g) as a gum (Found: C, 56·8; H, 7·9. $C_{13}H_{22}O_6$ requires C, 56·9; H, 8·1%), *m/e* 274 (M^+), $[\alpha]_D$ −183·7°, $\nu_{max.}$ 1750, 1245, 1175, and 1055 cm^{-1}.

In a similar manner methyl 4-*O*-acetyl-β-L-mycaroside (36β) (1 g) gave *methyl* 3-O-*acetyl*-4-O-*propionyl*-β-L-*mycaroside* (35β) (0·4 g) as a gum (Found: C, 56·8; H, 7·9%), *m/e* 243 (M^+ − 31), $[\alpha]_D$ −32·4°, $\nu_{max.}$ 1745, 1240, 1150, and 1045 cm^{-1}.

Similarly, methyl 4-*O*-propionyl-α-L-mycaroside (37α) (1 g) was acetylated with acetic anhydride (4 ml) to give *methyl* 4-O-*acetyl*-3-O-*propionyl*-α-L-*mycaroside* (38α) (0·8 g) as a gum (Found: C, 56·8; H, 7·9. $C_{13}H_{22}O_6$ requires C, 56·9; H, 8·1%), *m/e* 274 (M^+), $[\alpha]_D$ −180·2°, $\nu_{max.}$ 1750, 1240, 1190, and 1050 cm^{-1}; and methyl 4-*O*-propionyl-β-L-mycaroside (37β) (1 g) gave *methyl* 4-O-*acetyl*-3-O-*propionyl*-β-L-*mycaroside* (38β) (0·8 g) as a gum (Found: C, 56·7; H, 8·0%), *m/e* 274 (M^+), $[\alpha]_D$ −34·6°, $\nu_{max.}$ 1750, 1240, 1150, and 1050 cm^{-1}.

We thank Dr. M. Yudis, and his colleagues for analytical and spectral services, and the Morgan–Schaffer Corporation, Montreal, Canada, for the mass spectra.

[2/1699 *Received*, 18*th* ***July***, 1972]