Communications to the editor

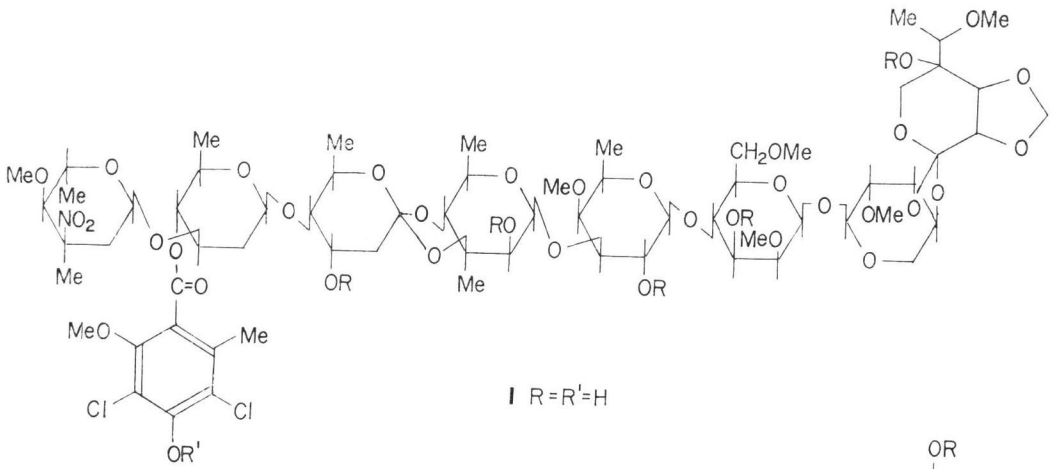
STRUCTURAL STUDIES ON CURAMYCINS

Sir:

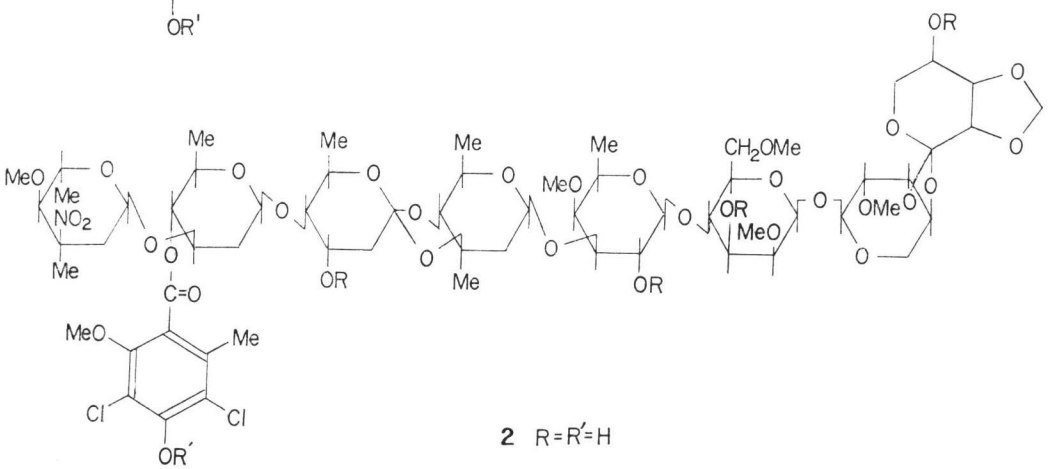
Curamycins[1,2], consisting of at least three potent antibiotics, are produced by *Streptomyces curacoi*. In this communication we wish to propose a tentative structure of curamycin A*, the major component of the above antibiotic complex.

It is known that curamycins belong to the group of oligosaccharide antibiotics. Extensive chemical degradation and spectroscopic evidence led to the structural elucidation of everninomicins B(**1**)[3], C(**2**)[4], D(**3**)[5], and 2(**4**)[6], the first among oligosaccharide antibiotics whose structures have been completely determined. Recently, the structures of flambamycin (**5**)[7] and avilamycins A(**6**) and C(**7**)[8], the other members of this group, have been reported. Early chemical degradation studies on curamycins[1] have shown curacin (**16**), L-lyxose(**17**), and curacose(**18**) (4-O-methyl-D-fucose) to be structural components of curamycin.

Curamycin A(**8**), $C_{59}H_{84}Cl_2O_{32}$, m.p. 192~194°C, ν_{max} 1715, 1735 cm^{-1} (carbonyl groups) is a colourless solid. On methylation with diazomethane curamycin A forms a crystalline monomethyl ether (**9**), $C_{60}H_{86}Cl_2O_{32}$, m.p. 204~206°C. The ^{13}C NMR spectrum of compound **9** shows signals at δ 205.1 (ketone), 169.2, 166.2 (esters), 154.2, 151.8, 133.1, 126.5, 126.0, 120.9 (aromatic), 118.9, 120.2 (orthoesters), 94.8, 96.1, 100.8, 101.5, 104.5 (anomeric), 96.9 (methylene dioxy), 59.1, 61.8, 62.0, 62.3, 60.6 (methoxyls),

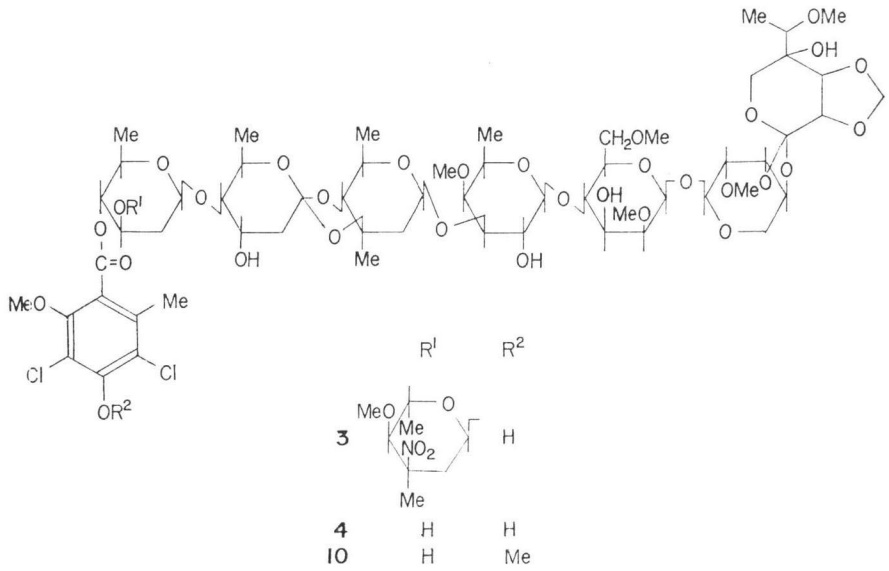


1 R=R'=H

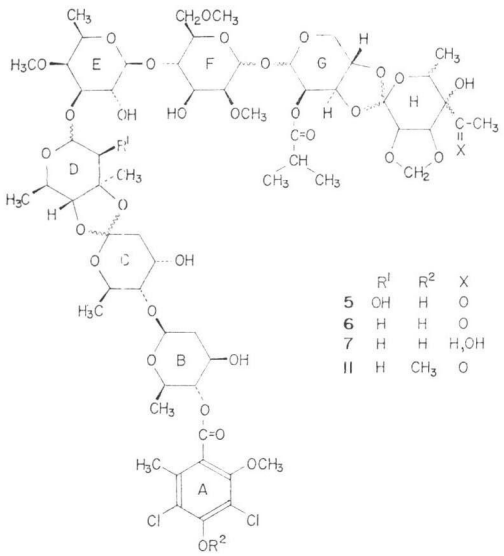


2 R=R'=H

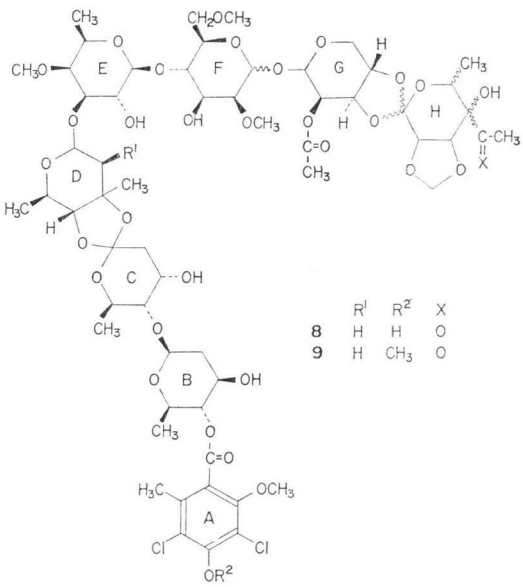
* Curamycin A was separated from the other curamycins by chromatography on a silica gel column.



	R^1	R^2
3		H
4	H	H
10	H	Me



	R^1	R^2	X
5	OH	H	O
6	H	H	O
7	H	H	H,OH
11	H	CH_3	O



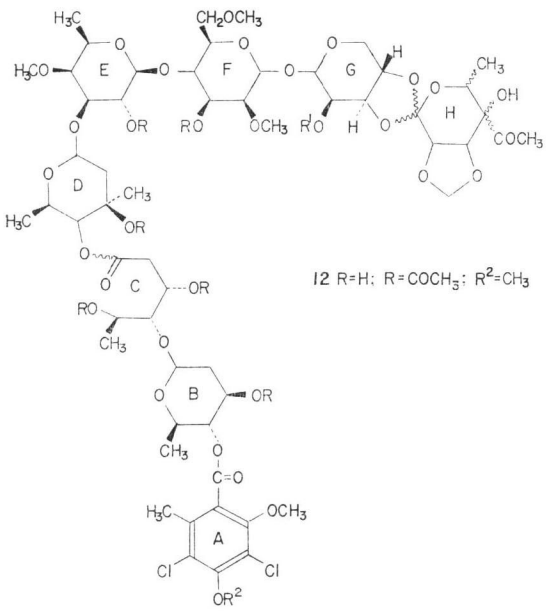
	R^1	R^2	X
8	H	H	O
9	H	CH_3	O

39.0, 40.1, 43.6 (methylene), 13.5, 16.1, 17.4, 17.6, 18.5, 19.7, 20.5, 25.3 (methyls).

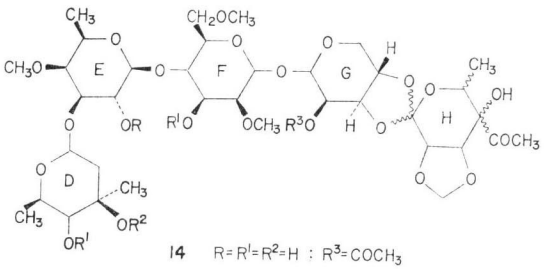
The above spectral data when compared with the CMR spectra of methyl ethers of everninomicin 2 **(10)**, avilamycin A **(11)**, and flambamycin **(5)** shows not only that curamycin A belongs to the oligosaccharide group of antibiotics but also the similarity of its structure to that of flambamycin and avilamycin A.

Methyl ether of curamycin A **(9)** on mild acidic hydrolysis (*p*-TSA/THF) yielded compound **(12)** which on treatment with diazomethane yielded lactone **(13)** and compound **(14)**. The above lactone is a colourless crystalline solid, $C_{22}H_{28}Cl_2O_{10}$(M$^+$522), m.p. 200~201°C, which was found to be identical (m.p., CD, nmr, ms) with an authentic sample of **13** prepared from the methyl ether of everninomicin 2(**10**).

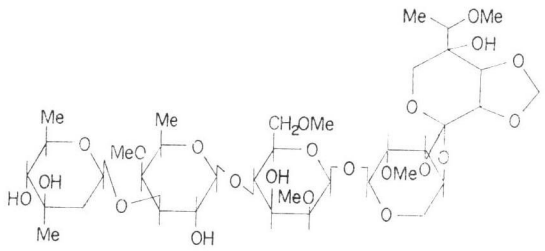
Compound **14** is a colourless crystalline solid, $C_{38}H_{60}O_{23}$, m.p. 261~263°C, ν_{max} 1710 (ketone), 1735 cm^{-1} (ester), δ 5.57 (H_2; broad singlet), 5.28 (1H; broad singlet), 5.14 (2H; broad singlet), 4.9, 4.75 (3H; m), 3.68, 3.62, 3.42 (methoxyls), 2.35 (3H; $\underline{CH_3}$–CO), 2.13 (3H; OCO–$\underline{CH_3}$),



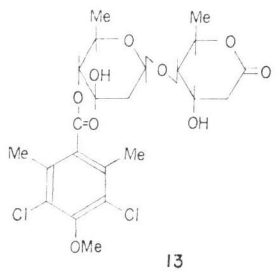
12 R=H; R=$COCH_3$; R^2=CH_3



14 R=R'=R^2=H : R^3=$COCH_3$



15



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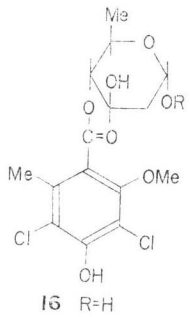
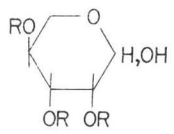
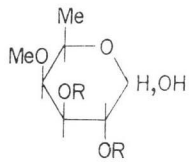


16 R=H



17 R=H



18 R=H

1.35~1.25 (three methyl groups), 1.10 (3H; J=7 Hz; $\underline{CH_3}$–CH). The ^{13}C NMR spectrum of compound **14** shows signals at δ 205.9 (ketone), 169.3 (ester), 119.1 (orthoester), 59.3, 61.9, 62.1 (methoxyls), 13.5, 16.2, 18.5, 20.4, 20.6, 25.2 (methyls).

Recently we reported a convenient method for the determination of the molecular weight of oligosaccharides using negative ion chemical ionization mass spectrometry (NCIMS)[9]. Compound **14** when subjected to NCIMS using CF_2Cl_2 as the regent gas displayed a pseudomolecular chloride adduct ion $(M+Cl)^-$ at *m/e* 919 and 921 corresponding to a molecular weight of 884 ($C_{38}H_{60}O_{23}$). A fragment ion at *m/e* 774, 776 corresponding to $(M-D+Cl)^-$ was the only other ion obtained in the high mass region of the spectrum. This is the type of fragmentation which we had observed in the case of the everninomicin antibiotics[9]. The tentative assignment of the structure of compound **14** is based on the above observations as well as a direct comparison of CMR and PMR spectra of **14** with those of olgose (**15**). In the light on the earlier degradation[2] of curamycin to **17**, and **18**, as well as 2,6-di-O-methyl-D-mannose, configuration of rings E, F, and G (except the anomeric carbons) can be assigned. The isolation of **13** by us from the degradation of curamycin A, defines the configuration of rings A, B, and C. The configuration of ring D is proposed on the basis of the close similarity of spectral data of curamycin A to the known compounds avilamycin A and everninomicin D which bear the same ring D. The stereochemistry of ring H remains unassigned.

To account for the formation of lactone (**13**) and compound **14** from the methyl ether of curamycin A(**9**) and the presence of two ortho-ester carbons in compound **9** we propose the structure of curamycin A as **8** and its methyl ether as **9**.

Further work, including X-ray analysis, is in progress to confirm the above structural assignments and to determine stereochemistry*. In a future communication we plan to report the structure of the two minor components of the curamycin complex.

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* The close similarity of the CMR spectra of **14** and **15** indicates very similar stereochemistry for these compounds.

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