# Mass Spectral Studies on Aminocyclitol Antibiotics

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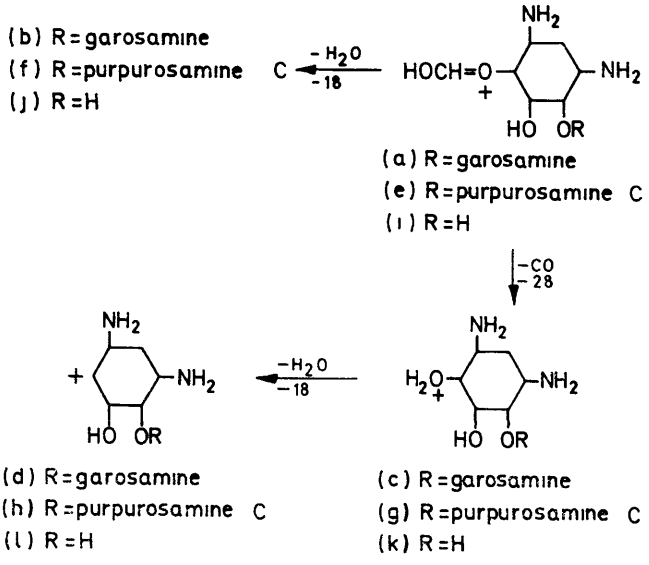
*Summary* Some key features of the mass spectral fragmentation patterns of aminocyclitol antibiotics are discussed

MASS spectrometry has been applied to aminocyclitol antibiotics as their *N*-acetyl-*O*-trimethylsilyl,[1] *N*,*O*-trimethylsilyl[2] and *N*-acetyl-per-*N*,*O*-methyl[3] derivatives and

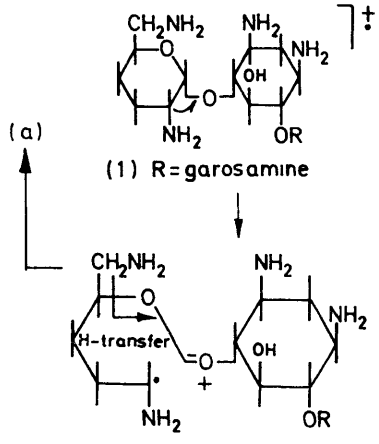
more recently the spectra of underivatised aminocyclitols[4] have provided useful structural information Previous work has for the most part emphasized only the expected glycosidic cleavages however we wish to draw attention to further useful information which can be drawn from spectra of antibiotics of the gentamicin [3] [4a] sisomicin,[4b] tobramycin,[5] and kanamycin family

In general underivatised aminocyclitols gave $(M + 1)^+$ peaks as the highest mass ions with smaller $M^+$ ions except in the case of sisomicin (**6**) where a strong $M^+$ ion was observed † In many cases these ions were sufficiently intense to permit unequivocal assignment of molecular formulae by accurate mass measurement whereas the usual microanalytical techniques gave poor results because of hydration Using carefully purified samples $(M + 1)^+$ peaks were easily discernable even in gentamicins A[6], B[7] and $X_2$[8] which contain numerous free hydroxy groups Three prominent series of fragment ions were observed for the gentamicins $C_{1a}$ $C_1$ $C_2$ B $X_2$ [(**1**)—(**5**)] sisomicin (**6**), gentamicin A (**7**), kanamycin A (**8**), and tobramycin (**9**), and are shown in Scheme 1, for gentamicin $C_{1a}$ (**1**) ‡ The




SCHEME 1

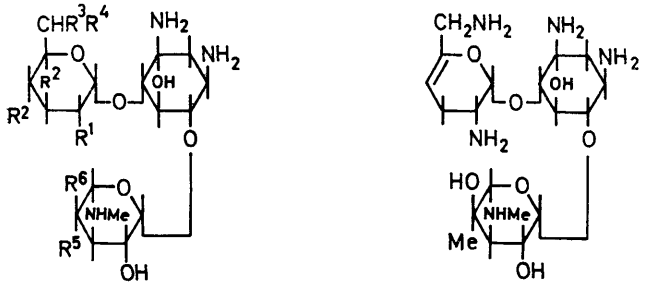
formation of the protonated formyl ions§ (a) and (e) may be rationalised by cleavage of the $C_1$–$C_2$ bonds in the respective sugar units followed by fission of the $C_5$–O bond




SCHEME 2

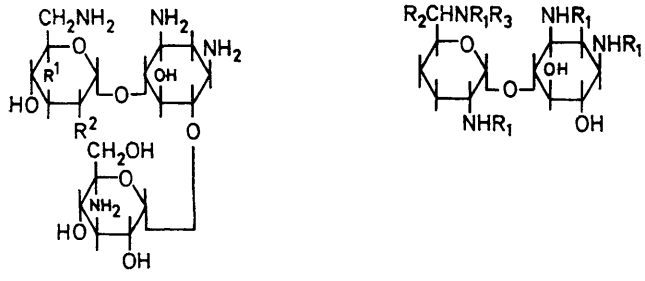
accompanied by proton transfer as outlined in Scheme 2 Subsequent losses of carbon monoxide and water from ions (a) and (e) give rise to prominent ions in the spectrum

The series of ions (i)—(l) are usually very intense Their formation is most easily explained by glycosidic cleavage of ions (a) and (e) accompanied by proton transfer to give ion (i) with subsequent losses of carbon monoxide and water as



| | $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ |
|---|---|---|---|---|---|---|
| (**1**) | $NH_2$ | H | $NH_2$ | H | Me | OH |
| (**2**) | $NH_2$ | H | NHMe | Me | Me | OH |
| (**3**) | $NH_2$ | H | $NH_2$ | Me | Me | OH |
| (**4**) | OH | OH | $NH_2$ | H | Me | OH |
| (**5**) | $NH_2$ | OH | OH | H | Me | OH |
| (**7**) | $NH_2$ | OH | H | OH | OH | H |

(**6**) Sisomicin



| | $R^1$ | $R^2$ |
|---|---|---|
| (**8**) | OH | OH |
| (**9**) | H | $NH_2$ |



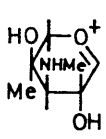
| | $R^1$ | $R^2$ | $R^3$ |
|---|---|---|---|
| (**10**) | H | H | H |
| (**11**) | H | Me | Me |
| (**12**) | H | Me | H |
| (**13**) | Ac | H | H |
| (**14**) | Ac | Me | Me |
| (**15**) | Ac | Me | H |

† Mass spectra were obtained using a Varian MAT CH5 spectrometer at 70 eV with a probe temperature of 230—250° The direct inlet technique was used High resolution measurements were carried out using an AEI MS 902B or MS 30 spectrometer

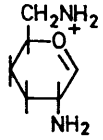
‡ The structures depicted for the ions represent one of several isomeric possibilities and are intended only to be illustrative of the processes involved

§ Ions of this type have also been recognised in the mass spectra of the megalomicin antibiotics due to cleavage of the desosamine moiety [9]

indicated. The pseudodisaccharide gentamines[3] (**10**)—(**12**) exhibit the ions (i)—(l) shown in Scheme 1 and their tetra-*N*-acetates (**13**)—(**15**) give similar ions displaced to appropriately higher mass. In the case of tetra-*N*-acetylgentamine $C_2$ (**15**) the loss of carbon monoxide (*m/e* 275 → *m/e* 247) is accompanied by an appropriate metastable transition (222·0 ± 0·2, theory 221·85).



(m)



(n)

The formation of the fragment ions outlined together with the ions (m) and (n) formed by the normal glycosidic cleavages may be used to determine the compositions of both the sugar and cyclitol units. The presence of the ions (a)—(h) may be used to demonstrate that the sugar units are glycosidically linked to the aglycone in antibiotics of unknown structure. The only aminocyclitol antibiotics examined to date which do not show the above fragments are those bearing a 2-deoxysugar[10] in which the initial $C_1$–$C_2$ cleavage (Scheme 2) is energetically less favourable.

High resolution mass measurements of selected compounds have confirmed the compositions of the fragment ions discussed. Considerable further information may be derived from study of the remaining fragment ions in the mass spectra, details of which will be given in the full publication.

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