

Studies in Organic Mass Spectrometry. III (1). Adenosine 8-Cyclonucleosides (2).

Masazumi Ikeda, Yasumitsu Tamura and Morio Ikehara

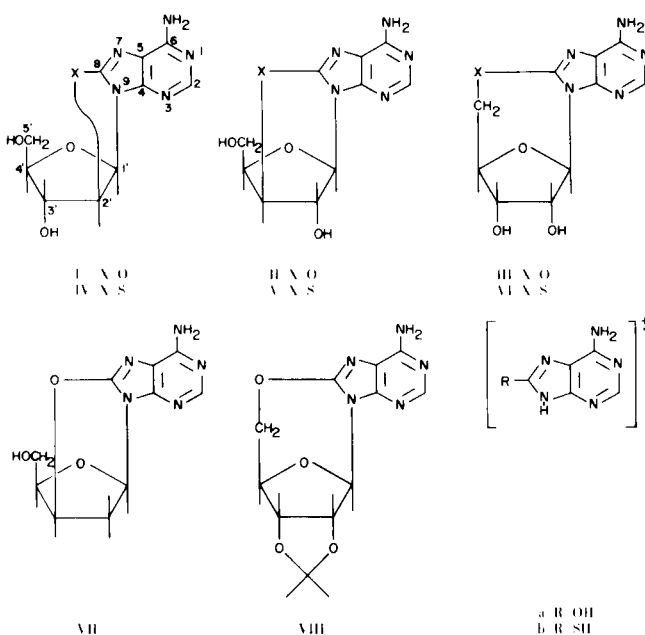
Faculty of Pharmaceutical Sciences, Osaka University

The mass spectra of purine 8-cyclonucleosides have been determined and compared with those of purine nucleosides. The mass spectra of the former are characterized not only by the presence of an intense molecular ion but also by the presence of the peaks corresponding to 8-oxy (or 8-thio) adenine and its protonated form due to a double and triple hydrogen transfer.

During the course of synthetic studies of some purine 8-cyclonucleosides (3), it was desirable to use mass spectrometry as an analytical method. We therefore examined the mass spectra of a series of 8-*O*- and 8-*S*-cycloadenosines with a view to reaching some generalizations about their behavior upon electron impact. Since the mass spectra of purine nucleosides have been extensively studied (4-5), it was also of interest to compare the mass spectra of the nucleosides and cyclonucleosides.

The relative abundances of some common ions in the spectra of cyclonucleosides are summarized in Table I. The compositions of these ions were established by exact mass measurements on I and IV.

In contrast to purine nucleosides (4-5) which show a small molecular ion peak, the mass spectra of the cyclonucleosides are characterized by a strong molecular ion peak which is frequently the base peak (see Fig. 1). In the low voltage spectra (13 ev) of I-III the molecular ion peak carries most (>80%) of the total ion current, reflecting the high stability of the ion radical.



The most important fragment ions in the mass spectra (see Fig. 1) of the three isomeric 8-*O*-cyclonucleosides (I-III) are intense peaks at masses 151 ($\text{C}_5\text{H}_5\text{N}_5\text{O}$) and 152 ($\text{C}_5\text{H}_6\text{N}_5\text{O}$), formulated as the 8-oxyadenine ion radical (*a*) and its protonated form (*a*+1). These two species are also observed in the spectra of the 2'-deoxy analog VII and even for the 2',3'-isopropylidene derivative VIII, and are shifted to *m/e* 167 ($\text{C}_5\text{H}_5\text{N}_5\text{S}$, *b*) and 168 ($\text{C}_5\text{H}_6\text{N}_5\text{S}$, *b*+1) in the mercapto series (IV-VI). Their formation necessarily involves a double and triple (6) hydrogen transfer to the charged species. This kind of hydrogen transfer behavior closely parallels that observed in purine nucleosides (4-5) except that a single and double hydrogen rearrangement takes place in the latter cases. It should be noted that the tendency for the rearrangement of three hydrogen atoms (formation of *a*+1 or *b*+1) is much more pronounced in the case of 8,5'-derivatives III or VI than it is for the 8,2'- and 8,3'-isomers. The species *a* (or *b*) decomposes further by expulsion of HCN to give the peak at *m/e* 124 ($\text{C}_4\text{H}_4\text{N}_4\text{O}$) (or *m/e* 140).

The other prominent common peaks in the upper mass range of I-III are those of masses 176 ($\text{C}_7\text{H}_6\text{N}_5\text{O}$) and 164 ($\text{C}_6\text{H}_6\text{N}_5\text{O}$), which are shifted to *m/e* 192 ($\text{C}_7\text{H}_6\text{N}_5\text{S}$) and 180 ($\text{C}_6\text{H}_6\text{N}_5\text{S}$), respectively, in the spectra of the mercapto-analogs (IV-VI). Although it is evident from the compositions of these ions that the 8-oxy- (or 8-thio-) adenine skeleton is retained in both the ions, it is not possible to deduce the structures of these ions without isotopic labeling experiments.

The following three peaks are characteristic of the spectra of 8,2'- and 8,3'-cyclonucleosides. (i) The minor but diagnostically important ion at *M*-31 corresponds to the elimination of CH_2OH (C-5') from the molecular ion. (ii) The prominent *M*-59 ion ($\text{C}_8\text{H}_8\text{N}_5\text{O}_2$ from I and $\text{C}_8\text{H}_8\text{N}_5\text{OS}$ from IV) is due to the total loss of $\text{C}_2\text{H}_3\text{O}_2$ from the molecular ion. Since the *m/e* 206 (*M*-59) ion in the mass spectrum of II is shifted to *m/e* 190 in the spectrum of the 2'-deoxy analog VII, the former must involve loss of C-4', C-5' and pentose ether oxygen. (iii) The *m/e* 188 ion ($\text{C}_8\text{H}_6\text{N}_5\text{O}$) in the spectra of I and

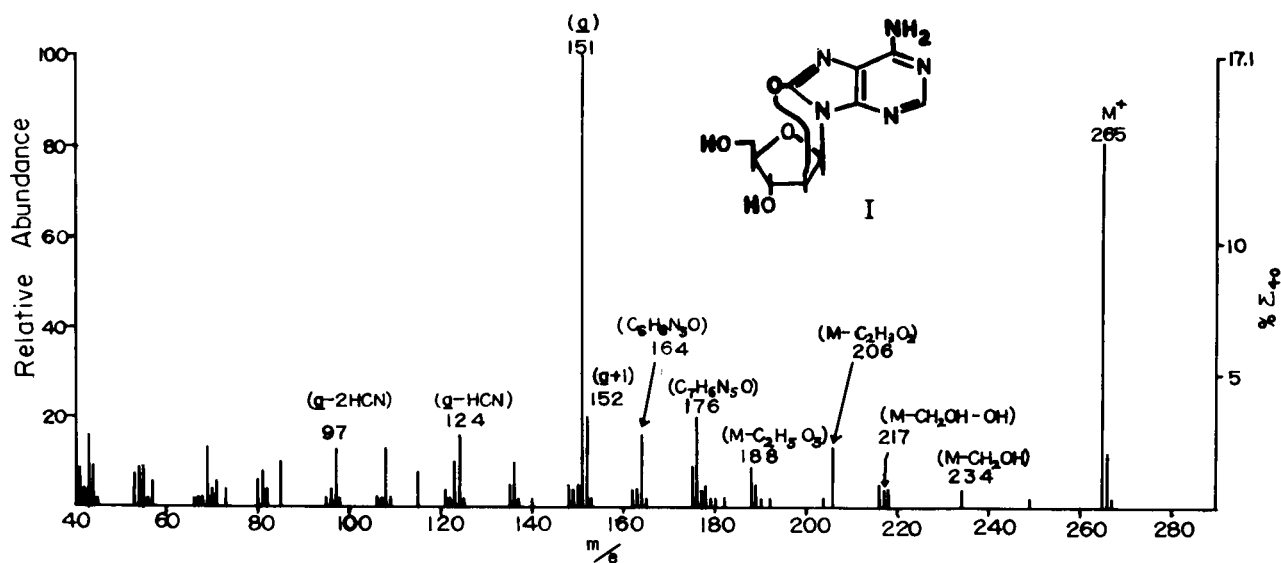


Fig. 1. Mass Spectrum of 8,2'-Anhydro-8-oxy-9- β -D-arabinofuranosyladenine (I).

TABLE I

Principal Mass Spectral Peaks in the Spectra (70 ev) of 8-O- and 8-S-Cycloadenosines (% Relative Abundance (a))

Compound	M	M-31	M-48	M-59	M-77	M-89	M-101	a+1 (b+1)	a (b)	a (b)- HCN	Other Peaks	% Σ_{40} / % RI
I	265 (81)	234 (4)	217 (4)	206 (13)	188 (9)	176 (20)	164 (16)	152 (15)	151 (100)	124 (16)	136 (b) (10)	0.17
II	265 (53)	234 (2)	---	206 (33)	188 (21)	176 (9)	164 (44)	152 (25)	151 (100)	124 (20)	136 (b) (21)	0.16
III	265 (84)	---	---	---	---	176 (14)	164 (8)	152 (100)	151 (95)	124 (15)		0.17
IV	281 (100)	250 (5)	233 (42)	222 (5)	204 (10)	192 (43)	180 (12)	168 (11)	167 (46)	140 (7)		0.16
V	281 (100)	250 (5)	---	222 (12)	204 (9)	192 (51)	180 (7)	168 (25)	167 (75)	140 (16)		0.13
VI	281 (67)	---	---	222 (2)	204 (2)	192 (16)	180 (4)	168 (39)	167 (100)	140 (10)		0.23
VII	249 (61)	218 (7)	---	190 (87)	---	---	---	152 (16)	151 (100)	124 (12)	176 (12) 163 (40)	0.14
VIII	305 (100)	---	---	206 (5)	188 (2)	176 (19)	164 (5)	152 (12)	151 (34)	124 (3)	290 (14)	0.19

(a) Ion intensities have been corrected for natural abundance of ^{13}C isotope. (b) Exact mass measurements on I and II indicated this ion to be $\text{C}_5\text{H}_4\text{N}_4\text{O}$.

II formally corresponds to a further loss of water from the m/e 206 ion, although the appropriate metastable peak was absent.

The mass spectra of the two isomeric 8,2'- and 8,3'-*O*-cyclonucleosides (I and II) are virtually identical. However, it is somewhat easier to distinguish between the similar isomers (IV and V) in the mercapto derivatives, since 8,2'-*S*-cyclonucleoside IV contains a characteristic peak at m/e 233 ($C_9H_7N_5OS$) due to loss of CH_2OH (C-5') and OH (at C-3') from the molecular ion, while this peak is absent from the spectrum of V.

EXPERIMENTAL

Low resolution mass spectra were obtained with a Hitachi RMU-6E mass spectrometer using direct sample insertion into the ion source, whose temperature was 200-250°. High resolution mass measurements were determined with a Hitachi RMU-6D and JEOLCO JMS-01SG mass spectrometer and are accurate to within 5 millimass units of the required values.

8,2'-Anhydro-8-oxy-9- β -*D*-arabinofuranosyladenine (I) (9), 8,3'-anhydro-8-oxy-9- β -*D*-xylofuranosyladenine (II) (10), 8,5'-anhydro-8-oxyadenosine (III) (11), 8,2'-anhydro-8-mercapto-9- β -*D*-arabinofuranosyladenine (IV) (12), 8,2'-anhydro-8-mercapto-9- β -*D*-xylofuranosyladenine (V) (12), 8,5'-anhydro-8-mercaptoadenosine (VI) (13), 8,3'-anhydro-8-oxy-9-(2-deoxy-*threo*-*D*-pentofuranosyl)adenine (VII) (14) and 2',3'-*O*-isopropylidene-8,5'-anhydro-8-oxyadenosine (VIII) (11,15) were synthesized according to the literature.

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