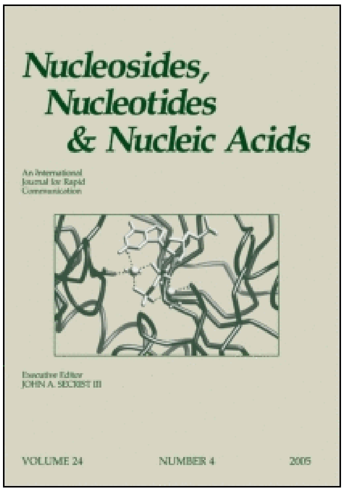


Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

Unimlecular Depurination of Substituted Deoxyadenosines by Fast Atom Bombardment Mass Spectrometry/Mass Spectrometry

Angelo Liguori[a]; Giovanni Sindona[a]; Nicola Uccella[a]
[a] Dipartimento di Chimica, University della Calabria, ARCAVACATA DI RENDE (CS), Italy

To cite this Article Liguori, Angelo , Sindona, Giovanni and Uccella, Nicola(1990) 'Unimlecular Depurination of Substituted Deoxyadenosines by Fast Atom Bombardment Mass Spectrometry/Mass Spectrometry', Nucleosides, Nucleotides and Nucleic Acids, 9: 3, 373 — 377

To link to this Article: DOI: 10.1080/07328319008045151

URL: http://dx.doi.org/10.1080/07328319008045151

NUCLEOSIDES & NUCLEOTIDES, 9(3), 373-377 (1990)

UNIMOLECULAR DEPURINATION OF SUBSTITUTED DEOXYADENOSINES BY FAST ATOM BOMBARDMENT MASS SPECTROMETRY/MASS SPECTROMETRY

Angelo Liguori, Giovanni Sindona* and Nicola Uccella
Dipartimento di Chimica, Università della Calabria
I-87030 ARCAVACATA DI RENDE (CS)- Italy

Abstract: The effect of benzoyl substitution on the unimolecular depurination of deoxyadenosine, in the gas-phase, has been evaluated. The glycosidic bond dissociation of the conjugated acids and bases of the isomeric species occurs remote from the charge sites.

The heterolysis of the glycosidic bond of nucleosides, known as depurination, causes, in aqueous acid media, the formation of neutral nucleobases and oxocarbenium ions derived from the sugar moiety.[1] N^6-benzoyl-2′-deoxyadenosine dissociates faster than the unprotected nucleoside, in the same environment, as consequence of a different protonation site.[2] All the kinetic data available in solution are in agreement with an A-1 mechanism, which does not involve the participation of the solvent in the transition state.[3] The unimolecular depurination of the conjugated acids of the four DNA nucleosides affords, in the gas-phase, protonated nucleobases and neutral sugar moieties.[4] This process requires the migration of a proton from the deoxyribose to the aglycone and does not involve the hydroxyl groups. A better understanding of this reaction mechanism has been achieved by examinining the reactivity of protonated isomeric benzoyl-deoxyadenosines, as well as the chemistry of their corresponding conjugated bases, in an isolated environment such as the high vacuum. The charged species have been produced by fast atom bombardment mass spectrometry (FABMS)[5] and their gaseous unimolecular dissociations have been investigated by MIKE and MIKE/CA[6], which are typical approaches of mass spectrometry/mass spectrometry (MS/MS) methodologies, widely applied in nucleic acid chemistry.[7]

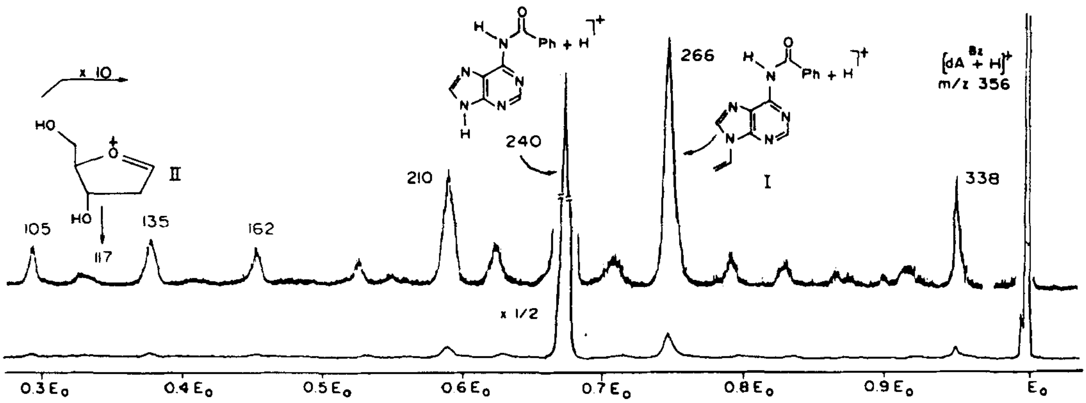
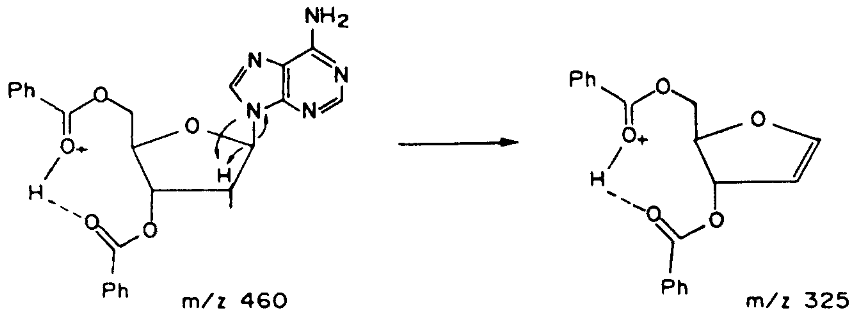


FIG. MIKE/CA spectrum of protonated N^6-benzoyl-2′-deoxyadenosine

Protonated adenine was formed from the spontaneous dissociations of the conjugated acid of 2′-deoxyadenosine, $[dA+H]^+$ (m/z 252), in the gas-phase (MIKE experiments), while, under collisonal activation (MIKE/CA experiments), the same precursor afforded, unimolecularly, 4% of oxocarbenium ions (II, fig.) and 8% of m/z 162, corresponding to the un-benzoylated structure I (fig.).[4] The cations $[dA^{Bz}+H]^+$, obtained by FAB from N^6-benzoyl-2′-deoxyadenosine, reacted similarly, however, when their internal energy was raised by collision with Helium, the preferred pathway of the unimolecular dissociations corresponded still to the formation of protonated benzoyladenine, in competition, to some extent, with the obtainment of species I at m/z 266. Traces of the oxonium ion II could be present in the reaction mixture (fig.).

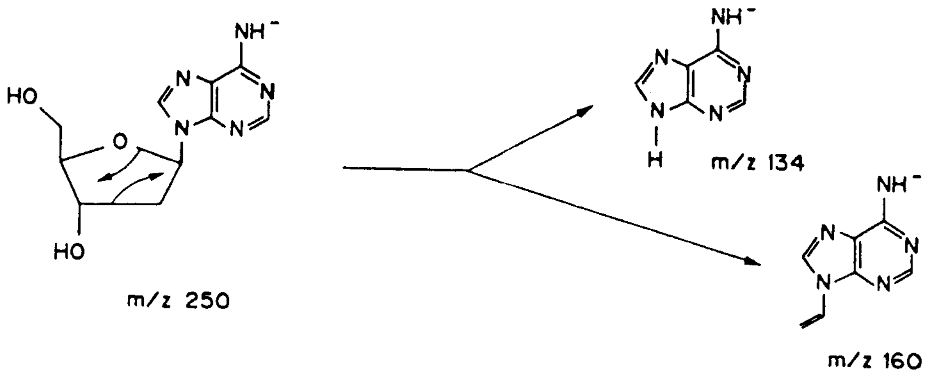
Under kinetic control, therefore, the releasing of protonated nucleobases is much more favoured than the formation of the oxocarbenium ion, when a benzoyl group is available on the adenine ring of dA. This result could suggest that dA and dA^{Bz} are protonated, in the gas-phase, at different nitrogen sites, in agreement with solution phase findings.[2] Actually, the proton affinity (PA) values of both nucleosides, experimentally determined from the unimolecular dissociations of their proton-bound dimers with triethylammine, showed that, in the gas-phase, dA^{Bz} is more basic than the unsubistuted nucleoside. Therefore, it can be assumed that the N^7 position of the purine is protonated and that the N^6-benzoyl group



Scheme 1

is involved, via intramolecular hydrogen-bonding, in the stabilization of the conjugated acid. The electron-withdrawing group on the heterocyclic ring weakens the glycosidic bond, thus promoting the formation of the observed products.

The conjugated acid of 5′-benzoyl-2′-deoxyadenosine [5′-BzdA+H]$^+$ gave rise, unimolecularly, to the formation of protonated adenine (m/z 136) and to the releasing of neutral adenine (m/z 221) with 86 and 14% relative yield respectively. This ratio was not modified under collisional activation, while the expected m/z 162 ion was formed. The species at m/z 221 might correspond to 5-benzoyl-oxocarbenium ions of type structure II (fig.), however, the enhanced rate of their formation, with respect to the unimolecular dissociation of the isomeric [dA^{Bz}+H]$^+$, is in contrast with the expected destabilizing effect of the electron-withdrawing group present on the 5′ position of the sugar moiety. This trend was even more pronounced in the depurination of protonated 3′,5′-dibenzoyl-2′-deoxyadenosine. The latter, in fact, gave rise to protonated adenine (m/z 136) and to the releasing of neutral adenine (m/z 325) with 6 and 94% yield, respectively. In this case, it can be assumed, therefore, that a preferential protonation occurs at one of the ester groups, whose basicity is enhanced by the possible intramolecular hydrogen bonding stabilization, and that the depurination corresponds to an unimolecular rearrangment occuring remote from the charge site (scheme 1). The reactivity of [5′BzdA+H]$^+$ could be due to the



Scheme 2

presence of mixtures of benzoyl and nucleobase protonated structures. The results above discussed are in agreement with previous observations[4] related to the depurination of unprotected 2′-deoxynucleosides, in fact, the unimolecular dissociation of the glycosidic bond of their conjugated acids, in the gas-phase and in the absence of solvent effect, does not proceed via the formation of oxocarbenium ions. Moreover, the depurination process seems to represent an intrinsic property of gaseous nucleosides which is not affected by the charge sites. Further insights into the reactivity of the examined molecules have been provided by the unimolecular reactions of the conjugated bases of dA and dA^{Bz}. Good yields of gaseous $[dA-H]^-$ (m/z 250) species can be obtained by FABMS in the negative ionization mode. The latter afforded unimolecularly (MIKE spectrum) the anions at m/z 232, 223, 160 and 134 with 4, 4, 11 and 81% relative yield. The lowest activation energy processes (scheme 2) were represented by charge-remote fragmentations which involve the same bonds as for the analogous protonated species. The conjugated base of dA^{Bz} (m/z 354) reacted similarly affording the anions at m/z 264 and 238 with 18 and 82% relative yield

It can be concluded that the depurination of the examined species does not correspond to a simple glycosidic bond heterolysis assisted by the hemiacetalic oxygen lon pairs of the sugar moiety. On the contrary, the process requires a proton rearrangement which does not seem to be much affected either by the structure of the reacting species or by the type and location of the charge site. The observed spontaneous dissociations of the conjugated acids and bases of the examined 2′-deoxyadenosines are to be related, therefore, to the intrinsic reactivity of these species in a not interacting environment.

REFERENCES

1 Oivanen, M.; Lonnberg, H.; Zhou, X.; Chattopadhyaya, J. Tetrahedron **1987**, 43, 1133.
2 Remaud, G.; Zhou, X.; Chattopadhyaya, J.; Oivanen, M.; Lonnberg, H. Tetrahedron **1987**, 43, 4453.
3 York, J.L. J. Org. Chem. **1981**, 46, 2171.
4 Greco, F.; Liguori, A.; Sindona, G.; Uccella, N. submitted for publication.
5 Barber, M.; Bordoli, R.S.; Sedgwick, R.D.; Tyler, A.N. J. Chem. Soc., Chem. Commun. **1981**, 325.
6 Beynon, J.H.; Cooks, R.G.; Baitinger, W.E.; Amy, J.W.; Ridley, T.V. Anal. Chem. **1973**, 45, 1023A.
7 Sindona, G. In "Spectroscopy of Inorganic Bioactivators. Theory and Applications-Chemistry, Physics, Biology and Medicine"; Theophanides, T. Ed.; Kluwer Academic Publishers: Dordrecht, 1989: pp.321-345.