

A technique to determine the thermal stability of uracil and uracil derivatives in a molecular beam



Todd M. Maddern^a, Vincent Jamier^{b,c}, Jessica R. Brunton^a, Michael J. Brunger^{a,d}, Cyril Papamicaël^c, Suzanne V. Smith^{b,e}, Stephen J. Buckman^{d,f,*}

^a School of Chemical and Physical Sciences, Flinders University, Adelaide, South Australia, Australia

^b Australian Nuclear Science and Technology Organisation, Lucas Heights, Australia

^c IRCOF de Rouen, rue Tesnière, Mont-Saint-Aignan, France

^d Institute of Mathematical Sciences, University of Malaya, Kuala Lumpur, Malaysia

^e Idaho State University, Idaho Accelerator Center, Department of Physics, Nuclear & Electrical Engineering, Pocatello ID 83209, USA

^f Research School of Physics and Engineering, Australian National University, Canberra, Australia

ARTICLE INFO

Article history:

Received 6 January 2016

Received in revised form

29 September 2016

Accepted 29 September 2016

Available online 1 October 2016

Keywords:

Jet

Beam

TOFMS

Uracil derivatives

PET

ABSTRACT

Uracil derivatives, especially synthesised for use in positron emission tomography studies, are heated to form a gas phase source and introduced into a vacuum system by seeding into a helium jet. Through time of flight mass spectroscopy, these uracil compounds are shown to have resisted any thermal dissociation during the heating phase of introduction into the jet. The successful introduction into a beam clearly demonstrates that dissociative electron attachment, or other scattering or spectroscopic studies, could be performed on these compounds with confidence that the parent molecule remains intact, at least at the temperatures considered in this study.

© 2016 Elsevier B.V. All rights reserved.

1. Introduction

Positron emission tomography (PET) provides a three-dimensional map of structures within a biological system [1]. The tomography is achieved by detection of gamma ray pairs emitted following the annihilation of a positron-electron pair created within a subject's body. The positrons are introduced into the subject by injecting an appropriate radionuclide into the circulation system. To facilitate safe passage through the subject, the radionuclide is chemically bonded either directly to, or indirectly through a bi-functional chelator, a biologically-compatible carrier molecule or targeting agent.

The spatial resolution achievable with PET is limited, in part, by the range of the positrons following emission from the radionuclide [2,3]. The further the positron is able to travel before annihilation, the lower the spatial resolution achievable with PET. Spatial resolution is thus potentially improved by using a radionuclide that

emits positrons with lower kinetic energy, as the stopping distance is reduced. Another potential way to improve spatial resolution is to reduce the range of the emitted positrons by increasing the electron density within close proximity to the radionuclide location, thereby increasing the probability that the positron will be annihilated closer to the point of emission.

One possible way to achieve this is by increasing the electron density within the bio-molecular carrier through the attachment of electron-rich atoms close to the positron emitting radionuclide. Halide atoms (i.e. F, Cl, Br and I) and aromatic groups are good examples of electron-rich species that could be attached to target agents and positioned close to the positron-emitting isotope.

Today, there are a number of ¹⁸F PET agents that incorporate uracil, one of the building blocks of the human body [4]. Uracil represents an ideal molecular template to study the annihilation process. A wide range of uracil derivatives (labelled 1a–e) incorporating halides such as F, Cl, Br and I atoms are already commercially available, and are shown in Fig. 1. Further substitution of the halide group with ethylene and/or benzene groups onto uracil could provide for a wider range of agents for studying this phenomenon. However, the latter more complex uracil-based compounds need to be synthesised in the laboratory.

* Corresponding author at: Research School of Physics and Engineering, Australian National University, Canberra, Australia.

E-mail address: stephen.buckman@anu.edu.au (S.J. Buckman).

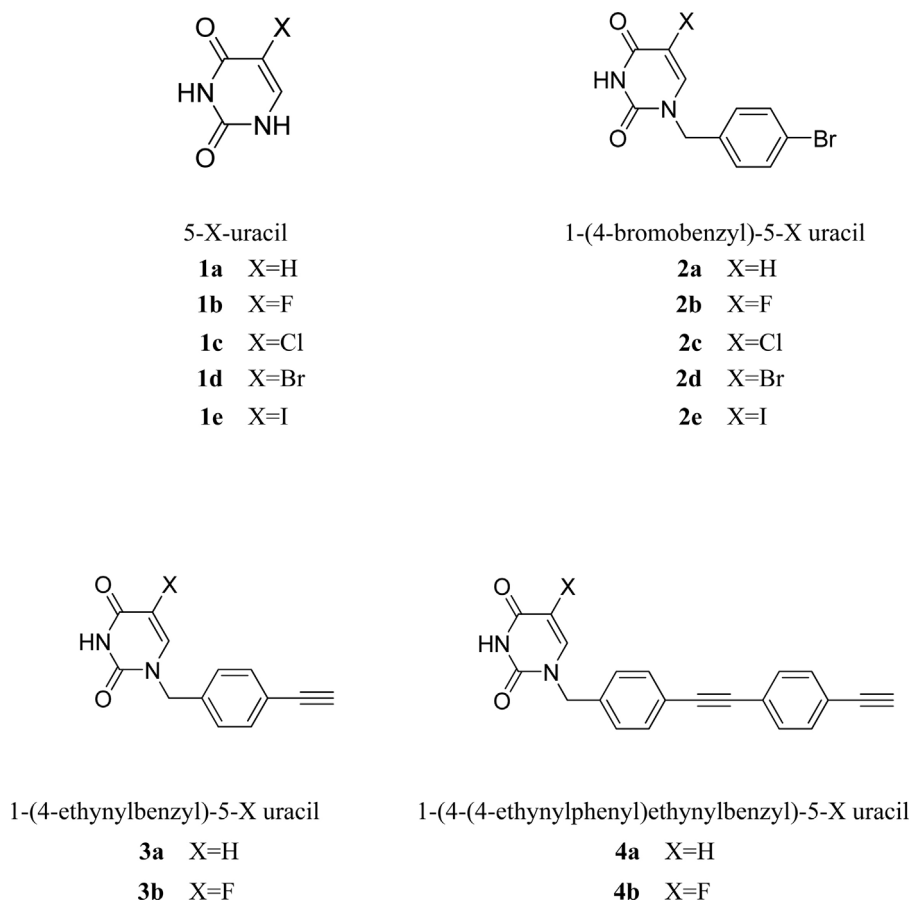


Fig. 1. Uracil derivatives, with varying electron densities, some of which were investigated in the present study.

A new series of uracil derivatives, labelled 2a–e, 3a,b and 4a,b, and illustrated in Fig. 1, have been synthesized using previously reported methods. [5,6]. They have been designed, for example, to study the effect that molecular structure and local electron density has on the cross section for Ps production, and subsequent annihilation, amongst other studies.

The principal motivation for the present measurements was to confirm that a gas phase beam of such uracil derivatives (and other biologically relevant molecules) could be effectively produced by thermal means, and that the purity of the beam was not compromised in the process. Given that uracil, and its derivatives (and other DNA bases and amino acids), exist as a solid at room temperature, beam experiments with such molecules require heating of the solid to produce sufficient vapour pressure for production of a beam, typically into a vacuum system. The likelihood that a particular molecule would dissociate during the heating phase thus needs to be determined to ensure the purity, or otherwise, of the beam. Once this is established, future experiments can be pursued to measure the effect that a particular uracil (or other biomolecule) compound has on positron annihilation probability. In our own laboratory this would be done by measurements of interaction cross sections for processes such as positronium (Ps) formation [7,8]. However, other measurements, such as low energy direct annihilation [9], would also potentially benefit from knowledge of the stability of such compounds at high production temperatures. Such experiments would involve crossing, within a vacuum system, a beam of positrons with a beam or gas cell containing the uracil derivative and then detecting the rate of positronium formation or gamma ray pair production resulting from annihilation. This paper reports a method to produce beams of the above mentioned

uracil compounds into a vacuum environment without incurring molecular dissociation.

It is also worth noting that the present study may be relevant to other contemporary areas of experimental charged-particle radiation physics. The past decade has seen an enormous flourish of papers dedicated to the study of low energy electron interactions with biomolecules [10–25]. This was prompted by the discovery of Sanche and co-workers [26], that sub-ionization-energy secondary electrons, which are formed in the body through thermalisation of high-energy ionizing radiation, can cause significant bond breaking in the molecular components of DNA. Many subsequent works have been concerned with studies of the principle mechanism responsible for this – dissociative attachment – and these measurements involve the interaction of low energy electrons with beams of biomolecules, such as those being studied here [10–27]. In all these measurements it has been largely assumed that at low enough production temperatures, the target molecules are stable and do not fragment or thermally dissociate in the beam. Specifically, in references [10–19] no mention for the possibility of thermal dissociation of the molecule under study was made, while in reference [20] it was addressed by simply stating, without references to support the assertion made, that thermal fragmentation was not an issue at the temperature those authors operated at. In references [21,22] a thermal decomposition temperature for the molecule in question was stated, but no references as to its origin were given. Abouaf et al. [23] and Kopyra and Abdoul-Corime [24] both address and discuss possible thermal fragmentation in their measurements, by reference to earlier similar experiments. However, on further checking, those earlier references actually do not provide any explicit evidence for why the temperature they operated at was free from such an effect. Finally, in their most recent study, Kopyra and Abdoul-

Download English Version:

<https://daneshyari.com/en/article/5134363>

Download Persian Version:

<https://daneshyari.com/article/5134363>

[Daneshyari.com](https://daneshyari.com)