Photochemistry and Vibrational Spectra of Matrix-Isolated Isoniazid

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Tuberculosis is still one of the most infectious diseases in the world [1]. At present, the accepted treatment of tuberculosis is achieved by drugs involving a combination of several molecules, including isoniazid, pyrazinamide, ethambutal and rifampicin. There are three main properties of antituberculosis drugs: bactericidal activity, sterilizing activity and the ability to prevent resistance [2]. Isoniazid (INH) is known to act as a bacteriostatic or bactericidal drug (depending on the concentration of the drug attained at the site of infection) against *Mycobacterium tuberculosis*. Being active only during bacterial cell division, it is still the most widely used drug in antituberculous regimens [1, 2].

In this study, INH was studied by matrix isolation infrared spectroscopy and DFT(B3LYP) and MP2 calculations. In the matrix isolation experiments, samples were prepared by co-deposition of INH (placed in a specially designed temperature variable mini-oven assembled inside the cryostat) and the inert gas, onto a cooled (10 K) CsI substrate. Irradiation of the matrices was carried out with a Hg(Xe) lamp at $\lambda > 235$ nm.

According to calculations at the DFT(B3LYP)/6-311G(d,p) level of theory, three minima were found on the potential energy surface, *TSk*, *CSk* and *TC*, with relative energies of 0.0, 20.4 and 22.6 kJ mol-1, respectively (see figure 1). In consonance with the theoretical results, only the *TSk* form could be isolated in both argon and xenon matrices. Assignment of the observed bands was carried out on the basis of the comparison with the theoretically predicted spectra and annealing experiments. After UV irradiation, the intensities of the bands corresponding to INH decreased significantly while new bands appeared in the spectrum, indicating that INH had been photolysed to several photoproducts, whose structures are discussed in this study. The knowledge of the photochemistry of the compound may help to develop better strategies for its management, preventing undesirable losses during its industrial production and processing.

Fig. 1: Conformers of isoniazid.

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