Ringing the Changes with Tetrazole: Hydrogen Bonding Studies

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Tetrazoles are acidic heterocycles and used in angiotensin II receptor antagonists for the treatment of high blood pressure. The binding mode is still controversial [1], as yet the only published crystal structure of a tetrazole-protein complex shows close contacts between two of the tetrazole nitrogen atoms and two lysine residues within the enzyme binding site. [2]

Tetrazoles are used as bioisosteric replacements for carboxylic acids in modern drug design. Transmembrane receptors are notoriously difficult to study, so model systems can provide further insight into non-covalent binding interactions.

This work describes the hydrogen-bonding patterns seen for readily available ionic model complexes, developing earlier studies of hydrogen-bonding tetrazolate anion [3] and illustrate how the tetrazole, or simple derivatives bind to acetamidine (arginine model), propranolol (an antihypertensive drug) and spermine (a natural hormone). These will be compared with analogous carboxylic acid complexes to provide insight into the hydrogen bonding interactions favoured by tetrazoles as well as difference in binding properties.

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