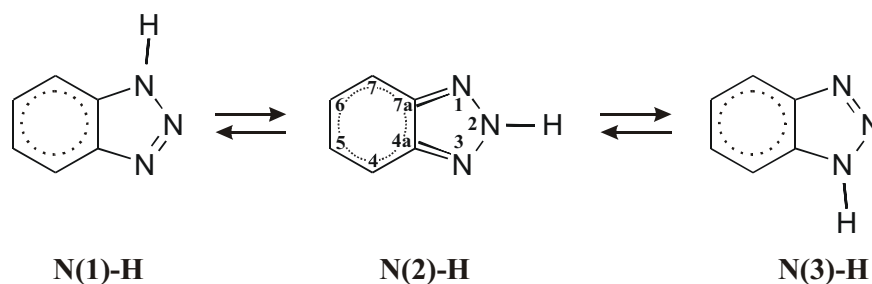


EXPERIMENTAL AND THEORETICAL STUDIES ON THE PROTOTROPIC TAUTOMERISM OF BENZOTRIAZOLE AND ITS DERIVATIVES SUBSTITUTED ON THE BENZENE RING

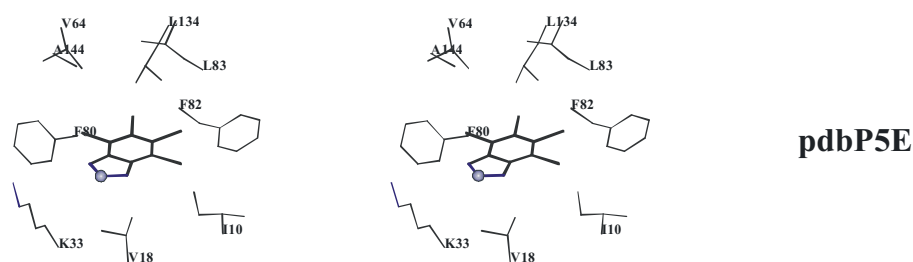
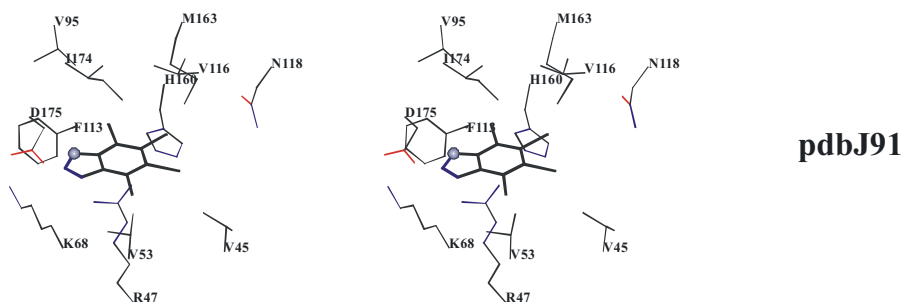
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The prototropic equilibrium of benzotriazole was followed by numerous experimental and theoretical methods. BT may exist in three forms, two of which, the N(1)-H and the N(3)-H, are degenerate in the absence of isotope labeling, or of asymmetric substitution on the benzene ring.

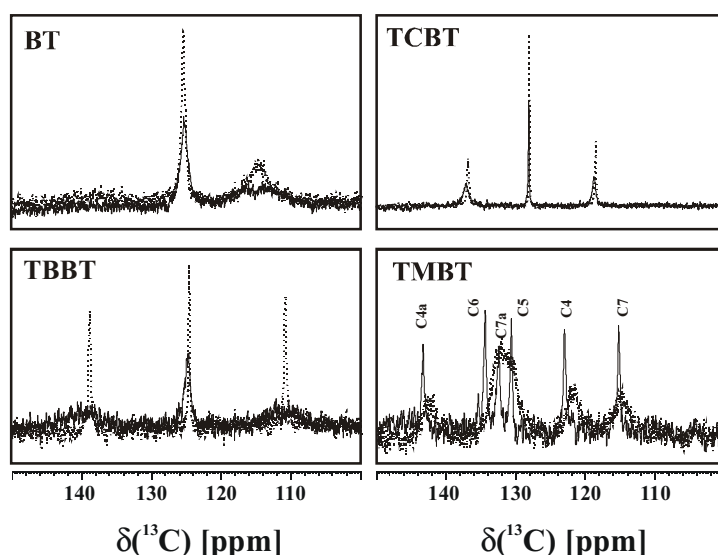


The prototropic equilibrium of BT derivatives interacting with biomolecules is less well known. There are, however, two examples of a BT derivative carrying an exchangeable proton, TBBT, bound to two different proteins, recorded in the Protein Data Bank, and according to the bond lengths, the two TBBT molecules differ in their prototropic forms.



The prototropic tautomerism in anhydrous DMSO of benzotriazole its six derivatives symmetrically substituted on the benzene ring /5,6-dichloro (DCBT), tetrachloro (TCBT), 4,7-dibromo (DBBT), tetrabromo (TBBT), 5,6-dimethyl (DMBT), tetramethyl (TMBT)/, and additionally 15 derivatives asymmetrically substituted, was followed by both experimental (^{13}C NMR and UV spectroscopy) and theoretical methods. In all of the analyzed symmetrical systems, predominance of the asymmetric form, N(1)/N(3) protonated, was found. The rates of the N(1)-H \leftrightarrow N(3)-H prototropic equilibrium, estimated by ^{13}C NMR techniques basing on the two state chemical exchange model, fail in the medium exchange regime of $300\div 3000\text{ s}^{-1}$, and are correlated with the spectroscopically determined pK_a values in aqueous medium.

For all the compounds, the anionic form is the putative rate-limiting intermediate state. Consequently, addition of 1% (v/v) of water to DMSO solution strongly affects the shape of resonance lines, as it is presented below for ^{13}C spectra of BT, TCBT, TBBT and TMBT (dotted lines). The increase of exchange rate results in the narrowing resonance lines of the compounds falling in medium exchange model in DMSO solution, while strong broadening is observed for the slowly exchanging TMBT



For the asymmetrically substituted molecules theoretical calculations pointed the existence at least two, closely populated forms. This agrees with the observed broadened resonance lines observed in the ^{13}C NMR spectra recorded in DMSO solution. As for symmetrical The resonance lines become narrower upon addition of the small amount of water.

Reference:

J. Poznański, A. Najda, M. Bretner, D. Shugar. Experimental (^{13}C NMR) and Theoretical (*ab initio* Molecular Orbital Calculations) Studies on the Prototropic Tautomerism of Benzotriazole and Some Derivatives Symmetrically Substituted on the Benzene Ring (2007) *J. Phys. Chem. A* **111**, 6501-6509

Acknowledgments

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