

C-H...O hydrogen bonds: historical overview and biological significance

Zygmunt S. Derewenda

The notion that polarized C-H groups can serve as donors in hydrogen bonds was first proposed in 1936 based on macroscopic properties of mixed solutions. Between 1938 and 1943 a series of papers from the Noyes Chemical Laboratory at the University of Illinois expanded on the original observations, taking advantage - among others - of the emerging data from infrared spectroscopy. Unfortunately, most probably due to World War II, this literature remains mostly unknown. The concept was re-introduced in 1962 by the New Zealand crystallographer, working at Birkbeck College in London, D. June Sutor, who based her conclusions based entirely on stereochemical information. Unfortunately, her work did not have much impact due to heavy criticism by the world-renowned expert on hydrogen bonds - Jerry Donohue. The field was once again revisited - this time conclusively - by Olga Kennard and Robin Taylor (Cambridge) who analyzed more accurate structure models obtained both by neutron and X-ray diffraction, to show convincingly that C-H groups serve as H-bond donors.

Although it has taken nearly half a century to gain acceptance, the field of C-H...X (mostly O) hydrogen bonds has expanded rapidly. Most notably, it has been shown that these interactions play a significant role in biological compounds, including proteins, their complexes with ligands and nucleic acids. In particular, these interactions are known today to play a critical role in the stabilization of the β -sheet secondary structure in proteins; to contribute to the specificity of the interactions of drugs with many targets; and are important in maintain the conformation of DNA. My talk will review the history of the field and focus on recent advances, based on the work published by our group, and - mostly - by other laboratories.