and her colleagues reported the crystal structure of rhombohedral 2 zinc insulin at 2.8 Å resolution, providing an atomic model for the protein.[49] In the intervening years, she revolutionized the field of X-ray crystallography by solving numerous atomic structures of compounds such as cholesteryl iodide,[50] establishing for the first time the relative stereochemistry of steroids, benzylpenicillin salts,[51] identifying the β-lactam substructure for the first time, and vitamin B_{12},[52] the first naturally occurring organometallic compound with biological significance (Figure 2.12). In 1964, Hodgkin received the Nobel Prize in chemistry for her contributions to the field.[53]

The remarkable work of Dorothy Crowfoot Hodgkin and the scientists that followed in her footsteps provided the scientific community with their first clear pictures of structures of biomolecules. Thousands of protein structures, both in the presence and absence of a ligand have been reported, and the information embedded within these structures has provided a detailed understanding of how drugs interact with their target proteins. The Protein Data Bank (http://www.rcsb.org/pdb/home/home.do), first established in 1971 with 7 structures, contains over 82,000 protein structures as of 2012.[54] Nucleic acid X-ray structures, the most famous of which is the Watson and Crick DNA structure introduced in 1953,[55] have also been exceptionally valuable tools in determining the molecular interaction required for normal, pathological, and drug-mediated biology. The Nucleic Acid Database (http://ndbserver.rutgers.edu/index.html), a more recently created publicly available database, was established in 1992 to provide the scientific community with access to three dimensional structures of nucleic acids, and contains over 6300 solved structures as of 2012.[56] Finally, The Cambridge Structural Database (http://www.ccdc.cam.ac.uk/products/csd/), founded in 1965,[57] focuses on small molecule crystal structures, and contains structural information on nearly 600,000 small molecules as of 2012.[58]

Molecular Modeling and Computational Chemistry

Although Heisenberg's 1925 paper on quantum mechanics[59] is widely considered to be the first publication in the field of computational chemistry and molecular modeling, it would take an additional 36 years for the concept of using computers to calculate and predict chemical properties and interactions to arrive. In 1961, James Hendrickson calculated the conformational energies of cycloheptanes using an IBM 709 computer (Figure 2.13) that was capable of "8000 additions/subtractions, 4000 multiplications/divisions, or 500 complex functions per second."[60] In essence, he launched the field of molecular modeling with a computer that had fewer capabilities and less capacity than most cellular telephones.