Summary

The field of experimental charge density determination faces at present a radical change that may be comparable to the development of X-ray structural analysis as a routine method of the structure determination of chemical compounds in the sixties. Within the framework of the present dissertation important methodological and experimental aspects could be contributed to this development. For the first time it could be proven that with the combination of synchrotron primary radiation/CCD area detection electronic properties are accessible in a short time and that the accuracy of these properties is comparable or even superior to that obtained with point detection, requiring measurement times of several weeks. This has been doubted so far. This result opened the perspective on the one hand to do comparable studies on a class of related compounds, on the other hand it seemed possible to perform charge density studies on larger systems of biological importance. In this thesis both perspectives were followed. The class of amino acids was successfully studied by comparable charge density determination. In addition, taking the example of an antithrombotic drug, it could be shown that even a conventional X-ray source combined with area detection, which is getting nowadays common laboratory equipment, is suitable for charge density determination of larger molecules. Quantitative results on the electronic level could be obtained due to fast experiments, whose time consumption is far less than that of comparable *ab initio* calculations. Therefore it is not exaggerated to say that with the introduction of area detection and the proof that accurate electronic properties are accessible in a very short time, a radical change in the field of experimental charge density determination could be reached.

On six amino acids extensive charge density studies were performed including a complete topological analysis of the charge density of all the intra- and intermolecular interactions. Before starting with this thesis, only one study in the class of amino acids of comparable extent had been published. An enhancement of resolution and accuracy could be reached. Two of the data sets belong to the most highly resolved so far in the field of charge density studies of organic compounds. For this class of compounds a high degree of reproducability and transferability of atomic and group properties could be found. The variance of these properties is even less than the one found when using *ab initio* calculations with different methods and basis sets. Therefore an experimental contribution to support the quantum theory of "*Atoms in Molecules*" was given. The results so obtained could serve as a basis to build a data base of electronic properties of this important class of compounds. This could be used as a tool for studies on compounds that contain amino acids as fragments, like the penicillines, or for studies on higher molecular systems like peptides and proteins.

With the antithrombotic drug Terbogrel it was shown that a larger compound of biological relevance could be characterized electronically with high accuracy. The chemically relevant classification of the bonds and the determination of the most reactive sites of this compound, that belongs to the largest topologically characterized molecules so far, are one of the main results. Besides the fact that there are only a few strong intermolecular interactions clear discrepancies were found in comparison with theoretical calculations. Because similarity and molecular recognition are realized to a high degree in the crystalline environment, this state is much better suited to simulate physiological conditions and to understand drug-receptor interactions than the isolated stationary state of a system. That is why the determination of dipole moments and the electrostatic potential as done in this thesis is so important. The topological analysis of the charge density performed in this thesis allows a quantitative characterization of chemical bonds. For the first time fine charge density reorganizations due to weak intermolecular interactions could be visualized with the help of the threedimensional experimental Laplacian function and therefore directions in which chemical interactions are favoured could be located and characterized. Besides the experimental contribution to the development in charge density determination introduced here this work also contributes to the fields of molecular modelling and drug design.