FIGURE 2.13 The IBM 709 computer, introduced in 1958, had less computer power than modern cellular phones. *Source: IBM 709 front panel at the Computer History Museum by Arnold Reinhold* http://en.wikipedia.org/wiki/IBM_709#mediaviewer/File:IBM_709_front_panel_at_CHM.agr.jpg.

A few years later (1966), Cyrus Levinthal described his efforts to combine computer simulations with molecular graphics to visualize and study the structures of proteins and nucleic acids,[61] marking the dawn of computer-aided drug design.

The impact of molecular modeling and computational chemistry grew as the computer industry became more and more sophisticated, but the overall premise of the field remained the same. Computers and software could be used to understand the relationship between structural features and physical/chemical properties, including those that were critical to drug function. In addition, knowledge of these relationships could be used to alter or improve the physical and chemical properties of compounds, such as biological activity, solubility, and metabolic stability. By the late 1970s, independent commercial ventures based on computer-assisted modeling were beginning to appear. Molecular Design Limited and Tripos (Figure 2.14) were the first of many organizations built to exploit the ever-growing understanding of molecular interaction with the goal of designing better molecules *in silico*. In 1984, computing capabilities and molecular modeling capabilities had grown to the point where protein simulation was possible and BioDesign launched the first commercial program designed for this purpose. Continued growth in computer power and changes in the drug discovery industry led to the development of additional software tools between 1984 and the present day. Tools designed to assess molecular diversity, design compound libraries, create screening sets based on molecular similarity, and automate the docking