Problems in total synthesis are defined by natural products possessing novel molecular architectures which provide unique opportunities for discovery and invention in chemistry, biology, and medicine. The artistry of total synthesis lies both in the originality and elegance by which the individual steps are orchestrated within the overall synthetic strategy and in the architecture of the designs of synthesized analogs with potential biological activity. Accomplishments in total synthesis of such complex molecules symbolize the state of the art of chemical synthesis and have a major impact by finding applications in everyday endeavors of researchers in drug discovery and development, chemical biology and material science, among other disciplines. A number of examples of total syntheses from our laboratories of bioactive natural products (see structures below) and associated discoveries and inventions in new synthetic technologies and chemical biology will be discussed.1–5