Chemists have a compelling curiosity to discover what compounds Nature provides, but to obtain this information it is necessary to isolate compounds from their natural source and to determine their structures. This is seldom an easy task, especially when the compound of interest is present at low concentrations such that enormous quantities of source material are required to extract even a few micrograms of the desired product. In this circumstance a high degree of skill and technology is required in both the isolation procedures and the subsequent investigations to establish the chemical structure.

A second objective is the total synthesis of the compound from smaller molecules. Indeed, in the classical approach to structure determination, a structure was assigned to a natural product through chemical degradation studies to smaller, identifiable molecules. However, the assigned structure was not regarded as fully confirmed until the compound was synthesized and shown to be identical in all respects (composition, configuration, conformation) with the natural compound. This approach persists, although the enormous impact of modern methods of separation and spectroscopic analysis has made it possible to determine structure beyond a reasonable doubt in almost all cases without recourse to synthesis.

Nevertheless, the synthesis of natural products continues to be important. It provides new methodology, new reactions and techniques. It also provides alternative sources of natural compounds and offers routes to related but unnatural analogs. In the case of a useful drug, the synthetic objective is to find a related structure that is more potent at lower dosages with fewer side effects than the natural compound.

Yet another area of investigation in natural-product chemistry concerns the way in which the compound is synthesized biologically - that is, the biosynthesis of the compound. These are experimentally difficult studies and involve first identifying the starting materials (biological precursors). This can be done by feeding the organism isotopically labeled compounds suspected of being precursors and then determining where and how much of the labeled material is incorporated into the natural product. Ultimately, each step in the synthesis should be elucidated and each enzyme isolated and the entire sequence reconstructed in a cell-free system. From experiments of this type we now have a rather good understanding of the biosynthesis of fatty acids, terpenes, and steroids.

Contributors and Attributions