

Scaffold-Building in Natural Products Biosynthesis: Two Case Studies

Nature has provided mankind with an arsenal of biologically active agents that are either used directly or used as an inspiration for drug development. A perusal of the current inventory of naturally occurring molecules reveals the use of molecular scaffolds conserved both within and across families of related metabolites. Two examples will be discussed: the reduced indane-containing metabolites and the thiopeptide antibiotics. The case study for the reduced indanes is indanomycin, a polyketide metabolite produced by the soil-dwelling bacterium, *Streptomyces antibioticus* NRRL 8167. The second example to be discussed is thiostrepton, a prototype for the thiopeptide antibiotics, produced by *Streptomyces laurentii* ATCC 31255. The biosynthetic gene clusters for both systems have now been isolated, and our efforts toward generating a firm understanding of how the molecular framework is assembled for each metabolite will be discussed.