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Lessons from the Total Synthesis of Hybrid Natural Products

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Natural products constitute a rich source of molecular diversity, which could be traced back to the Nature's engineering. For example, the polyketide biosynthetic pathway is a significant producer of various biologically active compounds, which has a branching point to two distinct classes of molecules, that is, macrolide anti biotics and polyaromatic compounds. The diversity is enhanced by various modification processes including oxidation/reduction, and becomes even more so by the hybridazation with the other classes of molecules, such as isoprenoid and carbohydrates. Importantly, such composite molecules are an attractive class of synthetic targets, because of the potentially unique biological activity profiles. However, the synthesis is generally by far challenging, due to the difficulties in assembling the molecular units of different properties. Over the years, we have been interested in the total synthesis of hybrid natural products. Our particular attention has been centered at the aromatic–sugar hybrids, such as the ravidomycins the benanomicins, and TAN-1085, which required efficient methods for (1) the *O*- and *C*-glycosidations, and (2) the construction of polyaromatic skeletons. In this presentation, strategies and tactics associated with the total synthesis of these hybrid natural products will be discussed.