Synthetic Studies on Biologically Active Compounds

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Morphine is a fascinating compound that has been used as an efficient analgesic and is indispensable in treating pains associated with cancer. However, morphine is strictly controlled by authorities due to its addictive nature. On the other hand, the structure of morphine is quite attractive from a synthetic point of view. Its complicated pentacyclic skeleton, including a quaternary carbon center, has stimulated extensive synthetic efforts. Hence, a number of synthetic studies and the total syntheses of morphine have been reported to date. Among them, the Pd-mediated total synthesis reported recently by Trost and coworkers seems quite versatile. In an effort to develop a novel morphine-type drug that is not addictive, we initiated our own studies of an efficient total synthesis of morphine, and we have successfully synthesized morphine using a Mizoroki-Heck reaction to form the quaternary carbon center and an intramolecular Mannich-type reaction to construct the B and D rings. Further studies on a more efficient and enantioselective total synthesis of morphine are currently underway, and our recent results will be also reported in this symposium.