Template assisted distal C–H functionalizations of arenes

Debabrata Maiti*

Indian Institute of Technology, Bombay
dmaiti@iitb.ac.in

A practical protocol to simplify natural product synthesis by site selective C–H functionalization had always been a coveted target for chemists. Most often, directing group assisted metallacycle formation has served as an efficient strategy in ensuring promising regioselectivity. In this regard wide variety of ortho-functionalization stands as an archetype. Despite significant progress, directing group-assisted selective distal C–H functionalization in arenes (at meta and para positions) had remained an unexplored venture mainly due to the formation of a geometrically constrained metallacyclic transition state. To address these issues, a novel class of cleavable and recyclable linker with nitrile based templates that direct efficient functionalization of distal para- and meta-C–H bonds are introduced. These directing templates allow the required flexibility in supporting the formation of an oversized 12-17 membered macrocyclic pre-transition state. Using this strategy, regioselective meta- and para-C–H functionalizations were performed on a series of important classes of arene substrates – including phenylacetic acid, benzyl sulphonyl, benzyl silyl and phenol systems. Applicability of these template based strategies have been demonstrated by synthesizing various natural products and complex molecules through post synthetic modifications. Such a benign distal C–H functionalization strategy is expected to streamline complex molecule synthesis in pharmaceutical and polymer industry.

References