LATE-STAGE DIVERSIFICATION THROUGH MANGANESE-CATALYZED C–H ACTIVATION: ACCESS TO ACYCLIC, HYBRID, AND STAPLED PEPTIDES

Nikolaos Kaplaneris, Torben Rogge, Rongxin Yin, Hui Wang, Giedre Sirvinskaite, and Lutz Ackermann*

Institut für Organische und Biomolekulare Chemie, Georg-August-Universität Göttingen, Tammannstraße 2, 37077 Göttingen, Germany

Non-natural peptides have emerged as increasingly potent scaffolds in medicinal chemistry and the pharmaceutical industry. As a consequence, the chemoselective assembly and modification of structurally complex peptides continues to be of utmost importance [1]. Significant recent momentum was gained through the development of palladium-catalyzed cross-couplings of peptides. A significantly more atom- and step-economic strategy relies on the direct activation of otherwise unreactive C–H bonds [2, 3], with recent transformative applications towards peptide modification [4]. As part of our program on sustainable C–H activation [4, 5], we reported on the first manganese-catalyzed C–H allylation of structurally complex peptides with easily accessible Morita–Baylis–Hillman adducts [6]. Notable features of our strategy include 1) an unprecedented manganese(I)-catalyzed peptide C–H alkylation, 2) the first metal-catalyzed peptide modification that installs synthetically useful $\alpha,\beta$-unsaturated esters, and 3) a uniquely versatile manganese catalyst that proved applicable to C–H fusion with peptides, natural products, steroids, drug molecules, and nucleobases, among others.