Highly chemoselective synthesis of indolizidine lactams by SmI_2-induced umpolung of the amide bond via aminoketyl radicals : efficient entry to alkaloid scaffolds.

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Streszczenie

Samarium(II) iodide enables a wide range of highly chemoselective umpolung radical transformations proceeding by electron transfer to carbonyl groups; however, cyclizations of important nitrogen-containing precursors have proven limited due to their prohibitive redox potential. Herein, we report the first reductive cyclizations of unactivated cyclic imides onto N-tethered olefins using SmI2 /H2 O. This new umpolung protocol leads to the rapid synthesis of nitrogen-containing heterocycles that are of particular significance as precursors to pharmaceutical pharmacophores and numerous classes of alkaloids. The reaction conditions tolerate a wide range of functional groups. Excellent chemoselectivity is observed in the cyclization over amide and ester functional groups. Such unconventional reactivity has important implications for the design and optimization of new bond-forming reactions by umpolung radical processes. The reaction advances the SmI2 cyclization platform to the challenging unactivated N-tethered acyl-type radical precursors to access nitrogen-containing architectures.

Słowa kluczowe

C−C coupling, amide bonds, nitrogen heterocycles, samarium, umpolung

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