Stereoselective cascade cyclizations with samarium diiodide to tetracyclic indolines - precursors of fluorostrychnines and brucine.

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Abstract

A series of γ-indolylketones with fluorine, cyano or alkoxy substituents at the benzene moiety was prepared and subjected to samarium diioidide-promoted cyclizations. The desired dearomatizing ketyl cascade reaction forming to new rings proceeded in all cases with high diastereoselectivity, but with differing product distribution. The annulated tetracyclic compounds were obtained in moderate to good yields, but as second product spirolactones were isolated in up to 29% yield. The reaction rate was influenced by the substituents at the benzene moiety of the substrate as expected, with electron-accepting groups accelerating and electron-donating groups decelerating the cyclization process. The intermediate samarium enolate of the tetracyclic products could be trapped by adding reactive alkylating agents as electrophiles delivering products with quarternary carbons. In the case of a dimethoxy-substituted tetracyclic cyclization product a reductive amination stereoselectively provided a pentacyclic compound that was N-protected and subjected to a regioselective elimination. The obtained pentacyclic product should be convertible into the

alkaloid brucine by four steps. The presented report shows that functionalized tetracyclic compounds with different substituents are rapidly available with the samarium diiodide cascade cyclization as crucial step. Hence analogs of the landmark alkaloid strychnine, e.g. with specific fluorine substitutions, should be easily accessible.

Involved units

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