Asymmetric Total Synthesis of Martinella Alkaloids

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Due to the novel hexahydropyrrolo[3,2-c]quinoline nuclei as well as their potential-use in medicinal chemistry, two alkaloids martinellic acid (1) and martinelline (2), isolated by Merck’s chemists from the root bark of tropical plant Martinella iquitosensis, have attracted considerable attention from synthetic community.

To date, however, there has only been one reported asymmetric total synthesis of (−)-martinellic acid (1) by Ma’s group, in which they pointed out that synthetic (−)-1 exhibits a considerably large value in its specific rotation compared with natural (−)-1, indicating that 1 may be partially racemic or a highly diluted solution was used when Merck’s chemists measured its specific rotation. Thus, the issue on the elucidation of the absolute configurations of 1 and 2 is still the subject of serious arguments. Herein, we describe the first asymmetric total synthesis of (−)-martinelline (2) and the second total synthesis of (−)-martinellic acid (1) employing the tandem Mukaiyama-Mannich reaction/aminal cyclization as a key step which support the suggestion of Ma’s group that natural Martinella alkaloids are partially racemic.