The synthesis of a 24-membered cyclic depsipeptide with an alternating sequence of phenyl-lactic acid and α-aminoisobutyric acid (Aib) is described. The linear precursor was prepared via the ‘azirine/oxazolone method’ using 2,2-dimethyl-3-amino-2H-azirines as building blocks for the α,α-disubstituted α-amino acid Aib. The macrolactonization leading to the cyclodepsipeptide was achieved by the ‘direct amide cyclization’, i.e., by treatment of a solution of the linear precursor in toluene with HCl gas.

Key words: Cyclodepsipeptides, Direct Amide Cyclization, Azirine/Oxazolone Method, Aminoisobutyric Acid, Crystal Structure