Synthesis of linear and cyclic opioid-based peptide analogs containing multiple *N*-methylated amino acid residues.

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A series of six novel opioid peptide analogs containing one to three N-methylamino acid residues, and six cyclic counterparts of these peptides were prepared by the solid-phase method. Introduction of two consecutive N-methylated amino acids, as well as cyclization of such conformationally constrained sequences, turned out to be challenging. The use of a recently reported triazine-based coupling reagent, 4-(4,6-dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholinium toluene-4-sulfonate, enabled the synthesis and cyclization of the designed analogs in acceptable yields and with a lesser amount of by-products than observed with the standard coupling reagents such as TBTU or HATU.

Słowa kluczowe

peptide synthesis, cyclization, coupling reagents, N-methylated amino acids

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