Preparation of novel deuterated cyclosporin A standards for quantitative LC-MS analysis.

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Streszczenie

The investigation on the synthesis ofα-C deuterated analogues of cyclosporin A (CsA) inN-meth-ylated amino acid residues was performed. The reaction based on our previous report (Bachoret al 2014 J Mass Spectrom 49, 43–49) proceeds in the presence of bases like TBD or MTBDat pH 13.4. The obtained results suggest the possibility of introduction of 3 deuterons, 2 at theα-C of sarcosine, and 1 at the chiralα-C atom of 2-N-methyl-(R)-((E)-2-butenyl)-4-methyl-L-thre-onine residue. The stability of the obtained isotopologues was analyzed both under neutral oracidic conditions, and the obtained results revealed that the introduced deuterons do notundergo back exchange. In addition, the co-elution of deuterated and non-deuterated formswas observed, which opens the possibility of application of the synthesized isotopologues forthe quantitative analysis utilizing isotope dilution strategy. The proposed strategy of the deuter-ated CsA analogues synthesis is rapid, cost-efficient, and does not require derivatization reagentsor further purification and may be useful in quantitative analysis of cyclosporin A and itsmetabolites.

Słowa kluczowe

cyclosporin A, hydrogen deuterium exchange, isotope dilution, liquid chromatography - mass spectrometry, N - methylamino acids

Adres publiczny

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