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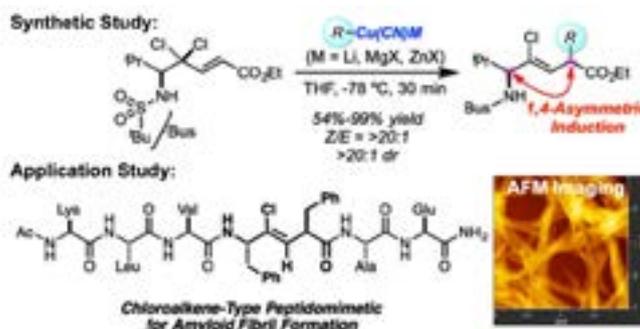
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Peptidomimetic study on amyloid fibril formation by alkene-type dipeptide isosteres

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Alkene-type dipeptide isosteres have emerged as ideal ground state mimetics of scissile peptide bonds. Although halo-substituted alkenes such as fluoroalkene and chloroalkene have been thought as one of the promising surrogates of peptide bonds, the lack of suitable synthetic methods toward those isosteres has hampered their application to pharmaceutical chemistry. To address this issue, we have identified a multi-gram preparative and diastereoselective synthetic approach toward (*Z*)-chloroalkene dipeptide isosteres [(*Z*)-CADIs]. A key to our approach is the use of 1,4-asymmetric induction strategy in the organocuprate-mediated allylic alkylation of allylic gem-dichlorides adjacent to the chiral center that is extremely useful for the diastereoselective synthesis of (*Z*)-CADIs in high yields with excellent (*Z*)-selectivity and diastereoselectivity (*Z*/*E* = >20:1, >20:1 *dr*). In this presentation, we will demonstrate the preparation of several peptidomimetics containing (*Z*)-CADIs by utilizing our synthetic approach, and explore the potentials of (*Z*)-CADIs as amide bond isosteres including the H-bonding ability of the (*Z*)-chloroalkene moiety, the tolerance to Fmoc-solid phase peptide synthesis conditions, and application to the peptides for amyloid fibril formation.



Biography

Tetsuo Narumi has completed his PhD from Kyoto University with Prof. Nobutaka Fujii. He spent a year in US as a JSPS Postdoctoral Fellow with Prof. Jeffrey W Bode at the University of Pennsylvania. In 2009, he began his academic career in Japan, at Tokyo Medical and Dental University with Prof. Hirokazu Tamamura. In 2013, he began his independent career at Shizuoka University, in Japan, as an Associate Professor in the Bioorganic Chemistry. He has published more than 50 papers in reputed journals and serves as a Leading Researcher in the field of Peptidomimetic Science.

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