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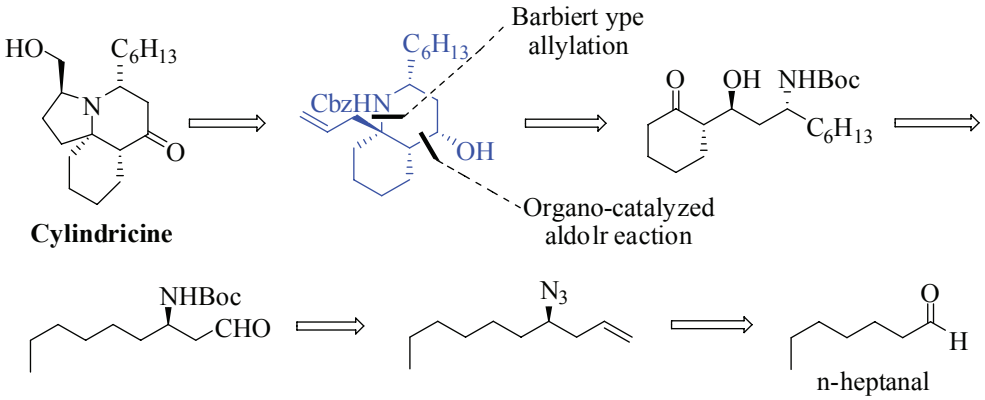
Studies towards the synthesis of marine alkaloid (+)-cylindricine

V. N. S. Murali Rampalli and S. Chandrasekhar
Indian Institute of Chemical Technology, India

Cylindricine was isolated from the marine ascidian (sea squirt) *Clavelina cylindrica*, It possesses a tricyclic skeleton with pyrrolo[2,1-j]quinoline framework. Cylindricine was found to be potent as a toxin. Here in we are reporting the synthesis of bicyclic quinolizidine moiety bearing a quaternary centre which is the key intermediate to achieve the total synthesis of Cylindricine. Heptanaldehyde was subjected to enantioselective Keck allylation to furnish the (S)-dec-1-en-4-ol, which was converted to its mesylate compound using MsCl and triethylamine. Displacement of the –OMs group with NaN3 provided (R)-4-azidodec-1-ene, followed by the reduction with LiAlH4 to furnish it's amine and then converted to it's t-Butyl carbamate, further subjected to one pot osmylation to afforded (R)-tert-butyl 1-oxononan-3-ylcarbamate. The aldehyde functionality underwent aldol reaction with cyclohexanone in presence of L-Proline as catalyst to give inseparable diastereomeric mixture of β-hydroxy ketones in 7:3 ratio which were separated by making their acetyl-derivatives (anti:syn = 7:3) and then deacetylated to give tert-butyl (1S,3R)-1-hydroxy-1-((S)-2-oxocyclohexyl)nonan-3-ylcarbamate, followed by treatment with TFA furnished an intramolecular imine, that undergoes a Barbier type allylation, to give the quinolizidine moiety bearing a quaternary centre. The free amine of this quinolizidine, was protected as its carbobenzyloxy ether.



Scheme 1: Retrosynthetic Analysis of Cylindricine

Biography

V. N. S. Murali obtained his Masters in Chemistry in the year 2006 from Andhra University. He specializes in synthesis of Natural products and bio-active small molecules. He is a Senior Research Fellow under CSIR and presently he is a researcher in the field of Natural products synthesis with Indian Institute of Chemical Technology-Hyderabad. He has 2 research articles published international journals to his credit. He has attended more than 8 national and international conferences.

muralivns1@gmail.com