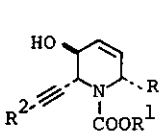
Application of an Oxygenative Nucleophile Introduction Reaction to 2-Alkynyl-1,2-dihydropyridine Derivatives

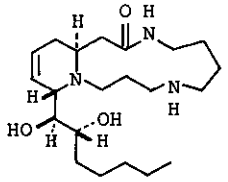
Masashi Ogawa and Mitsutaka Natsume
Research Foundation Itsuu Laboratory
Tamagawa 2-28-10, Setagaya, Tokyo 158, Japan

Variously functionalized 2,6-dialkylpiperidine derivatives are important as starting materials for the synthesis of natural products. We studied this time regioselective preparation of 1-alkoxycarbonyl-2-alkynyl-1,2-dihydropyridines, and submitted these to our $SnCl_2$-mediated oxygenative nucleophile introduction reaction. Alkynyl groups were completely intact to our reaction and formation of the desired compounds 1 was found to be satisfactory with respect to chemo- and stereoselective yields.

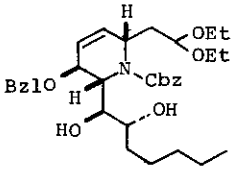
Conformational analysis of 1 led us to explore a stereoselective construction of the side chain of cannabisativine 2 and a possible intermediate 3 aiming at 2 was readily synthesized from 1 [$R^1=CH_2Ph$, $R^2=C_5H_{11}$, $R=CH_2CH(OEt)_2$] by (i) hydrogenation over Lindlar catalyst, (ii) O-benzyl protection, and (iii) glycol formation with OsO_4. Structure of 3 was proved by conversion into 4, whose ^1H nmr spectrum clearly demonstrated the stereochemical feature of oxygen-nitrogen arrangement.



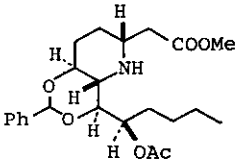
1



2



3



4