NATURAL PRODUCT SYNTHESIS STARTING FROM PYRIDINES

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Utility of our $SnCl_2$ mediated condensation reaction of carbon nucleophiles with endoperoxides derived from 1,2-dihydropyridines was further demonstrated by applying to the effective stereoselective synthesis of piperidine containing alkaloids as follows.

I. Synthesis of A Nuphar Alkaloid, Nupharolutine.[1]

Starting materials, 3-methylpyridine and 2-trimethylsilyloxy-2-butene, were selected so as to obtain condensation product 12, which was hydrogenated, followed by reaction with 3-furyl aldehyde to give 15. Removal of the ketone group completed a short synthesis of (±)-nupharolutine.

II. Synthesis of A Prosopis Alkaloid, Prosophylline.[2]

The endoperoxide derived from 2-vinyl-1-benzyloxycarbonyl-1,2-dihydropyridine was reacted with 1-trimethylsilyloxy-1,3-butadiene. The major product 27 was reduced with $Fe(CO)_5$-NaOH to afford 28. Introduction of benzyl group at the alcohol made it possible to differentiate the reactivity of vinyl function and the ring double bond. Thus, 29 was produced in the regioselective manner, and elongation of the side chain terminated the first synthesis of prosophylline.

III. Synthetic Approach to Equisetum Alkaloid, Palustrine.

A key intermediate 33 for the synthesis of (±)-palustrine was obtained in the stereospcific manner. Stereocontrolled formation of the hydroxypropyl side chain was achieved by reaction of Et_2CuLi on 21b. Copper chelate species C presumably played a definite role for conducting the attack of the carbanion to the aldehyde from the preferential face to afford the correct stereochemistry. 21b was synthesized by the condensation of 17 with ethyl vinyl ether, followed by the oxidative cleavage of the vinyl group, whose methodology was analogous to the above synthesis.

1. M. Natsume and M. Ogawa, Heterocycles, 15, 237 (1981).
2. M. Natsume and M. Ogawa, Heterocycles, 16, 973 (1981).