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SYNTHETIC ROUTE TOWARDS LEPADINS

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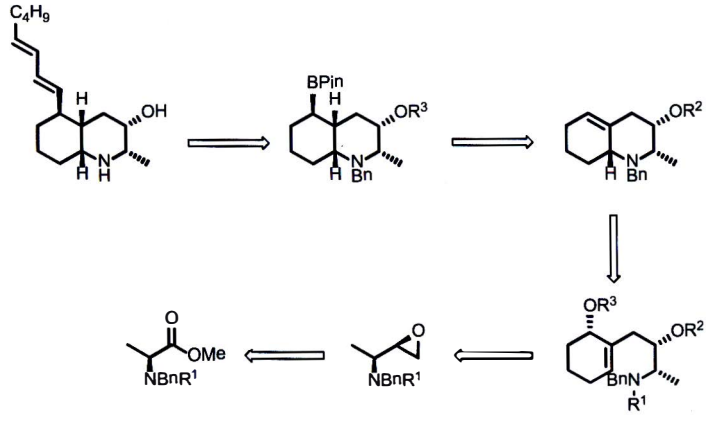
Lepadins are a class of *cis*-decahydroquinoline alkaloids isolated from several marine organisms: *Clavelina lepadiformis, Protheceraeus vittatus, Didemnum* sp., *Aplidium tabascum.* Eight representatives have been isolated during the period 1991–2002 [1, 2]. The lepadin alkaloids are characterized by a *cis*-decahydroquinoline ring containing a C-2 methyl group, a C-3 oxygenated (hydroxy or acyloxy) group and a C-5 eight carbon side chain.

Lepadins exhibit biological activity: cytotoxic, antiplasmodial, antitrypanosomal and neurological properties [3]. Further pharmacological research has been limited by the low quantities of samples available from natural sources. Previous syntheses of lepadins require many steps (18–40 steps) and that is why development of practical synthetic route towards these compounds is required.

We investigated a modular synthetic approach towards decahydroquinoline alkaloids. The main stages of our synthesis include epoxide preparation from orthogonally protected alanine methyl ester, the next stage is copper catalyzed epoxide coupling with bromo-cyclohexene derivative. Synthesis of octahydroquinoline core required development of novel Pd catalyzed amino-cyclization reaction.



Scheme 1. Retrosynthetic analysis of lepadin B

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References:

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