Thesis Title Synthetic Studies of 8-Oxoprotoberberine Alkaloids

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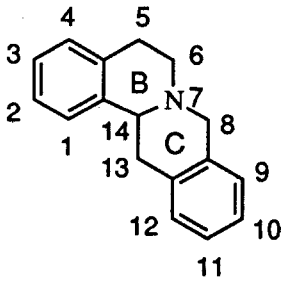
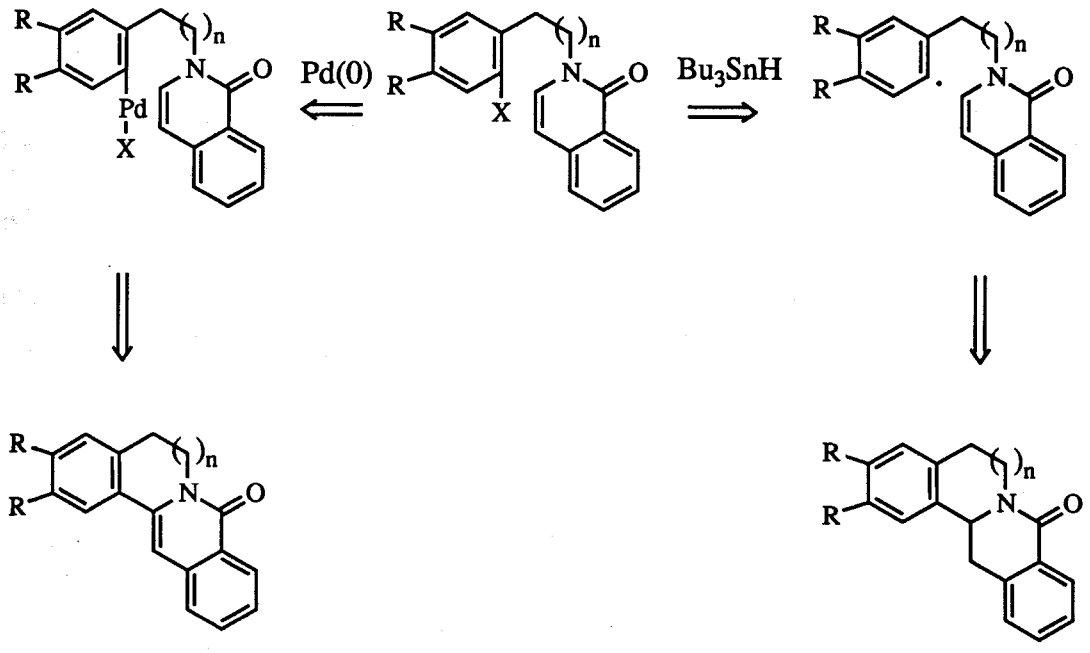
ABSTRACT

Derivatives of protoberberine alkaloids are natural products from numerous plants of Anonaceae, Berberidaceae, Convolvulaceae etc. which have four rings system as the main structure. In pharmacological studies, they posseses various biological activities such as antimicrobial, uterine contracting or stimulating and anticancer. Furthermore, protoberberine alkaloids act as very important precursors and can be transformed to other alkaloids such as protopine, spirobenzylisoquinoline, secoberbine, indenobenzanepine, benzo[c]-phenanthridine derivatives. So, in the past two decades, numerous studies of protoberberine alkaloids synthesis have been reported.



In our studies, we have devised a new synthetic route for the synthesis of 8-oxoprotoberberine derivatives, using as the key reaction, the formation of carbon 14 and 14a to cyclize ring B of the protoberberine skeleton using palladium (0) complex and tributyltin hydride in the presence of azobisbutyronitrile. We have utilized this new approach to successfully synthesized many 8-oxoprotoberberine alkaloids. In addition, we have also carried out the detailed investigation concerning the contributing factors which might govern the yields of products in the cyclization reactions such as substituents on the aromatic ring A, the magnitude of the ring size, base, acid and types of ligands of palladium (0) complex. The approach of our study was outlined as shown in scheme I.

Scheme I



n = 1 R = OCH_3 X = I
n = 1 R = H X = I
n = 1 R = H X = Br
n = 2 R = OCH_3 X = I