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ABSTRACT

The Reissert compounds have been used extensively for the synthesis of various heterocyclic compounds and alkaloids, especially the 1-benzylisoquinoline alkaloids. Their synthetic utilities are hampered by the sometimes low yield in the synthesis of the Reissert compounds and the multi-steps required for further transformations. We have solved the above problems by developing a high yield synthesis of the Reissert compounds and further reactions can be effected as a one-pot reaction. Many Reissert compounds have been successfully synthesized. A one-pot reaction for the synthesis of 1-benzylisoquinoline derivatives and 1-(α -hydroxybenzyl)isoquinoline (papaverinol) can be effected in good overall yield. The approach has also been successfully applied to the annulation of phenanthridine, with 2-chloromethylbenzoyl chloride.

The synthetic utility of dihydro Reissert compound was explored, however many attempts investigated failed to give the desired compounds. The problem was solved when we found that the presence of cyanide group was not necessary for the successful generation of the benzylic carbanion. The role of 'dipole-stabilized carbanion' is briefly discussed, followed by our successful attempts to use it as a means to synthesize 1-substituted-isoquinoline derivatives.

Analysis of the synthesis of berbine alkaloid in terms of carbon-carbon bond formation was presented. Three routes for the synthesis of 8-oxoberbine alkaloids have been developed. The first route involves the annulation of isoquinoline derivatives with 2-chloromethylbenzoyl chloride, the whole sequence of the reaction can be effected in a one reaction vessel. The second route involves the intramolecular alkylation of the dipole-stabilized carbanion derived from the appropriate amide of the isoquinoline derivative using bond α formation as the key step in the reaction. Various berbine alkaloids have been successfully synthesized by this route. The third route utilizes the chelation effect in ortho-lithiated benzamide. In terms of carbon-carbon bond formation this route involves the successive formation of bonds d, e, f. The approach has been successfully utilized for the synthesis of C-13 methylberbine alkaloid.