

THE SYNTHESIS OF HETEROCYCLIC COMPOUNDS VIA ARYL METAL HALIDES

Katsumi Chiba, Setsuko Kudo, Miwako Mori, and Yoshio Ban

Faculty of Pharmaceutical Sciences, Hokkaido University, 060 Sapporo, Japan

The synthesis of heterocycles by utilization of organometallic compounds such as Ni or Pd has been recently studied in this laboratory. The reactions promoted with palladium are very attractive, since a number of various nucleophiles should attack the olefins to afford the important products. In order to attempt the reaction of the aryl halide with a double bond within the molecule, N-(3-Phenyl-2-propenyl)-N-(2-bromobenzyl)benzylamine was heated with a catalytic amount of $\text{Pd}(\text{OAc})_2$ (2 mol %) and PPh_3 (4 mol %) in the presence of tetramethylethylenediamine (TMED 200 mol %) under the stream of nitrogen at 125° for 69 hr to furnish 1-benzyl-4-benzylidene-1,2,3,4-tetrahydroisoquinoline (7.6 %) and 4-benzylisoquinoline (27.3 %). N-(3-Carbomethoxy-2-propenyl)-2-bromoacetanilide was treated in the same way to give methyl 1-acetylinole-3-acetate in 43 % yield, which upon hydrolysis afforded indole-3-acetic acid quantitatively.

On the other hand, the insertion of CO by utilization of transition metal has been applied to exploit a new method of the synthesis of heterocyclic compounds. When N-(2-bromobenzyl)-N-benzylamine was heated with a catalytic amount of $\text{Pd}(\text{OAc})_2$ and PPh_3 in the presence of $n\text{-Bu}_3\text{N}$ under an atmospheric pressure of CO at 100° for 26 hr, 2-benzylisoindolin-1-one was obtained in a good yield (63 %). Similarly, N-benzyl-N-(2-bromophenethyl)amine afforded 2-benzyl-1,2,3,4-tetrahydroisoquinolin-1-one (65 %). With N-(2-bromobenzyl)-N-(2-bromophenethyl)amine, the formation of a five membered ring was predominant, in which the ratio of 2-(2-bromophenethyl)-isoindolin-1-one (38.5 %) and 2-(2-bromobenzyl)-1,2,3,4-tetrahydroisoquinolin-1-one (14.6 %) was approximately 4.7:2.