

THE SYNTHESIS OF HETEROCYCLIC COMPOUNDS VIA ARYL METAL HALIDES

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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 Pd(OAc)<sub>2</sub> (2 mol %) and PPh<sub>3</sub> (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-acetylindole-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 Pd(OAc)<sub>2</sub> and PPh<sub>3</sub> in the presence of n-Bu<sub>3</sub>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.