

THE SYNTHESIS OF HETEROCYCLIC COMPOUNDS BY USE OF ORGANOMETALLIC  
COMPLEX. THE SYNTHESIS OF OXINDOLE AND ISOQUINOLINE ALKALOIDS

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The heterocyclic compound was synthesized via arylmetal complex( $ArMXL_n$ ) which was prepared from aryl halide( $ArX$ ) and low valent metal( $ML_m$ ). In the extension of these studies, the natural alkaloids were synthesized.

1. The synthesis of heterocyclic compounds by the reaction of arylnickel complex ( $ArNiXL_n$ ) with internal double bond and the application of this method

*o*-Chloro-*N*-allyl-*N*-methylaniline was refluxed with  $MeMgBr$  in the presence of a catalytic amount of  $NiCl_2(PPh_3)_2$  in tetrahydrofuran for 30 min to give 1,3-dimethylindole in 53% yield. In the same manner, 1-methyl-4-methylene-1,2,3,4-tetrahydroquinoline (90%) and 1-methyl-5-methylene-2,3,4,5-tetrahydro-1*H*-1-benzazepine (62%) were obtained. When the functional group was present in the molecule, zerovalent nickel complex  $[Ni(PPh_3)_4]$  was used and many oxindole derivatives were prepared. Further extension of these studies, the natural alkaloid, [6-hydroxy-2'-(2-methylpropyl)-3,3'-spiro-tetrahydropyrrolidino-oxindole], was synthesized.

2. The synthesis of benzolactam by palladium catalyzed amidation and the total synthesis of sendaverine

It has been already reported that *o*-bromo-aminoalkylbenzene was heated with a catalytic amount of  $Pd(OAc)_2$  and  $PPh_3$  in the presence of  $n-Bu_3N$  in an atmosphere of carbon monoxide to give benzolactams. The substituents at the aromatic ring were not effected in this reaction and thus, *N*-benzyl-2-bromo-4,5-dimethoxyphenethylamine gave *N*-benzyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-one in good yield (78%). As the application of this synthetic method, the natural alkaloid, sendaverine, was synthesized.