

NICKEL-PHOSPHINE COMPLEX CATALYZED GRIGNARD COUPLING OF HETEROCYCLIC COMPOUNDS

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A general, versatile method for alkylation, alkenylation and arylation of haloheterocyclic compounds is reported.

Recently, Corriu and Masse [Chem. Commun., 144 (1972)] and we [J. Am. Chem. Soc., 94, 4374 (1972)] reported the selective carbon-carbon bond formation by cross-coupling of Grignard reagents with aromatic and olefinic halides in the presence of nickel complexes as catalysts. This paper describes the successful application of the nickel-phosphine complex catalyzed Grignard coupling to heterocyclic compounds. Thus, in the presence of a catalytic quantity of $[\text{Ni}(\text{dppp})\text{Cl}_2]$, $\text{dppp} = \text{Ph}_2\text{P}(\text{CH}_2)_3\text{PPh}_2$, 2-bromo-, 3-bromo-, and 2,5-dibromo-thiophene, 2-bromo-, 3-bromo-, 2,6-dichloro-, and 3,5-dichloro-pyridine, and 2-bromoquinoline reacted with *n*-butyl, trimethylsilylmethyl and/or 2-thienyl Grignard reagents at room temperature or at ether refluxing temperature during 2-44 hr to give coupling products in 35 - 100% yields, excepting the reaction of 2-bromothiophene with *n*-butylmagnesium bromide which gave mainly thiophene. Coupling reaction of the thienyl Grignard reagent with chloro- and bromo-benzene, 1-bromonaphthalene and vinyl chloride was also achieved under similar conditions.

The application of the present method is exemplified by one-step preparation of $[\text{n}](2,6)\text{pyridinophanes}$ by the reaction of 2,6-dichloropyridine with $\text{BrMg}(\text{CH}_2)_n\text{MgBr}$ ($n = 6 - 10, 12$). Racemic muscopolypyrindine, i.e., 2-methyl[10](2,6)pyridinophane, the *d*-form of which is one of the odoriferous constituents of natural musk from the musk deer (*Moschus moschiferus*) was obtained in 20% yield by the reaction of the di-Grignard reagent of racemic 2-methyl-1,10-dibromodecane with 2,6-dichloropyridine in the presence of $[\text{Ni}(\text{dppp})\text{Cl}_2]$.

The present method uses highly simple procedure, gives high yields of coupling products and should be widely applicable.