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Stereospecific Nickel-Catalyzed Cross-Coupling Reactions of Alkyl Grignard Reagents and Identification of Selective Anti-Breast-Cancer Agents

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Category

Metal-Mediated Synthesis

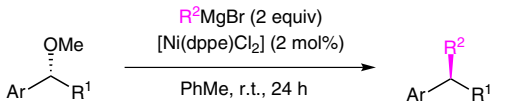
Key words

Grignard reagents

Kumada coupling

nickel

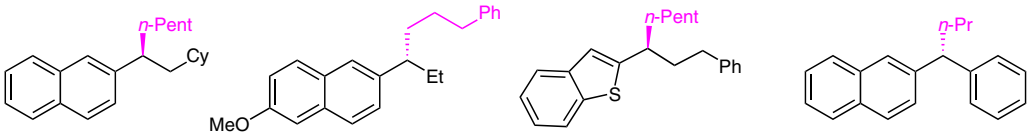
Stereospecific Kumada Cross-Coupling of Alkyl and Aryl Grignards



up to 93% yield
up to 97% ee

Ar = Naph, 6-MeONaph, benzothiophenyl, benzofuranyl
R^1 = Et, *i*-Bu, CH_2Cy, Bn, CH_2Bn, $(CH_2)_2CHCMe_2$
R^2 = various Alk, Ar

Selected examples:

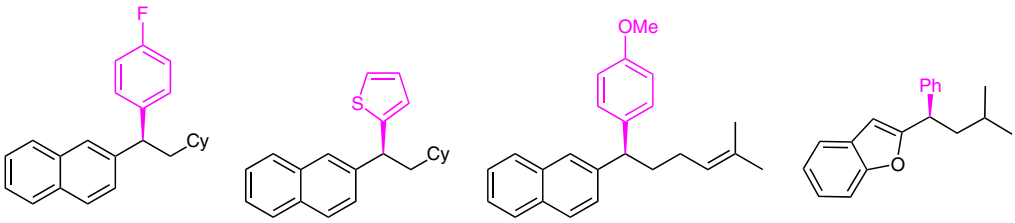


91% yield
97% ee
>99% es

88% yield
93% ee
>99% es

54% yield
96% ee
97% es

67% yield
91% ee
91% es



82% yield
87% ee
88% es

76% yield
93% ee
94% es

92% yield
88% ee
92% es

71% yield
95% ee
98% es

Significance: Herein, the authors report an efficient nickel-catalyzed cross-coupling reaction of long-chain alkyl and various aryl Grignards with benzylic ethers providing the corresponding products with high enantiospecificity. Furthermore, applying this reaction protocol, compounds that show promising inhibition of breast cancer cell proliferation could be prepared.

Comment: Decreasing the reaction concentration raised the efficiency of the transformation and less elimination byproduct was generated. Also, the use of more than two equivalents of Grignard reagent was disadvantageous for the reaction.

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