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Nickel(0)-Catalyzed Hydroalkylation of 1,3-Dienes with Simple Ketones
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Nickel-Catalyzed Enantioselective Hydroalkylation of 1,3-Dienes

Selected examples:

78% yield, er = 96:4^a

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91% yield, er = 96:4^a

91% yield
dr = 1.1:1, er = 90.5:9.5^a

70% yield
dr = 1.4:1, er = 90.5:9.5^a

40% yield, er = 86:14^b

^a (*S*)-DTBM-HO-BIPHEP was employed. ^b Performed with (*S*)-DTBM-MeO-BIPHEP and reacted at 90 °C.

Derivatization:

er = 96:4

(*R*)-(+)-flobufen
75% yield, er = 98:2

Significance: Transition-metal-catalyzed asymmetric addition of enols or enolates to unsaturated hydrocarbons remains an unanswered challenge. The authors have developed a regio- and stereo-selective hydroalkylation of 1,3-dienes by nickel catalysis.

Comment: This catalytic reaction provides a wide range of γ,δ -unsaturated ketones or esters in good yields and with high enantioselectivities. One product was easily converted into the nonsteroidal anti-inflammatory drug (*R*)-flobufen, which also exhibits immunomodulatory properties.

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