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Stereospecific Nickel-Catalyzed Cross-Coupling Reactions of Alkyl Ethers: Enantioselective Synthesis of Diarylethanes

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Asymmetric Synthesis of 1,1-Diarylethane Drugs

Significance: Syntheses of the sleep-inducing H₁-antihistamine **K** and the tubulin polymerization inhibitor **N** exemplify a general enantioselective synthesis of 1,1-diarylethanes using the stereospecific nickel-catalyzed cross-coupling reactions of alkyl ethers with methylmagnesium iodide. Further seven examples are reported giving yields of 70–96% and ee values of 85–99%.

Comment: The chiral diarylcarbinols (for example, **E**) were constructed via enantioselective addition of Et₂Zn to aryl aldehydes catalyzed by Ti(Oi-Pr)₄ and *ent*-BINOL (A. S. C. Chan and co-workers *Tetrahedron: Asymmetry* **1997**, *8*, 585) or by addition of arylzinc reagents catalyzed by *ent*-(1-methylpyrrolidin-2-yl)diphenylmethanol (A. L. Braga et al. *J. Org. Chem.* **2008**, *73*, 2879).

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