Catalytic Enantioselective γ-Alkylation of Carbonyl Compounds

Significance: The authors describe a new method for the catalytic enantioselective γ- (and δ-) alkylation of carbonyl compounds by cross-coupling of γ- (and δ-) haloamides with alkylboranes. The reaction is catalyzed by nickel and uses a commercially available chiral diamine ligand to achieve high enantiomeric excess.

Comment: The reaction conditions tolerate alkyl chlorides as well as alkyl bromides as suitable electrophilic cross-coupling partners. Also, an aryl metal, a boronate ester, and a secondary alkyl metal compound are able to undergo the stereoselective cross-coupling with good enantiomeric excess.

Selected examples:

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\begin{align*}
\text{Ph}_2\text{N} & \quad \text{O} & \quad \text{R}^1 = \text{NPh}_2, \text{N(OOMe)} & \quad \text{R}^2 = \text{Me, Et, n-Bu, Bn, f-Bu} & \quad \text{X} = \text{Cl, Br} \\
\text{Ph}_2\text{N} & \quad \text{O} & \quad \text{Et} & \quad \text{OMe} & \\
\text{Ph}_2\text{N} & \quad \text{O} & \quad \text{n-Bu} & \quad \text{OMe} & \\
\text{Me} & \quad \text{N} & \quad \text{O} & \quad \text{Et} & \\
\text{Ph}_2\text{N} & \quad \text{O} & \quad \text{Et} & \quad \text{OTBS} & \\
\end{align*}
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63% yield 85% ee
80% yield 89% ee
64% yield 90% ee
75% yield (with 25% KI) 86% ee
74% yield 91% ee