Category
Peptide Chemistry

Key words
palladium catalysis
Suzuki–Miyaura arylation
aziridinecarboxylates
aryl amino acids
asymmetric synthesis

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Asymmetric Synthesis of β²-Aryl Amino Acids through Pd-Catalyzed Enantiospecific and Regioselective Ring-Opening Suzuki–Miyaura Arylation of Aziridine-2-carboxylates
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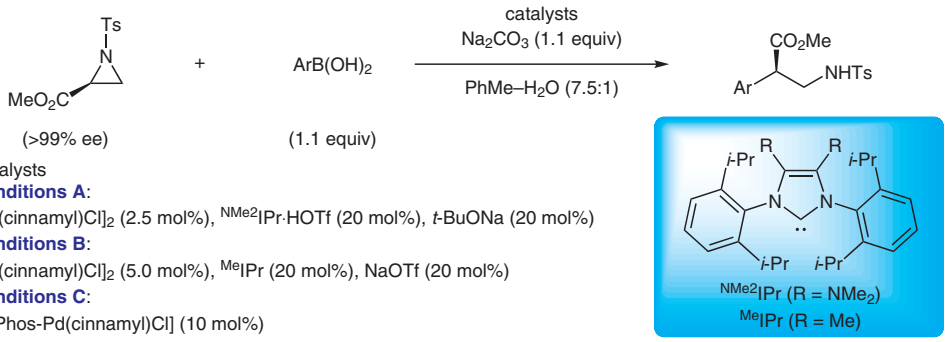
Synthesis of β²-Aryl Amino Acids with Palladium Catalysts

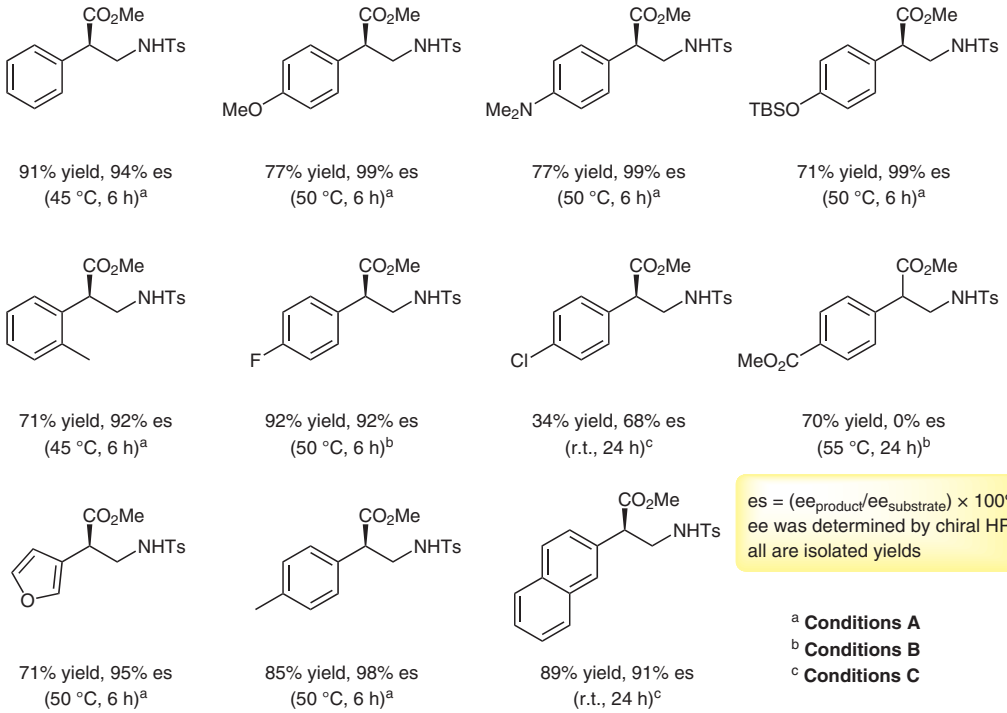


Catalysts

Conditions A:
[Pd(cinnamyl)Cl]$_2$ (2.5 mol%), ^{NMe2}IPr·HOTf (20 mol%), *t*-BuONa (20 mol%)

Conditions B:
[Pd(cinnamyl)Cl]$_2$ (5.0 mol%), ^{Me}IPr (20 mol%), NaOTf (20 mol%)

Conditions C:
[X-Phos-Pd(cinnamyl)Cl] (10 mol%)



91% yield, 94% es (45 °C, 6 h)[a]

77% yield, 99% es (50 °C, 6 h)[a]

77% yield, 99% es (50 °C, 6 h)[a]

71% yield, 99% es (50 °C, 6 h)[a]

71% yield, 92% es (45 °C, 6 h)[a]

92% yield, 92% es (50 °C, 6 h)[b]

34% yield, 68% es (r.t., 24 h)[c]

70% yield, 0% es (55 °C, 24 h)[b]

71% yield, 95% es (50 °C, 6 h)[a]

85% yield, 98% es (50 °C, 6 h)[a]

89% yield, 91% es (r.t., 24 h)[c]

es = ($ee_{product}/ee_{substrate}$) × 100%
ee was determined by chiral HPLC
all are isolated yields

[a] **Conditions A**
[b] **Conditions B**
[c] **Conditions C**

Significance: An efficient palladium-catalyzed method was developed for the enantiospecific and regioselective ring-opening Suzuki–Miyaura arylation of aziridine-2-carboxylates. Detailed mechanistic discussions and computational studies are provided.

Comment: The authors have developed a cross-coupling reaction of aziridine-2-carboxylates to give enantioenriched β²-aryl amino acids in moderate to excellent yields. The aziridine derivatives can be prepared from commercially available enantiopure serine. The method might be applicable to the synthesis of a variety of β-amino acid derivatives.

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