Ruthenium-Catalyzed Generation of N-Unsubstituted Imines

**Significance:** The authors report, that N-unsubstituted imines can be efficiently generated from alkyl azides using a ruthenium catalyst and fluorescent light. Furthermore, an allilation reaction in a one-pot fashion was achieved, leading to homoallylic imines.

**Comment:** The mild reaction conditions allow an asymmetric allilation of in situ generated benzaldimine from benzyl azide. Using the chiral allyl bis(isopinocampheyl)borane reagent at −78 °C furnishes the homoallylic amine in 87% yield with an enantiomeric excess of 89%.

**Selected examples:**

- **83% yield**
- **86% yield (syn/anti = 87:13)**
- **91% yield**
- **80% yield (syn/anti = 98:2)**
- **73% yield**
- **80% yield (single diastereomer)**
**Significance:** The authors report the new catalyst Pd-PEPPSI-Ipent\(^{\text{Cl}}\), which highly efficiently couples secondary alkylzinc reagents to (hetero)aryl bromides, chlorides and triflates. The corresponding alkylated aromatics are obtained in excellent yield and with high regioselectivity.

**Comment:** \(\beta\)-Hydride elimination (BHE) constitutes one of the main drawbacks for the cross-coupling of secondary alkyl reagents, especially if they react with electron-rich coupling partners. These problems are overcome by the new palladium-catalyst, which bears bulkier substituents and additionally, is characterized by a decreased electron density, thus favoring reductive elimination instead of BHE. Density functional theory (DFT) calculations support the theoretical selectivities.

---

**Pd-PEPPSI-Ipent\(^{\text{Cl}}\) – Selective Coupling of Secondary Organozinc Nucleophiles**

\[
\text{Ar} - X \xrightarrow{\text{Pd-PEPPSI-Ipent}^{\text{Cl}} (1 \text{ mol%)}} \xrightarrow{\text{THF–PhMe, 23 °C}} \text{Ar}^{\text{R}1\text{R}2} \quad \text{up to 99% yield} \]

\[
\text{Ar}^{\text{R}1\text{R}2} \quad \text{up to >99:1 n/r (normal to rearranged product)}
\]

**Selected examples:**

- **99% yield**

  n/r > 99:1

- **85% yield**

  n/r = 49:1

- **95% yield**

  n/r > 99:1

- **95% yield**

  n/r > 99:1

- **84% yield**

  n/r > 99:1
Palladium-Catalyzed β-Arylation of α-Amino Esters

**Significance:** A novel general β-arylation of protected alanine esters to yield synthetically useful (hetero)aryl alanine building blocks has been disclosed. The protocol utilizes a lithium amide to form an enolate that undergoes a palladium-catalyzed C–C coupling with various aromatic bromides.

**Comment:** Interestingly, the reaction could be extended to α-amino acids bearing other linear alkyl chains. Arylation occurs preferentially at the terminal Csp3–H bond, thus providing δ-, ε- and even ζ-arylated products. All products could be deprotected via hydrogenolysis to give the respective amines.
Enantioselective Fluoroallylboration of Aldehydes

Significance: An enantioselective fluoroallylboration of a variety of aldehydes with $B$-(3,3-difluoroallyl)disopinocampheylborane has been disclosed. The resulting 2,2-gem-difluorinated homoallylic alcohols have been obtained in good yield and high enantioselectivity.

Comment: The described reaction proceeds in one pot. After the synthesis of $B$-(3,3-difluoroallyl)disopinocampheylborane out of freshly prepared 1,1-difluoroallene, the aldehyde is added directly to the reaction mixture, followed by an oxidative workup.

Selected examples:

- 72% yield, 94% ee
- 71% yield, 93% ee
- 70% yield, 94% ee
- 76% yield, 97% ee
- 70% yield, 91% ee
- 69% yield, 92% ee

R = Ph, PMP, Naph, (CH$_2$)$_2$Ph, (E)-CH=CHPh, 2-furyl
**Significance:** A practical and straight-forward method for the preparation of indole-3-carboxylic acids has been reported. Deprotonation with LiOt-Bu under an atmospheric pressure of carbon dioxide furnishes a variety of indole-3-carboxylic acids in high yield.

**Comment:** The described reaction is very versatile since it tolerates various functional groups and has therefore a broad substrate scope. According to the authors, the large excess of LiOt-Bu suppresses the undesired decarboxylation side reaction.
Preparation and Rearrangement of $N$-Vinyl Nitrones: Synthesis of Spiroisoxazolines and Fluorene-Tethered Isoxazoles

**Org. Lett. 2012, 14, 5180–5183.**

**Significance:** Herein, the authors disclose the single-step, copper-mediated coupling of fluorene oximes and vinyl boronic acids, which undergo thermal rearrangement via [3+2] cycloaddition to form spiroisoxazolines. The corresponding $N$-vinyl nitrones and spiroisoxazolines are obtained in good yield.

**Comment:** In addition, this methodology may be applied to the synthesis of fluorene-tethered isoxazoles by treatment of $N$-vinyl nitrones with terminal or internal electron-deficient alkynes. The mechanism is supposed to proceed via [3+2] cycloaddition and subsequent elimination.

**Key words**
- boron
- copper
- fluorenone oxime
- $N$-vinyl nitrones
- [3+2] cycloaddition

**Selected examples:**

- $R^1 = \text{Et, Me, H, Ph, 4-O}_2\text{NC}_6\text{H}_4\text{H}, 4-\text{FC}_6\text{H}_4\text{H}, 4-\text{F}_3\text{CC}_6\text{H}_4$  
  $R^2 = \text{Et, Me, } n\text{-Bu, Ph}$  
  $R^1 + R^2 = 1\text{-cyclohexene derivatives, 1-cyclopentene, 1-cycloheptene, dihydropyran}$

![Diagram]

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Synthesis of Phenanthridine Derivatives via Oxidative Cyclization

**Significance:** A straightforward synthesis of a broad range of phenanthridine derivatives via a manganese-mediated annulation of 2-isocyanobiphenyls with organoboronic acids has been disclosed. This rapid and divergent reaction furnishes the corresponding phenanthridine derivatives in good yield.

**Comment:** The reported reaction shows a simple pathway for the synthesis of phenanthridine frameworks out of readily accessible starting materials. Furthermore, mechanistic studies indicate that the reaction proceeds by the intramolecular homolytic aromatic substitution of an imidoyl radical intermediate.
Direct Amination of Alkyl and Aryl Pinacol Boronates

Significance: Herein, the direct and stereospecific amination of various aryl and alkyl pinacol boronates with lithiated methoxyamine is disclosed. The corresponding (un)protected amines are obtained in very good yield and, in case of chiral compounds, with high enantiomeric excess.

Comment: Sensitive functional groups such as CN, OMe and CF₃ moieties are well tolerated with this methodology. In addition, this strategy might even be applied to gram-scale reactions without any further drawbacks.
Rhodium-Catalyzed Synthesis of Diaryl Sulfides Using $S_8$/Organopolysulfides

Significance: The rhodium-catalyzed reaction of sulfur or organopolysulfides with aryl penta- and monofluorides in the presence of tributylsilane is disclosed. The corresponding diaryl sulfides are obtained in moderate to good yield.

Comment: The mechanism is proposed to proceed via oxidative addition of the rhodium complex to the aryl fluoride and the SS–SS bond. After insertion of one sulfur atom, di-tert-butyl trisulfide is expelled and the rhodium–fluoride–aryl sulfide complex reacts with another aryl fluoride. The fluoride atoms are trapped with tributylsilane or triphenylphosphine and the corresponding diaryl sulfides are obtained after reductive elimination.

Selected examples:

- NO$_2$F
  - 42% yield (conditions A)

- Ph$_2$N
  - 18% yield (conditions A)

- PhS
  - 80% yield (conditions B)

- NO$_2$S
  - 53% yield (conditions B)

- ClS
  - 53% yield (conditions B)

- NC$_2$N
  - 71% yield (conditions B)
Iron-Catalyzed Hydromagnesiation of Diarylalkynes and Diynes

**Significance:** The authors report a novel iron-catalyzed hydromagnesiation of diarylalkynes in high yield with high stereoselectivity. Furthermore, alkenyl-magnesium compounds can be synthesized from diynes in a chemo-, regio- and stereoselective way.

**Comment:** The alkenylmagnesium intermediates can further be functionalized in a one-pot sequence. Reactions with allyl bromide, \(N,N\)-dimethylformamide and even nickel-catalyzed cross-couplings have been disclosed. The authors suggest a radical mechanism instead of a pure anionic mechanism.
Pentafluorinated β-Hydroxy Ketone Synthesis via Lithium-Mediated Aldol Reaction

Significance: A fast and mild synthesis of pentafluorinated β-hydroxy ketones has been disclosed. The reaction proceeds via a lithium-promoted aldol reaction of readily available difluoroenolate precursors with trifluoromethyl ketones furnishing the corresponding pentafluorinated β-hydroxy ketones in good to excellent yield.

Comment: The described reaction is very versatile since it proceeds under ambient temperature and tolerates a broad range of functional groups. Furthermore, the authors show that the reduction of the pentafluorinated β-hydroxy ketones furnishes quantitatively the corresponding 1,3-diols favoring the syn-isomer.

Selected examples:

- R₁ = Ph, 4-ClC₆H₄, Naph, (CH₂)₂Ph
  - R₂ = Ar, 2-thienyl, Bn

<table>
<thead>
<tr>
<th>R₁</th>
<th>R₂</th>
<th>Yield</th>
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<tbody>
<tr>
<td>Ph</td>
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<td>63%</td>
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<tr>
<td>Ph</td>
<td>Cl</td>
<td>84%</td>
</tr>
</tbody>
</table>

THF, 25 °C, 10 min

Li⁺ (2 equiv)

LHMDS (1.2 equiv)

(1 equiv)

R₁ = Ph, 4-ClC₆H₄, Naph, (CH₂)₂Ph
R₂ = Ar, 2-thienyl, Bn
Fluorination of Nickel(II)–Aryl Complexes with [¹⁸F]Fluoride

**Significance:** The authors report a one-step oxidative fluorination of aryllnickel complexes which enables a straight-forward and practical [¹⁸F] late-stage fluorination of molecules. Therefore, [¹⁸F]-labeled substances of high specific activity for PET imaging can be synthesized.

**Comment:** As the protocol can be performed using aqueous fluoride solutions, extensive drying procedures of fluoride, which are typical for radiochemistry, are not required. Furthermore, direct use of aqueous fluoride solutions increases the yield and prevents radioactive decay.
R. K. CHINNAGOLLA, M. JEGANMOHAN* (INDIAN INSTITUTE OF SCIENCE EDUCATION AND RESEARCH, PUNE, INDIA)

Regioselective Ortho-Arylation and Alkenylation of N-Alkyl Benzamides with Boronic Acids via Ruthenium-Catalyzed C–H Bond Activation: An Easy Route to Fluorenones Synthesis


Ruthenium-Catalyzed ortho-Arylation and Alkenylation of N-Alkyl Benzamides

**Significance:** The authors report a highly regioselective ruthenium-catalyzed ortho-arylation and alkenylation of various N-alkyl benzamides with different (hetero)aromatic and alkenyl boronic acids in the presence of silver salts. The corresponding benzamides are obtained in good to very good yield.

**Comment:** Noteworthy, this methodology may be applied to the synthesis of fluorenones by treatment of the biarylic coupling products with trifluoroacetic anhydride and hydrogen chloride.

**Selected examples:**

\[
\begin{align*}
& R^1 = \text{OMe, Me, I, Br, NO}_2, \text{CN, 1,3-dioxolane, Naph, thiényl} \\
& R^2 = \text{Me, Et, } \text{t-Bu} \\
& R^3 = \text{4-BrC}_6\text{H}_4, 4-\text{FC}_6\text{H}_4, \text{Tol, PMP,} \\
& \quad \text{4-HOC}_6\text{H}_4, 1-\text{Naph}, 3-\text{thienyl, various alkenyls}
\end{align*}
\]

**SYNFACTS Contributors:** Paul Knochel, Nadja M. Barl

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Copper-Catalyzed Amination of Silyl Ketene Acetals with \(N\)-Chloroamines

**Significance:** A copper-catalyzed amination reaction of silyl ketene acetals with \(N\)-chloroamines under mild reaction conditions has been developed. The formation of the corresponding \(\alpha\)-amino esters is catalyzed by a copper(I)–2,2′-bipyridyl complex which furnishes them in high yield.

**Comment:** According to the authors, the bulky silyl group disfavors the formation of unwanted by-products and improves the yield of the desired \(\alpha\)-amino ester. Furthermore, the facile availability of \(N\)-chloroamines from secondary amines with NCS permits a one-pot, two-step synthesis, especially if the \(N\)-chloroamine is too unstable for isolation.

**Selected examples:**

\[
\begin{align*}
\text{CuI (0.1 equiv)} \\
\text{bipy (0.1 equiv)} \\
\text{MeCN, 25 °C, 12 h} \\
\end{align*}
\]

- \(R^1 = \text{Ar, 3-thienyl}\)
- \(R^2 = R^3 = \text{Alk}\)
- \(\text{bipy = bipyridine}\)

<table>
<thead>
<tr>
<th>R^1</th>
<th>R^2</th>
<th>R^3</th>
<th>Yield</th>
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</table>
Metalation of 2-Phenylethylidimethylamine under Mild Conditions

**Significance:** The direct benzylic metalation of 2-phenylethylamine derivatives suffers from β-elimination. The authors found that benzylic metalation of 2-phenylethylidimethylamine can be performed at –78 °C with a mixture of t-BuLi and t-BuOK. The metalated species was found to be stable up to –40°C.

**Comment:** Interestingly, the metalation cannot be performed with a mixture of t-BuLi and t-BuOLi. Therefore, the potassium cation seems to be crucial for an efficient conversion. Theoretical and structural studies reveal that potassium is important for the lowering of the barrier of the initial deprotonation, as well as for stabilization of the labile anion.

\[
\begin{align*}
\text{Ph} & \text{NMe}_2 \\
1. \text{t-BuLi (1.7 equiv)} & \text{t-BuOK (1 equiv)} \\
\text{THF, –78 to –60 °C} & \\
2. \text{electrophile (E⁺) (1 equiv)} & \text{Ph} \text{NMe}_2 \\
\text{E = Bu, TMS, SiMePh₂, CPh₂OH, C(C₅H₁₀)OH} & \\
\text{up to 92% yield} & \text{E} \\
\end{align*}
\]

Selected examples:

- Ph\text{NMe}_2\text{Bu} with 92% yield
- Ph\text{NMe}_2\text{TMS} with 84% yield
- Ph\text{NMe}_2\text{SiMePh₂} with 60% yield
- Ph\text{NMe}_2\text{OH} with 74% yield
- Ph\text{NMe}_2\text{O₃Ph} with 84% yield

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