Nickel- or Palladium-Catalyzed Cross-Coupling Polycondensation

**Significance:** The authors describe a cross-coupling polycondensation of Grignard reagents and various aromatic ethers or ammonium salts to form π-conjugated polymers with high molecular weight through C–O or C–N bond cleavage. The reaction proceeds under mild conditions in the presence of commercially available Ni or Pd catalysts.

**Comment:** Interestingly, the optimized reaction conditions showed that the quality and purity of the organometallic compound critically influenced the yield and reactivity of this polycondensation. In the presence of mono-Grignard reagents, the chain-growth was terminated and the molecular weight was reduced.

**SYNFACTS Contributors:** Paul Knochel, Dorothée Ziegler

**DOI:** 10.1055/s-0037-1610104; Reg-No.: P07518SF
Negishi Coupling Reactions with [$^{11}$C]CH$_3$I: A Versatile Method for Efficient $^{11}$C–C Bond Formation

**Chem. Commun. 2018, 54, 4398–4401.**

**11C–C Bond Formation via Negishi Cross-Coupling**

**Significance:** The authors report a fast, efficient and general one-pot method for the synthesis of $^{11}$C-labelled compounds via a Negishi cross-coupling reaction. The method is based on the in situ formation of [$^{11}$C]CH$_3$ZnI by zinc insertion and the subsequent coupling with aryl halides or triflates.

**Comment:** The method was also successfully applied to the synthesis of $^{11}$C-thymidine, which is a biologically relevant compound with potential applications as a proliferation marker. The proposed irreversible formation of a nucleophilic $^{11}$C–Zn(II) reagent was shown by theoretical calculations.

Selected examples:

- **83% yield**
- **53% yield**
- **69% yield**
- **21% yield**
- **19% yield**
- **33% yield**
- **60% yield**
- **53% yield**

Yields refer to the calculated ratio between the area of the peak corresponding to [$^{11}$C]methylaryl and the sum of the areas of all peaks in the radiochromatogram.

**SYNFACTS Contributors:** Paul Knochel, Simon Graßl

SYNFACTS 2018, 14(07), 0736 Published online: 18.06.2018 DOI: 10.1055/s-0037-1610091; Reg-No.: P06218SF
Magnesium Ethoxide Mediated Synthesis of Amidines

**Significance:** The authors describe an intramolecular direct addition of alkyl amines to aryl nitriles using Mg(OEt)$_2$ as Lewis acid. The resulting amine is subsequently trapped with chloroacetaldehyde leading to a variety of functionalized condensed heterocycles.

**Comment:** The heterocyclic products were successfully derivatized. For example, treating benzoxazepine 1 with 1.5 equivalents of TMPMgCl·LiCl leads to the magnesiation of the phenyl ring. Subsequent trapping with I$_2$ affords the iodinated product in 73% yield.

SYNFACTS Contributors: Paul Knochel, Ferdinand H. Lutter

SYNFACTS 2018, 14(07), 0737 Published online: 18.06.2018

DOI: 10.1055/s-0037-1610993; Reg-No.: P/06418SF
Synthesis of Salicylidene Urea Derivatives by Snieckus–Fries-Type Rearrangement

**Significance:** Sanz and co-workers report an efficient 1,5-O→N-carbamoyl Snieckus–Fries-type rearrangement leading to salicylidene urea derivatives in very good yields.

**Comment:** In this work, the first O→N-carbamoyl migration of ortho-lithiated O-arylcarbamates is described. Reaction of the lithiated species with arylnitriles produces an N-lithiated imine, which then undergoes the carbamoyl translocation.

---

SYNFACTS Contributors: Paul Knochel, Moritz Balkenhohl
Syntacts 2018, 14(07), 0738  Published online: 18.06.2018
DOI: 10.1055/s-0037-1610097; Reg-No.: P06818SF
**Chemoselective Approach Towards α-Aryl and -Alkyl Selenomethylketones**

**Significance:** The authors report an easy and mild preparation of α-aryl and α-alkyl selenomethylketones via a selenium/lithium exchange and subsequent addition to Weinreb amides.

**Comment:** The transformation occurs under full retention of the stereochemistry and shows excellent chemoselectivity.

**Selected examples:**

- **92% yield**
- **86% yield**
- **88% yield**

- **88% yield**
- **85% yield**
- **90% yield**

- **89% yield**
- **84% yield**
- **87% yield**
Solid-State Enantioselective Arylation of Aldehydes in Batch and Continuous-Flow

**Significance:** Harada and co-workers developed a chiral silica-supported binaphthol catalyst, which, in the presence of a titanium source, efficiently catalyzes the enantioselective reaction of aryl organometallic species with aryl aldehydes. This leads to chiral secondary alcohols in high yields and excellent enantioselectivities.

**Comment:** Remarkably, the enantioselective arylation of aldehydes can also be performed under continuous-flow conditions using a convenient pipette reactor. After washing the immobilized catalyst, it can be readily reused for the reaction without loss of stereocontrol up to 14 cycles.

**Selected examples:**

| Reaction | Yield | Enantiomeric Excess |
|----------|-------|---------------------|
| 1.0 equiv of 1.0 equiv of Ti(O-i-Pr)4, 4.7 equiv of (R)-1 (10 mol%) | 97% | 95% ee |
| CH2Cl2, 0 °C, 4–5 h | 96% | 93% ee |
| 2.2 equiv of R1-i-C5H9MgBr | 85% | 83% ee |

**In situ generation of the aryltitanium reagent:**

1. 1-naphthaldehyde (1.0 equiv)
2. Ti(O-i-Pr)4 (0.4 equiv)
3. (R)-1 (5 mol%)
4. CH2Cl2, 0 °C, 3 h

| Reaction | Yield | Enantiomeric Excess |
|----------|-------|---------------------|
| 1-naphthaldehyde (1.0 equiv) | 93% | 86% ee | after the tenth reaction cycle of (R)-1
Metal Acetylide Elimination during the Transformation of Propargyl Amines

Significance: Andrews and co-workers describe a metal acetylide elimination of propargylamines by reaction with organometallic reagents such as n-BuLi, n-BuNa, n-BuMgCl or furyllithium, leading to unsymmetrical secondary amines.

Comment: Spectroscopic studies suggest that the reaction proceeds via a dimetalated intermediate. The IR spectrum of the dimetalated intermediate shows a bathochromic shift of 140 cm⁻¹ compared with the expected absorption band of a free amine.
Radical C–H Trifluoromethylation of Peptides

Significance: The authors report and compare two radical methods (stoichiometric oxidant or photoredox catalysis) to affect the trifluoromethylation of aryl C–H bonds in native unprotected peptides.

Comment: Derivatization of tyrosine and tryptophan side-chains under biocompatible conditions is possible with the reported method. Even fully unprotected peptides with up to 51 amino acids (e.g. insulin) have been successfully modified.
**Palladium-Catalyzed C–H Arylation**

**Significance:** The authors report a new palladium-catalyzed C–H arylation reaction of sulfinylthiophenes with various substituted (hetero)aryl bromides. Varying the reaction conditions allows the selective synthesis of 2-arylated or 2,5-diarylated thiophene derivatives in high yields.

**Comment:** Remarkably, the synthesis of sulfinylthiophenes bearing two different aryl moieties is also possible. Thus, using ‘Conditions B’ with a 2-arylthiophene, leads to the corresponding biarylated heterocycle in up to 85% yield.
X. YIANG, Z.-H. CAO, Y. ZHOU, F. CHENG, Z.-W. LIN, Z. OU, Y. YUAN, Y.-Y. HUANG*  
(WUHAN UNIVERSITY OF TECHNOLOGY, P. R. OF CHINA)  
Petasis-Type gem-Difluoroallylation Reaction Assisted by the Neighboring Hydroxyl Group in Amines  
*Org. Lett. 2018, 20, 2585–2589.

**Petasis Allylation Reaction Enabled by Hydroxyl Groups**

**Significance:** The authors report the preparation of racemic and chiral gem-difluoroallyl-
amines by a Petasis type reaction of gem-difluoroallylboronates, aldehydes and amino alcohols.

**Comment:** To clarify the origin of the regio- and stereoselectivity, a Zimmermann–Traxler model was proposed, in which the allylboronates adds to the C=N bond from its Re-face triggered by the chiral amino alcohols used as ligands.

**Proposed reaction pathway:**

**Selected examples:**

**Method A:**

| Compounds | Yields | Drs |
|-----------|--------|-----|
| ![Image](image1) | 98% | 94:6 |
| ![Image](image2) | 98% | 84:16 |

**Method B:**

| Compounds | Yields | Drs |
|-----------|--------|-----|
| ![Image](image3) | 88% | 84:16 |
| ![Image](image4) | 92% | >99:1 |
| ![Image](image5) | 80% | 90:10 |

**Key words**

- organoboron reagents
- Petasis reaction
- allylation

---

**SYNFACTS Contributors:** Paul Knochel, Dorothée Ziegler  
**Synfacts 2018, 14(07), 0744 Published online: 18.06.2018**

**DOI:** 10.1055/s-0037-1610102; **Reg-No.: P07318SF**
Intramolecular Alkylboration of Terminal Allenes

**Significance:** Ito and co-workers developed a regio- and diastereoselective intramolecular carbo-boration reaction of terminal allenes catalyzed by CuI, leading to alkenylboronates bearing a four-membered ring structure.

**Comment:** Based on mechanistic studies, in the oxidative addition step, the formation of the five-membered cupracycle A is kinetically favored compared with the seven-membered cupracycle B.
Cobalt-Catalyzed Borylation of Aryl Halides

Significance: Geetharani and co-workers developed a cobalt-catalyzed borylation reaction of various functionalized (hetero)aryl bromides and chlorides using B2pin2 as boron source leading to the (hetero)aryl boronates in good yields.

Comment: Mechanistically, cobalt (II) is first reduced to cobalt(I). Subsequent ligand exchange produces a CoI-OMe complex, which reacts with B2pin2 leading to a mixed cobalt–boryl intermediate. Oxidative addition of an aryl halide and subsequent reductive elimination gives the desired aryl boronate.
Generation of Grignard Reagents in Toluene

Significance: The Knochel group developed the organometallic reagents 1 and 2, which readily exchange a large variety ofaryl halides leading toaryl and heteroaryl magnesium reagents in toluene. These reagents react with several electrophiles, including epoxides and aziridines, in excellent yields.

Comment: The development of Grignard reagents in non-ethereal solvents such as toluene is of high industrial interest. Interestingly, these reagents also display an original reactivity, allowing a chlorine/magnesium exchange of electron-rich aryl halides.

SYNFACTS Contributors: Paul Knochel, Moritz Balkenhohl

Synfacts 2018, 14(07), 0747 Published online: 18.06.2018 DOI: 10.1055/s-0037-1610100; Reg-No.: P07118SF
Asymmetric Synthesis of β-Functionalized Ketones over an Immobilized Rh Catalyst

Significance: Uozumi and co-workers developed an efficient method to perform a resin-supported rhodium-catalyzed asymmetric 1,4-addition of arylboronic acids to enones. This results in β-functionalized ketones in high yields and excellent enantioselectivities.

Comment: Interestingly, the immobilized chiral rhodium catalyst (PS-PEG-diene*-Rh) was able to efficiently catalyze the reaction up to ten times without loss of catalytic activity or enantioselectivity. A continuous-flow setup also allowed easy scale up, yielding the desired product in good yield and excellent enantioselectivity on multigram scale.
Oxidative Trifluoromethylthioarylation of Styrenes Using Aryldiazonium Salts

Significance: The authors developed a copper-mediated trifluoromethylthiolation of various functionalized styrenes with (hetero)aryldiazonium salts. The use of 1,10-phenanthroline in combination with DMSO proved to be essential for obtaining the corresponding products in high yields.

Comment: The mechanism starts with the oxidation of the dimeric complex [(phen)CuSCF$_3$)$_2$ by an aryl diazonium salt leading to the corresponding copper(II) species and an aryl radical, which adds to a styrene. The formed benzylic radical could be trapped by [(phen)CuSCF$_3$)$_2$. Subsequent reductive elimination affords the product.