Palladium/Copper Bimetallic Catalyzed Decarboxylative C-C Bond Formations

vom Fachbereich Chemie der Technischen Universität Kaiserslautern zur Verleihung des akademischen Grades 'Doktor der Naturwissenschaften' eingereichte Dissertation

D 386

vorgelegt von

Jie Tang, M.Sc.

Betreuer

Prof. Dr. Lukas J. Gooßen

Kaiserslautern, 2016

Promotionskommission:

Vorsitzender:	Prof. Dr. Werner R. Thiel
Berichterstatter:	Prof. Dr. Lukas J. Gooßen
Berichterstatter:	Prof. Dr. Stefan Kubik

Datum der wissenschaftlichen Aussprache: 22.12.2016

Die vorliegende Arbeit entstand in der Zeit zwischen November 2012 und December 2016 in den Laboratorien des Fachbereichs Chemie an der Technischen Universität Kaiserslautern.

Eidesstattliche Erklärung

Hiermit versichere ich, dass ich die vorliegende Arbeit eigenständig verfasst, keine anderen als die angegebenen Quellen und Hilfsmittel verwendet und Literaturzitate kenntlich gemacht habe. Ich erkläre außerdem, dass diese Arbeit weder in gleicher noch in ähnlicher Form bereits in einem anderen Prüfungsverfahren vorgelegen hat.

Kaiserslautern, den 22.12.2016 Jie Tang

Jie Tang

To Yichen, Meng Chen & my parents

Acknowledgements

First and foremost, I would like to express my sincere gratitude to Prof. Dr. Lukas J. Gooßen for giving me the opportunity to carry out my Ph.D. work under his supervision. Appreciation goes to him for all his contribution of time, ideas, and funding to make my Ph.D. experience productive and stimulating. I am also thankful to Dr. Käthe Gooßen for all the help in finalizing my manuscripts.

I would like to thank Prof. Dr. Stefan Kubik and Prof. Dr. Werner R. Thiel for being in the examination committee of my dissertation.

China Scholarship Council, the DFG (SFB/TRR-88, "3MET") and DAAD are gratefully acknowledged for providing me with financial support to complete my Ph.D.

I am grateful to ISGS for all the support during my stay in Kaiserslautern.

Thanks to Agostino Biafora and Dagmar Hackenberger for fruitful discussions and hard work during our collaborative projects.

I am especially grateful to Dagmar Hackenberger for reviewing my thesis.

I would like to thank our secretary Frau Susanne Zeigner for her kind help during my work in TU Kaiserslautern.

I would like to thank Mrs. Müller from NMR facility, Mrs. Biel, Mrs. Dusch, Mrs. Ellmer and Mrs. Bergsträßer from the analytical department and Mr. Napast, Mr. Rahm, and Mr. Schröer from the chemical storage facility.

I am especially thankful to Andreas Fromm, Christoph Oppel, Patrizia Mamone, Matthias F. Grünberg, Sukalyan Bhadra, Grégory Danoun, Bingrui Song, Sabrina Baader, Benjamin Erb, Eugen Risto, Kai Pfister, Dagmar Hackenberger, Thilo Krause, Christian Matheis, Timo Wendling, Bilguun Bayarmagnai, Agostino Biafora, Dmitry Katayev, Liangbin Huang, Kevin Jouvin, Patricia Podsiadly, Minyan Wang, Martin Pichette Drapeau, Alexandre Aillerie, Janet Bahri, Stefania Trita, Fan Jia, Benjamin Exner, Philip Weber, Pratik Yadav, Guodong Zhang, Jacqueline Pollini, Daniel Eppel, Valentina Bragoni for providing me with an outstanding experience in and outside labs.

In the end, I owe my deepest gratitude to my parents and family members, especially my wife. They stood by my side in every aspect of my life. Without their support and encouragement, I would have not earned this degree.

Parts of this work have been published as following:

Publications

- **J. Tang**, D. Hackenberger, L. J. Gooßen, *Angew. Chem. Int. Ed.* **2016**, *55*, 11296-11299: Branched Arylalkenes from Cinnamates: Selectivity Inversion in Heck Reactions by Carboxylates as Deciduous Directing Groups.
- **J. Tang**, A. Biafora, L. J. Gooßen, *Angew. Chem. Int. Ed.* **2015**, **54**, 13130-13133: Catalytic Decarboxylative Cross-Coupling of Aryl Chlorides and Benzoates without Activating *ortho* Substituents.
- **J. Tang**, L. J. Gooßen, *Org. Lett.* **2014**, *16*, 2664-2667: Arylalkene Synthesis via Decarboxylative Cross-Coupling of Alkenyl Halides.

Abbreviations

Ac	Acetyl
acac	Acetylacetonate
Ar	Aryl
$AsPh_3$	Triphenylarsine
BINAP	Bis-(diphenylphosphino)-1,1'-binaphthaline
bpy	2,2'-Bipyridine
Bu	Butyl
*t*Bu	*tert*-Butyl
$^tBu_3P{\cdot}HBF_4$	Tri-*tert*-butylphosphonium tetrafluoroborate
Boc	Di-*tert*-butylldicarbonate
BrettPhos	2-(Dialkylphosphino)3,6-dimethoxy-2',4',6'-triisopropyl-1,1'-biphenyl
cat.	Catalyst
COD	1,5-Cycloctadiene
Cy	Cyclohexyl
CyJohnphos	(2-Biphenyl)dicyclohexylphosphine
DavePhos	2-Dicyclohexylphosphino-2'-(*N*,*N*-dimethylamino)biphenyl
dba	Dibenzylidene acetone
DBU	1,8-Diazabicyclo(5.4.0)undec-7-ene
DFT	Density functional theory
DIPEA	*N*,*N*-Diisopropylethylamine
DMA	*N*,*N*-Dimethylacetamide
DMF	*N*,*N*-Dimethylforamide
DMSO	Dimethylsulfoxide
dnpf	1,1'-bis[di(1-naphthyl)phosphino]ferrocene
dppf	1,1'-Bis(diphenylphosphino)ferrocene
dppp	1,1-Bis(diphenylphosphino)propane
R-DTBM-SEGPHOS	(*R*)-(-)-5,5'-Bis[di(3,5-di-tert-butyl-4-methoxyphenyl)phosphino]-4,4'-bi-1,3-benzodioxole
dtbbpy	4,4'-Di-*tert*-butyl-2,2'-bipyridyl

EI	Electron Ionization
Et	Ethyl
equiv.	Equivalent
F_6-acac	Hexafluoroacetylacetonate
FG	Functional group
GC	Gas chromatography
Het	Hetero
IPr	1,3-bis(2,6-diisopropyl)-phenyl-imidazol-2-ylidene
^{i}Pr	isopropyl
IR	Infrared
Johnphos	2-(Biphenyl)dialkylphosphine
L	Ligand
LED	Light-emitting diode
M	Metal
Me	Methyl
Mes.	Mesitylene
Ms	Methylsulfonyl
*n*Bu	*n*-Butyl
naph	Naphthyl
NHC	*N*-Heterocyclic carbene
Nf	1,1,2,2,3,3,4,4,4-Nonafluorobutane-1-sulfonyl
NMP	*N*-Methyl-2-pyrrolidone
Nu	Nucleophile
PCy_3	Tricyclohexyl phosphine
$PCyp_3$	Tricyclopentyl phosphine
Ph	Phenyl
Phen.	1,10-Phenanthroline
ppm	Parts per million
^{n}Pr	*n*-Propyl
quin.	Quinoline
r.t.	Room temperature
SET	Single electron transfer
SPhos	2-Dicyclohexylphosphino-2',6'-dimethoxybiphenyl

TBAC	Tetrabutylammonium chloride
TBAF	Tetrabutylammonium fluoride
TBHP	*tert*-Butyl hydroperoxide
TEMPO	2,2,6,6-Tetramethylpiperidinyloxyl
Tf	Trifluoromethanesulfonyl
TFA	Trifluoroacetic acid
THF	Tetrahydrofuran
TMS	Trimethylsilyl
Tol	Toluene
Ts	4-Toluenesulfonyl
X	Halide
Xantphos	4,5-Bis(diphenylphosphino)-9,9-dimethylxanthene
Xphos	2-(Dicyclohexylphosphino)-2',4',6'-isopropylbiphenyl

Structure Numbering

The chemical structures of each chapter are numbered separately for clarity and readability. Both in the results section and in experimental section, the number is composed of a second level chapter number followed by hyphen and a structure number of the molecule. For example, **5.1-3ba** represents compound **3ba** in chapter 5.1. Identical chemical structures in different chapters are represented by different numbers.

Table of Contents

Acknowledgements ... **ii**
Publications ... **iii**
Abbreviations ... **iv**
Structure Numbering ... **vii**
Table of Contents ... **viii**
1. Abstract ... **1**
2. Structure of the thesis ... **3**
3. Introduction ... **4**
3.1 Transition metal-catalyzed C-C bond formation reactions ... 4
3.1.1 Bimetallic catalyzed C-C bond formation reactions ... 5
3.1.1.1 Palladium based bimetallic catalyzed C-C bond formation ... 5
3.1.1.1.1 Bimetallic catalysis involving C-H bond activation ... 5
3.1.1.1.2 Bimetallic catalyzed cross-coupling reactions ... 8
3.1.1.1.3 Bimetallic catalyzed decarboxylative coupling reaction ... 11
3.1.1.1.4 Bimetallic catalyzed "cascade" reactions ... 11
3.1.1.2 Non-Pd based bimetallic catalyzed C-C bond formation ... 16
3.2 Decarboxylative cross-coupling reactions ... 17
3.2.1 Redox-neutral decarboxylative coupling reaction ... 18
3.2.1.1 Redox-neutral decarboxylative arylation reaction ... 18
3.2.1.1.1 Decarboxylative coupling of aryl halides ... 18
3.2.1.1.2 Decarboxylative coupling of aryl sulfonates ... 26
3.2.1.2 Decarboxylative alkenylation reaction ... 29
3.2.1.3 Decarboxylative alkynylation reaction ... 30
3.2.2 Challenges in redox-neutral decarboxylative coupling reaction ... 32
4. Aims of the research ... **33**
5. Results and discussion ... **35**
5.1 Catalytic decarboxylative cross-coupling of aryl chlorides and benzoates without activating *ortho* substituents ... 35
5.1.1 Restriction of decarboxylative arylation and the catalyst design ... 36
5.1.2 Protodecarboxylation studies ... 38
5.1.3 Optimization of the reaction conditions ... 39

5.1.4 Scope 41
5.1.5 Conclusions and outlook 44
5.2 Arylalkene synthesis 46
5.2.1 Arylalkene synthesis via decarboxylative cross-coupling of alkenyl halides 49
5.2.1.1 Decarboxylative coupling of alkenyl halides 49
5.2.1.2 Optimization of the reaction conditions 50
5.2.1.3 Scope 52
5.2.1.4 Application of decarboxylative coupling of alkenyl halides 55
5.2.1.5 Conclusions and outlook 55
5.2.2 Branched arylalkenes from cinnamates: selectivity inversion in Heck reactions by carboxylates as deciduous directing groups 57
5.2.2.1 1,1-Disubstituted alkene synthesis 58
5.2.2.2 Decarboxylative Heck coupling reaction 58
5.2.2.3 Protodecarboxylation studies 60
5.2.2.4 Optimization of the reaction conditions 60
5.2.2.5 Scope 62
5.2.2.6 One-pot 1,1-diarylalkene synthesis 65
5.2.2.7 Mechanistic studies 65
5.2.2.8 Conclusions and outlook 66
6. Experimental section 68
6.1. General techniques 68
6.2 Analytical methods 68
6.2.1 Thin layer chromatography 68
6.2.2 Gas chromatography 68
6.2.3 Mass spectroscopy 68
6.2.4 High-performance liquid chromatography 69
6.2.5 Infrared spectroscopy 69
6.2.6 Nuclear magnetic resonance spectroscopy 69
6.2.7 Elemental analysis 70
6.2.8 Melting point 70
6.3 High-throughput experiments 70
6.4 Catalytic decarboxylative cross-coupling of aryl chlorides and benzoates without activating *ortho* substituents 73
6.4.1 General procedure for the synthesis of potassium carboxylate salts 73

6.4.2 General procedure for the decarboxylative coupling 73
6.4.3 Sythesis of biaryls 73
6.5 Arylalkene synthesis 93
6.5.1 Arylalkene synthesis via decarboxylative cross-coupling of alkenyl halides 93
6.5.1.1 General procedure for the synthesis of potassium carboxylate salts 93
6.5.1.2 General procedure for the decarboxylative coupling 93
6.5.1.3 Synthesis and characterization of arylalkenes 93
6.5.2 Branched arylalkenes from cinnamates: selectivity inversion in Heck reactions by carboxylates as deciduous directing groups 106
6.5.2.1 General procedure for the decarboxylative Mizoroki-Heck coupling 106
6.5.2.2 Synthesis of 1,1-disubstituted alkenes 106
6.5.2.3 Procedure for the one-pot three-step process 124
7. Curriculum vitae 125
8. References 126

1. Abstract

Redox-neutral decarboxylative coupling reactions have emerged as a powerful strategy for C-C bond formation. However, the existing reaction conditions possess limitations, such as the coupling of aryl halides restricted to *ortho*-substituted benzoic acids; alkenyl halides were not applicable in decarboxylative coupling reaction. Within this thesis, the developments of Pd/Cu bimetallic catalyst systems are presented to overcome the limitations.

In the first part of the PhD work, a customized bimetallic Pd^{II}/Cu^{I} catalyst system was successfully developed to facilitate the decarboxylative cross-coupling of non-*ortho*-substituted aromatic carboxylates with aryl chlorides. The restriction of decarboxylative cross-coupling reactions to *ortho*-substituted or heterocyclic carboxylate substrates was overcome by holistic optimization of this bimetallic Cu/Pd catalyst system. All kinds of benzoic acids regardless of their substitution pattern now can be applied in decarboxylative cross-coupling reaction. This confirms prediction by DFT studies that the previously observed limitation to certain activated carboxylates is not intrinsic. The catalyst system also presents higher performance in the coupling of *ortho*-substituted benzoates, giving much higher yields than those previously reported. *ortho*-Methyl benzoate and *ortho*-phenyl benzoate which have never before been converted in decarboxylative coupling reactions, gave reasonable yields. These together further confirm the superiority of the new protocol.

In the second part of the PhD work, arylalkenes syntheses via two different Pd/Cu bimetallic-catalyzed decarboxylative couplings have been developed. This part consists of two projects: 2a) decarboxylative coupling of alkenyl halides; 2b) decarboxylative Mizoroki-Heck coupling of aryl halides with α,β-unsaturated carboxylic acids.

In project 2a, widely available, inexpensive, bench-stable aromatic carboxylic acids are used as nucleophile precursors instead of expensive and sensitive organometallic reagents that are commonly used in previously reported transition-metal catalyzed cross-couplings of alkenyl halides. With this protocol, alkenyl halides for the first time are used in decarboxylative coupling reaction, allowing regiospecific synthesis of a broad range of (hetero)arylalkenes in high yields. Unwanted double bond isomerization, a common side reaction in the alternative Heck reactions especially in the coupling of cycloalkenes or aliphatic alkenes, did not take place in this decarboxylative coupling reaction. Polysubstituted alkenes that hard to access with Heck reaction are also produced in good yields. The reaction can easily be scaled up to gram scale. The synthetic utility of this reaction was also demonstrated by synthesizing an important intermediate of fungicidal compound in high yield within 2 steps.

In project 2b, a Cu/Pd bimetallic catalyzed decarboxylative Mizoroki-Heck coupling of aryl halides with α, β-unsaturated carboxylic acids was successfully developed in which the

carboxylate group directs the arylation into its β-position before being tracelessly removed via protodecarboxylation. It opens up a convenient synthesis of unsymmetrical 1,1-disubstituted alkenes from widely available precursors. This reaction features good regioselectivity, which is complementary to that of traditional Heck reactions, and also presents excellent functional group tolerance. Moreover, a one-pot 3-step 1,1-diarylethylene synthesis from methyl acrylate was achieved, where solvent changes or isolation of intermediates are not required. This subproject presents an example of carboxylic acids utility in synthesizing valuable compounds which are hard to access via conventional methodologies.

2. Structure of the thesis

The present PhD work covers two major subject areas: 1) overcoming the limitation of decarboxylative coupling of halides to *ortho*-substituted benzoic acids; 2) synthesizing arylalkenes via decarboxylative couplings.

Since this work focuses on Pd/Cu bimetallic catalyzed decarboxylative C-C bond formations, a general introduction about this research field and especially in bimetallic catalyzed C-C bond formation and decarboxylative coupling reactions is presented (chapter 3).

Knowing the challenges in decarboxylative coupling reaction, aims of this work are presented in chapter 4.

In the following chapter 5, two main subjects are described. The first subject is introduced to overcome the limitation of decarboxylative coupling of halides to *ortho*-substituted benzoic acids. A Pd/Cu bimetallic catalyzed decarboxylative coupling of aryl chlorides with non-*ortho* substituted benzoates is presented in chapter 5.1. The second subject aims at arylalkenes synthesis via decarboxylative couplings. This subject consists of two subprojects: 1) decarboxylative coupling of alkenyl halides (chapter 5.2.1); 2) 1,1-disubstituted alkene synthesis via decarboxylative Mizoroki-Heck coupling reaction (chapter 5.2.2).

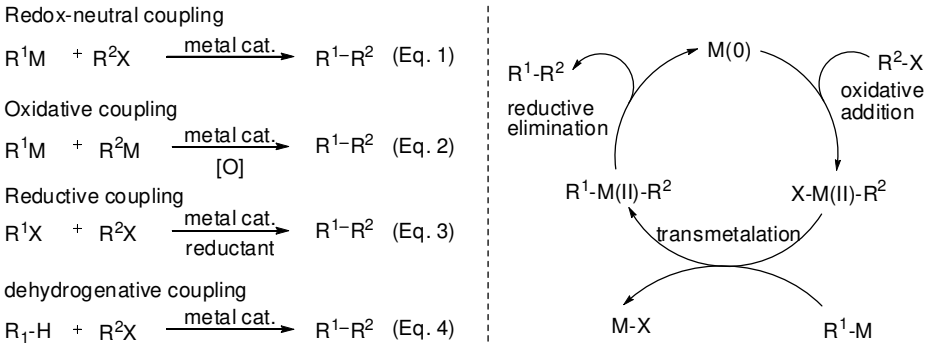
In the experimental section (chapter 6) the analytic methods, general procedures and full characterization of the compounds are presented.

3. Introduction

3.1 Transition metal-catalyzed C-C bond formation reactions

Transition-metal catalyzed C-C bond formation reactions have become one of the most powerful synthetic methodologies in modern organic synthesis.[1] In the past decades, it has allowed chemists to assemble complex molecular frameworks and provide new opportunities in total synthesis, medicinal chemistry, industrial process development, and materials science development. In 2010, the significance of this general class of reactions was recognized by the awarding of the Nobel Prize in chemistry jointly to Richard Heck, Ei-ichi Negishi, and Akira Suzuki "*for palladium-catalyzed cross-couplings in organic synthesis*".[2]

Transition-metal catalyzed C-C bond formation reactions can be classified into three models: redox-neutral coupling, oxidative coupling and reductive coupling. As shown in Scheme 1, a redox-neutral coupling reaction involves a formal nucleophilic substitution at aryl and alkenyl halides or pseudohalides by an organometallic reagent. The widely accepted mechanism for this coupling reaction contains three main parts: (1) oxidative addition of the C-X bond of electrophile R^2-X to the metal centre of the catalyst to form the intermediate R^2-M(II)-X; (2) transmetalation of nucleophile R^1-M to form the intermediate R^1-M(II)-R^2; (3) reductive elimination of intermediate R^1-M(II)-R^2 to release the coupling product R^1-R^2 and regenerate the low valent transition-metal species. [3]



Scheme 1. Transition-metal catalyzed cross-coupling reactions.

Oxidative coupling refers to the reaction that two nucleophiles are used as coupling partners.[4] In this case, these two nucleophiles are both electron-rich species and could not form chemical bonds directly unless an appropriate oxidant is introduced to remove the extra electrons. More recently, transition-metal catalyzed reductive couplings, the cross-coupling of two different electrophiles in the presence of a reductant, were also developed.[5] Recently, the development of dehydrogenative couplings of hydrocarbons, especially arenes bearing certain

directing groups, with all kinds of electrophiles, organometallic reagents or other hydrocarbons have also been reported.[6]

The previous decades have witnessed an extraordinary development of transition-metal catalyzed C-C bond formation reactions. Well-known reactions such as Kumada couplings, Mizoroki-Heck reactions, Negishi couplings, Stille couplings, Sonogashira reactions, Suzuki couplings, Hiyama couplings, etc. are developed to construct various C-C bonds.[7] In these transformations, a single transition metal, such as Pd, Ni, Cu, Co, Ru is usually used to promote the coupling reaction. On the contrary, bimetallic catalyzed C-C bond formations are relatively less developed.

Bimetallic catalysis usually refers to catalytic processes in which two transition metal catalysts are used in catalytic amounts and thus comprises two catalytic cycles and these two cycles are usually connected by a transmetalation step.[8] In this process, new metal reagents are formed in situ with one metal and its organic group is then transferred to a second metal catalyst. Subsequent reductive elimination delivers the cross-coupling product. Bimetallic catalysis possesses unique activity that allows accessing many difficult or unattainable transformations.

3.1.1 Bimetallic catalyzed C-C bond formation reactions

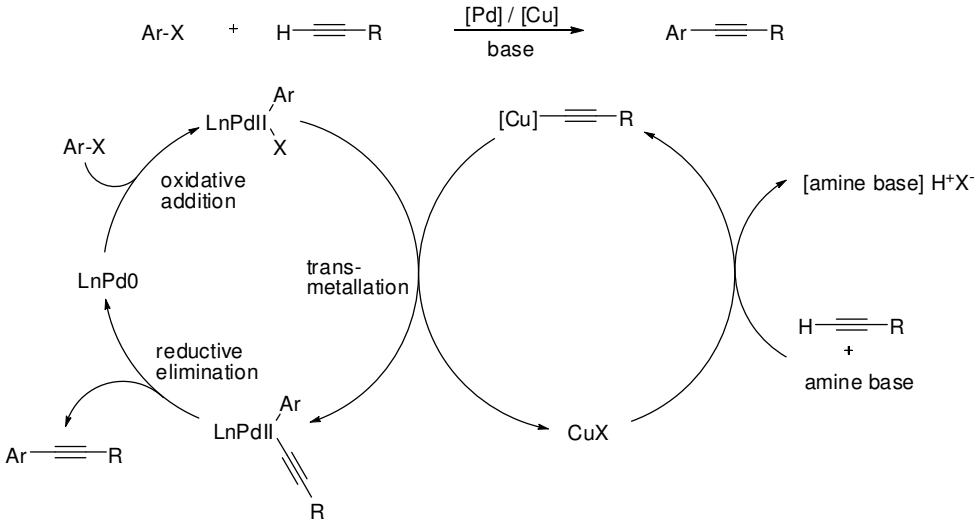
Different types of bimetallic catalyst systems have been developed for various transformations that previously were not or inefficiently promoted by monometallic catalysts. Considering the prevalence and importance of palladium catalysis, much effort has been devoted to combine palladium with other transition-metal catalysts, and to apply these bimetallic catalyst systems for the discovery of new methodologies. Besides palladium-based systems, other transition metals are also combined in bimetallic catalysts, such as gold or nickel.

3.1.1.1 Palladium based bimetallic catalyzed C-C bond formation

3.1.1.1.1 Bimetallic catalysis involving C-H bond activation

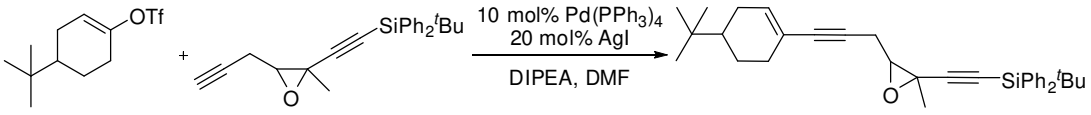
Among bimetallic catalyzed C-C bond formation reactions, palladium based bimetallic systems are under great investigation. One of the earliest examples is the Sonogashira reaction, where a Pd/Cu bimetallic catalyst was used. In 1975, Cassar[9] and Heck[10] independently disclosed the coupling of alkynes with in the presence of catalytic Ni(0) or Pd(0) complexes, which proceeded und under harsh reaction conditions, such as high temperatures. Sonogashira discovered that by adding catalytic amounts of copper catalyst along with a palladium catalyst,

the coupling of terminal alkynes and aryl halides could readily occur at room temperature (Scheme 2).[11] The role of the copper catalyst is to generate an alkynyl-copper species and thus facilitate the transmetalation to the organopalladium center, which is formed via oxidative addition of the aryl halide to the palladium catalyst. Subsequent reductive elimination delivers the cross-coupling product.



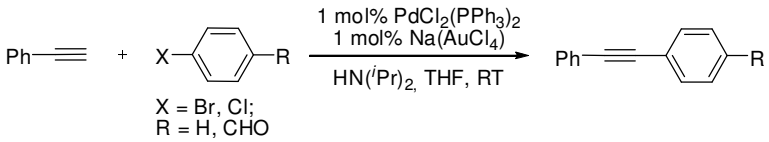
Scheme 2. Pd/Cu catalyzed Sonogashira coupling reaction.

The combination of a palladium catalyst with other metal salts, such as silver or gold-based catalyst has also been studied. In 1996, Pale *et al.* reported a coupling reaction between ethynyloxiranes and alkenyl triflates (Scheme 3).[12] Cu(I) salt that used in the classic Sonogashira reaction have a deleterious effect on the epoxyyne fragment. Due to the analogy in their electronic structure and some of their chemical properties, the authors reasoned that silver salts might be suitable as well. With this Pd/Ag catalyst, epoxyenynes can easily be prepared in good yields.



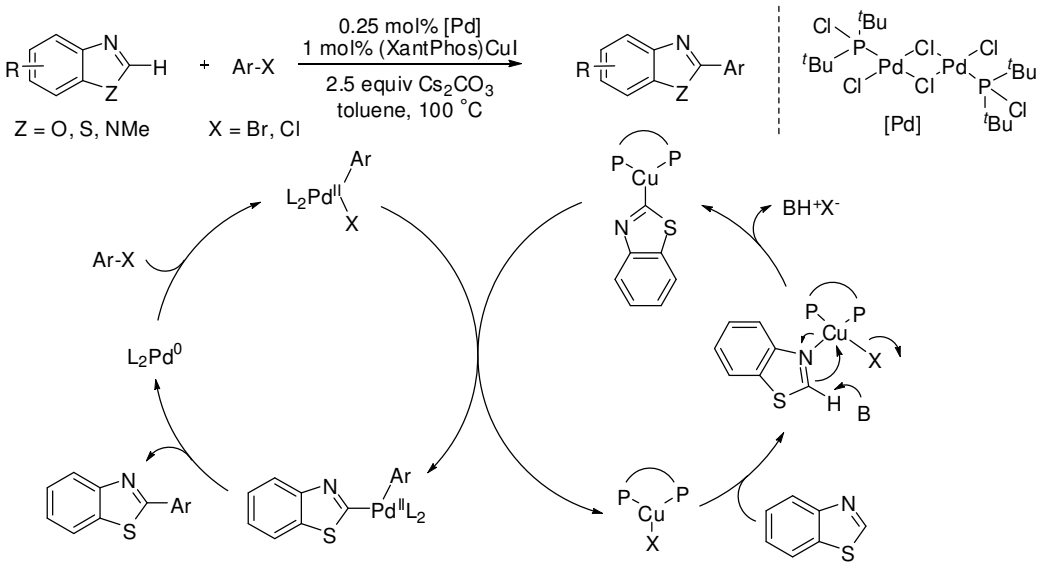
Scheme 3. Pd/Ag catalyzed Sonogashira coupling reaction.

The Laguna group used Au(I) ([AuCl(tht)]) and Au(III) ($Na[AuCl_4]$) complexes as co-catalysts in Sonogashira cross-coupling reactions of phenylacetylene with aryl halides (Scheme 4).[13] The authors highlighted that their system provided cleaner reactions, avoiding the homocoupling of phenylacetylene, and allowing for the use of technical grade solvents without previous purification or air exclusion.



Scheme 4. Pd/Au catalyzed Sonogashira coupling reaction.

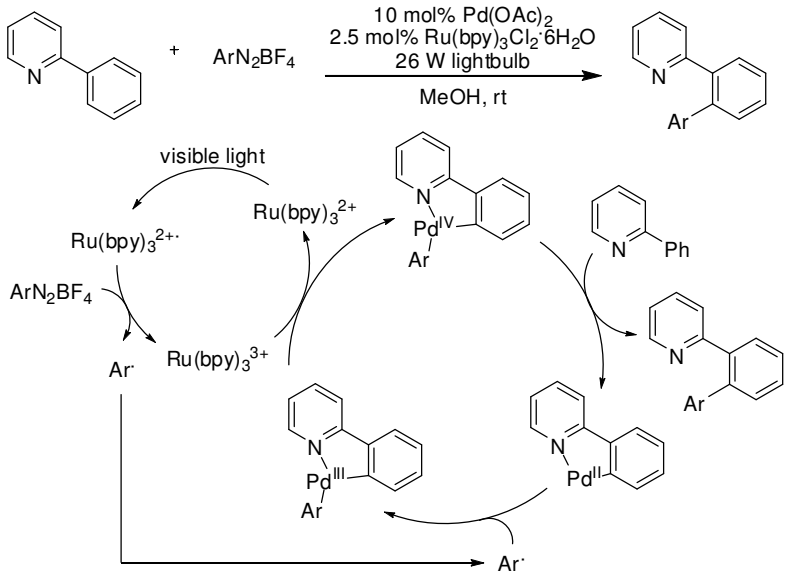
Recent decades have witnessed significant development of C-H activation functionalization, which presents an environmentally and atom-economically attractive approach. In most cases, mono transition-metal catalyst such as Pd, Ni, Cu, Rh, Ru are used. Considering the reaction mechanism, sometimes a stoichiometric oxidant such as $Cu(OAc)_2$ or Ag_2CO_3 is required for the reoxidation of low valent metal catalyst after reductive elimination. Concerning that Cu(I) salts are widely used as catalyst in direct C-H functionalization, such as Sonogashira reaction, in 2010, Huang and co-workers reported a direct arylation of heteroarenes with aryl halides by using Pd/Cu bimetallic catalyst, where both palladium and copper catalysts can be realized in catalytic amount (Scheme 5).[14] With only 0.25 mol% palladium catalyst and 1 mol% copper catalyst, the products can be afforded in good to high yields. At the same loading, neither palladium nor copper individually can catalyze this C-H arylation reaction. The authors proposed a mechanism in which an organocopper intermediate is formed via C-H activation of the heteroarene by a copper complex in the presence of a base. The following transmetalation to Pd(II) and reductive elimination gives the desired product and release both the copper and palladium catalyst.



Scheme 5. Pd/Cu catalyzed C-H arylation of heteroarenes.

Recently, visible-light photoredox catalysis has been becoming a hot topic. Photo catalysts that are usually seen as natural organic compounds, or transition metal based complexes,

exhibit both powerful oxidation and reduction ability. One of the earliest examples that merge photo catalyst and transition-metal catalyst was reported by the Sanford group in 2011. By using Ru/Pd bimetallic system, C-H arylation reaction with aryldiazonium salts was developed (Scheme 6). [15] With this protocol, C-H arylation can be achieved at room temperature. Mechanistically, the authors proposed that an aryl radical was generated with the light excited Ruthenium catalyst. This radical react with the palladacycle (generated via C-H activation) to form the Pd(III) intermediate, which undergoes single-electron oxidation to afford a Pd(IV) species. Reductive elimination delivers the final product and regenerates the Pd(II) catalyst.

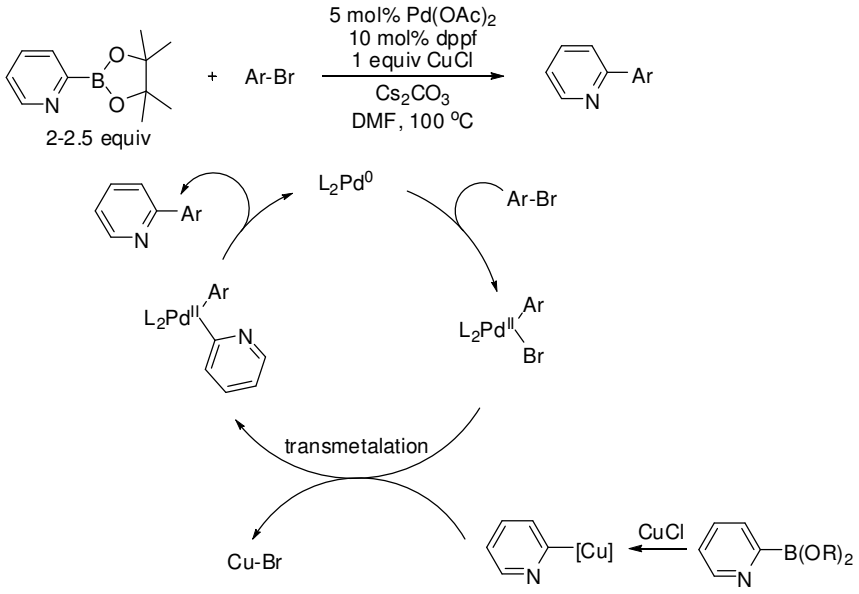


Scheme 6. Ru/Pd catalyzed C-H arylation with aryldiazonium salts**.**

3.1.1.1.2 Bimetallic catalyzed cross-coupling reactions

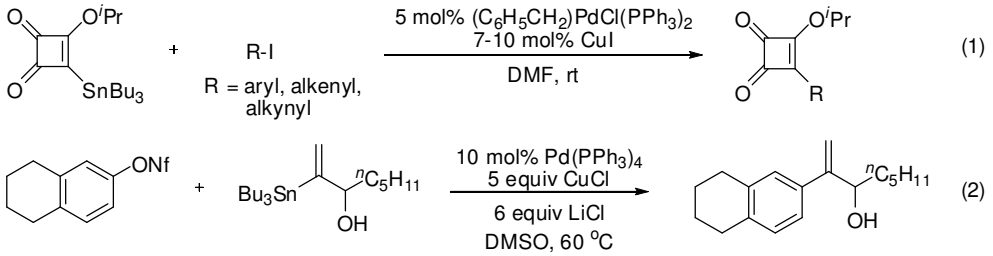
Transition-metal catalyzed cross-coupling reactions are well developed, however, there are some limitations in monometallic catalyzed transformations. With bimetallic catalysis, these limitations can be overcome. The representative application of bimetallic catalyzed cross-coupling reaction is Suzuki coupling. Since its discovery, Pd-catalyzed Suzuki coupling reaction has been developed as powerful tool for C-C bond formation. Although numerous reaction systems have been discovered for a wide range of coupling partners, the coupling of electron-deficient boronates such as 2-pyridyl boronate remains challenging. It is hypothesized that the transmetalation between palladium and electron-deficient 2-heterocyclic boronates is slow relative to the protodeboronation, leading to poor conversion. In 2009, Deng and Paone reported that addition of a Cu(I) catalyst can promote Suzuki reactions of electron-deficient 2-heterocyclic boronates in good yields (Scheme 7).[16] Based on mechanistic studies,

the authors proposed that the in situ generation of a more reactive organocopper species from the corresponding 2-heterocyclic boronic esters can sufficiently undergo transmetalation to the palladium catalyst, thus resulting in high yield of the product. However, due to the homocoupling of the 2-pyridyl copper species affording in 2,2'-bipyridines, an excess of boronate is still necessary for complete conversions.



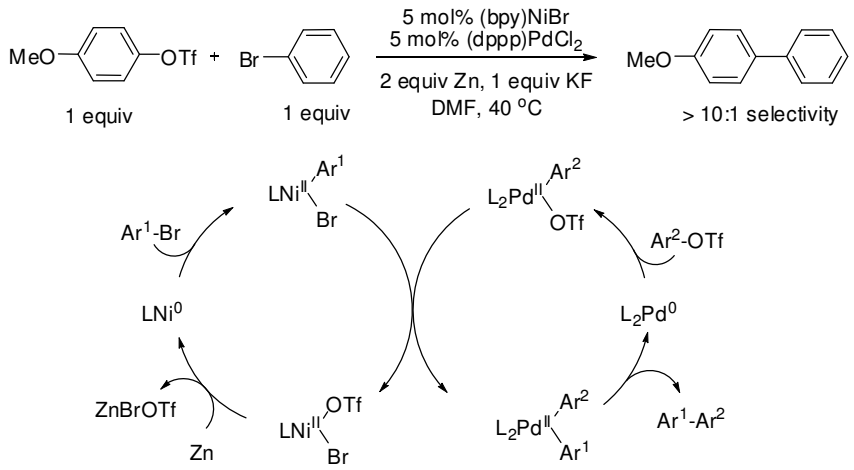
Scheme 7. Pd/Cu catalyzed Suzuki coupling of electron-deficient boronates.

Another example in bimetallic catalyzed coupling reaction is the Stille reaction. The Stille reaction that involves the coupling of an organostannanes with a variety of organic electrophiles is widely used in organic synthesis. However, this elegant coupling reaction displayed some limitations. For instance, the coupling of vinylstannanes usually results in low yield because of very low reaction rates. In 1990, the Liebeskind group found that the Pd-catalyzed Stille reaction of stannylcyclobutenedione took over 3 days to reach 50% at 100 °C. A dramatic improvement in the rate of the cross-coupling was observed when CuI was added as co-catalyst. In the presence of 7-10% CuI, stannylcyclobutenedione efficiently coupled at room temperature in excellent yield within 45 min (Scheme 8, Eq 1).[17] The authors reasoned that the addition of a copper catalyst leads to the formation of vinylcopper species, which rapidly undergo transmetalation to the palladium catalyst, thus facilitates the whole transmetalation from Sn to palladium and speeds up the cross-coupling reaction. The E.J. Corey group applied a similar strategy to promote the coupling of sterically hindered 1-substituted vinylstannanes although 5 equiv. of CuCl are required (Scheme 8, Eq 2).[18]



Scheme 8. Pd/Cu catalyzed Stille reaction.

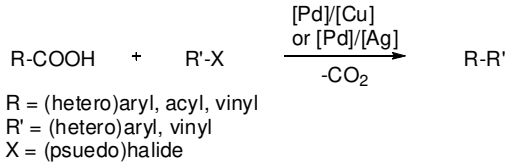
Recently, cross-electrophile coupling has been rapidly developed. Such a reaction avoids the need for preformed organometallic reagents. In this type of reaction, chemoselectivity has been a fundamental pursuit because both electrophiles can compete for oxidative addition with the metal catalyst, resulting in mixtures of cross-coupling and homocoupling products. Therefore, achieving selective cross-coupling is a prior challenge. A common method to address the challenge would be using an excess of the less reactive electrophile thus maximize cross-coupling product and suppress homocoupling of the more reactive electrophile. Difference in the rates of oxidative addition of electrophiles to different metal catalysts, and the different stability of the resulting metal complex opens up an opportunity for bimetallic catalyzed reductive cross-coupling reaction. It was found that most nickel complexes undergo oxidative addition more rapidly with aryl bromides than with the corresponding aryl triflates, while palladium catalyst favors the oxidative addition with aryl triflates.[19] Taking advantage of these findings, the Weix group reported Pd/Ni bimetallic catalyzed reductive cross-coupling of aryl triflates and aryl bromides, where aryl triflates and aryl bromides can be used in a 1:1 ratio (Scheme 9).[20] The authors reasoned that these two aryl electrophiles selectively undergo oxidative addition to palladium and nickel catalyst respectively. The aryl Pd(II) complex is relatively stable and unreactive towards homocoupling. The aryl Ni(II) complex is highly reactive, once formed, it undergoes rapid transmetalation with the aryl Pd(II) complex. Control experiments showed that this bimetallic catalysis exhibits much higher chemoselectivity.



Scheme 9. Ni/Pd catalyzed reductive cross-coupling reaction.

3.1.1.1.3 Bimetallic catalyzed decarboxylative coupling reaction

Another representing type of bimetallic catalysts that used in C-C and C-heteroatom bond formation is Pd/Cu or Pd/Ag catalyzed decarboxylative cross-coupling reaction (Scheme 10).[21] The reaction consists of copper or silver catalyzed decarboxylation cycle and palladium catalyzed coupling cycle, and these two cycles are connected by transmetalation. This type of coupling reaction will be discussed in details in chapter 3.2.

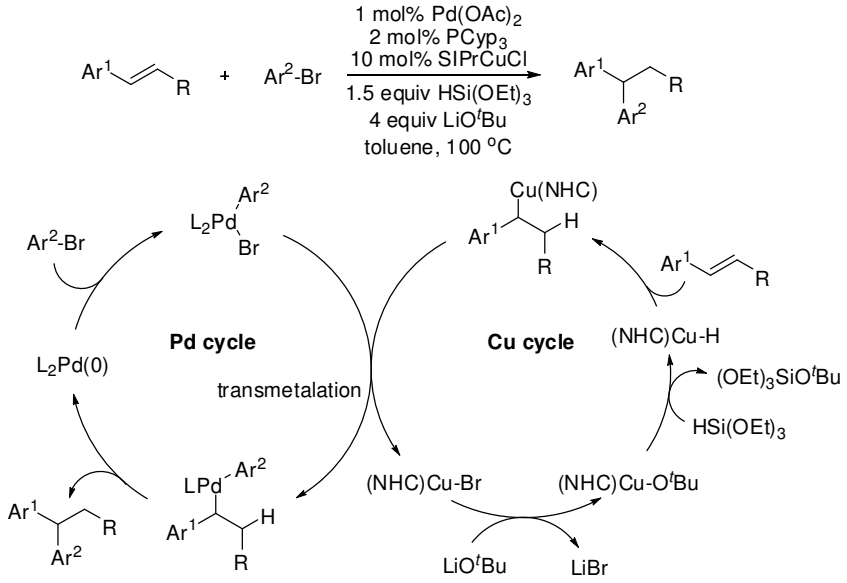


Scheme 10. Pd/Cu catalyzed decarboxylative coupling reactions**.**

3.1.1.1.4 Bimetallic catalyzed "cascade" reactions

In the above mentioned Suzuki and Stille reactions, a copper catalyst was used to facilitate the transmetalation of an organometal reagent to palladium catalyst, which undergoes reductive elimination to deliver the final coupling product. Another activating mode of bimetallic catalysis is that one transition metal catalyzes a first transformation and the resulting organometallic intermediate transfers its organo group to another transition metal catalyst, which undergoes a second transformation, thus resulting in more sophisticated compounds. This transformation is similar to cascade reaction. So we name it bimetallic catalyzed "cascade" reaction. In this type of reaction, more than one bond can be formed. For instance, copper is known to undergo olefin hydrocupration. The resulting alkylcopper species could either undergo direct functionalization or could transfer its organo group to another transition metal catalyst, such as palladium, which could couple with another reagent that copper

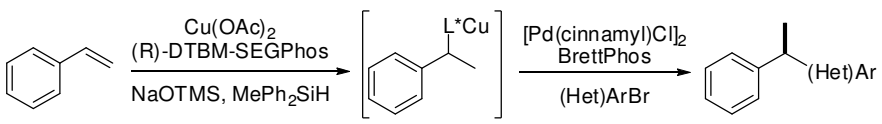
catalyst could not realize. In 2015, the Nakao group developed a hydroarylation of arylalkenes with aryl bromides and hydrosilanes by cooperative Pd/Cu catalysis, thus resulting in the highly regioselective formation of various 1,1-diarylalkanes (Scheme 11).[22] Both metals are essential to this transformation. If one leaves out palladium catalyst, the coupling partner will be limited to benzyl or alkyl halides.[23]



Scheme 11. Pd/Cu catalyzed hydroarylation of arylalkenes.

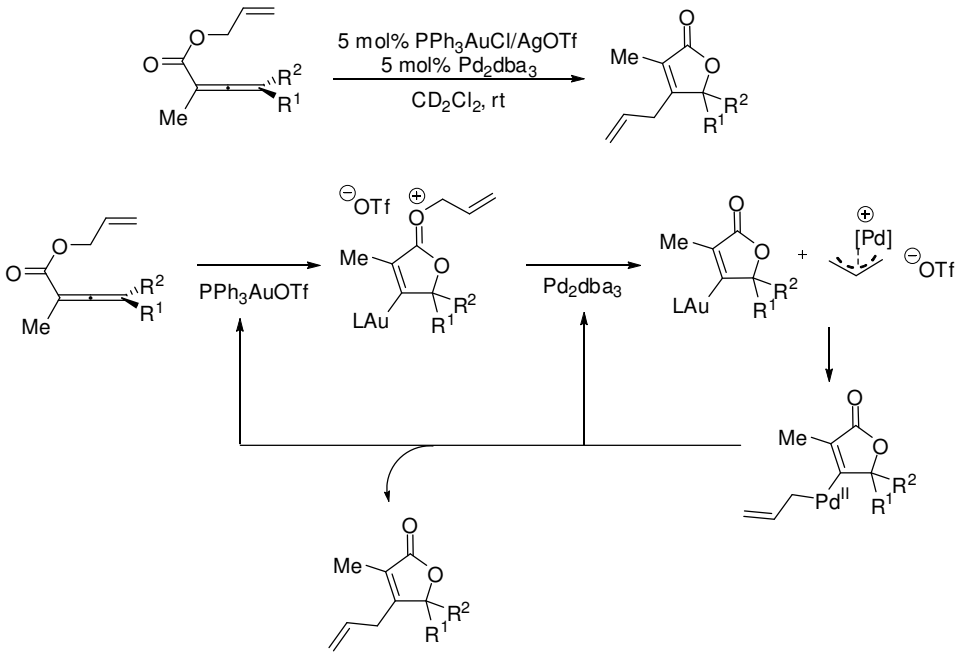
This reaction mechanism consists of Pd and Cu cycles. Initially, the copper hydride species is generated from the copper catalyst and $HSi(OEt)_3$. The regioselective hydrocupration of the 1-arylalkene with copper hydride species affords the alkylcopper intermediate, which undergoes transmetalation with $L_2Pd(Ar)Br$ to afford an aryl-alkyl Pd(II) species along with (NHC)CuBr. Reductive elimination of this Pd(II) species affords the final product and the Pd(0) catalyst. (NHC)CuBr reenters the catalytic cycle by reacting with LiO^tBu.

The Buchwald group almost simultaneously published an enantioselective fashion of this transformation by using a chiral bisphosphine ligand (Scheme 12).[24] In situ generated L*CuH species undergo enantioselective olefin hydrocupration to form a stereodefined Cu(I) intermediate, which further transmetalates with a Pd catalyst with high stereospecificity, ultimately leading to an enantioenriched coupling product.



Scheme 12. Pd/Cu catalyzed enantioselective synthesis of 1,1-diarylalkanes

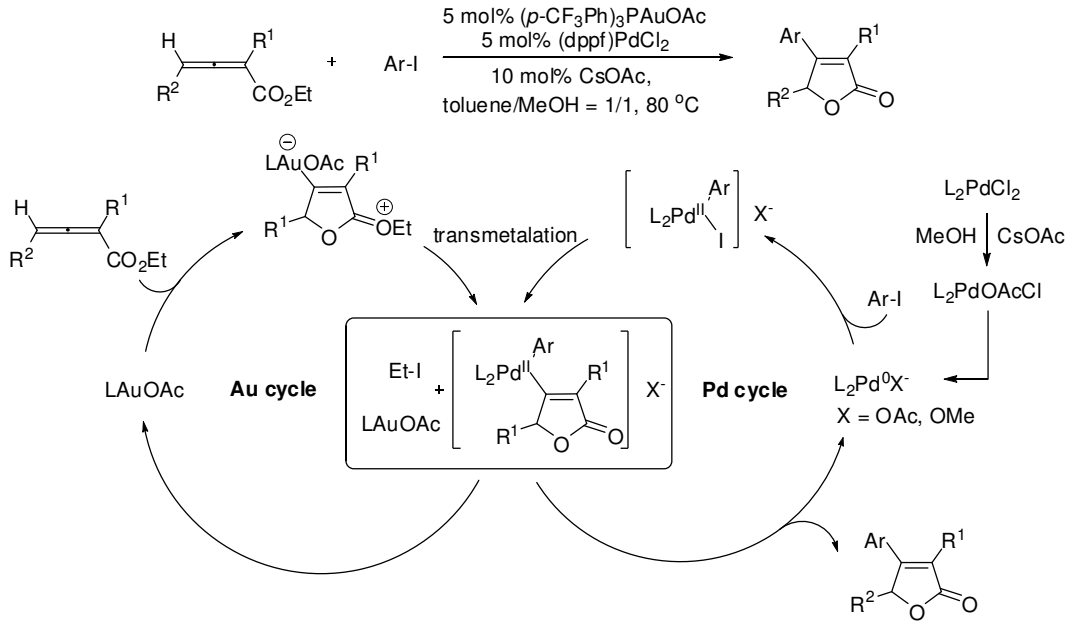
Gold catalysis has become a hot topic in organic chemistry. Recently, gold has been merged with other transition metals in catalysis that is particularly appealing for the synthesis of novel functionalized compounds. In 2009, the Blum group reported that the combination of carbophilic Lewis acidic gold and palladium catalyst could cooperatively catalyze cyclization/cross-coupling reaction for the synthesis of butenolides (Scheme 13).[25] The proposed mechanism showed that the cationic gold complex PPh_3AuOTf cyclizes allenoate to organogold oxocarbenium, activating the allyl group for oxidative addition by palladium catalyst through a bimetallic transition state. Transmetalation of a neutral vinylgold with π-allyl Pd complex affords allyl furanony a Pd(II) intermediate and regenerates the cationic gold catalyst. The substituted butenolide is then formed by reductive elimination from the allyl furanony Pd(II) intermediate. Control experiments showed that both metal catalysts are essential to reach high conversion. Furthermore, the mechanistic studies support that the gold intermediate lowers the oxidative addition barrier for palladium. In contrast to tandem catalyst system where each catalyst acts on the substrate separately, this catalyst system gold and palladium act cooperatively.



Scheme 13. Au/Pd catalyzed intermolecular cyclization/cross-coupling reaction.

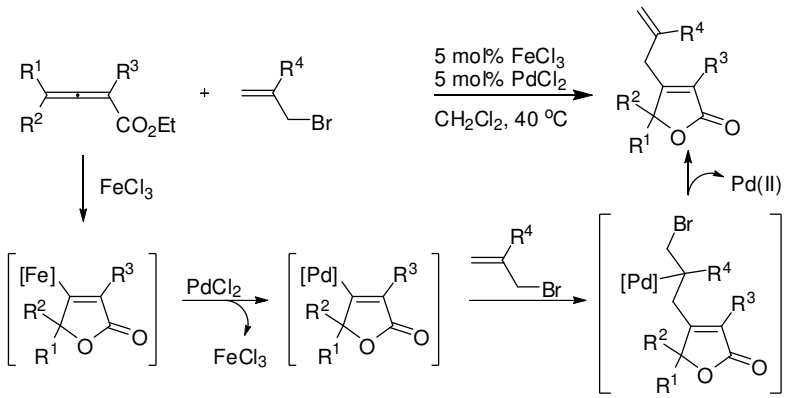
The above mentioned pioneer work by Blum *et al.* on the concept of Au-Pd "catalyzed catalysis" describes processes where the catalytic cycle of palladium can only be turned on once the catalytic cycle of gold has been initiated. More interestingly, comparable amounts of the desired product were also detected in the presence of Pd/Ag system, thus questioning the occurrence of an unambiguous Au-Pd catalytic transmetalation. Although Pd-catalyzed cross-

coupling of preformed organogold reagent is well known, the development of Pd/Au bimetallic catalyzed cross-coupling reaction where organogold species generated in situ with catalytic amounts of gold catalyst is still highly challenging, because 1) the gold and palladium intermediates generated in situ need to be stable toward protodemetalation or reaction with other species present in the reaction media; 2) in order to prevent competing homocoupling or decomposition reaction, a fine-tuning of the bimetallic catalyst is required to obtain a perfect balance between gold catalysis cycle and palladium catalyzed cross-coupling cycle; 3) the recycling of gold catalyst after the first turnover needs to be highly efficient, as formation of catalytically inactive neutral LAuX (X = halogen) complexes is thermodynamically driven, thus bringing gold catalyst re-enter into catalytic cycle is crucial. The Nevado group reported a Au-Pd bimetallic catalyzed cross-coupling of allenoates and (hetero)aryl iodides for the synthesis of butenolides (Scheme 14).[26] With fine adjusted catalyst system, Au-catalyzed cyclization of allenoates and the Pd-catalyzed cross-coupling of (hetero)aryl iodides join in key transmetalation step. More important, in the presence of catalytic amounts of CsOAc and co-solvent MeOH, catalytically competent LAu(I)OR species was generated. Based on mechanistic studies, the authors proposed that the reaction initiates by Au-catalyzed cyclization of allenoate, affording zwitterionic gold intermediate. At the same time, the (dppf)$PdCl_2$ precatalyst evolves in the presence of CsOAc to a Pd(0) anionic complex, which undergoes facile associative oxidative addition with Ar-I to form an aryl Pd(II) anionic complex. Au-Pd transmetalation affords the key aryl furanony Pd(II) intermediate along with catalytically active LAuOAc species, which could re-enter into Au cycle. Reductive elimination of the key aryl furanony Pd(II) intermediate produces the final product. This protocol alleviates the use of preformed organogold reagent, making it more practical.



Scheme 14. Au/Pd bimetallic catalyzed allenoate synthesis.

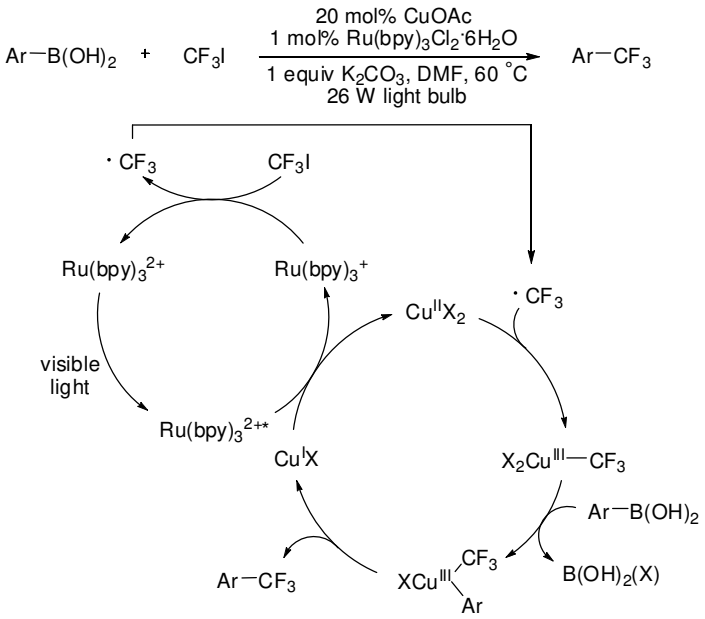
Iron is the second most abundant metal on Earth. Iron catalysts in organic synthesis present attractive potentials especially in industry due to their low cost and low toxicity. Attributing to its Lewis acidity, iron could function as gold in some allene involved transformations. The Ma group reported a Fe/Pd bimetallic catalyzed coupling of ethyl 2,3-allenoates with allyl bromides, which afforded various β-allylic substituted butenolides, although the yields are rather moderate (Scheme 15).[27] Similar to gold, $FeCl_3$ can also catalyze the cyclization of allenoates. The resulting furanonyl iron species undergoes transmetalation with $PdCl_2$ forming furanonyl Pd(II) species while regenerating $FeCl_3$. Subsequent carbopalladation with an allyl bromide followed by dehalopalladation affords the butenolide.



Scheme 15. Fe/Pd bimetallic catalyzed butenolides synthesis.

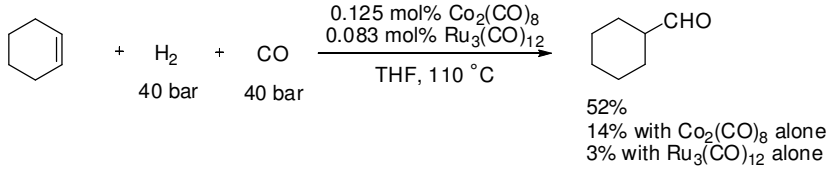
3.1.1.2 Non-Pd based bimetallic catalyzed C-C bond formation

Besides the most investigated palladium based bimetallic catalyst system, a few non-Pd based bimetallic catalyzed C-C bond formations have been developed. The Sanford group merged copper catalyst and Ru-based photocatalyst for trifluoromethylation of boronic acids (Scheme 16). [28] Different from previously developed Cu-catalyzed nucleophilic or electrophilic trifluoromethylation of boronic acids, where expensive trifluoromethylating reagents (e.g. Umemoto's or Togni's reagent) are used,[29] this protocol enables much cheaper CF_3I as the trifluoromethyl source. Besides, this reaction proceeds under much milder conditions, such as low reaction temperature and weak base. The reaction was proposed that photoexcited Ru(II) complex oxidizes Cu(I) catalyst to Cu(II) species. The resulting Ru(I) undergoes single-electron oxidation with CF_3I to generate CF_3 radical. This CF_3 radical then reacts with Cu(II) to generate a CF_3-Cu(III) intermediate. Subsequent transmetalation between Cu(III) and the arylboronic acid would afford (aryl)(CF_3)Cu(III) species, which could undergo reductive elimination to release the product and regenerate the Cu(I) catalyst.



Scheme 16. Ru/Cu catalyzed trifluoromethylation of boronic acids**.**

The Hidai group reported a Co/Ru bimetallic catalyzed hydroformation of olefins (Scheme 17).[30] This catalyst system not only significantly improves the yield but also enables the reaction rate 6 times faster than with $Co_2(CO)_8$ alone. Control experiment also showed that only trace amounts of product can be detected with $Ru_3(CO)_{12}$ alone. The role of ruthenium catalyst was believed to acting as a hydride agent on the acyl cobalt intermediate.

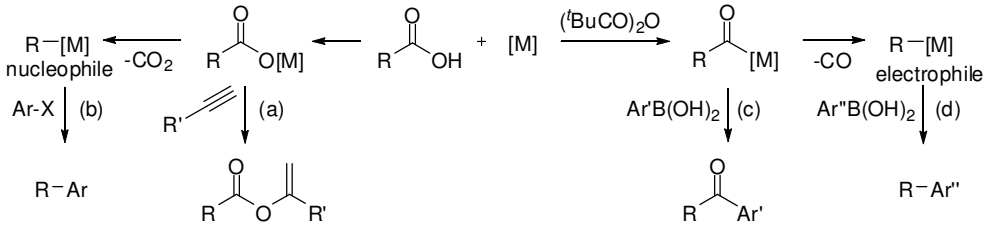


Scheme 17. Co/Ru catalyzed hydroformation of olefins**.**

3.2 Decarboxylative cross-coupling reactions

Transition metal catalyzed cross-coupling reaction has been well developed in C-C bond formation. Representative reactions include Suzuki reactions, Kumada couplings, Negishi couplings, Stille couplings, etc. However, multi-step preformed, sensitive and expensive organometallic reagents are used in these reactions. Moreover, over stoichiometric amounts of waste are produced both in the preparation and usage of these organometallic reagents.

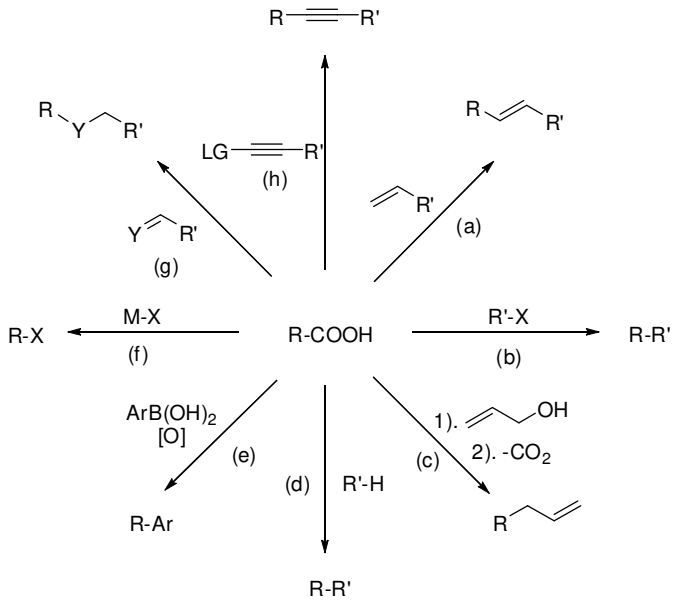
Carboxylic acids are widely available, low cost, bench stable and easy to handle, thus making them ideal and versatile starting materials for many important transformations: a) catalytic addition of carboxylic acids to alkenes or alkynes; b) decarboxylative couplings, in which carbon nucleophiles generated via CO_2 extrusion are coupled with electrophiles or nucleophiles; c) coupling of acyl metal species that generated by insertion of a metal catalyst into C-O bond of activated carboxylic acids derivatives, such as anhydrides; d) decarbonylative couplings, in which carbon electrophiles formed via the loss of CO from acyl metal species are coupled with nucleophiles (Scheme 18).[31] In this thesis, we will focus on decarboxylative coupling reactions.



Scheme 18. Transformations of carboxylic acids.

Within recent decades, decarboxylative cross-coupling reactions have emerged as a powerful new strategy for C-C and C-heteroatom bond formation.[21, 32] Their key advantage over couplings of organometallic reagents is that the carbon nucleophiles are generated in situ from widely available, bench stable carboxylic acids or their corresponding carboxylate salts by extrusion of CO_2. Various synthetic transformations have been developed based on this strategy, including decarboxylative Heck-type vinylation reaction (Scheme 19, a),[33] redox-neutral cross-coupling reaction (b),[21] allylation reaction (c),[34] C-H arylation and acylation

reaction (d),[35] oxidative coupling reaction (e),[36] decarboxylative halogenation reaction (f),[37] decarboxylative addition reaction (g),[38] and decarboxylative alkynylation reaction (h).[21]



Scheme 19. Decarboxylative coupling reactions.

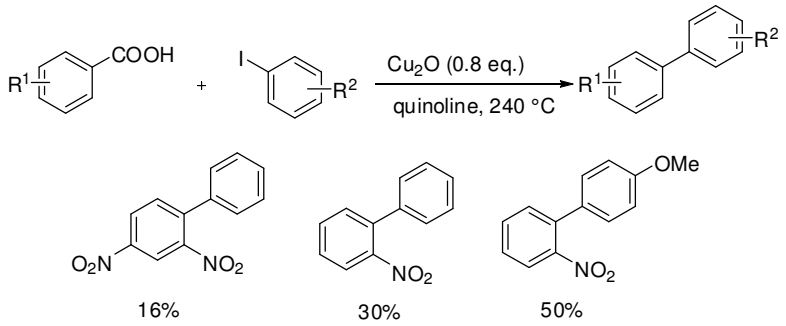
3.2.1 Redox-neutral decarboxylative coupling reaction

Redox-neutral decarboxylative cross-coupling reactions are among the most heavily investigated decarboxylative couplings. This type of reaction consists of decarboxylative arylation, alkenylation, and alkynylation.

3.2.1.1 Redox-neutral decarboxylative arylation reaction

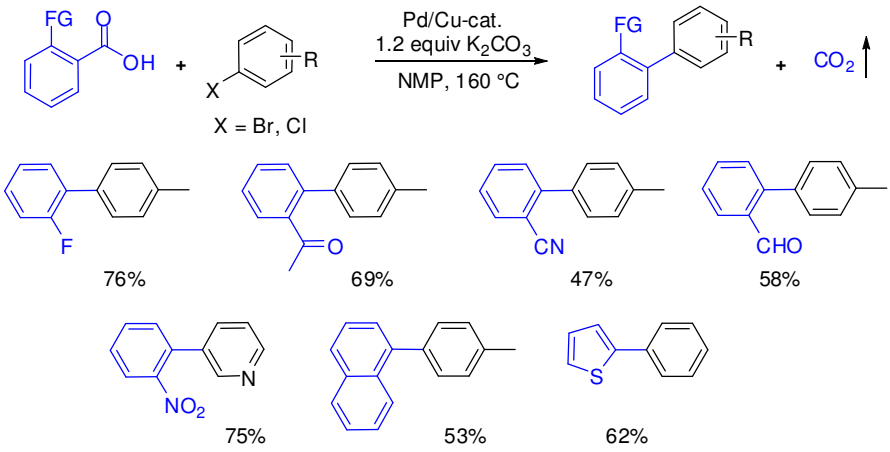
3.2.1.1.1 Decarboxylative coupling of aryl halides

In 1966, Nilsson reported the first Ullmann-type biaryl synthesis via copper mediated decarboxylative coupling of benzoic acids with aryl iodides (Scheme 20).[39] The products were formed in low to moderate yields along with substantial amounts of homocoupling byproducts. The harsh conditions and the intrinsic limitation of copper catalyzed Ullmann coupling reaction preclude its synthetic utility. However, this protocol verified the feasibility of decarboxylative coupling of benzoic acids.



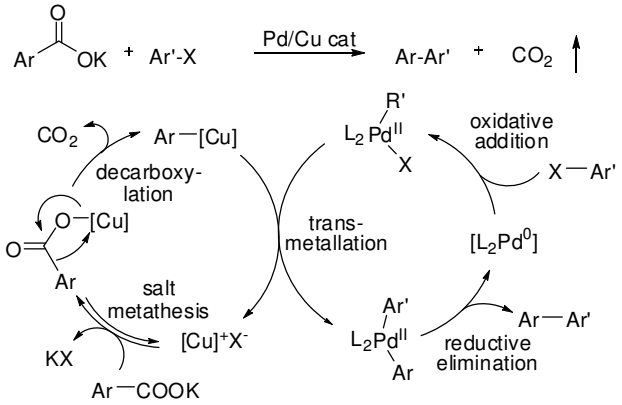
Scheme 20. Copper-mediated decarboxylative cross-coupling of benzoic acids

In 2006, Gooßen *et al.* discovered the first catalytic decarboxylative cross-coupling reaction of aromatic carboxylic acids with aryl halides, affording unsymmetrical biaryls in good yields (Scheme 21).[40] Compared to traditional biaryl synthesis via transition-metal catalyzed Kumada, Suzuki, or Negishi coupling reactions where preformed expensive and sensitive organometallic reagents were used, this protocol utilize (hetero)aromatic carboxylic acids as the nucleophilic precursor, thus presenting a much more economical and easy-operational alternative.



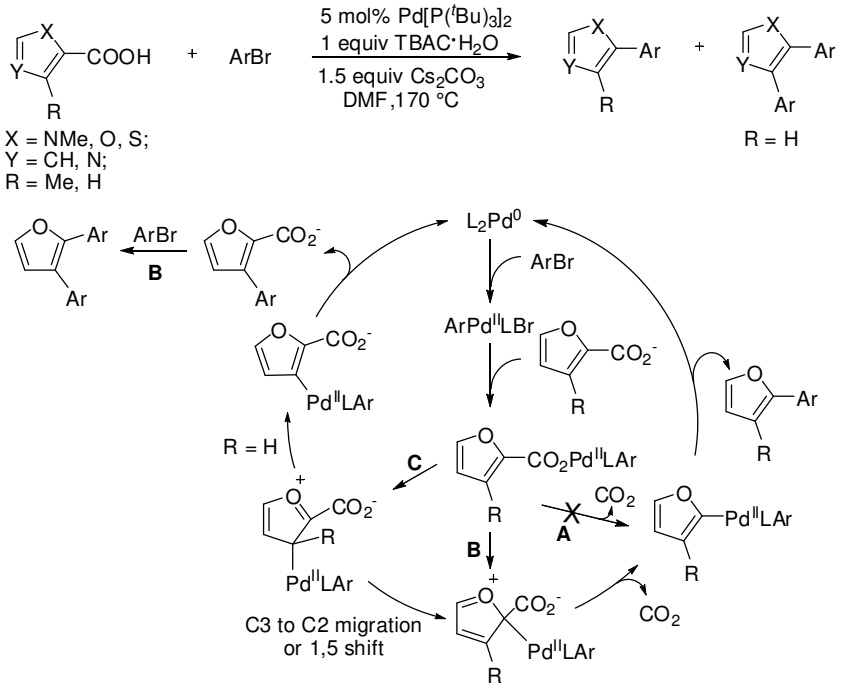
Scheme 21. Pd/Cu catalyzed decarboxylative biaryls synthesis.

This Pd/Cu bimetallic catalyzed decarboxylative cross-coupling reaction consists of two catalytic cycles, a Cu-catalyzed decarboxylation cycle and a Pd-catalyzed coupling cycle, which are connected at the transmetalation step. As depicted in Scheme 22, the proposed catalytic cycle starts with the salt metathesis between a copper catalyst and potassium benzoate, affording a copper benzoate. Subsequent decarboxylation produces an aryl copper species, which transfer its aryl group to a Pd(II) intermediate (generated via oxidative addition of aryl halide to Pd(0) catalyst), thus giving rise to a diaryl Pd(II) species and the regeneration of copper catalyst. The diaryl Pd(II) species undergoes reductive elimination to release the biaryl product, and to regenerate the Pd(0) catalyst.



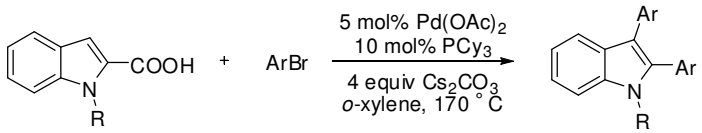
Scheme 22. Mechanism for the decarboxylative cross-coupling reaction.

In 2006, Bilodeau and Forgione disclosed the first Pd-catalyzed decarboxylative cross-coupling of five-membered heterocyclic carboxylic acids with aryl bromides (Scheme 23).[41] Various heterocyclic biaryls were synthesized in good yields. Compared to the direct C-H arylation of heteroarenes, where regioselectivity was problematic, good regioseletivity was observed in this case, thus showing the advantages of this protocol. Along with the main product, slight amounts of 2,3-diarylated heteroaromatic products could also be detected, although adding 1 equiv of tetrabutylammonium chloride hydrate could minimize the side reaction. The authors proposed that the coupling process of heteroaryl surrogates with aryl halides proceeds via electrophilic palladation pathways (paths B and C) instead of direct decarboxylation.[42]



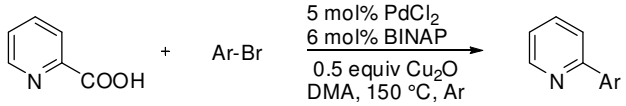
Scheme 23. Decarboxylative coupling of heteroaromatic carboxylic acids with aryl bromides.

The decarboxylative cross-coupling of indole-2-carboxylic acids with aryl halides has also been disclosed by Miura (Scheme 24).[43] This sequential *ortho*-arylation and *ipso*-decarboxylative arylation process features the synthesis of 2,3-diarylindoles, a highly luminescent solid blue emitter.



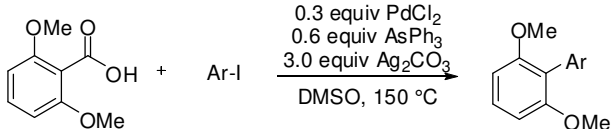
Scheme 24. Decarboxylative coupling of carboxyindoles with aryl bromides.

2-Arylpyridines are important heterocyclic structural motifs and their synthesis is of great interest for the organic community. Tremendous effort has been dedicated to develop efficient protocols for this compound class synthesis.[44] However, due to the instability and difficult-to-access of 2-pyridyl organometallics, their transition metal-catalyzed cross-coupling reactions to the access of 2-arylpyridine is still challenging. Burke's group developed an elegant coupling of air stable 2-pyridyl *N*-methyliminodiacetic acid (MIDA) boronate, however, this reagent possesses large leaving group and its synthesis is somewhat unsustainable.[45] As an alternative, 2-picolinic acid is air stable and nature abundant 2-pyridyl source. In 2013, Wu group reported Pd/Cu-catalyzed decarboxylative cross-coupling of 2-picolinic acid (Scheme 25).[46]. Although moderate yields were obtained, this process provides an efficient approach to this important compound class, presenting good synthetic utility.



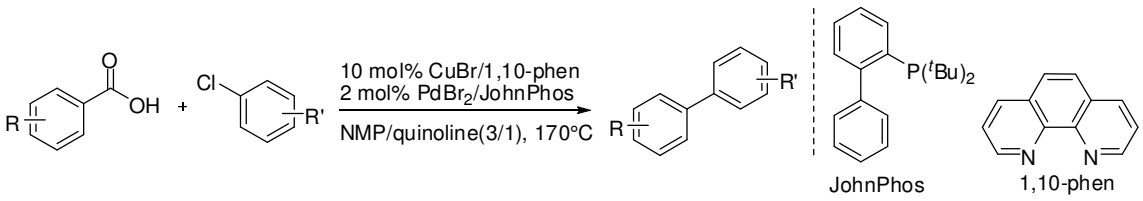
Scheme 25. Decarboxylative coupling of 2-picolinic acids with aryl bromides.

More active aryl iodides are of course applicable in decarboxylative biaryl synthesis. Becht and Wagner developed the coupling of aromatic carboxylic acids with aryl iodides by using $PdCl_2$ and unusual ligand $AsPh_3$ along with excessive Ag_2CO_3 (Scheme 26).[47] The silver catalyst is highly active towards the decarboxylation of *ortho*-methoxybenzoic acid. Thus in this protocol, the scope is mainly limited to *ortho*-methoxyl benzoic acids. In order to keep the decarboxylation and cross-coupling reaction in pace, 0.3 equiv of $PdCl_2$ is required. The use of large quantities of expensive palladium and silver salts limits its synthetic utility.



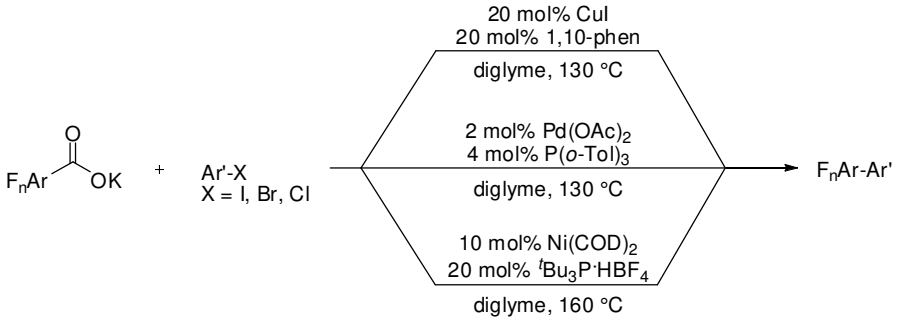
Scheme 26. Pd/Ag catalyzed decarboxylative coupling of aryl iodides.

Aryl chlorides are among the most attractive carbon electrophiles, particularly on industrial scale, because they are readily available in great structural diversity and at low cost. The aryl chlorides have also been demonstrated to be applicable to the decarboxylative cross-coupling reactions (Scheme 27).[48] Considering that the aryl C-Cl bond is much stronger than the corresponding C-Br bond,[49] the key to achieve the decarboxylative coupling of aryl chlorides is the choice of palladium catalyst along with electron-rich and sterically hindered phosphine ligand JohnPhos, allowing facial oxidative addition of palladium to aryl chlorides, thus furnishing the coupling process.



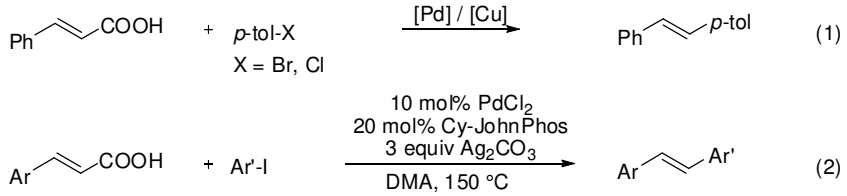
Scheme 27. Pd/Cu-catalyzed decarboxylative coupling of aryl chlorides.

Polyfluorobenzoic acids are particularly reactive in the presence of several transition metal catalysts. Copper [50], palladium [51] and nickel catalysts [52] are capable of promoting decarboxylative cross-couplings of fluorinated aromatic carboxylic acids with aryl halides (Scheme 28).



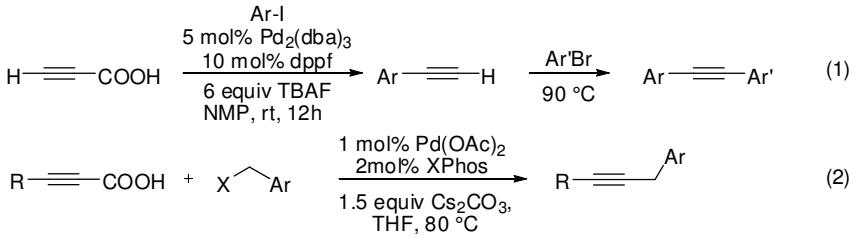
Scheme 28. Polyfluorobenzoates in decarboxylative cross-couplings.

The alkenyl carboxylic acids especially cinnamic acids are also applicable to decarboxylative cross-coupling reactions. In Gooßen's seminal works, with Pd/Cu bimetallic system, cinnamic acid has been successfully coupled with aryl bromides and chlorides affording a few examples of stilbenes in good yields (Scheme 29, Eq 1).[48,40b] In 2009, the Wu group reported their systematic study of decarboxylative coupling of cinnamic acids. A broader range of cinnamic acids were coupled with various aryl iodides. However, a stoichiometric amount of Ag_2CO_3 is required in this transformation (Scheme 29, Eq 2).[53]



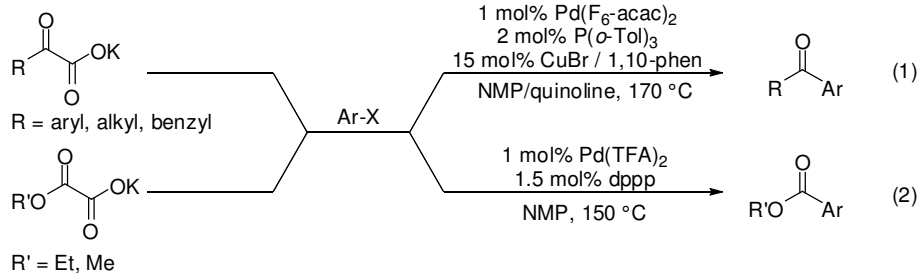
Scheme 29. Decarboxylative cross-coupling of cinnamic acids.

In 2008, the Lee group reported a convenient protocol for the synthesis of unsymmetrical diaryl alkynes starting from propiolic acid (Scheme 30, Eq 1).[54] This one-pot-reaction proceeds via Sonogashira coupling of the terminal alkyne with aryl iodide at room temperature followed by decarboxylative coupling with another aryl bromide at 90 °C. The Li group extended this reaction to the coupling of benzyl or allyl halides, affording alkyl substituted alkynes (Scheme 30, Eq 2).[55]



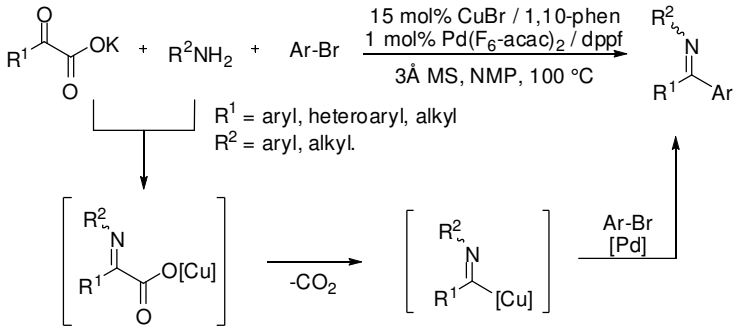
Scheme 30. The decarboxylative coupling of propiolic acids.

The Gooßen group demonstrated that acyl anions can be generated via Cu-catalyzed decarboxylation of α-oxocarboxylic acid, and the combination of this process with Pd-catalyzed coupling of aryl halides leads to a straightforward approach to aryl ketones (Scheme 31, Eq 1).[56] Unlike the conventional Friedel-Crafts acylations, which usually yields isomeric mixtures, this processes produce regiospecific ketones. Moreover, the use of readily accessible and bench stable α-oxocarboxylic acids alleviates multi-step generation of acyl nucleophiles. Inspired by this work, Fu and Liu developed Pd-catalyzed decarboxylative coupling of potassium oxalate monoesters with aryl halides, affording a broad range of benzoates (Scheme 31, Eq 2).[57]



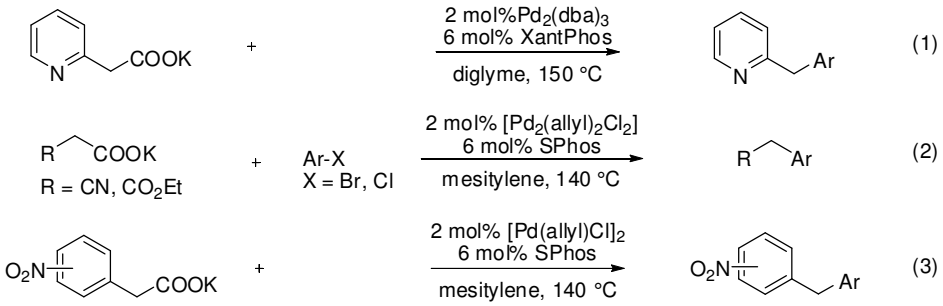
Scheme 31. Decarboxylative aryl ketone and ester synthesis.

Based on their decarboxylative ketone synthesis, the Gooßen group further developed a three-component decarboxylative coupling reaction to synthesize azomethines from α-oxocarboxylic acids, aryl halides and primary amines (Scheme 32).[58] The reaction was proposed to proceed via in situ generation of iminocarboxylates from α-oxocarboxylic acids and primary amines followed by Cu-catalyzed decarboxylation of iminocarboxylates and Pd-catalyzed coupling reaction. It is worth mentioning that this reaction occurs at 100 °C, which is 70 °C lower than the corresponding coupling of α-oxocarboxylic acids with aryl halides.



Scheme 32. Decarboxylative azomethine synthesis.

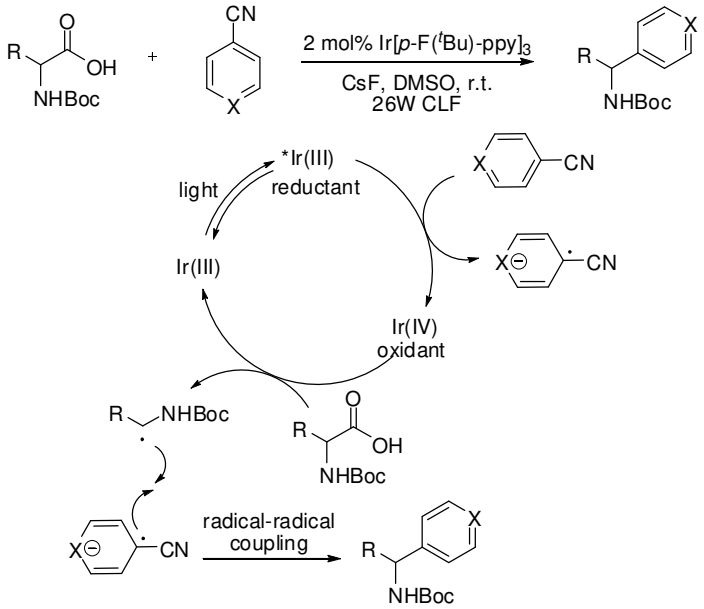
Activated aliphatic carboxylic acids such as α-pyridyl,[59] -cyano or -ethoxycarbonyl,[60] or nitroaryl carboxylic acids[61] can undergo decarboxylative cross-coupling with aryl halides, affording diarylmethanes with $C(sp^3)$-$C(sp^2)$ bond formation (Scheme 33, Eq 1-3).



Scheme 33. Decarboxylative coupling of activated aliphatic carboxylic acids.

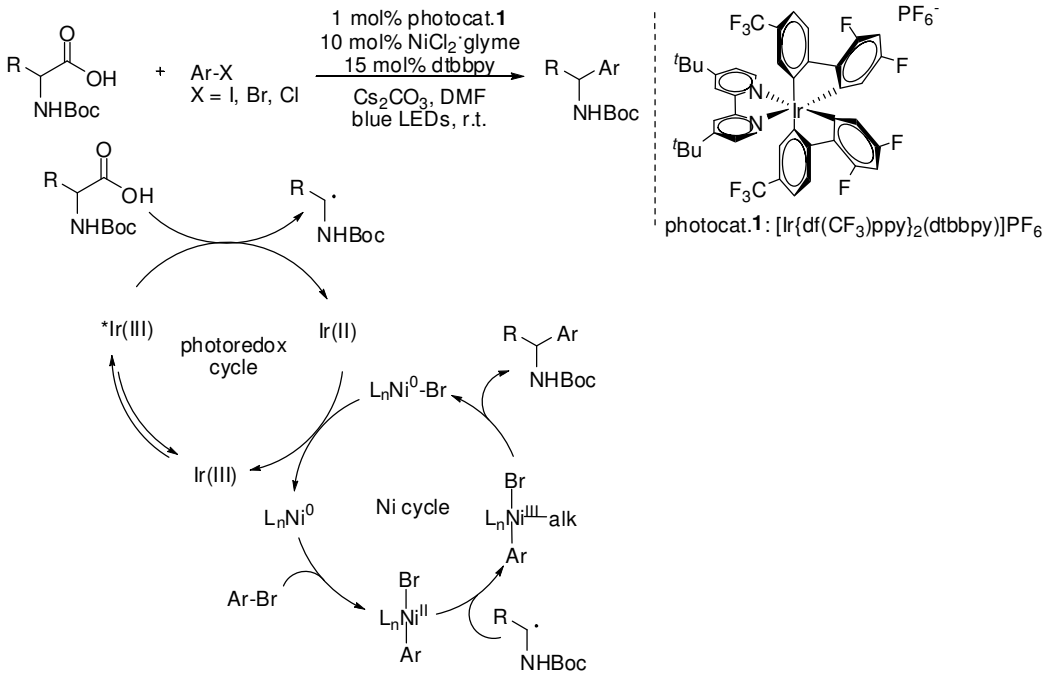
Recently, photo induced radical decarboxylation has been received much attention. Pioneering work was reported by the MacMillan group in 2014. A broad range of natural abundant amino acids were coupled with cyanoarenes in the presence of an iridium photocatalyst under irradiation at room temperature (Scheme 34).[62] The authors proposed that irradiation of the iridium(III) photocatalyst with visible light produces a long-lived photoexcited state *Ir(III), which would facile reduce cyanoarene via single electron transfer to generate the corresponding aryl radical anion and afford Ir(IV) complex. Oxidation of the amino acid by an Ir(IV) complex results in a carboxyl radical along with an Ir(III) complex.

Carboxyl radical would rapidly undergo decarboxylation to generate amino radical species. The final product was formed via radical-radical coupling between these two radical species.



Scheme 34. Decarboxylative arylation of α-amino acids.

This group later has successfully combined photoredox catalysis with Ni-catalyzed coupling strategy. Much broader aryl halides were employed in this Ir/Ni bimetallic catalyzed decarboxylative arylation of amino acids, promoting the utility of this protocol (Scheme 35).[63] In the presence of a Ni catalyst, the aryl halide would undergoes oxidative addition to form an aryl Ni(II) complex, which would further engage with an amino radical to from Ni(III) complex. Reductive elimination would release the product along with a Ni(I) species, which would reduce to Ni(0) catalyst with Ir(II) species. When a chiral ligand for the nickel catalyst was used, high enantioselective decarboxylative arylation of α-amino acids with aryl halides was realized.[64]



Scheme 35. Ir/Ni catalyzed decarboxylative arylation of amino acids with aryl halides.

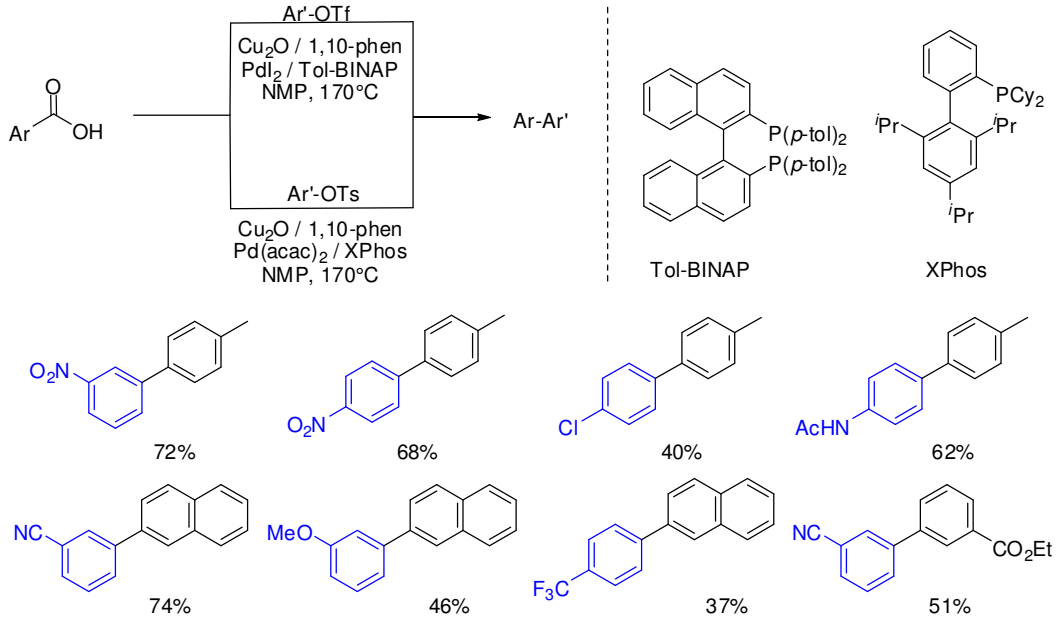
By merging iridium photoredox catalysis and palladium catalysis, Shang and Fu developed a decarboxylative coupling of α-oxocarboxylic acids with aryl halides, affording aryl ketones and amides at room temperature (Scheme 36).[65] Based on DFT calculations, the authors proposed a Pd(0)-Pd(II)-Pd(III) catalytic cycle combined with a photoredox catalysis cycle, which is similar to the above mentioned MacMillan's Ir/Ni mechanism.

Scheme 36. Ir/Pd catalyzed decarboxylative ketone and amide synthesis.

3.2.1.1.2 Decarboxylative coupling of aryl sulfonates

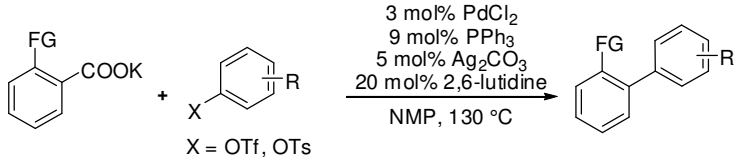
The decarboxylative cross-coupling of aryl bromides and chlorides, even with aryl iodide are both limited to specific carboxylic acids, namely the *ortho*-substituted benzoic acids or heteroaromatic carboxylic acids. This might result from the competition between halide ions and carboxylates in the coordination of the copper catalyst. The Gooßen group reasoned that if aryl triflates were used in decarboxylative coupling reaction, the weakly coordinating triflate ions released in the transmetalation step are unable to block the carboxylate out of the coordinating sphere of the copper catalyst. Based on this hypothesis, decarboxylative coupling

of aryl triflates was developed.[66] The substrate scope of decarboxylative coupling reaction for the first time covers the full range of substitution patterns including *meta*- and *para*-substituted benzoic acids. Considering the expense and the sensitivity of aryl triflates, this protocol has been successfully extended to the coupling of inexpensive and more robust aryl tosylates (Scheme 37).[67]



Scheme 37. Pd/Cu-catalyzed decarboxylative coupling of aryl triflates and tosylates.

Due to the fact that the proverbial stability of silver halides prevents the silver catalyst re-enters the decarboxylation cycle, stoichiometric amounts of silver catalyst are required in decarboxylative coupling of aryl halides. Silver catalyst can be realized in catalytic amounts by using arylsulfonates as the coupling partner. The Gooßen group reported a Pd/Ag catalyzed decarboxylative coupling of aryl triflates and tosylates (Scheme 38).[68] It is worth mentioning that the reaction proceeds readily at 120 °C so that transesterification between the aryl triflates and nucleophilic benzoates is suppressed. However, the silver-based system is ineffective for the coupling of *meta*- and *para*- substituted benzoates.

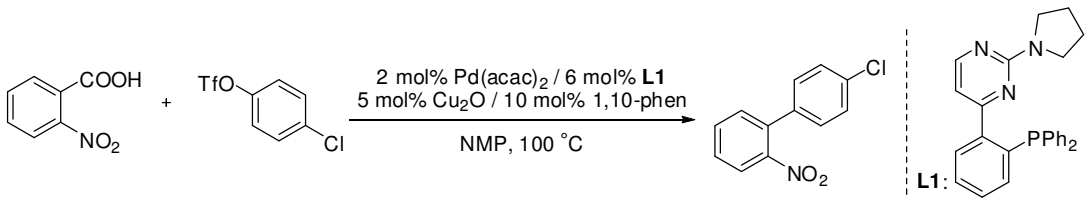


Scheme 38. Pd/Ag-catalyzed decarboxylative coupling of aryl triflates and tosylates.

Recent DFT-calculation based mechanism studies showed that the difference in reactivity between *ortho*- and non-*ortho*-substituted carboxylates in the reaction with aryl halides is not

caused by the salt metathesis step. Although the presence of excess bromide salt shifts the equilibrium of the salt metathesis step to the side of the copper bromide so that less copper carboxylate is available, which reduces the efficiency of the entire decarboxylation process, the low reactivity of non-*ortho*-substituted benzoate is probably caused by the higher barrier of the decarboxylation process. The decarboxylation of non-*ortho*-substituted benzoates requires more energy than that of *ortho*-substituted benzoates, high conversions of non-*ortho*-substituted benzoic acids cannot be achieved at temperatures where *ortho*-substituted derivatives decarboxylate.[69] If one could identify a new catalyst system that lower down the energy barrier, many variations would become possible, for instance, the decarboxylative coupling of non-*ortho* substituted benzoic acids with aryl halides.

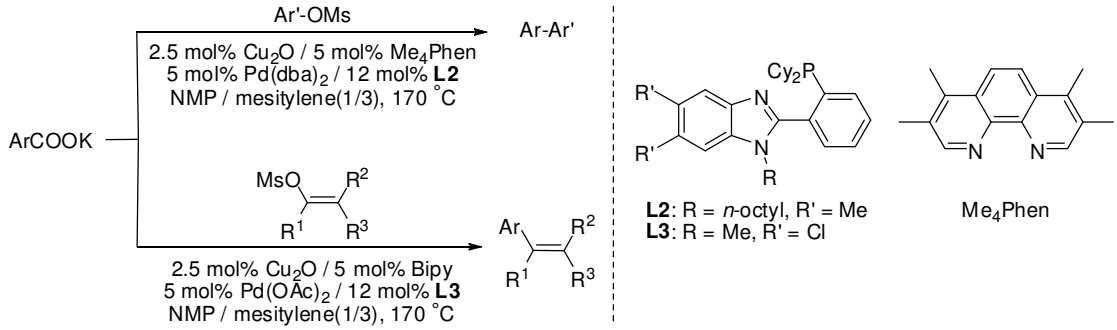
This mechanistic study also revealed that decarboxylation is not necessarily the rate-determining step. In some certain cases, such as for substrates that decarboxylate comparatively easily, the transmetalation becomes rate-limiting. 2-nitrobenzoic acid was found to decarboxylate in the presence of a copper catalyst at 100 °C. With this finding, the Gooßen group reported a Cu/Pd bimetallic catalyzed decarboxylative cross-coupling at much lower temperature (Scheme 39).[70] In this protocol, a bidentate aminopyrimidinyl phosphine was designed to bridge the palladium and copper centers and thereby facilitating the rate-determining transmetalation step. It allows the coupling of various substituted 2-nitro-benzoates with a broad range of aryl triflates at only 100 °C, which is 70 °C lower than previously reported protocol.



Scheme 39. Low temperature Pd/Cu-catalyzed decarboxylative coupling reaction.

Among the sulfonates, aryl and alkenyl mesylates are particularly attractive because they have the lowest molecular weight of all sulfonate leaving groups, thus possess great preparative- and industrial-scale synthesis utility. They are easily accessible by esterification of broadly available phenols or enolates with inexpensive methanesulfonyl chloride or anhydride. The notoriously hard-to-activate mesylates can only be cleaved with extremely active cross-coupling catalysts, such as nickel or palladium that bears sophisticated ligands. According to the mechanism, the decarboxylation catalyst copper or silver only undergoes transmetalation with palladium not nickel, therefore, palladium is the choice of coupling catalyst. Thus, the

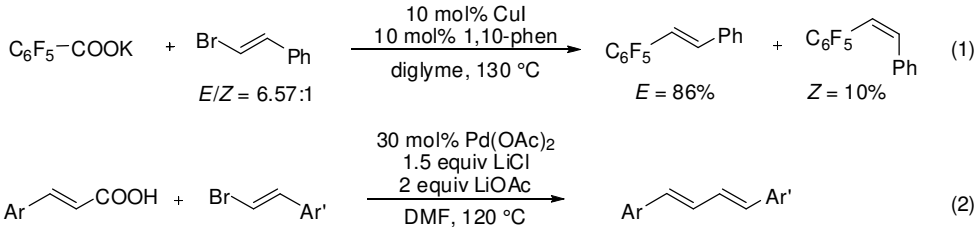
development of sophisticated ligands for the palladium catalyst became priority for the success of this transformation. The Gooßen group disclosed the first decarboxylative coupling of aryl- and alkenyl mesylates (Scheme 40).[71] Customized imidazolyl phosphine ligands were developed and efficiently promote the decarboxylative coupling or aryl- and alkenyl mesylates. Unfortunately, non-*ortho*-substituted benzoates are not active under these conditions.



Scheme 40. Pd/Cu-catalyzed decarboxylative coupling of mesylates.

3.2.1.2 Decarboxylative alkenylation reaction

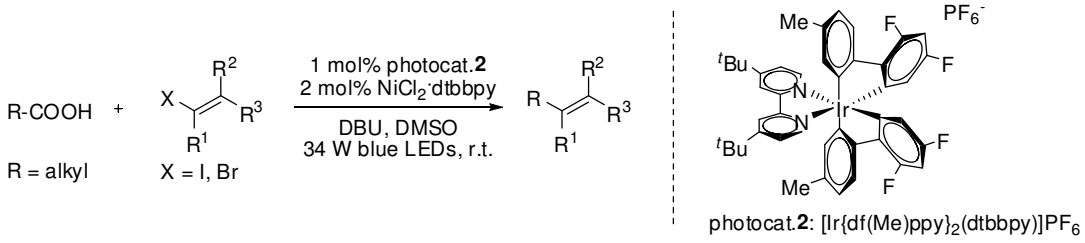
Compared to decarboxylative arylation, decarboxylative alkenylation is much less explored. In 2009, the Liu group disclosed the first single example, where potassium pentafluorobenzoate coupled with cinnamyl bromide in the presence of CuI as the catalyst (Scheme 41, Eq 1).[50] Almost simultaneously, the Miura group disclosed Pd-catalyzed decarboxylative coupling of cinnamic acids with broader cinnamyl bromides, affording conjugated olefins in good yields (Scheme 41, Eq 2).[72]



Scheme 41. Decarboxylative cross-coupling of cinnamic acids.

Just recently, the MacMillan group reported a decarboxylative cross-coupling of alkyl carboxylic acids with vinyl halides by synergistic merger of photoredox and nickel catalysis. A variety of α-oxy and α-amino acids, as well as simple hydrocarbon-substituted acids are coupled with vinyl iodides and bromides, giving rise to vinylation products in high efficiency under mild, operationally simple reaction conditions (Scheme 42).[73] The mechanism is similar to their previously reported decarboxylative arylation reaction, namely oxidative addition of

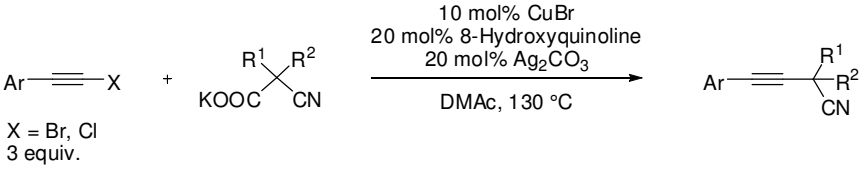
Ni(0) species into vinyl halide to generate vinyl Ni(II) intermediate, and interception of alkyl radical by vinyl Ni(II) intermediate to generate organometallic Ni(III) adduct. The subsequent reductive elimination affords the alkenylation product and Ni(I) species, which is reduced to Ni(0) by the reduced state of the photocatalyst.



Scheme 42. Decarboxylative vinylation of aliphatic acids.

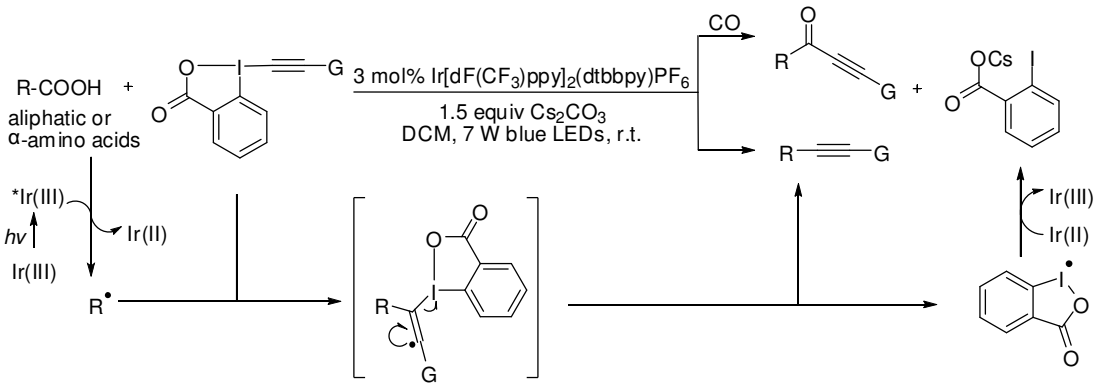
3.2.1.3 Decarboxylative alkynylation reaction

Decarboxylative alkynylations that have been reported are mostly under oxidative conditions, for instance $AgNO_3/K_2S_2O_8$ or CuBr/DTBP catalyzed decarboxylative alkynylation of aliphatic acids.[74] The first redox-neutral decarboxylative alkynylation was reported by the Xu group in 2013. Quaternary α-cyano acetate salts coupled with alkynyl halides in the presence of $CuBr/Ag_2CO_3$ catalyst system, affording butynenitriles in good yields (Scheme 43).[75] The yield dropped to half in the absence of Ag_2CO_3 and to less than 10% without CuBr. The authors didn't elucidate the role of Ag_2CO_3, however, it might help to promote decarboxylation step.[76]



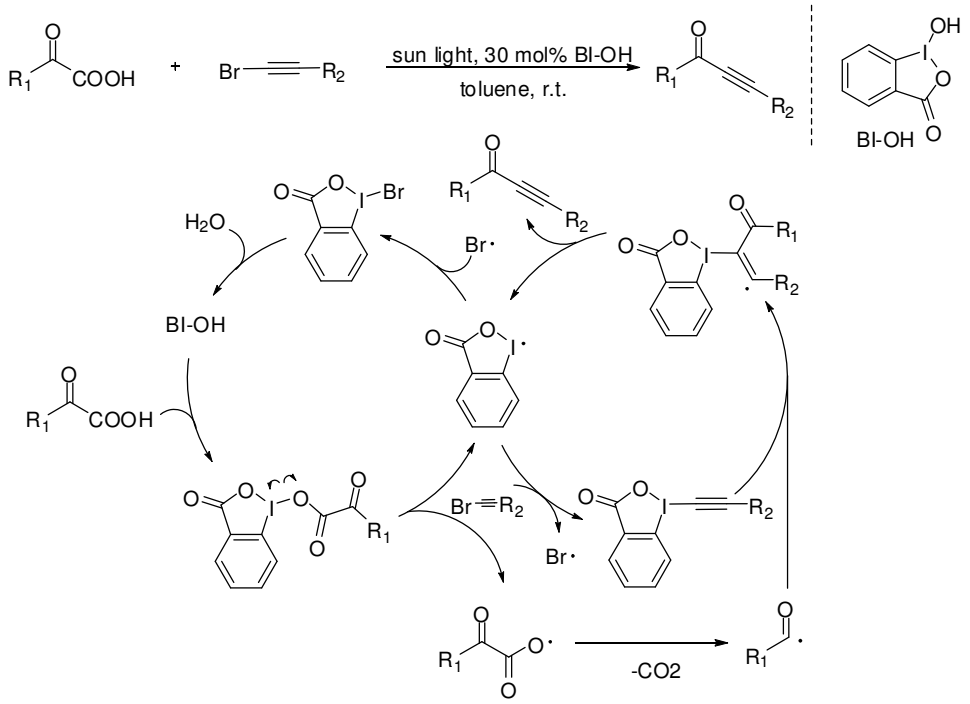
Scheme 43. The decarboxylative alkynylation of α-cyano acetate salts.

Recent rapid development of photo induced decarboxylation allows the alkynylation under milder redox-neutral conditions. Xiao and Waser independently reported an Ir-catalyzed photo induced decarboxylative alkynylation of aliphatic carboxylic acids with ethynylbenziodoxolone (EBX) reagent under blue LED irradiation. A broad range of aliphatic carboxylic acids including α-amino acids were converted to the corresponding alkynes in good yields. Moreover, under CO atmosphere, decarboxylative carbonylative alkynylation of carboxylic acids could be realized, allowing the preparation of ynones (Scheme 44).[77]



Scheme 44. Ir-catalyzed photo induced decarboxylative alkynylation.

Replacing aliphatic carboxylic acids with α-oxocarboxylic acids, ynones can also be approached via decarboxylative coupling with bromoacetylenes under sunlight (Scheme 45).[78] In this protocol, bromoacetylenes were used as the alkynyl source. Expensive but active ethynylbenziodoxolone reagent was generated in situ by adding catalytic amount of BI-OH. More important, an expensive photocatalyst is not required in this protocol, presenting significant synthetic utility. The reaction was initiated by the reaction between BI-OH and α-oxocarboxylic acids. The resulting intermediate undergoes homolytic cleavage by light irradiation to form an iodanyl radical and a carboxylate radical. The iodanyl radical reacts with bromoacetylenes to generate ethynylbenziodoxolone (EBX) reagent and the carboxylate radical undergoes decarboxylation to form an acyl radical. Addition of the acyl radical to EBX reagent affords the final product along with regeneration of the iodanyl radical. Subsequent radical coupling reaction between the Br radical and the iodanyl radical produces BI-Br, which finally undergoes hydrolysis to generate BI-OH.



Scheme 45. Light-driven transition metal free decarboxylative alkynylation.

3.2.2 Challenges in redox-neutral decarboxylative coupling reaction

Although the redox-neutral decarboxylative coupling reactions are under intensive investigation, there are still some obvious challenges that remain to be addressed. For instance, 1): the restriction of decarboxylative coupling of aryl halides to *ortho*-substituted benzoic acids need to be overcome; 2): decarboxylative coupling of alkenyl halides for the synthesis of arylalkenes need to be developed.

Recent developed decarboxylative coupling reactions provide an efficient strategy to access fundamental compounds via *ipso*-substitution, such as biaryls or stilbenes. As for other valuable compounds that are hard to produce via conventional methodologies, the potential of decarboxylative coupling reaction in synthesizing these compounds is much less explored. In this context, the carboxylate group could function as a deciduous directing group so that other functional groups could be introduced into its adjacent position before being tracelessly removed through protodecarboxylation.

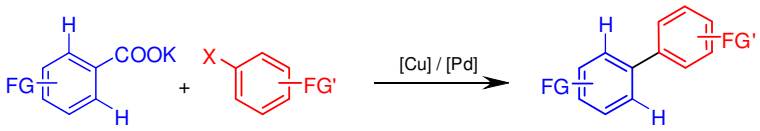
Within this PhD work, we focus to address these challenges.

4. Aims of the research

In the above chapter, bimetallic catalyzed C-C bond formation reactions as well as decarboxylative cross-coupling reactions have been reviewed. With bimetallic catalyst system, new transformation can be developed. One of the most important bimetallic catalyzed reactions is the decarboxylative coupling reaction. Compared to the well-developed traditional coupling reaction, where expensive and sensitive organometallic reagents are used, decarboxylative cross-coupling reactions exhibit advantages, since carboxylic acids are stable, inexpensive, and widely available in a large structural diversity. Although decarboxylative cross-coupling reactions are under heavily investigation, there are still many challenges that need to be addressed.

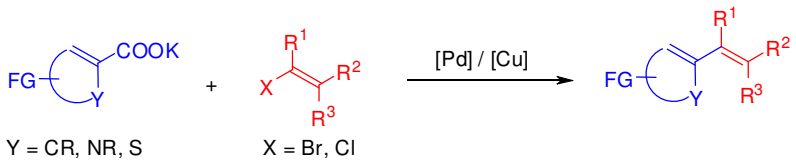
This thesis is divided into 2 main parts:

The 1st part is aimed to develop a new catalyst system, with which the restriction of decarboxylative cross-coupling reactions to *ortho*-substituted or heterocyclic carboxylate substrates can be overcome. Since recent DFT calculation based studies revealed that the previously observed limitation to certain activated carboxylates is not intrinsic, it is very likely to develop a catalyst system that enables decarboxylative cross-coupling of aryl halides with benzoates regardless of their substitution pattern.



Scheme 46. Decarboxylative cross-coupling of aryl halides with benzoates without activating *ortho*-substituents.

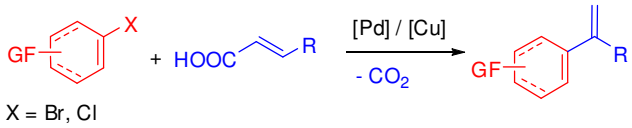
The objective of the 2nd part is to synthesize valuable arylalkenes via decarboxylative couplings. Decarboxylative coupling of alkenyl halides will be the first choice to fulfil the task. The goal is to develop a Cu/Pd bimetallic catalyst system to promote this desirable transformation.



Scheme 47. Decarboxylative coupling of alkenyl halides.

As a further pursuit for the synthesis of 1,1-disubstituted alkenes, we aimed to develop decarboxylative Mizoroki-Heck coupling of aryl halides with α,β-unsaturated carboxylic acids.

The carboxylate group will be used to direct the arylation into the β-position of α,β-unsaturated carboxylic acids before being tracelessly removed through protodecarboxylation.



Scheme 48. Decarboxylative Mizoroki-Heck coupling of aryl halides with α,β-unsaturated carboxylic acids.

5. Results and discussion

5.1 Catalytic decarboxylative cross-coupling of aryl chlorides and benzoates without activating *ortho* substituents

*Part of this work has been published: This Agreement between Jie Tang ("You") and John Wiley and Sons ("John Wiley and Sons") consists of your license details and the terms and conditions provided by John Wiley and Sons and Copyright Clearance Center. Those reproduced from the publication were written in italic.

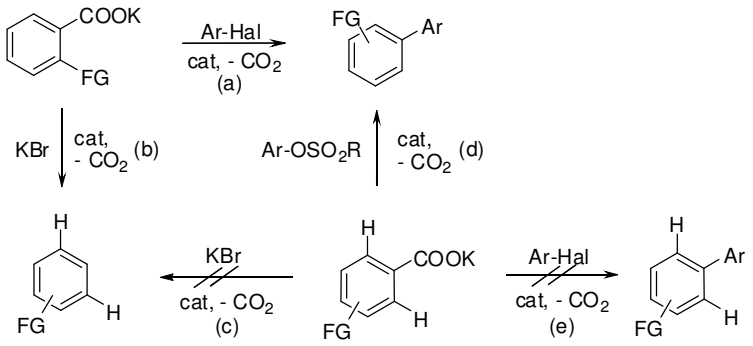
License Number	3962500426196
License date	Oct 05, 2016
Licensed Content Publisher	John Wiley and Sons
Licensed Content Publication	Angewandte Chemie International Edition
Licensed Content Title	Catalytic Decarboxylative Cross-Coupling of Aryl Chlorides and Benzoates without Activating *ortho* Substituents
Licensed Content Author	Jie Tang, Agostino Biafora, Lukas J. Goossen
Licensed Content Date	Sep 4, 2015
Licensed Content Pages	4
Type of use	Dissertation/Thesis
Requestor type	Author of this Wiley article
Format	Print and electronic
Portion	Full article
Will you be translating?	No

*This project was conducted in the collaboration with Mr. Agostino Biafora.

After I finished the first-round screening, he joined in this project. He synthesized some catalysts, tested the robustness of the screening conditions, and isolated half of the final products. He also corrected the manuscript and the supporting information that I wrote, and went through the publication submission process.

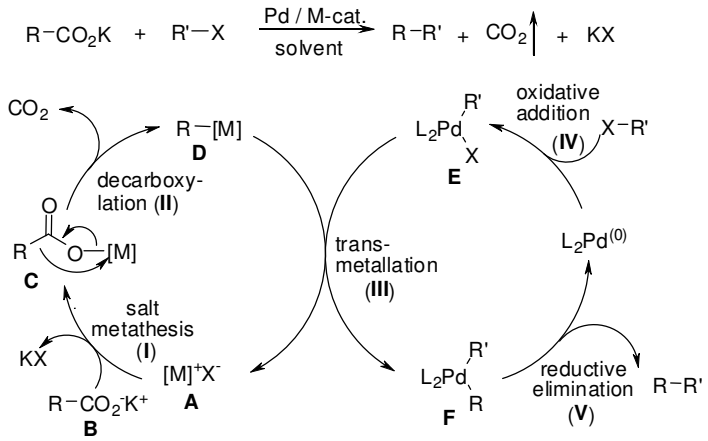
5.1.1 Restriction of decarboxylative arylation and the catalyst design

As reviewed in the previous chapter, the discovery of bimetallic Cu/Pd or Ag/Pd catalysts has enabled the efficient coupling of various aromatic and heteroaromatic carboxylates with aryl electrophiles.[21,79] However, for the first generation of decarboxylative arylation reaction, the reaction appeared to be limited to certain heterocyclic and mono- or di-*ortho*-substituted carboxylates (Scheme 1, a). *In protodecarboxylations, improved catalysts soon allowed surmounting the energetic barrier to decarboxylation even for meta- and para-substituted benzoates* (Scheme 1, b).[80] *Unfortunately, the addition of halide salts, as they form in a cross-coupling with aryl halides, completely suppresses protodecarboxylations of such non-activated benzoates* (Scheme 1, c).[40b]



Scheme 1. Scope and limitations of known decarboxylative couplings**.**

*Based on the mechanistic outline depicted in Scheme 2, it was initially hypothesized that the thermodynamically disfavored salt metathesis between copper or silver halides (**A**) and the potassium carboxylate (**B**) proceeds only when aided by coordinating groups in the ortho-position. This theory appeared to be supported by the successful coupling of non-ortho-substituted carboxylates with carbon electrophiles with non-coordinating sulfonate leaving groups (Scheme 1, d),[79d,e] for which the salt metathesis step (**I**) should be favorable. Unfortunately, the price and availability of these electrophiles somewhat limit the practical utility of these protocols.*



Scheme 2. Decarboxylative cross-coupling reaction. M = Cu, Ag; R = (hetero)aryl, vinyl, acyl; R' = (hetero)aryl; alkenyl.

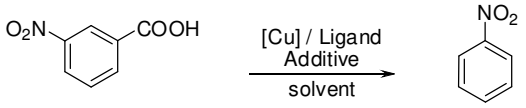
Overcoming the restriction to ortho-substituted benzoates for aryl halide substrates remained a prime target in the development of decarboxylative arylations (Scheme 1, e), because meta- and para-substituted biaryls are otherwise difficult to access from inexpensive precursors, whereas ortho-substituted biaryls can be synthesized in increasing diversity via ortho-C-H-arylations.[81]

*In-depth mechanistic studies confirmed the unfavorable position of the upstream salt metathesis equilibrium (**I**), but surprisingly revealed that it is almost unaffected by the substitution pattern of the benzoates.*[69] *Instead, the presence of σ-withdrawing groups in the ortho-position enables decarboxylative coupling reactions by reducing their rate-determining energy span by 4-8 kcal/mol overall, making them just feasible at manageable reaction temperatures.* [82] That is the reason why *ortho*-substituted benzoic acids can be highly converted in the coupling of aryl halides at temperatures where non-*ortho*-substituted derivatives don't. If we could identify a decarboxylation catalyst system that could lower down the decarboxylation step energy barrier of non-*ortho*-substitued benzoates to some extend, their conversion could still be realized. Moreover, *the transmetalation step (**III**) was found to have an energy barrier in the same high range as the salt metathesis/decarboxylation process. Improving the decarboxylation catalysts by introducing ligands that strongly stabilize intermediate **D** would facilitate its formation but reduce its reactivity in step **III**, once again disabling the overall process. Only a holistic optimization of all reaction steps together might enable the desired decarboxylative cross-coupling of non-activated benzoates with aryl halides using metal mediators only in catalytic amounts.*

5.1.2 Protodecarboxylation studies

*For the development of a decarboxylative arylation of benzoates without activating ortho-substituents, we set the focus on aryl chloride substrates, the most available and inexpensive among the aryl halides. Thus, we started by investigating the protodecarboxylation of 3-nitrobenzoic acid (**5.1-1a**). At 190 °C, quantitative yield was observed in the presence of the standard Cu_2O/1,10-phenanthroline catalyst (Table 1, entry 1), but when adding 1 equiv. of KCl,* the byproduct that would come from the coupling reaction, *the yield dropped to 14% (entry 2).*

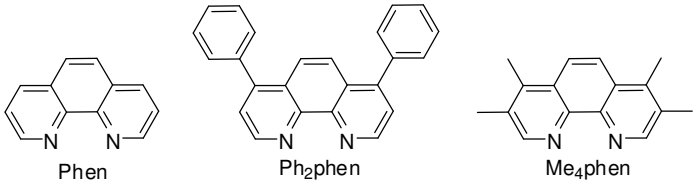
Table 1. Protodecarboxylation studies.[a]



5.1-1a **5.1-4**

entry	[Cu]	ligand	additive	solvent	T (^oC)	Yield (%)
1	Cu_2O	phen	-	NMP/quin.=3/1	190	99
2	”	”	KCl	”	”	14
3	”	”	KOTf	”	”	99
4	”	Ph_2phen	KCl	”	”	50
5	”	”	LiCl	”	”	0
6	”	”	NaCl	”	”	16
7	”	”	CsCl	”	”	30
8	”	”	$MgCl_2$	”	”	0
9	”	”	$CaCl_2$	”	”	trace
10	”	”	$^nBu_4NCl$	”	”	trace
11	**”**	**”**	**KCl**	**quin**	**”**	**99**
12	**”**	**Me_4phen**	**”**	**”**	**”**	**99**
13	”	”	KCl	”	170	50
14	Ag_2CO_3	-	”	”	190	0

[a]Reaction conditions: **5.1-1a** (0.5 mmol), Cu_2O or Ag_2CO_3 (5 mol %), ligand (10 mol %), additive (0.5 mmol), 3 mL of solvent, 190 ^oC, 16 h. Yields determined by GC analysis using *n*-tetradecane as the internal standard. NMP = *N*-methyl-2-pyrrolidone; quin. = quinoline.



The addition of other salts, e.g. NaCl, $^{n}Bu_4NCl$ or CsCl suppressed the protodecarboxylation to a comparably strong extend, whereas it was unaffected by the presence of potassium salts with weakly coordinating anions such as KOTf (entries 3-10). This confirms that it is mostly the anion and not the cation that affects the decarboxylation step.

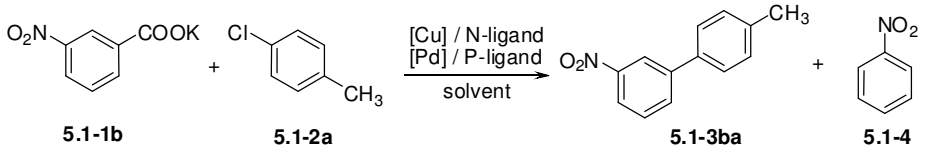
Previous mechanistic studies on protodecarboxylation showed that electron-rich ligand could improve the reactivity of the copper catalyst.[80] After in-depth optimization, a quantitative yield was finally achieved using either 3,4,7,8-tetramethyl-1,10-phenanthroline (Me_4phen) or 4,7-diphenyl-1,10-phenanthroline (Ph_2phen) as ligand in quinoline (entries 11-12). *This demonstrates that the decarboxylation barrier of non-activated carboxylates can be overcome with customized catalysts even when excess halide salt reduces the availability of copper carboxylate intermediates*. A lower reaction temperature gave inferior result suggesting a high decarboxylation energy barrier of this substrate (entry 13).

Silver-based catalysts were ineffective under these conditions (entry 15), because the proverbial stability of silver chloride shifts the salt exchange equilibrium away from the silver carboxylates. Also, the influence of ortho-substituents is particularly strong for silver, which catalyzes the decarboxylation of 2,6-dimethoxybenzoates under very mild conditions but is inactive for non-ortho-substituted benzoates.[79a,83]

5.1.3 Optimization of the reaction conditions

*Encouraged by the protodecarboxylation studies results, we went on to search for an effective decarboxylative cross-coupling catalyst for the model reaction of potassium 3-nitrobenzoate (**5.1-1b**) with 4-chlorotoluene (**5.1-2a**). Using a combination of the optimal protodecarboxylation catalyst (Cu_2O/Me_4phen) with a state-of-the-art cross-coupling system ($PdBr_2$/JohnPhos), only 15% yield of desired product was detected (Table 2, entry 1). The yield of **5.1-3ba** was even lower with other phenanthroline derivatives*, including 4,7-diphenyl-1,10-phenanthroline (entries 2-3). Even more electron rich 4,7-dimethoxyl-1,10-phenanthroline ($(MeO)_2$Phen) showed no activity, probably due to its decomposition to pyridone derivative, which is unable to act as ligand for copper (entry 4). *Remarkably, a large amount of protodecarboxylation product nitrobenzene **5.1-4** was formed (entries 1-3). This indicates that the decarboxylation step proceeds efficiently and suggests that the transmetalation step has become limiting*. The ratio of **5.1-3ba** to **5.1-4** improved when shifting to a more polar solvent mixture of quinoline/NMP, probably because polar solvent facilitate oxidative addition and transmetalation (entry 5). Among the copper source test, CuI was the optimal choice (entry 8), because with this copper catalyst, decarboxylation cycle and coupling cycle occurred at comparable rate.

Table 2. Optimization of the reaction conditions.[a]

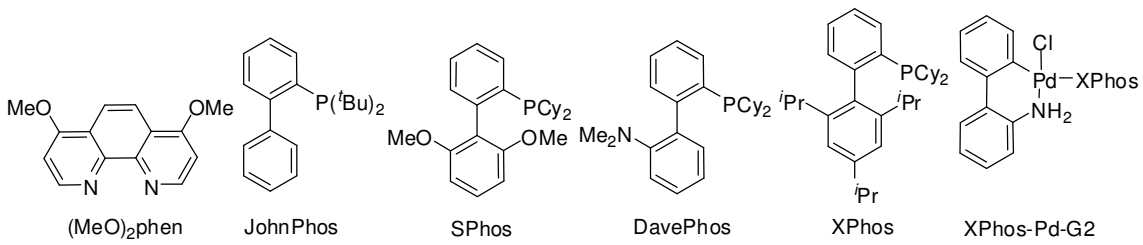


5.1-1b **5.1-2a** **5.1-3ba** **5.1-4**

Entry	[Cu]	N-ligand	[Pd]	P-ligand	solvent	Yield (%)	
						3ba	**4**
1	Cu_2O	Me_4Phen	$PdBr_2$	JohnPhos	quin.	15	70
2	”	Phen	”	”	”	4	60
3	”	Ph_2Phen	”	”	”	5	72
4	”	$(MeO)_2Phen$	”	”	”	0	18
5	”	Me_4Phen	”	”	quin./NMP=1/1	16	40
6	CuBr	”	”	”	”	12	42
7	CuCl	”	”	”	”	14	38
8	CuI	”	”	”	”	19	30
9	”	”	”	$^tBu_4P\cdot HBF_4$	”	17	28
10	”	”	”	PCy_3	”	8	28
11	”	”	”	SPhos	”	14	34
12	”	”	”	DavePhos	”	17	25
13	”	”	”	XPhos	”	36	23
14	”	”	PdI_2	”	”	37	24
15	”	”	$Pd(OAc)_2$	”	”	42	40
16	”	”	$Pd_2(dba)_3$	”	”	7	25
17	”	”	$Pd(allyl)_2Cl_2$	”	”	29	32
18	”	”	XPhos-Pd-G2	”	”	12	27
19	”	”	$(MeCN)_4Pd(BF_4)_2$	”	”	42	48
20	”	”	$(MeCN)_4Pd(OTs)_2$	”	”	53	50
21	”	”	$(MeCN)_4Pd(OTf)_2$	”	”	58	50
22[b]	”	”	”	”	”	**67**	**38**
23[b, c]	”	”	”	”	”	38	36
24[b, d]	”	”	”	”	”	30	33
25[b, e]	”	”	”	”	”	0	6
26[b, f]	”	”	”	”	”	0	trace
27[b]	”	”	-	-	”	0	25
28[b]	-	-	$(MeCN)_4Pd(OTf)_2$	XPhos	”	0	trace
29[b]	-	-	-	-	”	0	0

[a]Reaction conditions: **5.1-1b** (0.6 mmol), **5.1-2a** (0.5 mmol), Cu-source (10 mol %), N-ligand (10 mol %), Pd-source (2 mol %), P-ligand (5 mol %), 3 mL of solvent, 190 °C, 16 h. Yields

determined by GC analysis using *n*-tetradecane as the internal standard. NMP = *N*-methyl-2-pyrrolidone; quin. = quinoline. [b]5 ml of solvent. [c]180 °C. [d]170 °C. [e]150 °C. [f]100 °C.



The key improvement in the overall yield was achieved by optimizing the palladium co-catalyst. Electron-rich, bulky phosphine ligated palladium catalysts are known to activate aryl chlorides.[84] Among the phosphine ligand screening, XPhos was by far the most effective ligand in this reaction (entry 13). *Another major step upward resulted from the use of palladium precursors with weakly coordinating counter-ions*, i.e. $(MeCN)_4Pd(OTs)_2$ or $(MeCN)_4Pd(OTf)_2$ (entries 20-21). This highly electrophilic Pd(II) catalyst may facilitate the transmetalation of copper aryl species to the palladium complex, thus improving the coupling yield. *Finally, the cross-coupling catalyst was found to preserve its activity better at greater dilution* (entry 22), because less concentrated system disfavors palladium black aggregation. Control experiments showed that the yields sharply decrease at lower temperatures e.g. 38% at 180°C, 30% at 170°C, and 0% at 150°C (entries 23-26) and that both metals are essential for this transformation (entries 27-29).

5.1.4 Scope

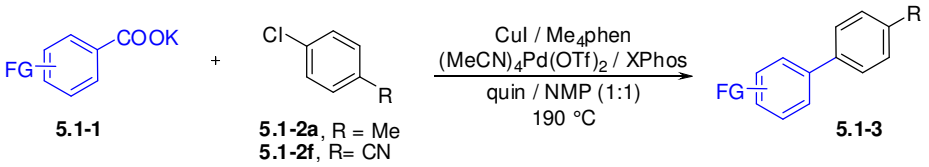
*With the optimal catalyst, a mixture of CuI, Me_4phen, $(MeCN)_4Pd(OTf)_2$, and XPhos in 1:1 quinoline/NMP, the desired product **5.1-3ba** was obtained in close to 70% yield after 16 hours at 190 °C, along with unreacted aryl chloride and the protodecarboxylation product **5.1-4**. Having thus found an effective protocol, we next investigated its scope.*

Under these conditions, a wide variety of benzoic acids with regardless of their substitution pattern were coupled with the model substrate 4-chlorotoluene (**5.1-2a**) in good yields (Table 3). *Electron-withdrawing substituents, such as nitro, cyano, fluoride, trifluoromethyl, trifluoromethoxy, sulfonyl and sulfonamide can be presented in any position of the aromatic ring. The catalyst reaches its performance limit for 3-phenoxy benzoate* (**5.1-3oa**). Even more electron-rich substrates gave unsatisfactory yields (**5.1-3pa**, **5.1-3qa**). However, the formation of protodecarboxylation byproducts indicates that the decarboxylation step proceeds well and this step is not limiting for any of the substrates.

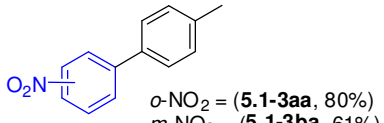
The yields obtained for ortho-substituted carboxylates are significantly higher than those previously reported (**5.1-3aa**, 80% vs 71%; **5.1-3da**, 76% vs 47%; **5.1-3ra**, 79% vs 65%; **5.1-**

3sa, 85% vs 40%),[48] *confirming the superiority of the new protocol*. The *ortho*-trifluoromethoxylbenzoate (**5.1-3ja**) was included for the first time in the decarboxylative couplings in good yield. *ortho-Methyl benzoate and ortho-phenyl benzoate (**5.1-3wf**, **5.1-3xf**), which have never before been converted in decarboxylative couplings, gave reasonable yields*. In these two cases, substantial amounts of protodecarboxylation products were detected, suggesting that there is a potential to improve the coupling yields.

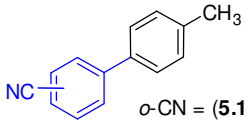
Table 3. Scope with regard to the aromatic carboxylates.[a]



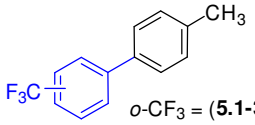
5.1-1 + **5.1-2a**, R = Me; **5.1-2f**, R= CN → **5.1-3**



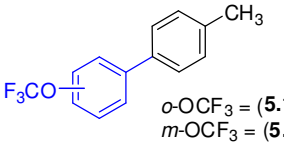
o-NO_2 = (**5.1-3aa**, 80%)
m-NO_2 = (**5.1-3ba**, 61%)
p-NO_2 = (**5.1-3ca**, 51%)



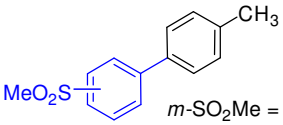
o-CN = (**5.1-3da**, 76%)
m-CN = (**5.1-3ea**, 70%)
p-CN = (**5.1-3fa**, 54%[b])



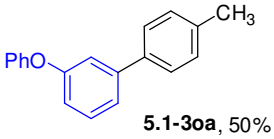
o-CF_3 = (**5.1-3ga**, 50%)
m-CF_3 = (**5.1-3ha**, 50%)
p-CF_3 = (**5.1-3ia**, 76%[b])



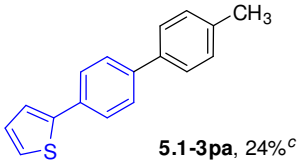
o-OCF_3 = (**5.1-3ja**, 80%)
m-OCF_3 = (**5.1-3ka**, 61%)
p-OCF_3 = (**5.1-3la**, 50%)



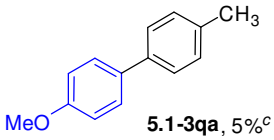
m-SO_2Me = (**5.1-3ma**, 60%)
p-SO_2Me = (**5.1-3na**, 88%[b])



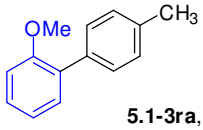
5.1-3oa, 50%



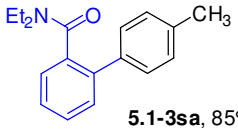
5.1-3pa, 24%[c]



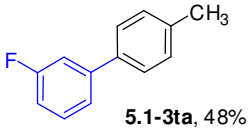
5.1-3qa, 5%[c]



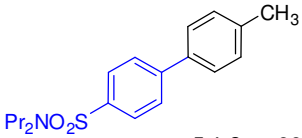
5.1-3ra, 79%



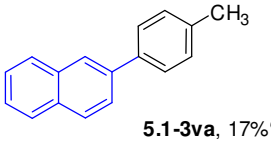
5.1-3sa, 85%



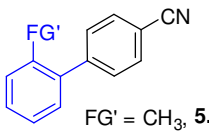
5.1-3ta, 48%



5.1-3ua, 88%



5.1-3va, 17%[c]

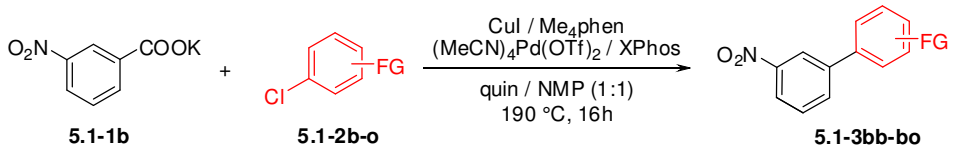


FG' = CH_3, **5.1-3wf**, 18%[d]
FG' = Ph, **5.1-3xf**, 32%[d]

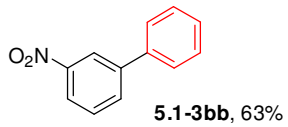
[a]Reaction conditions: **5.1-1a-v** (0.6-0.75 mmol), **5.1-2a** or **5.1-2f** (0.5 mmol), CuI (10 mol%), 3,4,7,8-tetramethyl-1,10-phenanthroline (10 mol%), $(MeCN)_4Pd(OTf)_2$ (2 mol%), XPhos (5 mol%), 5 mL of solvent, 190 °C, 16 h. Isolated yields. [b]32 h. [c]GC-yield. [d]4-chlorobenzonitrile (**5.1-2f**) used as coupling partner.

*The scope with regard to the electrophilic coupling partner was explored with potassium 3-nitrobenzoate (**5.1-1b**). As shown in Table 4, various aryl chlorides with common functionalities such as cyano, fluoro, trifluoromethyl, ether, sulfonyl, and ketone groups, as well as heterocyclic derivatives react smoothly.*

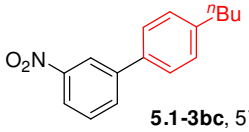
Table 4. Scope with regard to the aryl chlorides.[a]



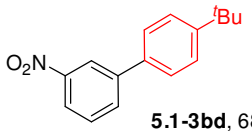
5.1-1b **5.1-2b-o** **5.1-3bb-bo**



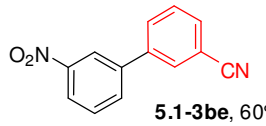
5.1-3bb, 63%



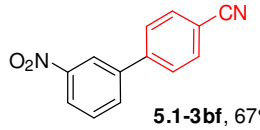
5.1-3bc, 57%



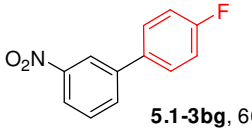
5.1-3bd, 68%



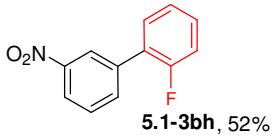
5.1-3be, 60%



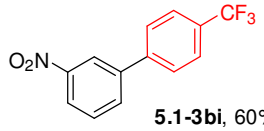
5.1-3bf, 67%



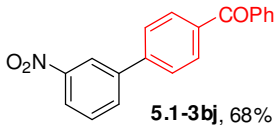
5.1-3bg, 66%



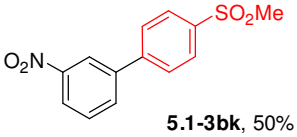
5.1-3bh, 52%



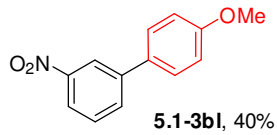
5.1-3bi, 60%



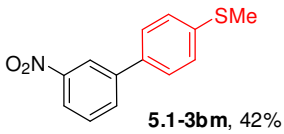
5.1-3bj, 68%



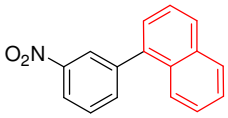
5.1-3bk, 50%



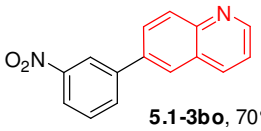
5.1-3bl, 40%



5.1-3bm, 42%



5.1-3bn, 43%



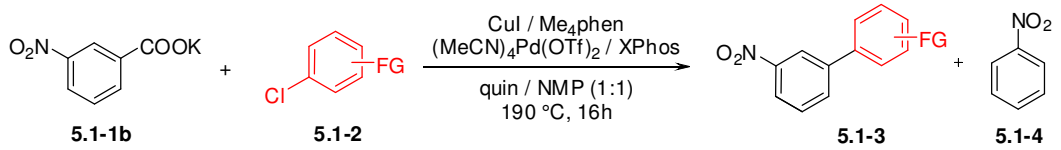
5.1-3bo, 70%

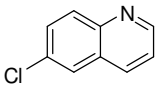
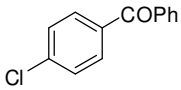
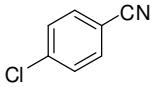
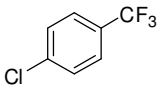
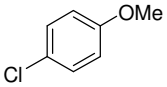
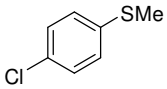
[a]Reaction conditions: **5.1-1b** (0.6 mmol), **5.1-2b-o** (0.5 mmol), CuI (10 mol%), 3,4,7,8-tetramethyl-1,10-phenanthroline (10 mol%), $(MeCN)_4Pd(OTf)_2$ (2 mol%), XPhos (5 mol%), 5 mL of solvent, 190 °C, 16 h. Isolated yields.

Notably, aryl chlorides bearing electron-donating groups gave lower ratios of decarboxylative coupling to protodecarboxylation than those bearing electron-withdrawing groups *(Table 5). A rationale for the observation that the oxidative addition becomes the selectivity-determining step can be derived from the energy span model, if one assumes that the transmetalation proceeds via the highest-energy transition state in the reaction profile, that protodecarboxylation always proceeds with the same speed, and that the transmetalation is unaffected by the substituent at the Pd-bound aryl group. The oxidative addition equilibrium, which should lie more on the side of the starting materials for electron-rich compared to*

electron-poor substrates, increases the rate-determining energy span for the former, so that the decarboxylative cross-coupling is more selective for the latter.

Table 5. Ratio between **5.1-3** and **5.1-4** using electron-rich or electron-poor aryl chlorides.[a]



5.1-2	**5.1-3** yield (%)	**5.1-4** yield (%)	Total (5.1-**3**+5.1-**4**) (%)	Ratio (5.1-**3**:5.1-**4**)
 **5.1-2o**	70	50	120	1.4:1
 **5.1-2j**	68	50	118	1.36:1
 **5.1-2e**	67	51	118	1.31:1
 **5.1-2i**	60	50	110	1.2:1
 **5.1-2l**	40	42	82	0.95:1
 **5.1-2m**	42	56	98	0.75:1

[a]Reaction conditions: **5.1-1b** (0.6 mmol), **5.1-2** (0.5 mmol), CuI (10 mol%), 3,4,7,8-tetramethyl-1,10-phenanthroline (10 mol%), $(MeCN)_4Pd(OTf)_2$ (2 mol%), XPhos (5 mol%), 5 mL of solvent, 190 °C, 16 h. Isolated yields.

5.1.5 Conclusions and outlook

In conclusion, a customized Pd^{II}/Cu^{I} bimetallic catalyst system was found to enable the decarboxylative cross-coupling of non-ortho-substituted aromatic carboxylates with aryl chlorides. This confirms predictions by DFT studies that the previously observed limitation to certain activated carboxylates is not intrinsic. The catalyst system also presents higher performance in the coupling of *ortho*-substituted benzoates, giving much higher yields than

those previously reported. *ortho*-Methyl benzoate and *ortho*-phenyl benzoate which have never before been converted in decarboxylative coupling reactions, gave reasonable yields. These together further confirm the superiority of the new procedure. However, this protocol also showed some limits. For example, this catalyst system promotes the coupling of electron-deficient benzoates in good yields, while it reaches its performance limit for electron-rich ones. Electron-rich aryl chlorides gave lower ratios of decarboxylative coupling to protodecarboxylation than electron-poor substrates. More importantly, the reaction proceeds at 190 °C. The next obvious challenge will be to develop a new catalyst system which allows the reaction to occur at greatly reduced temperatures. Considering that the decarboxylation step is no longer limiting, the catalysts with bridging ligands which facilitate the transmetalation step would probably be the choice to address this challenge.

5.2 Arylalkene synthesis

Aryl- and heteroarylalkenes are common structural motifs of natural products, bioactive substances and functional materials. Representing examples are depicted in Figure 1: Pawhuskins A, which is isolated from organic extracts of *Dalea purpurea*, with in vitro opioid receptor affinity; marine ascidian antibiotics Cadiolide A; photo- and thermochromic compound Spiropyrans; antimalarial active Trioxanes; 3-amino-2-phenylpropene (APP) derivatives which were characterized as novel bovine chromaffin vesicular monoamine transporter inhibitors.[85]

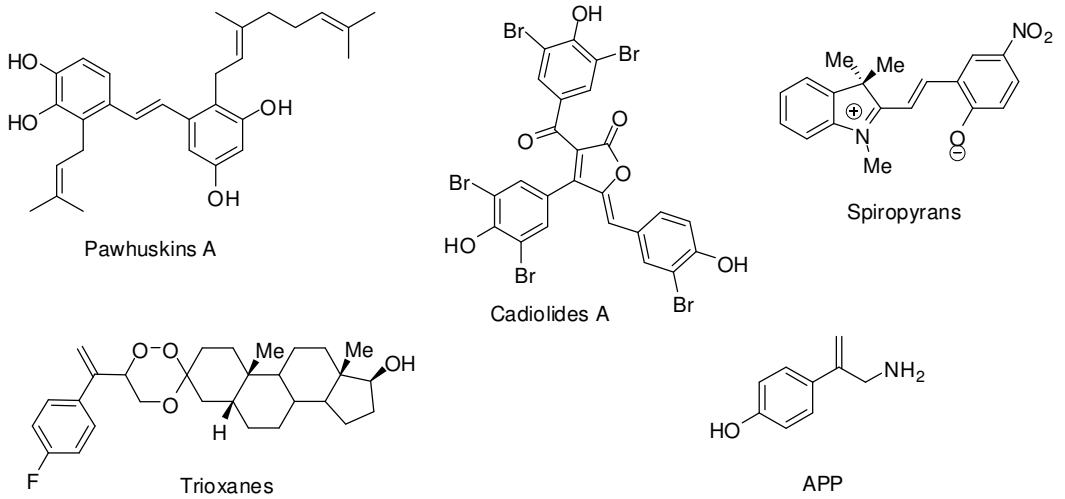


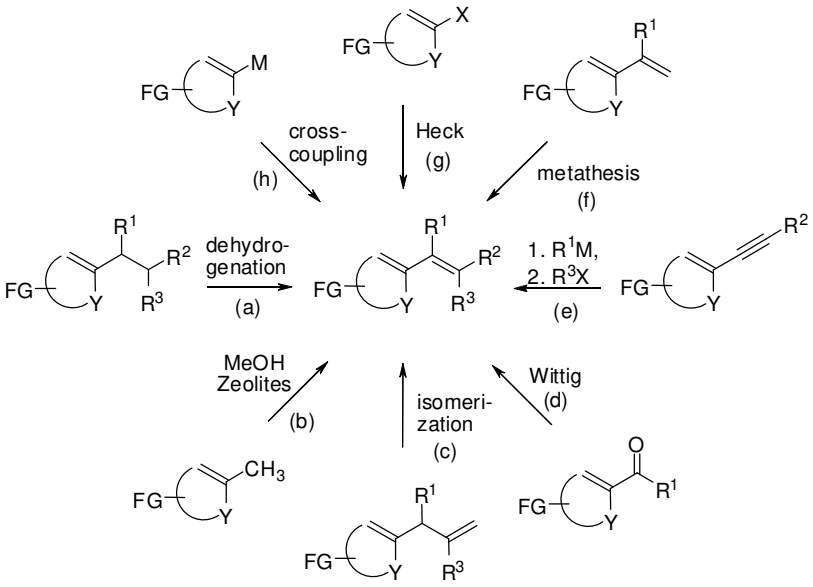
Figure 1. Examples of (hetero)aryl alkenes.

Efficient synthetic approaches to these important compounds are constantly pursued by organic chemists.[86] Traditionally, arylalkenes can be prepared via dehydrogenation reactions,[87] such as the dehydrogenation of ethylbenzene over a vanadium oxide-loaded MgO catalyst to afford styrene, the simplest arylalkene (Scheme 3, a), or via condensation of toluene with MeOH in the presence of Zeolites (b).[88] They can also be produced via isomerization of allylbenzenes (c).[89] Further established methods for the stereoselective synthesis of arylalkenes include Wittig or Peterson olefinations (d),[90] transition-metal catalyzed carbometalations of alkynes with aromatic metallic reagents (e),[91] as well as olefin metatheses (f).[92] These methodologies are somewhat limited in scope, waste-intensive, and/or require multistep syntheses of starting materials.

Nowadays, Mizoroki-Heck reactions of aryl halides or carboxylates have been well developed for the synthesis of arylalkenes (g).[93] However, existing reaction conditions for Mizoroki-Heck reaction of simple electron-neutral alkenes, such as aliphatic or cyclic olefins, are proved to be less efficient, usually leading to mixtures of double-bond isomers or low

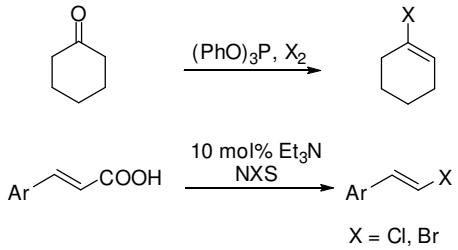
yields.[94] Moreover, regiospecific arylation of polysubstituted alkenes are difficult to access because the essential cis-Pd-H elimination pathway is usually not feasible.[95]

Transition metal-catalyzed cross-coupling reactions, such as Stille coupling reaction, Negishi reaction, and Suzuki coupling reaction are well developed for stereoselective synthesis of this compound class (h).[96] However, hard-to-access, expensive and sensitive preformed alkenyl metal reagents are required.



Scheme 3. Synthetic approaches to (hetero)arylalkenes.

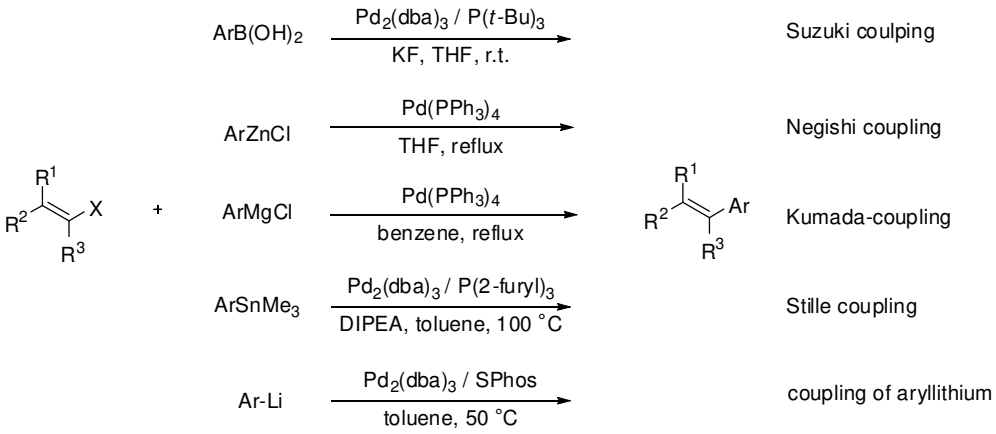
Alkenyl (pseudo)halides are substrates that ban be easily prepared in defined stereochemistries. [97] For instance, halogenation of enolizable ketones or Hunsdiecker decarboxylative halogenation of cinnamic acids allows alkenyl halides synthesis from readily available substrates (Scheme 4).



Scheme 4. Alkenyl halides synthesis.

Catalytic cross-couplings of alkenyl (pseudo)halides have found widespread application, especially for the synthesis of arylalkenes via coupling with arylmetallic reagents (Scheme 5).[96,98] However, the preformed organometallic reagents, e.g., (hetero)arylzinc, -boron, -tin, -

magnesium, or -lithium compounds, are often costly, hard to access, or sensitive to air and moisture.



Scheme 5. Arylalkene synthesis via coupling of alkenyl halide.

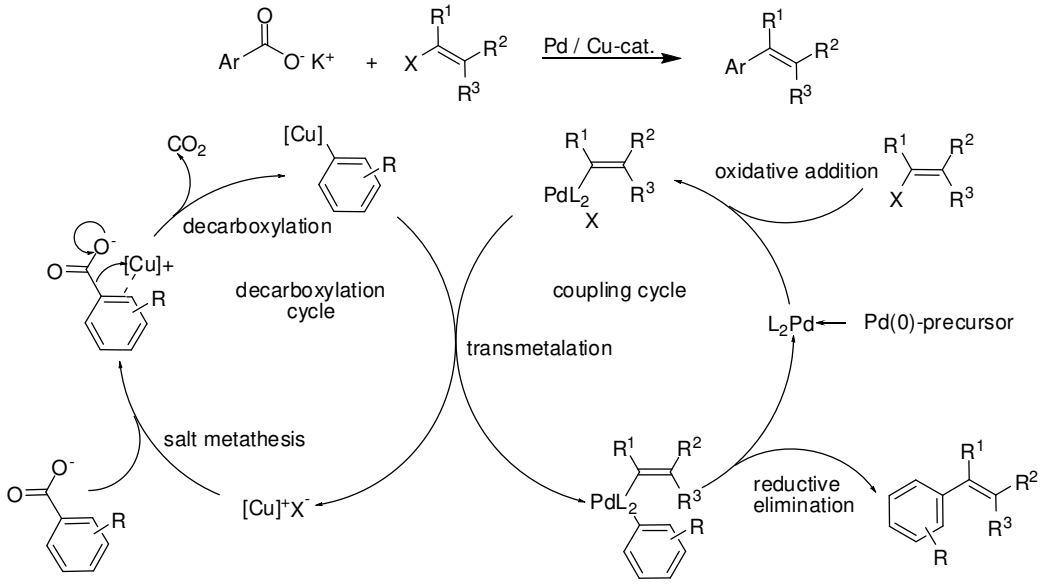
5.2.1 Arylalkene synthesis via decarboxylative cross-coupling of alkenyl halides

*Part of this work has been published: Reprinted (adapted) with permission from (COMPLETE REFERENCE CITATION). Copyright (2014) American Chemical Society. Those reproduced from the publication were written in italic.

5.2.1.1 Decarboxylative coupling of alkenyl halides

As reviewed in chapter 3, decarboxylative cross-coupling reactions have been emerged as a powerful new strategy for C-C and C-heteroatom bond formation.[21] However, among the electrophiles, *the substrate range of known catalyst systems does not seem to extend to the coupling of alkenyl halides*. Only two examples of alkenyl halides involved decarboxylative coupling have been reported: namely cinnamyl bromides coupled with cinnamic acids (Miura *et al.*)[72] and pentafluorobenzoic acid (Liu *et al.*).[50] *Myers' decarboxylative Heck reaction was the first example to give access to vinylarene products from benzoic acids,*[93e] *but the regiochemistry of the arylation step depends on the steric and electronic properties of the alkene, rather than being definable by a leaving group,* thus 1,2-substituted arylalkenes are usually obtained. Moreover, decarboxylative Heck coupling reactions require stoichiometric oxidant, such as Ag_2CO_3, further limits its practical utility.

An efficient and generally applicable protocol for the decarboxylative cross-coupling of alkenyl halides would be highly desirable, since it would allow the regiospecific synthesis of arylalkenes starting from simple, bench-stable and readily available (hetero)aromatic carboxylic acids, thus circumvent the use of expensive and sensitive aryl metal reagents. Based on the development of decarboxylative coupling reaction, we believed that such a process should be possible. As the outlined mechanism showed in Scheme 6, palladium inserts into the alkenyl halide bond via oxidative addition, and the resulted Pd(II) species undergoes transmetallation with aryl copper species that previously generated via decarboxylation to afford alkenyl aryl Pd(II) species. Subsequent reductive elimination of this Pd(II) species delivers the final product. *The key to success would be to synchronize the decarboxylation and cross-coupling cycles so that the key step transmetallation would occur smoothly*.

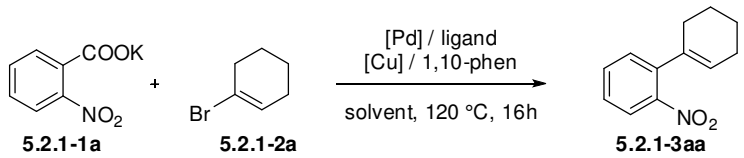


Scheme 6. Mechanistic blueprint for a decarboxylative alkenylation.

5.2.1.2 Optimization of the reaction conditions

*In our search for a suitable catalyst system, we chose the reaction of potassium 2-nitrobenzoate (**5.2.1-1a**) with 1-bromocyclohexene (**5.2.1-2a**) as a model and investigated various catalysts that had proven to give excellent yields in analogous couplings of **5.2.1-1a** with aryl bromides*.[40,99] However, as expected, *they displayed poor activity in the arylation of the cyclic alkenyl bromide* **5.2.1-2a**. *Using a combination of CuBr/1,10-phenanthroline and $Pd(acac)_2$ in a mixture of N-methylpyrrolidone (NMP) and quinolone, only 19% yield were obtained at 120 °C* (Table 7, entry 1). A large amount of protodecarboxylation product nitrobenzene was detected, indicating that decarboxylation was too fast. *A step-up in the yields was achieved by reducing the solvent polarity and, thus, slowing down the decarboxylation in relation to the cross-coupling step* (entry 2). *The addition of certain phosphine ligands such as the bidentate bis(diphenylphosphino)methane (dppm)*[99] *further improved the yield to 71%* (entry 3). *Copper sources containing halide ions were found to be particularly effective, and copper chloride provided the best yields* (entry 7). *Among the palladium precursors, $Pd(F_6\text{-}acac)_2$ proved to be the optimal choice* (entries 8-14). Phosphine ligand is critical for the success of this transformation. *An extensive ligand screening revealed that the moderately electron-donating, bulky ligand tri-1-naphthylphosphine [$P(1\text{-}naph)_3$] gave higher yields than all phosphines previously employed in the coupling of aryl halides* (entries 15-21). *This suggests that the oxidative addition, which is facilitated by particularly electron-rich ligands, is not rate determining for the coupling of alkenyl bromides*. On the contrary, the reductive elimination which is favored by sterically demanding phosphine ligand is probably the limiting step.

Table 7. Optimization of the reaction conditions.[a]



5.2.1-1a **5.2.1-2a** **5.2.1-3aa**

Entry	Cu-source	Pd-source	Ligand	Solvent	T(°C)	Yield (%)
1	CuBr	$Pd(acac)_2$	-	NMP/quin.=3/1	120	19
2	”	”	-	NMP/Mes.=1/3	”	48
3	”	”	dppm	”	”	71
4	Cu_2O	”	”	”	”	44
5	CuOAc	”	”	”	”	63
6	CuI	”	”	”	”	46
7	CuCl	”	”	”	”	73
8	”	$Pd(dba)_2$	”	”	”	71
9	”	PdI_2	”	”	”	63
10	”	$PdBr_2$	”	”	”	67
11	”	$PdCl_2$	”	”	”	68
12	”	$Pd(OAc)_2$	”	”	”	69
13	”	$Pd(PPh_3)_4$	”	”	”	64
14	”	$Pd(F_6\text{-acac})_2$	”	”	”	75
15	”	”	PPh_3	”	”	83
16	”	”	PCy_3	”	”	87
17	”	”	P(*t*-Bu)$_3$	”	”	79
18	”	”	P(2-furyl)$_3$	”	”	86
19	”	”	P(*p*-Tol)$_3$	”	”	81
20	”	”	P(*o*-Tol)$_3$	”	”	92
21	”	”	P(1-naph)$_3$	”	”	97
22	”	”	”	”	100	21
23	”	”	”	”	110	47
24	**”**	**”**	**”**	**”**	**130**	**99**
25	”	”	”	”	150	91
26	”	”	”	”	170	92
27[b, c]	”	”	”	”	”	74
28[c, d]	”	”	”	”	”	83

[a]Reaction conditions: **5.2.1-1a** (0.6 mmol), **5.2.1-2a** (0.5 mmol), Pd-source (1.0 mol %), phosphine ligand (2.0 mol %), Cu-source (10 mol %), 1,10-phen (10 mol %), 4 mL solvent, 16 h. Yields determined by GC analysis using *n*-tetradecane as the internal standard. 1,10-phen =1,10-phenanthroline; quin. = quinoline; Mes. = mesitylene; dppm = bis(diphenylphosphino)methane. [b]In situ generation of **5.2.1-1a** from the benzoic acid and K_3PO_4. [c]With 200 mg of 4 Å molecular sieves. [d]Without drying and degassing solvent.

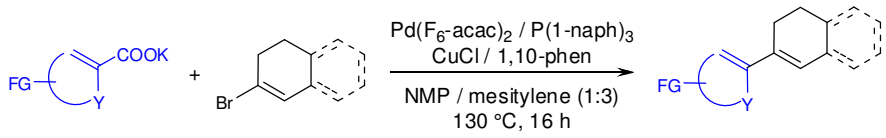
With the optimal catalyst system, 10 mol % CuCl, 1 mol % Pd(F_6-acac)$_2$ in NMP/mesitylene (1:3), full conversion of ***5.2.1-2a*** *and near-quantitative yield of the desired 1-cyclohexenyl-2-nitrobenzene (****5.2.1-3aa****) was achieved within 16 h at 130 °C (entry 24). Remarkably, considerable yield was obtained already at 100 °C, which is an extremely low temperature for a decarboxylative cross-coupling reaction* (entry 22). Higher reaction temperature gave same level of yields (entries 25-26). *The reaction was also successfully performed starting directly from the carboxylic acid and without drying or degassing solvent, which underlines its robustness* (entries 27-28).

5.2.1.3 Scope

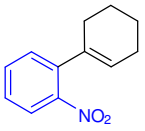
Having thus found an effective protocol for the decarboxylative coupling of alkenyl bromides, we next investigated its scope. For the less activated benzoates, 150 °C is required for higher conversion. This reaction proceeds at 130-150 °C, which is 20-40°C lower that previous reported decarboxylative arylation. *As can be seen from the examples in Table 8, ortho-substituted aromatic and heteroaromatic carboxylic acids smoothly reacted with 1-bromocyclohex-1-ene (****5.2.1-2a****) or the less volatile 3-bromo-1,2-dihydronaphthalene (****5.2.1-2h****) to give the corresponding (hetero)arylalkenes*. Common functionalities including electron-withdrawing and -donating groups, such as *ether, ketone, fluoro and trifluoromethyl groups were tolerated, and the reaction proceeds well even for sterically hindered o,o-disubstituted benzoic acids* (**5.2.1-3ea**).

*Non-ortho substituted benzoic acids (****5.2.1-3oa****) could not yet be converted*, which was expected since the presence of bromide salts shifts the equilibrium of the salt metathesis step to the side of the copper bromide so that less copper carboxylate is available. This reduces the efficiency of the entire decarboxylation process. More important, according to the DFT calculation study, the decarboxylation of non-*ortho*-substituted benzoates requires higher energy than that of *ortho*-substituted counterparts; therefore, non-*ortho*-substituted benzoates do not undergo decarboxylation where *ortho*-substituted benzoates can be decarboxylated. Decarboxylative coupling of alkenyl halides with non-*ortho* substituted benzoic acids is still challenging. To address this challenge, identifying an improved catalyst system and reaction conditions are required.

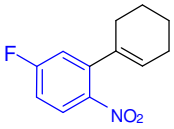
Table 8. Scope with regard to the aromatic carboxylates.[a]



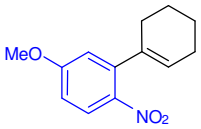
5.2.1-1 **5.2.1-2a** or **5.2.1-2h** **5.2.1-3**



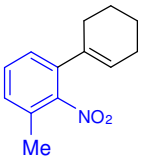
5.2.1-3aa, 92%



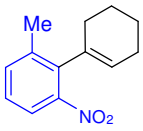
5.2.1-3ba, 82%



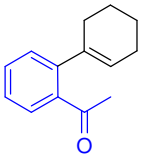
5.2.1-3ca, 94%



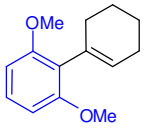
5.2.1-3da, 86%



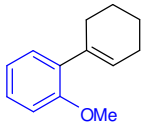
5.2.1-3ea,78%[b]



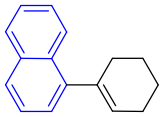
5.2.1-3fa, 71%[b]



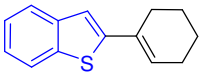
5.2.1-3ga, 43%[c,d]



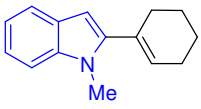
5.2.1-3ha, 51%[c,d]



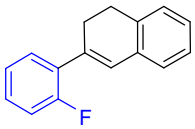
5.2.1-3ia, 47%[c,d]



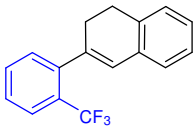
5.2.1-3ja, 75%



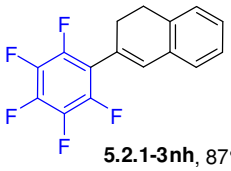
5.2.1-3ka, 59%



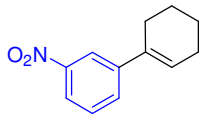
5.2.1-3lh, 63%[c,e]



5.2.1-3mh, 46%[c]



5.2.1-3nh, 87%[c]



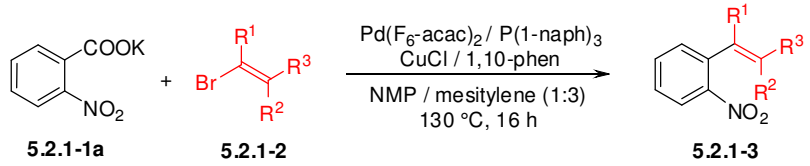
5.2.1-3oa, 0%

[a]Reaction conditions: **5.2.1-1** (0.6 mmol), **5.2.1-2** (0.5 mmol), $Pd(F_6\text{-acac})_2$ (1.0 mol %), $P(1\text{-naph})_3$ (2.0 mol %), CuCl (10. mol %), 1,10-phenanthroline (10 mol %), 4 mL of solvent, 130 °C, 16 h. Isolated yields. [b]24 h. [c]150 °C. [d]CuI/$PdBr_2$ as the catalyst. [e]NMP/mesitylene 2:1.

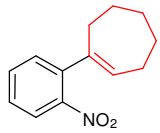
The reaction is also widely applicable with regard to the alkenyl bromides. As can be seen from the examples in Table 9, mono-, di-, and even trisubstituted alkyl bromides gave similarly high yields. Unwanted double bond isomerization, a common side reaction in the alternative Mizoroki-Heck reactions especially in the coupling of cycloalkenes, did not take place in this decarboxylative coupling reaction. Branched arylalkenes and polysubstituted alkenes that hard to access via Mizoroki-Heck reaction are obtained from moderate to high yields. *The reaction proved to be high yielding for products that are inaccessible via decarboxylative Heck reactions, e.g., cyclic arylalkenes or 2-arylalkenes, thus demonstrating the complementarity of both approaches. Only for highly volatile substrates, the isolated*

yields remained unsatisfactory at 0.5 mmol scale, since the product partly evaporated during work-up. The synthesis of ***5.2.1-3ac*** *in 80% yield on a gram scale demonstrates that the reaction can easily be scaled up.*

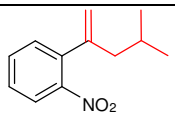
Table 9. Scope with regard to the alkenyl bromides.[a]



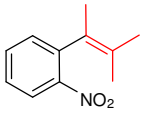
5.2.1-1a + **5.2.1-2** → **5.2.1-3**



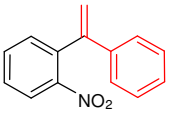
5.2.1-3ab, 74%



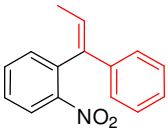
5.2.1-3ac, 92% (80%)[b]



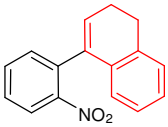
5.2.1-3ad, 70%



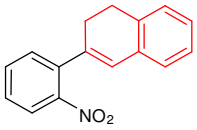
5.2.1-3ae, 39%



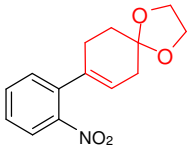
5.2.1-3af, 74%



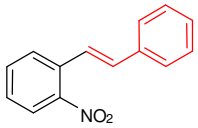
5.2.1-3ag, 68%



5.2.1-3ah, 97%



5.2.1-3ai, 97%

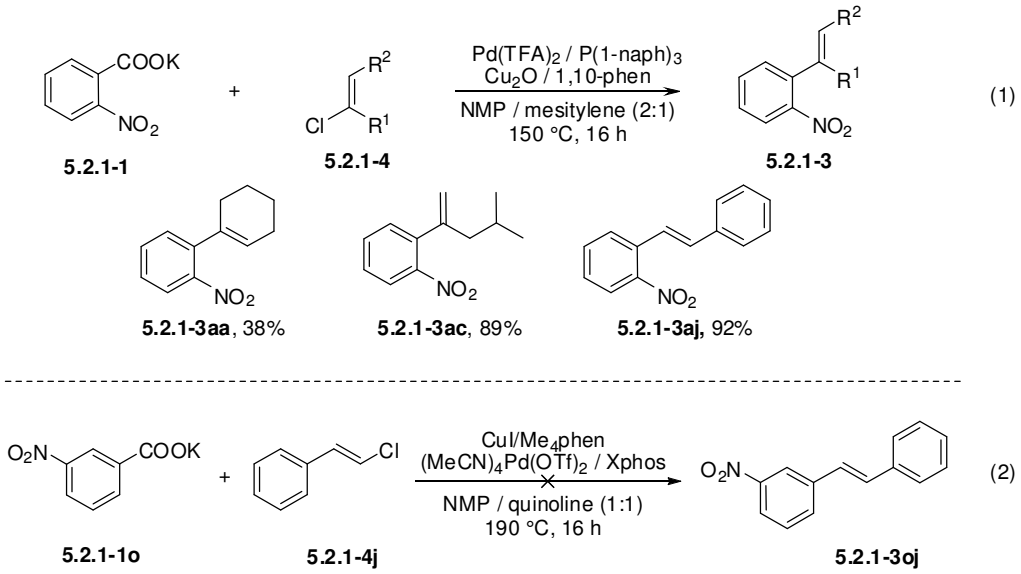


5.2.1-3aj, 92%

[a]Reaction conditions: **5.2.1-1a** (0.6 mmol), **5.2.1-2** (0.5 mmol), $Pd(F_6\text{-acac})_2$ (1.0 mol %), $P(1\text{-naph})_3$ (2.0 mol %), CuCl (10 mol %), 1,10-phenanthroline (10 mol %), 4 mL of solvent, 130 °C, 16 h. Isolated yields. [b]10 mmol scale.

*Further studies revealed that only minor adjustments were necessary to extend this reaction from alkenyl bromides to the less costly, but also less reactive alkenyl chlorides. Thus, representative alkenyl chlorides (****5.2.1-4****) were coupled with 2-nitrobenzoic acid (****5.2.1-1a****) to give the products up to 92% yield in the presence of 1 mol % Pd(TFA)$_2$, 3 mol % tri-1-naphthylphosphine, 3 mol % Cu_2O and 5 mol % 1,10-phenanthroline in NMP/mesitylene (2:1) at 150 °C (Scheme 7, eq. 1).* In chapter 5.1, we have developed a Pd/Cu bimetallic catalyst system that enables non-*ortho* substituted benzoic acids to couple with aryl chloride. Unfortunately, preliminary result showed that non-*ortho* substituted benzoic acid is not applicable in the coupling of alkenyl chloride even under the reaction conditions that developed in chapter 5.1 (Scheme 7, eq. 2). It might because of the high reaction temperature, the volatile vinyl chloride couldn't stay in the reaction mixture. More importantly, the protodecarboxylation product is detected along with substantial amount of alkenyl chloride

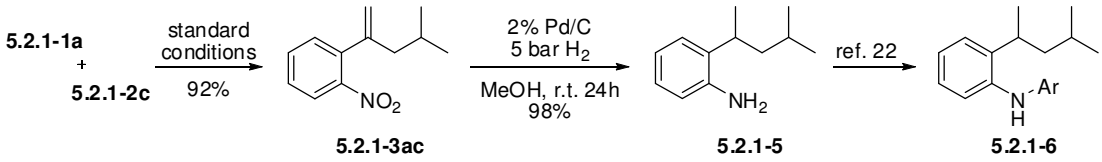
get recovered, which suggests that transmetalation may become the limiting step in this coupling reaction.



Scheme 7. Decarboxylative couplings of alkenyl chlorides.

5.2.1.4 Application of decarboxylative coupling of alkenyl halides

The obtained arylalkenes are valuable synthetic compounds. For instance, **5.2.1-3ac** can be converted in quantitative yield to 2-(4-methylpentan-2-yl)aniline **5.2.1-5**, a key intermediate for the synthesis of fungicidal compound **5.2.1-6** (Scheme 8). Thus, starting from cheap and bench-stable 2-nitrobenzoic acid, **5.2.1-5** can be accessed via decarboxylative coupling/hydrogenation in high yield. Compare to the previously reported synthetic route, in which **5.2.1-5** was obtained via multi-step synthesis under harsh conditions in low yield,[100] this protocol presents a highly efficient and economical alternative, thus demonstrating the superiority of this decarboxylative coupling of alkenyl halides.



Scheme 8. Synthetic utility of decarboxylative coupling of alkenyl halides.

5.2.1.5 Conclusions and outlook

In conclusion, an efficient and broadly applicable protocol for the decarboxylative cross-coupling of alkenyl halides with aromatic carboxylates has been developed. Compared to previously reported transition-metal catalyzed cross-couplings of alkenyl halides, where expensive and sensitive organometallic reagents were used, this protocol allows widely

available and stable aromatic carboxylic acid to be used as nucleophile precursor. With this protocol, alkenyl halides are for the first time used in decarboxylative coupling reaction, allowing regiospecific synthesis of a broad range of aryl- and heteroarylalkenes in high yields. This reaction can also easily scale up to gram scale. The synthetic utility of this reaction was also demonstrated by synthesizing an important intermediate of fungicidal compound in high yield within 2 steps.

However, the reaction is limited to *ortho*-substituted benzoic acids or heteroaryl carboxylic acids. The next challenge would be applying non-*ortho* substituted benzoic acids in this transformation. In section **5.2.1.4,** we have discussed that transmetalation step might be the limiting step. The next development would be targeting the transmetalation step, thus the above chapter mentioned bridging ligand that could facilitate this step provide a possible route to tackle this issue. As for the high temperature that also required by decarboxylation of non-*ortho* substituted benzoate, which would keep volatile vinyl chloride out of the reaction mixture, further studies can be directed towards the development of the ligand which could facilitate decarboxylation at strongly reduced reaction temperature. In this context, phenanthroline with stronger electron donating groups or other type of ligand such as aliphatic amine based ligand could be the choice to promote decarboxylation. The combination of bridging ligand and new ligand for copper catalyst may possible to enable the decarboxylative coupling of alkenyl chloride with non-*ortho* substituted benzoate.

5.2.2 Branched arylalkenes from cinnamates: selectivity inversion in Heck reactions by carboxylates as deciduous directing groups

*Part of this work has been published: This Agreement between Jie Tang ("You") and John Wiley and Sons ("John Wiley and Sons") consists of your license details and the terms and conditions provided by John Wiley and Sons and Copyright Clearance Center. Those reproduced from the publication were written in italic.

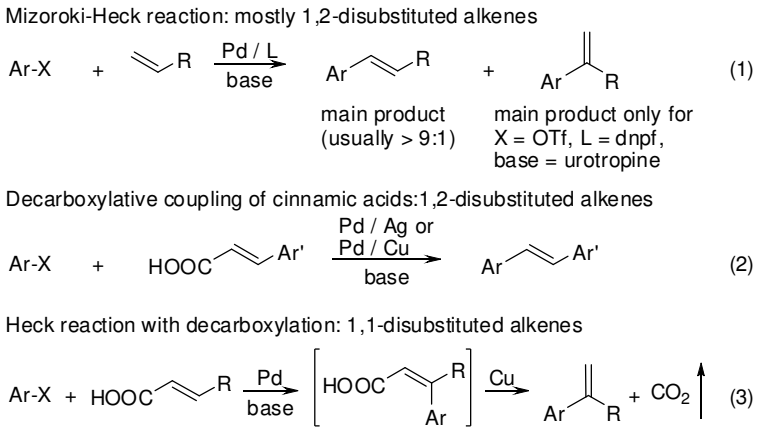
License Number	3962500619200
License date	Oct 05, 2016
Licensed Content Publisher	John Wiley and Sons
Licensed Content Publication	Angewandte Chemie International Edition
Licensed Content Title	Branched Arylalkenes from Cinnamates: Selectivity Inversion in Heck Reactions by Carboxylates as Deciduous Directing Groups
Licensed Content Author	Jie Tang, Dagmar Hackenberger, Lukas J. Goossen
Licensed Content Date	Aug 3, 2016
Licensed Content Pages	4
Type of use	Dissertation/Thesis
Requestor type	Author of this Wiley article
Format	Print and electronic
Portion	Full article
Will you be translating?	No

*This project was conducted in the collaboration with Miss Dagmar Hackenberger.
After I finished the first-round screening, she joined in this project. We carried out the final optimization together. The reaction scope was planned, isolated and characterized in close collaboration together with her in an overall ratio of approximately 2/3 (myself) to 1/3 (DH). She made major contributions in protodecarboxylation studies and the screening for the coupling of aryl chlorides. The two of us developed the one-pot 1,1-diarylethylene synthesis from methyl acrylate with equal contributions. After the initial draft by me, she and I co-wrote the manuscript and the supporting information.

5.2.2.1 1,1-Disubstituted alkene synthesis

1,1-Disubstituted alkenes are prevalent in natural[101] and synthetic products[102] with a wide spectrum of applications. *Traditional syntheses of this substructure, such as Wittig or Peterson olefinations,[103] arylations of alkynes,[104] olefin metathesis,*[105] are somewhat limited in scope, waste-intensive. Transition metal-catalyzed cross-couplings of preformed α-metalated vinylarenes[106] or 2-alkenyl electrophiles[107] are also well developed in regioselective synthesis of this compound class, however, multi-step synthesis of starting materials, and the use of expensive, sensitive organometal reagents are required, which undermine their utilities especially in industry. In chapter 5.2.1 we have described an excellent protocol for the synthesis of arylalkenes via decarboxylative coupling of alkenyl halides. 1,1-diarylalkene can be accessed, however, low yield was observed. Therefore, it is highly desirable to find alternative vinyl source to synthesize 1,1-diarylalkenes.

The selective synthesis of 1,1-diarylalkenes from widely available aryl (pseudo)halides via Heck-type reactions would be a welcome alternative.[108] However, electronic and steric factors usually determine the regiochemical outcome of the carbopalladation for simple hydrocarbons,[109-112] so that 1,2-diarylalkenes are obtained from styrenes (Scheme 9, Eq. 1).[113] This selectivity has successfully been shifted towards the 1,1-diarylakenes in very few cases only: Zou reported that aryl triflates react with selected styrenes with formation of 1,1-diarylakenes when using a urotropine base and the exceptionally bulky 1,1'-bis[di(1-naphthyl)phosphino]ferrocene (dnpf) ligand.[114]

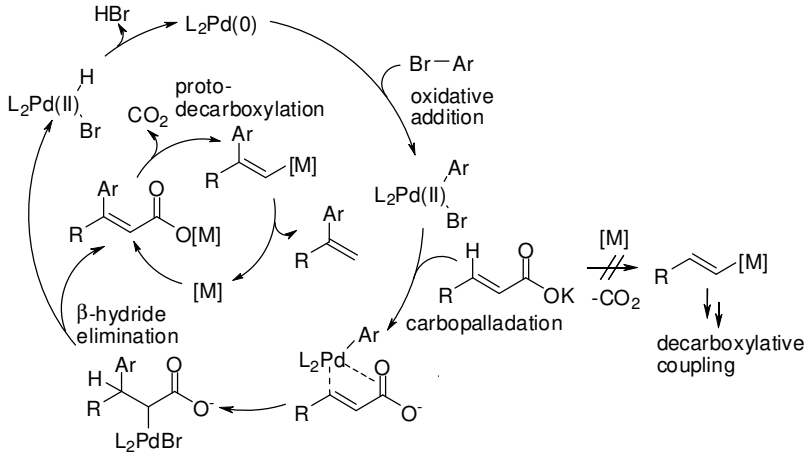


Scheme 9. Substituted alkene synthesis.

5.2.2.2 Decarboxylative Heck coupling reaction

Due to the wealth of methods for their preparation, *cinnamic acids are more widely available in greater structural diversity than styrenes*, thus making them attractive starting materials.[115] *In Heck couplings with aryl halides, the carboxylate group should direct the carbopalladation*

into its β-position,[116] leading to the intermediate formation of diarylacrylic acids. Their in situ conversion to the desired 1,1-diarylalkenes might be accomplished by an added copper or silver decarboxylation catalyst (Scheme 9, Eq. 3). *However, this attractive approach seemed to be out of reach, because the same catalyst combination is known to effectively promote a decarboxylative cross-coupling with formation of 1,2-diarylalkenes* (Scheme 9, Eq. 2).[40b,53]
The utility of carboxylates as directing groups that are tracelessly cleavable in situ has been demonstrated e.g. for C-H hydroxylations,[117] amidations,[118] (hydro)arylations[119] and alkoxylations.[120] Ideally, the carboxylate will act as a deciduous rather than a removable directing group, staying in place for only just as long as it is required to direct the metal catalyst into the α-position, but is destabilized by the newly formed bond to an extent that it is shed directly afterwards.



Scheme 10. Mechanistic outline for the envisioned process.

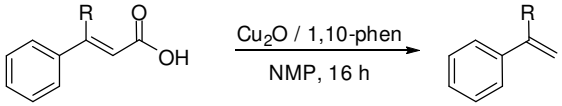
In order to switch the reaction of cinnamic acids with aryl halides from a decarboxylative coupling pathway to the desired Heck pathway with the carboxylate acting as a deciduous directing group, it is critical to identify a catalyst system that a) promotes the carbopalladation of cinnamic acids with unprecedented efficiency and b) efficiently mediates decarboxylation of diarylacrylic acids, but c) does not promote decarboxylation of cinnamates, thus blocking decarboxylative cross-coupling (Scheme 10).
Prerequisite a) already represented a substantial hurdle because the reactivity of the electron rich cinnamate salts formed under the basic conditions of a Heck process is low. Nájera and Fujiwara found that even under optimized conditions, cinnamic acids gave unsatisfactory yields (42%) at 120 °C, whereas the corresponding alkyl cinnamates reacted quantitatively.[121] However, these literature results demonstrate that both oxidative addition and carbopalladation should take place at temperatures below those required for most decarboxylative couplings (150-170°C), which give us an opportunity to improve the Heck

reaction of cinnamic acids at relative low reaction temperature where they don't undergo decarboxylation.

5.2.2.3 Protodecarboxylation studies

In order to probe whether prerequisites b) and c) could be fulfilled, we performed decarboxylation studies, and were delighted to find that an additional aryl group strongly activates the substrates towards CO_2 extrusion (Table 10). *Thus, β-tolylcinnamic acid underwent almost quantitative protodecarboxylation at 130°C in the presence of a Cu_2O catalyst, whereas under the same conditions, cinnamic acid showed < 5% conversion after 16 h* (entry 1). The table also shows that β-tolylcinnamic acid undergoes decarboxylation much faster than that of cinnamic acid (entries 2-4). Therefore, if we could identify a reaction condition, under which the Heck reaction outcompetes decarboxylative coupling, once the β-aryl cinnamic acid formed, it would undergo rapid decarboxylation to afford the desired product.

Table 10. Protodecarboxylation of cinnamic acids.[a]



5.2.2-1a', R = H,
5.2.2-1aa', R = *p*-tol

5.2.2-7, R = H
5.2.2-3aa, R = *p*-tol

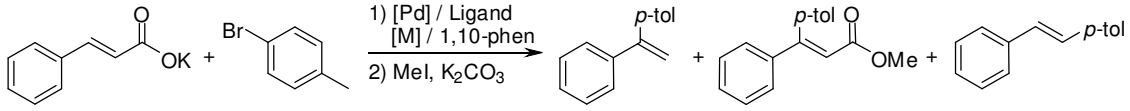
Entry	T (°C)	Yield (%)	
		5.2.2-7	**5.2.2-3aa**
1	130	trace	95
2	140	31	93
3	150	63	91
4	170	70	99

[a]Reaction condition: **5.2.2-1a'** or **5.2.2-1aa'** (0.3 mmol), Cu_2O (5 mol%), 1,10-phenanthroline (10 mol%), 1 mL NMP. Yields were determined by GC analysis with *n*-tetradecane as an internal standard.

5.2.2.4 Optimization of the reaction conditions

The above *preliminary experiments served to define a starting point for rational catalyst development. We chose the reaction of potassium cinnamate **5.2.2-1a** with 4-bromotoluene **5.2.2-2a** as a model to systematically investigate the influence of Heck and decarboxylation catalysts on the reaction outcome under various conditions* (Table 11). In order to differentiate all possible transformations, esterification with MeI was conducted after the decarboxylative Heck reaction.

Table 11. Optimization of the reaction conditions.[a]



5.2.2-1a **5.2.2-2a** **5.2.2-3aa** **5.2.2-4aa** **5.2.2-5aa**

Entry	[Pd]	P-ligand	[M]	solvent	T (°C)	Yield (%)		
						3aa	**4aa**	**5aa**
1	$Pd(acac)_2$	PPh_3	-	NMP/quin=1/1	130	4	12	10
2	"	"	CuBr	"	"	2	23	4
3	"	"	$Sc(OTf)_3$	"	"	6	40	12
4	"	"	$Pb(NO_3)_2$	"	"	6	30	11
5[b]	"	"	-	"	"	5	<1	<1
6	"	"	Ag_2CO_3	"	"	6	<1	12
7	"	"	CuBr	"	150	28	9	7
8	"	"	"	"	170	73	<1	12
9	"	P(*p*-tol)$_3$	"	"	"	76	"	14
10	**"**	**P(*o*-tol)$_3$**	**"**	**"**	**"**	**92**	**"**	**8**
11	"	PCy_3	"	"	"	76	"	12
12	"	$^tBu_3P{\cdot}HBF_4$	"	"	"	87	"	12
13	"	BINAP	"	"	"	78	"	13
14	"	Johnphos	"	"	"	77	"	11
15	"	Xphos	"	"	"	80	"	12
16	$Pd(F_6\text{-acac})_2$	P(*o*-tol)$_3$	"	"	"	85	"	13
17	$PdCl_2$	"	"	"	"	83	"	13
18	$PdBr_2$	"	"	"	"	82	"	12
19	$Pd(OAc)_2$	"	"	"	"	86	"	14
20	$Pd(dba)_2$	"	"	"	"	88	"	12
21	$Pd(acac)_2$	"	CuCl	"	"	90	"	10
22	"	"	Cu_2O	"	"	75	"	10
23	"	"	CuBr	NMP	"	25	"	11
24	"	"	"	NMP/mes=1/1	"	42	"	7
25[c]	"	"	CuBr/KOAc	NMP/quin=1/1	"	88	"	12
26[c]	"	"	$CuBr/K_2CO_3$	"	"	43	"	15
27[c]	"	"	CuBr	"	"	<1	"	<1
28	"	"	-	"	"	6	"	16
29	-	-	CuBr	"	"	<1	"	<1

[a]Reaction condition: **5.2.2-1a** (0.60 mmol), **5.2.2-2a** (0.5 mmol), [M] (10 mol%), 1,10-phenanthroline (10 mol%), [Pd] (2 mol%), P-ligand (5 mol%), 3 mL solvent (NMP / quinoline = 1/1), 16h. Yields were determined by GC analysis after esterification with MeI using *n*-tetradecane as internal standard. 1,10-phen =1,10-phenanthroline; quin = quinoline; Mes = mesitylene; BINAP = (±)-2,2′-Bis(diphenylphosphino)-1,1′-binaphthalene; Johnphos = (2-Biphenyl)di-tert-butylphosphine; Xphos = 2-Dicyclohexylphosphino-2′,4′,6′-triisopropyl-biphenyl. [b]Copper cinnamate was used instead of **5.2.2-1a**. [c]Starting from cinnamic acid.

Upon *subjecting substrates **5.2.2-1a** and **5.2.2-2a** to classical Mizoroki-Heck conditions (entry 1), only low conversion was observed, mostly to the non-decarboxylated Heck product **5.2.2-4aa**, along with decarboxylative cross-coupling product* **5.2.2-5aa**. *However, when adding copper(I) bromide, the selectivity for the branched product **5.2.2-4aa** increased sharply, indicating that the soft Lewis acid CuBr promotes the carbometallation step more strongly than the decarboxylation (entry 2). The addition of other Lewis acids, such as $Sc(OTf)_3$ or $Pb(NO_3)_2$, facilitated the Heck coupling even more strongly, but the selectivity was lower* (entries 3, 4). *This suggests that the role of the copper is mainly that of a soft Lewis acid. Starting from preformed copper cinnamate, lower yield was observed, which speaks against the intermediacy of this compound in the transformation* (entry 5). With Ag_2CO_3, unwanted **5.2.2-5aa** was formed as the main product (entry 6), which aligns with Wu's work.[53] In order to achieve higher conversion, we decided to elevate the reaction temperature. *Increasing the temperature led to preferential formation of decarboxylated product **5.2.2-3aa** over **5.2.2-4aa**, without sacrificing the selectivity for the branched over the linear product* **5.2.2-5aa** (entries 7, 8).

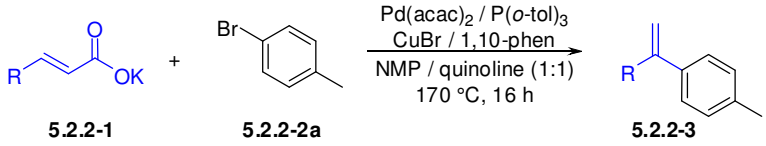
*Systematic variation of the phosphine ligand revealed that the moderately electron-donating, sterically demanding ligand tri-o-tolylphosphine ($P(o\text{-}tol)_3$) was most effective, giving greater than 10:1 selectivity for **5.2.2-3aa** at full conversion* (entries 9-15). *$Pd(acac)_2$ was found to be the optimal palladium precursor (entries 10, 16-20). Among the copper sources, copper halides and CuBr in particular were most effective (entries 21, 22). A solvent mixture of NMP and quinoline (1/1) gave the best results* (entries 23, 24). When starting directly from cinnamic acid, the addition of potassium acetate is required, whereas stronger bases retard the reaction (entries 25-27). *Control experiments confirmed that neither the palladium nor the copper catalyst alone is able to mediate this transformation* (entries 28, 29).

5.2.2.5 Scope

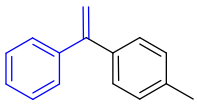
We next investigated the scope of the optimized protocol (2 mol% $Pd(acac)_2$, 5 mol% $P(o\text{-}tol)_3$, 10 mol% CuBr, 10 mol% 1,10-phenanthroline, NMP / quinoline (1:1), 170 °C, 16 h) with regard to the α,β-unsaturated carboxylic acids.

*Both electron-rich and electron-poor cinnamic acids reacted smoothly with 4-bromotoluene **5.2.2-2a** (Table 12). Common functionalities, such as halo, ester, ether, carbonyl, and even nitro and amino groups, regardless of their substitution position, were tolerated. The reaction also proceeded well with heterocyclic and alkyl-substituted allylic acids.*

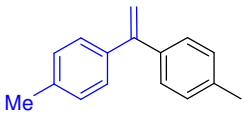
Table 12. Scope with regard to the carboxylates.[a]



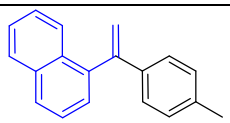
5.2.2-1 **5.2.2-2a** **5.2.2-3**



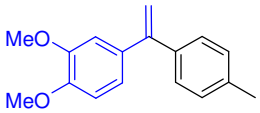
5.2.2-3aa, 92%



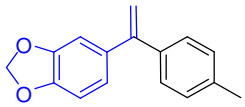
5.2.2-3ba, 90%



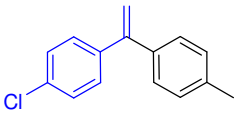
5.2.2-3ca, 58%



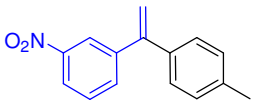
5.2.2-3da, 83%



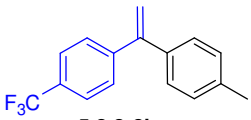
5.2.2-3ea, 40%



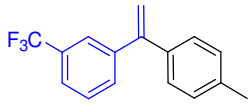
5.2.2-3fa, 67%



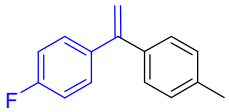
5.2.2-3ga, 74%



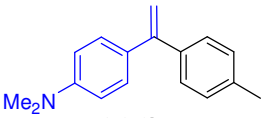
5.2.2-3ha, 82%



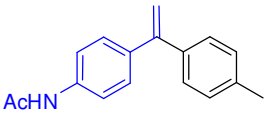
5.2.2-3ia, 94%



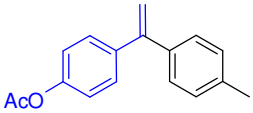
5.2.2-3ja, 74%



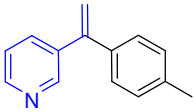
5.2.2-3ka, 82%



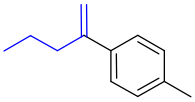
5.2.2-3la, 81%



5.2.2-3ma, 23%



5.2.2-3na, 72%



5.2.2-3oa, 81%

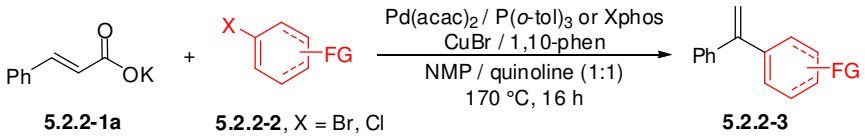
[a]Reaction conditions: **5.2.2-1** (1.20 mmol), **5.2.2-2a** (1.00 mmol), CuBr (10 mol%), 1,10-phenanthroline (10 mol%), $Pd(acac)_2$ (2 mol%), P(*o*-tol)$_3$ (5 mol%), 3 mL of solvent (NMP / quinoline = 1:1), 170 °C, 16 h. Yields of isolated products.

The reaction is also widely applicable with regard to the electrophilic coupling partner (Table 13). ortho-, meta-, and para-substituted aryl bromides bearing sensitive functionalities including ether, ester, carbonyl, thioether and tertiary amino groups were successfully converted. Besides aryl bromides, alkenyl bromide was also applicable in this reaction, affording 1,3-diene in moderate yield. The reaction reaches its performance limit in the coupling of heteroaryl bromides.

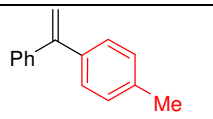
Aryl chlorides are particular attractive electrophiles especially for industrial-scale synthesis, because they are less expensive and possess the lowest molecular weight of all halide leaving groups. However, the much less reactive aryl chlorine bond needs to be activated. The choice of the ligand is of great importance in the coupling of aryl chlorides.[122] As expected, P(*o*-tol)$_3$ was not capable of promoting this transformation (Table 14, entry 1). A quick ligand screening revealed that Xphos is the choice for the success of this transformation (Table 14, entry 5). As shown in Table 13, various aryl chlorides bearing electron-donating or -withdrawing groups

are compatible in the decarboxylative Heck reaction, furnishing the products in the same level of yields.

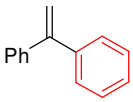
Table 13. Scope with regard to the electrophiles.[a]



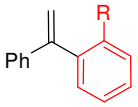
5.2.2-1a **5.2.2-2**, X = Br, Cl **5.2.2-3**



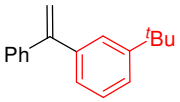
5.2.2-3aa, X = Br, 92%
X = Cl, 90%[b]



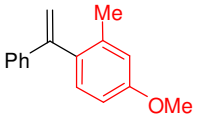
5.2.2-3ab, 73%



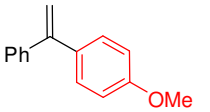
5.2.2-3ac, R = Me, 44%
5.2.2-3ad, R = Et, 57%



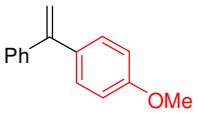
5.2.2-3ae, 90%



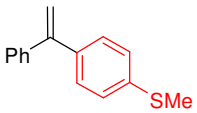
5.2.2-3af, 95%



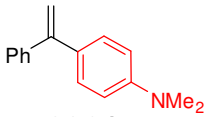
5.2.2-3ag, X = Br, 87%
X = Cl, 76%[b]



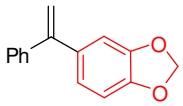
5.2.2-3ag, X = Br, 87%
X = Cl, 76%[b]



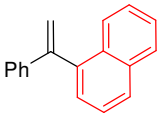
5.2.2-3ai, 64%



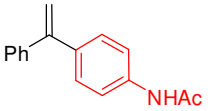
5.2.2-3aj, 82%



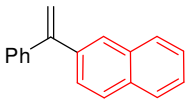
5.2.2-3ak, X = Br, 86%
X = Cl, 88%[b]



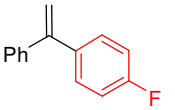
5.2.2-3al, X = Br, 66%
X = Cl, 40%[b]



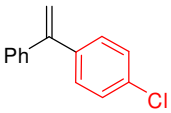
5.2.2-3am, 92%



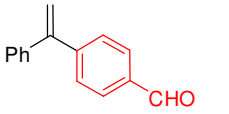
5.2.2-3an, 83%



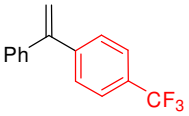
5.2.2-3ao, X = Br, 92%
X = Cl, 80%[b]



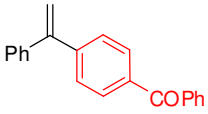
5.2.2-3ap, 70%



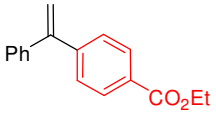
5.2.2-3aq, X = Br, 60%
X = Cl, 58%[b]



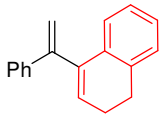
5.2.2-3ar, X = Br, 62%
X = Cl, 65%[b]



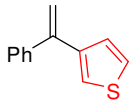
5.2.2-3as, X = Br, 66%
X = Cl, 63%[b]



5.2.2-3at, 50%



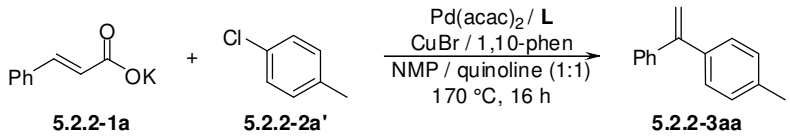
5.2.2-3au, 40%



5.2.2-3av, 29%

[a]Reaction conditions: **5.2.2-1a** (1.20 mmol), **5.2.2-2** (1.00 mmol), CuBr (10 mol%), 1,10-phenanthroline (10 mol%), $Pd(acac)_2$ (2 mol%), P(*o*-tol)$_3$ (5 mol%), 3 mL of solvent (NMP / quinoline = 1:1), 170 °C, 16 h. Yields of isolated products. [b]**5.2.2-1a** (0.60 mmol), **5.2.2-2** (0.5 mmol), CuBr (10 mol%), 1,10-phenanthroline (10 mol%), $Pd(acac)_2$ (2 mol%), XPhos (5 mol%), 3 mL of solvent (NMP / quinoline = 1:1), 170 °C, 16 h. Yields of isolated products. Xphos = 2-Dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl.

Table 14. Screening with ligands under optimal conditions.[a]



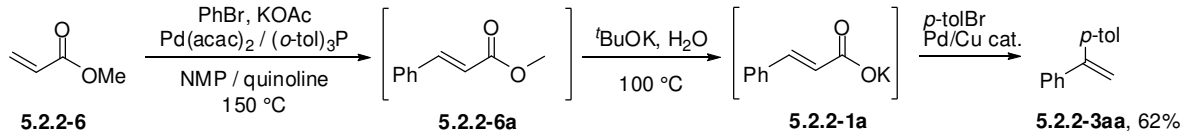
5.2.2-1a **5.2.2-2a'** **5.2.2-3aa**

Entry	Ligand	Yield (%)
1	P(*o*-tol)$_3$	6
2	Johnphos	19
3	Sphos	68
4	Davephos	19
5	**Xphos**	**90**

[a]Reaction conditions: **5.2.2-1a** (0.60 mmol), **5.2.2-2a'** (0.50 mmol), CuBr (10 mol%), 1,10-phenanthroline (10 mol%), Pd(acac)$_2$ (2 mol%), Ligand (5 mol%), 3 mL of solvent (NMP / quinoline = 1:1), 170 °C, 16 h. Yields were determined by GC analysis using *n*-tetradecane as internal standard. Johnphos = (2-Biphenyl)di-tert-butylphosphine; Sphos = 2-Dicyclohexylphosphino-2′,6′-dimethoxybiphenyl; Davephos = 2-Dicyclohexylphosphino-2′-(*N*,*N*-dimethylamino)biphenyl; Xphos = 2-Dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl.

5.2.2.6 One-pot 1,1-diarylalkene synthesis

Methyl acrylate **5.2.2-6** is a low costing and heavily investigated substrate in Mizoroki-Heck reaction. *The new decarboxylative Heck process was successfully combined with a traditional Heck coupling into a convenient one-pot synthesis of unsymmetrically substituted 1,1-diarylalkenes from two different aryl bromides and methyl acrylate. In the first step, a cinnamate salt was synthesized from the corresponding aryl bromide and methyl acrylate via Mizoroki-Heck reaction followed by the hydrolysis of the methyl cinnamate. Subsequently, without solvent change or isolation of intermediates, a decarboxylative Heck coupling furnishes the 1,1-diarylethylene in 62% overall yield* (Scheme 11).



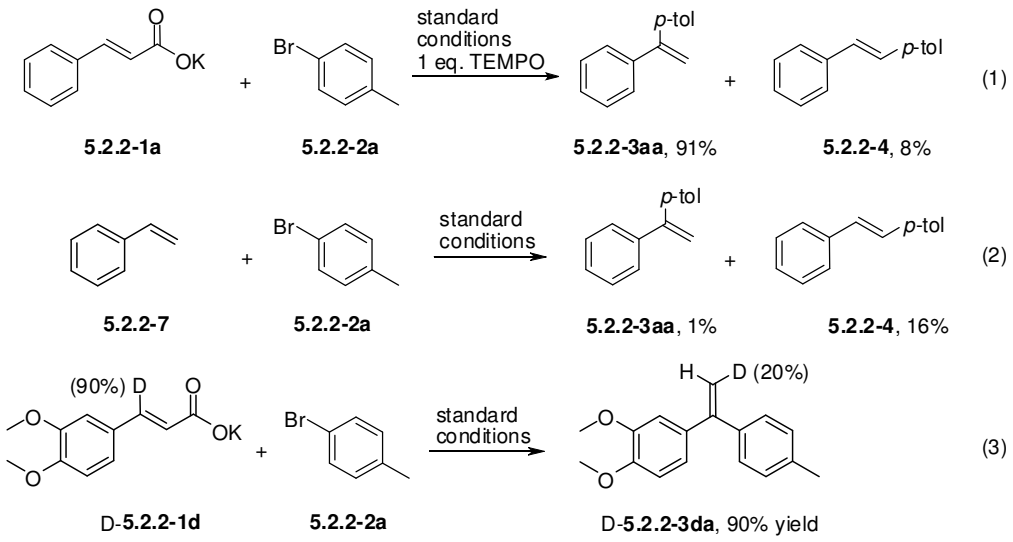
5.2.2-6 **5.2.2-6a** **5.2.2-1a** **5.2.2-3aa**, 62%

Scheme 11. One-pot 1,1-diarylethylene synthesis from methyl acrylate.

5.2.2.7 Mechanistic studies

A series of experiments was performed to shed more light on the reaction mechanism. The reaction occurred smoothly in the presence of the radical scavenger 2,2,6,6-tetramethylpiperidinyloxyl (TEMPO), thus suggesting that neither coupling nor decarboxylation proceed

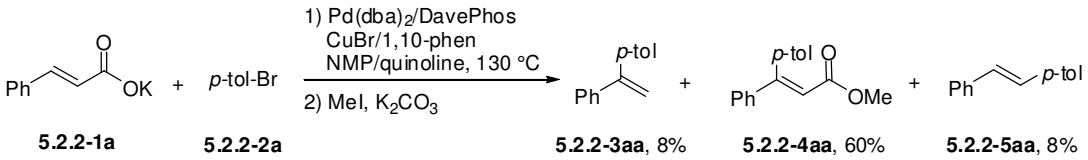
via a radical pathway (Scheme 12, Eq. 1).[123] *The reaction of styrene with 4-bromotoluene* ***5.2.2-2a*** *under the reaction conditions yielded the linear product* ***5.2.2-4aa*** *in high selectivity, which rules out a reaction pathway via protodecarboxylation followed by Heck reaction (Scheme 12, Eq. 2).* More interestingly, *when the reaction was performed with the deuterium-labelled starting material potassium (E)-3-(3,4-dimethoxyphenyl)-2-propenoate-3-d (D-**5.2.2-1d**), only 20% of the deuterium was incorporated in the original position of the carboxylate group (Scheme 12, Eq. 3).* This indicates that solvent is the major proton source for protodecarboxylation step and *that the Heck coupling and decarboxylation steps occur in a separate rather than concerted fashion.*



Scheme 12. Mechanistic studies.

5.2.2.8 Conclusions and outlook

In conclusion, a bimetallic Cu/Pd catalyzed decarboxylative Mizoroki-Heck coupling of aryl halides with α,β-unsaturated carboxylic acids was successfully developed in which the carboxylate group directs the arylation into its β-position before being tracelessly removed via protodecarboxylation. It *opens up a convenient synthesis of unsymmetrical 1,1-disubstituted alkenes from widely available precursors. Key advantages are the good regiochemical control, which is complementary to that of traditional Heck reactions, the use of cinnamates as source of the vinyl group, and the excellent functional group tolerance.* Moreover, a one-pot 3-step 1,1-diarylethylene synthesis from methyl acrylate was achieved, where solvent changes or isolation of intermediates are not required. The project presents an example of carboxylic acid utility in synthesizing valuable compounds which are hard to access via conventional methodologies.



5.2.2-1a **5.2.2-2a** **5.2.2-3aa**, 8% **5.2.2-4aa**, 60% **5.2.2-5aa**, 8%

Scheme 13. Synthesis of β-aryl cinnamic acid.

β-aryl cinnamic acids are useful compounds in pharmaceutical agent synthesis,[124] further development would be obtaining these compounds via coupling of cinnamic acids with aryl halides without protodecarboxylation. Preliminary result shows the feasibility of this concept (Scheme 13). However, protodecarboxylation can't be avoided with Cu/Pd catalyst system. The next step would be using other catalyst which is able to promote β-arylation but inactive towards protodecarboxylation. Considering our group's recent results in Ru-catalyzed *ortho*-C-H arylation of benzoic acids with aryl halides,[125] Ruthenium might be the candidate for this transformation. Another transformation that might be possible is that using carboxylate group as deciduous directing group to install other functional groups in the β-position of cinnamic acids. For instance, applying electrophilic carbamate reagents, β-amination/amidation might be realized in the presence of Pd/Cu or Rh/Cu catalysts, leading to α-amino/amido styrenes. Moreover, β-aryl cinnamic acids are more prone to decarboxylate under relatively lower reaction temperature, it opens an opportunity that after β-arylation of cinnamic acids, the carboxylate could function as a leaving group so that *ipso*-decarboxylative coupling with another coupling partner could occur smoothly, affording more sophisticated compounds. This one-pot transformation allows more than one bond to be formed.

6. Experimental section

6.1. General techniques

All commercially available chemicals were used without any further purification. Air and moisture sensitive chemicals were stored under nitrogen or argon. Reaction vessels were usually charged with solid starting materials and reagents, evacuated (oil pump ≤ 10-3 mbar) to remove oxygen and moisture, then backfilled with nitrogen. Solvents and liquid reagents were added under an atmosphere of nitrogen. Solvents were purified following standard literature techniques and stored over 3Å molecular sieves. Inorganic salts such as KF, K_2CO_3, or K_3PO_4 were dried under vacuum at 120 °C for 3 hours and stored under nitrogen. Copper salts were dried under vacuum at 60 °C for 1 hour.

6.2 Analytical methods

6.2.1 Thin layer chromatography

TLC was performed using analytical silica gel plates 60 F254 and analytical neutral alumina plates by Polygram Alox N/UV_{254} by Merk and Macherey-Nagel. The silica gel (230-400 mesh, 60 Å) used for column chromatography was purchased from Aldrich.

6.2.2 Gas chromatography

For GC-analysis a Hewlett Packard 6980 chromatograph was used. The carrier gas was nitrogen with a flow rate of 149 mL/min (0.5 bar pressure). The temperature of the injector was 220 °C. The split-ratio was 1:100. For separation, an Agilent HP-5-column with 5 % phenyl-methyl-siloxane (30 x 320 µm x 1.0 µm, 100/ 2.3-30-300/ 3) was used. The following temperature program was implemented: starting temperature 60 °C (2 min), linear temperature increase (30 °C min^{-1}) to 300 °C, end temperature 300 °C (13 min).

6.2.3 Mass spectroscopy

Mass spectrometry was performed using a Varian Saturn 2100 T GC-MS. The ionization was done by EI AGC. The intensities of the signals are relative to the highest peak. For fragments with isotopes, only the most intensive peak of the isotope is given. High resolution mass spectra were acquired on a GC-MS-TOF spectrometer using EI-ionization (Waters).

Electrospray ionization mass spectrometry (ESI-MS) was performed with a Bruker Esquire 3000plus ion trap instrument. The ion source was used in positive electrospray ionization mode. Scan speed was 13000 m/z / s in normal resolution scan mode (0.3 FWHM / m/z), scan

range was at least 50 to 1500 m/z. All spectra were accumulated for at least one minute. Sample solutions in toluene at concentrations of 0.007 M were continuously infused into the ESI chamber at a flow rate of 4 µL/min using a syringe pump. Nitrogen was used as drying gas with a flow rate of 3.0 L/min at 300 °C. The solutions were sprayed at a nebulizer pressure of 4 psi (275.8 mbar) and the electrospray needle was typically held at 4.5 kV. The instrument was controlled by the Bruker Esquire Control 5.3 software, and data analysis was performed using Bruker Data Analysis 3.4 software.

6.2.4 High-performance liquid chromatography

HPLC analysis was carried out using a Shimadzu HPLC equipped with a Merck KGaA reversed phase column LiChroCart©PAH C 18, with a particle diameter of 5 µm. The instrument was operated at a constant temperature of 60 °C and a pressure of 200 bar. Acetonitrile and water were used as eluents with a flow rate of 2 mL/min. Gradient: 15 % acetonitrile for 3 min linear increase to 85 % within 7 min, hold for 1 min, decrease to 15 % within 1 min. and hold for 50 seconds. 5 µL of sample were injected as standard amount into the Rheodyne. This amount can be varied manually through the Shimadzu sequence program Class-VP.

6.2.5 Infrared spectroscopy

Infrared spectra were recorded with a Perkin-Elmer Fourier Transform Infrared Spectrometer FT/IR. Solids were thoroughly ground and mixed with potassium bromide and pressed into a pellet. Liquids were measured as a thin film between sodium chloride plates. Absorbance bands are shown in wave numbers (cm^{-1}). Intensities are abbreviated: vs (very strong), s (strong), m (medium), w (weak) and b (broad).

6.2.6 Nuclear magnetic resonance spectroscopy

Proton-, fluorine-, phosphorus-, boron- and decoupled carbon-NMR spectra were recorded with a Bruker FT-NMR DPX 200, a DPX 400 and a Bruker Avance 600 spectrometer. The frequency and solvent used are described separately for each substance. Chemical shifts are given in units of the δ-scale in ppm. Shifts for ^{1}H-spectra are calibrated to the proton signal of the solvent used (chloroform: 7.25 ppm, dimethyl sulfoxide: 2.50 ppm, methanol: 3.35 ppm, water: 4.75 ppm), for ^{13}C-spectra respectively to the deuterated solvent (chloroform: 77.0 ppm, dimethyl sulfoxide: 37.7 ppm, methanol: 49.3 ppm). The atom numbering within products is not according to the IUPAC rules. The multiplicity of the signals is abbreviated by the following letters: Coupling constants are given in Hertz (Hz). Processing and interpretation

was performed with ACD/Labs 7.0 and ACD/Labs 12.0 software (Advanced Chemistry Development Inc.)

Signals are abbreviated as s (singlet), d (doublet), dd (doublet of doublet), ddd (doublet of doublet of doublet), td (triplet of doublet), q (quartet), quin (quintet), sext (sextet), hept (heptet), m (multiplet), br (broad).

6.2.7 Elemental analysis

CHNS-elemental analysis was performed with a Perkin-Elmer Elemental Analyzer EA 2400 CHNS.

6.2.8 Melting point

Melting points were measured in a glass capillary tube with a Mettler FP61 automatic measuring apparatus.

6.3 High-throughput experiments

In order to perform a large number of experiments, a specially manufactured setup was used. All reactions were carried out in 20 mL headspace vials that were closed and clamped shut with aluminum caps fitted with a Teflon-coated butyl rubber septum (both commercially available at Macherey & Nagel).

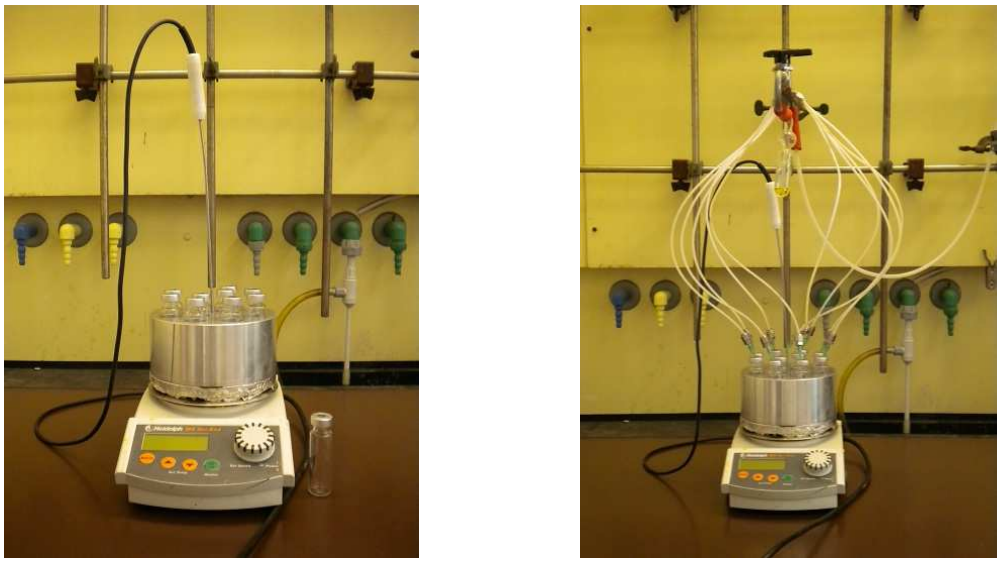


Figure 1. *Aluminum block, magnetic stirrer and vacuum distributer*

In an 8 cm high round aluminum block, which fits on the hot plate of a regular laboratory heater in diameter, 10 of these 20 mL headspace vials can be tempered between 25°C and 180 °C. An 11th smaller hole drilled in the middle of the block creates room to hold the thermometer of the heater. A similar setup was used for reactions in autoclaves, except that a

4 cm aluminum block containing 8 holes for 10 mL head space vials and a small hole for the thermometer. This aluminum block is designed to fit inside the autoclave. Figure 1 shows a magnetic stirrer, aluminum block and vacuum distributer (spider) (Fiture 1).

To correctly evacuate and refill 10 reaction vessels with inert gas at the same time, special vacuum distributors were manufactured to be connected to the Schlenk-line.

A steel tubing is linked to ten 3 mm Teflon tubes, which are equipped on the opposite end with adaptors for Luer-Lock syringe needles. The steel tubing can be connected to the Schlenk-line just like any other laboratory equipment by a steel olive and vacuum tubing. To perform 10 or more reactions in parallel, the following protocol was used. All solid substances were weighed in the reaction vessels, an oven-dried, hot 20 mm stir bar added and each vessel closed with a separate cap using flanging pliars. All 10 vessels were transferred to one of the aforementioned aluminum cases and evacuated using syringe needles connected to the vacuum steel tubing.

The reaction vessels were evacuated and refilled with nitrogen. Using standard sterile and Hamilton syringes all liquid reagents, stock solutions of reagents and solvents were added and the vessels were evacuated and refilled with nitrogen 3 times. After removal of the needles, the aluminum case was tempered to the desired temperature. Every temperature description is the case temperature, which only differs by maximum 2 °C from the actual reaction media temperature.

After the reaction time and subsequent cooling to room temperature, any over pressure was released with a needle and *n*-tetradecane was added as internal strandard with a Hamilton syringe. The reaction vials were opened carefully. 2 mL of ethyl acetate were added to dilute the reaction mixture, then mixed thoroughly with a disposable pipette to ensure a homogenous mixture. A 0.25 mL sample was collected and extracted with 2.5 mL of ethyl acetate and 2 mL of aqueous 1M HCl solution (acidic work up) or saturated potassium bicarbonate solution (basic work up). The organic layer was filtered through a pipette filled with a cotton plug and $NaHCO_3$ / magnesium sulfate (in case of acidic work up) or only $MgSO_4$, directly into a GC-vial. After analyzing sample the GC and, if necessary GC-MS, the contents of all work-up and analysis vials were recombined and the product isolated using standard procedures, deposed on silica-gel and purified by flash chromatography using a Combi Flash Companion-Chromatography apparatus from Isco-Systems.

The developed experimental setups and an electronic laboratory journal allowed a substantial amount of reactions to be performed during the course of this PhD. Approximately 4300 reactions would have consumed a much longer time when using standard laboratory

techniques. Preparative reactions were performed mostly in standard laboratory oven-dried glass ware. The following experimental section describes all reaction procedures and observations mentioned in chapters 2-6. Yields are isolated yields unless explicitly mentioned. All compounds were analyzed by melting point (for solids), ^{1}H-NMR, ^{13}C-NMR, ^{19}F-NMR (for fluorinated compounds), ^{31}P-NMR (for phosphorous-containing compounds), GC-MS or ESI-MS, IR spectroscopy, and elemental analysis or HR-MS.

6.4 Catalytic decarboxylative cross-coupling of aryl chlorides and benzoates without activating *ortho* substituents

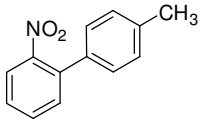
6.4.1 General procedure for the synthesis of potassium carboxylate salts

A 250 mL, two-necked, round-bottomed flask was charged with the carboxylic acid (20.0 mmol) and ethanol (20.0 mL). To this, a solution of potassium *t*-butoxide (2.24 g, 20.0 mmol) in ethanol (20.0 mL) was added dropwise over 2 h. After complete addition, the reaction mixture was stirred for another 1 h at room temperature. A gradual formation of a white precipitate was observed. The resulting solid was collected by filtration washed sequentially with ethanol (2 × 10.0 mL) and cold (0 °C) diethyl ether (10.0 mL), and dried in vacuum to provide the corresponding potassium salts of the carboxylic acids.

6.4.2 General procedure for the decarboxylative coupling

An oven-dried, nitrogen-flushed 20 mL crimp cap vessel was charged with the potassium carboxylate (0.60 mmol, 1.2 equiv.), $(MeCN)_4Pd(OTf)_2$ (5.7 mg, 0.01 mmol, 2.0 mol %), XPhos (12.3 mg, 0.025 mmol, 5.0 mol %), copper(I) iodide (9.7 mg, 0.05 mmol, 10.0 mol %), 3,4,7,8-tetramethyl-1,10-phenanthroline (11.9 mg, 0.05 mmol, 10.0 mol %), and aryl chloride (0.5 mmol). A degassed mixture of NMP (2.5 mL) and quinoline (2.5 mL) was added via syringe. The resulting solution was then stirred at 190 ºC for 16 h. After the reaction was complete, the mixture was cooled to room temperature, diluted with 1 N HCl and extracted with ethyl acetate (3 x 50 mL). The combined organic layers were washed with water and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (SiO_2, ethyl acetate/cyclohexane gradient) yielding the corresponding product.

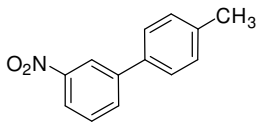
6.4.3 Synthesis of biaryls



4'-methyl-2-nitrobiphenyl (**5.1-3aa**) [CAS: 70680-21-6]

Compound **3aa** was prepared following general method from potassium 2-nitrobenzoate (**5.1-1a**) (154 mg, 0.75 mmol) and 4-chlorotoluene (**5.1-2a**) (64 mg, 60 µL, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). After the reaction, compound **5.1-3aa** was obtained by column chromatography as a yellow liquid (85 mg, 80%).

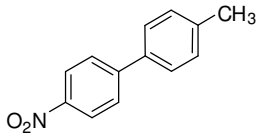
1H NMR (400 MHz, $CDCl_3$): δ = 7.84 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.61 (td, *J* = 7.5, 1.2 Hz, 1H), 7.49-7.44 (m, 2H), 7.27-7.22 (m, 4H), 7.00 (d, *J* = 8.5 Hz, 1H), 2.41 (s, 3H).
13C NMR (100 MHz, $CDCl_3$): δ = 149.38, 138.15, 136.26, 134.36, 132.16, 131.90, 129.43 (2C), 127.88, 127.72(2C), 124.00, 21.22 ppm.
IR: $\tilde{\nu}$ = 3027, 2922, 1614, 1522, 1475, 1353, 748 cm^{-1}.
MS (EI, 70 eV) m/z (%): 213 (75) [M+], 196 (60), 185 (100), 168 (86), 152 (50), 115 (44).
HRMS (EI-TOF) calcd for $C_{13}H_{11}NO_2$: 213.0790; found: 213.0787.



4'-methyl-3-nitrobiphenyl (**5.1-3ba**) [CAS: 53812-68-3]

Compound **5.1-3ba** was prepared following general method from potassium 3-nitrobenzoate (**5.1-1b**) (124 mg, 0.6 mmol) and 4-chlorotoluene (**5.1-2a**) (64 mg, 60 µL, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). After the reaction, compound **5.1-3ba** was obtained by column chromatography as a yellow solid (65 mg, 61%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.45 (t, *J* = 1.7 Hz, 1H), 8.18 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.91 (d, *J* = 7.8 Hz, 1H), 7.60 (t, *J* = 8.0 Hz, 1H), 7.54 (d, *J* = 8.2 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 2.44 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.69, 142.75, 138.53, 135.72, 132.77, 129.84 (2C), 129.60, 126.93 (2C), 121.67 (d, *J* = 3.6 Hz, 2C), 21.13 ppm.
IR: $\tilde{\nu}$ = 3029, 2922, 1528, 1511, 1345, 1294, 804, 738 cm^{-1}.
MS (EI, 70 eV) m/z (%): 213 (100) [M+], 167 (16), 152 (19), 139 (3), 115 (4).
HRMS (EI-TOF) calcd for $C_{13}H_{11}NO_2$: 213.0790; found: 213.0786.
M.p.: 76-77 °C.



4-methyl-4'-nitrobiphenyl (5.1-3ca) [CAS: 2143-88-6]

Compound **5.1-3ca** was prepared following general method from potassium 4-nitrobenzoate (**5.1-1c**) (135 mg, 0.6 mmol) and 4-chlorotoluene (**5.1-2a**) (64 mg, 60 µL, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). After the reaction, compound **5.1-3ca** was obtained by column chromatography as a yellow solid (55 mg, 51%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.29 (dt, *J* = 12.0, 4.0 Hz, 2H), 7.73 (dt, *J* = 8.0, 4.0 Hz, 2H), 7.54 (dt, *J* = 8.0, 4.0 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 2.44 (s, 3H).

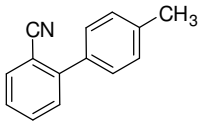
^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.56, 139.07, 135.83, 129.87 (2C), 127.47 (2C), 127.21 (2C), 124.09 (2C), 121.34, 21.21 ppm.

IR: $\tilde{\nu}$ = 3080, 2921, 1594, 1509, 1484, 1337, 1325, 821 cm^{-1}.

MS (EI, 70 eV) *m/z* (%): 213 (100) [M+], 183 (38), 165 (12), 155 (16), 115 (5).

HRMS (EI-TOF) calcd for $C_{13}H_{11}NO_2$: 213.0790; found: 213.0787.

M.p.: 139-140 °C.



4'-methylbiphenyl-2-carbonitrile (5.1-3da) [CAS: 114772-53-1]

Compound **5.1-3da** was prepared following general method from potassium 2-cyanobenzoate (**5.1-1d**) (139 mg, 0.75 mmol) and 4-chlorotoluene (**5.1-2a**) (64 mg, 60 µL, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). After the reaction, compound **5.1-3da** was obtained by column chromatography as a yellow solid (74 mg, 76%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.76 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.64 (td, *J* = 7.6, 1.3 Hz, 1H), 7.52 (dd, *J* = 7.8, 0.7 Hz, 1H), 7.48-7.46 (m, 2H), 7.43 (td, *J* = 7.6, 1.2 Hz, 1H), 7.31 (d, *J* = 8.0 Hz, 2H), 2.43 (s, 3H).

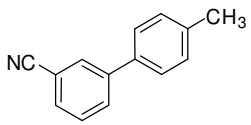
^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.57, 138.67, 135.30, 133.67, 132.67, 129.95, 129.41 (2C), 128.59 (2C), 127.22, 118.77, 111.28, 21.18 ppm.

IR: $\tilde{\nu}$ = 3059, 3022, 2916, 2225, 1595, 1517, 1478, 1441, 1184, 761 cm^{-1}.

MS (EI, 70 eV) *m/z* (%): 193 (100) [M+], 165 (31), 113 (3), 91 (4).

HRMS (EI-TOF) calcd for $C_{14}H_{11}N$: 193.0891; found: 193.0888.

M.p.: 81-82 °C.



4'-methylbiphenyl-3-carbonitrile (5.1-3ea) [CAS: 133909-96-3]

Compound **5.1-3ea** was prepared following general method from potassium 3-cyanobenzoate (**5.1-1e**) (111 mg, 0.6 mmol) and 4-chlorotoluene (**5.1-2a**) (64 mg, 60 µL, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). After the reaction, compound **5.1-3ea** was obtained by column chromatography as a white solid (68 mg, 70%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86 (t, *J* = 1.8 Hz, 1H), 7.81 (dt, *J* = 7.9, 1.4 Hz, 1H), 7.62 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.54 (t, *J* = 8.0 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 2.42 (s, 3H).

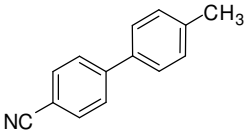
^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.34, 138.38, 135.96, 131.26 (2C), 130.47, 130.38, 129.82, 129.52, 126.88 (2C), 118.94, 112.86, 21.14 ppm.

IR: $\tilde{\nu}$ = 3033, 2919, 2228, 1515, 1474, 1386, 1263, 794 cm^{-1}.

MS (EI, 70 eV) *m/z* (%): 193 (100) [M+], 178 (10), 165 (17), 140 (4), 91 (7), 75 (5).

HRMS (EI-TOF) calcd for $C_{14}H_{11}N$: 193.0891; found: 193.0889.

M.p.: 63-64 °C.



4'-methylbiphenyl-4-carbonitrile (5.1-3fa) [CAS: 50670-50-3]

Compound **5.1-3fa** was prepared following general method from potassium 4- cyanobenzoate (**5.1-1f**) (111 mg, 0.6 mmol) and 4-chlorotoluene (**5.1-2a**) (64 mg, 60 µL, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). After the reaction, compound **5.1-3fa** was obtained by column chromatography as a white solid (53 mg, 54%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70 (q, *J* = 8.0 Hz, 4H), 7.50 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 5.62-5.60 (m, 1H), 2.43 (s, 3H).

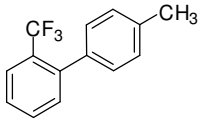
^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.57, 138.73, 136.23, 132.54 (2C), 129.81 (2C), 127.44 (2C), 127.03 (2C), 119.03, 110.49, 21.47 ppm.

IR: $\tilde{\nu}$ = 3026, 2918, 2224, 1644, 1603, 1494, 1396, 808 cm^{-1}.

MS (EI, 70 eV) *m/z* (%): 193 (100) [M+], 178 (8), 165 (19), 91 (6), 75 (5), 63 (8).

HRMS (EI-TOF) calcd for $C_{14}H_{11}N$: 193.0891; found: 193.0885.

M.p.: 101-102 °C.

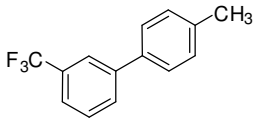


4-methyl-2'-(trifluoromethyl)biphenyl (5.1-3ga) [CAS: 145486-55-1]

Compound **5.1-3ga** was prepared following general method from potassium 2-trifluoromethylbenzoate (**5.1-1g**) (171 mg, 0.75 mmol) and 4-chlorotoluene (**5.1-2a**) (64 mg, 60 µL, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). After the reaction,

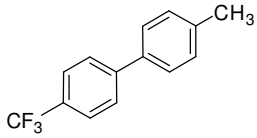
compound **5.1-3ga** was obtained by column chromatography as a colorless liquid (59 mg, 50%).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.76 (d, *J* = 7.6 Hz, 4H), 7.60-7.42 (m, 2H), 7.34 (dd, *J* = 7.5, 0.6 Hz, 1H), 7.24 (s, 4H), 2.43 (s, 3H).
^{19}F NMR (400 MHz, $CDCl_3$): δ = -56.83 ppm.
^{13}C NMR (50 MHz, $CDCl_3$): δ = 141.46 (q, *J* = 1.8 Hz, 1C), 137.30, 136.96, 132.14 (2C), 131.23, 128.80 (d, *J* = 1.5 Hz, 1C), 128.44 (2C), 127.11, 126.89 (d, *J* = 2.6 Hz, 1C), 126.01 (q, *J* = 5.2 Hz, 1C), 120.06 (d, *J* = 142.6 Hz, 1C), 21.20 ppm.
IR: $\tilde{\nu}$ = 3030, 2924, 1488, 1448, 1313, 1167, 1125, 1109, 1070, 1035, 767 cm^{-1}.
MS (EI, 70 eV) *m/z* (%): 236 (100) [M+], 215 (8), 196 (7), 167 (14), 91 (4).
HRMS (EI-TOF) calcd for $C_{14}H_{11}F_3$: 236.0813; found: 236.0818.



4-methyl-3'-(trifluoromethyl)biphenyl (5.1-3ha) [CAS: 97067-19-1]
Compound **5.1-3ha** was prepared following general method from potassium 3-trifluoromethylbenzoate (**5.1-1h**) (137 mg, 0.6 mmol) and 4-chlorotoluene (**5.1-2a**) (64 mg, 60 µL, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). After the reaction, compound **5.1-3ha** was obtained by column chromatography as a white solid (58 mg, 49%).

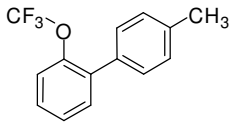
^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.83 (s, 1H), 7.79-7.74 (m, 1H), 7.61-9.49 (m, 4H), 7.29 (d, J = 8.2 Hz, 2H), 2.42 (s, 3H).
^{19}F NMR (400 MHz, $CDCl_3$): δ = -62.57 ppm.
^{13}C NMR (50 MHz, $CDCl_3$): δ = 141.92, 137.94, 136.87, 131.10 (d, *J* = 32.1 Hz, 1C), 130.20, 129.70 (2C), 129.16 (2C), 127.00 (2C), 123.87 (d, *J* = 232.7 Hz, 1C), 123.70 (q, *J* = 4.1 Hz, 1C), 21.11 ppm.
IR: $\tilde{\nu}$ = 3029, 2925, 1333, 1261, 1163, 1124. 1074, 796 cm^{-1}.
MS (EI, 70 eV) *m/z* (%): 236 (100) [M+], 167 (27), 152 (3), 91 (4), 69 (7).
HRMS (EI-TOF) calcd for $C_{14}H_{11}F_3$: 236.0813; found: 236.0816.
M.p.: 35-36 °C.



4-methyl-4'-(trifluoromethyl)biphenyl (5.1-3ia) [CAS: 97067-18-0]

Compound **5.1-3ia** was prepared following general method from potassium 4-trifluoromethylbenzoate (**5.1-1i**) (137 mg, 0.6 mmol) and 4-chlorotoluene (**5.1-2a**) (64 mg, 60 µL, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). After the reaction, compound **5.1-3ia** was obtained by column chromatography as a white solid (90 mg, 76%).

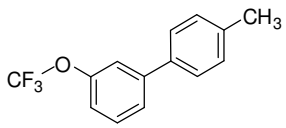
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69 (s, 4H), 7.51 (d, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 2.42 (s, 3H).
^{19}F NMR (400 MHz, $CDCl_3$): δ = -62.33 ppm.
^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.63, 138.14, 136.85, 129.69 (2C), 129.02 (q, *J* = 32.7 Hz, 1C), 127.15 (2C), 127.08 (2C), 125.64 (q, *J* = 3.6, 2C), 124.34, 21.13 ppm.
IR: $\tilde{\nu}$ = 2960, 2925, 1606, 1323, 1166, 1120, 1111, 1071, 809 cm^{-1}.
MS (EI, 70 eV) *m/z* (%): 236 (100) [M+], 217 (4), 167 (39), 91 (4), 69 (5).
HRMS (EI-TOF) calcd for $C_{14}H_{11}F_3$: 236.0813; found: 236.0809.
M.p.: 130-131 °C.



4'-methyl-2-(trifluoromethoxy)biphenyl (5.1-3ja)

Compound **5.1-3ja** was prepared following general method from potassium 2-trifluoromethoxybenzoate (**5.1-1j**) (147 mg, 0.6 mmol) and 4-chlorotoluene (**5.1-2a**) (64 mg, 60 µL, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). After the reaction, compound **5.1-3ja** was obtained by column chromatography as a colorless liquid (101 mg, 80%).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.66 (dd, , *J* = 7.9, 0.9 Hz, 1H), 7.60-7.42 (m, 2H), 7.34(d, *J* = 7.8 Hz, 1H), 7.24 (s, 4H), 2.43 (s, 3H).
^{19}F NMR (400 MHz, $CDCl_3$): δ = -57.03 ppm.
^{13}C NMR (50 MHz, $CDCl_3$): δ = 148.26 (d, *J* = 1.8 Hz, 1C), 137.43, 135.28, 133.91, 131.51, 129.07 (2C), 128.99 (2C), 128.33, 126.97, 123.02, 121.24 (d, *J* = 1.5 Hz, 1C), 21.19 ppm.
IR: $\tilde{\nu}$ = 3030, 2925, 2861, 1485, 1248, 1218, 1198, 1164, 817 cm^{-1}.
MS (EI, 70 eV) *m/z* (%): 252 (100) [M+], 183 (4), 167 (14), 69 (9).
HRMS (EI-TOF) calcd for $C_{14}H_{11}F_3O$: 252.0762; found: 252.0746.



4'-methyl-3-(trifluoromethoxy)biphenyl (5.1-3ka)

Compound **5.1-3ka** was prepared following general method from potassium 3-trifluoromethoxybenzoate (**5.1-1k**) (147 mg, 0.6 mmol) and 4-chlorotoluene (**5.1-2a**) (64 mg, 60 µL, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). After the reaction, compound **5.1-3ka** was obtained by column chromatography as a white solid (77 mg, 61%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.53-7.43 (m, 5H), 7.28 (d, *J* = 8.0 Hz, 2H), 7.19 (dt, *J* = 8.1, 1.0 Hz, 1H), 2.42 (s, 3H).

^{19}F NMR (400 MHz, $CDCl_3$): δ = -57.66 ppm.

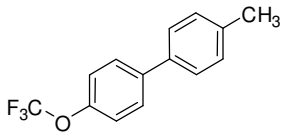
^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.67, 143.26, 137.90, 136.77, 129.98, 129.65 (2C), 126.95 (2C), 125.25, 121.80, 119.50, 119.22, 21.11 ppm.

IR: $\tilde{\nu}$ = 2925, 2867, 1606, 1588, 1474, 1262, 1203, 1150, 787 cm^{-1}.

MS (EI, 70 eV) *m/z* (%): 252 (100) [M+], 167 (3), 152 (2), 69 (3).

HRMS (EI-TOF) calcd for $C_{14}H_{11}F_3O$: 252.0762; found: 252.0756.

M.p.: 39-40 °C.



4-methyl-4'-(trifluoromethoxy)biphenyl (5.1-3la) [CAS: 1546954-83-9]

Compound **5.1-3la** was prepared following general method from potassium 4-trifluoromethoxylbenzoate (**5.1-1l**) (147 mg, 0.6 mmol) and 4-chlorotoluene (**5.1-2a**) (64 mg, 60 µL, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). After the reaction, compound **5.1-3la** was obtained by column chromatography as a white solid (63 mg, 50%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61-7.57(m, 2H), 7.47 (d, *J* = 8.0Hz, 2H), 7.29-7.26 (m, 4H), 2.42 (s, 3H).

^{19}F NMR (400 MHz, $CDCl_3$): δ = -57.81 ppm.

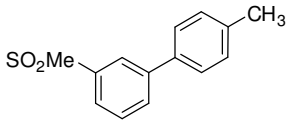
^{13}C NMR (100 MHz, $CDCl_3$) δ = 148.42 (d, *J* = 1.5 Hz, 1C), 139.90, 137.51, 136.95, 129.59 (2C), 128.21 (2C), 126.92 (2C), 121.19 (2C), 120.52 (d, *J* = 127.5 Hz, 1C), 21.08 ppm.

IR: $\tilde{\nu}$ = 3033, 2925, 1738, 1609, 1493, 1207, 1152, 806 cm^{-1}.

MS (EI, 70 eV) *m/z* (%): 252 (100) [M+], 183 (11), 167 (19), 155 (9), 115 (3), 69 (4).

HRMS (EI-TOF) calcd for $C_{14}H_{11}F_3O$: 252.0762; found: 252.0762.

M.p.: 98-99 °C.



4-methyl-3'-(methylsulfonyl)biphenyl (5.1-3ma)

Compound **5.1-3ma** was prepared following general method from potassium 3-methylsulfonylbenzoate (**5.1-1m**) (143 mg, 0.6 mmol) and 4-chlorotoluene (**5.1-2a**) (64 mg, 60 µL, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). After the reaction, compound **5.1-3ma** was obtained by column chromatography as a white solid (74 mg, 60%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.16 (t, *J* = 1.8 Hz, 1H), 7.90 (dt, *J* = 7.7, 1.4 Hz, 1H), 7.87 (dt, *J* = 7.8, 1.3 Hz, 1H), 7.64 (t, *J* = 8.0 Hz, 1H), 7.55-7.52 (m, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 3.11 (s, 3H), 2.43 (s, 3H).

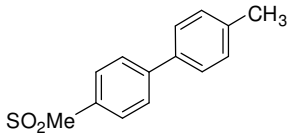
^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.66, 141.08, 138.39, 136.07, 131.99, 129.81 (2C), 129.78, 126.99 (2C), 125.59 (2C), 44.55, 21.14 ppm.

IR: $\tilde{\nu}$ = 3008, 2926, 1469. 1321, 1297, 1146, 958, 775 cm^{-1}.

MS (EI, 70 eV) *m/z* (%): 246 (100) [M+], 167 (27), 152 (12), 44 (9).

HRMS (EI-TOF) calcd for $C_{14}H_{14}O_2S$: 246.0715; found: 246.0714.

M.p.: 118-119 °C.



4-methyl-4'-(methylsulfonyl)biphenyl (5.1-3na) [CAS: 893738-58-4]

Compound **5.1-3na** was prepared following general method from potassium 4-methylsulfonylbenzoate (**5.1-1n**) (143 mg, 0.6 mmol) and 4-chlorotoluene (**5.1-2a**) (64 mg, 60 µL, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). After the reaction, compound **5.1-3na** was obtained by column chromatography as a white solid (108 mg, 88%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00 (m, 2H), 7.76 (m, 2H), 7.74-7.72 (m, 2H), 7.31 (d, *J* = 7.8 Hz,2H), 3.10 (s, 3H), 2.43 (s, 3H).

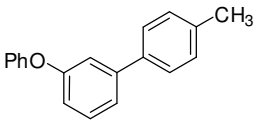
^{13}C NMR (100 MHz, $CDCl_3$): δ = 146.63, 138.77, 138.71, 136.18, 129.81 (2C), 127.87 (2C), 127.69 (2C), 127.20 (2C), 44.63, 21.17 ppm.

IR: $\tilde{\nu}$ = 3010, 2927, 1317, 1297, 1148, 1093, 954, 807 cm^{-1}.

MS (EI, 70 eV) *m/z* (%): 246 (100) [M+], 230 (30), 183 (36), 167 (22), 152 (12), 63 (8).

HRMS (EI-TOF) calcd for $C_{14}H_{14}O_2S$: 246.0715; found: 246.0714.

M.p.: 197-198 °C.



4'-methyl-3-phenoxybiphenyl (5.1-3oa)

Compound **5.1-3oa** was prepared following general method from potassium 3-phenoxybenzoate (**5.1-1n**) (151mg, 0.6 mmol) and 4-chlorotoluene (**5.1-2a**) (64 mg, 60 µL, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). After the reaction, compound **5.1-3oa** was obtained by column chromatography as a colorless liquid (65 mg, 50%).

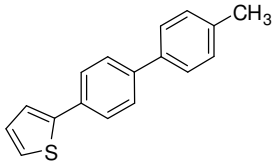
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47 (d, *J* = 8.0 Hz, 2H), 7.41-7.32 (m, 4H), 7.26-7.23(m, 3H), 7.12 (t, *J* = 8.0 Hz, 1H), 7.08-7.06 (m, 2H), 6.98 (ddd, *J* = 16.0, 8.0, 1.1 Hz, 1H), 2.40 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 157.60, 157.22, 143.02, 137.60, 137.41, 129.96, 129.76 (2C), 129.49 (2C), 126.93 (2C), 123.24, 121.86, 118.89 (2C), 117.43, 117.34, 21.09 ppm.

IR: $\tilde{\nu}$ = 3027, 2920, 1582, 1567, 1488, 1478, 1219, 903 cm^{-1}.

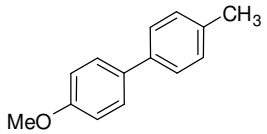
MS (EI, 70 eV) *m/z* (%): 260 (100) [M+], 232 (8), 217 (7), 165 (5), 152 (7), 77 (7).

HRMS (EI-TOF) calcd for $C_{19}H_{16}O$: 260.1201; found: 260.1199.



2-(4'-methylbiphenyl-4-yl)thiophene (5.1-3pa) [CAS: 1086406-13-4]

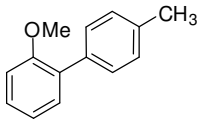
Compound **5.1-3pa** was prepared following general method from potassium 4-(thiophen-2-yl)benzoate (**5.1-1p**) (145 mg, 0.6 mmol) and 4-chlorotoluene (**5.1-2a**) (64 mg, 60 µL, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). The yield was determined by GC analysis using *n*-tetradecane as the internal standard.



4-methoxy-4'-methylbiphenyl (5.1-3qa) [CAS: 53040-92-9]

Compound **5.1-3qa** was prepared following general method from potassium 4-(thiophen-2-yl)benzoate (**5.1-1q**) (114 mg, 0.6 mmol) and 4-chlorotoluene (**5.1-2a**) (64 mg, 60 µL, 0.5

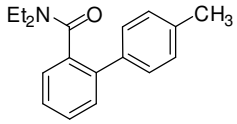
mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). The yield was determined by GC analysis using *n*-tetradecane as the internal standard.



2-methoxy-4'-methylbiphenyl (5.1-3ra) [CAS: 92495-53-9]

Compound **5.1-3ra** was prepared following general method from potassium 2-methoxybenzoate (**5.1-1r**) (143 mg, 0.75 mmol) and 4-chlorotoluene (**5.1-2a**) (64 mg, 60 µL, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). After the reaction, compound **5.1-3ra** was obtained by column chromatography as a yellow solid (79 mg, 79%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45 (d, *J* = 8.0 Hz, 2H), 7.34-7.30 (m, 2H), 7.24 (d, *J* = 7.9 Hz, 2H), 7.04 (td, *J* = 7.5, 1.2 Hz, 1H), 7.00 (d, *J* = 8.5 Hz, 1H), 3.82 (s, 3H), 2.41 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.47, 136.58, 135.55, 130.77, 130.66, 129.37 (2C), 128.72 (2C), 128.34, 120.76, 111.11, 55.50, 21.19 ppm
IR: $\tilde{\nu}$ = 3014, 2964, 2920, 1907, 1596, 1484, 1455, 1228, 1020, 757 cm^{-1}.
MS (EI, 70 eV) *m/z* (%): 198 (100) [M+], 183 (15), 155 (24).
HRMS (EI-TOF) calcd for $C_{14}H_{14}O$: 198.1045; found: 198.1044.
M.p.: 81-82 °C.

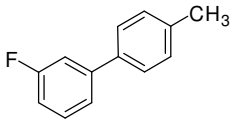


***N*,*N*-diethyl-4'-methylbiphenyl-2-carboxamide (5.1-3sa)** [CAS: 937166-55-7]

Compound **5.1-3sa** was prepared following general method from potassium 2-(diethylcarbamoyl)benzoate (**5.1-1s**) (195 mg, 0.75 mmol) and 4-chlorotoluene (**5.1-2a**) (64 mg, 60 µL, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). After the reaction, compound **5.1-3sa** was obtained by column chromatography as a yellow liquid (114 mg, 85%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.44-7.42 (m, 1H), 7.39-7.36 (m, 5H), 7.19 (d, *J* = 7.9 Hz, 2H), 3.78-3.72 (m, 1H), 3.07-3.01 (m, 1H), 3.00-2.94 (m, 1H), 2.70-2.64 (m, 1H), 2.38 (s, 3H), 0.93 (t, *J* = 7.1 Hz, 3H), 0.75 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.66, 138.31, 137.26, 136.89, 136.26, 129.36, 128.96, 128.86, 128.67, 127.26, 126.96, 42.22, 38.31, 21.14, 13.38, 11.99 ppm
IR: $\tilde{\nu}$ = 2920, 2932, 2871, 1623, 1456, 1425, 1288, 1220, 1089, 757 cm^{-1}.

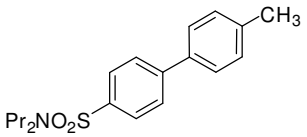
MS (EI, 70 eV) *m/z* (%): 266 (100) [M+], 195 (89), 165 (25), 152 (21), 72 (10).
HRMS (EI-TOF) calcd for $C_{18}H_{21}NO$: 267.1623; found: 267.1614.



3-fluoro-4'-methylbiphenyl (5.1-3ta) [CAS: 72093-42-6]

Compound **5.1-3ta** was prepared following general method from potassium 3-fluorobenzoate (**5.1-1t**) (109 mg, 0.6 mmol) and 4-chlorotoluene (**5.1-2a**) (64 mg, 60 µL, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). After the reaction, compound **5.1-3ta** was obtained by column chromatography as a white solid (45 mg, 48%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49 (d, *J* = 8.0 Hz, 2H), 7.42-7.35 (m, 2H), 7.30-7.26 (m, 3H), 7.07-6.99 (m, 1H), 2.42 (s, 3H).
^{19}F NMR (400 MHz, $CDCl_3$): δ = -113.27 ppm.
^{13}C NMR (100 MHz, $CDCl_3$) δ = 164.20 (d, *J* = 245.7 Hz, 1C), 143.44 (d, *J* = 8.1 Hz, 1C), 137.71, 137.07 (d, *J* = 1.5 Hz, 1C), 130.12 (d, *J* = 8.8 Hz, 1C), 129.58 (2C), 126.92 (2C), 122.53 (d, *J* = 2.9 Hz, 1C), 113.84 (d, *J* = 6.0 Hz, 1C), 113.66 (d, *J* = 6.0 Hz, 1C), 21.11 ppm.
IR: $\tilde{\nu}$ = 3032, 2919, 1611, 1588, 1567, 1485, 1473, 1183, 1160, 875 cm^{-1}.
MS (EI, 70 eV) *m/z* (%): 186 (100) [M+], 171 (9), 165 (31), 133 (6), 91 (8), 74 (6).
HRMS (EI-TOF) calcd for $C_{13}H_{11}F$: 186.0845; found: 186.0842.
M.p.: 40-41 °C.



4'-methyl-*N*,*N*-dipropylbiphenyl-4-sulfonamide (5.1-3ua)

Compound **5.1-3ua** was prepared following general method from potassium 4-(*N*,*N*-dipropylsulfamoyl)benzoate (**5.1-1u**) (194 mg, 0.6 mmol) and 4-chlorotoluene (**5.1-2a**) (64 mg, 60 µL, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). After the reaction, compound **5.1-3ua** was obtained by column chromatography as a white solid (147 mg, 88 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86 (d, *J* = 8.0 Hz, 2H), 7.69 (d, *J* = 8.0 Hz, 2H), 7.52 (d, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 3.13-3.10 (m, 4H), 2.43 (s, 3H), 1.64-1.54 (m, 4H), 0.90 (t, *J* = 8.0 Hz, 6H).

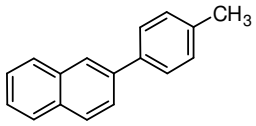
^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.98, 138.38, 138.35, 136.46, 129.73 (2C), 127.53 (2C), 127.27 (2C), 127.09 (2C), 50.11 (2C), 22.10 (2C), 21.16, 11.21 (2C) ppm.

IR: $\tilde{\nu}$ = 2965, 2873, 1468, 1332, 1324, 1151, 1092, 992, 807 cm^{-1}.

MS (EI, 70 eV) *m/z* (%): 331 (100) [M+], 302 (100), 231 (74), 183 (8), 167 (14), 152 (5).

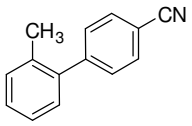
HRMS (EI-TOF) calcd for $C_{19}H_{25}NO_2S$: 331.1606; found: 331.1610

M.p.: 116-117 °C



2-*p*-tolylnaphthalene (5.1-3va) [CAS: 59115-49-0]

Compound **5.1-3va** was prepared following general method from potassium 2-naphthoate (**5.1-1v**) (126 mg, 0.6 mmol) and 4-chlorotoluene (**5.1-2a**) (64 mg, 60 µL, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). The yield was determined by GC analysis using *n*-tetradecane as the internal standard.



2'-methylbiphenyl-4-carbonitrile (5.1-3wf) [CAS: 189828-30-6]

Compound **5.1-3wf** was prepared following general method from potassium 2-methylbenzoate (**5.1-1w**) (131 mg, 0.75 mmol) and 4-chlorbenzonitrile (**5.1-2f**) (70 mg, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). After the reaction, compound **5.1-3wf** was obtained by column chromatography as a yellow solid (18 mg, 18%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.74-7.71 (m, 2H), 7.46-7.43 (m, 2H), 7.33-7.26 (m, 3H), 7.20 (d, *J* = 7.3 Hz, 1H), 2.26 (s, 3H).

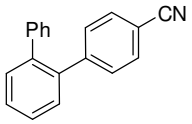
^{13}C NMR (100 MHz, $CDCl_3$): δ = 146.77, 139.97, 135.02, 131.95 (2C), 130.64, 129.98 (2C), 129.40, 128.27, 126.08, 118.95, 110.69, 20.30 ppm

IR: $\tilde{\nu}$ = 3062, 2924, 2853, 2227, 1608, 1482, 842, 759 cm^{-1}.

MS (EI, 70 eV) *m/z* (%): 193 (100) [M+], 178 (11), 165 (22), 74 (6), 50 (10).

HRMS (EI-TOF) calcd for $C_{14}H_{11}N$: 193.0891; found: 193.0890.

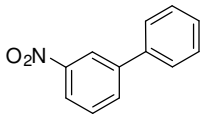
M.p.: 64-65 °C.



2'-phenylbiphenyl-4-carbonitrile (5.1-3xf) [CAS: 1071036-11-7]

Compound **5.1-3xf** was prepared following general method from potassium biphenyl-2-carboxylate (**5.1-1x**) (177 mg, 0.75 mmol) and 4-chlorbenzonitrile (**5.1-2f**) (70 mg, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). After the reaction, compound **5.1-3xf** was obtained by column chromatography as a yellow solid (41 mg, 32%).

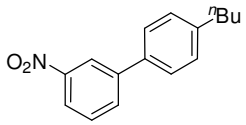
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.52-7.40 (m, 6H), 7.26-7.24 (m, 5H), 7.12-7.08 (m, 2H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 146.45, 140,65, 140.60, 138.60, 131.69 (2C), 130.85, 130.53 (2C), 130.23, 129.79 (2C), 128.56, 128.16 (2C), 127.75, 126.95, 118.95, 110.22 ppm
IR: $\tilde{\nu}$ = 3063, 2923, 2225, 1927, 1604, 1473, 1447, 830, 744 cm^{-1}.
MS (EI, 70 eV) *m/z* (%): 255 (100) [M+], 240 (11), 227 (5), 215 (4), 113 (7), 50 (8).
HRMS (EI-TOF) calcd for $C_{19}H_{13}N$: 255.1048; found: 255.1047.
M.p.: 118-119 °C.



3-nitrobiphenyl (5.1-3bb) [CAS: 2113-58-8]

Compound **5.1-3bb** was prepared following general method from potassium 3-nitrobenzoate (**5.1-1b**) (124 mg, 0.6 mmol) and chlorobenzene (**5.1-2b**) (57 mg, 52 µL, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). After the reaction, compound **5.1-3bb** was obtained by column chromatography as a white solid (63 mg, 63%).

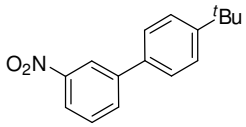
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.47 (t, *J* = 2.0 Hz, 1H), 8.22 (ddd, *J* = 8.0, 1.6, 1.0 Hz, 1H), 7.93 (ddd, *J* = 8.0, 1.6, 1.0 Hz, 1H), 7.66-7.61 (m, 3H), 7.54-7.49 (m, 2H), 7.47-7.43 (m, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.70, 142.86, 138.66, 133.03, 129.69, 129.15 (2C), 128.52, 127.15 (2C), 122.02, 121.95 ppm.
IR: $\tilde{\nu}$ = 3084, 2923, 1738, 1531, 1522, 1500, 1347, 1293, 730 cm^{-1}.
MS (EI, 70 eV) *m/z* (%): 199 (100) [M+], 152 (28), 141 (8), 115 (5), 76 (6).
HRMS (EI-TOF) calcd for $C_{12}H_9NO_2$: 199.0633; found: 199.0630.
M.p.: 57-58 °C.



4'-butyl-3-nitrobiphenyl (5.1-3bc)

Compound **5.1-3bc** was prepared following general method from potassium 3-nitrobenzoate (**5.1-1b**) (124 mg, 0.6 mmol) and 1-butyl-4-chlorobenzene (**5.1-2c**) (86 mg, 86 µL, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). After the reaction, compound **5.1-3bc** was obtained by column chromatography as a colorless liquid (73 mg, 57%).

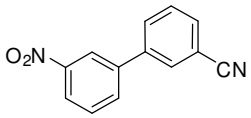
^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.46 (t, *J* = 1.9 Hz, 1H), 8.18 (ddd, *J* = 8.2, 2.2, 0.9 Hz, 1H), 7.92 (dt, *J* = 7.7, 1.3 Hz, 1H), 7.60 (t, *J* = 8.0 Hz, 1H), 7.57-7.55 (m, 2H), 7.32 (d, *J* = 8.2 Hz, 2H), 2.69 (t, *J* = 8.0 Hz, 2H), 1.69-1.62 (m, 2H), 1.45-1.36(m, 2H), 0.96 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (50 MHz, $CDCl_3$): δ = 148.71, 143.58, 142.84, 135.95, 132.82, 129.61, 129.22 (2C), 126.98 (2C), 121.72, 121.70, 35.28, 33.55, 22.36, 13.94 ppm.
IR: $\tilde{\nu}$ = 2956, 2928, 2858, 1529, 1515, 1346, 1101, 801 cm^{-1}.
MS (EI, 70 eV) *m/z* (%): 255 (73) [M+], 212 (100), 165 (10), 152 (3), 89 (2).
HRMS (EI-TOF) calcd for $C_{16}H_{17}NO_2$: 255.1259; found: 255.1263.



4'-*tert*-butyl-3-nitrobiphenyl (5.1-3bd)

Compound **5.1-3bd** was prepared following general method from potassium 3-nitrobenzoate (**5.1-1b**) (124 mg, 0.6 mmol) and 1-*tert*-butyl-4-chlorobenzene (**5.1-2d**) (86 mg, 86 µL, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). After the reaction, compound **5.1-3bd** was obtained by column chromatography as a colorless liquid (84 mg, 66%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.46 (t, *J* = 1.9 Hz, 1H), 8.19 (ddd, *J* = 8.2, 2.2, 0.9 Hz, 1H), 7.92 (ddd, *J* = 8.0, 1.6, 1.0 Hz, 1H), 7.63-7.57 (m, 3H), 7.54-7.52 (m, 2H), 1.39 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.76, 148.70, 142.69, 135.72, 132.83, 129.62, 126.79 (2C), 126.12 (2C), 121.74 (2C), 34.65, 31.27 (3C) ppm.
IR: $\tilde{\nu}$ = 2962, 2867, 1739, 1528, 1515, 1347, 834 cm^{-1}.
MS (EI, 70 eV) *m/z* (%): 255 (4) [M+], 240 (100), 212 (15), 194 (3), 165 (3), 152 (3), 57 (2).
HRMS (EI-TOF) calcd for $C_{16}H_{17}NO_2$: 255.1259; found: 255.1262.



3'-nitrobiphenyl-3-carbonitrile (5.1-3be) [CAS: 192699-67-5]

Compound **5.1-3be** was prepared following general method from potassium 3-nitrobenzoate (**5.1-1b**) (124 mg, 0.6 mmol) and 3-chlorobenzonitrile (**5.1-2e**) (70 mg, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). After the reaction, compound **5.1-3be** was obtained by column chromatography as a yellow solid (67 mg, 60%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.45 (t, *J* = 2.0 Hz, 1H), 8.30 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.92-9.90 (m, 2H), 7.88 (d, *J* = 7.9 Hz, 1H), 7.75 (d, *J* = 7.7 Hz, 1H), 7.70 (t, *J* = 8.0 Hz, 1H), 7.65 (t, *J* = 8.0 Hz, 1H).

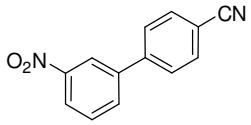
^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.78, 140.47, 139.92, 132.95, 131.91, 131.48, 130.69, 130.21, 130.08, 123.12, 121.98, 118.28, 113.48 ppm.

IR: $\tilde{\nu}$ = 3067, 2922, 2226, 1520, 1491, 1346, 1266, 892 cm^{-1}.

MS (EI, 70 eV) *m/z* (%): 224 (100) [M+], 178 (29), 166 (11), 151 (18), 75 (7).

HRMS (EI-TOF) calcd for $C_{13}H_8N_2O_2$: 224.0586; found: 224.0584.

M.p.: 176-177 °C.



3'-nitrobiphenyl-4-carbonitrile (**5.1-3bf**) [CAS: 39117-72-1]

Compound **5.1-3bf** was prepared following general method from potassium 3-nitrobenzoate (**5.1-1b**) (124 mg, 0.6 mmol) and 4-chlorobenzonitrile (**5.1-2f**) (69.5 mg, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). After the reaction, compound **5.1-3bf** was obtained by column chromatography as a yellow solid (77 mg, 67%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.48 (t, *J* = 1.9 Hz, 1H), 8.30 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.94 (d, *J* = 7.8 Hz, 1H), 7.83-7.81 (m, 2H), 7.76-7.74 (m, 2H), 7.70 (t, *J* = 8.0 Hz, 1H).

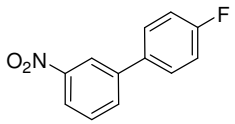
^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.81, 142.98, 140.80, 133.05, 132.95 (2C), 130.20, 127.88(2C), 123.33, 122.14, 118.38, 112.38 ppm.

IR: $\tilde{\nu}$ = 3083, 2924, 2225, 1607, 1519, 1506, 1350, 1293, 804 cm^{-1}.

MS (EI, 70 eV) *m/z* (%): 224 (100) [M+], 178 (32), 166 (9), 151 (20), 75 (6).

HRMS (EI-TOF) calcd for $C_{13}H_8N_2O_2$: 224.0586; found: 224.0581.

M.p.: 164-165 °C.



4'-fluoro-3-nitrobiphenyl (5.1-3bg) [CAS: 10540-32-6]

Compound **5.1-3bg** was prepared following general method from potassium 3-nitrobenzoate (**5.1-1b**) (124 mg, 0.6 mmol) and 1-chloro-4-fluorobenzene (**5.1-2g**) (67 mg, 54 µL, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). After the reaction, compound **5.1-3bg** was obtained by column chromatography as a yellow solid (73 mg, 67%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.42 (t, *J* = 1.9 Hz, 1H), 8.22 (ddd, *J* = 8.0, 2.0, 0.9 Hz, 1H), 7.89-7,87 (m, 1H), 7.64-7.59 (m, 3H), 7.23-7.17 (m, 2H).

^{19}F NMR (400 MHz, $CDCl_3$): δ = -133.42 ppm.

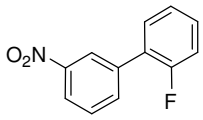
^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.33, 161.86, 148.70, 141.84, 134.81, 132.86, 129.79, 128.88 (d, *J* = 8.2 Hz, 1C), 122.04, 121.80, 116.28, 116.04 ppm.

IR: $\tilde{\nu}$ = 3087, 1606, 1528, 1508, 1476, 1346, 1228, 1165, 831 cm^{-1}.

MS (EI, 70 eV) *m/z* (%): 217 (100) [M+], 170 (29), 159 (15), 151 (3), 74 (4).

HRMS (EI-TOF) calcd for $C_{12}H_8FNO_2$: 217.0539; found: 217.0544.

M.p.: 66-67 °C.



2-fluoro-3'-nitrobiphenyl (5.1-3bh) [CAS: 80254-88-2]

Compound **5.1-3bh** was prepared following general method from potassium 3-nitrobenzoate (**5.1-1b**) (124 mg, 0.6 mmol) and 1-chloro-2-fluorobenzene (**5.1-2h**) (66 mg, 53 µL, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). After the reaction, compound **5.1-3bh** was obtained by column chromatography as a yellow solid (56 mg, 52%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.44 (t, *J* = 2.5 Hz, 1H), 8.25 (ddd, *J* = 8.3, 2.3, 1.0 Hz, 1H), 7.91 (dq, *J* = 7.7, 1.4 Hz, 1H), 7.64 (t, *J* = 8.0 Hz, 1H), 7.49 (td, *J* = 7.7, 1.8 Hz, 1H), 7.45-7.39 (m, 1H), 7.29 (td, *J* = 7.5, 1.3 Hz, 1H), 7.22 (ddd, *J* = 10.7, 8.2, 1.1 Hz, 1H).

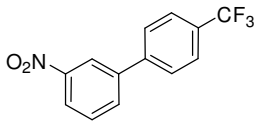
^{19}F NMR (400 MHz, $CDCl_3$): δ = -117.91 ppm

^{13}C NMR (100 MHz, $CDCl_3$) δ = 160.85, 158.38, 148.37, 137.39, 135.04 (d, *J* = 3.7 Hz, 1C), 130.48 (d, *J* = 2.9 Hz, 1C), 130.34 (d, *J* = 8.1 Hz, 1C), 129.37, 126.60 (d, *J* = 13.2 Hz, 1C), 124.31 (dd, *J* = 89.5. 3.7 Hz, 1C), 122.49, 116.40 (d, *J* = 22.7 Hz, 1C)

IR: $\tilde{\nu}$ = 3091, 2922, 2851, 1961, 1525, 1496, 1469, 1347, 1204, 741 cm^{-1}.

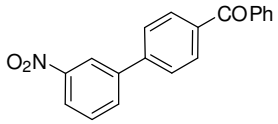
MS (EI, 70 eV) *m/z* (%): 217 (100) [M+], 170 (41), 159 (11), 151 (6), 133 (5), 85 (3).

HRMS (EI-TOF) calcd for $C_{12}H_8FNO_2$: 217.0539; found: 217.0540.
M.p.: 62-63 °C.



3-nitro-4'-(trifluoromethyl)biphenyl (5.1-3bi) [CAS: 1138479-19-2]
Compound **5.1-3bi** was prepared following general method from potassium 3-nitrobenzoate (**5.1-1b**) (124 mg, 0.6 mmol) and 4-chlorobenzotrifluoride (**5.1-2i**) (92 mg, 68 µL, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). After the reaction, compound **5.1-3bi** was obtained by column chromatography as a yellow solid (80 mg, 60%).

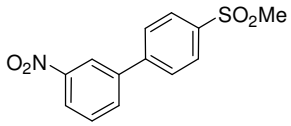
^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.48 (t, *J* = 1.9 Hz, 1H), 8.28 (ddd, *J* = 8.0, 1.6, 0.9 Hz, 1H), 7.94 (dt, *J* = 7.7, 1.3 Hz, 1H), 7.79-7.74 (m, 4H), 7.68 (t, *J* = 8.0 Hz, 1H).
^{19}F NMR (400 MHz, $CDCl_3$): δ = -62.60 ppm.
^{13}C NMR (50 MHz, $CDCl_3$): δ = 148.78, 142.13, 141.37, 133.14, 130.79, 130.47, 130.04, 127.56, 126.14 (q, J = 3.6 Hz, 1C), 125.33, 122.93, 122.62, 122.15 ppm.
IR: $\tilde{\nu}$ = 3081, 2923, 1618, 1531, 1514, 1346, 1322, 1159, 1110, 1068, 807 cm^{-1}.
MS (EI, 70 eV) *m/z* (%): 267 (100) [M+], 248 (9), 221 (3), 209 (9), 201 (21), 152 (18), 75 (3).
HRMS (EI-TOF) calcd for $C_{13}H_8F_3NO_2$: 267.0507; found: 267.0499.
M.p.: 59-60 °C.



(3'-nitrobiphenyl-4-yl)(phenyl)methanone (5.1-3bj) [CAS: 63242-13-7]
Compound **5.1-3bj** was prepared following general method from potassium 3-nitrobenzoate (**5.1-1b**) (124 mg, 0.6 mmol) and 4-chlorobenzophenone (**5.1-2j**) (109 mg, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). After the reaction, compound **5.1-3bj** was obtained by column chromatography as a yellow solid (102 mg, 68%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.53 (t, *J* = 2.0 Hz, 1H), 8.28 (ddd, *J* = 8.2, 2.2, 1.0 Hz, 1H), 7.99 (ddd, *J* = 8.0, 2.0, 1.0 Hz, 1H), 7.97-7.94 (m, 2H), 7.87-7.84 (m, 2H), 7.78-7.85 (m, 2H), 7.69 (t, *J* = 8.0 Hz, 1H), 7.66-7.62 (m, 1H), 7.56-7.51(m, 2H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.02, 148.77, 142.40, 141.65, 137.42, 137.34, 133.15, 132.66, 130.91 (2C), 130.01 (2C), 129.99, 128.40 (2C), 127.08 (2C), 122.84, 122.13 ppm.
IR: $\tilde{\nu}$ = 3088, 3066, 1651, 1603, 1522, 1511, 1347, 1279, 695 cm^{-1}.

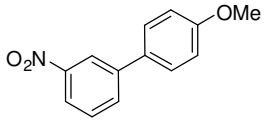
MS (EI, 70 eV) *m/z* (%): 303 (100) [M+], 286 (13), 226 (65), 152 (8), 105 (31), 77 (30).
HRMS (EI-TOF) calcd for $C_{19}H_{13}NO_3$: 303.0895; found: 303.0901.
M.p.: 139-140 °C.



4'-(methylsulfonyl)-3-nitrobiphenyl (5.1-3bk)

Compound **5.1-3bk** was prepared following general method from potassium 3-nitrobenzoate (**5.1-1b**) (124 mg, 0.6 mmol) and 4-chlorophenylmethylsulfone (**5.1-2k**) (97 mg, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). After the reaction, compound **5.1-3bk** was obtained by column chromatography as a yellow solid (69 mg, 50%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.50 (t, *J* = 1.9 Hz, 1H), 8.32 (ddd, *J* = 8.2, 2.1, 0.9 Hz, 1H), 8.11-8.08 (m, 2H), 7.96 (ddd, *J* = 7.8, 1.5, 1.1 Hz, 1H), 7.86-7.82 (m, 2H), 7.71 (t, *J* = 8.0 Hz, 1H), 3.13 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$) δ = 148.83, 144.05, 140.79, 140.49, 133.24, 130.21, 128.34 (2C), 128.19 (2C), 123.39, 122.30, 44.57
IR: $\tilde{\nu}$ = 3083, 3016, 2930, 1927, 1597, 1525, 1342, 1306, 1291, 1144, 1087, 967 cm^{-1}.
MS (EI, 70 eV) *m/z* (%): 277 (100) [M+], 262 (43), 214 (72), 198 (36), 152 (31), 43 (38).
HRMS (EI-TOF) calcd for $C_{13}H_{11}NO_4S$: 277.0409; found: 277.0408.
M.p.: 118-119 °C.

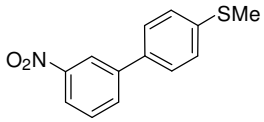


4'-methoxy-3-nitrobiphenyl (5.1-3bl) [CAS: 53059-31-7]

Compound **5.1-3bl** was prepared following general method from potassium 3-nitrobenzoate (**5.1-1b**) (124 mg, 0.6 mmol) and 4-chloroanisole (**5.1-2l**) (73 mg, 63 µL, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). After the reaction, compound **5.1-3bl** was obtained by column chromatography as a yellow solid (45 mg, 40%).

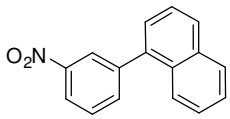
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.42 (t, *J* = 1.9, Hz, 1H), 8.16 (ddd, *J* = 8.0, 1.6, 1.0 Hz, 1H), 7.88 (d, *J* = 7.8 Hz, 1H), 7.61-7.57 (m, 3H), 7.05-7.02 (m, 2H), 3.89 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.04, 148.72, 142.46, 132.51, 131.06, 129.62, 128.27 (2C), 121.39, 121.36, 114.58 (2C), 55.41 ppm.
IR: $\tilde{\nu}$ = 3085, 2964, 2838, 1607, 1527, 1509, 1475, 1346, 1247, 1022, 804 cm^{-1}.

MS (EI, 70 eV) *m/z* (%): 229 (100) [M+], 183 (20), 168 (17), 139 (14), 128 (17), 74 (5).
HRMS (EI-TOF) calcd for $C_{13}H_{11}NO_3$: 229.0739; found: 229.0742.
M.p.: 75-76 °C.



methyl-(3'-nitrobiphenyl-4-yl)sulfane (5.1-3bm) [CAS: 1355247-56-1]
Compound **5.1-3bm** was prepared following general method from potassium 3-nitrobenzoate (**5.1-1b**) (124 mg, 0.6 mmol) and 4-chlorothioanisole (**5.1-2m**) (81 mg, 66 µL, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). After the reaction, compound **5.1-3bm** was obtained by column chromatography as a yellow solid (51 mg, 42%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.44 (t, *J* = 1.9 Hz, 1H), 8.19 (ddd, *J* = 8.0, 1.6, 1.0 Hz, 1H), 7.90 (ddd, *J* = 8.0, 1.6, 1.1 Hz, 1H), 7.61 (t, *J* = 8.0 Hz, 1H), 7.59-7.55 (m, 2H), 7.39-7.36 (m, 2H), 2.55 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.70, 142.12, 139.58, 135.06, 132.58, 129.71, 127.36 (2C), 126.72 (2C), 121.84, 121.48, 15.49 ppm.
IR: $\tilde{\nu}$ = 3074, 2922, 2852, 1594, 1525, 1497, 1344, 1102, 739 cm^{-1}.
MS (EI, 70 eV) *m/z* (%): 245 (100) [M+], 199 (18), 187 (3), 152 (32), 139 (5), 63 (3).
HRMS (EI-TOF) calcd for $C_{13}H_{11}NO_2S$: 245.0511; found: 245.0513.
M.p.: 95-96 °C.



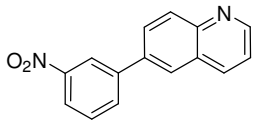
1-(3-nitrophenyl)naphthalene (5.1-3bn) [CAS: 94064-81-0]
Compound **5.1-3bn** was prepared following general method from potassium 3-nitrobenzoate (**5.1-1b**) (124 mg, 0.6 mmol) and 1-chloronaphthalene (**5.1-2n**) (83 mg, 70 µL, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). After the reaction, compound **5.1-3bn** was obtained by column chromatography as a yellow liquid (53 mg, 43%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.39 (t, *J* = 1.9 Hz, 1H), 8.32 (ddd, *J* = 8.0, 1.6, 1.0 Hz, 1H),7.95 (dd, *J* = 7.9, 4.6 Hz, 2H), 7.85 (dt, *J* = 7.6, 1.3 Hz, 1H), 7.78 (d, *J* = 8.4 Hz, 1H), 7.69 (t, *J* = 8.0 Hz, 1H), 7.59-7.44 (m, 4H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.29, 142.39, 137.47, 136.14, 133.76, 131.05, 129.22, 128.79, 128.55, 127.23, 126.71, 126.17, 125.32, 125.02, 124.85, 122.25 ppm.

IR: $\tilde{\nu}$ = 3060, 2922, 1737, 1524, 1508, 1345, 799 cm^{-1}.

MS (EI, 70 eV) *m/z* (%): 249 (100) [M+], 232 (14), 202 (42), 101 (6), 88 (3), 50 (4).

HRMS (EI-TOF) calcd for $C_{16}H_{11}NO_2$: 249.0790; found: 249.0789.



6-(3-nitrophenyl)quinoline (5.1-3bo)

Compound **5.1-3bo** was prepared following general method from potassium 3-nitrobenzoate (**5.1-1b**) (124 mg, 0.6 mmol) and 6-chloroquinoline (**5.1-2o**) (83 mg, 0.5 mmol) in a mixture of NMP (2.5 mL) and quinoline (2.5 mL). After the reaction, compound **5.1-3bo** was obtained by column chromatography as a yellow solid (90 mg, 71%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.99 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.61 (t, *J* = 1.9 Hz, 1H), 8.29-8.24 (m, 3H), 8.09 (d, *J* = 2.0 Hz, 1H), 8.06 (d, *J* = 7.8 Hz, 1H), 8.01 (dd, *J* = 8.8, 2.1 Hz, 1H), 7.70 (t, *J* = 8.0 Hz, 1H), 7.50 (dd, *J* = 8.3, 4.2 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.16, 148.83, 148.03, 142.02, 136.71, 136.36, 133.29, 130.59, 129.96, 128.52, 128.40, 126.18, 122.48, 122.27, 121.92 ppm.

IR: $\tilde{\nu}$ = 3028, 2970, 1740, 1523, 1500, 1342, 1291, 838 cm^{-1}.

MS (EI, 70 eV) *m/z* (%): 250 (100) [M+], 204 (18), 176 (6), 150 (2), 88 (4), 75 (3).

HRMS (EI-TOF) calcd for $C_{15}H_{10}N_2O_2$: 250.0742; found: 250.0747.

M.p.: 169-170 °C.

6.5 Arylalkene synthesis

6.5.1 Arylalkene synthesis via decarboxylative cross-coupling of alkenyl halides

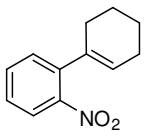
6.5.1.1 General procedure for the synthesis of potassium carboxylate salts

A 250 mL, two-necked, round-bottomed flask was charged with the carboxylic acid (20.0 mmol) and ethanol (20.0 mL). To this, a solution of potassium tert-butoxide (2.24 g, 20.0 mmol) in ethanol (20.0 mL) was added dropwise over 2 h. After complete addition, the reaction mixture was stirred for another 1 h at room temperature. A gradual formation of a white precipitate was observed. The resulting solid was collected by filtration washed sequentially with ethanol (2 x 10.0 mL) and cold (0 °C) diethyl ether (10.0 mL), and dried in vacuum to provide the corresponding potassium salts of the carboxylic acids.

6.5.1.2 General procedure for the decarboxylative coupling

An oven-dried, nitrogen-flushed 20 mL crimp cap vessel was charged with the potassium carboxylate (0.6 mmol, 1.2 equiv.), $Pd(F_6\text{-acac})_2$ (2.6 mg, 0.005 mmol, 1.0 mol %), tri-1-naphthylphosphine (4.25 mg, 0.01 mmol, 2.0 mol %), copper(I) chloride (5.1 mg, 0.05 mmol, 10 mol %), 1, 10-Phenanthroline (9.1 mg, 0.05 mmol, 10 mol %) and alkenyl bromide (0.5 mmol). A degassed mixture of NMP (1 mL) and mesitylene (3 mL) was added via syringe. The resulting solution was then stirred at 130 ºC for 16h. After the reaction was complete, the mixture was cooled to room temperature, diluted with sat. $NaHCO_3$ and extracted with ethyl acetate (3 × 20 mL). The combined organic layers were washed with water and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (SiO_2, ethyl acetate/hexane gradient) yielding the corresponding product.

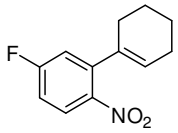
6.5.1.3 Synthesis and characterization of arylalkenes



1-cyclohexenyl-2-nitrobenzene (**5.2.1-3aa**) [CAS: 859219-19-5]

Compound **5.2.1-3aa** was prepared following the general method from potassium 2-nitrobenzoate (**5.2.1-1a**) (124 mg, 0.6 mmol) and 1-bromocyclohex-1-ene (**5.2.1-2a**) (83 mg, 59uL, 0.5 mmol) in a mixture of NMP (1 mL) and mesitylene (3 mL). Compound **5.2.1-3aa** was isolated by column chromatography as a yellow liquid (93 mg, 92%).

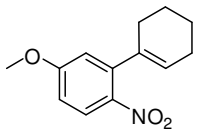
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.52 (td, *J* = 7.5, 1.3 Hz, 1H), 7.38-7.34 (m, 1H), 7.29 (dd, *J* = 7.7, 1.6 Hz, 1H), 5.65-5.62 (m, 1H), 2.26-2.21 (m, 2H), 2.18-2.13 (m, 2H), 1.81-1.74 (m, 2H), 1.73-1.65 (m, 2H);
^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.64, 139.49, 135.81, 132.36, 130.79, 127.31, 126.67, 123.84, 29.23, 25.40, 22.75, 21.67 ppm;
MS (EI, 70 eV) m/z (%): 204 (4) [M+], 186 (8), 158 (100), 130 (55), 91 (28), 77 (25).



2-cyclohexenyl-4-fluoro-1-nitrobenzene (5.2.1-3ba)

Compound **5.2.1-3ba** was prepared following the general method from potassium 2-nitro-5-fluoro-benzoate (**5.2.1-1b**) (135 mg, 0.6 mmol) and 1-bromocyclohex-1-ene (**5.2.1-2a**) (83 mg, 59uL, 0.5 mmol) in a mixture of NMP (1 mL) and mesitylene (3 mL). Compound **5.2.1-3ba** was isolated by column chromatography as a yellow liquid (91 mg, 82%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.89 (dd, *J* = 8.9, 5.1 Hz, 1H), 7.06-7.01 (m, 1H), 6.97 (dd, *J* = 8.8, 2.8 Hz, 1H), 5.66-5.63 (m, 1H), 2.23-2.18 (m, 2H), 2.17-2.12 (m, 2H), 1.80-1.72 (m, 2H), 1.71-1.62 (m, 2H);
^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.41, 162.87, 142.82 (d, *J* = 9.1 Hz, 1C), 135.38, 127.12, 126.67 (d, *J* = 10 Hz, 1C), 117.63 (d, *J* = 24 Hz, 1C), 114.29 (d, *J* = 24 Hz, 1C), 28.95, 25.29, 22.59, 21.53 ppm;
IR: *v* = 2936, 2861, 1735, 1580, 1525, 1347, 1264, 735 cm^{-1};
MS (EI, 70 eV) *m/z* (%): 222 (11) [M+], 204 (11), 176 (100), 148 (48), 138 (17), 109 (24), 75 (8).
EI-HRMS *m/z* calcd. for $C_{12}H_{12}FNO_2$: 221.0852, found: 221.0868.



2-cyclohexenyl-4-methoxy-1-nitrobenzene (5.2.1-3ca)

Compound **5.2.1-3ca** was prepared following the general method from potassium 2-nitro-5-methoxyl-benzoate (**5.2.1-1c**) (143 mg, 0.6 mmol) and 1-bromocyclohex-1-ene (**5.2.1-2a**) (83 mg, 59uL, 0.5 mmol) in a mixture of NMP (1 mL) and mesitylene (3 mL). Compound **5.2.1-3ca** was isolated by column chromatography as a yellow liquid (110 mg, 94%).

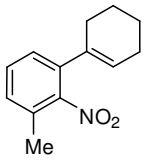
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.95 (d, *J* = 9.0 Hz, 1H), 6.83 (dd, *J* = 9.0, 2.8 Hz, 1H), 6.71 (d, *J* = 6.8 Hz, 1H), 5.62-5.60 (m, 1H), 3.89 (s, 3H), 2.22-2.14 (m, 4H), 1.82-1.75 (m, 2H), 1.73-1.66 (m, 2H);

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.75, 142.77, 141.32, 137.00, 126.80, 125.61, 115.67, 112.47, 55.80, 29.25, 25.32, 22.77, 21.74 ppm;

IR: *v* = 2935, 2837, 1574, 1512, 1339, 1293, 1246, 1206, 1095, 1029, 735 cm^{-1};

MS (EI, 70 eV) *m/z* (%): 234 (33) [M+], 216 (52), 188 (100), 160 (86), 106 (23), 63 (21).

EI-HRMS *m/z* calcd. for $C_{13}H_{15}NO_3$: 233.1052, found: 233.1056.



1-cyclohexenyl-3-methyl-2-nitrobenzene (5.2.1-3da)

Compound **5.2.1-3da** was prepared following the general method from potassium 2-nitro-3-methyl-benzoate (**5.2.1-1d**) (132 mg, 0.6 mmol) and 1-bromocyclohex-1-ene (**5.2.1-2a**) (83 mg, 59uL, 0.5 mmol) in a mixture of NMP (1 mL) and mesitylene (3 mL). Compound **5.2.1-3da** was isolated by column chromatography as a yellow liquid (93 mg, 86%).

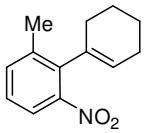
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30 (t, *J* = 8.0 Hz, 1H), 7.15 (d, *J* = 7.5 Hz, 1H), 7.10 (dt, *J* = 7.8, 0.8 Hz, 1H), 5.70-5.67 (m, 1H), 2.32 (s, 3H), 2.27-2.22 (m, 2H), 2.13-2.08 (m, 2H), 1.76-1.70 (m, 2H), 1.66-1.60 (m, 2H);

^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.41, 137.02, 134.17, 129.63, 129.25, 129.22, 127.86, 126.92, 29.34, 25.35, 22.71, 21.51, 17.46 ppm;

IR: *v* = 2931, 2860, 2837, 1736, 1526, 1435, 1370, 1265, 854, 736 cm^{-1};

MS (EI, 70 eV) *m/z* (%): 218 (6) [M+], 200 (9), 172 (100), 144 (36), 105 (20), 77 (12).

EI-HRMS *m/z* calcd. for $C_{13}H_{15}NO_2$: 217.1103, found: 217.1115



2-cyclohexenyl-1-methyl-3-nitrobenzene (5.2.1-3ea)

Compound **5.2.1-3ea** was prepared following the general method from potassium 2-nitro-6-methyl-benzoate (**5.2.1-1e**) (132 mg, 0.6 mmol) and 1-bromocyclohex-1-ene (**5.2.1-2a**) (83 mg, 59uL, 0.5 mmol) in a mixture of NMP (1 mL) and mesitylene (3 mL). Compound **5.2.1-3ea** was isolated by column chromatography as a yellow liquid (86 mg, 78%).

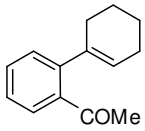
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.59 (m, 1H), 7.39 (dd, *J* = 7.5, 0.5 HZ, 1H), 7.25 (t, *J* = 8.0 HZ, 1H), 5.47-5.45 (m, 1H), 2.40-2.33 (m, 4H), 3.80 (s, 6H), 2.17-2.12 (m, 3H), 1.82-1.67 (m, 4H);

^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.94, 138.52, 137.89, 134.55, 133.71, 126.80, 126.07, 120.94, 29.07, 25.25, 22.58, 21.75, 19.36 ppm;

IR: *v* = 2930, 2859, 1735, 1527, 1448, 1437, 1357, 1265, 797, 739 cm^{-1};

MS (EI, 70 eV) *m/z* (%): 218 (9) [M+], 200 (23), 172 (100), 160 (46), 144 (70), 115 (32), 91 (22).

EI-HRMS *m/z* calcd. for $C_{13}H_{15}NO_2$: 217.1103, found: 217.1112.



1-(2-cyclohexenylphenyl)ethanone (5.2.1-3fa)

Compound **5.2.1-3fa** was prepared following the general method from potassium 2-acetylbenzoate (**5.2.1-1f**) (121 mg, 0.6 mmol) and 1-bromocyclohex-1-ene (**5.2.1-2a**) (83 mg, 59uL, 0.5 mmol) in a mixture of NMP (1 mL) and mesitylene (3 mL). Compound **5.2.1-3fa** was isolated by column chromatography as a yellow liquid (71 mg, 71%).

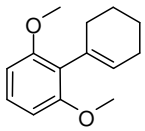
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.40 (td, *J* = 8.0, 1.5 Hz, 1H), 7.31-7.24 (m, 2H), 5.62-5.60 (m, 1H), 2.44 (s, 3H), 2.38-2.33 (m, 2H), 2.19-2.14 (m, 2H), 1.83-1.77 (m, 2H), 1.71-1.65 (m, 2H);

^{13}C NMR (100 MHz, $CDCl_3$): δ = 204.72, 143.22, 140.02, 137.83, 130.49, 128.87, 128.23, 127.78, 126.68, 30.07, 29.77, 25.81, 22.96, 21.74 ppm;

IR: *v* = 3057, 2929, 2858, 1683, 1594, 1437, 1266, 1244, 735 cm^{-1};

MS (EI, 70 eV) *m/z* (%): 200 (83) [M+], 185 (100), 171 (73), 157 (51), 145 (30), 115 (22), 43 (33).

EI-HRMS *m/z* calcd. for $C_{14}H_{16}O$: 200.1201, found: 200.1214.

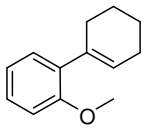


2-cyclohexenyl-1, 3-dimethoxybenzene (5.2.1-3ga)

Compound **5.2.1-3ga** was prepared following the general method from potassium 2, 6-dimethoxybenzoate (**5.2.1-1g**) (132 mg, 0.6 mmol) and 1-bromocyclohex-1-ene (**5.2.1-2a**) (83

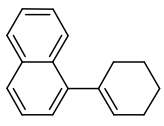
mg, 59uL, 0.5 mmol) in a mixture of NMP (1 mL) and mesitylene (3 mL). Compound **5.2.1-3ga** was isolated by column chromatography as a yellow liquid (47 mg, 43%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.16 (t, *J* = 8.3 Hz, 1H), 6.57 (d, *J* = 8.3 Hz, 2H), 5.57-5.54 (m, 1H), 3.79 (s, 6H), 2.23-2.14 (m, 2H), 1.79-1.68(m, 2H);
^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.69 (2C), 131.53, 127.42, 126.43, 122.53, 104.31 (2C), 56.11 (2C), 28.85, 25.46, 23.10, 22.18 ppm;
IR: *v* = 3007, 2926, 2835, 1586, 1469, 1431, 1247, 1113, 1107, 779, 729 cm^{-1};
MS (EI, 70 eV) *m/z* (%): 218 (100) [M+], 203 (33), 190 (22), 175 (19), 159 (18), 121 (11), 91 (11).
EI-HRMS *m/z* calcd. for $C_{14}H_{18}O_2$: 218.1307, found: 218.1301.



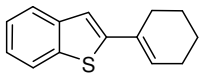
1-cyclohexenyl-2-methoxybenzene (5.2.1-3ha) [CAS: 22618-48-0]
Compound **5.2.1-3ha** was prepared following the general method from potassium 2-methoxybenzoate (**5.2.1-1h**) (114 mg, 0.6 mmol) and 1-bromocyclohex-1-ene (**5.2.1-2a**) (83 mg, 59uL, 0.5 mmol) in a mixture of NMP (1 mL) and mesitylene (3 mL). Compound **5.2.1-3ha** was isolated by column chromatography as a yellow liquid (48 mg, 52%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.23 (td, *J* = 7.8 Hz, 1H), 7.15 (dd, *J* = 7.5, 1.8 Hz, 1H), 6.93 (td, *J* = 7.4 Hz, 1H), 6.88 (d, *J* = 8.0 Hz, 1H), 5.80-5.77 (m, 1H), 3.84 (s, 3H), 2.40-2.37 (m, 2H), 2.24-2.20 (m, 2H), 1.79-1.69 (m, 4H);
^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.65, 137.53, 133.80, 129.55, 127.66, 126.11, 120.50, 110.69, 55.39, 28.77, 25.65, 23.03, 22.19 ppm;
IR: *v* = 2930, 2835, 1735, 1596, 1488, 1435, 1264, 1244, 1028, 737 cm^{-1};
MS (EI, 70 eV) *m/z* (%): 188 (100) [M+], 173 (25), 159 (28), 145 (20), 115 (11), 91 (9).



1-cyclohexenylnaphthalene (5.2.1-3ia) [CAS: 40358-51-8]
Compound **5.2.1-3ia** was prepared following the general method from potassium 1-naphthoate (**5.2.1-1i**) (126 mg, 0.6 mmol) and 1-bromocyclohex-1-ene (**5.2.1-2a**) (83 mg, 59uL, 0.5 mmol) in a mixture of NMP (1 mL) and mesitylene (3 mL). Compound **5.2.1-3ia** was isolated by column chromatography as a yellow liquid (49 mg, 47%).

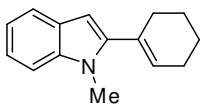
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.07-8.03 (m, 1H), 7.89-7.84 (m, 1H), 7.76 (d, *J* = 8.3 Hz, 1H), 7.52-7.43 (m, 3H), 7.29 (dd, *J* = 7.0, 1.5 Hz, 1H), 5.81-5.78 (m, 1H), 2.43-2.38 (m, 2H), 2.32-2.27 (m, 2H), 1.91-1.86 (m, 2H), 1.84-1.78 (m, 2H);
^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.08, 137.65, 133.74, 131.43, 128.22, 127.86, 127.23, 126.65, 125.83, 125.49, 125.41, 124.80, 31.04, 25.53, 23.22, 22.28 ppm;
IR: *v* = 3055, 2929, 2857, 2836, 1735, 1437, 1394, 1264, 1243, 798, 778, 738 cm^{-1};
MS (EI, 70 eV) *m/z* (%): 208 (100) [M+], 193 (6), 179 (17), 165 (31), 152 (6), 77 (3).



2-cyclohexenylbenzo[*b*]thiophene (5.2.1-3ja)

Compound **5.2.1-3ja** was prepared following the general method from potassium benzo[*b*]thiophene-2-carboxylate (**5.2.1-1j**) (131 mg, 0.6 mmol) and 1-bromocyclohex-1-ene (**5.2.1-2a**) (83 mg, 59uL, 0.5 mmol) in a mixture of NMP (1 mL) and mesitylene (3 mL). Compound **5.2.1-3ja** was isolated by column chromatography as a yellow liquid (80 mg, 75%).

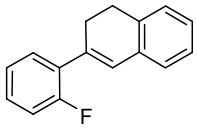
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.78-7.75 (m, 1H), 7.69 (dd, *J* = 7.0, 1.8 Hz, 1H), 7.34-7.26 (m, 2H), 7.14 (s, 1H), 6.35-6.32 (m, 1H), 2.55-2.50 (m, 2H), 2.30-2.25 (m, 2H), 1.86-1.80 (m, 2H), 1.74-1.68 (m, 2H);
^{13}C NMR (100 MHz, $CDCl_3$) δ = 146.75, 140.48, 138.24, 131.52, 127.05, 124.10, 124.01, 123.11, 121.94, 117.70, 26.93, 25.80, 22.59, 22.04 ppm;
IR: *v* = 2930, 2857, 2828, 1733, 1665, 1433, 1263, 816, 739, 724 cm^{-1};
MS (EI, 70 eV) *m/z* (%): 214 (100) [M+], 199 (17), 185 (21), 134 (6), 115 (3), 80 (3).
EI-HRMS *m/z* calcd. for $C_{14}H_{14}S$: 214.0816, found: 214.0822.



2-cyclohexenyl-1-methyl-1*H*-indole (5.2.1-3ka)

Compound **5.2.1-3ka** was prepared following the general method from potassium 1-methyl-1*H*-indole-2-carboxylate (**5.2.1-1k**) (128 mg, 0.6 mmol) and 1-bromocyclohex-1-ene (**5.2.1-2a**) (83 mg, 59uL, 0.5 mmol) in a mixture of NMP (1 mL) and mesitylene (3 mL). Compound **5.2.1-3ka** was isolated by column chromatography as a yellow liquid (63 mg, 59%).

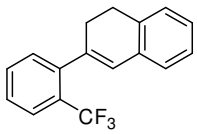
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.62-7.60 (m, 1H), 7.33 (dd, *J* = 8.3, 1.0 Hz, 1H), 7.25-7.21 (m, 1H), 7.15-7.11 (m, 1H), 6.40 (s, 1H), 5.97-5.94 (m, 1H), 3.75 (s, 3H), 2.43-2.39 (m, 2H), 2.33-2.27 (m, 2H), 1.88-1.81 (m, 2H), 1.79-1.73 (m, 2H);
^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.52, 137.95, 129.78, 129.33, 127.76, 121.11, 120.12, 119.44, 109.26, 99.30, 31.16, 29.45, 25.64, 22.88, 21.99 ppm;
IR: *v* = 3051, 2931, 2858, 1735, 1465, 1332, 1264, 1239, 736 cm^{-1};
MS (EI, 70 eV) *m/z* (%): 211 (100) [M+], 182 (14), 168 (8), 144 (6), 131 (5), 77 (2).
EI-HRMS *m/z* calcd. for $C_{15}H_{17}N$: 211.1361, found: 211.1363.



3-(2-fluorophenyl)-1,2-dihydronaphthalene (5.2.1-3lh)

Compound **5.2.1-3lh** was prepared following the general method from potassium 2-fluorobenzoate (**1l**) (107 mg, 0.6 mmol) and 3-bromo-1, 2-dihydronaphthalene (**5.2.1-2h**) (108 mg, 0.5 mmol) in a mixture of NMP (2 mL) and mesitylene (1 mL). Compound **5.2.1-3lh** was isolated by column chromatography as a colourless liquid (70 mg, 63%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.44 (td, *J* = 7.8, 2.0 Hz, 1H), 7.31-7.25 (m, 1H), 7.24-7.08 (m, 6H), 6.81 (s, 1H), 3.00-2.95 (m, 2H), 2.79-2.76 (m, 2H);
^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.34, 158.88, 135.14 (d, *J* = 1.8 Hz, 1C), 134.92, 134.33, 129.78 (d, *J* = 14.0 Hz, 1C), 128.72 (d, *J* = 4.0 Hz, 1C), 128.60, 128.52, 127.70 (d, *J* = 4.0 Hz, 1C), 127.25, 126.60 (d, *J* = 6.4 Hz, 1C), 124.06 (d, *J* = 4.0 Hz, 1C), 115.95 (d, *J* = 22.0 Hz, 1C), 28.14, 27.45 (d, *J* = 3.6 Hz, 1C) ppm;
IR: *v* = 3053, 3025, 2939, 1737, 1598, 1487, 1449, 1264, 1218, 739 cm^{-1};
MS (EI, 70 eV) *m/z* (%): 224 (100) [M+], 209 (6), 128 (7), 115 (12), 109 (31).
EI-HRMS *m/z* calcd. for $C_{16}H_{13}F$: 224.1001, found: 224.1000.

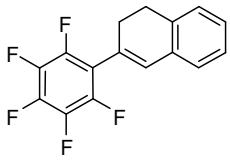


3-(2-(trifluoromethyl)phenyl)-1,2-dihydronaphthalene (5.2.1-3mh)

Compound **5.2.1-3mh** was prepared following the general method from potassium 2-(trifluoromethyl)benzoate (**5.2.1-1m**) (140 mg, 0.6 mmol) and 3-bromo-1,2-dihydronaphthalene (**5.2.1-2h**) (108 mg, 0.5 mmol) in a mixture of NMP (1 mL) and

mesitylene (3 mL). Compound **5.2.1-3mh** was isolated by column chromatography as a yellow liquid (63 mg, 46%).

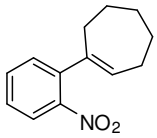
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72 (d, *J* = 7.8 Hz, 1H), 7.55 (t, *J* = 8.0 Hz, 1H), 7.42 (t, *J* = 8.0 Hz, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.23-7.20 (m, 3H), 7.12-7.10 (m, 1H), 6.45 (s, 1H), 3.00 (t, *J* = 8.2 Hz, 2H), 2.63 (t, *J* = 8.0 Hz, 2H);
^{19}F NMR (400 MHz, $CDCl_3$): d = -67.95 ppm;
^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.32 (q, *J* = 2.0 Hz, 1C), 138.60, 134.64, 134.06, 131.54, 130.18, 128.12, 127.38, 127.24, 127.17 (q, *J* = 1.5 Hz, 1C), 127.08, 126.58, 126.46, 126.19 (q, *J* = 5.1 Hz, 1C), 124.31 (d, *J* = 272 Hz, 1C), 29.34 (q, *J* = 1.5 Hz, 1C), 28.13 ppm;
IR: *v* = 2986, 2940, 2835, 1734, 1488, 1313, 1264, 1170, 1125, 1034, 735 cm^{-1};
MS (EI, 70 eV) *m/z* (%): 274 (100) [M+], 233 (8), 159 (4), 129 (5), 115 (17), 50 (3).
EI-HRMS *m/z* calcd. for $C_{17}H_{13}F_3$: 274.0969, found: 274.0984.



3-(perfluorophenyl)-1,2-dihydronaphthalene (5.2.1-3nh)

Compound **5.2.1-3nh** was prepared following the general method from potassium perfluorobenzoate (**5.2.1-1n**) (153 mg, 0.6 mmol) and 3-bromo-1, 2-dihydronaphthalene (**5.2.1-2h**) (108 mg, 0.5 mmol) in a mixture of NMP (1 mL) and mesitylene (3 mL). Compound **5.2.1-3nh** was isolated by column chromatography as a white solid (108 mg, 73%).

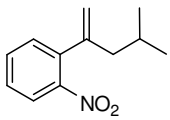
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.25-7.19 (m, 3H), 7.15-7.13 (m, 1H), 6.72 (s, 1H), 2.99 (t, *J* = 7.8 Hz, 2H), 2.64 (td, *J* = 8.0, 1.5 Hz, 2H);
^{19}F NMR (400 MHz, $CDCl_3$): d = -141.18, -156.61, -162.53 ppm;
^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.57-145.30 (m, IC), 143.11-142.85 (m, IC), 141.33-141.01 (m, 1C), 139.11-138.54 (m, 1C), 136.68-136.30 (m, 1C), 134.99, 133.08, 132.20 (q, *J* = 1.5 Hz, 1C), 128.28, 127.49, 127.00, 126.74, 125.25 (q, *J* = 1.5 Hz, 1C), 116.79 (m, IC), 27.86, 27.5 (t, *J* = 2.6 Hz, 1C) ppm;
IR: *v* = 3022, 2954, 1651, 1518, 1484, 1428, 1049, 981, 893, 757, 750 cm^{-1};
MS (EI, 70 eV) *m/z* (%): 296 (100) [M+], 281 (5), 127 (11), 115 (46), 77 (3), 50 (970).
EI-HRMS *m/z* calcd. for $C_{16}H_9F_5$: 296.0624, found: 296.0612.
M.p. 119-120 ^{o}C



1-cycloheptenyl-2-nitrobenzene (**5.2.1-3ab**)

Compound **5.2.1-3ab** was prepared following the general method from potassium 2-nitrobenzoate (**5.2.1-1a**) (124 mg, 0.6 mmol) and 1-bromocyclohept-1-ene (**5.2.1-2b**) (89 mg, 67uL, 0.5 mmol) in a mixture of NMP (1 mL) and mesitylene (3 mL). Compound **5.2.1-3ab** was isolated by column chromatography as a yellow liquid (80 mg, 74%).

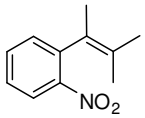
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81 (dd, *J* = 8.2, 1.4 HZ, 1H), 7.52-7.48 (m, 1H), 7.38-7.32 (m, 1H), 7.29 (dd, *J* = 7.5, 1.5 Hz, 1H), 5.84 (t, *J* = 6.5 Hz, 1H), 2.45-2.42 (m, 2H), 2.30-2.25 (m, 2H), 1.85-1.79 (m, 2H), 1.67-1.58 (m, 4H);
^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.89, 142.39, 141.25, 132.44, 131.94, 130.88, 127.13, 123.92, 34.50, 32.26, 29.03, 26.69, 26.59 ppm;
IR: *v* = 2924, 2850, 1739, 1606, 1525, 1447, 1350, 1265, 857, 738 cm^{-1};
MS (EI, 70 eV) *m/z* (%): 218 (7) [M+], 172 (100), 146 (60), 130 (72), 92 (38), 77(33).
EI-HRMS *m/z* calcd. for $C_{13}H_{15}NO_2$: 217.1103, found: 217.1114.



1-(4-methylpent-1-en-2-yl)-2-nitrobenzene (5.2.1-3ac)

Compound **5.2.1-3ac** was prepared following the general method from potassium 2-nitrobenzoate (**5.2.1-1a**) (124 mg, 0.6 mmol) and 2-bromo-4-methylpent-1-ene (**5.2.1-2c**) (82 mg, 70uL, 0.5 mmol) in a mixture of NMP (1 mL) and mesitylene (3 mL). Compound **5.2.1-3ac** was isolated by column chromatography as a yellow liquid (94 mg, 92%).

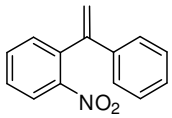
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (d, *J* = 8.0 Hz, 1H), 7.56-7.53 (m, 1H), 7.43-7.39 (m, 1H), 7.32 (d, *J* = 8.0 Hz, 1H), 5.19 (s, 1H), 5.07 (s, 1H), 2.24 (d, *J* = 7.0 Hz, 2H), 1.63-1.56 (m, 1H), 0.91 (s, 3H), 0.89 (s, 3H);
^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.40, 145.96, 138.36, 132.44, 131.15, 127.84, 124.07, 115.96, 45.96, 26.54, 22.39 (2C) ppm;
IR: *v* = 2956, 2923, 2853, 1741, 1529, 1465, 1350, 904, 854, 740 cm^{-1};
MS (EI, 70 eV) *m/z* (%): 206 (17) [M+], 190 (22), 162 (94), 120 (77), 91 (100), 77 (62), 43 (96).
EI-HRMS *m/z* calcd. for $C_{12}H_{15}NO_2$: 205.1103, found: 205.1111.



1-(3-methylbut-2-en-2-yl)-2-nitrobenzene (5.2.1-3ad)

Compound **5.2.1-3ad** was prepared following the general method from potassium 2-nitrobenzoate (**5.2.1-1a**) (124 mg, 0.6 mmol) and 2-bromo-3-methylbut-2-ene (**5.2.1-2d**) (77 mg, 60uL, 0.5 mmol) in a mixture of NMP (1 mL) and mesitylene (3 mL). Compound **5.2.1-3ad** was isolated by column chromatography as a yellow liquid (67 mg, 70%).

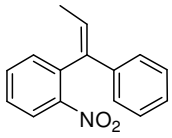
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.55 (td, *J* = 7.5, 1.3 Hz, 1H), 7.37 (m, 1H), 7.21 (dd, *J* = 7.8, 1.5 Hz, 1H), 1.97 (m, 3H), 1.79 (s, 3H), 1.40-1.39 (m, 3H);
^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.76, 140.12, 132.71, 131.20, 128.81, 127.09, 125.93, 123.88, 21.75, 20.16, 19.96 ppm;
IR: *v* = 2983, 2916, 2860, 1736, 1606, 1524, 1350, 1265, 859, 737 cm^{-1};
MS (EI, 70 eV) *m/z* (%): 192 (4) [M+], 149 (19), 134 (100), 104 (62), 77 (30), 43 (41).
EI-HRMS *m/z* calcd. for $C_{11}H_{13}NO_2$: 191.0946, found: 191.0945.



1-nitro-2-(1-phenylvinyl)benzene (5.2.1-3ae)

Compound **5.2.1-3e** was prepared following the general method from potassium 2-nitrobenzoate (**5.2.1-1a**) (124 mg, 0.6 mmol) and (1-bromovinyl)benzene (**5.2.1-2e**) (93mg, 0.5 mmol) in a mixture of NMP (1 mL) and mesitylene (3 mL). Compound **5.2.1-3ae** was isolated by column chromatography as a yellow liquid (44 mg, 39%).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.93 (d, *J* = 8.0 Hz, 1H), 7.67-7.59 (m, 1H), 7.53-7.43 (m, 2H), 7.31-7.22 (m, 5H), 5.75 (s, 1H), 5.32 (s, 1H);
^{13}C NMR (50 MHz, $CDCl_3$): δ = 146.44, 139.05, 136.93, 132.83, 132.45, 129.91, 128.65, 128.39 (2C), 128.16, 126.50 (2C), 124.35, 115.51 ppm;
IR: *v* = 2926, 1736, 1527, 1446, 1352, 1265, 908, 737 cm^{-1};
MS (EI, 70 eV) *m/z* (%): 225 (18) [M+], 224 (100), 208 (99), 180 (44), 152 (23), 105 (21), 77 (38).
EI-HRMS *m/z* calcd. for $C_{14}H_{11}NO_2$: 224.0712, found: 224.0726.



(*E*)-1-nitro-2-(1-phenylprop-1-enyl)benzene (5.2.1-3af)

Compound **5.2.1-3af** was prepared following the general method from potassium 2-nitrobenzoate (**5.2.1-1a**) (124 mg, 0.6 mmol) and (1-bromoprop-1-enyl)benzene (**5.2.1-2e**) (*E*:*Z* = 95:5) (93mg, 0.5 mmol) in a mixture of NMP (1 mL) and mesitylene (3 mL). Compound **5.2.1-3af** was isolated by column chromatography as a yellow liquid (89 mg, 74%) along with the expected 5% of the *Z* isomer.

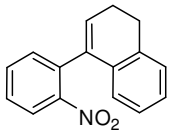
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.05 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.68 (td, *J* = 7.5, 1.5 Hz, 1H), 7.56-7.51 (m, 1H), 7.36 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.29-7.20 (m, 5H), 6.31 (q, *J* = 7.1 Hz, 1H), 1.66 (d, *J* = 7.0 Hz, 3H);

^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.36, 140.34, 138.42, 134.94, 132.90, 132.80, 128.30 (2C), 128.25 (2C), 127.16, 126.37, 125.11, 124.46, 15.52 ppm;

IR: *v* = 3029, 2914, 2855, 1735, 1607, 1522, 1494, 1441, 1347, 1241, 849, 756 cm^{-1};

MS (EI, 70 eV) *m/z* (%): 239 (15) [M+], 222 (100), 195 (74), 167 (58), 105 (78), 77 (64).

EI-HRMS *m/z* calcd. for $C_{15}H_{13}NO_2$: 239.0946, found: 239.0942.



4-(2-nitrophenyl)-1,2-dihydronaphthalene (5.2.1-3ag)

Compound **5.2.1-3ag** was prepared following the general method from potassium 2-nitrobenzoate (**5.2.1-1a**) (124 mg, 0.6 mmol) and 3-bromo-1, 2-dihydronaphthalene (**5.2.1-2g**) (105mg, 0.5 mmol) in a mixture of NMP (1 mL) and mesitylene (3 mL). Compound **5.2.1-3ag** was isolated by column chromatography as a yellow liquid (117 mg, 93%).

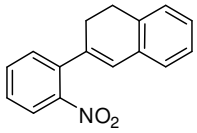
^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.06 (d, *J* = 8.0 Hz, 1H), 7.76-7.68 (m, 1H), 7.62-7.49 (m, 2H), 7.34-7.10 (m, 3H), 6.70 (d, *J* = 8.0 Hz, 1H), 6.11 (t, *J* = 4.6 Hz, 1H), 3.08-2.91 (m, 2H), 2.57-2.48 (m, 2H);

^{13}C NMR (50 MHz, $CDCl_3$): δ = 149.20, 136.61, 135.92, 135.67, 134.23, 132.89, 134.42, 128.28, 128.00, 127.68, 127.40, 126.43, 124.22, 123.61, 27.79, 23.38 ppm;

IR: *v* = 3058, 2938, 2832, 1735, 1526, 1350, 1265, 1044, 773 cm^{-1};

MS (EI, 70 eV) *m/z* (%): 251 (46) [M+], 234 (40), 222 (44), 206 (100), 179 (21), 115 (10), 76 (10).

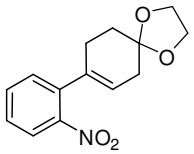
EI-HRMS *m/z* calcd. for $C_{16}H_{13}NO_2$: 251.0946, found: 251.0935.



3-(2-nitrophenyl)-1, 2-dihydronaphthalene (5.2.1-3ah)

Compound **5.2.1-3ah** was prepared following the general method from potassium 2-nitrobenzoate (**5.2.1-1a**) (124 mg, 0.6 mmol) and 4-bromo-1, 2-dihydronaphthalene (**5.2.1-2h**) (105mg, 0.5 mmol) in a mixture of NMP (1 mL) and mesitylene (3 mL). Compound **5.2.1-3ah** was isolated by column chromatography as a yellow liquid (122 mg, 97%).

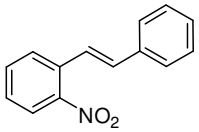
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97-7.94 (m, 1H), 7.63-7.59 (m, 1H), 7.48-7.44 (m, 1H), 7.22-7.18 (m, 3H), 7.13-7.11 (m, 1H), 6.54 (s, 1H), 3.03-2.99 (m, 2H), 2.58-2.54 (m, 2H);
^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.21, 138.05, 137.58, 134.84, 133.82, 132.94, 130.78, 128.04, 127.54, 127.37, 126.75, 126.60, 126.56, 124.41, 28.19, 27.88 ppm;
IR: *v* = 3064, 2939, 2890, 2832, 1735, 1606, 1521, 1345, 1264, 736 cm^{-1};
MS (EI, 70 eV) *m/z* (%): 251 (2) [M+], 234 (100), 216 (66), 204 (20), 91 (22), 77 (16).
EI-HRMS *m/z* calcd. for C $C_{16}H_{13}NO_2$: 251.0946, found: 251.0959.



8-(2-nitrophenyl)-1,4-dioxaspiro[4.5]dec-7-ene (5.2.1-3ai)

Compound **5.2.1-3ai** was prepared following the general method from potassium 2-nitrobenzoate (**5.2.1-1a**) (124 mg, 0.6 mmol) and 8-bromo-1, 4-dioxaspiro[4.5]dec-7-ene (**5.2.1-2i**) (105mg, 0.5 mmol) in a mixture of NMP (1 mL) and mesitylene (3 mL). Compound **5.2.1-3ai** was isolated by column chromatography as a yellow liquid (127 mg, 97%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (d, *J* = 8.0 Hz, 1H), 7.55-7.51 (m, 1H), 7.41-7.37 (m, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 5.54-5.53 (m, 1H), 4.03-4.02 (m, 4H), 2.48-2.43 (m, 4H), 1.93 (t, *J* = 6.3 Hz, 2H);
^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.26, 138.52, 135.61, 132.65, 130.93, 127.73, 124.09, 123.65, 107.34, 64.47(2C), 36.03, 31.31, 28.75 ppm;
IR: *v* = 2954, 2884, 1735, 1523, 1345, 1265, 1241, 1115, 1060, 1024, 866, 734 cm^{-1};
MS (EI, 70 eV) *m/z* (%): 262 (3) [M+], 244 (6), 172 (7), 115 (20), 99 (100), 86 (51).
EI-HRMS *m/z* calcd. for $C_{14}H_{15}NO_4$: 261.1001, found: 261.1000.



2-cyclohexenyl-4-fluoro-1-nitrobenzene (5.2.1-3aj)

Compound **5.2.1-3aj** was prepared following the general method from potassium 2-nitrobenzoate (**5.2.1-1a**) (124 mg, 0.6 mmol) and (*E*)-(2-bromovinyl)benzene (**5.2.1-2j**) (93 mg, 0.5 mmol) in a mixture of NMP (1 mL) and mesitylene (3 mL). Compound **5.2.1-3aj** was isolated by column chromatography as a yellow liquid (103 mg, 92%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.78-7.76 (m, 1H), 7.64-7.58 (m, 2H), 7.57-7.54 (m, 2H), 7.42-7.38 (m, 3H), 7.36-7.32 (m, 1H), 7.10 (d, *J* = 16.3, 1H);
^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.87, 138.38, 133.75, 133.01, 132.89, 128.72(2C), 128.52, 128.05, 127.86, 126.99(2C), 124.66, 123.37 ppm;
IR: *v* = 3076, 3022, 1603, 1570, 1532, 1449, 1345, 968, 859, 763, 699 cm^{-1};
MS (EI, 70 eV) *m/z* (%): 225 (2) [M+], 208 (33), 180 (26), 152 (23), 119 (88), 92 (100), 77 (32).
EI-HRMS *m/z* calcd. for $C_{14}H_{11}NO_2$: 225.0790, found: 225.0788.

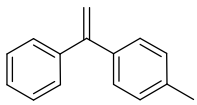
6.5.2 Branched arylalkenes from cinnamates: selectivity inversion in Heck reactions by carboxylates as deciduous directing groups

6.5.2.1 General procedure for the decarboxylative Mizoroki-Heck coupling

Method A: An oven-dried, nitrogen-flushed 20 mL crimp cap vessel was charged with $Pd(acac)_2$ (6.1 mg, 0.02 mmol, 2.0 mol%), (o-tol)$_3$P (15.7 mg, 0.05 mmol, 5.0 mol%), CuBr (14.6 mg, 0.10 mmol, 10.0 mol%), 1,10-phenanthroline (18.2 mg, 0.10 mmol, 10.0 mol%), and the potassium carboxylate (1.2 mmol, 1.2 equiv.). A degassed mixture of NMP and quinoline (1:1, 3.0 mL) and the aryl bromide (1.0 mmol, 1 equiv.) were added via syringe. The resulting solution was then stirred at 170 ºC for 16 h. After the reaction was complete, the mixture was cooled to room temperature, diluted with 1 N HCl (20 mL) and extracted with ethyl acetate (3 × 50 mL). The combined organic layers were washed with water and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (SiO_2, ethyl acetate/cyclohexane gradient) yielding the corresponding product.

Method B: An oven-dried, nitrogen-flushed 20 mL crimp cap vessel was charged with $Pd(acac)_2$ (3.1 mg, 0.01 mmol, 2.0 mol%), XPhos (12.3 mg, 0.025 mmol, 5.0 mol%), CuBr (7.3 mg, 0.05 mmol, 10.0 mol%), 1,10-phenanthroline (9.1 mg, 0.05 mmol, 10.0 mol%), and the potassium carboxylate (0.6 mmol, 1.2 equiv.). A degassed mixture of NMP and quinoline (1:1, 3.0 mL) and the aryl chloride (0.5 mmol, 1 equiv.) were added via syringe. The resulting solution was then stirred at 170 ºC for 16 h. After the reaction was complete, the mixture was cooled to room temperature, diluted with 1 N HCl (20 mL) and extracted with ethyl acetate (3 × 50 mL). The combined organic layers were washed with water and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (SiO_2, ethyl acetate/cyclohexane gradient) yielding the corresponding product.

6.5.2.2 Synthesis of 1,1-disubstituted alkenes

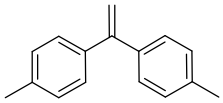


1-Methyl-4-(1-phenylvinyl)benzene (**5.2.2-3aa**) [CAS: 948-55-0]

Compound **5.2.2-3aa** was prepared following the general method A from potassium cinnamate (**5.2.2-1a**) (223 mg, 1.2 mmol) and 4-bromotoluene (**5.2.2-2a**) (175 mg, 126 µL, 1.0 mmol). **5.2.2-3aa** was isolated as a colorless liquid (178 mg, 92%).

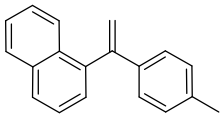
Compound **5.2.2-3aa** was prepared following the general method B from potassium cinnamate (**5.2.2-1a**) (112 mg, 0.6 mmol) and 4-chlorotoluene (**5.2.2-2a'**) (65 mg, 60 µL, 0.5 mmol). **5.2.2-3aa** was isolated as a colorless liquid (89 mg, 90%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.37-7.33 (m, 5H), 7.26 (d, J = 8.0 Hz, 2H), 7.16 (d, J = 9.0 Hz, 2H), 5.45 (d, J = 1.0 Hz, 1H), 5.43 (d, J = 1.3 Hz, 1H), 2.39 (s, 3H) ppm.
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 149.9, 141.7, 138.6, 137.5, 128.8, 128.3, 128.1, 128.1, 127.6, 113.6, 21.2 ppm.
IR: $\tilde{\nu}$ = 3086, 3053, 2924, 1659, 1606, 1509, 1492, 1327, 1028, 894, 825 cm^{-1}.
MS (EI, 70 eV) m/z (%): 194 (72) [M$^+$], 179 (100), 165 (8), 115 (9), 89 (5).
HRMS (EI-TOF) calcd. for $C_{15}H_{14}$: 194.1096; found: 194.1093.



4,4'-(Ethene-1,1-diyl)bis(methylbenzene) (**5.2.2-3ba**) [CAS: 2919-20-2]
Compound **5.2.2-3ba** was prepared following the general method A from potassium (*E*)-3-*p*-tolylacrylate (**5.2.2-1b**) (240 mg, 1.2 mmol) and 4-bromotoluene (**5.2.2-2a**) (175 mg, 126 µL, 1.0 mmol). **5.2.2-3ba** was isolated as a colorless liquid (188 mg, 90%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.26 (d, J = 8.0 Hz, 4H), 7.16 (d, J = 8.0 Hz, 4H), 5.40 (s, 2H), 2.39 (s, 6 H) ppm.
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 149.7, 138.8, 137.4, 128.8, 128.2, 113.0, 21.2 ppm.
IR: $\tilde{\nu}$ = 3028, 2922, 1725, 1654, 1607, 1511, 1312, 1277, 1177, 925 cm^{-1}.
MS (EI, 70 eV) m/z (%): 208 (99) [M$^+$], 193 (100), 178 (38), 115 (14), 89 (17).
HRMS (EI-TOF) calcd. for $C_{16}H_{16}$: 208.1252; found: 208.1250.



1-[1-(4-Methylphenyl)ethenyl]naphthalene (**5.2.2-3ca**) [CAS: 127236-58-2]
Compound **5.2.2-3ca** was prepared following the general method A from potassium (*E*)-3-(1-naphthalenyl)acrylate (**5.2.2-1c**) (284 mg, 1.2 mmol) and 4-bromotoluene (**5.2.2-2a**) (175 mg, 126 µL, 1.0 mmol). **5.2.2-3ca** was isolated as a colorless oil (142 mg, 58%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.87 (dd, J = 8.0, 5.2 Hz, 2H), 7.79 (d, J = 8.5 Hz, 1 H), 7.51 (dd, J = 8.0, 7.0 Hz, 1H), 7.48-7.42 (m, 2H), 7.34 (ddd, J = 8.3, 6.9, 1.5 Hz, 1H), 7.25-

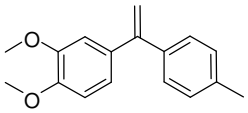
7.20 (m, 2H), 7.08 (d, *J* = 8.0 Hz, 2H), 5.96 (d, *J* = 1.5 Hz, 1H), 5.35 (d, *J* = 1.5 Hz, 1H), 2.33 (s, 3H) ppm.

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 148.0, 140.0, 138.2, 137.5, 133.6, 131.9, 129.1, 128.1, 127.8, 127.1, 126.5, 126.4, 125.8, 125.6, 125.4, 115.3, 21.1 ppm.

IR: $\tilde{\nu}$ = 3043, 2917, 1608, 1509, 1399, 896, 776 cm^{-1}.

MS (EI, 70 eV) m/z (%): 244 (100) [M$^+$], 243 (39), 229 (64), 228 (20), 152 (25), 91 (18).

HRMS (EI-TOF) calcd. for $C_{19}H_{16}$: 244.1252; found: 244.1260.



1,2-Dimethoxy-4-(1-*p*-tolylvinyl)benzene (**5.2.2-3da**) [CAS: 94752-74-6]

Compound **5.2.2-3da** was prepared following the general method A from potassium (*E*)-3-(3,4-dimethoxyphenyl)acrylate (**5.2.2-1d**) (275 mg, 1.2 mmol) and 4-bromotoluene (**5.2.2-2a**) (175 mg, 126 µL, 1.0 mmol). **5.2.2-3da** was isolated as a yellow solid (212 mg, 83%).

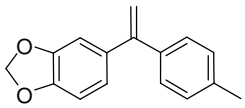
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.26 (d, *J* = 8.0 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 6.92-6.89 (m, 2H), 6.84 (d, *J* = 8.0 Hz, 1H), 5.37 (s, 2H), 3.91 (s, 3H), 3.85 (s, 3H), 2.38 (s, 3H) ppm.

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 149.5, 148.7, 148.5, 138.7, 137.5, 134.5, 128.8, 128.2, 120.8, 112.5, 111.4, 110.6, 55.9, 55.8, 21.2 ppm.

IR: $\tilde{\nu}$ = 3086, 2998, 2961, 2913, 2837, 1738, 1509, 1464, 1413, 1247, 1132, 1026, 899 cm^{-1}.

MS (EI, 70 eV) m/z (%): 254 (100) [M$^+$], 239 (29), 223 (12), 207 (8), 117 (11).

HRMS (EI-TOF) calcd. for $C_{17}H_{18}O_2$: 254.1207; found: 254.1306.



5-(1-*p*-Tolylvinyl)benzo[*d*][1,3]dioxole (**5.2.2-3ea**)

Compound **5.2.2-3ea** was prepared following the general method A from potassium (*E*)-3-(benzo[*d*][1,3]dioxol-5-yl)acrylate (**5.2.2-1e**) (230 mg, 1.2 mmol) and 4-bromotoluene (**5.2.2-2a**) (175 mg, 126 µL, 1.0 mmol). **5.2.2-3ea** was isolated as a colorless liquid (95 mg, 40%).

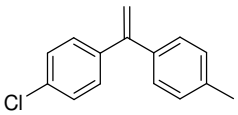
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.27-7.25 (m, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 6.88-6.83 (m, 2H), 6.79 (d, *J* = 8.0 Hz, 1H), 5.98 (s, 2H), 5.35 (d, *J* = 0.8 Hz, 2H), 2.39 (s, 3H) ppm.

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 149.4, 147.4, 147.2, 138.7, 137.5, 135.9, 128.8, 128.2, 122.0, 112.7, 108.7, 107.9, 101.0, 21.2 ppm.

IR: $\tilde{\nu}$ = 2894, 2776, 1725, 1652, 1603, 1501, 1485, 1436, 1230, 1034, 934 cm^{-1}.

MS (EI, 70 eV) m/z (%): 238 (100) [M$^+$], 223 (40), 193 (20), 180 (23), 165 (22), 63 (13).

HRMS (EI-TOF) calcd. for $C_{16}H_{14}O_2$: 238.0994; found: 238.0985.



1-Chloro-4-(1-*p*-tolylvinyl)benzene (5.2.2-3fa) [CAS: 69416-93-9]

Compound **5.2.2-3fa** was prepared following the general method A from potassium (*E*)-3-(4-chlorophenyl)acrylate (**5.2.2-1f**) (265 mg, 1.2 mmol) and 4-bromotoluene (**5.2.2-2a**) (175 mg, 126 µL, 1.0 mmol). **5.2.2-3fa** was isolated as a yellow liquid (152 mg, 67%).

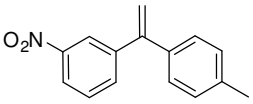
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.33-7.27 (m, 4H), 7.23-7.21 (m, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 5.45 (d, *J* = 1.3 Hz, 1H), 5.40 (d, *J* = 1.3 Hz, 1H), 2.39 (s, 3H) ppm.

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 148.8, 140.1, 138.1, 137.8, 133.5, 129.6, 128.9, 128.3, 128.1, 114.0, 21.2 ppm.

IR: $\tilde{\nu}$ = 3093, 3030, 2923, 2856, 1916, 1743, 1605, 1510, 1485, 1089, 1011, 897 cm^{-1}.

MS (EI, 70 eV) m/z (%): 230 (29) [M^+], 228 (100), 213 (23), 193 (63), 178 (57), 50 (13).

HRMS (EI-TOF) calcd. for $C_{15}H_{13}{}^{35}Cl$: 228.0706; found: 228.0697; $C_{15}H_{13}{}^{37}Cl$: 230.0676; found: 230.0699.



1-Nitro-3-(1-*p*-tolylvinyl)benzene (**5.2.2-3ga**) [CAS: 34564-93-7]

Compound **5.2.2-3ga** was prepared following the general method A from potassium (*E*)-3-(3-nitrophenyl)acrylate (**5.2.2-1g**) (277 mg, 1.2 mmol) and 4-bromotoluene (**5.2.2-2a**) (175 mg, 126 µL, 1.0 mmol). **5.2.2-3ga** was isolated as a yellow liquid (177 mg, 74%).

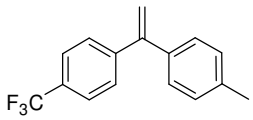
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.23 (t, *J* = 1.9 Hz, 1H), 8.18 (ddd, J = 8.0, 2.3, 1.0 Hz, 1H), 7.67 (dt, *J* = 7.7, 1.3 Hz, 1H), 7.51 (t, *J* = 8.0 Hz, 1H), 7.22-7.17 (m, 4H), 5.58 (d, *J* = 0.8 Hz, 1H), 5.52 (d, *J* = 0.8 Hz, 1H), 2.4 (s, 3H) ppm.

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 148.3, 148.0, 143.5, 138.3, 137.2, 134.2, 129.2, 129.1, 127.9, 123.0, 122.5, 115.8, 21.2 ppm.

IR: $\tilde{\nu}$ = 3084, 3047, 3027, 2920, 2863, 1744, 1510, 1346, 1084, 908 cm^{-1}.

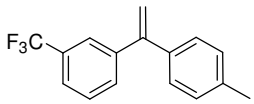
MS (EI, 70 eV) m/z (%): 239 (100) [M^+], 221 (16), 207 (14), 192 (20), 178 (27), 44 (43).

HRMS (EI-TOF) calcd. for $C_{15}H_{13}NO_2$: 239.0946; found: 239.0944.



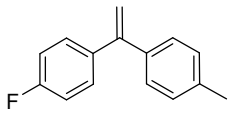
1-Methyl-4-(1-(4-(trifluoromethyl)phenyl)vinyl)benzene (**5.2.2-3ha**) [CAS: 1257310-40-9]
Compound **5.2.2-3ha** was prepared following the general method A from potassium (*E*)-3-(4-(trifluoromethyl)phenyl)acrylate (**5.2.2-1h**) (305 mg, 1.2 mmol) and 4-bromotoluene (**5.2.2-2a**) (175 mg, 126 µL, 1.0 mmol). **5.2.2-3ha** was isolated as a colorless liquid (215 mg, 82%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.61 (d, *J* = 8.3 Hz, 2H), 7.47 (d, *J* = 8.0 Hz, 2H), 7.24-7.17 (m, 4H), 5.55 (d, *J* = 0.8 Hz, 1H), 5.48 (d, *J* = 0.8 Hz, 1H), 2.40 (s, 3H) ppm.
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 148.8, 145.3, 137.96, 137.7, 129.6 (d, *J* = 33 Hz, 1C), 129.0, 128.6, 128.0, 125.1 (q, *J* = 3.7 Hz, 1C), 124.2 (d, *J* = 270 Hz, 1C), 115.2, 21.2 ppm.
^{19}F-NMR (400 MHz, $CDCl_3$): δ = -62.4 ppm.
IR: $\tilde{\nu}$ = 3028, 2970, 2925, 2875, 1741, 1614, 1509, 1320, 1164, 1124, 1110, 1060, 907, 855 cm^{-1}.
MS (EI, 70 eV) m/z (%): 262 (100) [M^+], 247 (48), 226 (13), 193 (29), 178 (29), 69 (10).
HRMS (EI-TOF) calcd. for $C_{16}H_{13}F_3$: 262.0969; found: 262.0979.



1-(1-*p*-Tolylvinyl)-3-(trifluoromethyl)benzene (**5.2.2-3ia**)
Compound **5.2.2-3ia** was prepared following the general method A from potassium (*E*)-3-(3-(trifluoromethyl)phenyl)acrylate (**5.2.2-1i**) (254 mg, 1.2 mmol) and 4-bromotoluene (**5.2.2-2a**) (175 mg, 126 µL, 1.0 mmol). **5.2.2-3ia** was isolated as a colorless solid (246 mg, 94%).

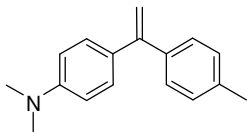
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.63 (s, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.46 (t, *J* = 8.0 Hz, 1H), 7.24-7.21 (m, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 5.54 (d, *J* = 1.0 Hz, 1H), 5.46 (d, *J* = 1.0 Hz, 1H), 2.40(s, 3H) ppm.
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 148.8, 142.5, 138.0, 137.7, 131.6 (d, *J* = 1.5 Hz, 1C), 130.59 (d, *J* = 31.0 Hz, 1C), 129.1, 128.6, 128.0, 125.0 (q, *J* = 3.7 Hz, 1C), 124.4 (q, *J* = 3.7 Hz, 1C), 122.8, 115.0, 21.2 ppm.
^{19}F NMR (400 MHz, $CDCl_3$): δ = -62.5 ppm.
IR: $\tilde{\nu}$ = 3012, 2925, 1735, 1511, 1439, 1312, 1338, 1296, 1165, 1149, 1119, 1069, 902 cm^{-1}.
MS (EI, 70 eV) m/z (%): 262 (100) [M^+], 247 (64), 193 (25), 178 (28), 69 (13).
HRMS (EI-TOF) calcd. for $C_{16}H_{13}F_3$: 262.0969; found: 262.0967.
m.p.: 66-67 °C.



1-Fluoro-4-(1-*p*-tolylvinyl)benzene (**5.2.2-3ja**) [CAS: 365-23-1]

Compound **5.2.2-3ja** was prepared following the general method A from potassium (*E*)-3-(4-fluorophenyl)acrylate (**5.2.2-1j**) (245 mg, 1.2 mmol) and 4-bromotoluene (**5.2.2-2a**) (175 mg, 126 µL, 1.0 mmol). **5.2.2-3ja** was isolated as a colorless liquid (156 mg, 74%).

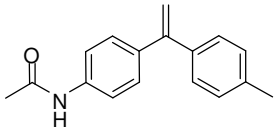
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.35-7.30 (m, 2H), 7.25-7.23 (m, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 7.06-7.00 (m, 2H), 5.43 (d, *J* = 1.3 Hz, 1H), 5.38 (d, *J* = 1.3 Hz, 1H), 2.39 (s, 3H) ppm.
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 163.7, 161.2, 148.9, 138.4, 137.7-137.7 (m, 1C), 129.9 (d, *J* = 8.0 Hz, 1C), 128.9, 128.1, 114.9 (d, *J* = 21.0 Hz, 1C), 113.5 (d, *J* = 2.0 Hz, 1C), 21.2 ppm.
^{19}F-NMR (400 MHz, $CDCl_3$): δ = -114.9 ppm.
IR: $\tilde{\nu}$ = 3047, 3027, 2924, 1659, 1601, 1506, 1222, 1157, 825 cm^{-1}.
MS (EI, 70 eV) m/z (%): 212 (100) [M^{+}], 211 (11), 197 (64), 196 (34), 177 (26), 50 (11).
HRMS (EI-TOF) calcd. for $C_{15}H_{13}F$: 212.1001; found: 212.0995.



***N*,*N*-Dimethyl-4-(1-*p*-tolylvinyl)aniline** (**5.2.2-3ka**) [CAS: 116330-41-7]

Compound **5.2.2-3ka** was prepared following the general method A from potassium (*E*)-3-(4-(dimethylamino)phenyl)acrylate (**5.2.2-1k**) (275 mg, 1.2 mmol) and 4-bromotoluene (**5.2.2-2a**) (175 mg, 126 µL, 1.0 mmol). **5.2.2-3ka** was isolated as a colorless liquid (196 mg, 82%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.30-7.25 (m, 4H), 7.17 (d, *J* = 8.0 Hz, 2H), 6.72 (d, *J* = 8.0 Hz, 2H), 5.36 (d, *J* = 1.5 Hz, 1H), 5.26 (d, *J* = 1.5 Hz, 1H), 2.99 (s, 6H), 2.40 (s, 3H) ppm.
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 150.1, 149.6, 139.3, 137.2, 129.0, 128.7, 128.3, 127.1, 111.9, 110.9, 40.5, 21.2 ppm.
IR: $\tilde{\nu}$ = 3082, 2891, 2807, 1742, 1611, 1520, 1443, 1362, 1230, 1199, 870 cm^{-1}.
MS (EI, 70 eV) m/z (%): 237 (100) [M^{+}], 222 (11), 178 (14), 44 (19).
HRMS (EI-TOF) calcd. for $C_{17}H_{19}N$: 237.1517; found: 237.1531.
m.p.:90-91 °C.



***N*-(4-(1-Tolylvinyl)phenyl)acetamide (5.2.2-3la)**

Compound **5.2.2-3la** was prepared following the general method A from potassium cinnamate (**5.2.2-1l**) (292 mg, 1.2 mmol) and 4-bromoacetanilide (**5.2.2-2a**) (175 mg, 126 µL, 1.0 mmol). **5.2.2-3la** was isolated as a colorless solid (204 mg, 81%).

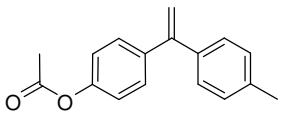
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.58 (br. s, 1H), 7.48 (d, J = 8.5 Hz, 2H), 7.30 (d, J = 8.5 Hz, 2H), 7.23 (d, J = 8.3 Hz, 2H), 7.15 (d, J = 7.8 Hz, 2H), 5.39 (s, 2H), 2.38 (S, 3H), 2.19 (s, 3H) ppm.

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 168.3, 149.2, 138.5, 137.6, 137.5, 137.3, 128.9, 128.8, 128.1, 119.5, 113.2, 24.6, 21.1 ppm.

IR: $\tilde{\nu}$ = 3291, 3029, 3922, 1736, 1658, 1591, 1528, 1369, 1314 cm^{-1}.

HRMS (EI-TOF) calcd. for $C_{17}H_{17}NO$: 251.1310; found: 251.1323.

m.p.: 125-126 °C.



1-Acetyloxy-4-(1-*p*-tolylvinyl)benzene (5.2.2-3ma)

Compound **5.2.2-3ma** was prepared following the general method A from potassium (*E*)-3-(4-acetyloxy)acrylate (**5.2.2-1m**) (293 mg, 1.2 mmol) and 4-bromotoluene (**5.2.2-2a**) (175 mg, 126 µL, 1.0 mmol). **5.2.2-3ma** was isolated as a colorless oil (57 mg, 23%).

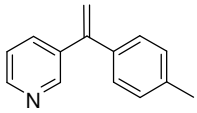
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.39-7.35 (m, 2H), 7.26 (d, J = 8.0 Hz, 2H), 7.17 (d, J = 8.0 Hz, 2H), 7.08-7.05 (m, 2H), 5.44 (d, J = 1.0 Hz, 1H), 5.41 (d, J = 1.0 Hz, 1H), 2.39 (s, 3H), 2.33 (s, 3H) ppm.

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 169.5, 150.2, 150.0, 139.3, 138.3, 137.6, 129.3, 128.9, 128.1, 121.2, 113.8, 21.1 (2C) ppm.

IR: $\tilde{\nu}$ = 3025, 2923, 1763, 1506, 1368, 1191, 1163, 1014, 909, 825 cm^{-1}.

MS (EI, 70 eV) m/z (%): 252 (34) [M^+], 210 (100), 207 (26), 195 (59), 44 (50), 43 (30), 40 (53).

HRMS (EI-TOF) calcd. for $C_{17}H_{16}O_2$: 252.1150; found: 252.1144.



3-(1-*p*-Tolylvinyl)pyridine (**5.2.2-3na**) [CAS: 857436-03-4]

Compound **5.2.2-3na** was prepared following the general method A from potassium (*E*)-3-(pyridin-3-yl)acrylate (**5.2.2-1n**) (225 mg, 1.2 mmol) and 4-bromotoluene (**5.2.2-2a**) (175 mg, 126 µL, 1.0 mmol). **5.2.2-3na** was isolated as a colorless liquid (140 mg, 72%).

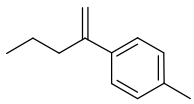
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.65 (s, 1H), 8.58 (d, *J* = 4.0 Hz, 1H), 7.63(dt, *J* = 8.0, 1.9 Hz, 1H), 7.29-7.26 (m, 1H), 7.24-7.22 (m, 2H), 7.19-7.17 (m, 2H), 5.56 (d, *J* = 0.8 Hz, 1H), 5.46 (d, *J* = 0.8 Hz, 1H), 2.39 (s, 3H) ppm.

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 149.2, 148.8, 146.7, 138.0, 137.4, 137.3, 135.6, 129.1, 127.8, 123.0, 115.1, 21.1 ppm.

IR: $\tilde{\nu}$ = 3085, 3026, 2921, 1609, 1565, 1510, 1473, 1412, 1021, 899, 824 cm^{-1}.

MS (EI, 70 eV) m/z (%): 195 (100) [M$^+$], 180 (70), 115 (14), 51 (20).

HRMS (EI-TOF) calcd. for $C_{14}H_{13}N$: 195.1049; found: 195.1047.



1-Methyl-4-(pent-1-en-2-yl)benzene (**5.2.2-3oa**) [CAS: 91176-31-7]

Compound **5.2.2-3oa** was prepared following the general method A from potassium (*E*)-hex-2-enoate (**5.2.2-1o**) (183 mg, 1.2 mmol) and 4-bromotoluene (**5.2.2-2a**) (175 mg, 126 µL, 1.0 mmol). **5.2.2-3oa** was isolated as a colorless liquid (130 mg, 81%).

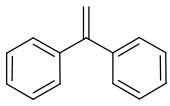
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.32 (d, *J* = 8.0 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 5.25 (s, 1H), 5.02 (s, 1H), 2.48 (t, *J* = 7.5 Hz, 2H), 2.36 (s, 3H), 2.40 (s, 3H), 1.53-1.44 (m, 2H), 0.93 (td, *J* = 7.4, 0.8 Hz, 3H) ppm.

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 148.2, 138.5, 136.9, 128.9, 126.0, 111.4, 37.4, 21.3, 21.1, 13.8 ppm.

IR: $\tilde{\nu}$ = 3085, 2959, 2930, 2872, 1739, 1626, 1513, 1455, 1377, 893 cm^{-1}.

MS (EI, 70 eV) m/z (%): 160 (18) [M$^+$], 145 (47), 132 (100), 117 (48), 115 (30), 91 (26).

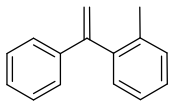
HRMS (EI-TOF) calcd. for $C_{12}H_{16}$: 160.1252; found: 160.1259.



1,1'-Ethenylidenebisbenzene (**5.2.2-3ab**) [CAS: 530-48-3]

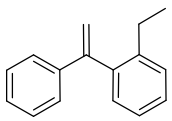
Compound **5.2.2-3ab** was prepared following the general method A from potassium cinnamate (**5.2.2-1a**) (223 mg, 1.2 mmol) and bromobenzene (**5.2.2-2b**) (159 mg, 106 µL, 1.0 mmol). **5.2.2-3ab** was isolated as a colorless liquid (132 mg, 73%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.40-7.30 (m, 10H), 5.51-45.47 (m, 2H) ppm.
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 150.0, 141.5, 128.2, 128.1, 127.7, 114.3 ppm.
IR: $\tilde{\nu}$ = 3080, 3056, 3029, 1610, 1574, 1492, 1444, 1328, 1027, 896 cm^{-1}.
MS (EI, 70 eV) m/z (%): 180 (100) [M^+], 179 (80), 178 (53), 165 (49), 73 (37), 50 (30), 44 (33).
HRMS (EI-TOF) calcd. for $C_{14}H_{12}$: 180.0939; found: 180.0942.



1-Methyl-2-(1-phenylvinyl)benzene (**5.2.2-3ac**) [CAS: 947-77-3]
Compound **5.2.2-3ac** was prepared following the general method A from potassium cinnamate (**5.2.2-1a**) (223 mg, 1.2 mmol) and 2-bromotoluene (**5.2.2-2c**) (171 mg, 120 µL, 1.0 mmol). **5.2.2-3ac** was isolated as a colorless liquid (86 mg, 44%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 9.30-9.17 (m, 9H), 5.77 (d, J = 1.3 Hz, 1H), 5.20 (d, J = 1.3 Hz, 1H) ppm.
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 149.4, 141.6, 140.6, 136.1, 130.04, 130.0, 128.3, 127.53, 127.5, 126.4, 125.7, 114.9, 20.1 ppm.
IR: $\tilde{\nu}$ = 3058, 3022, 2923, 1614, 1494, 1445, 1028, 901 cm^{-1}.
MS (EI, 70 eV) m/z (%): 194 (17) [M^+], 179 (100), 178 (56), 115 (15), 89 (14), 51 (15), 50 (18).
HRMS (EI-TOF) calcd. for $C_{15}H_{14}$: 194.1096; found: 194.1088.



1-Ethyl-2-(1-phenylvinyl)benzene (**5.2.2-3ad**) [CAS: 859315-62-1]
Compound **5.2.2-3ad** was prepared following the general method A from potassium cinnamate (**5.2.2-1a**) (223 mg, 1.2 mmol) and 1-bromo-2-ethylbenzene (**5.2.2-2d**) (227 mg, 170 µL, 1.0 mmol). **5.2.2-3ad** was isolated as a colorless liquid (120 mg, 57%).

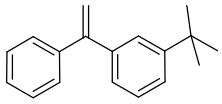
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.35-7.21 (m, 9H), 5.80 (d, J = 1.3 Hz, 1H), 5.23 (d, J = 1.3 Hz, 1H), 2.44 (q, J = 7.5 Hz, 2H), 1.06 (t, J = 7.5 Hz, 3H) ppm.

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 149.1, 142.1, 141.1, 140.8, 130.2, 128.4, 128.2, 127.7, 127.6, 126.5, 125.6, 114.9, 26.3, 15.2 cm^{-1}.

IR: $\tilde{\nu}$ = 3024, 2970, 2927, 2873, 1738, 1615, 1322, 1166, 1112, 1062, 905, 854 cm^{-1}.

MS (EI, 70 eV) m/z (%): 208 (100) [M$^+$], 193 (79), 178 (28), 130 (24), 115 (48), 44 (32).

HRMS (EI-TOF) calcd. for $C_{16}H_{16}$: 208.1252; found: 208.1245.



1-*tert*-Butyl-3-(1-phenylvinyl)benzene (**5.2.2-3ae**) [CAS: 1459147-48-8]

Compound **5.2.2-3ae** was prepared following the general method A from potassium cinnamate (**5.2.2-1a**) (223 mg, 1.2 mmol) and 1-bromo-3-*tert*-butylbenzene (**5.2.2-2e**) (213 mg, 170 µL, 1.0 mmol). **5.2.2-3ae** was isolated as a yellow liquid (212 mg, 90%).

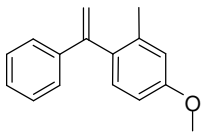
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.41-7.33 (m, 7H), 7.29 (t, *J* = 8.0 Hz, 1H), 7.15 (dd, *J* = 7.5, 1.0 Hz, 1H), 5.49 (s, 1H), 5.47 (s, 1H), 1.33 (s, 9H) ppm.

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 151.0, 150.4, 141.5, 141.08, 128.2, 128.1, 127.8, 127.6, 125.6, 125.3, 124.7, 114.0, 34.7, 31.3 ppm.

IR: $\tilde{\nu}$ = 3052, 3025, 2962, 1598, 1493, 1364, 1259, 890, 800, 776 cm^{-1}.

MS (EI, 70 eV) m/z (%): 236 (34) [M$^+$], 221 (100), 103 (26), 77 (7).

HRMS (EI-TOF) calcd. for $C_{18}H_{20}$: 236.1565; found: 236.1567.



4-Methoxy-2-methyl-1-(1-phenylvinyl)benzene (**5.2.2-3af**) [CAS: 24890-56-0]

Compound **5.2.2-3af** was prepared following the general method A from potassium cinnamate (**5.2.2-1a**) (223 mg, 1.2 mmol) and 2-bromo-5-methoxytoluene (**5.2.2-2f**) (207 mg, 228 µL, 1.0 mmol). **5.2.2-3af** was isolated as yellow liquid (213 mg, 95%).

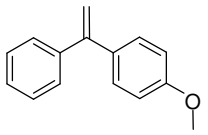
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.31-7.25 (m, 5H), 7.17 (d, *J* = 7.8 Hz, 1H), 6.80-6.77 (m, 2H), 5.75 (d, *J* = 1.5 Hz, 1H), 5.20 (d, *J* = 1.3 Hz, 1H), 3.85 (s, 2H), 2.05 (s, 3H) ppm.

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 158.9, 149.1, 141.0, 137.6, 134.2, 131.1, 128.3, 127.5, 126.5, 115.6, 114.9, 110.7, 55.2, 20.5 ppm.

IR: $\tilde{\nu}$ = 3083, 3025, 2953, 2834, 1605, 1572, 1498, 1444, 1293, 1238, 1163, 1040, 899, 807, 777 cm^{-1}.

MS (EI, 70 eV) m/z (%): 224 (100) [M+], 209 (95), 192 (13).

HRMS (EI-TOF) calcd. for $C_{16}H_{16}O$: 224.1201; found: 224.1211.



1-Methoxy-4-(1-phenylvinyl)benzene (**5.2.2-3ag**) [CAS: 4333-75-9]

Compound **5.2.2-3ag** was prepared following the general method A from potassium cinnamate (**5.2.2-1a**) (223 mg, 1.2 mmol) and 4-bromoanisole (**5.2.2-2g**) (189 mg, 127 µL, 1.0 mmol). **5.2.2-3ag** was isolated as a colorless solid (184 mg, 87%).

Compound **5.2.2-3ag** was prepared following the general method B from potassium cinnamate (**5.2.2-1a**) (112 mg, 0.6 mmol) and 4-chloroanisole (**5.2.2-2g'**) (73 mg, 63 µL, 0.5 mmol). **5.2.2-3ag** was isolated as a colorless solid (80 mg, 76%).

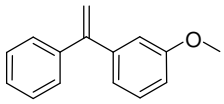
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.38-7.32 (m, 5H), 7.31-7.28 (m, 2H), 6.90-6.87 (m, 2H), 5.42 (d, J = 1.3 Hz, 1H), 5.37 (d, J = 1.3 Hz, 1H), 3.84 (s, 3H) ppm.

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 159.3, 149.5, 141.8, 136.0, 129.4, 128.3, 128.1, 127.6, 113.5, 112.9, 55.3 ppm.

IR: $\tilde{\nu}$ = 3095, 3031, 3005, 2952, 2835, 1737, 1598, 1505, 1242, 1177, 1026, 900, 840 cm^{-1}.MS (EI, 70 eV) m/z (%):

HRMS (EI-TOF) calcd. for $C_{15}H_{14}O$: 210.1045; found: 210.1039.

m.p.: 74-75 °C.



1-Methoxy-3-(1-phenylvinyl)benzene (**5.2.2-3ah**) [CAS: 34564-79-9]

Compound **5.2.2-3ag** was prepared following the general method A from potassium cinnamate (**5.2.2-1a**) (223 mg, 1.2 mmol) and 3-bromoanisole (**5.2.2-2h**) (191 mg, 129 µL, 1.0 mmol). **5.2.2-3ah** was isolated as a yellow liquid (170 mg, 81%).

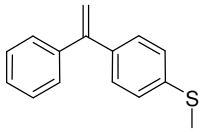
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.37-7.32 (m, 5H), 7.27 (t, J = 8.0 Hz, 1H), 6.94 (d, J = 7.5 Hz, 1H), 6.91-6.87 (m, 2H), 5.48(s, 2H), 3.81 (s, 3H) ppm.

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 159.4, 149.9, 143.0, 141.3, 129.1, 128.2, 128.1, 127.7, 120.9, 114.4, 113.9, 113.2, 55.2 ppm.

IR: $\tilde{\nu}$ = 3055, 3002, 2937, 2834, 1738, 1596, 1574, 1485, 1283, 1226, 1040, 893, 774 cm^{-1}.

MS (EI, 70 eV) m/z (%):

HRMS (EI-TOF) calcd. for $C_{15}H_{14}O$: 210.1045; found: 210.1040.



Methyl(4-(1-phenylvinyl)phenyl)sulfane (**5.2.2-3ai**) [CAS: 138534-58-4]

Compound **5.2.2-3ai** was prepared following the general method A from potassium cinnamate (**5.2.2-1a**) (223 mg, 1.2 mmol) and 4-bromothioanisole (**5.2.2-2i**) (207 mg, 1.0 mmol). **5.2.2-3ai** was isolated as a yellow liquid (146 mg, 64%).

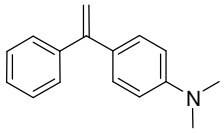
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.35-7.33 (m, 5H), 7.29-7.26 (m, 2H), 7.23-7.20 (m, 2H), 5.45 (d, J = 1.0 Hz, 1H), 5.42 (d, J = 1.0 Hz, 1H), 2.51 (s, 3H) ppm.

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 149.4, 141.4, 138.2, 138.0, 128.6, 128.3, 128.2, 127.7, 126.1, 113.87, 15.7 ppm.

IR: $\tilde{\nu}$ = 3091, 3017, 2921, 1741, 1590, 1489, 1392, 1078, 901, 830 cm^{-1}.

MS (EI, 70 eV) m/z (%): 226 (100) [M^+], 211 (10), 179 (31).

HRMS (EI-TOF) calcd. for $C_{15}H_{14}S$: 226.0816; found: 226.0757.



***N*,*N*-Dimethyl-4-(1-phenylethenyl)benzenamine** (**5.2.2-3aj**) [CAS: 22057-80-3]

Compound **5.2.2-3aj** was prepared following the general method A from potassium cinnamate (**5.2.2-1a**) (223 mg, 1.2 mmol) and 1-bromo-*N*,*N*-dimethylaniline (**5.2.2-2j**) (204 mg, 1.0 mmol). **5.2.2-3aj** was isolated as a yellow liquid (184 mg, 82%).

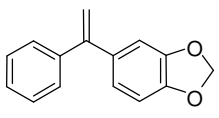
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.41-7.31 (m, 5 H), 7.28-7.24 (m, 2H), 6.71 (d, J = 8.0 Hz, 2 H), 5.40 (d, J = 1.3 Hz, 1 H), 5.27 (d, J = 1.3 Hz, 1 H), 2.99 (s, 6H) ppm.

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 150.2, 149.8, 142.2, 129.4, 129.0, 128.4, 128.0, 127.4, 111.9, 111.4, 40.5 ppm.

IR: $\tilde{\nu}$ = 3084, 3023, 2884, 2851, 2801, 1742, 1604, 1519, 1443, 1350, 1198, 946 cm^{-1}.

MS (EI, 70 eV) m/z (%): 223 (100) [M^+], 208 (25), 179 (8), 102 (7).

HRMS (EI-TOF) calcd. for $C_{16}H_{17}N$: 223.1361; found: 223.1364.

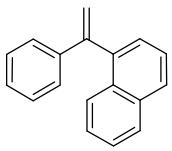


5-(1-Phenylethenyl)benzo[*d*][1,3]dioxole (**5.2.2-3ak**) [CAS: 51003-88-4]

Compound **5.2.2-3ak** was prepared following the general method A from potassium cinnamate (**5.2.2-1a**) (223 mg, 1.2 mmol) and 1-bromo-3,4-(methylenedioxy)benzene (**5.2.2-2k**) (207 mg, 124 µL, 1.0 mmol). **5.2.2-3ak** was isolated as a colorless liquid (192 mg, 86%).

Compound **5.2.2-3ak** was prepared following the general method B from potassium cinnamate (**5.2.2-1a**) (112 mg, 0.6 mmol) and 1-chloro-3,4-(methylenedioxy)benzene (**5.2.2-2k'**) (80 mg, 60 µL, 0.5 mmol). **5.2.2-3ak** was isolated as a colorless liquid (100 mg, 88%).

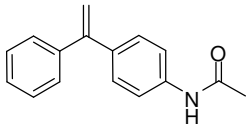
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.36-7.31 (m, 5H), 6.85-6.82 (m, 2H), 6.79 (d, J = 8.0 Hz, 1H), 5.98 (s, 2H), 5.40 (d, J = 1.0 Hz, 1H), 5.37 (d, J = 1.0 Hz, 1H) ppm.
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 149.6, 147.5, 147.2, 141.6, 135.7, 128.3, 128.1, 127.7, 122.0, 113.4, 108.6, 107.9, 101.1ppm.
IR: $\tilde{\nu}$ = 3024, 2887, 2778, 1485, 1439, 1231, 1097, 937, 917 cm^{-1}.
MS (EI, 70 eV) m/z (%): 224 (100) [M^+], 223 (18), 209 (17), 193 (14), 166 (22), 1645 (33).
HRMS (EI-TOF) calcd. for $C_{15}H_{12}O_2$: 224.0837; found: 224.0855.



1-(1-Phenylvinyl)naphthalene (**5.2.2-3al**) [CAS: 28358-65-8]
Compound **5.2.2-3al** was prepared following the general method A from potassium cinnamate (**5.2.2-1a**) (223 mg, 1.2 mmol) and 1-bromonaphthalene (**5.2.2-2l**) (211 mg, 142 µL, 1.0 mmol). **5.2.2-3al** was isolated as a yellow liquid (152 mg, 66%).

Compound **5.2.2-3al** was prepared following the general method B from potassium cinnamate (**5.2.2-1a**) (112 mg, 0.6 mmol) and 1-chloronaphthalene (**5.2.2-2l'**) (90 mg, 76 µL, 0.5 mmol). **5.2.2-3al** was isolated as a yellow liquid (47 mg, 40%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.87 (dd, J = 8.0, 4.0 Hz, 2H), 7.77 (d, J = 8.5 Hz, 1H), 7.52 (t, J = 8.0 Hz, 1H), 7.47-7.42 (m, 2H), 7.36-7.31 (m, 3H), 7.29-7.25 (m, 3H), 6.00 (d, J = 1.3 Hz, 1H), 5.41 (d, J = 1.3 Hz, 1H) ppm.
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 148.23, 141.02, 139.76, 133.65, 131.82, 128.35, 128.15, 127.92, 127.67, 127.21, 126.60, 126.40, 125.84, 125.65, 125.41, 116.23 ppm.
IR: $\tilde{\nu}$ = 3077, 3050, 3030, 2923, 2855, 1610, 1491, 1339, 1023, 906, 805 cm^{-1}.
MS (EI, 70 eV) m/z (%): 230 (100) [M^+], 228 (26), 207 (33), 152 (36), 44 (78).
HRMS (EI-TOF) calcd. for $C_{18}H_{14}$: 230.1096; found: 230.1082.



***N*-(4-(1-Phenylvinyl)phenyl)acetamide** (**5.2.2-3am**) [CAS: 22101-32-2]

Compound **5.2.2-3am** was prepared following the general method A from potassium cinnamate (**5.2.2-1a**) (223 mg, 1.2 mmol) and 4-bromoacetanilide (**5.2.2-2m**) (218 mg, 1.0 mmol). **5.2.2-3am** was isolated as a colorless solid (218 mg, 92%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.82 (br. s, 1H), 7.49 (d, J = 8.0 Hz, 2H), 7.33-7.29 (m, 7H), 5.42 (d, J = 8.0 Hz, 2H), 2.19 (s, 3H) ppm.

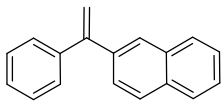
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 168.6, 149.3, 141.4, 137.4, 137.4, 128.7, 128.2, 128.1, 127.7, 119.6, 113.8, 24.5 ppm.

IR: $\tilde{\nu}$ = 3299, 3179, 3106, 3032, 2971, 1739, 1666, 1594, 1537, 1506, 1491, 1399, 1373, 1314, 1258, 1009, 897 cm^{-1}.

MS (EI, 70 eV) m/z (%): 237 (85) [M$^+$], 195 (100), 180 (65), 178 (15), 165 (17), 152 (11).

HRMS (EI-TOF) calcd. for $C_{16}H_{15}NO$: 237.1154; found: 237.1155.

m.p.: 119-120 °C.



2-[1-(Phenylethenyl]naphthalene (**5.2.2-3an**) [CAS: 28358-66-9]

Compound **5.2.2-3an** was prepared following the general method A from potassium cinnamate (**5.2.2-1a**) (223 mg, 1.2 mmol) and 2-bromonaphthalene (**5.2.2-2n**) (209 mg, 1.0 mmol). **5.2.2-3an** was isolated as a colorless oil (165 mg, 83%).

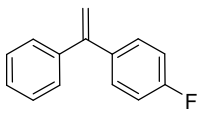
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.88-7.82 (m, 4H), 7.52-7.48 (m, 3H), 7.43-7.37 (m, 5H), 5.62 (s, 1H), 5.58 (s, 1H) ppm.

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 150.0, 141.5, 138.9, 133.3, 132.9, 128.4, 128.2, 128.2, 127.8, 127.7, 127.6, 127.3, 126.4, 126.1, 126.0, 114.8 ppm.

IR: $\tilde{\nu}$ = 3051, 3022, 1505, 1490, 901, 825 cm^{-1}.

MS (EI, 70 eV) m/z (%): 230 (100) [M$^+$], 229 (41), 228 (24), 215 (46), 51 (18), 44 (18).

HRMS (EI-TOF) calcd. for $C_{18}H_{14}$: 230.1096; found: 230.1077.

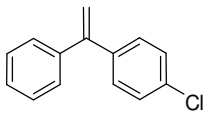


1-Fluoro-4-(1-phenylvinyl)benzene (**5.2.2-3ao**) [CAS: 395-21-1]

Compound **5.2.2-3ao** was prepared following the general method A from potassium cinnamate (**5.2.2-1a**) (223 mg, 1.2 mmol) and 4-bromofluorobenzene (**5.2.2-2o**) (177 mg, 111 µL, 1.0 mmol). **5.2.2-3ao** was isolated as a colorless liquid (182 mg, 92%).

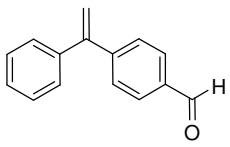
Compound **5.2.2-3ao** was prepared following the general method B from potassium cinnamate (**5.2.2-1a**) (112 mg, 0.6 mmol) and 4-chlorofluorobenzene (**5.2.2-2o'**) (67 mg, 54 µL, 0.5 mmol). **5.2.2-3ao** was isolated as a colorless liquid (79 mg, 80%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.39-7.30 (m, 7H), 7.04 (tt, J = 8.0, 4.0 Hz, 2H), 5.46 (d, J = 1.0 Hz, 1H), 5.43 (d, J = 1.0 Hz, 1H) ppm.
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 163.7, 161.3, 149.0, 141.3, 137.5, 129.9 (d, J = 8.1 Hz, 2C), 128.2 (d, J = 8.1 Hz, 2C), 127.9, 115.0 (d, J = 21.0 Hz, 2C), 114.2 (d, J = 1.5 Hz, 1C) ppm.
^{19}F NMR (400 MHz, $CDCl_3$): δ = -114.7 ppm.
IR: $\tilde{\nu}$ = 3047, 2926, 2854, 1737, 1601, 1504, 1222, 1158, 897, 840 cm^{-1}.
MS (EI, 70 eV) m/z (%): 198 (100) [M^+], 182 (63), 177 (25), 51 (15).
HRMS (EI-TOF) calcd. for $C_{14}H_{11}F$: 198.0845; found: 198.0843.



1-Chloro-4-(1-phenylethenyl)benzene (**5.2.2-3ap**) [CAS: 18218-20-7]
Compound **5.2.2-3ap** was prepared following the general method A from potassium cinnamate (**5.2.2-1a**) (223 mg, 1.2 mmol) and 1-bromo-4-chlorobenzene (**5.2.2-2p**) (191 mg, 116 µL, 1.0 mmol). **5.2.2-3ap** was isolated as a colorless liquid (150 mg, 70%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.40-7.25 (m, 9H), 5.47 (s, 1H), 5.46 (s, 1H) ppm.
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 149.0, 141.0, 139.9, 133.6, 129.5, 128.33, 128.26, 128.17, 127.9, 144.7 ppm.
IR: $\tilde{\nu}$ = 3056, 3028, 2971, 1739, 1661, 1598, 1487, 1445, 1366, 1229, 1217, 1090, 1012 cm^{-1}.
MS (EI, 70 eV) m/z (%): 216 (23) [M^+], 214 (78), 199 (11), 179 (100), 152 (10).
HRMS (EI-TOF) calcd. for $C_{14}H_{11}{}^{35}Cl$: 214.0549; found: 214.0543; $C_{14}H_{11}{}^{37}Cl$: 216.0520; found: 216.0524.

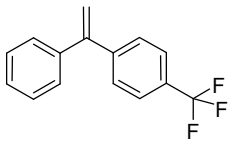


4-(1-Phenylvinyl)benzaldehyde (**5.2.2-3aq**) [CAS: 389582-37-0]

Compound **5.2.2-3aq** was prepared following the general method A from potassium cinnamate (**5.2.2-1a**) (223 mg, 1.2 mmol) and 4-bromobenzaldehyd (**5.2.2-2q**) (187 mg, 1.0 mmol). **5.2.2-3aq** was isolated as a colorless solid (126 mg, 60%).

Compound **5.2.2-3aq** was prepared following the general method B from potassium cinnamate (**5.2.2-1a**) (112 mg, 0.6 mmol) and 4-chlorobenzaldehyd (**5.2.2-2q'**) (70 mg, 59 µL, 0.5 mmol). **5.2.2-3aq** was isolated as a colorless solid (60 mg, 58%).

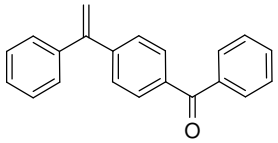
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 10.04 (s, 1H), 7.87 (dt, J = 8.0, 4.0 Hz, 2H), 7.52 (dd, J = 8.0, 4.0 Hz, 2H), 7.40-7.30 (m, 5H), 5.60 (dd, J = 4.8, 0.8 Hz, 2H) ppm.
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 191.9, 149.1, 147.6, 140.5, 135.6, 129.7, 128.6, 128.4, 128.2, 128.1, 116.5 ppm.
IR: $\tilde{\nu}$ = 3050, 2833, 2740, 1696, 1602, 1562, 1488, 1208, 913 cm^{-1}.
MS (EI, 70 eV) m/z (%): 237 (85) [M^+], 195 (100), 180 (65), 178 (15), 165 (17), 152 (11).
HRMS (EI-TOF) calcd. for $C_{15}H_{12}O$: 208.0888; found: 208.0883.
m.p.: 54-55 °C.



1-(1-Phenylethenyl)-4-(trifluoromethyl)benzene (**5.2.2-3ar**) [CAS: 345-88-0]
Compound **5.2.2-3ar** was prepared following the general method A from potassium cinnamate (**5.2.2-1a**) (223 mg, 1.2 mmol) and 1-bromo-4-(trifluoromethyl)benzene (**5.2.2-2r**) (227 mg, 142 µL, 1.0 mmol). **5.2.2-3ar** was isolated as a colorless oil (155 mg, 62%).

Compound **5.2.2-3ar** was prepared following the general method B from potassium cinnamate (**5.2.2-1a**) (112 mg, 0.6 mmol) and 1-chloro-4-(trifluoromethyl)benzene (**5.2.2-2r'**) (92 mg, 68 µL, 0.5 mmol). **5.2.2-3ar** was isolated as a colorless oil (80 mg, 65%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.61 (d, J = 8.3 Hz, 2H), 7.47 (d, J = 8.3 Hz, 2H), 7.40-7.31 (m, 5H), 5.58 (s, 1H), 5.53 (s, 1H) ppm.
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 149.0, 145.1, 140.6, 129.7 (q, J = 32 Hz, 1C), 128.5, 128.4, 128.1, 128.1, 125.2 (q, J = 3.7 Hz, 1C), 124.2 (q, J = 270 Hz, 1C), 115.9 ppm.
^{19}F-NMR (400 MHz, $CDCl_3$): δ = -62.5 ppm.
IR: $\tilde{\nu}$ = 3057, 2926, 2856, 1740, 1616, 1319, 1164, 1121, 1063, 1016, 905, 850 cm^{-1}.
MS (EI, 70 eV) m/z (%): 248 (100) [M^+], 233 (32), 227 (15), 179 (76), 151 (7).
HRMS (EI-TOF) calcd. for $C_{15}H_{11}F_3$: 248.0813; found: 248.0791.



Phenyl(4-(1-phenylvinyl)phenyl)methanone (**5.2.2-3as**) [CAS: 682748-25-0]

Compound **5.2.2-3as** was prepared following the general method A from potassium cinnamate (**5.2.2-1a**) (223 mg, 1.2 mmol) and 4-bromobenzophenone (**5.2.2-2s**) (269 mg, 1.0 mmol). **5.2.2-3as** was isolated as a yellow solid (188 mg, 66%).

Compound **5.2.2-3as** was prepared following the general method B from potassium cinnamate (**5.2.2-1a**) (112 mg, 0.6 mmol) and 4-chlorobenzophenone (**5.2.2-2s'**) (109 mg, 0.5 mmol). **5.2.2-3as** was isolated as a yellow solid (89 mg, 63%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.86-7.83 (m, 2H), 7.81 (dt, J = 8.0, 4.0 Hz, 2H), 7.63-7.59 (m, 1H), 7.53-7.46 (m, 4H), 7.41-7.34 (m, 5H), 5.59 (s, 2H) ppm.

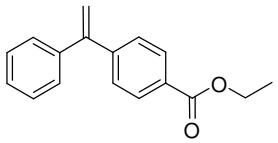
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 196.3, 149.3, 145.6, 140.7, 137.6, 136.7, 132.4, 130.1, 123.0, 128.3, 128.3, 128.2, 128.1, 128.0, 115.9 ppm.

IR: $\tilde{\nu}$ = 3096, 3050, 3029, 1648, 1595, 1442, 1311, 1274, 905, 859 cm^{-1}.

MS (EI, 70 eV) m/z (%): 284 (100) [M^+], 207 (69), 178 (17), 105 (24), 77 (25).

HRMS (EI-TOF) calcd. for $C_{21}H_{16}O$: 284.1201; found: 284.1199.

m.p.: 73-74 °C.



Ethyl 4-(1-phenylvinyl)benzoate (**5.2.2-3at**) [CAS: 679390-82-0]

Compound **5.2.2-3at** was prepared following the general method A from potassium cinnamate (**5.2.2-1a**) (223 mg, 1.2 mmol) and Ethyl 4-bromobenzoate (**5.2.2-2t**) (232 mg, 162 µL, 1.0 mmol). **5.2.2-3at** was isolated as a yellow liquid (126 mg, 50%).

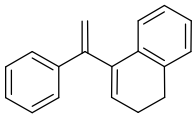
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.02 (dt, J = 8.0, 4.0 Hz, 2H), 7.42 (dt, J = 8.0, 4.0 Hz, 2H), 7.38-7.31 (m, 5H), 5.55 (dd, J = 5.5, 0.8 Hz, 2H), 4.40 (q, J = 7.0 Hz, 2H), 1.41 (t, J = 7.2 Hz, 3H) ppm.

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 166.4, 149.3, 145.9, 140.8, 129.7, 129.5, 128.3, 128.2, 128.0, 60.9, 14.3 ppm.

IR: $\tilde{\nu}$ = 3091, 3029, 2990, 2934, 1703, 1605, 1367, 1271, 1178, 1104, 1017, 907, 866, 777 cm^{-1}.

MS (EI, 70 eV) m/z (%): 252 (65) [M^+], 240 (41), 224 (21), 207 (100), 180 (30), 163 (40), 105 (49).

HRMS (EI-TOF) calcd. for $C_{17}H_{16}O_2$: 252.1150; found: 252.1159.



4-(1-Phenylvinyl)-1,2-dihydronaphthalene (**5.2.2-3au**)

Compound **5.2.2-3au** was prepared following the general method A from potassium cinnamate (**5.2.2-1a**) (223 mg, 1.2 mmol) and 4-bromo-1,2-dihydronaphthalene (**5.2.2-2u**) (209 mg, 1.0 mmol). **5.2.2-3au** was isolated as a colorless oil (93 mg, 40%) along with the approximate 5% of the s-cis isomer.

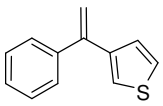
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.46-7.43 (m, 2H), 7.30-7.22 (m, 3H), 7.16 (d, J = 4.0 Hz, 2H), 7.08 (td, J = 7.3 Hz, 1H), 7.01 (td, J = 7.5 Hz, 1H), 6.93 (d, J = 8.0 Hz, 1H), 6.16 (t, J = 4.6 Hz, 1H), 5.66 (d, J = 1.8 Hz, 1H), 5.36 (d, J = 1.8 Hz, 1H), 2.89 (t, J = 8.0 Hz, 1H), 2.45-2.40 (m, 2H) ppm.

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 148.5, 140.0, 139.5, 136.1, 134.3, 128.7, 128.3, 127.6, 127.4, 126.7, 126.6, 126.3, 125.6, 114.8, 28.2, 23.4 ppm.

IR: $\tilde{\nu}$ = 3057, 3024, 2932, 2882, 2829, 14 93, 1484, 1446, 1022, 899 cm^{-1}.

MS (EI, 70 eV) m/z (%): 232.0 (100) [M^+], 231.1 (24), 217.1 (32), 128.0 (22), 77.0 (15), 51.0 (13).

HRMS (EI-TOF) calcd. for $C_{18}H_{16}$: 232.1252; found: 232.1259.



3-(1-Phenylethenyl)-thiophen (**5.2.2-3av**) [CAS: 75488-46-9]

Compound **5.2.2-3av** was prepared following the general method A from potassium cinnamate (**5.2.2-1a**) (223 mg, 1.2 mmol) and 3-bromothiophene (**5.2.2-2v**) (168 mg, 97 µL, 1.0 mmol). **5.2.2-3av** was isolated as a colorless oil (55 mg, 29%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.43-7.34 (m, 5H), 7.33-7.30 (m, 1H), 7.21-7.18 (m, 1H), 7.15-7.13 (m, 1H), 5.55 (d, J = 1.3 Hz, 1H), 5.35 (d, J = 1.3 Hz, 1H) ppm.

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 144.5, 142.5, 141.5, 128.2, 128.1, 127.8, 127.2, 125.4, 123.3, 113.4 ppm.

IR: $\tilde{\nu}$ = 3104, 3058, 3023, 1607, 1492, 1444, 1302, 1081, 1027, 891 cm^{-1}.

MS (EI, 70 eV) m/z (%):186.0 (100) [M^+], 185.1 (63), 184.2 (27), 171.1 (34), 50.0 (21) 44.9 (18).

HRMS (EI-TOF) calcd. for $C_{12}H_{10}S$: 186.0503; found: 186.0501.

6.5.2.3 Procedure for the one-pot three-step process

An oven-dried, nitrogen-flushed 20 mL crimp cap vessel was charged with $Pd(acac)_2$ (3.1 mg, 0.01 mmol, 2.0 mol%), (*o*-tol)$_3$P (7.8 mg, 0.025 mmol, 5.0 mol%) and potassium acetate (32.7 mg. 0.6 mmol). A degassed mixture of NMP and quinoline (1:1, 2.0 mL), bromobenzene (79.3 mg, 53 µL, 0.5 mmol) and methyl acrylate (43.5 mg, 46 µL, 0.5 mmol) were added *via* syringe. The resulting mixture was then stirred at 150 ºC for 16 h. After the reaction was complete, the mixture was cooled to room temperature. The vessel was opened inside a glove box and potassium *tert*-butoxide (137 mg, 1.1 mmol) was added. Outside the glove box water (10 mg, 10 µL, 0.55 mmol) was added *via* syringe. The resulting mixture was then stirred at 100 ºC for 2 h. After the reaction was complete, the mixture was cooled to room temperature. A degassed solution of $Pd(acac)_2$ (3.1 mg, 0.01 mmol, 2.0 mol%), P(*o*-Tol)$_3$ (7.8 mg, 0.025 mmol, 5.0 mol%), CuBr (7.3 mg, 0.05 mmol, 10.0 mol%), 1,10-phenanthroline (9.1 mg, 0.05 mmol, 10.0 mol%) in a mixture of NMP and quinoline (1:1, 1.0 mL) and 4-bromotoluene (**2a**) (85.5 mg, 62 µL, 0.5 mmol) were added *via* syringe. The resulting mixture was then stirred at 170 ºC for 16 h. After the reaction was complete, the mixture was cooled to room temperature, diluted with 1 N HCl (20 mL) and extracted with ethyl acetate (3 × 50 mL). The combined organic layers were washed with water and brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by column chromatography (SiO_2, ethyl acetate/cyclohexane gradient) yielding **5.2.2-3aa** as a colorless liquid (60 mg, 62%).

7. Curriculum vitae

Jie Tang

Education

11. 2012 - 12.2016	PhD in Organic Chemistry, TU Kaiserslautern under the supervision of Prof. Dr. Lukas. J. Gooßen.
09. 2007 - 07. 2010	M.S. in Applied Chemistry, under the supervision of Prof. Dr. Danqian Xu, Zhejiang University of Technology, with a thesis entitled "*Chiral amines-catalyzed asymmetric cascade reactions*".
09. 2003 - 07. 2007	B.A. in Chemical Engineering and Technology, Zhejiang University of Technology, with distinction (top 15%).
90.2000 - 07.2003	Xiangshan High School, Zhejiang

8. References

1 a) *Cross-Coupling Reactions: A Practical Guide*, Vol. 219 (Ed.: N. Miyaura), Springer, Berlin, **2002**; b) *Metal-Catalyzed Cross-Coupling Reactions* (Eds.: A. de Meijere, F. Diederich), Wiley-VCH, Weinheim, **2004**; c) *Transition Metal Reagents and Catalysis: Innovations in Organic Synthesis*. (Ed.: J. Tsuji), John Wiley & Sons Ltd., Chichester, **2000**; d) J. Magano, J. R. Dunetz, *Chem. Rev.* **2011**, *111*, 2177-2250.

2 C. C. C. Johansson Seechurn, M. O. Kitching, T. J. Colacot, V. Snieckus, *Angew. Chem. Int. Ed.* **2012**, *51*, 5062-5085.

3 a) M. Beller, *Chem. Soc. Rev.* **2011**, *40*, 4879-4890; b) N. Miyaura, A. Suzuki, *Chem. Rev.* **1995**, *95*, 2457-2483.

4 C. Liu, H. Zhang, W. Shi, A. Lei, *Chem. Rev*. **2011**, *111*, 1780-1824.

5 D. J. Weix, *Acc. Chem. Res*. **2015**, *48*, 1767-1775.

6 a) G. Dyker, *Handbook of C-H Transformations*, Wiley-VCH: Weinheim, **2005**; b) C. S. Yeung, V. M. Dong, *Chem. Rev.* **2011**, *111*, 1215-1292.

7 a) K. Tamao, K. Sumitani, M. Kumada, *J. Am. Chem. Soc*. **1972**, *94*, 4374-4376; b) R. F. Heck, J. P. Nolley, *J. Org. Chem*. **1972**, 37, 2320-2322; c) A. O. King, N. Okukado and E.Negishi, *J. Chem. Soc., Chem. Commun*. **1977**, 683-684; d) J. K. Stille, *Angew. Chem. Int. Ed.* **1986**, *25*, 508-524; e) K. Sonogashira, *J. Organomet. Chem*. **653**, 46-49; f) N. Miyaura, K. Yamada, A. Suzuki, *Tetrahedron Lett*. **1979**, *20*, 3437-3440; g) Y. Hatanaka, T. Hiyama, *J. Org. Chem*. **1988**, *53*, 918-920.

8 M. H. Pérez-Temprano, J. A. Casares, P. Espinet, *Chem. Eur. J*. **2012**, *18*, 1864-1884.

9 L. Cassar, *J. Organomet. Chem.* **1975**, *93*, 253-257.

10 H. A. Dieck, F. R. Heck, *J. Organomet. Chem.* **1975**, *93*, 259-263.

11 K. Sonogashira, Y. Tohda, N. Hagihara, *Tetrahedron Lett.* **1975**, *16*, 4467-4470.

12 P. Bertus, P. Pale, *Tetrahedron Lett*. 1996, 37, 2019-2022.

13 L. A. Jones, S. Sanz, M. Laguna, *Catal. Today* **2007**, *122*, 403-406.

14 J. Huang, J. Chan, Y. Chen, C. J. Borths, K. D. Baucom, R. D. Larsen, M. M. Faul, *J. Am. Chem. Soc.* **2010**, *132*, 3674-3675.

15 D. Kalyani, K. B. McMurtrey, S. R. Neufeldt, M. S. Sanford, *J. Am. Chem. Soc*. **2011**, *133*, 18566-18569.

16 J. Z. Deng, D. V. Paone, A. T. Ginnetti, H. Kurihara, S. D. Dreher, S. A. Weissman, S. R. Stauffer, C. S. Burgey, *Org. Lett.* **2009**, *11*, 345-347.

17 L. S. Liebeskind, R. W. Fengl, *J. Org. Chem*. **1990**, *55*, 5359-5364.

18 X. Han, B. M. Stoltz, E. J. Corey, *J. Am. Chem. Soc*. **1999**, *121*, 7600-7605.

19 a) K. Takashi, T. Hayashi, *Tetrahedron Lett*. **1997**, *38*, 7087-7090; b) C. E. I. Knappke, S. Grupe, D. Gartner, M. Corpet, C. Gosmini, A. J. von Wangelin, *Chem. Eur. J*. **2014**, *20*, 6828-6842.

20 L. K. G. Ackerman, M. M. Lovell, D. J. Weix, *Nature* **2015**, *524*, 454-457.

21 a) N. Rodríguez, L. J. Goossen, *Chem. Soc. Rev*. **2011**, *40*, 5030-5048; b) R. Shang, L. Liu, *Sci. China Chem*. **2011**, *54*, 1670-1687; c) J. Cornella, I. Larrosa, *Synthesis* **2012**, *44*, 653-676; d) W. I. Dzik, P. P. Lange, L. J. Gooßen, *Chem. Sci*. **2012**, *3*, 2671-2678; e) L. J. Gooßen, F. Collet, K. Gooßen, *Isr. J. Chem*. **2010**, *50*, 617-629.

22 K. Semba, K. Ariyama, H. Zheng, R. Kameyama, S. Sakaki, Y. Nakao, *Angew. Chem. Int. Ed.* **2016**, *55*, 6275-6279.

23 H. Yoshida, I. Kageyuki, K. Takaki, *Org. Lett*. **2013**, *15*, 952-955.

24 S. D. Friis, M. T. Pirnot, S. L. Buchwald, *J. Am. Chem. Soc*. **2016**, *138*, 8372-8375.

25 a) Y. Shi, K. E. Roth, S. D. Ramgren, S. A. Blum, *J. Am. Chem. Soc*. **2009**, *131*, 18022-18023; b) M.Al-Amin, K. E. Roth, S. A. Blum, *ACS Catal*. **2014**, 4, 622-629.

26 P. García-Domínguez, C. Nevado, *J. Am. Chem. Soc*. **2016**, *138*, 3266-3269.

27 B. Chen, S. Ma, *Chem. Eur. J.* **2011**, *17*, 754-757.
28 Y. Ye, M. S. Sanford, *J. Am. Chem. Soc.* **2012**, *134*, 9034-9037.
29 a) J. Xu, D.-F. Luo, B. Xiao, Z.-J. Liu, T.-J. Gong, Y. Fu, L. Liu, *Chem. Commun.* **2011**, *47*, 4300-4302; b) T. Liu, Q. Shen, *Org. Lett.* **2011**, *13*, 2342-2345.
30 M. Hidai, A. Fukuoka, Y. Koyasu, Y. Uchida, *J. Mol. Cat.* **1986**, *35*, 29-37.
31 L. J. Gooßen, N. Rodríguez, K. Gooßen, *Angew. Chem. Int. Ed.* **2008**, *47*, 3100-3120.
32 J. D. Weaver, A. Recio, A. J. Grenning, J. A. Tunge, *Chem. Rev.* **2011**, *111*, 1846-1913.
33 a) A. G. Myers, D. Tanaka, M. R. Mannion, *J. Am. Chem. Soc.* **2002**, *124*, 11250-11251; b) D. Tanaka, S. P. Romeril, A. G. Myers, *J. Am. Chem. Soc.* **2005**, *127*, 10323-10333; c) S. Zhang, Y. Fu, R. Shang, Q. Guo, L. Liu, *J. Am. Chem. Soc.* **2010**, *132*, 638-646; d) P. Hu, J. Kan, W. Su, *Org. Lett.* **2009**, *11*, 2341-2344; e) Z. Fu, S. Huang, W. Su, M. Hong, *Org. Lett.* **2010**, *12*, 4992-4995; f) L. J. Gooßen, B. Zimmermann, T. Knauber, *Beilstein J. Org. Chem.* **2010**, *6*, No. 43; g) Z.-M. Sun, J. Zhang, P. Zhao, *Org. Lett.* **2010**, *12*, 992-995.
34 a) I. Shimizu, T. Yamada, J. Tsuji, *Tetrahedron Lett.* **1980**, *21*, 3199-3202; b) T. Tsuda, Y. Chujo, S. Nishi, K. Tawara, T. Saegusa, *J. Am. Chem. Soc.* **1980**, *102*, 6381-6384;c) D. K. Rayabarapu, J. A. Tunge, *J. Am. Chem. Soc.* **2005**, *127*, 13510-13511; d) S. R. Waetzig, J. A. Tunge, *J. Am. Chem. Soc.* **2007**, *129*, 14860-14861; e) J. T. Mohr, D. C. Behenna, A. M. Harned, B. M. Stoltz, *Angew. Chem. Int. Ed.* **2005**, *44*, 6924-6927; f) N. Rodríguez, F. Manjolinho, M. F. Grünberg, L. J. Gooßen, *Chem. Eur. J.* **2011**, *17*, 13688-13691; g) M. F. Grünberg, L. J. Gooßen, *J. Organomet. Chem.* **2013**, *744*, 140-143; h) K. F. Pfister, M. F. Grünberg, L. J. Gooßen, *Adv. Synth. Catal.* **2014**, *356*, 3302-3306.
35 a) A. Voutchkova, A. Coplin, N. E. Leadbeater, R. H. Crabtree, *Chem. Commun.* **2008**, 6312-6314; b) C. Wang, I. Piel, F. Glorius, *J. Am. Chem. Soc.* **2009**, *131*, 4194-4195; c) L. Ackermann, R. Vicente, A. Kapdi, *Angew. Chem. Int. Ed.* **2009**, *48*, 9792-9826. J. Cornella, P. Lu, I. Larrosa, *Org. Lett.* **2009**, *11*, 5506-5509; d) J. Zhou, P. Hu, M. Zhang, S. Huang, M. Wang, W. Su, *Chem. Eur. J.* **2010**, *16*, 5876-5881; e) P.Hu, M. Zhang, X. Jie, W. Su, *Angew. Chem. Int. Ed.* **2012**, *51*, 227-231; f) F. Zhang, M. F. Greaney, *Angew. Chem. Int. Ed.* **2010**, *49*, 2768-2771. g) P. Fang, M. Li, H. Ge, *J. Am. Chem. Soc.* **2010**, *132*, 11898-11899; h) H. Wang, L-N. Guo, X.-H. Duan, *Org. Lett.* **2012**, *14*, 4358-4361; i) M. Li, H. Ge, *Org. Lett.* **2010**, *12*, 3464-3467; j) K. Yang, C. Zhang, P. Wang, Y Zhang, H. Ge, *Chem. Eur. J.* **2014**, *20*, 7241-7244; k) M. Yu, D. Pan, W. Jia, W. Chen, N. Jiao, *Tetrahedron Lett.* **2010**, *51*, 1287-1290; l) H.-P. Bi, L. Zhao, Y.-M. Liang, C.-J. Li, *Angew. Chem. Int. Ed.* **2009**, *48*, 792-795; m) H.-P. Bi, Q. Teng, M. Guan, W.-W. Chen, X. Yao, C.-J. Li, *J. Org. Chem.* **2010**, *75*, 783-788; n) H.-P. Bi, W.-W. Chen, Y.-M. Liang, C.-J. Li, *Org. Lett.* **2009**, *11*, 3246-3249; o) C. Wang, S. Rakshit, F. Glorius, *J. Am. Chem. Soc.* **2010**, *132*, 14006-14008.
36 a) J.-J. Dai, J.-H. Liu, D.-F. Luo and L. Liu, *Chem. Commun.* **2011**, *47*, 677-679; b) M. Yamashita, K. Hirano, T. Satoh and M. Miura, *Chem. Lett.* **2010**, 68-69; c) C. Feng, T.-P. Loh, *Chem. Commun.* **2010**, *46*, 4779-4781; d) Li, C. Wang, H. Ge, *Org. Lett.* **2011**, *13*, 2062-2064; e) J. Cornella, H. Lahlali, I. Larrosa, *Chem. Commun.* **2010**, *46*, 8276-8278; f) P. Hu, Y. Shang, W. Su, *Angew. Chem. Int. Ed.* **2012**, *51*, 5945-5949; g) K. Ouchaou, D. Georgin and F. Taran, *Synlett*, **2010**, 2083-2086; h) D. Katayev, B. Exner, L. J. Gooßen, *ChemCatChem* **2015**, *7*, 2028-2032.
37 a) H. Hunsdiecker, C. Hunsdiecker, E. Vogt, US 2176181, **1939**; b) H. Hunsdiecker, C. Hunsdiecker, *Ber. Dtsch. Chem. Ges.* **1942**, *75B*, 291-297; c) D. H. R. Barton, D. Crich, W. B. Motherwell, *Tetrahedron* **1985**, *41*, 3901-3924; d) D. H. R. Barton, B. Lacher, S. Z. Zard, *Tetrahedron* **1987**, *43*, 4321-4328; e) Y. Luo, X. Pan, J. Wu, *Tetrahedron Lett.* **2010**, *51*, 6646-6648; f) X. Peng, X.-F. Shao, Z.-Q. Liu, *Tetrahedron Lett.* **2013**, *54*, 3079-3081; g) Z. Fu, Z. Li, Y. Song, R. Yang, Y. Liu, H. Cai, *J. Org. Chem.* **2016**, *81*,

2794-2803; h) Z. Wang, L. Zhu, F. Yin, Z. Su, Z. Li, C. Li, *J. Am. Chem. Soc.* **2012**, *134*, 4258-4263; i) F. Yin, Z. Wang, Z. Li, C. Li, *J. Am. Chem. Soc.* **2012**, *134*, 10401-10404; j) X, Huang, W, Liu, J, M. Hooker, J. T. Groves, *Angew. Chem. Int. Ed.* **2015**, *54*, 5241-5245.

38 a) Z.-M. Sun, P. Zhao, *Angew. Chem. Int. Ed.* **2009**, *48*, 6726-6730; b) L. Yin, M. Kanai, M. Shibasaki, *J. Am. Chem. Soc.* **2009**, *131*, 9610-9611; c) J. Lindh, P. J. R. Sjöberg, M. Larhed, *Angew. Chem. Int. Ed.* **2010**, *49*, 7733-7737; d) Y.Luo, J. Wu, *Chem. Commun.* **2010**, *46*, 3785-3787; e) C. Li, B. Breit, *J. Am. Chem. Soc.* **2014**, *136*, 862-865.

39 a) M. Nilsson, *Acta Chem. Scand.* **1966**, *20*, 423-426; c) M. Nilsson, C. Ullenius, *Acta Chem. Scand.* **1968**, *22*, 1998-2002.

40 a) L. J. Gooßen, G. Deng, L. M: Levy, *Science* **2006**, *313*, 662-664; b) L. J. Gooßen, N. Rodríguez, B. Melzer, C. Linder, G. Deng, L. M. Levy, *J. Am. Chem. Soc.* **2007**, *129*, 4824-4833.

41 P. Forgione, M.-C. Brochu, M. St-Onge, K. H. Thesen, M. D. Bailey, F. Bilodeau, *J. Am. Chem. Soc.* **2006**, *128*, 11350-11351.

42 P. Forgione, M.-C. Brochu, N. Guimond, K. H. Thesen, F. Bilodeau, *J. Org. Chem.* **2010**, *75*, 1550-1560.

43 a) M. Miyasaka, A. Fukushima, T. Satoh, K. Hirano, M. Miura, *Chem. Eur. J.* **2009**, *15*, 3674-3677; b) F. A. Arroyave, J. R. Reynolds, *Org. Lett.* **2010**, *12*, 1328-1331.

44 a) T. R. Bailey, *Tetrahedron Lett.* **1986**, *27*, 4407-4410; b) A. F. Littke, L. Schwarz, G. C. Fu, *J. Am. Chem. Soc.* **2002**, *124*, 6343-6348; c) M. R. Luzung, J. S. Patel, J. Yin, *J. Org. Chem.* **2010**, *75*, 8330-8332; d) G. A. Molander, N. Ellis, *Acc. Chem. Res.* **2007**, *40*, 275-286.

45 a) D. M. Knapp, E. P. Gillis, M. D. Burke, *Org. Lett.* **2010**, *12*, 2314-2317; b) G. R. Dick, E. M. Woerly, M. D. Burke, *Angew. Chem. Int. Ed.* **2012**, *51*, 2667-2672.

46 X. Li, D. Zou, F. Leng, C. Sun, J. Li, Y. Wu, Y. Wu, *Chem. Commun.* **2013**, *49*, 312-314.

47 J.-M. Becht, C. Catala, C. L. Drian, A. Wagner, *Org. Lett.* **2007**, *9*, 1781-1783.

48 L. J. Gooßen, B. Zimmermann, T. Knauber, *Angew. Chem. Int. Ed.* **2008**, *47*, 7103-7106.

49 V. V. Grushin, H. Alper, *Top. Organomet. Chem.* **1999**, *3*, 193-226.

50 R. Shang, Y. Fu, Y. Wang, Q. Xu, H.-Z. Yu, L. Liu, *Angew. Chem. Int. Ed.* **2009**, *48*, 9350-9354.

51 R. Shang, Q. Xu, Y.-Y. Jiang, Y. Wang, L. Liu, *Org. Lett.* **2010**, *12*, 1000-1003.

52 L. W. Sardzinski, W. C. Wertjes, A. M. Schnaith, D. Kalyani, *Org. Lett.* **2015**, *17*, 1256-1259.

53 Z. Wang, Q. Ding, X. He, J. Wu, *Org. Biomol. Chem.* **2009**, *7*, 863-865.

54 J. Moon, M. Jeong, H. Nam, J. Ju, J. M. Moon, H. M. Jung, S. Lee, *Org. Lett.* **2008**, *10*, 945-948.

55 W.-W. Zhang, X.-G. Zhang, J.-H. Li, *J. Org. Chem.* **2010**, *75*, 5259-5264.

56 L. J. Gooßen, F. Rhoduphi, C. Oppel, N. Rodríguez, *Angew. Chem. Int. Ed.* **2008**, *47*, 3043-3045.

57 R. Shang, Y. Fu, J.-B. Li, S.-L. Zhang, Q.-X. Guo, L. Liu, *J. Am. Chem. Soc.* **2009**, *131*, 5738-5739.

58 a) F. Rudolphi, B. Song, L. J. Gooßen, *Adv. Synth. Catal.* **2011**, *353*, 337-342; b) F. Collet, B. Song, F. Rudolphi, L. J. Gooßen, *Eur. J. Org. Chem.* **2011**, 6486-6501.

59 R. Shang, Z.-W. Yang, Y. Wang, S.-L. Zhang, L. Liu, *J. Am. Chem. Soc.* **2010**, *132*, 14391-14393.

60 a) R. Shang, D.-S. Ji, L. Chu, Y. Fu, L. Liu, *Angew. Chem. Int. Ed.* **2011**, *50*, 4470-4474; b) P. Y. Yeung ,K. H. Chung, F. Y. Kwong, *Org. Lett.* **2011**, *13*, 2912-2915.

61 a) R. Shang, Z. Huang, L. Chu, Y.Fu, L. Liu, *Org. Lett.* **2011**, *13*, 4240-4243; b) Z. Xu, Q. Wang, J. Zhu, *Angew. Chem. Int. Ed.* **2013**, *52*, 3272-3276.

62 Z. Zuo, D. W. C. MacMillan, *J. Am. Chem. Soc*. **2014**, *136*, 5257-5260.

63 Z. Zuo, D. T. Ahneman, L. Chu, J. A. Terrett, A. G. Doyle, D. W. C. MacMillan, *Science,* **2014**, *345*, 437-440.

64 Z. Zuo, H. Cong, W, Li, J. Choi, G. C. Fu, D. W. C. MacMillan, *J. Am. Chem. Soc*. **2016**, *138*, 1832-1835.

65 W.-M. Cheng, R. Shang, H.-Z. Yu, Y. Fu, *Chem. Eur. J*. **2015**, *21*, 13191-13195.

66 L. J. Gooßen, N. Rodríguez, C. Linder, *J. Am. Chem. Soc.* **2008**, *130*, 15248-15249.

67 L. J. Gooßen, N. Rodríguez, P. P. Lange, C. Linder, *Angew. Chem. Int. Ed*. **2010**, *49*, 1111-1114.

68 L. J. Gooßen, P. P. Lange, N. Rodríguez, C. Linder, *Chem. Eur. J*. **2010**, *16*, 3906-3909.

69 A. Fromm, C. van Wüllen, D. Hackenberger, L. J. Gooßen, *J. Am. Chem. Soc*. **2014**, *136*, 10007-10023.

70 D. Hackenberger, B. Song, M. F. Grünberg, S. Farsadpour, F. Menges, H. Kelm, C. Groß, T. Wolff, G. Niedner-Schatteburg, W. R. Thiel, L. J. Gooßen, *ChemCatChem* **2015**, *7*, 3579-3588.

71 B. Song, T. Knauber, L. J. Gooßen, *Angew. Chem. Int. Ed*. **2013**, *52*, 2954-2958.

72 M. Yamashita, K. Hirano, T. Satoh, M. Miura, *Org. Lett.* **2010**, *12*, 592-595.

73 A. Noble, S. J. McCarver, D. W. C. MacMillan, *J. Am. Chem. Soc*. **2015**, *137*, 624-627.

74 a) X. Liu, Z. Wang, X. Cheng, C. Li, *J. Am. Chem. Soc*. **2012**, *134*, 14330-14333; b) H.-.Bi, L. Zhao, Y.-M. Liang, C.-J.Li, *Angew.Chem. Int. Ed*. **2009**, *48*,792-795.

75 Y.-S. Feng, Z.-Q. Xu, L. Mao, F.-F. Zhang, H.-J. Xu, *Org. Lett*. **2013**, *15*, 1472-1475.

76 a) S. Bhadra, W. Dzik, L. J. Gooßen, *Angew. Chem. Int. Ed*. **2013**, *52*, 2959-2962; b) S. Bhadra, W. I. Dzik, L. J. Gooßen, *J. Am. Chem. Soc*. **2012**, *134*, 9938-9941.

77 a) Q.-Q. Zhou, W. Guo, W. Ding, X. Wu, X. Chen, L.-Q. Lu, W.-J. Xiao, *Angew. Chem. Int. Ed.* **2015**, *54*, 11196-11199; b) F. Le Vaillant, T. Courant, J.Waser, *Angew. Chem. Int. Ed.* **2015**, *54*, 11200-11204.

78 H. Tan, H. Li, W. Ji, L. Wang, *Angew. Chem. Int. Ed*. **2015**, *54*, 8374-8377.

79 a) J.-M. Becht, C. Catala, C. Le Drian, A. Wagner, *Org. Lett*. **2007**, *9*, 1781-1783; b) L. J. Goossen, T. Knauber, *J. Org. Chem.* **2008**, *73*, 8631-8634; c) L. J. Goossen, N. Rodríguez, C. Linder, *J. Am. Chem. Soc*. **2008**, *130*, 15248-15249; d) L. J. Gooßen, N. Rodríguez, P. P. Lange, C. Linder, *Angew. Chem. Int. Ed*. **2010**, *49*, 1111-1114; e) B. Song, T. Knauber, L. J. Gooßen, *Angew. Chem. Int. Ed*. **2013**, *52*, 2954-2958.

80 L. J. Gooßen, N. Rodíguez, C. Linder, P. P. Lange, A. Fromm, *ChemCatChem* **2010**, *2*, 430-442.

81 a) X. Chen, K. M. Engle, D.-H. Wang, J.-Q. Yu, *Angew. Chem. Int. Ed*. **2009**; *48*, 5094-5115; b) T. W. Lyons, M. S. Sanford, *Chem. Rev*. **2010**, *110*, 1147-1169; c) D. A. Colby, R. G. Bergman, J. A. Ellman, *Chem. Rev*. **2010**, *110*, 624-655.

82 L. J. Gooßen, W. R. Thiel, N. Rodríguez, C. Linder, B. Melzer, *Adv. Synth. Catal*. **2007**, *349*, 2241-2246.

83 J.-M. Becht, C. Le Drian, *Org. Lett*. **2008**, *10*, 3161-3164.

84 a) D. W. Old, J. P. Wolfe, S. L. Buchwald, *J. Am. Chem. Soc*. **1998**, *120*, 9722-9723; b) A. F. Littke, C. Dai, G. C. Fu, *J. Am. Chem. Soc*. **2000**, *122*, 4020-4028.

85 a) G. Belofsky, A. N. French, D. R. Wallace, S. L. Dodson, J. Nat. Prod. 2004, 67, 26-30; b) C. Singh, M. Hassam, V. P. Verma, A. S. Singh, N. K. Naikade, S. K. Puri, P. R. Maulik, R. Kant, *J. Med. Chem.* **2012**, *55*, 10662-10673; c) R. P. Perera, D. S. Wimalasena, K. Wimalasena, *J. Med. Chem.* **2003**, *46*, 2599-2605; d) J. Boukouvalas, C. Thibault, *J. Org. Chem*. **2015**, *80*, 681-684; e) L. Eggers, V. Buss, *Angew. Chem. Int. Ed. Engl*. **1997**, *36*, 881-883.

86 a) O, Reiser, *Angew. Chem. Int. Ed*. 2006, 45, 2838-2840; b) A. B. Flynn, W. W. Ogilvie, *Chem. Rev*. **2007**, *107*, 4698-4745.

87 a) C. Kim, Y. Dong, L. Que, *J. Am. Chem. Soc.* **1997**, *119*, 3635-3636; b) Y. Sakurai, T. Suzaki, K. Nakagawa, N. Ikenaga, H. Aota, T. Suzuki, *J. Catal.* **2002**, *209*, 16-24; c) J. K. F. Buijink, J. J. M. van Vlaanderen, M. Crocker, F. G. M. Niele, *Catal. Today* **2004**, *93-95*, 199-204.

88 B. B. Tope, W. O. Alabi, A. M. Aitani, H. Hattori, S. S. Al-Khattaf, *Appl. Catal., A* **2012**, *443-444*, 214-220.

89 a) A. Zoran, Y. Sasson, J. Blum, *J. Org. Chem.* **1981**, *46*, 255-260; b) E. D'Incan, P. Viout, *Tetrahedron* **1984**, *40*, 3421-3424.

90 a) G. Wittig, U. Schöllkopf, *Chem. Ber.* **1954**, *87*, 1318-1330; b) G. Wittig, W. Haag, *Chem. Ber.* **1955**, *88*, 1654-1666; c) B. E. Maryanoff, A. B. Reitz, *Chem. Rev.* **1989**, *89*, 863-927; d) N. Britto, V. G. Gore, R. S. Mali, A. C. Ranade, *Synth. Commun.* **1989**, *19*, 1899-1910; e) T. Hanamoto, K. Nishiyama, H. Tateishi, M. Kondo, *Synlett* **2001**, *2001*, 1320-1322; f) D. J. Peterson, *J. Org. Chem.* **1968**, *33*, 780-784; g) D. J. Ager, *Synthesis* **1984**, *1984*, 384-398.

91 a) J. F. Normant, A. Alexakis, *Synthesis* **1981**, *1981*, 841-870; b) K. Itami, T. Kamei, J. Yoshida, *J. Am. Chem. Soc.* **2003**, *125*, 14670-14671; c) E. Negishi, G. Wang, H. Rao, Z. Xu, *J. Org. Chem.* **2010**, *75*, 3151-3182.

92 a) R. H. Grubbs, S. Chang, *Tetrahedron* **1998**, *54*, 4413-4450; b) A. Fürstner, *Angew. Chem. Int. Ed.* **2000**, *39*, 3012-3043.

93 a) I. P. Beletskaya, A. V. Cheprakov, *Chem. Rev.* **2000**, *100*, 3009-3066; b) R. F. Heck, J. P. Nolley, *J. Org. Chem.* **1972**, *37*, 2320-2322; c) K. Itami, M. Mineno, N. Muraoka, J. Yoshida, *J. Am. Chem. Soc.* **2004**, *126*, 11778-11779; d) S. Oi, K. Sakai, Y. Inoue, *Org. Lett.* **2005**, *7*, 4009-4011; e) A. G. Myers, D. Tanaka, M. R. Mannion, *J. Am. Chem. Soc.* **2002**, *124*, 11250-11251; f) P. Hu, J. Kan, W. Su, M. Hong, *Org. Lett.* **2009**, *11*, 2341-2344; g) Z.-M. Sun, J. Zhang, P. Zhao, *Org. Lett.* **2010**, *12*, 992-995; h) L. J. Gooßen, B. Zimmermann, T. Knauber, *Beilstein J. Org. Chem.* **2010**, *6*, No. 43; i) S.-L. Zhang, Y. Fu, R. Shang, Q.-X. Guo, L. Liu, *J. Am. Chem. Soc.* **2010**, *132*, 638-645.

94 a) A. de Meijere, F. E. Meyer, *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2379-2411; b) M. Ohff, A. Ohff, D. Milstein, *Chem. Commun.* **1999**, 357-358; c) C. G. Hartung , K. Köhler, M. Beller, *Org. Lett.* **1999**, *1*, 709-711; d) L. Kaganovsky, K.-B. Cho, D. Gelman, *Organometallics*, **2008**, *27*, 5139-5145.

95 a) M. Oestreich, *The Mizoroki-Heck Reaction*, Wiley, Hoboken, **2009**; b) I. P. Beletskaya, A. V. Cheprakov, *Chem. Rev.* **2000**, *100*, 3009-3066.

96 a) E. Negishi, X. Zeng, Z. Tan, M. Qian, Q. Hu, Z. Huang, In *Metal-Catalyzed Cross-Coupling Reactions*; A. de Meijere, F. Diederich, Eds.; Wiley-VCH Verlag GmbH: Weinheim, 2008; pp 815-889; b) N. Miyaura, A. Suzuki, *Chem. Rev.* **1995**, *95*, 2457-2483; c) J. K. Stille, *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508-524; d) S.-I. Murahashi, *J. Organomet. Chem.* **2002**, *653*, 27-33.

97 a) M. W. Renoll, *J. Am. Chem. Soc.* **1942**, *64*, 1115-1116; b) A. Spaggiari, D. Vaccari, P. Davoli, G. Torre, F. Prati, *J. Org. Chem.* **2007**, *72*, 2216-2219; c) J. P. Das, S. Roy, *J. Org. Chem.* **2002**, *67*, 7861-7864.

98 a) A. F. Littke, C. Dai, G. C. Fu, *J. Am. Chem. Soc.* **2000**, *122*, 4020-4028; b) R. B. Miller, M. I. Al-Hassan, *J. Org. Chem.* **1985**, *50*, 2121-2123; c) S.-I. Murahashi, M. Yamamura, K.-i. Yanagisawa, N. Mita, K. Kondo, *J. Org. Chem.* **1979**, *44*, 2408-2417; d) V. Farina, V. Krishnamurthy, W. J. Scott, in *Organic Reactions*, John Wiley & Sons, Inc., **2004**.

99 L. J. Gooßen, N. Rodríguez, C. Linder, B. Zimmermann, T. Knauber, *Org. Synth.* **2008**, *85*, 196-204.

100 a) Y. Yoshikawa, K. Tomiya, N. Tomura, H. Katsuta, O. Takahashi, S. Inami, Y. Yanase, J. Kishi, H. Kawashima, US005914344A, **1999**: *Substituted carboxanilide derivative and plant disease control agnet comprising same as active ingredient*; b) H.

Elbe, H. Rieck, R. Dunkel, P. Reinecke, U. Wachendorff-Neumann, A. Mauler-Machnik, K. Kuck, WO 2004005242 A1, **2004**: *Phenyl benzamides*.

101 a) P. Moosophon, S. Kanokmedhakul, K. Kanokmedhakul, K. Soytong, *J. Nat. Prod.* **2009**, *72*, 1442-1446; b) V. Rukachaisirikul, A. Rodglin, Y. Sukpondma, S. Phongpaichit, J. Buatong, J. Sakayaroj, *J. Nat. Prod.* **2012**, *75*, 853-858; c) M. S. Ali, S. Mahmud, S. Perveen, V. U. Ahmad, G. H. Rizwani, *Phytochemistry* **1999**, *50*, 1385-1389.

102 a) H. C. Kolb, M. S. VanNieuwenhze, K. B. Sharpless, *Chem. Rev*. **1994**, *94*, 2483-2547; b) C. Singh, M. Hassam, V. P. Verma, A. S. Singh, N. K. Naikade, S. K. Puri, P. R. Maulik, R. Kant, *J. Med. Chem.* **2012**, *55*, 10662-10673; c) S. P. Cook, A. Polara, S. J. Danishefsky, *J. Am. Chem. Soc.* **2006**, *128*, 16440-16441; d) S. Poplata, A. Trçster, Y.-Q. Zou, T. Bach, *Chem. Rev*. **2016**, 116, 9748-9815; e) S. J. Roseblade, A. Pfaltz, *Acc. Chem. Res*. **2007**, *40*, 1402-1411.

103 a) B. E. Maryanoff, A. B. Reitz, *Chem. Rev*. **1989**, *89*, 863-927; b) D. J. Peterson, *J. Org. Chem*. **1968**, *33*, 780-784.

104 a) C. H. Oh, H. H. Jung, K. S. Kim, N. Kim, *Angew. Chem. Int. Ed*. **2003**, *42*, 805-808; b) D. P. Ojha, K. R. Prabhu, *Org. Lett*. **2016**, *18*, 432-435.

105 a) R. H. Grubbs, S. Chang, *Tetrahedron* **1998**, *54*, 4413-4450; b) A. Fürstner, *Angew. Chem. Int. Ed*. **2000**, *39*, 3012-3043.

106 a) G. A. Molander, B. J. Rahn, D. C. Shubert, S. E. Bonde, *Tetrahedron Lett*. **1983**, *24*, 5449-5452; b) A. Gavryushin, C. Kofink,G. Manolikakes, P. Knochel, *Tetrahedron* **2006**, *62*, 7521-7533.

107 a) C.-L. Sun, Y. Wang, X. Zhou, Z.-H. Wu, B.-J. Li, B.-T. Guan, Z.-J. Shi, *Chem. Eur. J*. **2010**, *16*, 5844-5847; b) J. Tang, L. J. Gooßen, *Org. Lett*. **2014**, *16*, 2664-2667; c) A. L. Hansen, J.-P. Ebran, T. M. Gøgsig, T. Skrydstrup, *Chem. Commun*. **2006**, 4137-4139.

108 a) R. F. Heck, *Acc. Chem. Res*. **1979**, *12*, 146-151; b)W. Cabri, I. Candiani, *Acc. Chem. Res*. **1995**, *28*, 2-7.

109 a) M. Oestreich, *The Mizoroki-Heck Reaction*,Wiley, Hoboken, **2009**; b) I. P. Beletskaya, A. V. Cheprakov, *Chem. Rev*. **2000**, *100*, 3009-3066.

110 a) W. Cabri, I. Candiani, A. Bedeschi, R. Santi, *J. Org. Chem*. **1992**, *57*, 3558-3563; b) M.-P. Denieul, T. Skrydstrup, *Tetrahedron Lett*. **1999**, *40*, 4901-4904; c) D. Tsvelikhovsky, S. L. Buchwald, *J. Am. Chem. Soc.* **2010**, *132*, 14048-14051; d) L. F. Tietze, S. G. Stewart, M. E. Polomska, A. Modi, A. Zeeck, *Chem. Eur. J*. **2004**, *10*, 5233-5242.

111 For Heck reactions or vinylations of other substrates that selectively yield 1,1-disubstituted alkenes, see a) Y. Yang, K. Cheng, Y. Zhang, *Org. Lett*. **2009**, *11*, 5606-5609; b) C. Zheng, S. S. Stahl, *Chem. Commun*. **2015**, *51*, 12771-12775; c) C. Zheng, D. Wang, S. S. Stahl, *J. Am. Chem. Soc*. **2012**, *134*, 16496-16499; d) L. Qin, X. Ren, Y. Lu, Y. Li, J. (Steve) Zhou, *Angew. Chem. Int. Ed*. **2012**, *51*, 5915-5919; e) L. Qin, H. Hirao, J. (Steve) Zhou, *Chem. Commun*. **2013**, *49*, 10236-10238; f) J. Ruan, J. Xiao, *Acc. Chem. Res*. **2011**, *44*, 614-626; g) J. Ruan, J. A. Iggo, N. G. Berry, J. Xiao, *J. Am. Chem. Soc.* **2010**, *132*, 16689-16699; h) T. M. Gøgsig, A. T. Lindhardt, M. Dekhane, J. Grouleff, T. Skrydstrup, *Chem. Eur. J*. **2009**, *15*, 5950-5955; i) P. Hu, J. Kan, W. Su, M. Hong, *Org. Lett*. **2009**, *11*, 2341-2344.

112 a) L. J. Gooßen, J. Paetzold, L. Winkel, *Synlett* **2002**, 1721-1723; b) L. J. Gooßen, J. Paetzold, *Angew. Chem. Int. Ed*. **2002**, *41*, 1237-1241.

113 a) H. A. Dieck, R. F. Heck, *J. Am. Chem. Soc*. **1974**, *96*, 1133-1136; b) A. F. Littke, G. C. Fu, *J. Am. Chem. Soc*. **2001**, *123*, 6989-7000.

114 Y. Zou, L. Qin, X. Ren, Y. Lu, Y. Li, J. (Steve) Zhou, *Chem. Eur. J*. **2013**, *19*, 3504-3511.

115 a)W. H. Perkin, *J. Chem. Soc*. **1868**, *21*, 181-186; b)W. H. Perkin, *J. Chem. Soc*. **1877**, *32*, 660-674; c) K. E. Kolb, K.W. Field, P. F. Schatz, *J. Chem. Educ*. **1990**, *67*, A304; d) Sigma Aldrich offers about 150 cinnamic acids, whereas only about 80 styrenes are available.
116 R. Giri, J.-Q. Yu, J. Am. Chem. Soc. 2008, 130, 14082-14083.
117 Y.-H. Zhang, J.-Q. Yu, *J. Am. Chem. Soc*. **2009**, *131*, 14654-14655.
118 a) D. Lee, S. Chang, *Chem. Eur. J*. **2015**, *21*, 5364-5368; b) K.-H. Ng, F.-N. Ng, W.-Y. Yu, *Chem. Commun*. **2012**, *48*, 11680-11682.
119 a) Y. Zhang, H. Zhao, M. Zhang, W. Su, *Angew. Chem. Int. Ed*. **2015**, *54*, 3817-3821; b) J. Luo, S. Preciado, I. Larrosa, *J. Am. Chem. Soc*. **2014**, *136*, 4109-4112; c) J. Cornella, M. Righi, I. Larrosa, *Angew. Chem. Int. Ed*. **2011**, *50*, 9429-9432; d) X. Qin, D. Sun, Q. You, Y. Cheng, J. Lan, J. You, *Org. Lett*. **2015**, *17*, 1762-1765; e) H. A. Chiong, Q.-N. Pham, O. Daugulis, *J. Am. Chem. Soc*. **2007**, *129*, 9879-9884; f) H. Gong, H. Zeng, F. Zhou, C.-J. Li, *Angew. Chem. Int. Ed*. **2015**, *54*, 5718-5721; g) K. M. Engle, T.-S. Mei, M. Wasa, J.-Q. Yu, *Acc. Chem. Res*. **2012**, *45*, 788-802; h) K. Ueura, T. Satoh, M. Miura, *Org. Lett*. **2007**, *9*, 1407-1409; i) K. Ueura, T. Satoh, M. Miura, *J. Org. Chem*. **2007**, *72*, 5362- 5367; j) N. Y. P. Kumar, A. Bechtoldt, K. Raghuvanshi, L. Ackermann, *Angew. Chem. Int. Ed*. **2016**, *55*, 6929-6932; k) L. Huang, A. Biafora, G. Zhang, V. Bragoni, L. J. Gooßen, *Angew. Chem. Int. Ed*. **2016**, *55*, 6933-6937; l) L. Huang, D. Hackenberger, L. J. Gooßen, *Angew. Chem. Int. Ed*. **2015**, *54*, 12607-12611.
120 S. Bhadra,W. I. Dzik, L. J. Gooßen, *Angew. Chem. Int. Ed*. **2013**, *52*, 2959-2962.
121 a) L. Botella, C. Nájera, *J. Org. Chem*. **2005**, *70*, 4360-4369; b) C. Jia, W. Lu, T. Kitamura, Y. Fujiwara, *Org. Lett*. **1999**, *1*, 2097-2100.
122 a) D. W. Old, J. P. Wolfe, S. L. Buchwald, *J. Am. Chem. Soc*. **1998**, *120*, 9722-9723; b) A. F. Littke, C. Dai, G. C. Fu, *J. Am. Chem. Soc*. **2000**, *122*, 4020-4028; c) S. D. Walker, T. E. Barder, J. R. Martinelli, S. L. Buchwald, *Angew. Chem. Int. Ed*. **2004**, *43*, 1871-1876.
123 A. J. Borah, G. Yan, *Org. Biomol. Chem*. **2015**, *13*, 8094-8115.
124 a) E. J. E. Freyne, A. H. Raeymaekers, 0406958A2, **1991**: *Positive inotropic and lusitropic 3,5-dihydroimidazo[2,1-b]quinazolin-2(1H)-one derivatives*; b) U. Mueller, J. Dressel, P. Fey, R. Hanko, W. Huebsch, T. Kraemer, M. Mueller-Gliemann, M. Beuck, S. Kazda, A. Knorr, J.-P. Stasch, S. Wohlfeil, DE4220983A1, **1994**: *Preparation of (imidazolylmethyl)phenylpropionates, -cinnamates, and related compounds as angiotensin II antagonists*.
125 A. Biafora, T. Krause, D. Hackenberger, F. Belitz, L. J. Gooßen, *Angew. Chem. Int. Ed.* **2016**, 10.1002/anie.201607270.